

Fig. 1. View of the hydrogen-bonded pair of molecules constituting the asymmetric unit. Thermal ellipsoids of non-H atoms are drawn at the 50% probability level. Both orientations of the disordered ethyl group are shown.

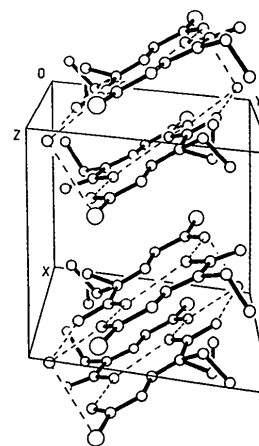


Fig. 2. View of the unit-cell contents.

the conformations of the two molecules. Additional hydrogen bonds connect this pair of molecules to the water of hydration and to other molecules. Details of the potential hydrogen-bonding interactions are included in Table 2. A number of these interactions are shown in Fig. 2, which depicts the unit-cell contents.

A search of the Cambridge Structural Database (Allen *et al.*, 1979) reveals numerous thiosemicarbazones, but none that are derivatives of simple monocarboxylic acids. Pyruvic acid thiosemicarbazone also crystallizes as a hemihydrate (Timken, Wilson & Hendrickson, 1985) and may well have a similar crystal structure.

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## Structure of *N,N*-Dimethyl[2-(2-ethoxyphenylcarbamoyloxy)-2-methylpropyl]-ammonium Chloride

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**Abstract.**  $C_{15}H_{25}N_2O_3^+ \cdot Cl^-$ ,  $M_r = 316.9$ , monoclinic,  $P2_1/c$ ,  $a = 13.228$  (9),  $b = 11.065$  (8),  $c = 11.556$  (10) Å,  $\beta = 96.32$  (7)°,  $V = 1681$  (2) Å<sup>3</sup>,  $Z = 4$ ,  $D_m = 1.25$  (1),  $D_x = 1.252$  Mg m<sup>-3</sup>,  $\lambda(Mo K\alpha) =$

$0.71069$  Å,  $\mu = 0.22$  mm<sup>-1</sup>,  $F(000) = 652$ ,  $T = 293$  K, final  $R = 0.045$  for 2708 unique observed reflections. The structure consists of discrete cations connected in pairs by hydrogen-bonded chloride

anions. The dimethylammonium group is oriented *gauche* with respect to the carbamate moiety, and the ethoxy group is approximately coplanar with the aromatic system. While the lone pair of electrons of the ethereal O atom is definitely delocalized through the adjacent phenyl ring, the results do not reveal any significant conjugation of the carbamate moiety with the aromatic system.

**Introduction.** The title compound is a member of a new series of *N,N*-dimethyl[2-(2-alkoxyphenyl-carbamoyloxy)-2-methylpropyl]ammonium chlorides exhibiting local anaesthetic activity (Gregáň, Račanská, Kettmann & Novomeský, 1991). Previous studies have indicated that local anaesthetics of the phenylcarbamate type share the features of having a  $\pi$ -excessive phenyl ring, a hydrophilic (amino) group and a hydrophobic group appropriately positioned relative to the aromatic ring (Remko & Scheiner, 1988). Consequently, the present crystal structure determination was undertaken to examine the three-dimensional disposition of these functional groups, which are assumed to define the interaction of the drug with the complementary biological system (receptor) and to deduce the effects of the substituents on the  $\pi$ -electron distribution of the phenyl ring. Another point of interest in the present structure was the hydrogen-bonding pattern of the protonated cation with the Cl<sup>-</sup> ions.

