Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

2-Ethyl-1,3-dioxo-2,3,3a,4,7,7a-hexahydro-1*H*-isoindole-4-carboxylic acid

Ilpo Mutikainen,[a]* Alexandros Kiriazis,[b] Tuomo Leikoski[b] and Jari Yli-Kauhaluoma[b]

[a]University of Helsinki, Department of Chemistry, Laboratory of Inorganic Chemistry, PO Box 55, FIN-00014 Helsinki, Finland, and [b]University of Helsinki, Faculty of Pharmacy, Division of Pharmaceutical Chemistry, PO Box 56, FI-00014 Helsinki, Finland
Correspondence e-mail: ilpo.mutikainen@helsinki.fi

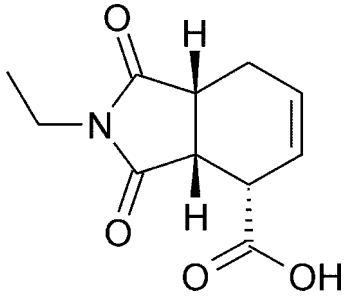
Received 1 June 2007; accepted 6 June 2007

Key indicators: single-crystal X-ray study; T = 173 K; mean σ(C–C) = 0.003 Å; R factor = 0.056; wR factor = 0.130; data-to-parameter ratio = 15.8.

The Diels–Alder cycloaddition reactions between deactivated dienes and electron-deficient dienophiles are generally known to be thermodynamically disfavoured but when low solvent volumes were used for the reaction, the cycloaddition of 4-(bromomethyl)phenoxymethyl polystyrene-bound (*E*)-1,3-butadiene-1-carboxylic acid with *N*-ethylmaleimide gave the title compound, $C_{11}H_{13}NO_4$, in good yield. The molecules are connected through hydrogen bonds between the carboxyl group and one exocyclic carbonyl oxygen. The title compound is interesting in medicinal chemistry since related compounds are known to increase the blood platelet count in thrombocytopenia and to possess anticonvulsant activity.

Related literature

For related literature, see: Bailleux *et al.* (1994); Kanai *et al.* (2000); Kiriazis *et al.* (2004); Morphy *et al.* (2002).



Experimental

Crystal data

$C_{11}H_{13}NO_4$
M_r = 223.22
Monoclinic, $P2_1/c$
a = 8.432 (1) Å
b = 8.588 (1) Å
c = 14.342 (2) Å
β = 94.07 (2)°
V = 1035.9 (2) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.11 mm^{-1}
T = 173 (2) K
0.25 × 0.11 × 0.10 mm

Data collection

Nonius KappaCCD diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.97, T_{max} = 0.99
7378 measured reflections
2350 independent reflections
1345 reflections with $I > 2\sigma(I)$
R_{int} = 0.078

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.056
$wR(F^2)$ = 0.130
S = 1.00
2350 reflections
149 parameters
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$ = 0.41 e Å^{-3}
$\Delta\rho_{min}$ = −0.25 e Å^{-3}

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

D—H···A	D—H	H···A	D···A	D—H···A
O1—H1A···O4^{i}	0.89 (3)	1.83 (3)	2.690 (2)	164 (2)

Symmetry code: (i) $x+1, y, z$.

Data collection: *COLLECT* (Nonius, 2002); cell refinement: *DIRAX* (Duisenberg, 1992); data reduction: *EVAL* (Nonius, 2002); program(s) used to solve structure: *SIR2002* (Burla *et al.*, 2003); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXTL* (Sheldrick, 1990); software used to prepare material for publication: *SHELXTL*.

The authors thank the National Technology Agency TEKES for financial support.

Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: BG2064).

