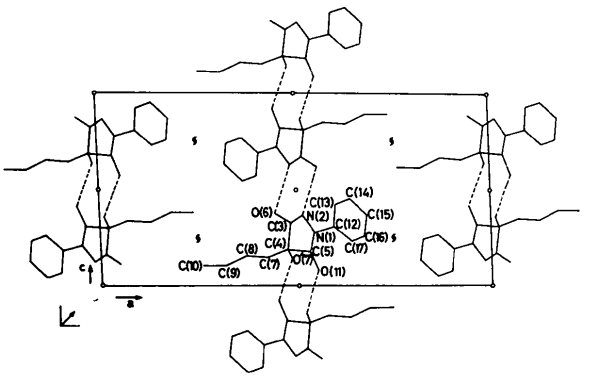

Fig. 2. The crystal structure of 4-hydroxymonophenylbutazone.

Table 2. *Hydrogen-bond parameters with e.s.d.'s in parentheses*

D···*A*		*l* (*D*···*A*)	*θ*(H–*D*···*A*)
N(2)	O(6^{i})	2·842 (4) Å	8 (3)°
O′(7)	O(11^{ii})	2·763 (3)	7 (3)

Key to symbols: *D* donor atom, *A* acceptor atom; symmetry codes: (i) 1–*x*, 2–*y*, 1–*z*; (ii) 1–*x*, 2–*y*, –*z*.

steric interactions between these two rings prevent coplanarity of the five-membered ring with either of them. In 4-hydroxymonophenylbutazone, however, one phenyl ring is replaced by an H atom, thus enabling the five- and the six-membered rings to be nearly coplanar. The planes of the two rings are inclined with respect to each other at 11·2°. This coplanarity presumably leads to the planarity of the hetero nitrogen atom N(1) through interactions involving π orbitals.

The crystal structure of the compound is shown in Fig. 2. The parameters of the hydrogen bonds that contribute to the stability of the structure are listed in Table 2. The molecules are arranged in infinite hydrogen-bonded columns parallel to the *c* axis. In these columns each molecule is involved in two pairs of parallel hydrogen bonds related by an inversion centre. One involves an N–H···O hydrogen bond between the hetero nitrogen atom N(2) and the carbonyl O atom O(6) [2·842 (4) Å], while the other contains an O–H···O hydrogen bond between the hydroxyl O′(7) and the carbonyl O(11) [2·763 (3) Å].

In the crystal, these hydrogen-bonded columns are packed together so that the crystal can be considered as made up of alternating hydrophilic and hydrophobic layers. The former contain primarily N and O atoms belonging to or attached to the five-membered rings whereas the latter contain phenyl and butyl groups.

References

CROMER, D. T. & WABER, J. T. (1965). *Acta Cryst.* **18**, 104–109.

DHANARAJ, V. & VIJAYAN, M. (1983). *Acta Cryst.* C**39**, 1398–1401.

FLOWER, R. J. (1974). *Pharmacol. Rev.* **26**, 33–67.

GERMAIN, G., MAIN, P. & WOOLFSON, M. M. (1971). *Acta Cryst.* A**27**, 368–376.

HAMILTON, W. C. (1959). *Acta Cryst.* **12**, 609–610.

KRISHNA MURTHY, H. M. & VIJAYAN, M. (1981). *Acta Cryst.* B**37**, 210–213.

SINGH, T. P. & VIJAYAN, M. (1977). *J. Chem. Soc. Perkin Trans.* 2, pp. 693–699.

STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.

VIJAYAN, M. (1983). *Proc. Indian Acad. Sci.* (*Chem. Sci.*), **92**, 463–471.

