SINTESIS SENYAWA IMINA DARI VANILIN DAN ANILINA DENGAN VARIASI JUMLAH KATALIS AIR JERUK NIPIS

SKRIPSI

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Untuk Memenuhi Salah Satu Persyaratan Dalam
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Saya yang bertanda tangan di bawah ini:

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Judul Penelitian	:"Sintesis Senyawa Imina dari Vanilin dan Anilina dengan Variasi Jumlah Katalis Air Jeruk Nipis"

Menyatakan dengan sebenar-benarnya bahwa hasil penelitian saya ini tidak terdapat unsur-unsur penjiplakan karya penelitian atau karya ilmiah yang pernah dilakukan atau dibuat oleh orang lain, kecuali yang secara tertulis dikutip dalam naskah ini dan disebutkan dalam sumber kutipan dan daftar pustaka.

Apabila ternyata hasil penelitian ini terbukti terdapat unsur-unsur jiplakan, maka saya bersedia untuk mempertanggung jawabkan, serta diproses sesuai peraturan yang berlaku.

Malang, 13 Januari 2016
Yang Membuat Pernyataan,

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KATA PENGANTAR

بِسْمِ ٱللَّهِ ٱلرَّحْمَٰنِ ٱلرَّحِيمِ

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Wassalamu'alaikum Wr.Wb.

Malang, Desember 2015

Penulis

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ABSTRAK

Al Hakimi, Nurush Shofi. 2015**. Sintesis Senyawa Imina Dari Vanilin Dan Anilina Dengan Variasi Jumlah Katalis Air Jeruk Nipis.** Pembimbing I: Ahmad Hanapi, M.Sc. Pembimbing II: Tri Kustono Adi, M.Sc. Konsultan: A.Ghanaim Fasya, M.Si.

Kata Kunci: Imina, Vanilin, Anilina, Jeruk Nipis.

Telah dilakukan sintesis senyawa imina dari vanilin dan anilina menggunakan katalis asam alami dari buah jeruk nipis (*Citrus aurantifolia*) dalam kondisi tanpa pelarut (*solvent free*). Penelitian dilakukan untuk mengetahui jumlah katalis air jeruk nipis yang optimum serta karakteristik produk yang dihasilkan. Variasi jumlah katalis jeruk nipis yang digunakan adalah 0,5; 1,0; 1,5; 2,0; dan 2,5 mL. Karakterisasi produk dilakukan dengan mengamati wujud, warna, titik lebur, serta identifikasi menggunakan FTIR dan KG-SM. Produk terbaik yang dihasilkan memiliki sifat-sifat antara lain: padatan, berwarna kuning, titik lebur = 150-152 C^o, dan rendemen terbaik sebesar 64,1234 % dengan nilai kemurnian senyawa target sebesar 74,74 %. Spektra IR: 2800-3500 cm^{-1} (OH), 3086 cm^{-1} (C-H sp2), 1515 cm^{-1} (C=C aromatik), 2937 cm^{-1} (C-H sp^3), 1428 cm^{-1} (-CH_3), 1285 dan 1030 cm^{-1} (C-O-C eter), 1584 cm^{-1} (–C=N), dan 875 dan 812 cm^{-1} (aromatik tersubtitusi). Spektra Massa: *m/z* 227 ($M^{\bullet+}$), *m/z* 226 ($M^{\bullet+}$–H), 211 ($M^{\bullet+}$–H–CH_3), *m/z* 197 ($M^{\bullet+}$–OCH_2), *m/z* 104 ($M^{\bullet+}$–CH_2O–fenil), *m/z* 77 ($M^{\bullet+}$–CH_2O–fenil–HCN).

ABSTRACT

Al Hakimi, Nurush Shofi. 2015**. Synthesis of Imine Compound From Vanillin And Aniline With Variation Amount Of Lime Juice Catalyst.** Supervisor I: Ahmad Hanapi, M.Sc. Supervisor II: Tri Kustono Adi, M.Sc. Consultant: A.Ghanaim Fasya, M.Si.

Keyword: Imine, Vanillin, Anilina, Lime.

Synthesis of imine compound from vanillin and aniline has been established by using natural acid from lime fruit (*Citrus aurantifolia*) as catalyst under the solvent free. The study was conducted to know the best result amount of lime juice catalyst and the characteristic of the product. A variety amount limes as catalyst were used are 0,5; 1,0; 1,5; 2,0; and 2,5 mL. The product was characterized by observing the shape, color, melted point, identifications using FTIR, and GC-MS. A physical characteristics of the best product: solids, with yellow color, melting point = 150 ^{o}C, yield = 64,1234 % with the purity value = 74,74 %. IR spectra: 2800-3500 cm^{-1} (OH), 3086 cm^{-1} (C-H sp^2), 1515 cm^{-1} (C=C aromatic), 2937 cm^{-1} (C-H sp^3), 1428 cm^{-1} ($-CH_3$), 1285 and 1030 cm^{-1} (C-O-C eter), 1584 cm^{-1} (C=N), 875 and 812 cm^{-1} (subtitutioned aromatic). Mass Spectra: *m/z* 227 ($M^{\bullet+}$), *m/z* 226 ($M^{\bullet+}$-H), *m/z* 211 ($M^{\bullet+}$-H-CH_3), *m/z* 197 ($M^{\bullet+}$-CH_2O), *m/z* 104 ($M^{\bullet+}$-CH_2O- phenyl), *m/z* 77 ($M^{\bullet+}$-CH_2O-phenyl-HCN).

الملخص

الحكيمي, نور الصفي. **تركيب الإمينن من فانيلين والأنيلين بأنواع عددمحفز الليمون** . المشريف الأولى: الأستاذ أحمد حنفي المجستير العالمي.المشريف الثاني: الأستاذ تري كوسطانو أدي المجستير العالمي. المستشارة: الأستاذأحمد غنائم فشى المجستير العالمي

الكلمات المفتحية: إمين, فانيلين, أنيلين, ليمون

قد تم الدراسة التجريبية عن تركيب الإمين من فانيلين والأنيلين باستخدام المحفز الحمض الطبيعي من ليمون (*Citrusaurantifolia*) بدون المذيب. هدفت هذه الدراسة لمعرفة التوصيف و نتائج عند تركيب الإمين من فانيلين والأنيلين بأنواع عدد ليمون. ومن أنواع عدد ليمون الذي يستعملها هي 0,5; 1,0; 1,5; 2,0; 2,5 mL. توصيف النتائج بملاحظة شكل و لون و نقطة الانصهار و هوية باستخدام FTIR و GC-MS. دلت النتائج إلي توصيف: الصلبة، الصفراء، نقطة الانصهار = 150 ^{o}C، % جملة النتاج = 64,1234 % مع قيمة النقاء= 74,74 %. IR spectra: 3500-2800 cm^{-1} (OH), 3086 cm^{-1} (C-H sp^2), 1515 cm^{-1} (C=C aromatic), 2937 cm^{-1} (C-H sp^3), 1428 cm^{-1} (-CH_3), 1285 و 1030 cm^{-1} (C-O-C eter), 812 cm^{-1} (subtitutioned aromatic). Mass Spectra: *m/z* 227 (M^{*+}), 1584 (C=N), 875 و *m/z* 226 (H-M^{*+}), *m/z* 211 (CH_3-H-M^{*+}), *m/z* 197 (CH_2O-M^{*+}), *m/z* 104 (-M^{*+}), *m/z* 77 (phenyl-CH_2O-HCN-phenyl-CH_2O-M^{*+}).

BAB I

PENDAHULUAN

1.1 Latar Belakang

ظَهَرَ الْفَسَادُ فِي الْبَرِّ وَالْبَحْرِ بِمَا كَسَبَتْ أَيْدِي النَّاسِ لِيُذِيقَهُمْ بَعْضَ الَّذِي عَمِلُوا لَعَلَّهُمْ يَرْجِعُونَ

Artinya: "Telah nampak kerusakan di darat dan di laut disebabkan karena perbuatan tangan manusia, supaya Allah merasakan kepada mereka sebagian dari (akibat) perbuatan mereka, agar mereka kembali (ke jalan yang benar)". (ar Rum: 41).

Hampir semua kerusakan alam seperti polusi udara, kebakaran hutan, pencemaran udara, dan pencemaran air, yang banyak kita jumpai sekarang ini adalah akibat dari ulah manusia. Hal ini karena hanya umat manusia saja yang dapat merusak lingkungan. Makhluk Allah seperti hewan, tumbunan, jin, malaikat, bahkan iblis pun tidak dapat melakukannya. Maka dari itu Allah memberikan bencana kepada umat manusia agar mereka sadar dan "kembali ke jalan yang benar".

Firman Allah SWT. dalam surat ar-Rum ayat 41 merupakan bentuk peringatan Allah kepada kita para manusia. Allah sengaja memperlihatkan kerusakan bukan untuk membuat kita takut, melainkan agar kita "*kembali (ke jalan yang benar)*". Sebagai ilmuan kimia tafsiran kata "*kembali (ke jalan yang benar)*" adalah kembali memikirkan alam dengan menerapkan penelitian-penelitian kimia yang ramah lingkungan (*Green Chemistry*). Apabila hal tersebut dilakukan, maka kita berharap agar kerusakan alam akan dapat dihindari. Alam

yang baik akan menjaga kita dan anak cucu kita dari kepunahan hingga hari kiamat kelak.

Green Chemistry sediri telah didefinisikan oleh Anastas dan Warner (1998), dalam beberapa prinsip, antara lain: mencegah terbentuknya limbah kimia dengan cara merancang sintesis atau analisis yang aman (bagi lingkungan dan peneliti) seperti menggunakan sedikit reagen dan pelarut serta mengurangi penggunaan reagen-reagen berbahaya, merancang penelitian yang efektif sehingga mengurangi pembentukan produk samping, meningkatkan efisiensi energi seperti melakukan reaksi pada suhu dan tekanan ruang, merancang penelitian yang produknya dapat terdegradasi dan tidak terakumulasi setelah digunakan, dan memperkecil potensi kecelakaan.

Di dalam penelitian ini akan dilakukan sintesis suatu imina dari senyawa vanilin dan anilina. Senyawa imina dan turunannya, merupakan senyawa yang keberadaanya sangat penting dalam bidang farmasi karena aktivitas biologinya cukup baik. Kegunaan senyawa ini sangat luas. Beberapa imina aromatis telah disintesis karena sangat berpotensi sebagai antioksidan, antimikroba, dan indikator asam-basa (Purwono dkk, 2013). Imina juga merupakan bahan baku dalam sintesis obat penenang, obat bius, obat kontrasepsi kehamilan, anti ketombe, analgesik, dan antiinflamasi (Vibhute *et al*., 2011).

Sintesis senyawa organik yang ekonomis, mudah, ramah lingkungan, dan hasil produk melimpah atau biasa disebut *green synthesis*, telah banyak dilakukan oleh ilmuwan kimia. Beberapa metode seperti metode penggerusan, telah dilakukan oleh Rahman *et al*., (2012) saat mensintesis senyawa aldol dan menghasilkan rendemen melebihi 95%. Pada tahun sebelumnya Naqvi *et al*.,

(2009) juga melakukan sintesis senyawa imina dalam pelarut air pada temperatur ruang dan tanpa menggunakan katalis dan memperoleh rendemen hingga 90%.

Upaya untuk melakukan *Green Synthesis* juga dilakukan oleh Zarei *et al*., (2011) dengan metode *solvent free*. Ia telah melakukan sintesis beberapa senyawa azo imina dari senyawa hasil reaksi *p*-anisidine dan *o*-vanilin dengan beberapa amina aromatis dan aril aldehida dengan sedikit air dan tanpa pelarut. Produk-produknya dikarakterisi menggunakan IR, Spektroskopi Massa, ^{1}H-NMR, ^{13}C-NMR dan menghasilkan rendemen senyawa azo imina hingga mencapai 100%.

Penelitian tentang sintesis senyawa imina sendiri, telah dilakukan oleh Purwono dkk (2013). Ia telah mereaksikan vanilin dan anilina dalam pelarut etanol dengan bantuan seperangkat alat refluks. Imina yang dihasilkan selanjutnya dikarakterisasi menggunakan IR, H-NMR, dan GC-MS. rendemen yang dihasilkan sebesar 82,17 %.

Secara umum reaksi pembentukan imina membutuhkan bantuan katalis asam (Fessenden *et al.,* 1997). Beberapa katalis asam seperti asam asetat (Hussain *et al*., 2014), asam klorida (Rublein, 1998), etanol (Purwono, 2013 dan Ibrahim *et al*., 2006), bahkan senyawaan logam transisi Cu, Ni, Mn, Fe, dan Co (Mobinikhaledi *et al*., 2009), telah digunakan dan menghasilkan produk imina dengan rendemen yang cukup baik.

Penggunaan katalis alami yang ramah lingkungan juga dilakukan oleh Patil *et al*., (2011 dan 2012). Katalis air buah lemon telah digunakan oleh Patil *et al*., (2011 dan 2012) dalam melakukan sintesis beberapa senyawa imina dari alkil benzaldehida dan alkil anilina. Perlakuan ini menghasilkan produk imina dengan rendemen sebesar 72–100 %. Karakterisasi produk dilakukan dengan bantuan IR

dan ^{1}H-NMR. Lebih lanjut Patil *et al*., (2011) juga menyatakan bahwa air buah nanas merupakan katalis yang sangat baik dalam reaksi Biginelli.

Upaya-upaya para peneliti inilah yang memberikan kesan sekaligus alasan mendasar untuk melakukan sintesis senyawa imina dari vanilin dan anilina yang ramah lingkungan. Metode yang digunakan adalah metode *solvent-free* dengan bantuan katalis asam alami dari air buah jeruk nipis. Hal ini juga merupakan salah satu upaya untuk mematuhi perintah Allah SWT. untuk tidak membuat kerusakan di muka bumi sebagaimana firman-Nya dalam surat al A'raf: 56.

1.2 Rumusan Masalah

1. Berapa jumlah katalis air buah jeruk nipis yang optimum pada reaksi pembentukan imina dari vanilin dan anilina?
2. Bagaimana karakteristik produk hasil reaksi pembentukan imina dari vanilin dan anilina dengan variasi jumlah katalis air jeruk nipis?

1.3 Tujuan

1. Untuk mengetahui jumlah katalis air buah jeruk nipis yang optimum pada reaksi pembentukan imina dari vanilin dan anilina.
2. Untuk mengetahui karakteristik produk hasil reaksi pembentukan imina dari vanilin dan anilina dengan variasi jumlah katalis air jeruk nipis.

1.4 Manfaat

Memberikan informasi kepada masyarakat kimia tentang metode *Green Synthesis* senyawa Imina dari vanilin dan anilina yang mudah, murah, dan ramah lingkungan.

1.5 Batasan Masalah

1. Reaksi pembentukan imina dari vanilin dan anilina dilakukan dalam kondisi tanpa pelarut (*Solvent free*).
2. Jeruk nipis (*Citrus aurantifolia*) yang digunakan merupakan jeruk nipis komersil yang banyak dijual di pasaran.
3. Karakterisasi senyawa produk terbatas hanya pada pengamatan wujud, warna, titik lebur, serta identifikasi menggunakan FTIR.
4. Karakterisasi senyawa produk menggunakan KG-SM hanya dilakukan pada produk dengan variasi terbaik.

BAB II

TINJAUAN PUSTAKA

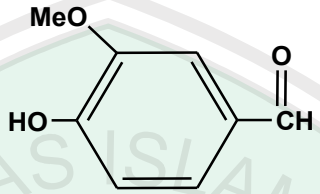
2.1 Vanilin

Vanilin adalah senyawa organik dengan rumus molekul $C_8H_8O_3$ yang banyak terkandung pada buah vanila (*Vanilla planifolia*). Tanaman vanili banyak ditemukan di Indonesia karena mereka dapat tumbuh dengan baik di kawasan tropis. Vanilin merupakan komponen utama hasil ekstraksi biji vanila. Senyawa inilah yang memberi aroma khas pada buah vanila. Isolasi vanilin dari buah vanila dapat terjadi melalui tahap hidrolisis dengan bantuan asam kuat. Proses hidrolisis ini akan memutuskan ikatan glikosida antara vanilin dan glukosa (Handayani dkk, 2011). Menurut Kumar *et al*. (2012), senyawa ini pertama kali disintesis dari eugenol yaitu komponen utama minyak atsiri pada cengkeh. Vanilin mempunyai wujud kristal berwarna putih dan banyak digunakan sebagai pewangi makanan.

Menurut Sarifudin dalam Budimarwanti (2007), vanilin dilihat dari struktur kimianya, merupakan senyawa fenolik tersubstitusi gugus metoksi pada posisi orto dan gugus aldehida pada posisi para, sehingga vanilin dapat dikelompokkan sebagai senyawa antioksidan. Hal ini juga didukung oleh penelitian yang dilakukan oleh Shyamala dkk, (2007) yang menyatakan bahwa vanilin memiliki aktivitas antioksidan meski aktivitasnya masih cukup rendah. Dibutuhkan vanilin dengan konsentrasi yang tinggi untuk menetralkan radikal bebas.

Di dalam sistem tata nama yang dirumuskan oleh komisi dari *the International Union of Pure and Applied Chemistry* (IUPAC), Vanilin memiliki

nama sistematik 4-hidroksi-3-metoksibenzaldehida. Nama ini merujuk pada gugus-gugus fungsi yang terdapat pada senyawa vanilin yakni aldehida, eter dan fenol. Ketiga gugus ini dapat membentuk ikatan hidrogen intramolekul dan atarmolekul (Kumar *et al*., 2013).

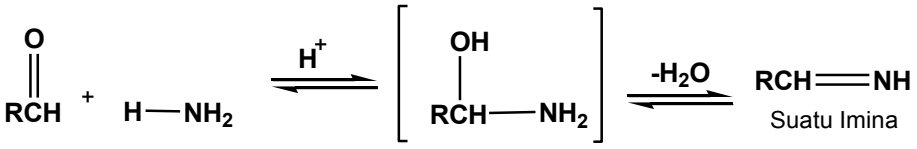


Gambar 2.1 Struktur Vanilin

Dari ketiga gugus fungsi yang ada (eter, hidroksi, dan aldehida), gugus aldehida pada vanilin adalah gugus yang paling reaktif, sebab terdapat ikatan ikatan C=O yang dapat dikenai reaksi adisi oleh nukleofil (Nu:$^-$). Adisi tersebut akan mengkonversi atom karbon karbonil yang terhibridisasi sp^2 menjadi sp^3. Zarei dan Jarrahpour (2011) menyatakan bahwa Gugus aldehida dapat bereaksi dengan amina primer membentuk ikatan C=N melalui reaksi pembetukan imina.

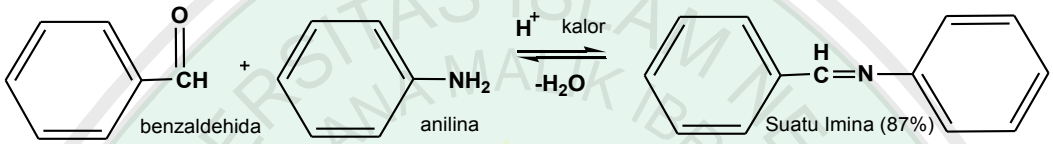
2.2 Reaksi Pembentukan Imina

Amoniak adalah suatu nukleofil yang dapat menyerang gugus karbonil dari suatu aldehida dalam suatu reaksi adisi-eliminasi. Reaksi ini dikatalisi oleh asam. Produknya adalah suatu imina, yakni suatu senyawa yang mengandung gugus C=N.



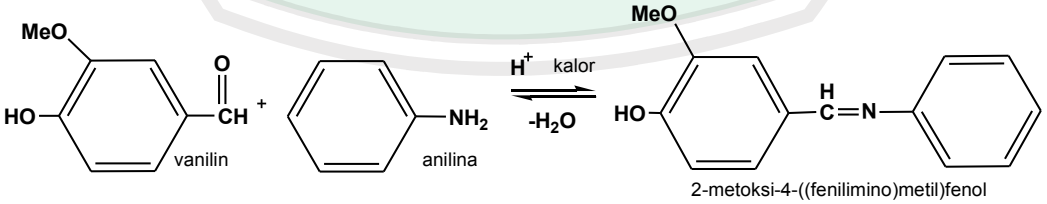
Gambar 2.2 Reaksi umum amoniak dengan suatu aldehida

Imina tak tersubstitusi dari amoniak bersifat tidak stabil dan akan berpolimerisasi jika didiamkan. Namun jika diganti dengan suatu *amina primer* (RNH_2), maka akan terbentuk imina tersubstitusi yang lebih stabil atau biasa disebut dengan basa Schiff. Aldehida aromatik (seperti benzaldehida) atau aril amina (seperti anilina) dapat bereaksi dan menghasilkan imina yang terstabilkan (Fessenden *et al.,* 1997).



Gambar 2.3 Reaksi pembentukan imina dari benzaldehida dan anilina

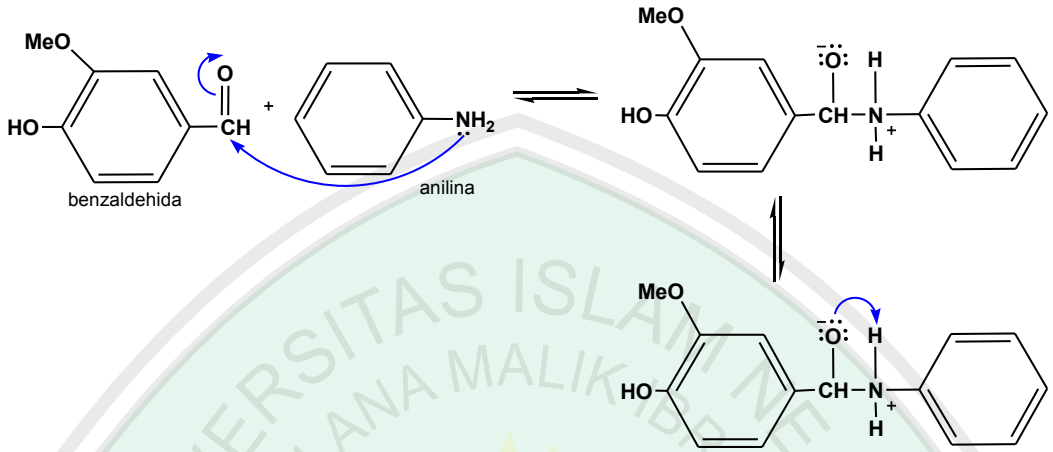
Imina yang terstabilkan akan lebih disukai sehingga dapat menggeser kesetimbangan kearah produk yang berimbas kepada kelimpahan produk yang sangat tinggi. Pada Gambar 2.3 reaksi antara benzaldehida dengan anilina memberikan produk dengan kelimpahan hingga 87%. Dengan reaksi yang serupa, maka dapat pula dibuat suatu reaksi antara vanilin dengan anilina menurut persamaan reaksi pada Gambar 2.4.



Gambar 2.4 Reaksi pembentukan imina dari vanilin dan anilina

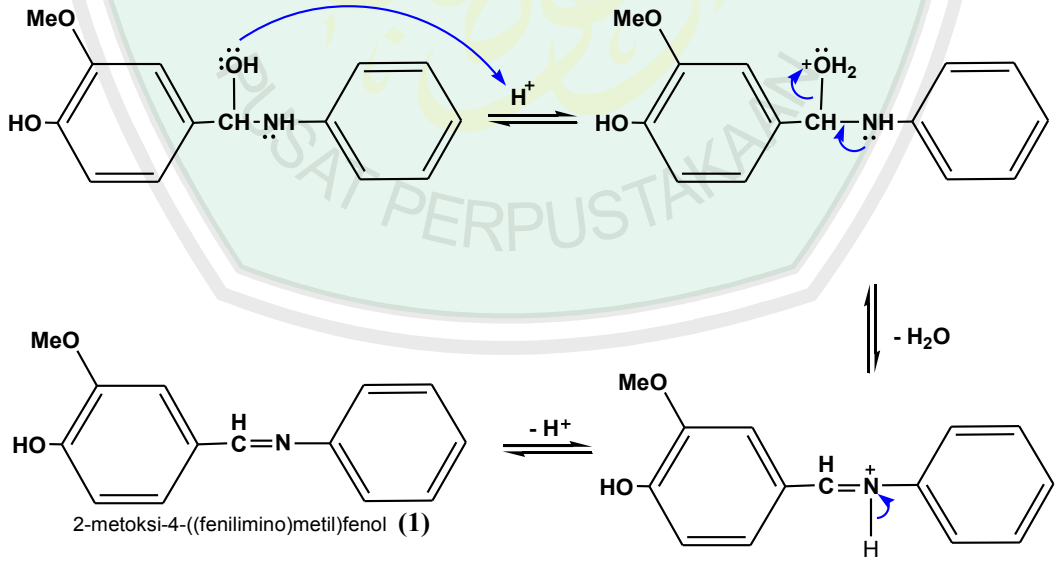
persamaan reaksi pembentukan imina pada Gambar 2.4 dapat terjadi menurut mekanisme reaksi yang terdiri dari dua tahapan yakni tahap adisi dan tahap eliminasi.

Tahap pertama adalah langkah adisi amina primer (sebagai nukleofilik) pada atom karbon –C=O dari vanilin.



Gambar 2.5 Mekanisme reaksi tahap pertama

Adapun tahap kedua adalah tahap eliminasi yang diawali dengan protonasi gugus –OH, kemudian akan terlepas sebagai molekul air yang merupakan gugus pergi yang baik.



Gambar 2.6 Mekanisme reaksi tahap kedua

Pembentukan imina sangat bergantung pada pH. Hal ini disebabkan karena tahap pertama adalah tahap adisi amina pada gugus karbonil. Apabila larutan terlalu asam, maka amina akan terprotonasi. Peristiwa ini akan menggangu proses

adisi pada tahap pertama, sehingga reaksi adisi menjadi sangat lambat dan menjadi tahap penentu laju reaksi.

Hal yang berbeda ditunjukkan saat reaksi eliminasi pada tahap kedua. Fessenden *et al*., (1997) menyatakan bahwa laju reaksi eliminasi tersebut akan meningkat seiring bertambahnya konsentrasi asam. Dengan demikian pengondisian pH sangat penting dilakukan agar keseluruhan tahap dapat berjalan dengan baik. Lebih lanjut Ia menyatakan bahwa pH optimum pada reaksi pembentukan imina adalah sekitar 3-4. Jadi dalam reaksi ini dibutuhkan suatu katalis asam yang dapat meningkatkan keasaman hingga pH optimum.

Beberapa katalis asam telah digunakan untuk mengkatalisi reaksi pembentukan imina. Katalis asam asetat telah digunakan Hussain *et al*. (2014), dalam mensintesis lima senyawa imina turunan dari Sulfametaksazol. Kelima senyawa tersebut telah berhasil teridentifikasi secara kualitatif oleh instrumen FTIR dan ^{1}H-NMR. Asam klorida digunakan oleh Rublein (1998) untuk mengkatalisis reaksi antara benzaldehida dan anilina. Sedangkan efisiensi katalis asam dari senyawaan logam transisi seperti Cu, Ni, Mn, Fe, dan Co, telah diteliti oleh Mobinikhaledi *et al*. (2009), dalam reaksi antara 2-aminobenzimidazol dan beberapa senyawa aromatik aldehida. Dari penelitian tersebut dihasilkan produk imina dengan kelimpahan hingga 89%.

Purwono dkk, pada tahun (2013) telah melakukan sistesis senyawa imina dari vanilin dan anilina dengan menggunakan pelarut etanol (pKa=16) sebagai sumber asamnya (Hart *et al*., 2003). Dari perlakuan tersebut dihasilkan produk reaksi dengan kelimpahan cukup tinggi yakni 82,17 %.

2.3 Metode *Green Synthesis*

Sintesis senyawa organik yang ekonomis, mudah, ramah lingkungan, dan hasil produk melimpah atau biasa disebut *Green Synthesis*, telah banyak dilakukan oleh para ilmuwan kimia. Beberapa metode seperti metode *solvent free* (Zarei *et al*., 2011), Penggerusan (Rahman *et al*., 2012), dan penggunaan katalis alami (Patil *et al*., 2012), kerap kali dikembangkan dalam laboratorium kimia.

2.3.1 Reaksi Tanpa Pelarut (*Solvent Free)*

Reaksi tanpa pelarut atau biasa dikenal dengan istilah *solvent free* adalah suatu metode reaksi yang dalam prosesnya sama sekali tidak melibatkan pelarut. Pelarut adalah suatu senyawa yang berwujud cair dan dapat melarutkan suatu senyawa berdasarkan kemiripan tingkat kepolarannya. Reaksi pelarutan senyawa bersifat dapat balik (reversibel). Pada reaksi pembentukan imina dari vanilin (*solid*) dengan anilina (*liquid*), anilina yang berwujud cair bukan merupakan pelarut, melainkan suatu reaktan meskipun reaksi antara vanilin dengan anilina bersifat reversibel. Reaksi tersebut menghasilkan produk baru yaitu suatu imina aromatis yang cukup stabil.

Metode *solvent free* termasuk dalam *Green Synthesis* karena dapat mengurangi penggunaan bahan kimia yaitu pelarut. Pelarut akan menjadi limbah di akhir reaksi. Metode *solvent free* merupakan salah satu metode yang kerap kali dilakukan para ilmuan kimia dalam upaya pengembangan *Green Synthesis*. Beberapa metode *solvent free* seperti metode radiasi *microwave* dan penggerusan dengan bantuan mortar merupakan metode yang sangat sering dilakukan.

\Naqvi *et al*. (2009), melakukan sintesis senyawa imina dengan metode radiasi *microwave* dengan hasil rendemen hingga 73 – 86 %. Rahman *et al*. (2012), juga telah menggunakan metode penggerusan saat mensintesis senyawa aldol. Ia mendapatkan produk dengan rendemen melebihi 95%. Metode serupa juga dilakukan oleh Zarei *et al*. (2011). Ia telah melakukan sintesis beberapa senyawa azo imina dari senyawa *p*-anisidine dan *o*-vanilin dengan variasi reaktan amina aromatis dan aril aldehida. Reaksi dilakukan hanya menggunakan sedikit air dan tanpa pelarut. Produk-produknya dikarakterisi menggunakan IR, Spektroskopi Massa, ^{1}H-NMR, ^{13}C-NMR dan menghasilkan rendemen senyawa azo imina hingga mencapai 100%.

2.3.2 Katalis Asam Alami dari Air Buah Jeruk Nipis

Jeruk nipis (*Citrus Aurantifolia*) sering disebut sebagai buah serba guna karena penggunaannya lebih banyak dibandingkan dengan jenis jeruk lain. Jeruk nipis mempunyai aroma yang kuat serta citarasa yang khas. Jeruk nipis memiliki sifat-sifat kimia yang berbeda dengan jenis buah jeruk yang lain, seperti kadar gula, pH yang sangat rendah dan rasa masam buah jeruk yang sangat tinggi. Struktur dan komposisi jeruk nipis hampir sama dengan lemon (Tessler dan Nelson, 1986)

Jeruk nipis memiliki beberapa nama yang berbeda di Indonesia, antara lain jeruk nipis (Sunda), jeruk pecel (Jawa), jeruk dhurga (Madura), lemo (Bali), mudutelong (Flores) dan lain sebagainya. Jeruk nipis merupakan tumbuhan obat dari famili *Rutaceae*. Dalam pengobatan tradisional jeruk nipis digunakan sebagai peluruh dahak dan obat batuk (Sarwono, 2001).

Secara taksonomi, tanaman jeruk nipis termasuk dalam klasifikasi sebagai berikut (Sarwono, 2001):

Gambar 2.7 Buah jeruk nipis
Sumber: Saraf, S. Textbook of oral pathology. USA: Jeypee Brothers Publishers; 2006:234 dalam Enda, 2012

- Kingdom : Plantae
- Divisi : Spermatophyta
- Subdivisi : Angiospermae
- Kelas : Dicotyledonae
- Ordo : Rutales
- Famili : Rutaceae
- Genus : Citrus
- Spesies : *Citrus aurantifolia* (*Cristm*.) *Swingle*

Buah jeruk nipis mengandung bahan kimia diantaranya asam sitrat sebanyak 7-7,6%, damar lemak, mineral, vitamin B1, minyak terbang (minyak atsiri atau essensial oil). Selain itu, jeruk nipis juga mengandung vitamin C sebanyak 27mg/100 g jeruk, Ca sebanyak 40mg/100 g jeruk dan pospat sebanyak 22mg. (Chutia *et al*., 2009 dan Hariana dalam Ermawati, 2008).

Patil *et al*., pada tahun 2012 telah melakukan sintesis beberapa senyawa imina dari beberapa alkil benzaldehida dan alkil anilina. Reaksi tersebut dilakukan dengan bantuan katalis asam alami dari air jeruk lemon (*Citrus limonium)*. Dari penelitian tersebut dihasilkan senyawa imina dengan kelimpahan yang cukup tinggi yakni 72 hingga 100%. Lebih lanjut Patil menjelaskan bahwa jeruk lemon memiliki tingkat keasaman yang cukup tinggi yakni pada kisaran pH = 2–3. Buah yang terdiri atas air (85%), karbohidrat (11.2 %), protein (1%), vitamin C (0.5 %), lemak (0.9 %), mineral (0.3 %), serat (1.6 %) dan beberapa asam organik. Lemon memiliki kandungan asam sitrat yang cukup tinggi yaitu antara 5-7%. Hal inilah yang menyebabkan jeruk lemon dapat bertindak sebagai katalis asam. Dengan demikian jeruk nipis juga diharapkan dapat digunakan sebagai katalis dalam

reaksi pembentukan imina dari vanilin dan anilina mengingat kandungan asam sirtratnya yang lebih tinggi dari jeruk lemon yaitu antara 7-7,6%.

2.4 Karakterisasi Senyawa Imina Hasil Sintesis

2.4.1 Identifikasi Menggunakan Spektrofotometri FTIR

Spektrofotometri *Fourier Transform Infrared* (FTIR) merupakan satu metode spektroskopi yang sangat sering digunakan dalam laboratorium sintesis kimia terutama dalam mensintesis senyawa organik. Spektroskopi FTIR merupakan hasil pengembangan Spektroskopi inframerah atau *Infra-Red (IR).* Sebenarnya Prinsip kerja Spektroskopi IR cukup sederhana, yaitu jika suatu radiasi gelombang elektromagnetik mengenai suatu materi, maka akan terjadi suatu interaksi, diantaranya berupa penyerapan energi (absorpsi) oleh atom-atom atau molekul-molekul dari materi tersebut. Absorpsi sinar ultraviolet dan cahaya tampak akan mengakibatkan tereksitasinya elektron. Sedangkan absorpsi radiasi inframerah, energinya tidak cukup untuk mengeksitasi elektron, namun dapat menyebabkan peningkatan amplitudo getaran (vibrasi) atom-atom pada suatu molekul (Fessenden *et al.,* 1997).

Penyerapan radiasi suatu senyawa pada gelombang IR sangat khas, karena senyawa tersebut hanya menyerap radiasi gelombang tertentu saja yang bergantung pada struktur senyawanya. Chatwal (1985) berpendapat bahwa absorpsi khas inilah yang mendorong pengembangan metode spektroskopi baik spektroskopi atomik maupun molekular. Spektroskopi inframerah telah memberikan sumbangsih besar bagi dunia ilmu pengetahuan terutama dalam upaya pemahaman gugus fungsi yang terdapat dalam suatu komponen serta unsur-

unsur penyusunnya. Spektroskopi inframerah yang sering kita jumpai biasanya dilengkapi dengan transformasi Fourier untuk analisis hasil spektrumnya. Spektroskopi inilah yang dinamakan *Fourier Transform Infra-Red* atau biasa disingkat FTIR.

Dalam prakteknya metode spektroskopi FTIR didasarkan atas perbedaan penyerapan radiasi inframerah atau absorbansi suatu materi. Absorbsi inframerah oleh suatu materi dapat terjadi jika telah memenuhi dua syarat, yaitu: kesesuaian antara frekuensi radiasi inframerah dengan frekuensi vibrasional molekul sampel dan perubahan momen dipol selama bervibrasi.

Menurut Setiadi (2008), dua senyawa yang berbeda tidak akan mempunyai bentuk serapan IR yang sama. Sebab setiap tipe ikatan memiliki sifat vibrasi dan lingkungan yang tidak sama dengan ikatan lainnya. Senyawa yang mempunyai gugus fungsi yang sama namun dalam lingkungan yang berbeda, akan menghasilkan serapan IR yang berbeda. Seperti contoh alkana dan alkena mempunyai serapan IR yang berbeda. Umumnya serapan –C-H tampak pada kisaran dibawah 3000 cm^{-1} sedangkan =C-H diatas 3000 cm^{-1}. Sedangkan serapan C=C berada pada daerah 1660-1600 cm^{-1}. Khusus pada senyawa aromatis, gugus C=C memberikan dua serapan pada 1600 cm^{-1}dan 1475 cm^{-1}.

Beberapa contoh lain yakni: gugus hidroksi (-OH) dari etanol yang mempunyai serapan khas melebar pada daerah 3550-3200 cm^{-1}, Sedangkan pada senyawa fenol, gugus –OH mempunyai serapan pada 3244 cm^{-1}; Gugus eter (C-O-C) tampak pada daerah 1150-1085 cm^{-1}, akan tetapi pada senyawa aromatis seperti anisol, vibrasi simetris eter menunjukkan serapan pada daerah 1046 cm^{-1}; Gugus karbonil (-C=O) pada aldehida, keton, asam karboksilat, ester, amida dan

laktam umumnya memberikan serapan tajam pada 1870-1540 cm^{-1}. Namun Gugus -C=O pada keton atau aldehid yang tersubtitusi oleh fenil akan menyerap radiasi IR pada 1686 cm^{-1} (Silverstein *et al.,* 2005).

Purwono dkk, (2013) dalam penelitiannya menyatakan bahwa senyawa 2-metoksi-4-((fenilimino)metil)fenol akan memberikan serapan IR gugus -O-H yang melebar pada rentang panjang gelombang 3000-3500 cm^{-1}, C_{sp2}-H aromatis pada 3086 cm^{-1} dan , C_{sp3}-H pada 2900 cm^{-1} dan 1427, C=N pada 1581 cm^{-1}, C=C aromatis pada 1512 cm^{-1}, C-O-C pada 1288-1026 cm^{-1},serta serapan aromatis tersubtitusi pada rentang 871-810 cm^{-1}.

2.4.2 Identifikasi Menggunakan Kromatografi Gas - Spektrometri Massa (KG- SM)

Identifikasi Menggunakan Kromatografi Gas - Spektrometri Massa (KG-SM) pada prinsipnya ialah pemisahan komponen-komponen dalam campurannya dengan kromatografi gas, kemudian tiap komponen yang terpisah dikonversi menjadi ion oleh spektroskopi massa untuk selanjutnya dideteksi oleh sensor yang dapat mendeteksi massa dari komponen tersebut. Hasil analisis kromatografi gas adalah suatu *kromatogram*, sedangkan hasil pemeriksaan spektrometri massa masing-masing senyawa disebut *spektrum*.

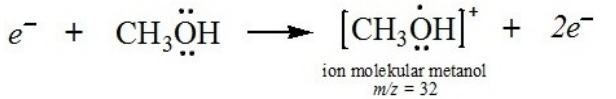
Kromatografi Gas (KG) merupakan suatu teknik pemisahan senyawa berdasarkan perbandingan distribusinya terhadap fasa diam dan fase gerak. komponen yang mudah menguap (dan stabil terhadap panas) akan bermigrasi melalui kolom yang berisi fase diam dengan suatu kecepatan yang tergantung pada rasio distribusinya (Rohman dan Gandjar, 2012). Senyawa yang lebih

terdistribusi pada fase diam akan tertahan dan keluar dari kolom dengan waktu lebih lama daripada senyawa yang terdistribusi pada fase gerak.

KG dapat digunakan untuk analisis secara kualitatif dan kuantitatif. Analisis kualitatif menunjukkan jumlah senyawa dalam sampel, sedangkan analisis kuantitatif menunjukkan kadar senyawa-senyawa dalam sampel tersebut. Secara kuantitatif, suatu senyawa dapat ditentukan persentase kadarnya (%) dengan menghitung luas puncak senyawa tersebut dalam kromatogram. Persentase relatif salah satu senyawa dalam sampel dapat dihitung dengan membandingkan luas komponen dengan jumlah luas semua sampel dengan Persamaan (2.1).

$$\% \text{ Komponen} = \frac{luas\ komponen}{jumlah\ luas\ semua\ sampel} \text{ x } 100\ \% \qquad \textbf{(2.1)}$$

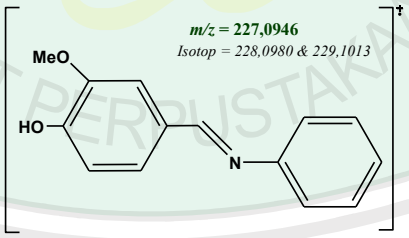
Spektrometri Massa (SM) merupakan metode analisis kualitatif yang berbeda dengan jenis spektroskopi yang lain karena prinsip kerja SM adalah mengkonversi suatu senyawa menjadi ion dan memilahnya berdasarkan rasio massa terhadap muatan (*m/z)*, kemudian jumlah relatif dari setiap ion yang ada ditentukan. Hart, *et al*. (2003), menyatakan bahwa setiap sampel yang dimasukkan dalam spektroskopi ini akan diuapkan dalam kevakuman tinggi dan terus-menerus dibom dengan elektron berenergi tinggi. Akibat pengeboman ini, elektron dari suatu molekul (M) membentuk radikal kation yang disebut ion molekular (*molecular ion)* $\mathbf{M}^{*+}$ (disebut juga ion induk, *parent ion*). Sebagai contoh metanol dapat membentuk ion molekular seperti Gambar 2.8.



Gambar 2.8 Pembentukan ion molekular dari senyawa metanol

Ion molekular kemudian akan dipecah berdasarkan pola fragmentasinya. Fragmen-fragmen inilah yang akan terbaca pada Spektra SM. Spektra tersebut dapat menunjukkan grafik perbandingan massa fragmen (*m/z*) dengan kelimpahan relatif masing-masing fragmen tersebut berdasarkan kestabilannya. Kestabilan suatu fragmen dipengaruhi oleh kemampuannya untuk beresonansi. Semakin stabil suatu fragmen maka kelimpahan relatifnya akan semakin tinggi. Fragmen-fragmen disusun menurut kenaikan *m/z* atau *m/e* dari kiri ke kanan dan intensitas puncak sebanding dengan kelimpahan relatif fragmen-fragmen (Supratman, 2010).

Senyawa 2-metoksi-4-((fenilimino)metil)fenol merupakan senyawa target sintesis yang didapat melalui mekanisme reaksi pembentukan imina. Apabila sintesis berhasil dan senyawa tersebut terbentuk, maka akan terbentuk fragmen yang memberikan puncak serapan pada spektra SM dengan bentuk ion molekular dan rasio *m/z* sebagaimana Gambar 2.9.



Gambar 2.9 Ion molekular dari senyawa 2-metoksi-4-((fenilimino)metil)fenol

BAB III

METODE PENELITIAN

3.1 Waktu dan Tempat Penelitian

Penelitian ini dilakukan pada bulan Agustus – Nopember 2015 di Laboratorium Jurusan Kimia Fakultas Sains dan Teknologi Universitas Islam Negeri (UIN) Malang dan Laboratorium Jurusan Kimia Fakultas Matemetika dan Ilmu Pengetahuan Alam (MIPA) Universitas Gadjah Mada (UGM) Yogyakarta.

3.2 Alat dan Bahan

3.2.1 Alat

Alat yang digunakan dalam penelitian ini adalah gelas arloji, *beakerglass* 100 mL, erlenmeyer 100 mL, gelas ukur 10 mL, pipet volume 1 mL, pipet tetes, pipa kapiler, bola hisap, spatula, pengaduk gelas, corong gelas, pengaduk magnet, neraca analitik, alat penentu titik lebur, kertas saring, gelas pengembang, oven, Spektrofotometer IR, dan KG-SM.

3.2.2 Bahan

Bahan yang digunakan dalam penelitian ini adalah Vanilin (4-hidroksi-3-metoksibenzaldehida) f.s, Anilina f.s, jeruk nipis komersil, kertas saring, kain saring, plat KLT, alumunium foil, etanol 96 %, etil asetat teknis, n-heksana teknis, aseton teknis dan akuades.

3.3 Tahapan Penelitian

Penelitian ini dilakukan dengan tahapan-tahapan sebagai berikut:

1. Preparasi katalis air jeruk nipis
2. Sintesis Senyawa imina dari vanilin dan anilina dengan variasi jumlah katalis asam dari air jeruk nipis.
3. Pemurnian dengan metode rekristalisasi
4. Monitoring menggunakan plat KLT
5. Karakterisasi senyawa imina hasil sintesis dengan FTIR dan KG-SM

3.4 Cara Kerja

3.4.1 Preparasi Katalis Asam Alami dari Air Buah Jeruk Nipis (*Citrus aurantifolia*)

Jeruk nipis segar dibelah menjadi dua kemudian diperas menggunakan pemeras jeruk yang telah dibersihkan. Air jeruk yang dihasilkan kemudian disaring bertahap dengan kain bersih dan kertas saring hingga mendapatkan air jeruk yang bersih dari padatan-padatan buah. Air jeruk nipis siap digunakan sebagai katalis (Patil *et* al.*,* 2011).

