Tetrahedron Letters No. 31, 2765 - 2766.
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0040-4039/78/0729-2765$02.00/0

PLANT INVESTIGATION 9. STEREOCHEMISTRY AND PARTIAL SYNTHESIS OF COROLLATADIOL[1]

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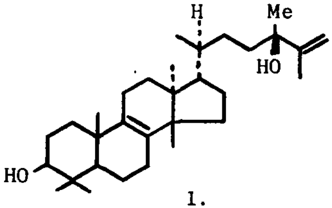
(Received in USA 10 April 1978; received in UK for publication 1 June 1978)

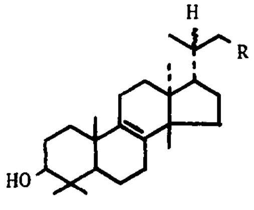
Corollatadiol (1), a new tetracyclic triterpene which we isolated from Euphorbia corollata or flowering spurge, was identified as a 3,24-dihydroxy-24-methyleupha-8,25-diene.[2] Although the basic ring system and stereochemistry had been elaborated during the overall structure proof, the two chiral points in the side chain at C-20 and C-24 remained undefined. We now wish to report the stereochemistry of these centers, thus establishing the full structure for corollatadiol (1), as well as the partial synthesis of 1 from tirucallol (2).

Since two well-known and rigidly documented triterpenes—tirucallol (2) and euphol (3)—which differ only in their C-20 stereochemistry are available, we chose to establish this chiral point in corollatadiol by comparison of tirucallenes and euphenes substituted analogously to dihydrocorollatadiol (4), mp 174-6°; $[\alpha]_D$-12°. Tirucallol acetate was acquired from gum mastic.[3] Hydroboration of the 24(25)-double bond followed by H_2O_2-NaOH yielded the C-24 alcohol 5, mp 185-6°; $[\alpha]_D$ -8.2°. Subsequent oxidation of 5 by CrO_3-pyridine to tirucallenone 6, mp 163-4°; $[\alpha]_D$-11°, and addition of MeLi to the resultant ketone moiety produced tirucallene analog 7, mp 173-4°; $[\alpha]_D$-14°. ORD spectra of the various derivatives 5-7 exhibited plain negative curves, and other spectroscopic properties were consistent with the structures.

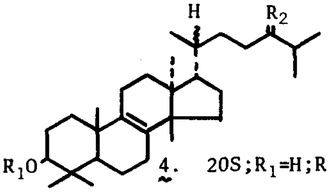
Replication of the above reactions with euphol acetate, secured from euphorbium resin,[4] led to euphenone 8, mp 123-4°; $[\alpha]_D$+21°. In addition, C-28 alcohol 9, mp 166-7°, ensued from the hydroboration step as a consequence of the presence of α-euphorbol 10 in the euphol sample. The euphene analog 11, mp 81-6°; $[\alpha]_D$+20°, was formed from 8 and MeLi. Since plain positive ORD spectra were observed for euphane derivatives 8 and 11, and the plain negative curve of 4



1.



2. 20S;R=CH_2CH=CMe_2
3. 20R;R=CH_2CH=CMe_2
12. R=$CH_2C(Me)$=CMe_2
13. R=CH=CH(Me)$CHMe_2$
14. 20S;R=$CH_2COC(Me)$=CH_2



4. 20S;R_1=H;R_2=OH,..Me
5. 20S;R_1=Ac;R_2=OH,H
6. 20S;R_1=Ac;R_2=O
7. 20S;R_1=H;R_2=OH,Me
8. 20R;R_1=Ac;R_2=O
9. 20R;R_1=Ac;R_2=OH,H
10. 20S;R_1=Ac;R_2=CH_2OH,H
11. 20S;R_1=H;R_2=CH_2

as well as its mp and optical rotation data more closely matched that of **7**, the C-20 configuration of **4** was tentatively considered to be 20S as in tirucallol (**2**).

To eliminate the C-24 chiral center of the synthetic analogs as a factor in the optical rotation data, dehydrative removal of the 24-hydroxyl moiety in **4**, **7**, and **11** was pursued. Dehydrations were performed on the corresponding 3-acetates with p-TSA in benzene at 60°, which was the optimum condition observed in model studies[5]. In all cases single TLC products were obtained; however, nmr and vpc indicated the presence of two closely related double bond isomers (likely **12** and **13**). Although they could not be readily separated, the consistency in the vpc and optical rotation data (see Table 1) of the product from the dehydration of tirucallene analog **7** with that from dihydrocorollatadiol (**4**) substantiated the 20S assignment.

Table 1. Analysis of C-24 Hydroxy Dehydration Products

Starting Compound	Vpc time (min) and (%) of isomers	$[\alpha]_D$	$[\phi]_{500}$	$[\phi]_{400}$	$[\phi]_{350}$
Dihydrocorollatadiol (**4**)	37(60) 43(40)	-5.0°	-55	-111	-194
Tirucallene analog **7**	36(61) 42(39)	-8.8°	-53	-106	-184
Euphene analog **11**	34(42) 39(58)	23°	+156	+260	+326

The configuration at C-24 was determined by the empirical circular dichroism method of Dillon and Nakanishi[6] using a 1.0 x 10^{-4}M solution of bis(hexafluoracetylacetonato)-copper (II) and corollatadiol (5.8 x 10^{-3}M) in CCl_4. Observation of a positive CD maximum at 345 nm (Θ=3600) predicated a clockwise arrangement of substituents of decreasing size around the C-24 chiral carbon as the OH moiety faces the observer and, therefore, a 24R configuration. The complete structure for corollatadiol is, hence, established as depicted by **1**.

The synthesis of corollatadiol (**1**) was begun by photooxygenation of tirucallol acetate (330 mg) according to a procedure by Morisaki _et al._[7] for demosterol. The crude product was separated by TLC and the major zone (120 mg) oxidized by CrO_3-pyridine. TLC of the oxidation product yielded **14** (10% yield); mp 163-5°; ν_{max} ($CHCl_3$) 1720, 1670, 1625 cm^{-1}; nmr 114(s,3H), 347(m,1H), 359Hz (m,1H); λ_{max} 218 nm (ε10,000). Addition of MeLi to the ketone group of **14** gave corollatadiol (**1**), mp 178-183°, which had the same vpc and TLC properties and spectroscopic data as material isolated[2] from _E. corollata_ although the mp's were somewhat different.

Acknowledgements. We thank the American Cancer Society (Grant IC-26) for partial support of this investigation.

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