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Structure of Thiamin Dinitrate

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Abstract. $C_{12}H_{18}N_4OS^{2+}.2NO_3^-$, $M_r = 390{\cdot}18$, triclinic, $P\bar{1}$, $a = 8{\cdot}9260\ (8)$, $b = 10{\cdot}201\ (1)$, $c = 10{\cdot}405\ (1)$ Å, $\alpha = 97{\cdot}897\ (8)$, $\beta = 105{\cdot}059\ (7)$, $\gamma = 104{\cdot}437\ (9)°$, $V = 865{\cdot}01$ Å^3, $Z = 2$, $D_m = 1{\cdot}494$, $D_x = 1{\cdot}498$ Mg m^{-3}, λ(Cu $K\alpha$) = 1·5418 Å, $\mu = 2{\cdot}086$ mm^{-1}, $F(000) = 408$, $T = 296$ K, $R = 0{\cdot}050$ for 2619 unique observed reflections. The structure was found to be in the characteristic *F* conformation and is similar to that of

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thiamin mononitrate [Yang (1983). PhD Thesis, University of Pittsburgh], with the additional nitrate ion linking the pyrimidine group of an adjacent molecule.

Introduction. The pyrophosphate ester of thiamin is a coenzyme for a number of biochemically important reactions. The basic mechanism of thiamin-catalyzed reactions was discovered by Breslow (1958). Since then, a variety of techniques have been applied in order to provide a more detailed description of the mechanism (Gallo, Mieyal & Sable, 1978; Sable & Gubler, 1982). Among these varied approaches have been numerous single-crystal X-ray diffraction analyses of thiamin, its catalytic reaction intermediates and analogues. On the basis of the structures of several intermediates, it was suggested that stacking interactions between the pyrimidine ring of thiamin and the substrate (pyruvate) might influence the conformation of the thiamin molecule (Pletcher, Sax, Blank & Wood, 1977). Suitable single crystals of the pyruvate adduct of thiamin or the pyruvate anion of thiamin have not yet been prepared. It was therefore decided to examine the nitrate salts of thiamin to see if this small planar anion would form any stacking interaction with the pyrimidine ring.

Thiamin mononitrate, the neutral-pH form (monovalent), was studied first. The exceptional diffracting quality of this crystal prompted a separate low-temperature charge-density study (Turano, Pletcher, Furey & Sax, 1982). Thiamin dinitrate, the low-pH form (divalent), was then examined and is reported here.

Experimental. Thiamin dinitrate (THDN) was prepared by adding excess dilute nitric acid to a solution of thiamin mononitrate (purchased from ICN Pharmaceuticals Inc., Cleveland, Ohio) and was isolated and crystallized from aqueous acetone as rods ($0\cdot1 \times 0\cdot2 \times 0\cdot6$ mm); D_m by flotation in CCl_4/C_6H_6 mixture.

Unit-cell parameters were obtained from a least-squares fitting of diffractometer setting angles for 12 centered reflections; each angle is the average of four separate measurements ($\pm 2\theta$, χ; $\pm 2\theta$, $180 + \chi$). Reflection data ($2\theta_{max}$ 127°; $h = 0$ to 10, $k = -11$ to 11, $l = -11$ to 11) were collected at room temperature on a Picker FACS-1 diffractometer using graphite-monochromated Cu $K\alpha$ radiation and a θ:2θ scan technique with a 2θ scan rate of 2° min^{-1} over a scan range of 2°. Background was measured for 20 s at each end of the scan range. Three standards, measured after every 50 reflections, showed no decrease in intensity and varied less than ±2%. Intensity data were placed on a uniform scale using the program *DATAPC* (Shiono, 1971). Lorentz and polarization factors were applied. The data were not corrected for absorption but a secondary-extinction correction (Zachariasen, 1963) was applied just before the final stage of refinement [I_o(corrected) $= I_o(1 + 2gI_c)$ where $g = 0\cdot18811 \times 10^{-4}$]. The assumed space group, $P\bar{1}$, indicated by an $N(Z)$ test and E statistics, resulted in satisfactory crystal-structure refinement. One hemisphere of reflection data with positive h was collected on a diffractometer. A large portion was recollected due to intermittent diffractometer failures. The merging R_{int} for 2144 duplicates among 4911 reflections was 0·020. Of the 2767 unique reflections 2619 exceeded $6\sigma(F)$ and were used in the subsequent structure solution and refinement {$\sigma(F)$ is given by $(\frac{1}{2}\mathrm{Lp}|F|)\sigma(I)_m$, $\sigma(I) = (I + k^2B)^{1/2}$; modified counting statistic $\sigma(I)_m = [(0\cdot02I)^2 + \sigma^2(I)]^{1/2}$; k = scan time/background time}.