3.4.2 Sintesis Senyawa Imina dari Vanilin dan Anilina Dengan Variasi Jumlah Katalis Air Jeruk Nipis

Sebanyak 10 mmol (0,9313 g) senyawa anilina dimasukkan ke dalam gelas beaker 100 mL. Selanjutnya ditambahkan 10 mmol (1,5215 g) vanilin dan 0,5 mL katalis air jeruk nipis. Campuran lalu diaduk secara merata menggunakan pengaduk gelas selama 30 menit, hingga terbentuk padatan keras berwarna kuning. Padatan yang terbentuk dimurnikan melalui proses rekristalisasi.

Perlakuan yang sama diulangi untuk variasi volume katalis 1,0; 1,5; 2,0 dan 2,5 mL (Patil *et* al*.,* 2011, termodifikasi).

3.4.3 Pemurnian dengan Metode Rekristalisasi

Padatan hasil sintesis ditambahkan dengan pelarut etanol 96 % dalam gelas beaker (Ibrahim *et* al, 2006). Dipanaskan campuran sambil diaduk-aduk hingga padatan larut sempurna. Apabila padatan masih belum larut, ditambahkan lagi etanol hingga padatan larut sempurna. Setelah padatan larut sempurna, larutan disaring dalam keadaan panas lalu kemudian didinginkan pada suhu ruang hingga 2 jam. Kristal yang dihasilkan selanjutnya disaring dengan kertas saring yang telah diketahui beratnya. Kristal dikeringkan dalam oven pada suhu 100 ^{o}C. Terakhir dilakukan perhitungan untuk mengetahui rendemen produk.

3.4.4 Monitoring Menggunakan Plat KLT

Kristal hasil pemurnian dicuplik (± 50 mg) ke dalam gelas alroji kemudian ditambahkan sedikit (0,1– 0,5 mL) kloroform hingga larut sempurna. Larutan kemudian ditotolkan pada plat KLT satu kali totolan. Senyawa standar anilina dan vanilin juga diberi perlakuan yang sama sebagai senyawa pembanding. Plat KLT selanjutnya dielusi menggunakan eluen etil asetat : n-heksana (3:10) yang telah dijenuhkan dalam desikator (Mhaske *et* al, 2014). Diamati perubahan *Rf* dan noda-noda yang terbentuk serta dibandingkan dengan *Rf* standar dari reaktan.

3.4.5 Karakterisasi Senyawa Imina Hasil Sintesis

3.4.5.1 Pengamatan Sifat Fisik

Padatan (kristal) kering yang telah dimurnikan diamati sifat fisiknya meliputi massa, warna, dan wujud produk. Titik lebur senyawa diamati dengan *Melting Point Aparratus*. Hasil pengamatan dicatat.

3.4.5.2 Identifikasi Menggunakan FTIR

Idenfikasi senyawa produk dilakukan di laboratorium analisis instrumen Jurusan Kimia Fakultas Sains dan Teknologi Universitas Islam Negeri (UIN) Malang. Spektrofotometer yang digunakan adalah Spektrofotometer FTIR Varian tipe FT 1000. Mula-mula dicampurkan senyawa produk dengan KBr lalu digerus dalam mortar agate. Selanjutnya campuran dipress dan dibentuk pelet, lalu pelet diletakkan di *cell holder* dalam instrumen FTIR dan dibuat spektrum IR pada rentang bilangan gelombang 4000 – 400 cm^{-1}.

3.4.5.2 Identifikasi Menggunakan KG-SM

Identifikasi produk terbaik hasil reaksi pembentukan imina menggunakan instrumen KG-SM dilakukan di Laboratorium Jurusan Kimia Fakultas Matemetika dan Ilmu Pengetahuan Alam (MIPA) Universitas Gadjah Mada (UGM) Yogyakarta. Produk dianalisis dengan spesifikasi teknis sebagai berikut:

Kolom	: Rtx-5MS	Pressure	: 35,6 kPa
Panjang	: 30 meter	Ion source Temp.	: 250^{o}C
ID	: 0,25 mm	Interface Temp.	: 310^{o}C
Eluen	: Helium	Solvent Cut Time	: 3 menit
Temp. Oven	: 150^{o}C	Start m/z	: 33
Temp. Injection	: 310^{o}C	End m/z	: 600

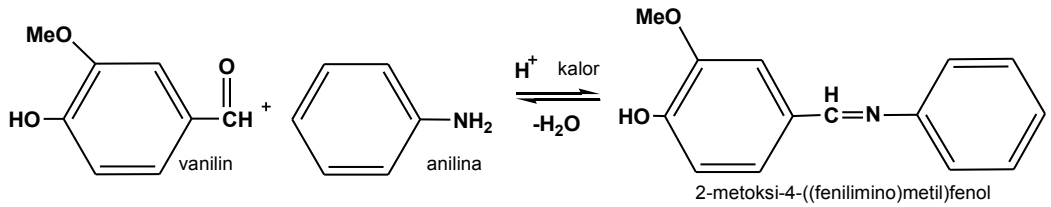
BAB IV

PEMBAHASAN

Pada Bab ini akan dilakukan pembahasan tentang hasil-hasil dari perlakuan dalam penelitian. Pembahasan akan dibagi menjadi enam sub-Bab yaitu: Sintesis senyawa imina dari vanilin dan anilina dengan variasi jumlah katalis asam dari air buah jeruk nipis, Monitoring dengan menggunakan metode KLT analitik, Analisis produk dengan metode Spektrofotometri FTIR, Penentuan produk hasil sintesis terbaik, Karakterisasi produk terbaik menggunakan KG-SM, dan diakhiri dengan integrasi antara *green chemistry* dan Islam.

4.1 Sintesis Senyawa Imina dari Vanilin dan Anilina dengan Variasi Jumlah Katalis Air Jeruk Nipis

Sintesis senyawa imina dari vanilin dan anilina diawali dengan menyampurkan 10 mmol vanilin (4-hidroksi-3-metoksi benzaldehida) dan 10 mmol anilina ke dalam gelas beaker. Katalis yang digunakan adalah air dari buah jeruk nipis yang umum dijual di pasaran. Campuran diaduk dengan pengaduk gelas selama 30 menit dalam kondisi tanpa pelarut (*Solvent Free*) pada suhu dan tekanan ruang. Variasi volume katalis yang digunakan yaitu 0,5 ; 1,0; 1,5; 2,0 dan 2,5 mL. Secara teori reaksi akan berjalan menurut persamaan reaksi pada Gambar 4.1(Fessenden *et al.,* 1997).



Gambar 4.1 Reaksi pembentukan imina dari vanilin dan anilina

Kelima produk hasil variasi perlakuan selanjutnya dimurnikan dengan metode rekristalisasi menggunakan pelarut etanol. Proses rekristalisasi dipilih karena wujud produk adalah padatan. Rekristalisasi dilakukan untuk menghilangkan sisa katalis jeruk nipis serta reaktan yang mungkin tersisa. Hasil pengamatan fisik dari kelima kristal produk setelah dimurnikan tersaji dalam Tabel 4.1.

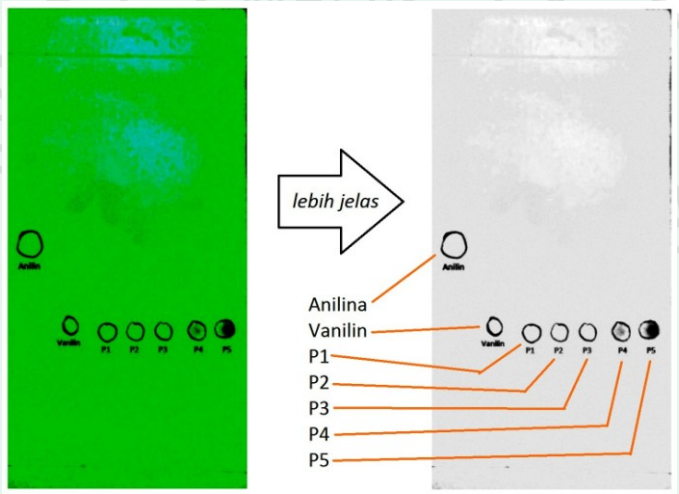
Tabel 4.1 Hasil akhir pengamatan fisik lima produk hasil variasi perlakuan

Pengamatan	**Variasi 1**	**Variasi 2**	**Variasi 3**	**Variasi 4**	**Variasi 5**
Vol. Katalis (mL)	0,5	1,0	1,5	2,0	2,5
Wujud	Padat	Padat	Padat	Padat	Padat
Warna	Kuning	Kuning Kecoklatan	Kuning Kecoklatan	Kuning Kecoklatan	Kuning Kecoklatan
Massa (gram)	1,459	1,386	1,104	0,928	0,8375
Titik Lebur (^{o}C)	150	152	150	152	152

Berdasarkan Tabel 4.1, kelima produk hasil variasi perlakuan memiliki kesamaan wujud yaitu padatan. Produk dari variasi 1 berwarna kuning, sedangkan pada variasi 2–5 berwarna kuning kecoklatan. Warna coklat yang muncul kemungkinan berasal dari sisa anilina yang tidak bereaksi. Terdapat kemiripan titik lebur kelima produk yaitu antara 150–152 ^{o}C. Hasil ini (wujud, warna, dan titik lebur) sesuai dengan sifat fisik dari senyawa 2-metoksi-4-((fenilimino)metil)fenol yang telah berhasil disintesis oleh Purwono, dkk (2013). Untuk massa produk mengalami penurunan seiring bertambahnya volume katalis air jeruk nipis. Hal ini sesuai dengan penelitian sebelumnya yang menyebutkan bahwa semakin bertambahnya katalis asam, akan membuat amina menjadi terprotonasi dan menurunkan kereaktifannya sebagai nukleofil (Yadav dan Mani, 2013).

4.2 Monitoring dengan Plat KLT

Monitoring reaksi dilakukan dengan cara menotolkan *starting material* (anilina dan vanilin) dan kelima produk hasil sintesis (yang telah dimurnikan) pada plat KLT GF_{254}. Eluen pengembang yang digunakan adalah etil asetat : n-heksana (3:10). Hasil monitoring produk pada Gambar 4.2 menunjukkan terbentuknya noda tunggal pada tiap-tiap produk (variasi 1–5) dengan nilai *Rf* yang tersaji pada Tabel 4.2.



Gambar 4.2 Kromatogram hasil monitoring menggunakan plat KLT

Tabel 4.2 Daftar nilai *Rf* Kromatogram hasil monitoring

Sampel	*Rf* (R_{sampel} : $R_{pelarut}$)
Anilina	0,53750
Vanilin	0,35000
P1	0,32500
P2	0,32500
P3	0,33125
P4	0,33750
P5	0,34375

Keterangan: P1 = Produk Var. 1; P2 = Produk Var. 2; P3 = Produk Var.3; P4 = Produk Var. 4; P5 = Produk Var. 5

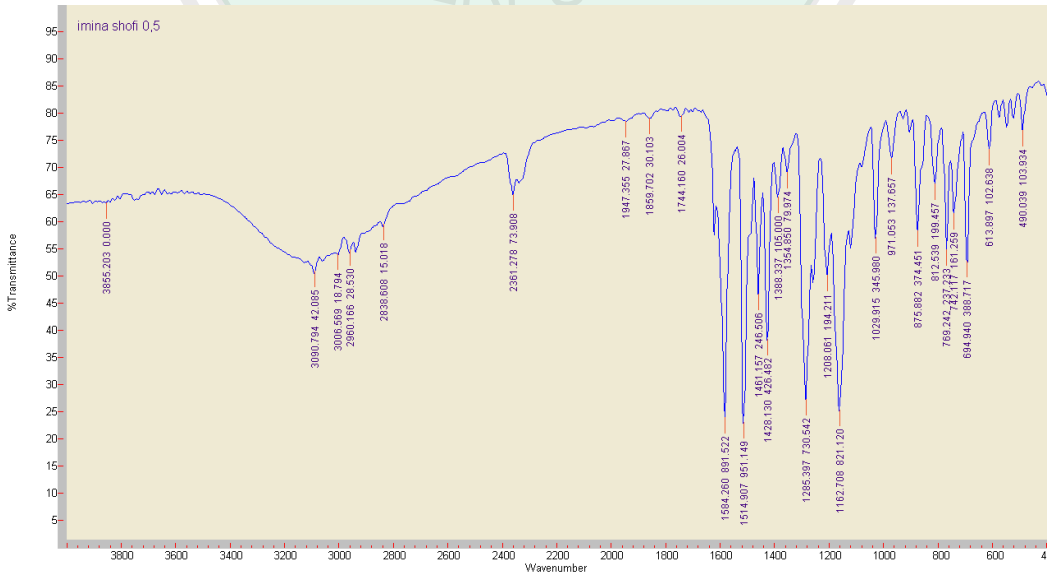
Berdasarkan Tabel 4.2, nilai *Rf* kelima produk sangat mirip dengan nilai *Rf* vanillin. Besar kemungkinan terjadi tumpang tindih antara noda vanilin dan

senyawa produk. Namun warna kuning yang tampak serta tidak munculnya noda lain pada daerah *Rf* anilina, mengasumsikan kemungkinan telah terbentuknya senyawa target. Setelah proses monitoring, masing-masing produk selanjutnya diuji lebih lanjut menggunakan metode spektrofotometri FTIR untuk mengetahui gugus fungsi yang ada.

4.3 Analisis Produk dengan Metode Spektrofotometri FTIR

Analisis FTIR kelima produk yang dihasilkan, dilakukan dengan menggunakan metode pelet KBr. Pembacaan pita serapan dilakukan pada bilangan gelombang 4000 – 400 cm^{-1}, dimana pada daerah tersebut umumnya serapan vibrasi gugus fungsi seringkali terjadi. Hasil analisis FTIR adalah suatu spektogram dari masing-masing produk dengan pita-pita serapan atau spektra-spektra yang selanjutnya akan diidentifikasi gugus fungsinya berdasarkan pada literatur yang telah ada.

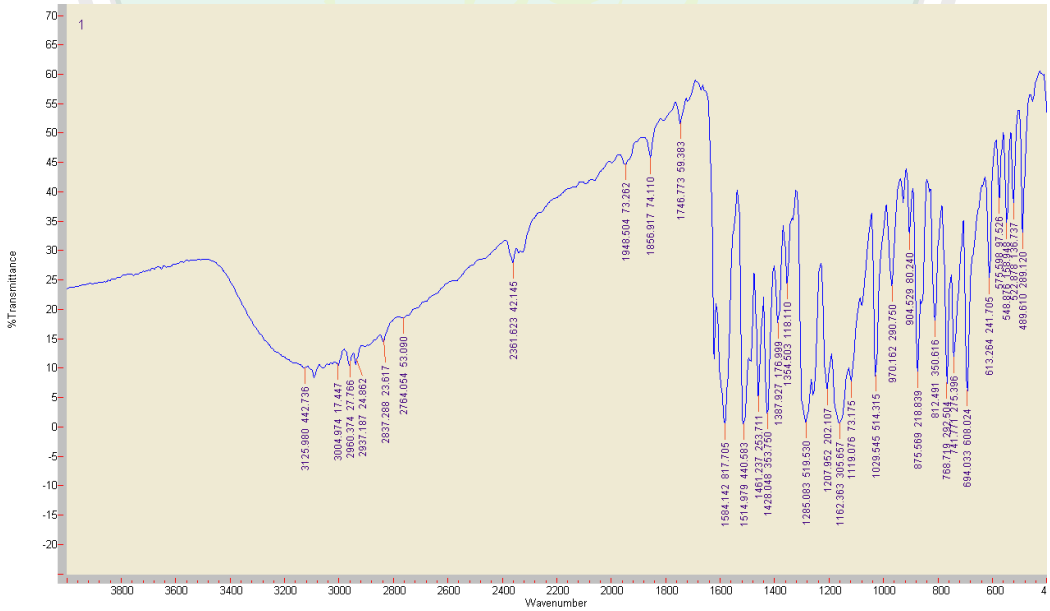
4.3.1 Identifikasi Spektra FTIR Produk 1 (katalis 0,5 mL)



Gambar 4.3 Spektogram produk 1 hasil analisis FTIR

Hasil spekta IR pada Gambar 4.2 menunjukkan adanya gugus –OH yang memunculkan pita serapan melebar yang khas pada daerah 2800-3400 cm^{-1}. Rentangan gugus C-H $_{sp2}$ aromatik memunculkan pita serapan lemah pada 3091 cm^{-1}, Ini didukung dengan adanya serapan pada 1515 cm^{-1} yang menunjukkan adanya gugus C=C aromatik. Serapan lemah pada 2935 cm^{-1} adalah akibat oleh rentangan C-H $_{sp3}$ dan didukung oleh adanya gugus metil (-CH_3) di pita serapan 1428 cm^{-1} (Purwono dkk., 2013). Munculnya serapan kuat pada daerah 1285 dan 1030 cm^{-1} menunjukkan adanya gugus C-O-C eter (Ibrahim et al, 2006). Terbentuknya gugus imina (-C=N-) ditunjukkan oleh serapan kuat pada daerah 1584 cm^{-1} (Naqvi *et al*, 2009). Pita serapan di derah 876 dan 813 cm^{-1} menunjukkan adanya senyawa aromatik tersubtitusi (Lambert, 1987).

4.3.2 Identifikasi Spektra FTIR Produk 2 (katalis 1,0 mL)

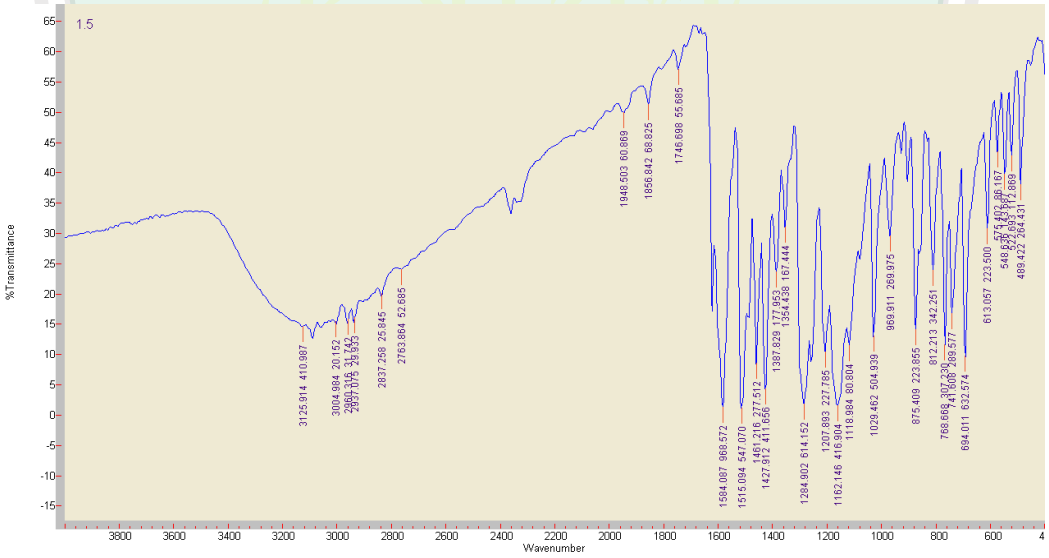


Gambar 4.4 Spektogram produk 2 hasil analisis FTIR

Hasil spekta IR menunjukkan adanya gugus –OH yang memunculkan pita serapan melebar yang khas pada daerah 2800-3500 cm^{-1}. Rentangan gugus C-H $_{sp2}$

aromatik memunculkan pita serapan lemah pada 3089 cm^{-1}, Ini didukung dengan adanya serapan pada 1515 cm^{-1} yang menunjukkan adanya gugus C=C aromatik. Serapan lemah pada 2937 cm^{-1} adalah akibat oleh rentangan C-H $_{sp3}$ dan didukung oleh adanya gugus metil ($-CH_3$) di pita serapan 1428 cm^{-1} (Purwono dkk., 2013). Munculnya serapan kuat pada daerah 1285 dan 1030 cm^{-1} menunjukkan adanya gugus C-O-C eter (Ibrahim et al, 2006). Terbentuknya gugus imina (-C=N-) ditunjukkan oleh serapan kuat pada daerah 1584 cm^{-1} (Naqvi *et al*, 2009). Pita serapan di derah 876 dan 812 cm^{-1} menunjukkan adanya senyawa aromatik tersubtitusi (Lambert, 1987).

4.3.3 Identifikasi Spektra FTIR Produk 3 (katalis 1,5 mL)

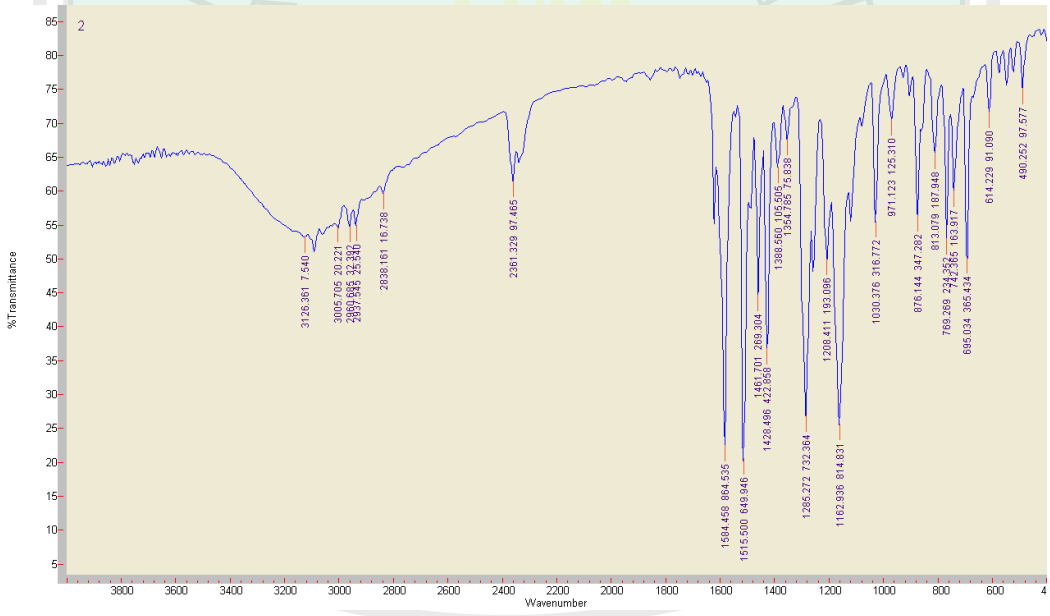


Gambar 4.5 Spektogram produk 3 hasil analisis FTIR

Hasil spekta IR menunjukkan adanya gugus –OH yang memunculkan pita serapan melebar yang khas pada daerah 2800-3500 cm^{-1}. Rentangan gugus C-H $_{sp2}$ aromatik memunculkan pita serapan lemah pada 3086 cm^{-1}, Ini didukung dengan adanya serapan pada 1515 cm^{-1} yang menunjukkan adanya gugus C=C aromatik.

Serapan lemah pada 2937 cm^{-1} adalah akibat oleh rentangan C-H $_{sp3}$ dan didukung oleh adanya gugus metil (-CH_3) di pita serapan 1428 cm^{-1} (Purwono dkk., 2013). Munculnya serapan kuat pada daerah 1285 dan 1030 cm^{-1} menunjukkan adanya gugus C-O-C eter (Ibrahim et al, 2006). Terbentuknya gugus imina (-C=N-) ditunjukkan oleh serapan kuat pada daerah 1584 cm^{-1} (Naqvi *et al*, 2009). Pita serapan di derah 875 dan 812 cm^{-1} menunjukkan adanya senyawa aromatik tersubtitusi (Lambert, 1987).

4.3.4 Identifikasi Spektra FTIR Produk 4 (katalis 2,0 mL)

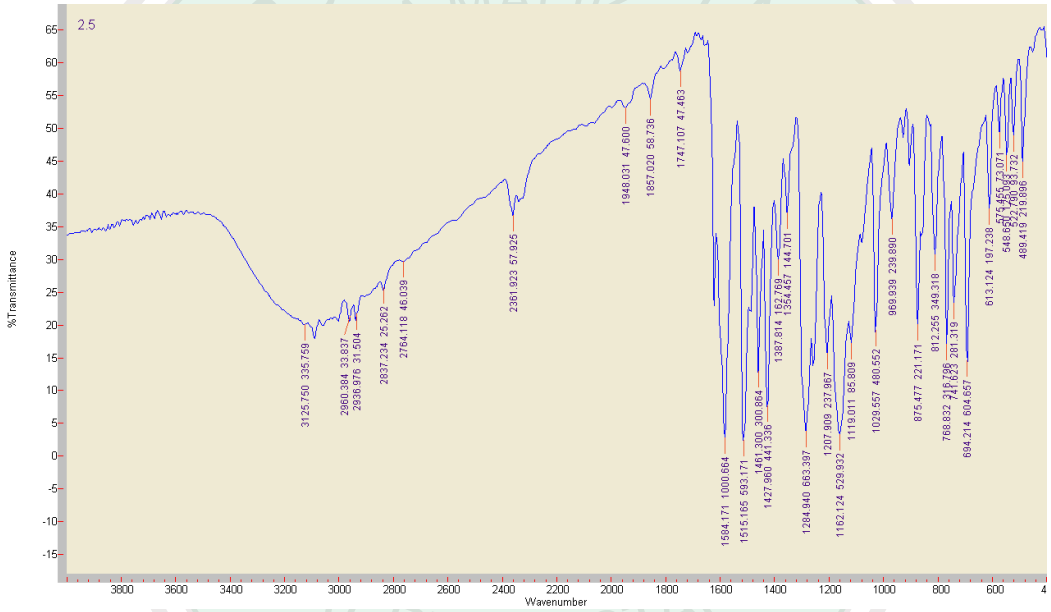


Gambar 4.6 Spektogram produk 4 hasil analisis FTIR

Hasil spekta IR menunjukkan adanya gugus –OH yang memunculkan pita serapan melebar yang khas pada daerah 2800-3500 cm^{-1}. Rentangan gugus C-H $_{sp2}$ aromatik memunculkan pita serapan lemah pada 3089 cm^{-1}, Ini didukung dengan adanya serapan pada 1516 cm^{-1} yang menunjukkan adanya gugus C=C aromatik. Serapan lemah pada 2938 cm^{-1} adalah akibat oleh rentangan C-H $_{sp3}$ dan didukung oleh adanya gugus metil (-CH_3) di pita serapan 1428 cm^{-1} (Purwono dkk., 2013).

Munculnya serapan kuat pada daerah 1285 dan 1030 cm^{-1} menunjukkan adanya gugus C-O-C eter (Ibrahim et al, 2006). Terbentuknya gugus imina (-C=N-) ditunjukkan oleh serapan kuat pada daerah 1584 cm^{-1} (Naqvi *et al*, 2009). Pita serapan di derah 876 dan 813 cm^{-1} menunjukkan adanya senyawa aromatik tersubtitusi (Lambert, 1987).

4.3.5 Identifikasi Spektra FTIR Produk 5 (katalis 2,5 mL)



Gambar 4.7 Spektogram produk 5 hasil analisis FTIR

Hasil spekta IR menunjukkan adanya gugus –OH yang memunculkan pita serapan melebar yang khas pada daerah 2800-3500 cm^{-1}. Rentangan gugus C-H $_{sp2}$ aromatik memunculkan pita serapan lemah pada 3086 cm^{-1}, Ini didukung dengan adanya serapan pada 1515 cm^{-1} yang menunjukkan adanya gugus C=C aromatik. Serapan lemah pada 2937 cm^{-1} adalah akibat oleh rentangan C-H $_{sp3}$ dan didukung oleh adanya gugus metil (-CH_3) di pita serapan 1428 cm^{-1} (Purwono dkk., 2013). Munculnya serapan kuat pada daerah 1285 dan 1030 cm^{-1} menunjukkan adanya gugus C-O-C eter (Ibrahim et al, 2006). Terbentuknya gugus imina (–C=N)

ditunjukkan oleh serapan kuat pada daerah 1584 cm^{-1} (Naqvi *et al*, 2009). Pita serapan di derah 875 dan 812 cm^{-1} menunjukkan adanya senyawa aromatik tersubtitusi (Lambert, 1987).

4.4 Penentuan Produk Sintesis Terbaik

Penentuan produk hasil sintesis terbaik (berdasarkan variasi volume katalis air jeruk nipis), perlu dilakukan untuk mengetahui produk dengan perlakuan mana yang lebih unggul. Berdasarkan rangkuman hasil interpretasi spektra IR pada Tabel 4.3, menunjukkan bahwa kelima senyawa ini memiliki spektra IR yang sangat mirip. Pita-pita serapan yang muncul juga memiliki bilangan gelombang yang berbeda sangat tipis dengan bentuk yang ekuivalen. Jadi dapat disimpulkan bahwa spektra IR yang dihasilkan oleh kelima produk (produk 1–5) adalah identik atau sama. Dengan hilangnya pita serapan gugus karbonil (–C=O) dari vanilin pada 1666 cm^{-1} serta terbentuknya pita serapan gugus imina (–C=N) pada panjang gelombang 1584 cm^{-1}, maka diduga kuat senyawa target (2-metoksi-4-((fenilimino)metil)fenol) telah berhasil terbentuk pada kelima produk yang dihasilkan dari lima variasi perlakuan.

Tabel 4.3 Gugus fungsi dan bilangan gelombang ($\bar{\upsilon}$) produk 1-5

$\bar{\upsilon}$ P1 (cm^{-1})	$\bar{\upsilon}$ P2 (cm^{-1})	$\bar{\upsilon}$ P3 (cm^{-1})	$\bar{\upsilon}$ P4 (cm^{-1})	$\bar{\upsilon}$ P5 (cm^{-1})	Gugus Fungsi
2800–3400	2800–3400	2800–3400	2800–3400	2800–3400	**-OH**
3091	3089	3086	3089	3086	**C-H** $_{sp2}$
1515	1515	1515	1516	1515	**C=C** aromatik
2935	2937	2937	2938	2937	**C-H** $_{sp3}$
1428	1428	1428	1428	1428	metil **(-CH_3)**
1285 dan 1030	1285 dan 1030	1285 dan 1030	1285 dan 1030	1285 dan 1030	**Eter (C-O-C)**
1584	1584	1584	1584	1584	**(-C=N-)**
876 dan 813	876 dan 812	875 dan 812	876 dan 813	875 dan 812	aromatik tersubtitusi

Keberhasilan suatu reaksi dapat ditentukan dari besarnya nilai rendemen yang didapatkan setelah proses pemurnian. Nilai rendemen dari beberapa variasi volume katalis air jeruk nipis disajikan pada Tabel 4.4:

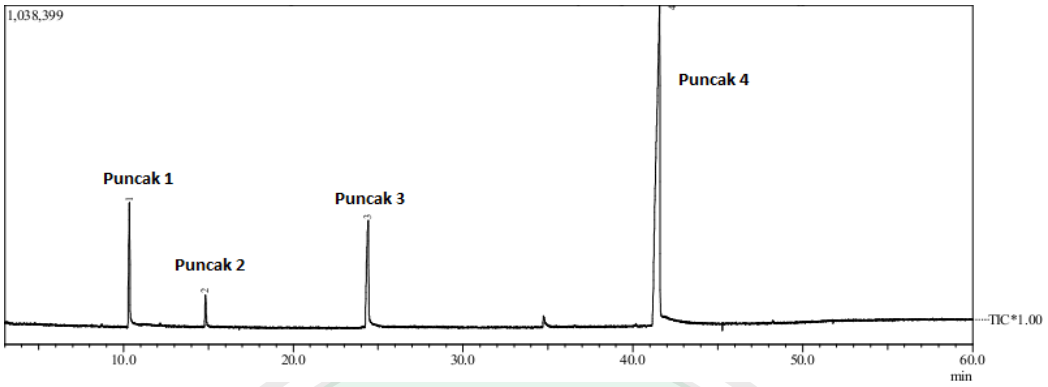
Tabel 4.4 Nilai rendemen produk tiap variasi volume katalis

Nama Produk	Volume Katalis Air Jeruk Nipis	Rendemen
P5	2,5 mL	36,8229 %
P4	2,0 mL	40,8469 %
P3	1,5 mL	48,5766 %
P2	1,0 mL	60,9847 %
P1	**0,5 mL**	**64,1234 %**

Data pada Tabel 4.4 menunjukkan bahwa nilai rendemen tertinggi terdapat Produk 1 dengan variasi katalis 0,5 mL. Jadi dapat dikatakan bahwa metode *Green synthesis* senyawa imina antara vanilin dan anilina terbaik adalah dengan menggunakan katalis air jeruk nipis sebanyak 0,5 mL. Nilai rendemen yang dihasilkan sebesar 64,1234 %. Hasil Rendemen terbaik selanjutnya dikarakterisasi lebih lanjut menggunakan instrumen KG-SM.

4.5 Karakterisasi Produk Terbaik (Produk 1) Menggunakan KG-SM

Analisis dengan Kromatografi Gas (KG) menghasilkan suatu kromatrogam yang memberikan informasi jumlah senyawa yang dapat dipisahkan dari sampel produk 1 yang telah dimasukkan. Gambar 4.8 menunjukkan bahwa KG berhasil memisahkan empat senyawa dari produk 1. Empat senyawa ini terwakili oleh empat puncak yang muncul pada kromatogram yang disajikan pada Gambar 4.8 beserta persentase luas area dan waktu retensi (*Rt*) pada Tabel 4.5.

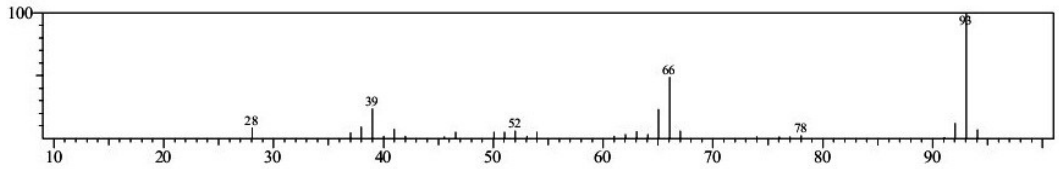


Gambar 4.8 Kromatogram hasil KG Produk 1

Tabel 4.5 Persentase luas area tiap puncak kromatogram

Puncak	Luas Area (%)	*Rt* (menit)
1	9,57	10,347
2	1,85	14,828
3	13,84	24,405
4	74,74	41,564
Total	100 %	-

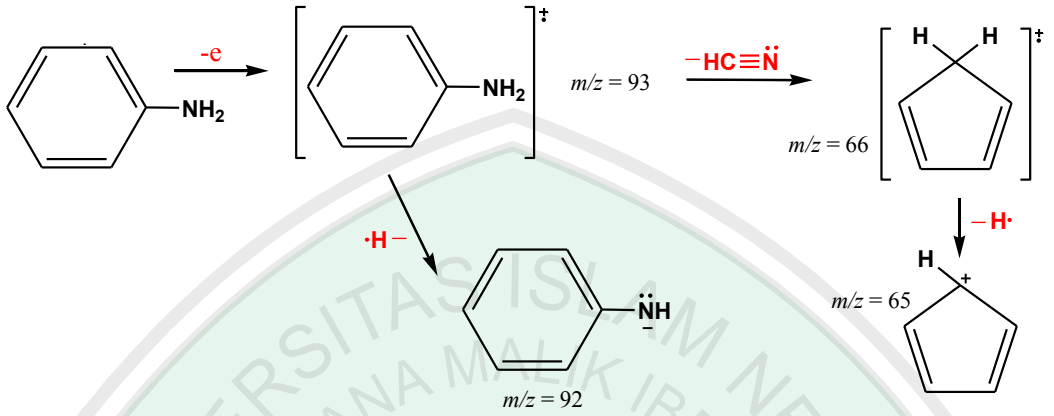
Berdasarkan nilai persentase luas area tiap puncak pada Tabel 4.5, terdapat empat puncak utama yakni puncak 1, 2, 3, dan 4. Puncak 1 dengan waktu retensi 10,347 menit dan persentase luas area 9,57 % memiliki spektra massa yang tersaji pada Gambar 4.9.



Gambar 4.9 Spektra massa Puncak 1

Hasil penelusuran *library*, diketahui bahwa spektra massa anilina (Lampiran 2) memiliki indeks kemiripan 96 % terhadap spektra puncak 1. Spektra massa pada Gambar 4.9 menunjukkan bahwa nilai *m/z* 93 merupakan puncak dasar sekaligus puncak ion molekular dengan kelimpahan relatif sebesar 100 %.

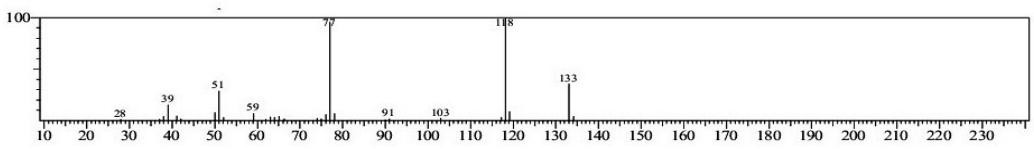
Nilai *m/z* 93 merupakan nilai yang sesuai dengan berat molekul anilina. Hal ini juga didukung oleh pola fragmentasi sebagaimana ditampilkan pada Gambar 4.10.



Gambar 4.10 Pola fragmentasi senyawa anilina

Anilina merupakan zat reaktan yang masih tersisa setelah proses sintesis. Senyawa anilina seharusnya sudah tidak ada dalam Produk 1 karena proses pemurnian telah dilakukan. Hal ini mengindikasikan bahwa proses pemurnian yang telah dilakukan masih kurang optimal. Penyebabnya bisa karena pemilihan pelarut, perbandingan volume pelarut, suhu pengendapan, dan lama waktu pengendapan.

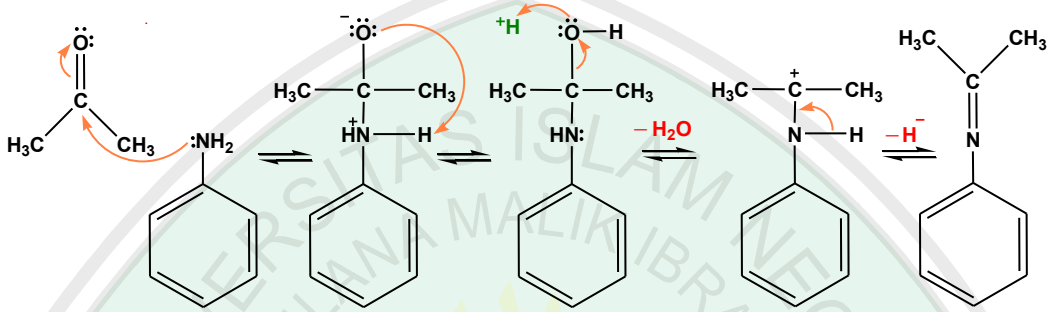
Puncak 2 dengan waktu retensi 14,828 menit dan persentase luas area 1,85 % memiliki spektra massa pada Gambar 4.11.



Gambar 4.11 Spektra massa Puncak 2

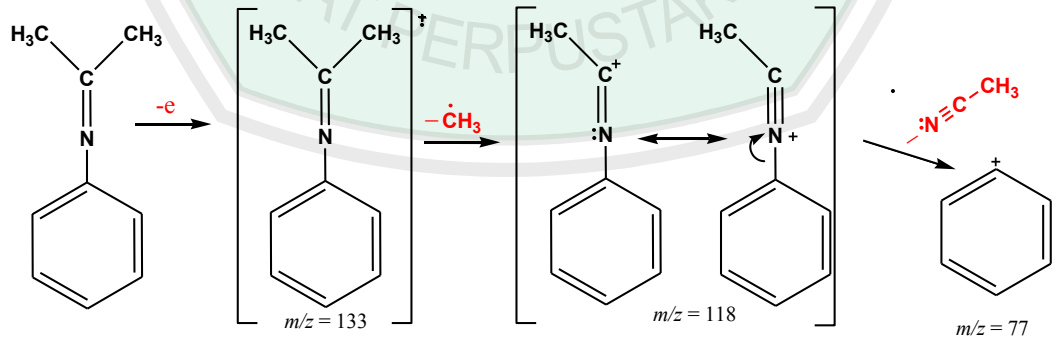
Hasil penelusuran *library* (Lampiran 2) menunjukkan bahwa tidak ada spektra massa yang sesuai dengan spektra Puncak 2. Spektra massa pada Gambar 4.11 menunjukkan bahwa nilai *m/z* 118 merupakan puncak dasar dengan kelimpahan relatif sebesar 100 %. Puncak ion molekular berada pada puncak *m/z*

133. Nilai ini (*m/z* 133) merupakan nilai yang sangat mirip dengan berat molekul senyawa N-(propan-2-ilidin)benzenamina. Senyawa ini diduga merupakan hasil dari reaksi pembentukan imina antara anilina dengan aseton menurut persamaan reaksi pada Gambar 4.12:



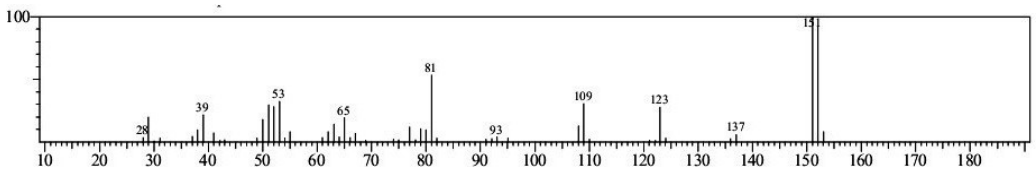
Gambar 4.12 Mekanisme reaksi pembentukan *N*-(propan-2-ilidin)benzenamina

Senyawa tersebut merupakan hasi samping (*by product*) yang tidak diharapkan terbentuk, sebab aseton adalah cairan yang digunakan untuk membersihkan sisa-sisa air dalam alat-alat gelas (erlenmeyer, pipet, gelas beaker dll.) setelah proses pencucian. Terbentuknya senyawa N-(propan-2-ilidin)benzenamina juga didukung oleh pola fragmentasi sebagaimana ditampilkan pada Gambar 4.13.



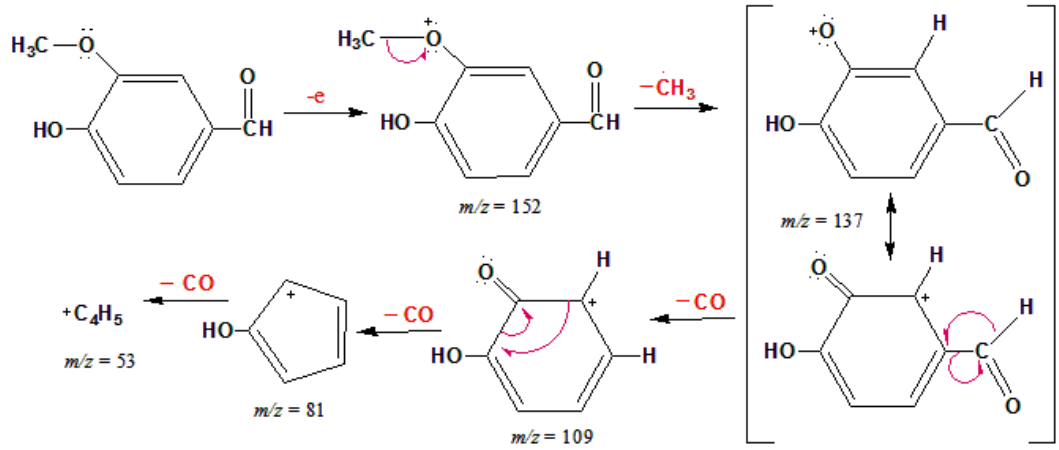
Gambar 4.13 Pola fragmentasi senyawa *N*-(propan-2-ilidin)benzenamina

Puncak 3 dengan waktu retensi 24,405 menit dan persentase luas area 13,84 % memiliki spektra massa yang tersaji pada Gambar 4.14.

