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NEW EPIMERIC DI-TRITERPENE QUINONE ETHERS. THEIR PARTIAL SYNTHESIS AND THAT OF NETZAHUALCOYENE FROM PRISTIMERIN AND DDQ

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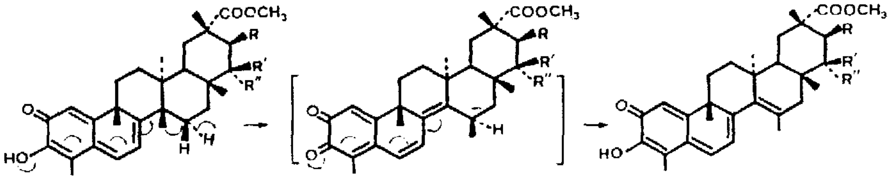
SUMMARY: Two new di-triterpene quinone ethers, 5 and 6, were isolated from the roots of Rzedowskia tolantonguensis and their structure was determined from NMR data and a partial synthesis, involving the reaction of pristimerin (1) with DDQ. Netzahualcoyene (2) and alcohol 4 were formed in this reaction favouring the theorized biogenetic pathway to triterpene quinones with a rearranged netzahualcoyene skeleton.

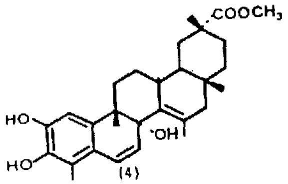
In our study of the flora used in Latin American folk medicine[1], biologically active[2] netzahualcoyone (3) and several other 14(15)-ene-quinone methides have been isolated[3]. Biosynthetically, these substances may be obtained by dehydrogenation and rearrangement of the corresponding quinone methides[3] (Scheme).



(1) R=R'= R"=H

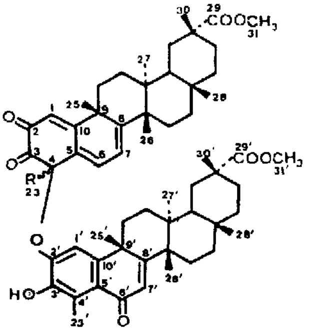
SCHEME

(2) R=R'=R"=H
(3) R=OH;R',R"=O



(4)

(5) R=α-Me
(6) R=β-Me



The roots of Rzedowskia tolantonguensis have now yielded pristimerin (1), netzahualcoyone (3) and two new epimeric di-triterpene quinone ethers. Pristimerin (1) was treated with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ)[4] (1:1 equiv.) in distilled dioxan at r.t. to give a mixture of four products, separated by preparative TLC. The physical and ^{1}H NMR data of the minor and least polar product were totally superimposable upon those of netzahualcoyene (2) isolated previously from Maytenus horrida[5]. The next least polar product, 4, contaminated with 2, had the molecular ion $|M|^+$ at m/z 480 and a fragment $|M-H_2O|^+$ at m/z 462. ^1H NMR showed the aromatic H-1 as a singlet at δ 6.60 and an AB benzylidenic system[6] as two doublets (J=9 Hz) at δ 6.25 (H- 7) and 6.43 (H-6), the 23-Me and 26-Me being observed as singlets at δ 2.26 and 1.70, respectively, all of which is in accordance with the structure proposed.

The two major and more polar products 5 and 6 had physical and spectral data completely superimposable upon those of the corresponding natural products. Both behaved as pure substances in TLC and HPLC, 5, $|\alpha|_D^{20}$ -143.6º $(CHCl_3)\lambda_{max}$ (EtOH) 255, 295, 335 and 385 nm, did not show the molecular ion in MS but had two fragments at m/z 480 (found, 480.2881, calc.for $C_{30}H_{40}O_5$, 480.2886) and m/z 464 (found, 464.2889, calc.for $C_{30}H_{40}O_4$, 464.2852). In the ^1H NMR[7], signals appeared for two carbomethoxy groups, twelve angular methyls and six protons at lowfield; the two doublets and the double doublet are analogous to those of the H-1, H-7 and H-6 protons of pristimerin although the chemical shifts are different. A broad singlet interchangeable with D_2O was assigned to the phenolic proton.

