

R. Malathi,<sup>a</sup> S. S. Rajan,<sup>a\*</sup>  
M. Sivarama Krishnan,<sup>b</sup> Geetha  
Gopalakrishnan<sup>b</sup> and G. Suresh<sup>b</sup><sup>a</sup>Department of Crystallography and Biophysics,  
University of Madras., Guindy Campus,  
Chennai 600 025, India, and <sup>b</sup>SPIC Science  
Foundation, Guindy, Chennai 600 032, India

Correspondence e-mail: ssrajansai@yahoo.com

## Key indicators

Single-crystal X-ray study  
 $T = 293$  K  
Mean  $\sigma(C-C) = 0.005$  Å  
 $R$  factor = 0.043  
 $wR$  factor = 0.127  
Data-to-parameter ratio = 8.2For details of how these key indicators were  
automatically derived from the article, see  
<http://journals.iucr.org/e>.

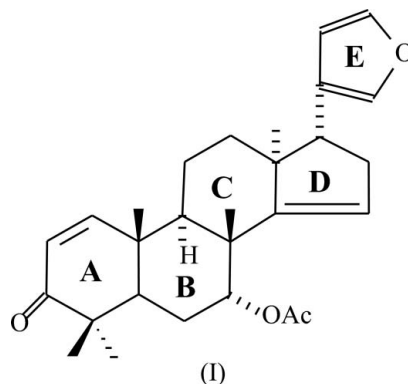
## Azadirone

The title compound [systematic name: (5 $\alpha$ ,7 $\alpha$ ,13 $\alpha$ ,17 $\alpha$ )-7-(acetyloxy)-21,23-epoxy-4,4,8-trimethyl-24-norchola-1,14,20,22-tetraen-3-one], C<sub>28</sub>H<sub>36</sub>O<sub>4</sub>, was isolated from uncrushed green leaves of *Azadirachta indica* A. Juss (neem) and has been reported to possess antifeedant activity against *Spodoptera litura* similar to nimonol extracted from neem leaves. Conformational differences from nimonol are seen in the orientation of the functional groups such as the acetoxy and furan rings. Weak intermolecular C—H···O hydrogen bonds help stabilize the crystal structure.

Received 11 October 2006  
Accepted 13 November 2006

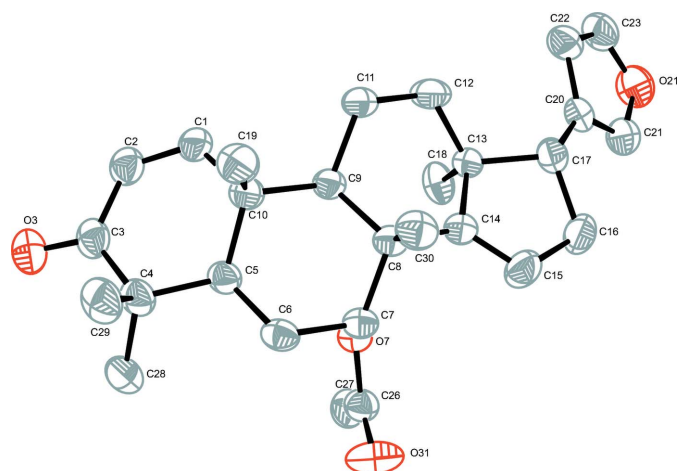
## Comment

The Neem leaf extracts have been shown to have insect antifeedant and insect growth regulatory activity (Schmutterer, 1995). The title compound, (I), has been isolated from uncrushed green neem leaves and differs from nimonol (Kabaleeswaran *et al.*, 2000) by the absence of a hydroxy group at position C6. This has resulted in differences in the conformations of rings and crystal packing but not in the levels of antifeedant activity (Suresh *et al.*, 2002).

