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An Efficient and Green Synthesis of Novel Azo Schiff Base and its Complex Under Ultrasound Irradiation

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ABSTRACT

An environmentally benign protocol for the synthesis of azo Schiff bases and its complex in short reaction time and high yield has been achieved. These Schiff base compounds have been characterized by C, H, N elemental analyses, FT-IR and ^{1}H NMR spectroscopy. The synthesized complex was characterized by atomic absorption spectrophotometry and elemental analyses.

Key words: Azo Schiff base, Green synthesis, Ultrasound irradiation.

INTRODUCTION

Schiff bases are well-known to have biological activates such as antibacterial[1-3], antifungal[4-5], antitumor[6-7], antiviral[8-10], anti bacterial[7], antifungal[7], anti-HIV-1[11], herbicidal[12] and anti-influenza A virus[13] activities.

Perhaps the most common method for preparing Schiff bases is the reaction of aldehydes and ketones with primary amines[14]. The reaction is generally carried out by refluxing the carbonyl compounds and amines in organic solvents. Recent years have witnessed a major drive to increase the efficiency of organic transformations while lowering the amount of waste materials Furthermore; the ultrasound assisted reactions are green methods in the organic synthesis which have numerous advantages: reduced pollution, low costs, and simplicity in process and handling[15-16].

EXPERIMENTAL

Materials and instruments

For the ultrasound reactions, ultrasound apparatus astra 3D (9.5 dm^3, 45 kHz frequency, input power with heating, 305W, number of transducers, 2) from TECNO-GAZ was used. Chemicals were purchased from Merck and Fluka and used as purchased. Melting points were measured on an Electro-thermal 9100 apparatus and are uncorrected. ^{1}H NMR spectra were obtained on a Bruker DRX 500Avance spectrometer in DMSO-d_6 as solvent and with TMS as internal standard. FT-IR spectra were recorded on a Shimadzu FT-IR-8400S spectrometer. Elemental analyses were recorded on a Carlo-Erba EA1110CNNO-S analyzer.

General Procedure for the synthesis of azo Schiff base

A mixture of azo-linked aldehydes (1mmol), aminopyrazole (1mmol) and 10 mL EtOH were placed into Pyrex-glass open vessel and irradiated in a water bath under silent condition by ultrasound (45 kHz) at 60°C for the required reaction times (5-15min). The progress of the reaction was monitored by TLC (EtOAc: petroleum ether 1:4). Then the reaction mixture was filtered to separate the product and recrystallized from EtOH. The pure products were collected in 85-96% yields.

4-((4-chlorophenyl)diazenyl)-2-((E)-(3-methyl-1H-pyrazol-5-ylimino)methyl) phenol 1

yellow solid, Mp 230 °C, IR (KBr): 3274, 2921, 1614, 1573, 1483, 1346, 1278, 1151 cm^{-1}. ^{1}HNMR (400 MHz, DMSO-d_6, ppm): δ_H 2.28 (3H, s), 6.33 (1H, s), 7.15 (1H, *J* = 8.8 Hz, d), 7.66 (2H, *J* = 8.6 Hz, d), 7.83 (2H, *J* = 8.6 Hz, d), 7.99 (1H, *J* = 2 Hz, *J* = 8.8 Hz, dd), 8.28 (1H, *J* = 2.4 Hz, d), 9.21 (1H, s), 12.66 (1H, s), 13.95 (1H, s). ^{13}C NMR (100 MHz, DMSO-d_6, ppm): δ_C 25.60, 95.36, 118.39, 119.93, 124.41, 127.38, 128.06, 130.05, 135.81, 140.71, 145.21, 151.03, 161.53. Anal. Calcd. for $C_{17}H_{14}ClN_5O$: C, 60.09; H, 4.15; N, 20.61. Found: C, 60.43; H, 4.11; N, 20.09.

