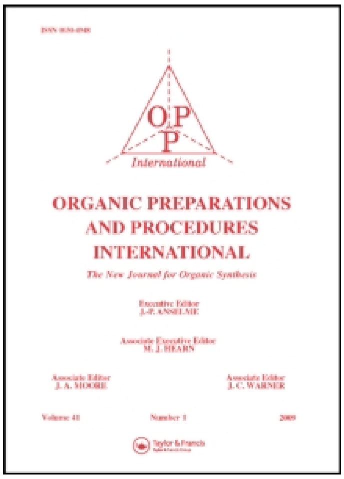

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ALKYLATION OF LITHIUM ALUMINUM HYDRIDE REDUCTION PRODUCTS OF AMIDES

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ALKYLATION OF LITHIUM ALUMINUM HYDRIDE REDUCTION PRODUCTS OF AMIDES

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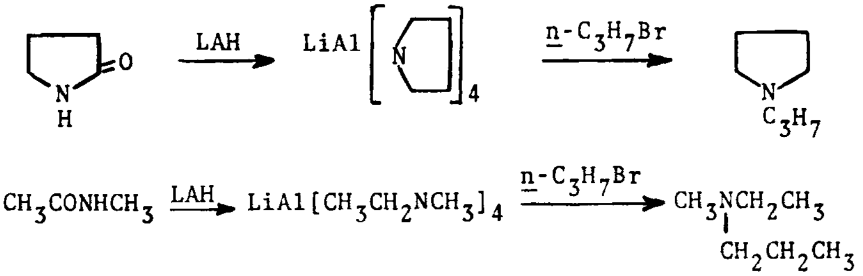
Tertiary amines have been prepared from lithium aluminum hydride reduction products of amides by treatment with esters[1,2] and are often by-products in such reduction if ethyl acetate is used to decompose the excess lithium aluminum hydride.[3] Based on these observations, a method[2] was developed for the preparation of tertiary amines by the alkylation of secondary amines with esters and lithium aluminum hydride. However, low yields of tertiary amines are obtained with esters other than ethyl acetate or ethyl benzoate owing to the condensation reactions of the esters. The present procedure using alkyl bromides obviates these difficulties.



$$CH_3CONHCH_3 \xrightarrow{LAH} LiAl[CH_3CH_2NCH_3]_4 \xrightarrow{\underline{n}\text{-}C_3H_7Br} CH_3\underset{\displaystyle CH_2CH_2CH_3}{N}CH_2CH_3$$

Treatment of the lithium aluminum hydride reduction product of 2-pyrrolidone with n-propyl bromide gave 1-n-propylpyrrolidine in a 53% yield. Similarly the alicyclic amide, N-methylacetamide, afforded a 28% yield of ethylmethyl-n-propylamine, in addition to a small amount(4%) of methyldi-n-propylamine. This latter product probably results from the reductive cleavage of the amide and subsequent dialkylation of the complex with n-propyl bromide.

Extension of the alkylation reaction to the reduction product from benzaldehyde failed; no ether was isolated using n-butyl bromide as the reagent.

EXPERIMENTAL

1-n-Propylpyrrolidine.- To a solution of lithium aluminum hydride(14.25g, 0.375 mole) in tetrahydrofuran (250ml) under nitrogen was added dropwise a solution of 2-pyrrolidone(42.5g, 0.50 mole) in tetrahydrofuran(150ml) over the period of one hour. The reaction mixture was then refluxed for 36 hrs, cooled to room temperature and treated with n-propyl bromide(61.5g, 0.50 mole) in tetrahydrofuran(100ml). The solution was refluxed for 23 hrs, hydrolyzed with water(50ml) and 6N hydrochloric acid(200ml) and steam distilled to remove the tetrahydrofuran. The solution was then made basic with 12N sodium hydroxide(200ml) and steam distilled again until the distillate was no longer basic. The distillate was acidified with hydrochloric acid and evaporated to dryness. Basification with a saturated solution of sodium hydroxide followed by extraction with pentane gave a brown liquid(44.2g). Vpc analysis on a 6' x 1/8" column containing 5% SE-30 on 100-120 Chromosorb P, (column temperature 79°, injection port 200°, detector 270°) indicated a 53% yield of 1-n-propylpyrrolidine, (retention time 1.2 min). The remainder of the product was mainly pyrrolidine (retention time 0.56 min). Fractional distillation gave 24.7g of 1-n-propylpyrrolidine, bp.120-32°, lit.[4] bp.130°; nmr(neat) δ2.15-2.54(m, 6H), 1.10-1.90(m, 6H), 0.84(t, 3, CH_3); picrate mp. 104-6°, lit.[4] mp. 105° did not depress the melting point of an authentic sample.

Ethylmethyl-n-propylamine.- N-Methylacetamide(73.1g) was reduced and alkylated in a similar fashion to that given above. Fractional distillation of the basic fraction using a 90cm spinning band column gave ethylmethyl-n-propylamine(25g), bp.90°, lit.[5] bp.91-92°. An additional 2.8g (retention time, 0.65 min) was detected in the intermediate fractions by vpc analysis on the SE-30 column (column temperature, 68°, injection port 165°, detector 240°); nmr(neat) δ2.12-2.54(m, 4H), 2.12(s, 3, NCH_3), 1.17-1.68(m, 2H), 0.70-1.17(two t, 6, $2CH_3$). The picrate melted at 94-95.5°, lit.[5] mp. 94.4-95.2°.

A higher boiling fraction contained methyl-di-n-propylamine(2.5g), bp.110°, lit.[6] bp.110-122°; nmr(neat) δ2.12-2.40(t, 4, $(NCH_2)_2$), 2.12(s, 3, NCH_3), 1.10-1.74(m, 4, $(C\text{-}CH_2\text{-}C)_2$), 0.90(t, 6, $(CH_3)_2$). An additional 1.37g (retention time, 1.35 min) was detected in the intermediate fractions by vpc analysis using the SE-30 column. The picrate melted at 92-94°, lit.[6] mp. 92-3°.

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