

Data collection

Enraf–Nonius CAD-4 diffractometer	$\theta_{\max} = 27^\circ$
ω - 2θ scans	$h = 0 \rightarrow 6$
Absorption correction: none	$k = 0 \rightarrow 15$
1391 measured reflections	$l = 0 \rightarrow 25$
1391 independent reflections	3 standard reflections
1195 observed reflections	frequency: 60 min
[$I > 2\sigma(I)$]	intensity decay: 3.85%

Refinement

Refinement on F^2	$(\Delta/\sigma)_{\max} = -0.119$
$R[F^2 > 2\sigma(F^2)] = 0.0391$	$\Delta\rho_{\max} = 0.231 \text{ e } \text{\AA}^{-3}$
$wR(F^2) = 0.1066$	$\Delta\rho_{\min} = -0.226 \text{ e } \text{\AA}^{-3}$
$S = 1.098$	Extinction correction: none
1391 reflections	Atomic scattering factors
126 parameters	from <i>International Tables for Crystallography</i> (1992), Vol. C, Tables 4.2.6.8 and 6.1.1.4)
All H-atom parameters refined	
$w = 1/[\sigma^2(F_o^2) + (0.0682P)^2 + 0.3024P]$	
where $P = (F_o^2 + 2F_c^2)/3$	

Table 1. Fractional atomic coordinates and equivalent isotropic displacement parameters (\AA^2)

$$U_{eq} = (1/3)\sum_i \sum_j U_{ij} a_i^* a_j$$

	x	y	z	U_{eq}
O1	0.2076 (2)	0.60536 (8)	0.02947 (5)	0.0335 (3)
O2	0.2496 (2)	0.76870 (9)	0.08009 (5)	0.0393 (3)
N1	-0.2827 (2)	0.58298 (9)	0.05647 (5)	0.0256 (3)
C1	0.1256 (2)	0.68583 (10)	0.06274 (6)	0.0256 (3)
C2	-0.1510 (2)	0.68180 (10)	0.08519 (6)	0.0250 (3)
C3	-0.1742 (3)	0.6678 (2)	0.16111 (7)	0.0433 (4)
C4	-0.3560 (3)	0.57210 (14)	0.17171 (7)	0.0428 (4)
C5	-0.3127 (3)	0.50003 (12)	0.11117 (8)	0.0405 (4)
OW1	0.1879 (3)	0.36355 (12)	0.20966 (8)	0.0529 (4)

Table 2. Selected torsion angles ($^\circ$)

O1—C1—C2—N1	-5.45 (15)	C3—C4—C5—N1	-39.6 (2)
O2—C1—C2—N1	175.42 (11)	C2—N1—C5—C4	34.71 (14)
N1—C2—C3—C4	-9.3 (2)	C5—N1—C2—C3	-15.75 (14)
C2—C3—C4—C5	30.4 (2)		

Table 3. Hydrogen-bonding geometry (\AA , $^\circ$)

D—H...A	H...A	D...A	H—D...A	D—H...A
N1—H1N1...O1 ⁱ	2.19 (2)	2.883 (1)	34 (1)	133 (1)
N1—H2N1...O1 ⁱⁱ	1.91 (2)	2.755 (1)	13 (1)	161 (2)
OW1—H1W...O2 ⁱⁱⁱ	2.05 (3)	2.859 (2)	1 (2)	179 (2)
OW1—H2W...OW1 ^{iv}	2.32 (3)	3.094 (2)	3 (2)	177 (3)

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

Data collection: Enraf–Nonius CAD-4 diffractometer software. Cell refinement: Enraf–Nonius CAD-4 diffractometer software. Data reduction: local program. Program(s) used to solve structure: *SHELXS86* (Sheldrick, 1985). Program(s) used to refine structure: *SHELXL93* (Sheldrick, 1993). Molecular graphics: *PLATON* (Spek, 1990), *PLUTO* (Motherwell, 1982).

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The computations were performed at the Supercomputer Education and Research Centre at the Institute.

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: HU1113). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

