ELAEODENDROSIDE D, E, H, I AND J: NEW CARDIAC STEROIDS FROM ELAEODENDRON GLAUCUM*

Kazutake Shimada, Tomoko Kyuno and Toshio Nambara
Pharmaceutical Institute, Tohoku University, Aobayama, Sendai 980, Japan
Itsuo Uchida[1]
Department of Chemistry, University of Virginia, Charlottesville,
Va. 22901, U. S. A.

Abstract--- Five new cardiac glycosides having an unusual sugar linkage, elaeodendroside D, E, H, I and J, were isolated from seeds of Elaeodendron glaucum Pers. and their structures were assigned on the basis of chemical correlation with elaeodendroside A, respectively. An improved procedure for cleavage of a glycoside having a doubly linked sugar was applied to characterization of elaeodendroside B and C. The probable structures of these two stereoisomers were proposed.

In the preceding papers we reported the isolation and structure elucidation of cardiac steroids named elaeodendroside A and elaeodendrogenin from seeds of Elaeodendron glaucum Pers. (Celastraceae)[2] by X-ray crystallography[3] and chemical means.[4] The probable structures of elaeodendroside B and C obtained from the same plant materials were also proposed.[4] The present paper describes the structures of elaeodendroside D, E, H, I and J which have been isolated by the method similar to that previously reported[3] and the application of an improved procedure for cleavage of a glycoside having a doubly linked sugar to characterization of elaeodendroside B and C.

Elaeodendroside D (6) was isolated as colorless prisms (from CH_2Cl_2-ether), mp 275 - 285° (decomp.), $[\alpha]_D^{10}$ +30.0° (c=0.10 in $CHCl_3$). Inspection of the high resolution mass spectrum, ^1H n.m.r. spectrum[5] and elemental analysis permitted us to assign the structure 6 to elaeodendroside D. The structure was definitely

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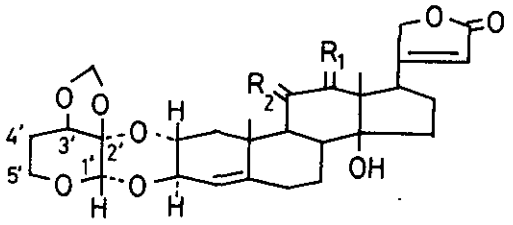
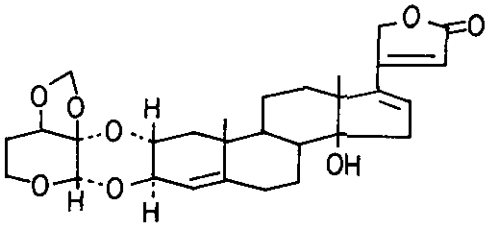
established by direct comparison with the synthetic sample derived from elaeodendroside A (1). Reduction of 1 with sodium borohydride gave the 11α,12ξ-diol (2) as a colorless amorphous substance (from acetone-ether), mp 206 - 210°, $[\alpha]_D^{21}$ +55.8° (c=0.43 in $CHCl_3$), together with the 12-epimer. Compound 2 was transformed into the monomesylate (3) in the usual manner. Treatment of 3 with sodium iodide and zinc dust in diglyme[6] provided the 12-ketone (4) as colorless prisms (from CH_2Cl_2-methanol), mp 296 - 300°, $[\alpha]_D^{10}$ +135.0° (c=0.10 in $CHCl_3$-methanol (3:1)). On the ^1H n.m.r. spectrum 4 exhibited the signals at δ 1.08 (3H, s, 18-CH_3) and 1.22 (3H, s, 19-CH_3), indicating the presence of an oxo group at C-12 rather than at C-11. The 12-ketone (4) was derivatized into the tosylhydrazone (5) which in turn was reduced with sodium cyanoborohydride in dimethylformamide-sulfolane (1:1)[7] at 105° for 4 hr. The yielded compound proved to be identical with elaeodendroside D (6) in all respects.

