# A Facile Synthesis of 4-Azatricyclo[4.3.1.1$^{3,8}$]undecane (4-Azahomoadamantane): A Novel Heterocyclic System

*V. L. Narayanan and L. Setescak*

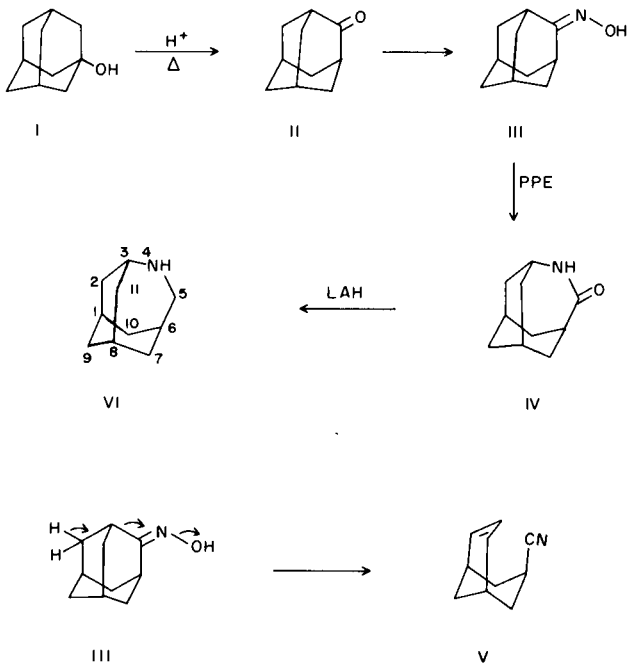
Squibb Institute for Medical Research

*Sir:*

The interesting chemistry (1) of adamantane and the biological activity of its derivatives (2) have stimulated a growing interest in recent years in the syntheses of "homo" (3) and "hetero" (4) adamantanes. We wish to report a convenient route to the synthesis of 4-azatricyclo-[4.3.1.1$^{3,8}$]undecane (VI), a novel heterocyclic system, for which we suggest the trivial name "4-azahomoadamantane".

Adamantanone (II), synthesized from 1-hydroxyadamantane (I) by the procedure of Geluk and Schlatmann (5), was converted to its oxime (III), m.p. 164-165.5°. Our initial attempts to synthesize the lactam (IV) by the Beckmann rearrangement of III by standard procedures (6) led to poor yields (<25%). Often an oily by-product (V), the result of a second order Beckmann rearrangement was obtained, λ max (chloroform) 4.4 μ (CN); τ (deuteriochloroform) 3.9-4.2, 6.2 (d), 7.5-8.8. The use of phosphorus pentachloride, on the other hand, led to chlorinated products. The desired lactam (IV) was successfully prepared in excellent yields by the following procedure. A solution of 0.015 mole of III and 10 g. of polyphosphate ester (PPE) in 10 ml. of chloroform was refluxed for 5-7 minutes. The reaction mixture was cooled, water added, and the two phase system stirred overnight to decompose the excess of PPE. The crude product was isolated from the chloroform layer as an off-white solid (81%). Crystallization from ether-hexane yielded 65% of pure 4-azatricyclo[4.3.1.1$^{3,8}$]undecan-5-one (IV), m.p. 298-300°, $M^+$ 165; λ max (Nujol) 3.0-3.3 (NH), 6.0 μ (C=O); τ (deuteriochloroform) 6.55-6.75 (NH), 7.2-7.4 (-C*H* adjacent to C=O), 7.7-8.5 (13*H*). Reduction of IV with lithium aluminum hydride in tetrahydrofuran yielded 53% of 4-azahomoadamantane (VI) isolated as the crystalline hydrochloride, m.p. >300°; λ max (Nujol) 3.3-4.1 ($NH_2^+$ and CH), no C=O at 6.0 μ; τ (deuteriochloroform) 0.6-0.8 ($NH_2^+$), 5.95-6.15 (1*H* adjacent to $NH_2^+$), 6.4-6.7 (C$H_2$ adjacent to $NH_2^+$), 7.6-8.5 (13*H*).

All new crystalline compounds gave satisfactory elemental analyses.




## REFERENCES

(1) R. C. Fort, Jr., and P. von R. Schleyer, *Chem. Rev.*, **64**, 277 (1964).

(2a) W. L. Davies, R. R. Grunert, R. F. Haff, J. W. McGahen, E. M. Newmager, M. Paulshock, J. C. Watts, T. R. Wood, E. C. Hermann, and C. E. Hoffmann, *Science*, **144**, 862 (1964); (b) K.

Gerzon, D. J. Tobias, Sr., R. E. Holmes, R. E. Rathbun, and R. W. Kattau, *J. Med. Chem.*, **10**, 603 (1967), and earlier papers.

(3a) B. R. Vogt, *Tetrahedron Letters*, 1579 (1967); (b) R. von R. Schleyer, and E. Wiskott, *ibid.*, 2845 (1967); (c) A. Nickon, G. D. Pandit, and R. O. Williams, *ibid.*, 2851 (1967); (d) B. R. Vogt, and J. R. E. Hoover, *ibid.*, 2841 (1967).

(4a) C. Ganter, and K. Wicker, *Helv. Chim. Acta*, **51**, 1599 (1968), and references therein; (b) A. C. Udding, Hans Wynberg, and J. Strating, *Tetrahedron Letters*, 5719 (1968).

(5) H. W. Geluk, and J. L. M. A. Schlatmann, *Tetrahedron*, **24**, 5361 (1968).

(6) L. G. Donaruma, and W. Z. Heldt in "Organic Reactions" Vol. II, A. C. Cope, Ed., John Wiley and Sons, Inc., New York, New York, p. 1 (1960). PPE was prepared according to the procedure of G. Schramm, H. Grotsch, and W. Pullmann, *Angew. Chem. Intern. Ed.*, **1**, 1 (1962).

Received April 15, 1969 New Brunswick, New Jersey 08903