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FOUR NOVEL 3,4-*SECO*-TRITERPENOIDS, ESPINENDIOLS A AND B, ESPINENOXIDE AND TRISNOR-ISOESPINENOXIDE FROM *EUPHORBIA SUPINA*

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Summary: Four novel 3,4-*seco*-triterpenoids named espinendiols A and B, espinenoxide and trisnor-isoespinenoxide were isolated from *Euphorbia supina* and their structures were established as 3,4-*seco*-D:B-*friedo*-B':A'-neogammacer-4(23)-en-3,5α-diol, 3,4-*seco*-D:B-*friedo*-B':A'-neogammacer-4(23)-en-3,5β-diol, 3,4-*seco*-D:B-*friedo*-B':A'-neogammacer-4(23)-en-3,5β-oxide and 3,4-*seco*-4,23,24-trisnor-D:B-*friedo*-B':A'-neogammacer-5(10)-en-3,5-oxide, respectively, on the basis of chemical, spectral and X-ray analytical evidence.

Euphorbia supina Rafin., which is documented as a folk medicine,[1] contained biogenetically interesting triterpene components[2-6] involving spirosupinanonediol[3] and neospirosupinanonediol.[6] Further investigation of the neutral benzene extract of the whole herb furnished four new *seco*-triterpenoids named espinendiols A (1a) and B (2a), espinenoxide (3) and trisnor-isoespinenoxide (4). This paper reports the structure elucidation of these compounds.

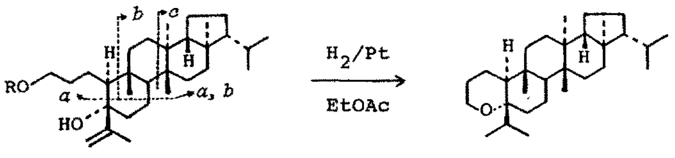
Espinendiols A (1a), mp. 194-196°, $[\alpha]^{23}_{D}$ + 90.7° (*c* 0.76, $CHCl_3$), and B (2a), mp. 192-193.5°, $[\alpha]^{23}$ - 17.1° (*c* 0.54, $CHCl_3$), were tetracyclic triterpenes which had the same molecular formulae of $C_{30}H_{50}O_2$ (HRMS) and the same functional groups of four tertiary methyls, one isopropyl, one isopropenyl, one hydroxymethyl and one tertiary hydroxyl in the IR, ^1H and ^{13}C NMR spectra (Tables 1 and 2). On usual acetylation, 1a gave a monoacetate (1b), while 2a afforded a different monoacetate (2b). Catalytic reduction of 1a furnished, with concomitant dehydration, a saturated oxide (1c) showing no any hydroxyl absorptions in the IR spectrum. On the other hand, alkaline hydrolysis of 2b afforded a conjugated diene (2c), λ^{EtOH}_{max} 205 and 228 nm (ε 4,000, 2,800), δ_H 1.82 (Me-24), 4.66 (*d*) and 4.79 (*dd*) ($>C=CH_2$) and 5.52 (1H, *m*, H-6), along with a small amount of 2a. Therefore the tertiary hydroxyl groups in 1a and 2a were located on the carbon attached to the isopropenyl group. In the EI-mass specrum, both 1a and 2a showed almost identical fragmentation, and 1a gave a prominent peak due to ion *a* at *m/z* 347.3309 $[C_{24}H_{43}O]^+$, besides four peaks at *m/z* 274.2655 (ion *b*), 259.2442 (*b* - Me), 231.2106 (*b* - C_3H_7) and 205.1936 (ion *c*) characteristic for those of simiarenol[7] (5) which has previously been isolated from this plant.[5] All these facts indicated that both 1a and 2a must be an epimeric pair of 3,4-*seco*-$\Delta^{4(23)}$-triterpene-3,5ξ-diol bearing D:B-*friedo*-B':A'-neogammacerane (adianane) skeleton in which the ring A suffered oxidative cleavage between C-3 and C-4. In addition, extensive ^1H and ^{13}C NMR measurements for 1a, 2a and 5 using 2D ^1H-^1H COSY, NOESY, 2D ^1H-^{13}C COSY and 2D long range ^1H-^{13}C COSY techniques suggested that 1a and 2a had the tertiary hydroxyl group at 5α and 5β position, respectively, in the structure proposed above.

