Probenecid, C₁₃H₁₉NO₄S의 結晶構造

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Crystal Structure of Probenecid, $C_{13}H_{19}NO_4S$

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요 약. Probenecid의 결정구조는 graphite-monochromated Mo-Kα 선을 사용하는 ENRAF-NONIUS CAD-4 자동 X-선 4축 회절기에서 수집된 2574개의 독립적 회절 반점들을 이용하여 결정되었다. 결정은 triclinic system에 속하고, 공간군은 P1이며, 단위세포 상수는 $a=7.535(2)$Å, $b=18.473(5)$Å, $c=5.317(9)$Å, $\alpha=92.00(5)°$, $\beta=99.02(5)°$, $\gamma=94.89(2)°$, $V=727.4(2)$Å³이었다. 이 밖의 다른 parameters로서, $Z=2$, $D_m=$ 1.310, $D_x=1.302$ gcm⁻³, $\mu=1.88$ cm⁻¹, $F(000)=304$, and $T=298$ K이었다. $5\sigma(F_o)$ 이상인 1209개의 반점들에 대한 최종 R 및 R_w는 각각 0.0676과 0.0630이었다. 질소원자 N(13)의 공간배열에서, 결합각의 합은 350.9이며, 질소 주위의 세 원자가 이루는 평면에서 0.268(6)Å 만큼 벗어나 있다. S(1)-C(4) 결합길이는 1.792(6)Å이며 C(4)-S(1)-N(13) 결합각은 106.5(3)°이다. 분자의 전체적인 형태는 황에 대하여 접혀진 구조를 나타내고 있다.

ABSTRACT. The crystal structure of Probenecid has been determined from 2574 independent reflections collected on an automatic ENRAF-NONIUS CAD-4 diffractometer using graphite-monochromated Mo-Kα radiation. The crystal is triclinic, space group P1 with unit cell dimensions $a=7.535(2)$Å, $b=18.473(5)$Å, $c=5.317(9)$Å, $\alpha=92.00(5)°$, $\beta=99.02(5)°$, $\gamma=94.89(2)°$, $V=727.4(2)$Å³, $Z=2$, $D_m=1.310$, $D_x=1.302$ gcm⁻³, $\mu=1.88$ cm⁻¹, $F(000)=304$, and $T=298$ K. Final $R=0.0676$ and $R_w=0.0630$ for 1209 reflections$>5\sigma$ (F_o). In the spacial arrangement about N(13), the sum of bond angles about nitrogen is 350.9° and the nitrogen lies only 0.268(6)Å out of S(1)-C(14)-C(17) plane. The S(1)-C(4) distance is 1.792(6)Å and the C(4)-S(1)-N(13) angle is 106.5(3)°. The overall conformation of the molecule is folded with respect to sulfur.

INTRODUCTION

The geometrical configuration of the sulfone group, X-SO₂-Y, has been studied in several molecules[1~4]. This study is to establish the crystal structure of the title compound and to compare the bond lengths, bond angles and the other geometrical properties for other sulfur containing compounds which have biological activities.

EXPERIMENTS

The transparent, rectangular parallelepiped crystals were grown from an ethanol solution at room temperature. The density was measured by flotation method in a mixture of carbon tetrachloride and n-hexane. The oscillation and Weissenberg photographs with Cu-Kα radiation $(\lambda=1.5418$Å$)$ did not show any symmetry and were used to calculate approximate lattice constants. The crystal with dimensions of 0.16×0.20×0.56 mm was sele-

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*Tables of anisotropic thermal parametrs, H atoms parameters, distances and angles involving H atoms, least-squares planes, the observed and calculated structure amplitudes are available as suplementary materials from the authors (total 12 pp.).

cted for the reflection data collection with graphite monochromated Mo-Kα radiation on an ENRAF-NONIOUS CAD-4 diffractometer. 25 reflections in the range $6<\theta<12°$ used to measure and refine the cell parameters. The intensity of 2622 unique reflections were measured by the ω-2θ scan mode with $\Delta\omega=(0.8+0.34\ \tan\theta)$ in indice range $1<\theta<25°$, $-9<h<9$, $0<k<20$, $-7<l<7$ and corrected for Lorentz-polarization factor. Absorption correction was not applied. Three intensity control reflections, (2, −6, −1), (2, −3, −1) and (0, −5, 1), were monitored every hour of exposure and showed only small random deviations (>2%).

