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N-[(1,3-Benzodioxol-5-yl)methyl]-benzenesulfonamide: an analogue of capsaicin

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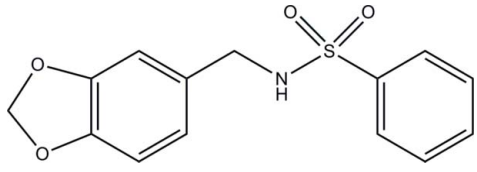
Key indicators: single-crystal X-ray study; T = 290 K; mean σ(C–C) = 0.003 Å; R factor = 0.051; wR factor = 0.149; data-to-parameter ratio = 14.7.

The title compound, $C_{14}H_{13}NO_4S$, an analogue of capsaicin, differs from the latter by having a 1,3-benzodioxole ring rather than a 2-methoxyphenol moiety, and having a benzenesulfonamide group instead of an aliphatic amide chain. The five-membered ring is in an envelope conformation with the methylene C atom lying 0.221 (6) Å out of the plane formed by the other four atoms. The dihedral angle between the phenyl ring and the mean plane of the 1,3-benzodioxole fused-ring system is 84.65 (4)°. In the crystal, molecules aggregate into supramolecular layers in the *ac* plane through C—H···O, N—H···O and C—H···π interactions.

Related literature

For background and the biological activity of capsaicin, see: Lee *et al.* (2011); Malagarie-Cazenave *et al.* (2011). For the synthesis and cytoxicity of the title compound, see: De Sá-Junior *et al.* (2013). For ring conformational analysis, see: Cremer & Pople (1975).



Experimental

Crystal data

$C_{14}H_{13}NO_4S$
M_r = 291.32
Orthorhombic, *Pbca*
a = 18.0158 (4) Å
b = 5.9346 (1) Å
c = 25.5480 (8) Å
V = 2731.51 (11) Å^3
Z = 8
Mo $K\alpha$ radiation
μ = 0.25 mm^{-1}
T = 290 K
0.25 × 0.22 × 0.20 mm

Data collection

Nonius KappaCCD diffractometer with Bruker APEXII CCD area-detector
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.930, T_{max} = 0.948
2652 measured reflections
2652 independent reflections
1860 reflections with $I > 2\sigma(I)$

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.051
$wR(F^2)$ = 0.149
S = 1.04
2652 reflections
181 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.26 e Å^{-3}
$\Delta\rho_{min}$ = −0.29 e Å^{-3}

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

*Cg*1 and *Cg*2 are the centroids of the C2–C7 and C9–C14 rings, respectively.

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1*N*···O2^{i}	0.99	2.00	2.945 (3)	157
C14—H14···O1^{ii}	0.93	2.59	3.486 (3)	161
C10—H10···*Cg*1^{iii}	0.93	2.74	3.563 (3)	147
C8—H8*B*···*Cg*2^{iv}	0.97	2.82	3.511 (3)	129

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

Data collection: *COLLECT* (Nonius, 1999); cell refinement: *SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO* (Otwinowski & Minor, 1997) and *SCALEPACK*; program(s) used to solve structure: *SIR97* (Altomare *et al.*, 1999); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 2012); software used to prepare material for publication: MarvinSketch (ChemAxon, 2010) and *publCIF* (Westrip, 2010).

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Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: TK5268).

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supplementary materials

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N-[(1,3-Benzodioxol-5-yl)methyl]benzenesulfonamide: an analogue of capsaicin

Stella H. Maganhi, Maurício T. Tavares, Mariana C. F. C. B. Damião and Roberto Parise Filho

