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AN IMPROVED AND FACILE SYNTHESIS OF SCHIFF BASES IN AQUEOUS MEDIUM

M. S. Singh [a] , A. K. Singh [a] , Pratibha Singh [a] & Ruchi Jain [a]
[a] Department of Chemistry, Faculty of Science, Banaras Hindu University, Varanasi, 221005, INDIA E-mail:

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OPPI BRIEFS

AN IMPROVED AND FACILE SYNTHESIS OF SCHIFF BASES IN AQUEOUS MEDIUM

Submitted by M. S. Singh*, A. K. Singh, Pratibha Singh and Ruchi Jain
(10/25/04)

Department of Chemistry, Faculty of Science
Banaras Hindu University, Varanasi-221005, INDIA
e-mail: singhms1960@rediffmail.com

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Schiff bases have been used as precursors and intermediates for the synthesis of a variety of organic compounds useful in analytical, medicinal, polymer and liquid crystalline materials[1] or as ligands for complexation. Previously Schiff bases have been synthesized by refluxing the mixture of amines and the carbonyl compounds in organic solvents under azeotropic conditions in order to remove the water formed.[2] In recent years, environmentally benign synthetic methods have received considerable attention and some solvent-free protocols have been developed.[3] Varma, Dahiya and Kumar[4] reported the clay-catalyzed synthesis of imines and enamines under solvent-free conditions using microwave irradiation. We report here the condensation reaction of salicylaldehyde (**1a**), *o*-hydroxyacetophenone (**1g**), *p*-tolualdehyde (**1k**) anisaldehyde (**1o**), *p*-chloroacetophenone (**1s**), 2-hydroxy-4-bromoacetophenone (**1t**) and *p*-(dimethylamino)acetophenone (**1u**) with diamines **2** in aqueous medium without catalyst to give imines **3a-u** in good to excellent yields in a very short time.[5]

The preparation of N,N'-ethylene*bis*(salicylideneimine) [**3a**] is a representative example of the general procedure employed. The compounds were characterized on the basis of satisfactory elemental analyses and spectral (IR, ^{1}H and ^{13}C NMR) studies (*Tables 1 and 2*). In compounds **3e**, **3n**, and **3r** the diamine used is *o*-phenylenediamine ($NH_2C_6H_4NH_2$) and in **3f**, the diamine is 4-methyl-*o*-phenylenediamine.

In contrast, the conventional method in organic solvents is less convenient. Mixtures of carbonyl compounds and amines in desired molar ratios are refluxed in benzene containing a small amount of benzenesulfonic acid as a catalyst for several hours under azeotropic conditions using Dean-Stark apparatus.[6] Apparently the condensation, which produces water as a by-product, is driven to completion by the separation of the products as insoluble oils or solids. It has been determined that the Schiff bases, which are soluble in water are not formed under these conditions. The reaction works both with water soluble and insoluble starting materials.

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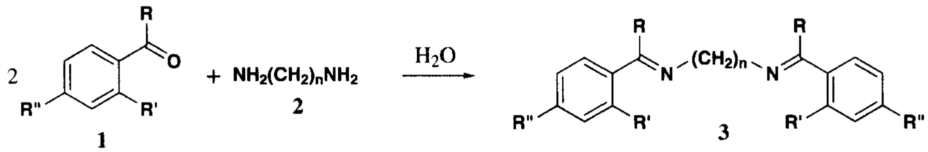

	R	R'	R''	$NH_2(CH_2)_nNH_2$		R	R'	R''	$NH_2(CH_2)_nNH_2$
a)	H	OH	H	n = 2	l)	H	H	CH_3	n = 3
b)	H	OH	H	n = 3	m)	H	H	CH_3	n = 4
c)	H	OH	H	n = 4	n)	H	H	CH_3	$(CH_2)_n = C_6H_4$
d)	H	OH	H	n = 0	o)	H	H	OCH_3	n = 2
e)	H	OH	H	$(CH_2)_n = C_6H_4$	p)	H	H	OCH_3	n = 3
f)	H	OH	H	$(CH_2)_n = 4\text{-Me•}C_6H_3$	q)	H	H	OCH_3	n = 4
g)	CH_3	OH	H	n = 2	r)	H	H	OCH_3	$(CH_2)_n = C_6H_4$
h)	CH_3	OH	H	n = 3	s)	CH_3	H	Cl	n = 2
i)	CH_3	OH	H	n = 4	t)	CH_3	OH	Br	n = 2
j)	CH_3	OH	H	n = 0	u)	CH_3	H	NMe_2	n = 2
k)	H	H	CH_3	n = 2					

