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SYNTHESIS OF B-HOMOAPORPHINE SKELETON
STERIC REQUIREMENTS IN THE FORMATION OF THE PHENANTHRO[10,1-b,c]AZEPINE SYSTEM

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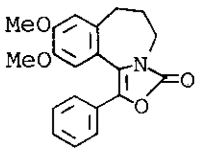
B-Homoaporphine skeletons (4a and b) were prepared via two routes; the photocyclization of the 1-phenyloxazolo[4,3-a][2]benzazepin-3-one (1) and the Friedel-Crafts-type cyclization of 2-oxophenanthro[9,10-d]-oxazoline-3-propionic acid (6c).

Previously[1], we have reported the photocyclization of various 4,5-diaryl-4-oxazolin-2-ones and its unsuccessful application to the aporphine synthesis. These results suggested that severe steric requirements in the formation of the four-ring system had to be overcome for the development of a new synthetic route. In the present communication, we described the formation of B-homoaporphine skeleton (4a) via the route of cyclization of the oxazolone (1) which contained a seven-membered ring.

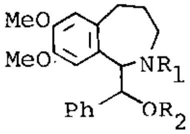
Reduction of 1-benzoyl-4,5-dihydro-7,8-dimethoxy-3H-2-benzazepine[2] with lithium aluminum hydride gave the amino-alcohol[3](2a), which was acylated with ethyl chloroformate to afford the carbamate[3](2b) in 90 % yield. Hydrolysis of the carbamate[3](2b) with KOH-MeOH gave two products, the cis-dihydrooxazolone (3a) and the single hydroxycarbamate (2c), in 56 and 41 % yields respectively. Heating the hydroxycarbamate (2c) in the presence of p-TsOH gave the trans-dihydrooxazolone (3b) in 90 % yield. The structures of the cis- and trans-dihydrooxazolones (3a and b) were readily established from their n.m.r. spectra, which showed δ 6.40 (1H, s, 11-H), 6.27 (1H, s, 8-H), 5.80 (1H, d, J=8Hz, 1-H), and 5.30 (1H, d, J=8Hz, 11b-H) in the cis-isomer (3a) and 6.70 (1H, s, 11-H), 6.27 (1H, s, 8-H), 5.30 (1H, d, J=8Hz, 1-H), and 4.80 (1H, d, J=8Hz, 11b-H) in the trans-isomer (3b), respectively.

Both dihydrooxazolones(3a and b) were then dehydrogenated to give an identical oxazolone (1) with remarkably different reaction rates, which were 2.5 h. with 90 % yield in the case of the cis-isomer (3a) and 6 h. with 45 % yield in the trans-isomer (3b).

Under the same condition reported previously[1], irradiation of a methanolic solution of the oxazolone (1) afforded the photocyclized phenanthrene (4a) in 20 % yield which showed the n.m.r. signals at δ 9.67 (1H, m), 8.07 (1H, m), 7.80-7.30 (2H, m), and 7.17 (1H, s) for five aromatic protons, thus proved the formation of B-homoaporphine skeleton. This result clearly suggested that a seven-membered ring eased steric congestion existing in the formation of an aporphine-type ring system to a great extent.



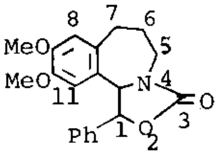
(1)



(2a) $R_1=R_2=H$

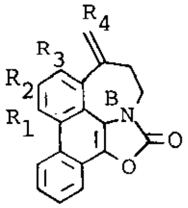
(2b) $R_1=R_2=CO_2Et$

(2c) $R_1=CO_2Et$, $R_2=H$



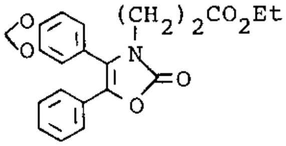
(3a) cis

(3b) trans

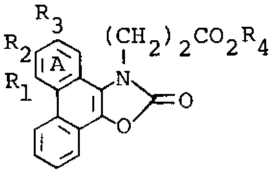


(4a) $R_1=R_2=OMe$, $R_3=H$, $R_4=H_2$

(4b) $R_1=H$, $R_2=OCH_2O=R_3$, $R_4=O$



(5)



(6a) $R_1=OCH_2O=R_2$, $R_3=H$, $R_4=Et$

(6b) $R_1=H$, $R_2=OCH_2O=R_3$, $R_4=Et$

(6c) $R_1=R_4=H$, $R_2=OCH_2O=R_3$

To prove this steric requirements in this type of ring system, we then investigated another approach to the B-homoaporphines via the cyclization of ring B as a final step. Irradiation of the oxazolone (5), which was prepared from benzoin as described previously[1], afforded two photocyclized phenanthrenes (6a and b) in 7 and 63 % yields respectively.

Inspection of the Dreiding model of (6b) showed that the ester group is favorably situated within a reaching distance from the benzene ring (A) to undergo cyclization, therefore being susceptible to facile cyclization. Treatment[4] of the carboxylic acid (6c), which was prepared from (6b) upon hydrolysis, with $POCl_3$ afforded the azepinone (4b) in 85 % yield, which has also a B-homoaporphine skeleton. Therefore it would be concluded that there would be a considerably severe congestion in the aporphine ring system, which could be reduced by enlarging the size of one of the rings to seven, thus facilitating the formation of B-homoaporphines.

Synthesis of B-homoaporphine has been relatively unexploited except the work by Berney et al.[5]

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3 The products (2a and b) were obtained as unseparable diastereomeric mixtures.

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