

## References

- GOLDSMITH, D. G. & THOTTATHIL, J. (1982). *J. Org. Chem.* In preparation.
- GRANT, D. F., KILLEAN, R. C. G. & LAWRENCE, J. L. (1969). *Acta Cryst.* B25, 374–376.
- HOSAZAWA, S., KATO, N. & MUNAKATA, K. (1974). *Tetrahedron Lett.* pp. 3753–3756.
- JOHNSON, C. K. (1965). *ORTEP*. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee.
- KUBO, I., LEE, Y.-W., BALOGH-NAIR, V., NAKANISHI, K. & CHAPYA, A. (1976). *Chem. Commun.* pp. 949–950.
- RUBIN, B., EPSTEIN, J. & BROOKS, L. (1983). In the press.
- SHELDRIK, G. M. (1976). *SHELX 76* Program for crystal structure determination. Univ. of Cambridge, England.

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## Structure of *N*-[1-(2-Hydroxy-2-phenylethyl)-4-piperidyl]-*N*-phenylpropanamide Hydrochloride (R4333\*), an Analgesic of the Fentanyl Family

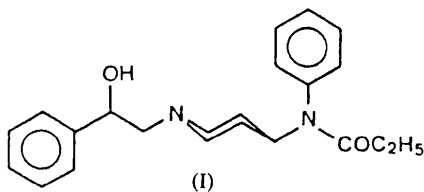
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**Abstract.** C<sub>22</sub>H<sub>28</sub>N<sub>2</sub>O<sub>2</sub>·HCl, *P*2<sub>1</sub>/*c*, *a* = 12.104 (5), *b* = 11.560 (5), *c* = 15.013 (5) Å, β = 101.14 (5)°, *M<sub>r</sub>* = 388.9, *D<sub>m</sub>* = 1.25 (1), *D<sub>x</sub>* = 1.25 (2) Mg m<sup>-3</sup>, *Z* = 4, *T* = 293 K, *R* = 0.06 for 2538 reflexions. The conformation is similar to that found for other compounds of the fentanyl family. Packing is governed by van der Waals interactions; the chloride ion does not contribute to the formation of intermolecular H bonds.

**Introduction.** The crystal structure determination of the title compound (I) is part of a more general study of conformations for narcotic analgesics, particularly those of the fentanyl family. Some of these compounds are very potent analgesics (Van Daele, De Bruyn, Boey, Sanezuk, Agten & Janssen, 1976); in particular R4333 was revealed as being more than 150 times more active than meperidine (Janssen & Van Der Eycken, 1968). Crystals have been obtained from a chloroform/ethanol mixture slowly evaporated. The space group was determined by photographs. Final cell dimensions and intensities were measured on a Nonius CAD-4 four-circle computer-controlled diffractometer.



\* Janssen Pharmaceutica internal code number.

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Table 1. *Instrumental settings for the data collection*

Source Cu <i>K</i> α	λ = 1.54178 Å
Graphite monochromator	
Scan ω-2θ	
Δ2θ = 0.80 + 0.30 tg θ (°)	
Aperture = 2.5 + 0.5 tg θ (mm)	
Confidence level: 2.5 σ, where σ <sup>2</sup> = <i>S</i> + <i>B</i> + (0.03 <i>S</i> ) <sup>2</sup> , <i>S</i> being the scan and <i>B</i> the background count	
2 ≤ θ ≤ 70°	
Total number of independent reflexions	3921
Total observed reflexions	2538

The instrumental settings are listed in Table 1. No corrections were applied for absorption.