References

- Ashida, T. & Kakudo, M. (1974). *Bull. Chem. Soc. Jpn.* **47**, 1129–1133.
- Fox, R. O. & Rosenstein, P. D. (1976). *Am. Crystallogr. Assoc. Abstr.* p. 50.
- Kayushina, R. L. & Vainshtein, B. K. (1966). *Soviet Phys. Crystallogr.* **10**, 698–706.
- Motherwell, W. D. S. (1982). *PLUTO. Program for Plotting Molecular and Crystal Structures*. Chemical Crystallography Laboratory, Univ. of Cambridge, England. (Modified by J. L. Sussman & N. H. F. Beebe.)
- Nair, C. M. K. & Vijayan, M. (1981). *J. Indian Inst. Sci.* **63**, 81–103.
- Prasad, G. S. & Vijayan, M. (1993). *Acta Cryst.* **B49**, 348–356.
- Sheldrick, G. M. (1985). *SHELXS86. Program for the Solution of Crystal Structures*. Univ. of Göttingen, Germany.
- Sheldrick, G. M. (1993). *SHELXL93. Program for Refinement of Crystal Structures*. Univ. of Göttingen, Germany.
- Soman, J. & Vijayan, M. (1989). *J. Biosci.* **14**, 111–125.
- Spek, A. L. (1990). *Acta Cryst.* **A46**, C-34.
- Suresh, S., Prasad, G. S. & Vijayan, M. (1994). *Int. J. Prot. Pep. Res.* **43**, 139–145.
- Suresh, C. G. & Vijayan, M. (1983). *Int. J. Prot. Pep. Res.* **22**, 129–143.
- Vijayan, M. (1988). *Prog. Biophys. Mol. Biol.* **52**, 71–99.

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Ethyl 6,7-Bis(trifluoromethyl)isocoumarin-3-carboxylate: Formed by a Novel Diels–Alder Cycloaddition Involving Two Different α,β -Unsaturated Esters

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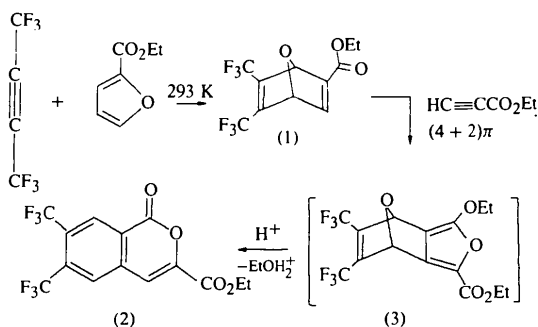
Abstract

In common with other isocoumarin-based molecules, the planar fused ring system [maximum deviation 0.05 (2) \AA] in the title molecule, ethyl 1-oxo-6,7-bis(trifluoromethyl)-1*H*-2-benzopyran-3-carboxylate, C₁₄H₈F₆O₄, contains a non-delocalized double bond

[C=C 1.34 (2) Å]. Pairs of molecules form π -bonded dimers, centred on inversion points at $y = \frac{1}{4}$ and $\frac{3}{4}$ [closest interplanar C...C approach 3.59 (3) Å]. Consequently, the crystal structure is composed of alternating aromatic ($y = \frac{1}{4}$ or $\frac{3}{4}$) and aliphatic zones ($y = 0$ or $\frac{1}{2}$).

Comment

The structure determination was carried out as part of a general investigation of the chemistry of acetylenes of type $\text{CF}_3\text{C}\equiv\text{CR}$ and their Diels–Alder cycloadducts (Abubakar, 1990; Suliman, 1990; Abubakar, Booth, Suliman & Tipping, 1992; Suliman, 1993). In particular, unequivocal structural proof was required that the product of the reaction of the norbornadiene derivative (1) with ethyl propynoate was the isocoumarin (2).



Compound (2) is considered to have been formed *via* novel Diels–Alder cycloaddition involving two different α,β -unsaturated esters, *i.e.* the C=C–C=O system in (1) functioned as the diene component and the acetylene triple bond in the propynoate as the dienophile. This afforded the 1:1 adduct (3) which then underwent acid-catalysed elimination of ethanol to give (2); the mechanism has been fully explained previously (Abubakar, Booth, Suliman & Tipping, 1992).

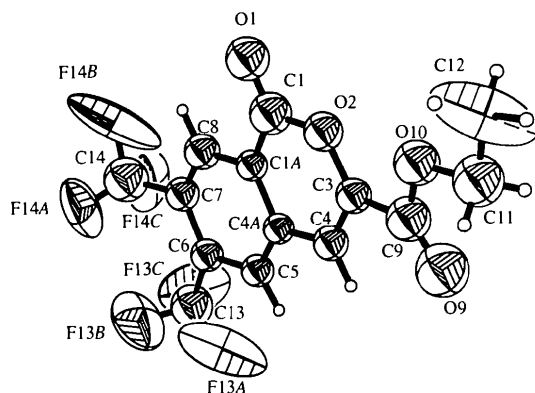


Fig. 1. The title molecule (ORTEP); Johnson, 1976) showing the atomic numbering scheme. Ellipsoids are drawn at the 50% probability level.

Experimental

A mixture of ethyl 2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene-5-carboxylate (1.50 g, 4.97 mmol) and ethyl propynoate (0.50 g, 5.10 mmol), heated at 423 K (7 d) in a Rotaflo tube (*ca* 250 cm³) gave material (1.80 g) which was purified by dry-column flash chromatography [silica Kieselgel 60H, eluant petroleum ether (b.p. 313–333 K)/CH₂Cl₂ 1:1 v/v] to afford the title compound (2) (1.48 g, 4.18 mmol, 84%; found C 47.8, H 2.5, F 31.9%, M^+ 354; C₁₄H₈F₆O₄ requires C 47.5, H 2.3, F 32.3%, M 354; m.p. 465–467 K) (see scheme above). Compound (2) was recrystallized from *n*-C₅H₁₂/CH₂Cl₂ (1:1 v/v).