Conclusive evidence for the structure was obtained from its X-ray analysis.[8] Figure 1 shows the ORTEP diagram of 1a. Consequently, 1a was proved to be 3,4-*seco*-D:B-*friedo*-B':A'-neogammacer-4(23)-en-3,5α-diol and then 2a to be the 5β-epimer of 1a.

Compound 3, $C_{30}H_{50}O$, M^+ at *m/z* 426.0950, mp. 215-218°, $[\alpha]_D^{23}$ + 7.8° (*c* 0.32, $CHCl_3$), showed ^1H and ^{13}C NMR signals of four tertiary methyls, one isopropyl, one isopropenyl and one methylene group attached to an etheral oxygen (Tables 1 and 2), while no hydroxyl band has been observed in the IR spectrum. Close similarity of its EI-MS, ^1H and ^{13}C NMR spectra with those of 2a suggested that it must be an oxide produced by dehydration of either 1a or 2a. Owing to a poor yield of 3 from this plant, the structure was proved by its single crystal X-ray analysis.[8] Compound 3 gave two crystallographically independent molecules, 3A and 3B, per asymmetric unit. Figure 2 shows ORTEP plots of both molecules. The C-5α isopropenyl group is in the opposite direction in 3A and 3B due to restriction of its rotation by 1α and 3α hydrogenes. Thus, compound 3 was confirmed to be 3,4-*seco*-D:B-*friedo*-B':A'-neogammacer-4(23)-en-3,5β-oxide in which the oxide and the B-rings had *cis* juncture. Although there remains some doubt that 3 is an artefact produced during the extraction and isolation of compound, the coexistence of the following compound suggested that it may also be a natural product.

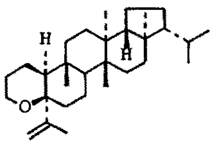
Compound 4, $C_{27}H_{44}O$, M^+ at *m/z* 384.3389, mp. 209-213°, $[\alpha]_D^{23}$ - 2.9° (*c* 0.63, $CHCl_3$), showed ^1H and ^{13}C NMR signals due to four tertiary methyls, one isopropyl, one methylene group attached to an etheral oxygen and two *sp*^{2} carbons arose from a tetrasubstituted double bond with the oxygen function (Tables 1 and 2). Thus, 4 must have a $-CH_2O-\overset{|}{C}=\overset{|}{C}-$ grouping in the molecule. Despite the absence of an isopropenyl signal in the ^1H and ^{13}C NMR spectra, similarity of the methyl resonances with those of 1a, 2a and 3 indicated that 4 must be 3,4-*seco*-4,23,24-trisnor-D:B-*friedo*-B':A'-neogammacer-5(10)-en-3,5-oxide. Detailed assignments of its ^1H and ^{13}C NMR signals employing 2D ^1H-^1H COSY, NOESY, 2D ^1H-^{13}C COSY and 2D long range ^1H-^{13}C COSY experiments supported well the proposed structure.

So far 3,4-*seco*-adianane triterpenes have not yet been reported in the literature. Particular interest is the isolation of compound 4, as well as its precursors, 1a and 2a, in this work. For the biogenesis of 1a and 2a, a route from simiarenone[7] via their 3,5-hemiketal are suggested. Formation of 4 may proceed from 1a and 2a through oxidative fission of the isopropenyl at C-5, enolization and subsequent dehydration. Up to now, a considerable



1a R = H
1b R = Ac

1c



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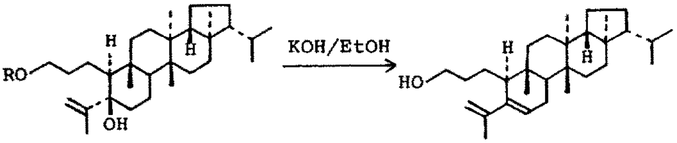

2a R = H
2b R = Ac

2c

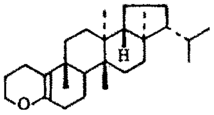

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Table 1. 300 MHz ^{1}H NMR chemical shifts of 1a, 1b, 1c, 2a, 2b, 2c, 3, 4 and 5 in $CDCl_3$.