2-((E)-(3-methyl-1H-pyrazol-5-ylimino)methyl)-4-((4-nitrophenyl)diazenyl)phenol 2

IR (KBr): 3407, 3213, 3132, 1614, 1434, 1517, 1361, 1286 cm^{-1}. ^{1}HNMR (400 MHz, DMSO-d_6, ppm): δ_H 2.07 (3H, s), 6.30 (1H, s), 7.12 (1H, *J* = 8.7 Hz, d), 8.01 (3H, *J* = 8.2 Hz, d), 8.39 (2H, *J* = 8.2 Hz, d), 8.30 (1H, *J* = 3 Hz, d), 9.18 (1H, s), 12.64 (1H, s), 14.16 (1H, s). ^{13}C NMR (100 MHz, DMSO-d_6, ppm): δ_C 23.46, 93.43, 119.10, 124, 125.90, 128.08, 128.93, 129.46, 143.51, 144.74, 145.71, 148.85, 156.16, 161.31. Anal. Calcd. for $C_{17}H_{14}N_6O_3$: C, 58.28; H, 4.03; N, 23.99. Found: 58.65; H, 4.25; N, 23.09.

2-((E)-(3-methyl-1H-pyrazol-5-ylimino)methyl)-4-(phenyldiazenyl)phenol 3

IR (KBr): 3438, 3089, 2974, 1614, 1560, 1490, 1436, 1282 cm^{-1}. ^{1}HNMR (400 MHz, DMSO-d_6, ppm): δ_H 2.05 (3H, s), 6.33 (1H, s), 7.15 (1H, *J* = 8.8 Hz, d), 7.55-7.62 (3H, m), 7.87 (2H, *J* = 7.2 Hz, m), 7.99 (1H, *J* = 2 Hz, *J* = 8.8 Hz, dd), 8.28 (1H, s), 9.21 (1H, s), 12.65 (1H, s). ^{13}C NMR (100 MHz, DMSO-d_6, ppm): δ_C 25.6, 96.30, 107.15, 116.12, 118.91, 122.69, 123.32, 123.71, 124.91, 129.92, 138.43, 139.66, 155.41, 161.30. Anal. Calcd. for C17H15N5O: C, 66.87; H, 4.95; N, 22.94. Found: 66.35; H, 4.75; N, 22.42.

4-((4-bromophenyl)diazenyl)-2-((E)-(3-methyl-1H-pyrazol-5-ylimino)methyl) phenol 4

IR (KBr): 3448, 3274, 1614, 1558, 1278, 1151, 1002 cm^{-1}. ^{1}HNMR (400 MHz, DMSO-d_6, ppm): δ_H 2.28 (3H, s), 6.35 (1H, s), 7.15 (1H, *J*= 8.8 Hz, d), 7.80 (4H, br), 7.99 (1H, *J*= 8.8 Hz, d), 8.28 (1H, s), 9.20 (1H, s), 12.66 (1H, s). ^{13}C NMR (100 MHz, DMSO-d_6, ppm): δ_C 23.83, 95.35, 118.44, 119.91, 122.36, 124.64, 127.39, 128.91, 132.99, 140.43, 145.20, 151.33, 161.24. Anal. Calcd. for $C_{17}H_{14}BrN_5O$: C, 53.14; H, 3.67; N, 18.23. Found: C, 53.37; H, 3.73; N, 18.96.

4-((2-chlorophenyl)diazenyl)-2-((E)-(3-methyl-1H-pyrazol-5-ylimino)methyl) phenol 5

IR (KBr): 3429, 3128, 2928, 1616, 1502, 1456, 1325, 1280, 1054 cm^{-1}. ^{1}HNMR (400 MHz, DMSO-d_6, ppm): δ_H 2.28 (3H, s), 6.35 (1H, s), 7.17 (1H, *J* = 8.8 Hz, d), 7.48-7.57 (2H, m), 7.67-7.72 (2H, m), 8.01 (1H, *J* = 2 Hz, *J* = 8.8 Hz, dd), 8.31 (1H, *J* = 2.4 Hz, d), 9.23 (1H, s), 12.66 (1H, s), 14.08 (1H, s). ^{13}C NMR (100 MHz, DMSO-d_6, ppm): ´$_C$ 95.41, 118.04, 118.64, 119.87, 127.32, 128.56, 128.97, 131.17, 132.51, 133.86, 140.76, 145.54, 148.46, 156.16, 161.62, 164.64. Anal. Calcd. for $C_{17}H_{14}ClN_5O$: C, 60.09; H, 4.15; N, 20.61. Found: C, 60.56; H, 4.01; N, 20.45.

