SYNTHESIS AND STRUCTURAL STUDY OF 3-CYANO-2-(ETHOXYCARBONYL)-*N*-(4- FLUOROBENZYL) CYCLOPENTANAMMONIUM CHLORIDE $C_{16}H_{20}ClFN_2O_2$

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ABSTRACT: The salt $C_{16}H_{20}ClFN_2O_2$ crystallizes in the monoclinic system, space group $P2_1/c$. The parameters of the unit cell are: a = 6.038(1) Å, b = 20.140(1) Å, c = 14.180(1) Å, β = 101,00(1)° and Z = 4. The structure is built up from $(C_{16}H_{20}FN_2O_2)^+$ cations and Cl^- anions linked by N-H..Cl hydrogen bond. The organic cation has a benzyl group linked to the ammonium group $(NH_2)^+$ which is attached to a 2,3-disubstituted five membered ring.

RESUME: Le sel $C_{16}H_{20}ClFN_2O_2$ cristallise dans le système monoclinique, groupe d'espace $P2_1/c$ avec a = 6,038(1) Å, b = 20,140(1) Å, c = 14,180(1) Å, β = 101,00(1)° et Z = 4. La structure moléculaire montre que la molécule est formée d'un cation organique $C_{16}H_{20}FN_2O_2^+$ et d'un ion Cl^- liés par une liaison hydrogène de type N-H..Cl. Le cation organique est formé d'un groupe benzyle lié à un groupe $(-NH_2)^+$ qui est lié à un cycle à cinq atomes de carbone.

INTRODUCTION

Cyclopentane skeletons are often encountered in many natural and organic molecules, which may have antibiotic [1] and hormonal [2] properties. In a recent contribution to valorize some functional five-membered ring from Baylis-Hillman adducts, we have established a strategy for the synthesis of 1,2,3-trisubstituted cyclopentanes with three stereogenic centers. The conjugate addition of primary amine to racemic ethyl 5-cyanocyclopent-1-enecarboxylate in a polar protic solvent such as ethanol at reflux, to provide pure viscous brown oil in 92% yield. The resulting product was treated by an aqueous solution of hydrochloric acid (2M) to get a white precipitate. The spectroscopic data using ^1H and ^{13}C NMR failed to define the number of diastereoisomers obtained then the relative stereochemistry of the three substituted five-membered ring. To solve the problem of different configurational diastereomers, we have used the X-ray diffraction via the use of a single crystal isolated from hydrochloride salt $C_{16}H_{20}ClFN_2O_2$ in water.

SYNTHESIS

To a solution of ethyl 5-cyanocyclopent-1-enecarboxylate (3 mmol) in absolute ethanol (5mL) was added dropwise 4-fluorobenzylamine (4.50 mmol). The mixture was stirred at reflux for 10 days. After reaction completion (TLC monitoring), the mixture was concentrated under vacuum and the crude material was purified by chromatography on silica gel (AcOEt/Petroleum ether, 4:6) to give with high diastereoselectivity, pure ethyl 2-(benzylamino)-5-cyanocyclopentanecarboxylate in 92% yield. The obtained oil was treated with 2M aqueous hydrochloric acid solution aqueous until acidic pH. The resulting ammonium salt is filtered off then recrystallized in water. Slow evaporation of the solvent gave the formation of a crystal structure which was able to select a single crystal.

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STRUCTURAL STUDY OF CRISTAL SALT $C_{16}H_{20}ClFN_2O_2$

Collection and data processing

A crystal dimensions 0.2 x 0.2 x 0.2 mm are used for the structural study. The recording of diffracted intensities was performed on an automatic four-circle diffractometer Enraf-Nonius brand type CAD-4, using the K_α radiation of molybdenum (l = 0.71073 Å). The structure was solved by direct methods implemented by the program SHELXS [3] and refined by full matrix least squares (SHELXL-97) [4]. The conditions for collecting intensities are summarized in Table I. The reduced atomic coordinates and thermal agitation anisotropic factors are given in Tables II and III. Main geometrical characteristics are shown in Table IV.

Table I: Crystallographic data and conditions for collecting intensities of $C_{16}H_{20}ClFN_2O_2$.