Comparison of the chemical shifts of the methyls in pristimerin, zeylasterone 2,3-dimethyl ether[8] and 5,(Table 1) shows that in one segment of 5 the 23-Me of pristimerin has been shifted to δ 1.37 (assigned to a methyl on an oxygen-bearing carbon) indicating an ether bridge between the C-4 of one part of the molecule and the phenolic group of the other. In the other section of 5 the 23-Me has been shifted to δ 2.75 suggesting the existence of a grouping similar to that of zeylasterone 2,3-dimethyl ether[8] with the carbonyl at C'-6 facing the 23'-Me and the singlet protons at δ 6.20 and 6.73 assignable to H-7' and H-1'

Table 1: ^1H NMR (200 MHz) Data (δ, $CDCl_3$, Chemical Shifts in ppm Relative to Me_4Si) for the Methyls of Pristimerin (1). 5,6 and Zeylasterone 2,3-Dimethyl Ether[8]

	1	5[a]		6[a]		Zeylasterone 2,3-Dimethyl Ether
		H	H*	H	H*	
23-Me	2.21	1.37,	2.72	1.41,	2.73	2.66
25-Me	1.48	1.48,	1.57	1.47,	1.58	1.60
26-Me	1.26	1.26,	1.26	1.27,	1.25	1.32
27-Me	1.10	1.05,	1.08	1.06,	1.08	1.12
28-Me	1.18	1.16,	1.16	1.16,	1.16	1.18
30-Me	0.53	0.52,	0.54	0.53,	0.54	0.60

a The values of the pairs H and H* may be interchanged.

respectively. The UV and IR data[9] also agree with this structure[10].

The ^{13}C NMR (Table 2) signal at 91.2 ppm was assigned to C-4 while the 14-CH$_3$, 14CH$_2$, 7CH, 25-C (four C-O and 5 C=O) and a phenolic proton confirmed the molecular formula $C_{60}H_{78}O_9$. A NOESY experiment on 5 confirmed the assignment of the methyls and established the configuration at C-4, no n.O.e. effect being observed between C-23 and C-25.

Table 2: ^{13}C NMR (50 MHz) Data (δ, CDCl$_3$, Chemical Shifts in ppm Relative to Me$_4$Si) of Pristimerin (1) and Ethers 5 and 6

	1[3]	5[a]		6[a]	
		C	C'	C	C'
1	119.0(d)	110.8(d),	114.9(d)	11.3(d)	115.3(d)
2	178.4(s)	179.2(s),	173.4(s)	188.0(s)	174.0(s)
3	146.1(s)	171.3(s),	145.3(s)	171.5(s)	144.7(s)
4	117.0(s)	91.2(s),	124.0(s)	92.1(s)	124.0(s)
5	127.5(s)	128.5(s),	132.0(s)	127.7(s)	130.1(s)
6	133.9(d)	129.0(d),	189.6(s)	126.7(d)	189.0(s)
7	118.1(d)	117.4(d),	126.3(d)	116.2(d)	126.2(d)
8	169.9(s)	164.5(s),	151.3(s)	161.4(s)	150.5(s)
9	42.9(s)	38.8(s),	44.0(s)	38.2(s)	41.9(s)
10	164.7(s)	137.7(s)	151.3(s)	137.7(s)	151.0(s)
11	33.6(t)	33.0(t)	34.1(t)	33.0(t)	34.2(t)
12	29.7(t)	29.5(t)	29.7(t)	29.7(t)	29.8(t)
13	39.4(s)	39.1(s)	39.3(s)	39.0(s)	39.9(s)
14	45.0(s)	44.5(s)	44.5(s)	44.7(s)	44.2(s)
15	28.7(t)	28.7(t)	29.4(t)	28.7(t)	28.6(t)
16	36.4(t)	36.5(t)	36.5(t)	36.4(t)	36.5(t)
17	30.6(s)	30.7(s)	30.7(s)	30.6(s)	30.6(s)
18	44.4(d)	44.8(d)	44.8(d)	44.5(d)	44.7(d)
19	30.9(t)	30.9(t)	31.0(t)	30.9(t)	31.0(t)
20	40.4(s)	40.6(s)	40.7(s)	40.5(s)	40.5(s)
21	29.9(t)	29.8(t)	30.0(t)	29.9(t)	29.9(t)
22	34.8(t)	34.9(t)	35.1(t)	34.9(t)	34.9(t)
23	10.2(q)	24.7(q)	13.3(q)	22.5(q)	12.8(q)
25	38.3(q)	37.8(q)	40.2(q)	37.6(q)	37.7(q)
26	21.6(q)	21.0(q)	22.5(q)	20.9(q)	22.2(q)
27	18.3(q)	18.3(q)	18.6(q)	18.3(q)	18.6(q)
28	31.6(q)	31.7(q)	31.7(q)	31.6(q)	31.6(q)
29	178.7(s)	179.0(s)	179.0(s)	179.0(s)	179.0(s)
30	32.7(q)	33.0(q)	33.0(q)	32.7(q)	32.8(q)
31	51.6(q)	51.6(q)	51.8(q)	51.5(q)	51.5(q)

