Tetranortriterpenoids and Related Substances. Part 20.[1] New Tetranortriterpenoids from the Seeds of *Chukrasia tabularis* (Meliaceae); Simple Esters of Phragmalin and 12α-Acetoxyphragmalin

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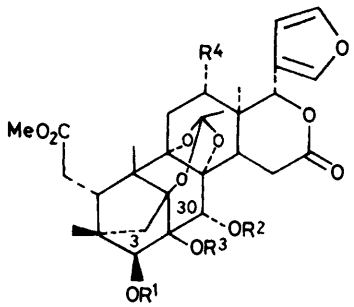
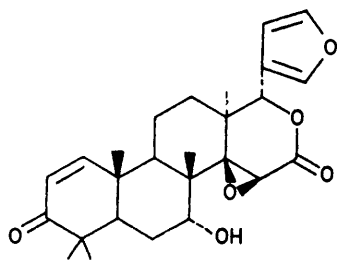
Four new tetranortriterpenoids isolated from the light petroleum extract of the seeds of *Chukrasia tabularis* (Meliaceae) have been identified as the 3,30-di-isobutyrates (1) and (2) and the 3-isobutyrate 30-propionates (3) and (4) of phragmalin and 12α-acetoxyphragmalin. Two compounds (12) and (13) with a modified furan ring were also obtained from the extract.

EXTRACTION of the seeds of *Chukrasia tabularis* (Meliaceae) with light petroleum and concentration of the solution afforded a precipitate containing a complex mixture. The major components were four closely related tetranortriterpenoids, A—D, which were eventually obtained crystalline by extensive preparative t.l.c. We now present chemical and spectroscopic evidence to show that A and B are the 3,30-di-isobutyrates (1) and (2) and C and D the 3-isobutyrate 30-propionates (3) and (4) of phragmalin (5)[2] and 12α-acetoxyphragmalin (6). The known 7-deacetoxy-7-hydroxygedunin (7) was also isolated.

The spectroscopic properties (see Tables 1 and 2) of compounds A (1), $C_{37}H_{48}O_{13}$, and C (3), $C_{36}H_{46}O_{13}$, indicated that they had the same tetranortriterpenoid nucleus and differed only in attached ester groups. The presence of three tertiary methyl groups, an orthoacetate, and a methoxycarbonyl group suggested that they were phragmalin (5) derivatives. This was readily confirmed by alkaline hydrolysis in each case to yield phragmalin (5), identified by comparison with an authentic specimen and by conversion into the known mono-, di-, and tri-acetates (8)—(10).[2] The nature of the attached ester groups was elucidated in several ways. First, ^{1}H n.m.r. examination of the volatile acids[3] released on hydrolysis showed that compound A (1) gave





(7)

(1) $R^1 = R^2 = Pr^iCO$, $R^3 = R^4 = H$
(2) $R^1 = R^2 = Pr^iCO$, $R^3 = H$, $R^4 = OAc$
(3) $R^1 = Pr^iCO$, $R^2 = EtCO$, $R^3 = R^4 = H$
(4) $R^1 = Pr^iCO$, $R^2 = EtCO$, $R^3 = H$, $R^4 = OAc$
(5) $R^1 = R^2 = R^3 = R^4 = H$
(6) $R^1 = R^2 = R^3 = H$, $R^4 = OAc$
(8) $R^1 = Ac$, $R^2 = R^3 = R^4 = H$
(9) $R^1 = R^2 = Ac$, $R^3 = R^4 = H$
(10) $R^1 = R^2 = R^3 = Ac$, $R^4 = H$
(11) $R^1 = R^2 = R^3 = H$, $R^4 = OH$

[1] Part 19, B. Sabata, J. D. Connolly, C. Labbé, and D. S. Rycroft, *J.C.S. Perkin I*, 1977, 1875.

[2] R. R. Arndt and W. H. Baarschers, *Tetrahedron*, 1972, **28**, 2333.

[3] D. H. Calam and D. A. H. Taylor, *J. Chem. Soc.* (*C*), 1966, 949.

rise to 2 mol. equiv. of isobutyric acid, whereas compound C gave 1 mol. equiv. each of isobutyric and propionic acids. Secondly, the mass spectrum of (1) showed a characteristic cleavage for an isobutyrate (*m/e* 71) whereas (3) had peaks for cleavage of both isobutyrate and propionate (*m/e* 57). These findings were confirmed by the ^{13}C n.m.r. spectra of (1) and (3) (see Table 2). The ^{1}H n.m.r. data in Table 1 demonstrated that the hydroxy-groups at both C-3 and C-30 of the phragmalin nucleus were acylated. It follows, therefore, that compound A is phragmalin 3,30-di-isobutyrate (1) and compound C is the corresponding isobutyrate propionate.

