Conversion of aldehydes to amides *via* dimethyl sulfoxide oxidation of the corresponding α-aminonitriles

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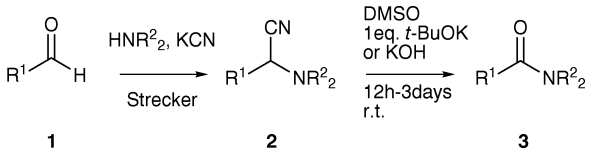
Unsaturated, aryl and heteroaryl *N*-dialkyl-α-aminonitriles are easily oxidized at room temperature to their corresponding tertiary *N*-dialkylamides by using dimethyl sulfoxide and bases like Bu^{t}OK or KOH. The reaction offers an efficient two-step conversion of aldehydes to *N*-dialkyamides.

Owing to their ease of operation and effectiveness, oxidations with activated dimethyl sulfoxide (DMSO) are regularly employed in organic synthesis. A variety of different reactions such as the Kornblum,[1] Pfitzner-Moffat,[2] Swern[3] and Corey-Kim[4] reactions, amongst others[5] have become classical procedures, especially those utilised for the conversion of alcohols to carbonyl compounds.

Only a few methods for the direct conversion of aldehydes to their corresponding amides have been reported so far, through electrophilic amination of *O*-(trimethylsilyl) aldehyde cyanohydrins,[6] and through radical-mediated oxidation of aldehydes to acid bromides.[7] Two papers have also reported a base-catalysed O_2-autoxidation of α-aminonitriles.[8]

We now wish to report a new DMSO-based reaction, the oxidation of unsaturated, aryl and heteroaryl *N*-dialkyl-α-aminonitriles to their corresponding *N*-dialkylamides. Since the α-aminonitriles are easily accessible from the parent aldehydes, the reaction allows an efficient two-step conversion of aldehydes to tertiary amides.

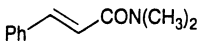
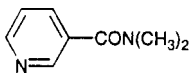
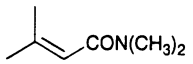
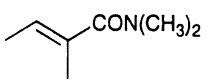
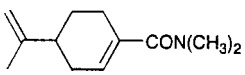
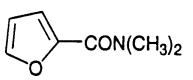
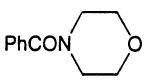
The oxidation was performed by simply adding the α-aminonitriles **2** (obtained from the aldehydes **1** by Strecker synthesis[9]) to a DMSO solution containing one equivalent of potassium *tert*-butoxide or potassium hydroxide, and subsequently stirring at room temperature for 12 h–3 days (Scheme 1).† After work-up and purification by distillation or chromatography, the *N*-dialkylamides **3a**–**h** were isolated in satisfactory yields and were fully characterized (Table 1). A relatively broad range of dialkylaminonitriles bearing a heterocycle (furyl, pyridyl), an aromatic or an unsaturated chain could be



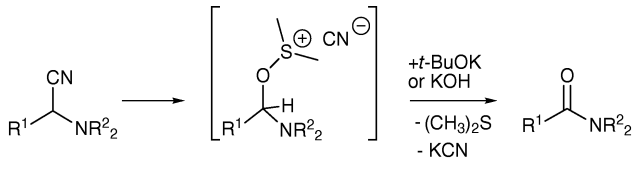
1 2 3

Scheme 1

Table 1 Reaction conditions and yields for the oxidation of the α-aminonitriles **2** to the amides **3**

Entry	Amide	Reaction time[a]	Yield[b](%)	Physical characteristics[c]/°C Torr^{-1}
3a		3 days	64 (50)	m.p.: 95–97 (Lit.[10] 95–96)
3b		3 days	79 (66)	m.p.: 47–49 (Lit.[11] 48–49)
3c		12 h	89 (70)	m.p.: 40 (Lit.[10] 41–43)
3d		3 days[d]	43 (30)	Oil[12]
3e		3 days	56 (50)	Oil[13]
3f		3 days	66 (44)	See typical procedure
3g		3 days	91 (76)	b.p.: 55–60/0.05 (Lit.[6]–)
3h		3 days	68 (65)	b.p.: 83–84 (Lit.[14]–)

[a] **2** (5 mmol), Bu^{t}OK (5 mmol), DMSO (15 ml), room temperature. [b] Value in parentheses is calculated from **1**. [c] Uncorrected. The spectroscopic data are in accordance with the literature data. [d] **2** (5 mmol), KOH (5 mmol), DMSO (15 ml), room temperature.



Scheme 2

transformed, but attempts to carry out the oxidation on aminonitriles bearing alkyl chains (**R** = C_5H_{11}, Et, **Bu**^{t}) were unsuccessful.

DMSO was unambiguously implicated in the oxidation process since no transformation occurred in its absence. In addition, dimethyl sulfide resulting from the reduction of DMSO was clearly detected by its characteristic odour. We also ensured that oxygen was not involved in the process, by carrying out all the reactions in dry and degassed DMSO, under an argon atmosphere.

Bearing this in mind, a reasonable mechanism for the oxidation might involve the formation of an alkoxysulfonium intermediate **A** (Scheme 2) after substitution of the cyanide by DMSO in the α-aminonitriles **2**. This intermediate **A** could then form the final products through the corresponding sulfonium ylide, intramolecular proton transfer and loss of dimethyl sulfide, as is usually described for related reactions.[5]

In summary, the transformations of Scheme 1 are experimentally simple, mild and efficient and the second step constitutes a new application of DMSO in oxidation reactions.

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Notes and references

† Typical procedure for the preparation of **3f**: Under an argon atmosphere, **Bu**^{t}OK (0.56 g, 5 mmol) was dissolved in 10 ml of degassed DMSO and stirred at room temperature for 10 min. A solution of the aminonitrile **2f** (1.02 g, 5 mmol) in 5 ml of DMSO was added dropwise and the resulting mixture stirred at room temperature for 3 days. After adding 30 ml of ether, the organic phase was washed with 5% aqueous solution of KOH to eliminate the residual DMSO. The organic layer was washed with a saturated solution of $NaHCO_3$, dried over $MgSO_4$ and the solvent removed *in vacuo*. Purification by column chromatography (neutral alumina, activity grade III, ether) and distillation (73 °C/0.01 Torr) afforded the amide **3f**, isolated as a yellow oil (0.64 g, 66%). IR (neat): 3090, 3000–2840, ν(CO) 1630, 1500, 1400, 1190, 1070, 890 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.51 (s, 3H), 1.51–2.4 (m, 7H), 2.95 (s, 6H), 4.68 (m, 2H), 5.77 (m, 1H); MS : *m/z* (%) 193 (M^+, 96), 192 (16), 178 (17), 165 (50), 164 (36), 152 (34), 150 (27), 149 (53), 148 (24), 147 (27), 126 (18), 121 (42), 113 (24), 111 (11), 105 (30), 93 (96), 91 (34), 82 (45), 81 (46), 80 (11), 79 (86), 77 (31), 72 (100), 67 (18), 55 (19), 53 (58), 45 (11), 44 (26), 41 (24) ; anal. calcd for $C_{12}H_{19}NO$ (193.29): C, 74.57; H, 9.9; N, 7.25. Found: C, 74.10; H, 10.2; N, 7.38%.

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