A New Method for the Synthesis of Unsymmetric Azines: Alkylidene Group Exchange between Azines and Imines

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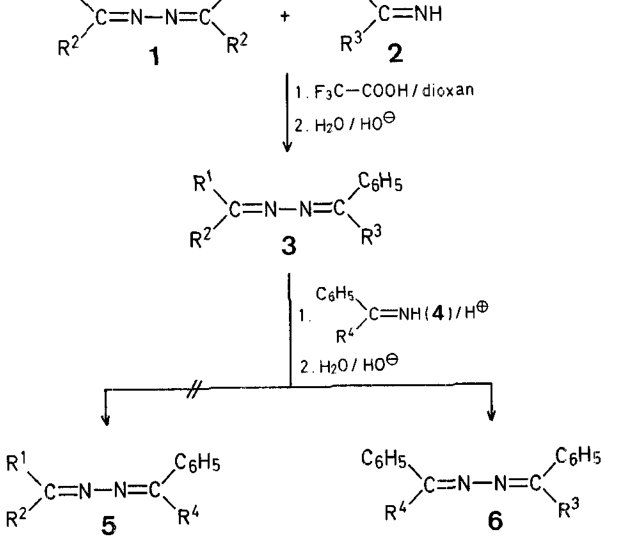
Exchange reactions between iminic compounds are known but scarcely found in the literature[1,2] and rarely provide a process of interest from the synthetic point of view[3]. In this context we report our results on the reaction of azines unsubstituted at the imino nitrogen atom.



Symmetric azines **6** ($R^3 = R^4$) and unsymmetric azines **3** and **6** ($R^3 \neq R^4$) are obtained in good yields in a simple process, which involves one or two steps, respectively, by reacting azines derived from aliphatic aldehydes or ketones **1** (R^1, R^2 = H, alkyl) with imines **2** or **4** derived from aryl ketones[4] (R^3, R^4 = alkyl, aryl) in dioxan solution at 100 °C using trifluoroacetic acid as the catalyst in a 1 : 1 : 0.05 molar ratio (Table 1). It is noteworthy that aryl substituted alkylidene groups in azines **3** do not participate in the exchange reaction. This enables a direct route to the unsymmetrical compounds as indicated in the transformation of **3** into **6** (see Scheme).

Azines are usually synthesised by reaction of carbonyl compounds with hydrazine or hydrazones[5]. While the symmetrical compounds are easily obtained in this manner, the method fails totally or partially when the preparation of the unsymmetrical azines is attempted[6], except for hydrazones of diaryl ketones. However, more complex procedures for unsymmetric azines are known[7]. For the above reasons our procedure should be the one of choice for some of these compounds.

Table 1. Azines **3** and **6** ($R^1 = CH_3$) from Imines **2** and Azines **1**

Product No.	R^2	R^3	R^4	Reaction Time [h]	Yield [%]	m.p. [°C] or b.p. [°C]/torr	
						found	reported
3a	CH_3	n-C_3H_7	—	4	76	74°/0.01	—
3b	CH_3	C_2H_5	—	3	83	66°/0.01	—
3c	CH_3	C_6H_5	—	6	90	97°/0.01	148–150°/0.4[8]
3d	C_2H_5	C_2H_5	—	4	80	83°/0.01	—
3e	C_2H_5	C_6H_5	—	5	80	109°/0.01	135°/1[8]
3f	H	C_2H_5	—	6	71	81°/0.01	—
6a	CH_3	C_6H_5	C_2H_5	8	80	76–78°	77–79°
6b	CH_3	C_6H_5	C_6H_5	10	75	163–164°	163–165°[5,8]
6c	C_2H_5	C_2H_5	C_2H_5	7	78	66–68°	66–67°[8]
6d	H	C_2H_5	C_2H_5	7	75	66–68°	66–67°[8]

Table 2. Characterisation of Compounds **3** and **6**

Product	Molecular Formula[a]	I.R. (film) $\nu_{C=N}$ [cm^{-1}]	^{1}H-N.M.R. ($CDCl_3$/TMS_{int}) δ [ppm]
3a	$C_{13}H_{18}N_2$ (202.3)	1640	0.8–1.1 (t, CH_3); 1.3–1.7 (m, CH_2); 1.9 (s, CH_3); 2.1 (s, CH_3); 2.6–2.9 (t, CH_2); 7.3–8.0 (m, H_{arom})
3b	$C_{12}H_{16}N_2$ (188.3)	1630	0.9–1.2 (t, CH_3); 1.9 (s, CH_3); 2.1 (s, CH_3); 2.6–3.0 (q, CH_2); 7.3–8.0 (m, H_{arom})
3c	—	1645	1.96 (s, CH_3); 2.02 (s, CH_3); 7.1–7.8 (m, H_{arom})
3d	$C_{13}H_{18}N_2$ (202.3)	1638	0.95–1.15 (t, CH_3); 1.1–1.3 (t, CH_3); 1.9 (s, CH_3); 2.2–2.6 (q, CH_2); 2.6–3.0 (q, CH_2); 7.3–8.0 (m, H_{arom})
3e	—	1650	0.85–1.04 (t, CH_3); 1.90 (s, CH_3); 2.14–2.40 (q, CH_2); 7.3–7.7 (m, H_{arom})
3f	$C_{11}H_{14}N_2$ (174.2)	1640	0.9–1.2 (t, CH_3); 2.1 (d, CH_3); 2.75–3.10 (q, CH_2); 7.1–8.0 (m, H_{arom}); 7.7–7.9 (q, CH)
6a	—	1600, 1575	1.0–1.3 (t, CH_3); 2.8–3.2 (q, CH_2); 7.1–7.8 (m, H_{arom})
6b	—	1595, 1575	7.1–7.8 (m, H_{arom})
6c, d	—	1610	1.0–1.3 (t, CH_3); 2.7–3.1 (q, CH_2); 7.2–8.0 (m, H_{arom})

[a] Satisfactory microanalyses obtained for all products: C ±0.24, H ±0.09, N ±0.16.

Azine (3c) Derived from Acetone and Benzophenone:

Trifluoroacetic acid (0.1 g, 1 mmol) is added under argon to a mixture of **1** ($R^1 = R^2 = CH_3$; 2.24 g, 20 mmol) and **2** ($R^3 = C_6H_5$; 3.62 g, 20 mmol) in dioxan. The mixture is heated at 100 °C for 6 h, hydrolysed with 1 normal aqueous potassium hydroxide (100 ml) and then extracted with ether (2 × 60 ml). The dry organic layer is evaporated and the oily residue distilled; yield: 4.24 g (90%); b.p. 97–98 °C/0.01 torr (Lit.[8], b.p. 148–150 °C/0.4 torr).

$C_{16}H_{16}N_2$	calc.	C 81.37	H 6.79	N 11.87
(236.3)	found	81.13	6.75	11.99

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I.R. (film): $\nu = 1645, 790, 715$ cm^{-1}.

^{1}H-N.M.R. (CDCl$_3$/TMS$_{int}$): $\delta = 1.96$ (s, CH$_3$); 2.02 (s, CH$_3$); 7.1–7.8 ppm (m, H$_{arom}$).

M.S.: $m/e = 236$ (M$^+$).

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[6] For instance, in the reaction between propiophenone (1 mol), ($R^3 = C_2H_5$) and hydrazine hydrate (1 mol) followed by treatment of the resulting hydrazone with an excess of acetone, the unsymmetrical azine **3b** was obtained in only 24% yield.

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