1. Comment

Capsaicin is the common name of *trans*-8-methyl-*N*-vanillyl-6-nonenamide, the main pungent component produced by hot red and chili peppers (Lee *et al.*, 2011). It is a product of secondary metabolism from several species of the genus *Capsicum* (Malagarie-Cazenave *et al.* 2011) The beneficial effects of capsaicinoids are well known, such as their antitumoral activity. Thus, by rational approaches, the capsaicinoid structure could be used as an important prototype for the design of novel analogues. With this in mind, we intended to design a capsaicin-like analogue with potential activity against cancer cells. The title molecule, (I), *N*-(benzo[*d*][1,3]dioxol-5-ylmethyl)benzenesulfonamide was designed by converting the vanillyl system on the capsaicinoid structure to a benzodioxol group, and modifying the alkyl-lipophilic chain by an aromatic ring. The amide bond was replaced by a sulfonamide bond using bioisosteric concepts. Molecule (I) showed relevant cytotoxicity against MCF7 breast cancer cell line presenting an IC_{50} = 32 μM (De Sá-Junior *et al.*, 2013). The compound, Fig. 1, shows an envelope configuration in the 1,3-dioxole five membered ring, with the C7 atom lying 0,221 (6) Å out of the plane formed by the other four atoms. The ring puckering parameters are q2 = 0.140 (3) Å and $\varphi 2$ = 145.7 (1)^o (Cremer & Pople, 1975). The crystal packing of (I), Table 1, is sustained by N—H···O and C—H···π interactions, leading to supramolecular layers in the *ac* plane.

2. Experimental

The synthesis has been already described (De Sá-Junior *et al.*, 2013). Crystals were obtained by slow evaporation from a hexane/chloroform (4:1) solution.

3. Refinement

The H atoms were geometrically placed (C–H = 0.93–0.97 Å) and refined as riding with U_{iso}(H) = 1.2U_{eq}(C). The N—H H atom was located in a difference map and placed in that position with U_{iso}(H) = 1.2U_{eq}(N).

The data collection was not ideal but, in spite of that, the structure is unambiguous and fine.

Computing details

Data collection: *COLLECT* (Nonius, 1999); cell refinement: *SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO* (Otwinowski & Minor, 1997) and *SCALEPACK*; program(s) used to solve structure: *SIR97* (Altomare *et al.*, 1999); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 2012); software used to prepare material for publication: MarvinSketch (ChemAxon, 2010) and *publCIF* (Westrip, 2010).

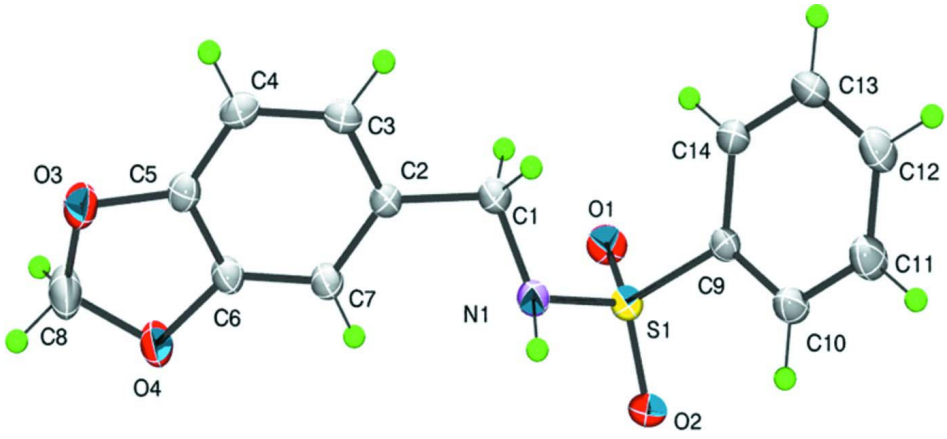

Figure 1

Molecular structure of the title compound showing atom labels and 50% displacement ellipsoids.

N-[(1,3-Benzodioxol-5-yl)methyl]benzenesulfonamide

Crystal data

$C_{14}H_{13}NO_4S$
$M_r = 291.32$
Orthorhombic, *Pbca*
Hall symbol: -P 2ac 2ab
$a = 18.0158$ (4) Å
$b = 5.9346$ (1) Å
$c = 25.5480$ (8) Å
$V = 2731.51$ (11) Å^3
$Z = 8$
$F(000) = 1216$
$D_x = 1.417$ Mg m^{-3}
Melting point = 350.1–350.6 K
Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
Cell parameters from 3351 reflections
$\theta = 1.4$–$27.1°$
$\mu = 0.25$ mm^{-1}
$T = 290$ K
Irregular, colourless
0.25 × 0.22 × 0.20 mm

