Supplementary Material (ESI)

Lewis Base-catalyzed Three-Component Strecker Reaction On Water. An Efficient Manifold for the Direct α-Cyanoamination of Ketones and Aldehydes

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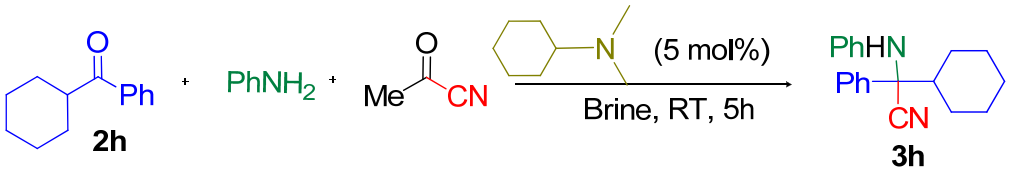
General remarks. ^{1}H NMR and ^{13}C NMR spectra of $CDCl_3$ solutions were recorded either at 400 and 100 MHz or at 500 and 125 MHz (Bruker Ac 200 and AMX2-500), respectively. FT-IR spectra were measured in chloroform solutions using a Perkin Elmer FT-IR Spectrum BX spectrophotometer. Mass spectra (low resolution) (EI/CI) were obtained with a Hewlett-Packard 5995 gas chromatograph/mass spectrometer. High-resolution mass spectra were recorded with a Micromass Autospec mass spectrometer. Microanalyses were performed with a Fisons Instruments EA 1108 carbon, hydrogen, and nitrogen analyzer. Analytical thin-layer chromatography plates used were E. Merck Brinkman UV-active silica gel (Kieselgel 60 F254) on aluminum. Flash column chromatography was carried out with E. Merck silica gel 60 (particle size less than 0.020 mm) using appropriate mixtures of ethyl acetate and hexanes as eluent. Melting points are uncorrected. Compounds **3b-g** and **3i-t** have been fully described elsewhere.



2-Cyclohexyl-2-phenyl-2-(phenylamino)acetonitrile (3h). To a stirred (250 rpm) salt-saturated aqueous solution (brine) (7 ml) is sequentially added acetyl cyanide (0.1 ml;1.4 mmol), N,N-dimethyl cylclohexylamine (0.004 ml; 0.037 mmol), Cyclohexyl phenyl ketone (**2h)** (0,132 g; 0.70 mmol) and aniline (0,065 g, 0.70 mmol)(dropwise) to form a biphasic system. The stirring rate is increased to 1200 rpm and after a few minutes, the biphasic system breaks into small drops. After 24 h the reaction is quenched by addition of dichloromethane and the organic materials are recovered in dichloromethane. Concentration and flash chromatography (ethyl acetate-hexanes:

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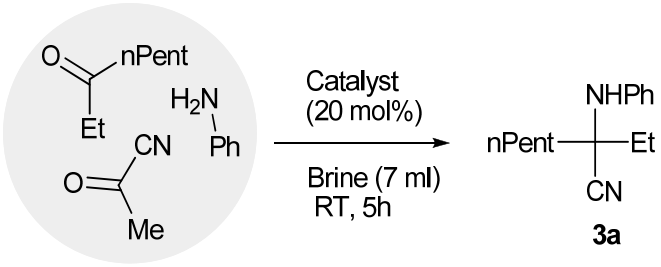
20/80) yields pure compound **3h**. Crystalline (needles, CH_2Cl_2), ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.05-1.35 (m, 6H), 3.75 (s, 3H), 1.6-2.10 (m, 5H), 6.51 (d, ^3J(H,H)=8.1 Hz, 2H), 6.75 (t, ^3J(H,H)=7.4 Hz, 1H), 7.03-7.1 (m, 1H), 7.32-7.40 (m, 3H), 7.51-7.56 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 25.8, 26, 26.1, 27.6, 28, 49.8, 65.6, 115.7, 119.6 (x2C),126.6 (x2C), 128.4, 128.6 (x2C), 128.9 (x3C), 137, 143.7; IR ($CHCl_3$, cm^{-1}): 3435 (NH), 2230,5 (CN); Anal. Calcd. for $C_{20}H_{22}N_2$: C, 82.72; H, 7.64; N, 9.65. Found: C, 82.77; H, 7.83; N, 9.28; m.p. 215.1-216.4ºC.

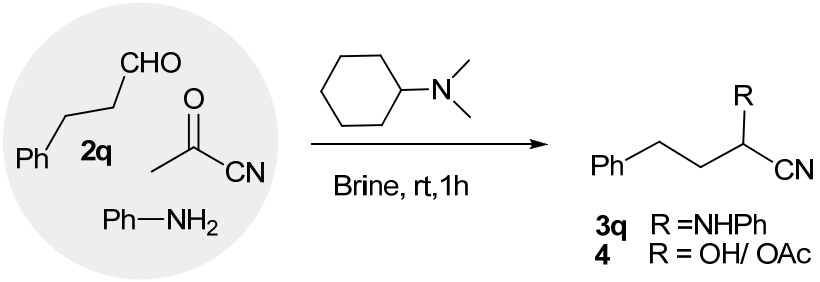
Table 1. Lewis Base-catalyzed three-component reaction of 3-octanone (**2a**), aniline and acetyl cyanide on brine.[a]



Entry	Catalyst	pKa	AcCN (equiv.)	Yield (%)[b]
1	N,N-dimethyl cyclohexylamine	10.7	1	49
2	N,N-dimethyl cyclohexylamine	10.7	2	≥95
3	N,N-diisopropyl ethylamine	11	2	85
4	DABCO	8.7	2	78
5	Pyridine	5.2	2	87
6	Quinine	7.7	2	89
7	None		2	≤10%

[a] See general procedure for experimental details.[b] Yields of analytically pure products.

Table 2. Chemoselective formation of α-aminonitriles **3q**.[a]



Entry	**2q** (equiv.)	Aniline (equiv.)	Catalyst (mol%)	Yield(%)[b]	**3q**:**4**
1	1	1	5	70	100:0
2	2	1	5	≥95	100:0
3	2	1	100	≥95	100:0

[a] See general procedure for experimental details. [b]Yields of analytically pure products.