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ISOLATION AND STRUCTURE DETERMINATION OF TWO NOVEL LATHYRANES FROM *JATROPHA CURCUS*

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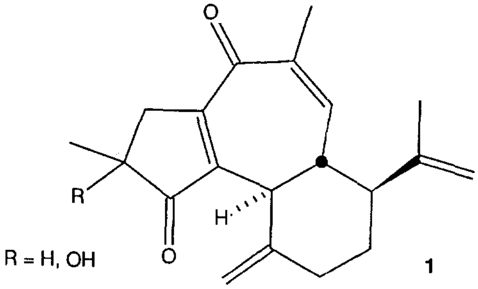
Summary: Two new lathyranes have been isolated from *Jatropha curcus* and characterized by NMR spectroscopy and x-ray diffraction.

Two recent reports have dealt with diterpenes from the plant *Jatropha curcus*. Hecker *et al.*[1] discussed several phorbol derivatives and we have described the curcusones (**1**).[2] In this paper we report two new lathyrane diterpenes- curculathyranes A (**2**) and B (**3**).



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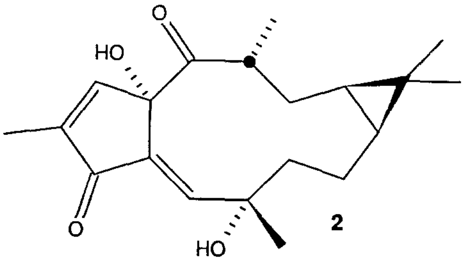

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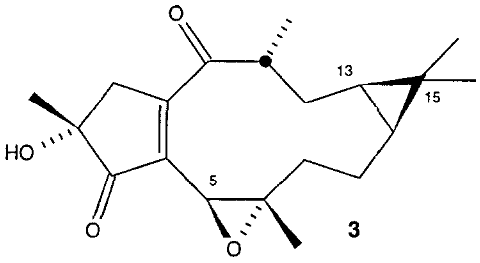

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Following our previously described[2] isolation scheme, compounds **2** and **3** were obtained. The initial structural characterization of **2** and **3** was done spectroscopically. Both compounds had the elemental composition $C_{20}H_{28}O_4$ (m/z calcd. 332.1987, detd. 332.1979 (**2**), 332.1990 (**3**)) by high-resolution mass spectrometry. ^{13}C NMR spectroscopy for **3** showed five methyl (δ 28.8q, 26.2q, 18.5q, 17.7q, 15.0q), four methylene (43.1t, 40.3t, 26.5t, 19.5t), four methine (55.7d, 43.6d, 28.2d, 23.4d), two carbonyl (207.6s, 164.9s), two alkene (134.1s, 108.4s) and three quaternary (75.4s, 60.8s, 18.1s) carbons. ^1H NMR spectroscopy provided further structural information by giving evidence for one alcohol group (δ 1.55, br s, D_2O exchangeable, 1H) and a cyclopropane ring (δ 0.54, 1H; δ 0.10, 1H). The unassigned oxygen was believed to belong to an epoxide ring. With these assignments, five sites of unsaturation had been accounted for; therefore, **3** was determined to have a fourteen carbon bicyclic structure.

Since the spectroscopic data for **3** did not closely match that for previously described compounds, **3** was subjected to x-ray diffraction analysis after recrystallization from methylene chloride. Preliminary x-ray photographs displayed monoclinic symmetry with accurate lattice constants of **a**= 11.2420(40), **b**= 6.6979(20), **c**= 12.1033(80)Å, and **β**= 80.710(40)° determined from a least squares fit of fifteen diffractometer measured 2Θ-values. Systematic extinctions and an approximate density indicated the space group $P2_1$ with two molecules in the unit cell. All unique diffraction maxima with $2\Theta < 114^\circ$ were collected on a computer-controlled four-circle diffractometer using variable speed 1° ω-scans and graphite monochromated Cu K$\bar{\alpha}$ radiation (1.54178Å). A total of 1394 reflections was collected and after correction for Lorentz, polarization, and background effects, 761 (55%) were judged observed ($|F_o| > 3\sigma(F_o)$). A phasing model was easily found using direct methods. Block-diagonal least-squares refinements with anisotropic nonhydrogen and isotropic hydrogen atoms have converged to a conventional crystallographic residual of 0.067 for the observed data.[3] Figure **1a** is a computer generated perspective drawing of the final x-ray model without hydrogens; the conventional chemical drawing is given as **3**. The structure shown in **3** is consistent with all the spectroscopic data.[4]