Data collection

Nonius KappaCCD with Bruker APEXII CCD area detector diffractometer
Radiation source: fine-focus sealed tube
Graphite monochromator
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
$T_{min} = 0.930$, $T_{max} = 0.948$
2652 measured reflections
2652 independent reflections
1860 reflections with $I > 2\sigma(I)$
$R_{int} = 0.000$
$\theta_{max} = 26.0°$, $\theta_{min} = 1.6°$
$h = 0 \rightarrow 22$
$k = 0 \rightarrow 7$
$l = -31 \rightarrow 0$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.051$
$wR(F^2) = 0.149$
$S = 1.04$
2652 reflections
181 parameters
0 restraints
Primary atom site location: structure-invariant direct methods
Secondary atom site location: difference Fourier map
Hydrogen site location: inferred from neighbouring sites
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0843P)^2 + 0.6245P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.26$ e Å^{-3}
$\Delta\rho_{min} = -0.29$ e Å^{-3}

Special details

Geometry. All s.u.'s (except the s.u. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell s.u.'s are taken into account individually in the estimation of s.u.'s in distances, angles and torsion angles; correlations between s.u.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell s.u.'s is used for estimating s.u.'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 $F^2 > 2\sigma(F^2)$ 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 (Å²)

	x	*y*	*z*	U_{iso}*/U_{eq}
C1	0.14422 (14)	0.0794 (4)	0.26877 (9)	0.0610 (6)
H1A	0.1939	0.1190	0.2574	0.073*
H1B	0.1283	−0.0507	0.2487	0.073*
C2	0.14588 (11)	0.0187 (4)	0.32636 (9)	0.0493 (5)
C3	0.17158 (12)	−0.1926 (4)	0.34057 (10)	0.0561 (6)
H3	0.1836	−0.2958	0.3145	0.067*
C4	0.17986 (13)	−0.2546 (4)	0.39256 (10)	0.0596 (6)
H4	0.1975	−0.3962	0.4019	0.071*
C5	0.16096 (13)	−0.0985 (4)	0.42922 (9)	0.0550 (6)
C6	0.13417 (14)	0.1100 (4)	0.41568 (9)	0.0559 (6)
C7	0.12552 (13)	0.1742 (4)	0.36469 (8)	0.0547 (6)
H7	0.1069	0.3154	0.3559	0.066*
C8	0.1485 (2)	0.1023 (6)	0.50195 (12)	0.0966 (11)
H8A	0.1936	0.1721	0.5148	0.116*
H8B	0.1132	0.0948	0.5306	0.116*
C9	0.09760 (11)	0.2425 (4)	0.15195 (8)	0.0492 (5)
C10	0.02961 (13)	0.2300 (4)	0.12712 (10)	0.0625 (6)
H10	−0.0093	0.3224	0.1377	0.075*
C11	0.01987 (15)	0.0799 (5)	0.08658 (11)	0.0748 (8)
H11	−0.0258	0.0719	0.0697	0.090*
C12	0.07628 (17)	−0.0566 (5)	0.07097 (11)	0.0805 (8)
H12	0.0689	−0.1577	0.0436	0.097*
C13	0.14451 (16)	−0.0459 (5)	0.09547 (11)	0.0806 (9)
H13	0.1830	−0.1390	0.0845	0.097*
C14	0.15560 (13)	0.1045 (5)	0.13662 (10)	0.0647 (7)
H14	0.2013	0.1120	0.1535	0.078*
O1	0.18306 (9)	0.4975 (3)	0.20769 (7)	0.0703 (5)
O2	0.04895 (10)	0.5823 (3)	0.20637 (6)	0.0654 (5)
O3	0.16399 (11)	−0.1167 (3)	0.48341 (7)	0.0764 (6)
O4	0.11841 (13)	0.2327 (3)	0.46019 (6)	0.0841 (6)
N1	0.09406 (10)	0.2681 (3)	0.25825 (7)	0.0558 (5)
H1N	0.0405	0.2323	0.2630	0.067*
S1	0.10836 (3)	0.42069 (10)	0.20672 (2)	0.0518 (2)

