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Ethyl 4-methyl-9*H*-carbazole-3-carboxylate

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Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.004 Å
R factor = 0.065
wR factor = 0.200
Data-to-parameter ratio = 12.2

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

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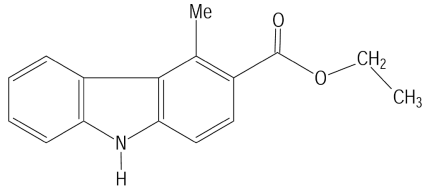
The title compound, $C_{16}H_{15}NO_2$, consists of a carbazole skeleton with carboxyethyl and methyl groups at positions 3 and 4, respectively. Molecules are linked about inversion centres by N—H···O hydrogen bonds [N···O 2.897 (3) Å] to form centrosymmetric dimers.

Comment

Tetrahydrocarbazole derivatives can be considered to be synthetic precursors of cyclic indole-type alkaloids of biological interest (Phillipson & Zenk, 1980; Saxton, 1983; Abraham, 1975). They have tricyclic ring systems, as in the strychnose type of indole alkaloids (Bosch & Bonjoch, 1988). Synthesis of indole-type alkaloids by substitution at different positions is currently under investigation (Patır *et al.*, 1997).



(I)

The structures of tetrahydrocarbazole derivatives having different substituents at different positions of the carbazole core have been the subject of much interest in our laboratory. These include 2-(1,2,3,4-tetrahydrocarbazol-2-yl)butylamine, (II) (Hökelek *et al.*, 2001*a*), 4-methylcarbazole-3-carboxylic acid, (III) (Hökelek *et al.*, 2001*b*), 1-benzyloxy-1,2,3,4-tetrahydrocarbazole, (IV) (Hökelek *et al.*, 2000), *N*-(1,2,3,4-tetrahydrocarbazole-1-yl)-2-methoxyacetamide, (V) (Hökelek & Patır, 2000*a*), 2,3-dihydro-3-ethyl-9-(phenylsulfonyl)carbazole-4(1*H*)-one, (VI) (Hökelek & Patır, 2000*b*), *N*-(2,2-dimethoxyethyl)-*N*-(9-methoxymethyl-1,2,3,4-tetrahydrospiro-[carbazole-1,2′-[1,3]dithiolan]-4-yl)benzamide, (VII) (Hökelek & Patır, 1999), 9-acetonyl-3-ethylidene-1,2,3,4-tetrahydrospiro[carbazole-1,2′-[1,3]dithiolan]-4-one, (VIII) (Hökelek *et al.*, 1999), spiro[carbazole-1(2*H*),2′-[1,3]dithiolan]-4(3*H*)-one, (IX) (Hökelek *et al.*, 1998), *N*-(2-methoxymethyl)-*N*-(2,3,4,9-tetrahydrospiro[1*H*-carbazole-1,2-(1,3)dithiolan]-4-yl)benzenesulfonamide, (X) (Patır *et al.*, 1997), 2,3-dihydro-9-(phenylsulfonyl)carbazole-4(1*H*)-one, (XI), and 1,2,3,4-tetrahydrocarbazole-1-spiro-2′-[1,3]dithiolane (XII) (Hökelek *et al.*, 1994).

Carbazole derivatives with different substituents at positions 1 and 2 (carbazole numbering) constitute the basic core of the hyellazoles and of carbazomycine. These structural features are also present in the [4,3-*b*]-substituted carbazole

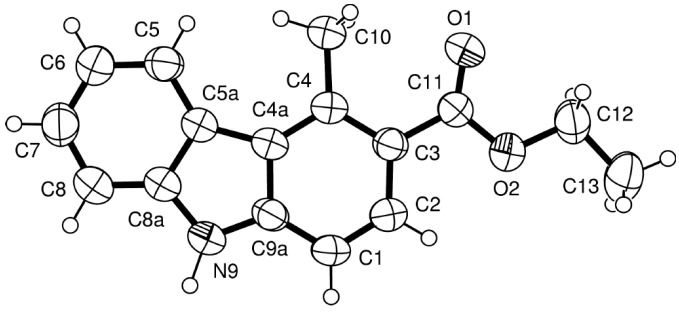


Figure 1
An *ORTEP*-3 (Farrugia, 1997) drawing of the title molecule with the atom-numbering scheme. The displacement ellipsoids are drawn at the 50% probability level.

alkaloids ellipticine and olivacine (Kansal & Potier, 1986; Ishikura *et al.*, 2000). Olivacine, ellipticine and their 9-oxygenated derivatives have attracted much interest due to their antitumour activities, and many elegant methods for the synthesis of ellipticine and related pyrido-carbazole alkaloids have been reported (Harada *et al.*, 1997). The title compound, (I), is an intermediate in the total synthesis of 5-demethylellipticine (Ergün *et al.*, 1998).

The present structure determination of (I) was undertaken in order to understand the effects of carboxyethyl and methyl groups on the geometry of the carbazole skeleton, and to compare the results with those of previously reported tetrahydrocarbazole derivatives.

