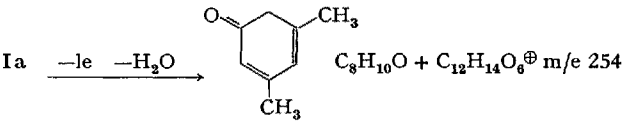
The remaining hydroxyl groups were readily acetylated and are therefore secondary hydroxyls attached at positions 6 and 15 in the molecule as shown. Additional evidence for the attachment of 1 of the hydroxyls at position 6 was obtained by analysis of the mass spectrum of bruceine G. An abundant peak at m/e 254 could be assigned to the fragment $C_{12}H_{14}O_6^{\oplus}$ which forms by the fragmentation of the molecule across the 5–6 and 9–10 bonds as shown.



This is very similar to the fragmentation found for other bruceines[3] however occurs closer to ring A due to the presence of the hydroxyl at position 6. (The lactone at 7 in other bruceines promotes cleavage of the 6–7 bond.)

We have no direct evidence which proves that the stereochemistry of the ring junctions is as shown, however it is reasonable to assume that these related compounds (bruceines) arise via similar biogenetic routes[13] and that their gross stereochemistry is alike. Also, it is reasonable to assume that the configuration of the hydroxyls at 6 and 15 is equatorial due to their facile acetylation with acetic anhydride/pyridine[14].

Zusammenfassung. Aus den Samen von *Brucea sumatrana* wurden die beiden neuen Stoffe Brucein D und G isoliert. Für die letztere Verbindung wird eine Strukturformel vorgeschlagen.

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29 April 1968.

[13] For a review see J. Polonsky, Planta med., Suppl. 107 (1966).

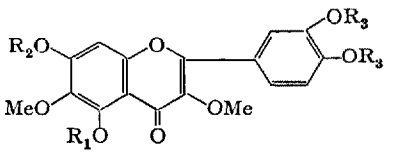
[14] The authors would like to thank the National Research Council of Canada (grant No. A-1863) and Poulenc Ltd. for their support of this research.

The Syntheses of Axillarin and its Related Compounds

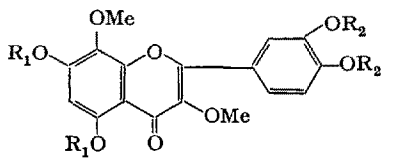
Axillarin (quercetagetin 3,6-dimethyl ether) was first isolated from the leaves of cocklebur (*Xanthium pensylvanicum*)[1] and later from the flowers and leaves of *Iva axillaris* Pursh. ssp. *robustor*[2]. Its structure was assigned to 5,7,3′,4′-tetrahydroxy-3,6-dimethoxyflavone (I)[1,2]. Axillarin 7-methyl ether (II) was also isolated from the leaves of *Cyanoestegia microphylla*[3]. The synthetic approaches to those compounds, however, had remained unsuccessful. 5,7,3′,4′-Tetrahydroxy-3,8-dimethoxyflavone (III), an isomer of I was isolated from *Ricirocarpus muricatus* Muell. Arg.[4] and was synthesized[5]. The present paper deals with the first syntheses of I and II, and a new synthesis of III from 2,4,6-trihydroxy-3,ω-dimethoxyacetophenone (IV) in a manner similar to that described earlier[6,7].