Crystal data

C₁₄H₈F₆O₄
 $M_r = 354.21$
 Monoclinic
 C2/c
 $a = 27.511 (5) \text{ \AA}$
 $b = 6.666 (3) \text{ \AA}$
 $c = 17.351 (3) \text{ \AA}$
 $\beta = 115.30 (3)^\circ$
 $V = 2876 (3) \text{ \AA}^3$
 $Z = 8$
 $D_x = 1.636 \text{ Mg m}^{-3}$

Mo K α radiation

$\lambda = 0.71069 \text{ \AA}$

Cell parameters from 25 reflections

$\theta = 12.60\text{--}21.96^\circ$

$\mu = 0.1602 \text{ mm}^{-1}$

$T = 296 \text{ K}$

Needle

0.40 × 0.15 × 0.15 mm

Colourless

Data collection

CAD-4 diffractometer

$\omega/2\theta$ scans

Absorption correction:

none

4626 measured reflections

2002 independent reflections

521 observed reflections

$[I > 2\sigma(I)]$

$R_{\text{int}} = 0.032$

$\theta_{\text{max}} = 23.0^\circ$

$h = -30 \rightarrow 27$

$k = 0 \rightarrow 7$

$l = 0 \rightarrow 18$

3 standard reflections

monitored every 150

reflections

intensity decay: insignificant

Refinement

Refinement on F^2

$R = 0.068$

$wR = 0.042$

$S = 1.93$

521 reflections

132 parameters

H-atom parameters not

refined

$w = 1/\sigma^2(F)$

$(\Delta/\sigma)_{\text{max}} = 0.09$

$\Delta\rho_{\text{max}} = 0.35 \text{ e \AA}^{-3}$

$\Delta\rho_{\text{min}} = -0.37 \text{ e \AA}^{-3}$

Extinction correction: none

Atomic scattering factors

from *International Tables*

for *X-ray Crystallography*

(1974, Vol. IV)

Table 1. Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (\AA^2)

U_{iso} for all atoms except C12 and the F atoms, for which $U_{\text{eq}} = (1/3)\sum_i\sum_j U_{ij}a_i^*a_j^*a_i\cdot a_j$.

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{eq}}/U_{\text{iso}}$
O1	0.2786 (5)	0.937 (2)	0.7496 (9)	0.077 (6)
O2	0.2983 (5)	0.663 (3)	0.7020 (8)	0.061 (5)
O9	0.3183 (6)	0.203 (3)	0.616 (1)	0.105 (7)
O10	0.3588 (5)	0.343 (3)	0.7447 (8)	0.073 (5)
C1	0.2648 (10)	0.830 (4)	0.690 (2)	0.073 (9)
C1a	0.2172 (8)	0.834 (4)	0.610 (1)	0.041 (7)
C3	0.2870 (9)	0.516 (4)	0.642 (1)	0.049 (7)
C4	0.2417 (9)	0.520 (4)	0.570 (1)	0.052 (7)
C4a	0.2038 (8)	0.680 (4)	0.550 (1)	0.041 (7)

C5	0.1570 (8)	0.698 (4)	0.475 (1)	0.048 (7)
C6	0.1198 (9)	0.851 (4)	0.464 (1)	0.050 (7)
C7	0.1346 (10)	1.003 (4)	0.526 (1)	0.055 (8)
C8	0.1814 (8)	0.988 (4)	0.598 (1)	0.058 (8)
C9	0.3216 (9)	0.322 (5)	0.665 (2)	0.073 (9)
C11	0.3956 (9)	0.160 (5)	0.771 (1)	0.087 (10)
C12	0.432 (1)	0.198 (4)	0.854 (2)	0.17 (1)
C13	0.070 (1)	0.835 (7)	0.381 (2)	0.09 (1)
C14	0.093 (2)	1.163 (7)	0.520 (2)	0.10 (1)
F13A	0.0688 (7)	0.706 (3)	0.334 (1)	0.19 (1)
F13B	0.0299 (6)	0.825 (4)	0.3952 (9)	0.17 (1)
F13C	0.0605 (8)	0.994 (3)	0.334 (1)	0.18 (1)
F14A	0.0503 (6)	1.126 (2)	0.513 (1)	0.14 (1)
F14B	0.1160 (7)	1.293 (3)	0.579 (1)	0.22 (1)
F14C	0.0860 (7)	1.276 (3)	0.451 (1)	0.14 (1)

Table 2. Selected geometric parameters (Å, °)