The positions of all the non-H atoms were located using *MULTAN*78 (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978). The β-hydroxyl side chain was disordered due to rotations about two bonds [C(5)–C(5α) and C(5α)–C(5β)]. *SHELX*76 (Sheldrick, 1976) was used to refine the relative occupancies of the two positions of the side chain such that they summed to unity (refined occupancies are 0·64 and 0·36). Nine of the 21 H atoms were located in difference maps. The rest were generated by *SHELX*76 using idealized stereochemistry. Subsequent refinements were carried out using the program *QWKREF* (Furey, Wang & Sax, 1982). The refinement converged to an R of 0·050, wR of 0·063 and S of 1·22. The weighting scheme was $w = 1/[\sigma^2(F_o)]$ and the quantity minimized was $\sum w||F_o| - k|F_c||^2$ where k is a single scale factor. The initial e.s.d.'s for the structure factors were derived from counting statistics, but were eventually replaced by ones making $|F_o - F_c|/\sigma(F_o)$ independent of $|F_o|$ [*NANOVA*, Turano (1979); based on the algorithm of Lalancette, Cefola, Hamilton & LaPlaca (1967)]. The assignments for $\sigma(F_o)$ are: for $0 < F_o \le 12\cdot0$, $\sigma(F_o) = 0\cdot007F_o + 0\cdot409$; and for $12\cdot0 < F_o \le 100\cdot0$, $\sigma(F_o) = 0\cdot041F_o - 0\cdot080$. The atomic scattering factors were taken from *International Tables for X-ray Crystallography* (1974); the H scattering factors are for bonded atoms. The highest peaks in the final difference Fourier map occur near the disordered side chain which has relatively high thermal factors (residual density is 0·89 e Å^{-3}). The final atomic coordinates with their e.s.d.'s are listed in Table 1. The shift to e.s.d. ratios in final cycles of refinement are less than 0·02.

Discussion. An *ORTEP* (Johnson, 1971) drawing of thiamin dinitrate is shown in Fig. 1.* The labeling scheme conforms with the accepted chemical nomenclature and utilizes the standard we adopted for

* Lists of structure factors, anisotropic thermal parameters, refined H-atom positions, close contacts, least-squares planes and torsion angles have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 43264 (20 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

thiamin structures. The bond distances and angles are listed in Table 2. Their values are similar to those of other protonated forms of thiamin such as thiamin pyrophosphate hydrochloride (Pletcher & Sax, 1972). The bond lengths of the two nitrates, which are situated in different environments, also show some degree of variation. The molecule assumes the preferred *F* conformation (Shin, Pletcher, Sax & Blank, 1979). Fig. 2 shows the packing diagram with the hydrogen-bonding networks that link the different molecules together.

The distance between the S and the nitrate O in THDN is 3·168 Å which is significantly shorter (76σ) than the van der Waals contact distance of 3·32 Å (Bondi, 1964). The interaction between S and negative ions or electronegative atoms has been observed in a number of other thiamin structures and it has been suggested to have mechanistic importance in C(2)-substituted thiamin (Sax, Pulsinelli & Pletcher, 1974). The C···O close contacts are similar to those in other thiamin structures.

Table 1. *Fractional atomic coordinates* ($\times 10^4$) *and equivalent isotropic temperature factors for THDN, with e.s.d.'s in parentheses*

