Communications to the Editor

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THE ISOLATION OF A NEW CLASS OF ISOFLAVONOID METABOLITES FROM SOPHORA TOMENTOSA L.

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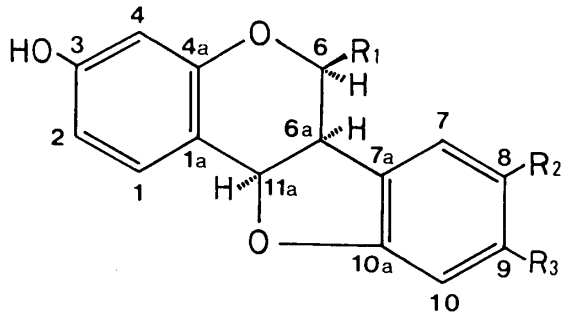
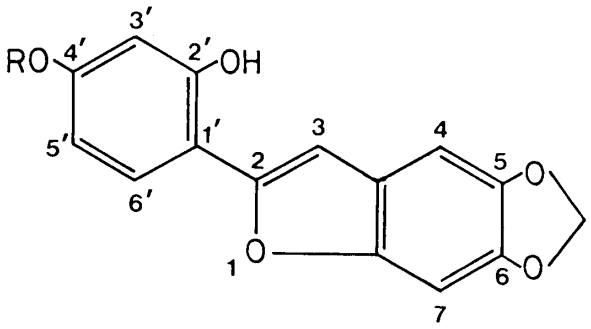
Two new pterocarpans named sophoracarpans A and B were isolated from Sophora tomentosa L. (Leguminosae), and their respective structures have been elucidated as 6β,9-dimethoxy-3-hydroxypterocarpan (I) and 3-hydroxy-6β-methoxy-8,9-methylenedioxypterocarpan (III).

KEYWORDS ——— 6-methoxypterocarpan; sophoracarpan A; sophoracarpan B; Sophora tomentosa; Leguminosae

Sophora tomentosa L. is a leguminous shrub which occurs abundantly along the seashore throughout tropical Asia and extends north to the Ryukyu and Bonin Islands of Japan. This plant is of medicinal value in Eastern Malaysia as a remedy for cholera and diarrhea, and as an antidote after eating poisonous fishes and other marine animals. In the Philippines it is regarded as anticholeric and is a common remedy for stomach disorders. Although a number of flavonoids, including isoflavonoids, have been isolated from this plant to date,[1] none of those





(I) $R_1=R_3=OMe$ $R_2=H$ **sophoracarpan A**

(II) $R_1=R_2=H$ $R_3=OMe$ **medicarpin**

(III) $R_1=OMe$ $R_2=R_3=OCH_2O$ **sophoracarpan B**

(IV) R=H

(V) R=Me

compounds have been identified with the pharmacological properties attributed in traditional use to this crude drug. As part of our continuing research dealing with biologically active principles from Asian herbal medicines,[2] we selected this plant as a subject for chemical investigation. In this communication we report the isolation and structural elucidation of a new class of isoflavonoid metabolites from the aerial parts of this plant collected in Taiwan.

Sophoracarpan A was obtained as optically active crystals,[3] and its structure was elucidated as (I) on the basis of the following evidence. The molecular formula $C_{17}H_{16}O_5$ was determined by high resolution mass spectroscopy.[4] The UV spectrum exhibits an absorption maximum at 287nm indicating that it is a phenolic compound.[4] The IR spectrum indicates the absence of a functional group such as carbonyl. The ^{13}C-NMR spectrum[5] closely resembles that of medicarpin (II),[6] differing only in chemical shifts of C-6 and C-6a in the pterocarpan structure. The hemiacetal nature of C-6 is indicated by a chemical shift of 102.6ppm, characteristic of the hemiacetal carbon, and a marked downfield shift (5.9ppm) of the adjacent C-6a. The ^1H-NMR spectrum[7] reveals the presence of the three resonances (δ4.92; δ3.62; δ5.66) on the two hetero rings, which are assignable to 6-H, 6a-H and 11a-H respectively. These assignments are further confirmed by ^1H-^{13}C selective decoupling experiments in which irradiating the 6-H proton at δ4.92 collapsed the doublet C-6 signal at δ102.6 to a sharp singlet. This strongly suggests that it is a hemiacetal proton (6-H) rather than 11a-H. Thus the stereochemical figure of sophoracarpan A is illustrated as (B) in Fig. 1 based on the magnitude of the coupling constants ($J_{6\text{-}6a}$=5.5Hz; $J_{6a\text{-}11a}$=8.5Hz). Further proof of the structure was provided by results of an NOE (Nuclear Overhauser Effect) study in which the irradiation of 6a-H resulted in a substantial NOE on the methine protons at 11a-H and 6-H (16% and 8% respectively).[8] This indicates that the methine proton (6-H) is cis with respect to the neighboring methine proton (6a-H); that is, the methoxy group at C-6 is β-oriented.

