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A cocrystal of clusiacitran A, clusiacitran B, fluorinated clusiacitran A and fluorinated clusiacitran B (0.45:0.45:0.05:0.05)

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Key indicators

Single-crystal X-ray study
T = 100 K
Mean σ(C–C) = 0.003 Å
Disorder in main residue
R factor = 0.057
wR factor = 0.135
Data-to-parameter ratio = 13.7

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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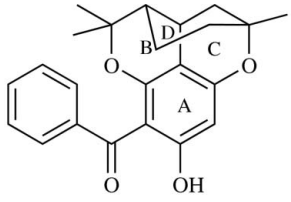
The title cocrystal, $0.45C_{23}H_{24}O_4{\cdot}0.45C_{23}H_{24}O_4{\cdot}0.05C_{23}H_{23}FO_4{\cdot}0.05C_{23}H_{23}FO_4$, is a disordered mixture of four compounds, *viz*. clusiacitran A [(9-hydroxy-1,5,5-trimethyl-6,15-dioxatetracyclo[9.3.$10^{4,13}$.$0^{7,12}$]pentadeca-7,9,-11-trien-8-yl)(phenyl)methanone], clusiacitran B [(9-hydroxy-1,5,5-trimethyl-6,15-dioxatetracyclo[9.3.$10^{4,13}$.$0^{7,12}$]pentadeca-7,9,11-trien-10-yl)(phenyl)methanone], fluorinated clusiacitran A {(10-fluoro-9-hydroxy-1,5,5-trimethyl-6,15-dioxatetracyclo[9.3.$10^{4,13}$.$0^{7,12}$]pentadeca-7,9,11-trien-8-yl)(phenyl)-methanone} and fluorinated clusiacitran B, {(10-fluoro-9-hydroxy-1,5,5-trimethyl-6,15-dioxatetracyclo[9.3.$10^{4,13}$.$0^{7,12}$]-pentadeca-7,9,11-trien-10-yl)(phenyl)methanone}, which were isolated from *Garcinia schomburgkiana* Pierre. In all the components, the cyclohexane rings adopt half-chair conformations. O—H···O intramolecular hydrogen bonds are observed. In the crystal structure, the molecules are linked *via* C—H···O intermolecular interactions, forming chains along the *b* axis.

Comment

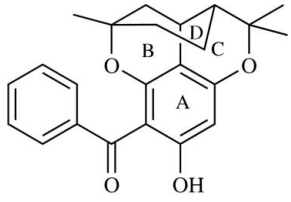
The structure analysis of the title compound, (I), has been undertaken as a part of our ongoing crystallographic investigations of biologically active compounds from natural products (Chantrapromma *et al.*, 2005; Chantrapromma, Boonnak *et al.*, 2006; Chantrapromma, Boonsri *et al.*, 2006; Chantrapromma, Fun *et al.*, 2006). The title compound is a cocrystal of a pair of regioisomers clusiacitran A/clusiacitran B and minor components of fluorinated clusiacitran A/fluorinated clusiacitran B. The title compound was isolated from *Garcinia schomburgkiana* Pierre, a plant belonging to the *Clusiaceae* (Guttiferae) family which was collected from Songkla province in southern Thailand. The traditional ethnomedicinal uses of the leaves, roots and fruits are as an expectorant, in the treatment of coughs, improvement of menstrual blood quality, treatment of diabetes and as a laxative. The crude hexane extract of the stems of this plant exhibited antimalarial activity with EC_{50} 2.2 µg ml^{-1}. Further investigation of this crude product yielded clusiacitran A, (I), and clusiacitran B, (II), which had previously been isolated from *Clusia multiflora* (Gonzalez *et al.*, 1995). However, refinement revealed a cocrystal with (I) and (II) as major components (0.45:0.45) but with minor components, (III) and (IV) (each 0.05), in which the H atom attached to C10 has been replaced by an F atom.

