

STUDIES IN SYNTHETIC PHOTOCHEMISTRY - II¹
SYNTHESIS OF CHELILUTINE AND SANGUILUTINE

S.V. Kessar, Y. P. Gupta, (Miss) K. Dhingra, G.S.Sharma and (Miss) S.Narula
Department of Chemistry, Panjab University, Chandigarh-160014 (India)

(Received in UK 8 March 1977; accepted for publication 14 March 1977)

A number of pentaalkoxy naphthaphenanthridine alkaloids have been isolated² and over the past few years three types of structures³ have been proposed^{4,5,6a}. However, recently Ishii et al^{6b} have shown that the methylenedioxy amide IX, secured through an unambiguous synthesis, is identical with the material obtained on oxidation of chelirubine (VIIIc, $R_1-R_2=CH_2O$, $R_6-R_7=CH_2$, $R_3=R_5=H$, $R_4=OCH_3$). We now report total synthesis of the alkaloids chelilutine (VIIIa, $R_1=CH_3$, $R_2=R_4=OCH_3$, $R_3=R_5=H$, $R_6-R_7=CH_2$, $X=Cl$) and sanguilutine (VIIIb, $R_1=CH_3$, $R_2=R_4=OCH_3$, $R_3=R_5=H$, $R_6=R_7=CH_3$, $X=Cl$) and confirm that in the methoxy series also a similar oxygenation pattern is present.

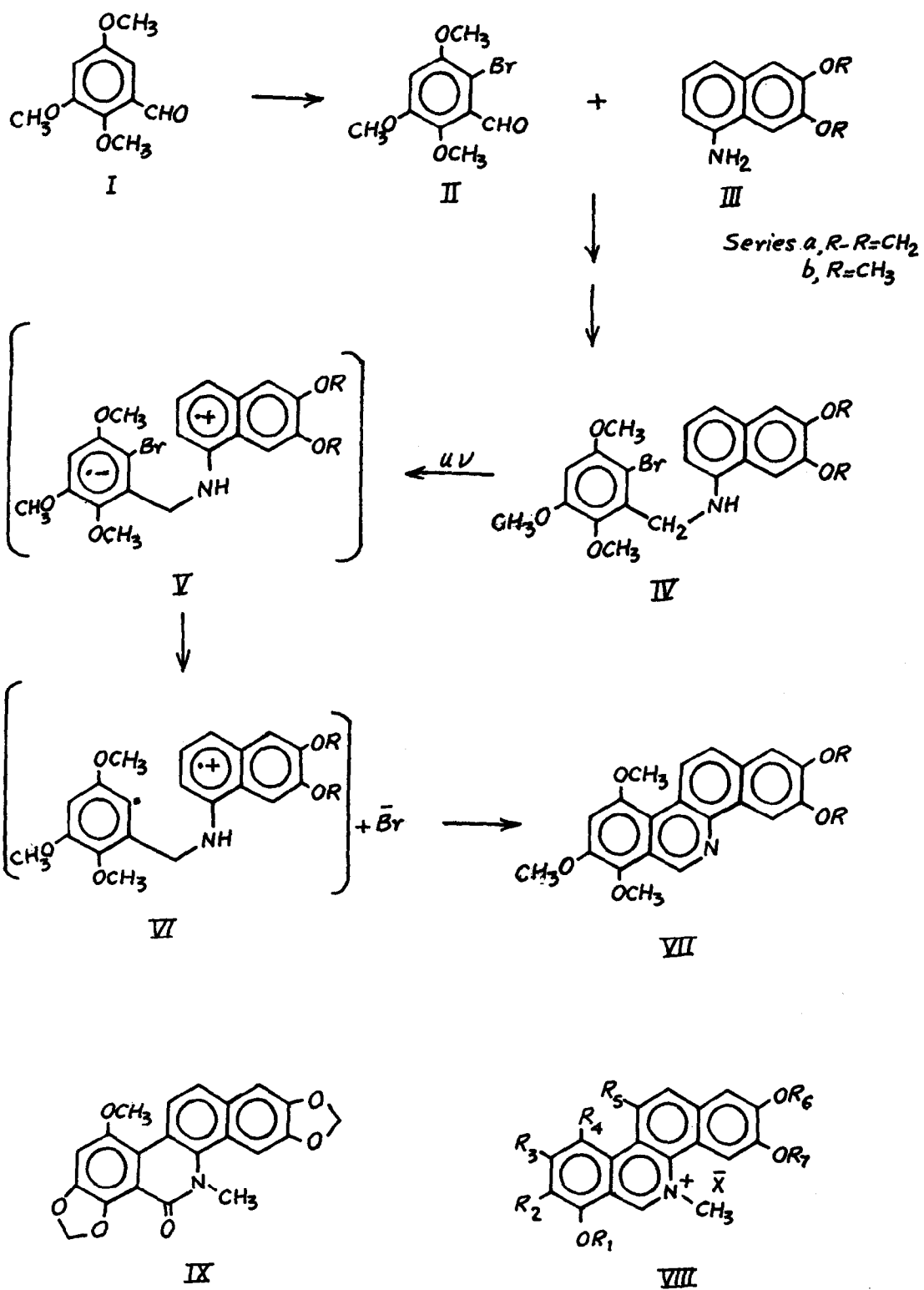
Since the established routes⁷ to naphthaphenanthridine alkaloids seemed unsuitable for the synthesis of penta-oxygenated members, a novel procedure for effecting the crucial ar-ar linkage (IV \rightarrow VII) has been utilised in the present work. It is known⁸ that photolysis of aryl halides in the presence of aniline derivatives leads to phenylation of the base, presumably through an electron transfer process. However, complex mixture are obtained and yields, including the intramolecular case⁹, are poor. We thought that the naphthylamine moiety may be more suitable for such a reaction. Here, as compared to benzene, the lower ionisation potential¹⁰ could facilitate the electron transfer process (IV \rightarrow V). Further, the cyclisation step (VI \rightarrow VII) also may be more competitive with side reactions as it entails¹¹ a smaller sacrifice of resonance energy^{12,13}.

