Synthesis and structure of 1-(4-chlorophenyl)-3-(5-methyl-1,3-dioxan-5-yl)-(1,2),(3,4)-diepoxybutane

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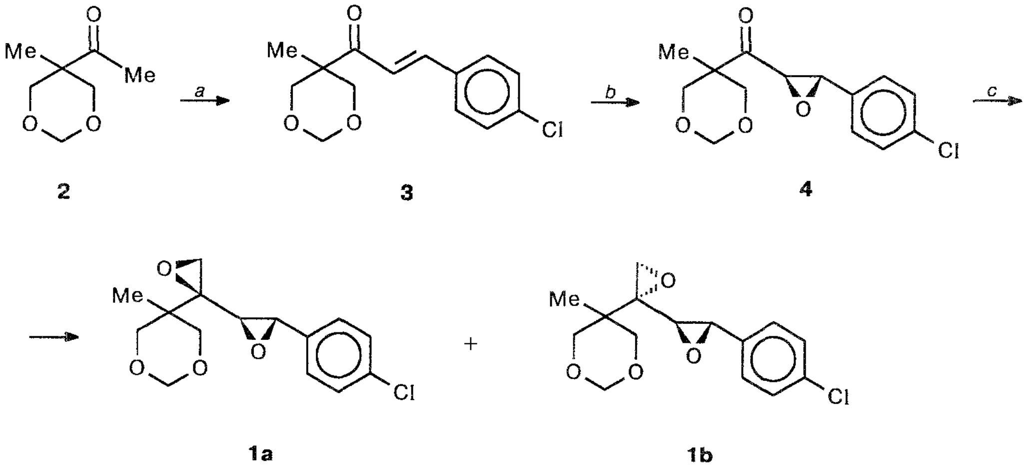
The synthesis and X-ray structural study of 1-(4-chlorophenyl)-3-(5-methyl-1,3-dioxan-5-yl)-(1,2),(3,4)-diepoxybutane are described.

Key words: oxirane, synthesis, molecular structure; X-ray structural analysis.

Oxiranes obtained by methyleneoxiranation of a series of aliphatic and carbocyclic ketones are used for preparing (1*H*-1,2,4-triazol-1-ylmethyl)alkanols, which exhibit high fungicidal activity.[1,2] Oxyranyl-containing triazolylalkanols also exhibit fungicidal properties.[3,4] These compounds are formed as a mixture of diastereoisomers[3] that differ substantially in activity.[4] In this connection, it is of interest to synthesize the corresponding dioxiranes and to determine their spatial structures.

In this work, we performed the synthesis and X-ray structural analysis of one of these dioxiranes, 1-(4-chlorophenyl)-3-(5-methyl-1,3-dioxan-5-yl)-(1,2),(3,4)-diepoxybutane (**1**). Condensation of 5-acetyl-5-methyl-1,3-dioxane (**2**) with 4-chlorobenzaldehyde under the action of sodium methoxide[5] afforded α,β-unsaturated ketone (**3**), which was oxidized with H_2O_2 to monoepoxide (**4**). The latter was converted to a mixture of diastereoisomers **1a,b** under the action of dimethylsulfonium methylide[6] generated from $Me_3S^+MeSO_4^-$.

Scheme 1



Reagents and conditions: *a*. 4-ClC_6H_4CHO, MeONa/MeOH, 20 °C, ~16 h; *b*. H_2O_2, NaOH—H_2O, 50 °C, 1.5 h; *c*. $Me_3S^+MeSO_4^-$/CH_2Cl_2, NaOH—H_2O, 20 °C, ~12 h

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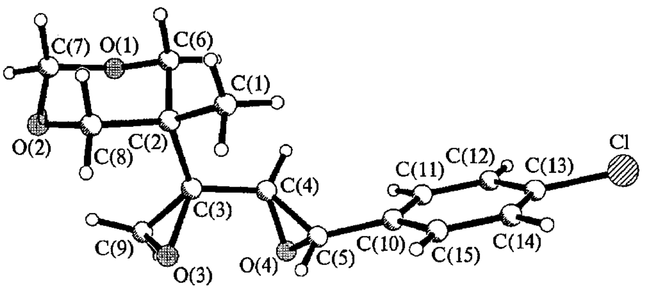

Fig. 1. The structure of molecule **1a**.