Baruah et al.[9] have recently reported the isolation of two new 6-methoxypterocarpans and established the conformation of MeO at C-6 as α based on the analysis of resonances attributed to the hetero rings. These resonances are in

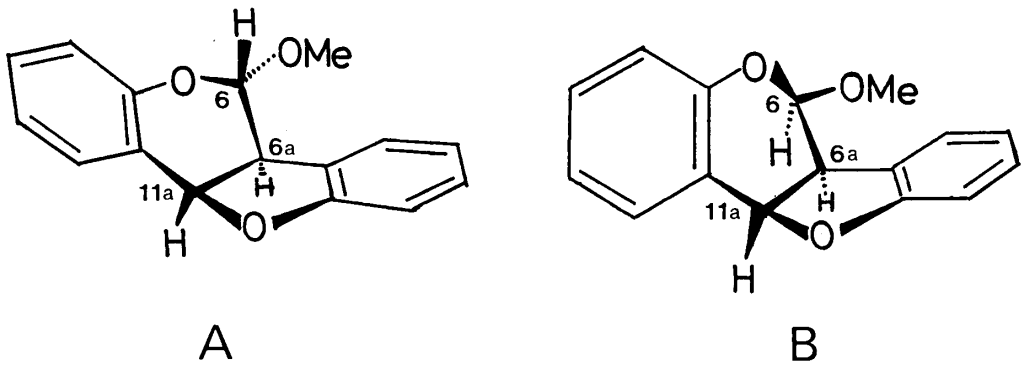


Fig. 1. Possible Conformations for 6α- and 6β-Methoxypterocarpans

good conformity with those of sophoracarpan A. Unfortunately the structures should be reviewed since the authors deduced them from wrong assignments of the proton signals in the hetero rings.[10]

The ^{1}H-NMR spectrum also reveals the presence of six protons in the aromatic region, which constitute ABX and A'B'X'.[11] The assignment of ABX to the D-ring was based on the observation of a long range coupling (0.8Hz) between 6a-H and the signal at δ7.21 (A). Irradiating the aromatic methoxy protons at δ3.73 furnished 9% and 13% NOE on the signals at δ6.44 (B) and δ6.32 (X) respectively, thus confirming the location of another methoxy group on the D-ring.

Sophoracarpan B was obtained in a small amount in an amorphus form. The spectroscopic results[12] reveal the close relationship of this compound to sophoracarpan A, and indicate that the structure is 6β-methoxymaackiain (III).

6-Methoxypterocarpan is a new class of isoflavonoid metabolite and only four natural compounds of this type are known, including sophoracarpans A and B. Komatsu et al.[1] have reported the isolation of 2-arylbenzofuran derivatives (IV) and (V) from the same plant. In view of the biogenetic origin of these compounds, their isoflavonoid nature is obvious from their structural feature (the presence of 2'-OH) and the fact that they are of leguminous origin.[13] A biosynthesis sequence involving loss of C-6 from a coumestan, by chemical analogy with alkaline degradation of coumestans, is generally postulated for 2-arylbenzofurans, but lacks experimental proof. Although the role of the 6-methoxypterocarpan in the biosynthesis scheme of the isoflavonoid is speculative, it is of considerable interest to note that 6-methoxypterocarpans were isolated from the same plant species that contains 2-arylbenzofurans and a pterocarpan with related substitution patterns.

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2) This is the second report on this series. Previous report: T. Kinoshita, S. Tatara and U. Sankawa, Chem. Pharm. Bull., **33**, 1770 (1985).

3) Sophoracarpan A: colorless needles, mp 163-5°C (MeOH-H_2O). $[\alpha]_D^{25}$-110° (c=0.33, MeOH).

4) UV λ_{max}^{MeOH} nm(log ε): 283sh(3.89), 287(3.92). High resolution MS: Calcd for $C_{17}H_{16}O_5$: 300.0995. Found: 300.0965. m/z: 300(M^+, 21%), 269(M^+-OCH_3, 30%), 268(M^+-CH_3OH, base peak), 267(93%).