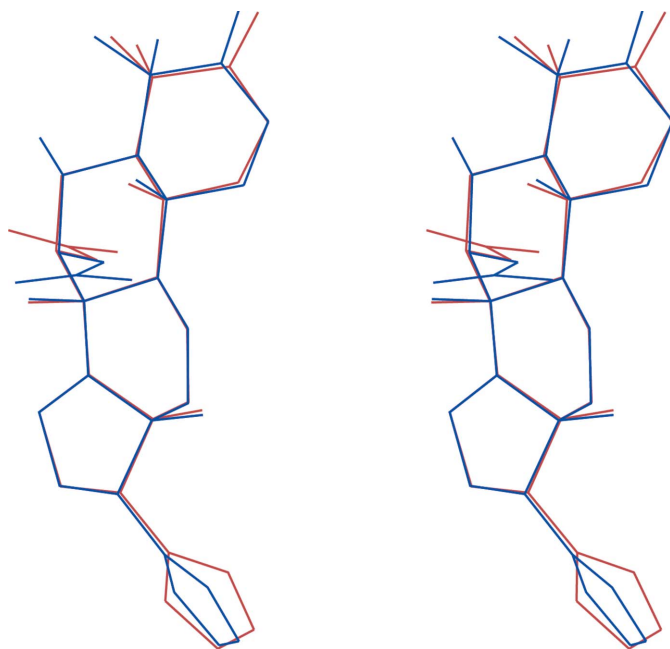


The molecular structure is shown in Fig. 1 and illustrates that the furan ring *E* as well as the acetoxy group attached to atom C7 exhibit larger than normal displacement ellipsoids. For the acetoxy group the anisotropic displacement gradually increases from atom C7 to the terminal atoms O31/C27. A similar trend is seen in the furan ring from atom C20 to atoms O21/C23. However no disordered sites were modelled for these groups, even though some very slight rotational disorder about the C7—O7 and C17—C20 bonds may exist.

The orientation (Klyne & Prelog, 1960) of the furan ring (*E*) with respect to ring *D*, as denoted by the torsion angle C16—C17—C20—C22, is *ap* in the title compound [ $-177.9$  ( $4^\circ$ )] as well as in nimonol [ $-158.6$  ( $5^\circ$ )]. The acetoxy group attached to C7 is in the ( $-$ )*sc* orientation with respect to ring *B* [the



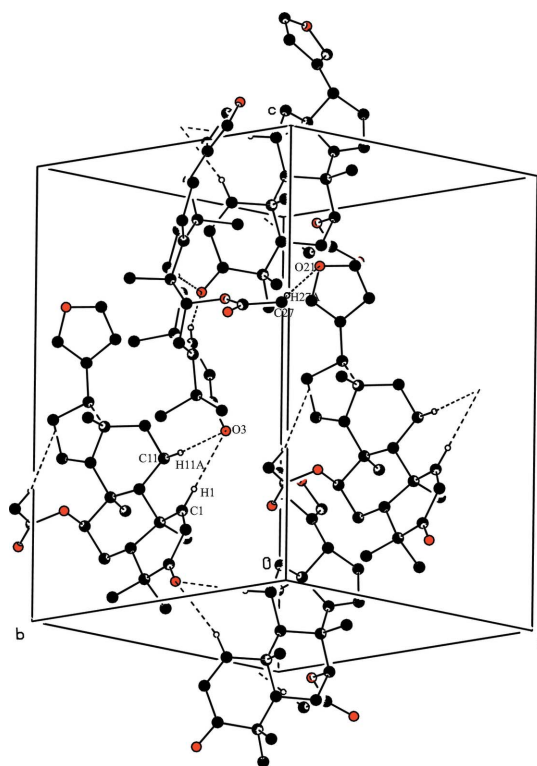
**Figure 1**  
The molecular structure of (I), showing 30% probability displacement ellipsoids and the atomic numbering scheme. H atoms have been omitted.



**Figure 2**  
Stereoscopic view of superimposed line diagrams of (I) (red) and nimonol (blue).

$C6-C7-O7-C26$  torsion angle is  $-85.6(3)^\circ$  while it is  $(-y, x - y - 1, \frac{1}{3} + z)$  in nimonol [ $-108.9(3)^\circ$ ]. The conformational differences between nimonol and (I) are illustrated in Fig. 2.

In (I) ring A is in a sofa conformation, as evident from the ring puckering amplitudes [ $Q_T = 0.445(4) \text{ \AA}$ ,  $\theta = 56.7(6)^\circ$ ,  $\varphi_2 = -116.6(7)^\circ$ ] (Cremer & Pople, 1975) and atom C5 deviates by  $-0.502(4) \text{ \AA}$  from the plane of rest of the other atoms of the ring. Ring B adopts a chair conformation [ $Q_T = 0.578(4) \text{ \AA}$ ,  $\theta = 6.2(4)^\circ$ ,  $\varphi_2 = -2.6(3.5)^\circ$ ]. The puckering occurs at C5 and C8 and these atoms deviate from the plane of the other four atoms by  $0.705(4)$  and  $-0.635(4) \text{ \AA}$ , respectively. Ring C is in a boat conformation [ $Q_T = 0.640(4) \text{ \AA}$ ,  $\theta = 80.1(4)^\circ$ ,  $\varphi_2 =$



**Figure 3**  
Part of the crystal structure of (I) with weak  $C-H \cdots O$  hydrogen bonds shown as dashed lines. H atoms not involved in these interactions have been omitted.