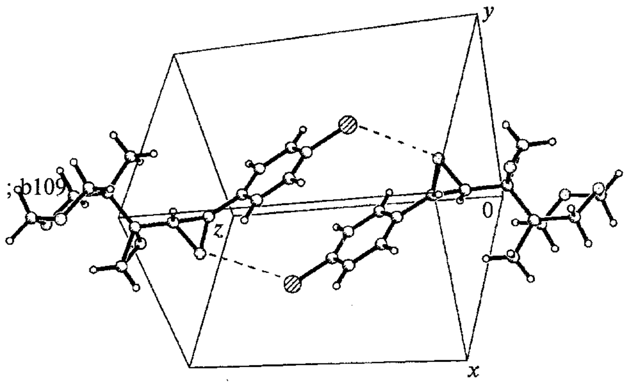

Fig. 2. The crystal structure of compound **1a**.

Diepoxide **1a** was isolated by recrystallization (Scheme 1).

The structure of compound **1a** was established by X-ray structural analysis (Fig. 1). The bond lengths and bond angles are listed in Tables 1 and 2; atomic coordinates are given in Table 3.

Conventionally, molecule **1a** can be characterized by its four fragments: dioxane (A), 2,2-disubstituted (B) and 2,3-disubstituted (C) oxirane, and chlorophenyl fragments (D). The dihedral angles between fragments A—B, B—C, and C—D are 32.4, 58.2, and 101.3°, respectively. The C(2)—C(3)—C(4)—C(5), C(3)—C(4)—C(5)—C(10), and O(3)—C(3)—C(4)—O(4) torsion angles are 107.1, −151.1, and 41.0°, respectively. The 1,3-dioxane fragment has the normal chair conformation. The C(7) and C(1) atoms deviate from the O(1)O(2)C(6)C(8) plane by 0.64 and 0.66 Å, respectively. The chlorophenyl fragment is planar within 0.009 Å.

The HC(4)—C(4)—C(5)—HC(5) torsion angle is 156.3°, which is indicative of the *trans* orientation of H atoms with respect to the C(4)—C(5) bond. This is an important structural characteristic because it must remain constant when the 2,2-disubstituted oxirane cycle is cleaved by triazole. The chlorophenyl group and the H atom at the C(4) atom are in *cis* positions. The HC(4)—C(4)—C(5)—C(10) torsion angle is 3.0°.

The principal interatomic distances and bond angles agree well with the data in the literature on compounds containing oxirane fragments.[7]

The molecules are packed in the crystal to form centrosymmetric dimers (Fig. 2). The Cl...O(4) intermolecular contact is 3.6 Å. The dimers are separated by distances exceeding the sums of the van der Waals radii.

Table 1. Bond lengths in molecule **1a**

Bond	d/Å	Bond	d/Å
Cl—C(13)	1.738(3)	O(1)—C(6)	1.422(3)
O(1)—C(7)	1.395(4)	O(2)—C(7)	1.408(4)
O(2)—C(8)	1.426(3)	O(3)—C(3)	1.441(3)
O(3)—C(9)	1.449(3)	O(4)—C(4)	1.432(2)
O(4)—C(5)	1.447(3)	C(1)—C(2)	1.538(3)
C(2)—C(3)	1.531(3)	C(2)—C(6)	1.531(3)
C(2)—C(8)	1.528(4)	C(3)—C(4)	1.499(3)
C(5)—C(10)	1.484(3)	C(10)—C(11)	1.387(3)
C(10)—C(15)	1.390(3)	C(11)—C(12)	1.379(4)
C(12)—C(13)	1.386(3)	C(13)—C(14)	1.380(3)
C(14)—C(15)	1.384(3)		

Table 2. Bond angles in molecule **1a**

Angle	φ/deg	Angle	φ/deg	Angle	φ/deg
C(6)—O(1)—C(7)	110.7(2)	O(2)—C(8)—C(2)	112.8(2)	O(3)—C(3)—C(9)	59.7(1)
C(3)—O(3)—C(9)	61.3(1)	C(5)—C(10)—C(11)	121.9(2)	C(4)—C(3)—C(9)	117.9(2)
C(1)—C(2)—C(3)	108.5(2)	C(11)—C(10)—C(15)	119.1(2)	O(4)—C(4)—C(5)	59.9(1)
C(3)—C(2)—C(6)	110.4(2)	C(11)—C(12)—C(13)	119.0(2)	O(4)—C(5)—C(4)	58.8(1)
C(3)—C(2)—C(8)	112.6(2)	Cl—C(13)—C(14)	119.2(2)	C(4)—C(5)—C(10)	122.78(1)
O(3)—C(3)—C(2)	116.2(2)	C(13)—C(14)—C(15)	119.5(2)	O(1)—C(7)—O(2)	111.9(2)
C(2)—C(3)—C(4)	115.0(2)	C(7)—O(2)—C(8)	111.4(2)	O(3)—C(9)—C(3)	59.1(1)
C(2)—C(3)—C(9)	123.0(2)	C(4)—O(4)—C(5)	61.3(1)	C(5)—C(10)—C(15)	119.0(2)
O(4)—C(4)—C(3)	116.6(2)	C(1)—C(2)—C(6)	110.1(2)	C(10)—C(11)—C(12)	121.1(2)
C(3)—C(4)—C(5)	121.5(2)	C(1)—C(2)—C(8)	108.1(2)	Cl—C(13)—C(12)	119.8(2)
O(4)—C(5)—C(10)	117.3(2)	C(6)—C(2)—C(8)	107.0(2)	C(12)—C(13)—C(14)	121.0(2)
O(1)—C(6)—C(2)	110.9(2)	O(3)—C(3)—C(4)	112.0(1)	C(10)—C(15)—C(14)	120.4(2)