TABLE 1

^{1}H n.m.r. spectra * of phragmalin and related compounds

	(1)	(2)	(3)	(4)	(5)	(6)	(9)	(10)	(11)	(14)
H-21	7.52	7.48	7.52	7.46	7.50	7.52	7.51	7.50	7.64	
H-22	6.42	6.43	6.46	6.42	6.46	6.42	6.44	6.42	6.58	7.28
H-23	7.42	7.40	7.43	7.42	7.39	7.42	7.40	7.38	7.46	6.91
H-17	5.54	5.59	5.52	5.56	5.58	5.55	5.48	5.53	5.63	5.48
H-30	5.91	6.02	5.88	5.99	4.74	4.56	5.91	6.29	4.68	5.94
H-3	4.66	4.68	4.61	4.59	3.56	4.70	4.64	5.09	3.54	4.65
H-12		4.60 (q, *J* 4 and 12 Hz)		4.66 (q, *J* 4 and 12 Hz)					4.0 (t, *J* 8 Hz)	
CO_2Me	3.69	3.72	3.70	3.72	3.69	3.70	3.69	3.69	3.69	3.75
O–MeC(–O)–O	1.65	1.60	1.65	1.60	1.61	1.62	1.67	1.70	1.61	1.65
12α-OAc		1.66		1.65						
	0.90	0.90	0.91	0.92	0.98	0.94	0.93	0.95	0.98	0.94
CMe †	1.04	1.12	1.05	1.13	1.04	1.06	1.11	1.11	1.07	1.06
	1.14	1.18	1.13	1.20	1.13	1.14	1.17	1.19	1.13	1.16

* Chemical shifts in p.p.m. downfield from internal Me_4Si; solvent $CDCl_3$. † Skeletal methyl groups only

TABLE 2

^{13}C n.m.r. spectra * of phragmalin and related compounds

Carbon no.	(1)	(2)	(3)	(4)	(5)	(8)	(9)	(10)	(14)
1 [a]	87.2	86.1	87.1	86.0	86.9	86.7	87.2	86.9	87.2
2	79.8	80.0	79.5	79.8	78.6	77.8	79.4	85.3	80.0
3	83.1	83.2	83.4	83.8	83.1	83.0	83.4	81.1	82.9
4 [b]	45.4	45.4	45.4	45.4	45.8	45.6	45.4	46.2	45.8
5	36.8	35.9	36.7	35.9	35.9	36.9	36.4	35.5	36.5
6	33.3	33.5	33.5	33.5	34.3	33.8	33.5	33.3	34.2
8 [a]	86.4	85.7	86.2	85.5	86.4	86.2	86.2	86.0	86.2
9 [a]	85.5	85.3	85.5	85.3	84.4	84.1	85.6	85.3	85.8
10 [b]	45.2	45.1	45.2	45.1	45.8	45.4	45.3	45.8	45.5
11	25.2	31.7	25.2	31.7	25.3	25.2	25.3	25.4	25.3
12	29.1	69.1	29.2	69.1	29.3	29.0	29.2	29.2	27.9
13	34.4	38.9	34.4	38.7	34.3	34.6	34.4	34.4	35.0
14	42.7	43.8	42.8	43.8	42.5	42.2	42.9	43.2	42.7
15	26.6	26.8	26.6	26.8	27.4	27.2	26.7	26.6	26.3
17	78.5	76.6	78.7	76.9	79.1	78.3	78.8	78.6	77.1
20	121.3	120.9	121.2	120.9	121.6	121.6	121.2	121.2	135.4
21	140.6	141.0	140.5	141.0	140.6	140.3	140.7	140.8	167.6
22	109.7	109.9	109.7	109.9	109.7	109.7	109.7	109.8	147.2
23	142.9	143.0	142.9	143.0	142.7	143.1	143.1	143.0	92.1
29	39.5	39.8	39.5	39.8	39.5	39.6	39.4	40.2	39.5
30	70.7	70.2	70.9	70.3	68.9	69.2	71.2	69.3	70.4
CO_2Me	51.9	51.7	51.9	51.7	52.0	52.1	52.0	52.1	52.4
O–MeC(–O)–O	119.0	119.1	118.9	119.1	118.9	119.1	119.1	119.1	119.0
O–MeC(–O)–O	21.1	21.1	21.1	21.1	21.3	21.2	21.1	21.1	21.2
18	19.5	14.0	19.6	14.0	20.2	19.9	19.7	19.6	20.0
19 [c]	16.3	16.2	16.3	16.2	15.8	16.0	16.2	16.6	16.1
28 [c]	14.4	14.0	14.5	14.0	14.8	14.5	14.5	14.6	14.7
	19.5	19.7	19.3	19.5					19.6
Me_2CHCO	19.3	19.3	18.3	18.4					19.3
	18.2	18.4							18.1
	18.0	17.9							18.0
Me_2CHCO	34.4(2)	34.6(2)	34.3	34.7					34.6(2)
$MeCH_2CO$			8.62	8.62					
$MeCH_2CO$			27.7	27.9					
*Me*CO		20.1		20.1		20.9	21.2(2)	21.7	20.7
								21.6	
								21.1	
CO att. to posn. 7	172.9	172.1	172.9	172.1	173.4	172.9	172.8	172.7	172.5
CO att. to posn. 16	170.1	169.7	170.1	169.7	172.0	171.3	170.8	170.3	169.3
CO att. to posn. 3	176.5	177.3	176.6	177.5		170.3	170.3	170.3	177.0
CO att. to posn. 30	174.9	174.9	172.3	172.5			169.0	168.6	175.2
CO att. to posn. 12/2/23		169.2		169.2				170.2	168.7