$55.6(4)^\circ$ ]. Atoms C9 and C13 deviate from the C8/C11/C12/C14 plane by  $0.685(4)$  and  $0.382(3) \text{ \AA}$ , respectively. Ring D is in an envelope conformation [ $q_2 = 0.345(5) \text{ \AA}$ ,  $\varphi = -32.8(9)^\circ$ ] with atom C17 as the flap, which deviates by  $0.546(4) \text{ \AA}$  from the plane of the remaining four atoms. The furan ring (E) adopts a planar conformation [ $q_2 = 0.028(9) \text{ \AA}$ ,  $\varphi = -162(9)^\circ$ ]. Rings A/B and B/C are *trans* fused while the rings C/D are quasi-*trans* fused, as can be seen from the endocyclic torsion angles [ $C12-C13-C14-C8 = 32.3(4)^\circ$  and  $C17-C13-C14-C15 = -22.1(4)^\circ$ ] of the ring junction atoms. The fusion and the ring conformations are similar to those in nimonol.

The crystal structure is stabilized by weak  $C-H \cdots O$  hydrogen bonds (Table 1 and Fig. 3). A C(5) chain motif (Bernstein *et al.*, 1995) running along the *b* axis is formed by donor atom C1 of an  $\alpha,\beta$  enone group and the enone carbonyl O3 at  $(-y, x - y - 1, \frac{1}{3} + z)$ . In addition, there is an  $R_2^2(7)$  ring formed through the bifurcated hydrogen bond with O3 at  $(-y, x - y - 1, \frac{1}{3} + z)$  as an acceptor with atoms C1 and C11 as donors. A C(12) chain is generated with atom C27 as a donor and O21 at  $(-x + y, -x, z - \frac{1}{3})$  as an acceptor. Studies reveal that small changes in the conformations described above do not affect the antifeedant activity of the title compound.

## Experimental

Fresh uncrushed green leaves of *Azadirachta indica* A. Juss (Neem) (5 kg) were soaked in hexane (25 l) for 24 h and the decanted *n*-hexane extract was concentrated to 1 l *in vacuo*. The hexane extract

was partitioned with 95% MeOH–water. The methanol layer was concentrated to dryness *in vacuo* resulting in a residue (16 g). The methanol extract (1.5 g) obtained was dissolved in methanol (2 ml) and was loaded on a Lobar column (Merck, 60 mm) and eluted with ethyl acetate/hexane (1:4). The polarity was increased progressively to 100% ethyl acetate followed by a methanol wash. A single compound was eluted between fractions 16–24 (1:4 ethyl acetate/hexane) (TLC monitored, 30% ethyl acetate in hexane) which, on solvent evaporation, yielded (I) (120 mg). Good diffraction quality crystals were obtained from a solution of (I) in ethyl acetate/hexane (1:1) by slow evaporation.

Crystal data

C<sub>28</sub>H<sub>36</sub>O<sub>4</sub>  $D_x = 1.193 \text{ Mg m}^{-3}$   
 $M_r = 436.57$  Cu  $K\alpha$  radiation  
 Trigonal,  $P3_1$   $\mu = 0.62 \text{ mm}^{-1}$   
 $a = 10.818 (3) \text{ \AA}$   $T = 293 (2) \text{ K}$   
 $c = 17.984 (5) \text{ \AA}$  Rod, colourless  
 $V = 1822.7 (10) \text{ \AA}^3$   $0.39 \times 0.28 \times 0.15 \text{ mm}$   
 $Z = 3$

Data collection

Enraf–Nonius CAD-4 diffractometer 2387 independent reflections  
 $\omega/2\theta$  scans 1996 reflections with  $I > 2\sigma(I)$   
 Absorption correction:  $\psi$  scan  $R_{\text{int}} = 0.080$   
 (North *et al.*, 1968)  $\theta_{\text{max}} = 72.1^\circ$   
 $T_{\text{min}} = 0.852, T_{\text{max}} = 0.909$  3 standard reflections  
 7386 measured reflections every 200 reflections  
 intensity decay: 2%

Refinement

Refinement on  $F^2$   $w = 1/[\sigma^2(F_o^2) + (0.0689P)^2 + 0.0034P]$   
 $R[F^2 > 2\sigma(F^2)] = 0.043$  where  $P = (F_o^2 + 2F_c^2)/3$   
 $wR(F^2) = 0.127$   $(\Delta/\sigma)_{\text{max}} = 0.001$   
 $S = 1.02$   $\Delta\rho_{\text{max}} = 0.15 \text{ e \AA}^{-3}$   
 2387 reflections  $\Delta\rho_{\text{min}} = -0.14 \text{ e \AA}^{-3}$   
 290 parameters  
 H-atom parameters constrained

**Table 1**  
 Hydrogen-bond geometry ( $\text{\AA}, ^\circ$ ).

$D-H \cdots A$	$D-H$	$H \cdots A$	$D \cdots A$	$D-H \cdots A$
$C1-H1 \cdots O3^i$	0.93	2.52	3.431 (4)	166
$C11-H11A \cdots O3^i$	0.97	2.66	3.628 (5)	175
$C27-H27A \cdots O21^{ii}$	0.96	2.76	3.684 (6)	162

Symmetry codes: (i)  $-y, x - y - 1, z + \frac{1}{3}$ ; (ii)  $-x + y, -x, z - \frac{1}{3}$ .

