Acerogenin A, a Novel Cyclic Diarylheptanoid

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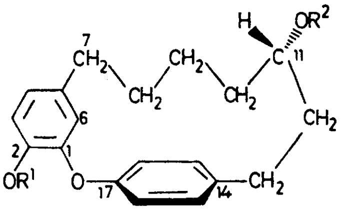
Summary Acerogenin A, a diaryl ether-type diarylheptanoid was isolated and characterized as (I).

ACEROGENIN A (I), $C_{19}H_{22}O_3$, m.p. 151—152 °C, $[\alpha]^{20}_{D}$ + 57·3°, was isolated as the aglycone of a glucoside from the stem bark of *Acer nikoense* Maxim. (Aceraceae), a Japanese folk medicine. It has λ_{max} (EtOH) 278 nm (ϵ 2390), ν_{max} (KBr) 3460, 3170, 2935, 2853, 1593, 1517, and 1500 cm^{-1}, indicating the presence of hydroxy-groups and aromatic rings. It affords a monomethyl ether (II), m.p. 124—125 °C, $[\alpha]^{20}_{D}$ + 36·1°, and a diacetate (III), m.p. 116—118 °C, $[\alpha]^{20}_{D}$ + 21·7°. The methyl ether (II) was oxidized with chromic acid to give an optically inactive ketone (IV), m.p. 124—125 °C. On further oxidation with permanganate, the ketone (IV) yielded a dicarboxylic acid, m.p. 298—300 °C, which was identified as 3-carboxy-6-methoxyphenyl 4-carboxyphenyl ether.[1] This proves not only the presence of a diphenyl ether structure in the molecule (I) but also the location of the substituents on the aromatic rings.



(I) $R^1 = R^2 = H$, 11(*S*)
(II) $R^1 = Me$, $R^2 = H$
(III) $R^1 = R^2 = COMe$
(IV) $R^1 = Me$, 11-oxo
(V) $R^1 = Me$, $R^2 =$ tetrahydropyranyl

The ^1H and ^{13}C n.m.r. spectra‡ of (IV) showed signals at $\delta(^1H)$ 1·09 (9-H_2), 1·37 (8-H_2), 1·90 (10-H_2), 2·44 (7-H_2), 2·61 (12-H_2), and 2·96 (13-H_2) (all m); 5·65 (6-H, d, *J* 2 Hz), 6·63 (4-H, dd, *J* 2 and 8 Hz), and 6·82 (3-H, d, *J* 8 Hz) (1,2,5-trisubstituted benzene); 7·01 (16- and 18-H) and 7·20 (15- and 19-H) (AA′BB′ q, *J* 9 Hz, 1,4-disubstituted benzene); $\delta(^{13}C)$ 20·5, 27·6, 31·5, 32·3, 44·6, and 46·2 (6 × CH_2), 112·7, 117·7, 122·2, 123·9, and 130·8 (7 × Ar*C*H); 133·9 and 137·3 (2 × Ar*C*–C); 147·1, 151·2, and 157·2 (3 × Ar*C*–O), and 212·0 (>*C*=O). In the ^1H n.m.r. spectrum of the 10,12-tetradeuteriated ketone [10,12-$^2H_4$]-(IV), the C-10 and C-12 proton signals were not observed, the coupling pattern of the 9-H_2 signal was simplified, and the 13-H_2 multiplet became a broad singlet. In ^1H double-resonance experiments on [10,12-$^2H_4$]-(IV), the 7-H_2 and 9-H_2 signals changed into two broad singlets upon irradiation of the 8-H_2 protons. On irradiation at δ 1·09 (9-H_2), the intensity of the 6-H signal increased by 13%. This NOE showed that the C-6 and C-9 protons are close to each other. These findings indicate structure (IV) for the ketone.

In order to confirm the assignment of structure (I), including its configuration at C-11, the diphenyl ether linkage of the tetrahydropyranyl ether derivative (V) of (II) was reductively cleaved with lithium in liquid ammonia.[2] The phenol, $C_{20}H_{26}O_3$, m.p. 80·5—81·5 °C, $[\alpha]_D^{20}$ − 7·5°, obtained after removal of the tetrahydropyranyl group, was identified as (−)-*O*-methylcentrolobol[3] [(*S*)-(−)-1-(*p*-hydroxyphenyl)-7-(*p*-methoxyphenyl)heptan-3-ol], establishing the structure of acerogenin A as (I).

The 6-H signals in (I)—(IV) were observed at abnormally high fields, because this proton is located above the plane of the other benzene ring.[4] A Dreiding model of (IV) shows that the planes of the two benzene rings are approximately perpendicular to each other.

Acerogenin A (I) is the first example of a diphenyl ether type diarylheptanoid. A series of diarylheptanoids[5] including biphenyl[6] and diphenyl ether types, might be interesting from biosynthetic considerations.

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‡ N.m.r. spectra for $CDCl_3$ solutions were recorded on a Varian XL-100 spectrometer using Me_4Si as internal standard.

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