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A NEW SYNTHESIS OF BENZO[C]PHENANTHRIDINE DERIVATIVE

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4-Substituted isocarbostyril derivative (V) was reduced with lithium aluminum hydride to give the 1,2-dihydro-4-substituted isoquinoline which was heated with hydrochloric acid to give two cis-hexahydrobenzo[c]phenanthridine derivatives (VI) and (VII or VIII).

The benzo[c]phenanthridine ring system is found in a few alkaloids[1]. Several methods have been described[2,3,4] for the construction of the ring system.

In connection with our studies on reaction of isocarbostyril derivatives[5], we have investigated the synthesis of dibenzo-[c]phenanthridine derivatives, which involve new synthesis of 4-substituted isocarbostyril derivative (V) from 4-substituted homophthalimide derivative (III).

4-(3,4-Dimethoxyphenacyl)-2-methylhomophthalimide (III), m.p. 155-156° ; ir νmax (nujol) 1700 and 1650 cm^{-1} ; mass m/e

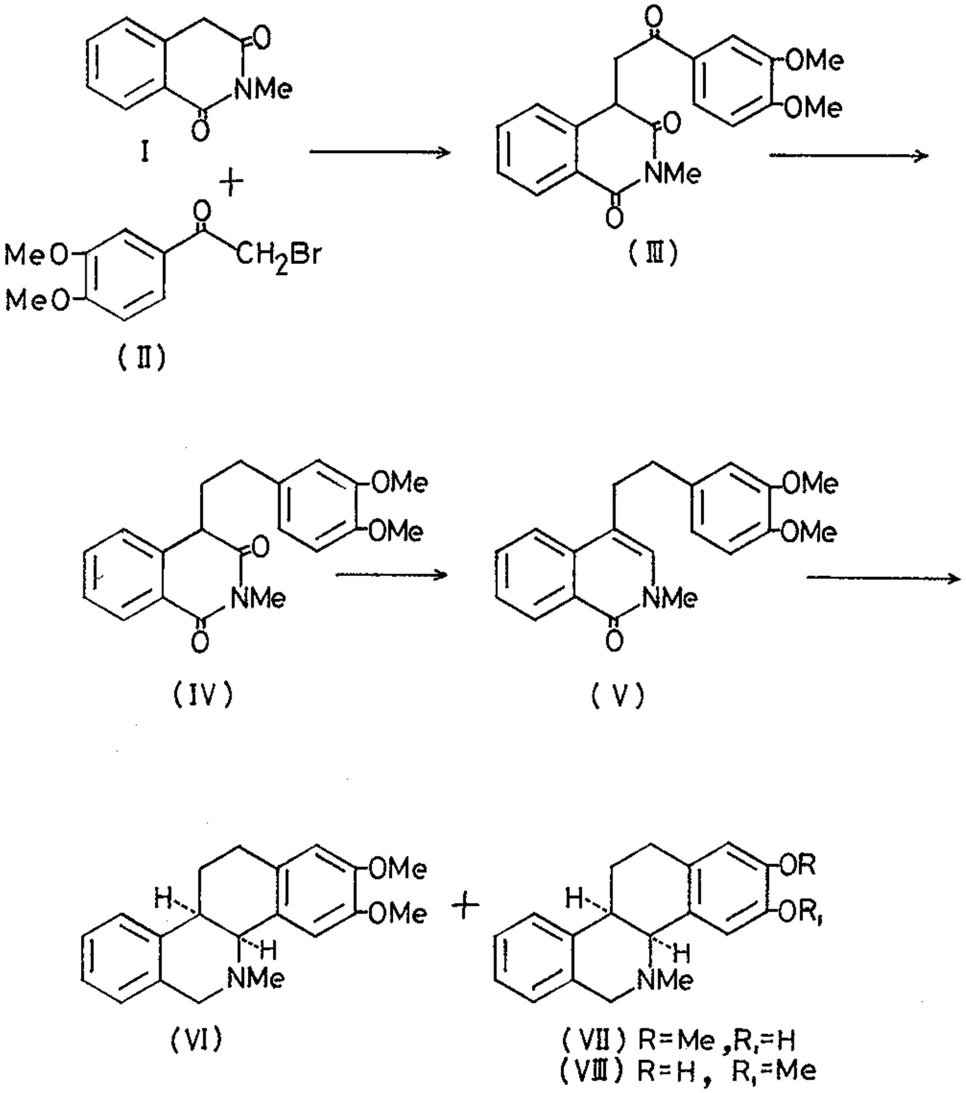
353 (M^+) and nmr δ($CDCl_3$) 3.42 (3H, s, N-CH_3), 3.84 (3H, s, O-CH_3), 3.91 (3H, s, O-CH_3) and 4.01 (2H, d, J=4Hz, CH_2) was prepared in 70-80% yield by treating 2-methylhomophthalimide (I) with 3,4-dimethoxyphenacyl bromide (II) in the presence of sodium ethoxide.

