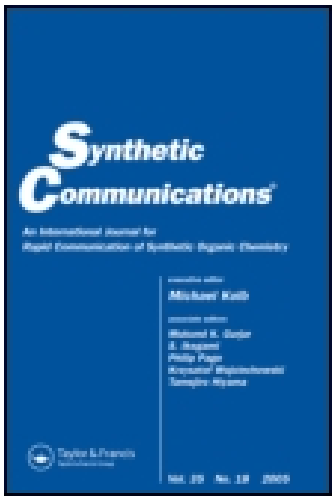

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NOVEL SYNTHESIS OF UNSYMMETRICAL AZINES FROM SEMICARBAZONES AND ALDEHYDES

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NOVEL SYNTHESIS OF UNSYMMETRICAL AZINES FROM SEMICARBAZONES AND ALDEHYDES

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ABSTRACT

A new synthesis of unsymmetrical azines utilizing semicarbazones and aldehyde is described.

In general, symmetrical azines are easily prepared by condensation of hydrazine with appropriate carbonyl compounds (1). In this manner, it is difficult to obtain pure unsymmetrical substituted azines in good yield (2). The methods involving synthesis of unsymmetrical azines have received much attention recently. Some routes, such as the alkylidene group exchange between azines and imines (3), N-(diethoxyphosphinyl)-hydrazone with carbonyl compounds (4), and Zirconium "metalloazines" and aldehydes (5), have been proposed. These methods suffer from the fact that the starting substances are not commercially available. Herein, we wish to report a new, simple, and convenient process for preparing unsymmetrical azines from aromatic aldehyde semicarbazones and aromatic aldehydes (Scheme 1, Table 1).

The reaction was performed with semicarbazones and aldehydes in DMF under reflux.

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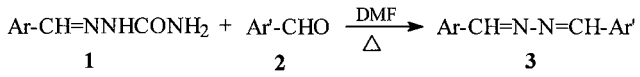


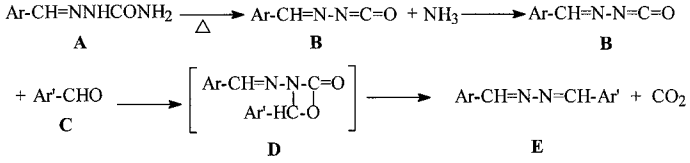
Scheme 1.

Table 1. Preparation of Unsymmetrical Azines

Compd.	Ar	Ar′	Reaction Time (h)	Yield (%)	m.p. (°C)
3a	4-Cl-Ph	4-OCH_3-Ph	16	87	130.5–131.5
3b	4-NO_2-Ph	4-OCH_3-Ph	16	87	203.7–204.5
3c	4-F-Ph	4-OCH_3-Ph	16	84	90.0–91.0
3d	2-Cl-Ph	4-OCH_3-Ph	16	79	74.5–75.2
3e	2,4-$(Cl)_2$-Ph	4-OCH_3-Ph	16	78	152.5–153.4
3f	4-Cl-Ph	4-CH_3-Ph	16	92	153.0–154.0
3g	4-NO_2-Ph	4-CH_3-Ph	16	90	193.5–194.0
3h	4-F-Ph	4-CH_3-Ph	16	80	119.0–120.0
3i	2-Cl-Ph	4-CH_3-Ph	16	72	106.0–106.5
3j	2,4-$(Cl)_2$-Ph	4-CH_3-Ph	16	73	178.0–179.0

RESULTS AND DISCUSSION

Because the formation of NH_3 and CO_2 has been observed during the reaction, the suggested reaction mechanism is as follows (Scheme 2).



Scheme 2.

At first, the ammonia is released from semicarbazones **A** under reflux to form intermediate **B**. Subsequently, a four-membered cyclic transition state **D** is suggested for the cycloaddition reaction of **B** with the aromatic aldehydes **C**, and finally carbon dioxide and unsymmetrical azines **E** are obtained by fragmentation of ring **D**.

A mixture of unsymmetrical and symmetrrical azines is produced when using aromatic aldehyde semicarbazones with an electron-donating group. The mechanism for the formation of symmetrical azine is similar to that outlined above (Scheme 3).