References

Bailleux, V., Vallee, L., Nyuts, J.-P. & Vamecq, J. (1994). *Chem. Pharm. Bull.* **42**, 1817–1821.
Burla, M. C., Camalli, M., Carrozzini, B., Cascarano, G. L., Giacovazzo, C., Polidori, G. & Spagna, R. (2003). *J. Appl. Cryst.* **36**, 1103.
Duisenberg, A. J. M. (1992). *J. Appl. Cryst.* **25**, 92–96.
Kanai, F., Murakata, I., Yamashita, K., Shiotsi, Y., Akinaga, S. & Tamaoki, T. (2000). Jpn. Patent 044 562 .
Kiriazis, A., Leikoski, T., Mutikainen, I. & Yli-Kauhaluoma, J. (2004). *J. Comb. Chem.* **6**, 283–285.
Morphy, J. R., Rankovic, Z. & York, M. (2002). *Tetrahedron Lett.* **43**, 5973–5975.
Nonius (2002). *COLLECT* and *EVAL*. Nonius BV, Delft, The Netherlands.
Sheldrick, G. M. (1990). *SHELXTL*. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.
Sheldrick, G. M. (1996). *SADABS*. University of Göttingen, Germany.
Sheldrick, G. M. (1997). *SHELXL97*. University of Göttingen, Germany.

  doi:10.1107/S1600536807027900

supplementary materials

Acta Cryst. (2007). E**63**, o3240 [**doi:10.1107/S1600536807027900**]

2-Ethyl-1,3-dioxo-2,3,3a,4,7,7a-hexahydro-1*H*-isoindole-4-carboxylic acid

I. Mutikainen, A. Kiriazis, T. Leikoski and J. Yli-Kauhaluoma

Comment

The Diels-Alder cycloaddition reactions between deactivated dienes and electron-deficient dienophiles are generally known to be thermodynamically disfavoured. We have recently found that when low solvent volumes (Morphy *et al.*, 2002) were used for the reaction, the disfavoured cycloaddition of the 4-(bromomethyl)-phenoxymethyl polystyrene-bound (*E*)-1,3-butadiene-1-carboxylic acid with *N*-ethylmaleimide (PhMe, rt, 2 d) gave the *endo* cycloadduct in 40% yield (Kiriazis *et al.*, 2004). The hexahydro-1,3-dioxoisoindole structure of the cycloadduct is very interesting in medicinal chemistry. For example, the related compounds are known to increase the blood platelet count in thrombocytopenia (Kanai *et al.*, 2000) and to possess anticonvulsant activity (Bailleux *et al.*, 1994).

Experimental

Polystyrene-bound 1,3-butadiene-1-carboxylic acid (1.4 mmol/g, 600 mg) was treated with *N*-ethylmaleimide (8.4 mmol, 1.05 g) in toluene (1.0 ml) at room temperature for 48 h. Cleavage with TFA-CH_2Cl_2 1:4 (8 ml) over 2 h at room temperature and purification by successive trituration with hexane, Et_2O and EtOAc gave the *endo* cycloadduct (75 mg, 40%) as white crystals, mp 156–158 °C.

Refinement

The H atom connected to the carboxylate oxygen was situated from the difference map and refined isotropically. Other H atoms were introduced at calculated positions and allowed to ride, with C—H = 0.95–1.00 Å, U_{iso}=1.2/1.5× U_{eq}(carrier).

Figures

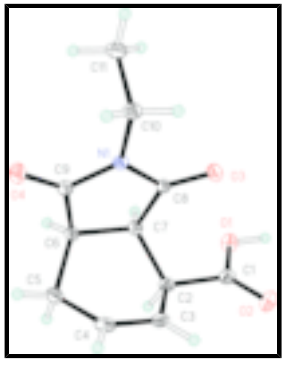


Fig. 1. View of the molecule. Thermal ellipsoids are drawn at 30% probability.

