PELLETIER, S. W., DECAMP, W. H., HERALD, D. L. JR, PAGE, S. W. & NEWTON, M. G. (1977). *Acta Cryst.* B**33**, 716–722.

PELLETIER, S. W., DJARMATI, Z., LAJŠIĆ, S. & DECAMP, W. H. (1976). *J. Am. Chem. Soc.* **98**, 2617–2625.

PELLETIER, S. W. & KEITH, L. H. (1970). *Chemistry of the Alkaloids*, edited by S. W. PELLETIER, pp. 503–505. New York: Van Nostrand–Reinhold.

PELLETIER, S. W., MODY, N. V., JONES, A. J. & BENN, M. H. (1976). *Tetrahedron Lett.* **16**, 3025–3028.

PRZYBYLSKA, M. (1961). *Acta Cryst.* **14**, 424–434.

PRZYBYLSKA, M. (1976). *Acta Cryst.* B**32**, 1638–1642.

STEWART, J. M. (1976). XRAY 76. Tech. Rep. TR-446. Computer Science Center, Univ. of Maryland, College Park, Maryland.

Acta Cryst. (1981). B**37**, 383–387

Structure of the Asthma Drug Beclomethasone Dipropionate

BY WILLIAM L. DUAX, VIVIAN CODY AND PHYLLIS D. STRONG

Medical Foundation of Buffalo, Inc., 73 High Street, Buffalo, New York 14203, *USA*

(*Received* 29 *July* 1980; *accepted* 1 *October* 1980)

Abstract

Beclomethasone dipropionate, 9α-chloro-16β-methyl-3,20-dioxo-1,4-pregnadiene-11β,17,21-triol 17,21-dipropionate, $C_{28}H_{37}ClO_7$, crystallizes as the monohydrate in the orthorhombic space group $P2_12_12_1$ [a = 14·152 (2), b = 16·268 (1), c = 12·0849 (7) Å, λ = 1·5418 Å, T = 271 K, V = 2782·2 Å^3, Z = 4, ρ_x = 1·29 Mg m^{-3}]. Final R = 0·056 for 1842 observed reflections. The overall conformation of the molecule is similar to that of other anti-inflammatory steroids. The progesterone side chain takes up one of two conformations common to 16β-substituted steroids. There is a tightly bound water molecule linking the C(11) hydroxyl and the carbonyl O of the 21-propionate group. The 5000-fold enhancement in anti-asthmatic properties appears to be due primarily to the fact that the drug can be administered in aerosol form. The presence of the propionate groups and to some extent the bound water account for the efficacy of this means of administration.

Introduction

Asthma can be combated with drugs that antagonize the chemical mediators causing it and by β-adrenergic stimulants, anti-cholinergics, phosphodiesterase inhibitors, steroids, and prostaglandins. Steroids have been used to block the inflammation of the bronchial tubes, which is the end result of many pulmonary allergic responses. Although the mechanism of the anti-inflammatory effect of cortisol is not fully understood, its effect appears to be related to its ability to stabilize membranes of cellular lysosomes so that they rupture only with difficulty and to decrease the formation of bradykinin, a powerful vasodilating substance (Guyton, 1976). Whether these effects are achieved by direct interaction or are mediated by specific receptor interaction remains uncertain.

Beclomethasone dipropionate, the title compound, is an asthma drug found to be 5000 times more potent than most other steroids. Because the drug is administered in aerosol form (Smith, Clegg, Cook & Butler, 1975) many side effects that have accompanied the use of systemic steroids are avoided.

The structure determination was undertaken in order to examine the effects of the dipropionate substitution on the conformation of the already crowded D ring and side chains, and to compare its conformation with those of other steroidal anti-inflammatory agents.

Crystallographic diffraction data were measured on a specimen crystal of dimensions 0·10 × 0·12 × 0·40 mm on an Enraf–Nonius CAD-4 automated diffractometer using Ni-filtered Cu $K\alpha$ radiation. The lattice parameters were refined by a least-squares fit to measured 2θ values for 22 reflections in the interval $50° < 2\theta < 78°$. Integrated relative intensities for 3212 independent reflections with $2\theta < 150°$ were measured as ω–2θ scans; 1842 of these reflections were measured to be observed above background ($I > 2\sigma_I$).