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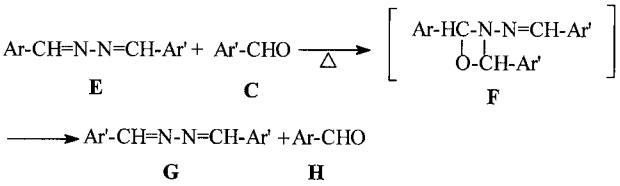
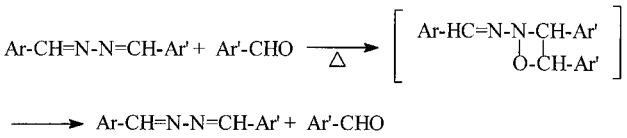


Ar = Ph, 4-CH_3Ph, 4-$N(CH_3)_2$, 4-OH-Ph; Ar′ = 4-CH_3O-Ph

Scheme 3.

First, unsymmetrical azines **E** are prepared. Next, the four-membered cyclic interimediate **F** is formed by cycloaddition reaction of aldehyde **C** and the imine group in azine **E** with electron-donating group, because the electron charge density of this imine is higher than one without an electron-donating group. The cleavage of ring **F** produces aldehyde **H** and symmetrical azine **G**.

When the electron-donating group is replaced by an electron-withdrawing group, the exchanging reaction between the aldehyde and imine always occurs on the imine with 4-methoxybenzaldehyde. As a result, the unsymmetrical azines are retained (Scheme 4).



Ar = 4-Cl-Ph , 4-NO_2-Ph , 4-F-Ph , 2-Cl-Ph , 2,4-$(Cl)_2$-Ph ;

Ar' = 4-CH_3O-Ph , 4-CH_3-Ph

Scheme 4.

EXPERIMENTAL

Melting points are uncorrected. They were determined on a WRS-1 digital melting point apparatus made by Shanghai Physical Optical Instrument Factory (SPOIF), China. IR spectra were measured in KBR on a PE-580B spectrometer. Elemental analyses were carried out on a Foss Heraeus CHN-O-RAPID element analysis instrument. ^{1}HNMR were recorded at Bruker AC-100SC, using $CDCl_3$ as solvent and TMS as internal reference.

General Procedure

The mixture of aromatic aldehyde semicarbazones (2.5 mmol) and aromatic aldehydes (10 mmol) in 20 mL DMF are refluxed for 16 h. After cooling, water (200 mL) is added to the reaction mixture. The precipitate is allowed to stand overnight, collected by suction filtration, washed with petroleum ether, and dried at room temperature.

3a: IR, $\nu_{C=N}$ (cm^{-1}), 1654, ^{1}HNMR, δ (ppm), 3.87 (s, 3H), 6.98 (d, 2H, J = 9.0 Hz), 7.42, (d, 2H, J = 8.0 Hz), 7.78 (d, 2H, J = 9.0 Hz), 7.83 (d, 2H, J = 8.0 Hz), 8.61 (s, 1H), 8.66 (s, 1H). Anal. calcd. for $C_{15}H_{13}ClN_2O$, C, 66.06, H, 4.80, N, 10.27. Found, C, 66.39, H, 4.80, N, 10.28.

3b: IR, $\nu_{C=N}$ (cm^{-1}), 1625, ^{1}HNMR, δ (ppm), 3.88 (s, 3H), 6.99 (d, 2H, J = 8.7 Hz), 7.83 (d, 2H, J = 8.7 Hz), 7.99 (d, 2H, J = 8.6 Hz), 8.31 (d, 2H, J = 8.6 Hz), 8.65 (s, 1H), 8.71 (s, 1H). Anal. calcd. for $C_{15}H_{13}N_3O_3$, C, 63.60, H, 4.63, N, 14.83. Found, C, 63.77, H, 4.46, N, 14.65.

3c: IR, $\nu_{C=N}$ (cm^{-1}), 1657, ^{1}HNMR, δ (ppm), 3.87 (s, 3H), 6.97 (d, 2H, J = 8.7 Hz), 7.18 (d, 2H, J = 8.7 Hz), 7.76–7.91 (d, d, 4H, J = 8.7 Hz, J = 8.7 Hz), 8.62–8.64 (d, 2H). Anal. cacld. for $C_{15}H_{13}FN_2O$, C, 70.30, H, 5.11, N, 10.93. Found, C, 70.26, H, 5.19, N, 10.89.