2-Ethyl-1,3-dioxo-2,3,3a,4,7,7a-hexahydro-1*H*-isoindole-4-carboxylic acid

Crystal data

$C_{11}H_{13}NO_4$	$F_{000} = 472$
$M_r = 223.22$	$D_x = 1.431$ Mg m^{-3}
Monoclinic, $P2_1/c$	Mo $K\alpha$ radiation $\lambda = 0.71073$ Å
Hall symbol: -P 2ybc	Cell parameters from 257 reflections
$a = 8.432$ (1) Å	$\theta = 2.2$–17.9º
$b = 8.588$ (1) Å	$\mu = 0.11$ mm^{-1}
$c = 14.342$ (2) Å	$T = 173$ (2) K
$\beta = 94.07$ (2)º	Needle, colorless
$V = 1035.9$ (2) Å^3	0.25 × 0.11 × 0.10 mm
$Z = 4$	

Data collection

Nonius Kappa CCD diffractometer	2350 independent reflections
Radiation source: fine-focus sealed tube	1345 reflections with $I > 2\sigma(I)$
Monochromator: graphite	$R_{int} = 0.078$
$T = 173$(2) K	$\theta_{max} = 27.5$º
ω scans	$\theta_{min} = 5.3$º
Absorption correction: multi-scan (SADABS; Sheldrick, 1996)	$h = -9 \rightarrow 10$
$T_{min} = 0.97$, $T_{max} = 0.99$	$k = -11 \rightarrow 11$
7378 measured reflections	$l = -18 \rightarrow 12$

Refinement

Refinement on F^2	Secondary atom site location: difference Fourier map
Least-squares matrix: full	Hydrogen site location: inferred from neighbouring sites
$R[F^2 > 2\sigma(F^2)] = 0.056$	H atoms treated by a mixture of independent and constrained refinement
$wR(F^2) = 0.130$	$w = 1/[\sigma^2(F_o^2) + (0.0571P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$S = 1.00$	$(\Delta/\sigma)_{max} < 0.001$
2350 reflections	$\Delta\rho_{max} = 0.41$ e Å^{-3}
149 parameters	$\Delta\rho_{min} = -0.25$ e Å^{-3}
Primary atom site location: structure-invariant direct methods	Extinction correction: none

Special details

Geometry. All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes.

Refinement. Refinement of F^2 against ALL reflections. The weighted *R*-factor *wR* and goodness of fit S are based on F^2, conventional *R*-factors *R* are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\text{sigma}(F^2)$ is used only for calculating *R*-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. *R*-factors based on F^2 are statistically about twice as large as those based on F, and R– factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}
O1	1.20615 (19)	0.12766 (19)	0.18956 (12)	0.0291 (5)
H1A	1.305 (3)	0.108 (3)	0.2114 (19)	0.040 (8)*
O2	1.20296 (19)	−0.1224 (2)	0.14398 (13)	0.0344 (5)
O3	1.01229 (17)	−0.02571 (19)	0.33666 (12)	0.0275 (4)
O4	0.48321 (17)	0.0661 (2)	0.28732 (12)	0.0337 (5)
N1	0.74206 (19)	0.0088 (2)	0.33060 (13)	0.0191 (5)
C1	1.1350 (3)	0.0004 (3)	0.15529 (17)	0.0230 (6)
C2	0.9591 (2)	0.0274 (3)	0.12836 (17)	0.0208 (5)
H2A	0.9518	0.0958	0.0718	0.025*
C3	0.8682 (3)	−0.1201 (3)	0.10316 (16)	0.0244 (6)
H3A	0.9225	−0.2159	0.0965	0.029*
C4	0.7109 (3)	−0.1129 (3)	0.09050 (17)	0.0271 (6)
H4A	0.6509	−0.2048	0.0771	0.032*
C5	0.6282 (3)	0.0415 (3)	0.09743 (17)	0.0272 (6)
H5A	0.5127	0.0242	0.1009	0.033*
H5B	0.6436	0.1039	0.0408	0.033*
C6	0.6941 (2)	0.1316 (3)	0.18465 (16)	0.0208 (5)
H6A	0.6670	0.2445	0.1772	0.025*
C7	0.8756 (2)	0.1135 (3)	0.20590 (15)	0.0184 (5)
H7A	0.9244	0.2190	0.2154	0.022*
C8	0.8919 (2)	0.0247 (3)	0.29702 (16)	0.0187 (5)
C9	0.6239 (2)	0.0690 (3)	0.27090 (16)	0.0216 (5)
C10	0.7154 (3)	−0.0611 (3)	0.42150 (17)	0.0251 (6)
H10A	0.8034	−0.1338	0.4396	0.030*
H10B	0.6151	−0.1214	0.4164	0.030*
C11	0.7061 (3)	0.0629 (3)	0.49656 (18)	0.0313 (6)
H11A	0.6884	0.0130	0.5564	0.047*
H11B	0.6180	0.1340	0.4793	0.047*
H11C	0.8061	0.1215	0.5024	0.047*

