Phytochemistry, Vol. 34, No. 3, pp. 859–860, 1993
Printed in Great Britain.

0031-9422/93 $6.00+0.00

ABSOLUTE CONFIGURATION OF EREMOPHILENOLIDES FROM *HERTIA CHEIRIFOLIA*

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(*Received* 25 *January* 1993)

Key Word Index—*Hertia cheirifolia*; Compositae; eremophilenolides; tetrahydroligularenolide; absolute configuration.

Abstract—The absolute configurations of 8α-methoxy-10β-hydroxyeremophilenolide and 8β,10β-dihydroeremophilenolide from *Hertia cheirifolia* were determined by transformation into (−)tetrahydroligularenolide.

INTRODUCTION

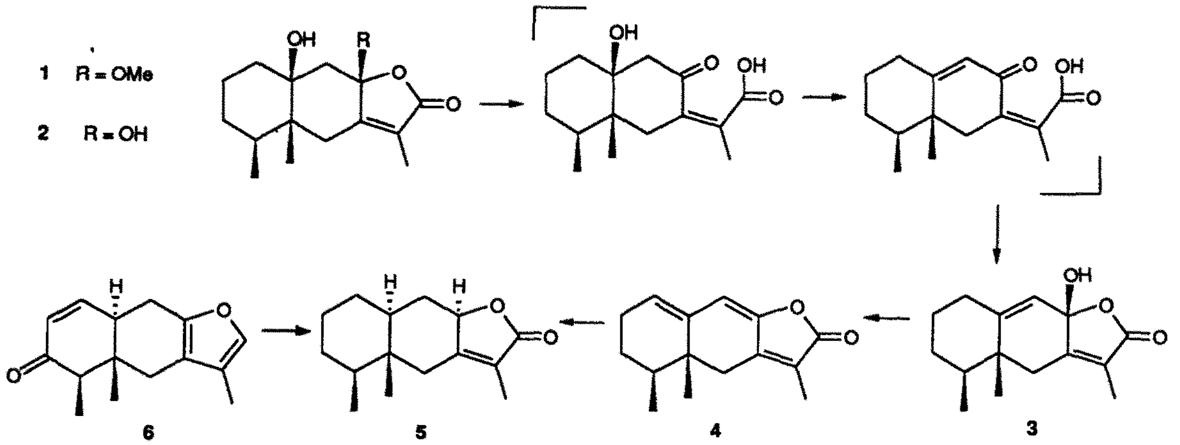
In two previous communications [1, 2], we reported the isolation from *Hertia cherifolia* of a series of novel eremophilenolides characterized by a tertiary hydroxyl group at the A/B ring junction. In the absence of chemical correlations, the absolute configurations were only tentatively given. We now report chemical reactions performed in order to link the *Hertia* eremophilenolides to sesquiterpenes of known absolute configuration.

Starting materials were 8β-methoxy-10β-hydroxyeremophilenolide (**1**) and 8β-dihydroxyeremophilenolide (**2**) (**6** in ref. [2]) which were interconverted under base catalysis. The main compound from prolonged treatment was 8β-hydroxy-9,10-dehydroeremophilenolide (**3**), which arises from **2** by lactone ring opening and β-hydroxy elimination from the intermediate β-hydroxy ketone. Structure **3** relies on spectral data, $[M]^+$ at m/z 248 (weak intensity) and the ^{1}H NMR spectrum. Compound **3** was smoothly dehydrated by trifluoroacetic acid in methylene chloride into a diene, identified with ligularenolide (**4**). Our diene had $[\alpha]_D = -326°$; literature reports $-332°$ for this compound [3] (an earlier publication erroneously described ligularenolide with $[\alpha]_D = 33°$ [4]). To secure the identification, our ligularenolide was hydrogenated to yield tetrahydroligularenolide (**5**) with $[\alpha]_D = -82°$ (lit. $-92°$ [3]). Since **4** and **5** were chemically linked to furanoligularenone (**6**) of known absolute configuration, this settles the point of the absolute configuration of the *Hertia* eremophilenolides.