Structure which was solved by direct methods using SHELXS[5] with 616 E values>1.2 and the phase set with a highest combined figure of merit resulted in all 19 non-H atoms being which was located from a subsequent Fourier map. Hydrogen atoms were located from five successive anisotropic full-matrix refinement based on difference Fourier maps using SHELX[6]. The structure involving H atoms was resulted in a final $R=0.068$, $R_w=0.063$, $w=2.8178[\sigma^2(|F_o|)+0.000602(|F_o|)^2]$ from 1209 reflections over 5σ $(|F_o|)$, where σ $(|F_o|)$'s were based on counting statistics. Total 172 variables were refined and maximum shift/e.s.d.'s were <0.01. $\Delta\rho$ excursions in final ΔF synthesis were −0.58 to 0.54 eÅ^{-3}. Scattering factors of SHELX[6] were used. All computations were performed on a CYBER 930 NOS/VE computer.

RESULTS AND DISCUSSION

A stereoscopic ORTEP[7] drawing of the Probenecid in the asymmetric unit together with the
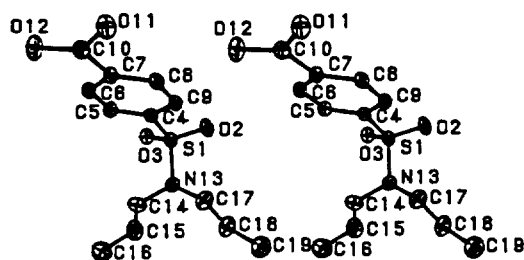

Fig. 1. An ORTEP drawing of probenecid with atomic numbering scheme.

atomic numbering scheme is shown in *Fig.* 1. The final atomic parameters are listed in *Table* 1. The bond lengths, bond angles and some selected torsion angles are listed in *Table* 2.

The phenyl-ring atoms are coplanar within ± 0.007Å with C-C bond lengths varing from 1.375(9) to 1.413(9)Å and endocyclic C-C-C bond angles from 118.4(5) to 122.1(5)° (mean 120.0(6)Å). The bond angle pattern is in fair agreement with the values expected for the angular deviations from the ideal value of 120°[8]. The CO_2 group is markedly rotated by 6.4° with respect to the benzene ring and the displacements of C(10), O(11) and O(12) from the benzene plane are −0.102(6), −0.007(5) and −0.238(5)Å, respectively. The two C-O bond lengths are nearly equal, being 1.269(8) and 1.242 (9)Å and the corresponding C-C-O angles are 116. 5(6) and 119.1(5)°.

The S-O lengths of 1.428(5) and 1.432(5)Å indicate a π-bond character of over 60%[9]. The angular disposition of the bonds about the S stom deviates significantly from that of a regular tetrahedron

Table 1. Fractional atomic coordinates and equivalent isotropic values of the anisotropic thermal parameters for non-H atoms (coordinates are $\times10^4$; $U_{eq}=1/3\sum_{\sum_{ij}a_i^*a_j^*a_ia_j}$ are $\text{Å}^2\times10^3$) with e.s.d.'s in parantheses

atom	x	y	z	U_{eq}
S(1)	5252(2)	2773(1)	0970(3)	53
O(2)	6983(6)	3138(3)	0850(9)	71
O(3)	4030(6)	2525(3)	−1295(8)	62
C(4)	4088(8)	3351(3)	2800(11)	45
C(5)	2215(9)	3285(3)	2354(12)	51
C(6)	1311(8)	3688(4)	3908(13)	51
C(7)	2282(8)	4144(3)	5859(11)	42
C(8)	4127(8)	4218(3)	6266(12)	47
C(9)	5070(8)	3814(4)	4692(12)	48
C(10)	1264(10)	4541(3)	7650(12)	49
O(11)	2200(6)	4995(3)	9284(9)	63
O(12)	−402(6)	4416(3)	7408(8)	65
N(13)	5605(8)	2057(3)	2609(11)	61
C(14)	4002(11)	1567(4)	2840(15)	79
C(15)	4064(13)	831(5)	1686(21)	112
C(16)	2499(15)	322(5)	2005(24)	138
C(17)	7080(11)	2127(5)	4807(14)	79
C(18)	8457(11)	1623(5)	4533(18)	100
C(19)	9861(13)	1666(6)	6819(20)	115

Table 2. The bond lengths, bond angles and selected torsion angles

a) bond length (Å)

S(1)-O(2)	1.428(5)	S(1)-O(3)	1.432(5)
S(1)-C(4)	1.792(6)	S(1)-N(13)	1.627(6)
C(4)-C(5)	1.388(9)	C(4)-C(9)	1.375(9)
C(5)-C(6)	1.386(9)	C(6)-C(7)	1.384(9)
C(7)-C(8)	1.367(8)	C(7)-C(10)	1.520(9)
C(8)-C(9)	1.413(9)	C(10)-O(11)	1.269(8)
C(10)-O(12)	1.242(9)	N(13)-C(14)	1.470(10)
N(13)-C(17)	1.475(10)	C(14)-C(15)	1.479(12)
C(15)-C(16)	1.479(14)	C(17)-C(18)	1.472(12)
C(18)-C(19)	1.476(13)		

b) bond angles (°)

