

ORMOSIA ALKALOIDS, PART I: STRUCTURE OF  
ORMOJANINE AND ORMOSANINE

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Recently, several publications appeared dealing with alkaloids contained in Ormosia jamaicensis (1,2), O. panamensis (3) and O. dasycarpa (4). Three of these compounds were identified with lupin alkaloids of known structure: angustifoline (1,2,5,6), epihydroxylupanine (2,5) and (-)-sparteine (4). However, none of the reports contained any significant advances towards the structure elucidation of the  $C_{20}$ -alkaloids present in large quantities in plants of this genus (2,3).

We now report the results of our study of two  $C_{20}$ -alkaloids of Ormosia jamaicensis Urb., ermojanine,  $C_{20}H_{31}N_3$ , m.p. 124-126°, and ormosanine,  $C_{20}H_{35}N_3$ , m.p. 179-181°(2).\*

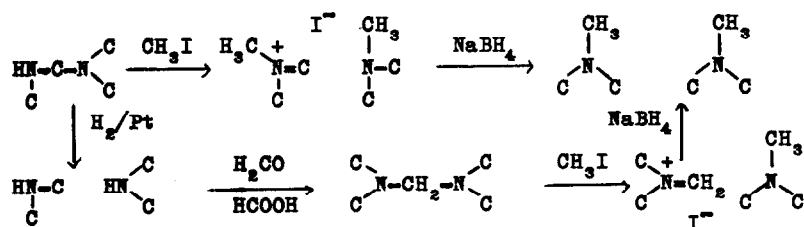
Ormojanine. The compound contains 3 basic N's (1 secondary, 2 tertiary) and no C-CH<sub>3</sub> or N-alkyl groups. It has a trisubstituted double-bond (NMR doublet for 1H at

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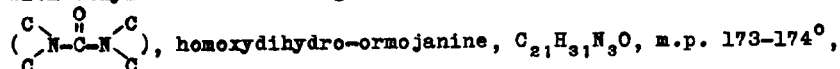
\* All compounds described in this communication gave satisfactory elemental analysis.

4.56 p.p.m.,  $J$  6 cps.).<sup>\*</sup> Controlled hydrogenation of ormojanine gave dihydro-ormojanine,  $C_{20}H_{33}N_3$ , m.p. 127-129°, still containing the double-bond but having two secondary nitrogens. Continued hydrogenation saturated the double-bond to give tetrahydro-ormojanine,  $C_{20}H_{35}N_3$ , m.p. 107-109°.

The nature of the unstable C-N bond was solved in the following way. Treatment of ormojanine with  $CH_3I$  in benzene followed by filtration through basic amberlite gave an unstable enamine (NMR, IR), which on reduction with  $NaBH_4$  yielded dimethyldihydro-ormojanine,  $C_{22}H_{37}N_3$ , m.p. 120-122°. Reaction of dihydro-ormojanine with  $CH_2O/HCOOH$  bridged the secondary nitrogen atoms to give homodihydro-ormojanine,  $C_{21}H_{33}N_3$ , which on methylation with  $CH_3I$  in benzene followed by a reduction with  $NaBH_4$  gave a compound identical in all respects with dimethyldihydro-ormojanine. These two sequences prove the presence of the grouping N-C-N in ormojanine and can be illustrated by the following scheme:



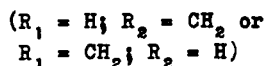
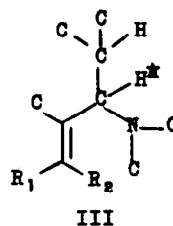
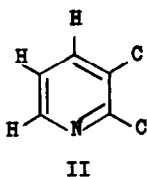
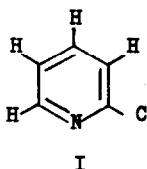
Treatment of dihydro-ormojanine and tetrahydro-ormojanine with ethyl chloroformate gave the corresponding ureas



<sup>\*</sup> NMR spectra were run at 60 mc in  $CDCl_3$  with  $Si(CH_3)_4$  as an internal reference.

and homoxytetrahydro-ormojanine,  $C_{21}H_{33}N_3O$ , m.p. 203-205°, respectively. Their IR carbonyl absorption (1640  $cm^{-1}$  in  $CCl_4$ ) indicates that the two secondary N's are separated by at least three C atoms. The urea grouping was found to be stable to a vigorous acid and basic hydrolysis, indicating an unstrained planar arrangement.