**Experimental.** Single crystals were grown from an ethanol/water solution and a colourless crystal of dimensions 0.75 × 0.40 × 0.20 mm was selected.  $D_m$  determined by flotation. Systematic absences  $0k0$  for  $k$  odd and  $h0l$  for  $l$  odd were determined from Weissenberg photographs. A Syntex P<sub>2</sub> diffractometer with graphite-monochromated Mo  $K\alpha$  radiation was used for the collection of the intensity data ( $h = 0$  to 17,  $k = 0$  to 14,  $l = -14$  to 14). The unit-cell parameters and their e.s.d.'s were determined by a least-squares refinement of 15 reflections with  $15 < 2\theta < 45^\circ$ . The  $\theta$ - $2\theta$  scan mode was used with the scan rate ranging from 2.0 to 29.3° min<sup>-1</sup>, depending on intensity. The background time to scan time used was 1.0, and the scan range was from -1.0 to +1.0 ( $2\theta$ ) about the  $K\alpha$  doublet. Two check reflections (211, 232) were measured after every 98 reflections and no significant systematic fluctuation was observed. The intensities were corrected for Lorentz-polarization effects but not for absorption. Of the 3870 unique ( $R_{\text{int}} = 0.025$ ) reflections measured ( $2\theta_{\text{max}} = 55^\circ$ ), 2708 with  $I > 2\sigma(I)$  were considered observed. The structure was solved by direct methods using MULTAN80 (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1980) and refined by block-diagonal least-squares methods with anisotropic thermal parameters for the non-H

Table 1. Final atomic coordinates ( $\times 10^4$ ) and equivalent isotropic thermal parameters with e.s.d.'s in parentheses

$$B_{\text{eq}} = (4/3)\sum_i \sum_j \beta_{ij} \mathbf{a}_i \cdot \mathbf{a}_j$$

|       | x        | y        | z        | $B_{\text{eq}}(\text{\AA}^2)$ |
|-------|----------|----------|----------|-------------------------------|
| C(1)  | 1410 (1) | 4827 (1) | 3070 (1) | 3.51 (3)                      |
| C(2)  | 1037 (1) | 4071 (1) | 3867 (1) | 3.82 (4)                      |
| C(3)  | 133 (1)  | 3462 (2) | 3559 (2) | 5.25 (5)                      |
| C(4)  | -358 (1) | 3597 (2) | 2467 (2) | 6.06 (6)                      |
| C(5)  | 12 (1)   | 4328 (2) | 1682 (2) | 6.28 (6)                      |
| C(6)  | 899 (1)  | 4958 (2) | 1983 (1) | 4.82 (5)                      |
| C(7)  | 2334 (1) | 6351 (1) | 4182 (1) | 3.11 (3)                      |
| C(8)  | 3482 (1) | 7757 (1) | 5237 (1) | 2.93 (3)                      |
| C(9)  | 4559 (1) | 8159 (1) | 5136 (1) | 3.18 (3)                      |
| C(10) | 2831 (1) | 8849 (1) | 4896 (1) | 4.41 (5)                      |
| C(11) | 3342 (1) | 7298 (2) | 6431 (1) | 4.03 (4)                      |
| C(12) | 6368 (1) | 7925 (2) | 5727 (2) | 4.97 (5)                      |
| C(13) | 5518 (1) | 6415 (1) | 4478 (1) | 3.87 (4)                      |
| C(14) | 1138 (1) | 3473 (2) | 5827 (2) | 6.43 (6)                      |
| C(15) | 1864 (2) | 3559 (3) | 6880 (2) | 8.00 (8)                      |
| N(1)  | 2318 (1) | 5482 (1) | 3384 (1) | 3.48 (3)                      |
| N(2)  | 5395 (1) | 7273 (1) | 5430 (1) | 3.08 (3)                      |
| O(1)  | 1618 (1) | 6697 (1) | 4634 (1) | 4.26 (3)                      |
| O(2)  | 3287 (1) | 6804 (1) | 4382 (1) | 3.09 (2)                      |
| O(3)  | 1598 (1) | 3971 (1) | 4906 (1) | 4.81 (3)                      |
| Cl(1) | 5676 (0) | 5667 (0) | 7609 (0) | 3.91 (1)                      |