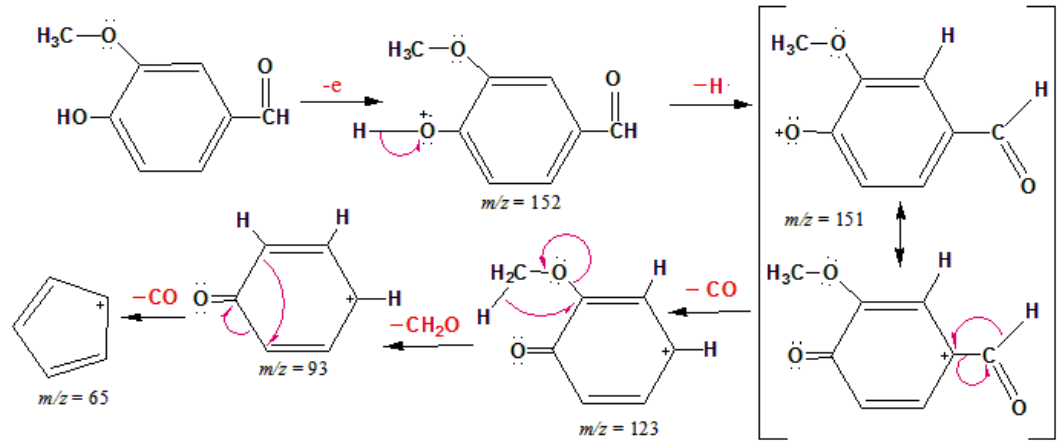


Gambar 4.14 Spektra massa Puncak 3

Hasil penelusuran *library*, diketahui bahwa spektra massa vanilin (Lampiran 2) memiliki indeks kemiripan 95 % terhadap spektra Puncak 3. Spektra massa pada Gambar 4.12 menunjukkan bahwa nilai *m/z* 151 dengan kelimpahan relatif sebesar 100 % merupakan puncak dasar. Puncak ion molekular berada pada *m/z* 152. Nilai *m/z* 152 merupakan nilai yang sesuai dengan berat molekul vanilin. Hal ini juga didukung oleh pola fragmentasi sebagaimana ditampilkan pada Gambar 4.15.



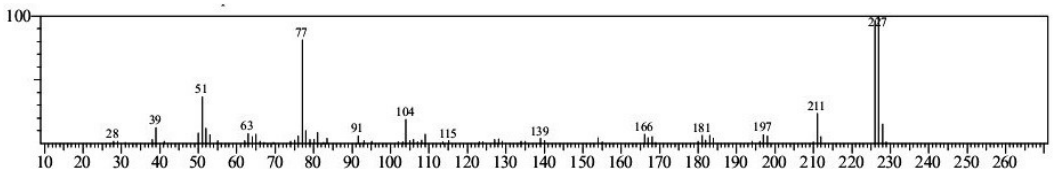
Pola Fragmentasi yang lain:



Gambar 4.15 Pola fragmentasi vanilin

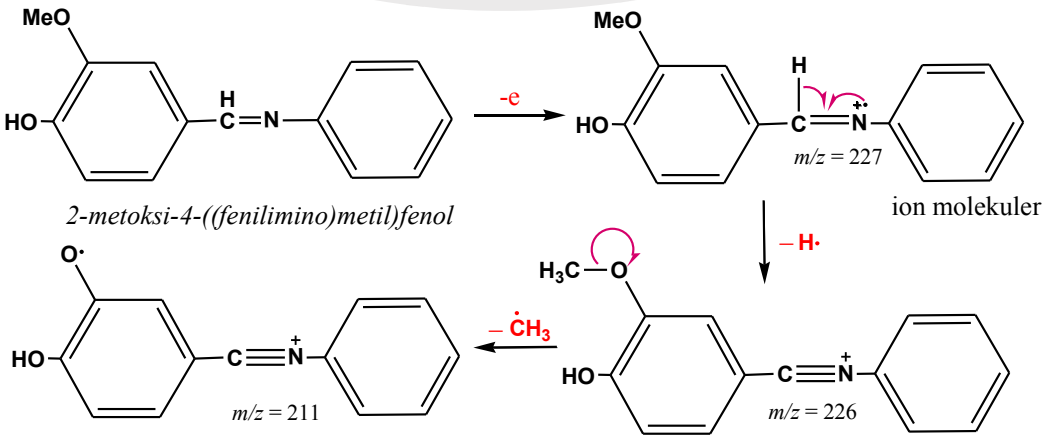
Vanilin juga merupakan zat reaktan yang masih tersisa setelah proses sintesis. Sama dengan anilina, vanilin seharusnya juga sudah hilang dari Produk 1 setelah proses pemurnian dilakukan. Hal ini juga mengindikasikan bahwa proses pemurnian yang telah dilakukan masih kurang optimal.

Puncak 4 dengan waktu retensi 41,567 menit dan persentase luas area 74,74 % memiliki spektra massa yang tersaji pada Gambar 4.16.

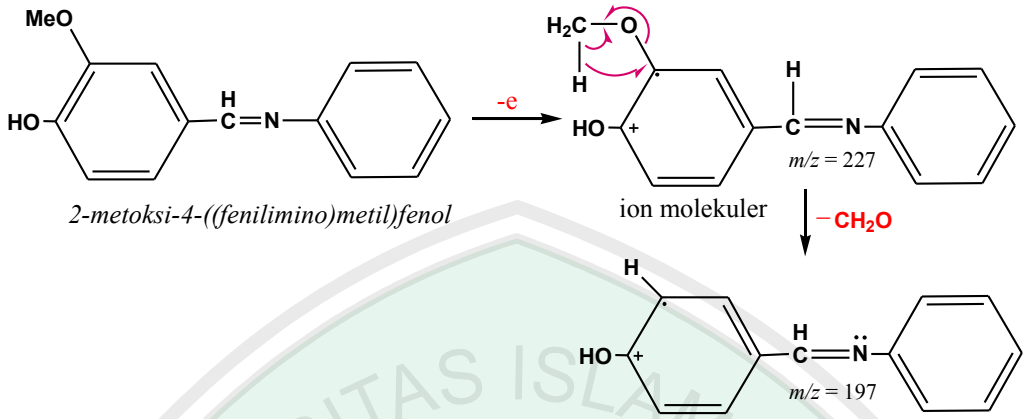


Gambar 4.16 Spektra massa Puncak 4

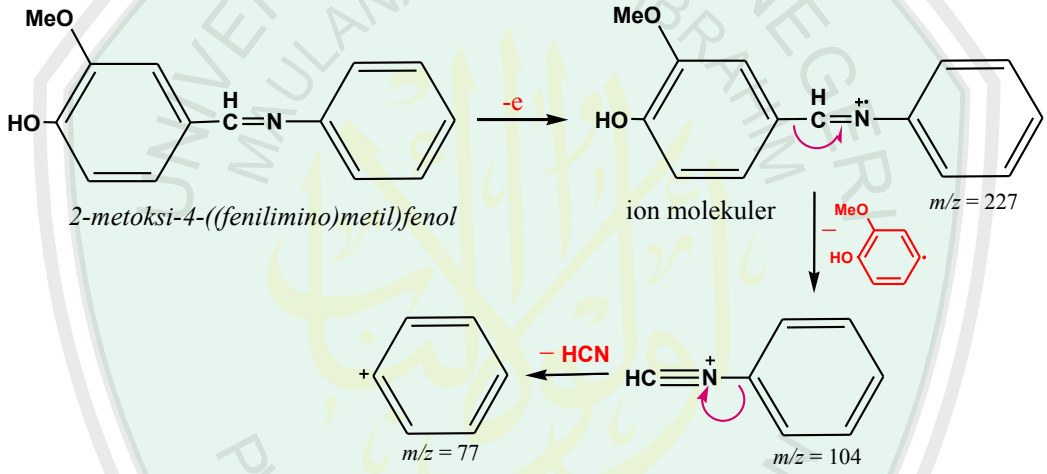
Spektra massa pada Gambar 4.16 menunjukkan bahwa nilai *m/z* 227 dengan kelimpahan relatif sebesar 100 % merupakan puncak dasar sekaligus puncak ion molekular. Berdasarkan penelusuran *library*, tidak ditemukan spektra senyawa yang sesuai dengan puncak 4. Namun nilai *m/z* 227 merupakan nilai yang sesuai dengan bentuk ion molekular ($M^{\bullet+}$) dari senyawa target yaitu 2-metoksi-4-((fenilimino)metil)fenol. Pola fragmentasi yang tersaji pada Gambar 4.17 juga menguatkan dugaan bahwa puncak 4 merupakan senyawa target sintesis.



Pola fragmentasi yang lain:



Pola fragmentasi yang lain:



Gambar 4.17 Pola fragmentasi senyawa 2-metoksi-4-((fenilimino)metil)fenol

Puncak 4 atau puncak senyawa target memiliki jumlah luas area tertinggi yaitu 74,74 %. Jadi di dalam 100 % rendemen hasil sintesis, terkandung 74,74 % senyawa target 2-metoksi-4-((fenilimino)metil)fenol serta 25,26 % pengotor meliputi 9,57 % anilin; 13,84 % vanilin; dan 1,85 % *by product*. Dengan demikian prosentase (%) hasil reaksi dapat diketahui yaitu 74,74 % dari jumlah rendemen terbaik yang didapat (64,1234 %), yakni sebesar 47,9258 %.

4.6 Tinjauan *Green Chemistry* dalam Islam

Sintesis kimia juga merupakan unit bidang kimia yang mempunyai potensi besar untuk mencemari lingkungan, sebab keberadaan limbah merupakan hal wajar dalam proses produksi. Misalkan proses produksi senyawa imina sebagai obat antibakteri dalam suatu industri farmasi mempunyai nilai efektifitas produksi sebesar 80%. Pada saat produksi, metode sintesis yang digunakan adalah metode konvensional yang membutuhkan pelarut kloroform dengan perbandingan reaktan: pelarut = 1:10. Maka dalam produksi 1000 g senyawa imina akan dihasilkan 200 g limbah reaktan serta 10.000 g limbah pelarut. Apabila industri tersebut membuat 2000 g senyawa imina per hari, maka dalam satu bulan saja, akan dihasilkan setidaknya 12.000 g limbah reaktan dan 600.000 g limbah pelarut. Limbah-limbah tersebut merupakan zat-zat kimia berbahaya yang dapat merusak lingkungan apabila dibuang langsung tanpa melalui proses pengolahan terlebih dahulu. Adanya metode sintesis ramah lingkungan merupakan solusi sintesis yang baik dalam kaitannya menjaga lingkungan.

Allah dengan tegas melarang umat manusia untuk berbuat kerusakan lingkungan. Firman Allah di dalam surat al A'raf: 56 mengatakan:

وَلاَتُفْسِدُوا فِي ٱلأَرْضِ بَعْدَ إِصْلاَحِهَا

Artinya: "Dan janganlah kamu membuat kerusakan di muka bumi, sesudah (Allah) memperbaikinya". (QS. al A'raf: 56)

Lebih lanjut Allah menegaskan dalam surat al Baqarah ayat 60:

كُلُواْ وَاشْرَبُواْ مِن رِّزْقِ اللَّهِ وَلاَ تَعْثَوْاْ فِي الأَرْضِ مُفْسِدِينَ

Artinya: "Makan dan minumlah rezki (yang diberikan) Allah, dan janganlah kamu berkeliaran di muka bumi dengan berbuat kerusakan". (QS. al Baqarah: 60)

Manusia tidak dapat hidup tanpa adanya alam semesta. Allah memperkenankan kita untuk memanfaatkan alam untuk memenuhi kehidupan kita, seperti makan, minum, atau mencari nafkah. Tetapi kita dilarang untuk merusaknya. Larangan ini mengandung makna dalam tentang betapa besarnya kasih sayang Allah kepada umat manusia. Larangan bertujuan agar manusia dapat menjaga keseimbangan alam dengan baik, sehingga manusia dapat hidup lebih lama di bumi.

Sifat dari alam semesta ini adalah tidak kekal (*fana'*). Peristiwa alamiah yang terjadi di alam semesta ini (gempa, gunung meletus, tsunami, dll.) selalu menuju pada kerusakan yang irreversibel dengan peningkatan entropi yang lebih tinggi (hukum termodinamika II). Untungnya Allah memberikan kita nikmat berupa hari kiamat, sehingga kita tidak sampai merasakan seramnya kehancuran dunia. Manusia dapat berperan aktif untuk mempercepat atau memperlambat datangnya hari kiamat dengan cara merusak atau menjaga alam semesta ini.

Di dalam sudut pandangan ilmu fiqih, larangan Allah dalam surat al A'raf ayat 56 dan al-Baqarah 60, dapat dijadikan sebagai dasar yang kuat untuk menarik suatu hukum. Larangan dalam kaidah ushul fiqih dikenal dengan istilah *an-Nahyu* (النهي). Terdapat dua kaidah ushul fiqih yang sesuai untuk menarik suatu hukum dari dua firman Allah tersebut, yaitu (Hakim, 1927):

الأصل فى النهى للتحريم

"Hukum asal dalam suatu larangan menunjukkan arti haram".

النهى عن الشيئ أمربضده

"*Larangan terhadap sesuatu berarti perintah kebalikannya"*.

Dua kaidah ini apabila diaplikasikan ke dalam firman Allah tentang larangan merusak lingkungan maka akan didapatkan hukum sementara bahwa merusak lingkungan adalah haram dan menjaga lingkungan adalah wajib. Larangan keras merusak lingkungan juga disampaikan oleh Rasulullah Saw. dalam hadis yang berbunyi:

عَنْ سَعِيْدٍ بْنِ زَيْدٍ رضي الله عنه قال سَمِعْتُ رَسُولَ اللَّهِ صَلَّى اللَّهُ عَلَيْهِ وَسَلَّمَ يَقُولُ مَنْ ظَلَمَ مِنَ الْأَرْضِ شَيْئًا طُوِّقَهُ مِنْ سَبْعِ أَرَضِيْنَ (رواه البخاري)

Artinya: *"Dari Sa'id ibn Yazid ra ia berkata: Saya mendengar Rasulullah saw bersabda: Barang siapa melakukan kezhaliman terhadap sesuatu pun dari bumi, niscaya Allah akan membalasnya dengan borgolan tujuh kali bumi yang ia zhalimi"*. (HR. Bukhari).

Di dalam Undang-Undang Dasar Negara Republik Indonesia Tahun 1945 Pasal 33 ayat (3) juga dituliskan bahwa, "*Bumi dan air dan kekayaan alam yang terkandung di dalamnya dikuasai oleh negara dan dipergunakan untuk sebesar-besar kemakmuran rakyat*". Lebih lanjut Pemerintah Indonesia juga mengeluarkan Undang-Undang RI Nomor 32 Tahun 2009 tentang Pertambangan Mineral dan Batubara. Di dalam Pasal 97 disebutkan bahwa, "*Tindak pidana dalam undang-undang ini merupakan kejahatan*". Bagi orang yang dengan sengaja merusak lingkungan akan dipenjara maksimal 10 tahun dan dikenakan denda paling banyak 10 milyar. Dengan adanya dasar-dasar hukum tersebut, maka dapat diambil dua buah kesimpulan hukum yaitu:

1. Merusak lingkungan hukumnya **haram**
2. Menjaga lingkungan hukumnya **wajib**

Green Chemistry adalah suatu upaya untuk menciptakan kegiatan kimia yang ramah lingkungan. Aspek *green chemistry* adalah meminimalisasi zat berbahaya, optimalisasi penggunaan katalis, penggunaan reagen yang tidak beracun, penggunaan sumber daya yang dapat diperbaharui, penggunaan pelarut yang ramah lingkungan dan dapat didaur ulang. *Green chemistry* bertujuan mengembangkan proses kimia dan produk kimia yang ramah lingkungan (Ulfah dkk, 2013).

Green chemistry adalah pemikiran mengenai kimia untuk menyelamatkan lingkungan dari pencemaran. *Green chemistry* bukanlah cabang ilmu kimia baru, tetapi cara pandang atau strategi dalam kaitannya memanfaatkan kimia yang ramah lingkungan. Pada penelitian ini telah dilakukan sintesis suatu senyawa 2-metoksi-4-((fenilimino)metil)fenol yang ramah lingkungan atau biasa disebut *green synthesis.* Upaya *green synthesis* yang digunakan adalah proses sintesis yang bebas dari pelarut (*free solvent*) serta penggunaan katalis asam alami dari air buah jeruk nipis. Semoga *green synthesis* ini dapat berperan aktif dalam menjaga lingkungan dengan cara meminimalisis limbah proses sintesis seperti pelarut serta katalis yang berbahaya. Menjaga lingkungan adalah suatu kewajiban, maka upaya mengembangkan *green synthesis* juga merupakan suatu kewajiban bagi segenap kimiawan, terutama kimiawan muslim.

BAB V

PENUTUP

5.1 Kesimpulan

1. Jumlah katalis air buah jeruk nipis terbaik dalam reaksi pembentukan imina tanpa pelarut antara vanilin dan anilina adalah 0,5 mL.
2. Produk terbaik yang dihasilkan memiliki sifat fisik berupa padatan, berwarna kuning, titik lebur = 150 C^{o}, dan rendemen sebesar 64,1234 % dengan nilai kemurnian sebesar 74,74 %. Produk memiliki spektra IR khas senyawa imina (C=N) pada 1584 cm^{-1}. Spektra Massa *m/z* 227 (M^{*+}) muncul sebagai puncak ion molekuler senyawa target sintesis 2-metoksi-4-((fenilimino)metil)fenol.

5.2 Saran

1. Perlu dilakukan penelitian lanjutan tentang metode pemurnian yang baik, waktu reaksi terbaik, variasi jumlah katalis di bawah 0,5 mL, agar didapatkan rendemen yang lebih baik dengan tingkat kemurnian lebih tinggi.
2. Perlu juga dilakukan penelitian menggunakan asam sitrat buatan sebagai katalis pembanding.
3. Perlu dilakukan penelitian untuk menentukan eluen yang sesuai saat monitoring menggunakan plat KLT.

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ALCHEMY *Journal of Chemistry*

Research Article

Synthesis of Imine Compound From Vanillin And Aniline With Variation Amount of Lime Juice Catalyst

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ABSTRACT

Synthesis of imine compound from vanillin and aniline has been established by using natural acid from lime fruit (*Citrus aurantifolia*) as catalyst under the solvent free. The study was conducted to know the result and characteristics of the imine product. The variation amount lime juice catalyst were used are 0,5; 1,0; 1,5; 2,0; and 2,5 mL. The product was characterized by observing the shape, color, melting point, identificated by using FTIR, and GC-MS. The physical characteristics of the best product: solids, yellow, melting point = 150 ^{o}C, yield = 64,1234 % with the purity value = 74,74 %. IR spectra: 2800-3500 cm^{-1} (OH), 3086 cm^{-1} (C-H sp2), 1515 cm^{-1} (C=C aromatic), 2937 cm-1 (C-H sp3), 1428 cm-1 (-CH3), 1285 and 1030 cm-1 (C-O-C eter), 1584 cm-1 (C=N), 875 and 812 cm-1 (substitued aromatic). Mass Spectra: m/z 227 (M^{*+}), m/z 226 (M^{*+}), +-H), m/z 211 (M^{*+}), -H-CH_3), m/z 197 (M^{*+}-CH_2O), m/z 104 (M^{*+}-CH_2O- phenyl), m/z 77 (M^{*+}-CH_2O-phenyl-HCN).

Keywords: Imine, Vanillin, Anilina, Lime

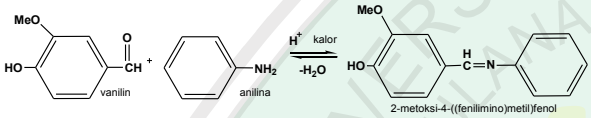
Telah dilakukan sintesis senyawa imina dari vanilin dan anilina menggunakan katalis asam alami dari buah jeruk nipis (Citrus aurantifolia) dalam kondisi tanpa pelarut (solvent free). Penelitian dilakukan untuk mengetahui hasil reaksi pembentukan imina antara vanilin dan anilina dengan variasi jumlah katalis jeruk nipis serta karakteristik produk yang dihasilkan. Variasi jumlah katalis jeruk nipis yang digunakan adalah 0,5; 1,0; 1,5; 2,0; dan 2,5 mL. Karakterisasi produk dilakukan dengan mengamati wujud, warna, titik lebur, serta identifikasi menggunakan FTIR dan KG-SM. Produk terbaik yang dihasilkan memiliki sifat-sifat antara lain: padatan, berwarna kuning, titik lebur = 150-152 Co, dan rendemen terbaik sebesar 64,1234 % dengan nilai kemurnian senyawa target sebesar 74,74 %. Spektra IR: 2800-3500 cm-1 (OH), 3086 cm-1 (C-H sp2), 1515 cm-1 (C=C aromatik), 2937 cm-1 (C-H sp3), 1428 cm-1 (-CH3), 1285 dan 1030 cm-1 (C-O-C eter), 1584 cm-1 (–C=N), dan 875 dan 812 cm-1 (aromatik tersubtitusi). Spektra Massa: m/z 227 (M^{*+}), m/z 226 (M^{*+}-H), 211 (M^{*+}-H-CH_3), m/z 197 (M^{*+}-OCH_2), m/z 104 (M^{*+}-CH_2O-fenil), m/z 77 (M^{*+}-CH_2O-fenil-HCN).

Kata Kunci: Imina, Vanilin, Anilina, Jeruk Nipis

1. Pendahuluan

Senyawa imina dan turunannya, merupakan senyawa yang sering disintesis. Kegunaan senyawa ini sangat luas. Senyawa imina berpotensi besar sebagai antioksidan, antimikroba, dan indikator asam-basa (Purwono dkk, 2013). Imina juga merupakan bahan baku dalam sintesis obat penenang, obat bius, obat kontrasepsi kehamilan, anti ketombe, analgesik, dan anti inflamasi (Vibhute et al., 2011).

Purwono dkk. (2013) telah melakukan sintesis senyawa imina dari vanilin dan anilina dengan pelarut etanol dalam refluks. Reaksi pembentukan imina antara vanilin dan anilina dapat berlangsung menurut persamaan reaksi pada Gambar 1:



Gambar 1. Reaksi pembentukan imina antara vanilin dan anilina

Imina yang dihasilkan selanjutnya dikarakterisasi menggunakan IR, H-NMR, dan GC-MS. rendemen yang dihasilkan sebesar 82,17 %.

Sintesis senyawa organik yang ekonomis, mudah, ramah lingkungan, dan hasil produk melimpah atau biasa disebut green synthesis, telah banyak dilakukan oleh ilmuwan kimia. Beberapa metode seperti metode penggerusan, telah dilakukan oleh Rahman et al., (2012) saat mensintesis senyawa aldol dan menghasilkan rendemen melebihi 95%. Pada tahun sebelumnya Naqvi et al., (2009) juga melakukan sintesis senyawa imina dalam pelarut air pada temperatur ruang dan tanpa menggunakan katalis dan memperoleh rendemen hingga 90%.

Penggunaan katalis alami dari air buah lemon telah dilakukan oleh Patil et al., (2011 dan 2012) dalam sintesis beberapa senyawa imina dari alkil benzaldehida dan alkil anilina. Perlakuan ini menghasilkan produk imina dengan rendemen sebesar 72–100 %. Karakterisasi produk dilakukan dengan bantuan IR dan 1H-NMR. Lebih lanjut Patil et al., (2011) juga menyatakan bahwa air buah nanas merupakan katalis yang sangat baik dalam reaksi Biginelli.

Penelitian-penelitian tersebut merupakan salah satu upaya untuk mematuhi perintah Allah SWT. untuk tidak membuat kerusakan di muka bumi sebagaimana firman-Nya dalam surat al A'raf: 56). Jadi sintesis senyawa imina dari vanilin dan anilina dalam kondisi tanpa pelarut, dengan bantuan air buah jeruk nipis sebagai katalis asam alami, juga merupakan upaya pengembangan metode sintesis yang ramah lingkungan (*green synthesis*).

2. Bahan dan Metode

2.1. Bahan

Bahan yang digunakan dalam penelitian ini adalah Vanilin f.s (Merck), Anilina f.s (Merck), jeruk nipis komersil, dan, plat KLT GF_{254}.

2.2. Preparasi Katalis Asam dari Buah Jeruk Nipis (Citrus Aurantifolia)

Jeruk nipis segar dibelah kemudian diperas. Air jeruk yang dihasilkan kemudian disaring hingga mendapatkan air jeruk yang bersih dari padatan-padatan buah. Air jeruk nipis siap digunakan sebagai katalis (Patil et al., 2011).

2.3. Sintesis senyawa imina dari vanilin dan anilina dengan variasi jumlah katalis air jeruk nipis

Sintesis diawali dengan menyampurkan 10 mmol (0,9313 g) senyawa anilina dengan 10 mmol (1,5215 g) vanilin dan 0,5 mL katalis air jeruk nipis. Campuran lalu diaduk secara merata menggunakan pengaduk gelas selama 30 menit hingga terbentuk padatan berwarna kuning. Perlakuan yang sama diulangi untuk variasi volume katalis 1,0; 1,5; 2,0 dan 2,5 mL. Padatan yang terbentuk dimurnikan melalui proses rekristalisasi. Monitoring reaksi dilakukan dengan menggunakan plat KLT.

2.3. Karakterisasi produk

Padatan murni diamati sifat fisiknya (wujud,warna, massa, dan ttik lebur) lalu diidentifikasi dengan spektrofotometer FT-IR Varian tipe FT 1000. Produk terbaik selanjutnya dianalisis dengan KG-SM -QP2010S Shimadzu.

3. Hasil dan Pembahasan

Tabel 1. Hasil akhir pengamatan fisik lima produk hasil variasi perlakuan

Pengamatan	P1	P2	P3	P4	P5
Variasi Vol. Katalis (mL)	0,5	1,0	1,5	2,0	2,5
Wujud	Padatan	Padatan	Padatan	Padatan	Padatan
Warna	Kuning	Kuning Kecoklatan	Kuning Kecoklatan	Kuning Kecoklatan	Kuning Kecoklatan
Massa (gram)	1,459	1,386	1,104	0,928	0,8375
Titik Lebur (°C)	150	152	150	152	152
Rendemen (%)	64,1234	60,9847	48,5766	40,8469	36,8229

Keterangan: V1 = Produk Variasi 1; V2 = Produk Variasi 2; P3 = Produk Variasi 3; P4 = Produk Variasi 4; P5 = Produk Variasi 5

Berdasarkan Tabel 1, sifat fisik kelima produk memiliki kemiripan titik leleh yaitu antara 150–152 oC. Produk dari variasi 1 berupa padatan kuning, sedangkan pada variasi 2–5 padatan bewarna kuning kecoklatan. Warna coklat yang muncul kemungkinan berasal dari sisa anilina yang tidak bereaksi. Hasil ini (wujud, warna, dan titik lebur) sesuai dengan sifat fisik dari senyawa 2-metoksi-4-((fenilimino)metil) fenol yang telah berhasil disintesis oleh Purwono, dkk (2013). Massa produk menurun seiring bertambahnya volume katalis. Hal ini terjadi karena semakin bertambahnya katalis asam, akan membuat amina menjadi terprotonasi dan menurunkan kereaktifannya sebagai nukleofil (Yadav dan Mani, 2013).

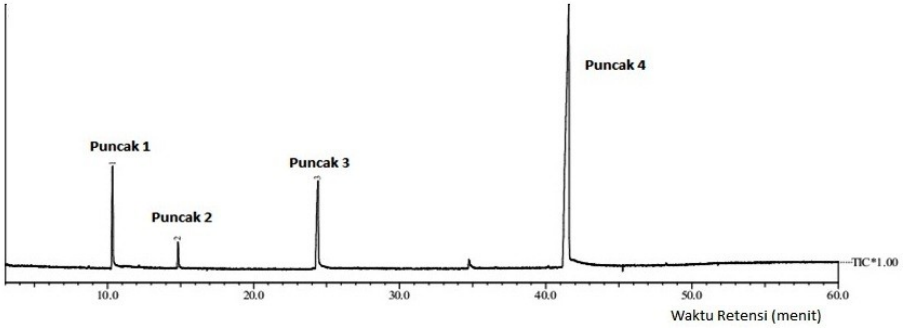
3.1 Analisis Dengan Spektrofotometer FTIR

Tabel 2. Gugus fungsi dan bilangan gelombang ($\bar{\upsilon}$) produk 1-5 Hasil FTIR

$\bar{\upsilon}$ P1 (cm^{-1})	$\bar{\upsilon}$ P2 (cm^{-1})	$\bar{\upsilon}$ P3 (cm^{-1})	$\bar{\upsilon}$ P4 (cm^{-1})	$\bar{\upsilon}$ P5 (cm^{-1})	Gugus Fungsi
2800–3400	2800–3400	2800–3400	2800–3400	2800–3400	**-OH**
3091	3089	3086	3089	3086	**C-H** $_{sp2}$
1515	1515	1515	1516	1515	**C=C** aromatic
2935	2937	2937	2938	2937	**C-H** $_{sp3}$
1428	1428	1428	1428	1428	metil **(-CH_3)**
1285 dan 1030	1285 dan 1030	1285 dan 1030	1285 dan 1030	1285 dan 1030	**Eter (C-O-C)**
1584	1584	1584	1584	1584	**(-C=N-)**
876 dan 813	876 dan 812	875 dan 812	876 dan 813	875 dan 812	aromatik tersubtitusi

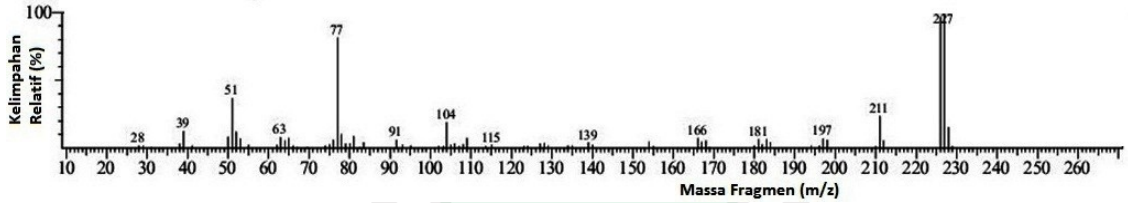
Tabel 2 menunjukkan bahwa kelima produk memiliki Pita-pita serapan pada bilangan gelombang yang hampir sama. Hilangnya serapan –C=O dari vanilin pada 1666 cm-1 serta terbentuknya pita serapan gugus imina (–C=N) pada panjang gelombang 1584 cm-1, menandakan bahwa senyawa imina telah berhasil terbentuk. Produk terbaik dipilih berdasarkan nilai rendemen. Nilai rendemen tertinggi terdapat pada produk dengan variasi jumlah katalis 0,5 mL (Tabel 1). Selanjutnya Produk 1 (P1) akan dikarakterisasi lebih lanjut menggunakan KG-SM.

3.2 Karakterisasi produk terbaik menggunakan KG-SM



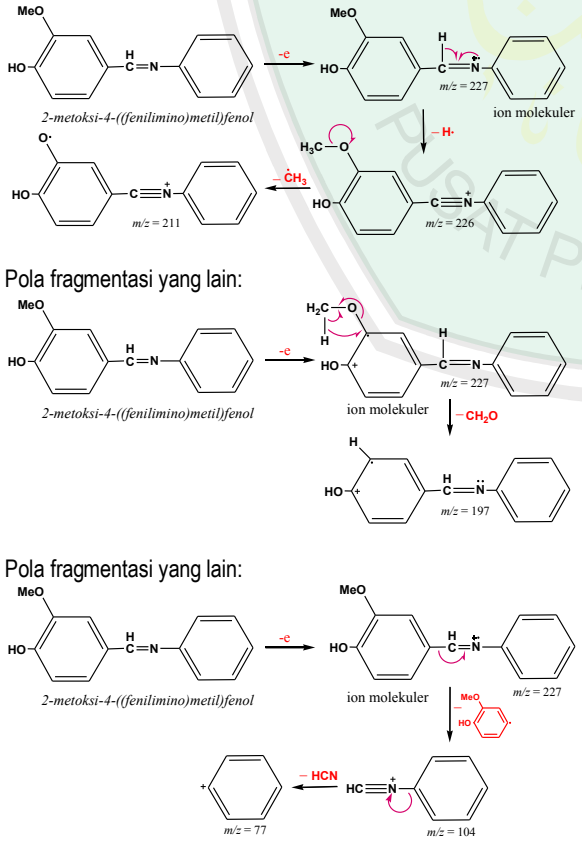
Gambar 2. Kromatogram hasil analisis KG Produk 1

Gambar 2 menunjukkan bahwa KG berhasil memisahkan produk 1 menjadi empat senyawa yang terwakili oleh empat puncak yang muncul. Dari hasil penelusuran library serta pengamatan pola fragmentasi SM, diketahui bahwa puncak 1 merupakan senyawa anilina, puncak 2 adalah by produk, dan puncak 3 adalah senyawa vanillin. senyawa target berada pada puncak 4 dengan waktu retensi 41,567 menit dan persentase luas area 74,74 %. Spektra massa puncak 4 tersaji pada Gambar 3.



Gambar 3. Spektra massa puncak 4

Spektra massa pada Gambar 3 menunjukkan bahwa nilai *m/z* 227 dengan kelimpahan relatif sebesar 100 % merupakan puncak dasar sekaligus puncak ion molekuler. Berdasarkan penelusuran *library*, tidak ditemukan spektra senyawa yang sesuai dengan puncak 4. Namun nilai *m/z* 227 merupakan nilai yang sesuai dengan bentuk ion molekuler (M^{*+}) dari senyawa target yaitu 2-metoksi-4-((fenilimino)metil)fenol. Pola fragmentasi yang tersaji pada Gambar 4 juga menguatkan dugaan bahwa puncak 4 merupakan senyawa target sintesis.



Gambar 4. Pola fragmentasi senyawa 2-metoksi-4-((fenilimino)metil)fenol

IV. Kesimpulan

Jumlah katalis asam alami dari buah jeruk nipis terbaik dalam reaksi pembentukan imina tanpa pelarut antara vanilin dan anilina adalah 0,5 mL. Produk terbaik yang dihasilkan memiliki sifat fisik berupa padatan berwarna kuning, titik lebur = 150 ^{o}C, dan rendemen sebesar 64,1234 % dengan nilai kemurnian sebesar 74,74 %. Produk memiliki spektra IR khas senyawa imina (C=N) pada 1584 cm^{-1}. Spektra Massa *m/z* 227 (M^{*+}) muncul sebagai puncak ion molekuler senyawa target sintesis 2-metoksi-4-((fenilimino) metil)fenol.

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SYNTHESES OF AZO-IMINE DERIVATIVES FROM VANILLIN AS AN ACID BASE INDICATOR

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ABSTRACT

*Preparations of azo, imine and azo-imine derivatives from vanillin as an indicator of acid-base titration have been carried out. The azo derivative of 4-hydroxy-3-methoxy-5-(phenylazo)benzaldehyde **2** was produced by diazotitation reaction of vanillin in 37.04% yield. The azo product was then refluxed with aniline in ethanol to yield azo-imine derivatives, 2-methoxy-6-(phenylazo)-4-((phenylimino)methyl)phenol **1** in 82.21% yield. The imine derivative, 2-methoxy-4-((phenylimino)methyl)-phenol **3** was obtained by refluxing of vanillin and aniline mixture in ethanol solvent and produced 82.17% yield. The imine product was then reacted with benzenediazonium chloride salt. However, the products indicated hydrolyzed product of 4-hydroxy-3-methoxy-5-(phenylazo)benzaldehyde **2** in 22.15% yield. The 2-methoxy-4-((phenylimino)methyl)phenol **2** could be used as an indicator for titration of NaOH by $H_2C_2O_4$ with maximum concentration of $H_2C_2O_4$ 0.1 M while the target compound **1** could be used as titration indicator for titration of NaOH with $H_2C_2O_4$ with same result using phenolphthalein indicator.*

Keywords: *vanillin; indicator of acid-base titration; azo-imine group*

ABSTRAK

*Telah dilakukan sintesis turunan senyawa azo, imina dan azo-imina dari vanilin sebagai indikator titrasi asam-basa. Sintesis turunan azo, 4-hidroksi-3-metoksi-5-(fenilazo)benzaldehida **2** dilakukan dengan reaksi diazotasi vanilin dengan rendemen 37,04%. Produk azo selanjutnya direfluks dengan anilina dalam pelarut etanol menghasilkan turunan azo-imina, 2-metoksi-6-(fenilazo)-4-((fenilimino)metil)fenol **1** dengan rendemen 82,21%. Sintesis turunan imina dilakukan dengan merefluks campuran vanilin dan anilina dalam pelarut etanol menghasilkan 2-metoksi-4-((fenilimino)metil)fenol **3** dengan rendemen 82,17%. Produk imina selanjutnya direaksikan dengan garam benzenadiazonium klorida. Namun produk yang terbentuk adalah produk hidrolisis 4-hidroksi-3-metoksi-5-(fenilazo)benzaldehida **2** dengan rendemen 22,15%. Senyawa 2-metoksi-4-((fenilimino)metil)fenol dapat dijadikan sebagai indikator untuk titrasi NaOH oleh $H_2C_2O_4$ dengan konsentrasi maksimum $H_2C_2O_4$ 0,1 M, sedang senyawa target mempunyai hasil yang sama dengan menggunakan indikator fenolftaline.*

Kata Kunci: *vanillin; indikator titrasi asam-basa; gugus azo-imin*

INTRODUCTION

Recently, attempts to synthesize for acid-base titration indicator from the natural products of phenol has become our concerns [1] The indicator compounds from phenol natural product compounds have been obtained by extending of delocalization of electron through chromophoric group [2]. The investigation also showed the increases in the visible absorption through the addition of base and acid. We were interested to introduce azo and imine groups together into vanillin as a targeted compound **1**. The azo derivatives have been used for dyes synthesis [3,4], metal ion sensor [5] and pH measurement [6]. The imine derivatives have been used for pigments [7], titration indicator [8] and fluorometry reagent [9].

The target compound **1** would be synthesized by two routes. First route, the aldehyde group in vanillin is converted to imine derivative by Schiff-base imine formation and then reacted diazotization with benzenediazonium ion [10]. The second route, vanillin is reacted by benzenediazonium ion and then converted to imine derivatives. All of imine, azo and imine-azo product derivatives contain chromophoric group. They will be examined the change in the color of solution through the addition of base and acid.

In this paper, the targeted compound **1** is subjected to examine stabilization in acid and base. The

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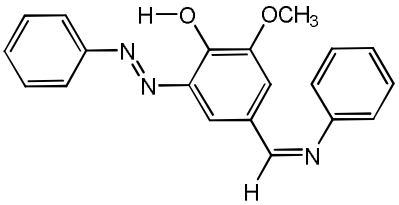


Fig 1. The structure of the designed potential acid-base titration indicator (1)

azo group indicates stabilization in acid and base condition while the imine could be hydrolyzed in base condition [11]. Such phenomenon is unexpected for indicator compounds. Therefore, it seems quite challenging to observe the study of their acid-base equilibrium in order to establish whether it could be used as an acid-base indicator.

EXPERIMENTAL SECTION

Materials

All reagents and solvents were purchased from E.Merck, unless otherwise specified. The materials used in this study were: vanillin, aniline, HCl 37% w/v, $NaNO_2$, NaOH, $CHCl_3$, $NaHCO_3$, Na_2SO_4 anhydrous, ethanol, phenolphthalein indicator, KH_2PO_4, Na_2HPO_4, silica gel 60 (0.040 to 0.063 mm), buffer solution pH 2 to 13.

Instrumentation

Infrared spectra were recorded with Shimadzu Prestige-21FTIR Spectrophotometer. ^{1}H-NMR spectra were recorded on JEOL JNM-MY60 spectrometer. Mass spectra were performed on Shimadzu QP-QP-5000 and 2010. Melting point was recorded with uncorrected Electrothermal-9100.

Procedure

Synthesis of 4-hydroxy-3-methoxy-5-(phenylazo) benzaldehyde (2)

Aniline (1.49 g, 16 mmol) was dissolved in a mixture of HCl 37% w/v (4.73 mL, 48 mmol) and distilled water (4.73 mL) in beaker glass 250 mL. The solution was cooled in an ice bath until a temperature to 0–5 °C. $NaNO_2$ (1.21 g, 17.6 mmol) was dissolved in aquadest (6 mL) and chilled in an ice bath. The solution of $NaNO_2$ was added dropwise into the solution of aniline-HCl, stirring and temperature maintained at 0–5 °C to produce benzenediazonium chloride salt solution. The solution was kept for several minutes with the temperature maintained at 0–5 °C. Vanillin (2.43 g, 16 mmol) was dissolved in NaOH solution 10% (w/v) (7.5 mL). The solution was cooled in an ice bath until a temperature of 0–5 °C. Solution of cooled benzenediazonium chloride was added slowly to the solution of sodium-vanillin, stirring constantly until it forms a gel. The gel was then separated by extraction using chloroform (3 x 25 mL) and the organic layer was neutralized with $NaHCO_3$ solution. The organic layer was dried with anhydrous Na_2SO_4. The solvent of chloroform was evaporated with Büchi evaporator and residue was purified by using column chromatography with silica gel absorbent and chloroform eluent. After evaporating of the chloroform eluent, product was obtained as red solid, yield 37.04%, m.p. 132–133 °C. IR cm^{-1}: 3425 (O-H); 3055 (C_{sp2}-H aromatic); 2931 (C_{sp3}-H); 1674 (C=O); 1604 (C=C aromatic); 1525 (-N=N-), and 864 (aromatic substituted). ^{1}H-NMR: δ/ppm 14.2 (O-H,s,1H), 9.95 (CHO,s,1H), 7.8 (aromatic,m,7H), 3.9 (OCH_3,s,3H); m/z: 256 (30%), 179 (10%), 151 (30%), 77 (100%).

Synthesis of 2-methoxy-4-((phenylimino)methyl) phenol (3)

Vanillin (0.28 g, 3 mmol) and ethanol (25 mL) was introduced to the base-round three neck flask capacity 100 mL equipped with magnetic stirrer, a thermometer and condenser. Aniline (0.46 g, 3 mmol) was added to the flask and refluxed for 30 min. The result was cooled to room temperature and dried with anhydrous Na_2SO_4. Solvent was evaporated with evaporator Büchi and residue was added with aquadest until the precipitate formed. The precipitation was filtered and then dried in desiccators. The product was characterized as yellow powder (82.17%), m.p. 150–152 °C, IR cm^{-1}: 3500 (O-H); 3086 (C_{sp}^2-H aromatic); 2900 (C_{sp3}-H); 1581 (C=N); 1512 (C=C aromatic); 871 (aromatic substituted). ^{1}H-NMR: δ/ppm 8.36 (-CH=N,s,1H); 7.6 ppm (O-H,s,1H); 7.27 (Ar,m,8H), 3.9 (OCH_3,s,3H); m/z: 227 (100%), 197 (10%), 104 (20%), 77 (80%).

Synthesis of 2-methoxy-6-(phenylazo)-4-((phenyl imino)methyl)phenol (1)

The compound of 4-hydroxy-3-methoxy-5-(phenylazo)benzaldehyde **2** (0.19 g (0.75 mmol)) and ethanol (15 mL) was introduced into the base-round three neck flask capacity 100 mL equipped with a magnetic stirrer, thermometers and condenser. Aniline (0.07 g, 0.75 mmol) was added to the flask and refluxed for 30 min. The result was cooled to room temperature. Solvent was evaporated with evaporator Büchi. The residue was added with aquadest and stirred until the precipitate formed. Precipitate was filtered and washed with aquadest and dried in desiccators. The product was obtained as brown powder (82.21%), m.p. 144–146 °C, IR cm^{-1}: 3433 (O-H); 3070 (C_{sp}^2-H aromatic); 2931 (C_{sp3}-H); 1627 (C=N), 1589 (N=N); 1489 (C=C aromatic); 864

(aromatic substituted). ^{1}H-NMR: δ/ppm 14.0 (O-H,s,1H), 8.6 (-CH=N,s,1H), 7.62 (Ar,m,8H), 4.1 (OCH_3,s,3H).

Test for solution color change of 4-hydroxy-3-methoxy-5-(phenylazo)benzaldehyde (2), 2-methoxy-4-((phenylimino)methyl)phenol (3) and 2-methoxy-6-(phenylazo)-4-((phenylimino)methyl)phenol (1)

Buffer solutions were prepared with variations of pH 2–13. The solution of 4-hydroxy-3-methoxy-5-(phenylazo)benzaldehyde **2** was prepared by dissolving of compound **2** (0.05 g) in 5 mL of ethanol. Each buffer solution (2.5 mL) was put into a test tube and then added 2 drops of a solution of compound **2**. The same treatments were performed for compounds of 2-methoxy-4-((phenylimino)methyl)phenol **3** and 2-methoxy-6-(phenylazo)-4-((phenylimino)-methyl)phenol (**1**). Color change was recorded.

Test for color stability of compounds 2-methoxy-4-((phenylimino)methyl)phenol (3) and 2-methoxy-6-(phenylazo)-4-((phenylimino)methyl)phenol (1) in the acid

Titration of NaOH solution was performed with a solution of oxalic acid ($H_2C_2O_4$) at various concentrations in the Table 1 using indicators of 2-methoxy-4-((phenylimino)methyl)phenol **3** and 2-methoxy-6-(phenylazo)-4-((phenylimino)methyl)phenol **1**. After equivalent point reached, the stability of change of color solution was recorded.

Test as a titration indicator of 2-methoxy-4-((phenylimino)methyl)phenol (3) and 2-methoxy-6-(phenylazo)-4-((phenylimino)methyl)phenol (1)

Titration was performed against NaOH solution using oxalic acid solution. The solution of NaOH was taken for 5 mL and added 2 drops of solution methoxy-2-4-((phenylimino)methyl)phenol **3**. The solution was then titrated with standard solution of 0.05 M oxalic acid until the color changes. The same treatment performed for 2-methoxy-6-(phenylazo)-4-((phenylimino)methyl)phenol **1**. Each titration was performed for three times and recorded the volume of a solution of 0.05 M oxalic acid required for titration. The same treatment performed on phenolphthalein indicators as comparative indicators.