O2—C1	1.40 (2)	C4—C4a	1.42 (2)
O2—C3	1.36 (2)	C4a—C5	1.39 (2)
C1a—C8	1.38 (2)	C5—C6	1.40 (2)
C3—C4	1.34 (2)	C6—C7	1.41 (2)
C3—C9	1.55 (3)	C7—C8	1.36 (2)
C1—O2—C3	122 (2)	C1a—C4a—C4	116 (2)
O1—C1—O2	114 (2)	C1a—C4a—C5	118 (2)
O2—C1—C1a	115 (3)	C4—C4a—C5	126 (3)
C1—C1a—C4a	123 (3)	C4a—C5—C6	121 (2)
C1—C1a—C8	117 (3)	C5—C6—C7	118 (2)
C4a—C1a—C8	120 (2)	C6—C7—C8	120 (3)
O2—C3—C4	121 (2)	C1a—C8—C7	122 (3)
C3—C4—C4a	123 (2)		

The low number of significant reflections meant that only the peripheral atoms could be refined anisotropically. The high vibrational amplitudes displayed by the terminal groups, possibly an indication of disorder, explained the low number of observed reflections and the relatively high *R* factor of 0.096 obtained when all 2002 independent reflections were used.

Data collection: *CAD-4 Software* (Enraf-Nonius, 1989). Cell refinement: *CAD-4 Software*. Data reduction: *TEXSAN PROCESS* (Molecular Structure Corporation, 1985). Program(s) used to solve structure: *SHELXS86* (Sheldrick, 1985). Program(s) used to refine structure: *TEXSAN LS*. Molecular graphics: *ORTEPII* (Johnson, 1976). Software used to prepare material for publication: *TEXSAN FINISH*. Literature survey: *CSSR* (1984).

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: L11134). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

References

- Abubakar, A. B. (1990). PhD thesis, Univ. of Manchester, England.
 Abubakar, A. B., Booth, B. L., Suliman, N. N. E. & Tipping, A. E. (1992). *Fluorine Chem.* **56**, 359–371.
CSSR (1984). *Crystal Structure Search and Retrieval Instruction Manual*. SERC Daresbury Laboratory, Warrington, England.
 Enraf-Nonius (1989). *CAD-4 Software*. Version 5.0. Enraf-Nonius, Delft, The Netherlands.
 Johnson, C. K. (1976). *ORTEPII*. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.
 Molecular Structure Corporation (1985). *TEXSAN. TEXRAY Structure Analysis Package*. MSC, 3200A Research Forest Drive, The Woodlands, TX 77381, USA.
 Sheldrick, G. M. (1985). *SHELXS86. Program for the Solution of Crystal Structures*. Univ. of Göttingen, Germany.
 Suliman, N. N. E. (1990). MSc thesis, Univ. of Manchester, England.
 Suliman, N. N. E. (1993). PhD thesis, Univ. of Manchester, England.

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Structural Studies of Intermediates in the Synthesis of Mifepristone (RU 486). IV. An α -Epoxy Steroid

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Abstract

Crystallographic characterization of the title compound, 5 α ,10 α -epoxy-3,3-ethylenedioxy-17 β -hydroxy-17 α -(1-propynyl)-9(11)-estrene, C₂₃H₃₀O₄, establishes the configuration of the epoxy O atom as 5 α ,10 α and locates the double bond between C9 and C11. The asymmetric unit contains two crystallographically independent molecules which are related by a pseudo twofold screw axis. The presence of an epoxy O atom between C5 and C10 causes strain in the molecules, and this is reflected in the distortion of bond angles around several tetrahedral C atoms. The propynyl group is oriented perpendicular to the steroid skeleton. The molecular structure is stabilized by a network of O—H···O hydrogen bonds.

Comment

The title 5 α ,10 α -epoxy steroid, (III), is a key intermediate in the synthesis of mifepristone (RU 486), (I), the first steroidal antiprogestosterone drug for non-surgical abortion in clinical use (Ulmann & Dubois, 1989; Heikinheimo, Ylikorkala & Lahteenmaki, 1990). The antagonistic activity of RU 486 is due to the 11 β -dimethylaminophenyl substitution (Benhamou *et al.*, 1992). Crystallographic characterization has established the configuration of the epoxy O atom as 5 α ,10 α and has located the double bond between C9 and C11. Fig. 1 depicts the conformation of the two crystallographically independent molecules, 1 and 2, present in the asymmetric unit, which are related by a pseudo twofold screw axis. The bond distances, angles and relevant torsion angles are in satisfactory agreement with accepted values (Duax, Griffin, Strong & Wood, 1989). The high e.s.d.'s of the bond lengths may be due to the poor ratio of the number of observations to parameters, a consequence of having two molecules in the asymmetric unit and the relatively weak diffracting properties of the crystal. That