ω–2θ scans	$h = 0 \rightarrow 6$
Absorption correction: none	$k = 0 \rightarrow 14$
	$l = -27 \rightarrow 27$
2865 measured reflections	2 standard reflections
2797 independent reflections	frequency: 120 min
1386 observed reflections $[I > 2\sigma(I)]$	intensity decay: none

Refinement

Refinement on F	$(\Delta/\sigma)_{max} = 0.23$
$R = 0.044$	$\Delta\rho_{max} = 0.6$ e Å^{-3}
$wR = 0.053$	$\Delta\rho_{min} = -0.4$ e Å^{-3}
$S = 2.3$	Extinction correction: none
1386 reflections	Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV, Tables 2.2B and 2.3.1)
223 parameters	
All H-atom parameters refined except H11*B* which was not refined	
$w = 1/\sigma^2(F)$	

Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters* (Å^2)

$U_{eq} = (1/3)\Sigma_i\Sigma_j U_{ij} a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	U_{eq}
C1	0.6510 (6)	0.2527 (3)	0.5213 (2)	0.041
C2	0.7487 (7)	0.3245 (3)	0.5662 (2)	0.043
C3	0.9105 (6)	0.2825 (3)	0.6118 (2)	0.040
C4	0.9737 (7)	0.1654 (3)	0.6179 (2)	0.047
C5	0.8763 (9)	0.0965 (4)	0.5695 (2)	0.057
C6	0.7225 (8)	0.1383 (3)	0.5228 (2)	0.051
C7	0.6773 (10)	0.3801 (5)	0.4144 (2)	0.059
C8	1.1001 (8)	0.1639 (4)	0.7289 (2)	0.058
C9	0.8259 (9)	0.1867 (6)	0.7510 (2)	0.075
C10	1.2456 (11)	0.0061 (5)	0.6587 (3)	0.079
C11	1.0771 (17)	−0.0869 (5)	0.6793 (3)	0.110
N1	1.0388 (6)	0.3703 (3)	0.6496 (1)	0.052
N2	1.1107 (7)	0.1187 (3)	0.6661 (2)	0.061
O1	0.3417 (5)	0.2130 (3)	0.4285 (1)	0.073
O2	0.2740 (5)	0.3922 (2)	0.4863 (1)	0.063
O3	1.2762 (5)	0.3600 (3)	0.6618 (1)	0.073
O4	0.9096 (6)	0.4537 (3)	0.6643 (1)	0.077
S	0.45238 (17)	0.30780 (9)	0.46148 (4)	0.049

Table 2. *Selected geometric parameters* (Å, °)

C1—C2	1.377 (5)	C7—S	1.753 (6)
C1—C6	1.384 (6)	C8—C9	1.491 (7)
C1—S	1.757 (4)	C8—N2	1.467 (6)
C2—C3	1.371 (5)	C10—C11	1.452 (10)
C3—C4	1.410 (5)	C10—N2	1.490 (7)
C3—N1	1.462 (5)	N1—O3	1.228 (5)
C4—C5	1.412 (6)	N1—O4	1.216 (5)
C4—N2	1.366 (5)	O1—S	1.430 (4)
C5—C6	1.364 (6)	O2—S	1.442 (3)
C4—C3—N1	122.0 (3)	O3—N1—O4	122.8 (4)
C3—C4—C5	114.0 (4)	C8—N2—C4	123.4 (4)
C3—C4—N2	124.8 (4)	C10—N2—C4	119.8 (4)
O3—N1—C3	118.6 (4)	C8—N2—C10	116.1 (4)
O4—N1—C3	118.5 (3)		
C6—C1—S—O1	13.2 (3)	C2—C1—S—O2	−40.1 (3)
C2—C1—S—C7	74.2 (4)		

Data collection: *CAD*-4 *Software* (Enraf–Nonius, 1989). Cell refinement: *CAD*-4 *Software*. Data reduction: *GX* (Mallinson & Muir, 1985). Program(s) used to solve structure: *MITHRIL* (Gilmore, 1984). Program(s) used to refine structure: *GX*. Molecular graphics: *ORTEP*II (Johnson, 1971; Mallinson & Muir, 1985). Software used to prepare material for publication: *GX*.

