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.

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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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Jacoby, Boon, Darling & Willette, 1981; Iorio & Casey, 1978; Lawson, Cheng, Uyeno, Toll, DeGraw & Loew, 1985). These compounds exhibit mixed analgesic agonist and antagonist activity. The agonist/antagonist potency ratios are dependent on the position of the phenyl-ring substituent and the nature of substituents at the 2 and 3 C atoms of the piperidine ring.

In addition, the 3-phenylpiperidines possess a chiral centre at C3, which is another significant factor in the observed agonist/antagonist potency ratios of these compounds. G. H. Loew and coworkers isolated optical isomers of 3-(*m*-OH)phenyl-3-methylpiperidines and studied receptor binding affinities and analgesic and narcotic antagonist potencies of these isomers. These studies showed that while receptor affinities do not vary, all of the antagonist activity resides in the (+)-isomer of each enantiomeric pair (Lawson *et al.*, 1985). We report the X-ray single-crystal study of the (+)-L-tartrate salt of 3-(*m*-OCH_3)phenyl-3-methylpiperidine, undertaken to confirm the absolute configuration and to examine the conformational correlates of agonism and antagonism in this class of analgesic compounds.

Experimental. Plate-shaped crystal, 0·07 × 0·17 × 0·33 mm. Ni-filtered Cu $K\alpha$ radiation was used for measuring 1660 independent reflections. Picker FACS1 system was used for data collection, θ–2θ scan technique, scan rate = 1° min^{-1}, $2\theta_{max} = 125°$, h: 0→8, k: 0→8, l: 0→35, crystal mounted along **b**. No absorption or extinction corrections were applied. Three standards measured every 100 reflections, intensity variation = 2%. 12 reflections used for measuring lattice parameters, $2\theta > 45°$.

The crystal data were reduced as usual. Trials with routine runs of *MULTAN*80 (Main *et al.*, 1980) did not solve the structure. Choosing different starting reflections and inputting a planar six-membered ring with *meta*-related O and C atoms as a partial structure did not help. The result always showed two seven-atom fragments, and had relatively high ψ_0 values (>1·96). Structure-factor calculations based on the fragments resulted in high R values (47%) and subsequent Fourier maps did not reveal additional parts of the structure.

The program *RANTAN* (Yao, 1982) was successful in solving the structure. Of 190 phase sets calculated, the one with the best figures-of-merit and lowest ψ_0 (1·35) resulted in an E map which gave the positions of the 25 non-H atoms (R = 23·7%).

Anisotropic refinement reduced R to 8·99%, and all H atoms but one were identified in subsequent difference Fourier maps. Further refinement, in which H-atom positional parameters were varied but their thermal parameters were fixed isotropically, resulted in convergence at $R = 0{\cdot}055$ and $wR = 0{\cdot}060$ for 1045 reflections with $I \geq 3\sigma(I)$. Refinement was based on F with individual weights $w = 1/\sigma^2(F)$ where $\sigma(F)$'s were calculated from counter intensity statistics. The shift/e.s.d. ratio in the final cycle is ≤0·22, and the goodness-of-fit is 1·7187. $\Delta\rho$ in the final difference map is 0·22 e $Å^{-3}$ and the peaks were deemed as spurious. Real f from Cromer & Mann (1968), f' and f'' from *International Tables for X-ray Crystallography* (1974), scattering factors for H from Stewart, Davidson & Simpson (1965). Final parameters are shown in Table 1.*

