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SHORT COMMUNICATION

PSEUDOGUIANOLIDES OF *GAILLARDIA AMBLYODON**

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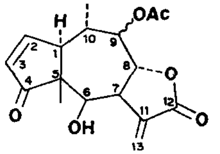
Abstract—The structure of amblyodin, a new pseudoguainolide from *Gaillaridia amblyodon* Gay, has been established. Gaillardipinnatin, previously isolated from *G. pinnatifida* Torr., was also isolated.

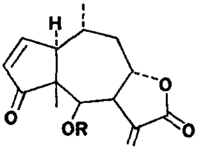
INTRODUCTION

The distribution of *Gaillardia amblyodon* Gay is relatively limited and confined to Southeast Texas inland from Galveston.[1] In 1960 one of us (W.H.) received a small collection of this species through the courtesy of Professor B. L. Turner and isolated two new sesquiterpene lactones in very small amounts. Recent refinement of analytical techniques now enables us to report their structures.

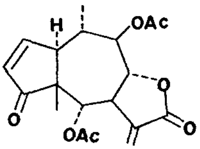
Amblyodin, the substance isolated in somewhat larger amount, had formula $C_{17}H_{20}O_6$ (elemental analysis, high resolution mass spectrum). The NMR spectrum (90 mHz) exhibited the typical doublets of an exocyclic methylene group conjugated with a lactone (H-13a and H-13b of formula I), the α- and β-protons of a cyclopentenone function (H-3 and H-2) obviously spincoupled to each other and to a proton (H-1) at 2·77 ppm, a slightly broadened doublet (after D_2O exchange) at 4·53 ppm (H-6), and a two proton multiplet (H-8 and H-9) centered at 4·85 ppm, one of whose components was the hydrogen under the acetate function revealed by a singlet at 2·16 ppm. The presence of a methyl singlet at 1·29 and a methyl doublet at 1·21 ppm suggested immediately that amblyodin was a pseudoguaianolide with the gross structure shown in formula (I).



(I)



(II) a R = H
b R = Ac



(III)

This was verified by spin-decoupling experiments which revealed the coupling constants listed in Table 1. Irradiation at the frequency of H-1 collapsed the signals of H-2 and H-3 to doublets and affected a broad signal at 2·1 ppm (H-10) partially hidden under the acetate signal. Irradiation at the frequency of H-10 simplified the signal of H-1, collapsed the methyl doublet and altered, but did not resolve the H-8, H-9 multiplet centered at 4·85 ppm. This signal was also affected by irradiation at the frequency of the H-7 resonance (3·22

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* Part XI in the series "Constituents of *Gaillardia* Species". For Part X see K. Aota, C. N. Caughlan, M. T. Emerson, W. Herz, S. Inayama and M.-Ul-Haque, *J. Org. Chem.* **35**, 1448 (1970).

[1] S. F. Biddulph, *Res. Studies, Washington State Coll.* **12** (4), 195 (1944).

ppm) whose identity was established by irradiation at the frequency of H-13a and H-13b. Irradiation at the frequency of H-7 also collapsed the doublet of H-6 to a singlet.

As regards stereochemistry a detailed comparison of chemical shifts and coupling constants with those of other pseudoguaianolides of similar gross structure revealed that amblyodin belonged to the mexicanin I (IIa) and linifolin A (IIb) series (0–6 β, 0–8 α). Although the strong coupling of H-8 and H-9 and the complexity of H-7 and H-10 interfered with direct determination of $J_{7,8}$, $J_{8,9}$ and $J_{9,10}$ even after decoupling, the magnitude of $J_{7,13a}$ and $J_{7,13b}$ (> 3 Hz) is strongly indicative of a *trans*-fused lactone function[2] and the observed value for $J_{6,7}$ of 4·5 Hz is also highly characteristic of the β-oriented 6-hydroxyl group in the mexicanin I series.[3]

TABLE 1. NMR SPECTRA OF COMPOUNDS I AND III*

	I†	III‡
H-1	2·77 ddd (11, 2·7, 2·0)	3·13 ddd (11, 3, 2)
H-2	7·64 dd (6·0, 2·0)	7·72 dd (6·5, 2)
H-3	6·19 dd (6, 2·7)	6·16 dd (6·5, 3)
H-6	4·53 d (4·5)	5·64 d (8)
H-7	3·22 c	3·22 tt (10, ~3)
H-8	4·85 c§	4·64 t (9·5)
H-9	4·85 c	4·98 t (9·5)
H-10	2·17 c††	2·1 c
H-13a	6·41 d (3·7)	6·20 d (3·5)
H-13b	5·69 d (3·1)	5·89 d (3·0)
H-14**	1·21 d (6·4)	1·24 d (7)
H-15**	1·29	1·27
Ac	2·16	2·16, 1·98

* Run at 90 mHz in $CDCl_3$ solution on a Bruker NMR spectrometer using TMS as internal standard. Multiplicities are indicated by the usual symbols: d, doublet; t, triplet; c, complex signal whose center is given. Unmarked signals are singlets.

† Figures in parentheses are coupling constants measured by spin decoupling.

‡ Chemical shifts and line separations given here differ slightly from those reported in ref. 6 due to changes in instrumentation.

§ Center of AB system where A and B were each coupled to one other proton.

** Three protons.

†† Partially obscured by acetate.