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: HA1134). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

References

Enraf–Nonius (1989). *CAD*-4 *Software*. Version 5.0. Enraf–Nonius, Delft, The Netherlands.
Gilmore, C. J. (1984). *J. Appl. Cryst.* **17**, 42–46.
Johnson, C. K. (1971). *ORTEP*II. Report ORNL-3794, revised. Oak Ridge National Laboratory, Tennessee, USA.
Mallinson, P. R. & Muir, K. W. (1985). *J. Appl. Cryst.* **18**, 51–53.

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KR-25003, a Potent Analgesic Capsaicinoid

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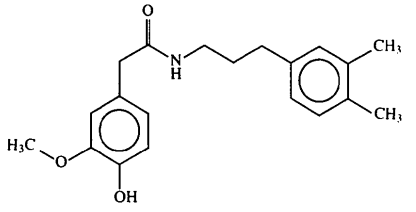
Abstract

The crystal structure of *N*-[3-(3,4-dimethylphenyl)propyl](4-hydroxy-3-methoxyphenyl)acetamide, $C_{20}H_{25}NO_3$, was determined to a final R value of 0.047. The vanilloid, amide and dimethylphenyl groups of the compound are nearly perpendicular with respect to one another. The overall conformation in the crystalline state is somewhat different from that of other capsaicinoids. The molecules are stabilized by intermolecular hydrogen bonds.

Comment

Capsaicin, the pungent principle component of red pepper, is well known to have analgesic activity in animal species (Suzuki & Iwai, 1984). It has a different mechanism of action from the usual analgesics such as narcotic or non-steroidal anti-inflammatory drugs (NSAIDs). Although the undesirable side effects of natural capsaicin prevent its direct utilization in medicinal preparations for humans, the strong analgesic effect of the capsaicinoids, natural as well as synthetic, has been studied in detail (Dray, 1992).

We have synthesized and studied a number of structural analogues of capsaicin (Park, Ha, Choi, Kim, Lim & Lee, 1991; Park, Ha, Kim & Choi, 1991). The crystallographic study of the title compound, KR-25003, was undertaken in order to provide three-dimensional information concerning the functional groups that were believed to be important in its analgesic activity, and also to establish the reliable structure–activity relationship necessary for the understanding of the mode of action and/or the design of new members of the non-narcotic analgesics. Details of the synthetic work have been published elsewhere (Park, Ha, Choi, Kim, Lim & Lee, 1991).



KR-25003

The molecular geometry of KR-25003 shows no significant differences from that expected. The capsaicinoid is composed of three major functional moieties, namely, a vanilloid, an amide and a hydrophobic side chain or equivalent. In the crystal, the vanilloid group of the title compound is nearly perpendicular to the plane of the amide [dihedral angle 105.5 (4)°], which in turn is also perpendicular to the dimethylphenyl group [dihedral angle 94.9 (5)°] (Fig. 1). The overall conformation of the compound in the crystalline state, however, is not entirely similar to those of other capsaicinoids having similar structure and bioactivity, *e.g.* capsaicin (Park, Park, Choi & Kim, 1995*a*), KR-21042 (Park, Park, Choi & Kim, 1995*b*) and KR-25018 (Park, Park & Kim, 1995). This suggests that there may be conformational changes between the capsaicinoid and its receptor during their interaction in the biosystem.

The methoxy group of the vanilloid moiety is important for strong bioactivity (Dray, 1992; Park, Ha, Choi, Kim, Lim & Lee, 1991) and, in the present case, it is nearly coplanar with the phenyl ring [C7—O2—C5—C6 9.4 (3)°], presumably for effective overlap of the lone pair of electrons of the O atom with the π-electron system of the ring. The C5—O2 bond length is significantly shorter than that of O2—C7. Such tendencies have also been observed in structures having a methoxyaryl moiety (Kim, Kim & Park, 1993; Kim, Park & Lah, 1990; Kistenmacher & Marsh, 1972).

Molecules of KR-25003 are connected by intermolecular hydrogen bonds between the phenolic HO1 atom of the vanilloid moiety and the amide O3(x, $y-1$, z) atom of a neighbouring molecule. The O···O hydrogen bond length is 2.71 (1) Å, with an internal angle O1—HO1···O3 of 166 (4)°.