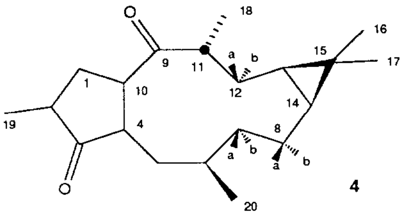
Comparison of the ^1H and ^{13}C NMR spectra for **2** and **3** showed that the two compounds must have the same general structure (see Table 1). Differences appeared to involve the formal epoxide ring opening of **3** to give a second carbon-carbon double bond and a second alcohol moiety. At least two tentative structures were consistent with the available spectral data and a definite assignment could not be made. Therefore, **2** was also subjected to x-ray diffraction analysis after recrystallization from methylene chloride. Preliminary x-ray photographs displayed monoclinic symmetry with accurate lattice constants of **a**= 23.2225(71), **b**= 6.5102(20), **c**= 12.4751(40)Å, and **β**= 98.488(25)°. Systematic extinctions and an approximate density indicated the space group C2

Table 1

^1H AND ^{13}C NMR ASSIGNMENTS[1]

Assignment	General	δ, ppm (J, Hz)[2] Curculathyrane A	Curculathyrane B
H1	1H	6.83s	a 2.56dd(3.8,18.7) b 3.11dd(4.4,18.7)
H5	1H	6.61s	3.73dd(1.9,3.3)
H7	1H,ddd	1.64(n.d.)[3] 1.68(4.2,14.2,15.2)	a 2.34(4.0,8.4,12.0) b 1.81(4.9,8.4,14.9)
H8	1H,dddd	1.85(n.d.) 1.93(n.d.)	0.99(n.d.) 1.28(14.1,n.d.)
H11	1H,tdd	2.87(n.d.)	3.14(n.d.)
H12	1H,ddd	1.36(n.d.) 1.47(n.d.)	a 2.09(4.9,9.3,10.6) b 1.12(2.7,4.0,9.5)
H13	1H,ddd	0.62(7.8,7.8,n.d.)	0.54(4.9,8.6,8.6)
H14	1H,ddd	0.41(9.4,9.4,n.d.)	0.10(8.6,8.6,n.d.)
H16,H17	3H,s	0.97, 0.64	0.98, 0.86
H18	3H,d	1.06(6.8)	1.08(6.7)
H19	3H	1.96d(1.3)	1.34s
H20	3H,s	1.31	1.24
HO-C2	1H,br s,exch	----------	1.55
HO-C6	1H,br s,exch	3.26	-----------
HO-C10	1H,br s,exch	5.26	-----------
C3	s	146.7	164.9
C5	d	----------	55.7
C7	t	41.6	-----------
C8,12	t	29.7, 19.6	26.5, 19.5
C9	s	195.8	207.6
C11	d	38.2	43.6
C13,14	d	27.0, 19.5	28.2, 23.4
C15	s	18.0	18.1
C16,17,18	q	17.0, 15.0, 10.9	18.5, 17.7, 15.0
C19,20	q	29.1, 28.4	28.8, 26.2
$R_1R_2\overset{*}{C}=$	s	134.1, 108.4	134.1, 108.4
$R_1H\overset{*}{C}=$	d	151.6, 144.0	-----------
$R_1R_2R_3O\overset{*}{C}$	s	84.3, 76.1	75.4, 60.8
$-\overset{*}{C}H_2-$	t	----------	43.1, 40.3

1 See 4 for numbering and hydrogen designations
2 ^1H NMR: 400 MHz; ^{13}C NMR: 100 MHz, multiplicity determined by DEPT
3 n.d.= not determinable