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0200 (8)	0.0271 (9)	0.0400 (12)	−0.0019 (8)	0.0004 (7)	0.0025 (9)
O2	0.0329 (9)	0.0281 (10)	0.0428 (12)	0.0084 (8)	0.0069 (8)	−0.0017 (9)
O3	0.0229 (8)	0.0337 (10)	0.0256 (10)	0.0041 (7)	−0.0020 (7)	0.0018 (8)
O4	0.0199 (8)	0.0499 (12)	0.0315 (11)	0.0012 (8)	0.0033 (7)	0.0026 (9)
N1	0.0222 (9)	0.0199 (11)	0.0154 (11)	−0.0004 (8)	0.0033 (8)	0.0012 (8)
C1	0.0276 (12)	0.0247 (13)	0.0173 (13)	−0.0012 (11)	0.0065 (10)	0.0037 (11)
C2	0.0249 (11)	0.0215 (13)	0.0165 (13)	0.0021 (10)	0.0035 (9)	0.0024 (10)
C3	0.0329 (13)	0.0208 (12)	0.0195 (14)	0.0024 (11)	0.0011 (10)	−0.0047 (11)
C4	0.0347 (13)	0.0241 (13)	0.0221 (14)	−0.0067 (11)	0.0004 (10)	−0.0058 (11)
C5	0.0259 (12)	0.0341 (15)	0.0210 (14)	−0.0010 (11)	−0.0028 (10)	−0.0003 (12)
C6	0.0215 (11)	0.0191 (11)	0.0214 (13)	0.0027 (10)	−0.0017 (9)	−0.0013 (11)
C7	0.0201 (11)	0.0158 (11)	0.0192 (13)	−0.0024 (9)	0.0011 (9)	−0.0010 (10)
C8	0.0203 (11)	0.0162 (12)	0.0191 (13)	0.0006 (10)	−0.0013 (9)	−0.0054 (10)
C9	0.0216 (11)	0.0220 (13)	0.0209 (14)	0.0018 (10)	−0.0006 (10)	−0.0041 (11)
C10	0.0307 (12)	0.0260 (13)	0.0193 (14)	0.0005 (11)	0.0057 (10)	0.0025 (11)
C11	0.0345 (13)	0.0380 (15)	0.0215 (15)	−0.0024 (12)	0.0020 (11)	−0.0011 (12)

Geometric parameters (Å, °)

O1—C1	1.325 (3)	C4—H4A	0.9500
O1—H1A	0.89 (3)	C5—C6	1.541 (3)
O2—C1	1.217 (3)	C5—H5A	0.9900
O3—C8	1.208 (3)	C5—H5B	0.9900
O4—C9	1.226 (2)	C6—C9	1.508 (3)
N1—C9	1.368 (3)	C6—C7	1.547 (3)
N1—C8	1.391 (3)	C6—H6A	1.0000
N1—C10	1.467 (3)	C7—C8	1.511 (3)
C1—C2	1.523 (3)	C7—H7A	1.0000
C2—C3	1.511 (3)	C10—C11	1.520 (3)
C2—C7	1.546 (3)	C10—H10A	0.9900
C2—H2A	1.0000	C10—H10B	0.9900
C3—C4	1.327 (3)	C11—H11A	0.9800
C3—H3A	0.9500	C11—H11B	0.9800
C4—C5	1.505 (3)	C11—H11C	0.9800
C1—O1—H1A	111.1 (18)	C9—C6—H6A	109.5
C9—N1—C8	112.67 (19)	C5—C6—H6A	109.5
C9—N1—C10	124.08 (17)	C7—C6—H6A	109.5
C8—N1—C10	123.24 (18)	C8—C7—C2	111.26 (18)
O2—C1—O1	124.0 (2)	C8—C7—C6	104.42 (17)
O2—C1—C2	123.9 (2)	C2—C7—C6	113.64 (18)
O1—C1—C2	112.1 (2)	C8—C7—H7A	109.1
C3—C2—C1	113.65 (19)	C2—C7—H7A	109.1
C3—C2—C7	108.91 (17)	C6—C7—H7A	109.1
C1—C2—C7	112.04 (18)	O3—C8—N1	123.7 (2)