The intensities were reduced to structure factor amplitudes, and phase angles sufficient for location of the nonhydrogen atoms were derived using the direct-methods program *MULTAN* (Germain, Main & Woolfson, 1971) in conjunction with the negative-quartet figure of merit (DeTitta, Edmonds, Langs & Hauptman, 1975). 31 of 37 H atoms on the steroid and

0567-7408/81/020383-05$01.00

Table 1. *Atomic coordinates* ($\times 10^4$, *for* H $\times 10^3$) *and isotropic thermal parameters* ($\times 10$) *for beclomethasone dipropionate*

The isotropic thermal parameters for the H atoms are $B_{iso} = 4{\cdot}0$ Å^2. For the non-hydrogen atoms $B_{iso} = \frac{4}{3}\sum_i \sum_j b_{ij}\,\mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	B_{iso} (Å^2)		x	y	z	B_{iso} (Å^2)
C(1)	5777 (3)	7124 (2)	7195 (3)	39 (1)	C(20)	10303 (2)	4514 (2)	8089 (3)	36 (1)
C(2)	4851 (3)	7144 (3)	7211 (3)	43 (1)	C(21)	10206 (3)	3915 (3)	7130 (4)	43 (1)
C(3)	4338 (3)	7182 (2)	8256 (4)	45 (1)	C(22)	10905 (3)	4620 (2)	5665 (3)	41 (1)
C(4)	4893 (3)	7247 (2)	9270 (3)	37 (1)	C(23)	11718 (3)	4642 (3)	4870 (4)	54 (1)
C(5)	5840 (3)	7235 (2)	9252 (3)	33 (1)	C(24)	11530 (4)	5088 (4)	3833 (4)	66 (2)
C(6)	6414 (3)	7267 (2)	10299 (3)	39 (1)	C(25)	8860 (3)	3279 (2)	8941 (3)	35 (1)
C(7)	7067 (3)	6532 (2)	10382 (3)	36 (1)	C(26)	7991 (3)	2777 (3)	8790 (4)	49 (1)
C(8)	7668 (2)	6418 (2)	9354 (3)	29 (1)	C(27)	8034 (4)	1920 (3)	9077 (6)	87 (2)
C(9)	7052 (2)	6384 (2)	8282 (3)	27 (1)	C(16*M*)	10574 (3)	4849 (3)	10531 (4)	51 (1)
C(10)	6406 (2)	7182 (2)	8194 (3)	33 (1)	Cl(9)	6226 (1)	5520 (1)	8417 (1)	35 (1)
C(11)	7626 (3)	6172 (2)	7232 (3)	31 (1)	O(3)	3464 (2)	7172 (2)	8287 (3)	62 (1)
C(12)	8290 (2)	5435 (2)	7380 (3)	29 (1)	O(11)	8099 (2)	6898 (2)	6896 (2)	42 (1)
C(13)	8916 (2)	5507 (2)	8418 (3)	29 (1)	O(17)	8725 (1)	4054 (1)	8591 (2)	33 (1)