Table 2. Bond lengths ( $\text{\AA}$ ) and angles ( $^\circ$ ) with e.s.d.'s in parentheses

|                |           |                  |           |
|----------------|-----------|------------------|-----------|
| C(1)—C(2)      | 1.376 (2) | O(2)—C(8)        | 1.449 (2) |
| C(2)—C(3)      | 1.384 (2) | C(8)—C(9)        | 1.509 (2) |
| C(3)—C(4)      | 1.362 (3) | C(8)—C(10)       | 1.511 (2) |
| C(4)—C(5)      | 1.348 (3) | C(8)—C(11)       | 1.501 (2) |
| C(5)—C(6)      | 1.376 (3) | C(9)—N(2)        | 1.490 (2) |
| C(6)—C(1)      | 1.367 (2) | N(2)—C(12)       | 1.482 (2) |
| C(1)—N(1)      | 1.416 (2) | N(2)—C(13)       | 1.476 (3) |
| N(1)—C(7)      | 1.332 (2) | C(2)—O(3)        | 1.344 (2) |
| C(7)—O(1)      | 1.193 (2) | O(3)—C(14)       | 1.396 (3) |
| C(7)—O(2)      | 1.353 (2) | C(14)—C(15)      | 1.467 (3) |
| C(1)—C(2)—C(3) | 119.1 (1) | O(2)—C(8)—C(9)   | 105.1 (1) |
| C(2)—C(3)—C(4) | 119.7 (2) | O(2)—C(8)—C(10)  | 110.6 (1) |
| C(3)—C(4)—C(5) | 121.2 (2) | O(2)—C(8)—C(11)  | 110.5 (1) |
| C(4)—C(5)—C(6) | 119.8 (2) | C(9)—C(8)—C(10)  | 105.1 (1) |
| C(5)—C(6)—C(1) | 120.0 (2) | C(9)—C(8)—C(11)  | 112.5 (1) |
| C(6)—C(1)—C(2) | 120.2 (1) | C(10)—C(8)—C(11) | 112.7 (1) |
| C(2)—C(1)—N(1) | 119.7 (1) | C(8)—C(9)—N(2)   | 118.2 (1) |
| C(6)—C(1)—N(1) | 120.1 (1) | C(9)—N(2)—C(12)  | 109.7 (1) |
| C(1)—N(1)—C(7) | 119.7 (1) | C(9)—N(2)—C(13)  | 113.2 (1) |
| N(1)—C(7)—O(1) | 125.6 (1) | C(12)—N(2)—C(13) | 108.8 (1) |
| N(1)—C(7)—O(2) | 109.2 (1) | C(1)—C(2)—O(3)   | 116.3 (1) |
| O(1)—C(7)—O(2) | 125.1 (1) | C(3)—C(2)—O(3)   | 124.5 (1) |
| C(7)—O(2)—C(8) | 118.6 (1) | C(2)—O(3)—C(14)  | 118.0 (1) |
|                |           | O(3)—C(14)—C(15) | 107.9 (2) |

atoms and isotropic thermal parameters for the H atoms (all H atoms were located from a  $\Delta\rho$  map). 290 parameters refined. The final error indices were  $R = 0.045$ ,  $wR = 0.064$  and  $S = 1.41$ . The largest shift/e.s.d. ratio in the final cycle of refinement was 0.06. The function minimized was  $\sum w(\Delta F)^2$ , where  $w = 1$  if  $|F_o| < 15$  and  $w = 15/|F_o|$  if  $|F_o| \geq 15$ , in order to make  $w(\Delta F)^2$  approximately independent of  $|F_o|$  and  $\sin\theta/\lambda$ . The max. and min. heights in the final  $\Delta\rho$  synthesis were 0.23 and  $-0.25 \text{ e \AA}^{-3}$ , respectively. Scattering factors for neutral atoms were taken from *International Tables for X-ray Crystallography* (1974, Vol. IV). All calculations except

*MULTAN* were performed with local version of *NRC* (1973).

**Discussion.** Final atomic coordinates of non-H atoms and equivalent isotropic  $B$ 's are listed in Table 1,\* bond distances and angles in Table 2. The numbering scheme is shown in Fig. 1, which also displays the overall conformation of the molecule.