Compound (I) (Fig. 1) contains a carbazole skeleton with carboxyethyl and methyl groups as substituents at positions 3 and 4, respectively. The carboxyethyl group has an electron-withdrawing effect, while the methyl group interacts with atom O1 [O1$\cdots$H10*C*(C10) 2.484 (2) Å], causing increases in the exocyclic angles C4—C4a—C5a [133.6 (2)°], C5—C5a—C4a [135.1 (3)°] and C3—C4—C10 [123.0 (3)°] and decreases in the endocyclic angles C3—C4—C4a [117.6 (2)°] and C5—C5a—C8a [117.9 (3)°]. As can be seen from the packing diagram (Fig. 2), there are intermolecular hydrogen bonds between the carbonyl O atoms and the indole N—H groups of neighbouring molecules [O1$^{i}\cdots$H9(N9) 1.89 (4) Å and N9—H9$\cdots$O1^{i} 170 (3)°; symmetry code: (i) x, y+1, z]. These intermolecular hydrogen bonds cause dimerization of the substituted carbazole molecules. Dipole–dipole and van der Waals interactions are also effective in the molecular packing. The intermolecular interactions may also cause increases in the angles C5a—C8a—C8 [123.1 (3)°], C1—C9a—N9 [128.7 (3)°] and C1—C2—C3 [123.4 (3)°] of the tetrahydrocarbazole skeleton.

The absence of any protecting group at atom N9 causes shortening of the C—N bonds [N9—C8a 1.397 (4) Å and N9—C9a 1.360 (4) Å]. These may be compared with corresponding values: 1.376 (4) and 1.391 (4) Å in (VII), 1.377 (2) and 1.396 (2) Å in (VIII), 1.382 (2) and 1.355 (3) Å in (IX), 1.390 (10) and 1.404 (9) Å in (X), 1.423 (5) and 1.412 (5) Å in (XI), and 1.372 (5) and 1.392 (5) Å in (XII).

The carboxyethyl and methyl groups in (I) cause notable changes in the geometry of the carbazole core leading to

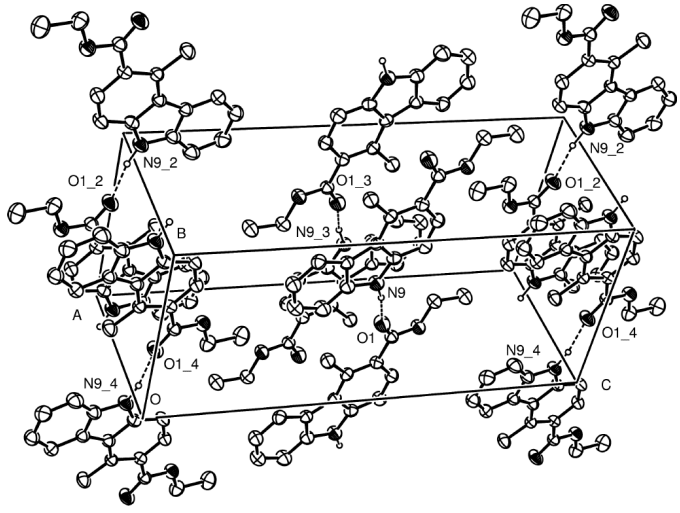


Figure 2
The packing diagram for (I). Hydrogen bonds are shown as dashed lines and H atoms not involved in hydrogen bonding have been omitted.

increases in the angles C2—C3—C4, C4—C4a—C5a, C3—C4—C4a, C1—C9a—N9 and C4a—C5a—C5 and decreases in C4—C4a—C9a and N9—C8a—C8 angles (Table 1), compared with the corresponding values in compounds (II), (VII), (VIII), (IX) (XI) and (XII) (Table 2).

In conclusion, the types of groups, electron-releasing or electron-donating, and their substitution positions, have a significant effect on the geometry of the carbazole system.

An examination of the deviations from the least-squares planes through the individual rings shows that rings *A* (C5a/C5—C8/C8a), *B* (C4a/C5a/C8a/N9/C9a) and *C* (C1—C4/C4a/C9a) are nearly coplanar. The dihedral angles between the mean least-squares planes are *A*/*B* = 0.65 (11), *A*/*C* = 1.20 (10), and *B*/*C* = 0.58 (12)°. Ring C has a local pseudo-twofold axis running along the midpoints of the C1—C2 and C4—C4a bonds.

Experimental

The title compound, (I), was prepared from a mixture of ethyl 1,2-dihydro-4-methylcarbazole-3-carboxylate (1.5 g, 5.88 mmol), decalin (25 ml) and Pd/C (0.25 g, 10% Pd), which was refluxed for 6 h under an argon atmosphere. The catalyst was separated by filtration and the solvent was removed under reduced pressure. The crude product was purified by column chromatography, using silica gel and benzene. The solvent was evaporated and the residue was crystallized from ethanol (yield 1.35 g, 90%), m.p. 455 K.

