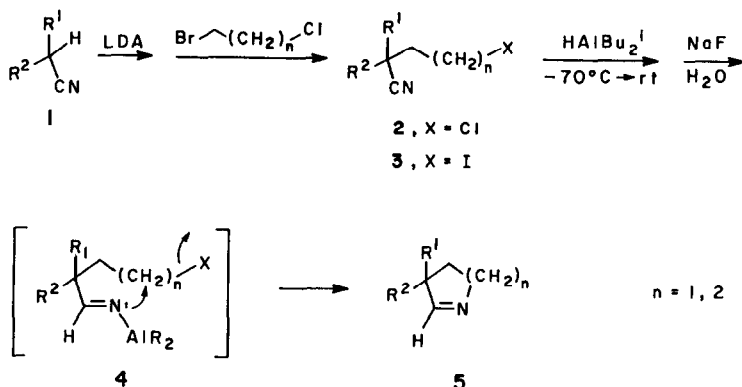


A CONVENIENT SYNTHESIS OF  $\Delta^1$ -PYRROLINES AND  $\Delta^1$ -PIPERIDEINES

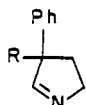
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**Summary:** Imines 5 are formed in excellent yield from the reaction of nitriles 2 with diisobutylaluminum hydride.

Cyclic imines such as 5 are useful intermediates for preparing azacyclics that contain pyrrolidine or piperidine rings.<sup>1</sup> In connection with another study,<sup>2</sup> we required a convenient synthesis of 3,3-disubstituted- $\Delta^1$ -pyrrolines (5, n=1). In this Letter we report that  $\Delta^1$ -pyrrolines of this type, as well as the related  $\Delta^1$ -piperideines, can be readily prepared from nitrile precursors<sup>3</sup> by the two step sequence outlined in the Scheme.



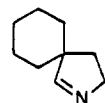
Alkylation of the lithium salt of 1 with 1-bromo-3-chloropropane (6) or 1-bromo-2-chloroethane (7), under standard conditions,<sup>4</sup> provided nitriles 2. When R<sup>1</sup> was Ph, yields for this step were 85-95%, while alkylation of cyclohexanecarbonitrile or cyclopentanecarbonitrile with 6 or 7 proceeded in yields of 65-70% or 30-40%, respectively. Treatment of 2 with 1 equiv or *i*-Bu<sub>2</sub>AlH (THF, -78°→23°C) followed by workup<sup>5</sup> with NaF (4 equiv) and H<sub>2</sub>O (3 equiv) gave cyclic imines 5 in excellent yields. For the preparation of  $\Delta^1$ -piperideines, conversion of 2 to iodide 3 (NaI, 2-butanone, 80°C) prior to the reduction-cyclization step afforded 5 (n=2) in better overall yields. The imines<sup>6</sup> we have prepared by this procedure are shown below.



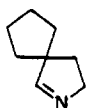
**8**, R = nC<sub>4</sub>H<sub>9</sub> 78%

**9**, R = CH<sub>2</sub>CH<sub>2</sub>CH<sup>Z</sup>=CHSiMe<sub>3</sub> 86%

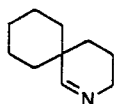
**10**, R = CH<sub>2</sub>CH<sub>2</sub>CH<sup>E</sup>=CHSiMe<sub>3</sub> 80%



**11** 81%

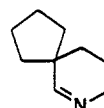


**12** 85%



**13** 54%

75% (via iodide)



**14** 63%

84% (via iodide)

**Typical Procedure:** Neat *i*-Bu<sub>2</sub>AlH (0.52 mL, 2.9 mmol) was added to a stirring solution of **2** [500 mg, 2.91 mmol; R<sup>1</sup>, R<sup>2</sup> = (CH<sub>2</sub>)<sub>5</sub>, n=1] and toluene (10 mL) at -70°C. This solution was maintained at -70°C for 1 h, allowed to warm to room temperature, and after an additional 1 h was cooled to 0°C and NaF (490 mg, 11.7 mmol) was added. The resulting mixture was stirred rapidly for 0.5 h and then H<sub>2</sub>O (0.16 mL, 8.8 mmol) was added. This mixture was stirred rapidly for 45 min at 0°C and 1 h at room temperature. The insoluble fluoroaluminate salts were removed by filtration, and the concentrated filtrate was purified by chromatography on silica gel (2:1 hexane-ethyl acetate) to give 320 mg (81%) of 2-azaspiro[4.5]dec-1-ene (**11**): <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 7.33 (br s, CH=N), 3.86 (dt, J=2.3, 7.2 Hz, CH<sub>2</sub>N), 1.7-1.2 (m, 10 H); IR (CHCl<sub>3</sub>) 1640 cm<sup>-1</sup> (C=N); MS (isobutane CI) m/z 138 (100%).

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#### References and Notes

- For examples, see Stevens, R.V. In "The Total Synthesis of Natural Products"; John Wiley: New York, 1977; Vol. 3, pp 439-543.
- Overman, L.E.; Burk, R.M. following Letter in this issue.
- The related preparation of cyclic imines with alkyl substituents at C-2 from the reaction of nitriles with organolithium reagents has been described: Larcheveque, M.; Debal, A.; Cuvigny, T. Bull. Soc. Chim. Fr. **1974**, 1710.
- Arseniyadis, S.; Kyler, K.S.; Watt, D.S. Org. React. **1984**, **31**, 1.
- Yamamoto, H.; Maruoka, K. J. Am. Chem. Soc. **1981**, **103**, 4186.
- Imine products were characterized by their <sup>1</sup>H and <sup>13</sup>C NMR, IR, and mass spectra. Imines **11**, **13**, and **14** have been described previously: Smolanoft, J.R. U.S. Patent 4 374 991 A, **1983**; Chem. Abstr. **1983**, **98**, 198045 and U.S. Patent 4 400 512 A, **1983**; Chem. Abstr. **1984**, **100**, 6316.

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