$$B_{eq} = \tfrac{4}{3}\sum_i\sum_j \beta_{ij}\mathbf{a}_i.\mathbf{a}_j.$$

	x	*y*	*z*	B_{eq}(Å^2)
S(1)	4796 (1)	6875 (1)	9318 (1)	3·7
C(2)	6035 (3)	8019 (3)	10738 (3)	3·0
N(3)	7550 (2)	8006 (2)	10983 (2)	2·5
C(3,5′)	8938 (3)	9034 (3)	12079 (3)	3·0
C(4)	7800 (3)	7055 (2)	10019 (2)	2·8
C(4α)	9458 (4)	6957 (3)	10121 (3)	4·4
C(5)	6391 (3)	6344 (2)	9030 (3)	3·1
C(5α)	6190 (4)	5367 (3)	7734 (3)	4·0
C(5β)	6874 (10)	6100 (10)	6753 (8)	4·3
C(5β′)	6121 (18)	6129 (19)	6576 (14)	4·5
O(5γ)	6154 (5)	7099 (4)	6320 (3)	4·4
O(5γ′)	7479 (9)	7318 (6)	6827 (6)	4·0
N(1′)	7957 (3)	11937 (2)	13929 (2)	3·3
C(2′)	7429 (3)	11382 (3)	14888 (3)	3·1
C(2′α)	6876 (4)	12261 (3)	15830 (3)	4·6
N(3′)	7396 (3)	10125 (2)	15022 (2)	3·3
C(4′)	7847 (3)	9327 (2)	14122 (2)	2·8
N(4′α)	7743 (4)	8052 (2)	14293 (3)	3·9
C(5′)	8390 (3)	9857 (2)	13073 (2)	2·7
C(6′)	8425 (3)	11183 (3)	13026 (3)	3·2
N(1″)	3274 (3)	9852 (2)	11288 (2)	3·5
O(1″)	4544 (3)	10109 (3)	12227 (2)	5·6
O(2″)	2990 (3)	8966 (3)	10242 (3)	6·4
O(3″)	2276 (3)	10512 (2)	11345 (2)	4·7
N(1‴)	8818 (3)	15070 (2)	13140 (2)	3·4
O(1‴)	9080 (4)	16258 (2)	12955 (3)	6·8
O(2‴)	9459 (3)	14282 (2)	12658 (3)	6·6
O(3‴)	7883 (3)	14665 (2)	13794 (3)	5·2

Table 2. *Bond lengths* (Å) *and angles* (°) *between non*-H *atoms, with e.s.d.'s in parentheses*

S(1)–C(2)	1·674 (3)	C(2′)–C(2′α)	1·496 (4)
S(1)–C(5)	1·724 (3)	C(2′)–N(3′)	1·303 (3)
C(2)–N(3)	1·313 (3)	N(3′)–C(4′)	1·360 (3)
N(3)–C(4)	1·398 (3)	C(4′)–N(4′α)	1·321 (3)
C(4)–C(5)	1·354 (4)	C(4′)–C(5′)	1·423 (3)
C(4)–C(4α)	1·485 (4)	C(5′)–C(6′)	1·353 (4)
C(5)–C(5α)	1·503 (4)	C(6′)–N(1′)	1·347 (4)
C(5α)–C(5β)	1·510 (9)	N(1″)–O(1″)	1·231 (3)
C(5α)–C(5β′)	1·517 (17)	N(1″)–O(2″)	1·239 (3)
C(5β)–O(5γ)	1·399 (8)	N(1″)–O(3″)	1·252 (3)
C(5β′)–O(5γ′)	1·423 (18)	N(1‴)–O(1‴)	1·228 (3)
N(3)–C(3,5′)	1·491 (3)	N(1‴)–O(2‴)	1·222 (3)
C(3,5′)–C(5′)	1·497 (3)	N(1‴)–O(3‴)	1·237 (3)
N(1′)–C(2′)	1·343 (4)		

C(2)–S(1)–C(5)	91·3 (1)	N(1′)–C(2′)–N(3′)	122·3 (2)
N(3)–C(2)–C(4)	112·4 (2)	N(1′)–C(2′)–C(2′α)	117·9 (2)
C(2)–N(3)–C(4)	114·3 (2)	N(3′)–C(2′)–C(2′α)	119·8 (2)
C(2)–N(3)–C(3,5′)	123·6 (2)	C(2′)–N(3′)–C(4′)	118·8 (2)
C(4)–N(3)–C(3,5′)	121·5 (2)	N(3′)–C(4′)–C(5′)	121·1 (2)
N(3)–C(4)–C(5)	111·2 (2)	N(3′)–C(4′)–N(4′α)	115·7 (2)
N(3)–C(4)–C(4α)	120·8 (2)	C(5′)–C(4′)–N(4′α)	123·2 (2)
C(5)–C(4)–C(4α)	127·9 (2)	C(4′)–C(5′)–C(6′)	116·3 (2)
C(4)–C(5)–S(1)	110·7 (2)	C(4′)–C(5′)–C(3,5′)	123·2 (2)
C(4)–C(5)–C(5α)	127·1 (3)	C(6′)–C(5′)–C(3,5′)	120·4 (2)
S(1)–C(5)–C(5α)	121·7 (2)	C(5′)–C(6′)–N(1′)	120·8 (2)
C(5)–C(5α)–C(5β)	112·6 (4)	O(1″)–N(1″)–O(2″)	120·4 (2)
C(5)–C(5α)–C(5β′)	110·1 (6)	O(1″)–N(1″)–O(3″)	120·9 (3)
C(5α)–C(5β)–O(5γ)	114·7 (5)	O(2″)–N(1″)–O(3″)	118·3 (3)
C(5α)–C(5β′)–O(5γ′)	114·5 (10)	O(1‴)–N(1‴)–O(2‴)	119·9 (2)
N(3)–C(3,5′)–C(5′)	112·5 (2)	O(1‴)–N(1‴)–O(3‴)	119·9 (2)
C(2′)–N(1′)–C(6′)	120·6 (2)	O(2‴)–N(1‴)–O(3‴)	120·1 (2)