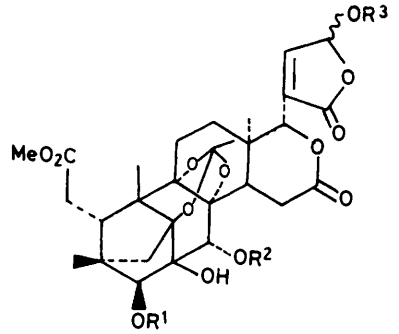
* Chemical shifts in p.p.m. downfield from internal Me_4Si; solvent $CDCl_3$.

[a–c] These assignments may be interchanged.

The question of the position of attachment of the propionate in compound C is less easily settled. We favour C-30 on the basis of the assignments of the carbonyl carbon signals in the ^{13}C n.m.r. spectra of the series of compounds in Table 2. The carbonyl carbon atom of an ester group attached to C-30 resonates at higher field than that in the corresponding C-3 ester [*cf.* (8), (9), and (10)]. This difference is enhanced by the substitution effect [4] on going from isobutyrate to propionate [*cf.* (1) and (3)]. These assignments are consistent with structure (3), phragmalin 3-isobutyrate 30-propionate, for compound C.

The spectroscopic properties of compounds B (2), $C_{39}H_{50}O_{15}$, and D (4), $C_{38}H_{48}O_{15}$, were very similar to those of A and C (see Tables 1 and 2) suggesting the same phragmalin nucleus. On hydrolysis both compounds afforded acetic acid in addition to isobutyric (B and D) and propionic (D) acids. The presence of the acid residues was confirmed by the mass spectral data and the ^{13}C n.m.r. spectra of (2) and (4). These results indicated that B and D were acetoxyphragmalin derivatives. The secondary nature and the position of attachment of this extra oxygen substituent in the phragmalin skeleton of (2) and (4) were readily determined from the ^1H and ^{13}C n.m.r. spectra. Both compounds had an additional *CH*OAc group [δ_C 69.1 (d); δ_H 4.60 (B) or 4.66 (D) (q, J 4 and 12 Hz)] relative to A and C and an acetate methyl resonance at abnormally high field (δ_H 1.66). These data require a 12α-acetate group, since in this position it comes under the shielding influence of the furan ring.[5,6] The ^{13}C spectra of (2) and (4) further confirmed this assignment. The introduction of a 12α-oxygen substituent caused a downfield shift [relative to (1) and (3)] of the signals due to C-12 (40 p.p.m.), C-11 (6.5 p.p.m.), and C-13 (4.5 p.p.m.) and an upfield shift [7] of those due to C-18 (5.5 p.p.m.) and C-17 (2 p.p.m.). Thus compound B is 12α-acetoxyphragmalin 3,30-di-isobutyrate (2) and compound D is 12α-acetoxyphragmalin 3-isobutyrate 30-propionate (4). Hydrolysis of both (2) and (4) yielded 12α-hydroxyphragmalin (11), which has not been described previously.

