Homogeneous Catalysis Involving Lanthanoid(III) Ions: Formation of 4-Substituted-2,6-dimethylpyrimidines

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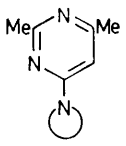
Summary Lanthanum(III) perchlorate has been found to catalyse a novel reaction between cyclic secondary amines and acetonitrile giving 4-substituted-2,6-dimethylpyrimidines.

PREVIOUS studies have established that polydentate aliphatic amines form high-co-ordinate, thermodynamically stable complexes with lanthanoid(III) ions in acetonitrile.[1] Extending our investigations to monodentate cyclic secondary amines, we have discovered that a catalytic quantity of anhydrous $La(ClO_4)_3$† in acetonitrile catalyses a novel reaction between the amine and solvent, resulting in the evolution of ammonia with formation of 4-substituted-2,6-dimethylpyrimidines (**1**). The catalytic activity demonstrated by the La^{III} ion in these systems is surprising in the light of the previous studies cited above. Furthermore, a

† $Pr(ClO_4)_3$ has also been used as a catalyst and it is expected that all Ln^{III} ions are catalytically active in this system.

survey of the literature reveals the limited use of Ln^{III} ions as catalysts in organic reactions, *e.g.*, the hydrolysis of esters[2] and the decarboxylation of acids.[3]



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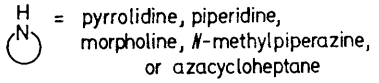
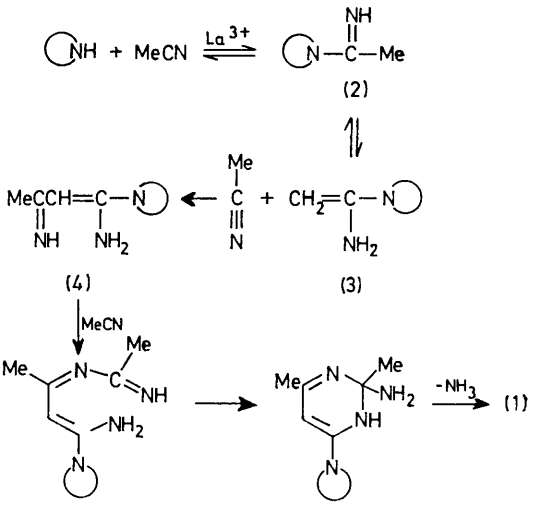


The pyrimidines (**1**) were prepared by refluxing an acetonitrile (400 mmol) solution containing the amine (100 mmol) and $La(ClO_4)_3$ (2 mmol) under nitrogen. The rate of conversion, as monitored by n.m.r. spectroscopy, is dependent upon the mole ratio of amine to metal-ion; *e.g.*, after 48 h, 14, 37, and 50% conversions for ratios of 100 : 1, 50 : 1, and 25 : 1, respectively.‡ The products were collected by vacuum distillation, and characterized by their elemental analyses and spectral data. 4-Morpholino-2,6-dimethylpyrimidine was also compared with an authentic sample.

A mechanism accounting for the formation of the pyrimidines is shown in the Scheme. The n.m.r. spectrum of a typical reaction mixture reveals initial formation of an amidine (**2**), with eventual dimunition of the amidine signals and a corresponding growth of peaks characteristic of (**1**). The amidine intermediate can be isolated by vacuum distillation of the reaction mixture prior to the formation of significant quantities of pyrimidine.§ A tautomerism, *viz.* (**2**) ⇌ (**3**), is required to account for the formation of the C–C bond of the pyrimidine.

The role of the La^{III} ion in these systems appears twofold: namely, (i) to promote amidine formation, and (ii) to assist in the ring-formation steps. The activity of the metal ion in



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the first role may be to increase polarization of the CN bond of acetonitrile thus facilitating attack by the amine. In the absence of the catalyst no amidine is formed. That the metal ion promotes ready deuteriation of Me and C=NH protons of the amidine upon dissolution in CD_3CN containing La^{III} ion supports the proposed equilibrium, (**2**) ⇌ (**3**). Refluxing the amidine in acetonitrile results in extensive dissociation and formation of only traces of pyrimidine, thus confirming the involvement of the lanthanoid ion in the ring-formation steps. The La^{III} ion may effect ring closure by catalysing the addition of intermediates such as (**3**) and (**4**) to acetonitrile.

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‡ The optimum conditions have not been explored.

§ The amidines were characterized by elemental analysis and n.m.r. data. Although amidines have been synthesized using Lewis acid catalysts such as $AlCl_3$, $FeCl_3$ and $ZnCl_2$, pyrimidine formation in these systems has not been reported (S. R. Sandler and W. Karo, 'Organic Functional Group Preparation,' Vol. III, Academic Press, New York, 1972, p. 205).

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[3] A. Wood, *Trans. Faraday Soc.*, 1966, **62**, 1231; E. Gelles and K. S. Pitzer, *J. Amer. Chem. Soc.*, 1955, **77**, 1974.