Table 1. Physical and Analytical Data of Schiff Bases **3a-u**

Cmpd.	Yield[a] (%)	mp (°C)	*lit.* mp (°C)	Reaction time (min)	Analysis Calcd (Found) C	H
3a	99	125-126[7]	126-127	10	71.64 (71.48)	5.97 (5.83)
3b	98	52-53	53-54	12	72.34 (72.12)	6.38 (6.18)
3c	99	81-82	82-83	06	72.97 (72.63)	6.76 (6.43)
3d	83	209-211[8]	210-211	60	70.00 (69.84)	5.04 (5.24)
3e	95	164-165	165-166	25	75.95 (75.73)	5.06 (5.27)
3f	65	110-111	109-110	90	76.36 (76.42)	5.45 (5.87)
3g	93	185-186[9]	186-187	20	72.97 (72.78)	6.76 (6.48)
3h	93	121-122	121-122	15	73.55 (73.38)	7.09 (7.27)
3i	92	194-96	194-195	10	74.07 (74.33)	7.40 (7.67)
3j	86	176-178	177-178	130	71.64 (71.86)	5.97 (5.62)
3k	97	156-157	156-158	05	91.81 (81.98)	7.57 (7.89)
3l	95	56-57	57-58	15	82.01 (82.36)	7.91 (8.23)
3m	96	98-99	99-100	05	82.19 (82.43)	8.22 (8.56)
3n	86	232(dec.)	233 (dec.)	10	84.62 (84.97)	6.41 (6.73)
3o	99	118-119	119-120	05	72.97 (73.32)	6.76 (7.13)
3p	89	78-80	79-80	90	73.55 (73.97)	7.09 (7.47)
3q	97	108-109	108-110	10	74.07 (74.43)	7.41 (7.79)
3r	95	260-262	261-262	15	76.74 (76.43)	5.81 (6.13)
3s	68	177-178[10]	178-179	60	64.86 (64.98)	5.41 (5.13)
3t	52	84-85	85-86	150	51.18 (51.43)	4.27 (4.53)
3u	85	175-176[10]	176-177	12	74.53 (74.87)	8.07 (8.41)

a) Yields of the crude products.

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The IR spectra display bands at ~1638cm^{-1} (C=N) and ~3706 cm^{-1} (OH). The ^{1}H NMR spectra of **3a-u** display aromatic protons at δ 6.75-8.08. The azomethine protons appear as singlet around δ 8.84 in all compounds. There are no azomethine protons in compounds **3g-j** and **3s-u**. The methyl and methoxy groups of compounds **3k** to **3r** exhibit sharp singlet at δ ~2.23 and δ ~3.46, respectively. The phenolic OH groups show broad singlets at δ 11.56-13.14, which are D$_2$O exchangeable. The ^{13}C NMR spectra exhibited the expected number of signals for the *ortho*, *meta*, and *para* carbons. Carbons attached to nitrogen and oxygen reveal signals in the region δ 155.9-159.7 and 152.46-153.74, respectively.