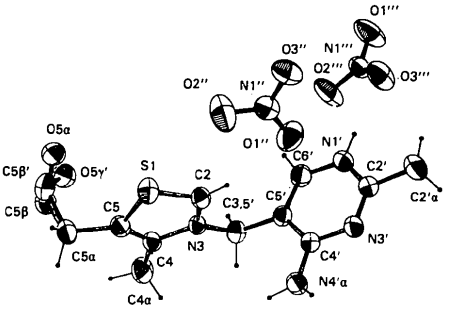

Fig. 1. *ORTEP* drawing (Johnson, 1971) of THDN. Thermal ellipsoids are shown at a 50% probability level for non-H atoms; C(5β) and O(5γ) are disordered.

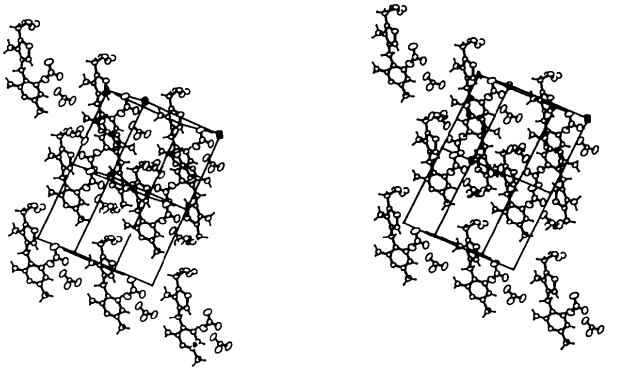

Fig. 2. Stereoview of the molecular packing in THDN crystals (two cells).

In THDN one of the nitrate ions, which is in the plane of the thiazolium ring, hydrogen-bonds to C(2)—H and forms a close contact with S(1). The O(1'') nitrate O of this same nitrate group is close to the plane of the pyrimidine ring (the perpendicular distance is 2·92 Å). This nitrate also forms a stacking interaction with a centrosymmetrically related thiazolium ring with O(3'') situated over the ring nearly midway between S(1) and N(3) at a distance of 2·88 Å from the ring plane. The other nitrate ion, which is approximately in the plane of the pyrimidine ring, spans the pyrimidine group of two molecules linking N(1') and C(6') of one pyrimidine to N(4'α) of another. However, there is no stacking interaction between the nitrate and pyrimidine ring.

A review of the literature (Pletcher, Sax, Turano & Chang, 1982) shows that the conformation of thiamin seen in the solid state is either the *F* or the *S* form. Turano *et al.* (1982) demonstrated by a charge-density analysis of thiamin mononitrate the existence of a weak interaction between the ionizable hydrogen H(2) and the π electrons of the pyrimidine ring. They concluded that this weak attractive intramolecular force gives a slight advantage in energy to the *F* form. In this study the *F* conformation also prevails. In addition to the interaction between H(2) and the π electrons, the nitrate ion in linking the two rings in the molecule may provide additional stability to the *F* form in this case.

References

BONDI, A. (1964). *J. Phys. Chem.* **68**, 441–451.

BRESLOW, R. (1958). *J. Am. Chem. Soc.* **80**, 3719–3726.