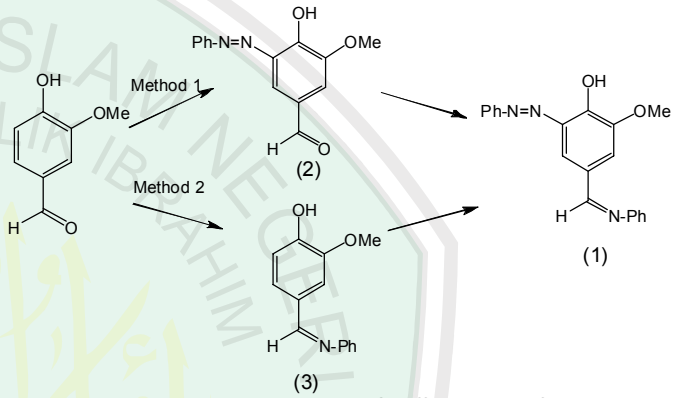
RESULT AND DISCUSSION

The target compound **1** was prepared by two methods as shown in Scheme 1.

Method 1, the target compound **1** has been obtained in good yield. The structure elucidation for the compound **1** has been indicated the existing of C=N band (1627 cm^{-1}) and N=N band (1589 cm^{-1}). The ^{1}H-NMR also supported the existing of -CH=N- peak (δ 8.6 ppm). These spectra were really different compared

Table 1. Variation of NaOH concentration and $H_2C_2O_4$.

Indicator compounds			
2-methoxy-4-((phenylimino)methyl) phenol **3**		2-methoxy-6-(phenylazo)-4-(phenylimino)methyl)phenol **1**	
[NaOH]	[$H_2C_2O_4$]	[NaOH]	[$H_2C_2O_4$]
0.50 M	0.50 M	0.50 M	0.50 M
0.15 M	0.15 M	0.25 M	0.25 M
0.10 M	0.10 M	0.05 M	0.05 M
0.05 M	0.05 M	-	-



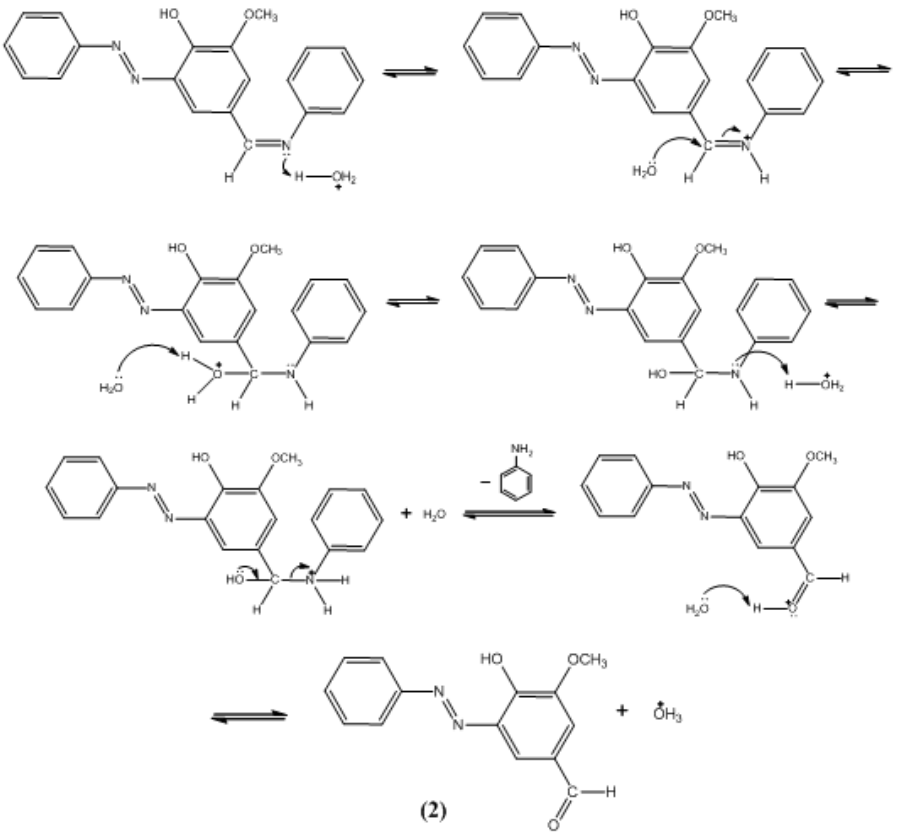
Method 1: i. Diazotization reaction, ii. Schiff base imine formation
Method 2: i. Schiff base imine, ii. Diazotization

Scheme 1. Route synthesis to produce the target compound **1**

spectra of compound **2**. IR spectra indicated specific vibration for the CHO band (1674 cm^{-1}) and N=N band (1525 cm^{-1}). The ^{1}H-NMR showed the specific for CHO peak (δ 9.95 ppm,s,1H) and aromatic (δ 7.8 ppm,m,7H). The molecular ion was indicated m/z 256 corresponding molecular weight for compound **2**.

Synthesis in method 2 has been started by formation of imine derivative. Compound **3** has been produced in good yield. The IR spectra of this compound showed very specific of C=N band (1581 cm^{-1}) and also supported by ^{1}H-NMR spectra of -CH=N- peak (δ 8.36 ppm). The molecular ion was shown m/z 227 indicating molecular weight for compound **3**. Following step of diazotization reaction produced compound **2** rather than compound **1**. This reaction indicated that the imine group was hydrolyzed in acid condition during diazotization reaction. Hydrolysis mechanism could be predicted after formation of compound **1** then the imine group was converted to carbonyl derivative as a product of compound **2**.

The color change of buffer solution at various pH after addition of solution of compound **2** showed light brown at pH < 5, light yellow at pH 6–7 and orange at pH > 7 as shown in Fig. 2. The color change of buffer solution at various pH after addition of solution of compound **3** showed colorless at pH < 6, yellowish at



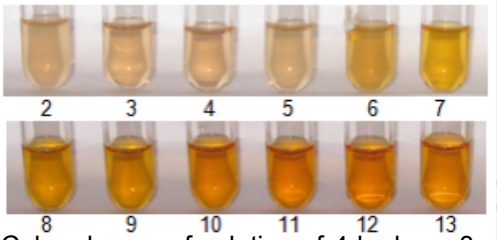


Fig 2. Color change of solution of 4-hydroxy-3-methoxy-5-(phenylazo)benzaldehyde (**2)** at various buffer solution with pH 2–13

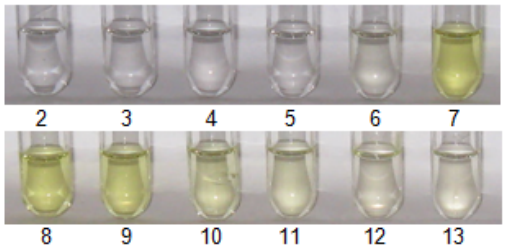


Fig 3. Color change of solution of 2-methoxy-4-((phenylimino)methyl)phenol **3** at various buffer solution with pH 2–13

pH 7–9 and light green at pH > 10.

The color change of buffer solution at various pH after addition of solution of compound **1** showed light brown at pH < 4, yellow at pH 5–8 and orange at pH > 10.

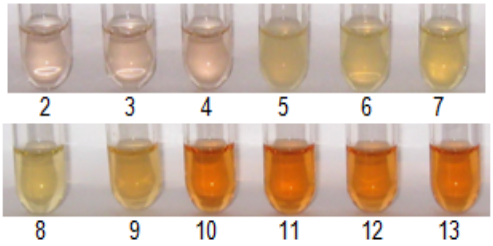


Fig 4. Color change of solution of 2-methoxy-6-(phenylazo)-4-((phenylimino)methyl)phenol **1** at various buffer solution with pH 2–13

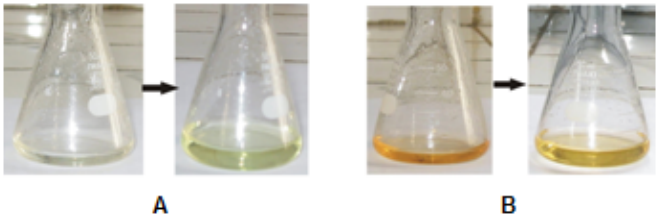


Fig 5. A. Color change with indicator compounds **3,** and B color change with indicator compound **1**

Based on this color change examination, compound **1** and **3** will be further examined for acid-base titration indicator compounds. Compound **2** failed to give sharp color change at range 1–2 pH scale as a

Table 2. Color stability after equivalent point for NaOH solution titrated by $H_2C_2O_4$ solution

Concentration (M)		Indicator compound **1**		Indicator compound **3**	
NaOH	$H_2C_2O_4$	Color Change	Color stability (second)	Color Change	Color stability (second)
0.50	0.50	Orange to Yellow	Permanent	Light green to Yellowish	2–3
0.25	0.25	Orange to Yellow	Permanent	-	-
0.15	0.15	-	-	Light green to Yellowish	10.86
0.10	0.10	-	-	Light green to Yellowish	63.93
0.05	0.05	Oranye to Yellow	Permanent	Light green to Yellowish	100.98

Table 3. Results of NaOH titration with $H_2C_2O_4$ solution (0.05 M) using phenolphthalein, compound **3** and **1** as titration indicators

Indicator compounds	Average Volume of $H_2C_2O_4$ solution (mL) ± *S.D*	Color change
2-methoxy-6-(phenylazo)-4-((phenylimino)methyl)phenol **(1)**	4.87 ± 0.06	Orange to Yellow (Fig. 5B)
2-methoxy-4-((phenylimino)-methyl)phenol **(3)**	4.83 ± 0.06	Light green to Yellowish (Fig. 5.A)
Phenolphthalein	4.87 ± 0.06	Pink to colorless

titration indicator pH. Compound **1** will be tried for equivalent point at pH 6-8 in acid-base titration while compound **3** will be examined for equivalent point at pH 7–9.

Color Stability Test

Color stability was conducted by determining of discoloration time at equivalent point in titration. Since range of pH giving color change between 6–8 for compound **1** and 7-9 for compound **3**, titration of NaOH solution with $H_2C_2O_4$ solution will be chosen for examination of color stability at equivalent point. Various concentration both solutions has also been varied. Result of color stability of equivalent point for titration of NaOH solution with $H_2C_2O_4$ solution has been recorded in Table 2.

From the Table 2, indicator compound **1** showed color stabilization up to 0.5 M in this experiment. Compound **3** did not show color stabilization on equivalent point for range $H_2C_2O_4$ concentration of 0.15–0.5 M (short color stabilization less then 10 sec) but the color is stable enough for concentration up to 0.1 M.

Application as an Acid-Base Titration Indicator

Application of compound **1** and **3** as a titration indicator will be compared with standard indicator phenolphthalein in titration of NaOH solution with $H_2C_2O_4$ solution (0.05 M). The color change for titration was shown in figure 5 and result of titration has been written in Table 3.

Table 3 indicated that target compound **1** can be used as a acid-base titration indicators with same accuracy with phenolphthalein. For compound **3** has accuracy less than 0.81% compared with standard indicator of phenolphthalein.

CONCLUSION

The target compound **1** could be synthesized by reaction of vanillin with diazotitation then imine formation giving 2-methoxy-6-(phenylazo)-4-((phenylimino)methyl)phenol. The target compound **1** could be used as titration indicator for titration of NaOH with $H_2C_2O_4$ with same result using phenolphthalein indicator.

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Natural Acid Catalyzed Synthesis of Schiff Base under Solvent-free Condition: As a Green Approach

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ABSTRACT

The reaction of primary aromatic amines with aryl aldehydes is found to be catalyzed by lemon juice as natural acid under solvent-free conditions to give the corresponding Schiff bases in good yields. This eco-friendly reaction has many advantages like economical, environmental, mild reaction conditions and simple work-up with high product yield.

Keywords: Schiff base, imines, lemon juice, natural acid.

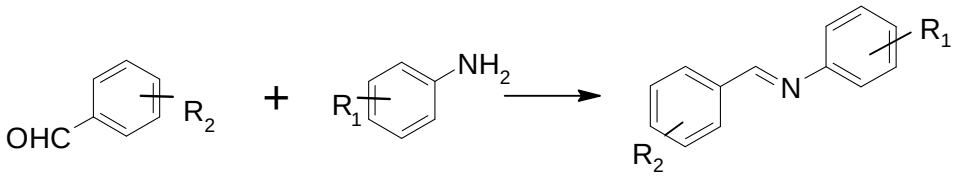
INTRODUCTION

Development of non-hazardous synthetic methodologies for organic synthesis is one of the latest challenges to organic chemists. The growing concern for the environment demands the development of eco-friendly and economic processes wherein even less hazardous byproducts are not desirable. Organic reactions under solvent-free conditions have gained in popularity in recent years[1] since the majority of solvents are either toxic or flammable and add considerably to the cost of an overall synthesis. These solvent-free reactions usually need shorter reaction times, simpler reactors, resulting simpler and more efficient work up procedures, more improved selectivities and easier separations and purifications than conventional solvents[2,3].

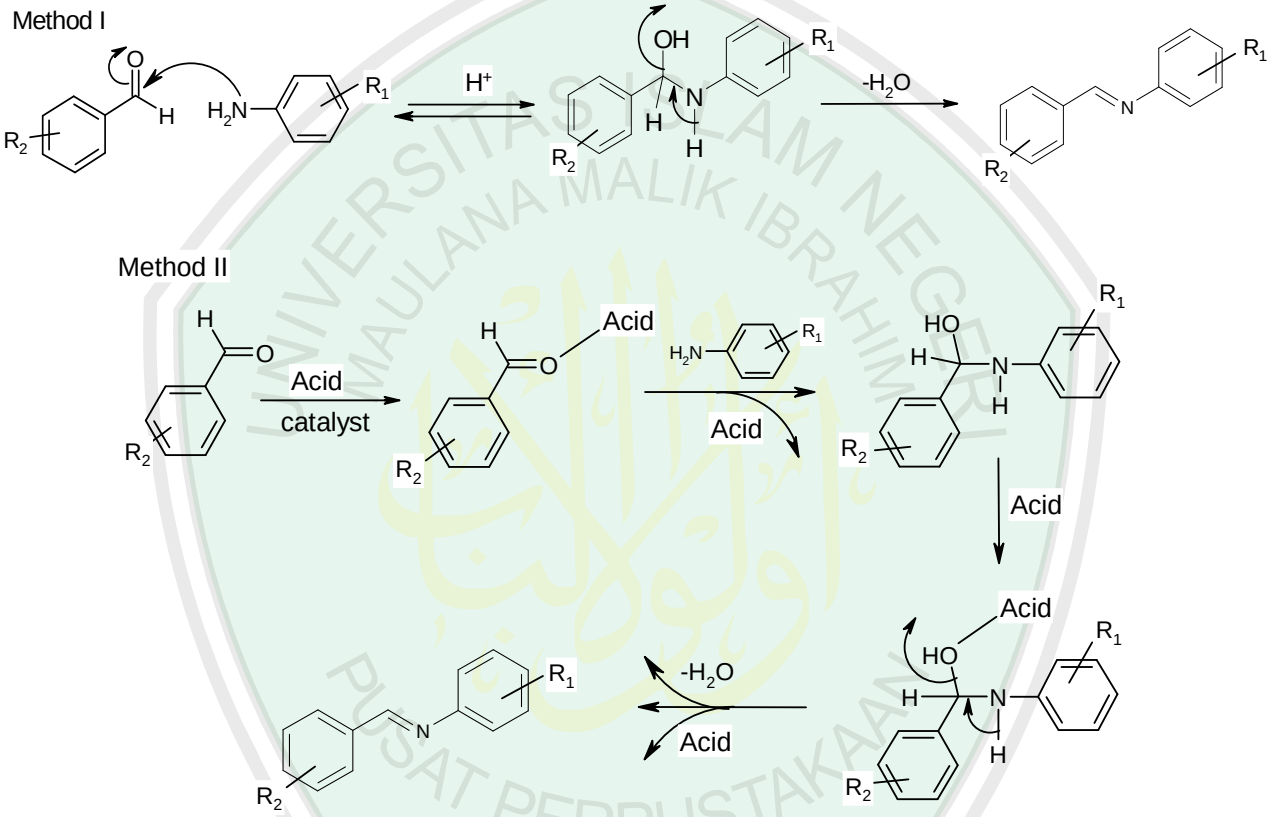
The formation of carbon–nitrogen double bond plays important role in organic synthesis. This can be achieved by the reaction of aldehydes and amines in acidic medium which leads to synthesis of Schiff bases (imines). Schiff bases have attracted considerable attention of organic chemists due to their significant biological activities like anticancer[4], antitumor[5], anti-inflammatory agents[6], insecticidal[7], antibacterial[8], antituberculosis[9], antimicrobial[10], anticonvulsant[11] activity. The Schiff bases are also used as versatile components in nucleophilic addition with organometallic reagents[12] and in cycloaddition reactions[13,14].

If we focus on the mechanism of transformation of aldehydes and amines in to Schiff bases, two synthetic methods are possible which are mechanized in Scheme-II. In method I, there is nucleophilic attack of primary amine on carbonyl carbon affords hydroxyl compound which on dehydration gives Schiff bases. The formation of Schiff bases in the second step largely depends upon the rate of removal of water from reaction mixture. Originally, the classical synthetic route for synthesis of Schiff bases was reported by Schiff[15] which involves condensation of primary amines with carbonyl compounds under azeotropic distillation[16] with the simultaneous removal of water. The removal of water during this condensation also conventionally facilitated by using molecular sieves or a Dean-Stark apparatus[17]. In the literature, for removal of water in situ dehydration method has been employed by using dehydrating solvents such as tetramethyl orthosilicate[18] and trimethyl orthoformate[19].

Scheme I : Schiff bases synthesis



Scheme II: Mechanism for acid catalyzed Schiff base synthesis



To overcome the difficulties in the removal of water, alternative method II has been employed in which Lewis acid is used as catalyst which accelerates nucleophilic attack of amines on carbonyl carbon as well as serving as dehydrating agent for removal of the water in the second step. Several modified methods for synthesis of Schiff bases have been reported in the literature in which Lewis acids were used as catalysts such as $ZnCl_2$[20], $TiCl_4$[21], alumina[22], P_2O_5[23] and also by using materials like Hydrotalcite [24].

Environmental-friendly methods for the synthesis of Schiff bases have been reported in the literature. Hossein et al[25] have reported the solvent less synthesis of Schiff base catalysed by P_2O_5/Al_2O_3, resulting in quantitative yields of the product. Varma et al[26] have reported the solvent-free synthesis of Schiff base under microwave conditions using montmorillonite K-10 as a solid support. The synthesis of imines catalyzed by CaO under microwave conditions has been also reported by Gopalakrishnan et al[27]. L. Ravishankara et al have reported Cerium(III) catalyzed synthesis of Schiff bases[28]. Bendale et.al. have reported Schiff base synthesis by using UV chamber, sonicator and also by grinding method[29].

The methodologies reported above have some disadvantages such as prolonged reaction time, the high reaction temperatures, an excess of costly dehydrating reagents/catalysts, moisture sensitive catalysts, and special apparatus, etc. Considering these facts, we have decided to synthesize Schiff bases of various substituted aldehydes and aromatic amines by employing Lemon juice as green catalyst for green approach.

Citrus aurantium, *Citrus indica*, *Citrus limonium* are some important species of citrus family commonly known as lemon. The lemon is indigenous to the north-west regions of India. It is now widely grown in all tropical and

subtropical countries. In India it is also cultivated in home gardens. For the present work, we have used extract of *Citrus limonium* species of lemon as natural catalyst for synthesis of Schiff bases. The main ingredients of lemon juice are moisture (85%), carbohydrates (11.2 %), citric acid (5-7%), protein (1%), vitamin-C (0.5 %), fat (0.9 %), minerals (0.3 %), fibers (1.6 %) and some other organic acids. As lemon juice is acidic in nature (pH ≈ 2-3) and percentage of citric acid (5-7%) is more than other acids, it works as acid catalyst for Schiff bases formation.

RESULTS AND DISCUSSION

It is observed that the condensation between a carbonyl compound and an amine leading to the formation of Schiff bases should be a facile reaction due to the good electrophilic and nucleophilic characteristic properties of the carbonyl and amine groups respectively.

Logically, we focused our attention on protonation of heteroatom in organic transformation by natural acids. Recently, we reported that Lemon Juice as Natural Catalyst efficiently catalyzes the Knoevenagel and Biginelli reactions [30,31]. To our satisfaction we found that the use of stoichiometric amount of Lemon Juice resulted in quantitative yield of the corresponding Schiff base at room temperature within 15 min to 2 hrs (Table 1). However, no result was obtained when condensation is carried without employing catalyst, if one of the reactant is deactivated by electronic effect. The role of Lemon juice in catalyzing the reaction was demonstrated by the lack of Schiff base formation when the reaction is carried out in the absence of catalyst.

To establish the scope and limitations of Lemon Juice as a catalyst for Schiff base formation, structurally diverse carbonyl compounds were treated with variously substituted amines such as aniline, 4-methylaniline, 4-methoxyaniline, 4-bromoaniline and 4-nitroaniline under the catalytic influence of lemon juice and the results are summarized in Table 1.

Table 1: Physical characterization of Schiff's bases

Entry	Product		Time	Yield	m.p. ^{0}C		Ref.
	R_1	R_2	min	%	Found	Reported	
1	H	H	60	89	65-67	66-68	31
2	H	4-OH	60	89	191-194	--	--
3	H	2-OH	45	90	47-49	--	--
4	H	4-OCH_3	90	93	84-85	80-82	31
5	H	4-$N(CH_3)_2$	90	97	78-82	--	--
6	H	4- NO_2	60	85	65-70	--	--
7	4-CH_3	H	25	90	112-115	--	--
8	4-CH_3	4-OH	50	94	210-212	--	--
9	4-CH_3	2-OH	30	94	102-105	--	--
10	4-CH_3	4-OCH_3	45	92	93-95	--	--
11	4-CH_3	4-$N(CH_3)_2$	30	84	92-95	--	--
12	4-CH_3	4- NO_2	50	83	121-125	128-130	31
13	4-OCH_3	H	20	96	154-157	--	--
14	4-OCH_3	4-OH	42	93	215-220	--	--
15	4-OCH_3	2-OH	15	91	145-149	--	--
16	4-OCH_3	4-OCH_3	30	84	142-145	--	--
17	4-OCH_3	4-$N(CH_3)_2$	55	93	132-135	--	--
18	4-OCH_3	4- NO_2	30	100	68-72		
19	4-Br	H	120	82	61-62	63-65	31
20	4-Br	4-OH	90	87	169-170	--	--
21	4-Br	2-OH	65	88	175-177	--	--
22	4-Br	4-OCH_3	120	no reaction	--	--	--
23	4-Br	4-$N(CH_3)_2$	145	78	189-192	--	--
24	4-Br	4- NO_2	110	80	172-175	176-178	31
25	4-NO_2	H	180	75	138-140	141-143	31
26	4-NO_2	4-OH	85	42	158-161	--	--
27	4-NO_2	2-OH	90	85	158-162	--	--
28	4-NO_2	4-OCH_3	300	no reaction	--	--	--
29	4-NO_2	4-$N(CH_3)_2$	180	72	178-182	--	--
30	4-NO_2	4- NO_2	150	81	110-117	--	--

The treatment of aniline with 4-dimethylaminobenzaldehyde and 4-nitrobenzaldehyde afforded the corresponding Schiff bases in 97% and 85% yields in 1.5 hr, respectively (entries 5, 6), and a quantitative yield was obtained during the reaction of 4-methoxyaniline with 4-nitrobenzaldehyde in 0.5h (entry 18) at room temperature in the presence of the catalyst.

The presence of the methoxy group in 4-methoxybenzaldehyde reduces the electrophilicity of the carbonyl carbon through resonance, and the strong electron withdrawing property of the nitro group in 4-nitroaniline decreases the nucleophilicity of the amine group. The less nucleophilic amines such as 4-nitroaniline and less electrophilic aldehydes such as 4-methoxybenzaldehyde, p-bromobenzaldehyde, 4-hydroxybenzaldehyde, and 2-hydroxybenzaldehyde were employed. Good results are obtained in the later two cases (entry 26, 27) while reactions were not forwarded in case of 4-methoxybenzaldehyde and p-nitroaniline (entry 28) and p-bromoaniline (entry 22) even at improved reaction condition. It was also observed that if one of the reactant is deactivated by its substituent, comparatively more reaction time is required to complete (TLC) the reaction.

MATERIALS AND METHODS

All aldehydes and anilines were obtained from commercial source and used without purification. Melting points were measured on open capillary method and on DBK-programmable melting point apparatus. IR spectra were obtained in potassium bromide wafers on Bruker ALPHA FT-IR Spectrometer. ^{1}H NMR spectra were measured with a Avance-300 NMR spectrophotometer using $CDCl_3$ as solvent and TMS as internal standard. Purity of the products was checked by TLC.

General Procedure for Extraction of Lemon Juice:
Fresh lemon was cut by using knife and then pieces were pressed manually using domestic presser to extract juice. Then juice was then filtered through cotton/muslin cloth and then through filter paper to remove solid material and to get clear juice which was used as a catalyst.

Synthesis of 4-methyl-N-[(2-hydoxyphenyl)methylidene]aniline 9 :
The synthesis of **9** is described as a representative example: A mixture of 2-hydoxybenzaldehyde (1.22 g, 10 mmol) and p-toluidine (1.08 g, 10 mmol) and 1/2 ml lemon juice was stirred at room temperature for 30 minutes with monitoring by TLC. Then the reaction mixture was filtered and the pure yellow crystalline product recovered by recrystallization with ethanol. Its identity was confirmed by IR, NMR spectrum and its melting point. Yield 94%; mp 102^{0}C; IR (KBr): 3320 (-OH), 1642 (C=N) cm^{-1}; ^{1}H NMR ($CDCl_3$): 2.4 (s, 3H, -CH_3), 6.9 (m, 1H, Ar-H), 7.0 (d, 1H, Ar-H),7.2 (m, 4H, Ar-H), 7.4(m, 2H, Ar-H), 8.6 (s, 1H, =CH), 13.4 (s, 1H, -OH).

The experimental procedure is followed for appropriate time to synthesize all the products listed in Table 1. Spectral characterization data for selected Schiff bases were reported in Table 2.

Table 2. Selected characterization data for some Schiff's bases

Compound	^{1}H NMR chemical shift =C-H (ppm)	IR Stretch of C=N (cm^{-1})
1	8.4	1625
2	8.6	1640
6	8.4	1650
9	8.6	1642
14	8.5	1634
20	8.6	1645
25	8.5	1640
27	8.5	1645
30	8.4	1640

CONCLUSION

In this article, we are reporting a new eco-friendly route with good yield for the synthesis of Schiff bases by using Lemon Juice, and the products can be purified by recrystallization using appropriate solvents. This solvent-free approach is nonpolluting and does not employ any toxic materials, quantifying it as a green approach for the synthesis of Schiff bases. In addition to this, compared to traditional methods, this new method is cleaner, safer and more eco-friendly, involving mild reaction conditions and simple workup. The reaction conditions such as reaction time, use of hazardous solvents can be reduced by maintaining good yield of product.

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Natural Acid Catalyzed Multi-component Reactions as a Green Approach

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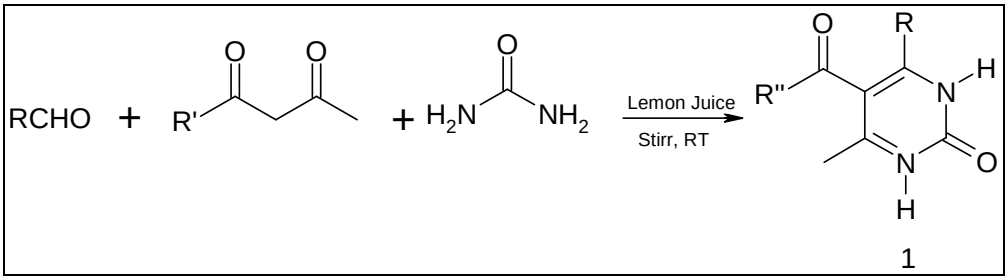
ABSTRACT

An efficient, esuriently, three-component, one-pot condensation between aldehydes, diketones and urea for synthesis of dihydropyrimidinone derivatives in excellent yields is reported.

Keywords: Natural catalyst, diketones, lemon juice, dihydropyrimidinone, Biginelli.

INTRODUCTION

Development of non-hazardous synthetic methodologies for organic reactions is one of the latest challenges to the organic chemists. The growing concern for the environment demands the development of eco-friendly and economic processes wherein even less hazardous byproducts are not desirable. Lemon juice as natural catalyst, due to its acidic nature (pH=2.4) has been found to be a suitable replacement for various homogeneous acid catalysts. Number of organic reactions are reported in literature by employing natural catalyst like clay [1,2], phosphates [3,4,5], etc. In continuation of our research work in application of lemon juice as natural catalyst, here, we report a clean, solvent free and single-step cyclocondensation reaction of aldehydes, diketones and urea (**Scheme 1**) with high yields.



Scheme 1

Dihydropyrimidinone and its derivatives are found in a large family of natural products with broad biological activities, due to which they become important classes of organic compounds. They generally possess intriguing therapeutic and pharmacological properties [6]. Several of their functionalized derivatives are used as calcium channel modulators [6,7], Ca-antagonists [8] and vasodilative, antihypertensive [9]. In 1893, Biginelli reported the synthesis of dihydropyrimidinone, which is acid catalyzed, a one-pot three component reaction between an aldehydes, β-ketoester and urea. However, this method suffered from drawbacks like the lower yields and longer reaction time. The reaction remained unfocused in the last century. But due to important biological properties of dihydropyrimidinones, the interest in their synthesis has been increased in the last two decades. Much effort has been made recently to improve and modify this reaction. This gave inspiration to organic chemists to find out more suitable protocol and simpler methods for the synthesis of dihydropyrimidinones.

Attempts to synthesize dihydropyrimidinones by the Biginelli reaction over various homogeneous catalysts such as $Mg(NO_3)_2$ [10], lanthanum chloride heptahydrate [11], oxalic acid [12] have been reported. Recently Lewis acid catalyzed Biginelli reactions have been extensively reported in the literature. This involved the use of Lewis acids like DDQ [13], $InBr_3$ [14], $Yb(OTf)_3$ [15], $CaCl_2$ [16], $Y(OAc)_3$ [17], $Cu(OTf)_2$ [18], $BF_3.Et_2O/Cu(OAc)_2$ [19], $ZnCl_2$ [20], Metal triflimides $Ni(NTf_2)_2$ [21], polymer supported ytterbium reagents [22], the Bronsted acids such as *p*-TSA [23], tungstate sulphuric acid [24] almost neutral catalyst $Zn(BF_4)_2$ [25]. Heterogeneous catalysts such as KSF (montmorillonite) [26], zeolites like HZSM-5,HY,MCM-41 [27] have also been employed. Synthesis of dihydrapyrimidones can also be catalyzed by ionic liquids [28,29]. The limitations in using the above mentioned catalysts were such as long reaction time, elevated reaction temperature, harsh reaction conditions, use of expensive reagents, moderate yields of the products, use of harmful organic solvents and toxic and hazardous transition metals (**Table 1**). Apart from these, the heterogeneous catalysts were required in stoichiometric amounts. Furthermore, when aliphatic aldehydes were used low yields of dihydropyrimidinones were realized [30].

Table 1. Comparison for different catalysts used for synthesis of dihydropyrimidone ($R = p\text{-}OCH_3C_6H_4$)

Entry	Catalyst	Time	Temperature	Yield (%)
1	p-TSA [23]	1 hr	Refluxed in EtOH	90
2	$ZnCl_2$ [20]	30 sec	MW Irradiation	94
3	$Zn(BF)_4$ [25]	4 hrs	Stirring at RT	71
4	$Y(OAC)_3$ [17]	4½ hrs	115^0C	89
5	$Mg(NO_3)_2$ [10]	45 min	Refluxed	90
6	$CaCl_2$ [16]	2 hrs	Refluxed in EtOH	98
7	$InBr_3$ [14]	7 hrs	Refluxed in EtOH	97
8	$Pb(NO_3)_2$ [31]	180 min	Refluxed in CH_3CN	89
9	P_2O_5 [32]	1.5 hr	Refluxed at 100^0C	94
10	Citric acid [33]	1 hr	80^0C	79
11	Lemon Juice	2 hrs	Stirring at RT	91

Citrus aurantium, Citrus indica, Citrus limonium are some important species of citrus family commonly known as lemon. The lemon is indigenous to the north-west regions of India. It is now widely grown in all tropical and subtropical countries. In India it is also cultivated in home

gardens. For the present work, we have used extract of *Citrus limonium* species of lemon as natural catalyst for synthesis of dihydropyrimidinones. The main ingredients of this extract are moisture (85%), carbohydrates (11.2%), citric acid (5-7%), protein (1%), vitamin-C (0.5%), fat (0.9%), minerals (0.3%), fibers (1.6%) and some other organic acids. As lemon juice is acidic in nature (pH about 2-3) and percentage of citric acid (5-7%) is more than other acids, it will be worked as acid catalyst for cyclocondensation.

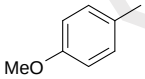
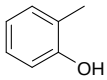
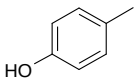
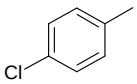
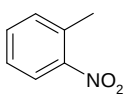
MATERIAL AND METHODS

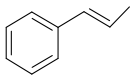
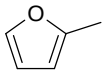
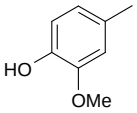
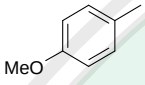
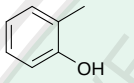
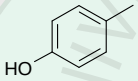
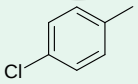
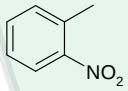
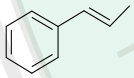
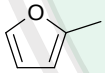
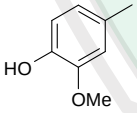
Procedure for synthesis of 5-ethoxycarbonyl-6-methyl-4-(4-methoxyphenyl)-3,4-dihydropyrimidin-2(1H)-one. The synthesis of 5-ethoxycarbonyl-6-methyl-4-(4-methoxyphenyl)-3,4-dihydropyrimidin-2(1*H*)-one is described as a representative example: The mixture of 10 mmol (1.36g) of p-methoxybenzaldehyde, 10 mmol (1.30g) of ethyl acetoacetate, 10 mmol (0.6 g) of urea and 1 ml Lemon Juice was stirring for 2 hours at room temperature with monitoring by TLC. Then the reaction mixture was filtered, washed with water and the pure yellow crystalline solid recovered by crystallization with ethanol. Its identity was confirmed by IR and NMR and its melting point. This procedure is followed for the synthesis of all the dihydropyrimidinones listed in Table 2.

RESULT AND DISCUSSION

We, herein, report a one-pot synthesis of dihydropyrimidinone using a lemon juice as natural catalyst under solvent-free conditions. To the best of our knowledge, there are no earlier reports of lemon juice as catalyst for Biginelli reaction. This also shows that high acidity is required to facilitate the cyclocondensation for dihydropyrimidinone synthesis. In addition to its simplicity, this catalyst resulted in higher yields for different aromatic aldehydes (**Table 2**).

Table 2: Lemon Juice catalyzed synthesis of dihydropyrimidinones

Entry	R	R^1	Time (hours)	Yield (%)	M.P.	
					Found	Reported
1		OEt	1.5	89	205	202 [25]
2		OEt	2	91	201	203 [25]
3		OEt	2	85	203	201 [25]
4		OEt	1	90	221	226 [25]
5		OEt	2.5	89	215	218 [17]
6		OEt	4	92	212	215 [25]
7		OEt	2	90	210	208 [25]

8		OEt	1	92	230	232 [25]
9		OEt	4-5	89	200	203-205 [31]
10		OEt	1.5	90	214	215 [34]
11	H	OEt	1	54	234	-
12		Me	2	91	231	233 [25]
13		Me	2	94	172	166 [25]
14		Me	2.5	89	221	-
15		Me	2.5	91	254	-
16		Me	2	98	242	-
17		Me	4.5	95	276	-
18		Me	2	92	232	234-236 [31]
19		Me	4	90	240	-
20		Me	2.5	89	196	-
21		Me	1	94	228	-
22	H	Me	2	61	230	-

CONCLUSION

We have developed an eco-friendly and economic process for the synthesis of dihydropyrimidinone by lemon juice as a catalyst higher good yields. This solvent free approach is nonpolluting and does not employ any toxic materials, quantifying it as a green approach to this cyclocondensation reaction. In addition to this, it involved mild reaction conditions and simple workup.

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Green Synthesis of Schiff Bases by Using Natural Acid Catalysts

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Abstract: ***The utilization of green chemistry techniques are dramatically reduces chemical wastes and reaction time as recently have been proven in several organic syntheses and chemical transformations. To illustrate these advantages in the synthesis of organic heterocycles, various environmentally benign protocols that involve greener alternatives have been studied. The objective of present research work has also used green methodologies for synthesis of Schiff bases. Conventionally synthesis of Schiff base is carried out with or without acid catalyst and sometimes by refluxing the mixture of aldehyde (or ketone) and amine in organic medium. Present synthesis involves the use of fruit juice of Citrus limetta, Vitis lanata and aqueous extract of Mangifera indica as natural acid catalysts. The synthesized product was identified by its physical properties, melting point, TLC and characterized by Mass spectrometry. Compared with traditional methods, these methods were more convenient and provided higher yield (75-93%), shows maximum efficiency, held without generation of pollution in shorter reaction time, safer to analyst, low cost and simple to run.***

Keywords: Green chemistry, Schiff bases, natural acid catalysts, mass spectrometry.

1. Introduction

Green chemistry is the branch of chemistry that involves tools techniques and technologies. It is helpful to chemists and chemical engineers in research, development and production, for development of more ecofriendly and efficient products which may also have significant financial benefits. It is going to now become an essential tool in the synthetic chemistry[1]. It is a new way of looking at organic synthesis and the design of drug molecules, offering important environmental and economical advantages over traditional synthetic processes[2]. **The recent interest in green chemistry has posed a new challenge for organic synthesis in that** new reaction conditions need to be found which reduce the emission of volatile organic solvents and the use of hazardous toxic chemicals[3]. They improve selectivity, reduces reaction time, and simplifies separation and purification of products than the conventional methods.[4]

Schiff bases, known as Imines are compounds containing azomethine group -(HC=N)- and represented by the general formula R3R2C=NR1. They are the condensed products of aldehydes or ketones and were first reported by Hugo Schiff in 1864[5]. Originally, the classical synthetic route for synthesis of Schiff bases was reported by Schiff which involves condensation of primary amines with carbonyl compounds[6] under azeotropic distillation with the simultaneous removal of water. Interests in these compounds are largely due to their structural similarities with natural biological substances and relatively simple procedures of synthesis as well as synthetic flexibility that enable the design of suitable structural properties. They are well known intermediate for the preparation of azetidinone, thiazolidinone, formazone, arylacetamide, metal complexes and many other derivatives[7]. The Schiff bases constitute one of the most active classes of the compounds possessing diversified biological applications such as antitubercular, anticancer, antibacterial, anti-inflammatory, antifungal, antitumor, diuretic, insecticidal, herbicidal, anthelmintic, anti-HIV, antiproliferative, anticonvulsant, antihypertensive and antiparasitic activities[8]. The Schiff's base derivatives have been extensively investigated for more than a century and employed in different aspects including magneto chemistry, non-linear optics**,** photo physical studies, catalysis, materials chemistry, chemical analysis**,** absorption and transport of oxygen[9].

Due to these beneficial properties, concern for the environmental demands and strong interest in the development of green chemistry, new sustainable catalysts and new environmentally benign processes[10] have been investigated which are both economically and technologically feasible[11]. Present study also involves some eco-friendly and inexpensive natural catalysts like grapes (*Vitis lanata*) juice, sweet lemon(*Citrus limetta*) juice and aqueous extract of mango *(Mangifera indica*) for the synthesis of Schiff bases.

2. Literature Survey

1) **Cimerman *et al*., (2000)** studied that Schiff bases are condensation products of ketones or aldehydes with primary amines and were first reported by Hugo Schiff in 1864.
2) **Ahluwalia and Kidwai, (2004)** illustrated that Green chemistry is chemistry for the environment. It is really a philosophy and way of thinking that can help chemistry in research and production to develop more eco-friendly solutions.
3) **Ibrahim *et al*., (2006)** synthesized a series of ten Schiff bases by condensation of a variety of aromatic amines with some aniline (or derivative) and aromatic aldehyde derivatives. These Schiff base have been characterized by IR, H NMR in addition to elemental analysis.
4) **Chamarthi *et al*., (2012)** synthesized a library of Schiff base derivatives (12 compounds) under conventional conditions in ethanol as well as ultrasonic conditions in aqueous medium without using any catalyst.
5) **Patil *et al*., (2012)** revealed that the reaction of primary aromatic amines with aryl aldehydes is found to be

catalyzed by lemon juice as natural acid solvent-free conditions to give the corresponding Schiff bases in good yields.

6) **Pawar *et al.*, (2012)** explained about the important and interesting roles of Schiff bases are an intermediate in the biologically transmutation reaction.
7) **Aslam *et al.*, (2013)** explained that Schiff bases having azomethine group and their metal complexes are widely used for industrial purposes and also reveal a wide range of biological applications.
8) **Kajal *et al.*, (2013)** summarized information on the diverse biological activities and also highlights the recently synthesized numerous Schiff bases as potential bioactive core.
9) **Pal, (2013)** illustrated about the role of naturally available fruit juice in organic synthesis has attracted the interest of chemists, particularly from the view of green chemistry.

3. Material and Methods

a) Preparation of catalyst: Grapes, sweet lime and unripe mango fruits were procured locally, then grapes were pressed into fruit juicer and filtered with cotton to get liquid juice. While sweet lime fruits was peeled off with knife and fruit slices were pressed into fruit juicer to get semisolid mass which was then filtered with cotton to get liquid juice to used as catalyst[12].

The upper shell of unripe Mango fruit was removed and the hard fleshy green material (5 g) was boiled with water (100 ml), cooled and filtered with muslin cloth to get clear liquid portion to used as catalyst for the synthesis[11].

b) Synthesis of Schiff bases with grapes juice sweet lemon juice and aq. extract of unripe mango under solvent free condition by stirring method: The equimolar amount of benzaldehyde (0.1 mol) with aniline (0.1 mol) was taken in different beakers. In those reaction mixtures natural acid catalyst i.e. grapes juice were added in variable amounts (0.5 ml, 1 ml, 1.5 ml, 2.0 ml, 2.5 ml) and then kept for 5-10 minutes. Further each reaction mixture was stired for 2 - 4 minutes at room temperature pale yellow solid crude product was appear after completion of reaction which was washed with dislilled water and purified by recrystallization with minimum amount of ethanol. The same procedure is repeated with sweet lemon juice and aqueous extract of mango. Melting point of the products were measured by open capillary method which was further identified and purified with the help of TLC and confirmed by using mass spectra.

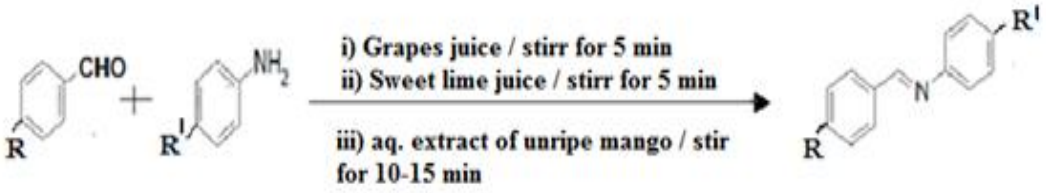

Figure 1: Reaction for Schiff base synthesis in presence of acid catalysts

4. Result and Discussion

If we focus on the mechanism of transformation of aldehydes and amines into Schiff bases, there is nucleophilic attack of primary amine on carbonyl carbon affords hydroxyl compound which on dehydration gives Schiff bases. The formation of Schiff bases in the second step largely depends upon the rate of removal of water from the reaction mixture.

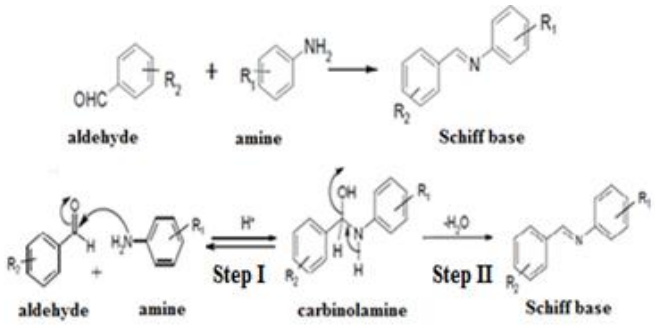

Figure 2: General reaction and mechanism for Schiff base synthesis in acidic solvent media

In the I step of the mechanism the amine reacts with the aldehyde or ketone to give an unstable addition compound called carbinolamine. Then in the II step carbinolamine loses water by either acid or base catalyzed pathways. Since the carbinolamine is an alcohol, it favors to undergo acid catalyzed dehydration. It is observed that the condensation between a carbonyl compound and an amine leading to the formation of Schiff bases should be a facile reaction due to the good electrophilic and nucleophilic characteristic properties of the carbonyl and amine groups respectively. Formation of carbilonamine and protonation occurs in the same step if the reaction takes place in acidic solvent media while in the acid catalysed mechanism the protonation occurs before the formation carbilonamine.