4-((4-iodophenyl)diazenyl)-2-((E)-(3-methyl-1H-pyrazol-5-ylimino)methyl)phenol 6

IR (KBr): 3419, 1610, 1560, 1469, 1276, 1101 cm^{-1}. ^{1}HNMR (400 MHz, DMSO-d_6, ppm): δ_H 2.28 (3H, s), 6.33 (1H, s), 7.15 (1H, *J* = 9 Hz, d), 7.66 (2H, *J* = 8.6 Hz, d), 7.99 (2H, *J* = 8.6 Hz, d), 8.01 (1H, *J* = 8.8 Hz, *J* = 2 Hz, dd) ,8.28 (1H, *J* = 2.4 Hz, d), 9.21 (1H, s), 12.66 (1H, s), 14.00 (1H, s). Anal. Calcd. for $C_{17}H_{14}IN_5O$: C, 47.35; H, 3.27; N, 16.24. Found: C, 47.76; H, 3.11; N, 16.61.

2-((E)-(3-methyl-1H-pyrazol-5-ylimino)methyl)-4-(p-tolyldiazenyl)phenol 7

IR (KBr): 3502, 3163, 3082, 2968, 1606, 1568, 1446, 1278. ^{1}HNMR (400 MHz, DMSO-d_6, ppm): δ_H 2.28 (3H, s), 2.41 (3H, s), 6.33 (1H, s)

7.14 (1H, *J* = 8.8 Hz, d), 7.40 (2H, *J* = 8.4 Hz, d), 7.77 (2H, *J* = 8.4 Hz, d), 7.96 (1H, *J* = 2 Hz, *J* = 8.8 Hz, d), 8.24 (1H, *J* = 2 Hz, d), 9.21 (1H, s), 12.65 (1H, s), 13.85 (1H, s). ^{13}C NMR (100 MHz, DMSO-d_6, ppm): δ_C 21.48, 25.60, 95.32, 118.25, 119.86, 122.56, 122.77, 127.21, 127.61, 130.43, 141.58, 145.35, 150.51, 161.75. Anal. Calcd. for $C_{18}H_{17}N_5O$: C, 67.70; H, 5.37; N, 21.93;. Found: C, 67.30; H, 5.83; N, 21.11.

4-((3-chlorophenyl)diazenyl)-2-((E)-(3-methyl-1H-pyrazol-5-ylimino)methyl) phenol 8

IR (KBr): 3274, 3448, 2925, 1652, 1558, 1458, 1217, 756 cm^{-1}. ^{1}HNMR (400 MHz, DMSO-d_6, ppm): δ_H 2.09 (3H, s), 6.33 (1H, s), 7.67-7.71 (2H, m), 7.96 (2H, m), 8.08 (1H, *J* = 9.2 Hz, d), 8.28 (1H, *J* = 9.2 Hz, d), 8.89 (1H, s), 9.21 (1H, s), 13.41 (1H, s). ^{13}C NMR (100 MHz, DMSO-d_6, ppm): δ_C 25.60, 95.43, 120.66, 121.37, 122.97, 123.62, 129.84, 131.33, 131.82, 132.66, 132.79, 135.01, 138.36, 147.46, 149.72, 152.08, 161.34. Anal. Calcd. for $C_{17}H_{14}ClN_5O$: C, 60.09; H, 4.15; N, 20.61;. Found: C, 60.39; H, 4.16; N, 20.81.

2-((E)-(3-methyl-1H-pyrazol-5-ylimino)methyl)-4-((2-methyl-4-nitrophenyl) diazenyl)phenol 9

IR (KBr): 3274, 3149, 3191, 2991, 1614, 1519, 1434, 1575, 1342, 1288, 1115 cm^{-1}. ^{1}HNMR (400 MHz, DMSO-d_6, ppm): δ_H 2.25 (3H, s), 2.69 (3H, s), 6.26 (1H, s), 7.08 (1H, br), 7.60 (1H, br), 7.92 (1H, br), 8.08 (1H, br), 8.21 (2H, br), 9.10 (1H, s), 12.62 (1H, s), 14.13 (1H, s). ^{13}C NMR (100 MHz, DMSO-d_6, ppm): δ_C 17.89, 23.50, 95.81, 117.29, 118.97, 120.12, 127.04, 127.65, 129.92, 130.01, 139.10, 141.07, 146.05, 148.51, 154.21, 155.12, 157.46, 161.72. Anal. Calcd. for $C_{18}H_{16}N_6O_3$: C, 59.34; H, 4.43; N, 23.07. Found: C, 59.35; H, 4.82; N, 23.49.