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0711 (16)	0.0610 (14)	0.0509 (14)	0.0106 (12)	0.0004 (11)	−0.0038 (11)
C2	0.0490 (12)	0.0500 (13)	0.0487 (13)	−0.0012 (10)	0.0018 (9)	−0.0018 (10)
C3	0.0558 (13)	0.0492 (14)	0.0632 (15)	0.0037 (10)	0.0044 (11)	−0.0060 (11)
C4	0.0576 (14)	0.0483 (12)	0.0728 (17)	0.0033 (11)	−0.0017 (12)	0.0047 (11)
C5	0.0579 (13)	0.0551 (13)	0.0519 (13)	−0.0040 (10)	−0.0008 (10)	0.0085 (11)
C6	0.0698 (15)	0.0511 (13)	0.0467 (13)	0.0008 (11)	0.0029 (11)	−0.0035 (10)
C7	0.0679 (14)	0.0463 (12)	0.0497 (13)	0.0031 (11)	0.0018 (11)	0.0017 (10)
C8	0.156 (3)	0.084 (2)	0.0500 (16)	0.010 (2)	−0.0048 (18)	0.0069 (15)
C9	0.0487 (12)	0.0559 (12)	0.0431 (12)	0.0012 (10)	0.0049 (9)	0.0026 (9)
C10	0.0515 (13)	0.0768 (16)	0.0592 (14)	0.0030 (12)	0.0026 (11)	−0.0098 (12)
C11	0.0678 (17)	0.0909 (19)	0.0657 (17)	−0.0066 (14)	−0.0029 (13)	−0.0167 (15)
C12	0.099 (2)	0.0810 (18)	0.0619 (17)	0.0034 (17)	−0.0010 (15)	−0.0185 (14)
C13	0.091 (2)	0.089 (2)	0.0620 (17)	0.0302 (17)	0.0082 (15)	−0.0123 (15)
C14	0.0592 (14)	0.0821 (17)	0.0526 (14)	0.0156 (12)	−0.0001 (11)	−0.0023 (12)
O1	0.0522 (10)	0.0763 (12)	0.0823 (13)	−0.0131 (9)	0.0035 (8)	−0.0066 (9)
O2	0.0653 (11)	0.0623 (11)	0.0686 (11)	0.0126 (8)	0.0045 (8)	−0.0066 (8)
O3	0.1040 (14)	0.0704 (12)	0.0548 (11)	0.0079 (10)	−0.0014 (9)	0.0142 (8)
O4	0.1363 (18)	0.0690 (12)	0.0471 (10)	0.0244 (11)	−0.0015 (10)	−0.0023 (9)
N1	0.0522 (11)	0.0670 (12)	0.0482 (11)	0.0010 (9)	0.0026 (8)	0.0001 (9)
S1	0.0522 (4)	0.0525 (4)	0.0507 (4)	−0.0022 (2)	0.0016 (2)	−0.0017 (2)

Geometric parameters (Å, º)

C1—N1	1.464 (3)	C8—H8B	0.9700
C1—C2	1.515 (3)	C9—C10	1.382 (3)
C1—H1A	0.9700	C9—C14	1.384 (3)
C1—H1B	0.9700	C9—S1	1.765 (2)
C2—C3	1.385 (3)	C10—C11	1.377 (3)
C2—C7	1.395 (3)	C10—H10	0.9300
C3—C4	1.386 (3)	C11—C12	1.360 (4)
C3—H3	0.9300	C11—H11	0.9300
C4—C5	1.361 (3)	C12—C13	1.381 (4)
C4—H4	0.9300	C12—H12	0.9300
C5—C6	1.372 (3)	C13—C14	1.393 (4)
C5—O3	1.390 (3)	C13—H13	0.9300
C6—C7	1.366 (3)	C14—H14	0.9300
C6—O4	1.380 (3)	O1—S1	1.4210 (17)
C7—H7	0.9300	O2—S1	1.4372 (18)
C8—O3	1.411 (4)	N1—S1	1.6186 (19)
C8—O4	1.425 (3)	N1—H1N	0.9947
C8—H8A	0.9700		
N1—C1—C2	111.85 (18)	C10—C9—C14	120.5 (2)
N1—C1—H1A	109.2	C10—C9—S1	119.57 (17)
C2—C1—H1A	109.2	C14—C9—S1	119.74 (18)
N1—C1—H1B	109.2	C11—C10—C9	119.5 (2)
C2—C1—H1B	109.2	C11—C10—H10	120.2

