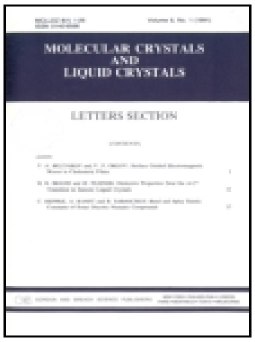


Molecular Crystals and Liquid Crystals

ISSN: 1542-1406 (Print) 1563-5287 (Online) Journal homepage: http://www.tandfonline.com/loi/gmcl20

Molecular and Crystal Structures of α,α,β-Trimethylfuranylxanthone from Cratoxylum formosum ssp. pruniflorum: A Partial Racemate

Nawong Boonnak, Suchada Chantrapromma & Hoong-Kun Fun

To cite this article: Nawong Boonnak, Suchada Chantrapromma & Hoong-Kun Fun (2015) Molecular and Crystal Structures of α,α,β-Trimethylfuranylxanthone from Cratoxylum formosum ssp. pruniflorum: A Partial Racemate, Molecular Crystals and Liquid Crystals, 606:1, 165-175, DOI: 10.1080/15421406.2014.905044

To link to this article: http://dx.doi.org/10.1080/15421406.2014.905044

Mol. Cryst. Liq. Cryst., Vol. 606: pp. 165–175, 2015
Copyright © Taylor & Francis Group, LLC
ISSN: 1542-1406 print/1563-5287 online
DOI: 10.1080/15421406.2014.905044

Molecular and Crystal Structures of α,α,β-Trimethylfuranylxanthone from *Cratoxylum formosum* ssp. *pruniflorum*: A Partial Racemate

NAWONG BOONNAK,[1,*] SUCHADA CHANTRAPROMMA,[2,*]
AND HOONG-KUN FUN[3,4]

[1]Department of Chemistry, Faculty of Science, Thaksin University, Pattalung, Thailand
[2]Faculty of Science, Department of Chemistry, Prince of Songkla University, Hat-Yai, Songkhla, Thailand
[3]X-ray Crystallography Unit, School of Physics, Universiti Sains Malaysia, USM, Penang, Malaysia
[4]Department of Pharmaceutical Chemistry, College of Pharmacy, King Saud University, Riyadh, Saudi Arabia

*The title xanthone known as Formoxanthone C (**1**) was isolated from the green fruits of* Cratoxylum formosum *ssp.* pruniflorum. *Compound **1** crystallized out in* $P2_1/c$ *space group, indicating that **1** exists both enantiomers. The unit cell parameters are* $a = 13.8038(2)$, $b = 14.6712(2)$, $c = 9.4686(1)$ Å, $\beta = 95.358(1)^\circ$, $V = 1909.19(4)$ Å^3, *and* $Z = 4$. *The α,α,β-trimethyldihydrofuran ring was in an envelope conformation and disordered over two sites with 0.628(1) and 0.372(1) occupancies for the major and minor components, respectively, which corresponded to the less furan ring strain and the steric hindrance between the two methyl substituents (at positions 1′ and 2′) on the furan ring of the major component than that of the minor component. The crystal structure is stabilized by intermolecular O—H···O hydrogen bonds and weak C—H···O interactions.*

Keywords Crystal structure; formoxanthone C; α,α,β-trimethyldihydrofuran; partial racemate; xanthone; X-ray

Introduction

Cratoxylum formosum ssp. *pruniflorum*, belonging to the family Guttiferae, is widely distributed in northern and north-eastern parts of Thailand [1]. Decoction of the fresh or dried leaves from this plant has been used in folk medicine as stomach and diuretic tonics [2]. Previous reports [3–5] have revealed that tri- and tetra-oxygenated xanthones were mainly produced as major components from plants of Cratoxylum genus. Moreover, several

---

[*]Address correspondence to Nawong Boonnak and Suchada Chantrapromma, Faculty of Traditional Thai Medicine, Prince of Songkla University, Hat-Yai, Songkhla 90112, Thailand and Faculty of Science, Department of Chemistry, Prince of Songkla University, Hat-Yai, Songkhla 90112, Thailand. E-mail: suchada.c@psu.ac.th; nawongb@yahoo.com

Color versions of one or more of the figures in the article can be found online at www.tandfonline.com/gmcl.

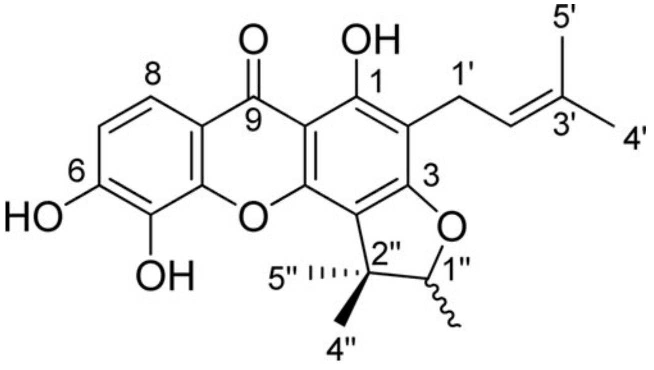


Figure 1. Schematic diagram of formoxanthone C (**1**).

isolated xanthones were reported to possess various interesting biological activities [4, 6–8]. The bioactivity-guided fractionation of the CH_2Cl_2 crude extract of *C. formosum* spp. *pruniflorum* green fruits afforded compound **1** (Fig. 1), which known as formoxanthone C [6] [systematic name: 5,9,10-trihydroxy-1,1,2-trimethyl-4-(3-methylbut-2-enyl)-1*H*-furo[2,3-*c*]xanthen-6(2*H*)-one]. Our nitric oxide inhibitory activity study resulted that compound **1** exhibits potent nitric oxide inhibitory activity with IC_{50} value of 4.3 μM [9] and also showed strong antibacterial activity against methicillin-resistant *Staphylococcus aureus* (MRSA) ATCC43300, *Enterococcus faecalis* TISTR459, vancomycin-resistant *Enterococcus faecalis* (VRE) ATCC51299, *Bacillus subtilis*, and *Salmonella typhi* with an MIC value of 4.67 μg/mL^{-1} [9]. It is well documented that bioactivities are related to the structure of the compound thereby making the correct characterization and identification of compounds of paramount importance. Of all the various physical methods that are important in helping to elucidate structure, single crystal X-ray diffraction is a powerful technique and undoubtedly the most far reaching and complete method. To study in more details of the molecular structure of **1** and to establish the conformation of the α,α,β-trimethyldihydrofuran ring, its molecular and crystal structures by single crystal X-ray diffraction was studied. The results reported here show that **1** exists in both enantiomers and also in two conformations with 62.8% for the major and 37.2% for the minor components.