4-((4-methoxyphenyl)diazenyl)-2-((E)-(3-methyl-1H-pyrazol-5-ylimino)methyl) phenol 10

IR (KBr): 3274, 3448, 1652, 1558, 1458, 1382, 1217 cm^{-1}. ^{1}HNMR (400 MHz, DMSO-d_6, ppm): δ_H 2.40 (3H, s), 3.74 (3H, s), 6.20 (1H, s), 7.16 (1H, *J* = 8.8 Hz, d), 7.53 (2H, *J* = 8.4 Hz, d), 7.91 (2H, *J* = 8.4 Hz, d), 8.44 (1H, *J* = 8.4 Hz, d), 8.66 (1H, s), 9.48 (1H, s), 13.60 (1H, s) ppm. Anal. Calcd. for $C_{18}H_{17}N_5O_2$: C, 64.47; H, 5.11; N, 20.88. Found: C, 64.49; H, 5.61; N, 20.73.

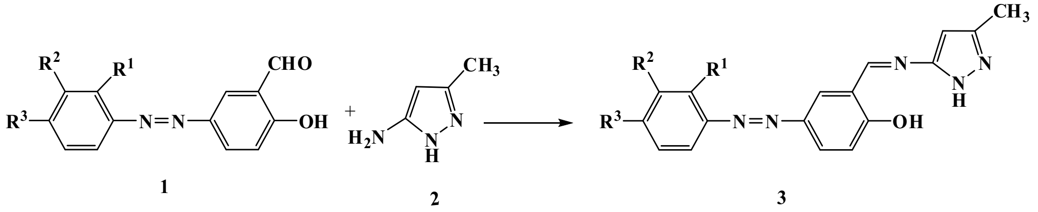
Preparation of complex 4i under ultrasound irradiation

A mixture of Schiff base **3i** (2mmol), $Cu(OAc)_2$ (1mmol) and 10 mL EtOH were placed into Pyrex-glass open vessel and irradiated in a water bath under silent condition by ultrasound (45kHz) at 60°C for the required reaction times (15min). The progress of the reaction was monitored by TLC (EtOAc: petroleum ether 1:4). Then the reaction mixture was filtered to separate the product and recrystallized from EtOH. The pure products were collected in 98% yields. Anal. Calcd. for $C_{36}H_{32}Ac_2CuN_{12}O_8^{2-}$: C, 33.46; H, 2.56; N, 13.42. Found: C, 33.83; H, 2.52; N, 13.15.

RESULTS AND DISCUSSION

As part of our going interest for the development of efficient and environmentally friendly procedures for the synthesis of heterocyclic and pharmaceutical compounds[17-20] we wish to report the first ultrasound assisted synthesis of novel derivatives of Schiff bases (Scheme 1).

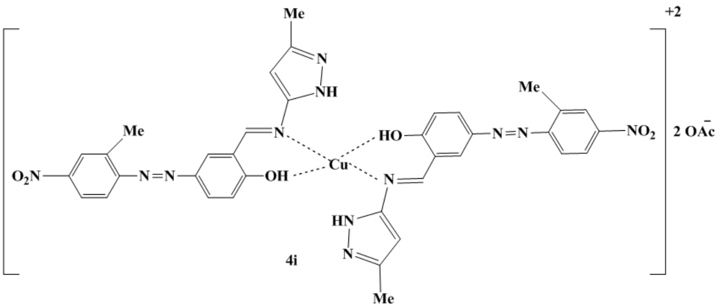
In an initial endeavor, 1a and 5-methyl-3-aminopyrazole were refluxed in 10 mL ETOH. After 7 h only, 73 % of expected product after purification



Scheme 1: Synthesis of azo-linked Schiff bases

of crude product was obtained. To improve the product yields and to optimize the reaction condition, the same reaction was carried out in the presence of ultrasonic's irradiation. We found that the best results were obtained under ultrasound irradiation at 60 ˚C in EtOH. As indicated in Table 1, ultrasonic irradiation accelerates the reaction, the reaction time decreases from 7 h to 8min (Entry 1, Table 1). Also, under ultrasonic irradiation the yield of product is higher. The results are summarized in table 1. The higher yield and less reaction time during ultrasonic irradiation in the presence of the catalyst can be attributed to implosive collapse of the cavitations period of the sound waves. When the formed bubbles burst, it results in high temperature and high pressure which facilitate the intermolecular reaction.

