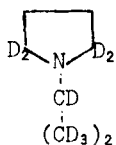


## NOTES

SYNTHESIS OF CERTAIN SPECIFICALLY DEUTERATED TERTIARY AMINES  
WITH SPECIAL REFERENCE TO DEUTERATED N-ALKYLPYRROLIDINES

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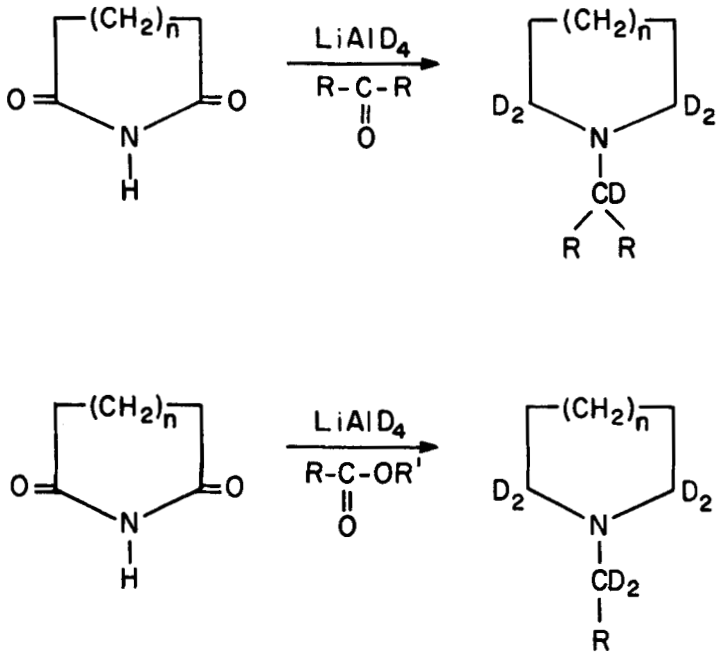
The preparation of several N-alkylpyrrolidines by reductive alkylation of pyrrolidine with esters, ketones or aldehydes in the presence of lithium aluminum hydride was in progress here when a paper appeared by Khanna, Dixit, and Anand on the N-alkylation of secondary amines with esters and lithium aluminum hydride (1). The synthesis of certain deuterium labelled N-alkylpyrrolidines by this method is quite convenient. For example, I can be prepared in one step from succinimide,



I

lithium aluminum deuteride and acetone-D<sub>6</sub>.\*

The alternative preparation involves nitrosation of pyrrolidine, base catalyzed exchange in the 2 and 5 positions, denitrosation and alkylation with isopropyl-D<sub>7</sub> iodide which must itself be prepared from acetone-D<sub>6</sub> by reduction to isopropyl-D<sub>7</sub> alcohol and reaction with



$n = 2, 3$

$R = CH_3, CD_3, CH_3CD_2, CD_3CD_2$  etc.

FIGURE I

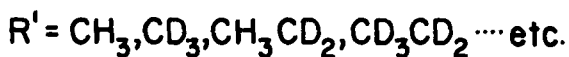
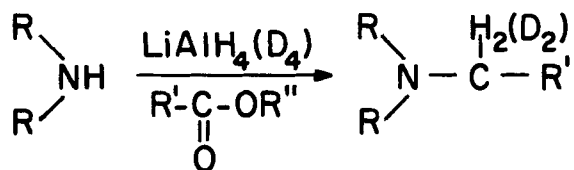
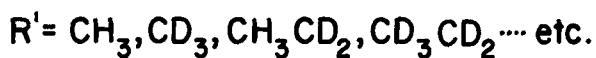
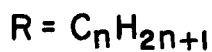
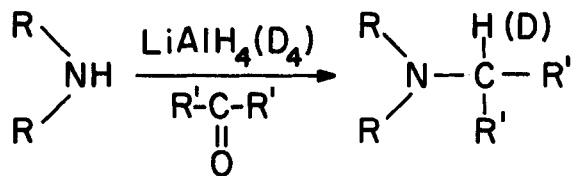
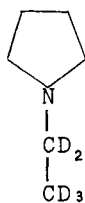


FIGURE 2

hydriodic acid. With esters N-alkylpyrrolidines labelled on the first and second carbon atoms are readily accessible.

Thus II was conveniently prepared from ethyl acetate-D<sub>3</sub>,



II

pyrrolidine and lithium aluminum deuteride.

A wide variety of combinations is possible and have been exploited as sources of specifically labelled N-alkylpyrrolidines for IR spectroscopic studies (2). These possibilities are indicated in the Figures. A mechanism for this reaction was proposed in reference 1.

#### EXPERIMENTAL

##### N-Isopropyl-D<sub>7</sub>-pyrrolidine-2,5-D<sub>4</sub>

Lithium aluminum deuteride (4.2 g; 0.1 mole) was added cautiously in portions to a stirred solution of succinimide (7.1 g; 0.1 mole) in tetrahydrofuran (125 ml). Acetone-D<sub>6</sub> (8.0 g; 0.125 mole) was added dropwise and the reaction mixture was heated overnight under reflux. Most of the solvent was distilled off under reduced pressure and the cold residue was basified with 5N sodium hydroxide. The amine was then removed by steam distillation until the distillate was neutral. The distillate was neutralized with 1 N hydrochloric acid and evaporated to dryness under reduced pressure. The syrupy residue was treated with pellets of potassium hydroxide. The liberated

amine was distilled into a trap on a vacuum line and fractionated in a suitable column. After a forerun of 2 mls, b.p. 97°C, the pure amine distilled at 120°C. Yield: 6.5 g (55%). The band of medium intensity at 2770  $\text{cm}^{-1}$  in IR observed in all protiated N-alkylpyrrolidines is absent (4).

N-Isopropyl-D<sub>6</sub>-pyrrolidine

This compound was prepared in the same manner from pyrrolidine, lithium aluminum hydride and acetone-D<sub>6</sub>. Unlike the above compound it showed a strong band at 2770  $\text{cm}^{-1}$  (4).

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