Irradiation of IV indeed gave the tetracyclic base VII smoothly as described below.

Treatment of the Grignard reagent from 2,3,5-trimethoxy-bromobenzene (readily obtained from 5-bromovanillin through a Baeyer-Villiger oxidation and methylation) with dimethylformamide gave the aldehyde I¹⁴ which on bromination in carbon tetrachloride afforded the bromo compound II¹⁵ (C₁₀H₁₁BrO₄, m.p. 105-6°). The Schiff base obtained on its condensation with 6,7-methylenedioxy-naphthylamine¹ (IIIa) was reduced with sodium borohydride to get the compound IVa (C₂₁H₂₀BrNO₅, m.p. 142-43°). Irradiation (4 hrs, N₂) of a 0.001M solution of IVa in acetonitrile-water (9:1) containing sodium hydroxide (0.002 molar) with a 100 watt medium pressure mercury lamp (pyrex filter) gave the phenanthridine VIIa (C₂₁H₁₇NO₅, m.p. 183-5°, m/e 363 M⁺) in 50 % isolated yield. Conversion to the methosulphate followed by crystallisation from dilute HCl furnished the compound VIIIa, m.p. 197-98° (decomp.), which was found to be identical with the alkaloid chelilutine¹⁶ (undepressed m.m.p. 197-98°, same R_f value in a number of solvent systems).

Starting with the dimethoxynaphthylamine IIIb, a similar sequence of steps gave the tetracyclic base VIIb (C₂₂H₂₁NO₅, m.p. 162°, m/e 379 M⁺). It was elaborated to VIIIb, m.p. 137-38°, identical with the alkaloid sanguilutine¹⁶.

The above type photocyclisation was carried out with a few other naphthyl substrates also. It was found that alkoxy substituents, on either side, accelerate the reaction and preparatively bromides are superior to chlorides as well as iodides. Curiously¹⁷, presence of air during irradiation of IV increased the rate of its disappearance and of product formation though not the chemical yield. This is not a consequence of oxidation of IV to the corresponding Schiff base as the latter compound was not detected during the reaction. Further, a separate experiment showed it to be inert under the irradiation conditions. The synthetic scope and mechanism of this photocyclisation are currently under investigation.



References & Foot-Notes

1. Part I of this series, S.V.Kessar, G.Singh and (Miss) P.Balakrishnan, Tetrahedron Letters, 2269 (1974).
2. J. Slavik, L. Slavikova, Coll. Czech. Chem. Commun., 20, 21 (1955); 25, 1667 (1960).
3. Structure VIII, R₂ and R₅ or R₃ and R₄, or R₂ and R₄ as alkoxy groups.
4. J. Slavik, L. Dolejs, V. Hanus and A.D.Cross, Coll. Czech. Chem. Commun., 33, 1619 (1968).
5. M. Onda, K. Abe, K. Yonezawa and N. Esumi, Chem. Pharm. Bull., 18, 1435 (1968).
- 6a. H. Ishii, T. Deushi and K.I. Harada, The 16th Symposium on the Chemistry of Natural Products, Osaka, Oct., 1972, Symposium Papers, p.327.
b. H. Ishii, K.I. Harada, T. Ishida and K. Nakajima, Tetrahedron Letters, 319 (1975).
7. S.F. Dyke, B.J. Moon and M. Sainsbury, Tetrahedron, 24, 1467 (1968) and references therein. Of the two new routes developed in this laboratory one (S.V.Kessar, M. Singh, P. Balakrishnan, Ind. J. Chem., 12, 323 (1974) was inherently inapplicable and the other (ref. 1) failed for the present purpose.
8. C. Pac, T. Tosa and H. Sakurai, Bull. Chem. Soc. Japan, 45, 1169 (1972); M. Grodowski and T. Latowski, Tetrahedron, 30, 767 (1974).
9. K. Mizuno, C. Pac and H. Sakurai, Bull. Chem. Soc. Japan, 46, 3316 (1973).
10. Steven L. Murev, "Handbook of Photochemistry", Marcel Dekker, Inc., New York, p. 199 (1973).
11. The product of ring closure of VI should be dihydro compound in which the aromaticity of one naphthalene ring is destroyed. Its subsequent rearrangement and oxidation would lead to VII.
12. J. March, "Advanced Organic Chemistry" McGraw Hill Book Co., New York, p. 56, 391 (1968).
13. We are investigating the utility of naphthylamines as ET reagents in photoreaction in general.
14. Cf. J.R. Merchant, R.M. Naik and A.J. Mountwalla, J. Chem. Soc., 4142 (1957)
15. Satisfactory elemental analysis was obtained for all new compounds.
16. We are very grateful to Prof. J. Slavik for authentic samples and for a re-recording of the m.p. of sanguilutine chloride.
17. For example of an anomalous effect of oxygen on a photocyclisation see G. Fischer, E. Fischer, K.H. Grellmann, H. Linschitz and A. Temizer, J. Am. Chem. Soc., 96, 6267 (1974).