Elaeodendroside E (12) was separated as colorless prisms (from CH_2Cl_2-methanol), mp 283 - 290° (decomp.), $[\alpha]_D^{21}$ +7.9° (c=0.14 in $CHCl_3$). The high resolution mass spectrum and elemental analysis lent a support to assign a molecular formula $C_{31}H_{40}O_{10}$ to 12. On the ^1H n.m.r. spectrum 12 exhibited the signals at δ 0.98 (3H, s, 18-CH_3), 1.15 (3H, s, 19-CH_3), 2.00 (3H, s, $OCOCH_3$), 2.60 (1H, dd, J=17, 10 Hz, 15α-H), 3.25 (1H, d, J=10 Hz, 17α-H) and 5.60 (1H, t, J=10 Hz, 16α-H). These data suggested the presence of an acetoxyl group at the 16β-position.[8] Hydrolysis of 12 with potassium bicarbonate in methanol under mild condition afforded 13 as colorless prisms (from ether), mp 289 - 291° (decomp.), $[\alpha]_D^{24.5}$ +34.5° (c=0.17 in $CHCl_3$). Compound 13 was readily and quantitatively transformed into the cyclic phenylboronate, colorless needles (from acetone), mp 300° (decomp.), mass spectrum m/e 616 (M^+),615, indicating the existence of a cis-diol structure.[9] Being adsorbed on alumina in benzene at 60° for 5 hr, 12 was converted into 14, colorless prisms (from ether), mp 293 - 295° (decomp.), $[\alpha]_D^{15.5}$ +166.7° (c=0.12 in $CHCl_3$), UV λ_{max}^{MeOH} 270 nm. Upon partial hydrogenation over 5% palladium-on-charcoal for 30 min, 14 provided 17α-elaeodendroside D as a colorless amorphous substance (from acetone-ether), mp 254 - 258°, $[\alpha]_D^{20}$ +55.8° (c=0.22 in $CHCl_3$), together with a small amount of elaeodendroside D (6). The major product was also obtained from 6 by the procedure described by Merkel et al.[10] On the basis of these evidences elaeodendroside E was unequivocally identified as 16β-acetoxyelaeodendroside D (12). Elaeodendroside H (14) was also obtained from the natural source[11] and its structure was confirmed by direct

comparison with the Δ^{16} compound derived from 12.

Elaeodendroside I (10) was separated as colorless leaflets (from acetone-ether), mp 299 - 300° (decomp.), $[\alpha]_D^{21}$ +44.3° (c=0.14 in $CHCl_3$), ^1H n.m.r. spectrum δ 0.95 (3H, s, 18-CH_3), 1.32 (3H, s, 19-CH_3), 2.50 (1H, dd, J=3.2, 14 Hz, 1β-H) and 2.90 (1H, d, J=10 Hz, 17α-H). The high resolution mass spectrum and elemental analysis provided a molecular formula $C_{29}H_{38}O_9$. Oxidation of 10 with pyridinium chlorochromate in dichloromethane gave the 11-ketone (9) as colorless prisms (from ethyl acetate), mp >300°, $[\alpha]_D^{19}$ +66.7° (c=0.08 in $CHCl_3$), ^1H n.m.r. spectrum