5) ^{13}C-NMR(acetone-d_6, 25MHz) δ: 46.2(C-6a), 56.1, 57.1(OCH_3), 80.1(C-11a), 97.3(C-10), 102.6(C-6), 105.0(C-4), 107.4(C-8), 111.2(C-2), 114.3(C-1a), 119.6(C-7a), 126.7(C-7), 132.3(C-1), 154.4(C-4a), 160.0(C-3), 161.9(C-10a), 162.4(C-9).

6) A. A. Chalmers, Tetrahedron, **33**, 1735 (1977).

7) ^{1}H-NMR(acetone-d_6, 400MHz) δ: 3.47(3H, s, 6-OCH_3), 3.62(1H, br dd, J=8.5 and 5.5Hz, 6a-H), 3.73(3H, s, 9-OCH_3), 4.92(1H, d, J=5.5Hz, 6-H), 5.66(1H, d, J=8.5Hz, 11a-H), 6.32(1H, d, J=2.3Hz, 10-H), 6.36(1H, d, J=2.4Hz, 4-H), 6.44(1H, dd, J=2.3 and 8.4Hz, 8-H), 6.56(1H, dd, J=2.4 and 8.4Hz, 2-H), 7.21(1H, dd, J=0.8 and 8.4Hz, 7-H), 7.27(1H, d, J=8.4Hz,1-H), 8.52(1H, br s, 3-OH). The irradiation of the signal at δ3.62 collapsed the double doublet signal at δ7.21 to a doublet.

8) This was further substantiated by a positive NOE in the difference spectrum.

9) P. Baruah, N. C. Barua, R. P. Sharma, J. N. Baruah, P. Kulanthaivel and W. Hertz, Phytochemistry, **23**, 443 (1984).

10) In ref. 9, the authors assigned signals at δ4.76 and δ5.67 respectively to 11a-H and 6-H of 6α-methoxy-homopterocarpin. Apparently this was inconsistent with any previously reported chemical shifts for these protons. The authors may have confused δ with τ for these two signals.

11) ABX: δ7.21(7-H); δ6.44(8-H); δ6.32(10-H). A'B'X': δ7.27(1-H); δ6.56(2-H); δ6.36(4-H). This grouping is confirmed by spin decoupling experiments.

12) $[\alpha]_D^{25}$-135°(c=0.15, MeOH). UV λ_{max}^{MeOH} nm(log ε): 282sh(3.72), 287(3.76), 310(3.89). High resolution MS: Calcd for $C_{17}H_{14}O_6$: 314.0789. Found: 314.0779. m/z: 314(M^+, 27%), 283(M^+-OCH_3, 23%), 282(M^+-CH_3OH, base peak), 281(58%). ^{1}H-NMR(acetone-d_6, 400MHz) δ: 3.54(3H, s, 6-OCH_3), 3.64(1H, br dd, J=5.5 and 8.5Hz, 6a-H), 4.98(1H, d, J=5.5Hz, 6-H), 5.69(1H, d, J=8.5Hz, 11a-H), 5.95(1H, d, J=1Hz, -OCH(H)O-), 5.97(1H, d, J=1Hz, -OCH(H)O-), 6.39(1H, s, 10-H), 6.42(1H, d, J=2.4Hz, 4-H), 6.61(1H, dd, J=2.4 and 8.3Hz, 2-H), 6.90(1H, d, J=0.7Hz, 7-H), 7.31(1H, d, J=8.3Hz, 1-H), 8.57(1H, br s, 3-OH). The irradiation of the signal at δ3.64 collapsed the doublet at δ6.90 to a sharp singlet. ^{13}C-NMR(acetone-d_6, 25MHz) δ: 46.9(C-6a), 57.2(OCH_3), 80.1(C-11a), 94.1(C-10), 102.6(C-6 and $-OCH_2O-$, overlapped), 105.0(C-4), 106.8(C-7), 111.2(C-2), 114.3(C-1a), 118.7(C-7a), 132.3(C-1), 142.9(C-8), 149.4(C-9), 154.5(C-10a), 155.6(C-4a), 160.1(C-3).

13) P. M. Dewick, "The Flavonoid: Advances in Research," ed. by J. B. Harborne and T. J. Mabry, Chapman and Hall, New York, 1982, Chapter X.

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