Solventless Synthesis of Imines Derived from Diphenyldisulphide Diamine or *p*-Vanillin

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Abstract: A solventless synthesis can reduce environmental contamination and can be more convenient than solvent-based synthesis. A series of Schiff bases were synthesized in high yield > 90% under solvent free conditions with negligible waste. All the synthesized products were characterized on the basis of spectral, elemental analysis and melting points and were compared with the data of the products obtained from classical method

Keywords: Solvent –free, Imines, Diphenyldisulphide diamine, *p*-Vanillin.

Introduction

Recently, great efforts have been made on developing chemical technologies that can reduce or eliminate the use of organic solvents in synthesis. Large-scale use of organic solvents has been proved to be environmental hazards¹. Schiff base compounds are well known because of their wide applications and are useful intermediates in organic synthesis^{2,3}. These types of compounds have normally been synthesized by traditional methods using organic solvents. Recently, a few papers reported modern synthetic protocols where benign solvents (water or supercritical CO₂)^{4,5}, recyclable reactions medium (PPG)⁶ and solvent-less conditions⁷⁻¹⁰ have been used. These conditions are so simple as to be considered almost facile yet generate products in good yields, which give them attractive green chemistry metrics.

Herein, we report a simple and versatile route to mono and bis-imine Schiff bases in good yields. This study investigates the synthesis and characterization of imine products using solvent free conditions and compared with products obtained from traditional methods.

Experimental

Melting points were uncorrected and were determined on a Stuart Scientific Electric melting point apparatus. Aldrich and BDH chemicals were used. Furan 2-carboxaldehyde was distilled prior to use. IR spectra (KBr) were recorded on a Mattson 1000 FT IR spectrometer in the range 400–4000 cm^{-1} . ^1H and ^{13}C NMR spectra were recorded on a Bruker spectrometer at 250 MHz. Elemental analyses were obtained with a LECO 932 CHNS Mattson 1000 Spectrophotometer. Magnetic susceptibility of the complexes was performed at room temperature in Sherwood scientific magnetic balance.

General experimental procedure

In a typical solventless experiment the aldehyde (2 equivalents) was added to the diphenyldisulphides diamine (1 equivalent) and the mixture was grinded in a mortar and pestle at room temperature for 5 to 20 min afforded the *bis*-imine product as a paste or a solid. The paste after leaving for half an hour solidified into a solid. If required, analytically pure product can be obtained by washing with hot ethanol or diethyl ether or recrystallised from ethanol.

For compounds (**9–12**) for vanillin the solid after grinding was dissolved in minimum amount of ethanol and poured on ice. Analytically pure compound was washed with hot water.

The analyses (mp, IR, NMR, CHNS data) of compounds were consistent with literature values^{11–13}.

N, N' (1,1'-Dithiobisphenylene) bisbenzyldeimine (**1**)

Colour: yellow; ^1H NMR (CDCl_3): δ H 8.51(s, 2H), 8.01–7.87(m, 4H), 7.57–7.54(m, 6H), 7.28–7.22(m, 8H); ^{13}C NMR: δ C 160.1, 149.0, 136.1, 132.1, 131.7, 129.2, 128.8, 127.0, 126.0, 118.3; $\text{C}_{26}\text{H}_{20}\text{N}_2\text{S}_2$ found (Calc.) C 73.05(73.5), H 4.2(4.7), N 6.9(6.6), S 15.5(15.1).

N, N' (1,1'-Dithiobisphenylene) bis-2-chlorobenzyldeimine (**2**)

Colour: yellow; ^1H NMR (CDCl_3): δ H 8.98(s, 2H), 8.40(d, 2H), 7.66(d, 2H), 7.26–6.58(m, 12H); ^{13}C NMR: δ C 156.5, 136.2, 135.2, 132.5, 130.7, 130.0, 129.4, 129.2, 127.4, 127.3, 127.1, 126.1, 117.5; $\text{C}_{26}\text{H}_{18}\text{Cl}_2\text{N}_2\text{S}_2$ found (Calc.) C 62.8(63.2), H 3.5(3.6), N 5.9(5.7), S 13.5(13.0).

N, N' (1,1'-Dithiobisphenylene) bis-2-nitrobenzyldeimine (**3**)

Colour: yellow; ^1H NMR (CDCl_3): δ H 8.59(s, 2H), 8.36(m, 4H), 8.15(m, 4H), 7.64(m, 2H), 7.26–7.13(m, 6H), ^{13}C NMR: δ C 157.0, 149.5, 147.8, 141.4, 132.5, 129.7, 128.1, 127.3, 127.1, 126.1, 124.1, 117.0; $\text{C}_{26}\text{H}_{18}\text{N}_4\text{O}_4\text{S}_2$ found (Calc.) C 61.3(60.6), H 3.1(3.5), N 10.8(10.8), S 12.0(12.4).