Experimental

General Experimental Procedures

Melting points were determined with a Fisher–John melting point apparatus. Optical rotations were measured on a JASCO P-1020 digital polarimeter. UV-Vis and IR spectra were recorded on SPECORD S 100 (Analytikjena) and Perkin–Elmer FTS FT-IR spectrophotometer, respectively. The ^{1}H and ^{13}C NMR spectra were recorded on a 300 MHz Bruker FT-NMR Ultra Shield^{TM} spectrometer in $CDCl_3$ with TMS as an internal standard. Chemical shifts are reported in δ (ppm) and coupling constants (J) are expressed in hertz. Quick column chromatography (QCC) and column chromatography (CC) were carried out on silica gel 60 F_{254} (Merck) and silica gel 100 (Merck), respectively.

Extraction and Isolation

Air-dried green fruits of *C. formosum* ssp. *pruniflorum* (5.0 kg) were extracted with CH_2Cl_2 and CH_3OH (each 2 × 20 L, for a week) successively at room temperature and further evaporated under reduced pressure to afford the crude extracts of CH_2Cl_2 (31.42 g) and CH_3OH (65.74 g), respectively. The crude CH_2Cl_2 extract (31.42 g) of the green fruits of *C. formosum* ssp. *pruniflorum* was further subjected to QCC on silica gel using hexane as a first eluent and then increasing the polarity with acetone to give 14 fractions (F1–F14). Fraction F10 was separated by QCC eluting with a gradient of acetone-hexane to give 17 subfractions (F10A–F10Q). Subfraction F10N was separated by CC and eluted with a gradient of EtOAc-hexane to give eight subfractions (F10N1–F10N8). Subfraction F10N6 was separated by CC and eluted with $CHCl_3$ to give the compound **1.** Yield: yellow solid 15.2 mg, m.p.: 152–154°C; $[\alpha]^{25}_{D} = -44.8$ (*c* 0.05, $CHCl_3$); UV-Vis (CH_3OH) λ_{max} (log ε) 258 (4.51), 276 (4.44), 392 (3.85) nm; FT-IR (KBr) ν_{max} 3440, 1646, 1624 cm^{-1}; ^1H NMR ($CD_3OD+CDCl_3$, 300 MHz, ppm) δ: 13.40 (1H, s, OH), 7.63 (1H, d, $J = 8.1$ Hz, H-8), 6.85 (1H, br s, H-7), 5.28 (1H, br t, $J = 7.2$ Hz, H-2′), 4.52 (1H, q, $J = 6.6$ Hz, H-1″), 3.29 (2H, d, $J = 7.2$ Hz, CH_2-1′), 1.77 (3H, s, CH_3-5′), 1.68 (3H, s, CH_3-4′), 1.59 (3H, s, CH_3-5″), 1.41 (3H, dd, J = 6.6, 1.2 Hz, CH_3-3″), and 1.31 (3H, s, CH_3-4″). ^{13}C NMR ($CD_3OD+CDCl_3$, 75 MHz) δ: 164.5 (C-1), 110.6 (C-2), 168.0 (C-3), 115.9 (C-4), 135.9 (C-5), 149.7 (C-6), 115.9 (C-7), 121.1 (C-8), 184.5 (C-9), 154.9 (C-4a), 154.1 (C-5a), 118.2 (C-8a), 106.8 (C-9a), 25.6 (C-1′), 125.6 (C-2′), 135.9 (C-3′), 29.6 (C-4′), 21.6 (C-5′), 44.4 (C-1″), 47.9 (C-2″), 18.2 (C-3″), 25.1 (C-4″), and 29.6 (C-5″).

Preparation of Single Crystal for Structure Determination

Yellow block-shaped single crystals of formoxanthone C suitable for X-ray diffraction study were obtained from CH_2Cl_2–CH_3OH (4:1 v/v) solution by slow evaporation at room temperature after several days. A suitable single crystal was selected optically for the diffraction study.

A single crystal of dimensions 0.35 mm × 0.30 mm × 0.17 mm was used. Crystallographic data were collected at 100.0 (1) K with the Oxford Cryosystem Cobra low-temperature attachment. The data were collected using a Bruker Apex2 CCD diffractometer with a graphite monochromated Mo Kα ($\lambda = 0.71073$ Å) radiation at a detector distance of 5 cm using *APEX2* [10]. The collected data were reduced using *SAINT* program [10], and the empirical absorption corrections were performed using *SADABS* program [10]. The structures were solved by direct methods and refined by least-squares using the *SHELXTL* software package [11]. All nonhydrogen atoms were refined anisotropically. Hydroxy H atoms were located in different maps and refined isotropically, whereas the remaining H atoms were placed in calculated positions with C–H = 0.93 Å for aromatic, 0.98 Å for CH, 0.97 Å for CH_2, and 0.96 Å for CH_3. The $U_{iso}(H)$ values were constrained to be $1.5U_{eq}$ of the carrier atoms for methyl H atoms and $1.2U_{eq}$ for hydroxyl and the other H atoms. The final refinement converged well. Materials for publication were prepared using *SHELXTL* [11], *PLATON* [12], and *Mercury* [13]. The α,α,β-trimethylfuran ring was found to be disordered over two sites with a 0.628(1): 0.372(1) refined site occupancy ratio. The crystal data of formoxanthone C (CCDC 910092) are summarized in Table 1.

