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# ISOLATION AND STRUCTURE DETERMINATION OF FOUR NOVEL DITERPENES FROM *JATROPHA CURCUS*

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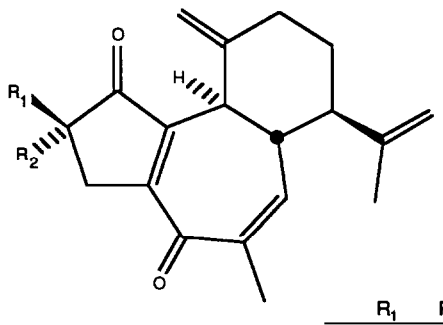
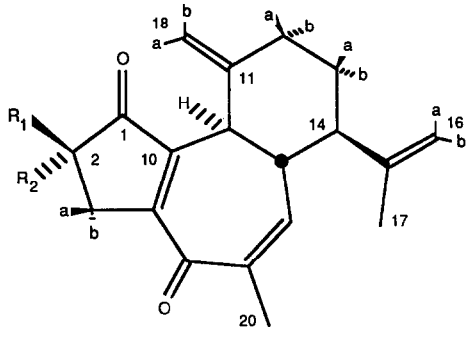
Summary: Four novel diterpenes have been isolated from *Jatropha curcus* and the structures have been determined by NMR spectroscopy and x-ray diffraction. All four compounds are structurally related and belong to the crotophorbolane class of compounds.

The roots from the plants of the genus *Jatropha* have yielded numerous novel diterpenes,[1] including jatrophone[2] and the jatropholones.[3] The previously unexamined *J. curcus* has also proven to be a rich source of novel compounds, and we wish to report four new diterpenes that have been trivially named curcusones A-D.




| | $R_1$ | $R_2$ |
|---|---|---|
| **1** | Me | H |
| **2** | H | Me |
| **3** | Me | OH |
| **4** | OH | Me |



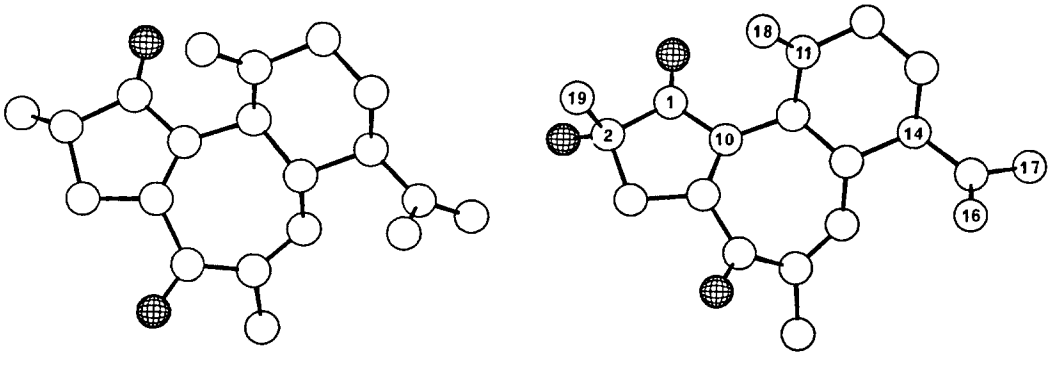

**5**

The dried ground roots of *J. curcus* (1.6 kg) were soaked in hexane (5L) for seven days; this was repeated three times. The mixtures were combined, filtered, and evaporated to near dryness. Jatropholone (0.431g) precipitated out and was removed by filtration. The filtrate was chromatographed on a silica gel column with 5:1 hexane:ethyl acetate as the eluant. Three

fractions, *i-iii*, were obtained. After solvent evaporation, fraction *i* was separated further into two compounds by preparative liquid chromatography ($SiO_2$,5:1 hexane:ethyl acetate) to give curcusone A (**1**,0.211g) and curcusone B (**2**,0.203g) after recrystallization from hexane. Fractions *ii* and *iii*, treated similarly, each yielded one compound, curcusones C (**3**,0.017g) and D (**4**,0.065g) respectively. Ultraviolet (UV), mass spectroscopy (MS), infrared (IR), and nuclear magnetic resonance spectroscopy (NMR) data indicated all four compounds were structurally related and that curcusones A and B and curcusones C and D were epimeric pairs. Further evidence for the epimeric nature of A and B was their ready interconversion in the presence of water.