Table 3. Atomic coordinates ($\times 10^4$, $\times 10^3$ for H atoms) and equivalent isotropic thermal parameters ($U \times 10^3$/Å^2) in molecule **1a**

Atom	*x*	*y*	*z*	*U*
Cl	7816(1)	3081(1)	5837(1)	68(1)
O(1)	49(3)	−136(2)	−2058(2)	64(1)
O(2)	1240(3)	1235(2)	−3318(2)	70(1)
O(3)	2432(2)	3979(2)	−799(1)	51(1)
O(4)	1450(2)	3886(2)	1606(1)	55(1)
C(1)	5313(4)	1444(3)	−1049(3)	75(1)
C(2)	3113(3)	1418(2)	−1457(2)	43(1)
C(3)	2081(3)	2627(2)	−570(2)	36(1)
C(4)	2294(3)	2721(2)	749(2)	40(1)
C(5)	3637(3)	3824(2)	1542(2)	43(1)
C(6)	1955(4)	10(2)	−1479(2)	53(1)
C(7)	328(5)	−76(3)	−3256(3)	76(1)
C(8)	3186(4)	1530(3)	−2762(2)	62(1)
C(9)	387(3)	3300(2)	−914(2)	48(1)
C(10)	4636(3)	3629(2)	2614(2)	41(1)
C(11)	3583(3)	3023(3)	3435(2)	51(1)
C(12)	4536(4)	2846(3)	4424(2)	54(1)
C(13)	6577(4)	3299(2)	4601(2)	46(1)
C(14)	7658(3)	3902(2)	3795(2)	49(1)
C(15)	6684(3)	4073(2)	2805(2)	46(1)
H(1)	601(4)	239(2)	−111(2)	8(1)
H(2)	599(4)	72(2)	−162(2)	8(1)
H(3)	526(4)	138(3)	−17(2)	8(1)
H(4)	206(4)	187(2)	101(2)	5(1)
H(5)	435(4)	452(2)	117(2)	5(1)
H(6.1)	281(4)	−75(3)	−198(2)	7(1)
H(6.2)	167(4)	−9(3)	−60(2)	6(1)
H(7.1)	134(4)	−84(3)	−375(2)	8(1)
H(7.2)	−110(4)	−19(2)	−371(2)	9(1)
H(8.1)	406(4)	73(3)	−325(2)	8(1)
H(8.2)	366(4)	250(3)	−274(2)	7(1)
H(9.1)	−3(4)	298(3)	−179(2)	6(1)
H(9.2)	−56(4)	371(3)	−30(3)	6(1)
H(11)	213(4)	275(2)	332(2)	8(1)
H(12)	379(4)	244(3)	501(2)	6(1)
H(14)	915(4)	424(3)	392(2)	7(1)
H(15)	752(4)	448(2)	220(2)	6(1)

Experimental

The starting 5-acetyl-5-methyl-1,3-dioxane was prepared according to the known procedure.[8] Melting points were not corrected. The ^{1}H NMR spectra were recorded on a Varian XL-400 spectrometer (400 MHz) in $(CD_3)_2CO$; TMS was used as the internal standard.

3-(4-Chlorophenyl)-1-(5-methyl-1,3-dioxan-5-yl)prop-2-en-1-one (3). A solution of MeONa (2 mL, 4.2 mmol) in MeOH was added to a solution of ketone **2** (6.0 g, 41.7 mmol) and 4-chlorobenzaldehyde (6.44 g, 45.8 mmol) in 10 mL of MeOH at ~20 °C with stirring. The mixture was kept at 20 °C for 16 h; the precipitate formed was filtered off and recrystallized from EtOH to give α,β-unsaturated ketone **3** (7.8 g, 70 % yield); m.p. is 121—122.5 °C. Found (%): C, 63.2; H 5.7; Cl, 13.4. $C_{14}H_{15}ClO_3$. Calculated (%): C, 63.0; H, 5.7; Cl, 13.3. ^{1}H NMR (δ, *J*/Hz): 1.11 (s, 3 H, Me); 3.71, 4.36 (both d, 4 H, OCH_2CCH_2O, AX system, $^2J = -11.6$); 4.76, 4.79 (both d, 2 H, OCH_2O, AB system, $^2J = -6.1$); 7.48, 7.58 (both d, 2 H, HC=CH, AB system, $J = 15.6$); 7.46, 7.77 (m, 4 H, ArH, AA'BB' system).