C(14)	8281 (2)	5648 (2)	9429 (3)	30 (1)	O(20)	11043 (2)	4861 (2)	8245 (3)	48 (1)
C(15)	8959 (2)	5554 (2)	10396 (3)	36 (1)	O(21)	10957 (2)	3982 (2)	6366 (2)	43 (1)
C(16)	9556 (3)	4799 (2)	10081 (3)	33 (1)	O(22)	10257 (2)	5092 (2)	5678 (2)	50 (1)
C(17)	9439 (2)	4689 (2)	8796 (3)	30 (1)	O(25)	9601 (2)	3045 (1)	9330 (2)	41 (1)
C(18)	9659 (2)	6189 (2)	8286 (3)	36 (1)	O(1*W*)	9285 (2)	6592 (2)	5120 (3)	56 (1)
C(19)	6970 (3)	7990 (2)	8073 (4)	43 (1)					
H(1)	609 (2)	711 (2)	655 (3)		H(19*C*)	725 (2)	802 (2)	731 (3)	
H(2)	451 (2)	715 (2)	660 (3)		H(21*A*)	956 (2)	397 (2)	682 (3)	
H(4)	454 (2)	733 (2)	1001 (3)		H(21*B*)	1025 (2)	342 (2)	751 (3)	
H(6*A*)	592 (2)	736 (2)	1093 (3)		H(23*A*)	1184 (2)	409 (2)	472 (3)	
H(6*B*)	672 (2)	780 (2)	1028 (3)		H(23*B*)	1225 (2)	485 (2)	523 (3)	
H(7*A*)	664 (2)	601 (2)	1048 (3)		H(24*A*)	1133 (2)	572 (2)	400 (3)	
H(7*B*)	746 (2)	657 (2)	1101 (3)		H(24*B*)	1215 (2)	508 (2)	330 (3)	
H(8*B*)	811 (2)	685 (2)	923 (3)		H(24*C*)	1105 (2)	482 (2)	352 (3)	
H(11*A*)	720 (2)	604 (2)	671 (3)		H(26*A*)	773 (2)	290 (2)	798 (3)	
H(12*A*)	790 (2)	499 (2)	741 (3)		H(26*B*)	751 (3)	306 (2)	920 (3)	
H(12*B*)	869 (2)	540 (2)	666 (3)		H(27*A*)	858 (2)	169 (2)	872 (3)	
H(14*A*)	787 (2)	514 (2)	942 (3)		H(27*B*)	809 (2)	185 (2)	996 (3)	
H(15*A*)	867 (2)	548 (2)	1099 (3)		H(27*C*)	740 (2)	161 (2)	880 (3)	
H(15*B*)	936 (2)	603 (2)	1033 (3)		H(16*MA*)	1056 (2)	492 (2)	1120 (3)	
H(16*A*)	922 (2)	434 (2)	1038 (3)		H(16*MB*)	1087 (2)	429 (2)	1043 (3)	
H(18*A*)	1013 (2)	615 (2)	875 (3)		H(16*MC*)	1091 (2)	534 (2)	1026 (3)	
H(18*B*)	995 (2)	612 (2)	753 (3)		H(11O)	836 (2)	684 (2)	648 (3)	
H(18*C*)	934 (2)	670 (2)	825 (3)		H(1*W*)	951 (2)	687 (2)	499 (3)	
H(19*A*)	657 (2)	849 (2)	823 (3)		H(2*W*)	955 (2)	630 (2)	542 (3)	
H(19*B*)	753 (2)	805 (2)	865 (3)						