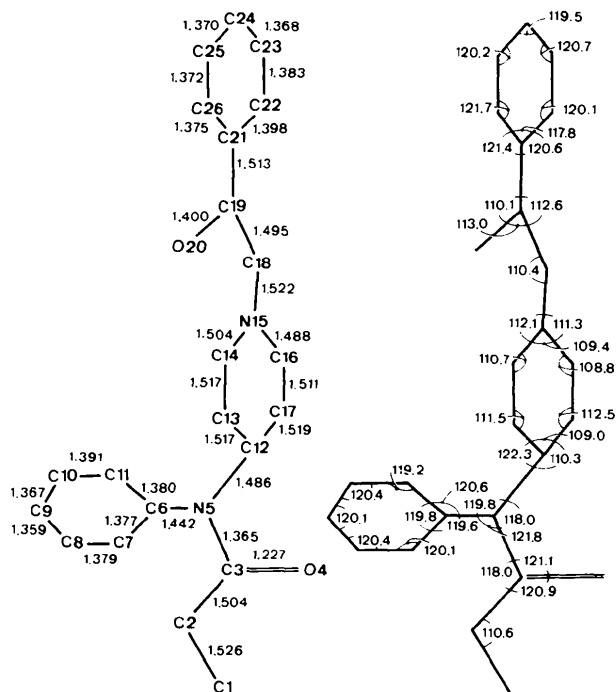
The structure was solved with *MULTAN 78* (Main, Woolfson, Lessinger, Germain & Declercq, 1978). All non-H atoms were located on the most probable *E* map computed with the 208 largest ⟨*E*⟩. Refinement was performed (Sheldrick, 1976) by Fourier maps and full-matrix anisotropic least squares for non-H atoms. Their final coordinates are listed in Table 2. H-atom coordinates were calculated but not refined. The final  $R = \sum ||F_o| - |F_c|| / \sum |F_o| = 0.06$  for the observed reflexions.‡

‡ Lists of structure factors, anisotropic thermal parameters and H atom coordinates have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 36976 (14 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 2. Final coordinates ( $\times 10^4$ ) and  $U_{eq}$  values with e.s.d.'s in parentheses

$$U_{eq} = (U_{11} U_{22} U_{33})^{1/3} (\text{\AA}^2 \times 10^3, \times 10^4 \text{ for Cl}).$$

	x	y	z	$U_{eq}$
C(1)	3478 (7)	476 (7)	3465 (6)	96 (5)
C(2)	3539 (4)	1502 (6)	4112 (4)	67 (4)
C(3)	2447 (3)	1639 (4)	4438 (3)	46 (3)
O(4)	1554 (2)	1322 (3)	3968 (2)	49 (2)
N(5)	2481 (3)	2120 (3)	5273 (2)	41 (2)
C(6)	3503 (3)	2599 (4)	5796 (3)	41 (2)
C(7)	3856 (4)	3679 (4)	5583 (3)	52 (3)
C(8)	4820 (4)	4155 (5)	6090 (4)	63 (3)
C(9)	5432 (4)	3562 (5)	6799 (3)	62 (3)
C(10)	5085 (4)	2494 (6)	7023 (3)	59 (3)
C(11)	4113 (4)	1999 (5)	6522 (3)	52 (3)
C(12)	1402 (3)	2259 (4)	5594 (3)	37 (2)
C(13)	1528 (4)	3013 (4)	6435 (3)	44 (3)
C(14)	441 (4)	3070 (4)	6794 (3)	48 (3)
N(15)	59 (3)	1877 (3)	6995 (2)	47 (2)
C(16)	-145 (4)	1179 (5)	6146 (3)	55 (3)
C(17)	944 (4)	1086 (4)	5800 (3)	50 (3)
C(18)	-979 (4)	1906 (6)	7428 (3)	60 (3)
C(19)	-645 (4)	1854 (5)	8439 (3)	58 (3)
O(20)	-165 (3)	792 (3)	8753 (3)	83 (3)
C(21)	-1608 (3)	2143 (4)	8910 (3)	44 (2)
C(22)	-1893 (4)	1398 (4)	9564 (3)	54 (3)
C(23)	-2722 (4)	1708 (5)	10036 (3)	59 (3)
C(24)	-3267 (4)	2746 (5)	9876 (3)	59 (3)
C(25)	-2990 (4)	3482 (5)	9238 (3)	63 (3)
C(26)	-2172 (4)	3179 (4)	8764 (3)	53 (3)
Cl	2063 (1)	546 (1)	8175 (1)	663 (8)

Fig. 2. Atom numbering, bond lengths (Å) and angles ( $^{\circ}$ ). The e.s.d.'s are  $\leq 0.013$  Å and  $0.5^{\circ}$ , respectively.