Treatment of dihydro-ormojanine with Pd-charcoal in  $C_6H_6$  at 200° gave a 50% yield of an oily pyridine,  $C_{20}H_{23}N_3$ . Its UV spectrum (infl. 256 m $\mu$ ,  $\lambda_{max}$  262 m $\mu$ ,  $\epsilon$  5,600 and 268 m $\mu$ ,  $\epsilon$  5,300, infl. 278 m $\mu$ ) shows the presence of two isolated pyridine rings. The position of these maxima together with the position and splitting pattern of seven aromatic H's found in its NMR spectrum (two broadly split  $\alpha$  H's, three  $\beta$  H's, two  $\gamma$  H's) indicate the presence of pyridines (I) and (II) in the molecule. The third nitrogen in the dehydrogenation product was found to be tertiary.

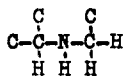


A Hofmann degradation of homoxydihydro-ormojanine gave a crystalline diene,  $C_{22}H_{33}N_3O$ , m.p. 135-138°. Its UV spectrum indicates a transoid arrangement of double-bonds (UV max. of hydrochloride: 243 m $\mu$ ,  $\epsilon$  16,600; free base max. at 225 m $\mu$ ,  $\epsilon$  11,600 and 253 m $\mu$ ,  $\epsilon$  11,700) and the NMR

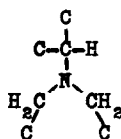
spectrum shows the presence of two vinylic H's (1H at 3.85 p.p.m., singlet; 1H at 4.79 p.p.m., triplet). Partial structure (III) describing the environment of the tertiary N in ormojanine explains the Hofmann degradation and the fact that the NMR spectra of ormojanine and its double-bond containing derivatives show an H at 6.7 p.p.m. (double deshielding; see H<sup>\*</sup> in III).

Ormosanine. The alkaloid (C<sub>20</sub>H<sub>35</sub>N<sub>3</sub>) contains three basic nitrogens (2 secondary, 1 tertiary) and no C-CH<sub>3</sub> or N-alkyl groups and no double-bonds; it is therefore pentacyclic. It undergoes bridging reactions analogous to those described for ormojanine. Treatment with CH<sub>2</sub>O/HCOOH gave homo-ormosanine, C<sub>21</sub>H<sub>35</sub>N<sub>3</sub>, m.p. 148-149°, while reaction with COCl<sub>2</sub> yielded the corresponding urea, homoxyormosanine, C<sub>21</sub>H<sub>33</sub>N<sub>3</sub>O, m.p. 178-180° (IR max. 1640 cm<sup>-1</sup> in CCl<sub>4</sub>).

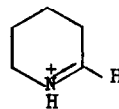
NMR study provided important information about the environment of the nitrogen atoms. While ormosanine shows no absorption below 7 p.p.m., the corresponding N,N'-diacetyl derivative, C<sub>24</sub>H<sub>39</sub>N<sub>3</sub>O<sub>2</sub>, m.p. 164-166°, has six deshielded hydrogen atoms (5.06-6.7 p.p.m.) in its NMR spectrum. The comparison of the NMR spectra of the N,N'-diacetyl, the N-monoacetyl and the N,N'-dinitroso derivatives indicated that both secondary nitrogens in ormosanine have the environment IV.



IV



V



VI

Treatment of homoxyormosanine with BrCN gave the von Braun product,  $C_{22}H_{33}N_4BrO$ , m.p. 184-186°, which on reaction with KOAc gave the cyanoacetate,  $C_{24}H_{36}N_4O_3$ . Hydrolysis of the acetate with  $K_2CO_3$  yielded the cyanoalcohol,  $C_{22}H_{34}N_4O_2$ , m.p. 225-227°. The NMR study of these three compounds showed that the von Braun product contains the grouping  $-CH_2Br$  and three H's  $\alpha$  to the cyanamide group. The tertiary N in ormosanine is thus present in the grouping V.

By far the most prominent peak in the mass-spectrum of ormosanine is one at  $m/e$  84. We consider that it is given by the ion VI and that the formation of this ion together with the finding of the pyridine grouping I in the dehydrogenation product of dihydro-ormojanine strongly suggests the presence of an  $\alpha$ -monosubstituted piperidine in both alkaloids under investigation.

Skeletal Structure. Treatment of either ormosanine or tetrahydro-ormojanine with Pd-charcoal at 280° in a sealed tube, followed by an extensive product purification by counter-current distribution and  $Al_2O_3$ -chromatography gave a 5-10% yield of an oily quinoline, picrate m.p. 108-110°. The analysis and NMR integration indicated the empirical formula  $C_{19-20}H_{27-28}N$ . The NMR spectrum (in  $CCl_4$ ) contained the following peaks: 1.48 p.p.m. (1H, doublet, J 2 cps.), 2.42 p.p.m. (1H, doublet, J 2 cps.), 2.85 p.p.m. (2H's, sharp singlet), 6.88 p.p.m. (2H's, triplet, J 6 cps.), 7.32 p.p.m. (4H's, triplet, J 6 cps.), 8.2-8.6 p.p.m. (8-10H's, multiplet) and 9.0 p.p.m. (9H's, 2 triplets, J 6 cps.). A comparison of the aromatic region with model compounds showed