	1a	1b	1c	2a	2b	2c	3	4	5
H-23	4.90*t* 1.4 5.15*br.s*	4.92*t* 1.4 5.14*br.s*	1.08*d* 6.5	4.87*t* 1.5 5.10*d* 1.5	4.87*t* 1.5 5.09*d* 1.5	4.66*d* 2.8 4.79*dd* 2.8, 1.5	4.93*br.s* 4.97*t* 1.5	-	1.05*s*
Me-24	1.94*d* 0.8	1.91*d* 0.8	1.41*d* 6.5	1.79*d* 0.8	1.78*d* 0.8	1.82*s*	1.73*s*	-	1.14
Me-25	0.86	0.85	1.03	1.04	1.04	0.85	1.31	0.98	0.89
Me-26	0.89	0.88	0.90	0.97	0.94	0.98	0.93	0.92	1.01
Me-27	0.97	0.96	0.96	0.97	0.97	0.93	0.96	0.96	0.93
Me-28	0.79	0.79	0.79	0.80	0.80	0.78	0.79	0.80	0.78
Me-29	0.88*d* 6.5	0.88*d* 6.5	0.88*d* 6.5	0.89*d* 6.5	0.89*d* 6.5	0.89*d* 6.5	0.88*d* 6.5	0.89*d* 6.5	0.88*d* 6.5
Me-30	0.82*d* 6.5	0.82*d* 6.5	0.83*d* 6.5	0.83*d* 6.5	0.83*d* 6.5	0.83*d* 6.5	0.83*d* 6.5	0.83*d* 6.5	0.83*d* 6.5
H-3	3.65*ddd* 12, 5.2, 5 3.65*ddd* 12, 9, 4.2	4.06*m*	3.62*m*	3.54*t* 6.3	3.95*m*	3.57*t* 6.3	3.63*m*	3.74*td* 10.5, 2.8 4.00*dtd* 10.5, 5, 1.5	3.47*m*
H-6	-	-	-	-	-	5.52*dt* 6.2, 2.2	-	-	5.62*dt* 6.2, 2.2

Table 2. 74.5 MHz ^{13}C NMR chemical shifts of 1a, 1b, 2a, 2b, 3, 4 and 5 in $CDCl_3$.

C	1a	1b	2a	2b	3	4	5
1	20.74	21.96	17.51	17.54	18.06	18.54	18.09
2	34.68	32.32	35.46	31.23	21.75	23.21	27.79
3	61.84	65.16	63.57	65.03	61.70	65.19	76.38
4	149.89	150.03	151.21	150.04	151.10	-	40.99
5	76.78	76.59	78.43	78.41	78.48	144.94	141.99
6	42.00	41.96	39.07	39.14	40.82	28.80	122.01
7	21.22	20.99	21.13	21.38	17.97	17.85	24.04
8	49.54	48.87	49.13	49.18	48.07	44.62	44.30
9	39.63	41.96	38.83	38.87	38.44	36.59	34.85
10	60.83	63.41	54.99	55.05	47.21	115.94	50.02
11	33.93	34.56	34.34	34.33	36.05	31.26	34.18
12	28.41	28.41	28.41	28.44	28.61	28.46	28.94
13	39.01	39.37	38.98	38.97	38.75	39.10	38.65
14	40.28	40.27	40.10	40.13	39.69	40.07	40.28
15	29.36	29.28	29.20	29.22	29.93	29.04	29.11
16	35.68	35.63	35.63	35.66	35.52	35.56	35.44
17	42.77	42.74	42.71	42.74	42.68	42.28	42.38
18	51.65	51.65	51.70	51.69	51.69	51.71	51.77
19	19.95	19.93	19.87	19.90	18.87	19.98	19.92
20	28.27	28.41	28.10	28.16	28.41	28.46	28.33
21	60.15	60.11	60.08	60.10	60.10	60.16	60.05
22	30.76	30.77	30.88	30.83	30.80	30.81	30.80
23	114.47	114.40	110.69	110.77	117.73	-	29.11
24	23.45	23.08	20.67	20.63	19.08	-	25.50
25	18.07	18.52	19.67	19.70	22.61	23.21	17.89
26	16.24	16.13	16.21	16.24	16.47	16.29	15.77
27	15.65	15.57	15.57	15.56	15.27	15.52	15.00
28	16.50	16.42	16.41	16.44	16.69	16.51	16.07
29	21.95	21.96	21.95	21.94	21.92	21.97	21.93
30	22.88	22.90	22.90	22.90	22.89	22.87	22.92
OCO<u>Me</u>	-	22.90	-	20.20	-	-	-
O<u>C</u>OMe	-	171.25	-	171.16	-	-	-

