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Succinimido 4-(*N*-maleimidomethyl)cyclohexanecarboxylate

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Key indicators

Single-crystal X-ray study
T = 295 K
Mean σ(C–C) = 0.003 Å
R factor = 0.043
wR factor = 0.132
Data-to-parameter ratio = 17.6

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

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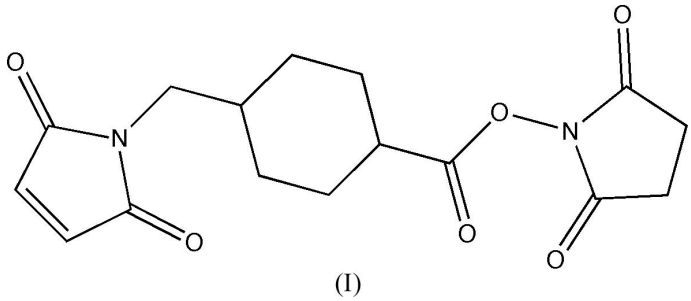
The title compound {alternative name: 2,5-dioxo-3-pyrrolidin-1-yl 4-[(2,5-dioxo-3-pyrrolin-1-yl)methyl]cyclohexanecarboxylate}, $C_{16}H_{18}N_2O_6$, crystallizes as discrete molecules separated by normal van der Waals interactions. The succinimide ester and maleimide subunits occupy equatorial positions on the cyclohexane ring.

Comment

The title compound (SMCC), (I), is a heterobifunctional linking reagent that finds considerable utility for the bioconjugation of chemical and biological species and is reactive to reagents possessing both amine and sulfhydryl functional groups (Bieniarz *et al.*, 1996). We have used a simple two-step procedure to synthesize the target material in reasonable yields (41%). Recrystallization yielded highly pure crystalline material suitable for single-crystal X-ray diffraction studies. The structure of (I) consists of discrete molecules (Fig. 1). Bond lengths are in accord with conventional values (Allen *et al.*, 1987). The succinimide ester and maleimide subunits occupy equatorial positions on the cyclohexane ring.



(I)

Experimental

trans-4-{[(3-Carboxy-1-oxo-2-propenyl)amino]methyl}cyclohexanecarboxylic acid (7.402 g, 29 mmol) and *N*-hydroxysuccinimide (3.696 g, 32 mmol) were dissolved in dry dimethylformamide (50 ml) and cooled to 273 K under an atmosphere of nitrogen. *N*,*N*-Dicyclohexylcarbodiimide (DCC) (10.542 g, 51 mmol) was added to the solution and the reaction stirred for a further hour at 273 K. After warming to room temperature (296 K), the reaction was stirred for an additional 48 h. Precipitated dicyclohexylurea (DCU) was removed by filtration. Water (200 ml) was added to the filtrate and the solution was extracted with $CHCl_3$ (4 × 250 ml). The combined organic layers were dried ($MgSO_4$), filtered and the solvent removed *in vacuo* to yield a red oil. The oil was dissolved in dichloromethane (200 ml) and subsequently precipitated by the careful addition of

hexane to yield a white solid that was collected by filtration and characterized as succinimido 4-(*N*-maleimidomethyl)cyclohexanecarboxylate (4.03 g, 12 mmol, 41%). A small quantity of the product was recrystallized from $(CH_3)_2CO/CH_3OH$ to yield crystals suitable for single-crystal X-ray diffraction studies (m.p. 444–447 K). ESMS+: 357 (*M*Na$^+$, 50%), 341 (*M*Li$^+$, 30%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.01 (*s*, 2H), 3.26 (*d*, 2H), 2.80 (*s*, 4H), 2.68 (*tt*, 1H), 1.99 (*m*, 2H), 1.67 (*m*, 2H), 1.59 (*m*, 1H), 1.38 (*dddd*, 2H), 1.04 (*dddd*, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 171.24, 170.85, 170.19, 134.37, 42.73, 39.39, 35.65, 28.55, 27.78, 25.41.