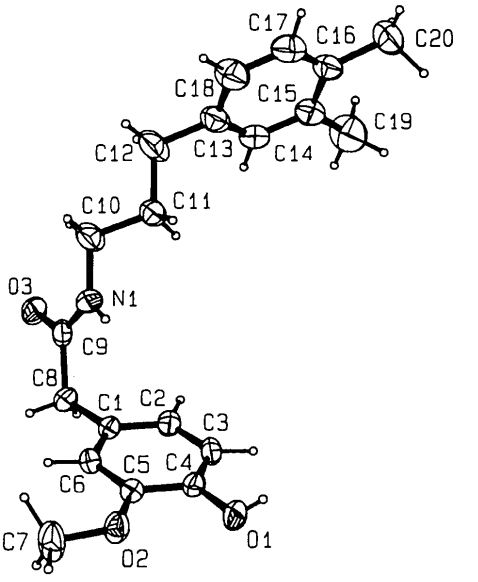


Fig. 1. *ORTEP*II (Johnson, 1976) drawing of KR-25003 with the atomic numbering scheme. The displacement ellipsoids are drawn at the 50% probability level. H atoms are drawn as small circles of arbitrary radii.

Experimental

Colourless prismatic crystals were grown by slow evaporation from a mixture of ethyl acetate and *n*-hexane at room temperature.

Crystal data

$C_{20}H_{25}NO_3$
M_r = 327.42
Triclinic
$P\bar{1}$
a = 7.964 (1) Å
b = 8.859 (1) Å
c = 13.229 (2) Å
α = 86.34 (1)°
β = 73.71 (1)°
γ = 88.25 (1)°
V = 894.0 (2) Å^3
Z = 2
D_x = 1.216 Mg m^{-3}
D_m = 1.21 Mg m^{-3}
D_m measured by flotation in KI solution

Cu $K\alpha$ radiation
λ = 1.5418 Å
Cell parameters from 25 reflections
θ = 12.8–33.2°
μ = 0.571 mm^{-1}
T = 293 K
Prism
0.34 × 0.28 × 0.21 mm
Colourless

Data collection

Enraf–Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: none
3522 measured reflections
3371 independent reflections
3014 observed reflections [$F > 3\sigma(F)$]

R_{int} = 0.016
θ_{max} = 70.0°
$h = 0 \rightarrow 9$
$k = -10 \rightarrow 10$
$l = -16 \rightarrow 16$
3 standard reflections
frequency: 60 min
intensity decay: 0.41%

Refinement

Refinement on F	Unit weights applied
$R = 0.047$	$(\Delta/\sigma)_{max} = 0.107$
$wR = 0.048$	$\Delta\rho_{max} = 0.198$ e Å^{-3}
$S = 0.537$	$\Delta\rho_{min} = -0.253$ e Å^{-3}
3014 reflections	Atomic scattering factors from *SHELX*76 (Sheldrick, 1976)
317 parameters	
All H-atom parameters refined	

Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters* (Å^2)

$U_{eq} = (1/3)\sum_i\sum_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	U_{eq}
O1	0.8274 (2)	0.2655 (2)	0.6225 (1)	0.050 (1)
O2	1.0589 (2)	0.4393 (2)	0.6625 (1)	0.049 (1)
O3	0.6994 (2)	1.1177 (2)	0.4878 (1)	0.061 (1)
N1	0.8109 (3)	0.9075 (2)	0.4054 (1)	0.047 (1)
C1	0.7555 (3)	0.7321 (2)	0.6019 (2)	0.036 (1)
C2	0.6329 (3)	0.6386 (2)	0.5826 (2)	0.043 (1)
C3	0.6554 (3)	0.4820 (2)	0.5893 (2)	0.042 (1)
C4	0.7985 (3)	0.4183 (2)	0.6153 (1)	0.034 (1)
C5	0.9214 (3)	0.5115 (2)	0.6364 (2)	0.033 (1)
C6	0.8995 (3)	0.6673 (2)	0.6287 (2)	0.035 (1)
C7	1.1712 (4)	0.5325 (3)	0.6986 (3)	0.073 (1)
C8	0.7294 (4)	0.9018 (2)	0.5975 (2)	0.049 (1)
C9	0.7460 (3)	0.9825 (2)	0.4913 (2)	0.041 (1)
C10	0.8285 (4)	0.9729 (3)	0.2992 (2)	0.058 (1)
C11	0.7364 (4)	0.8787 (3)	0.2392 (2)	0.050 (1)
C12	0.7338 (5)	0.9569 (3)	0.1339 (2)	0.071 (1)
C13	0.6511 (3)	0.8642 (3)	0.0689 (2)	0.054 (1)
C14	0.4758 (4)	0.8269 (3)	0.1042 (2)	0.054 (1)
C15	0.3944 (3)	0.7448 (3)	0.0451 (2)	0.054 (1)
C16	0.4929 (4)	0.6990 (3)	−0.0532 (2)	0.057 (1)
C17	0.6674 (4)	0.7357 (3)	−0.0881 (2)	0.064 (1)
C18	0.7469 (4)	0.8167 (3)	−0.0280 (2)	0.063 (1)
C19	0.2038 (4)	0.7075 (5)	0.0884 (3)	0.082 (1)
C20	0.4126 (6)	0.6099 (4)	−0.1219 (3)	0.085 (1)