N, N' (1,1'-Dithiobisphenylene) bisfurfurylimine (**4**)

Colour: yellow; ^1H NMR (CDCl_3): δ H 8.28(s, 2H), 7.68–7.61(m, 4H), 7.15(td, 4H), 7.05(m, 4H), 6.5 (m, 2H); ^{13}C NMR: δ C 177.9, 152.2, 148.9, 147.9, 146.1, 131.9, 127.0, 126.9, 126.0, 117.2, 116.7, 112.4; $\text{C}_{26}\text{H}_{18}\text{N}_4\text{O}_4\text{S}_2$ found (Calc.) C 66.1(65.3), H 3.9(3.9), N 7.4(6.9).

N, N' (1,1'-Dithiobisphenylene) bis-*o*-anisalimine (**5**)

Colour: yellow; ^1H NMR (CDCl_3): δ H 8.97(s, 2H), 8.33(d, 2H), 7.85–7.82(d, 2H), 7.56–7.43(m, 2H), 7.22–7.13(m, 6H), 7.01–7.04(d, 2H), 6.58(d, 2H), 3.9(s, 6H); ^{13}C NMR: δ C 159.7, 156.0, 149.6, 132.2, 131.7, 128.2, 126.8, 126.7, 126.3, 125.7, 121.1, 118.5, 111.2, 55.6; $\text{C}_{28}\text{H}_{24}\text{N}_2\text{O}_2\text{S}_2$ found (Calc.) C 69.0(69.4), H 4.3(4.9), N 6.2(5.8).

N, N' (1,1'-Dithiobis phenylene) bis p-anisalimine (6)

Colour: yellow; ^1H NMR (CDCl_3): δH 8.42(s, 2H), 8.05(d, 4H), 7.65 (d, 2H), 7.16-6.99 (m, 10H), 3.89 (s, 6H); ^{13}C NMR: δC 162.6, 159.3, 149.2, 132.0, 131.0, 129.2, 126.8, 126.5, 125.8, 117.2, 114.4, 114.3, 55; $\text{C}_{28}\text{H}_{24}\text{N}_2\text{O}_2\text{S}_2$ found (Calc.) C 68.8(69.4), H 4.6(4.9), N 6.2 (5.8), S 13.8(13.2).

N, N' (1,1'-Dithiobis phenylene) bis pyridylimine (7)

Colour: yellow; ^1H NMR (CDCl_3): δH 8.67-8.65(d, 2H), 8.60(s, 2H), 8.34-8.30(d, 2H), 7.82-7.75(t, 2H), 7.62-7.58(d, 2H), 7.36-7.31(t, 2H), 7.19-7.04(m, 6H); ^{13}C NMR: δC 160.4, 154.5, 149.7, 147.8, 136.8, 132.7, 127.9, 127.1, 126.0, 125.5, 122.2, 117.3; $\text{C}_{24}\text{H}_{18}\text{N}_4\text{S}_2$ found (Calc.) C 68.2(67.6), H 4.2(4.2), N 13.4(13.1), S 15.5(15.0).

N, N' (1,1'-Dithiobis phenylene) bis-cinnamaldehydimine (8)

Colour: yellow; ^1H NMR (CDCl_3): δH 8.03-8.00(d, 2H), 7.28-7.34 (m, 6H), 7.20-7.11(m, 8H), 6.87-6.94(m, 5H), 6.75-6.72 (m, 2H), 6.44(dd, 1H); $\text{C}_{30}\text{H}_{22}\text{N}_2\text{S}_2$ found (Calc.) C 75.2(75.6), H 5.4(5.1), N 6.4(5.9).

N-Phenyl-vanillaldimine (9)

Colour: cream; ^1H NMR (CDCl_3): δH 8.43(s, 1H) 7.52 (d, 1H), 7.41-7.31(m, 3H), 7.21-7.18(m, 3H), 6.96-6.87 (d, 1H) 3.38 (s, 3H); ^{13}C NMR: δC 161.4, 153.2, 151.4, 149.2, 130.4, 129.1, 126.6, 125.4, 122.1, 116.6, 111.6, 56.8; $\text{C}_{14}\text{H}_{13}\text{NO}_2$ found (Calc.) C 73.8(74.0), H 5.7(5.7), N 6.2(6.2).

N-p-Tolylvanillaldimine (10)

Colour: yellow ^1H NMR (CDCl_3): δH 8.43(s, 1H) 7.50 (s, 1H), 7.32-7.29(d, 1H), 7.19-7.10(m, 4H), 6.89-6.86 (d, 1H), 3.83(s, 3H), 2.30(s, 3H); ^{13}C NMR: δC 160.5, 151.3, 150.5, 149.2, 135.8, 130.9, 129.2, 125.2, 122.0, 116.6, 111.6, 56.8, 21.8; $\text{C}_{15}\text{H}_{15}\text{NO}_2$ found (Calc.) C 74.2(74.7), H 6.3(6.2), N 5.7(5.8).

