

Aluminium chloride and sodium iodide (AlCl₃-NaI): a versatile dehydrating agent†

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AlCl₃-NaI is an efficient reagent for dehydration of oximes, amides and the Beckmann rearrangement of ketoximes to anilides; it forms isoquinoline derivatives **8(a–c)** by cyclodehydrating amides **7(a–c)** in very good yields at room temperature.

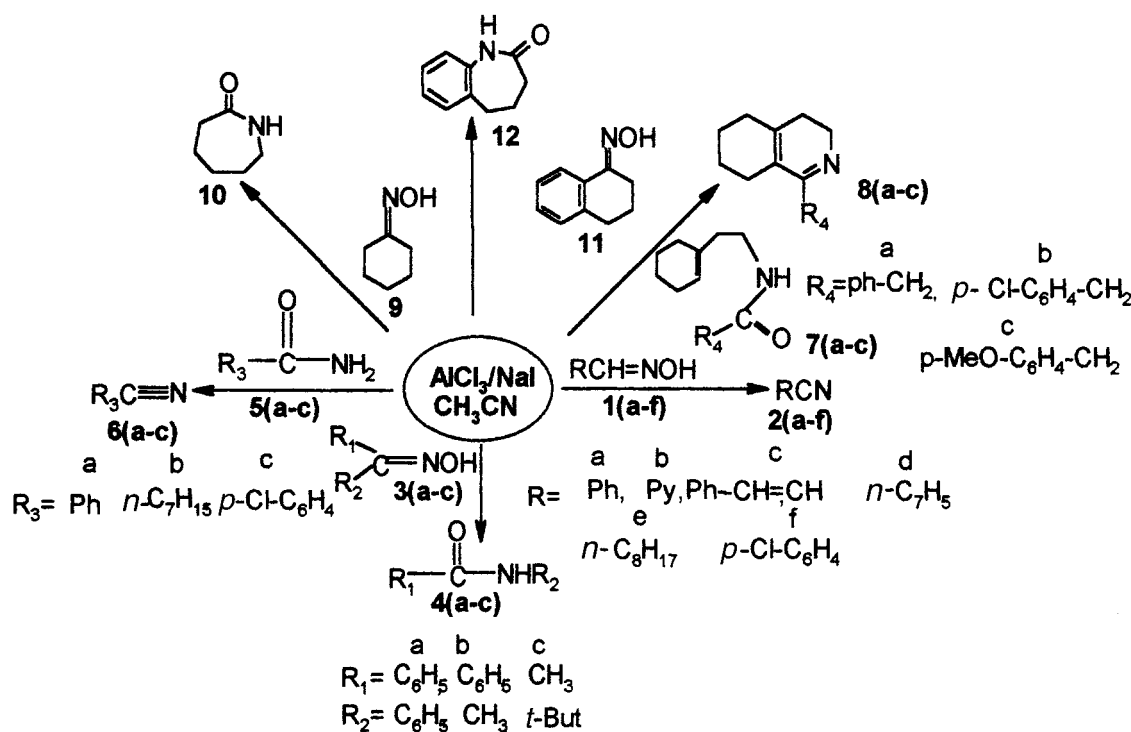
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Compounds and nitrile group functionality play an important role in organic syntheses.¹ Many synthetic² and biologically active compounds³ are derived from nitrile group participation.

A number of methods have been developed for the conversion of aldoximes and amides into nitriles using dehydrating agents such as: 4,6-diphenyl-2-methylthiopyrylium tetrafluoroborate,⁴ Vilsmeier reagents,⁵ sulphuryl chloride fluoride,⁶ phosphorus tri-iodide,⁷ chlorosulfonyl isocyanate,⁸ trifluoroacetic anhydride,⁹ iodotriethoxyphosphoranes,¹⁰ benzene-sulfonyl chloride,¹¹ diphosphorus tetraiodide,¹² phosphoryl halide and imidazolide,¹³ selenium dioxide,¹⁴ phosphorus trichloride,¹⁵ chlorodimethylsulfonium chloride,¹⁶ triflic anhydride,¹⁷ dicyclohexylcarbodi-mide,¹⁸ phenyl chlorosul-fite,¹⁹ phosphonitrile chloride,²⁰ carbenes,²¹ 1,1-dicarbonyl-di-imidazole,²² cyanuric chloride.²³