Chemical formula	$C_{16}H_{20}ClFN_2O_2$
Molar mass	326,79 g.mol^{-1}
Temperature	298(2) K
Wavelength	0,71073 Å
Crystal system, space group	monoclinique, $P2_1/c$
Cell parameters	a = 6,038(1) Å
	b = 20,140(1) Å β = 101,00(1)°
	c = 14,180(1) Å
Volume	1692,7(3) Å^3
Groups forms	Z = 4
Calculated density	D_x = 1,282 Mg/m^3
Absorption coefficient	μ = 0,243 mm^{-1}
Dimensions of the crystal	0,20 x 0,20 x 0,20 mm
Angular field of collection	θ: 2,02° - 26,96°
Miller Indices	-6<h<0, -1<k<21, -14<l<14
Collected reflections	3629
Settings	258
Reliability factors [I > 2σ(I)]	R_1 = 0,0453 wR_2 = 0,1051

Description and discussion of the structure

The functionalized ammonium hydrochloride, subject of this study consists of an organic cation $(C_{16}H_{20}FN_2O_2)^+$ and an anion Cl^- linked by hydrogen bonding type Cl…NH (Figure 1).

The benzylammonium cation is attached to the C1 carbon of the cyclopentane while on the phenyl group was attached a fluorine atom at the para position.

On the C2 carbon of the cyclopentane is attached a second functionnal group such as ethoxycarbonyl ($CO_2C_2H_5$) and cyano group at the C3 carbon.

The three stereogenic carbons C1, C2 and C3 on the five-membered ring are respectively bonded to hydrogen H1, H2 and H3. H1 and H3 are on the same side of the ring (*cis position*) while H1 and H2 then H2 and H3 are alternatively on either side of the ring (*trans position*).

The carbon atoms (C10, C11, C12, C13, C14, C15 and C16) of the benzyl group are on an average plane equation: -2,71(1) x + 17,28(2) y – 2,27(2) z = 8,16(2).

The dihedral angle formed by the atoms (C1, C5, C6 and C7) is 84.9 (4)°, that formed by (C1, C7, C2 and N2) is -104.7 (4)°.

The hydrogen atom H12 $(NH_2)^+$ is a weak hydrogen bonding with Cl^- type N-H...Cl to ensure the cohesion of the structure bond lengths of the C=O, C-O, C≡N and C-F which are comparable to those found in related organic structures [5-7].

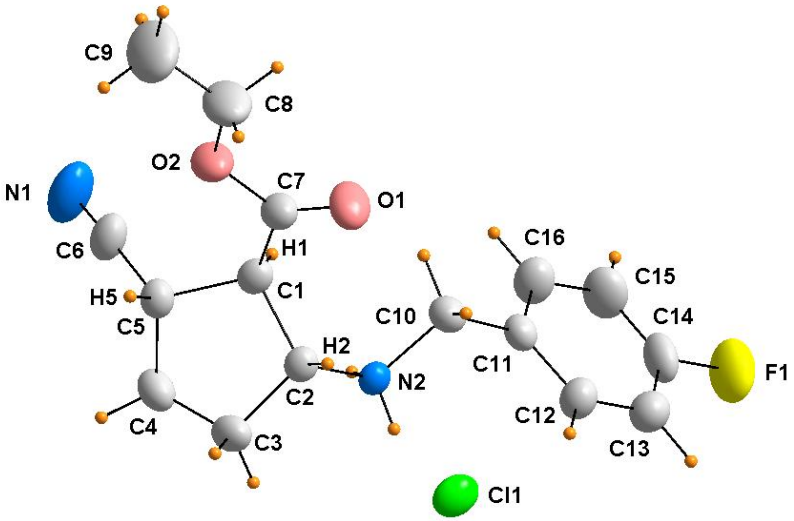

Figure1: Ortep view of the ammonium salt $C_{16}H_{20}ClFN_2O_2$**.**
The ellipsoids of thermal agitation have around 50 % probability of presence.

Table II: reduced atomic coordinates and thermal agitation factors equivalents Ueq ($Å^2$) of $C_{16}H_{20}ClFN_2O_2$.

