Tetrahedron Letters No.42, pp. 4139-4142, 1967. Pergamon Press Ltd. Printed in Great Britain.

TRANSANNULAR REACTIONS IN THE DIBENZO[a,d]CYCLOHEPTENE SERIES - I.

THE SYNTHESIS OF 10,5-(IMINOMETHANO)-5H-DIBENZO[a,d]CYCLOHEPTENES.

T.A. Dobson, M.A. Davis, A-M. Hartung and J.M. Manson.

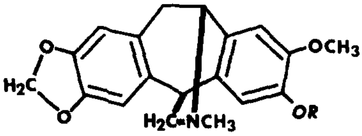
Ayerst Laboratories, Montreal, Canada.

(Received in USA 19 July 1967)

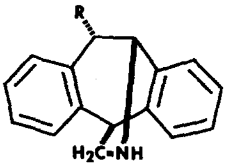
The recent identification (1) of the alkaloids amurensine Ia and amurensinine Ib prompts us to report a convenient synthesis of their parent ring system IIa, 10,5-(iminomethano)-5H-dibenzo[a,d]cycloheptene. This method is particularly useful for preparing 11-substituted derivatives of IIa and is based on the ready transannular interaction of suitable 5,10-disubstituted dibenzo[a,d]-cycloheptene derivatives III (2).

Addition of bromine to the readily available amide IV (3) gave the anti-11-bromo-iminolactone hydrobromide V, yellow needles, m.p.220-224° dec., I.R. max. (nujol) 1675 (C=N), 1105 cm^{-1} (ether). Hydrolysis of V with aqueous alcohol gave the anti-11-bromolactone VIa, m.p. 160-161° (from ethanol), I.R. max. ($CHCl_3$) 1765 cm^{-1} (lactone). The overall yield for these two steps was 95%. The stereochemistry of V and VIa was assigned on mechanistic grounds, i.e. participation of the amide group in the addition of bromine to IV (4). The potential trans-bromohydrin system of VIa was demonstrated by its ready reaction with liquid ammonia to give the syn-epoxyamide VII, m.p. 191-193° (from ethanol, 98% yield), I.R. max. ($CHCl_3$) 3445 (NH), 1690 cm^{-1} (amide).

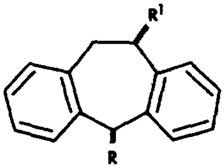
The structure of VII was supported by its ready catalytic hydrogenation to give the syn-11-hydroxyamide IIIa, m.p. 163-165° dec. (from dioxane-hexane, 95% yield), I.R. max. (nujol) 3450 (OH), 3320 (NH), 1683 cm^{-1} (amide), which evolved ammonia at room temperature with concommitant formation of the lactone VIb, m.p. 169-171° (from methanol), I.R. max.



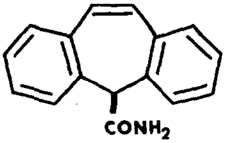
Ia, R=H
b, R=CH$_3$



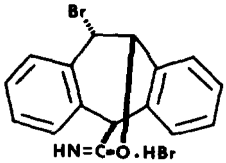
IIa, R=H
b, R=OH



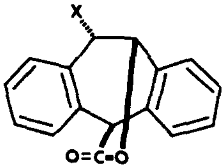
IIIa, R=CONH$_2$; R^1=OH
b, R=CON$_3$; R^1=H