both H atoms of the water molecule were located in a difference electron density map prepared at an intermediate stage of least-squares refinement of the structural parameters. In the final cycles of full-matrix least-squares refinement, positional parameters for all the atoms and anisotropic thermal vibration parameters for the nonhydrogen atoms were varied. The quantities $(1/\sigma_F^2)$, where σ_F was as defined by Stout & Jensen (1968) but with an instrumental instability factor of 0·06, were used to weight the least-squares differences for the observed data; unobserved data were given zero weight. The final values of the residual $\sum ||F_o| - |F_c||/\sum |F_o|$ were 0·056 for the observed data and 0·073 for all the measured data. Final positional parameters are listed in Table 1.*

Discussion

The bond lengths and valence angles (Fig. 1) are comparable to those observed in similar steroid

* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 35670 (17 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

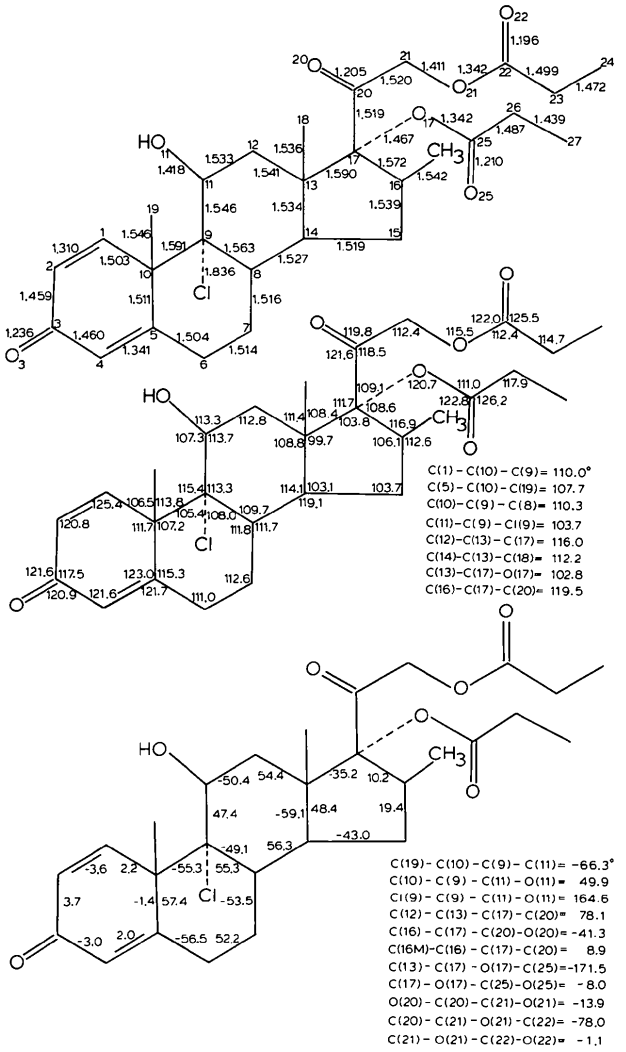

Fig. 1. Bond distances (Å, σ range = 0·007–0·008 Å), bond angles (°, σ range = 0·3–0·4°), and torsion angles (°, σ range = 0·4–0·6°) for beclomethasone. A torsion angle α–β–γ–δ is positive if, when viewed down the β–γ bond, the α–β bond will eclipse the γ–δ bond when rotated less than 180° in a clockwise direction.

structures (Duax & Norton, 1975). The *A* ring is planar due to the 1,4-diene-3-one composition and the *B* and *C* rings have normal chair conformations. The overall shape of the steroid skeleton is nearly identical to that of dexamethasone (Rohrer & Duax, 1977), another anti-inflammatory steroid having 1,4-diene-3-one composition and a 9α-fluorine substituent.

The most interesting feature of the structure is the water molecule that bridges the hydroxyl at C(11) and the carbonyl O atom of the 21-propionate group (Fig. 2). This water molecule is also hydrogen bonded to the carbonyl O of the 17α-propionate group of a symmetry-related molecule. A water molecule bridges O(11) and the carbonyl O atom of a 21-acetate

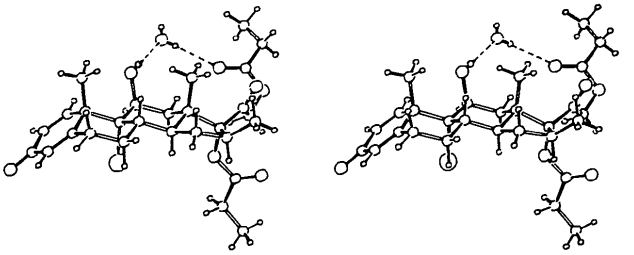

Fig. 2. Stereo *ORTEP* (Johnson, 1970) drawing illustrating the hydrogen-bonded water bridge in beclomethasone.

Table 2. *Hydrogen-bond geometry in beclomethasone*

Donor (*D*)	Acceptor (*A*)	*D*···*A*	*D*–H	H···*A*	∠*D*–H···*A*
O(11)	O(1)	2·770 (8) Å	0·63 (8) Å	2·14 (8) Å	176 (6)°
O(1)	O(22)	2·881 (8)	0·71 (8)	2·23 (6)	155 (6)
O(1)	O(25)	2·917 (8)	0·57 (8)	2·44 (6)	144 (6)

substituent in a nearly identical fashion in dexamethasone acetate (Terzis & Theophanides, 1975). The geometry of the hydrogen bonds in the title compound is given in Table 2. The correlation between the valence angle C(9)–C(11)–O(11) and the torsion angle C(9)–C(11)–O(11)–H(O11) previously noted in 9α-substituted structures (Weeks & Duax, 1976) is also observed here [C(9)–C(11)–O(11)–H(O11) = −179°]. In view of the fact that the crystal was open to the air and no deterioration was detected during the data collection it would appear that the water molecule is tightly bound. This intramolecular water bridge may influence the conformation of the progesterone side chain discussed below and may also influence the lipid solubility of the structure.