Refinement of the Flack (1983) parameter resulted in the value of  $-0.0 (3)$  which does not throw much light on the absolute configuration of (I) (Flack & Bernardinelli, 2000). Hence 2383 Friedel equivalents were merged before the final refinement. The enantiomer employed in the refined model was in good agreement with the accepted configuration of limonoids (Henderson *et al.*, 1968; Narayanan *et al.*, 1964; Harris *et al.*, 1968). The CH and CH<sub>3</sub> atoms were constrained to an ideal geometry ( $C-H = 0.98$  and  $0.96 \text{ \AA}$ ) with  $U_{\text{iso}}(H) = 1.2U_{\text{eq}}(C)$  and  $1.5U_{\text{eq}}(C)$ , but were allowed to rotate freely about the C–C bonds. All remaining H atoms were placed in geometrically idealized positions ( $C-H = 0.93-0.97 \text{ \AA}$ ) and constrained to ride on their parent atom with  $U_{\text{iso}}(H) = 1.2U_{\text{eq}}(C)$ .

Data collection: CAD-4 EXPRESS (Enraf–Nonius, 1994); cell refinement: CAD-4 EXPRESS; data reduction: XCAD4 (Harms & Wocadlo, 1995); program(s) used to solve structure: SHELXS97 (Sheldrick, 1997); program(s) used to refine structure: SHELXL97 (Sheldrick, 1997); molecular graphics: ORTEPIII (Burnett & Johnson, 1996); software used to prepare material for publication: SHELXL97 (Sheldrick, 1997) and PARST97 (Nardelli, 1995).

RM thanks CSIR (India) for a research associateship.

References

Bernstein, J., Davis, R. E., Shimoni, L. & Chang, N.-L. (1995). *Angew. Chem. Int. Ed. Engl.* **34**, 1555–1573.  
 Burnett, M. N. & Johnson, C. K. (1996). ORTEPIII. Report ORNL-6895. Oak Ridge National Laboratory, Tennessee, USA.  
 Cremer, D. & Pople, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354–1358.  
 Enraf–Nonius, (1994). CAD-4 EXPRESS. Enraf–Nonius, Delft, The Netherlands.  
 Flack, H. D. (1983). *Acta Cryst.* **A39**, 876–881.  
 Flack, H. D. & Bernardinelli, G. (2000). *J. Appl. Cryst.* **33**, 1143–1148.  
 Harms, K. & Wocadlo, S. (1995). XCAD4. University of Marburg, Germany.  
 Harris, M., Henderson, R., McCrindle, R., Overtone, K. H. & Turner, D. W. (1968). *Tetrahedron*, **24**, 1517–1519.  
 Henderson, R., McCrindle, R., Melera, A. & Overtone, K. H. (1968). *Tetrahedron*, **24**, 1525–1527.  
 Kabaleeswaran, V., Malathi, R., Rajan, S. S., Suresh, G. & Narashiman, N. S. (2000). *Acta Cryst.* **C56**, 82–84.  
 Klyne, W. & Prelog, V. (1960). *Experientia*, **15**, 521–523.  
 Narayanan, C. R., Pachapurkar, R. V., Pradhan, S. K., Shah, V. R. & Narasimhan, N. S. (1964). *Chem. Ind. (London)*, pp. 322–324.  
 Nardelli, M. (1995). *J. Appl. Cryst.* **28**, 659.  
 North, A. C. T., Phillips, D. C. & Mathews, F. S. (1968). *Acta Cryst.* **A24**, 351–359.  
 Schmutterer, H. (1995). *The Neem Tree: Source of Unique Natural Products for Integrated Pest Management, Medicine, Industry and Other Purposes*, edited by H. Schmutterer, pp. 127–129. Weinheim: VCH.  
 Sheldrick, G. M. (1997). SHELXS97 and SHELXL97. University of Göttingen, Germany.  
 Suresh, G., Gopalakrishnan, G., Wisley, D., Pradeep Singh, N. D., Malathi, R. & Rajan, S. S. (2002). *J. Agric. Food. Chem.* **50**, 4484–4490.