* Lists of structure factors, anisotropic thermal parameters and bond angles involving H atoms have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 43344 (13 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. *Atomic coordinates* (×10⁴ *or* ×10³ *for* H *atoms*) *and equivalent isotropic thermal parameters*

	x	y	z	B_{eq}*(Å²)
C1	−1807 (12)	219 (10)	3220 (3)	2·70
C2	−45 (13)	618 (11)	3304 (3)	3·37
C3	747 (13)	2003 (12)	3089 (3)	3·55
C4	−138 (14)	2998 (12)	2798 (3)	3·83
C5	−1897 (13)	2626 (13)	2706 (3)	4·18
C6	−2735 (13)	1224 (13)	2932 (3)	3·67
C7	−2708 (11)	−1274 (10)	3480 (3)	2·92
C8	−2692 (13)	−722 (10)	3960 (3)	2·91
N9	−3321 (10)	−2153 (9)	4260 (2)	2·77
C10	−2204 (14)	−3754 (12)	4224 (3)	3·51
C11	−2243 (15)	−4412 (12)	3754 (3)	3·71
C12	−1604 (15)	−2974 (12)	3435 (3)	3·90
C13	−4625 (14)	−1588 (15)	3327 (4)	4·44
O14	2489 (10)	2252 (9)	3205 (2)	5·01
C15	3227 (18)	3863 (18)	3120 (5)	5·88
C16	7472 (12)	−4234 (9)	492 (3)	2·34
C17	7905 (10)	−2366 (10)	619 (2)	2·26
C18	7067 (11)	−1134 (9)	292 (3)	2·44
C19	7299 (11)	738 (10)	452 (3)	2·75
O20	8809 (8)	−5262 (7)	429 (2)	3·08
O21	5941 (8)	−4682 (7)	448 (2)	3·81
O22	9751 (8)	−2043 (7)	645 (2)	3·38
O23	7645 (8)	−1447 (6)	−139 (2)	2·75
O24	6655 (8)	1140 (7)	807 (2)	3·42
O25	8098 (8)	1766 (6)	179 (2)	2·94
H2	69 (12)	1 (11)	358 (3)	
H4	26 (13)	380 (12)	258 (3)	
H5	−262 (12)	310 (12)	251 (3)	
H6	−414 (13)	125 (12)	291 (3)	
H8*a*	−125 (13)	−35 (12)	408 (3)	
H8*b*	−345 (13)	24 (12)	398 (3)	
H10*a*	−263 (13)	−458 (12)	442 (3)	
H9*a*	−336 (13)	−166 (12)	453 (3)	
H9*b*	−472 (14)	−243 (12)	426 (3)	
H10*b*	−100 (13)	−344 (13)	433 (3)	
H11*a*	−137 (13)	−530 (11)	371 (3)	
H11*b*	−355 (14)	−462 (12)	371 (3)	
H12*a*	6 (12)	−276 (11)	345 (3)	
H12*b*	−169 (13)	−342 (11)	312 (3)	
H13*a*	−463 (14)	−198 (13)	304 (3)	
H13*b*	−526 (12)	−240 (13)	356 (3)	
H13*c*	−517 (13)	−43 (12)	326 (3)	
H15*a*	338 (13)	394 (12)	275 (3)	
H15*b*	436 (14)	403 (14)	319 (3)	
H15*c*	251 (15)	469 (12)	320 (3)	
H17	734 (9)	−219 (9)	98 (2)	
H18	577 (11)	−148 (10)	29 (3)	
H22	1039 (13)	−278 (13)	53 (3)	
H23	905 (13)	−114 (12)	−13 (3)	

* B_{eq} for H atoms fixed at 5·65 Å² except 3·5 Å² for H17 and H18 [B_{eq} calculated from $B_{eq} = \frac{4}{3}(\beta_{11}a^2 + \beta_{22}b^2 + \beta_{33}c^2 + \beta_{12}ab\cos\gamma + \beta_{13}ac\cos\beta + \beta_{23}bc\cos\alpha)$].

Discussion. Fig. 1 shows the bond lengths and angles together with the atom-numbering scheme used in this study. Bond angles involving H atoms have been deposited. Fig. 2 is a stereoscopic drawing of the 3-(*m*-OCH_3)phenyl-3-methylpiperidine cation and the tartrate anion. N9 is protonated and displays tetrahedral coordination. While one of the two H atoms of the tartrate carboxyl groups has been given up to protonate N9, the remaining H could not be located in electron-density difference maps. However, since the distances C16—O20 = 1·29 (1) Å and C19—O25 = 1·29 (1) Å are both significantly longer than C16—O21 = 1·21 (1) Å and C19—O24 = 1·23 (1) Å, it may be assumed that the position of the unlocated H atom is disordered between bonding proximities of O20 and O25.