**Discussion.** A stereoview of the molecule is represented in Fig. 1. Fig. 2 gives bond lengths and angles with estimated standard deviations and atomic numbering.

The N side chain of the piperidyl group is in a pseudo-equatorial position. This moiety adopts an extended conformation as can be deduced from the torsion-angle values listed in Table 3.

According to the already known structures for analogues (Humblet, 1978), the presence of the 2-hydroxy group [O(20)] does not influence the orientation of this side chain. Moreover, the conformation of the 4-anilinpiperidine moiety is similar to that observed for other compounds of this family. Fig. 3 and Table 4 illustrate the structural analogies between the title compound and other fentanyl derivatives such

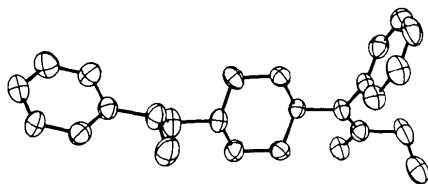


Fig. 1. Drawing of the molecule with thermal ellipsoids (50% probability).

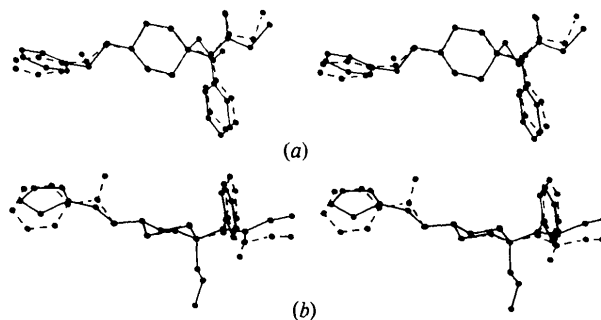
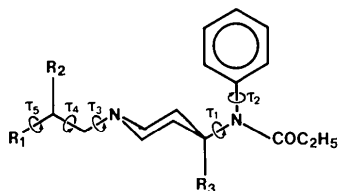


Fig. 3. Stereoviews of pairs of fentanyl derivatives after a least-squares fitting of their piperidyl moiety (OSIRIS graphics program; Michel, 1978); see Table 4 for planar formula. (a) R4333 (dotted lines) and R30490; (b) R4333 (dotted lines) and R30730.

Table 3. Torsion angles with e.s.d.'s ( $^{\circ}$ )

C(1)–C(2)–C(3)–N(5)	151.4 (6)
C(2)–C(3)–N(5)–C(6)	6.5 (6)
O(4)–C(3)–N(5)–C(6)	-173.9 (4)
C(12)–N(5)–C(6)–C(7)	-94.8 (6)
C(3)–N(5)–C(12)–C(13)	-168.5 (4)
C(14)–N(15)–C(18)–C(19)	-95.0 (8)
N(15)–C(18)–C(19)–C(21)	167.4 (4)
C(18)–C(19)–C(21)–C(22)	127.8 (7)
C(12)–C(13)–C(14)–N(15)	57.0 (6)
C(13)–C(14)–N(15)–C(16)	-60.6 (6)
C(14)–N(15)–C(16)–C(17)	61.0 (7)
N(15)–C(16)–C(17)–C(12)	-59.8 (7)
C(16)–C(17)–C(12)–C(13)	55.3 (6)
C(17)–C(12)–C(13)–C(14)	-53.1 (6)

Table 4. Main torsion angles (°) for three known fentanyl derivatives



	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>		
R4333	Phenyl	—OH	—H		
R30490	Phenyl	—H	—C—O—CH <sub>3</sub>		
R30730	Thienyl	—H	—C—O—CH <sub>3</sub>		
	τ <sub>1</sub>	τ <sub>2</sub>	τ <sub>3</sub> *	τ <sub>4</sub>	τ <sub>5</sub>
R4333	—169	—95	22	167	128
R30490	—180	—83	43	170	101
R30730	—162	—87	49	163	35

\* From the orientation of the nitrogen lone pair.

as R30490\* (Koch, De Ranter, Rolies & Dideberg, 1976) and R30730\* (Peeters, Blaton & De Ranter, 1979).