Results and Discussion

Spectroscopic Properties

The UV-Vis spectrum showed absorption bands of a xanthone at 258, 276, and 392 nm. The FT-IR spectrum exhibited the hydroxyl group at 3440 cm^{-1} and conjugated carbonyl group at 1646 cm^{-1}. The ^1H NMR spectrum ($CD_3OD+CDCl_3$) exhibited a chelated hydroxyl proton at δ 13.40 (1H, *s*), a pair of *ortho*-coupled aromatic protons at δ 7.63

Table 1. Crystal data and structure refinement for formoxanthone C

CCDC reference no.	CCDC 910092
Empirical formula	$C_{23}H_{24}O_6$
Formula weight	396.43
Crystal system, space group	Monoclinic, $P2_1/c$
Temperature (K)	100.0(1)
a, b, c (Å)	13.8038(2), 14.6712(2), 9.4686(1)
β (°)	95.358(1)
V(Å^3)	1909.19(4)
Z	4
Calculated density (Mg/m^{-3})	1.379
Radiation type, wavelength (Å)	Mo Kα, 0.71073
Absorption coefficient (mm^{-1})	0.098
Crystal form, color	block, yellow
Crystal size (mm)	0.35 × 0.30 × 0.17
Diffractomemter	CCD area detector diffractomemter
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0619$, $wR_2 = 0.1550$
R indices (all data)	$R_1 = 0.0804$, $wR_2 = 0.1655$
Reflections collected / unique	29475/4383 [R(int) = 0.0391]
θ range for data collection (°)	2.03−27.50
Limiting indices	$-17 <= h <= 17$, $-16 <= k <= 19$, $-12 <= l <= 11$
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	4383/0/298
Completeness to $\theta = 27.50$	100.0%
F(000)	840
Extinction method	None
Goodness-of-fit on F^2	1.101
Largest difference in peak and hole (e Å^{-3})	0.782 and −0.325

(1H, d, $J = 8.1$ Hz, H-8) and 6.85 (1H, br s, H-7), an isoprenyl side chain at δ 5.28 (1H, br t, $J = 7.2$ Hz, H-2′), 3.29 (2H, d, $J = 7.2$ Hz, H_2-1′), 1.77 (3H, s, CH_3-5′), and 1.68 (3H, s, CH_3-4′). Moreover, the presence of a α,α,β-trimethyldihydrofuran ring was suggested by the following ^{1}H NMR spectral data at δ 4.52 (1H, q, $J = 6.6$ Hz, H-1″), 1.59 (3H, s, CH_3-5″), 1.41 (3H, dd, $J = 6.6, 1.2$ Hz, CH_3-3″), and 1.31 (3H, s, CH_3-4″), respectively.

Crystal Structure

The X-ray diffraction of compound **1** was studied and revealed its molecular structure, which was shown in Figs. 2 and 3. The chemical structure of **1** showed that it contains one chiral center at C-1″ (Fig. 1). However, compound **1** crystallized out in the centrosymmetric space group $P2_1/c$ which clearly indicated that the compound contained both enantiomers [(1′*S*)-**1** and (1′*R*)-**1**] which can be clearly seen in the crystal packing in Fig. 4. Therefore, compound **1** was a racemic mixture. Bond lengths, angles, and torsion angles of **1** are listed in Table 2 and hydrogen bonds are listed in Table 3.