Column chromatography of the total light petroleum extract afforded a polar fraction from which a crystalline mixture of two compounds (12) and (13) was obtained. They were difficult to separate. Both compounds lacked the β-substituted furan ring characteristic of most tetranortriterpenoids. The spectroscopic properties of (12) and (13) and of their acetates (14) and (15) readily disclosed their similarity to (1) and (3), with an α-substituted γ-hydroxy(or acetoxy)-butenolide system replacing the furan ring. Tetranortriterpenoids with an oxidatively modified furan ring are well known.[8] It is possible, in this case, that compounds (12) and (13) are artefacts formed on prolonged exposure of the light petroleum extract to Glasgow sunshine.



(12) $R^1 = R^2 = Pr^iCO$, $R^3 = H$
(13) $R^1 = Pr^iCO$, $R^2 = EtCO$, $R^3 = H$
(14) $R^1 = R^2 = Pr^iCO$, $R^3 = Ac$
(15) $R^1 = Pr^iCO$, $R^2 = EtCO$, $R^3 = Ac$

EXPERIMENTAL

For general experimental details see refs. 1 and 8.

Extraction.—Powdered seeds (3 kg) of *Chukrasia tabularis* were extracted with light petroleum (Soxhlet). Concentration of the solution resulted in precipitation of a gum (25 g) which was filtered off and chromatographed over alumina (grade IV) using increasing proportions of chloroform in light petroleum as eluant. The fractions eluted with chloroform were combined to give a mixture (10 g) of four compounds, A—D, of similar polarity. They were subjected to careful multiple preparative t.l.c. 7 : 3 (CCl_4–EtOAc as solvent). Subsequent crystallisation afforded (in increasing order of polarity): (a) *compound A* (1) (*phragmalin di-isobutyrate*) (0.85 g), m.p. 224—228° (needles from ether–light petroleum); $\nu_{max.}$ (CCl_4) 3 578 and 1 748 cm^{-1}; *m/e* 682 ($M^+ - 18$) (Found: C, 63.6; H, 7.1. $C_{37}H_{48}O_{13}$ requires C, 63.4; H, 6.85%); (b) *compound B* (2) (*12α-acetoxyphragmalin di-isobutyrate*) (0.3 g), m.p. 226—229° (needles from ether–light petroleum); $\nu_{max.}$ (CCl_4) 3 578 and 1 748 cm^{-1}; *m/e* 740 ($M^+ - 18$) (Found: C, 62.0; H, 6.80. $C_{39}H_{50}O_{15}$ requires C, 61.75; H, 6.6%); (c) *compound C* (3) (*phragmalin 3-isobutyrate 30-propionate*) (0.6 g), m.p. 195—200° (needles from CCl_4–light petroleum); $\nu_{max.}$ (CCl_4) 3 578 and 1 748 cm^{-1}; *m/e* 668 ($M^+ - 18$) (Found: C, 53.0; H, 5.45. $C_{36}H_{46}O_{13},CCl_4$ requires C, 53.0; H, 5.5%); (d) *compound D* (4) (*12α-acetoxyphragmalin 3-isobutyrate 30-propionate*) (0.5 g), m.p. 214—216° (needles from ether–light petroleum); $\nu_{max.}$ (CCl_4) 3 578 and 1 748 cm^{-1}; *m/e* 726 ($M^+ - 18$) (Found: C, 61.25; H, 6.55. $C_{38}H_{48}O_{15}$ requires C, 61.3; H, 6.45%).

