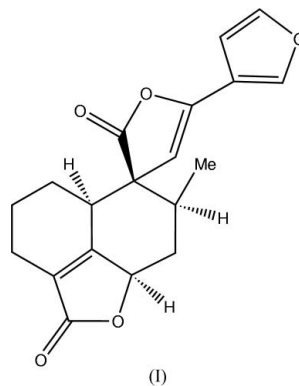


**ent-(8*S*,10*R*)-15,16-Epoxy-19-norcleroda-4,11,13(16),14-tetraene-18,6(*R*):20,12-diolactone (isocrotocaudin)**Ikram M. Said,<sup>a</sup> Ainal F. A. Noor,<sup>a</sup> Yana M. Syah,<sup>b</sup> Jalifah Latif,<sup>a</sup> Nurziana Ngah<sup>a</sup> and Bohari M. Yamin<sup>a\*</sup><sup>a</sup>School of Chemical Sciences and Food Technology, Universiti Kebangsaan Malaysia, 43600 Bangi, Selangor, Malaysia, and<sup>b</sup>Department of Chemistry, Institut Teknologi Bandung, Bandung, IndonesiaCorrespondence e-mail:  
bohari@pkriscc.ukm.my**Key indicators**Single-crystal X-ray study  
*T* = 298 K  
Mean  $\sigma(\text{C}-\text{C}) = 0.005 \text{ \AA}$   
*R* factor = 0.056  
*wR* factor = 0.113  
Data-to-parameter ratio = 8.6For details of how these key indicators were automatically derived from the article, see <http://journals.iucr.org/e>.

The title compound,  $\text{C}_{19}\text{H}_{18}\text{O}_5$ , is a diastereoisomer of crotocaudin, both being isolated from the plants of genus *Croton*. In isocrotocaudin, the furan moiety makes a dihedral angle with the adjacent lactone of  $13.53 (17)^\circ$ . The cyclohexyl ring of the diterpene moiety adopts a chair confirmation. The weak intermolecular  $\text{C}-\text{H}\cdots\text{O}$  hydrogen bonds link the molecules into linear chains along the *c* axis.

**Comment**

Isocrotocaudin, (I), and its diastereoisomer crotocaudin were isolated as minor components mainly from the plants of genus *Croton*, a tropical shrub native to the West Indies and northern South America. Their stereochemistry and absolute configurations were studied by NMR spectroscopic and circular dichroism measurements and established as *ent*-(8*S*,10*R*)-15,16-epoxy-19-norcleroda-4,11,13(16),14-tetraene-18,6(*R*):20,12-diolactone (Chatterjee *et al.*, 1978) and *ent*-(8*S*,10*S*)-15,16-epoxy-19-norcleroda-4,11,13(16),14-tetraene-18,6(*S*):20,12-diolactone (Chatterjee *et al.*, 1977) for isocrotocaudin and crotocaudin, respectively. The two isomers are differentiated by the  $\alpha\alpha$  and  $\beta\beta$  orientation of the H atoms at atoms C6 and C10, respectively. From the chemical shift values, it was concluded that both isomers have the same  $\beta\beta$  configuration of the C17-methyl group. However, on the basis of biogenetic and partial synthesis of these compounds from the natural 19-nor-neo-clerodane montanin (Malakov *et al.*, 1978), which is known to possess an 8*R* configuration (Fujita *et al.*, 1973), a compound similar to (I) was obtained (Lourenco *et al.*, 1991). Therefore, the 8*S* configuration was proposed for isocrotocaudin and crotocaudin. During our work on the local *Croton* plants, a few small crystals of (I) were found in the solid extract.