Packing is only governed by van der Waals interactions. Surprisingly, the Cl<sup>-</sup> ion does not contribute to the formation of intermolecular hydrogen bonds. Indeed, Cl<sup>-</sup> is bound to the piperidyl nitrogen [Cl—N(15) 3.120 (20) Å], which is of course protonated, and to the hydroxy group [Cl—O(20)

\* Janssen Pharmaceutica internal code number.

3.002 (9) Å] of the same molecule by means of an intramolecular bridge. No other hydrogens are available for hydrogen bonding; moreover, all contact distances from Cl<sup>-</sup> are greater than 3.50 Å.

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#### References

- HUMBLET, C. (1978). Dissertation doctorale. Facultés Univ. de Namur, Belgium.
- JANSSEN, P. A. J. & VAN DER EYCKEN, C. A. M. (1968). *Drugs Affecting the Central Nervous System*, edited by A. BURGER & M. DEKKER, Vol. 2, pp. 25–60. New York: Marcel Dekker.
- KOCH, M. H. J., DE RANTER, C. J., ROLIES, M. & DIDEBERG, O. (1976). *Acta Cryst.* B32, 2529–2531.
- MAIN, P., WOOLFSON, M. M., LESSINGER, L., GERMAIN, G. & DECLERCQ, J. P. (1978). *MULTAN 78. A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*. Univs. of York, England, and Louvain-la-Neuve, Belgium.
- MICHEL, A. (1978). *OSIRIS* graphics program. Department of Chemistry, Facultés Univ., B-5000 Namur, Belgium.
- PEETERS, O. M., BLATON, N. M. & DE RANTER, C. J. (1979). *Acta Cryst.* B35, 999–1001.
- SHELDRIK, G. M. (1976). *SHELX 76*. Program for crystal structure determination. Univ. of Cambridge, England.
- VAN DAELE, P. G. H., DE BRUYN, M. F. L., BOEY, J. M., SANEZUK, S., AGTEN, J. J. M. & JANSSEN, P. A. J. (1976). *Arzneim.-Forsch.* 26, 1521–1551.

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## Tetrachlorophthalic Anhydride (TCPA), a Refinement

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**Abstract.** C<sub>8</sub>Cl<sub>4</sub>O<sub>3</sub>, *M<sub>r</sub>* = 285.9, monoclinic, *P*2<sub>1</sub>/*n*, *a* = 13.459 (4), *b* = 5.789 (1), *c* = 12.342 (2) Å, β = 91.18 (1)°, *V* = 961.4 (6) Å<sup>3</sup> at 294 K, *Z* = 4, *D<sub>m</sub>* = 2.00, *D<sub>x</sub>* = 2.00 Mg m<sup>-3</sup>, μ(Mo *K*α) = 1.217 mm<sup>-1</sup>. The atomic parameters of tetrachlorophthalic anhydride (TCPA), which had been determined photographically [Rudman (1971). *Acta Cryst.* B27, 262–269], were refined with diffractometer data. The refinements by block-diagonal least squares gave a final *R* value of 0.050 for 1835 independent reflections. All the chemically equivalent bond distances are almost equal within the e.s.d.'s. The results are in agreement

with Rudman's own refinement within the e.s.d.'s [Sake Gowda & Rudman (1982). *Acta Cryst.* B38, 2842–2845], which has been reported independently of this paper.

**Introduction.** In a series of structure determinations of electron donor–acceptor complexes containing TCPA as an electron acceptor, it was necessary to refine the atomic parameters of the TCPA molecule, which had been determined by Rudman based on photographic data (Rudman, 1971). After this paper was submitted, we were informed of the independent refinement of