Atom	x/a	y/b	z/c	Ueq.
Cl1	0,2542(2)	0,5443(1)	0,4327(1)	0,054(1)
O1	0,5270(6)	0,6650(2)	0,1891(2)	0,070(1)
O2	0,6767(5)	0,6239(1)	0,0694(2)	0,067(1)
N1	1,2211(7)	0,5296(2)	0,0989(3)	0,090(1)
N2	0,7508(5)	0,5687(2)	0,3958(2)	0,035(1)
F1	1,0209(5)	0,7379(2)	0,7814(2)	0,097(1)
C1	0,7831(6)	0,5734(2)	0,2198(2)	0,039(1)
C2	0,6589(6)	0,5440(2)	0,2960(2)	0,037(1)
C3	0,6842(8)	0,4689(2)	0,2905(3)	0,053(1)
C4	0,8744(8)	0,4563(2)	0,2376(3)	0,052(1)
C5	0,8499(6)	0,5125(2)	0,1642(3)	0,042(1)
C6	1,0575(7)	0,5233(2)	0,1259(3)	0,057(1)
C7	0,6466(7)	0,6262(2)	0,1594(3)	0,049(1)
C8	0,532(1)	0,6687(3)	0,0035(3)	0,098(2)
C9	0,590(1)	0,6640(3)	-0,0879(3)	0,124(2)
C10	0,7277(7)	0,6421(2)	0,4087(3)	0,046(1)
C11	0,8143(6)	0,6643(2)	0,5097(2)	0,040(1)
C12	0,6870(8)	0,6540(2)	0,5796(3)	0,053(1)
C13	0,7555(8)	0,6785(2)	0,6709(3)	0,060(1)
C14	0,9520(8)	0,7131(2)	0,6900(3)	0,060(1)
C15	1,0842(7)	0,7240(2)	0,6241(3)	0,072(1)
C16	1,0131(7)	0,6988(2)	0,5331(3)	0,060(1)

Table III: Factors anisotropic thermal agitation U_{ij} (x 10^3) of $C_{16}H_{20}ClFN_2O_2$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
Cl1	28(1)	77(1)	55(1)	7(1)	7(1)	0(1)
O1	92(2)	61(2)	55(2)	5(2)	7(2)	30(2)
O2	102(2)	56(2)	42(2)	10(1)	11(2)	9(2)

N1	62(3)	134(4)	81(3)	-27(3)	32(2)	-10(3)
N2	31(2)	40(2)	34(2)	-1(2)	9(1)	-1(1)
F1	115(2)	110(2)	57(2)	-32(2)	-6(2)	1(2)
C1	35(2)	46(2)	36(2)	-2(2)	4(2)	-6(2)
C2	30(2)	43(2)	35(2)	-2(2)	3(2)	-2(2)
C3	68(3)	46(3)	45(3)	-3(2)	6(2)	-12(2)
C4	61(3)	43(3)	49(3)	-4(2)	1(2)	6(2)
C5	40(2)	46(2)	40(2)	-6(2)	5(2)	1(2)
C6	52(3)	75(3)	46(3)	-14(2)	13(2)	-3(2)
C7	63(3)	47(3)	35(2)	-1(2)	6(2)	-2(2)
C8	175(8)	68(4)	49(3)	19(3)	18(3)	18(4)
C9	200(7)	118(5)	47(3)	-4(3)	5(4)	18(5)
C10	50(3)	41(2)	46(2)	0(2)	7(2)	-1(2)
C11	42(2)	35(2)	39(2)	-4(2)	2(2)	3(2)
C12	55(3)	59(3)	46(3)	-5(2)	12(2)	-2(2)
C13	70(3)	61(3)	52(3)	-1(2)	16(2)	-2(2)
C14	75(3)	54(3)	45(3)	-18(2)	-5(2)	8(3)
C15	58(3)	79(3)	77(3)	-23(3)	8(3)	-19(3)
C16	48(3)	73(3)	59(3)	-14(3)	11(2)	-11(2)

Table IV: Bond lengths (Å) and angles (°) of $C_{16}H_{20}ClFN_2O_2$.

O1-C7	1,194(4)	C5-C6	1,475(5)
O2-C7	1,323(4)	C5-H5	0,99(3)
O2-C8	1,461(6)	C8-C9	1,408(6)
N1-C6	1,132(5)	C8-H18	0,9700
N2-C10	1,500(5)	C8-H28	0,9700
N2-C2	1,503(4)	C9-H19	0,9600
N2-H12	0,96(4)	C9-H29	0,9600
N2-H22	0,84(3)	C9-H39	0,9600
F1-C14	1,377(4)	C10-C11	1,496(5)
C1-C7	1,508(5)	C10-H110	0,99(3)
C1-C2	1,546(5)	C10-H210	0,96(4)
C1-C5	1,553(5)	C11-C16	1,373(5)
C1-H1	0,88(3)	C11-C12	1,380(5)
C2-C3	1,524(5)	C12-C13	1,373(6)
C2-H2	0,92(3)	C12-H112	0,95(5)
C3-C4	1,508(6)	C13-C14	1,358(6)
C3-H13	0,93(4)	C13-H113	1,03(4)
C3-H23	1,01(4)	C14-C15	1,357(6)
C4-C5	1,525(5)	C15-C16	1,376(6)
C4-H14	0,96(4)	C15-H115	0,9300
C4-H24	0,98(4)	C16-H116	0,97(4)