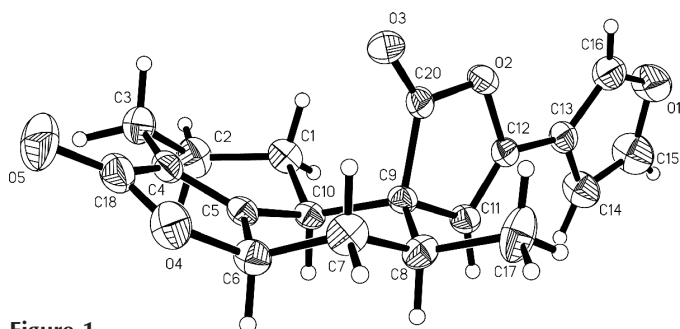


The X-ray investigation gave a molecular structure of the isocrotocaudin diastereoisomer (Fig. 1) with both H atoms attached to C6 and C10 occupying the axial positions – a  $\beta\beta$

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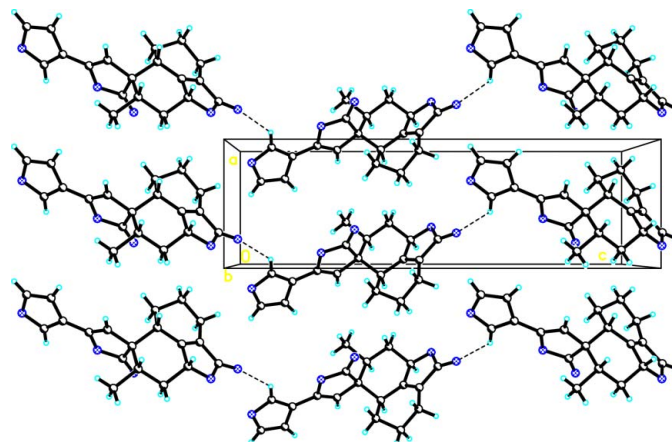
**Figure 1**  
The molecular structure of (I), shown with 50% probability displacement ellipsoids.

orientation or  $6R,10R$  configuration. The C17-methyl group attached to atom C8 is in an equatorial position indicating a  $\beta$  orientation or  $8S$  configuration. In addition, the C9–C20 bond is in the opposite direction to the C10–H10 bond and therefore has an  $\alpha$ -orientation. The relative configurations at the chiral centres are  $6R, 8S, 9S$  and  $10R$ , which is in agreement with the absolute configuration proposed by Chatterjee *et al.* (1978). All bond lengths (Table 1) and angles in (I) are in normal ranges (Allen *et al.*, 1987). The furan (O1/C13/C14/C15/C16) and lactones (C9/C11/C12/O2/C20 and C4/C5/C6/O4/C18) are essentially planar, with a maximum deviation for atom C6 of 0.030 (3) Å. The C5–C10 cyclohexyl ring has a chair conformation [ $Q = 0.506$  (3) Å,  $\theta = 169.0$  (3) and  $\varphi_2 = 333.0$  (16)° (Cremer & Pople, 1975)] and the fused C1–C5/C10 ring has a distorted sofa conformation [ $Q = 0.493$  (3) Å,  $\theta = 124.9$  (3) and  $\varphi_2 = 216.6$  (4)°] induced by the presence of the  $\alpha,\beta$ -unsaturated ketone function attached to the ring. The furan ring makes a dihedral angle with the adjacent lactone ring of 13.53 (17)°.

There is a weak intramolecular hydrogen bond, C7–H7B...O3 (Table 2), which may contribute to the planarity of the lactone rings. In the crystal structure, the molecules are linked by weak intermolecular C–H...O hydrogen bonds (Table 2) into linear chains along the  $c$  axis (Fig. 2).

## Experimental

The *Croton* species was collected from Lintang Village, Terengganu, on the East Coast of Peninsular Malaysia. The voucher specimen (AZZ004-6) was deposited at The Herbarium of Universiti Kebangsaan Malaysia (UKMB). The air-dried and powdered leaves of *Croton caudatus* Geisel (dry weight 1.0 kg) were soaked in ethyl acetate (2.0 l) for 5 d at room temperature. The mixture was filtered and concentrated under reduced pressure to give a crude extract (100 g, 10%). The ethyl acetate extract was subjected to flash chromatography followed by column chromatography using silica as stationary phase and eluted initially with petroleum ether followed by increasing amounts of ethyl acetate in petroleum ether. Each fraction was monitored by thin-layer chromatography; fractions that appeared similar were combined to yield 20 major fractions, denoted F1–F20. Fraction F17 (0.9 g, 0.10%) was concentrated by evaporation to give a colourless solid with fine crystals on the top surface [m.p. 485.5–486.8 K (literature value: 485 K) and NMR data are in agreement with the reported values (Chatterjee *et al.*, 1978)].