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1: R_1=O, R_2=H,OH

2: R_1=H,OH, R_2=H,OH

3: R_1=H,OH, R_2=H,OMs

4: R_1=O, R_2=H,H

5: R_1=NNHTs, R_2=H,H

6: R_1=R_2=H,H

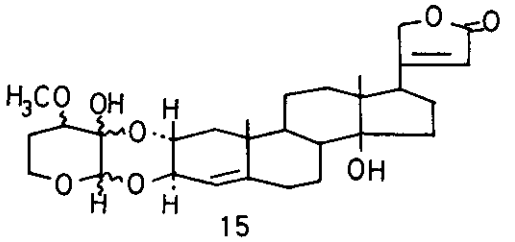
7: R_1=H,OH, R_2=O

8: R_1=H,OAc, R_2=O

9: R_1=H,H, R_2=O

10: R_1=H,H, R_2=H,OH

11: R_1=H,H, R_2=H,OAc



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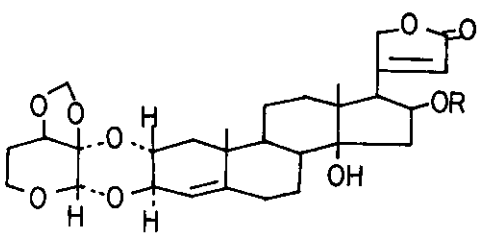
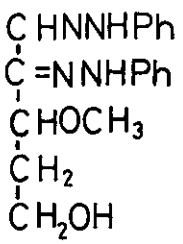


12: R=Ac

13: R=H



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δ 0.90 (3H, s, 18-CH_3), 1.32 (3H, s, 19-CH_3) and 2.50 (1H, dd, J=3, 14Hz, 1β-H).[12] The structural assignment was definitely established by direct comparison with the synthetic sample obtained from 1. Being adsorbed on alumina for a week,[13,14] 1 underwent ketol rearrangement to yield 7 as colorless prisms (from ether), mp 274 - 276° (decomp.), $[\alpha]_D^{19}$ +10.0° (c=0.05 in $CHCl_3$). Subsequent acetylation with acetic anhydride and pyridine afforded the 12-monoacetate (8) as a colorless amorphous substance (from acetone-ether), mp 200 - 204°, $[\alpha]_D^{20}$ +22.2° (c=0.09 in $CHCl_3$). Elimination of the acetoxyl group by reduction with zinc dust in acetic acid[15] yielded the 11-ketone (9) which was entirely identical with the compound derivable from 10. The configurational assignment of the 11α-hydroxyl group in 10 was supported by the chemical shift of angular methyl groups in ^1H n.m.r. spectrum[16] and the fact that 10 was easily converted into the acetate (11), colorless prisms (from acetone), mp >300°, $[\alpha]_D^{20}$ +15.4° (c=0.07 in $CHCl_3$). Based upon these data elaeodendroside I was unambiguously identified as 10.

Elaeodendroside J (7) was also isolated from the natural source and its structure was confirmed by direct comparison with the authentic sample obtainable from 1. The two isomeric 11,12-ketols, compound 1 and 7, were readily convertible each other when adsorbed on silica gel overnight.

In the previous paper, we reported that treatment of elaeodendroside B and C with acetic anhydride and pyridine gave elaeodendrogenin acetate. However, their sugar moiety including the position of a methoxyl group has not yet been characterized.[4] Treatment of elaeodendroside B and C with phenylhydrazine in a 1:2.2 molar ratio in boiling ethanol containing sodium acetate[17,18] afforded desacetylelaeodendrogenin as colorless prisms (from methanol), mp 262 - 266°, $[\alpha]_D^{20}$ -3.1° (c=0.16 in methanol) and the osazones (16) as colorless prisms (from ether), mp 135 - 138°, mass spectrum m/e 326 (M^+). The osazones formed from elaeodendroside B and C showed specific rotations, $[\alpha]_D^{14}$ +15.9° (c=0.19 in $CHCl_3$) and $[\alpha]_D^{14.5}$ -16.4° (c=0.19 in $CHCl_3$), respectively. Elaeodendroside B gave desacetylelaeodendrogenin and elaeodendroside C when refluxed in pyridine for 6-8 hr. In addition, elaeodendroside B was transformed into 2'- and 3'-deuterated elaeodendroside C by treatment with deuteriomethanol-deuterium oxide (10:1) in the presence of sodium carbonate at 60-70° for 1 hr. These evidences together with the previous findings[4] permitted us to assign the structure 15 to elaeodendroside B and C which are stereoisomers involving the methoxyl group at the 3'-position.

Further studies on the complete structures of elaeodendroside B and C and

other cardiac steroids are being conducted in these laboratories. The details will be reported elsewhere in the near future.

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