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SHORT COMMUNICATIONS

Crystal Hydrates $LnCl_3 \cdot 6H_2O$ and $Ln(NO_3)_3 \cdot 6H_2O$ as Catalysts in the Synthesis of 2,3,5-Trialkylpyridines by Reaction of Ammonia with Aliphatic Aldehydes

R. G. Bulgakov, S. P. Kuleshov, A. R. Makhmutov, and U. M. Dzhemilev

Institute of Petroleum Chemistry and Catalysis, Russian Academy of Sciences,
pr. Oktyabrya 141, Ufa, 450075 Bashkortostan, Russia
e-mail: ink@anrb.ru

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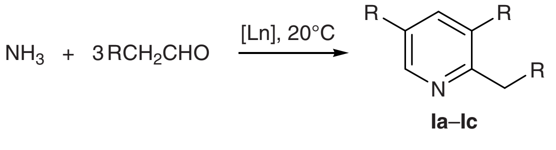
Systems based on Zr, Fe, Cr, Co, Ni, Pd, and Mg complexes and Et_3Al are efficient catalysts in the synthesis of alkyl-substituted pyridines [1]. Disadvantages of these systems include high reaction temperature (180–200°C) and pressure and the use of flammable and explosive Et_3Al. By contrast, trifluoromethanesulfonate lanthanide complexes $Ln(OTf)_3$ ensure preparation of pyridine bases at room temperature in the absence of Et_3Al [2–4]. However, almost stoichiometric amounts (up to 50%) of $Ln(OTf)_3$ are necessary to attain the maximal yield (40–80%) of the target products. Therefore, search for new more effective catalysts for the synthesis of alkyl-substituted pyridines is an important problem. We previously found [5] that $LnCl_3 \cdot 6H_2O$ crystal hydrates exhibit a high catalytic activity in the synthesis of alkyl-substituted quinolines and phenanthrolines at 20°C. In the present work we examined the catalytic activity of $LnCl_3 \cdot 6H_2O$ and $Ln(NO_3)_3 \cdot 6H_2O$ ([Ln]) in the synthesis of 2,3,5-trialkylpyridines **I** by reaction of ammonia with aliphatic aldehydes.

Compounds **I** were formed in up to 82% yield at 20°C (see Experimental) in polar solvents (dimethylform-amide and dimethyl sulfoxide) in the presence of [Ln]. The process is characterized by complete conversion of ammonia, and a catalytic amount of [Ln] (2 mol %) is sufficient to catalyze the reaction.



Ia–Ic

R = Et (**a**), Pr (**b**), Bu (**c**); [Ln] = $LnCl_3 \cdot 6H_2O$, $Ln(NO_3)_3 \cdot 6H_2O$; Ln = Pr, Nd, Tb.

Apart from the corresponding pyridines, the reaction mixtures contained unidentified tarry materials (18–26%) which remained in the still residue after vacuum fractionation; presumably, they were formed by crotonization of the initial aldehydes. With rise in temperature, the yield of the target products decreased, while the amount of tars increased. The aldehyde and solvent nature only slightly influenced the selectivity and the yield of compounds **I**. In the reaction of ammonia with butyraldehyde, the examined lanthanide catalysts can be arranged in the following series with respect to the yield of pyridine **Ia** (%): $PrCl_3 \cdot 6H_2O$ (82) > $NdCl_3 \cdot 6H_2O$ (78) > $TbCl_3 \cdot 6H_2O$ (61); $Pr(NO_3)_3 \cdot 6H_2O$ (80) > $Nd(NO_3)_3 \cdot 6H_2O$ (77) > $Tb(NO_3)_3 \cdot 6H_2O$ (60). Thus $PrCl_3 \cdot 6H_2O$ possesses the strongest catalytic activity. The catalytic activity weakens as the lanthanide ionic radius decreases.

After addition of aldehyde to an aqueous ammonia solution (before addition of catalyst), it is necessary to separate the organic phase from aqueous, and the catalyst should be added to the organic phase. Our attempts to carry out the process in a one-pot mode, by mixing in succession a solution of catalyst, aqueous ammonia, and aldehyde, resulted in precipitation of $Ln(OH)_3$, and the catalysis became ineffective.

Thus lanthanide crystal hydrates $LnCl_3 \cdot 6H_2O$ and $Ln(NO_3)_3 \cdot 6H_2O$ make it possible to perform condensation of ammonia with aldehydes under mild conditions (20°C) and ensure preparation of trialkyl-substituted pyridines **I** in up to 82% yield. The examined catalysts are more advantageous than Ln(OTf)$_3$ due to their low cost and accessibility; they exhibit catalytic effect at much lower concentration and provide direct formation of substituted pyridines rather than of the corresponding pyridinium salts.