EXPERIMENTAL

General. ^{1}H NMR spectra were measured at 300 MHz on a Bruker AC 300 instrument. Mass spectra were recorded on a Jeol DNM 300 spectrometer in the electron impact mode. IR spectra were recorded on a NICOLET FT IR 10 DX spectrometer.

Compound **3**. Sodium (100 mg; 4.3 mmoles) was added to MeOH (9 ml). After reaction and cooling to ambient



temp., a soln of **1** (152 mg, 0.6 mmole) in 4 ml of MeOH was added and the mixt. was stirred for 4 hr. The reaction mixt. was poured into H_2O and neutralized with diluted MeCOOH. Extraction with EtOAc, drying ($MgSO_4$) and evapn of the solvent gave the crude material (124 mg) which was purified by flash chromatography. Solvent: CH_2Cl_2–MeOH (9:1). Unreacted **1** (14.5 mg, 9.5%) was eluted first, followed by **2** (47.7 mg) and **3** (41 mg). Mp 140–142° dec. $[\alpha]_D -51°$ ($CHCl_3$; *c* 0.8). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3610, 1760, 1610. MS, *m/z* (rel. int.): 248 $[M]^+$ (4), 230 (8), 220 (45), 204 (28), 203 (100), 175 (18), 119 (22), 105 (18), 91 (25). ^1H NMR ($CDCl_3$, 300 MHz): δ 5.54 (*s*, H-9), 4.4 (*s*, OH), 2.65 (*d*, *J* = 12.5 Hz, H-6b), 2.35 (*br d*, *J* = 12.5 Hz, H-6a), 1.76 (*d*, *J* = 0.5 Hz, 3H, Me-13), 0.87 (*d*, *J* = 6.7 Hz, 3H, Me-15), 0.81 (*s*, 3H, Me-14).

Compound **4**. Trifluoroacetic acid (0.2 ml) was added to a soln of **3** (20 mg, 0.08 mmol) in CH_2Cl_2 (5 ml) and the mixt. was stirred for 45 min at room temp. The yellow soln was diluted with H_2O and neutralized (Na_2CO_3). The organic layer was sepd, the aq. layer was further extracted with CH_2Cl_2, and the combined organic layers were dried over $MgSO_4$. Removal of solvent gave **4** (12.3 mg). Mp 128–130°. $[\alpha]_D = -326°$ ($CHCl_3$; *c* 0.54). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1760, 1650, 1620. ^1H NMR ($CDCl_3$, 300 MHz): δ 5.94 (*s*, H-9), 5.80 (*t*, *J* = 4, 11 Hz, H-1), 2.84 (*d*, *J* = 16.5 Hz, H-6b), 2.35 (*m*, H-6a), 1.91 (*d*, *J* = 1.8 Hz, 3H, Me-13), 1.0 (*d*, *J* = 6.7 Hz, 3H, Me-15), 0.97 (*s*, 3H, Me-14).

Compound **5**. A soln of **4** (12 mg) in MeOH (5 ml) was added to a suspension of Pd/C (1.5 mg) in MeOH (2 ml). The mixt. was stirred for 12 hr in H_2 atmosphere at room temp. Filtration and removal of solvent gave 7.8 mg of **5**. The yellow material is recrystallized from Et_2O. Mp 107–108°, $[\alpha]_D -82°$ ($CHCl_3$; *c* 0.43). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1760, 1740, 1680. ^1H NMR ($CDCl_3$, 300 MHz): δ 4.65 (*m*, 1H, H-8), 2.75 (*d*, *J* = 14.5 Hz, H-6b), 2.15 (*m*, H-6a), 1.85 (*d*, *J* = 1.5 Hz, 3H, Me-13), 0.97 (*d*, *J* = 6 Hz, 3H, Me-15), 0.60 (*s*, 3H, Me-14).

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