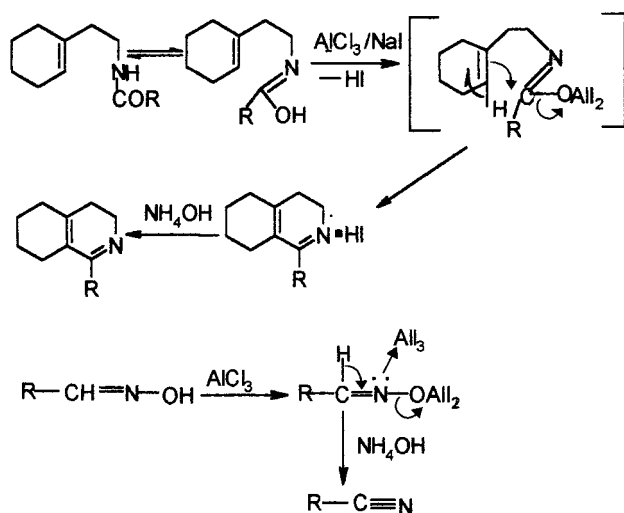
The chemistry of aluminium has received renewed interest and in recent years the versatility of aluminium iodide has been demonstrated.²⁴ However, the chemistry of aluminium chloride in presence of sodium iodide is less explored.^{25,26} A continuation of our interests in aluminium chemistry²⁷ has led us to report here, the novel utility of AlCl₃-NaI in acetonitrile as a mild, efficient and versatile dehydrating reagent for the conversion of aldoximes and amides into nitriles and ketoximes into anilides (Beckmann rearrangement)²⁸ and the intramolecular cyclodehydration of amides to isoquinolines (Scheme 1).

Addition of 1 equivalent of benzaldoxime (**1a**, R = Ph) to 2 equivalents of AlCl₃ = NaI and reflux under anhydrous condition in acetonitrile for 2.5 h, gave benzonitrile (**2a**) in 95% yield. Substituted aromatic and aliphatic oximes afforded corresponding **2(b–f)** in high yields (Table 1).



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† This is a Short Paper, there is therefore no corresponding material in *J. Chem. Research (M)*.



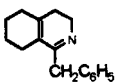
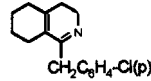
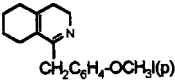

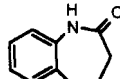
It was observed that the reagent was applicable to aliphatic, aromatic and heterocyclic aldoximes. Both (*E*) and (*Z*) iso-

mers of oximes could be converted into nitriles [in most cases the oximes used were a mixture of (*E*) and (*Z*) isomers]. When the reagent was treated with benzophenone and acetophenone oximes interestingly the Beckmann rearrangement occurred and gave benzanilide and acetanilide respectively **4(a-b)**.

Moreover, when the reagent was reacted with amides **5a-5c**, it gave nitriles in fair to good yields **6a-6c**, and in the case of amides **7a-7c**, it was observed that intramolecular cyclodehydration occurred quantitatively to produce synthetically useful reduced isoquinoline derivatives **8a-8c** [intermediate for anti-tussive drug Dextromethorphan and its analogues]. Therefore, it is hoped that it would be an efficient alternative²⁹ reagent for the Bischler Napieralski Reaction where hazardous reagents like P_2O_5 , $POCl_3$, $POCl_3/P_2O_5$ have been used.³⁰ The above conversions did not proceed at all in the absence of NaI even at reflux temperature.

Regarding the mechanism of the above reaction, it is proposed that sodium iodide reacts with aluminium chloride to generate aluminium iodide *in situ*, which participated in the dehydration of oximes, or amides to nitriles, and in the intramolecular cyclodehydration of amides **7a-7c** to produce isoquinoline derivatives as shown below (Scheme 2).