Substituted 2,3,5-trialkylpyridines. A glass finger reactor equipped with a magnetic stirrer was charged with 60 mmol of the corresponding aldehyde and cooled to 0°C, 1.5 ml (20 mmol) of 25% aqueous ammonia was added, and the mixture was vigorously stirred for 1–2 min. The mixture was allowed to settle down, the upper organic layer was withdrawn, a solution of 0.4 mol of the catalyst in 2 ml of DMF or DMSO was added to the organic phase, and the mixture was stirred for 24 h at 20°C. The product was extracted into diethyl ether (3×50 ml), the extracts were combined and dried over MgSO$_4$, the solvent was distilled off, and the residue was subjected to fractional distillation under reduced pressure.

3,5-Diethyl-2-propylpyridine (Ia). Yield 82% (DMF), 80% (DMSO), bp 75–78°C (1 mm). ^{1}H NMR spectrum, δ, ppm: 0.98 m (3H, CH$_3$), 1.18 m (6H, CH$_3$), 1.32 m (2H, CH$_2$), 2.54–2.66 m (4H, CH$_2$), 2.72 q (2H, CH$_2$), 7.25–8.21 d (2H, 4-H, 6-H). ^{13}C NMR spectrum, δ$_C$, ppm: 14.06 q (C^{13}), 14.70 q (C^{11}), 15.19 q (C^9), 22.79 t (C^{12}), 24.89 t (C^8), 25.47 t (C^{10}), 36.30 t (C^7), 135.29 d (C^4), 136.07 s (C^3), 136.36 s (C^5), 145.83 d (C^6), 157.04 s (C^2). Found, %: C 81.92; H 10.25; N 7.83. C$_{12}$H$_{19}$N. Calculated, %: C 81.35; H 10.73; N 7.92.

2-Butyl-3,5-dipropylpyridine (Ib). Yield 77% (DMF), bp 80–82°C (1 mm). ^{1}H NMR spectrum, δ, ppm: 0.90 m (9H, CH$_3$), 1.40 m (2H, CH$_2$), 1.53 m (6H, CH$_2$), 2.53 m (4H, CH$_2$), 2.63 m (2H, CH$_2$), 7.17–8.15 d (2H, 4-H, 6-H). ^{13}C NMR spectrum, δ$_C$, ppm: 13.11 q (C^{16}), 13.60 q (C^{13}), 14.25 q (C^{10}), 22.90 t (C^{15}), 23.31 t (C^{12}), 24.23 t (C^9), 25.07 t (C^{14}), 28.63 t (C^8), 31.46 t (C^{11}), 34.30 t (C^7), 133.23 d (C^4), 135.54 s (C^3), 136.82 s (C^5), 141.47 d (C^6), 158.10 s (C^2). Found, %: C 81.93; H 11.55; N 6.52. C$_{15}$H$_{25}$N. Calculated, %: C 82.19; H 11.42; N 6.39.

3,5-Dibutyl-2-pentylpyridine (Ic). Yield 74% (DMF), bp 105–108°C (1 mm). ^{1}H NMR spectrum, δ, ppm: 0.92 m (9H, CH$_3$), 1.32 m (14H, CH$_2$), 2.50 q (4H, CH$_2$), 2.70 m (2H, CH$_2$), 7.10–8.20 d (2H, 4-H, 6-H). ^{13}C NMR spectrum, δ$_C$, ppm: 13.07 q (C^{19}), 13.07 q (C^{15}), 14.11 q (C^{11}), 22.26 t (C^{18}), 22.26 t (C^{14}), 22.49 t (C^{10}), 28.40 t (C^8), 30.44 t (C^{12}), 32.64 t (C^{17}), 32.87 t (C^9), 33.01 t (C^{13}), 33.52 t (C^{16}), 34.56 t (C^7), 135.22 d (C^4), 136.28 s (C^3), 136.55 s (C^5), 145.89 d (C^6), 159.06 s (C^2). Found, %: C 82.27; H 11.93; N 5.80. C$_{18}$H$_{31}$N. Calculated, %: C 82.76; H 11.88; N 5.36.

The ^{1}H and ^{13}C NMR spectra were recorded on a Jeol FX 90Q spectrometer using CDCl$_3$ as solvent and tetramethylsilane as internal reference. The elemental compositions were determined on a Carlo Erba 106 analyzer.

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