3d: IR, $\nu_{C=N}$ (cm^{-1}), 1619, ^{1}HNMR, δ (ppm), 3.87 (s, 3H), 6.97 (d, 2H, J = 8.5 Hz), 7.25–7.40 (m, 3H), 7.82 (d, 2H, J = 8.5 Hz), 8.14–8.22 (q, 1H), 8.63 (s, 1H), 9.09 (s, 1H). Anal. cacld. for $C_{15}H_{13}ClN_2O$, C, 66.06, H, 4.80, N, 10.27. Found, C, 66.34, H, 4.78, N, 10.25.

3e: IR, $\nu_{C=N}$ (cm^{-1}), 1719, ^{1}HNMR, δ (ppm), 3.88 (s, 3H), 6.98 (d, 2H, J = 8.2 Hz), 7.38 (d, 1H, J = 8.7 Hz), 7.45 (s, 1H), 7.82 (d, 2H, J = 8.2 Hz), 8.14 (d, 1H, J = 8.7 Hz), 8.62 (s, 1H) 9.02 (s, 1H). Anal cacld. for $C_{15}H_{12}Cl_2N_2O$, C, 58.65, H, 3.94, N, 9.12. Found, C, 58.19, H, 3.77, N, 9.09.

3f: IR, $\nu_{C=N}$ (cm^{-1}), 1654, ^{1}HNMR, δ (ppm), 2.41 (s, 3H), 7.26 (d, 2H, J = 8.0 Hz), 7.41 (d, 2H, J = 8.5 Hz), 7.70–7.82 (d, d, 4H, J = 8.0 Hz, J = 8.5 Hz), 8.61–8.63 (d, 2H). Anal. cacld. for $C_{15}H_{13}ClN_2$, C, 70.18, H, 5.10, N, 10.91. Found, C, 69.80, H, 4.78, N, 10.85.

3g: IR, $\nu_{C=N}$ (cm^{-1}), 1628, ^{1}HNMR, δ (ppm), 2.42 (s, 3H), 7.29 (d, 2H, J = 8.0 Hz), 7.76 (d, 2H, J = 8.0 Hz), 7.99 (d, 2H, J = 8.4 Hz), 8.30 (d, 2H, J = 8.4 Hz), 8.66–8.96 (d, 2H). Anal. calcd. for $C_{15}H_{13}N_3O_2$ C, 67.40, H, 4.90, N, 15.72. Found, C, 67.00, H, 4.69 N, 16.02.

3h: IR, $\nu_{C=N}$ (cm^{-1}), 1654, ^{1}HNMR, δ (ppm), 2.42 (s, 3H), 7.14–7.30 (q, 4H), 7.70–7.83 (q, 4H), 8.64 (d, 2H). Anal. cacld. for $C_{15}H_{13}FN_2$, C, 74.98, H, 5.45, N, 11.66. Found, C, 74.93, H, 5.75, N, 11.64.

3i: IR, $\nu_{C=N}$ (cm^{-1}), 1654, ^{1}HNMR, δ (ppm), 2.42 (s, 3H), 7.23–7.40 (m, 5H), 7.72–7.80 (d, 2H), 8.17–8.22 (q, 1H), 8.64 (s, 1H), 9.09 (s, 1H). Anal. cacld., for $C_{15}H_{13}ClN_2$, C, 70.18, H, 5.10 N, 10.91. Found, C, 70.13, H, 4.99, N, 10.89.

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3j: IR, $\nu_{C=N}$ (cm^{-1}), 1718, ^{1}HNMR, δ (ppm), 2.42 (s, 3H), 7.24–7.36 (d,d, 3H, J = 8.0 Hz, J = 8.5 Hz), 7.45 (s, 1H), 7.75 (d, 2H, J = 8.0 Hz), 8.14 (d, 1H, J = 8.5 Hz), 8.63 (s, 1H), 9.01 (s, 1H). Anal. calcd. for $C_{15}H_{12}Cl_2N_2$, C, 61.87, H, 4.15, N, 9.62. Found, C, 61.89, H, 3.97, N, 9.75.

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