The piperidine ring has a chair conformation and is approximately perpendicular to the phenyl ring (angle between normals to the phenyl ring plane and the mean plane of the piperidine ring is 87°). The molecular conformation of 3-(*m*-OCH_3)phenyl-3-methylpiperidine is very similar to the low-energy conformation postulated to be the antagonist pharmacophore for 3-arylpiperidines from quantum chemical calculations (Loew, Burt & Hashimoto, 1981), the only difference being a 180° rotation of the phenyl ring about the C1—C7 bond. The crystal-structure conformation may, of course, be influenced by intermolecular hydrogen bonding (Table 2). As rotational freedom about C1—C7 is possible, and as the energy difference between the two 180° conformations is presumably small, the present result is not inconsistent with the previous calculated low-energy-conformation conclusions.

Table 2. *Intermolecular hydrogen bonding*

	O···O or N···O distance (Å)	O···H distance (Å)	∠O—H···O or ∠N—H···O (°)
O22—H22···O23	2·902 (8)	2·16 (10)	153 (10)
O23—H23···O21	2·793 (8)	1·84 (10)	144 (7)
N9—H9*a*···O25	2·818 (8)	1·98 (9)	152 (8)
N9—H9*b*···O24	2·841 (10)	1·84 (10)	153 (7)
N9—H9*a*···O21	2·879 (9)	2·47 (10)	108 (7)
N9—H9*b*···O21	2·879 (9)	2·46 (9)	101 (6)
O20···O25	2·464 (7)	H not located	

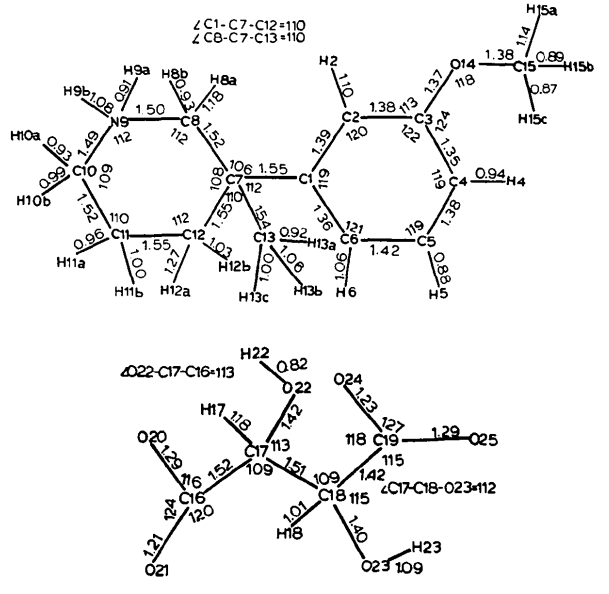

Fig. 1. Bond lengths (Å) and angles (°) of 3-(*m*-OCH_3)phenyl-3-methylpiperidinium hydrogen tartrate. Standard e.s.d.'s for C—C, C—O and C—N bonds are ≤0·01 Å, for C—H and N—H bonds ≤0·1 Å, and for bond angles ≤1°.

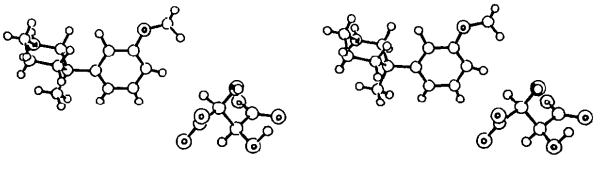

Fig. 2. Stereoscopic drawing of 3-(*m*-OCH_3)phenyl-3-methylpiperidinium hydrogen tartrate.