C3—C2—H2A	107.3	O3—C8—C7	127.59 (19)
C1—C2—H2A	107.3	N1—C8—C7	108.66 (18)
C7—C2—H2A	107.3	O4—C9—N1	122.9 (2)
C4—C3—C2	118.6 (2)	O4—C9—C6	127.3 (2)
C4—C3—H3A	120.7	N1—C9—C6	109.74 (17)
C2—C3—H3A	120.7	N1—C10—C11	111.22 (19)
C3—C4—C5	119.7 (2)	N1—C10—H10A	109.4
C3—C4—H4A	120.2	C11—C10—H10A	109.4
C5—C4—H4A	120.2	N1—C10—H10B	109.4
C4—C5—C6	110.73 (19)	C11—C10—H10B	109.4
C4—C5—H5A	109.5	H10A—C10—H10B	108.0
C6—C5—H5A	109.5	C10—C11—H11A	109.5
C4—C5—H5B	109.5	C10—C11—H11B	109.5
C6—C5—H5B	109.5	H11A—C11—H11B	109.5
H5A—C5—H5B	108.1	C10—C11—H11C	109.5
C9—C6—C5	110.30 (18)	H11A—C11—H11C	109.5
C9—C6—C7	104.05 (18)	H11B—C11—H11C	109.5
C5—C6—C7	113.84 (17)		
O2—C1—C2—C3	11.0 (3)	C9—N1—C8—O3	−176.9 (2)
O1—C1—C2—C3	−171.04 (19)	C10—N1—C8—O3	4.7 (3)
O2—C1—C2—C7	135.0 (2)	C9—N1—C8—C7	3.2 (3)
O1—C1—C2—C7	−47.1 (2)	C10—N1—C8—C7	−175.14 (19)
C1—C2—C3—C4	171.3 (2)	C2—C7—C8—O3	51.0 (3)
C7—C2—C3—C4	45.7 (3)	C6—C7—C8—O3	174.0 (2)
C2—C3—C4—C5	2.6 (3)	C2—C7—C8—N1	−129.13 (18)
C3—C4—C5—C6	−46.2 (3)	C6—C7—C8—N1	−6.2 (2)
C4—C5—C6—C9	−78.7 (2)	C8—N1—C9—O4	179.7 (2)
C4—C5—C6—C7	37.8 (3)	C10—N1—C9—O4	−2.0 (3)
C3—C2—C7—C8	68.7 (2)	C8—N1—C9—C6	1.3 (3)
C1—C2—C7—C8	−57.9 (2)	C10—N1—C9—C6	179.67 (19)
C3—C2—C7—C6	−48.8 (2)	C5—C6—C9—O4	−60.9 (3)
C1—C2—C7—C6	−175.39 (19)	C7—C6—C9—O4	176.6 (2)
C9—C6—C7—C8	6.6 (2)	C5—C6—C9—N1	117.4 (2)
C5—C6—C7—C8	−113.5 (2)	C7—C6—C9—N1	−5.1 (2)
C9—C6—C7—C2	128.0 (2)	C9—N1—C10—C11	−82.9 (3)
C5—C6—C7—C2	7.9 (3)	C8—N1—C10—C11	95.3 (2)

Hydrogen-bond geometry (Å, °)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O1—H1A···O4^{i}	0.89 (3)	1.83 (3)	2.690 (2)	164 (2)

Symmetry codes: (i) *x*+1, *y*, *z*.

Fig. 1