N-o-Hydroxyphenyl (vanillaldimine) (11)

Colour: brown; ^1H NMR (DMSO-d_6): δH 8.82(s, 1H), 7.26(d, 2H), 7.08(d, 2H), 6.95-6.86(m, 3H), 6.34(s, 1H), 5.58(s, 1H), 3.81(s, 3H) $\text{C}_{14}\text{H}_{13}\text{NO}_3$ found (Calc.) C 68.5(69.1), H 5.0(5.4), N 6.0(5.76).

4-[(4-Hydroxy-3-methoxy benzylidene (amino) benzoic acid (12)

Colour: orange; ^1H NMR (DMSO-d_6): δH 9.74(s, 1H), 7.66(d, 1H), 7.41(d, 1H), 7.38(s, 1H), 7.19(t, 1H), 6.95 (d, 1H), 6.71(d, 2H), 6.47(t, 1H), 3.81(s, 3H) $\text{C}_{15}\text{H}_{13}\text{NO}_4$ found (Calc.) C 66.8(66.4), H 4.5(4.8), N 5.8(5.2).

Results and Discussion

In the past we have reported the synthesis of a number of Schiff bases using the classical method¹¹. On the other hand, an alternative method having green chemistry approach might lead to the formation of imines eliminating the generation of the hazardous substances. Herein, the synthesis of Schiff bases using mechanochemistry, which deals with the use of grinding to promote reactions between solid-solid or solid-liquid reactants were demonstrated.

Reactions of diphenyldisulphide diamine with aldehydes or *p*-vanillin with amines were achieved by simply grinding together the starting materials in the molar ratio 1:2. Some of the reaction mixtures after grinding become viscous liquids or paste even where all reagents are solids. In some cases the melt phase stiffens within minutes to yield a sticky solid that hardens further on standing. The reactions were completed within 5-20 min with good yields comparable with classical methods. Reaction mixtures of vanillin were poured in ice after grinding. The product precipitated after 2 days on standing.

The synthesized products were characterized on the basis of their IR, NMR, elemental analysis and melting points (Table 1) and were compared with the data of products obtained from classical method¹¹⁻¹³.

The Schiff bases (**1-12**) showed a strong signal in the region 1620 cm⁻¹, assigned to the azomethine group. The NMR data (¹H and ¹³C) are reported in the experimental section. The comparison of the ¹H NMR spectrum of **7** (Figure 1) obtained from both green and classical methods¹⁴ was comparable, hence confirming that the same product was formed. To the best of our knowledge the synthesis of **8** has not been reported. The ¹H NMR of **8** (Figure 2) showed the azomethine proton as a doublet at δ 8.02 and the aromatic protons at 6.87-7.35 ppm. One of the olefinic protons appeared at δ 6.44 as doublet of doublet while the other olefin proton was merged with the aromatic protons. The peaks at 7.8 and 6.2 ppm indicated the formation of another isomer of the Schiff base **8**. This may be due to resonance of the conjugated system.

Table 1. Solvent free synthesis of imines derivatives.

Entry	Product	Yield %	M.P, °C
		Green (Classical)	Green (Classical)
1	<i>N, N'</i> (1,1'-Dithiobisphenylene) bis benzyldeimine	93(85)	138(140)
2	<i>N, N'</i> (1,1'-Dithiobisphenylene) bis-2-chlorobenzyldeimine	97(98)	172(173)
3	<i>N, N'</i> (1,1'-Dithiobisphenylene) bis-2-nitrobenzyldeimine	94(61)	164(168)
4	<i>N, N'</i> (1,1'-Dithiobisphenylene) bisfurfurylimine	94(83)	106(108)
5	<i>N, N'</i> (1,1'-Dithiobisphenylene) bis- <i>o</i> -anisalimine	94	163
6	<i>N, N'</i> (1,1'-Dithiobis phenylene) bis <i>p</i> -anisalimine	96	169(172)
7	<i>N, N'</i> (1,1'-Dithiobis phenylene) bis pyridylimine	92(80)	136(140)
8	<i>N, N'</i> (1,1'-dithiobisphenylene) bis-cinnamaldehydimine	98	138
9	<i>N</i> -Phenyl-vanillaldimine	90(89)	154(155)
10	<i>N-p</i> -Tolylvanillaldimine	92	154(158)
11	<i>N-o</i> -Hydroxyphenyl (vanillaldimine)	91	154(158)
12	4-[(4-Hydroxy-3-methoxy benzylidene (amino) benzoic acid	89	164

Scheme 1. Synthesis route to imines. **Figure 1.** ^1H NMR spectra of **7** obtained from (a) green chemistry and (b) the classical method.

Figure 2. ^1H NMR spectra of compound **8**.

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