Crystal data

$C_{16}H_{18}N_2O_6$
M_r = 334.32
Orthorhombic, *Pbca*
a = 20.203 (5) Å
b = 17.021 (6) Å
c = 9.643 (3) Å
V = 3316.0 (18) Å^3
Z = 8
D_x = 1.339 Mg m^{-3}
Mo Kα radiation
Cell parameters from 25 reflections
θ = 12.7–17.3°
μ = 0.10 mm^{-1}
T = 295 K
Prism, colorless
0.50 × 0.30 × 0.30 mm

Data collection

Rigaku AFC-7*R* diffractometer
ω scans
Absorption correction: none
4776 measured reflections
3816 independent reflections
1926 reflections with $I > 2\sigma(I)$
R_{int} = 0.032
θ_{max} = 27.5°
$h = 0 \rightarrow 26$
$k = -10 \rightarrow 22$
$l = -5 \rightarrow 12$
3 standard reflections
every 150 reflections
intensity decay: 0.1%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.043
$wR(F^2)$ = 0.132
S = 1.01
3816 reflections
217 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0582P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.15 e Å^{-3}
$\Delta\rho_{min}$ = −0.23 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

O1—C1	1.203 (3)	O6—C16	1.206 (3)
O2—C4	1.206 (2)	N1—C1	1.379 (3)
O3—N1	1.387 (2)	N1—C4	1.376 (2)
O3—C5	1.395 (2)	N2—C12	1.463 (2)
O4—C5	1.187 (3)	N2—C13	1.389 (3)
O5—C13	1.202 (3)	N2—C16	1.380 (3)
N1—O3—C5	112.53 (14)	N1—C4—C3	105.55 (16)
O3—N1—C1	121.31 (15)	O3—C5—O4	121.40 (18)
O3—N1—C4	122.07 (15)	O3—C5—C6	109.01 (15)
C1—N1—C4	116.49 (16)	O4—C5—C6	129.57 (19)
C12—N2—C13	125.11 (16)	N2—C12—C9	113.96 (15)
C12—N2—C16	124.65 (16)	O5—C13—N2	124.8 (2)
C13—N2—C16	110.20 (16)	O5—C13—C14	129.4 (2)
O1—C1—N1	124.28 (19)	N2—C13—C14	105.81 (18)
O1—C1—C2	130.10 (19)	O6—C16—N2	125.10 (17)
N1—C1—C2	105.62 (16)	O6—C16—C15	128.83 (19)
O2—C4—N1	124.30 (18)	N2—C16—C15	106.06 (18)
O2—C4—C3	130.14 (18)		

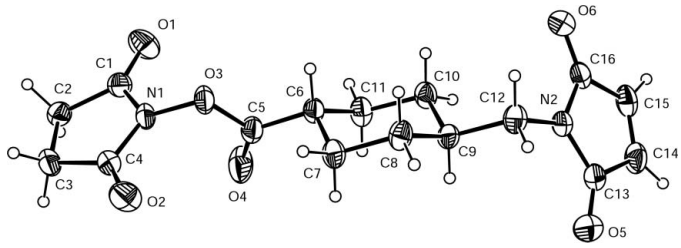


Figure 1
View of the title compound with the atom-numbering scheme. Displacement ellipsoids for non-H atoms are drawn at the 30% probability level. H atoms are shown as spheres of arbitrary radii.

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

D—H···A	D—H	H···A	D···A	D—H···A
C2—H2A···O2^{i}	0.95	2.50	3.381 (3)	154
C2—H2B···O6^{ii}	0.95	2.58	3.033 (3)	109
C3—H3A···O6^{iii}	0.95	2.52	3.335 (3)	144
C12—H12A···O6	0.95	2.60	2.913 (3)	100
C14—H14···O1^{iv}	0.95	2.42	3.330 (3)	160

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

H atoms were constrained in riding-model approximation, with C—H distances set at 0.95 Å. U_{iso}(H) values were set at 1.2U_{eq} of the parent atom.

Data collection: *MSC/AFC-7 Diffractometer Control Software for Windows* (Molecular Structure Corporation, 1999); cell refinement: *MSC/AFC-7 Diffractometer Control Software for Windows*; data reduction: *TEXSAN for Windows* (Molecular Structure Corporation, 2001); program(s) used to solve structure: *TEXSAN for Windows*; program(s) used to refine structure: *TEXSAN for Windows* and *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3* (Farrugia, 1997); software used to prepare material for publication: *TEXSAN for Windows* and *PLATON* (Spek, 2003).

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