According to the Allan-Robinson's flavone synthesis, the ketone (IV) with 3,4-dibenzyloxybenzoic anhydride and potassium 3,4-dibenzyloxybenzoate gave a mixture of flavones, which was used for next acetylation step without purification. After usual acetylation, the reaction products were purified by recrystallization from methanol to give 5,7-diacetoxy-3′,4′-dibenzyloxy-3,6-dimethoxyflavone (V) (m.p. 135–136.5°, UV λ_{max}^{EtOH} nm (log ε): 252 (4.32), 350 (4.21). Found: C, 69.08; H, 4.80. $C_{35}H_{30}O_{10}$ requires: C, 68.84; H, 4.95%) in 26% yield from IV. Treatment of V with dilute alkali gave 3′,4′-dibenzyloxy-5,7-dihydroxy-3,6-dimethoxyflavone (VI) (m.p. 147.5 to 148.5°, UV λ_{max}^{EtOH} nm (log ε): 255 (4.27), 273 (4.23), 347 (4.35). Found: C, 70.66; H, 4.76. $C_{31}H_{26}O_8$ requires: C, 70.71; H, 4.98%). The residue, obtained from the methanolic filtrate, hydrolyzed its acetoxy groups with alkali to phenolic compounds, from which 3′,4′-dibenzyloxy-5,7-dihydroxy-3,8-dimethoxyflavone (VII) (m.p. 180 to 181.5°, UV λ_{max}^{EtOH} nm (log ε): 258 (4.28), 277 (4.32), 339 (4.21), 355 (4.20). Found: C, 70.99; H, 4.97. $C_{31}H_{26}O_8$ requires: C, 70.71; H, 4.98%) was isolated by repeated recrystallization from ethyl acetate in 18% yield from IV.

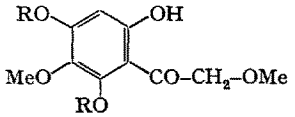
Debenzylation of VI with hydrogen yielded axillarin (I) (m.p. 207–208° and 217–218° (208–209° sinter), IR 3380, 3130, 1652, 1602 cm^{-1} (Nujol), UV λ_{max}^{EtOH} nm (log ε): 259 (4.25), 295 (3.91), 358 (4.32). Found: C, 58.86; H, 3.96.



I $R_1 = R_2 = R_3 = H$
II $R_1 = R_3 = H$ $R_2 = Me$
V $R_1 = R_2 = Ac$ $R_3 = C_6H_5CH_2$
VI $R_1 = R_2 = H$ $R_3 = C_6H_5CH_2$
VIII $R_1 = R_2 = R_3 = Et$
X $R_1 = R_2 = Ac$ $R_2 = Me$



III $R_1 = R_2 = H$
VII $R_1 = H$ $R_2 = C_6H_5CH_2$



IV R = H
IX R = Et

$C_{21}H_{18}O_{10}$ requires: C, 58.96; H, 4.08%) (natural one[8], m.p. 207.5–209°, IR 3390, 3130, 1653, 1604 cm^{-1} (Nujol), UV λ_{max}^{EtOH} nm (log ε): 259 (4.26), 296 (3.92), 355 (4.33)) (lit. m.p. 207–209°[1], 211–213°[2], 199–200°[9]), whose identity with natural one was confirmed by mixed m.p. determination and UV- and IR-spectral comparison. Synthetic axillarin gave, with acetic anhydride, tetraacetate (m.p. 161–161.5°) and, with diethyl sulphate, tetraethyl ether (VIII) (m.p. 110–111.5°) (lit.[2] m.p. 108–110°), which was also prepared from 2,4-diethoxy-6-hydroxy-3,ω-dimethoxyacetophenone (IX) and 3,4-diethoxybenzoic anhydride by unambiguous method.

Partial methylation of VI, followed by debenzylation yielded axillarin 7-methyl ether (II) (m.p. 237–238°, IR 3380, 1651, 1603, 1593 cm^{-1} (Nujol), UV λ_{max}^{EtOH} nm (log ε): 260 (4.32), 356 (4.37). Found: C, 60.21; H, 4.47. $C_{18}H_{16}O_8$ requires: C, 60.00; H, 4.48%) (lit.[3] m.p. 235–236°, UV λ_{max}^{EtOH} nm (log ε): 271 (4.29), 360 (4.31)). Its triacetate (X) (m.p. 158–159°) (lit.[3] m.p. 159–160°) was prepared by acetylation.

On the other hand, debenzylation of VII afforded the tetrahydroxyflavone (III) (m.p. 297–299°, IR 3440, 3360, 3290, 1657, 1616 cm^{-1}, UV λ_{max}^{EtOH} nm (log ε): 262 (4.32), 274.5 (4.37), 298 (3.97), 368 (4.25). Found: C, 58.87; H, 3.83. $C_{21}H_{18}O_{10}$ requires: C, 58.96; H, 4.08%) (natural compound[10], m.p. 296–298°) (lit.[4] m.p. 301–303°), whose identity with natural compound was confirmed by mixed m.p. determination and UV-spectral comparison. Its tetraacetate (m.p. 157–158°) (lit.[4] m.p. 149–150°) and tetraethyl ether (m.p. 124.5–125.5°) (lit.[4] m.p. 125–126°) were prepared by a usual method.