O(3)-S(1)-O(2)	121.4(3)	C(4)-S(1)-O(2)	107.8(3)
C(4)-S(1)-O(3)	107.4(3)	C(5)-C(4)-S(1)	118.6(4)
C(6)-C(5)-C(4)	118.7(6)	C(7)-C(6)-C(5)	119.8(6)
C(8)-C(7)-C(6)	121.4(6)	C(8)-C(9)-C(4)	118.4(5)
C(9)-C(4)-S(1)	119.1(5)	C(9)-C(4)-C(5)	122.1(5)
C(9)-C(8)-C(7)	119.6(6)	C(10)-C(7)-C(6)	118.8(5)
C(10)-C(7)-C(8)	119.7(5)	O(11)-C(10)-C(7)	116.5(6)
O(12)-C(10)-C(7)	119.1(5)	O(12)-C(10)-O(11)	124.4(6)
N(13)-S(1)-O(2)	106.7(3)	N(13)-S(1)-O(3)	106.1(3)
N(13)-S(1)-C(4)	106.5(3)	C(14)-N(13)-S(1)	116.3(5)
C(15)-C(14)-N(13)	112.5(7)	C(16)-C(15)-C(14)	113.1(8)
C(17)-N(13)-S(1)	117.7(5)	C(17)-N(13)-C(14)	116.9(6)
C(18)-C(17)-N(13)	112.0(7)	C(19)-C(18)-C(17)	111.3(8)

c). selected torsion angles (°)

O(2)-S(1)-C(4)-C(5)	153.6(6)	O(2)-S(1)-C(4)-C(9)	−30.1(5)
O(3)-S(1)-C(4)-C(5)	21.2(5)	O(3)-S(1)-C(4)-C(9)	−162.5(6)
N(13)-S(1)-C(4)-C(5)	−92.2(6)	N(13)-S(1)-C(4)-C(9)	84.1(5)
O(2)-S(1)-N(13)-C(17)	37.9(5)	C(8)-C(1)-C(10)-O(11)	8.1(6)
O(3)-S(1)-N(13)-C(14)	−‰45.4(5)	O(3)-S(1)-N(13)-C(17)	168.6(6)
C(4)-S(1)-N(13)-C(14)	68.9(5)	C(4)-S(1)-N(13)-C(17)	−77.1(5)
S(1)-N(13)-C(14)-C(15)	118.0(8)	C(17)-N(13)-C(14)-C(15)	−95.7(8)
S(1)-N(13)-C(17)-C(18)	−120.1(8)	C(14)-N(13)-C(17)-C(18)	94.0(8)

with the largest deviations in O-S-O and O-S-N angles. The significant widening of the O-S-O angle (121.4(3)°) from the ideal tetrahedral value may be the result of the non-bonding interactions between the short S-O bonds[10]. The S-C (1.792(6) Å) bond length is slightly shorter than the sum (1.82Å) of Pauling's covalent radii and the S-N (1.627(6)Å) is markedly shorter than the sum (1.74 Å). In the spacial arrangement about N(13), the sum of bond angles about nitrogen is 350.9Å and the nitrogen lies only 0.268(6)Å out of S(1)-C (14)-C(17) plane. This suggests that the N(13) is

sp^2 hybridized in order to allow the remaining filled p orbital to participate more effectively in d-p π bonding with S(1)[11].

The average bond lengths of 1.474(10) [N-CH₂], 1.476(12) [CH₂-CH₂] and 1.478(14) [CH₂-CH₃]Å in the dipropylamine moiety agree well with the corresponding average values of 1.490(8), 1.494(9) and 1.512(10)Å in bis-dipropylammonium tetrachlorocuprate(II) (DPACC)[12] within 2σ.

A PLUTO[13] stereoview of the unit cell is shown in *Fig.* 2. The molecules appears to form a intermolecular hydrogen bond O(11)-H⋯O(2)* of le-

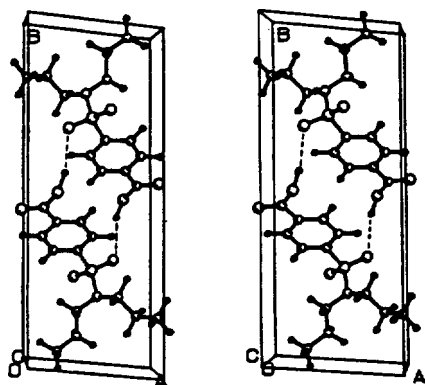*Fig.* 2. A stereoscopic PLUTO molecular packing drawing of Probenecid. The dashed lines denote the intermolecular hydrogen bonds.

ngth 2.428(6)Å and angle 155.7° related by 2-fold axis parallel to the c axis. Adjacent molecules parallel to a and b axis are bound together by van der Waals forces.

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