Logically, in this work the protonation of heteroatom in organic transformation was done with natural acid i.e. fruit juices. All the fruit juices contain many organic acids like citric acid, tartaric acid, malic acid, oxalic acid, succinic acid and amino acids amongst these organic acids, citric acid is the major constituent in many fruit extracts. Thus these organic acids are responsible for acidic nature of fruit juices and provide a desirable pH to catalyze the condensation reaction have used in the synthesis of Schiff bases.

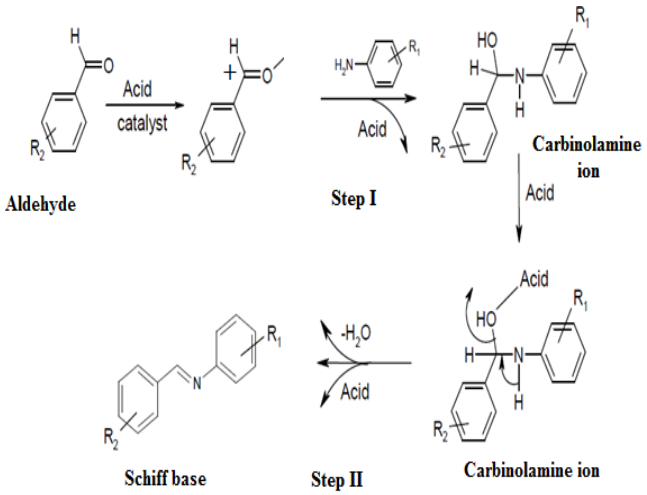

Figure 3: Mechanism for Schiff base synthesis in the presence of acid catalyst

Yields of the N-benzylidene aniline (Sb I) and 4-chloro-N-benzylidene aniline (Sb II)in the presence of different catalysts:

N-benzylidene aniline (Sb I) and 4-chloro-N- benzylidene aniline (Sb II) was successfully synthesized by green catalysts which have been used and good to excellent yield of the product was obtained. The data shows that the acid catalysts are effectively catalyze the synthesis of Schiff bases and even very small amount of natural acids provide quantitative yield of the product.

Table 1: Comparative yields of N-benzylidene aniline (Sb I) and 4-chloro-N-benzylidene aniline (Sb II) in the presence of different catalysts

Title / S. No.	Name of catalyst	Amount of catalyst (ml)	Percentage yield (Sb I)	Percentage yield (Sb II)
1	Grape juice	0.5	93.60	88.54
2	Sweet lemon juice	0.5	88.13	79.19
3	Aqueous extract of Mango	0.5	91.11	82.18

The yields of Sb I is always more than Sb II because the electrophilicity of the carbonyl carbon of Sb II reduces due to the presence of the electron-donating substituent group i.e. Cl through resonance and M+ effect (mesomeric effect). From this perspective it has been clear that the yield of the Schiff bases is depend upon the electrophilicity of carbonyl carbon of benzaldehyde and nucleophilicity of aniline[12]. Electrophilicity of benzaldehyde increases if any electron attracting substituent group attached to it and decreases if benzaldehyde has any electron donating group in its structure while the nucleophilicity of aniline is increases due to electron donating group and decreases in the presence of electron withdrawing group.

4.4: Effect of catalyst loading on the product yield

Different yields of the product obtained with variable amount of acid catalysts are summarized in Table no. 2 and Table no. 3

Table 2: Yields of the N-benzylidene aniline o(Sb I) obtained with different amount of natural acid catalysts

Title / S. No	Amount of catalyst (ml)	Product yield obtained with grapes juice		Product yield obtained with sweet lemon juice		Product yield obtained with aqueous extract of unripe mango	
		Product Yield (gm)	Percentage yield	Product Yield (gm)	Percentage yield	Product yield (gm)	Percentage yield
1	0.5	2.2468	93.60	2.1345	88.93	2.1868	91.11
2	1	2.1376	89.07	2.0516	85.48	2.0935	87.23
3	1.5	2.0192	84.13	1.9448	81.02	1.9776	82.40
4	2	1.8890	78.71	1.8328	76.37	1.8523	77.18
5	2.5	1.7649	73.54	1.7101	71.25	1.7073	71.14

Table 3: Yields of the 4-chloro-N-benzylidene aniline (Sb II) obtained with different amount of natural acid catalysts

Title / S.No	Amount of catalyst (ml)	Product yield obtained with grapes juice		Product yield obtained with sweet lemon juice		Product yield obtained with aqueous extract of unripe mango	
		Product Yield (gm)	Percentage yield	Product Yield (gm)	Percentage yield	Product yield (gm)	Percentage yield
1	0.5	1.8593	88.54	1.6642	79.24	1.7257	82.18
2	1	1.7150	81.67	1.5315	72.93	1.5481	73.72
3	1.5	1.5579	74.19	1.3887	66.13	1.3685	65.17
4	2	1.3983	66.59	1.2816	61.03	1.2306	58.60
5	2.5	1.2553	59.78	1.1862	56.48	1.1258	52.98

The data clearly show that on increasing the amount of acid catalysts product yields were decreasing because of acid concentration cannot be too high due to the basicity of amines. If the amine is protonated and becomes non-

neucleophilic, equilibrium is pulled to the left and carbinolamine formation cannot occur. Therefore, many Schiff bases synthesis are best carried out at mildly acidic pH[13.]

4.5 Characterization of the products:

Both of the products are stable at room temperature and non hygroscopic. They decompose at high temperature, insoluble in water and soluble in ethanol. Thus Characterization of products was done with its physical properties, melting points, TLC and mass spectra. TLC was performed with chloroform and methanol (1:9) provided a single spot on TLC plate which shows purity of products.

Table 4: Physical characteristics of products

S. No.	Products Name and chemical formula	Product color	Product smell	Physical state	Solubility	Melting point	Rf value
1	N-benzylidene aniline ($C_{13}H_{11}N$)	Pale yellow	Disagre-eable	Crystal-line solid	Both are Insoluble in distilled water, soluble in	54 ^{0}C	0.620
2	4-chlro-N-benzylidene aniline ($C_{13}H_{10}NCl$)	Pale yellow	Disagre-eable	Crystal-line solid	methanol, ethanol, and chlorofom	62^{0}C	0.623

Spectral characterization: It is done with mass spectra of the product. Mass spectrometry is the most accurate method for determining the molecular mass of the compound and its elemental composition. The mass spectrum is a plot representing the m/z values of the various ions (parent as well as fragment ions) against their corresponding relative abundance. In this technique, molecules are bombarded with a beam of energetic electrons. The molecules are ionized and broken up into many fragments, some of which are positive ions. Each kind of ions has a particular ratio of mass to charge, i.e. m/z ratio (value).

Mass spectra of N-benzylidene aniline (Sb I) shows a molecular ion peak at 182.1 with 100 % relative abundance so it is also the base peak of spectra which corresponds to the one additional molecular weight of the synthesized compound because calculated molecular weight of the compound is 181.23 gm/mol. Then with the peak have been described as molecular ion peak another fragment ion peak is clearly visible at 183.1 m/z value which is an isotopic peak for ^{13}C with 13 % relative abundance.

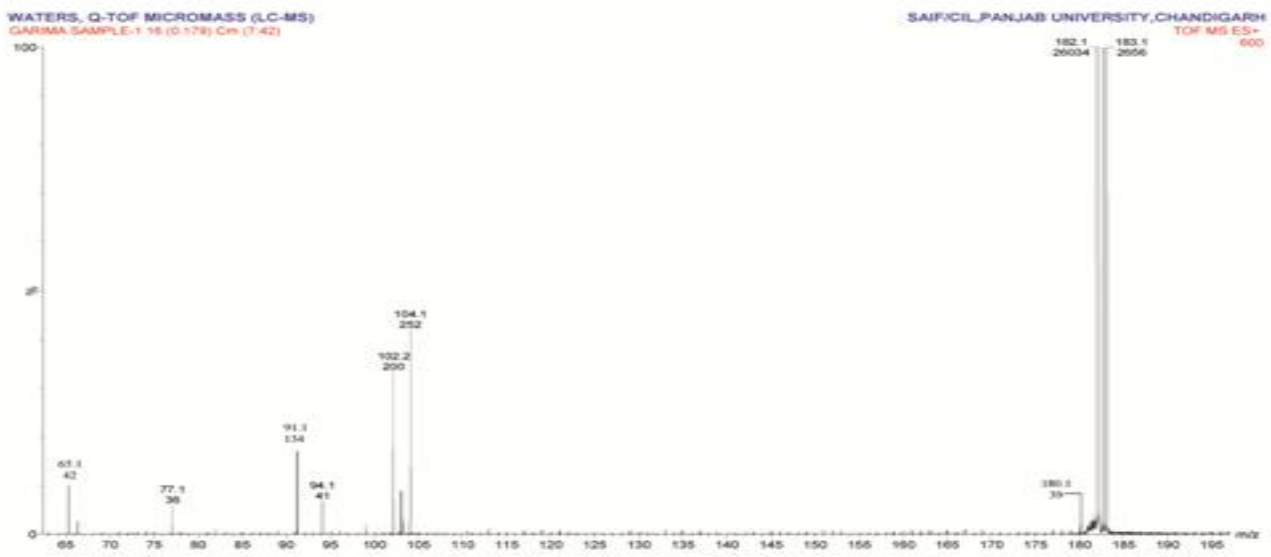

Fig. 4: Mass spectra for N-benzylidine aniline obtained with grapes juice shows fragment ion peaks

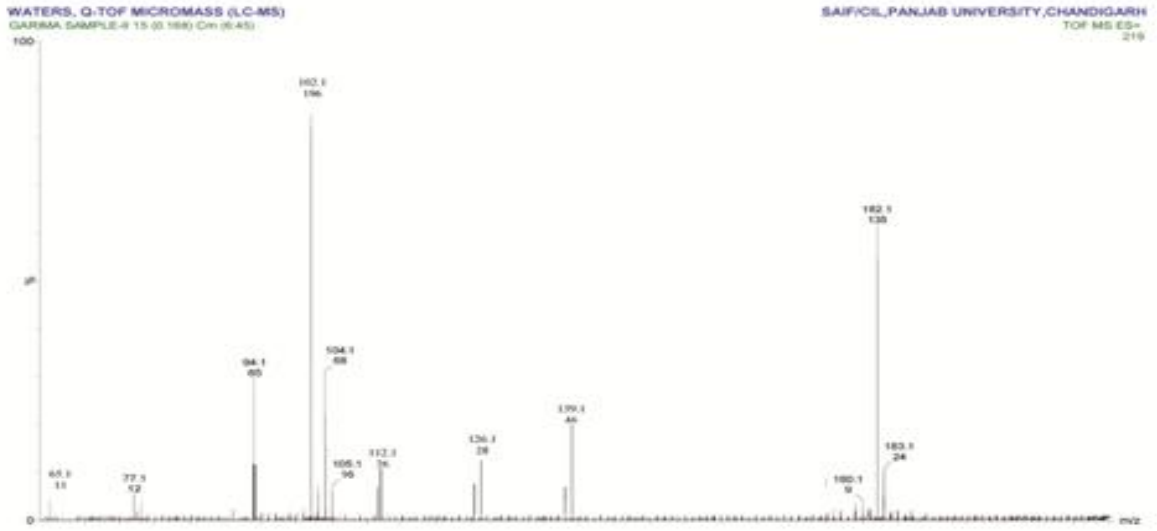

Fig. 6: Mass spectra for 4-chloro-N-benzylidine aniline obtained with grapes juice shows fragment ion peaks

Fig. 5: Mass spectra for N-benzylidine aniline obtained with grapes juice shows molecular ion peak and base peak

Fig. 7: Mass spectra for 4-chloro-N-benzylidine aniline obtained with grapes juice shows molecular ion peak and base peak

In the spectra of 4-chloro-N-benzylidene aniline (Sb II) molecular ion peak observed at the m/z 216.0 with 100 % abundance which correspond to the $(M + H)^+$ ion i.e. one additional molecular weight of the respective compound because calculated molecular weight of the compound is 215.68 gm/mol, it is also the most abundant peak of spectra so the molecular ion peak and base peak both are also same. With this molecular ion peak one extra peak also seen at m/z 218.0 with 24.5 % relative abundance which produced due to the isotopic form of chlorine into it.[14]

5. Summary and Conclusion

The present work focuses the importance of fruit juice as natural and biocatalyst in organic transformations. The growing interest of fruit juice in organic synthesis is mainly due to their acidic properties, enzymatic activity, benign environmental character, inexpensive, and commercial availability. The catalytic activity including the application of fruit juices in various organic transformations such as formation of C-C, C-N bonds in different synthetically important organic compounds have been studied. Although many observations have not received by application of fruit juice in synthesis of natural products or complex structured molecules in details, it is believed that in near future the chemistry of natural catalysts will continue to attract significant research activity. Therefore, the present review would serve the need of organic chemists in searching new applications of fruit juice for organic synthesis.

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Fruit Juice: A Natural, Green and Biocatalyst System in Organic Synthesis

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Abstract -The role of naturally available fruit juice in organic synthesis has attracted the interest of chemists, particularly from the view of green chemistry. This review summarizes the versatile synthetic applications of fruit juice as a biocatalyst in different chemical transformations. Fruit juice of lemon, pineapple, tamarind, *Acacia concinna*, *Sapindum trifolistus*, and coconut is extensively used in organic synthesis. Lemon juice catalyzed reactions including Knoevenagel condensation, three-component synthesis of dihydropyrimidinones, triazoles, synthesis of schiff bases, and bis-, tris- and tetraindoles are reported. Pineapple juice and tamarind juice has been used for the synthesis of dihydropyrimidinones and bis-, tris- and tetraindoles respectively. Anilides and aldamines were also synthesized by *Acacia concinna* fruit juice and *Sapindum trifolistus* fruit juice respectively. Coconut juice was used as a biocatalyst for reduction of carbonyl compounds and hydrolysis of esters, amides and anilides. Application of fruit juice as a natural and biocatalyst allows mild and highly selective transformation and synthesis in a facile and environmentally friendly manner. Moreover, fruits are inexpensive and easily available in the market, and its juice can be extracted easily which can be used as catalyst in the organic transformations.

Keywords - Fruit Juice, Environmentally Friendly, Economic, Biocatalyst, Organic Synthesis

1. Introduction

In recent years, organic research is mainly focused on the development of greener and eco-friendly processes which involve in the use of alternative reaction media to replace toxic and expensive catalysts or volatile and hazardous solvents like benzene, toluene and methanol, commonly used in organic synthesis. Nowadays, many organic transformations have been carried out in water [1-3]. It is unique solvent because it is readily available, inexpensive, nontoxic, safer, and environmentally benign. The applications of an aqueous extract of different fruit juice have witnessed a rapid development. This growing interest in fruit juice is mainly because of its biocatalysts, environmentally benign character, nonhazardous and cost effectiveness. In literature, number of organic reactions are reported in which natural catalysts like clay [4-6], phosphates [7, 8], gold [8], animal bone [9] are employed. In recent years, chemical reactions using plant cell cultures and part of plants as biocatalysts have received great attention [10-12]. This crescent interest is due to the wide biotechnological potential of the enzymetic reactions. The biocatalytical transformations using edible plants [13], plant root [14, 15], plant tubers [16] and plant leave [17] extract can be applied in many organic reactions. Fruit juice is also naturally occurring which was used as a biocatalysts in organic synthesis. Fruit juice is now being routinely used in organic synthesis as homogeneous catalysts for various selective transformations of simple and complex molecules. The purpose of the present review is to summarize the utility of different fruit juice with emphasis on recent synthetic applications; Literature coverage is through till 2013.

2. Fruit Juice of Lemon

The lemon is a small evergreen tree and the tree's ellipsoidal yellow fruits. *Citrus limonium*, *Citrus indica*, *Citrus aurantium* are some important species of citrus family. The lemon is indigenous to the north-west regions of India. It is now widely grown in all tropical and subtropical countries. In India it is also cultivated in home gardens. Lemon juice [18] obtained from lemon is sour in taste. The use of lemon juice, pulp and zest in our day-to-day life can not be understated. Lemon juice is used to make lemonade, soft drinks, and cocktails. It is used for deodorize the garbage, freshen the room and fridge. The juice is used to control the high blood pressure, arthritis and rheumatism, asthma, prevent kindny stone etc.

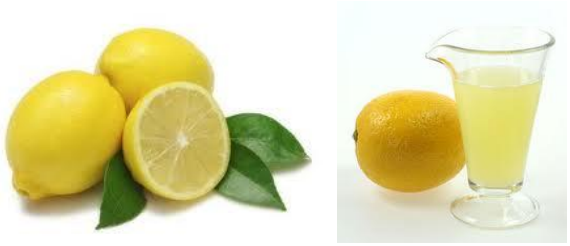


Fig.1. Photography of Fruit and Lemon Juice of *Citrus Limon*

2.1. Composition of Lemon Juice

The main ingredients of the extract of *Citrus limonium* species of lemon are moisture (85%), carbohydrates (11.2%), citric acid (5-7%), protein (1%), ascorbic acid or vitamin-C (0.5%), fat (0.9%), minerals (0.3%), fibres (1.6%) and some other organic acids [18]. The juice is soluble in water. Due to presence of citric acid and ascorbic acid, lemon juice is acidic (pH= 2-3) in nature, and thus it works as acid catalyst in organic reactions.

2.2. General Procedure for Extraction of Lemon Juice

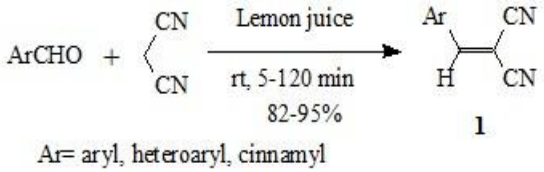
Fresh lemon was cut by using knife and then pieces were pressed in a fruit juicer to get the juice extract. Then the juice was filtered through cotton/muslin cloth and then through filter paper to remove solid material and to get clear juice which as used as a catalyst.

2.3. Applications of Lemon Juice in Organic Synthesis

Most people are familiar with the traditional uses for lemon juice such as culinary, medicinal and industrial purposes. Nowadays the lemon juice has played an important role in organic synthesis. Lemon juice was reported to catalyze Knoevenagel condensation reaction to synthesise arylidene-malononitriles which shows antibacterial and antifungal activity [19]. Dihydropyrimidinones are interesting intriguing therapeutic and pharmacological properties [20, 21]. 1, 2, 4-Triazole derivatives are found to be associated with various biological activities such as anticonvulsant [22], antifungal [23], anticancer [24] and antibacterial [25]. Schiff bases exhibit significant biological activities like antitumor [26], anti-inflammatory agents [27], antituberculosis [28] and antimicrobial [29] activities. Bis-, and tris (indolyl) methanes are used to prevent bladder cancer growth, mammary tumor growth and also shows numerous activities [30a]. Tetraindolyl derivatives [30b] are used in the treatment of fibromyalgia, chronic fatigue and irritable bowel syndrome. These important compounds have efficiently been synthesised using naturally occurring biocatalyst, lemon juice.

2.3.1. Knoevenagel Condensation Reaction

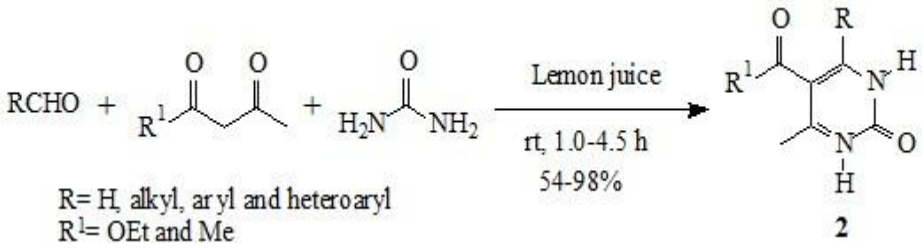
The Knoevenagel condensation [31] of aldehydes with active methylene compounds is an important method used for the synthesis of pharmaceutically important organic compounds. Deshmukh and his co-workers [18] showed that lemon juice can act as an efficient homogeneous acid catalyst for the knoevenagel condensation reaction under solvent-free conditions. Thus, when various aldehydes and malononitrile were mixed with lemon juice and the mixture were stirred at room temperature for 5-120 min afforded the condensation product **1** in good yields (Scheme 1). The new approach for knoevenagel condensation by lemon juice is nonpolluting and does not employ any toxic material, quantifying it is a green method.



Scheme 1. Lemon juice catalyzed Knoevenagel condensation

2.3.2. Synthesis of Dihydropyrimidinone

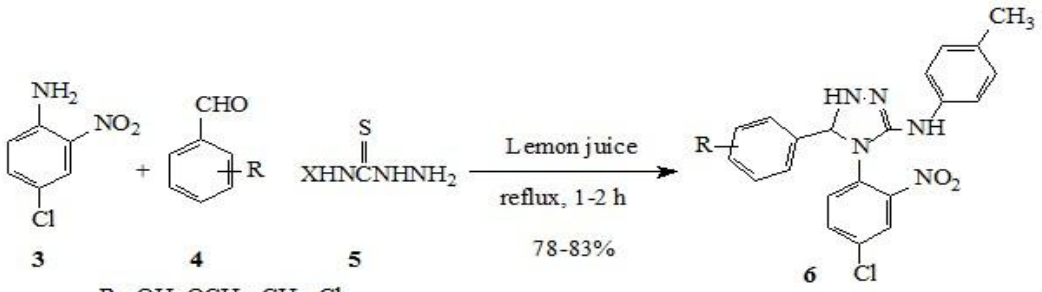
Patil *et al*. reported an efficient one-pot, three component Biginelli type synthesis of dihydropyrimidinone (**2**) under solvent-free conditions from aldehydes,1,3-dicarbonyl compounds and urea at room temperature using extract of lemon juice (*Citrus limonium* species) as natural catalyst (Scheme 2) [32]. Compared with the other methods for multicomponent synthesis of 3, 4-dihydropyrimidinones this new procedure using lemon juice offers better yields, non-polluting and green approach to this biocycloconensation reaction.



Scheme 2. Three-component synthesis of dihydropyrimidinones catalyzed by lemon juice

2.3.3. Synthesis of Triazoles

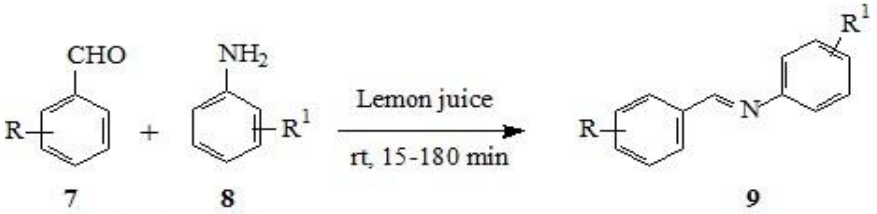
A three component one-pot clean biocyclocondensation reaction was reported by Sachdeva et al. using biocatalyst lemon juice of *Citrus limonium* species of lemon. Thus, substituted-2*H*-1,2,3-triazole phenol derivatives (**6**) were synthesized by Sachdeva et al. using lemon juice in aqueous ethanol in reflux by the reaction of 4-chloro-2-nitro aniline (**3**) and aromatic aldehydes (**4**) with thiosemicarbazide (**5**) in high yield (Scheme 3) [33]. Citric acid (5-7%) present in lemon juice (pH= 2-3) works as acid catalyst for the synthesis of triazole derivatives. The use of water as a green solvent and the use of lemon juice as a natural catalyst offer a convenient, non-toxic, and inexpensive reaction medium for the environ-economic synthesis of triazole derivatives. Synthesized compounds **6** were found to be excellent fluorescent materials and potent fungicidal agents.



Scheme 3. Three-component synthesis of triazole derivatives catalyzed by lemon juice

2.3.4. Synthesis of Schiff Base

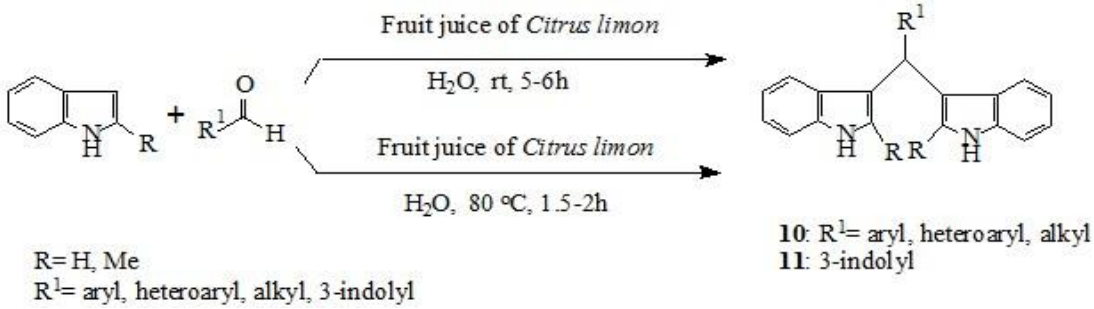
Lemon juice is a powerful and selective natural acid catalyst for condensation reaction. Patil and his coworker have reported a mild and selective imine **9** formation of aryl aldehyde (**7**) and aromatic primary amine (**8**) using lemon juice (C*itrus limonium* species) at room temperature in 25-300 min in good to excellent yields (42-100%) (Scheme 4) [34]. It was found that electron withdrawing groups attached to aromatic aldehydes and electron donating groups attached to aromatic amines facilities the reaction. However no result was obtained when condensation is carried without employing lemon juice. The role of lemon juice is catalyzing the reaction was demonstrated by the lack of schiffs base formation when the reaction is carried out in absence of catalyst.



Scheme 4. Lemon juice catalyzed synthesis of Schiff bases

2.3.5. Synthesis of Bis-, Tris- and Tetraindoles

Pal and coworkers [35] observed that lemon juice can be utilized for the biocondensation of indoles and aldehydes for the synthesis of bis-, and tris (indolyl) methanes (Scheme 5). Thus, when a mixture of indoles and aldehydes were treated in fruit juice of *Citrus limon*-water mixture at pH 3 in stirring at room temperature for 5-6 h or refluxed at 80 ℃ for 1.5-2.0 h afforded compounds **10** and **11** in excellent yields without column chromatographic separation.

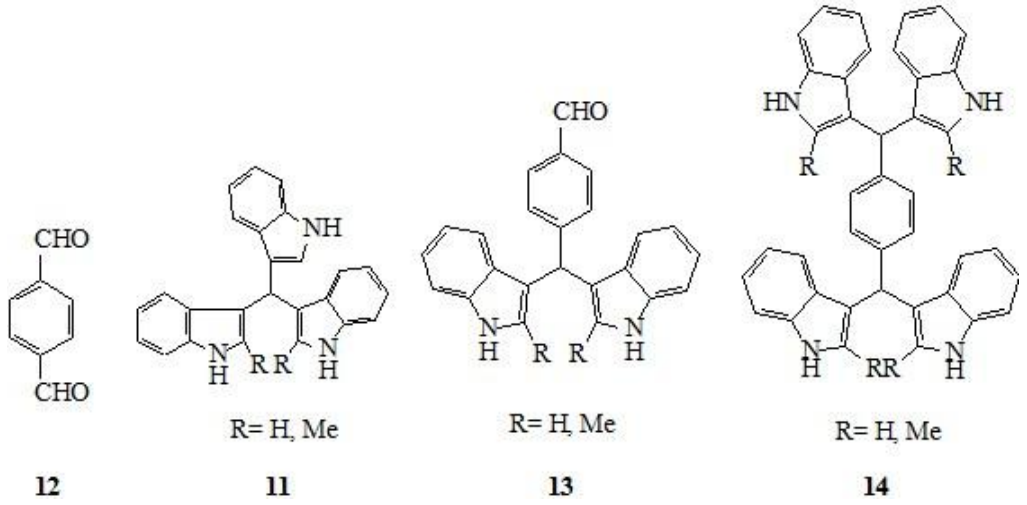


Scheme 5. Lemon juice catalyzed synthesis of bis- and tris (indolyl) methanes

This method proved to be chemoselective as only aldehydes reacts with indoles while ketones did not give corresponding products. The use of lemon juice as biocatalyst and water as solvent in this reaction makes the method is inexpensive and green as complete elimination of toxic solvent, catalysts, and inorganic support.

Microwave-assisted [36] efficient, rapid and eco-friendly synthesis of bis-, tris (indolyl) methanes (**10** and **11** respectively) and di-bis (indolyl) methanes (**14**) by the reaction of indoles and aldehydes in presences of lemon juice (*Citrus limon*) as biocatalysts under solvent-free conditions was reported by Pal. Various substituted aromatic, heteroaromatic and aliphatic aldehydes smoothly reacts with indoles to give corresponding products **10**, **11** in excellent yields. Terephthaldialdehydes (**12**) containinig two aldehyde functional groups react with indoles in 1:2 ratio gave p-bis- indolylmethane benzaldehyde (**13**) and in 1:4 ratio gave p-di (bis- indolylmethane) benzene (**14**) in good yield (Figure 2).

The same biocondensation reaction was demonstrated by Pal in his another paper using aqueous ethanol as solvent under ultrasound irradiation [37] in high yield within 15-25 min.



12 11 13 14

Figure 2. Structure of Terephthaldialdehydes (**12**) and Lemon Juice Catalyzed Synthesized Compounds (**11**, **13** and **14**)

3. Fruit Juice of Pineapple

Pineapple (*Ananas comosus*) is sometimes called the King of Fruit [38]. Pineapple is grown extensively in Hawaii, Philippines, Caribbean area, Malaysia, Austrilia, Thiland, Maxico, Kenya and South Africa. Pineapple has long been one of the most popular of the non-citrus tropical and subtropical fruits, largely because of its attractive flavour and sugar-acid balance [39].

Fig.3. Fruit and Pineapple Juice of *Ananas Comosus*

3.1. Composition of Pineapple Juice

The main ingredient of 100 g pineapple contain water (85.3 – 87.0 g), protein (0.4 – 0.7 g), fat (0.2 – 0.3 g), total carbohydrate (11.6 – 13.7 g), fiber (0.4 – 0.5 g), ash (0.3 – 0.4 g), calcium (17 – 18 mg), phosphorous (8 – 12 mg), iron (0.5mg), sodium (1 – 2 mg) and potassium (125 – 146 mg). It contains 12 – 15% sugars of which two-third in the form of sucrose and rest are glucose and fructose and 0.6 – 1.2% acid of which 87% is citric and 13% is malic acid [40,41]. The composition of the juice varies with geographical, cultural and seasonal harvesting and processing.

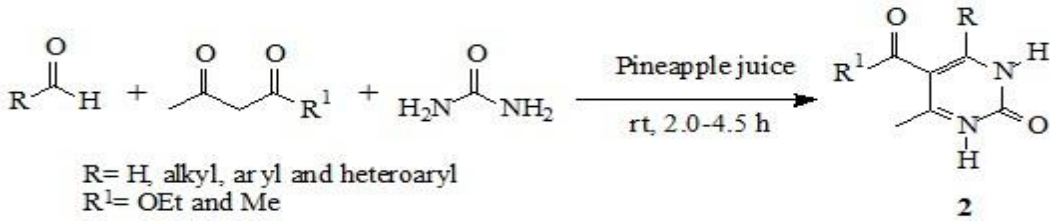
3.2. General Procedure for Extraction of Pineapple juice

The crown and stem portion of the fresh pineapple (*Ananas comosus*) were removed and the skin was peeled using knife. Then the fruit was sliced and the fruit slices pressed in a fruit juicer for one or two minutes to get the semisolid mass which was then filtered through to get liquid pineapple juice. The extract of the pineapple is acidic having pH 3.7 and the acidity percentage is 53.5% and hence it will be worked as acid catalyst in organic reactions.

3.3. Application of Pineapple Juice in Organic Synthesis: Preparation of Dihydropyrimidinone

Patil and his groups [42] synthesized a series of dihydropyrimidinone (DHPMs) derivatives **2** in presence of pineapple juice as a natural catalyst in good to excellent yields using a three component reaction sequence. Thus, an equimolar quantities of an aldehydes, ethyl acetoacetate and urea is stirred in presence of pineapple juice at room temperature for

2-5.5 h produced **2** (Scheme 6). Due to acidic nature (pH 3.7) pineapple juice acts as a catalyst in the formation of DHPMs. This solvent-free approach is totally nonpolluting having several advantages such as shorter reaction time, mild reaction conditions, simple work-up and reduces environmental impact.



Scheme 6. Pineapple juice catalyzed synthesis of dihydropyrimidinones

4. Fruit Juice of Tamarind

Tamarind (*Tamarind indica*) is a leguminous tree in the family Fabaceae indigenous to tropical Africa. The tamarind tree produces edible, pod-like fruit which are used extensively in cuisines around the world. It has long been one of the most popular non-citrus tropical and sub-tropical fruit, largely because of its attractive flavor and refreshing sugar-acid balance. The fruit juice is also used as traditional medicine and metal polises.

Fig.4. Photography of Fruit and Tamarind Juice of *Tamarindus Indica*

4.1. Composition of Tamarind Fruit Juice

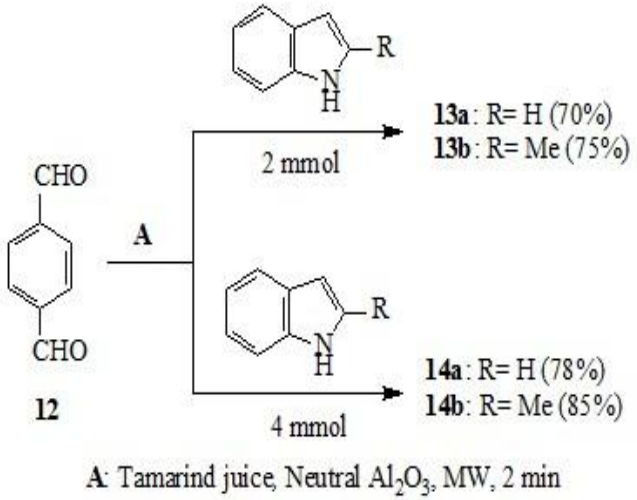
The main ingredient of 100 g of pulp of tamarind fruit [43] contain water (15-30%), protein (2-9%), fat (0.5-3%), total carbohydrate (56-82%), edible fiber (2.2-18.3%), ash (2.1-3.3%), calcium (81-466mg), phosphorous (86-190 mg), iron (1.3-10.9 mg), sodium (23-28 mg), potassium (62-570 mg). It also contains 41-58% sugar of which 25-45% is in the form of reducing sugars and 16% is in the form of non-reducing sugars and tartaric acid is (8-18%) and ascorbic acid is (3-9 mg). The composition of the tamarind fruit juice varies with geographical, cultural and seasonal harvesting and processing. An aqueous extract of tamarind fruit juice is acidic having pH 3 and acidity percentage is 50.3% and hence it will be worked as an acid catalyst in acid catalyzed reactions.

4.2. General Procedure for Extraction of Tamarindus Indica Fruit Juice

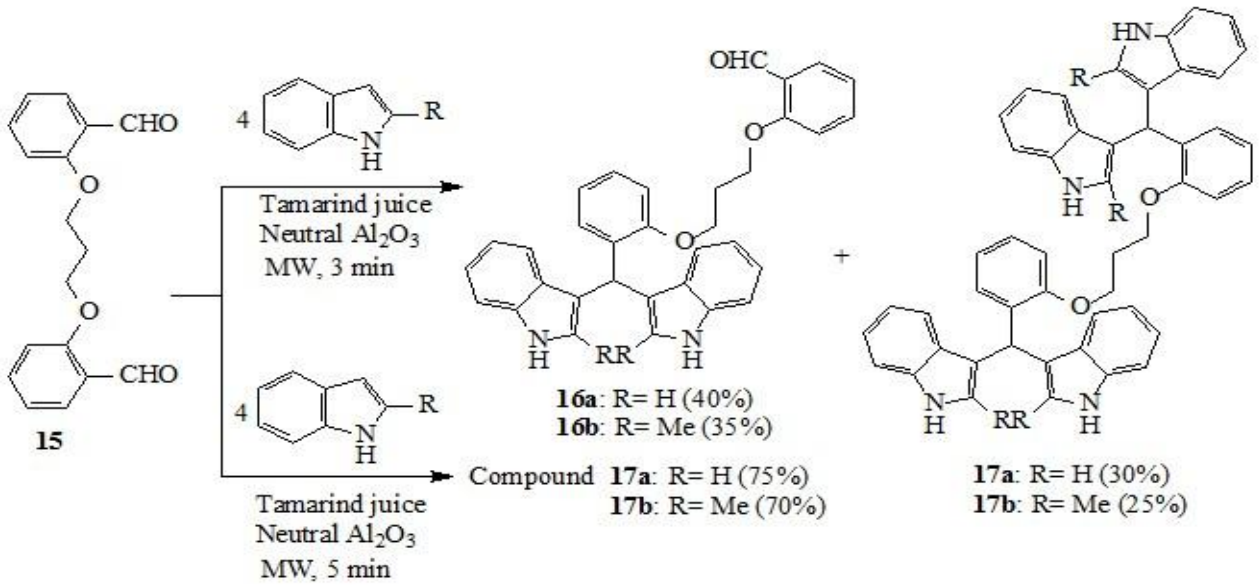
The upper shell and inner grain of unripe tamarind fruit were removed with the help of a knife. The hard green material (pulp, 10 g) was boiled with water (50 mL), cooled and it was centrifuged. The clear portion of the aqueous extract (pH 3) of tamarind fruit was used as catalyst for the reaction.

4.3. Application of Tamarind Juice in Organic Synthesis: Preparation of Bis-, Tris- and Tetraindoles

Tamarind (*Tamarindus indica)* fruit juice has been applied as a biocatalyst for the first time for rapid synthesis of bis-, tris(indolyl)methanes and tetraindolyl compounds by Pal [44] in excellent yields by electrophonic substitution reaction of indoles with aldehydes using microwave irradiation under solvent-free conditions.



Scheme 7. Reaction of lemon juice with terephthaldialdehyde and indoles under solvent-free conditions



Scheme 8. Preparation of bis (indolyl) methane benzaldehyde and di-bis (indolyl) methane derivatives

Aromatic as well as aliphatic monoaldehydes and 3-formyl indole afforded bis- and tris (indolyl) methanes (**10** and **11**) respectively with indoles in presence of tmarind juice under microwave irradiation. Dialdehyde, such as terephthaldialdehyde (**12**) when reacted with indoles in 1:2 ratios gave p-bis (indolyl) methane benzaldehydes (**13**) and in 1:4 rations afforded p-di (bis-indolylmethane) benzene (**14**) in good yields within 2 min under the similar reaction conditions (Scheme 7).

The condensation of 4 equivalents of indoles with 1 equivalent of 2, 2'-di (formylphenoxy) propane (**15**) gave compounds **16** and **17** in 3 min under the similar reaction conditions (Scheme 8). It was also found that on increasing the reaction time to 5 min, only compounds **17** was obtained in good yield. The catalytic role of tamarind fruit extract in the above process was clearly evident from the observation that in its absence a little reaction took place. Neutral alumina was acted as solid support only.

5. Fruit Juice of *Acacia Concinna*

Acacia concinna fruit is a member of Leguminosae, subfamily Mimosacaea. *Acacia concinna* is a medicinal plant that grows in tropical rainforests of southern Asia, and its fruits are used for washing hair, for promoting hair growth, as an expectorant, emetic and pugitive [45]. Aqueous extracts of this fruit has been in use as detergent since a long time in India. Various properties of *Acacia concinna* fruit are due to the presence of saponins [46] in it. Saponins have surfactant properties similar to dodecylbenzene sulfonates [47].

Fig.5. Photography of *Acacia Concinna* Fruit and Juice

5.1. Composition of Acacia Concinna Fruit Juice

The pods of *Acacia concinna* have been found to contain the saponin of acaciac acid, a trihydroxymonocarboxylic acid belonging to the tetracyclic triterpene group [48].The aqueous extract of these pods of fruits shows acidic (pH 2.1) which is due to presence of acaciac acid with molecular formula $C_{30}H_{48}O_5$.

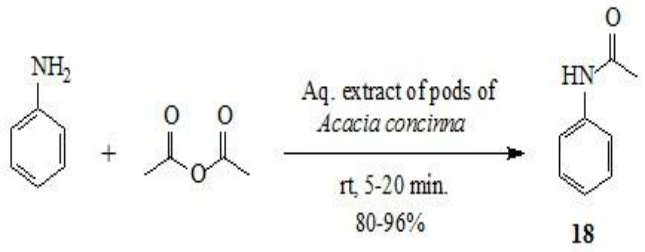
5.2. General Procedure for Extraction of Acacia Concinna Fruit Juice

100 g dry pods of Acacia concinna fruit was soaked in 1000 ml distilled water for 12 h. The material was then filtered through Whatman filter paper and filtrate was used as a catalyst. The aqueous extract of the juice is acidic in nature (pH 2.1) due to presence of acaciac acid which promted chemists to use as catalyst in organic synthesis.

5.3. Application of Acacia Concinna Fruit Juice in Organic Synthesis: Preparation of Acetanilides

A facile, efficient, cost-effective and green protocol was reported by Mote *et al*. [49] for the synthesis of acetanilides **18** in good to excellent yields by reaction of aromatic primary amines and acetic anydried, catalyzed by aqueous extract of pods of acacia concinna fruit at room temperature (Scheme 9). The acetylation reaction was completed within very short

time (5-20 min) using this juice as natural catalyst and the rate enhancement in aqueous extract of pods of acacia concinna fruit can be attributed due to its surfactant property and acidic nature (pH 2.1). The saponin which are high acidic solubalize the reactant species strongly by hydrogen bond formation in aqueous solution. This increases number of favorable collision between the reactant species. Further encapsulation of hydrophobic end of the product in micellar cages drives the equillibrium towards product side which increase the speed as well as yields of products.



Scheme 9. Acylation of amines with Ac_2O catalyzed by Pods of *Acacia concinna* fruit

6. Fruit Juice of *Sapindum Trifolistus*

Sapindus trifiliatus is known as soapnut tree or three-leaf soapberry that grows in South India. The shell is of a red color and become darker after they are harvested and dried. Aqueous extract of the pericarp of this fruit have been used as detergent since a long time in India [50]. It is also known to possess various pharmacological activities [51].

Fig.6. Photography of Fruit and Juice of *Sapindum Trifolistus*

6.1. Composition of Sapindum Trifolistus Fruit Juice

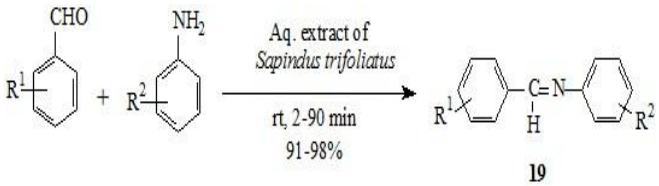
The pericarp of this fruit is known to contain 10-11.5% of saponins [52]. These saponins have a common structural skeleton containing a pentacyclic triterpenoid part substituted with different carbohydrate side chains [53]. The aqueous extract of the pericarp of Sapindus trifoliatus fruits shows an acidic (pH 3.8), which is due to the presence of a COOH group in the triterpenoid part. This acidic nature of the aqueous extract prompted organic chemists to use it as a catalyst in acid-catalyzed reactions.

6.2. General Method for Extraction of Sapindum Trifolistus Fruit Juice

The dry pericarp of the *Sapindus trifoliatus* fruit (100 g) was soaked in water (400 ml) for 12 h. The material was then macerated with the water in which it was soaked and filtered. The filtrate, *i.e*., the aqueous extract, was kept below 5 ℃ and used as catalyst for 15 days.

6.3. Applications of Sapindum Trifolistus Fruit Juice in Organic Synthesis: Preparation of Aldamines

Pore and his group [54] were demonstrated the catalytic efficiency of the aqueous extract of the pericarp of Sapindus trifoliatus fruits in the chemoselective synthesis towards aldamines (**19**) (Scheme 10). Thus, when a mixture of aromatic aldehydes and aromatic amines were stirred in presence of this fruit extract produced aldamines in good yields whereas aromatic ketone and aromatic amines did not yield ketamines under comparable reaction conditions indicating chemoselective catalysis of the extract. The mild conditions, high yields, and short reaction times not only make this protocol a valuable alternative to the conventional methods, but it also become significant under the roof of environmentally greener and safer processes.



Scheme 10. Synthesis of aldamines catalyzed by aqueous extract of *Sapindus trifoliatus*

7. Fruit Juice of Coconut

Cocos nucifera is a member of the family Arecaceae (palm family). Coconut juice is a pleasant and refreshing beverage derived from the fruit of *Cocos nucifera*. Its juice is also called "coconut water", and is widely consumed as a nourishing soft drink in tropical and subtropical countries as it is flavorful, sweet, and contains antioxidants. Coconut water is the clear liquid inside green young coconuts. In early, development serves as a suspension for the endosperm of the coconut during theirn nuclear phase of development. As growth continues the endosperm mature into their cellular phase and deposit into the rind of the coconut meat. The juice is used for the treatment of high blood pressure, hypertension

and diarrhea related dehydration.