Bond distances and angles within the 2-methylpropylammonium moiety are comparable to those reported for a number of similar compounds in which the amino N atom is protonated. The arrangement of the phenylcarbamate and amino groups around the C(8)—C(9) bond is *gauche*, similar to those in other structures containing the O—C—C—N fragment (Pavelčík, Remko, Čížmárik & Majer, 1986; Dexter, 1972). Although the *gauche* conformation brings the N(2) atom close to O(2) [2.961 (2) Å] there is no indication for hydrogen-bond formation between these atoms [as given below, the N(2)<sup>+</sup>—H moiety is involved in a hydrogen-bond interaction with a chloride anion].

The ethoxy group lies approximately in the plane of the phenyl ring [torsion angle C(3)—C(2)—O(3)—C(14) =  $-16.6$  (2)°]; this coplanar conformation can be attributed to some degree of conjugation between the ether O(3) atom and the phenyl ring, a feature well known from the structures of aromatic alkoxy compounds (Domiano, Nardelli, Balsamo, Macchia & Macchia, 1979). This is evidenced by a shortening of the C(2)—O(3) bond [1.344 (2) Å] from the value of 1.406 (4) Å reported for a C( $sp^2$ )—O single bond (Ammon, Mazzochi, Regan & Colicelli, 1979) and by a widening of the C(2)—O(3)—C(14) valence angle [118.0 (2)°] from its normal tetrahedral value, both essentially suggesting an  $sp^2$  character for O(3).

In the carbamate moiety, the mean plane through N(1), C(7), O(1) and O(2) makes an angle of

69.5 (1)° with the plane of the phenyl ring. The C(1)—N(1) bond length of 1.416 (2) Å is not far from the value of 1.425 Å found for a pure C( $sp^2$ )—N single bond (Adler, Goode, King, Mellor & Miller, 1976). Moreover, the N(1)—C(7) bond distance [1.332 (2) Å] is close to the range 1.32–1.33 Å usually observed for the N—C(=O) bond in amides. All these facts indicate that, in contrast to the ethoxy group, the carbamate moiety is not involved in conjugation with the phenyl ring. This is also consistent with the literature data on various *N*-phenylcarbamates (see *e.g.* Laidlaw, Miura, Panetta & Metzger, 1988) which suggest that the carbamate group can act as both a  $\pi$ -electron donor and an acceptor, depending on the ( $\sigma$  and  $\pi$ ) charge and hence the substitution pattern of the phenyl ring. In our series of compounds, having a slightly negatively charged phenyl ring due to  $\pi$  donation from the ether O atom, the carbamate group appears to have essentially no effect on the charge distribution of the phenyl ring. Thus, the lone pair on the amide N atom is delocalized though conjugation with the ester group rather than with the phenyl ring.

Examination of the unit-cell packing reveals that both of the two potential hydrogen-bond donors of the cation are involved in hydrogen-bonding interactions with two different Cl<sup>-</sup> anions related by a centre of symmetry, thus leading to the formation of centrosymmetric dimers. The details of the geometry of these hydrogen bonds are: N(2)<sup>+</sup>—H...Cl, N—H 0.90 (2), N...Cl 3.070 (1), H...Cl 2.22 (2) Å, N—H...Cl 159 (2)°; N(1)—H...Cl(1 -  $x$ , 1 -  $y$ , 1 -  $z$ ), N—H 0.83 (2), N...Cl 3.262 (1), H...Cl 2.44 (2) Å, N—H...Cl 172 (2)°. The dimers are packed by van der Waals forces.

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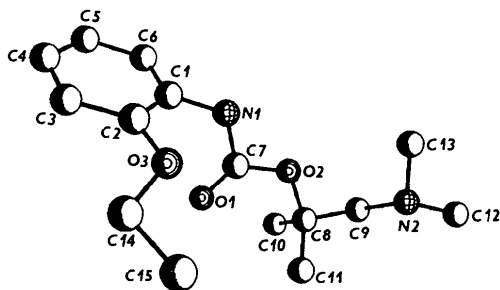


Fig. 1. A perspective view of the title cation and the numbering of the atoms.