Furanoeremophilan-14β,6α-olide, a New Furanosesquiterpene Lactone from *Ligularia Hodgsoni* Hook, f. The Structure and Nuclear Overhauser Effects

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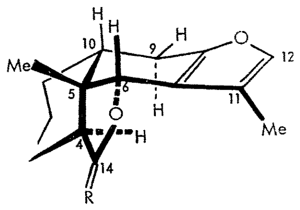
DURING chemical investigations on the genus *Ligularia* (Compositae), we have isolated a new furanosesquiterpene lactone, furanoeremophilan-14β,6α-olide (I), $C_{15}H_{18}O_3$, M^+ 246, m.p. 136—138°, $[\alpha]_D$ $-47°$ (dioxan), from the roots of *L. Hodgsoni* Hook, f. The presence of a β-methyl-substituted furan moiety and a γ-lactone are indicated by the positive Ehrlich test, the i.r. ($\nu_{max.}$ 1767, 1634, and 1563 cm.$^{-1}$) and ^{1}H n.m.r. (see Table) spectra. Reduction of (I) with $LiAlH_4$ gave a diol (II), $C_{15}H_{22}O_3$, m.p. 197—198°, $\nu_{max.}$ 3200 cm.$^{-1}$, which is readily converted into an ether (III), $C_{15}H_{20}O_2$, M^+ 232, m.p. 114—115°, $[\alpha]_D$ $-65°$ (dioxan). In its ^{1}H n.m.r. the methylene protons in the α-position to the ether oxygen show the AB pattern of an ABX spin system (see the Table); this suggests that the carbon atom in the β-position to the ether oxygen bears one proton. The presence of a tertiary methyl group and a proton on carbon bearing ether-type oxygen are also shown in the ^{1}H n.m.r. spectra of (I) and (III).

Applications of spin-decoupling and intramolecular nuclear Overhauser effects (NOE)[1] suggest the stereostructure shown for (I). The ^{1}H n.m.r. spectral data on (I) are listed in the Table.† The fact that 6-H is only coupled weakly ($J < 2$ Hz.) to the two allylic protons, 9α-H and 9β-H, suggests that 6-H is adjacent to the furan ring, and that the other neighbour, C-5, bears no proton. The presence of an NOE between 6-H and the tertiary methyl group implies that the latter is situated at C-5 and *cis* to 6-H. An NOE observed between 6-H and the β-methyl group on the furan ring indicates that C-6 is attached to the other β-position of the furan ring. On triple irradiation at the resonance frequencies of 6-H and 12-H in perdeuterioacetone, the signals of 9α-H and 9β-H exhibit the AB part of an ABX spin system, which gave $J_{9\alpha,9\beta}$ $-17{\cdot}3$, $J_{9\alpha,10}$ 11·3, and $J_{9\beta,10}$ 5·9 Hz. Therefore, the carbon atom adjacent to C-9 bears *one* proton that adopts a *trans* or an



(A)

R = O or H_2

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† The ^{1}H n.m.r. spectra were taken with a Varian HA-100 spectrometer operating at 100 MHz. in the frequency-swept and internal $SiMe_4$-locked mode, for $\sim$5% (w/v) degassed solutions in $CDCl_3$ and (or) perdeuterioacetone. ^{1}H n.m.d.r. and n.m.t.r. experiments were performed using the same spectrometer with two Hewlett–Packard HP-200ABR audio-oscillators and an HP-5212A electronic counter. Accuracies are about $\pm 0{\cdot}01$ p.p.m. for chemical shifts, $\pm 0{\cdot}2$ Hz. for coupling constants, and $\pm 2\%$ for NOE values.

TABLE

^{1}*H N.m.r. spectral data on* (I) *and* (III)

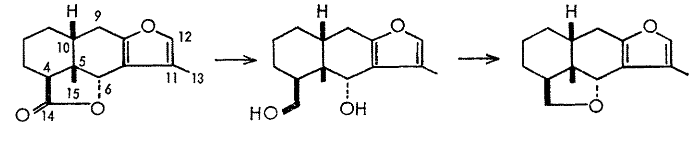
Chemical shifts (δ, p.p.m.)

