Tetrahedron Letters, Vol. 33, No. 26, pp. 3761-3764, 1992
Printed in Great Britain

0040-4039/92 $5.00 + .00
Pergamon Press Ltd

Monocarpin, a New Cycloartane from *Monocarpia marginalis*

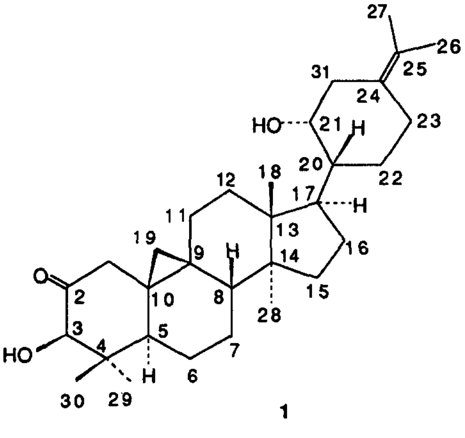
Kamaliah Mahmood[a], Mary Pais*[b], Catherine Fontaine[b], Hapipah M. Ali[a], A. Hamid. A. Hadi[a], Bruno David[b] and Eric Guittet[b]

[a] Department of Chemistry, University of Malaya, 59100 Kuala Lumpur, Malaysia.
[b] Institut de Chimie des Substances Naturelles, CNRS, 91198 Gif-sur-Yvette, France.

Abstract: *Monocarpin 1, a new cycloartane derivative, was isolated from the trunk bark of Monocarpia marginalis J. Sinclair and its structure elucidated primarily by 2D NMR.*

A number of cycloartane triterpenoids have been found in various plant species often in the form of glycosides[1]. We have isolated a triterpenoid belonging to this series, monocarpin 1, having an unknown combination of oxygen functions in ring A and a unique C-17 side chain, from the trunk bark of a Malaysian Annonaceae[2] *Monocarpia marginalis* J. Sinclair.

Monocarpin was extracted from the bark using petroleum ether and purified by repeated chromatography on silica gel. 1 crystallized from methanol affording small needles, mp 203°C, $[\alpha]_D$ - 4 ($CHCl_3$, c = 0.5). The molecular formula $C_{31}H_{48}O_3$ was deduced by HREIMS (M^+, m/z 468.3587, calcd 468.3603). In addition, two fragmentation peaks at m/z 450 (M-18) and m/z 329 (M - side chain, HREIMS 329.2465, calcd 329.2480) were observed in the mass spectrum. The IR spectrum exhibited absorptions at 3500 and 1720 cm^{-1} suggesting the presence of hydroxyl groups and a carbonyl function. In the ^{13}C NMR spectrum, this carbonyl resonated at δ 210.9 and two hydroxymethines were observed at δ 79.0 and 83.2. In the ^1H NMR spectrum, the CH groups geminal to the hydroxyls appeared at δ 3.86 as a broad singlet and at



1

δ 4.05 as a doublet (J = 4 Hz). Deuterium exchange resulted in the collapse of the signal at δ 4.05 into a sharp singlet accompanied by the disappearance of the OH doublet (J = 4 Hz) at δ 3.46.

Indications of the cycloartane skeleton were provided by the characteristic ^{1}H and ^{13}C resonances of the cyclopropyl moiety : two doublets at high field (δ_H 0.46 and 0.62, J = 4.5 Hz) correlated (HETCOR) to a carbon at 28.9, assigned to CH_2-19, and two signals at δ_C 19.7 and 28.2 assigned to the quarternary carbons C-9 and C-10, and further by the presence in the ^{1}H NMR spectrum of four methyl singlets at δ_H 0.68, 1.11, 0.94, 0.97 (δ_C 15.2, 25.5, 18.5, 19.6). Two additional methyl singlets appeared at lower field (δ 1.66 and 1.77 ppm) suggesting that they were α to a double bond situated in the side chain. No olefinic proton signals were observed, but the ^{13}C NMR spectrum showed two sp^2 quaternary carbons at δ 125.9 and 126.8. These data were consistent with a gem dimethyl group located on a tetrasubstituted double bond.