The progesterone side-chain orientation is normally restricted to a region over the *D* ring; the torsion angle C(16)–C(17)–C(20)–O(20) in 84 structures having 20-one substitution is observed to be between 0 and −41° (Duax, Griffin, Rohrer & Weeks, 1980). Substitution at the 17α and 21 positions further restricts the conformational flexibility of the 17α side chain to the −16 to −35° portion of this range. The progesterone side chain in beclomethasone is observed to be at one extreme of this range [C(16)–C(17)–C(20)–O(20) = −41·3°]. This could be attributed to one or a combination of the following factors, the substitution of 21-propionate, the 17α-propionate, or the 16-methyl, the water-bridging of the 11-hydroxyl and the 21-propionate, or the influence of crystal-packing forces. Since there are too few examples of propionate substitution to draw conclusions concerning its influence, the effect of acetate substitution will be considered as a plausible analogue. The addition of a 17α-acetate group alone does not shift the 17β side chain to the position observed in the beclomethasone.

In 17α-acetate-substituted structures observed crystallographically (Chandross & Bordner, 1974, 1975; Duax, Cody & Hazel, 1977; Duax, Cody, Griffin, Hazel & Weeks, 1978; Bordner, Hennessee & Saxe, 1978; Bordner, Hennessee & Ellis, 1978) the C(16)–C(17)–C(20)–O(20) torsion angles are within the range −18 to −33°.

The 21-propionate substitution alone does not appear to be responsible for the restriction of the 17β-side-chain orientation either. In four structures having a 21-acetate substituent (Declercq, Germain & Van Meerssche, 1972; Kierstead, Blount, Fahrenholtz, Farone, LeMahiere & Rosen, 1970; Williams, Moore, Li & Blount, 1979; Tseikinsky, Rybakov, Simonov & Petropavlov, 1979), the C(16)–C(17)–C(20)–O(20) torsion angles have the values −32, −33, −23 and −30°.

The 17β-side-chain conformation observed in beclomethasone is one of two conformers that appears to be stabilized by 16β-methyl substitution. In 16β-methylprogesterone (Weeks, Strong & Osawa, 1976) the C(16)–C(17)–C(20)–O(20) torsion angle is −108° and in crystals of 16β-methyl-20-oxo-5-pregnen-3β-yl acetate conformational isomers occur in which this angle is −46·6 and −110·0° (Campsteyn, Dideberg, Dupont & Lamotte, 1979). Furthermore, 16β-bromo substitutions have a comparable influence upon the progesterone side chain. The C(16)–C(17)–C(20)–O(20) torsion angle is −129° in 16β-bromo-17α-hydroxy-11,20-dioxo-5α-pregnan-3β-yl acetate (Ohrt, Haner, Cooper & Norton, 1968) and −46° in 16β-bromo-3β,17α-dihydroxy-5α-pregnane-11,20-dione (Ohrt, Cooper & Norton, 1969). Campsteyn *et al.* (1979) have proposed that a broad energy minimum lies between the two observed conformations of 16β-methyl-20-oxo-5-pregnen-3β-yl acetate. The fact that not one of the 88 steroid structures having the possibility of free rotation about the C(17)–C(20) bond has a C(16)–C(17)–C(20)–O(20) torsion angle in the range from −47 to −110° suggests that conformations in this range are of substantially higher energy relative to the range between 0 and −40°. It seems evident that upon 16β substitution of a methyl or bromine, steric interaction excludes all of the normal conformational range except that where C(16)–C(17)–C(20)–O(20) is near −40°. Furthermore, this conformation appears to be of comparable energy to a second form in which C(16)–C(17)–C(20)–O(20) is near −115° (at least in 16β-substituted structures). There is no evidence to suggest that a broad minimum extends between these two conformations. On the contrary, the conformations of all reported crystal structures of 16β-substituted structures are evidence against such a proposal.

It would appear then that the 16β-methyl substitution is responsible for narrowing the conformational preference of beclomethasone to conformers in which C(16)–C(17)–C(20)–O(20) is approximately −40 or −115° and that the propionate groups may contribute to the further stabilization of the former. The fact that a water molecule is simultaneously hydrogen bonded to O(11) and the carbonyl group of the 21-propionate also supports this suggestion. Subtle details of the conformation of the steroid skeleton and the 17β side chain are consistent with previously observed patterns. Intramolecular interactions are seen to play a determining role in defining conformation, and crystal-packing forces appear to have little influence upon the observed conformation, with the possible exception of the water molecule stabilizing one of the two conformational isomers observed in 16β-substituted structures.