Catalytic reduction of this compound (III) on 5% palladium charcoal in acetic acid containing perchloric acid at 60° and atmospheric pressure gave 4-(3,4-dimethoxyphenethyl)-2-methylhomophthalimide (IV) in 90% yield as an oil, ir νmax (film) 1700 and 1650 cm^{-1} ; mass m/e 339 (M^+) and nmr δ($CDCl_3$) 2.48 (4H, m, CH_2-CH_2), 3.30 (3H, s, N-CH_3), 3.85 (6H, s, O-CH_3x2) and 4.00 (1H, t, J=4Hz, C_4-H).

Treatment of the imide (IV) with sodium borohydride afforded the 3,4-dihydro-3-hydroxyisocarbostyril, which was then acidified with 10% hydrochloric acid to give the isocarbostyril (V), m.p. 133-134° ; ir νmax (nujol) 1650 cm^{-1} ; mass m/e 323 (M^+) and nmr δ($CDCl_3$) 2.90 (4H, s, CH_2-CH_2), 3.50 (3H, s, N-CH_3), 3.84, 3.86 (6H, s, O-CH_3x2) and 6.78 (1H, s, C_3-H).

4-(3,4-Dumethoxyphenethyl)-2-methylisocarbostyril (V) was treared with lithium aluminum hydride to give 1,2-dihydro-4-substituted isoquinoline, which was heated with concentrated hydrochloric acid to give two compounds, which were separated by column chromatography on silica gel with chloroform as eluent.

The first compound was obtained in 40% yield, m.p. 120-122° ;


I
(Ⅱ)
(Ⅲ)
(IV)
(V)
(VI)
(VII) R=Me, R1=H
(VIII) R=H, R1=Me

ir νmax (nujol) 1600 cm^{-1} ; mass m/e 309 (M^+) and nmr δ($CDCl_3$) 2.40 (3H, s, N-CH_3), 3.58, 4.00 (2H, ABq, J=20Hz, C_6-H), 3.60 (1H, d, J=4.5Hz, 4b-H), 3.85, 3.90 (6H, s, O-CH_3x2) and 6.60, 6.93 (2H, s, C_1-H and C_4-H).

The nmr spectrum of the product (VI) also supported the benzo[c]phenanthridine structure and the coupling constant shown by the 4b-proton suggested that BC ring junction was cis.

A similar result of the coupling constant of 4b-proton in the benzo[c]phenanthridine was reported by Ninomiya et al.[6]

The compound (VI) was determined as cis-4b,5,6,10b,11,12-hexahydro-2,3-dimethoxy-5-methylbenzo[c]phenanthridine.

The second compound was obtained in 50% yield, a single product, m.p. 250-252° ; ir νmax (nujol) 3450 and 1600 cm^{-1} ; mass m/e 295 (M^+) and nmr δ($CDCl_3$) 2.30 (3H, s, N-CH_3), 3.68 (1H, d, J=4.5Hz, 4b-H), 3.70, 3.97 (2H, ABq, J=20Hz, C_6-H_2), 3.80 (3H, s, O-CH_3) and 6.60, 6.93 (2H, s, C_1-H and C_4-H).

The mass and nmr spectra of the second product were indicated demethylation of the benzo[c]phenanthridine (VII or VIII).

The position of demethylation was not determined yet.

REFERENCES

1 R.H.F. Manske, and H.L. Holmes, The Alkaloids Vol IV; Chap 35, Academic Press, New York (1954).

2 A.S. Bailey, and R. Robinson, *J. Chem. Soc.,* 1950, 1375.

A.S. Bailey, R. Robinson, and R.S. Staunton, *J. Chem. Soc.,* 1950, 2277.

3 S.F. Dyke, M. Sainsbury, and B.J. Moon, *Tetrahedron,* 1968, **24**, 1467.

4 W.J. Gensler, S.F. Lawless, A.L. Bluhm, and H. Dertouzos, *J. Org. Chem.*, 1975, **40**. 733.

5 H. Iida, K. Kawano, T. Kikuchi, and F. Yoshimizu, *J. Pharm. Soc.,* Japan, 1967, **96**, 176.

6 I. Ninomiya, T. Naito, T. Kiguchi, and T. Mori, *J. Chem. Soc.,* Perkin 1, 1973, 1696.

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