Structural characterization of the new compounds began with curcusone B. Elemental composition for **2** was determined by high-resolution MS to be $C_{20}H_{24}O_2$ (m/z calcd. 296.1776, detd. 296.1769). $^{13}C$ NMR (100MHz, $CDCl_3$) showed the presence of two carbonyls at $\delta$ 211.9s and 198.5s. Furthermore, $^{13}C$ NMR provided evidence for two exo methylenes (113.2t, 108.1t), six other $sp^2$ carbons (158.4s, 148.8s, 148.6s, 146.8s, 140.8s, 136.5d), as well as three methyl (19.4q, 18.7q, 14.6q), three methylenes (36.5t, 36.2t, 34.9t), and four methine (51.7d, 45.8d, 43.6d, 39.6d) groups. $^1H$ NMR comfirmed these general assignments. Six sites of unsaturation had been accounted for and therefore, curcusone B must be tricyclic.

Since the spectroscopic data for **2** did not match that for well-known classes of compounds, curcusone B was subjected to x-ray diffraction analysis after recrystallization from chloroform. Preliminary x-ray photographs displayed orthorhombic symmetry with accurate lattice constants of **a**= 10.3156(17), **b**= 10.5026(14), and **c**= 16.0326(23) Å determined from a least-squares fit of fifteen diffractometer measured $2\theta$-values. Systematic extinctions and an approximate density indicated the space group $P2_12_12_1$ with four molecules in a unit cell. All unique diffractions with $2\theta<114^\circ$ were collected on a computer-controlled four-circle diffractometer using variable speed $1^\circ$-scans and graphite monochromated Cu K$\bar{\alpha}$ radiation (1.54178Å). A total of 1367 reflections were collected and after correction for Lorentz, polarization, and background effects, 830 (61%) 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 0.068 for the observed data.[4] Figure 1a is a




**1a** **1b**

Figure 1: Computer generated perspective drawings of (a) curcusone B and (b) curcusone C. Hydrogens are omitted for clarity, and no absolute configuration is implied.

computer generated perspective drawing of the final x-ray model without hydrogens; a conventional chemical drawing is given in **2**. The structure shown in **2** is consistent with $^1$H NMR (see Table 1). From spectroscopic and chemical evidence, **1**[5] was deduced to be the C-2 epimer of **2**.[6] Based on MS and NMR, **3**[7] and **4**[8] appeared to be the C-2 hydroxylated analogs of **1** and **2**. The relative stereochemistry at the chiral centers was not readily assignable for either hydroxylated compound; therefore, curcusone C (**3**) was also subjected to x-ray diffraction analysis using methods similar to those for **2**.[4,9] The computer-generated drawing is given in Figure 1b.

The four novel diterpenes from *Jatropha curcus* belong to the class of crotophorbolanes, of which crotophorbolone[10] itself is the only previously reported natural product. Work on the chemistry and biology of the plant is continuing.

**ACKNOWLEDGEMENTS.** The Cornell workers wish to thank NIH CA24487 for financial assistance.

## REFERENCES

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2. S.M. Kupchan, C.W. Sigel, M.J. Matz, J.A.S. Renauld, R.C. Haltiwanger, and R.F. Bryan. *J. Am. Chem. Soc.* **92**, 4476-77(1970).

3. K.K. Purushothaman and S. Chandrasekharan. *Tetrahedron Lett.* **11**, 979-80(1979).

4. All crystallographic calculations were done on a PRIME 9950 computer operated by the Cornell Chemistry Research Computing Facility. For a listing of principal programs employed see: H-N. Chou, Y. Shimizu, G. Van Duyne, and J. Clardy. *Tetrahedron Lett.* **26**, 2865-68(1985). Cyrstallographic data have been deposited with the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge, ENGLAND CB2 1EW and are available from them.