The definitive structure of monocarpin was deduced from careful analysis of the 2D NMR spectra including DQF-COSY[3], HETCOR, HOHAHA[4] and HMBC[5]. The protons H-1α and H-1β gave an isolated spin system (two doublets at δ 2.62 and 2.06, J gem = 14 Hz) and HMBC correlations together with chemical shift considerations allowed the localization of the keto group in ring A at position 2 and the hydroxyl group (δ_H 3.86, δ_C 83.2) at the normal 3 position. Three other spin systems corresponding to (H-5, H-6, H-7, H-8)[6], (H-11, H-12) and (H-15, H-16, H-17, H-20, H-21, H-31, H-22, H-23) were identified from the DQF-COSY spectrum aided by the HETCOR experiment. In addition, CH_3-18 and CH_3-28 showed homonuclear four bond couplings to H-12α and one H-15 respectively. HMBC and NOESY[7] correlations (Table 1) further supported the structure and stereochemistry of the polycyclic part of the molecule with OH-3 in the β position.

The structure of the side chain ring was confirmed by HOHAHA and HMBC correlations. The HOHAHA spectrum showed that H-17 has relay correlations to H-20, H-22 and H-23 and the HMBC spectrum demonstrated an unambiguous correlation between H-31 and the olefinic carbons C-24 and C-25. The downfield shifts observed for H-23e (2.68 ppm, br d, J_{gem} = 10 Hz) and H-31e (2.06 ppm, br d, J_{gem} = 13 Hz) supported their position α to the C-24 - C-25 double bond.

The structure of monocarpin could be alternatively automatically deduced from the COSY-DQF, HETCOR and HMBC informations using the SYDASIA expert system developped in our laboratory[8].

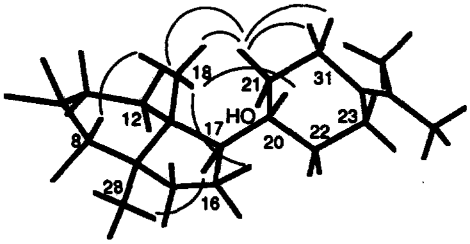


Fig. 1. NOESY correlations for Monocarpin **1** (ring C, D and side chain)

A large vicinal coupling between H-20 and H-22a indicated their trans diaxial orientation. A small coupling was measured between H-20 and H-21 (broad singlet at δ 4.05) suggesting that H-21 is equatorial. The relative configuration at C-20 and C-21 is thus established. The 17-β stereochemistry of the side chain

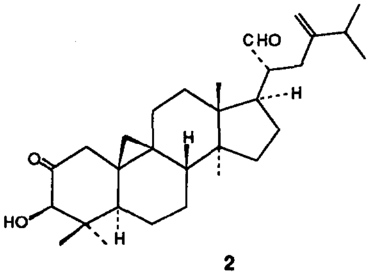
Table 1. ^{1}H- and ^{13}C-NMR Data for Monocarpin 1[a]