In the other study, we concentrated on the synthesis of novel complex of this Schiff base in the reflux condition and ultrasound irradiation. The structure of synthesized complex 4i was shown in Scheme 2.



Scheme 2: The structure of synthesized complex 4i

All of compounds summarized in table 1 were characterized by spectroscopic methods (IR,^{1}H NMR, ^{13}C NMR) and elemental analysis. In the ^{1}H NMR spectra of azo-linked Schiff bases 3a-j, imines C-H proton of resonated at 6.2-6.3 ppm and in the ^{13}C NMR spectra of azo-linked Schiff bases 3a-j, imines C-H carbon of resonated at 95 ppm.

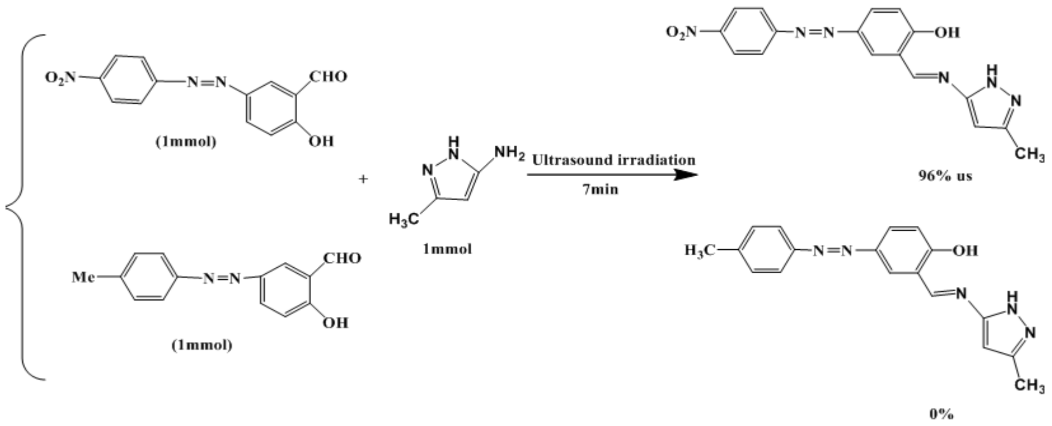
Following these results, we further investigated the potential of this procedure for

Table 1: Ultrasound assisted synthesis of Schiff bases and complex

Entry	R^1	R^2	R^3	product	Reflux condition		Ultrasound		m.p.
					Time (h)	Yield (%)[1]	Time (min)	Yield (%)[1]	(°C)
1	H	H	Cl	3a	7	73	8	89	230
2	H	H	NO_2	3b	7	77	7	96	198
3	H	H	H	3c	8	76	12	85	197
4	H	H	Br	3d	7	79	10	98	200
5	Cl	H	H	3e	9	70	12	91	211
6	H	H	I	3f	7	76	7	95	201
7	H	H	CH_3	3g	9	78	12	85	210
8	H	Cl	H	3h	8	77	10	89	200
9	NO_2	H	CH_3	3i	7	79	5	91	215
10	H	H	OCH_3	3j	9	75	10	86	199
11	NO_2	H	CH_3	4i	3	88	15	98	>250

[1.]Isolated Yield.

the selective synthesis of azo-linked Schiff bases of different types of azo-linked aldehydes with pyrazolamines. The results showed that ultrasound irradiation is able to discriminate between aromatic compounds containing electron donating and electron withdrawing groups, a transformation that is difficult to accomplish via conventional methods (Scheme 3).



Scheme 3: The ability of ultrasound irradiation to discriminate of various substituted azo

CONCLUSION

Finally, we develop an efficient, green, fast and convenient procedure for the synthesis of azo-linked Schiff bases through electrophilic substitution of azo-linked aldehydes and pyrazole amine under ultrasound irradiation. This procedures offer advantages such as reduced reaction time, mild reaction condition, productivity and higher yield, ease of execution and economic viability. To the best of our knowledge, the process described herein represents the first example of ultrasound assisted synthesis of azo-linked Schiff bases and its complex.

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