number of ring-A-degraded triterpenes have been found from recent and fossil sediments and petroleum except for 3,4-*seco*-3-nor-olean-12-en-1-ol,[9] which has been isolated once from the leaf wax of several *Hoya* species (Ascrepiadaceae), and their biosynthetic pathways have also been discussed on the basis of geochemical, photochemical, and biochemical aspects.[10] Although Baas pointed out that at least part of the degradation of the A-ring may occur in the plants,[10] this investigation presented clear evidence that the degradation of the A-ring occured in the plant body itself without any other influences.

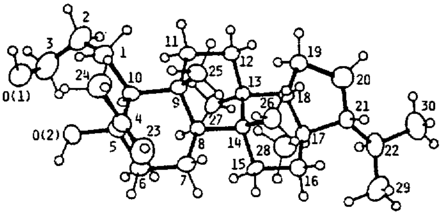
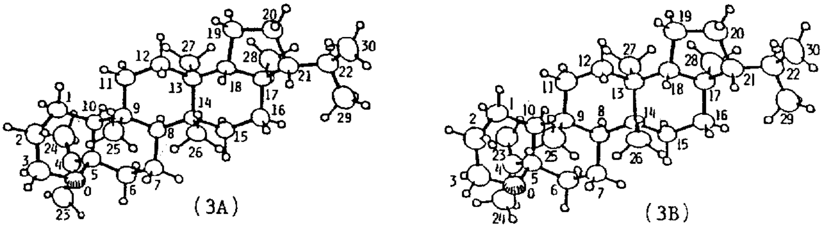


Fig. 1. The ORTEP diagram of 1a.



(3A) (3B)

Fig. 2. ORTEP plots of 3A and 3B.

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8) *Crystal data of* 1a: $C_{30}H_{52}O_2$, M = 444.743, monoclinic, space group $P2_1$, a = 12.337(4), b = 7.225(2), c = 16.145(5)Å, β = 111.36(3)°, U = 1340.3 (8)$Å^3$, Dx = 1.102 g cm^{-3}, Z = 2. *Crystal data of* 3: $C_{30}H_{50}O$, M = 426.728, monoclinic, space group $P2_1$, a = 13.447(15), b= 12.355(13), c = 15.954(11)Å, β = 105.91(5)°, U = 2549.0(43)$Å^3$, Dx = 1.112 g cm^{-3}, Z = 4. A total of 2491 and 4227 independent reflection intensities up to 2θ = 130° for 1a and 3, respectively, were measured on a Rigaku automatic four-circle diffractometre with graphite monochromated Cu-*Kα* radiation. Structures of 1a and 3 were solved by the direct method. The hydrogen atoms were located from a difference Fourier synthesis. Structures of 1a and 3 were refined by the brock-diagonal least squares to R = 0.073 and 0.085, respectivery. Atomic co-ordinates, bond lengths and angles, thermal paramerers, and observed and calculated structure factors of both crystals have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

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