Table 2. Spectral Data of Schiff Bases **3a-u**

Cmpds	IR (cm^{-1})	^{1}H NMR (δ)	^{13}C NMR (δ)
3a	1640(C=N), 3710(O–H)	8.08-6.86(m, 8H, Ar), 8.86(s, 2H, CH=N), 3.86(t, J = 8.2 Hz, 4H, NCH$_2$), 12.35(s, 2H, OH)	159.73, 153.72, 134.34, 133.67, 126.78, 120.34, 116.42, 56.84
3b	1635(C=N), 3705(O–H)	7.94-6.74(m, 8H, Ar), 8.66(s, 2H, CH=N), 3.78(t, J = 8.0 Hz, 4H, NCH$_2$), 1.24(m, 2H, CH$_2$),12.76(s, 2H, OH)	159.34, 152.94, 134.42, 133.54, 126.56, 121.26, 116.48, 57.32, 28.46
3c	1640(C=N), 3712(O–H)	7.98-6.92(m, 8H, Ar), 8.74(s, 2H, CH=N), 3.82(t, J = 8.4 Hz, 4H, NCH$_2$), 1.30(m, 4H, CH$_2$), 12.54(s, 2H, OH)	158.28, 153.26, 134.57, 133.43, 126.43, 121.47, 117.46, 57.21, 27.62
3d	1632(C=N), 3698(O–H)	8.04-6.96(m, 8H, Ar), 8.56(s, 2H, CH=N), 11.56(s, 2H, OH)	157.72, 152.92, 135.56, 133.67, 127.34, 122.34, 116.84
3e	1637(C=N), 3718(O–H)	8.02-6.84(m, 12H, Ar), 8.66(s, 2H, CH=N), 13.46(s, 2H, OH)	158.14, 152.46, 141.34, 134.54, 133.37, 127.42, 120.24, 116.74
3f	1635(C=N), 3707(O–H)	8.00-6.94(m, 11H, Ar), 8.64(s, 2H, CH=N), 13.46(s, 2H, OH), 2.21(s, 3H, ArCH$_3$)	159.34, 153.86, 134.76, 133.82, 127.14, 120.62, 116.48, 21.47
3g	1628(C=N), 3702(O–H)	7.94-6.78(m,8H,Ar), 2.76(s,6H,CH$_3$), 3.84(t, J=8.2 Hz, 4H,NCH$_2$), 12.56(s,2H,OH)	159.74, 152.46, 141.37, 133.59, 127.36, 121.58, 57.86, 33.78
3h	1638(C=N), 3706(O–H)	7.92-6.84(m, 8H, Ar), 2.68(s, 6H, CH$_3$), 3.78(t, J = 8.4 Hz, 4H, NCH$_2$), 1.28(m, 2H, CH$_2$),12.64(s, 2H, OH)	159.42, 152.68, 141.67, 133.27, 127.62, 121.34, 57.24, 33.64, 28.37
3I	1644(C=N), 3716(O–H)	7.90-6.87(m, 8H, Ar), 2.86(s, 6H, CH$_3$), 3.74(t, J = 8.4 Hz, 4H, NCH$_2$), 1.34(m, 4H, CH$_2$),12.48(s, 2H, OH)	158.46, 153.36, 140.47, 134.59, 127.18, 121.23, 57.62, 27.58
3j	1634(C=N) 3712(O–H)	8.06-6.92(m,8H,Ar), 2.76(s,6H,CH$_3$), 12.56(s,2H,OH)	158.74, 153.68, 141.38, 134.39, 127.47, 121.74, 58.34
3k	1633(C=N)	8.02-6.88(m, 8H, Ar), 8.42(s, 2H, CH=N), 3.74(t, J = 8.2 Hz, 4H, NCH$_2$), 2.23(s, 6H, CH$_3$)	159.34, 154.38, 140.56, 133.42, 126.54, 121.47, 58.62, 21.28
3l	1636(C=N)	7.94-6.82(m, 8H, Ar), 8.62(s, 2H, CH=N), 3.88(t, J = 8.2 Hz, 4H, NCH$_2$), 1.24(m, 2H, CH$_2$), 2.32(s, 6H, CH$_3$)	158.47, 153.54, 141.37, 133.76, 126.21, 121.84, 58.94, 28.24, 21.72

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Table 2. Continued...