Table 2. Selected bond lengths (Å), angles, and torsion angles (°) for **1**

Bond lengths							
$O_{1—13}$	1.361(2)	C_7-H_{7A}	0.93	$C_{16}-H_{16D}$	0.96
O_1-C_{12}	1.372(2)	C_8-C_9	1.406(3)	$C_{16}-H_{16E}$	0.96
O_2-C_{10}	1.270(2)	C_8-H_{8A}	0.9300	$C_{16}-H_{16F}$	0.96
O_3-C_1	1.350(3)	C_9-C_{13}	1.398(3)	$C_{17}-H_{17A}$	0.96
$O_3-H_1O_3$	0.78(3)	C_9-C_{10}	1.459(3)	$C_{17}-H_{17B}$	0.96
O_4-C_3	1.355(3)	$C_{10}-C_{11}$	1.435(3)	$C_{17}-H_{17C}$	0.96
O_4-C_{15A}	1.499(5)	$C_{11}-C_{12}$	1.412(3)	$C_{18A}-H_{18A}$	0.96
O_4-C_{15B}	1.629(8)	$C_{14}-C_{18A}$	1.449(6)	$C_{18A}-H_{18B}$	0.96
O_5-C_5	1.369(2)	$C_{14}-C_{17}$	1.493(4)	$C_{18A}-H_{18C}$	0.96
$O_5-H_1O_5$	0.82(3)	$C_{14}-C_{15B}$	1.566(8)	$C_{18B}-H_{18D}$	0.96
O_6-C_6	1.361(3)	C_8-H_{8A}	0.93	$C_{18B}-H_{18E}$	0.96
$O_6-H_1O_6$	0.84(3)	C_9-C_{13}	1.398(3)	$C_{18B}-H_{18F}$	0.96
C_1-C_2	1.390(3)	$C_{14}-C_{15A}$	1.628(5)	$C_{19}-C_{20}$	1.517(3)
C_1-C_{11}	1.430(3)	$C_{14}-C_{18B}$	1.661(10)	$C_{19}-H_{19A}$	0.97
C_2-C_3	1.394(3)	$C_{15A}-C_{16}$	1.472(6)	$C_{19}-H_{19B}$	0.97
C_2-C_{19}	1.514(3)	$C_{15A}-H_{15A}$	0.98	$C_{20}-C_{21}$	1.323(4)
C_3-C_4	1.394(3)	$C_{15A}-H_{16E}$	1.4613	$C_{20}-H_{20A}$	0.93
C_4-C_{12}	1.376(3)	$C_{15B}-C_{16}$	1.426(9)	$C_{21}-C_{23}$	1.503(4)
C_4-C_{14}	1.515(3)	$C_{15B}-H_{15D}$	0.98	$C_{21}-C_{22}$	1.504(4)
C_5-C_6	1.391(3)	$C_{15B}-H_{16B}$	1.4382	$C_{22}-H_{22A}$	0.96
C_5-C_{13}	1.399(3)	$C_{16}-H_{16A}$	0.96	$C_{22}-H_{22B}$	0.96
C_6-C_7	1.405(3)	$C_{16}-H_{16B}$	0.96	$C_{22}-H_{22C}$	0.96
C_7-C_8	1.372(3)	$C_{16}-H_{16C}$	0.96	$C_{23}-H_{23A}$	0.96
Bond angles							
$C_{13}-O_1-C_{12}$	119.47(16)	$O_6-C_6-C_7$	117.99(19)	$C_{18A}-C_{14}-C_{17}$	117.9(4)
$C_3-O_4-C_{15A}$	105.0(2)	$C_5-C_6-C_7$	120.26(19)	$C_{18A}-C_{14}-C_4$	110.3(3)
$C_3-O_4-C_{15B}$	105.0(3)	$C_8-C_7-C_6$	120.4(2)	$C_{17}-C_{14}-C_4$	113.6(2)
$O_3-C_1-C_2$	118.17(19)	$C_7-C_8-C_9$	120.69(19)	$C_{17}-C_{14}-C_{15B}$	128.3(5)
$O_3-C_1-C_{11}$	119.86(19)	$C_{13}-C_9-C_8$	118.15(19)	$C_{18A}-C_{14}-C_{15A}$	114.9(3)
$C_2-C_1-C_{11}$	121.97(19)	$C_{13}-C_9-C_{10}$	119.02(18)	$C_{17}-C_{14}-C_{18B}$	96.5(4)
$C_1-C_2-C_3$	115.65(19)	$C_8-C_9-C_{10}$	122.83(18)	$C4-C_{14}-C_{18B}$	113.6(4)
$C_1-C_2-C_{19}$	123.0(2)	$O_2-C_{10}-C_{11}$	121.38(19)	$C_{15B}-C_{14}-C_{18B}$	103.8(5)
$C_3-C_2-C_{19}$	121.3(2)	$O_2-C_{10}-C_9$	121.81(19)	$C_{15A}-C_{14}-C_{18B}$	135.0(4)
$O_4-C_3-C_2$	121.6(2)	$C_{11}-C_{10}-C_9$	116.81(18)	$C_{16}-C_{15A}-O_4$	111.2(4)
$O_4-C_3-C_4$	112.87(19)	$C_{12}-C_{11}-C_1$	118.06(19)	$C_{16}-C_{15A}-C_{14}$	116.2(4)
$C_2-C_3-C_4$	125.6(2)	$C_{12}-C_{11}-C_{10}$	119.82(19)	$O_4-C_{15A}-C_{14}$	105.2(3)
$C_{12}-C_4-C_3$	116.99(19)	$C_1-C_{11}-C_{10}$	122.09(18)	$C_{16}-C_{15B}-C_{14}$	123.2(7)
$C_{12}-C_4-C_{14}$	131.3(2)	$O_1-C_{12}-C_4$	116.63(18)	$C_{16}-C_{15B}-O_4$	106.6(6)
$C_3-C_4-C_{14}$	111.64(19)	$O_1-C_{12}-C_{11}$	121.73(18)	$C_{14}-C_{15B}-O_4$	102.1(5)
$O_5-C_5-C_6$	122.87(18)	$C_4-C_{12}-C_{11}$	121.64(19)	$C_2-C_{19}-C_{20}$	114.59(19)
$O_5-C_5-C_{13}$	118.59(18)	$O_1-C_{13}-C_9$	122.95(18)	$C_{21}-C_{20}-C_{19}$	126.8(2)
$C_6-C_5-C_{13}$	118.50(18)	$O_1-C_{13}-C_5$	115.17(17)	$C_{20}-C_{21}-C_{23}$	122.2(2)
$O_6-C_6-C_5$	121.72(19)	$C_9-C_{13}-C_5$	121.88(19)	$C_{20}-C_{21}-C_{22}$	123.6(2)
$C_{13}-O_1-C_{12}$	119.47(16)	$O_6-C_6-C_7$	117.99(19)	$C_{23}-C_{21}-C_{22}$	114.2(2)
Torsion angles							
$O_3-C_1-C_2-C_3$	−177.11(18)	$C_8-C_9-C_{10}-O_2$	2.5(3)	$C_{12}-C_4-C_{14}-C_{18B}$	−51.0(5)
$C_{11}-C_1-C_2-C_{19}$	−178.10(19)	$O_3-C_1-C_{11}-C_{10}$	0.9(3)	$C_3-C_4-C_{14}-C_{18B}$	127.3(5)
$C_{15A}-O4-C3-C_4$	19.2(3)	$O_2-C_{10}-C_{11}-C_1$	−0.8(3)	$C_3-O_4-C_{15A}-C_{16}$	−156.5(3)
$C_{15B}-O_4-C_3-C_4$	−17.3(5)	$C_{13}-O_1-C_{12}-C11$	3.0(3)	$C_{18A}-C_{14}-C_{15A}-C_{16}$	35.8(5)
$C_1-C_2-C_3-O_4$	177.97(19)	$C_{14}-C_4-C_{12}-O1$	1.7(3)	$C_{17}-C_{14}-C_{15A}-C_{16}$	−92.9(4)
$C_{19}-C_2-C_3-C_4$	179.0(2)	$O_5-C_5-C_{13}-C_9$	−175.31(18)	$C_4-C_{14}-C_{15A}-C_{16}$	151.4(4)
$O_4-C_3-C_4-C_{14}$	0.6(3)	$C_3-C_4-C_{14}-C_{18A}$	101.3(4)	$C_{18B}-C_{14}-C_{15B}-C_{16}$	98.3(9)
$C_2-C_3-C_4-C_{14}$	−179.7(2)	$C_{12}-C_4-C_{14}-C_{17}$	58.0(4)	$C_3-O_4-C_{15B}-C_{16}$	157.0(5)
$O_5-C_5-C_6-O_6$	−4.0(3)	$C_3-C_4-C_{14}-C_{17}$	−123.8(3)	$C_1-C_2-C_{19}-C_{20}$	116.0(2)
$C_{13}-C_5-C_6-O_6$	178.57(18)	$C_{12}-C_4-C_{14}-C_{15B}$	−161.4(5)	$C_3-C_2-C_{19}-C_{20}$	−64.7(3)
$O_5-C_5-C_6-C_7$	177.96(19)	$C_3-C_4-C_{14}-C_{15B}$	16.8(5)	$C2-C19-C20-C_{21}$	−81.2(3)
$O_6-C_6-C_7-C_8$	179.39(19)	$C_{12}-C_4-C_{14}-C_{15A}$	163.9(3)	$C_{19}-C_{20}-C_{21}-C_{23}$	−176.2(2)
$C_{13}-C_9-C_{10}-O_2$	−177.14(18)	$C_3-C_4-C_{14}-C_{15A}$	−17.9(3)	$C_{19}-C_{20}-C_{21}-C_{22}$	4.0(4)