Fig.7. Photography of Fruit and Coconut Juice of *Cocos Nucifera*

7.1. Composition of Coconut Juice

The main ingredients [55-57] per 100 g of coconut juice of *Cocos nucifera* are water (94.99 g), carbohydrates (3.71 g), protein (0.72 g or 1.2%), fat (0.2 g), ascorbic acid or vitamin-C (2.4 mg or 3%) as a water soluble antioxidant, pantothenic acid (0.043 mg or 1%), electrolytes; such as pottasium (250 mg or 5%), sodium (105 mg); minerals such as magnesium (25 mg or 7%), phosphorous (20 mg or 3%), calcium (24 mg) and iron (0.29 mg or 2%). The juice contains cytokinins which promote plant cell division and growth, showed significant anti-ageing, anti-carcinogenic, and anti-thrombotic effects. Coconut water is composed of many naturally occurring bioactive enzymes such as acid phosphatase, catalase, dehydrogenase, diastase, peroxidase, RNA-polymerase etc. Due to presence of ascorbic acid and pantothenic acid, coconut juice is low acidic in nature.

7.2. General Method for Extraction of Coconut Juice

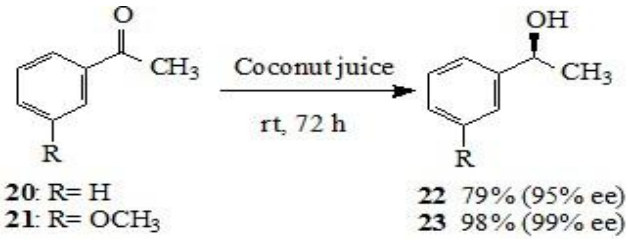
The coconut juice (water) was obtained by perforating the fruit with a metallic sharp object (knife). The coconut juice was filtered using Whatman 47 mm filter paper for the elimination of solid residues. The clear filtrate was used as catalyst in the reaction.

7.3. Applications of Coconut Juice in Organic Synthesis

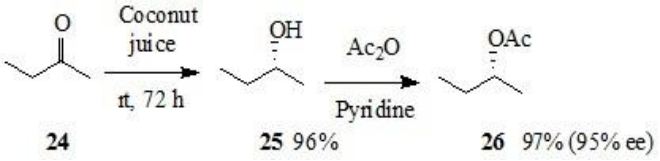
Coconut juice also represents a very important class of biocatalyst in organic synthesis. The use of coconut juice as a biocatalyst for selective reduction of aromatic and aliphatic carbonyl compounds and dimerisation of aromatic nitro compounds has been reported. The coconut juice is also effectively hydrolyzed esters, amides and anilides under mild conditions.

7.3.1. Reduction of Carbonyl Compounds

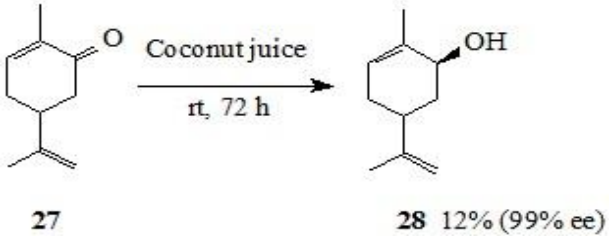
Fonseca *et al*. [58] developed a simple and green method for the selective bioredeuction of aliphatic and aromatic aldehydes and ketones in high yields using coconut juice as natural catalysts. When various carbonyl compounds such as **20**, **21**, **24** and **27** were added to the freshly prepared coconut juice of *Cocos nucifera* and the mixture were shaken (160 rpm) at room temperature for 72 h, gave corresponding alcohols. Enantioselectivity, induced by coconut juice, was oserved in the reduction of the pro-chiral ketones **20**, **21** where the alcohols **22** (79%) and **23** (98%) and the ee ranging from 95% to 99%, respectively.



Scheme 11. Enantioselective reduction of aromatic ketone using coconut juice

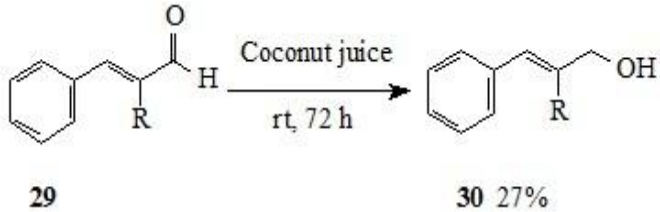


Scheme 12. Enantioselective reduction of aliphatic ketone using coconut juice



Scheme 13. Chemo- and stereoselective reduction of α, β-unsaturated ketone using coconut juice

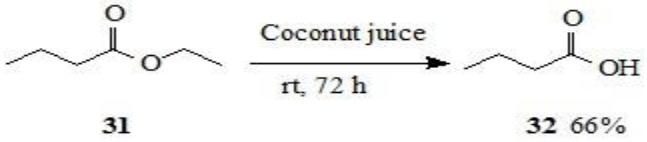
Aliphatic ketone **24** enantioselectively produced alcohol **25** (96%) and the ee was determined as 95% of its acylated derivatives **26**. Chemoselectivity was also observed for the reduction of α, β-unsaturated ketones x using coconut juice. The chemoselective reduction of **27** yielded **28** in low yield (12%); however, with high ee (99%) and "S" configuration. A regioselective reaction was observed using coconut juice. The compound **29** was reduced selectively at the carbonyl functional group, yielded only the corresponding alcohol **30** (27%), without modification of the double bond.



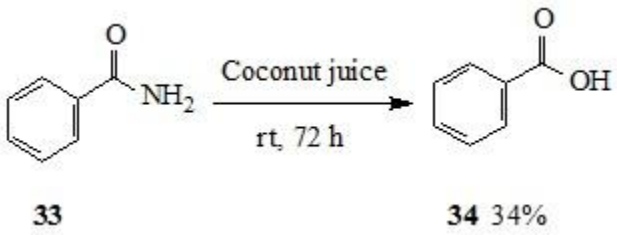
Scheme 14. Regioselective reduction of α, β-unsaturated aldehyde using coconut juice

7.3.2. Hydrolysis of Ester, Amide and Anilides

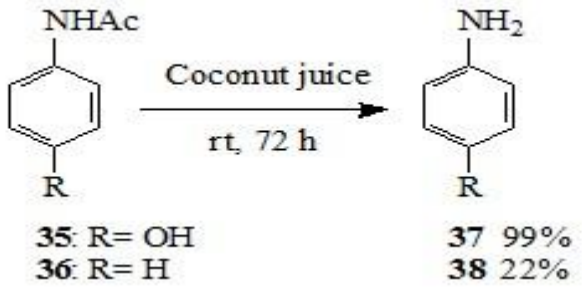
Hydrolysis of ester and amide with water has been accomplished using coconut juice. Fonseca and co-workers [58] reported that coconut juice acts as a biocatalyst for the hydrolysis of **31** and **33**. Bioconversion of ester **31** and amide **33** to the corresponding acids **32** (66%) and **34** (34%) were observed after 3 days under constant stirring at room temperature. The enzymatic anilide hydrolysis of **35** and **36** by coconut juice is quite effective for 4-hydroxyacetanilide yielding **37** (99%). However, hydrolysis proceeds much lower yield with unsubstituted anilide **36**, which producing aniline **38** in only 22%.



Scheme 15. Hydrolysis of ester using coconut juice



Scheme 16. Hydrolysis of amide using coconut juice



Scheme 17. Hydrolysis of anilides using coconut juice

8. Conclusions

This review focuses the importance of fruit juice as a natural and biocatalyst in organic transformations. The growing interest of fruit juice in organic synthesis is mainly due to their acidic properties, enzymatic activity, benign environmental character, inexpensive, and commercial availability. The catalytic activity including the application of fruit juice in various organic transformations such as formation of C-C, C-N bonds and breaking of C-O, C-N bonds in different synthetically important organic compounds have been studied. Although many observations have not received by application of fruit juice in synthesis of natural products or complex structured molecules in details, it is believed that in near future the fruit juice chemistry will continue to attract significant research activity. Therefore, the present review would serve the need of organic chemists in searching new applications of fruit juice for organic synthesis.

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Rammohan Pal was born in 1978 in Kolkata, India. He obtained his B.Sc. in 1999 and M.Sc. in 2001 in Chemistry from University of Calcutta, India. He worked as a DBT-project fellow at the Biological Department of Chemistry, Indian Association for the Cultivation of Sciences (IACS), Kolkata and as a UGC-JRF at the Natural Product Laboratory, Indian Institute of Chemical Technology (IICT), Hyderebad, India. He carried out his predoctoral research work at the Department of Chemistry, Jadavpur University under the supervision of Prof. Asok Kumar Mallik. He received his Ph.D. degree in 2011 from Jadavpur University on synthesis and reactions of some nitrogen heterocycles. He has published over 26 scientific papers. His current research interests cover the development of synthetic methodology, green chemistry and synthesis of heterocyclic compounds. Presently, he is an Assistant Professor of Organic Chemistry at the Acharya Jagadish Chandra Bose College, Kolkata, India.

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Pineapple Juice as a Natural Catalyst: An Excellent Catalyst for Biginelli Reaction

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Abstract

An efficient and greener synthesis of a series of dihydropyrimidinone (DHPMs) derivatives were accomplished via three-component one-pot cyclocondensation between substituted aryl aldehydes, diketone/ketoester and urea. This solvent free approach is totally nonpolluting having several advantages such as shorter reaction time, mild reaction conditions, simple workup and reduced environmental impact.

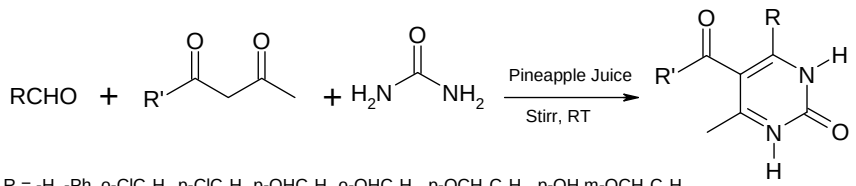
Keywords: Biginelli, Natural Catalyst, Pineapple Juice, Dihydropyrimidinone.

1. Introduction

Among the challenges for chemists include discovery and development of non-hazardous and simple environmentally safe chemical processes for selective synthesis by identifying alternative reaction conditions and solvents for much improved selectivity, energy conservation and even less hazardous waste generation are not desirable and inherently safer chemical products. Therefore, to address depletion of natural resources and preservation of ecosystem it is just urgent to adopt so called "greener technologies" to make chemical agents for well being of human health. Due to acidic nature (pH = 3.7) pineapple juice as a natural catalyst has been found to be a suitable replacement for various homogeneous acid catalysts.

In literature number organic reactions are reported in which natural catalyst like clay [1-3], phosphates [4,5], gold [5], animal bone [6] etc. are employed. In continuation of our research work in application of natural acids as catalyst, here, we report a solvent free one pot cyclocondensation reaction of substituted aryl aldehydes, diketone/ketoester and urea (**Scheme 1**) with good yields.

Pineapple (*Ananas comosus*) is sometimes called the *King of Fruit* [7]. Pineapple is grown extensively in Hawaii, Philippines, Caribbean area, Malaysia, Taiwan, Thailand, Australia, Mexico, Kenya and South Africa. Pineapple has long been one of the most popular of the non-citrus tropical and subtropical fruits, largely because of its attractive flavour and refreshing sugar-acid balance [8]. For the present work, we have used extract of *pineapple* as natural catalyst for synthesis of dihydropyrimidinone (DHPMs). The main ingredients of 100 g pineapple contain 47 - 52 calories, water (85.3 - 87.0 g), protein (0.4 - 0.7 g), fat (0.2 - 0.3 g), total carbohydrate (11.6 - 13.7 g), fiber (0.4 - 0.5 g), ash (0.3 - 0.4 g), calcium (17 - 18 mg), phosphorus (8 - 12 mg), iron (0.5 mg), sodium (1 - 2 mg) and potassium (125 - 146 mg) [9]. It also contains 12% - 15% sugars of which two-third is in the form of sucrose and the rest are glucose and fructose and 0.6% - 1.2% acid of which 87% is citric acid and 13% is malic acid [10,11]. The composition of the juice varies with geographical, cultural and seasonal harvesting and processing.



R = -H, -Ph, o-ClC_6H_4, p-ClC_6H_4,p-OHC_6H_4,o-OHC_6H_4, p-$OCH_3C_6H_4$, p-OH m-$OCH_3C_6H_3$, -$CH{=}CHC_6H_4$, o-$NO_2C_6H_4$, -C_4H_3O(furfural)

R' = OEt, Me

Scheme 1. Synthesis of dihydropyrimidinones.

The extract of pineapple is acidic having pH 3.7 and the acidity percentage is 53.5% and hence it will be worked as acid catalyst for cyclocondensation. Therefore, we have used this extract as natural catalyst for synthesis of DHPMs.

The Italian chemist Pietro Biginelli (1893, University of Florence) for the first time reported on the acid-catalyzed cyclocondensation reaction of ethyl acetoacetate, benzaldehyde, and urea [12]. The three components reaction mixture in ethanol was simply heated with a catalytic amount of HCl at reflux temperature and the product that precipitated on cooling the reaction mixture was identified as 3,4-dihydropyrimidin-2(1H)-one. This reaction is nowadays referred to as the Biginelli reaction, Biginelli condensation or as the Biginelli dihydropyrimidine synthesis. However, this method is suffered from drawbacks of the longer reaction time and lower yields, hence reaction remained unfocused in the last century. But due to important biological properties of DHPMs, the interest in their synthesis has been increased in the last two decades. Much effort has been made recently to improve and modify this reaction. This gave inspiration to organic chemists to find out more suitable protocol and simpler methods for the synthesis of DHPMs.

DHPM and its derivatives are found in a large family of natural products with broad biological activities, due to which they become important classes of organic compounds. They generally possess intriguing therapeutic and pharmacological properties [13-15]. Several of their functionalized derivatives are used as calcium channel modu- lators [13-16], Ca-antagonists [16-18] and vasodilative, antihypertensive [19].

For Biginelli reaction, large number of methods have been reported to synthesize DHPMs by altering catalyst. Of them various homogeneous catalysts such as $Mg(NO_3)_2$ [20], $Pb(NO_3)_2$ [21], $LaCl_3{\cdot}7H_2O$ [22], P_2O_5 [23]. Recently Lewis acids like DDQ [24], $InBr_3$ [25], $CaCl_2$ [26], $Y(OAc)_3$ [27], $ZnCl_2$ [28], $RuCl_3$ [29], Metal triflimides $Ni(NTf_2)_2$ [30] etc. have been extensively reported in the literature Biginelli reactions. Apart from these, the Bronsted acids such as *p*-TSA [31], almost neutral catalyst $Zn(BF_4)_2$ [32] also reported. Heterogeneous catalysts such as E4a [33], SiO_2-Cl [34], AMA [35], KSF(montmorillonite) [36], zeolites like HZSM-5, HY, MCM-41 [37] have also been employed. Synthesis of DHPMs can also be catalyzed by ionic liquids [38].

The limitations in using the above mentioned catalysts were such as long reaction time, elevated reaction temperature, harsh reaction conditions, use of expensive reagents, moderate yields of the products, use of harmful organic solvents and toxic and hazardous transition metals (**Table 1**).

2. Results and Discussion

Herein, we, report a single step synthesis of DHPMs using a pineapple juice as natural catalyst under solvent-free conditions. As per literature survey, there are no earlier reports of pineapple juice as catalyst for Biginelli reaction. In addition to its clean and simplicity, this catalyst resulted in higher yields for different aromatic aldehydes (**Table 2**).

3. Conclusions

We have developed an eco-friendly and economic process for the synthesis of DHPMs by pineapple juice as a catalyst with good yields. This solvent free approach is totally nonpolluting and there no any use of toxic materials, quantifying it as a green approach to this cyclocon densation reaction. In addition to this, it involved mild.

4. Experimental Section

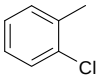
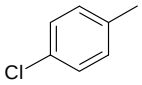
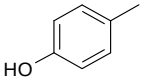
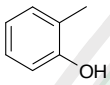
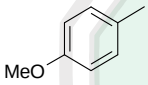
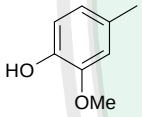
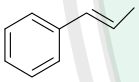
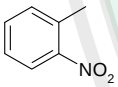
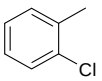
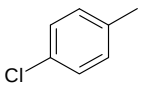
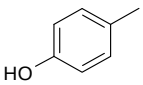
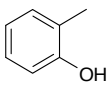
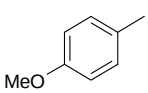
4.1 General Process for Preparation of Pineapple Juice

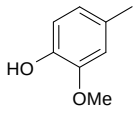
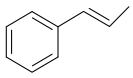
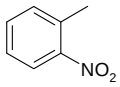
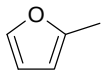
Fresh pineapple (*Ananas comosus*) was procured locally. The crown and stem portions were removed and the skin reaction conditions and simple workup was peeled using

Table 1. Comparison for different catalysts used for synthesis of DHPMs (R = p-$OCH_3C_6H_4$).

Entry	Catalyst	Time	Temperature	Yield (%)
1	p-TSA [31]	1 hr	Refluxed in EtOH	90
2	$RuCl_3$ [29]	4.5 hr	Reflux in N_2 atm	82
3	$Zn(BF)_4$ [32]	4 hr	Stirring at RT	71
4	$Y(OAC)_3$ [27]	4.5 hr	115˚C	89
5	$Mg(NO_3)_2$ [20]	45 min	Refluxed	90
6	$CaCl_2$ [26]	2 hr	Refluxed in EtOH	98
7	$InBr_3$ [25]	7 hr	Refluxed in EtOH	97
8	$Pb(NO_3)_2$ [21]	180 min	Refluxed in CH_3CN	89
9	P_2O_5 [23]	1.5 hr	Refluxed at 100˚C	94
10	SA & SSA [39]	10 min	Reflux 120˚C	86
11	E4a [33]	8 hr	Heated at 80˚C	91
12	AMA [35]	35 min	Heated at 60˚C in EtOH	96
13	Yattria-Zirconia Lewis acid [40]	6 hr	Aq. CH_3CN 60˚C	92
14	Silica chloride [34]	3 hr	Heated at 80˚C	90
15	Pineapple	3.5 hr	Stirring at RT	82

Table 2. Pineapple Juice catalyzed synthesis of DHPMs.

Entry	R	R^1	Time (hours)	Yield (%)	M.P.	
					Found	Reported
1	H	OEt	3.5	60	232	-
2		OEt	2.5	82	207	202 [32]
3		OEt	3.5	81	216	218 [27]
4		OEt	4.5	85	213	215 [32]
5		OEt	2	86	222	226 [32]
6		OEt	3.5	79	202	201 [32]
7		OEt	3.5	82	203	203 [32]
8		OEt	2.5	85	215	215 [41]
9		OEt	2	89	230	232 [32]
10		OEt	3.5	87	209	208 [32]
11		OEt	5	88	204	203 - 205 [21]
12	H	Me	3.5	61	230	--
13		Me	3.5	90	232	233 [32]
14		Me	3	92	240	-
15		Me	5.5	93	277	-
16		Me	3	90	256	-
17		Me	4	88	220	-
18		Me	3	93	172	166 [32]

19		Me	2	92	232	-
20		Me	5	89	243	-
21		Me	2.5	91	230	234 - 236 [21]
22		Me	4.5	90	197	-

knife. Then the fruit was sliced and the fruit slices pressed in a fruit juicer for one to two minutes to get the semisolid mass which was then filtered through cotton to get liquid pineapple juice.

4.2 General Procedure for Synthesis of 5-Ethoxycarbonyl-6-methyl-4-(4-methoxyphenyl)-3,4-dihydropyrimidin-2(1H)-one

The synthesis of 5-ethoxycarbonyl-6-methyl-4-(4-methoxyphenyl)-3,4-dihydropyrimidin-2(1*H*)-one is described as a representative example : The equimolar quantities of p-metho-xy- benzaldehyde (1.36 g, 10 mmol), ethyl acetoacetate, (1.30 g, 10 mmol) and urea (0.6 g, 10 mmol) in 1 ml pineapple juice were stirred for 3.5 hours at room temperature with monitoring by TLC. Then the reaction mixture was filtered, washed with little water. The yellow solid obtained was then recrystallized with ethanol to get fine yellow crystals of 5-ethoxycarbonyl-6-methyl-4-(4-methoxyphenyl)-3,4-dihydropyrimidin-2(1H)-one. The formation of the compound was confirmed by IR, NMR and its melting point.

This procedure is followed for the synthesis of all the DHPMs listed in **Table 2**.

4.3 Spectral Data for Representative Compounds

5-*ethoxycarbonyl*-6-*methyl*-4-(4-*methoxyphenyl*)-3,4-*dihydropyrimidin*-2(1*H*)-*one* (Compound 7 **Table 2**):

IR ($CHCl_3$, cm^{-1}): max 3230, 1720, 1690 cm^{-1}.

^1H NMR ($CDCl_3$): 1.14 (s, 3H, $-OCH_2CH_3$), 2.32 (s, 3H, $-CH_3$), 3.78 (s, 3H, $-OCH_3$), 4.05 (s, 2H, $-OCH_2CH_3$), 5.34 (s, 1H,-NH), 5.90 (s, 1H,-NH), 6.84 (s, 2H, Ar-H), 7.21 (s, 2H, Ar-H), 8.42 (s, 1H, -CH) **(Figure 1)**.

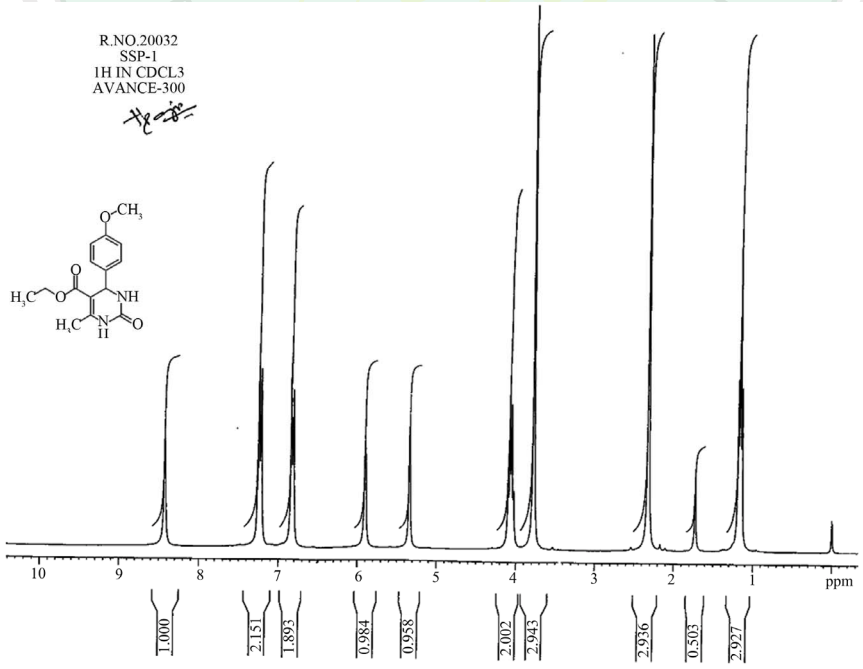


Figure 1. NMR Spectrum (1).

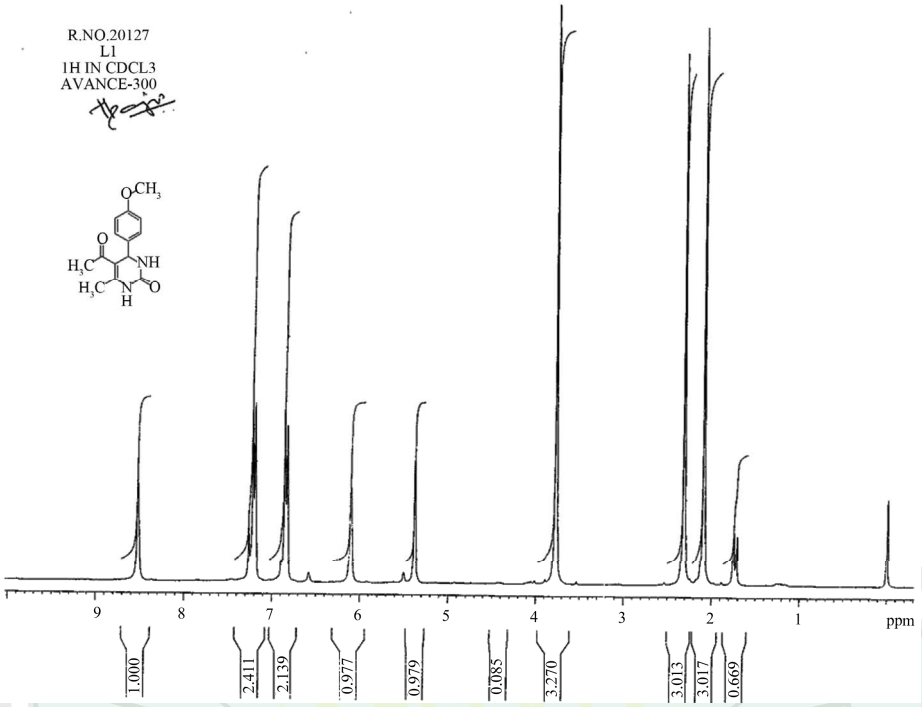


Figure 2. NMR Spectrum (2).

5-*acetyl*-6-*methyl*-4-(4-*methoxyphenyl*)-3,4-*dihydropyri midin*-2(1*H*)-*one* (Compound 18 **Table 2**)

IR ($CHCl_3$, cm^{-1}): max 3235, 1721, 1692 cm^{-1}.

^1H NMR ($CDCl_3$): 2.09 (s, 3H, $-CH_3$), 2.32 (s, 3H, $-CH_3$), 3.77 (s, 3H, $-OCH_3$), 5.37 (s, 1H, -NH), 6.10 (s, 1H, -NH), 6.85 (s, 2H, Ar-H), 7.21 (s, 2H, Ar-H), 8.52 (s, 1H, -CH) **(Figure 2)**.

5. Acknowledgements

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6. References

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Synthesis of Schiff Bases via Environmentally Benign and Energy-Efficient Greener Methodologies

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Abstract: Non classical methods (water based reaction, microwave and grindstone chemistry) were used for the preparation of Schiff bases from 3-chloro-4-fluoro aniline and several benzaldehydes. The key raw materials were allowed to react in water, under microwave irradiation and grindstone. These methodologies constitute an energy-efficient and environmentally benign greener chemistry version of the classical condensation reactions for Schiff bases formation.

Keywords: Schiff bases, Microwave irradiation, Grinding, Greener chemistry approaches.

Introduction

Among the challenges for chemists include discovery and development of novel and simple environmentally safe chemical processes for selective synthesis by identifying alternative reaction conditions and solvents for much improved selectivity, energy conservation and less or no toxic waste generation and inherently safer chemical products. Therefore, to address depletion of natural resources and preservation of ecosystem it is just urgent to adopt so called "greener technologies" to make chemical agents for well being of human health. Schiff's bases are reported to show characteristic biological activities including antibacterial, antifungal, anticancer and herbicidal properties[1-6]. Other application of Schiff's bases includes industrial synthesis of high value life saving beta lactam[7] antibiotics from class of penicillins and cephalosporins.

In recent years, environmentally benign synthetic methods have received considerable attention. Verma *et al*[8] reported synthesis of enamines and imines under microwave irradiation accompanied with solvent less conditions. Kaupp *et al*[9] reported the synthesis of Schiff bases using water as a solvent. In continuation of our ongoing program[12-13] towards

ecofriendly green synthesis, it was thought worthwhile to synthesize Schiff bases utilizing greener methodologies.

Experimental

Melting points were determined in open capillary tubes and are uncorrected (Table 1). The purity of the compound was checked on silica-gel-coated Al plates (Merck). IR spectra were recorded in KBr on a Perkin Elmer Spectrum RX-1 FT-IR spectrophotometer. ^{1}H-NMR spectra was measured on Advance Bruker DRX-300 and JEOL AL300 FTNMR using solution in hexadeuterio dimethyl sulfoxide (DMSO) with trimethyl silane (TMS) as the internal standard, chemical shifts are given in δ (ppm). The values are recorded in the Table 2. Nitrogen was estimated by Dumas method. Microwave irradiations were carried out in an unmodified IFB domestic microwave oven. All chemicals were of analytical grade.

General procedure

3 Different greener methodologies that were adopted and studied for preparing Schiff bases are described below (Scheme 1).

Water based synthesis (Method A)

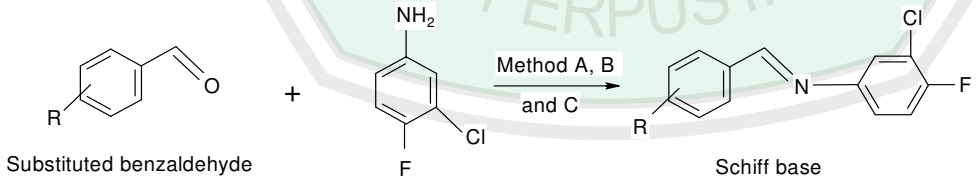
A mixture of 3-chloro-4-fluoro aniline (5 mmol, 0.71 g) and substituted benzaldehydes[1-9] (5 mmol) was stirred in 10 mL water for 30 min at room temperature in a few minutes, the temperature of the reaction mixture rises due to the heat evolved during this exothermic reaction, but it should not allowed to exceed 20 ^{o}C above the room temperature. The crystalline product so obtained was filtered, washed with water and dried. The product was obtained in good yield (80-90%).

Microwave "jump start" synthesis (Method B)

A mixture of 3-chloro-4-fluoro aniline (0.145 g, 0.1 mmol), substituted benzaldehydes[1-9] (0.1 mmol), and piperidine (0.02 mmole) were taken in DMSO (3 mL) in a round bottom flask. Reaction mixture was irradiated in MW oven for 3-6 min. On cooling the reaction mixture, a good yield (73-86%) of Schiff bases was obtained which was recrystallized from absolute ethanol.

Grindstone "friction activated" synthesis (Method C)

A mixture of 3-chloro-4-fluoro aniline (1 mmol, 0.15 g) and substituted benzaldehydes[1-9] (1 mmol) was grinded in a mortar with a pestle made of porcelain for 5-10 min. The mixture turns pasty after few minutes of grinding. Leave the reaction mixture for overnight. The solid product thus obtained (53-70%) was recrystallized from absolute ethanol.



Scheme 1.

Results and Discussion

Formation of Schiff base is an exothermic reaction. So rather than providing energy in the form of heat, their synthesis has been scaled up towards green chemistry domain by circumventing the use of water as a solvent, microwave irradiations and friction activated

synthesis by grinding. And out of the above adopted greener methodologies, water based reactions have a great virtue as water is the abundantly available solvent, indeed a cheaper medium for reactions. Reactions in aqueous media are not only environmentally benign but easy to handle and devoid of any corrosive or carcinogenic effect. Moreover, in this protocol, the products obtained are in high yield, pure and easily isolable. In conclusion, from our point of view, water has been proved here as a suitable "green solvent" for the synthesis of Schiff bases and increase in % yield is in following order: Method C < Method B < Method A.

Table 1. Physical and analytical data of compounds.

S.No	Aldehydes*	M.P, ^oC	Colour	N, % Found, Calcd.	Yield, %		
					A	B	C
1	3,4-Di-OCH_3 BD	110	White	4.38(4.43)	81.37	73.64	57.00
2	2-Cl BD	63	Peach	2.96(2.98)	82.00	77.10	53.72
3	4-Cl BD	124	White	2.96(2.99)	90.00	79.52	68.40
4	Piperonal	88	White	3.22(3.24)	89.36	84.30	65.16
5	Vanillin	86	White	5.57(5.52)	87.20	85.12	69.23
6	2-OH BD	138	Yellow	3.58(3.60)	87.79	79.00	70.25
7	4-OH BD	172	Cream	3.58(3.62)	84.65	83.42	63.80
8	3-NO_2 BD	140	White	10.05(9.98)	89.72	84.89	64.32
9	2-OH-1-ND	122	Yellow	4.63(4.68)	85.81	86.14	55.93

Note: BD=Benzaldehyde, ND=Naphthaldehyde*

Table 2. Characterization (IR and ^1H NMR) data of compounds.

Compd No.	IR (ν in cm^{-1})	^1H NMR (δ in ppm)
1	1018 (C-Cl), 1264-1138 (C-F), 1576 (-CH=N-), 1620 (Ar-(C-C)), 2935(-OCH_3).	2.51 (DMSO), 3.36 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3), 7.54-7.24(m, 6H, Ar-H), 8.54(s, 1H, -CH=N-).
3	1057 (C-Cl), 1412-1171 (C-F), 1571 (-CH=N-), 1617 (Ar-(C-C)).	2.51 (DMSO), 7.33-7.95(m, 7H, Ar-H), 8.67(s, 1H, -CH=N-)
6	976 (C-O), 1052 (C-Cl), 1273-1150 (C-F), 1494 (-OH), 1510 (-CH=N-), 1618 (Ar-(C-C)).	2.51 (DMSO), 6.96-7.54(m, 7H, Ar-H), 8.96(s, 1H, -CH=N-), 12.59(s, 1H, OH).

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Green and efficient synthesis of azo Schiff bases

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Abstract

Pure azo Schiff bases were readily and conveniently accessible in high yields by mixing of the reagents either as aqueous slurry, or by grinding at room temperature. This method, unlike a classical method, needs neither harsh conditions nor organic solvents. The satisfactory results were obtained with excellent yields, short reaction time, and operational simplicity in the experimental procedure. Comparison of time and yield in this green method with the classical methods is also performed.

Keywords: Azo Schiff bases; imines; solvent-free; green chemistry; grinding

1. Introduction

Azo dyes constitute one of the largest and most varied groups of synthetic organic dyes in use today [1]. Azo compounds are highly important, well-known and widely used substances in the textile, paper, coloring agents for foods and cosmetics industries. Other applications include emerging technologies like liquid crystals, organic photoconductors and non-linear optics [2-3]. Azo compounds serve as important analytical tools by providing a strongly chromophoric label, the concentration of which is easily determined by colorimetric, spectrophotometric or spectrofluorimetric methods. Besides, azo compounds are important analytical aid compounds serving as pH indicators, complexometric indicators and to a lesser extent, pre-concentration reagents [4]. The pharmacological use of azo compounds originates from the discovery of the antibacterial action of Prontosil on streptococcal infections by Dogmagk [5]. Furthermore, azo compounds were reported to show a variety of biological activities including antibacterial [6], antifungal [7], pesticidal [8], antiviral [9] and anti-inflammatory [10] activities.

Recently heterocyclic azo compounds have been used in the Mitsunobu reaction [11]. Usually, azo compounds were synthesized by diazotization of the amine in mineral acid at about 0 °C [12-15].

Schiff bases are used as substrates in the preparation of a large amount of bioactive and industrial compounds [16-20].

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In addition, Schiff bases are well-known to have biological activites such as antibacterial [21-22], antifungal [23-24], antitumor [25-26], antiviral [27-28], anti-HIV-1 [29], antiproliferative [30], herbicidal [31] and anti-influenza A virus [32] activities. It has been suggested that azomethine linkage (C=N) might be responsible for the biological activities of Schiff bases [33]. Also, Schiff base ligands have been recognized as 'privileged ligands' and they are able to coordinate with various metals and stabilize them in various oxidation states, enabling the applications of Schiff base metal complexes in a large variety of useful catalytic transformations [34-36]. Some Schiff bases have been reported as effective corrosion inhibitors for metal alloys in acidic media [37-39].

Perhaps the most common method for preparing Schiff bases is the reaction of aldehydes and ketones with primary amines [40]. The reaction is generally carried out by refluxing the carbonyl compounds and amines in organic solvents by separating the water as formed with an azeotroping agent or by anhydrous Na_2SO4 and $MgSO_4$ [41-45].

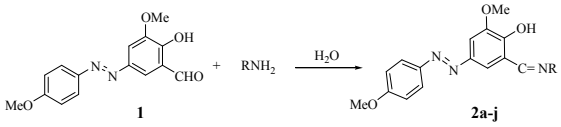
Recent years have witnessed a major drive to increase the efficiency of organic transformations while lowering the amount of waste materials. Many organic solvents are hazardous and can be deleterious to human health. They are volatile and cause an environmental threat by polluting the atmosphere [46-47]. The replacement of volatile organic solvents in organic reaction processes is an important green chemistry goal. The use of water as a biodegradable, nonflammable and readily available resource is attractive [48-50]. Furthermore, the solvent-free reaction or solid-state

reaction are green methods in the organic synthesis which have numerous advantages: reduced pollution, low costs, and simplicity in process and handling [51-52]. Mechanochemistry can be as simple as grinding two reactants in a mortar pestle and mortar or more complex, as with the use of commercially available ball mills [53-55].

Some new azo Schiff bases in organic solvents have been previously reported by the authors [56]. According to the above facts and in embracing the principles of green chemistry, herein we report two clean, simple and versatile routes to mono and bis azo Schiff bases in water or by grinding.

2. Results and discussion

Azoaldehyde **1** was prepared from *p*-anisidine and 2-hydroxy-3-methoxybenzaldehyde (*o*-vanillin) in aqueous medium at 0-5 ^{o}C according to a reported method and was purified by recrystallization from warm 95% ethanol.[56] Then azoaldehyde **1** reacted with amines in a small amount of water at room temperature to produce azo Schiff bases **2a-j** in excellent yields (Scheme 1, Table 1). The crystalline solids formed were collected by filtration, washed with water and dried in a desiccator to give pure products. The structures of the target compounds were well characterized by IR, ^{1}H NMR, ^{13}C NMR and MS Spectra.



Scheme 1. Synthesis of azo Schiff bases **2a-j** in water suspension

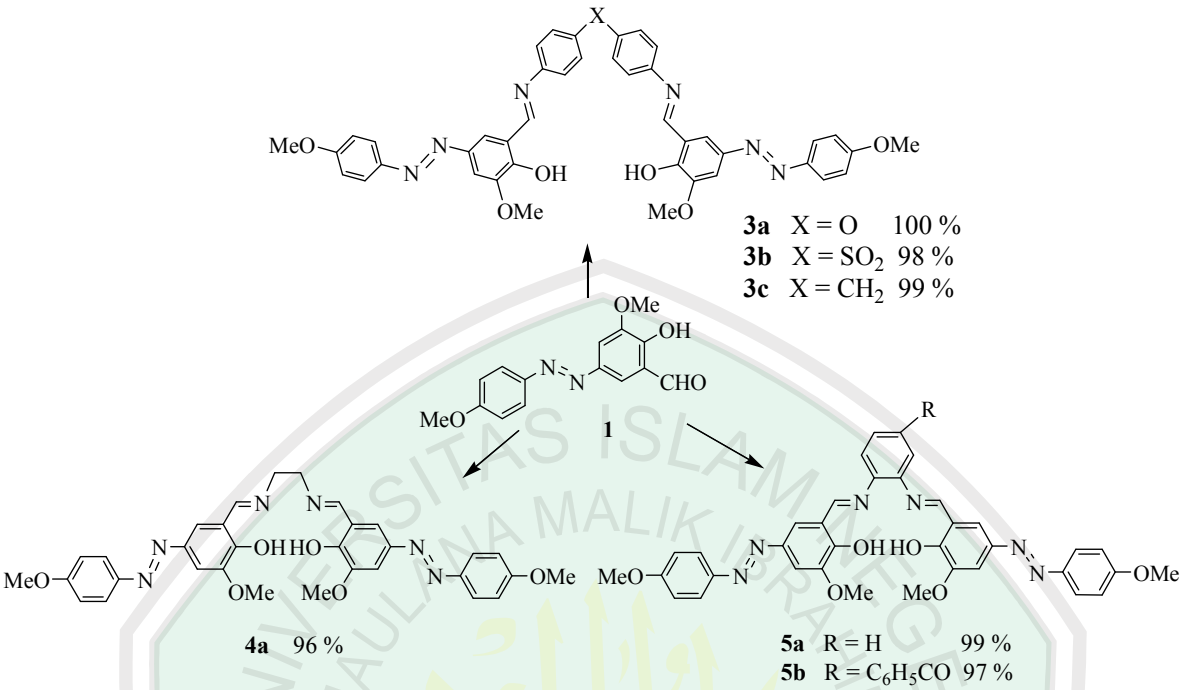
Comparison of this method with the conventional methods (e.g. refluxing in ethanol) showed the priority due to saving time and energy. Because of the low nucleophilicity of 4-chloroaniline and 4-nitroaniline, the yields of **2i-j** were moderate (Entry 9-10). When the mentioned reactions were performed in the presence of K_2CO_3 as a base, the yield increased and the time decreased (Entry 11-12). After these successful results, the bis azo Schiff bases **3a-c, 4a** and **5a-b** were synthesized using azoaldehyde **1** and the corresponding bis amine at room temperature for 1 hour (Scheme 2).

Condensation reaction of aldehydes and *p*-amino azobenzene in a water suspension medium was also found to produce azo Schiff bases **6a-g** quite efficiently. *p*-Amino azobenzene reacted with equimolar of different aldehydes in water suspension at room temperature to give azo Schiff bases **6a-g** in high yields at lower time than refluxing ethanol (Scheme 3, Table 2). All the synthesized products were characterized on the basis of their IR, ^{1}H NMR, ^{13}C NMR and Mass Spectra.

Table 1. Synthesis of azo Schiff bases **2a-j**

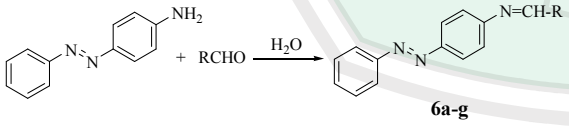
Entry	Product	R	Refluxing ethanol		Aqueous slurry	
			Time/min	Yield %	Time/min	Yield %
1	**2a**	4-$MeOC_6H_4$	120	99	30	100
2	**2b**	3-$MeOC_6H_4$	180	99	30	99
3	**2c**	4-MeC_6H_4	180	99	45	98
4	**2d**	3-MeC_6H_4	180	98	45	99
5	**2e**	C_6H_5	480	99	45	97
6	**2f**	$C_6H_5CH_2$	480	98	45	98
7	**2g**	3-HOC_6H_4	360	98	30	98
8	**2h**	2,4-di$MeOC_6H_3$	120	99	30	100
9	**2i**	4-ClC_6H_4	600	78	120	65
10	**2j**	4-$NO_2C_6H_4$	600	71	120	53
11	**2i**	4-ClC_6H_4	-	-	45	93[a]
12	**2j**	4-$NO_2C_6H_4$	-	-	45	90[a]

[a] The reaction was performed in the presence of K_2CO_3.



Scheme 2. Synthesis of bis azo Schiff bases **3a-c**, **4a** and **5a-b** in water suspension

We next decided to prepare azo Schiff bases by grinding corresponding amines and aldehydes without solvents in a mortar. When different amines and azoaldehyde **1** were ground together at room temperature, the reaction starts immediately, usually with gentle heat production but without melting because azo Schiff bases have high melting points. Indication of softening for some seconds followed by immediate hardening was visually observed only in synthesis with benzyl amine. The mixture was ground together for 1 min and was kept for 90 min.



Scheme 3. Synthesis of azo Schiff bases **6a-g** in water suspension

On the basis of these successful results, synthesis of bis azo Schiff bases **3a-c, 4a**, **5a-b** and azo Schiff bases **6a-g** were also performed by mechanochemical method (grinding of reactants together) at room temperature (Table 3). The water produced in the reaction was removed at 70 ^{o}C under vacuum.

Comparison of this method to the conventional method (refluxing ethanol) showed that the synthesis of azo Schiff bases in solvent-free method is faster and more inexpensive than the conventional method since in the former method, the reactions proceeded at room temperature with high yields. It is noteworthy that azo Schiff bases **2i-j** were obtained in excellent yields by grinding without the need for any base. This method has the following merits: high yield, easy separation and purification, simple instruments, mild condition, and no solvents.

3. Experimental

General: All required chemicals were purchased from Merck, Fluka and Acros chemical companies. IR spectra were run on a Shimadzu FT-IR 8000 spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ using a Bruker Avance DPX instrument (^{1}H NMR 250 MHz, ^{13}C NMR 62.9 MHz). Chemical shifts were reported in ppm (δ) downfield from TMS. All of the coupling constants (*J*) are in Hertz. The mass spectra were recorded on a Shimadzu GC-MS QP 1000 EX instrument. Melting points were determined in open capillaries with Buchi 510 melting point apparatus and are not corrected. Thin-layer chromatography was carried out on silica gel 254 analytical sheets obtained from Fluka. Azoaldehyde **1** (2-hydroxy-3-methoxy-5(4-methoxyphenylazo) benzaldehyde) was synthesized *via* the reported procedures [56]. Spectral data for **2a-b**, **2d-g** and **3a-b** have been previously reported [56].