Cmpds	IR (cm^{-1})	^{1}H NMR (δ)	^{13}C NMR (δ)
3m	1630(C=N)	8.05-6.74(m, 12H, Ar), 8.42(s, 2H, CH=N), 1.32(m, 4H, CH_2), 2.28(s, 6H, CH_3)	158.82, 154.74, 141.72, 133.67, 126.62, 121.37, 116.43, 58.64, 27.42, 21.54
3n	1628(C=N)	7.84-6.68(m, 12H,Ar), 8.62(s, 2H, CH=N), 2.36(s, 6H, CH_3)	159.52, 153.54, 141.42, 133.23, 126.87, 121.63, 116.86, 57.42
3o	1633(C=N)	7.96-6.71(m, 8H, Ar), 8.56(s, 2H, CH=N), 3.72(t, J = 8.4 Hz, 4H, NCH_2), 3.36(s, 6H, OCH_3)	159.34, 153.68, 141.82, 133.96, 126.42, 121.26, 116.42, 57.78, 55.42
3p	1627(C=N)	8.02-7.12(m, 8H, Ar), 8.48(s, 2H, CH=N), 3.76(t, J = 8.0 Hz, 4H, NCH_2), 1.22 (m, 2H, CH_2), 3.52(s, 6H, OCH_3)	158.74, 153.68, 133.48, 126.23, 121.16, 116.28, 58.42, 55.34, 27.63
3q	1612(C=N)	7.98-6.70(m, 12H, Ar), 8.46(s, 2H, CH=N), 1.28(m, 4H, CH_2), 3.48(s, 6H, OCH_3)	159.52, 153.12, 141.18, 133.34, 126.28, 121.46, 116.82, 58.84, 54.62, 28.64
3r	1643(C=N)	7.82-6.70(m, 12H, Ar), 8.52(s, 2H, CH=N), 3.42(s, 6H, OCH_3)	159.21, 152.78, 140.48, 133.24, 127.94, 121.12, 58.46
3s	1634(C=N)	7.96-6.64(m, 8H, Ar), 2.58(s, 6H, CH_3), 3.56(t, J = 8.2 Hz, 4H, NCH_2)	158.91, 152.46, 141.24, 133.76, 128.54, 121.62, 58.84, 27.76
3t	1632(C=N) 3710(O–H)	8.06-7.02(m, 6H, Ar), 2.52(s, 6H, CH_3), 3.68(t, J = 8.2 Hz, 4H, NCH_2), 13.14(s, 2H, OH)	159.46, 153.27, 134.74, 133.25, 126.47,120.16,116.58, 57.94, 34.48
3u	1640(C=N)	7.84-6.72(m, 8H, Ar), 2.56(s, 6H, CH_3), 3.74(t, J = 8.0 Hz, 4H, NCH_2), 2.42(s, 12H, NMe_2)	156.34, 152.96, 134.24, 133.46, 127.48, 120.45, 58.23, 54.12, 28.46

Our method has the advantage that neither acid catalyst nor hazardous aromatic solvents for azeotropic water separation are required. The products were isolated and purified by simple filtrations and washing, in much better yields than previously reported. The crude materials were recrystallized from suitable solvents to give the pure imines.

EXPERIMENTAL SECTION

The chemicals were purchased from Aldrich and E-Merck, and used as supplied. All solvents (AR or extra pure grade) were further purified by literature methods.[11] Melting points were determined using a calibrated thermometer by Remi Digital Melting Point apparatus and are uncorrected. The progress of the reactions was monitored by TLC on silica gel plates. Infrared spectra were recorded as KBr discs on a FT-IR Perkin-Elmer model RX-I spectrophotometer. Elemental analyses were performed by the Central Drug Research Institute, Lucknow. NMR (^{1}H and ^{13}C) spectra were recorded on a Bruker AM 270 instrument.

Typical Procedure for the Preparation of N,N'-Ethylene bis(Salicylideneimine) (3a). A mixture of salicylaldehyde (244 mg, 2.00 mmol) and ethylenediamine (60 mg, 1.00 mmol) was stirred in a 25 mL of distilled water at room temperature for 10 minutes. The yellow crystalline solid product formed was collected, washed with water and dried in a vacuum oven to give 270 mg (99%) of N,N'-ethylenebis(salicylideneimine). The crude yellow crystals were recrystallized from ethanol to give (258 mg, 95%) of pure imine as yellow prisms, mp. 125-126°C. The purity of the imine was checked by TLC and mixture melting point.[7]

In the case of **3f**, the product does not precipitate out of water instead it separates as a light brown viscous liquid is obtained; upon treatment with acetone, it gives a yellow solid that is recrystallized from methanol to give the pure imine (58%).

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