Zusammenfassung. Axillarin (5,7,3′,4′-Tetrahydroxy-3,6-dimethoxyflavon), 5,3′,4′-Trihydroxy-3,6,7-trimethoxyflavon und 5,7,3′,4′-Tetrahydroxy-3,8-dimethoxyflavon wurden synthetisiert.

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Department of Chemistry, Faculty of Science, Hiroshima University, Hiroshima and Department of Applied Chemistry, Faculty of Engineering, University of Tokushima (Japan), 11 April 1968.

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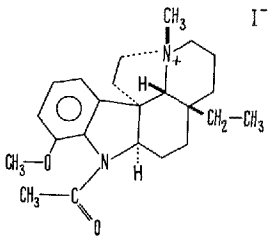
[6] K. FUKUI, T. MATSUMOTO, S. NAKAMURA, M. NAKAYAMA and T. HORIE, Experientia *24*, 108 (1968); Bull. chem. Soc. Japan *41*, No. 6 (1968).
[7] K. FUKUI, M. NAKAYAMA and T. HORIE, Experientia *24*, 417 (1968).
[8] Natural axillarin and its tetraethyl ether, kindly supplied by Prof. W. HERZ, the Florida State University, were measured in this laboratory.
[9] D. K. BHADWAJ, S. NEELAKANTAN and T. R. SESHADRI, Indian J. Chem. *4*, 417 (1966).
[10] The natural pigment and its acetate, kindly supplied by Prof. P. R. JEFFERIES, the University of Western Australia, were measured in this laboratory.

The Absolute Configuration of (-)-Aspidospermine

We report a confirmation of previous assignments of absolute configuration to the *Aspidosperma* alkaloids by use of the X-ray anomalous scattering effect from crystals of (–)-aspidospermine N(b)-methiodide. The X-ray anomalous scattering effect already has been used elegantly in demonstrating the stereospecificity of the transannular cyclization of quebrachamine to aspidospermine[1]. This work resulted in establishing the absolute configuration of 7-ethyl-5-desethyl-aspidospermidine[2]. However, although crystal structures have been reported for a number of *Aspidosperma* and related alkaloids[3–6], including (–)-aspidospermine N(b)-methiodide[7], there has been no previous X-ray determination of absolute configuration of a derivative which is closely related to a naturally occurring *Aspidosperma* alkaloid. Absolute configurations have been inferred from chemical inter-relationships and from optical rotatory dispersion data[8–11].

The determination of absolute configuration is particularly important for these alkaloids, because they are known to occur naturally in 2 series which differ in that their skeletal structures are enantiomeric. Some of these alkaloids, such as (–)-aspidospermine, have so far been found in only 1 series, while others, such as pyrifolidine, have been found to occur in both[11]. It has been suggested that these 2 series arise from a non-asymmetric intermediate in *Aspidosperma* alkaloid biosynthesis[12].

From the data in the Table, the absolute configuration of (–)-aspidospermine N(b)-methiodide is established as (I), from which the absolute configuration of the free base follows.



(I)

It should be noted that the atomic parameters reported by MILLS and NYBURG give the correct absolute configuration provided that these are referred to a right-handed set of crystal axes, as in Figures 1 and 2 of their paper[7]. In their Figure 3, the axial set is left-handed, so that the molecular ion shown has the incorrect absolute configuration.

In the present work, crystals of (–)-aspidospermine N(b)-methiodide[13] were found to be morphologically similar to those described by MILLS and NYBURG[7]. The reported crystal data were assumed (a = 24.3, b = 8.50, c = 11.1 Å; space group $P2_12_12_1$ with 4 molecules in the unit cell). A needle-like crystal of square cross section (0.2 × 0.2 mm) was cut to a length of 0.3 mm and mounted