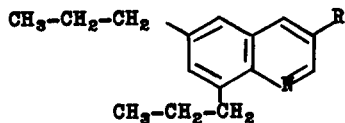
that the quinoline is 3,6,8-trisubstituted. All other substituted quinolines gave clearly different splitting patterns. The presence of only 3 methyl groups (NMR) showed that all side-chains are unbranched, while the absence of any methyl resonance at 8.7 p.p.m. showed that all chains are longer than ethyl.

A careful analysis by v.p.c. (25% Silicone SE-30 on Chromosorb-W; 12 ft. x 1/8" o.d. column; 280°; N<sub>2</sub>-40 ml./min.) showed that the "natural" quinoline is actually a mixture of two compounds (ratio 1.65:1; retention times 14 min. 37 sec. and 11 min. 57 sec., respectively), although the corresponding quinoline had been recrystallized 15 times, with the m.p. remaining constant for the last 5 crystallizations. Since a preparative separation proved difficult, it was decided to solve the problem synthetically. It has now been found that a mixture of 3-n-pentyl-6,8-dipropylquinoline (VII) (1.65 parts) with 3-n-butyl-6,8-dipropylquinoline (VIII) (1 part) is identical in all respects (v.p.c., NMR, IR, UV, picrate m.p.) with the natural mixture, while the 6-butyl and pentyl and 8-pentyl isomers show distinct differences.\* In particular, the 11-12  $\mu$  region in the IR, the NMR methyl region and the picrate m.p.'s are distinctly different in the three series. Furthermore, 8-pentyl-3,6-dipropylquinoline was found to have a longer retention time than the higher boiling component of the dehydrogenation product in v.p.c. (13 sec. difference in

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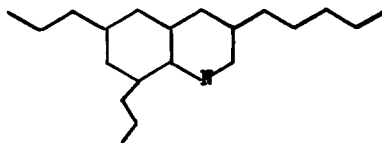
\* The quinoline synthesis will be reported in a separate publication.

a 4 min. run).



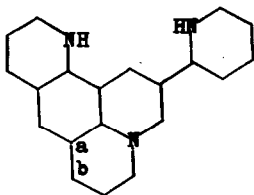
VII: R = n-pentyl;

VIII: R = n-butyl

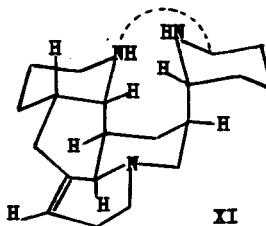


IX

Quinoline (VII) contains all the C-atoms present in the two alkaloids. The relatively high yield of both dehydrogenations and the fact that the reaction conditions were mild enough to preserve long aliphatic chains (7) strongly suggest carbon skeleton (IX) for the two Ormosia alkaloids under investigation. It now remains to add two nitrogen atoms in a way which takes account of all the described chemical data. Only total structure X for tetrahydro-ormejanine and ormosanine completely satisfies these conditions. Structure X also gives a good explanation for the finding that, in addition to the quinolines, the dehydrogenation of both tetrahydro-ormejanine and ormosanine gave pyridine and  $\beta$ -picoline as determined by v.p.c. and picrate crystallisation.



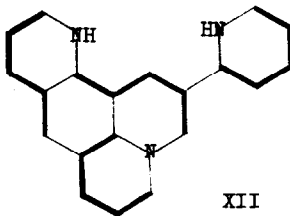
X



XI

Based on partial structure (III), the double-bond in dihydro-ormojanine must be at  $C_a-C_b$ . The requirement of a cyclic urea formation naturally places severe restrictions upon the configuration of X. Dihydro-ormojanine must have the stereostructure XI. Ormojanine itself is then XI with an additional C-N bond as indicated by the dotted line. (The use of the alternative NH for this bond is prohibited on steric grounds.) It appears from the study of atomic models that the two saturated compounds possessing structure (X), tetrahydro-ormojanine and ormosanine, can only differ in the configuration at  $C_a$  with the configuration at all the remaining asymmetric carbons identical with XI.

Biogenesis. It is interesting to note that in analogy to all lupin alkaloids, the  $C_{20}$  Ormosia alkaloids satisfy the following conditions: a) molecular composition  $(C_5N)_x + C_5$ ; b) straight-chain  $C_5$  building units; c) nitrogen atoms only joined to the ends of chains; d) new C-C bonds only formed between  $C_1$  of one chain and  $C_2$  of another (aldol or Mannich condensation).





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