Table 1 Synthesis of nitriles, anilides and isoquinolines

Entries	Products	Yields/% ^a	Reaction time/h	b.p. (C/Torr) found	or	m.p./°C reported
2a	Ph-CN	95	2.5	b.p. 68-69/10		b.p. 69-70/10 ¹⁴
2b	Ph-CH = CH-CN	90	2.0	b.p. 108-109		b.p. 95/1.5 ⁶
2c	3-Py-CN	92	2.5	mp. 50-1 (PE)		m.p. 50 ^b
2d	<i>n</i> -C ₇ H ₁₅ -CN	85	3.0	b.p. 79-80/10		b.p. 79/10 ¹¹
2e	<i>n</i> -C ₈ H ₁₇ -CN	80	3.0	b.p. 222-223		b.p. 221-224 ^b
2f	4-Cl-C ₆ H ₄ -CN	92	1.5	m.p. 89-91		m.p. 90-92 ^b
4a	Ph-CO-NH-Ph	85	3.5	m.p. 162-165		m.p. 164-166 ^b
4b	Ph-CO-NH-CH ₃	94	2.5	m.p. 110-115		m.p. 113-115 ^b
4c	Me-CO-NH-t-but	Nil	8.0	-		-
6a	Ph-CN	96	1.5	b.p. 68-69/10		b.p. 69-70/10 ¹⁴
6b	<i>n</i> -C ₇ H ₁₅ -CN	91	2.0	b.p. 79-80/10		b.p. 79/10 ¹¹
6c	4-Cl-C ₆ H ₄ -CN	88	1.5	m.p. 90-91		m.p. 90-92 ^b
8a		90	2.5 ^c	-		-
8b		92	3.5 ^c	-		-
8c		91	3.2 ^c	-		-
10		85	2.2	m.p. 71-72		m.p. 70-72 ^b
12		82	2.4	m.p. 135-141		m.p. 142-143 ³¹

^aThe structures of the compounds were determined by IR, ¹H NMR and mass spectrometer analyses, ^bcompared with the authentic samples from Aldrich chemicals, ^cthe spectral data of the compounds **8a-8c** are given below.^{32,29}

8a: IR (KBr cm^{-1}), 1650, 1450, 3000; ¹H NMR (60 MHz, $CDCl_3$ δ ppm) 1.00-1.73 (m, 12H), 3.10 (s, 2H), 3.60 (s, 3H), 6.20 (m, 5H); Mass M^+ 225.

8b: IR (KBr cm^{-1}), 1650, 1450, 3000; ¹H NMR (60 MHz, $CDCl_3$ δ ppm) 1.00-1.72 (m, 12H), 3.10 (s, 2H), 3.60 (s, 3H), 6.60 (d, 2H), 7.00 (d, 2H); Mass M^+ 259.

8c: IR (KBr cm^{-1}), 1650, 1450, 2995; ¹H NMR (60 MHz, $CDCl_3$ δ ppm) 1.00-1.70 (m, 12H), 3.10 (s, 2H), 3.60 (s, 3H), 6.50 (d, 2H), 6.90 (d, 2H); Mass M^+ 255.

Experimental

M.p.s. were determined on a Buchi apparatus. Mass spectra were recorded in Finnigan-MAT (INCIOS -50) spectrophotometer. IR spectra were recorded on a Perkin Elmer 237 B spectrophotometer and ¹H NMR spectra were recorded on Varian T-60/90 MHz spectrometers. Commercially available anhydrous aluminium chloride and sodium iodide [Aldrich] were used directly. Acetonitrile was used after distillation over phosphorus pentoxide. Oximes and amides were prepared following standard procedures.

Typical procedure: Anhydrous aluminium chloride (0.264 g, 2 mmol) and sodium iodide (0.900 gm, 6 mmol) was added to dry acetonitrile (25 ml) and the mixture stirred magnetically for half hour at room temperature under nitrogen. Benzaldoxime **1a** (0.121 g, 1 mmol) was added and stirring was continued under reflux for another 2.5 h. The progress of the reaction was monitored by TLC. The reaction mixture was poured into ice cold ammonical water solution (10%) and extracted with diethyl ether. The organic layer was washed with water (2 × 100 ml), dried and the solvent was distilled off under reduced pressure to give **2a**, 0.098 g, 95% yield. Similarly, the compounds [**2b–2f**, **4a–4c**, **6a–6c**, **10** and **12**] were prepared (Table 1). The compounds **8a–8c** were prepared by stirring the reaction mixture at room temperature and worked-up as above.

In conclusion, it may be stated that we have discovered a new, mild, efficient and versatile dehydrating agent for amides and oximes which may have wide applications in organic synthesis in the future.

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