The asymmetric unit of the cocrystal (Fig. 1) consists of a disordered mixture of clusiacitran A and fluorinated clusiacitran A (Fig. 2), clusiacitran B and fluorinated clusiacitran B (Fig. 3), giving effectively one molecule overall. In all the four components, atoms C12 and C13 deviate from the mean plane

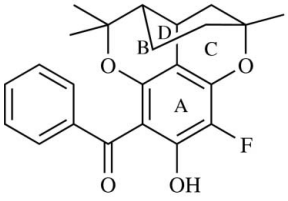
through the benzene ring *A* by −0.088 (2) and 0.072 (2) Å, respectively, and the cyclohexane ring *D* adopts a half-chair conformation. In clusiacitran A and fluorinated clusiacitran A, the pyran ring *B* is in a half-chair conformation, with Cremer & Pople (1975) puckering parameter Q = 0.665 (3) Å, θ = 65.2 (2)° and φ = 206.2 (3)°, and ring *C* is in a screw-boat conformation, with Q = 0.585 (3) Å, θ =53.0 (2)° and φ = 280.9 (3)°, whereas in clusiacitran *B* and fluorinated clusiacitran *B*, both pyran rings *B* and *C* adopt half-chair conformations, with Q = 0.647 (3) Å, θ = 125.6 (3)° and φ = 98.3 (3)° for ring *B* and Q = 0.604 (3) Å, θ = 112.8 (3)° and φ = 26.0 (3)° for ring *C*. The dihedral angle between the phenyl (C1–C6) and benzene (C8–C13) rings is 52.45 (8)°. Bond lengths and angles show normal values (Allen *et al.*, 1987).



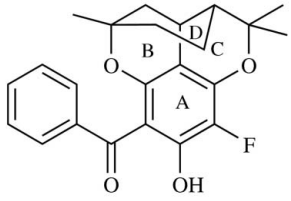
(I)



(II)



(III)



(IV)

An intramolecular O—H···O hydrogen bond is observed in the molecular structure (Table 1). In the crystal structure, the screw-related molecules are linked *via* C—H···O intermolecular interactions, forming chains along the *b* axis (Fig. 4).

Experimental

The air-dried powdered stems of *Garcinia schomburgkiana* Pierre (19.0 kg) were extracted twice with hexane (35 l) at room temperature. The crude extract (106.89 g) was subjected to flash column chromatography over silica gel, eluted with hexane and three further solvents in order of increasing polarity, CH_2Cl_2, EtOAc and CH_3OH, to give 13 fractions (G1–G13). Fraction G3 (48.20 g) was further purified by column chromatography, eluted with hexane–EtOAc (1:0 to 1:4), to afford a yellow solid of the title compound. Yellow needle-shaped single crystals of the title compound were obtained by recrystallization from $CHCl_3$–hexane (4:1 *v*/*v*) after several days. The ^{1}H and ^{13}C NMR spectra displayed resonances for a composite of a

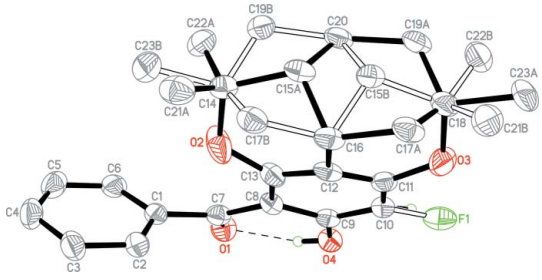


Figure 1
The asymmetric unit of (I), showing 40% probability displacement ellipsoids and the atomic numbering. All H atoms except those attached to O4 and C10 are omitted for clarity. The dashed line indicates a hydrogen bond.

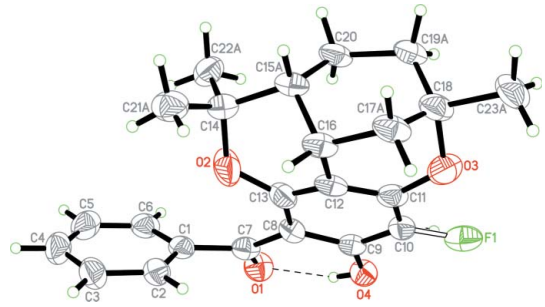


Figure 2
The disordered structure of clusiacitran A and fluorinated clusiacitran A, showing 50% probability displacement ellipsoids and the atomic numbering. The O—H···O hydrogen bond is shown as a dashed line.

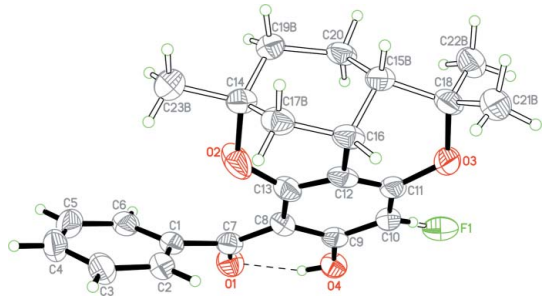


Figure 3
The disordered structure of clusiacitran B and fluorinated clusiacitran B, showing 40% probability displacement ellipsoids and the atomic numbering. The O—H···O hydrogen bond is shown as a dashed line.