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Structure of 11β-[4-(Dimethylamino)phenyl]-17β-hydroxy-17α-(2-propenyl)-estra-4,9-dien-3-one

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Abstract. $C_{29}H_{37}NO_2$, $M_r = 431{\cdot}62$, orthorhombic, $P2_12_12_1$, $a = 11{\cdot}3527\ (9)$, $b = 12{\cdot}035\ (1)$, $c = 17{\cdot}594\ (1)$ Å, $V = 2403{\cdot}8\ (3)$ Å^3, $Z = 4$, $D_x = 1{\cdot}192$ g cm^{-3}, $\lambda(\text{Cu } K\alpha) = 1{\cdot}54184$ Å, $\mu(\text{Cu } K\alpha) = 5{\cdot}4$ cm^{-1}, $F(000) = 936$, room temperature, $R = 0{\cdot}060$ for 1817 unique reflexions with $I \geq 2{\cdot}5\sigma(I)$. The overall conformation of the title compound is slightly more bent than that of the 17α-(1-propynyl) parent compound but compared with other $\Delta^{4,9}$ steroids the molecular skeleton is rather flat. The *A* and *B* rings are statistically disordered (1:2), which is indicative of the flexibility of the steroid skeleton. The molecules are hydrogen-bonded head-to-tail.

Introduction. The title compound is the 17α-(2-propenyl) analogue of RU 38 486 {11β-[4-(dimethylamino)phenyl]-17β-hydroxy-17α-(1-propynyl)estra-4,9-dien-3-one; Sakiz, Euvrard & Baulieu (1984)}, which is the lead compound in studies aimed at finding new drugs with antiprogestational and antiglucocorticoid activities (*e.g.* Neef, Beier, Elger, Henderson & Wiechert, 1984) and whose structure was reported recently (van Geerestein, Kanters, van der Sluis & Kroon, 1986). In contrast with RU 38 486, which suffered from serious crystallization problems, the title compound could be readily crystallized and here we report its X-ray analysis.

Experimental. Crystals (ORG 30761) obtained through the Scientific Development Group of Organon, Oss, The Netherlands, were prepared by slow evaporation from acetone at room temperature. Data measured on a crystal of approximate dimensions $0{\cdot}15 \times 0{\cdot}45 \times 0{\cdot}28$ mm on an Enraf–Nonius CAD-4 diffractometer with Ni-filtered Cu $K\alpha$ radiation; lattice parameters refined by least-squares fitting of four alternative settings [*SET*4; de Boer & Duisenberg (1984)] of eight symmetry-related reflexions (668, $\bar{6}68$ *etc.*) with $\theta = \pm 41{\cdot}3°$; ω–2θ scan mode, $\Delta\omega = (0{\cdot}50 + 0{\cdot}15\tan\theta)°$, 2528 independent reflexions measured up to $\theta = 70°$, *h,k,l* (max. range 13, 14, 21), 1817 of these considered observed [$I \geq 2{\cdot}5\sigma(I)$] and used for structure refinement. Three periodically measured standard reflexions ($\bar{2}11$, 111, 201) showed intensity variations less than 0·5%; Lp corrections, no correction for absorption or secondary extinction.

Structure solved by direct methods using a preliminary version of *SHELXS*84 (Sheldrick, 1984). Default run gave no solution, possibly due to the fact that only 4941 unique triples were found using 265 largest *E* values, sorted according to $|E|$. The ratio of phase relations to unknown phases was increased by sorting 300 largest *E* values according to the estimated α, which resulted in 9544 triplets. Best *E* map of this run gave all 32 non-H atoms as the 32 highest peaks.

Anisotropic refinement, using *SHELX*76 (Sheldrick, 1976), resulted in very large values for the $U(1,1)$ component of the temperature tensor for atoms C(2), C(6) and C(7), indicating an unrealistic mean-square amplitude of vibration of about 1 Å, and short bond distances involving these atoms [*e.g.* C(6)–C(7) = 1·33 Å]. During subsequent refinement the bond lengths involving these atoms, which were assigned fixed isotropic thermal parameters, were constrained to realistic values. The difference map revealed one satellite peak for C(2), and for C(6) and C(7) as well, indicating a statistical disorder over two positions, here labelled *A* and *B*. The coordinates of

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