Position	δ C	δ H (J, Hz)	(^{1}H)-^{13}C	NOESY
1α	46.8	2.62 d (14)	2,10	1β,3,5
β		2.06 d	2,3,4,10	11β,19α
2	210.9			
3	83.2	3.86 d (4)	4,29,30	5,29
4	45.9			
5	46.5	1.90 m	4,9,10	7α
6α	21.1	1.70 m		6β, 7β
β		0.86 ddd (14)	9	8,19β
7α	25.5	1.40 m		7β
β		1.20 m		
8	47.6	1.58 m	7,9,14,19	15,18,19β
9	19.7			
10	28.2			
11α	26.8	1.95 m		11β, 12α
β		1.08 m		
12α	31.7	1.70 m		
β		1.90 m		21
13	45.2			
14	48.8			
15a	35.5	1.25 m	16	
b		1.30 m		
16α	26.8	1.32 m	13,15	16β
β		1.85 m		18
17	46.8	1.90 m		20,28
18	19.6	0.97 s	12,13,14	20,21
19α	28.9	0.46 d (4.5) 4,9,10	4,9,10	19β
β		0.62 d (4.5) 4,9,10	4,9,10	
20	44.8	1.48 m		
21	69.0	4.05 br s		31a, 31e
22a	27.9	1.62 m		27
e		1.20 m		
23a	30.1	1.62 m		23b
e		2.68 br d (10)		
24	126.8			
25	125.9			
26	20.2	1.70 s	24, 25	
27	20.2	1.66 s	24, 25	
28	18.5	0.94 s	15, 13, 14	
29	25.5	1.11 s	3, 4, 29	30
30	15.2	0.68 s	3, 4, 30	
31a	37.8	1.93 m	23e, 24, 25	31b
e		2.06 br d (13)		
OH		3.46 d (4)		

[a] $CDCl_3$, 400MHz; assignments based on DQF-COSY, HETCOR and HMBC.

was deduced from the NOESY spectrum (Table 1 and Fig.1). The R-configuration was tentatively assigned to C-20 from NOE correlations between H-18/H-20, H-18/H-21 and H-12β/21 assuming the preferred conformation shown in Fig.1. Molecular models show that such a conformation insures minimum interaction between the side chain and rings C and D.

The side chain of monocarpin has an extra carbon (C-31) located on C-24 in comparison with a normal terpenoid, but the same feature is often found in the cycloartane serie[1]. The precursor of 1 in the plant could possibly be the aldehyde **2** giving rise to **1** through an internal Prins cyclisation. The same type of biogenetic origin has been previously proposed for other natural compounds.[9,10]



2

REFERENCES AND NOTES

1. For reviews see : Isaev, M.I.; Gorovits, M.B.; Abubakirov, N.K., ; *Chem. Nat. Compd.*, **1985**, *21*, 399; Conolly, J.D.; Hill, R.A., *Nat. Prod. Rep.* **1989**, *6*, 475; Pfander, H.; Stoll, H., *ibid..*, **1991**, *8*, 69.
2. This work was carried out as part of a collaborative program on Malaysian plants, between CNRS (France) and the University of Malaya (Malaysia).[9] *Monocarpia marginalis* was collected near Mersing, Johor, Malaysia. Voucher specimens (DB 87) were deposited at the Museum d'Histoire Naturelle in Paris and at the Herbarium of Department of Chemistry, University of Malaya, Kuala Lumpur, Malaysia.
3. Shaka, A.J.; Freeman, R., *J. Magn. Res.* **1985**, *65*, 169.
4. Bax, A; Davis, D.G., *J. Magn. Res.* **1985**, *65*, 355.
5. Bax, A.; Summers, M.F., *J. Amer. Chem. Soc.* **1986**, *108*, 2093.
6. This sequence was also supported by HOHAHA showing relay correlations from H-5 to H-6α, H-7α, H7-β and H-8.
7. Bodenhausen, G.; Kogler, H.; Ernst, R.R., *J. Magn. Reson.* **1984**, *58*, 370.
8. Ekondzi, A.; Guittet, E., to be published.
9. Kretschmar, H.C; Barnels, Z.J.; Erman, W. F., *Tetrahedron Lett.***1970**, 37, 4145.
10. Païs, M.; Djakouré, L.A.; Jarreau, F.X.; Goutarel, R, *Tetrahedron* **1977**, *33*, 1449.
11. Teo, L.E.; Pachiaper, G.; Chan, K.C.; Hadi, H.A.; Weber, J.F.; Deverre, J.R.; David, B.; Sévenet, T., *J. Ethnopharmacol.* **1990**, *28*, 63.

(Received in France 6 March 1992)