Table 2. *Selected geometric parameters* (Å, °)

O1—C4	1.368 (2)	N1—C9	1.322 (3)
O2—C5	1.368 (2)	N1—C10	1.456 (3)
O2—C7	1.430 (3)	C1—C8	1.511 (3)
O3—C9	1.245 (2)	C8—C9	1.508 (3)
C5—O2—C7	116.0 (2)	O3—C9—N1	122.4 (2)
C9—N1—C10	123.4 (2)	O3—C9—C8	118.8 (2)
C1—C8—C9	118.1 (2)	N1—C9—C8	118.8 (2)

Intensity data were collected with a scan width of $\Delta\omega = (1.2 + 0.15\tan\theta)°$ (estimated from ω–θ plots). The counter aperture was also adjusted as a function of θ. The horizontal aperture width ranged from 2.0 to 3.1 mm, while the vertical one was set at 4 mm. All reflections were corrected for the usual Lp effects and decay compensation was applied.

Data collection: *CAD*-4 *Software* (Enraf–Nonius, 1989). Cell refinement: *CAD*-4 *Software* (Enraf–Nonius, 1989). Data reduction: *MolEN* (Fair, 1990). Program(s) used to solve structure: *MULTAN*84 (Main, Germain & Woolfson, 1984). Program(s) used to refine structure: *SHELX*76 (Sheldrick, 1976). Molecular graphics: *ORTEP*II (Johnson, 1976). Software used to prepare material for publication: *MolEN* (Fair, 1990).

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Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry, including H-atom geometry, have been deposited with the IUCr (Reference: AS1152). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

References

Dray, A. (1992). *Life Sci.* **51**, 1759–1765.
Enraf–Nonius (1989). *CAD*-4 *Software*. Version 5. Enraf–Nonius, Delft, The Netherlands.
Fair, C. K. (1990). *MolEN. An Interactive Intelligent System for Crystal Structure Analysis*. Enraf–Nonius, Delft, The Netherlands.
Johnson, C. K. (1976). *ORTEP*II. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.
Kim, Y. B., Kim, J. A. & Park, I. Y. (1993). *Arch. Pharm. Res.* **16**, 134–139.
Kim, Y. B., Park, I. Y. & Lah, W. R. (1990). *Arch. Pharm. Res.* **13**, 166–173.
Kistenmacher, T. J. & Marsh, R. E. (1972). *J. Am. Chem. Soc.* **94**, 1340–1345.
Main, P., Germain, G. & Woolfson, M. M. (1984). *MULTAN*84. *A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*. Univ. of York, England.
Park, N.-S., Ha, D.-C., Choi, J.-K., Kim, H.-S., Lim, H.-J. & Lee, B.-Y. (1991). *Korean J. Med. Chem.* **1**, 36–43.
Park, N.-S., Ha, D.-C., Kim, H.-S. & Choi, J.-K. (1991). *Korean J. Med. Chem.* **1**, 2–7.
Park, N.-S., Park, I. Y., Choi, J. & Kim, Y. B. (1995*a*). In preparation.
Park, N.-S., Park, I. Y., Choi, J.-K. & Kim, Y. B. (1995*b*). In preparation.
Park, N.-S., Park, I. Y. & Kim, Y. B. (1995). In preparation.
Sheldrick, G. M. (1976). *SHELX*76. *Program for Crystal Structure Determination*. Univ. of Cambridge, England.
Suzuki, T. & Iwai, K. (1984). *The Alkaloids*, Vol. XXIII, edited by A. Brossi, pp. 227–299. Orlando: Academic Press.

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Stereochemistry of Asymmetric β-Lactam Formation Involving Achiral Glyoxylamide Derivatives

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Abstract

The crystals of three glyoxylamide compounds, *N*,*N*-diisopropyl(*o*-methylphenyl)glyoxylamide, $C_{15}H_{21}NO_2$, *N*,*N*-diisopropyl(*p*-methylphenyl)glyoxylamide, $C_{15}H_{21}$-