Table 2. Synthesis of azo Schiff bases **6a-g**

Entry	Product	R	Refluxing ethanol		Aqueous slurry	
			Time/min	Yield %	Time/min	Yield %
1	**6a**	4-$NO_2C_6H_4$	300	96	30	98
2	**6b**	4-ClC_6H_4	300	91	30	98
3	**6c**	2-OHC_6H_4	300	95	45	99
4	**6d**	4-$MeOC_6H_4$	300	89	45	96
5	**6e**	4-MeC_6H_4	300	84	45	91
6	**6f**	C_6H_5	390	83	45	94
7	**6g**	$C_6H_5CH_2$	390	80	45	90

General procedure for the preparation of azo Schiff bases in water

Solid starting materials were finely powdered before use. A mixture of aldehyde (2.5 mmol) and amine (2.5 mmol) was stirred in a small amount of water (5 ml) at room temperature for the mentioned time. In the case of bis azo Schiff bases 5.0 mmol aldehyde was used. The crystalline powder formed was collected by filtration, washed with water and dried in a desiccator to give azo Schiff bases. If the reaction need a base, K_2CO_3 (0.41 g, 3.0 mmol) was added to the reaction mixture. The same procedure was used in the synthesis of bis azo Schiff bases with amine (2.5 mmol) and aldehyde (5.0 mmol).

General procedure for the solvent-free synthesis of azo Schiff bases

All solvent-free reactions were performed by grinding together 5.0 mmol of the pure amine with 5.0 mmol of the pure aldehyde in a mortar for one min and keeping the mixture at room temperature for 1.5 h in order to be formed quantitatively. The water produced in the reaction was removed at 70 ^oC under vacuum. The same procedure was used in the synthesis of bis azo Schiff bases with amine (5.0 mmol) and aldehyde (10.0 mmol).

4-((4-Methoxyphenyl)diazenyl)-2-methoxy-6-((*p*-tolylimino)methyl)phenol (**2c**): Red solid. mp: 139-141 ^oC. IR (KBr) (cm^{-1}): 1417 (N=N), 1612 (C=N), 3211-3637 (OH). ^1H NMR ($CDCl_3$) δ 2.31 (Me, s, 3H), 3.79, 3.82 (2OMe, s, 6H), 6.80-7.83 (ArH, m, 10H), 8.36 (HC=N, s, 1H), 14.29 (OH, br, 1H). ^{13}C NMR ($CDCl_3$) δ 20.5 (Me), 55.3, 55.7 (OMe), 108.4-158.7 (aromatic carbons), 162.2 (HC=N). GC-MS *m/z* = 375 [M^+].

4-((4-Methoxyphenyl)diazenyl)-2-((2,4-dimethoxyphenylimino)methyl)-6-methoxyphenol (**2h**): Dark red solid. mp: 176-178 ^oC. IR (KBr) (cm^{-1}): 1422 (N=N), 1609 (C=N), 3196-3618 (OH). ^1H NMR ($CDCl_3$) δ 3.78, 3.83, 3.85, 3.88 (4OMe, s, 12H), 6.93-7.86 (ArH, m, 9H), 8.42 (HC=N, s, 1H), 14.33 (OH, br, 1H). ^{13}C NMR ($CDCl_3$) δ 55.7, 55.9, 56.2, 56.6 (OMe), 110.4-156.9 (aromatic carbons), 161.5 (HC=N). GC-MS *m/z* = 421 [M^+].

4-((4-Methoxyphenyl)diazenyl)-2-((4-chlorophenylimino)methyl)-6-methoxyphenol (**2i**): Light brick red solid. mp: 126-128 ^oC. IR (KBr) (cm^{-1}): 1414 (N=N), 1615 (C=N), 3219-3642 (OH). ^1H NMR ($CDCl_3$) δ 3.80, 3.83 (2OMe, s, 6H), 6.88-7.93 (ArH, m, 10H), 8.30 (HC=N, s, 1H), 14.38 (OH, br, 1H). ^{13}C NMR ($CDCl_3$) δ 55.1, 55.5 (OMe), 106.3-155.6 (aromatic carbons), 163.4 (HC=N). GC-MS *m/z* = 397 [M^+, ^{37}Cl], 395 [M^+, ^{35}Cl].

4-((4-Methoxyphenyl)diazenyl)-2-methoxy-6-((4-nitrophenylimino)methyl)phenol (**2j**): Crimson solid. mp: 182-184 ^oC. IR (KBr) (cm^{-1}): 1344, 1520 (NO_2), 1419 (N=N), 1610 (C=N), 3203-3635 (OH). ^1H NMR ($CDCl_3$) δ 3.86, 3.90 (2OMe, s, 6H), 6.93-8.11 (ArH, m, 10H), 8.46 (HC=N, s, 1H), 14.29 (OH, br, 1H). ^{13}C NMR ($CDCl_3$) δ 55.5, 55.8 (OMe), 114.0-158.6 (aromatic carbons), 163.9 (HC=N). GC-MS *m/z* = 406 [M^+].

Bis[5-(4-methoxyphenylazo)-2-hydroxy-3-methoxybenzaldehyde]-4,4′-diiminophenyl methane (**3c**): Dark red solid. mp: 217-219 ^oC. IR (KBr) (cm^{-1}): 1422 (N=N), 1617 (HC=N), 3244-

Table 3. Synthesis of azo Schiff bases **2a-j**, **3a-c**, **4a**, **5a-b** and **6a-g** by solvent-free method

Product	Yield %	Product	Yield %	Product	Yield %
2a	100	**2i**	90	**6a**	100
2b	100	**2j**	91	**6b**	100
2c	100	**3a**	100	**6c**	100
2d	98	**3b**	95	**6d**	99
2e	96	**3c**	98	**6e**	100
2f	93	**4a**	98	**6f**	97
2g	98	**5a**	100	**6g**	98
2h	100	**5b**	97	-	-

3666 (OH). ^{1}H NMR ($CDCl_3$) δ 3.82, 3.86 (4OMe, s, 12H), 3.93 (CH_2, s, 2H), 6.84-7.89 (ArH, m, 20H), 8.39 (2HC=N, s, 2H), 14.31 (2 OH, br, 2H). ^{13}C NMR ($CDCl_3$) δ 42.7 (CH_2), 55.8, 56.2 (OMe), 107.1-159.5 (aromatic carbons), 163.6 (HC=N).

6,6'-(Ethane-1,2-diylbis(azan-1-yl-1-ylidene))bis(methan-1-yl-1-ylidene))bis(2-methoxy-4-((4-methoxyphenyl)diazenyl)phenol) (**4a**): Dark orange solid. mp: 191-193 ^{o}C. IR (KBr) (cm^{-1}): 1415 (N=N), 1622 (HC=N), 3217-3653 (OH). ^{1}H NMR ($CDCl_3$) δ 3.77, 3.82 (4OMe, s, 12H), 3.89 (2 CH_2, s, 4H), 6.76-7.62 (ArH, m, 12H), 8.48 (2HC=N, s, 2H), 14.19 (2 OH, br, 2H). ^{13}C NMR ($CDCl_3$) δ 55.4, 55.7 (OMe), 58.9 (CH_2), 113.7-156.5 (aromatic carbons), 165.1 (HC=N).

Bis[5-(4-methoxyphenylazo)-2-hydroxy-3-methoxybenzaldehyde]-1,2-phenylene diimine (5a): (**3c**): Dark red solid. mp: 185-187 ^{o}C. IR (KBr) (cm^{-1}): 1426 (N=N), 1605 (HC=N), 3163-3672 (OH). ^{1}H NMR ($CDCl_3$) δ 3.81, 3.86 (4OMe, s, 12H), 6.97-7.88 (ArH, m, 16H), 8.66 (2HC=N, s, 2H), 13.94 (2 OH, br, 2H). ^{13}C NMR ($CDCl_3$) δ 55.6, 55.9 (OMe), 105.5-156.9 (aromatic carbons), 163.3 (HC=N).

(3,4-Bis{[2-hydroxy-3-methoxy-5-(4-methylphenylazo)benzylidene]-amino}phenyl)phenyl methanone (5b): Red solid. mp: 140-142 ^{o}C. IR (KBr) (cm^{-1}): 1419 (N=N), 1605 (HC=N), 1659 (C=O), 3155-3650 (OH). ^{1}H NMR ($CDCl_3$) δ 3.87, 3.91 (4OMe, s, 12H), 6.91-7.85 (ArH, m, 20H), 8.70 (2HC=N, s, 2H), 13.89 (2 OH, br, 2H). ^{13}C NMR ($CDCl_3$) δ 55.9, 56.4 (OMe), 105.7-154.2 (aromatic carbons), 162.8 (HC=N), 195.6 (C=O).

(4-Nitrobenzylidene)-4-(phenyldiazenyl)aniline (6a): Red solid. mp: 171-173 ^{o}C. IR (KBr) cm^{-1}: 1341, 1534 (NO_2), 1411 (N=N), 1606 (C=N). ^{1}H NMR ($CDCl_3$) δ 6.81-8.14 (ArH, m, 13H), 8.72 (HC=N, s, 1H). ^{13}C NMR ($CDCl_3$) δ 114.6-155.2 (aromatic carbons), 161.3 (HC=N). GC-MS m/z = 330 [M^+]

(4-Chlorobenzylidene)-4-(phenyldiazenyl)aniline (6b): Orange solid. mp: 156-158 ^{o}C. IR (KBr) cm^{-1}: 1415 (N=N), 1609 (C=N). ^{1}H NMR ($CDCl_3$) δ 6.89-8.03 (ArH, m, 13H), 8.61 (HC=N, s, 1H). ^{13}C NMR ($CDCl_3$) δ 117.5-153.9 (aromatic carbons), 161.9 (HC=N). GC-MS m/z = 321 [M^+, ^{37}Cl], 319 [M^+, ^{35}Cl].

2-((4-(Phenyldiazenyl)phenylimino)methyl)phenol (**6c**)**:** Orange solid. mp: 162-164 ^{o}C. IR (KBr) cm^{-1}: 1423 (N=N), 1609 (C=N), 3137-3623 (OH). ^{1}H NMR ($CDCl_3$) δ 6.76-8.04 (ArH, m, 13H), 8.47 (HC=N, s, 1H), 13.75 (OH, br, 2H). ^{13}C NMR ($CDCl_3$) δ 115.8-159.9 (aromatic carbons), 162.4 (HC=N). GC-MS m/z = 301 [M^+].

***N*-(4-Methoxybenzylidene)-4-(phenyldiazenyl)aniline (6d):** Red solid. mp: 140-142 ^{o}C. IR (KBr) cm^{-1}: 1416 (N=N), 1614 (C=N). ^{1}H NMR ($CDCl_3$) δ 3.80 (OMe, s, 3H), 6.87-8.02 (ArH, m, 13H), 8.63 (HC=N, s, 1H). ^{13}C NMR ($CDCl_3$) δ 55.5 (OMe), 117.1-158.5 (aromatic carbons), 163.0 (HC=N). GC-MS m/z = 315 [M^+].

***N*-(4-Methylbenzylidene)-4-(phenyldiazenyl)aniline** (**6e**)**:** Dark orange solid. mp: 149-151 ^{o}C. IR (KBr) cm^{-1}: 1413 (N=N), 1607 (C=N). ^{1}H NMR ($CDCl_3$) δ 2.27 (Me, s, 3H), 6.92-7.91 (ArH, m, 13H), 8.67 (HC=N, s, 1H). ^{13}C

NMR ($CDCl_3$) δ 21.1 (Me), 112.8-154.3 (aromatic carbons), 161.7 (HC=N). GC-MS m/z = 299 [M^+].

***N*-Benzylidene-4-(phenyldiazenyl)aniline (6f):** Orang solid. mp: 155-157 ^oC. IR (KBr) cm^{-1}: 1414 (N=N), 1619 (C=N). ^1H NMR ($CDCl_3$) δ 6.76-7.88 (ArH, m, 14H), 8.57 (HC=N, s, 1H). ^{13}C NMR ($CDCl_3$) δ 119.4-156.8 (aromatic carbons), 162.5 (HC=N). GC-MS m/z = 285 [M^+].

4-(Phenyldiazenyl)-*N*-(2-phenylethylidene)aniline (6e): Light orange solid. mp: 119-121 ^oC. IR (KBr) cm^{-1}: 1411 (N=N), 1624 (C=N). ^1H NMR ($CDCl_3$) δ 3.26 (CH_2, d, 2H, J = 5.9), 6.93-7.80 (ArH, m, 14H), 8.26 (HC=N, t, 1H, J = 5.9). ^{13}C NMR ($CDCl_3$) δ 33.7 (CH_2), 117.3-154.5 (aromatic carbons), 161.8 (HC=N). GC-MS m/z = 299 [M^+].

4. Conclusions

In conclusion, we have developed convenient, fast and green procedures for the synthesis of azo Schiff bases that requires neither organic solvent nor refluxing condition. The yields were excellent and reactions were fast.

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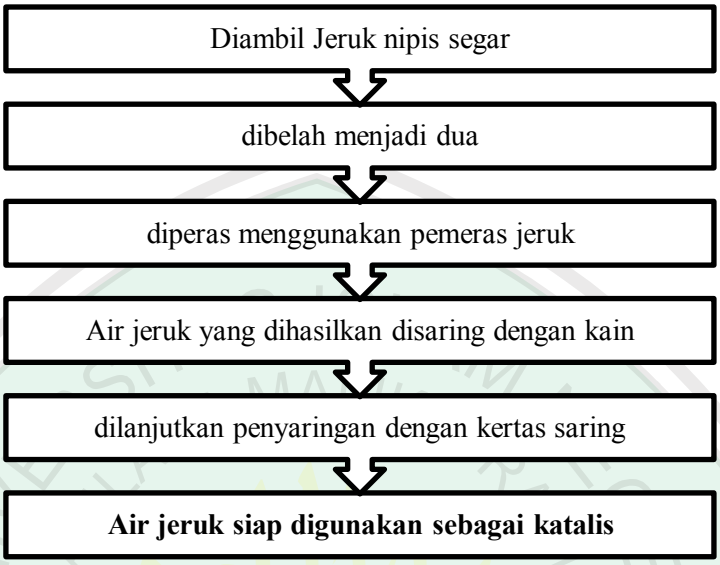
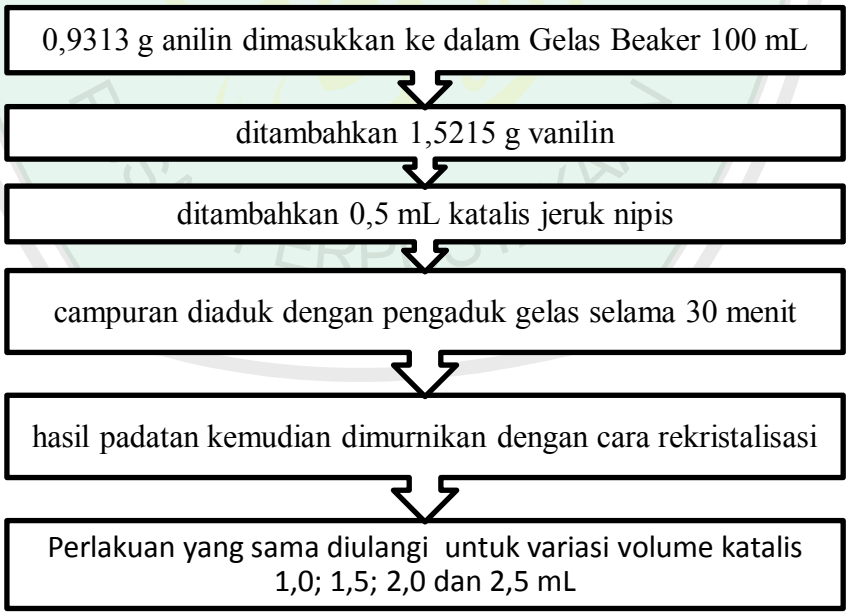
Lampiran 1. Diagram Alir

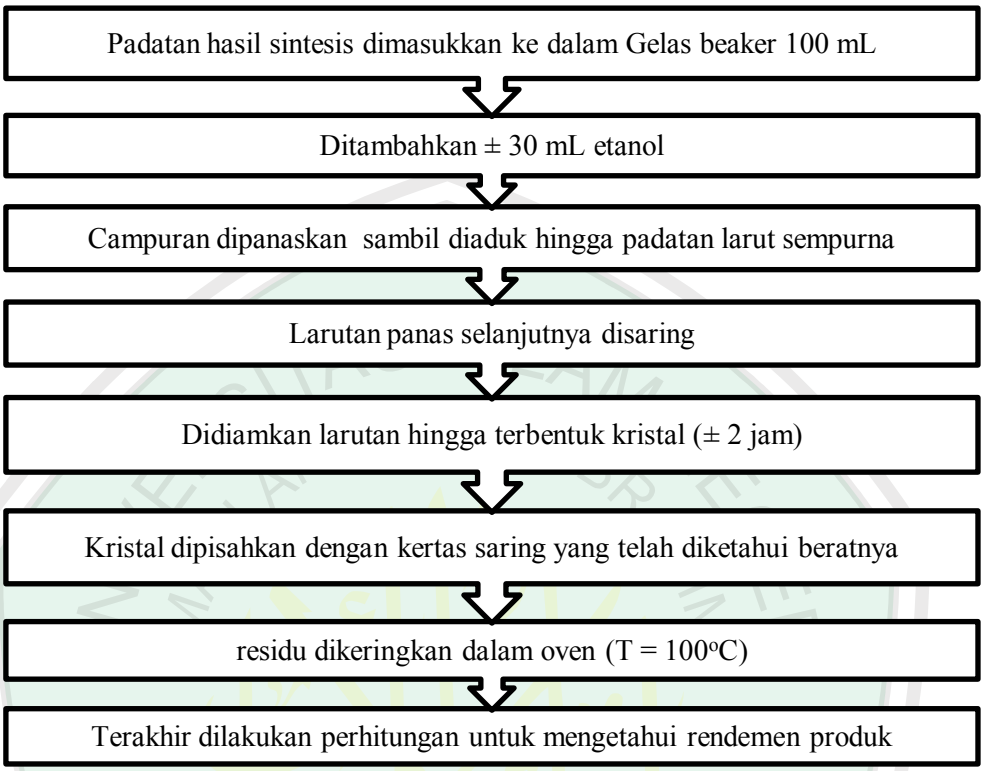
L.1.1 Preparasi katalis asam dari jeruk nipis (*Citrus aurantifolia*)



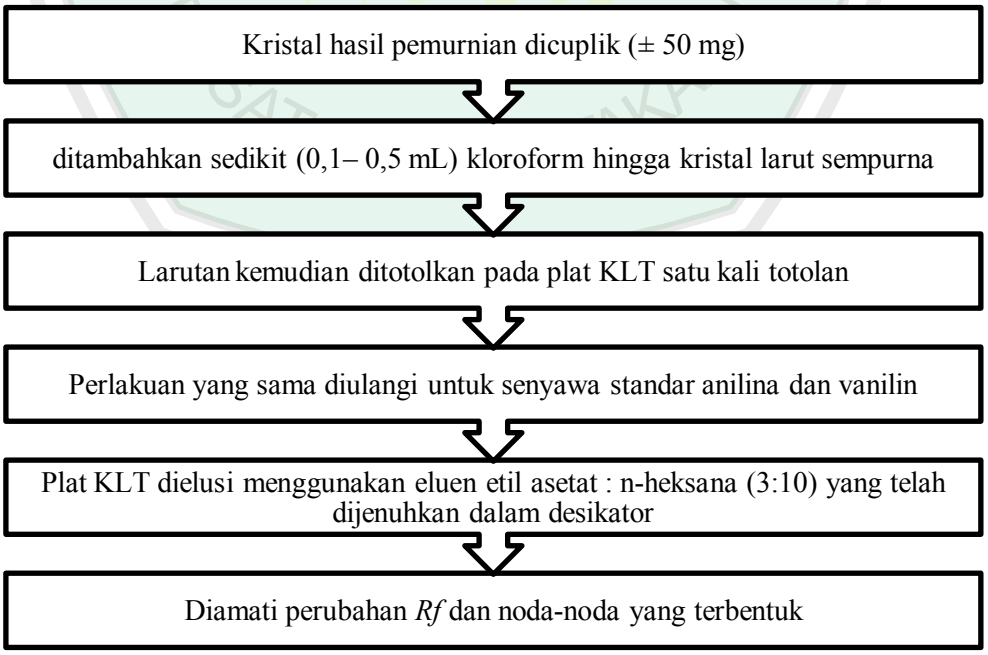
L.1.2 Reaksi pembentukan imina antara vanilin dan aniline dengan variasi jumlah katalis air jeruk nipis



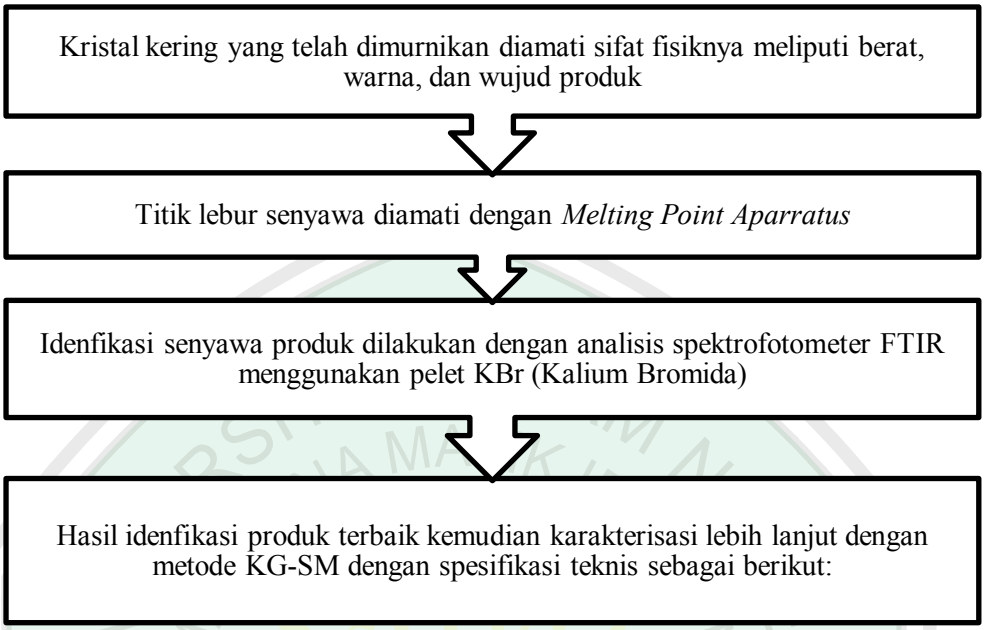
L.1.3 Pemurnian dengan metode rekristalisasi



L.1.4. Monitoring menggunakan plat KLT



L.1.5 Karakterisasi senyawa produk hasil sintesis



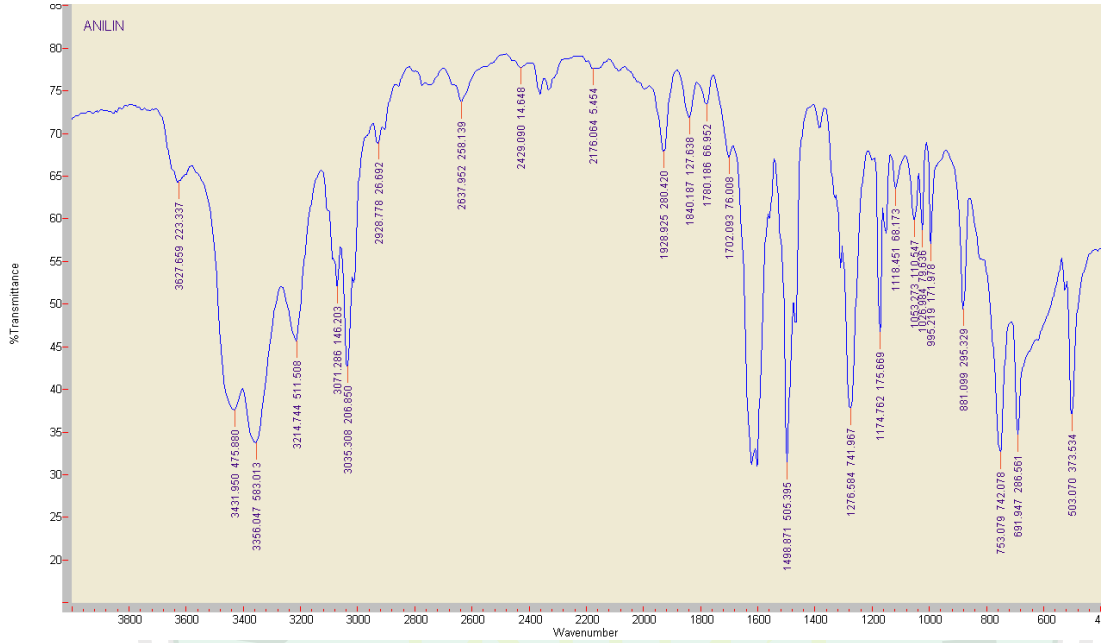
Kolom	: Rtx-5MS
Panjang	: 30 meter
ID	: 0,25 mm
Eluen	: Helium
Temp. Oven	: 150^{o}C
Temp. Injection	: 310^{o}C

Pressure	: 35,6 kPa
Ion source Temp.	: 250^{o}C
Interface Temp.	: 310^{o}C
Solvent Cut Time	: 3 menit
Start m/z	: 33
End m/z	: 600

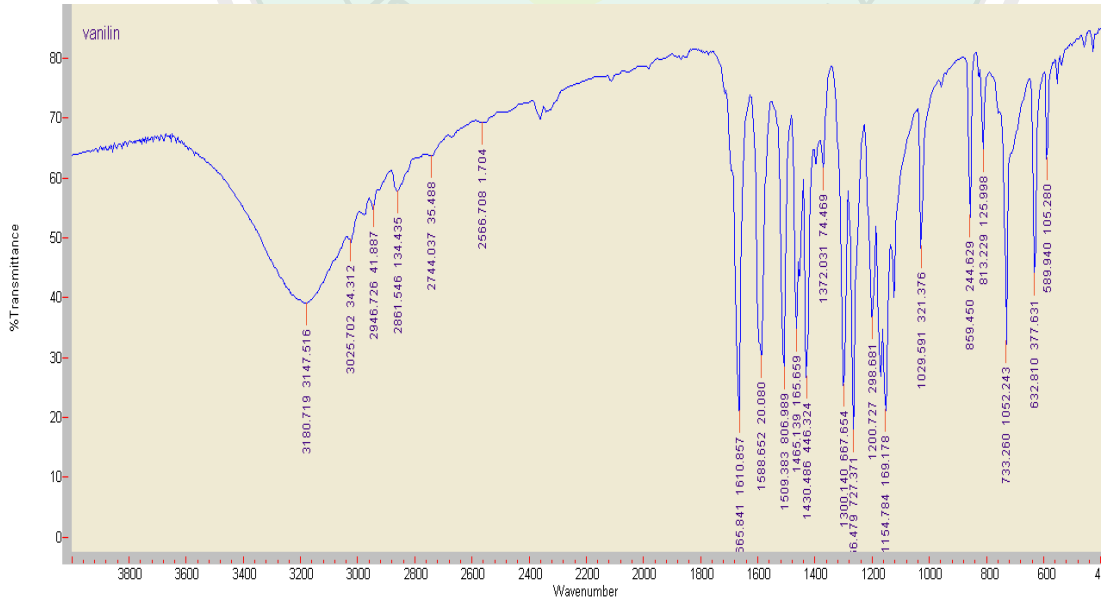
Lampiran 2. Hasil analisis FTIR dan KG-SM

L.2.1 Hasil analisis FTIR

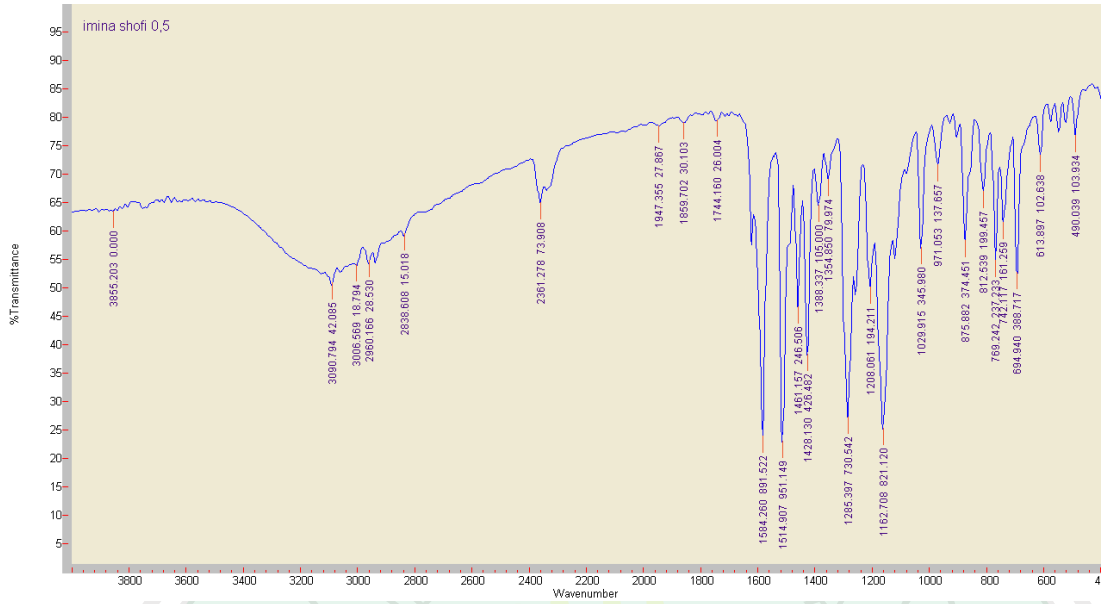
L.2.1.1 Hasil analisis FTIR senyawa Anilina



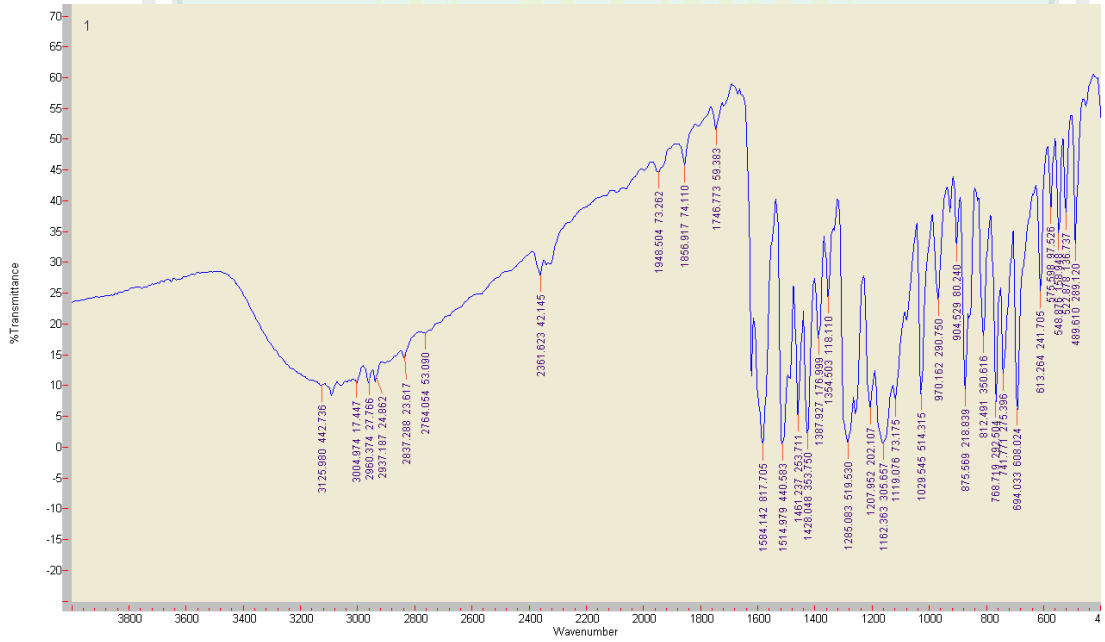
L.2.1.2 Hasil analisis FTIR senyawa Vanilin



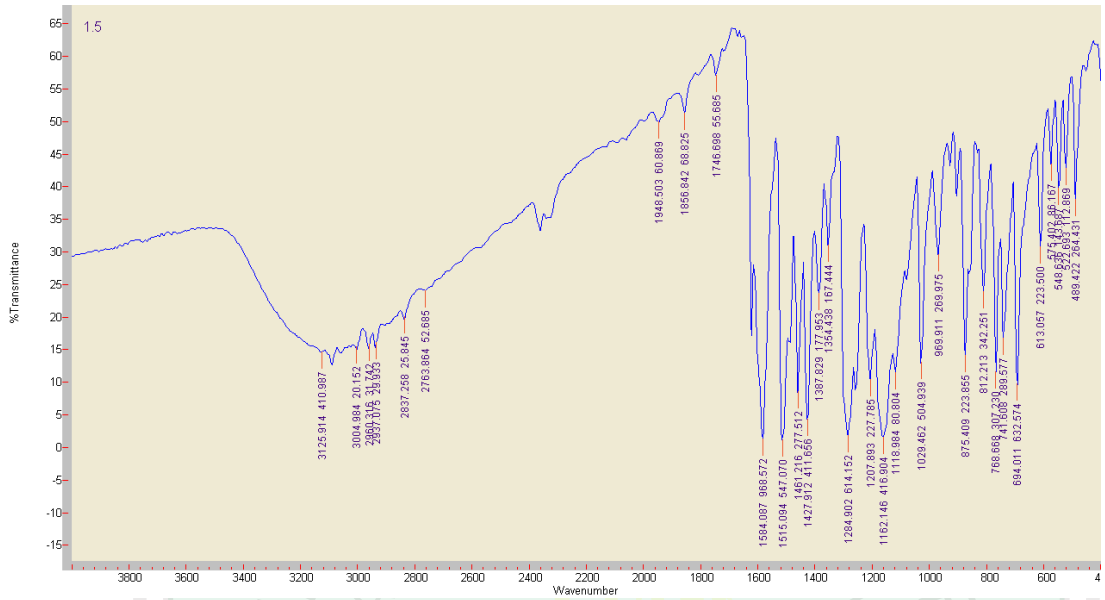
L.2.1.3 Hasil analisis FTIR produk 1 (katalis 0,5 mL)



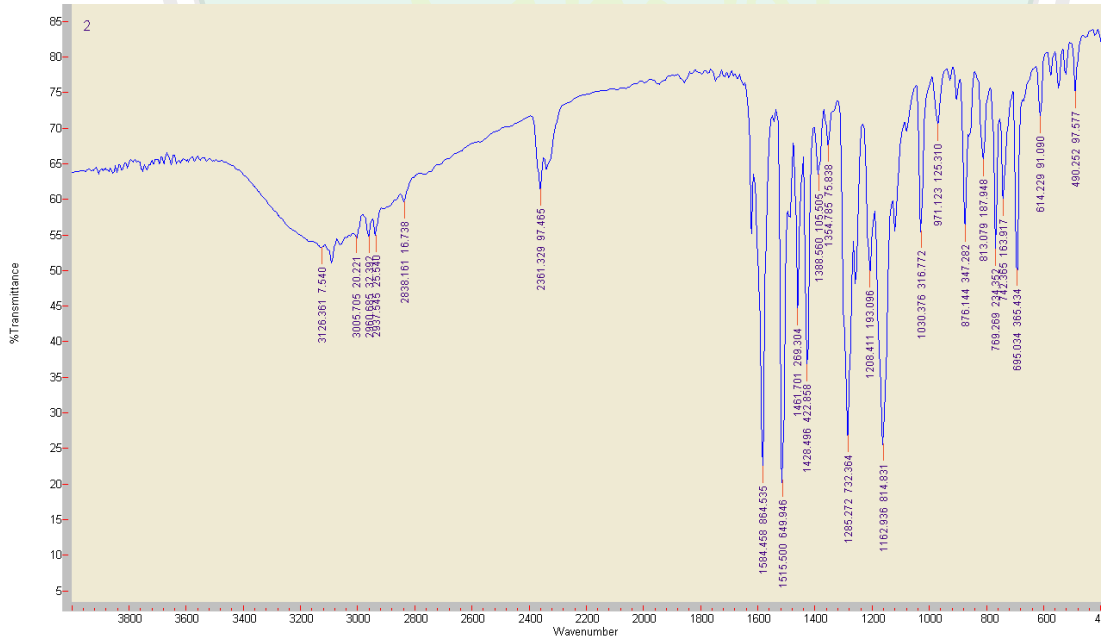
L.2.1.3 Hasil analisis FTIR produk 2 (katalis 1,0 mL)



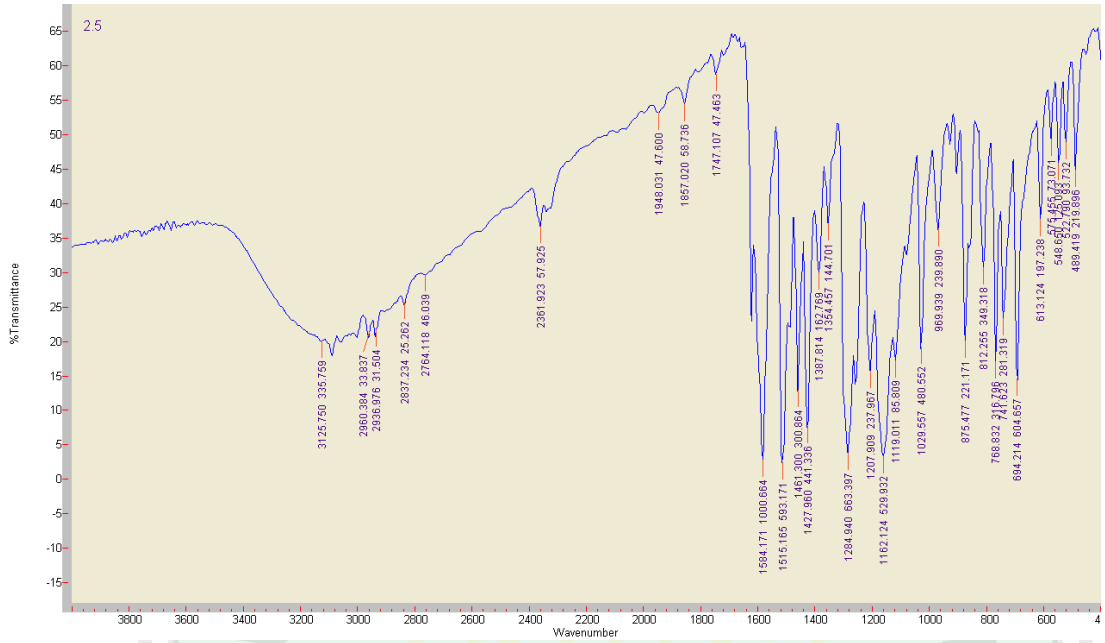
L.2.1.3 Hasil analisis FTIR produk 3 (katalis 1,5 mL)



L.2.1.3 Hasil analisis FTIR produk 4 (katalis 2,0 mL)



L.2.1.3 Hasil analisis FTIR produk 5 (katalis 2,5 mL)



L.2.1 Hasil analisis KG-SM produk terbaik

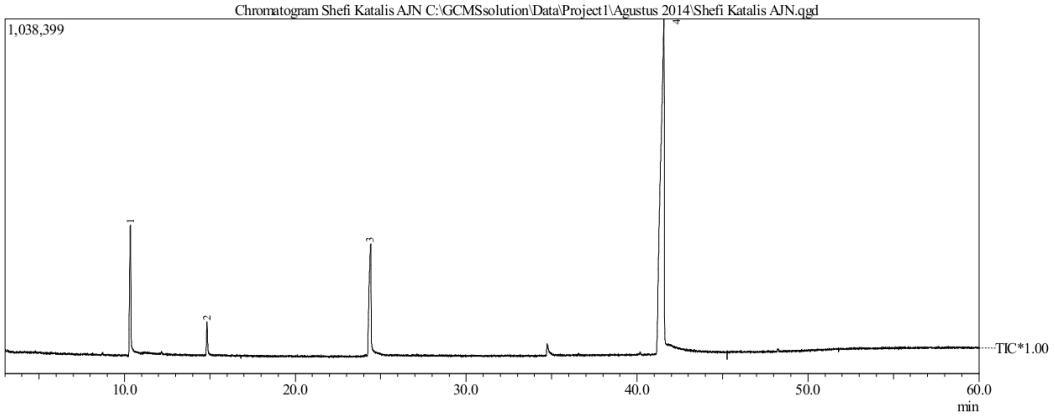
C:¥GCMSsolution¥Data¥Project1¥Agustus 2014¥Shefi Katalis AJN.qgd 11/3/2015

Lab.Kimia Organik FMIPA - UGM

Sample Information

Analyzed by	: Admin
Sample Name	: Shefi Katalis AJN
Sample ID	: 10.15.55.3
Data File	: C:\GCMSsolution\Data\Project1\Agustus 2014\Shefi Katalis AJN.qgd
Method File	: C:\GCMSsolution\Data\Project1\Agustus 2014\organik baru.qgm
Tuning File	: C:\GCMSsolution\System\Tune1\September 15 2015.qgt

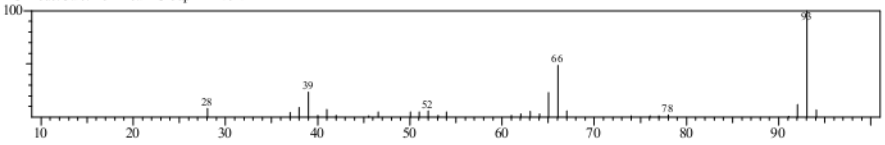
Chromatogram Shefi Katalis AJN C:\GCMSsolution\Data\Project1\Agustus 2014\Shefi Katalis AJN.qgd



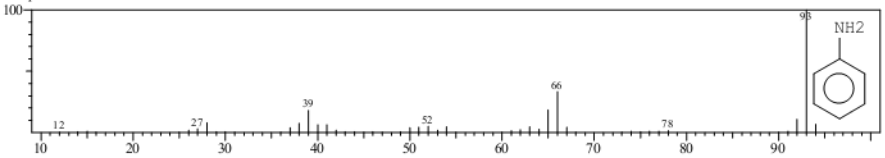
Peak Report TIC

Peak#	R.Time	I.Time	F.Time	Area	Area%	Height	Name
1	10.347	10.250	10.425	1723729	9.57	365251	
2	14.828	14.767	14.900	334203	1.85	90309	
3	24.405	24.225	24.500	2493496	13.84	312132	
4	41.564	41.150	41.650	13465118	74.74	949858	
				18016546	100.00	1717550	

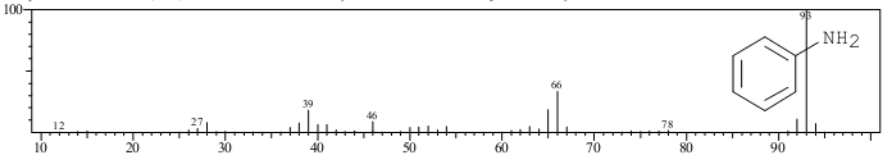
Library
<<Target>>
Line#:1 R.Time:10.350(Scan#:1027) MassPeaks:29
RawMode:Averaged 10.342-10.358(1026-1028) BasePeak:93.05(113010)
BG Mode:Calc. from Peak Group 1 - Event 1



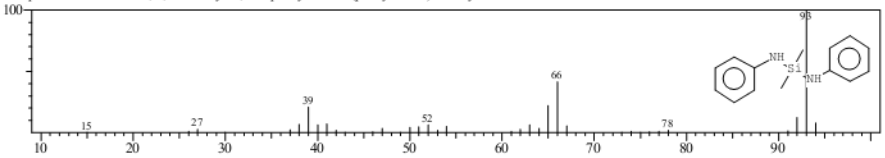
Hit#:1 Entry:803 Library:NIST12.LIB
SI:96 Formula:C6H7N CAS:62-53-3 MolWeight:93 RetIndex:0
CompName:Aniline



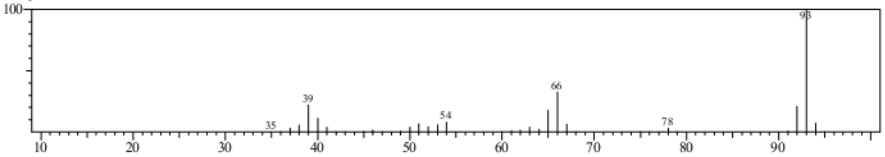
Hit#:2 Entry:3794 Library:WILEY229.LIB
SI:95 Formula:C6 H7 N CAS:62-53-3 MolWeight:93 RetIndex:0
CompName:Benzenamine (CAS) Aniline $$ C.I. 76000 $$ Anyvim $$ Blue Oil $$ Aminophen $$ Phenylamine $$ Aminobenzene $$ Benzene, amino- $$