5. Chemical and spectral data for **1** not included in text: m.p.= 124-25° ($CHCl_3$); $[\alpha]_D^{22}$= -510° ($CH_2Cl_2$); IR (Nujol) 1710, 1650 $cm^{-1}$; HRMS m/z calcd. 296.1776, detd. 296.1769; EIMS m/z 296 ($M^+$, 15%), 281 ($M^+$-15, 11%), 268 ($M^+$-28, 33%), 253 ($M^+$-43, 21%), 108 ($M^+$-188, 100%); UV $\lambda_{max}$ (EtOH) 206 (log $\epsilon$ 3.9862), 257 (log $\epsilon$ 4.0097) nm.

6. Chemical and spectral data for **2** not included in text: m.p.= 122-3° ($CHCl_3$); $[\alpha]_D^{22}$= -610° ($CH_2Cl_2$); IR (Nujol) 1710, 1650, 1635 $cm^{-1}$; EIMS m/z 296 ($M^+$, 26%), 281 ($M^+$-15, 16%), 268 ($M^+$-28, 41%), 253 (M+-43, 27%), 108 ($M^+$-188, 100%); UV $\lambda_{max}$ (EtOH) 206 (log $\epsilon$ 3.9236), 255 (log $\epsilon$ 3.9362) nm.

7. Chemical and spectral data for **3** not included in text: m.p.= 204-5° ($CHCl_3$); $[\alpha]_D^{24}$= -432° ($CH_2Cl_2$); IR (Nujol) 3420, 1720, 1650 $cm^{-1}$; HRMS m/z calcd. 312.1725, detd. 312.1711; EIMS m/z 312 ($M^+$, 2.6%), 284 ($M^+$-28, 1.9%), 269 ($M^+$-43, 2.1%), 255 ($M^+$-57, 2.0%), 243 ($M^+$-69, 9.5%), 43 ($M^+$-269, 100%); UV $\lambda_{max}$ (EtOH) 208 (log $\epsilon$ 4.0149), 258 (log $\epsilon$ 3.9606) nm.

8. Chemical and spectral data for **4** not included in text: m.p.= 158-60° ($CHCl_3$); $[\alpha]_D^{22}$= -518° ($CH_2Cl_2$); IR (Nujol) 3470, 1720, 1650, 1630 $cm^{-1}$; HRMS m/z calcd. 312.1725, detd. 312.1712; EIMS m/z 312 ($M^+$, 1.1%), 284 ($M^+$-28, 1.2%), 269 ($M^+$-43, 1.8%), 255 ($M^+$-57, 2.3%), 243 ($M^+$-69, 8.8%), 108 ($M^+$-204, 100%); UV $\lambda_{max}$ (EtOH) 204 (log $\epsilon$ 4.0505), 260 (log $\epsilon$ 3.9413) nm.

9. X-ray diffraction information for **3**: monoclinic $P2_1$ space group; **a**= 7.9560(17)Å, **b**= 12.5838 (30)Å, **c**= 8.7833(14)Å, $\beta$= 99.867(15)°; 1345 data points collected, 1207 observed (90%); final crystallographic residual= 0.053.

10. K.L. Stuart and M. Barrett. *Tetrahedron Lett.* **28**, 2399-400(1969). The isolation procedure is not given, and crotophorbolone may be an artifact.