The appearance of the combined H-8, H-9 multiplet before and after irradiation at the frequencies of H-7 and H-10 in different solvents at 90 mHz did not permit a unique solution for $\Delta\nu_{8,9}{}^{\tau}$ $J_{8,9}$, $J_{7,8}$ and $J_{9,10}$. Hence the stereochemistry at C-9 is left undefined until additional amblyodin becomes available for further studies.

The identification of the second substance from *G. amblyodon* which was obtained only in milligram quantities was complicated by the circumstance that the peak of highest mass

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[2] Z. SAMEK, *Tetrahedron Letters* 671 (1970).

[3] W. HERZ, C. M. GAST and P. S. SUBRAMANIAM, *J. Org. Chem.* **33**, 2780 (1968).

number in the high resolution mass spectrum had the composition $C_{17}H_{20}O_6$, identical with that of amblyodin, but actually corresponded, as was discovered subsequently, to the loss of ketene from the molecular ion $C_{19}H_{22}O_7$. The NMR spectrum, recorded with the aid of a computer, revealed that the substance contained two acetate functions and was identical with gaillardipinnatin, a minor constituent of *G. pinnatifida* Torr.,[4] for which formula III exclusive of stereochemistry at C-9, has been deduced earlier.[5] Direct comparison of the samples established identity.[6]

The observed coupling constants $J_{8,9}$ and $J_{9,10}$ in the 90 mHz NMR spectrum of gaillardipinnatin (Table 1) are best satisfied by a β-oriented 7-acetoxyl group on the 7-membered ring in the chair conformation, less so by an α-oriented 7-acetoxyl in a distorted boat. The former seems preferable on energetic grounds (model).

EXPERIMENTAL

M.ps were determined in capillaries and are uncorrected. IR spectra were run in $CHCl_3$; MS on a MS 902 high resolution mass spectrometer at 70 meV.

Extraction of Gaillardia amblyodon. A collection of 250 g of *G. amblyodon* Gay, collected by Professor B. L. Turner during the first week of May 1960 near Gonzales, Texas, was extracted with $CHCl_3$ in the usual manner.[7] The crude gum, wt 6 g, was taken up in 20 ml of hot benzene and chromatographed over 75 g of alumina (Alcoa F-20). The material was eluted successively with benzene (200 ml), benzene–$CHCl_3$ 3:1 (3 fractions, 75 ml each), $CHCl_3$ (15 fractions, 75 ml each), and $CHCl_3$–MeOH 10:1 (4 fractions, 150 ml each). Fractions 2–4 gave a small amount of crystalline material which was recrystallized from acetone-ether, yield of slightly impure gaillardipinnatin 10 mg, m.p. 247–250°, IR bands 3500, 1760 and 1650 (conjugated γ-lactone), 1745, 1705 and 1580 cm^{-1} (cyclopentenone). Found: apparent MW (high resolution MS) 320·1237 (10·3%). Calcd for $C_{17}H_{20}O_6$: 320·1259. This actually corresponds to the loss of C_2H_2O from the molecular ion. Other significant peaks in the high MW region were 302·1165 (33·6%, M–$C_2H_4O_2$, 260·1050 (base peak, M–$C_2H_4O_2$–C_2H_2O), and 242·0942 (83%, M–$C_2H_4O_2$). Direct comparison with authentic material from *G. pinnatifida* established identity.

Fractions 5–9 also yielded solid material which was combined and recrystallized from acetone-ether, diisopropyl ether and again from acetone-ether, yield of amblyodin 60 mg, m.p. 220–222°, IR bands 3500, 1760 and 1650 (conjugated γ-lactone), 1750 (sh, ester), 1695 and 1575 cm^{-1} (cyclopentenone). (Found: C, 63·64; H, 6·18; MW. (by MS), 320·1261 (3·1%). Calcd for $C_{17}H_{20}O_6$: C, 63·74; H, 6·29; MW. 320·1259.) Other significant peaks in the high MW region were 305·1028 [1·5% M–CH_3], 278·1158 [2·8%, M–C_2H_2O], 260·1054 [12·8%, M–H_2O–C_2H_2O or M–$C_2H_4O_2$], 245·0829 [4·0%, M–CH_3–$C_2H_4O_2$] and 242·0901 [4·1%, M–H_2O–$C_2H_4O_2$].

Acknowledgement—This work was supported in part by a grant from the United States Public Health Service (RG-GM-05814).

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[4] W. Herz, S. Rajappa, M. V. Lakshmikantham and J. J. Schmid, *Tetrahedron* **22**, 693 (1966). On p. 698 of this reference, the empirical formula of gaillardipinnatin is misprinted as $C_{19}H_{22}O_7$ and NMR signals at 4·94 q and 4·64 t are, again by misprint, assigned to H-7 and H-8 instead of to H-8 and H-9.

[5] W. Herz, S. Rajappa, S. K. Roy, J. J. Schmid and R. N. Mirrington, *Tetrahedron* **22**, 1907 (1966).

[6] The m.p. of gaillardipinnatin from *G. pinnatifida* was 270° (dec), whereas the sample from *G. amblyodon* melted in the range 247–250°. Although m.p.s of sesquiterpene lactones are notoriously unreliable, the difference was undoubtedly due to the difficulties inherent in purifying the small amount of material from *G. amblyodon*. This was also indicated by the NMR spectrum which exhibited a few impurity peaks in the methylene region.

[7] W. Herz and G. Högenauer, *J. Org. Chem.* **27**, 905 (1962).

Key Word Index—Gaillardia amblyodon; Compositae; pseudoguianolides; amblyodin: gaillardipinnatin.