Investigations Toward the Total Syntheses of Proaporphine and Homoproaporphine Alkaloids

By WILLIAM V. CURRAN

(Lederle Laboratories Division, American Cyanamid Co., Pearl River, New York 10965)

Summary A synthetic approach to the proaporphine and homoproaporphine alkaloids which was successful in the latter series is presented.

PROAPORPHINE and homoproaporphine alkaloids are an interesting group of isoquinoline type compounds which have only recently been described.¹ We describe a synthetic approach to these systems.²

crystalline enol ether (6) in good yield by a modified Birch reduction:⁴ white crystals, m.p. 78—80°; i.r. (CHCl₃) 1660 and 1690 cm⁻¹ (enol ether bands); n.m.r. (CDCl₃) δ 2·44 (s, 3H, NCH₃), 3·54 (s, 3H, enol OCH₃), 3·84 (s, 3H, aromatic OCH₃), 4·63 (m, 1H, olefinic H), 5·41 (m, 1H, olefinic H), 6·55 (s, 1H, ArH), and 6·64 (s, 1H, ArH) p.p.m. Treatment of this compound with hot phosphoric acid gave two compounds which were separated by liquid-liquid



Isoquinoline (1),³ was subjected to the Dryden modification of the Birch reduction⁴ to afford the white crystalline enol ether (3) (68%): m.p. 111—113.5°; i.r. (CHCl₃), 3540 (OH), 1670, and 1695 cm⁻¹ (enol ether bands); n.m.r. (CDCl₃) δ 2.43 (s, 3H, NMe), 3.55 (s, 3H, enol OMe), 3.85 (s, 3H, ArOMe), 4.62 (m, 1H, olefinic H), 5.40 (m, 1H, olefinic H), 6.54 (s, 1H, ArH), and 6.67 (s, 1H, ArH) p.p.m. Treatment of (3) with hot phosphoric acid afforded (±)tetrahydrohomoglaziovine (4) as the principal product: white crystals, m.p. 206—211° decomp.; i.r. (KBr) 1710 (C=O); n.m.r. (CDCl₃) δ 2.43 (s, 3H, NMe), 3.84 (s, 3H, COMe), and 6.50 (s, 1H, ArH) p.p.m. The structure of this compound δ -50 (s, 1H, ArH) p.p.m. The structure of this compound the previously described dienone (5)⁵ gave the same compound (i.r. and t.l.c.).

The benzylisoquinoline $(2)^6$ was also converted into a

partition chromatography on Celite. Neither was (\pm) -tetrahydroglaziovine (9) as they were not identical to

TABLE.	Acid	cyclization	products	from ((6)	
		-				

Molecular ion (m/e)	Major isomer 301	Minor isomer 301
i.r. $v(CHCl_3)/cm^{-1}$ u.v. $\lambda_{max}(EtOH)/nm (\epsilon)$ δ (p.p.m. in CDCl ₃)	3660, 1710, 1630 288(3600) 2·47(3H, s, NMe) 3·82(3H, s, OMe) 6·50(1H, s, Ar)	3660, 1710, 1625 288(3300) 2·54(3H, s, NMe) 3·84(3H, s, OMe) 6·52(1H, s, Ar)

authentic (9) obtained by catalytic hydrogenation of (\pm) -glaziovine (10).⁷ The two compounds (a major and minor isomer) have been assigned structures (7) and (8), having aporphine-type skeletons, but the available evidence does

CHEMICAL COMMUNICATIONS, 1971

not allow exact stereochemical formulation.[†] Their principal physical characteristics are listed in the Table. Both compounds exhibit only one unsplit aromatic proton proving that a Friedel-Crafts type cyclization has taken place. Other types of acid treatment on the enol ether (6)did not afford any of the spiro-compound (9). Further details will be presented elsewhere.

We thank Mr. L. Brancone and staff for elemental

analyses, which were satisfactory for all compounds reported, Mr. W. Fulmor and staff for spectral data, Dr. P. J. Kohlbrenner and Mr. I. Jones for the preparation of some of the intermediates, and Mr. C. Pidacks, Dr. C. A. Strueli, and Mr. R. Mills for chromatographic analyses. We also thank Dr. L. Goldman for discussions.

(Received, March 15th, 1971; Com. 233.)

† All structures reported with chiral centres are racemates.

¹ For recent reviews see K. L. Stuart and M. P. Cava, *Chem. Rev.*, 1968, 68, 321; K. Bernauer and W. Hofheinz, 'Progress in the Chemistry of Natural Products,' vol. XXVI, Springer-Verlag, New York, 1969, p. 245.

- Cnemistry of Natural Products, vol. XXVI, Springer-Verlag, New York, 1969, p. 245.
 ² For other syntheses in this area not involving radical-coupling reactions see K. Bernauer, Helv. Chim. Acta, 1968, 68, 1119;
 J. W. Huffman and C. E. Oplinger, Tetrahedron Letters, 1969, 5243; F. Schneider and K. Bernauer, Helv. Chim. Acta, 1970, 53, 938.
 ³ T. Kametani, S. Takano, and T. Kobseri, J. Chem. Soc. (C), 1969, 9.
 ⁴ H. L. Dryden, Jun., G. M. Webber, R. R. Burtner, and J. A. Lella, J. Org. Chem., 1961, 26, 3237.
 ⁵ T. Kametani, H. Yagi, F. Satoh, and K. Fukumoto, J. Chem. Soc. (C), 1968, 271.
 ⁶ T. Kametani, S. Takano, H. Iida, and M. Shinbo, J. Chem. Soc. (C), 1969, 298.
 ⁷ T. Kametani and H. Yagi, J. Chem. Soc. (C), 1967, 2182.