HETEROCYCLIC COMPOUNDS

Synthesis of 2 : 3-Dihydro-2 : 4-Dimethylfuro-(2, 3-b) Quinolines

BY JOSEPH P. JOHN AND P. SHANMUGAM

(Department of Organic Chemistry, University of Madras, Madras-25)

Received January 25, 1962

(Communicated by Dr. K. N. Menon, F.A.Sc.)

The structural determinations of the alkaloids, Lunasine\(^1\) (I), Lunacrine\(^2-3\) (II) and Lunine\(^3\) (III) of the genus \(L^\text{nasia}\) were recently made and they were all found to be derivatives of dihydrofuro-(2, 3-b)-quinoline\(^*\) (IV). All these alkaloids have an alkyl substituent (-isopropyl) in the 2-position. It would be of interest to prepare 2 : 3-dihydrofuro-(2, 3-b)-quinolines having an alkyl substituent in the 2-position. This paper describes the synthesis of 2 : 4-dimethyl-2 : 3-dihydrofuro-(2, 3-b)-quinolines starting from the appropriate \(o\)-aminoacetophenones.

The \(o\)-aminoacetophenone is reacted with 3-pentenoyl chloride and the resulting amide (V) is then ring-closed to give the carbostyril (VI). The carbostyril, on heating with polyphosphoric acid, furnished the dihydrofuroquinoline (VII). This seems to be an attractive route for the synthesis of 2 : 3-dihydrofuro-(2, 3-b)-quinolines. The u.v. absorption of the dihydrofuroquinoline is almost identical with that of the corresponding dihydro-

\* Ring numbering as in Chemical Abstracts.
furoquinoline without a substituent in the 2-position prepared by one of us (P.S.8) (VIII).

![Chemical structure and reaction diagram]

The following dihydrofuroquinolines were made starting from the appropriate o-aminoacetophenones:

(a) 2:3-dihydro-2:4-dimethylfuro-(2, 3-b)-quinoline:
   (VII, \( R_1 = R_2 = R_3 = H \));

(b) 2:3-dihydro-6:7-dimethoxy-2:4-dimethylfuro-(2, 3-b)-quinoline:
   (VII, \( R_1 = R_2 = \text{OCH}_3, \ R_3 = H \));

(c) 2:3-dihydro-7:8-dimethoxy-2:4-dimethylfuro-(2, 3-b)-quinoline:
   (VII, \( R_1 = H, \ R_2 = R_3 = \text{OCH}_3 \));

(d) 2:3-dihydro-2:4-dimethyl-7-methoxyfuro-(2, 3-b)-quinoline:
   (VII, \( R_1 = R_3 = H, \ R_2 = \text{OCH}_3 \))

**EXPERIMENTAL**

(a) 2: Dihydro-2: 4-dimethylfuro-(2, 3-b)-quinoline (VII, \( R_1 = R_2 = R_3 = H \)).—3-Pentenoyl chloride [prepared from 3-pentenoic acid] (2 g.)
and thionyl chloride] was added to a well-cooled solution of o-aminoacetophenone (2·7 g.) in benzene (25 ml.) containing pyridine (2·5 ml.). It was shaken well during addition and allowed to stand overnight and was poured into water. The benzene layer was separated and successively washed with dilute hydrochloric acid, water, sodium bicarbonate solution and finally with water. After drying over anhydrous magnesium sulphate, the solvent was removed under reduced pressure. The residue was then treated with 5% alcoholic potash and allowed to stand overnight. It was poured into water and acidified with hydrochloric acid. The carbostyril (VI, R₁ = R₂ = R₃ = H) that separated was collected and crystallised from ethanol, m.p. 227–28° C. Found: C, 77·9; H, 6·59; C₁₃H₁₃ON requires C, 78·39; H, 6·53. Yield 3 g.

The carbostyril was then heated with polyphosphoric acid (prepared from 5 g. of phosphorus pentoxide and 5 c.c. of phosphoric acid) on a steam-bath for 4 hours. After cooling, it was poured into water, filtered and the clear filtrate was basified with ammonia. The base was collected, dissolved in dilute hydrochloric acid and reprecipitated with ammonia. The base was dried and crystallised from petroleum ether (40–60°) containing a little benzene, m.p. 119–20° C. Yield 1·4 g. Found: C, 78·36; H, 6·53; C₁₃H₁₃ON requires C, 78·39; H, 6·53%. I.R. in CHCl₃—1930 cm.⁻¹ It was found to be identical with the sample prepared by Raman¹⁰ by reacting the sodio-derivative of acetoacetanilide with allyl bromide and cyclising the resulting product with polyphosphoric acid, mixed m.p. 119–20° C. They have identical u.v. absorption: λ 272, ε 5073; λ 313, ε 5723; λ 326, ε 6389.