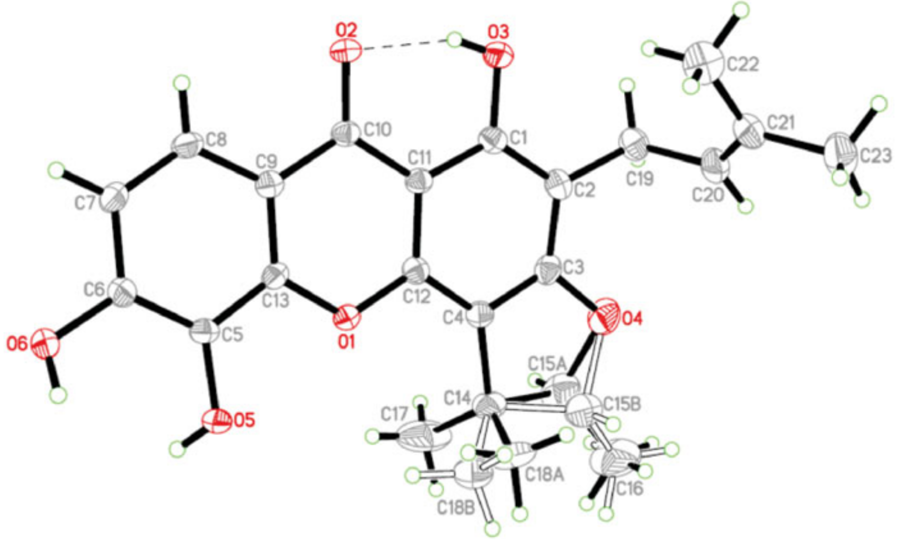
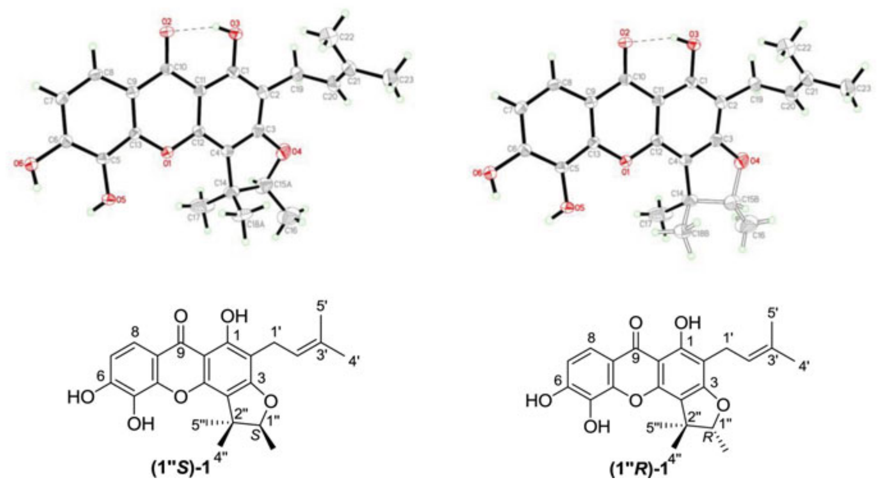


Figure 2. Molecular structure of **1**, showing displacement ellipsoids drawn at 30% probability level and the atom-labeling scheme. Open bond is a minor component. Intramolecular O—H···O hydrogen bond was drawn as a dashed line.

From the X-ray molecular structure in Fig. 2, the three-ring system of xanthone skeleton [C_1–C_{13}/O_1] is essentially planar. The O_3, O_5, and O_6 hydroxyl O atoms lie close to their attached benzene rings with deviations +0.023(2) Å, −0.031(2) Å, and −0.008(2) Å for atoms O_3, O_5, and O_6, respectively, and the torsion angles O_3–C_1–C_2–C_3 =



(a) major conformational component (62.8%)

(b) minor conformational component (37.2 %)

Figure 3. The molecular structure of (**1**) showing; (**a**) major and (**b**) minor conformational components.

Table 3. Hydrogen bond lengths (Å) and angles (°) for **1**

D−H···A	D−H	H···A	D···A	D−H···A
$O_3-H_1O_3\cdots O_2$	0.77(3)	1.85(3)	2.583(2)	157(3)
$O_5-H_1O_5\cdots O_2{}^a$	0.82(4)	1.82(4)	2.636(2)	169(3)
$O_6-H_1O_6\cdots O_5{}^b$	0.84(3)	1.99(3)	2.779(2)	158(3)
$C_{17}-H_{17A}\cdots O_2{}^c$	0.96	2.60	3.520(4)	161
$C_{22}-H_{22A}\cdots O_3$	0.96	2.59	3.519(3)	163

Symmetry codes: [a] $-x$, $-1/2 + y$, $1/2 - z$; [b] $-x$, $-y$, $1 - z$; [c] x, $1/2 - y$, $-1/2 + z$.

−177.11(18)°, O_5–C_5–C_6–C_7 = 177.96(19)°, and O_5–C_5–C_6–C_7 = 179.39(19)°. The *α*,*α*,*β*-trimethyldihydrofuran (C_3–C_4/C_{14}–C_{18}/O_4) moiety was found to be disordered over two sites of the major and minor conformational components with occupancy ratio of 0.628(1) and 0.372(1), respectively. It was interesting to note that this occupancy ratio corresponds to the dihydrofuran ring strain and steric hindrance between the two methyl substituents at positions 1″ and 2″ on the dihydrofuran ring.

