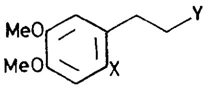
Intramolecular Photoarylation of Enamino-ketones: Simple Synthesis of Hexahydroapoerysopine Dimethyl Ether

By HIDEO IIDA,* TATSUTOSHI TAKARAI, and CHIHIRO KIBAYASHI
(*Tokyo College of Pharmacy, Horinouchi, Hachioji, Tokyo* 192-03, *Japan*)

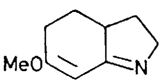
Summary A novel synthesis of hexahydroapoerysopine dimethyl ether (**11**), by photolytic intramolecular arylation of the 6′-iodo- and 7-bromo-derivatives of 1,2,3,3a,4,5-hexahydro-*N*-(3,4-dimethoxyphenethyl)indol-6-one (**6**) and (**8**) to 2,3-dihydroapoerysopin-1(3a*H*)-one (**9**), followed by reduction with $LiAlH_4$ to *cis*-2,3,3a,12c-tetrahydroapoerysopine (**10**) and then hydrogenation, is reported.

TREATMENT of tetrahydroerythraline under acidic conditions followed by reaction with diazomethane yields an optically active base, hexahydroapoerysopine.[1] We have now devised a new synthesis of the title compound (**11**)† from the key intermediate (**9**) obtained by photolysis of halogen-containing enamino-ketones.‡ Our results represent a convenient one-step preparation of enamino-ketones from the imino-enol ether (**5**) and a new intramolecular arylation.

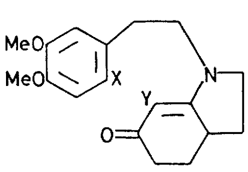
Iodination (I_2, CF_3CO_2Ag, $CHCl_3$) of 3,4-dimethoxyphenethyl alcohol[2] gave the iodo-alcohol (**1**)§ (84%), m.p. 52—54 °C, which was then chlorinated ($SOCl_2$, $PhNEt_2$, C_6H_6) to afford the phenethyl chloride (**2**) (85%), m.p. 76—78 °C. This was then converted into the corresponding iodide (**3**) (95%), m.p. 55—57 °C, by treatment with NaI–MeCOEt complex. Heating (**3**) and the imino-enol ether (**5**) (obtained readily from Birch reduction of 6-methoxyindoline)[3] in refluxing toluene provided the iodo-enamino-ketone (**6**) (55%), m.p. 129—130 °C. Irradiation of (**6**) in dioxan containing Et_3N with a 100 W high-pressure mercury lamp and Pyrex filter produced the tetracyclic compound (**9**) (50%) as a syrup, *m/e* 299 (100%, M^+); δ ($CDCl_3$) 6·50 (1H, s, 9-H) and 7·21 (1H, s, 12-H), together with the photoreduction product (**7**) (30%), m.p. 44—45 °C. The latter product (**7**), which could be prepared alternatively from the imino-enol ether (**5**) and the phenethyl iodide (**4**)[2]



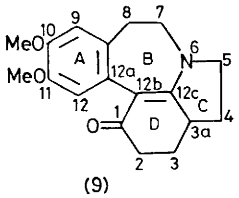
(1) X = I, Y = OH
(2) X = I, Y = Cl
(3) X = Y = I
(4) X = H, Y = I



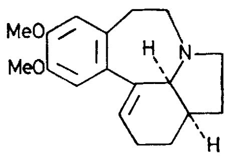
(5)



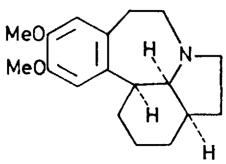
(6) X = I, Y = H
(7) X = Y = H
(8) X = H, Y = Br



(9)



(10)



(11)

---

† The synthesis of an apoerysopinone derivative *via* acid-promoted reaction of a halogenated enamide was reported by A. Mondon and H.-U. Menz, *Tetrahedron*, 1964, **20**, 1729.

‡ For a related cyclisation, the photochemical formation of a pyrrolobenzazepinone from an enamide was recently described (I. Tse and V. Snieckus, *J.C.S. Chem. Comm.*, 1976, 505).

§ Satisfactory analytical and spectral data were obtained for all new compounds.

in the same way as described for (**6**), was allowed to react with an equimolecular amount of Br_2 in $CHCl_3$ to give the bromo-enamino-ketone (**8**) (75%), m.p. 127—129 °C. By similar irradiation in MeCN, (**8**) underwent photocyclisation and photoreduction, to give (**9**) (38%) and (**7**) (13%), respectively.

Reduction of (**9**) with $LiAlH_4$ in tetrahydrofuran afforded the *cis* dimethyl ether (**10**) (62%), m.p. 80—82 °C. The stereochemical assignment for (**10**) was based on its n.m.r. spectrum in which the 12c-H–3a-H coupling constant (*J* 6·5 Hz) indicated that the C/D-ring junction is *cis*. Hydrogenation of (**10**) in AcOH over Adams catalyst at 2·5 atm yielded hexahydroapoerysopine dimethyl ether (**11**) (43%) as a syrup, picrate m.p. 233—234 °C; it is thought that hydrogen adds to the less hindered α-side of the compound resulting in a B/D *cis* fusion, in analogy with previous work.[3]

We thank the Ministry of Education, Japan, for financial support (to C.K.).

(*Received*, 9*th May* 1977; *Com.* 438.)

---

[1] V. Prelog, K. Wiesner, H. G. Khorana, and G. W. Kenner, *Helv. Chim. Acta*, 1949, **32**, 453; E. W. Warnhoff, in 'Molecular Rearrangements,' ed. P. de Mayo, Interscience, New York, 1964, part 2, p. 846.

[2] M. Barash and J. M. Osbond, *J. Chem. Soc.*, 1959, 2157.

[3] H. Iida, S. Aoyagi, and C. Kibayashi, *J.C.S. Perkin I*, 1975, 2502.