3-(4-Chlorophenyl)-1-(5-methyl-1,3-dioxan-5-yl)-2,3-epoxypropan-1-one (4). A 30 % H_2O_2 solution (3.4 g) was added to a vigorously stirred mixture of enone **3** (6.5 g, 24.5 mmol) and NaOH (0.4 g) in 100 mL of MeOH at such a rate that the temperature of the reaction mixture remained within the range 25—30 °C. After 2 h, the crystals formed were filtered off, the mother liquor was evaporated by 3/4 volume and cooled to 0 °C. The crystals formed were isolated, combined with the first portion, washed with water, then with MeOH, and air dried. Oxirane **4** was obtained in 87.8 % yield (5.85 g); m.p. 119—121 °C. Found (%): C, 59.8; H, 5.5; Cl, 12.5. $C_{14}H_{15}ClO_4$. Calculated (%): C, 59.5; H, 5.4; Cl, 12.5. ^{1}H NMR (δ, *J*/Hz): 1.05 (s, 3 H, Me); 3.60, 4.33 (both d, 2 H, OCH_2C, AX system, $^2J = -11.4$); 3.66, 4.43 (both d, 2 H, OCH_2, AX system, $^2J = -11.9$); 3.90, 4.28 (both d, 2 H, HC—CHO, AB system, $^3J = 2.0$); 4.68, 4.85 (both d, 2 H, OCH_2O, AB system, $^2J = -6.0$); 7.38, 7.44 (m, 4 H, ArH, AA'BB' system).

1-(4-Chlorophenyl)-3-(5-methyl-1,3-dioxan-5-yl)-(1,2),(3,4)-diepoxybutane (1a,b). $Me_3S^+MeSO_4^-$ (6.02 g, 32 mmol) and a 50 % NaOH solution (50 mL) were added to a solution of monoepoxide **4** (3.96 g, 14 mmol) in 100 mL of CH_2Cl_2. The mixture was stirred for 12 h at ~20 °C and poured into water; the organic layer was isolated, dried with Na_2SO_4, and evaporated. Diepoxides **1a,b** were obtained in 73.4 % yield (3.05 g) as a 76 : 24 mixture of diastereoisomers (according to the results of ^{1}H NMR).

The predominant diastereoisomer, **1a**, m.p. 101—102 °C, was isolated in the pure form by double recrystallization of the mixture from hexane. Found (%): C, 61.0; H, 6.0; Cl, 11.2. $C_{15}H_{17}ClO_4$. Calculated (%): C, 60.7; H, 5.8; Cl, 12.0. ^{1}H NMR (δ, *J*/Hz): 1.05 (s, 3 H, Me); 2.79, 3.07 (both d, 2 H, C—CH_2O, AB system, $^2J = -11.6$); 3.56, 3.59 (both d, 2 H, OCH_2C, AB system, $^2J = -11.6$); 3.87, 4.06 (both d, 2 H, OCH_2C, AB system, $^2J = -11.9$); 3.61, 3.80 (both d, 2 H, HC—CHO, AB system, $^3J = 2.0$); 4.69, 4.72 (2 H, OCH_2O, AB system, $J = 6.0$); 7.33, 7.40 (4 H, ArH, AA'BB' system).

A single crystal of diepoxide **1a** was grown from an 80 % aqueous EtOH solution at 20 °C. X-ray structural analysis was performed on a four-circle automated Syntex PI diffractometer (Mo-Kα radiation, graphite monochromator). The colorless transparent crystals belong to the triclinic system: $a = 6.594(2)$, $b = 9.956(3)$, $c = 11.457$ Å, $\alpha = 106.30(2)°$, $\beta = 87.67(2)°$, $\gamma = 94.99(2)°$, $V = 719.1(8)$ Å^3, $Z = 2$, $d_{calc} = 1.347$ g cm^{-3}, the space group is $P\bar{1}$.

The structure was refined using 1816 independent reflections with $I \geq 3\sigma(I)$. The structure was solved by direct methods using the SHELXTL program (see Ref. 9) and refined with anisotropic temperature factors for non-hydrogen atoms. All H atoms were located from the difference electron density synthesis and refined isotropically. The final values of *R* factors are as follows: $R = 0.038$ and $R_w = 0.054$. Atomic coordinates are given in Table 3.

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