

Hexamethyldisilazane as an amination agent: one-pot synthesis of isoamarine and its pyridine analogue

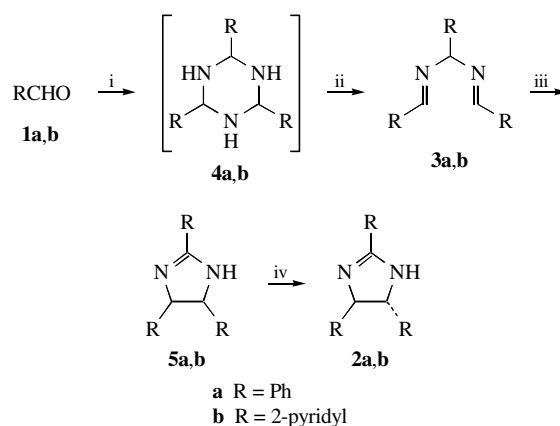
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The ability of hexamethyldisilazane to convert aldehydes into Schiff bases was adapted to the one-pot syntheses of isoamarine and its pyridine analogue.

Here, the conversion of a non-enolisable aldehyde function into a Schiff base with hexamethyldisilazane (HMDS) under LiBr catalysis *via* amination–dehydration is reported.¹ The choice of aldehydes is connected with the synthesis of vicinal diamines such as diphenylethylenediamine and its pyridine analogue. For these purposes, two aldehydes (benzaldehyde **1a** and 2-pyridinecarboxaldehyde **1b**) were used as starting materials for the synthesis of isoamarine **2a**[†] and its pyridine analogue **2b**[‡] as intermediates for the corresponding vicinal diaryl ethylenediamines. The reported procedure for 1,2-diphenylethylenediamine-1,2 includes reduction and hydrolysis of **2a**.² The multistage synthesis of **2a** is known,³ where the first product is bis-Schiff base **3a**[§] formed by deamination of a probable unstable trimeric Schiff base, *sym*-triazine **4a**. Corresponding *sym*-triazine **4b**, a derivative of aldehyde **1b**, is a stable compound.⁴ In the case of **1a**, when HMDS is an amination agent, we found that the sequence **1a** → **4a** → **3a** → **5a** → **2a** can be performed with a high yield by a one-pot procedure. Moreover, if **3a**, **5a** or **2a** is the aim product, the reaction may be stopped at any intermediate stage by changing the conditions (Scheme 1). For example, if the first intermediate of aldehyde amination by HMDS (compound **3a**) is to be isolated, the reaction is performed in a THF or diethyl ether solution with no basic catalyst added. Transformation to cyclic products requires a basic catalyst and thermal treatment. The kinetic product of cyclization, *cis*-imidazoline **5a**, may be ob-



Scheme 1 Reagents and conditions: i, HMDS, NH₃, – H₂O, DMSO, LiBr cat.; ii, – NH₃, heat; iii, heat; iv, NaOH cat.

tained by the thermal process in DMSO with sodium hydroxide catalysis under mild conditions. The reaction of HMDS with aldehyde **1b** is of special interest. Here, no catalyst addition is required, the reaction is exothermic and gives, depending on conditions, either intermediate bis-Schiff base **3b**^{||} or pyridoisoamarine **2b**. The conversion of **3b** into cyclic product **2b** is to be noted. Contrary to the conversion of **3a** into a cyclic product, where a thermal or catalytic reaction gives different products, *cis*-**5a** or *trans*-**2a**, compound **3b** gives the same isomer (probably, *trans*-**2b**) by either catalytic (NaOH) or thermal process, although the latter is much slower (*ca.* 30% conversion after 1 h at 140 °C). Deep colour formation at the NaOH-catalysed conversion of **3b** into **2b** indicates different structures of transition states for **2a** and **2b**.

References

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^{||} **Synthesis of 3b.** A solution of **1b** (0.1 mol, 9.52 ml), 0.1 mol of HMDS (20.9 ml) in 20 ml DMSO was stirred under argon. The temperature spontaneously raised to *ca.* 90 °C with ammonia evolution and when the exothermal stage subsided, this temperature was kept for additional 20 min. On cooling, the two-phase reaction mixture gave copious crystals. After filtration and washing with dioxane and toluene, the yield of **3b** was 7.4 g (86%), mp 149–150 °C. ¹H NMR (DMSO) δ: 7.7 (br. s, 1H), 6.9–8.7 (m, 12H), 5.6 (br. s, 2H).

[†] **Synthesis of 2a**, one-pot procedure. To a solution of **1a** (0.1 mol, 10.13 ml) and 0.1 g of LiBr in 20 ml of DMSO (argon) HMDS (0.11 mol, 23.05 ml) was added with stirring. The spontaneous temperature raise was accompanied by ammonia evolution (*T* ~ 50 °C). After the exothermal stage NaOH (1 g) was added, and siloxane was distilled off by a gradual raise of temperature to 120–130 °C. After 2 h at 130 °C the cooled mixture was poured onto aqueous ammonia (50 ml), and the suspension was left to stand overnight. The product was filtered off, washed with ammonia, acetone and hexane and dried on the filter. The yield of **2a** was 8.15 g (83%), mp 198–201 °C. ¹H NMR (CDCl₃) δ: 7.97–7.26 (m, 15H), 4.93 (s, 2H, CH), 1.7 (br. s 1H NH).

[‡] **Synthesis of 2b.** One-pot procedure. A mixture of **1b** (0.1 mol, 9.52 ml), 0.1 mol of HMDS (20.9 ml) and 20 ml of DMSO was stirred under argon. The temperature gradually raised to *ca.* 90 °C (30 min) with ammonia evolution. When the temperature started to drop, the mixture was heated to 90 °C for 15 min. To the cooled heterogeneous mixture (the upper layer of siloxane) 1.2 g NaOH was added to immediately give a deep red colour. By gradual heating up to 135 °C, siloxane was distilled off and, after 1 h at 130 °C, the cooled mixture was treated with 1.8 ml of AcOH and then 30 ml of ammonia. After 12 h at room temperature, the suspension was filtered, washed with ammonia (2×10 ml), the filter cake was dried by suction and washed with diethyl ether (2×10 ml). After drying, the product was dissolved in 60 ml of hot toluene and filtered through a silica gel bed. On cooling, the precipitated crystals of **2b** were filtered off and washed with toluene and hexane. Total yield 6.8 g, mp 132–133 °C. ¹H NMR (DMSO) δ: 8.0 (br. s, 1H, NH), 7.2–8.7 (m, 12H, Py), 5.25 (s, 2H, CH).

[§] **Synthesis of 3a.** The mixture of 0.1 mol of **1a**, 0.1 g LiBr, 0.1 mol of HMDS and 20 ml of THF was stirred under argon at 50–80 °C until evolution of ammonia subsided (*ca.* 2 h). The solvent was removed on a rotary evaporator, and the residue was dissolved in hot hexane. The solution was filtered through a silica gel bed and cooled. After filtration, the yield of **3a** was 9.33 g (94%), mp 101–102 °C. ¹H NMR (DMSO) δ: 6.05 (s, 1H, CH), 7.3–7.9 (m, 15H, ArH), 8.7 (s, 2H, CH).