H1A—C1—H1B	107.9	C9—C10—H10	120.2
C3—C2—C7	120.2 (2)	C12—C11—C10	120.7 (2)
C3—C2—C1	118.4 (2)	C12—C11—H11	119.6
C7—C2—C1	121.3 (2)	C10—C11—H11	119.6
C2—C3—C4	121.8 (2)	C11—C12—C13	120.3 (3)
C2—C3—H3	119.1	C11—C12—H12	119.8
C4—C3—H3	119.1	C13—C12—H12	119.8
C5—C4—C3	116.9 (2)	C12—C13—C14	119.9 (2)
C5—C4—H4	121.6	C12—C13—H13	120.0
C3—C4—H4	121.6	C14—C13—H13	120.0
C4—C5—C6	121.9 (2)	C9—C14—C13	119.0 (2)
C4—C5—O3	128.5 (2)	C9—C14—H14	120.5
C6—C5—O3	109.6 (2)	C13—C14—H14	120.5
C7—C6—C5	122.1 (2)	C5—O3—C8	104.8 (2)
C7—C6—O4	128.0 (2)	C6—O4—C8	104.6 (2)
C5—C6—O4	109.9 (2)	C1—N1—S1	118.62 (15)
C6—C7—C2	117.0 (2)	C1—N1—H1N	114.4
C6—C7—H7	121.5	S1—N1—H1N	111.9
C2—C7—H7	121.5	O1—S1—O2	119.43 (12)
O3—C8—O4	108.9 (2)	O1—S1—N1	108.42 (11)
O3—C8—H8A	109.9	O2—S1—N1	105.06 (10)
O4—C8—H8A	109.9	O1—S1—C9	108.06 (10)
O3—C8—H8B	109.9	O2—S1—C9	108.26 (10)
O4—C8—H8B	109.9	N1—S1—C9	106.99 (11)
H8A—C8—H8B	108.3		

N1—C1—C2—C3	160.6 (2)	C10—C9—C14—C13	0.5 (4)
N1—C1—C2—C7	−22.4 (3)	S1—C9—C14—C13	175.8 (2)
C7—C2—C3—C4	−1.8 (3)	C12—C13—C14—C9	−0.5 (4)
C1—C2—C3—C4	175.2 (2)	C4—C5—O3—C8	171.9 (3)
C2—C3—C4—C5	0.5 (3)	C6—C5—O3—C8	−8.6 (3)
C3—C4—C5—C6	0.7 (4)	O4—C8—O3—C5	14.5 (3)
C3—C4—C5—O3	−179.9 (2)	C7—C6—O4—C8	−171.0 (3)
C4—C5—C6—C7	−0.6 (4)	C5—C6—O4—C8	9.3 (3)
O3—C5—C6—C7	179.8 (2)	O3—C8—O4—C6	−14.8 (4)
C4—C5—C6—O4	179.0 (2)	C2—C1—N1—S1	155.52 (16)
O3—C5—C6—O4	−0.5 (3)	C1—N1—S1—O1	−53.6 (2)
C5—C6—C7—C2	−0.6 (4)	C1—N1—S1—O2	177.62 (16)
O4—C6—C7—C2	179.8 (2)	C1—N1—S1—C9	62.69 (19)
C3—C2—C7—C6	1.8 (3)	C10—C9—S1—O1	−149.4 (2)
C1—C2—C7—C6	−175.1 (2)	C14—C9—S1—O1	35.3 (2)
C14—C9—C10—C11	−0.4 (4)	C10—C9—S1—O2	−18.7 (2)
S1—C9—C10—C11	−175.7 (2)	C14—C9—S1—O2	165.94 (19)
C9—C10—C11—C12	0.3 (4)	C10—C9—S1—N1	94.0 (2)
C10—C11—C12—C13	−0.3 (5)	C14—C9—S1—N1	−81.3 (2)
C11—C12—C13—C14	0.4 (5)		

Hydrogen-bond geometry (Å, º)

Cg1 and Cg2 are the centroids of the C2–C7 and C9–C14 rings, respectively.

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1*N*···O2^{i}	0.99	2.00	2.945 (3)	157
C14—H14···O1^{ii}	0.93	2.59	3.486 (3)	161
C10—H10···*Cg*1^{iii}	0.93	2.74	3.563 (3)	147
C8—H8*B*···*Cg*2^{iv}	0.97	2.82	3.511 (3)	129

Symmetry codes: (i) −*x*, *y*−1/2, −*z*+1/2; (ii) −*x*+1/2, *y*−1/2, *z*; (iii) −*x*, *y*+1/2, −*z*+1/2; (iv) *x*, −*y*−1/2, *z*−1/2.