	(I) CDCl$_3$	(I) (CD$_3$)$_2$CO	(III) CDCl$_3$
5-Methyl	1·26	1·24	1·16
11-Methyl	2·03	2·01	2·03
9β-H	~2·7	2·62	2·48
9α-H		2·76	2·64
6β-H	5·08	5·08	4·63
14β-H	—	—	3·53
14α-H	—	—	3·91
12-H	7·06	7·19	7·01

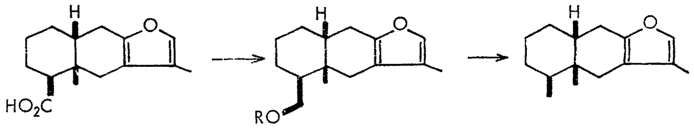
Nuclear Overhauser effects (%, in CDCl$_3$)

Observed proton	Saturated proton	(I)	(III)
12-H	11-Methyl	22	17
6β-H	11-Methyl	6	7
6β-H	5-Methyl	28	23
14β-H	5-Methyl	—	8
14α-H	5-Methyl	—	−2

eclipsed conformation with respect to one of the C-9 methylene protons. Triple irradiation on 12-H and the 11-methyl signals determined the two homoallylic couplings $J_{6,9\alpha}$ 1·8 and $J_{6,9\beta}$ 1·2 Hz.[2] These two large J values imply that 6-H has a quasi-axial conformation. Interpretation of the ^{1}H n.m.r. spectral data on (III) (Table) is in full accord with that of the data on (I); this shows that no stereochemical change occurred on transformation of (I) to (III). On saturation of the signal due to the 5-methyl group by double irradiation, the signal due to one of the methylene protons, 14β-H, at δ 3·53 p.p.m. ($J_{4,14\beta}$ 11·3 and $J_{14\alpha,14\beta}$ −7·4 Hz.) shows a substantial increase in area, whereas the other 14α-H signal at δ 3·91 p.p.m. ($J_{4,14}$ 7·3 and $J_{14\alpha,14\beta}$ −7·4 Hz.) appears unaffected. This observation determined the assignment of 14-H methylene signals and the α-configuration of 4-H.



(I) (II) (III)



(IV) (V) (VI)

The above ^{1}H n.m.r. spectroscopic evidence for (I) and (III) is satisfactorily accommodated by the stereostructure (A), which is compatible with the biogenetic isoprene rules for sesquiterpenoids. Confirmatory evidence for the carbon skeleton and the absolute configuration were afforded by the following transformation. Hydrogenolysis of (I) over 10% Pd–C in EtOH gave a carboxylic acid (IV), $C_{15}H_{20}O_3$, (methyl ester: oil, $\nu_{C=O}$ 1730 cm.$^{-1}$, absence of ν_{OH}), which was subsequently converted into a mono-alcohol (V; R = H), oil, ν_{OH} ~3400 cm.$^{-1}$. Reduction of the tosylate (V; R = Ts) with LiAlH$_4$ furnished furanoeremophilane (VI), $C_{15}H_{22}O$, oil, $[\alpha]_D$ −12° (CDCl$_3$). Its spectroscopic data are in complete accord with those of an authentic sample of furanoeremophilane.‡[3]

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[1] F. A. L. Anet and A. J. R. Bourn, *J. Amer. Chem. Soc.*, 1965, **87**, 5250; M. C. Woods, H.-C. Chiang, Y. Nakadaira, and K. Nakanishi, *ibid.*, 1968, **90**, 522; K. Tori, M. Ohtsuru, I. Horibe, and K. Takeda, *Chem. Comm.*, 1968, 943; R. A. Bell and J. K. Saunders, *Canad. J. Chem.*, 1968, **46**, 3421, and references cited therein.

[2] J. T. Pinhey and S. Sternhell, *Tetrahedron Letters*, 1963, 275.

[3] H. Ishii, T. Tozyo, and H. Minato, *J. Chem. Soc.* (*C*), 1966, 1545.