**Figure 2**  
Packing diagram viewed down the  $b$  axis. The dashed lines denote C–H...O hydrogen bonds.

### Crystal data

$C_{19}H_{18}O_5$   
 $M_r = 326.33$   
Orthorhombic,  $P2_12_12_1$   
 $a = 6.677$  (2) Å  
 $b = 10.794$  (3) Å  
 $c = 22.608$  (7) Å  
 $V = 1629.4$  (8) Å<sup>3</sup>  
 $Z = 4$   
 $D_x = 1.330$  Mg m<sup>-3</sup>

Mo  $K\alpha$  radiation  
Cell parameters from 743 reflections  
 $\theta = 1.8$ – $26.0^\circ$   
 $\mu = 0.10$  mm<sup>-1</sup>  
 $T = 298$  (2) K  
Needle, colourless  
 $0.42 \times 0.10 \times 0.09$  mm

### Data collection

Bruker SMART APEX CCD area-detector diffractometer  
 $\omega$  scans  
Absorption correction: multi-scan (SADABS; Sheldrick, 1996)  
 $T_{\min} = 0.960$ ,  $T_{\max} = 0.991$   
8831 measured reflections

1866 independent reflections  
1583 reflections with  $I > 2\sigma(I)$   
 $R_{\text{int}} = 0.035$   
 $\theta_{\max} = 26.0^\circ$   
 $h = -8 \rightarrow 8$   
 $k = -13 \rightarrow 13$   
 $l = -18 \rightarrow 27$

### Refinement

Refinement on  $F^2$   
 $R[F^2 > 2\sigma(F^2)] = 0.056$   
 $wR(F^2) = 0.113$   
 $S = 1.18$   
1866 reflections  
217 parameters  
H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.0462P)^2 + 0.3404P]$   
where  $P = (F_o^2 + 2F_c^2)/3$   
 $(\Delta/\sigma)_{\max} < 0.001$   
 $\Delta\rho_{\max} = 0.16$  e Å<sup>-3</sup>  
 $\Delta\rho_{\min} = -0.13$  e Å<sup>-3</sup>

**Table 1**  
Selected bond lengths (Å).

O1–C16	1.350 (5)	O4–C6	1.439 (4)
O1–C15	1.354 (5)	O5–C18	1.202 (4)
O2–C20	1.372 (4)	C4–C5	1.316 (4)
O2–C12	1.411 (4)	C11–C12	1.312 (4)
O3–C20	1.196 (4)	C13–C16	1.334 (5)
O4–C18	1.365 (5)	C14–C15	1.323 (5)

**Table 2**  
Hydrogen-bonding geometry (Å, °).

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
C7–H7B...O3	0.97	2.56	3.172 (4)	121
C16–H16A...O5 <sup>i</sup>	0.93	2.49	3.223 (4)	136

Symmetry codes: (i)  $\frac{3}{2} - x, 1 - y, \frac{1}{2} + z$ .

After their location in a difference map, all H atoms were placed in ideal positions and allowed to ride on their parent C atoms, with C—distances of 0.93–0.98 Å and  $U_{\text{iso}}$  values set at  $1.2U_{\text{eq}}$  of the parent atom. Due to the absence of any significant anomalous scatterers in the molecule, Friedel pairs were merged before the final refinement and the absolute configuration was assigned in accordance with the literature (Chatterjee *et al.*, 1978).

Data collection: *SMART* (Siemens, 1996); cell refinement: *SAINTE* (Siemens, 1996); data reduction: *SAINTE*; program(s) used to solve structure: *SHELXTL* (Sheldrick, 1997); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL*, *PARST* (Nardelli, 1995) and *PLATON* (Spek, 2003).

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