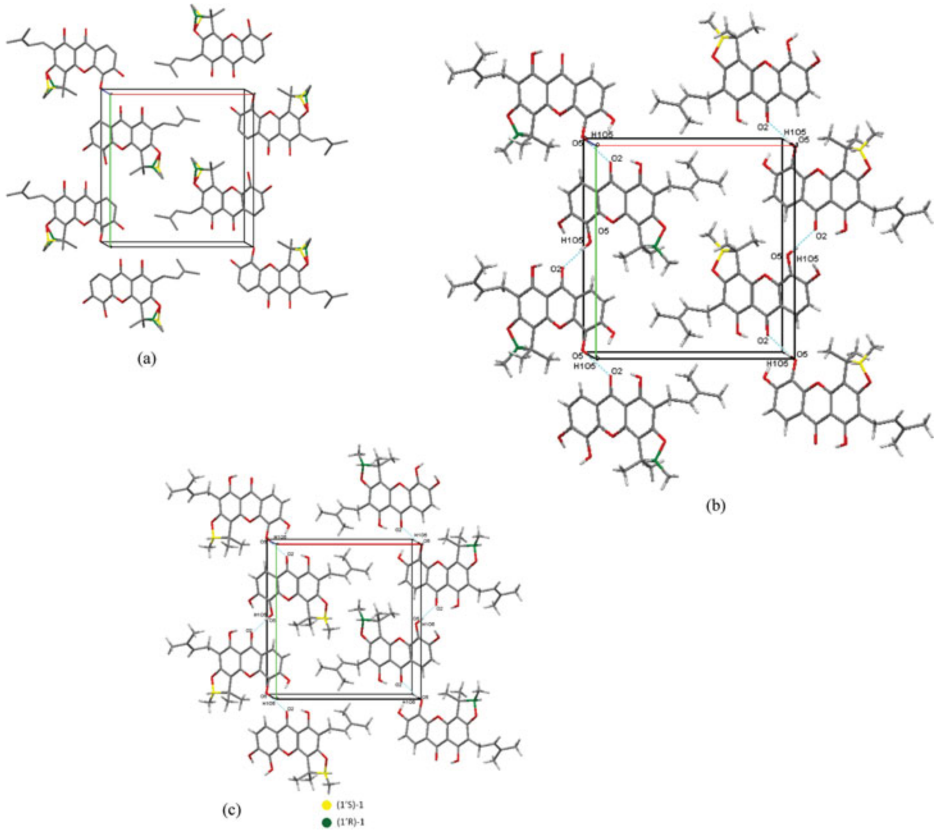
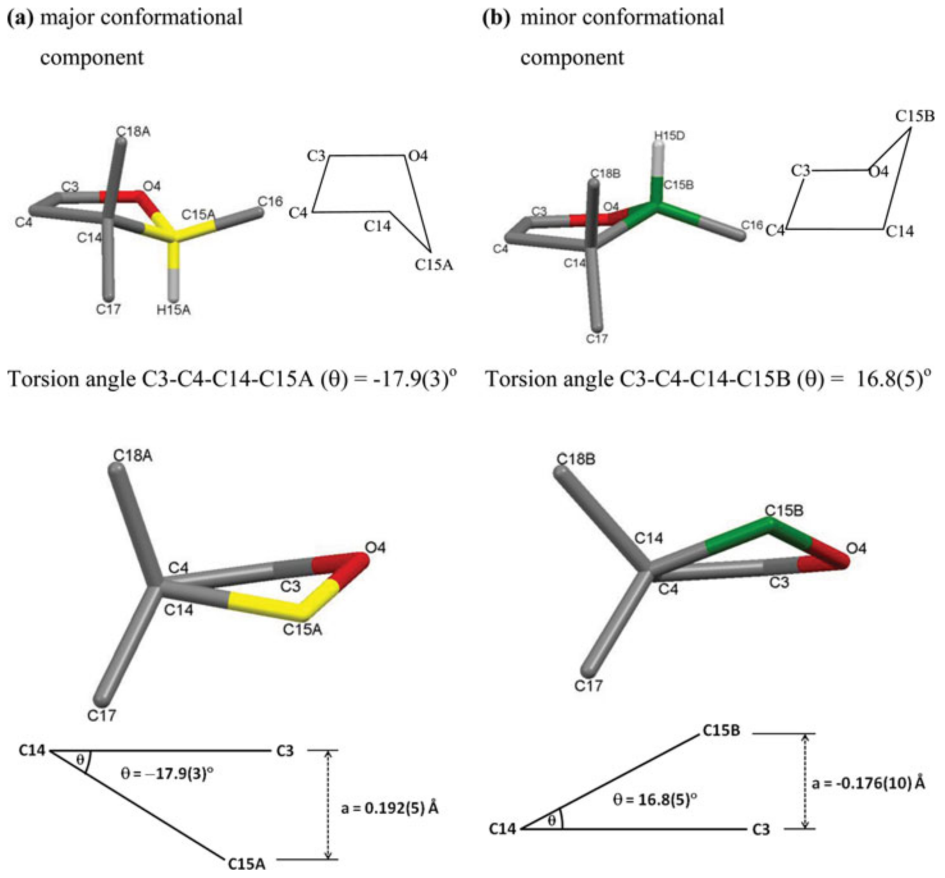


Figure 4. The crystal packing of **1**, showing the existence of both (1″S)-1 and (1″R)-1 (**a**) both major and minor conformational components, (**b**) only the major conformational component and (**c**) only the minor conformational component. H atoms were omitted for clarity.


(a) major conformational component

(b) minor conformational component

Torsion angle C3-C4-C14-C15A (θ) = -17.9(3)°

Torsion angle C3-C4-C14-C15B (θ) = 16.8(5)°

Figure 5. The torsion angles of C_3-C_4-C_{14}-$C_{15A/5B}$ and the puckering values of atom C_{15} in the (**a**) major and (**b**) minor conformational components, showing the strain of the dihydrofuran ring of **1**.

To understand the existence of the major and minor confirmational components, two important criteria's in each component need to be considered which are the dihydrofuran ring strain and the steric hindrance between the two methyl groups at position 1″ and 2″ or at atoms C_{14} and C_{15}. For the dihydrofuran ring strain, the dihydrofuran ring of both components was in an envelope conformation with the different puckering values of atom C_{15}, in which the major component (A), atom C_{15A} having the deviation of 0.192(5) Å from the mean plane of $C_3/C_4/C_{14}/O_4$ (see Fig. 5a) and with puckering parameters $Q = 0.305(3)$ Å and $\phi = 141.4(6)^\circ$ [14] and the torsion angle C_3–C_4–C_{14}–$C_{15A} = -17.9(3)^\circ$, whereas the minor component (B), the puckering atom C_{15B} having the deviation of −0.176(10) Å from the mean plane of $C_3/C_4/C_{14}/O_4$ (see Fig. 5b) and with puckering parameters $Q = 0.278(5)$ Å and $\phi = 323.3(10)^\circ$ [14] and the torsion angle C_3–C_4–C_{14}–$C_{15B} = 16.8(5)^\circ$. It can be seen that the dihydrofuran ring with puckering value of 0.192(5) Å and the torsion angle C_3–C_4–C_{14}–$C_{15A} = -17.9(3)^\circ$ should have less strain than that of the one with the puckering value of −0.176(10) Å and the torsion angle C_3–C_4–C_{14}–$C_{15B} = 16.8(5)^\circ$. It can be concluded that the former component should exist as a major component, whereas the latter one as minor conformational component due to the dihydrofuran ring strain.