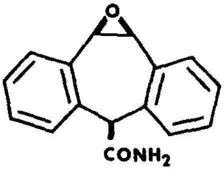
IV



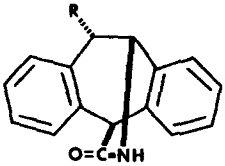
V



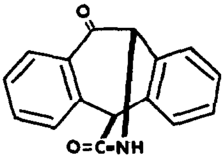
VIa, X=Br
b, X=H



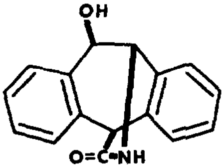
VII



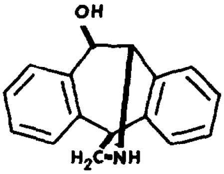
VIIIa, R=OH
b, R=H



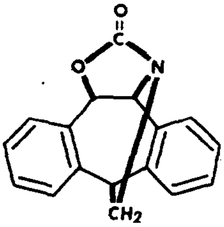
IX



X



XI



XII

($CHCl_3$) 1740 cm^{-1} (lactone). *

Treatment of the epoxyamide VII with ammonium hydroxide at 140° gave the anti-11-hydroxylactam VIIIa, m.p. 260-262° dec. (from ethanol, 70% yield), I.R. max. (nujol) 1670 cm^{-1} (lactam). The same product was obtained from the reaction of the bromolactone VIa with ammonium hydroxide at 140°, and from the reaction of the epoxyamide VII with sodium hydride in dioxane.

Chromic acid oxidation of VIIIa gave the ketolactam IX, m.p. 197-199° (from ethanol, 95% yield), I.R. max, ($CHCl_3$) 3425, 3200 (NH), 1685 cm^{-1} (ketone and lactam). Reduction of IX with sodium borohydride gave VIIIa demonstrating that VIIIa and IX had the same skeleton. Catalytic hydrogenation of IX gave the syn-11-hydroxylactam X, m.p. 260-263° (from methanol, 90% yield), I.R. max. (nujol) 1665 cm^{-1} (lactam). Hydrogenolysis of both VIIIa and X with sodium in liquid ammonia gave the lactam VIIIb, m.p. 242-245° (from ethanol, 95% yield), I.R. max. (nujol) 1675 cm^{-1} (lactam). The same product was also obtained, in poor yield, from the photolysis of the acid azide IIIb. Reduction of VIIIb with lithium aluminium hydride gave IIa, isolated as its hydrochloride salt, m.p. > 280° (from ethanol, 81% yield), I.R. max. (nujol) 2700, 2605, 2450 (NH^+), 1590, 1457, 757 cm^{-1}.

Reduction of VIIIa with lithium aluminium hydride gave the anti-hydroxy compound IIb, m.p. 130-134° (from benzene-hexane, 80% yield), I.R. max. ($CHCl_3$) 3570 (OH), 3325, 1020 cm^{-1}. and similar reduction of X gave the epimeric syn-hydroxy compound XI, m.p. 191-193° (from methanol, 85% yield), I.R. max. (nujol) 3300 (OH), 1488, 1308, 748 cm^{-1}. The configuration assigned to IIb (and therefore the configuration assigned to its parent hydroxylactam VIIIa) was supported by its I.R. spectrum since the hydroxyl absorption maximum of this compound was concentration-dependent.

Definitive chemical evidence for the configuration of XI was obtained from its reaction with phosgene. The product, which was non-basic, was XII, m.p. 226-228° dec. (from ethanol, 50% yield), I.R. max. ($CHCl_3$) 1758 cm^{-1} (carbonyl). (Found: C, 77.59; H, 5.00; N, 5.17; M.W. (mass spectroscopy) 263. $C_{17}H_{13}NO_2$ requires: C, 77.55; H, 4.98; N, 5.32%. M.W. 263. Inspection of Drieding molecular models of IIb and XI showed that only the latter compound

---

* The anti-hydroxy epimer of IIIa, prepared by hydroboration of IV, is stable up to 140°. Furthermore, attempts to prepare the anti-epoxyamide epimer of VII, by epoxidation of IV, gave the anti-hydroxylactone VIc.

could form XII.

A more detailed account of this work will be published elsewhere.

REFERENCES.

1. F. Šantavý, L. Hruban and M. Maturová, Collection Czech. Chem. Commun. 31, 4286 (1966).

2. J. Rigaudy and L. Nédélec, Bull. Soc. Chim. France, 643, 648. (1959); G.L. Buchanan and D.B. Jhaveri, J. Org. Chem., 26, 4295 (1961).

3. M.A. Davis, S.O. Winthrop, R.A. Thomas, F. Herr, M-P. Charest and R. Gaudry, J. Med. Chem., 7, 88 (1964).

4. P.N. Craig, J. Amer. Chem. Soc., 74, 129 (1952).