(b) 2 : 3-Dihydro-6 : 7-dimethoxy-2 : 4-dimethyl-(2 : 3)-quinoline (VII, R₁ = R₂ = OCH₃, R₃ = H).—The carbostyril (VI, R₁ = R₂ = OCH₃; R₃ = H) was prepared from 3 : 4-dimethoxy-6-aminoacetophenone (2 g.) and 3-pentenoyl chloride (from 1 g. of the acid) as in the previous case. Crystallised from ethanol, m.p. 273–74° C. Yield 1·8 g. Found: C, 69·50; H, 6·63; C₁₅H₁₇O₃N requires C, 69·5; H, 6·56.

The carbostyril was cyclised as in the previous case to give the furoquinoline (VII, R₁ = R₂ = OCH₃; R₃ = H). Crystallised from ethanol, m.p. 169–70° C. Yield 1·5 g. Found: C, 69·54; H, 6·56; C₁₅H₁₇NO₃ requires C, 69·50; H, 6·56. I.R. in CHCl₃—1934 cm.⁻¹

U.V. absorption: λ 276, ε 3996; λ 328, ε 13130; λ 343, ε 16000.

U.V. absorption of VIII (R₁ = R₂ = OCH₃, R₃ = H): λ 277, ε 4013; λ 329, ε 13240; λ 343, ε 16280.
(c) 2: 3-Dihydro-7: 8-dimethoxy-2: 4-dimethylfuro-(2: 3-b)-quinoline (VII, $R_1 = H; R_2 = R_3 = OCH_3$).—The carbostyril (VI, $R_1 = H; R_2 = R_3 = OCH_3$) was prepared from 2-amino-3; 4-dimethoxyacetophenone (2 g.) and 3-pentenoyl chloride (from 1 g. of the acid) as before. Crystallised from ethanol, m.p. 214-16° C. Yield 1.2 g. Found: C, 69.29; H, 6.67; $C_{15}H_{17}NO_3$ requires C, 69.50; H, 6.56.

The carbostyril was then cyclised to give the base VII ($R_1 = H; R_2 = R_3 = OCH_3$); crystallised from light petrol (40-60°) containing little benzene, m.p. 150-51° C. Yield 0.8 g. Found: C, 69.71; H, 6.67; $C_{15}H_{17}NO_3$ requires C, 69.50; H, 6.56.

I.R. in CHCl$_3$—1939 cm.$^{-1}$

U.V. absorption: $\lambda 278, \varepsilon 3769; \lambda 319, \varepsilon 9065; \lambda 333, \varepsilon 10510.$

U.V. absorption of VIII ($R_1 = H; R_2 = R_3 = OCH_3$): $\lambda 277, \varepsilon 3905; \lambda 319, \varepsilon 8511; \lambda 333, \varepsilon 9906.$

(d) 2: 3-dihydro-2: 4-dimethyl-7-methoxyfuro-(2: 3-b)-quinoline (VII, $R_1 = R_3 = H; R_2 = OCH_3$).—The carbostyril (VI, $R_1 = R_3 = H; R_2 = OCH_3$) was prepared from 2-amino-4-methoxyacetophenone (3.3 g.) and 3-pentenoyl chloride (from 2 g. of the acid); crystallised from ethanol, m.p. 214-15° C. Yield 2.2. Found C, 73.25; H, 6.55; $C_{14}H_{15}NO_2$ requires C, 73.36; H, 6.56.

The carbostyril was then cyclised as before to give the base (VII, $R_1 = R_3 = H; R_2 = OCH_3$); crystallised from light petrol (40-60°) containing little benzene, m.p. 125-26° C. Yield 1.4 g. Found: C, 73.24; H, 6.66; $C_{14}H_{15}NO_2$ requires C, 73.36; H, 6.56.

I.R. in CHCl$_3$—1926 cm.$^{-1}$

U.V. absorption: $\lambda 276, \varepsilon 3938; \lambda 319, \varepsilon 10800; \lambda 333, \varepsilon 15620.$

U.V. absorption of VIII ($R_1 = R_3 = H; R_2 = OCH_3$): $\lambda 276, \varepsilon 3687; \lambda 318 \varepsilon 10000; \lambda 333, \varepsilon 14120.$

ACKNOWLEDGEMENT

Our thanks are due to Dr. K. N. Menon and Dr. S. Swaminathan for their encouragement. We thank Dr. Alfred Bernhadt of Max-Plank Institute, W. Germany, for the micro-analysis, and Dr. V. Mahadeven for the u.v. data, reported here. We are grateful to the University of Madras for the Fellowship to one of us (J. P. J.).
REFERENCES

1. Price, J. R. 

2. Goodwin, S. and Horning, E. C. 

3. ———, Shoolery, J. N. and Johnson, L. F. 

4. Price, J. R. 
   *Austr. J. Chem.*, 1959, **589-600**.

5. Goodwin, S., Shoolery, J. N. and Horning, E. C. 

6. Price, J. R. 

7. Rapoport, H. and Holden, K. G. 

8. Shanmugam, P. 

   *J. Chem. Soc.*, 1933, **557**.

10. Raman, P. S. 