Table 4. Torsion angles (°) in the α,α,β-trimethyldihydrofuran ring of the major and minor conformational components

Major component		Minor component	
Torsion angles	(°)	Torsion angles	(°)
C_{18A}–C_{14}–C_{15A}–C16	35.80	C_{17}–C_{14}–C_{15B}–C_{16}	−11.70
C_{17}–C_{14}–C_{15A}–C16	−92.90	C_{18B}–C_{14}–C_{15B}–C_{16}	98.30
C_{17}–C_{14}–C_{15A}–H_{15A}	28.54	C_{18B}–C_{14}–C_{15B}–H_{15D}	−28.70
C_4–C_{14}–C_{15A}–H_{15A}	−87.18	C_4–C_{14}–C_{15B}–H_{15D}	89.11
C_4–C_{14}–C_{15A}–O_4	27.93	C_4–C_{14}–C_{15B}–O_4	−24.61
C_{18A}–C_{14}–C_{15A}–O_4	−87.63	C_{17}–C_{14}–C_{15B}–O_4	107.57

In addition, the steric hindrance between the methyl substituents on the dihydrofuran ring can be indicated by the torsion angles which were summarized in Table 4 and Fig. 6. The key is to consider the torsion angle (Fig. 6); the torsion angle C_{18A}–C_{14}–C_{15A}–C_{16} of the major component (A) was 35.80° (Table 4 and Fig. 6a), whereas the torsion angle at C_{17}–C_{14}–C_{15B}–C_{16} of the minor component (B) was −11.70° (Table 4 and Fig. 6b). The component with the wider torsion angle (35.80°) has definitely less steric hindrance than the narrow one (−11.70°). It is suggested that the former component with the wider torsion angle should exist as the major component, whereas the latter one as the minor component. In addition, to avoid steric hindrance in the molecule of **1**, the 3-methylbut-2-enyl moiety (C_{19}–C_{23}) is rotated by 73.10(12)° with respect to the C_1–C_4/C_{11}–C_{12}

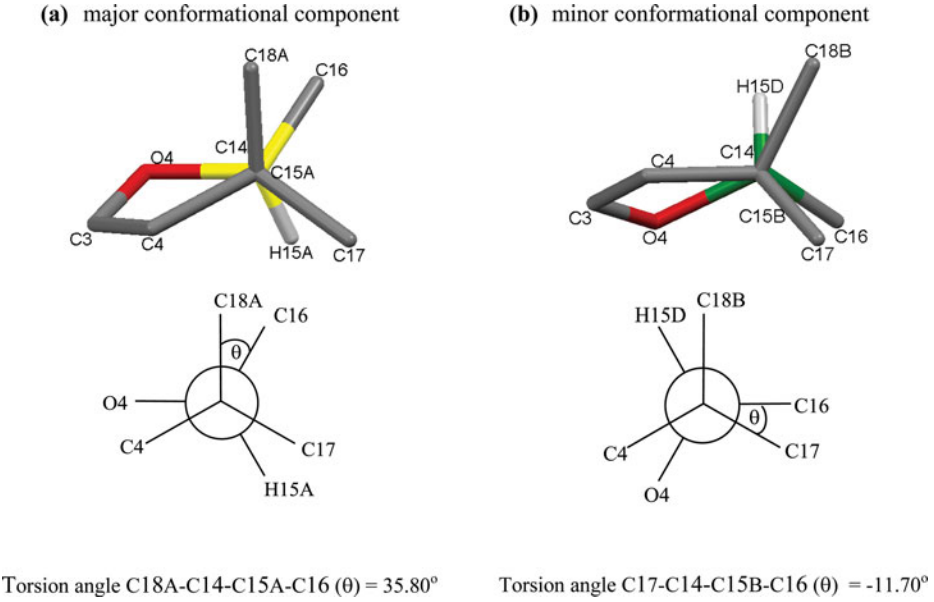


Figure 6. Conformations of the α,α,β-trimethyldihydrofuran ring and the substituent groups, showing the steric hindrance between the two methyl groups at positions C_{14} and C_{15} in the (**a**) major and (**b**) minor conformational components of **1.**

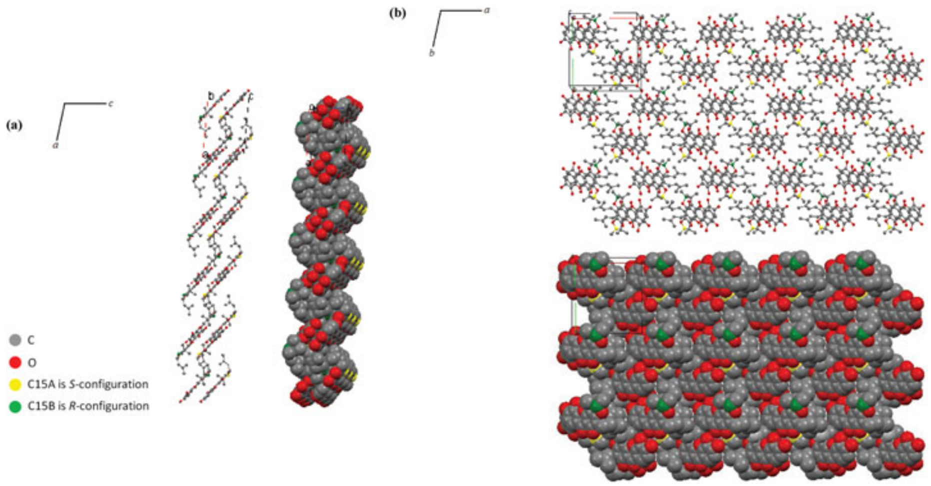


Figure 7. The crystal packing of **1**, H atoms were omitted for clarity**;** (**a**) showing the screw chains (**b**) showing the 2D network parallel to the *ab* plane.

ring. The orientation of the 3-methylbut-2-enyl moiety (C_9–C_{23}) at atom C_2 can be indicated by the torsion angle of C_2–C_{19}–C_{20}–C_{21} = $-81.2(3)^\circ$, C_{19}–C_{20}–C_{21}–C_{22} = $4.01(4)^\circ$, and C_{19}–C_{20}–C_{21}–C_{23} = $-176.2(2)^\circ$ (Table 2). Intramolecular O_2–$H_1O_3\cdots O_2$ hydrogen bond (Table 3 and Fig. 2) generate S(6) ring motif [15] which help to stabilize the planarity of the xanthone ring system.