Since beclomethasone does not exhibit any conformational feature that is dramatically different from other steroidal anti-inflammatory agents the 5000-fold enhancement in potency must be attributed almost solely to the fact that the drug is delivered directly to the lungs in aerosol form. The propionate substituents mask two hydroxyl groups, enhance lipophilicity and promote rapid membrane absorption. The water bridge brought to light by the structure determination may also serve to mask the 11-hydroxyl commonly present in the anti-inflammatory steroids. The bound water is in turn shielded by the 21-propionate side chain and the steroid as a whole retains a lipophilic surface.

The sample of beclomethasone dipropionate was generously supplied by Dr Thomas Popper and Dr Irving Tabachnick of Schering Corporation. This work was supported in part by Grant No. AM-26546 from the National Institute of Arthritis, Metabolism and Digestive Diseases, DHEW. We would like to thank Miss Gloria Del Bel, Mrs Brenda Giacchi, Miss Deanna Hefner, Mrs Estelle Robel and Miss Melda Tugac for technical assistance.

References

BORDNER, J., HENNESSEE, G. L. A. & ELLIS, H. B. JR (1978). *Cryst. Struct. Commun.* **7**, 489–492.

BORDNER, J., HENNESSEE, G. L. A. & SAXE, P. W. (1978). *Cryst. Struct. Commun.* **7**, 485–488.

CAMPSTEYN, H., DIDEBERG, O., DUPONT, L. & LAMOTTE, J. (1979). *Acta Cryst.* B**35**, 2971–2975.

CHANDROSS, R. J. & BORDNER, J. (1974). *Acta Cryst.* B**30**, 1581–1585.

CHANDROSS, R. J. & BORDNER, J. (1975). *Acta Cryst.* B**31**, 928–931.

DECLERCQ, J. P., GERMAIN, G. & VAN MEERSSCHE, M. (1972). *Cryst. Struct. Commun.* **1**, 59–62.

DETITTA, G. T., EDMONDS, J. W., LANGS, D. A. & HAUPTMAN, H. (1975). *Acta Cryst.* A**31**, 472–479.

DUAX, W. L., CODY, V., GRIFFIN, J. F., HAZEL, J. & WEEKS, C. M. (1978). *J. Steroid Biochem.* **9**, 901–907.

DUAX, W. L., CODY, V. & HAZEL, J. (1977). *Steroids*, **30**, 471–480.

DUAX, W. L., GRIFFIN, J. F., ROHRER, D. C. & WEEKS, C. M. (1980). *Lipids*, **15**, 783–792.

DUAX, W. L. & NORTON, D. A. (1975). *Atlas of Steroid Structure*. New York: Plenum.

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

GUYTON, A. C. (1976). *Textbook of Medical Physiology*, pp. 1027–1028. Toronto: Saunders.

JOHNSON, C. K. (1970). *ORTEP*. Report ORNL-3794, 2nd revision. Oak Ridge National Laboratory, Tennessee.

KIERSTEAD, R. W., BLOUNT, J., FAHRENHOLTZ, K. E., FARONE, A., LEMAHIERE, R. A. & ROSEN, P. (1970). *J. Org. Chem.* **35**, 4141–4145.

OHRT, J. M., COOPER, A. & NORTON, D. A. (1969). *Acta Cryst.* B**25**, 41–51.

OHRT, J. M., HANER, B. A., COOPER, A. & NORTON, D. A. (1968). *Acta Cryst.* B**24**, 312–319.

ROHRER, D. C. & DUAX, W. L. (1977). *Cryst. Struct. Commun.* **6**, 123–126.

SMITH, J. M., CLEGG, R. T., COOK, N. & BUTLER, A. (1975). *Br. Med. J.* p. 255.

STOUT, G. H. & JENSEN, L. H. (1968). *X-ray Structure Determination*, p. 457, equation H14. New York: Macmillan.

