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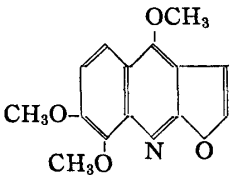
Furoquinolines. X.* Synthesis of Dihydroskimmianine.

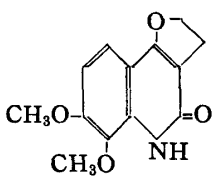
Asahina and Inubuse[1] assigned the structure (I) for skimmianine, conforming to the structural determination of dictamnine.[2] Recently, evidences for the linear structure of skimmianine were provided by ultraviolet spectrum[3] as well as by synthesis[4] of 3-ethyl-4,7,8-trimethoxycarbostyril, which was obtained by reductive degradation by Ohta,[5] and also by synthesis of methyl skimmianinate.[6]

We have now succeeded in the synthesis of dihydroskimmianine, which was obtained by reduction of skimmianine with PdO and hydrogen.[7] By this synthesis the linear tricyclic structure for skimmianine was unequivocally established.

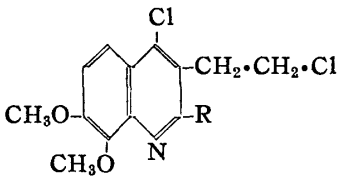
2,3-Dimethoxyaniline, which was prepared by decarboxylation[8] of 3,4-dimethoxyanthranilic acid obtained through methyl 3,4-dimethoxyanthranilate,[4] was condensed with diethyl 2-(2-ethoxyethyl)malonate to form 2,3-dihydro-6,7-dimethoxyfuro[3,2-*c*]quinolin-4(5*H*)-one (II), m.p. 221~222°, by refluxing in diphenyl ether for 4.5 hours. By heating with $POCl_3$[9] for 3 hours, (II) was derived to 3-(2-chloroethyl)-2,4-dichloro-7,8-dimethoxyquinoline (III), m.p. 117~118°. When refluxed with glacial AcOH during 3 hours, (III) afforded crystals melting at 215~222°. It seems that the crystals thereby obtained are a mixture of 4-chloro-3-(2-chloroethyl)-7,8-dimethoxycarbostyril (IV) and 4-chloro-2,3-dihydro-7,8-dimethoxyfuro[2,3-*b*]quinoline (V), judging from the experience of the dictamnine synthesis by T. Sato and M. Ohta.[10] Boiling of the crystal mixture thus obtained with 10% methanolic NaOH solution[11] for 2 hours yielded 2,3-dihydro-4,7,8-trimethoxyfuro[2,3-*b*]quinoline (VI), m.p. 165°(picrate, m.p. 184°), which was quite identical with dihydroskimmianine, m.p. 195°(formerly, m.p. 163°), derived from the natural alkaloid.



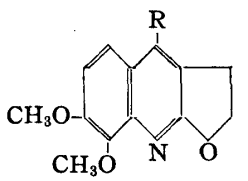
(I)



(II)



(III) R=Cl
(IV) R=OH



(V) R=Cl
(VI) R=OCH_3

Tokyo College of Pharmacy
Kashiwagi 2-Chome
Shinjuku-ku, Tokyo

Tatsuo Ohta (太田達男)
Yo Mori (森 陽)

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1) Y. Asahina, M. Inubuse: Ber., **63**, 2052(1930).
2) Y. Asahina, T. Ohta, M. Inubuse: Ber., **63**, 2045(1930).
3) T. Ohta, T. Miyazaki, Y. Mori: Ann. Rept. Tokyo Coll. Pharm., **4**, 255(1954).
4) T. Ohta, Y. Mori: *Ibid.* **5**, 336(1955).
5) T. Ohta: J. Pharm. Soc. Japan, **73**, 63(1953).
6) R.F. C. Brown: Australian J. Chem., **8**, 121(1955).
7) T. Ohta, T. Miyazaki, Y. Mori: J. Pharm. Soc. Japan, **74**, 708(1954).
8) C.S. Gibson *et al.*: J. Chem. Soc., **111**, 69(1917).
9) *cf.* M.F. Grundon, *et al.*: *Ibid.*, **1955**, 4284.
10) T. Sato, M. Ohta: J. Chem. Soc. Japan, **77**, 1630(1956).
11) *cf.* T. Ohta, Y. Mori: Ann. Rept. Tokyo Coll. Pharm., **4**, 261(1954).