Crystal data

$C_{16}H_{15}NO_2$
M_r = 253.29
Monoclinic, $P2_1/c$
a = 7.292 (1) Å
b = 9.020 (1) Å
c = 19.583 (2) Å
β = 92.798 (9)°
V = 1286.4 (3) Å^3
Z = 4
D_x = 1.308 Mg m^{-3}
Cu $K\alpha$ radiation
Cell parameters from 25 reflections
θ = 10–18°
μ = 0.69 mm^{-1}
T = 293 (2) K
Rod-shaped, colourless
0.30 × 0.25 × 0.20 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
Non-profiled ω scans
Absorption correction: ψ scan (North *et al.*, 1968)
T_{min} = 0.812, T_{max} = 0.871
2612 measured reflections
2612 independent reflections
1320 reflections with $I > 2\sigma(I)$
θ_{max} = 74.1°
$h = 0 \rightarrow 9$
$k = -11 \rightarrow 0$
$l = -24 \rightarrow 24$
3 standard reflections
frequency: 120 min
intensity decay: 1%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.065
$wR(F^2)$ = 0.200
S = 0.93
2141 reflections
176 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.1415P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.23 e Å^{-3}
$\Delta\rho_{min}$ = −0.22 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

C4a—C4	1.394 (4)	C4—C10	1.498 (4)
C4a—C9a	1.411 (4)	C11—C3	1.470 (4)
C4a—C5a	1.453 (4)	C2—C1	1.359 (4)
O1—C11	1.204 (3)	C9a—N9	1.360 (4)
O2—C11	1.350 (3)	C9a—C1	1.402 (4)
C8a—C8	1.383 (4)	C5a—C5	1.409 (4)
C8a—C5a	1.391 (4)	C5—C6	1.376 (4)
C8a—N9	1.397 (4)	C6—C7	1.374 (5)
C4—C3	1.424 (4)	C8—C7	1.384 (5)
C4—C4a—C9a	120.8 (3)	C2—C3—C4	119.4 (3)
C4—C4a—C5a	133.6 (2)	C1—C2—C3	123.4 (3)
C9a—C4a—C5a	105.5 (2)	N9—C9a—C1	128.7 (3)
C8—C8a—C5a	123.1 (3)	C1—C9a—C4a	121.3 (3)
C8—C8a—N9	128.1 (3)	C8a—C5a—C5	117.9 (3)
C4a—C4—C3	117.6 (2)	C8a—C5a—C4a	107.1 (2)
C3—C4—C10	123.0 (3)	C5—C5a—C4a	135.1 (3)
C9a—C4a—C4—C3	−0.4 (4)	C4—C4a—C9a—C1	−0.4 (4)
C4a—C4—C3—C2	−0.2 (4)	C3—C2—C1—C9a	−2.5 (5)
C4—C3—C2—C1	1.7 (5)	C4a—C9a—C1—C2	1.8 (4)

Table 2
Comparison of bond angles (°) in the carbazole core of (I) with the corresponding values in the related compounds (II), (VII), (VIII), (IX), (XI) and (XII).

Angles	(I)	(II)	(VII)	(VIII)	(IX)	(XI)	(XII)
C2—C3—C4	119.4 (3)	112.2 (2)	109.9 (2)	115.1 (2)	114.7 (2)	114.6 (5)	110.5 (4)
C4—C4a—C5a	133.6 (2)	130.8 (2)	128.6 (2)	127.5 (2)	130.9 (2)	130.4 (4)	129.9 (4)
C3—C4—C4a	117.6 (2)	110.1 (2)	109.0 (2)	114.6 (2)	115.9 (2)	116.5 (4)	110.1 (4)
C1—C9a—N9	128.7 (3)	123.1 (2)	126.7 (2)	127.5 (2)	126.4 (2)	126.8 (4)	125.0 (3)
C4a—C5a—C5	135.1 (3)	135.1 (2)	134.7 (2)	134.0 (3)	134.7 (2)	132.2 (4)	133.6 (4)
C4—C4a—C9a	120.8 (3)	122.3 (2)	124.2 (3)	124.5 (2)	122.0 (2)	121.5 (4)	124.0 (4)
N9—C8a—C8	128.1 (3)	129.2 (2)	129.1 (2)	129.4 (3)	129.8 (2)	131.0 (4)	130.8 (4)

Atom H9 was located in a difference map and refined isotropically; the positions of the remaining H atoms were calculated geometrically at distances of 0.93 (CH), 0.97 (CH_2) and 0.96 (CH_3) Å from the corresponding C atoms, and a riding model was used during the refinement process.

Data collection: *CAD*-4 *EXPRESS* (Enraf–Nonius, 1994); cell refinement: *CAD*-4 *EXPRESS*; data reduction: *XCAD*4 (Harms & Wocadlo, 1995); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*-3 for Windows (Farrugia, 1997); software used to prepare material for publication: *WinGX* publication routines (Farrugia, 1999).

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