TERZIS, A. & THEOPHANIDES, T. (1975). *Acta Cryst.* B**31**, 796–801.

TSEIKINSKY, V. M., RYBAKOV, V. B., SIMONOV, V. I. & PETROPAVLOV, N. N. (1979). *Sov. J. Bioorg. Chem.* **5**, 1537–1542.

WEEKS, C. M. & DUAX, W. L. (1976). *Acta Cryst.* B**32**, 2819–2825.

WEEKS, C. M., STRONG, P. & OSAWA, Y. (1976). *Cryst. Struct. Commun.* **5**, 745–748.

WILLIAMS, J. R., MOORE, R. H., LI, R. & BLOUNT, J. F. (1979). *J. Am. Chem. Soc.* **101**, 5019–5025.

Acta Cryst. (1981). B**37**, 387–394

Structural Studies of Benzene Derivatives. IX.* The Structures of *p*-Fluoroaniline and *p*-Cyanoaniline Hydrochlorides

BY MARCELLO COLAPIETRO, ALDO DOMENICANO, CLARA MARCIANTE AND GUSTAVO PORTALONE

Istituto di Chimica Farmaceutica e Tossicologica, Università di Roma, Città Universitaria, 00185 *Roma, Istituto di Strutturistica Chimica del CNR 'Giordano Giacomello',* 00016 *Monterotondo Stazione and Gruppo di Chimica Biologica e Strutturistica Chimica, Università di Roma, Città Universitaria,* 00185 *Roma, Italy*

(*Received* 29 *July* 1980; *accepted* 8 *September* 1980)

Abstract

The crystals of the title compounds, $C_6H_7FN^+.Cl^-$ and $C_7H_7N_2^+.Cl^-$, are triclinic, space group $P\bar{1}$, $Z = 2$, with unit cells of closely related dimensions: $a = 4{\cdot}266$ (1), $b = 5{\cdot}865$ (1), $c = 13{\cdot}635$ (2) Å, $\alpha = 91{\cdot}90$ (1), $\beta = 90{\cdot}05$ (2), $\gamma = 99{\cdot}15$ (2)° (*p*-fluoroaniline hydrochloride), and $a = 4{\cdot}267$ (2), $b = 5{\cdot}967$ (1), $c = 14{\cdot}555$ (3) Å, $\alpha = 91{\cdot}64$ (2), $\beta = 92{\cdot}18$ (2), $\gamma = 99{\cdot}59$ (2)° (*p*-cyanoaniline hydrochloride). The structures were determined from 1768 and 1856 counter intensities and refined to final R values of 0·0421 and 0·0374, respectively. Apart from minor deviations from planarity, the benzene rings have *mm* symmetry. The deviations from 6/*mmm* symmetry are highly significant, and involve bond distances as well as angles. The internal angles at the *ipso* positions of the rings are all >120° [$\alpha_{NH_3^+} = 121{\cdot}8$ (2), 122·5 (2); $\alpha_F = 123{\cdot}2$ (2); $\alpha_{CN} = 121{\cdot}0$ (2)°], due to the strongly σ-electron-withdrawing properties of the NH_3^+, F and CN substituents. The crystal structures of the two compounds are essentially the same. The NH_3^+ groups and Cl^- ions are connected in infinite ribbons through $Cl^-\cdots H{-}N$ hydrogen bonds, 3·15–3·32 Å long. Adjacent ribbons are joined in layers through additional, longer $Cl^-\cdots H$ contacts.

Introduction

As part of a research project aimed at measuring the effect of different *para* substituents on the geometry of the anilinium cation we have determined the crystal structures of *p*-fluoroaniline and *p*-cyanoaniline hydrochlorides (hereafter referred to as *p*-fluoro and *p*-cyano derivatives). Previous work has included X-ray diffraction studies of *p*-phenylenediamine dihydrochloride (Domenicano, Foresti Serantoni & Riva di Sanseverino, 1977) and *p*-aminobenzoic acid hydrochloride (Colapietro, Domenicano & Portalone, 1980). A preliminary communication of the present work has been given (Colapietro, Domenicano, Marciante & Portalone, 1980).

* Part VIII: Di Rienzo, Domenicano & Riva di Sanseverino (1980).

0567-7408/81/020387-08$01.00