[a] The values of the pairs C and C' may be interchanged.

6, $|\alpha|_D$ +260º ($CHCl_3$), λ_{max} (EtOH) 255, 295, 335 and 2385 nm, m/z 480(found 480.2191, calc. for $C_{30}H_{40}O_5$, 480.2962); m/z 464 (found 464.2960, calc. for $C_{30}H_{40}O_4$, 464.2994). The IR was virtually superimposable upon that of 5. The ^{1}H NMR differs from the same spectrum for 5 in that the H-6 and H-7 protons register lower chemical shifts. NOESY experiments show a n.O.e. effect between 23-Me and 25-Me and between 23-Me and H-1' which establishes the configuration at C-4 and the fact that in solution, as predicted on Dreiding models, the two triterpenic portions of the ether are perpendicular to each other which also accounts for the deshielding of H-6 and H-7 by the π orbitals of Ring A'.

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REFERENCES

1 González A.G. Fraga B.M. González C.M. Ravelo A.G. Ferro E. Domínguez X.A. Martínez M.A. Fayos J. Perales A. & Rodríguez M.L. Tetrahedron Lett. 24 3033 (1983)

2 González A.G. Ravelo A.G. Bazzocchi I.L. Jiménez J. González C.M. Luis J.G. Ferro E.A. Gutierrez A. Moujir L. & de Las Heras F.G. Il Farmaco 43 451 (1988)

3 Chandrasiri H. Gunatilaka A.A.L. Kumar V. Weeratunga G. Tezuka Y.& Kikuchi T. Tetrahedron Lett. 29 387 (1988)

4 González A.G. Rodríguez C.M. & Luis J.G. J. Chem. Research (S) 114 (1988)

5 González A.G. González C.M. Ferro E.A. Ravelo A.G. & Domínguez X.A. J. Chem.Res. (S) 20 (1988)

6 González A.G. Rodríguez C.M. & Luis J.G. Phytochemistry 26 2133 (1987)

7 ^{1}H NMR (200 MHz) in $CDCl_3$ (J in Hz): 5, see Table 1 for methyls; δ 3.47 3.58 (each 3H, s, 2xCOOMe), 5.14 (1H, br s, -OH), 6.08(1H, d, 6.8, H-7), 6.08 (1H, d, 1.3, H-1), 6.20 (1H, s, H-7'), 6.50 (1H, dd, 6.8, 1.3,H-6), 6.73 (1H, s, H-1'); 6, see Table 1 for methyls; δ 3.53, 3.59 (each 3H, s, 2xCOOMe), 5.10 (1H, s, OH), 5.93 (1H, d, 6.8, H-7), 6.08 (1H, d, 1.3, H-1), 6.23 (1H, dd, 6.8, 1.3, H-6), 6.24 (1H, s, H-7'), 6.80 (1H, s, H-1-).

8 Gamlath C.B. Gunaherath K.B. & Gunatilaka A.A.L. J.Chem.Soc.Perkin 1 2849 (1987)

9 IR determined in $CHCl_3$ 5, 3430, 2940, 1710, 1650, 1625, 1590, 1580, 1560, 1530, 1460, 1370, 1300, 1200, 1150, 1100, 1050, 1040, 1020 and 1010 cm^{-1}.

10 Details of the mechanistic formation of 5 and 6 will be given later.

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