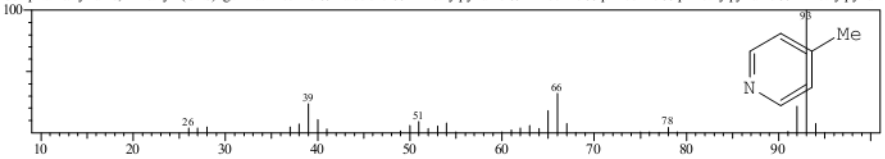
Hit#:3 Entry:32331 Library:NIST62.LIB
SI:95 Formula:C14H18N2Si CAS:13435-09-1 MolWeight:242 RetIndex:0
CompName:Silanediamine, 1,1-dimethyl-N,N'-diphenyl- $$ Bis(phenylamino)dimethylsilane



Hit#:4 Entry:3805 Library:WILEY229.LIB
SI:92 Formula:C6 H7 N CAS:0-00-0 MolWeight:93 RetIndex:0
CompName:4-METHYLPYRIDINE $$



Hit#:5 Entry:3781 Library:WILEY229.LIB
SI:92 Formula:C6 H7 N CAS:108-89-4 MolWeight:93 RetIndex:0
CompName:Pyridine, 4-methyl- (CAS) .gamma.-Picoline $$ Ba 35846 $$ 4-Methylpyridine $$ 4-Picoline $$ p-Picoline $$ p-Methylpyridine $$ 4-Methylpyridineate $$ .gamma.-Methylpyridine $$



<< Target >>
Line#:2 R.Time:14.825(Scan#:1564) MassPeaks:28
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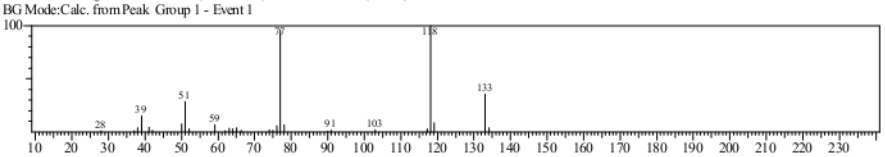
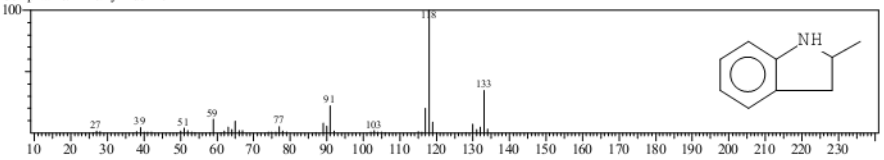
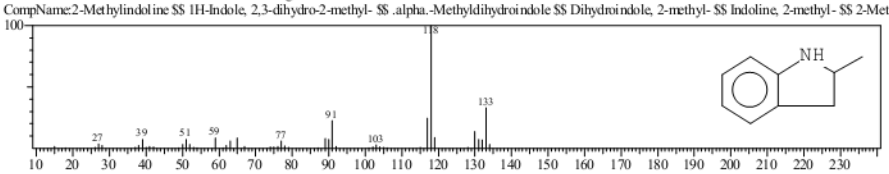
BG Mode:Calc. from Peak Group 1 - Event 1



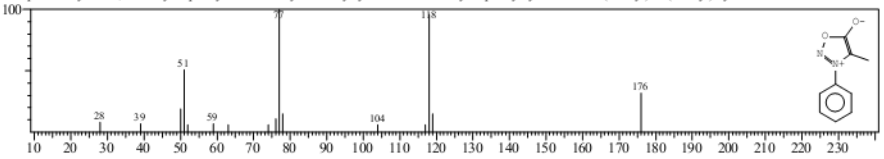
Hit#:1 Entry:3216 Library:NIST12.LIB
SI:80 Formula:C9H11N CAS:6872-06-6 MolWeight:133 RetIndex:0
CompName:2-Methylindoline



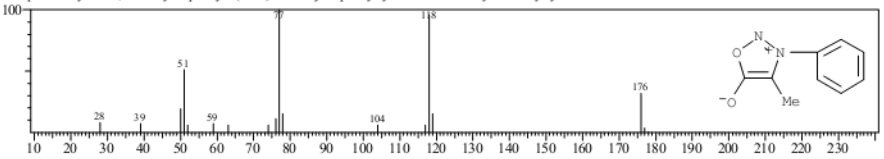
Hit#:2 Entry:5987 Library:NIST62.LIB
SI:80 Formula:C9H11N CAS:6872-06-6 MolWeight:133 RetIndex:0
CompName:2-Methylindoline $$ 1H-Indole, 2,3-dihydro-2-methyl- $$ .alpha.-Methyldihydroindole $$ Dihydroindole, 2-methyl- $$ Indoline, 2-methyl- $$ 2-Methyl-2,3-dihydroindole $$ 2,3-Dihydro-2-methylir



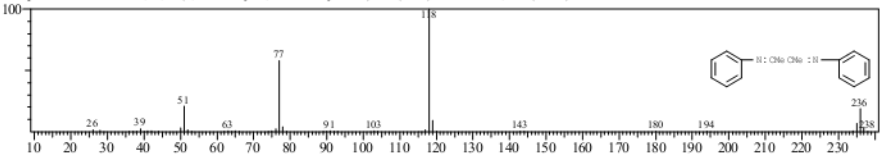
Hit#:3 Entry:16633 Library:NIST62.LIB
SI:79 Formula:C9H8N2O2 CAS:3483-16-7 MolWeight:176 RetIndex:0
CompName:Sydnone, 4-methyl-3-phenyl- $$ 3-Phenyl-4-methylsydnone $$ 4-Methyl-3-phenylsydnone $$ N-(Phenyl)-C-(methyl)-sydnon



Hit#:4 Entry:47426 Library:WILEY229.LIB
SI:79 Formula:C9 H8 N2 O2 CAS:3483-16-7 MolWeight:176 RetIndex:0
CompName:Sydnone, 4-methyl-3-phenyl- (CAS) 4-Methyl-3-phenylsydnone $$ 3-Phenyl-4-methylsydnone $$



Hit#:5 Entry:98374 Library:WILEY229.LIB
SI:78 Formula:C16 H16 N2 CAS:5393-49-7 MolWeight:236 RetIndex:0
CompName:Benzenamine, N,N'-(1,2-dimethyl-1,2-ethanediylidene)bis- (CAS) DIACETYL, BIS(ANIL) $$



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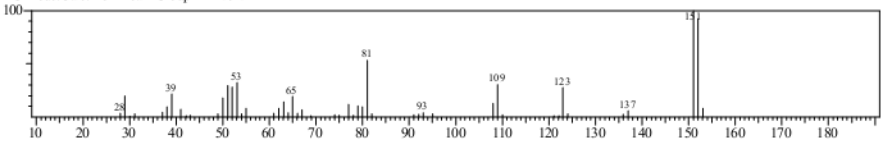
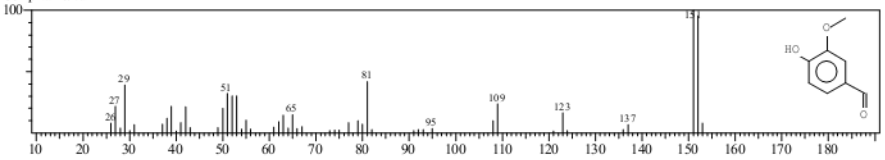
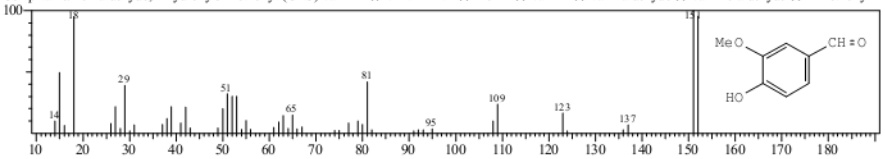
BG Mode:Calc. from Peak Group 1 - Event 1



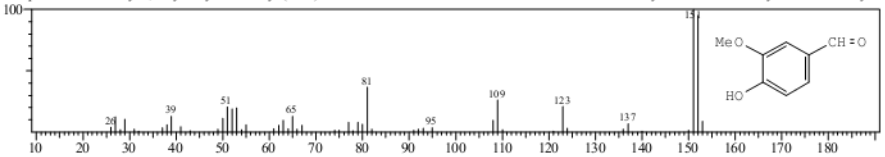
Hit#:1 Entry:4680 Library:NIST12.LIB
SI:95 Formula:C8H8O3 CAS:121-33-5 MolWeight:152 RetIndex:0
CompName:Vanillin



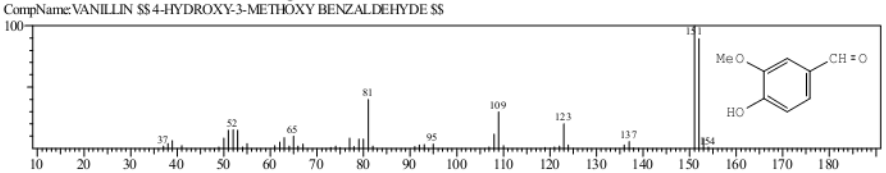
Hit#:2 Entry:28900 Library:WILEY229.LIB
SI:94 Formula:C8 H8 O3 CAS:121-33-5 MolWeight:152 RetIndex:0
CompName:Benzaldehyde, 4-hydroxy-3-methoxy- (CAS) Vanillin $$ VANILLINE $$ Lioxin $$ Vanilin $$ Vanillaldehyde $$ Vanillic aldehyde $$ 2-Methoxy-4-formylphenol $$ 4-Formyl-2-methoxyphenol $$ p-



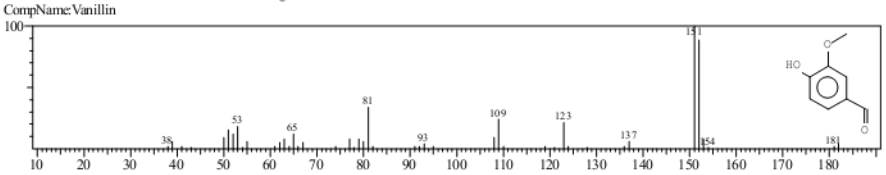
Hit#:3 Entry:28893 Library:WILEY229.LIB
SI:93 Formula:C8 H8 O3 CAS:121-33-5 MolWeight:152 RetIndex:0
CompName:Benzaldehyde, 4-hydroxy-3-methoxy- (CAS) Vanillin $$ VANILLINE $$ Lioxin $$ Vanilin $$ Vanillaldehyde $$ Vanillic aldehyde $$ 2-Methoxy-4-formylphenol $$ 4-Formyl-2-methoxyphenol $$ p-



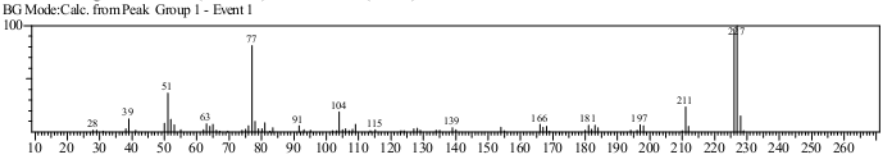
Hit#:4 Entry:28933 Library:WILEY229.LIB
SI:90 Formula:C8 H8 O3 CAS:121-33-5 MolWeight:152 RetIndex:0
CompName:VANILLIN $$ 4-HYDROXY-3-METHOXY BENZALDEHYDE $$



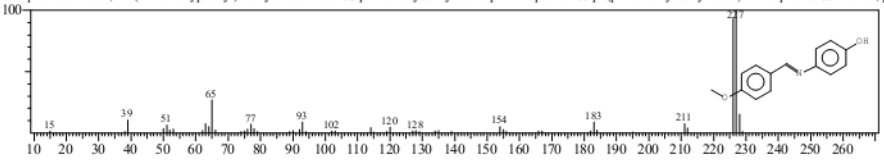
Hit#:5 Entry:4682 Library:NIST12.LIB
SI:88 Formula:C8H8O3 CAS:121-33-5 MolWeight:152 RetIndex:0
CompName:Vanillin



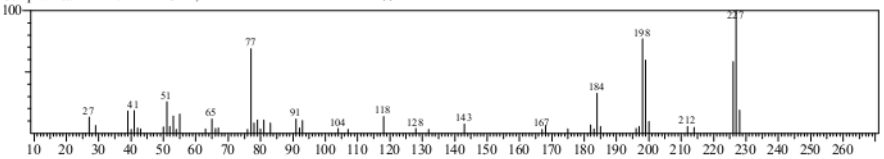
<< Target >>
Line#:4 R.Time:41.567(Scan#:4773) MassPeaks:72
RawMode:Averaged 41.558-41.575(4772-4774) BasePeak:227.00(143170)
BG Mode:Calc. from Peak Group 1 - Event 1



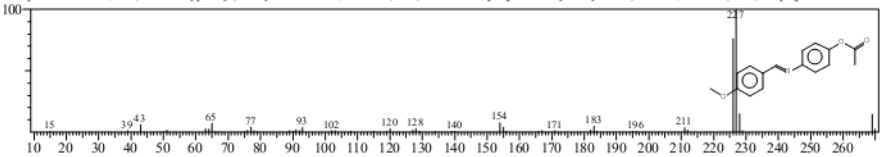
Hit#:1 Entry:29353 Library:NIST62.LIB
SI:77 Formula:C14H13NO2 CAS:3230-39-5 MolWeight:227 RetIndex:0
CompName:Phenol, 4- (4-methoxyphenyl)methylene amino - $$ p-Methoxybenzylidene p-aminophenol $$ p- (p-Methoxybenzylidene)amino phenol $$ Phenol, p-((p-methoxybenzylidene)amino)-



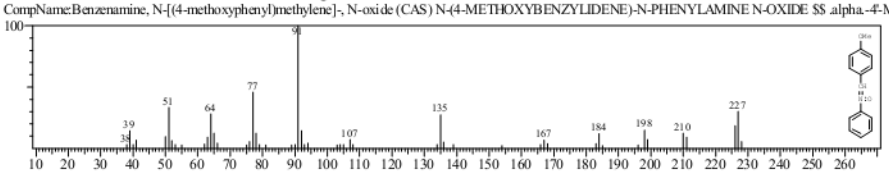
Hit#:2 Entry:90797 Library:WILEY229.LIB
SI:71 Formula:C15 H17 N O CAS:0-00-0 MolWeight:227 RetIndex:0
CompName:.ALPHA.-PYRIDONE, N-PHENYL-TETRAMETHYL- $$



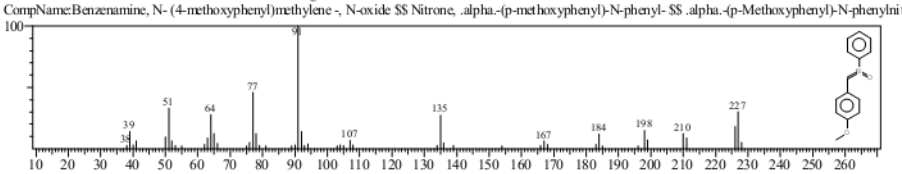
Hit#:3 Entry:37580 Library:NIST62.LIB
SI:70 Formula:C16H15NO3 CAS:10484-13-6 MolWeight:269 RetIndex:0
CompName:Phenol, 4- (4-methoxyphenyl)methylene amino -, acetate (ester) $$ Phenol, p- (p-methoxybenzylidene)amino -, acetate (ester) $$ p-(p-Anisilideneamino)phenyl acetate $$ p-(Anisylideneamino)pheny



Hit#:4 Entry:90713 Library:WILEY229.LIB
SI:68 Formula:C14 H13 N O2 CAS:3585-93-1 MolWeight:227 RetIndex:0
CompName:Benzenamine, N-[(4-methoxyphenyl)methylene]-, N-oxide (CAS) N-(4-METHOXYBENZYLIDENE)-N-PHENYLAMINE N-OXIDE $$ .alpha.-4'-Methoxyphenyl N-phenylnitrone $$ .alpha.-(p-Me



Hit#:5 Entry:29351 Library:NIST62.LIB
SI:68 Formula:C14H13NO2 CAS:3585-93-1 MolWeight:227 RetIndex:0
CompName:Benzenamine, N- (4-methoxyphenyl)methylene -, N-oxide $$ Nitrone, .alpha.-(p-methoxyphenyl)-N-phenyl- $$ .alpha.-(p-Methoxyphenyl)-N-phenylnitrone $$ .alpha.-4'-Methoxyphenyl N-phenylni



Lampiran 3. Perhitungan

L.3.1 Massa reaktan yang harus diambil (pra-Penelitian)

L.3.1.1 Vanilin (1) yang harus diambil

Rumus molekul senyawa **(1)** = $C_8H_8O_3$

BM senyawa **(1)** = 152.1473 g/mol

Mol senyawa **(1)** = 0,01 mol

Massa senyawa **(1)** = mol x BM

= 0,01 mol x 152.1473 g/mol

= 1,5215 g

L.3.1.2 Anilina (2) yang harus diambil

Rumus molekul senyawa **(2)** = $C_6H_5NH_2$

BM senyawa **(2)** = 93,1265 g/mol

BJ senyawa **(2)** = 1.0216 g/mL

Mol senyawa **(2)** = 0,01 mol

Volume senyawa **(2)** $= \frac{\text{mol x BM}}{BJ}$

$= \frac{0{,}01 \text{ mol x } 93{,}1265 \text{ g/mol}}{1.0216 \ g/mL}$

= 0,9116 mL atau 0,9313 g

L.3.1.3 Perbandingan Stoikiometri Massa Senyawa 2-metoksi-4-((fenilimino) metil)fenol (3) yang diharapkan terbentuk

Reaksi = senyawa **(1)** + senyawa **(2)** → senyawa **(3)** + air

Reaksi	senyawa **(1)**	+	senyawa **(2)**	→	senyawa **(3)**
Mula-mula	0,01 mol		0,01 mol		-
Bereaksi	0,01 mol		0,01 mol		0,01 mol
Setimbang	-		-		0,01 mol

Rumus molekul senyawa **(3)** = $C_{14}H_{13}O_2N$

BM senyawa **(3)** = 227,2585 g/mol

Mol senyawa **(3)** = 0,01 mol

Massa senyawa **(3)** = mol x BM
= 0,01 mol x 227,2585 g/mol
= 2,2726 g

L.3.2 Perbandingan stoikiometri & perhitungan rendemen produk (paska Penelitian)

Rumus umum untuk menetukan jumlah mol suatu senyawa adalah sebagai berikut:

$$\mathbf{n} = \frac{\mathbf{m}}{\mathbf{Mr}}$$

Keterangan:

n = Jumlah mol (mol)

m = massa (gram)

Mr = Massa atom relatif (gram/mol)

Sedangkan untuk menetukan rendemen suatu senyawa dalam persen (%) menggunakan persamaan berikut:

$$\text{rendemen (\%)} = \frac{\mathbf{m}\ \text{Produk hasil sintesis}}{\mathbf{m}\ \text{Produk Teoritis}} \text{x } 100\ \%$$

Keterangan:

m Produk hasil sintesis = massa produk yang diperoleh saat sintesis **(gram)**

m Produk Teoritis = massa produk yang diperoleh melalui proses perhitungan teoritis **(gram)**

L.3.2.1 Perhitungan Rendemen Produk 1 (0,5 mL)

Diketahui:

- **m** Anilina = **0,934 gram**
- **m** Vanilin = **1,521 gram**
- **m** Produk hasil sintesis = **1,459 gram** *(setelah proses pemurnian)*
- **Mr** Anilina = **093,13 gram/mol**

- **Mr** Vanilin = **152,15 gram/mol**
- **Mr** Produk hasil sintesis = **227,27 gram/mol**

Ditanya:

- **m** Produk teoritis (gram) ?
- Rendemen (%) ?

Jawaban:

$$\mathbf{n}\ \text{Vanilin} = \frac{\mathbf{m}\ \text{Vanilin}}{\mathbf{Mr}\ \text{Vanilin}} = \frac{\mathbf{1{,}521\ gram}}{\mathbf{152{,}15\ gram/mol}} = \mathbf{0{,}009997\ mol}$$

$$\mathbf{n}\ \text{Anilina} = \frac{\mathbf{m}\ \text{Anilina}}{\mathbf{Mr}\ \text{Anilina}} = \frac{\mathbf{0{,}934\ gram}}{\mathbf{93{,}13\ gram/mol}} = \mathbf{0{,}010032\ mol}$$

	Vanilin	+	Anilin	<=>	Produk
Mula-mula:	**0,009997 mol**		**0,010032 mol**		
Reaksi :	**0,009997 mol**		**0,009997 mol**		**0,009997 mol**
Setimbang:	**-**		**0,000035 mol**		**0,009997 mol**

- *"Apabila reaksi berjalan sempurna (100%) maka **n** Produk = **0,009997 mol**"*

m Produk teoritis = **n** Produk x **Mr** Produk
= **0,009997 mol** x **227,26 gram/mol**
= **2,2753 gram**

$$\text{rendemen}\ (\%) = \frac{\mathbf{m}\ \text{Produk hasil sintesis}}{\mathbf{m}\ \text{Produk Teoritis}} \text{ x } 100\ \% = \frac{\mathbf{1{,}459\ gram}}{\mathbf{2{,}2753\ gram}} \text{ x } 100\ \% = \mathbf{64,\ 1234\ \%}$$

L.3.2.2 Perhitungan Rendemen Produk 2 (1,0 mL)

Diketahui:

- **m** Anilina = **0,932 gram**
- **m** Vanilin = **1,522 gram**
- **m** Produk hasil sintesis = **1,386 gram** *(setelah proses pemurnian)*
- **Mr** Anilina = **93,13 gram/mol**
- **Mr** Vanilin = **152,15 gram/mol**
- **Mr** Produk hasil sintesis = **227,27 gram/mol**

Ditanya:

- **m** Produk teoritis (gram) ?
- Rendemen (%) ?

Jawaban:

$$\mathbf{n}\ \text{Vanilin} = \frac{\mathbf{m}\ \text{Vanilin}}{\mathbf{Mr}\ \text{Vanilin}} = \frac{\mathbf{1{,}522\ gram}}{\mathbf{152{,}15\ gram/mol}} = \mathbf{0{,}0100003\ mol}$$

$$\mathbf{n}\ \text{Anilina} = \frac{\mathbf{m}\ \text{Anilina}}{\mathbf{Mr}\ \text{Anilina}} = \frac{\mathbf{0{,}934\ gram}}{\mathbf{93{,}13\ gram/mol}} = \mathbf{0{,}0100075\ mol}$$

	Vanilin	+	Anilin	<=>	Produk
Mula-mula:	**0,0100003 mol**		**0,0100075 mol**		
Reaksi :	**0,0100003 mol**		**0,0100003 mol**		**0,0100003 mol**
Setimbang:	**-**		**0,0000072 mol**		**0,0100003 mol**

- *"Apabila reaksi berjalan sempurna (100%) maka **n** Produk = **0,0100003 mol**"*

m Produk teoritis = **n** Produk x **Mr** Produk
= **0,0100003 mol** x **227,26 gram/mol**
= **2,2727 gram**

$$\text{rendemen}\ (\%) = \frac{\mathbf{m}\ \text{Produk hasil sintesis}}{\mathbf{m}\ \text{Produk Teoritis}} \text{ x } 100\ \% = \frac{\mathbf{1{,}386\ gram}}{\mathbf{2{,}2727\ gram}} \text{ x } 100\ \% = \mathbf{60,\ 9847\ \%}$$

L.3.2.3 Perhitungan Rendemen Produk 3 (1,5 mL)

Diketahui:

- **m** Anilina = **0,939 gram**
- **m** Vanilin = **1,522 gram**
- **m** Produk hasil sintesis = **1,104 gram** *(setelah proses pemurnian)*
- **Mr** Anilina = **93,13 gram/mol**
- **Mr** Vanilin = **152,15 gram/mol**
- **Mr** Produk hasil sintesis = **227,27 gram/mol**

Ditanya:

- **m** Produk teoritis (gram) ?
- Rendemen (%) ?

Jawaban:

$$\mathbf{n}\ \text{Vanilin} = \frac{\mathbf{m}\ \text{Vanilin}}{\mathbf{Mr}\ \text{Vanilin}} = \frac{\mathbf{1{,}522\ gram}}{\mathbf{152{,}15\ gram/mol}} = \mathbf{0{,}0100003\ mol}$$

$$\mathbf{n}\ \text{Anilina} = \frac{\mathbf{m}\ \text{Anilina}}{\mathbf{Mr}\ \text{Anilina}} = \frac{\mathbf{0{,}939\ gram}}{\mathbf{93{,}13\ gram/mol}} = \mathbf{0{,}0100827\ mol}$$

	Vanilin	+	Anilin	<=>	Produk
Mula-mula:	**0,0100003 mol**		**0,0100827 mol**		
Reaksi :	**0,0100003 mol**		**0,0100003 mol**		**0,0100003 mol**
Setimbang:	**-**		**0,0000824 mol**		**0,0100003 mol**

- *"Apabila reaksi berjalan sempurna (100%) maka **n** Produk = **0,0100003 mol**"*

  m Produk teoritis = **n** Produk x **Mr** Produk
  = **0,0100003 mol** x **227,26 gram/mol**
  = **2,2727 gram**

$$\text{rendemen (\%)} = \frac{\mathbf{m}\ \text{Produk hasil sintesis}}{\mathbf{m}\ \text{Produk Teoritis}} \text{ x } 100\ \% = \frac{\mathbf{1{,}104\ gram}}{\mathbf{2{,}2727\ gram}} \text{ x } 100\ \% = \mathbf{48{,}5766\%}$$

L.3.2.4 Perhitungan Rendemen Produk 4 (2,0 mL)

Diketahui:

- **m** Anilina = **0,938 gram**
- **m** Vanilin = **1,521 gram**
- **m** Produk hasil sintesis = **0,928 gram** *(setelah proses pemurnian)*
- **Mr** Anilina = **93,13 gram/mol**
- **Mr** Vanilin = **152,15 gram/mol**
- **Mr** Produk hasil sintesis = **227,27 gram/mol**

Ditanya:

- **m** Produk teoritis (gram) ?
- Rendemen (%) ?

Jawaban:

$$\mathbf{n}\ \text{Vanilin} = \frac{\mathbf{m}\ \text{Vanilin}}{\mathbf{Mr}\ \text{Vanilin}} = \frac{\mathbf{1{,}521\ gram}}{\mathbf{152{,}15\ gram/mol}} = \mathbf{0{,}009997\ mol}$$

$$\mathbf{n}\ \text{Anilina} = \frac{\mathbf{m}\ \text{Anilina}}{\mathbf{Mr}\ \text{Anilina}} = \frac{\mathbf{0{,}938\ gram}}{\mathbf{93{,}13\ gram/mol}} = \mathbf{0{,}010072\ mol}$$

	Vanilin	+	Anilin	<=>	Produk
Mula-mula:	**0,009997 mol**		**0,010072 mol**		
Reaksi :	**0,009997 mol**		**0,009997 mol**		**0,009997 mol**
Setimbang:	**-**		**0,000075 mol**		**0,009997 mol**

- *"Apabila reaksi berjalan sempurna (100%) maka **n** Produk = **0,009997 mol**"*

  m Produk teoritis = **n** Produk x **Mr** Produk
  = **0,009997 mol** x **227,26 gram/mol**
  = **2,2719 gram**

$$\text{rendemen}\ (\%) = \frac{\mathbf{m}\ \text{Produk hasil sintesis}}{\mathbf{m}\ \text{Produk Teoritis}} \text{ x } 100\ \% = \frac{\mathbf{0{,}928\ gram}}{\mathbf{2{,}2719\ gram}} \text{ x } 100\ \% = \mathbf{40{,}8469\ \%}$$

L.3.2.5 Perhitungan Rendemen Produk 4 (2,5 mL)

Diketahui:

- **m** Anilina = **0,9488 gram**
- **m** Vanilin = **1,5227 gram**
- **m** Produk hasil sintesis = **0,8375 gram** *(setelah proses pemurnian)*
- **Mr** Anilina = **93,13 gram/mol**
- **Mr** Vanilin = **152,15 gram/mol**
- **Mr** Produk hasil sintesis = **227,27 gram/mol**

Ditanya:

- **m** Produk teoritis (gram) ?
- Rendemen (%) ?

Jawaban:

$$\mathbf{n}\ \text{Vanilin} = \frac{\mathbf{m}\ \text{Vanilin}}{\mathbf{Mr}\ \text{Vanilin}} = \frac{\mathbf{1{,}5227\ gram}}{\mathbf{152{,}15\ gram/mol}} = \mathbf{0{,}010008\ mol}$$

$$\mathbf{n}\ \text{Anilina} = \frac{\mathbf{m}\ \text{Anilina}}{\mathbf{Mr}\ \text{Anilina}} = \frac{\mathbf{0{,}9488\ gram}}{\mathbf{93{,}13\ gram/mol}} = \mathbf{0{,}010188\ mol}$$

	Vanilin	+	Anilin	<=>	Produk
Mula-mula:	**0,010008 mol**		**0,010188 mol**		
Reaksi :	**0,010008 mol**		**0,010008 mol**		**0,010008 mol**
Setimbang:	**-**		**0,000180 mol**		**0,010008 mol**

- *"Apabila reaksi berjalan sempurna (100%) maka **n** Produk = **0,010008 mol**"*

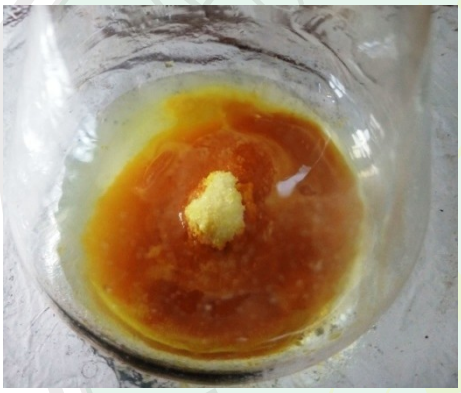
  m Produk teoritis = **n** Produk x **Mr** Produk
  = **0,010008 mol** x **227,26 gram/mol**
  = **2,2744 gram**

$$\text{rendemen (\%)} = \frac{\textbf{m Produk hasil sintesis}}{\textbf{m Produk Teoritis}} \text{ x } 100\ \% = \frac{\textbf{0,8375 gram}}{\textbf{2,2744 gram}} \text{ x } 100\ \% = \textbf{36,8229 \%}$$

Lampiran 4. Dokumentasi

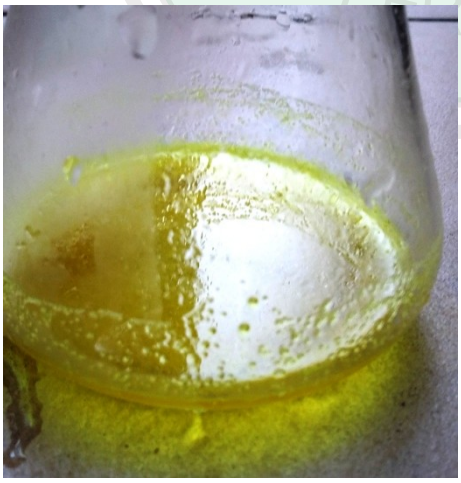
Gambar 1: Senyawa anilina (kiri) dan Vanilin (kanan) sebagai *starting material*

Gambar 2: Katalis asam alami dari buah jeruk nipis setelah proses preparasi



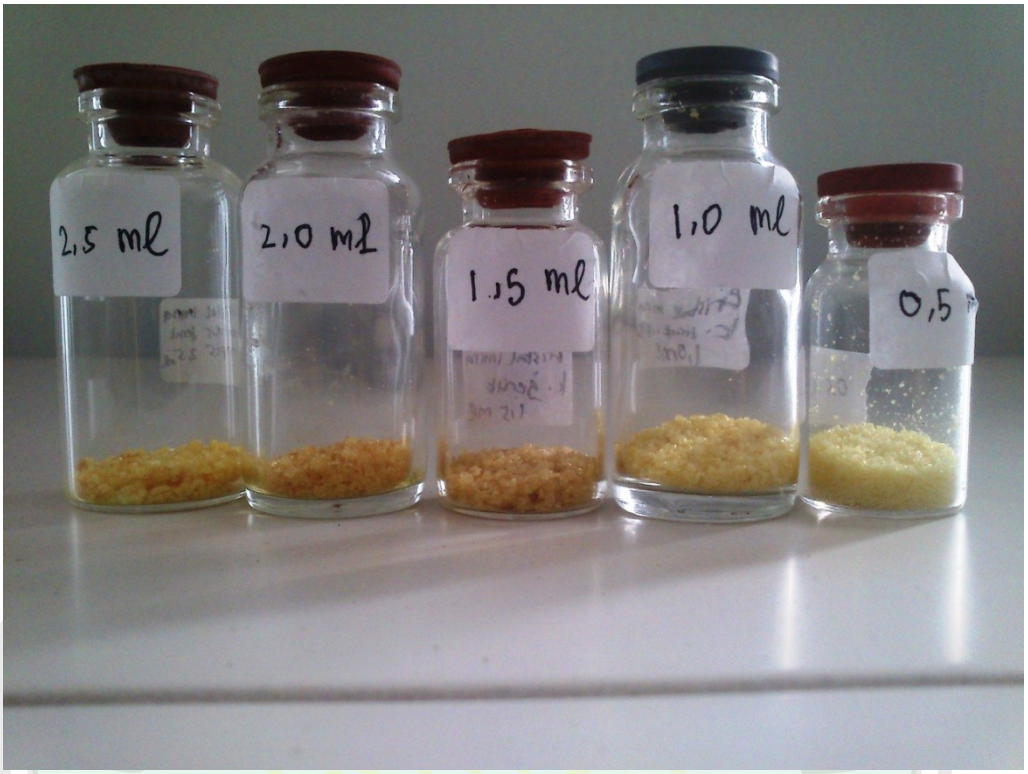
Gambar 4: Campuran anilina, vanilin, dan Katalis sebelum pengadukan

Gambar 3: Campuran anilina, vanilin, dan Katalis setelah beberapa saat pengadukan

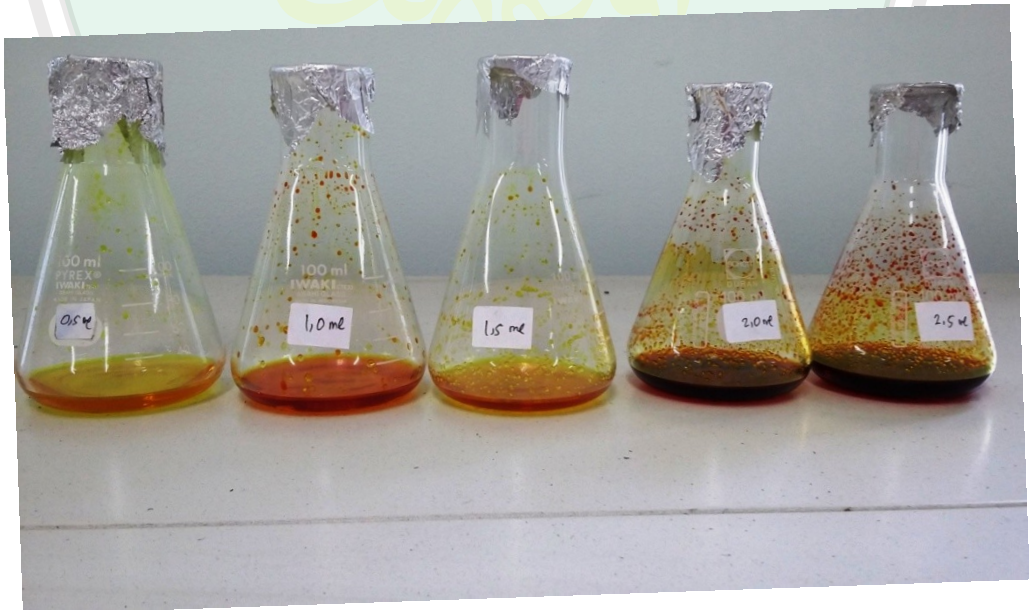


Gambar 5: Proses rekristalisasi

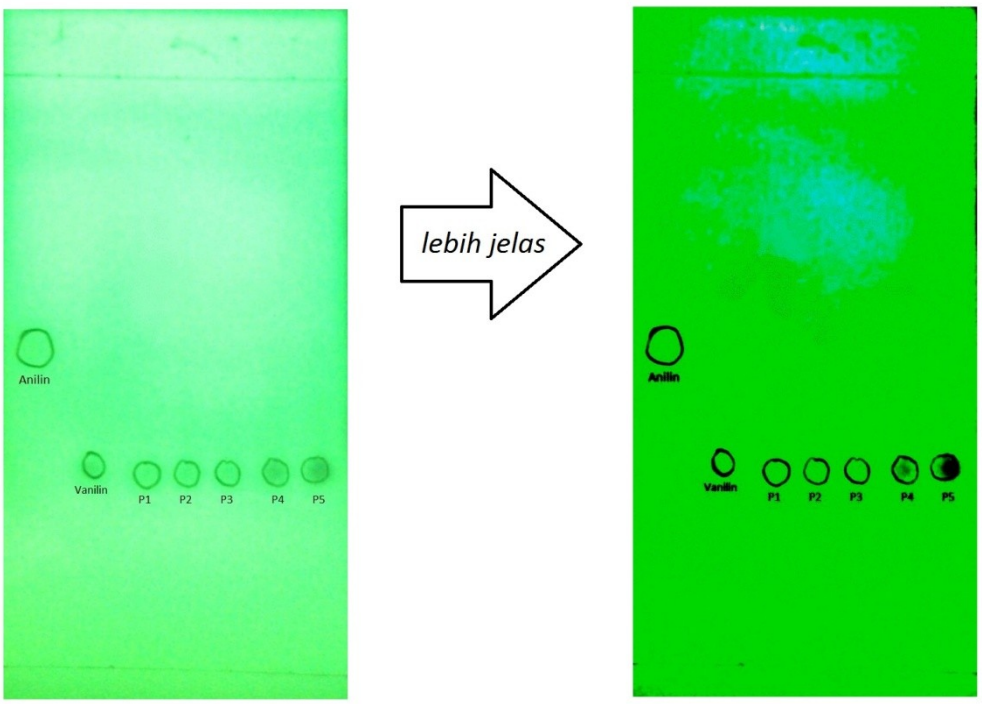
Gambar 6: Proses pembentukan kristal



Gambar 7: Kristal tiap variasi volume katalis yang telah dipisahkan dan dikeringkan (dari kanan ke kiri: 0,5 mL; 1,0 mL; 1,5 mL; 2,0 mL; 2,5 mL)



Gambar 8: Filtrat sisa proses rekristalisasi tiap variasi volume katalis (dari kanan ke kiri: 0,5 mL; 1,0 mL; 1,5 mL; 2,0 mL; 2,5 mL)



Gambar 9: Hasil elusi tiap produk hasil sintesis (kiri ke kanan: anilina; vanilina; Produk (1 0,5 mL) Produk 2 (1,0 mL); Produk 3 (1,5 mL); Produk 4(2,0 mL); Produk 5 (2,5 mL))

Sintesis Senyawa Imina dari Vanilin dan Anilina

Dengan Variasi Jumlah Katalis Air Jeruk Nipis

Latar Belakang

Senyawa imina aromatis dan turunannya, merupakan senyawa yang sering disintesis karena berpotensi besar sebagai antioksidan, antimikroba, dan indikator asam-basa (Purwono dkk, 2013). Imina merupakan bahan baku dalam sintesis obat penenang, obat bius, obat kontrasepsi kehamilan, anti ketombe, analgesik, dan anti inflamasi (Vibhute *et al.,* 2011).

Sintesis ramah lingkungan (*green synthesis*) telah banyak dilakukan. Beberapa metode seperti metode penggerusan (Rahman *et al.,* 2012); sintesis dalam pelarut air tanpa katalis (Naqvi *et al.,* 2009); dan penggunaan katalis alami dari air buah lemon (Patil *et al.,* 2011 dan 2012) telah memberikan hasil yang cukup baik dengan perolehan rendemen hingga 100%.

Metode Penelitian

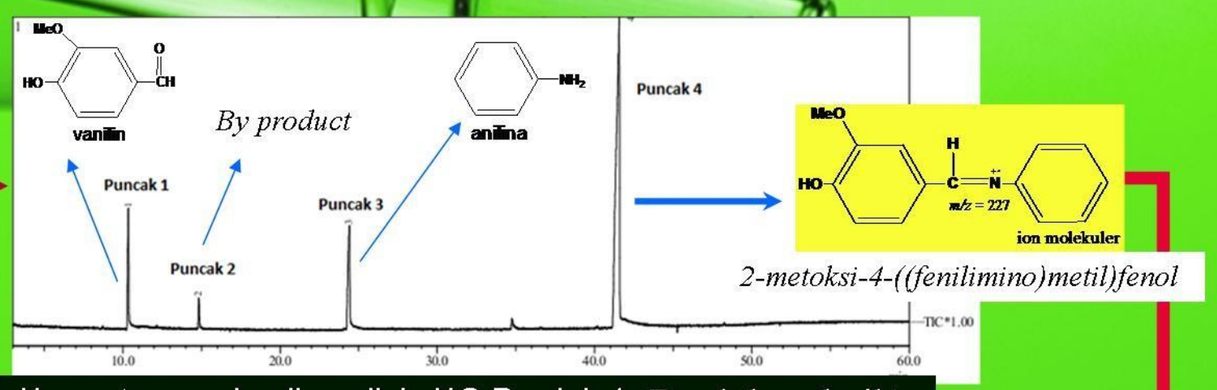
Tujuan

- Mengetahui jumlah katalis air buah jeruk nipis yang optimum pada reaksi pembentukan imina dari vanilin dan anilina.
- Mengetahui karakteristik produk hasil reaksi pembentuk-an imina dari vanilin dan anilina dengan variasi jumlah katalis air jeruk nipis.

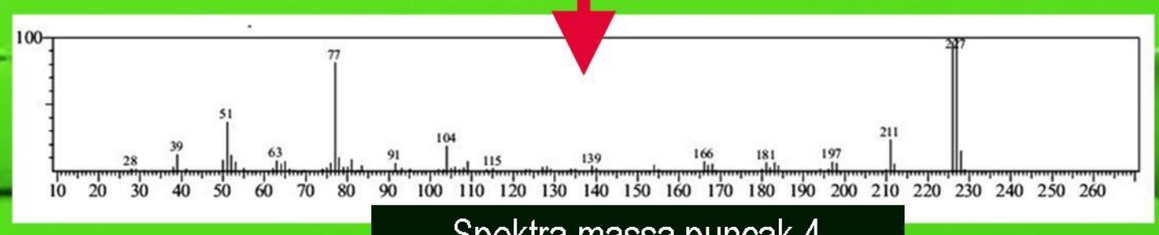
Hasil

pengamatan fisik lima produk hasil variasi perlakuan

Pengamatan	Variasi 1	Variasi 2	Variasi 3	Variasi 4	Variasi 5
Vol. Katalis (mL)	0,5	1,0	1,5	2,0	2,5
Wujud	Padatan	Padatan	Padatan	Padatan	Padatan
Warna	Kuning	Kuning Kecoklatan	Kuning Kecoklatan	Kuning Kecoklatan	Kuning Kecoklatan
Massa (gram)	1,459	1,386	1,104	0,928	0,8375
Titik Lebur (°C)	150	152	150	152	152
Rendemen (%)	64,1234	60,9847	48,5766	40,8469	36,8229



Kromatogram hasil analisis KG Produk 1 (Produk terbaik)



Spektra massa puncak 4

Gugus fungsi dan bilangan gelombang (ῡ) produk 1-5 Hasil FTIR

ῡ P1 (cm^{-1})	ῡ P2 (cm^{-1})	ῡ P3 (cm^{-1})	ῡ P4 (cm^{-1})	ῡ P5 (cm^{-1})	Gugus Fungsi
2800–3400	2800–3400	2800–3400	2800–3400	2800–3400	-OH
3091	3089	3086	3089	3086	C-H $_{sp2}$
1515	1515	1515	1516	1515	C=C aromatic
2935	2937	2937	2938	2937	C-H $_{sp3}$
1428	1428	1428	1428	1428	metil (-CH_3)
1285 dan 1030	1285 dan 1030	1285 dan 1030	1285 dan 1030	1285 dan 1030	Eter (C-O-C)
1584	**1584**	**1584**	**1584**	**1584**	(-C=N-)
876 dan 813	876 dan 812	875 dan 812	876 dan 813	875 dan 812	aromatik tersubtitusi

Kesimpulan

Jumlah katalis air buah jeruk nipis terbaik dalam reaksi pembentukan imina tanpa pelarut antara vanilin dan anilina adalah 0,5 mL. Produk terbaik yang dihasilkan memiliki sifat fisik padatan berwarna kuning, titik lebur = 150 °C, dan rendemen sebesar 64,1234 % dengan nilai kemurnian sebesar 74,74 %. Produk memiliki spektra IR khas senyawa imina pada 1584 cm^{-1} (–C=N). Spektra Massa m/z 227 (M^{*+}) muncul sebagai puncak ion molekuler senyawa target sintesis 2-metoksi-4-((fenilimino) metil)fenol.

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1) Nurush Shofi al Hakimi, 2) Ahmad Hanapi, 3) A.Ghanaim Fasya