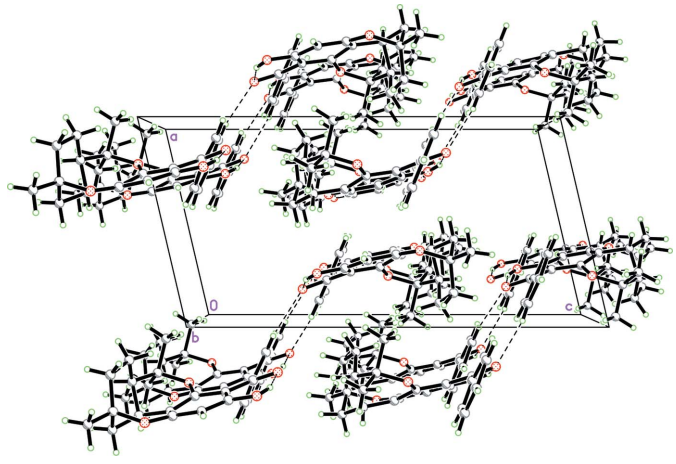


Figure 4
The crystal packing, viewed down the *b* axis. Hydrogen bonds are shown as dashed lines. Only the component clusiacitran A is shown here.

pair of regioisomeric cytriylidene derivatives (ratio 1:1). The assignment of the compounds as clusiacitran A and clusiacitran B isomers was made by the comparison of their ^{1}H and ^{13}C NMR spectroscopic data with the published data (Gonzalez *et al.*, 1995). The presence of an F atom with partial occupancy was consistent with the chemical analysis. Analysis found: C 75.46, H 06.54, O 17.61; calculated for $C_{23}H_{23.90}F_{0.10}O_4$: C 75.39, H 06.57, O 17.47.

Crystal data

$0.45C_{23}H_{24}O_4{\cdot}0.45C_{23}H_{24}O_4{\cdot}0.05C_{23}H_{23}FO_4{\cdot}0.05C_{23}H_{23}FO_4$
M_r = 366.24
Monoclinic, $P2_1/c$
a = 9.6691 (2) Å
b = 10.5583 (2) Å
c = 18.9279 (3) Å
β = 103.160 (1)°
V = 1881.59 (6) Å^3
Z = 4
D_x = 1.293 Mg m^{-3}
Mo $K\alpha$ radiation
μ = 0.09 mm^{-1}
T = 100.0 (1) K
Needle, yellow
0.42 × 0.13 × 0.11 mm

Data collection

Bruker SMART APEX2 CCD area-detector diffractometer
ω scans
Absorption correction: multi-scan (*SADABS*; Bruker, 2005)
T_{min} = 0.986, T_{max} = 0.991
22779 measured reflections
4330 independent reflections
2691 reflections with $I > 2\sigma(I)$
R_{int} = 0.047
θ_{max} = 27.5°

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.057
$wR(F^2)$ = 0.135
S = 1.05
4330 reflections
317 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0489P)^2 + 0.5555P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.25 e Å^{-3}
$\Delta\rho_{min}$ = −0.22 e Å^{-3}
Extinction correction: *SHELXTL*
Extinction coefficient: 0.0036 (7)

Table 1
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
O4—H1*O*4···O1	0.82	1.79	2.5211 (19)	148
C5—H5*A*···O1^{i}	0.93	2.43	3.333 (3)	163

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

H atoms were placed in calculated positions, with O—H = 0.82 Å and C—H = 0.93–0.96 Å. The U_{iso} values were were set equal to $1.5U_{eq}$ of the carrier atom for hydroxyl and methyl H atoms and $1.2U_{eq}$ for the remaining H atoms. From the refined occupation factors of the various disordered components, the ratio of clusiacitran A, clusiacitran B, fluorinated clusiacitran A and fluorinated clusiacitran B is found be 0.450 (2):0.450 (2):0.050 (2):0.050 (2).

Data collection: *APEX2* (Bruker, 2005); cell refinement: *APEX2*; data reduction: *SAINT* (Bruker, 2005); program(s) used to solve structure: *SHELXTL* (Sheldrick, 1998); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL* and *PLATON* (Spek, 2003).

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