## $^1H$ AND $^{13}C$ NMR ASSIGNMENTS FOR CURCUSONES A-D[1]

| Assignment | General | 1 | 2 | 3 | 4 |
|---|---|---|---|---|---|
| | | $\delta$, ppm (J, Hz)[2] | | | |
| H2 | 1H,ddd | 2.42(n.d.)[3] | 2.47(7.4,7.4,3.3) | ----- | ----- |
| H3a | 1H,ddd | 2.79(18.5,6.8,3.6) | 2.13(18.7,3.4,3.4) | ----- | ----- |
| | 1H,dd | ----- | ----- | 2.65(18.6,4.0) | 3.08(18.0,2.8) |
| H3b | 1H,ddd | 2.58(18.5,2.3,2.3) | 3.29(18.7,7.4,2.3) | ----- | ----- |
| | 1H,dd | ----- | ----- | 3.10(18.6,2.5) | 2.66(18.0,2.9) |
| H7 | 1H,m | 5.83(5.0,n.d.) | 5.84(5.2,n.d.) | 5.86(5.0,n.d.) | 5.94(n.d.) |
| H8 | 1H,m | 2.57(n.d.) | 2.56(n.d.) | 2.60(n.d.) | 2.63(n.d.) |
| H9 | 1H,m | 3.11(12.2,n.d.) | 3.12(12.1,n.d.) | 3.14(11.0,n.d.) | 3.14(11.8,4.0,n.d. |
| H12a | 1H,ddd | 2.41(n.d.) | 2.39(12.7,4.4,4.4) | 2.41(12.0,4.4,2.2) | 2.43(12.8,5.1,2.9) |
| H12b | 1H,ddd | 2.25(12.7,12.7,4.3) | 2.23(12.7,12.7,4.4) | 2.23(12.0,12.0,3.9) | 2.28(12.8,12.8,5.0 |
| H13a | 1H,dddd | 1.44(12.5, 12.5,12.5,3.8) | 1.44(12.5, 12.5,12.5,4.4) | 1.45(n.d.) | 1.49(12.8, 12.8,12.8,5.0 |
| H13b | 1H,m | 1.86(n.d.) | 1.85(n.d.) | 1.87(n.d.) | 1.89(5.3,3.0,n.d.) |
| H14 | 1H,ddd | 2.32(12.5,12.5,3.8) | 2.32(12.5,12.5,3.8) | 2.32(12.4,12.4,3.8) | 2.34(11.7,11.7,3.4 |
| H16a | 1H,s | 4.73 | 4.72 | 4.75 | 4.78 |
| H16b | 1H,s | 4.17 | 4.18 | 4.18 | 4.42 |
| H17 | 3H,s | 1.56 | 1.56 | 1.56 | 1.59 |
| H18a | 1H,d | 4.81(2.3) | 4.80(2.3) | 4.82(2.3) | 4.85(1.3) |
| H18b | 1H,s | 4.79 | 4.79 | 4.80 | 4.83 |
| H19 | 3H,d | 1.22(7.8) | 1.17(7.4) | ----- | ----- |
| | 3H,s | ----- | ----- | 1.41 | 1.39 |
| H20 | 3H,dd | 1.81(2.3,2.3) | 1.81(2.3,2.3) | 1.82(2.3,2.3) | 1.85(2.3,2.3) |
| H0 | 1H | ----- | ----- | 2.51($D_2O$ exch.) | 2.13($D_2O$ exch.) |
| C1 | s | 212.5 | 211.9 | 211.9 | 208.9 |
| C2 | d | 39.0 | 39.6 | ----- | ----- |
| | s | ----- | ----- | 74.5 | 72.9 |
| C3 | t | 36.1 | 36.2 | 43.4 | 42.9 |
| C5 | s | 198.9 | 198.5 | 198.0 | 197.1 |
| C7 | d | 136.3 | 136.5 | 136.6 | 137.2 |
| C14 | d | 51.7 | 51.7 | 51.9 | 51.4 |
| C19 | q | 17.6 | 14.6 | 26.2 | 24.0 |
| $R_1R_2C=$ | s | 160.4 | 158.4 | 157.8 | 158.0 |
| | | 148.7 | 148.8 | 146.4 | 147.9 |
| | | 147.5 | 148.6 | 146.3 | 146.6 |
| | | 146.8 | 146.8 | 145.1 | 145.6 |
| | | 141.0 | 140.8 | 140.9 | 140.6 |
| $H_2C=$ | t | 113.2 | 113.2 | 113.3 | 113.3 |
| | | 108.1 | 108.1 | 108.1 | 108.9 |
| $H_2CR_1R_2$ | t | 36.5 | 36.5 | 36.6 | 36.3 |
| | | 34.5 | 34.4 | 34.5 | 34.2 |
| $H_3C-$ | q | 19.4 | 19.4 | 19.6 | 19.7 |
| | | 18.6 | 18.7 | 18.8 | 18.7 |

1 See 5 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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