Preparative t.l.c. of the later fractions afforded 7-deacetoxy-7-hydroxygedunin (7) (50 mg), m.p. 249—255°, identified by direct comparison (m.p., n.m.r., mass spectra) with an authentic sample.[9]

A sample (32 g) of the total light petroleum extract was chromatographed over silica gel in light petroleum, with increasing amounts of chloroform in light petroleum as eluant. The early fractions containing fatty material were discarded. The later fractions were combined (10.24 g)

[4] A. B. Terent'ev, V. I. Dostovalova, and R. Kh. Friedlina, *Org. Magnetic Resonance*, 1977, **9**, 301.
[5] J. D. Connolly, D. A. Okorie, and D. A. H. Taylor, *J.C.S. Perkin I*, 1972, 1145.
[6] R. Hanni, C. Tamm, V. Gullo, and K. Nakanishi, *J.C.S. Chem. Comm.*, 1975, 563.
[7] H. Beierbeck and J. K. Saunders, *Canad. J. Chem.*, 1976, **54**, 2985.
[8] K. K. Purushothaman, S. Chandrasekharan, J. D. Connolly, and D. S. Rycroft, *J.C.S. Perkin I*, 1977, 1873, and references therein.
[9] A. Akisanya, C. W. L. Bevan, T. G. Halsall, J. W. Powell, and D. A. H. Taylor, *J. Chem. Soc.*, 1961, 3705.

and rechromatographed over silica gel in chloroform. The intermediate fractions contained a mixture of compounds (1)—(4) (4 g). The final fraction (0.5 g), eluted with MeOH, was chromatographed (preparative t.l.c.) and the main band crystallised from MeOH–ether–light petroleum to give a mixture, m.p. 242—248 °C, of compounds (12) and (13). Separation was difficult but careful preparative t.l.c. afforded pure *compound* (12), m.p. 243—250° (from ether–MeOH), *m/e* 714 ($M^+ - 18$), δ 7.28 (H-22), 6.36 (H-23), 5.94 (H-30), 5.46 (H-17), 4.65 (H-3), 3.75 (CO_2Me), 2.67 (OH), and 1.65 [O–CMe(–O)–O]. The corresponding *acetate* (14), prepared by treatment with Ac_2O–pyridine at room temp. for 1 min, was crystallised from MeOH–ether and had m.p. 218—220°, *m/e* 756 ($M^+ - 18$) (Found: C, 60.25; H, 6.6. $C_{39}H_{50}O_{16}$ requires C, 60.45; H, 6.45%). The second component of the mixture, compound (13), was not obtained entirely pure but had *m/e* 700 ($M^+ - 18$), δ 7.28 (H-22), 6.30 (H-23), 5.92 (H-30), 5.46 (H-17), 4.60 (H-3), 7.38 (CO_2Me), and 1.66 [O–CMe(–O)–O]. Acetylation yielded the *acetate* (15), m.p. 203—210° (from MeOH–ether), *m/e* 742 ($M^+ - 18$), δ 7.28 (H-22), 6.91 (H-23), 5.92 (H-30), 5.49 (H-17), 4.60 (H-3), 3.78 (CO_2Me), 2.68 (OH), 2.17 (OAc), and 1.66 [O–CMe(–O)–O]. Acetylation of the mixture of (12) and (13) followed by preparative t.l.c. led to a more efficient separation.

Alkaline Hydrolysis of Compound A (1).—Compound A (1) (100 mg) was dissolved in 5% KOH–MeOH (10 ml) and the solution refluxed for ½ h. Addition of water, acidification with 6M-HCl, and extraction with chloroform gave a gum which was dissolved in MeOH and treated with an excess of ethereal diazomethane. Preparative t.l.c. and crystallisation from MeOH–ether yielded phragmalin (5) (57 mg) as needles, m.p. 148—153°, with the same spectroscopic properties as an authentic specimen.[2] A similar result was obtained on hydrolysis of compound C (3).

Alkaline Hydrolysis of Compound D (4).—Compound D (4) (97 mg) was hydrolysed and methylated as above. Preparative t.l.c. and crystallisation from MeOH–ether afforded 12α-*hydroxyphragmalin* (11) (60 mg) as needles, m.p. 160—170° (Found: C, 58.35; H, 6.5. $C_{29}H_{36}O_{12},H_2O$ requires C, 58.9; H, 6.45%).

Hydrolysis of compound B (2) gave a similar result.

Acetylation of Phragmalin.—Phragmalin (100 mg) was refluxed in acetyl chloride for 3 h. Preparative t.l.c. afforded phragmalin monoacetate (8) (42 mg), m.p. 248—255° (from MeOH–ether), and phragmalin diacetate (9) (35 mg), m.p. 234—238° (from MeOH–ether). Longer reaction times led to the formation *inter alia* of phragmalin triacetate (10), m.p. 165—173° (from MeOH–ether–light petroleum). These compounds had the expected spectroscopic properties (see Tables 1 and 2).

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