C(7)-O(2)-C(8)	114,9(4)	O(2)-C(8)-H(18)	109,9
C(10)-N(2)-C(2)	114,5(3)	C(9)-C(8)-H(28)	109,9
C(10)-N(2)-H(12)	106(2)	O(2)-C(8)-H(28)	109,9
C(2)-N(2)-H(12)	108(2)	H(18)-C(8)-H(28)	108,3
C(10)-N(2)-H(22)	110(2)	C(8)-C(9)-H(19)	109,5
C(2)-N(2)-H(22)	111(2)	C(8)-C(9)-H(29)	109,5
H(12)-N(2)-H(22)	107(3)	H(19)-C(9)-H(29)	109,5
C(7)-C(1)-C(2)	112,4(3)	C(8)-C(9)-H(39)	109,5
C(7)-C(1)-C(5)	115,8(3)	H(19)-C(9)-H(39)	109,5

C(2)-C(1)-C(5)	105,0(3)	H(29)-C(9)-H(39)	109,5
C(7)-C(1)-H(1)	107(2)	C(11)-C(10)-N(2)	112,8(3)
C(2)-C(1)-H(1)	109(2)	C(11)-C(10)-H(110)	111,8(18)
C(5)-C(1)-H(1)	108(2)	N(2)-C(10)-H(110)	108,1(18)
N(2)-C(2)-C(3)	110,7(3)	C(11)-C(10)-H(210)	113(2)
N(2)-C(2)-C(1)	112,9(3)	N(2)-C(10)-H(210)	108(2)
C(3)-C(2)-C(1)	106,1(3)	H(110)-C(10)-H(210)	103(3)
N(2)-C(2)-H(2)	104,1(18)	C(16)-C(11)-C(12)	118,9(4)
C(3)-C(2)-H(2)	115,0(18)	C(16)-C(11)-C(10)	120,8(4)
C(1)-C(2)-H(2)	108,2(18)	C(12)-C(11)-C(10)	120,1(4)
C(4)-C(3)-C(2)	106,6(3)	C(13)-C(12)-C(11)	121,0(4)
C(4)-C(3)-H(13)	114(2)	C(13)-C(12)-H(112)	119(3)
C(2)-C(3)-H(13)	112(2)	C(11)-C(12)-H(112)	120(3)
C(4)-C(3)-H(23)	111(2)	C(14)-C(13)-C(12)	117,8(4)
C(2)-C(3)-H(23)	107(2)	C(14)-C(13)-H(113)	125(2)
H(13)-C(3)-H(23)	106(3)	C(12)-C(13)-H(113)	117(2)
C(3)-C(4)-C(5)	103,3(3)	C(15)-C(14)-C(13)	123,5(4)
C(3)-C(4)-H(14)	114(2)	C(15)-C(14)-F(1)	118,5(4)
C(5)-C(4)-H(14)	111(2)	C(13)-C(14)-F(1)	118,0(4)
C(3)-C(4)-H(24)	111(2)	C(14)-C(15)-C(16)	117,8(4)
C(5)-C(4)-H(24)	107(2)	C(14)-C(15)-H(115)	121,1
H(14)-C(4)-H(24)	110(3)	C(16)-C(15)-H(115)	121,1
C(6)-C(5)-C(4)	112,5(3)	C(11)-C(16)-C(15)	121,0(4)
C(6)-C(5)-C(1)	113,1(3)	C(11)-C(16)-H(116)	117(2)
C(4)-C(5)-C(1)	103,9(3)	C(15)-C(16)-H(116)	121(2)
C(6)-C(5)-H(5)	106(2)	O(1)-C(7)-C(1)	124,2(4)
C(4)-C(5)-H(5)	111(2)	O(2)-C(7)-C(1)	111,2(4)
C(1)-C(5)-H(5)	110(2)	C(9)-C(8)-O(2)	109,0(5)
N(1)-C(6)-C(5)	177,2(5)	C(9)-C(8)-H(18)	109,9
O(1)-C(7)-O(2)	124,6(4)		

The cifdep file that collected the structural data of this sample was introduced in "Cambridge Crystallographic Data Centre" referenced CCDC 923497.

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