The intra- and intermolecular hydrogen bonds (Table 3) were analyzed with the program *PLATON* [12]. In the crystal structure of **1**, the molecules are linked by O_5—$H_1O_5\cdots O_2$ hydrogen bonds (Fig. 3 and Table 3) into screw chains (Fig. 7a). These screw chains are further linked into two dimensional network parallel to the *ab* plane (Fig. 7b) by O_6–$H_1O_6\cdots O_5$ hydrogen bonds (Table 3) and are stacked along the *c*-axis by $\pi \ldots \pi$ interactions with the centroid—centroid distances of $Cg_1 \ldots Cg_2{}^d$ = 3.7520(11) Å and $Cg_1 \ldots Cg_3{}^c$ = 3.7891(11) Å; Cg_1, Cg_2, and Cg_3 are the centroids of C_9–C_{13}/O_1, C_1–C_4/C_{11}–C_{12} and C_5–C_9/C_{13} rings, respectively, with symmetry codes: $c = x, 1/2 - y, -1/2 + z$, and $d = x, 1/2 - y, 1/2 + z$. The crystal structure is consolidated and stabilized by intra- and intermolecular O–H… O hydrogen bonds together with C–H… O interactions. Details of these interactions bond lengths and bond angles are listed in Table 3. The importance of hydrogen bonds in natural products was well documented as it was known that the numbers and positions of hydrogen donors are important and related to their bioactivities. Compound **1** which is a natural product bearing a rich source of hydrogen bond donors (CH and OH) and acceptors (O) and possesses potent nitric oxide inhibitory activity and antibacterial activities [9]. Hydrogen bonds are essential to maintain the bioactive conformation and for recognition of the binding sites of the corresponding receptors [16].

Acknowledgments

NB and SC thank the Prince of Songkla University for the research facilities. The useful discussions by Assoc. Prof. Dr. Chatchanok Karalai are gratefully acknowledged.

Funding

The authors sincerely thank the Universiti Sains Malaysia for the APEX DE2012 grant No. 1002/PFIZIK/910323. The authors extend their appreciation to the Deanship of Scientific Research at King Saud University for the research group project No. RGP VPP-207.

This manuscript has not been published elsewhere and that has not been submitted simultaneously for publication elsewhere.

Supplementary Material

CCDC 910092 contains the supplementary crystallographic data for this article. These data can be obtained free of charge at http://www.ccdc.cam.ac.uk/data_request/cif, or by e-mailing data_request@ccdc.cam.ac.uk, or by contacting the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; Fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk.

References

[1] Smitinand, T. (2001). *Thai Plant Names*, Prachachon Press: Bangkok, Thailand, p. 152.

[2] Kitanov, G. M., Assenov, I., & The Van, D. (1988). *Pharmazie.*, *43*, H12.

[3] Boonnak, N., Karalai, C., Chantrapromma, S., Ponglimanont, C., Fun, H.-K., Kanjana-Opas, A., & Laphookhieo, S. (2006). *Tetrahedron.*, *62*, 8850.

[4] Boonnak, N., Karalai, C., Chantrapromma, S., Ponglimanont, C., Fun, H.-K., Kanjana-Opas, A., Chantrapromma, K., & Kato, S. (2009). *Tetrahedron.*, *65*, 3003.

[5] Boonnak, N., Karalai, C., Chantrapromma, S., Ponglimanont, C., Kanjana-Opas, A., Chantrapromma, K., & Kato, S. (2010). *Chem. Pharm. Bull.*, *58*, 386.

[6] Boonsri, S., Karalai, C., Ponglimanont, C., Kanjana-Opas, A., & Chantrapromma, K. (2006). *Phytochem.*, *67*, 723.

[7] Mahabusarakam, W., Nuangnaowarat, W., & Taylor, W. C. (2006). *Phytochem.*, *67*, 470.

[8] Phongpaichit, S., Nilrat, L., Tharavichitkul, P., Bunchoo, S., Chuaprapaisilp, T., & Wiriyachitra, P. (1994). *Songklanakarin. J. Sci.Technol.*, *16*, 399.

[9] Boonnak, N., Khamthip, A., Karalai, C., Chantrapromma, S., Ponglimanont, C., Kanjana-Opas, A., Tewtrakul, S., Chantrapromma, K., Fun, H.-K., & Kato, S. (2012). *Aust. J. Chem.*, *63*, 1550.

[10] Bruker (2009). *APEX 2, SAINT and SADABS*. Bruker AXS Inc., Madison, Wisconsin, USA.

[11] Sheldrick, G. M. (2008). *Acta Cryst.*, *A64*, 112.

[12] Spek, A. L. (2009) *Acta Cryst., D65*, 148.

[13] Macrae, C. F., Edginton, P. R., McCabe, P., Pidcook, E., Shields, G. P., Taylor, R., Towler, M., & van de Streek, J. (2006). *J. Appl. Cryst.*, *39*, 453.

[14] Cremer, D., & Pople, J. A. (1975). *J. Am. Chem. Soc.*, *97*, 1354.

[15] Bernstein, J., Davis, R. E., Shimoni, L., & Chang, N. L. (1995), *Angew. Chem. Int. Ed. Engl.*, *34*, 1555.

[16] Zhang, B., Salituro, G., Szalkowshi, D., Li, Z. H., Zhang, Y., Royo, I., Vilella, D., Diez, M. Y., Pelaez, F., Ruby, C., Kendall, R. L., Mao, X. Z., Griffin, P., Calaycay, J., Zierath, J. R., Heck, J. V., Simith, R. G., & Moller, D. E. (1999). *Science.*, *28*, 974.