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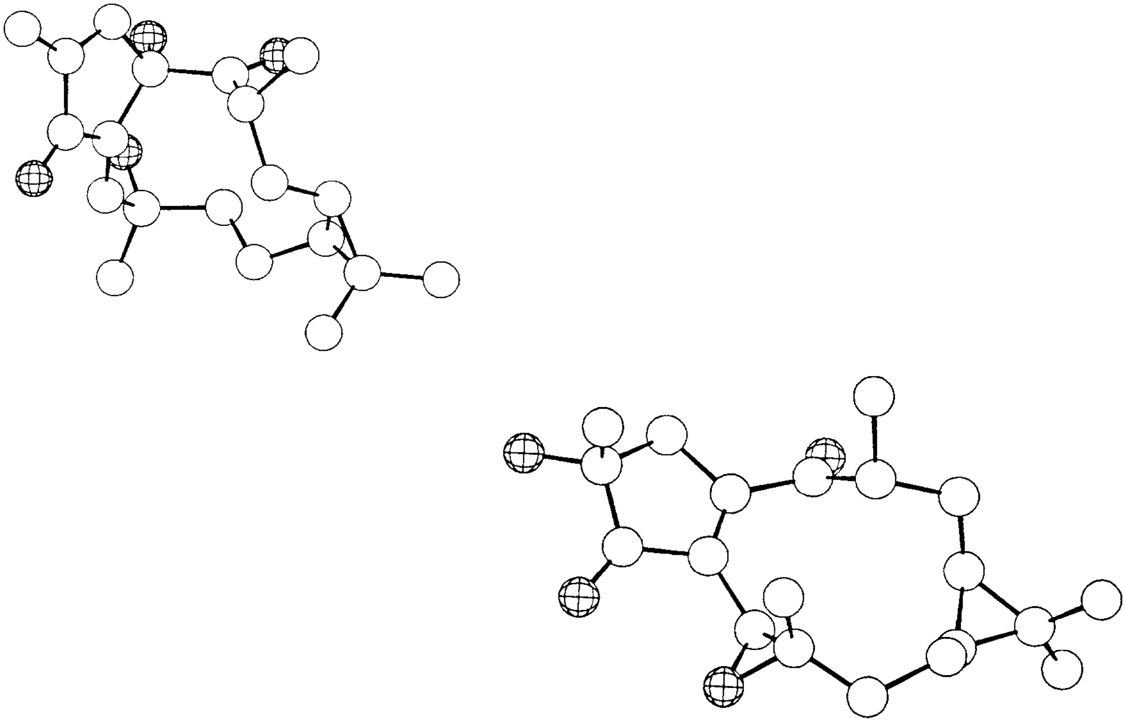

Figure 1. Computer-generated perspective drawings of curculathyranes A (**2**, top) and B (**3**, bottom). Hydrogens are omitted for clarity and no absolute configuration is implied.

with four molecules in a unit cell. A total of 1428 reflections was collected and after correction for Lorentz, polarization, and background effects, 994 (70%) were judged observed ($|F_o|>3\sigma(F_o)$). Solution and refinement were similar to **3** and a conventional crystallographic residual of 0.060 was obtained for the observed data.[3] The computer-generated perspective drawing without the hydrogens is given in Figure **1b**. The structure shown in the conventional chemical drawing **2** is consistent with all spectroscopic data.[5]

The substitution pattern of **2** and **3** suggests that the curculathyranes may be the biosynthetic precursors of the curcusones (**1**). For 3, a scheme to accomplish this begins with the protonation of the epoxide oxygen followed by breaking the C5-O, rather than the C6-O, bond to form a secondary carbocation. A bond is then formed between C13 and C5 with a simultaneous cyclopropane ring opening to give a tertiary carbocation at C15. Finally loss of a methyl proton forms a terminal double bond.[6] This gives the curcusane (crotophorbolane) carbon skeleton; further dehydration across the C6-C20 bond and dehydrogenation across the C11-C12 bond gives the curcusones themselves.

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REFERENCES

1. W. Adolf, H.J. Opferkuch, and E. Hecker. *Phytochemistry*. **23**, 129-132(1984).

2. W. Naengchomnong, Y. Thebtaranonth, P. Wiriyachitra, K.T. Okamoto, and J. Clardy. *Tetrahedron Lett.* **27**, 2439-42(1986). The absolute stereochemistry of the curcusones (**1**) is not known. The structure shown here is the enantiomer of that given in the above reference.

3. All crystallographic calculations were done on a PRIME 9955 computer operated by the Cornell Chemistry Research Computing Facility. For a listing of the principal programs employed see: E. Fahy, R.J. Andersen, G.D. Van Duyne, and J. Clardy. *J. Org. Chem.* **51**, 57-61(1986). Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge, ENGLAND CB2 1EW and are available from them.

4. Chemical and spectral data for **3** not included in text: m.p.= 178-179° ($CHCl_3$); $[\alpha]_D^{22}$= 0.0° (CH_2Cl_2, c= 1.22 x 10^{-1}); IR (Nujol) 3480, 2925, 2850, 1720, 1690 cm^{-1}; EIMS m/z 332 (M^+, 1.1%), 275 (M^+-57, 25.7%), 263 (M^+-69, 10.6%); UV λ_{max} (EtOH) 272 (log ϵ 3.5625) nm.

5. Chemical and spectral data for **2** not included in text: m.p. 168-170° ($CHCl_3$); $[\alpha]_D^{22}$= -385° (CH_2Cl_2, c= 1.05 x 10^{-1}); IR (Nujol) 3300, 2920, 2850, 1720, 1690, 1460, 1370 cm^{-1}; EIMS m/z 332 (M^+, 5.8%), 314 (M^+-18, 57.4%), 271 (M^+-61, 39.2%), 257 (M^+-75, 36.3%); UV λ_{max} (EtOH) 272 (log ϵ 3.6285) nm.

6. For background information on intramolecular diterpene cyclization see: W. Adolf and E. Hecker. *Isr. J. Chem.* **16**, 75-83(1977), and references therein.

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