FUREY, W. JR, WANG, B. C. & SAX, M. (1982). *J. Appl. Cryst.* **15**, 160–166.

GALLO, A. A., MIEYAL, J. J. & SABLE, H. Z. (1978). *Bioorganic Chemistry*, Vol. 4, pp. 147–177. New York: Academic Press.

International Tables for X-ray Crystallography (1974). Vol. IV. Birmingham: Kynoch Press. (Present distributor D. Reidel, Dordrecht.)

JOHNSON, C. K. (1971). *ORTEP*II. Report ORNL-3794, revised. Oak Ridge National Laboratory, Tennessee.

LALANCETTE, R. A., CEFOLA, M., HAMILTON, W. C. & LAPLACA, S. J. (1967). *Inorg. Chem.* **6**, 2127–2134.

MAIN, P., HULL, S. E., LESSINGER, L., GERMAIN, G., DECLERCQ, J.-P. & WOOLFSON, M. M. (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, Belgium.

PLETCHER, J. & SAX, M. (1972). *J. Am. Chem. Soc.* **94**, 3998–4005.

PLETCHER, J., SAX, M., BLANK, G. & WOOD, M. (1977). *J. Am. Chem. Soc.* **99**, 1396–1403.

PLETCHER, J., SAX, M., TURANO, A. & CHANG, C. H. (1982). *Ann. N.Y. Acad. Sci.* **378**, 454–458.

SABLE, H. Z. & GUBLER, C. J. (1982). Editors. *Ann. N.Y. Acad. Sci.* **378**, 1–470.

SAX, M., PULSINELLI, P. & PLETCHER, J. (1974). *J. Am. Chem. Soc.* **96**, 155–165.

SHELDRICK, G. M. (1976). *SHELX*76. Program for crystal structure determination. Univ. of Cambridge, England.

SHIN, W., PLETCHER, J., SAX, M. & BLANK, G. (1979). *J. Am. Chem. Soc.* **101**, 2462–2469.

SHIONO, R. (1971). *DATAPC*. Tech. Rep. 49. Department of Crystallography, Univ. of Pittsburgh, Pittsburgh, PA 15260.

TURANO, A. (1979). *NANOVA*. Univ. of Pittsburgh, Pittsburgh, PA 15260.

TURANO, A., PLETCHER, J., FUREY, W. & SAX, M. (1982). *Ann. N.Y. Acad. Sci.* **378**, 91–106.

YANG, D. S. C. (1983). PhD Thesis, Univ. of Pittsburgh, Pittsburgh, PA 15260.

ZACHARIASEN, W. H. (1963). *Acta Cryst.* **16**, 1139–1144.

Acta Cryst. (1987). C**43**, 316–319

Structure and Absolute Configuration of a Phenylpiperidine Analgesic 3-(*m*-Methoxyphenyl)-3-methylpiperidinium Hydrogen Tartrate

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Abstract. $C_{13}H_{20}NO^+.C_4H_5O_6^-$, $M_r = 355{\cdot}39$, orthorhombic, $P2_12_12_1$, $a = 7{\cdot}534$ (3), $b = 7{\cdot}677$ (3), $c = 30{\cdot}437$ (7) Å, $V = 1760{\cdot}4$ Å^3, $Z = 4$, $D_x = 1{\cdot}34$ Mg m^{-3}, λ(Cu $K\alpha$) = 1·5418 Å, $\mu = 0{\cdot}875$ mm^{-1}, $F(000) = 760$, $T = 291$ K, $R = 0{\cdot}055$ for 1045 observed reflections. The N atom is protonated and displays tetrahedral coordination. The piperidine ring has a chair conformation and is approximately perpendicular to the phenyl ring. Absolute configuration is confirmed and the molecular conformation in the crystal structure is compared with the calculated low-energy conformation postulated to be the antagonist pharmacophore.

Introduction. The discovery by Kugita, Inoue, Oine, Hayashi & Nurimoto (1964) and Kugita, Oine, Inoue & Hayashi (1965) of the analgesic properties of phenylpiperidines has led to the synthesis and pharmacological studies of several series of 3- and 4-phenylpiperidines (Jacoby, Nieforth & Willette, 1974;

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