



Synthesis and Crystal Structure of (5-Ethyl-2-methyl-2-phenyl-1,3-dioxan-5-yl)methanol

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A new compound (5-ethyl-2-methyl-2-phenyl-1,3-dioxan-5-yl)methanol, obtained from the reaction of 2,2-bis(hydroxymethyl)butanol with acetophenone, has been synthesized and characterized by IR and ¹H NMR. Single crystal X-ray diffraction analyses indicated that the title compound belongs to tetragonal system with space group I4(1)/a with a = 29.921(2) Å, b = 29.921(2) Å, c = 5.9627(9) Å. Mr = 236.30, V = 5338.1(10) Å³, Dc = 1.176 g/cm³, Z = 16, μ = 0.081 mm⁻¹, F(000) = 2048, R = 0.0595, wR = 0.1645. In the title compound, the 1,3-dioxane ring adopts a chair conformation and the phenyl substituent occupies an equatorial site. In the crystal, adjacent four molecules are connected by O-H...O hydrogen bonding interactions into a tetramer.

Keywords: 1,3-Dioxane, Acetophenone, Synthesis, Crystal structure.

INTRODUCTION

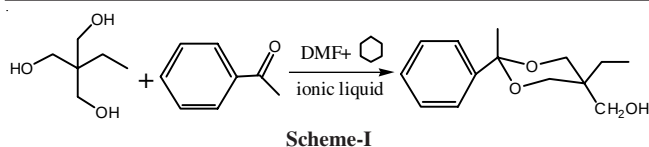
Acetal compounds have many characters such as aroma¹ and chemical stability², which are used widely in fragrances and food flavors^{3,4}. Acetal compounds are stable in neutral and alkaline conditions and will degrade and generate a material of small molecules in acidic conditions. Polyfunctional branched compounds are the new class of compounds with a wide range of applications. The synthesis of these compounds rich in raw materials and simple manufacturing process, in the synthesis of fine chemicals and other industries have shown important uses and has great potential for development⁵⁻⁷. Ionic liquids as a catalyst have especial advantages in the synthesis of acetal compounds in 21st century green⁸. To our knowledge the report of 2,2-dimethylolbutyric acetal (ketone) was rare. Herein, in this paper, a novel compounds (5-ethyl-2-methyl-2-phenyl-1,3-dioxan-5-yl)methanol was synthesized by using 2,2-bis(hydroxymethyl) butanol with acetophenone as raw material, ionic liquid as catalyst, DMF and cyclohexane as solvent and its structure has been characterized.

EXPERIMENTAL

The ionic liquid of 1-acetyl-3-methylimidazole hydrogen sulfate was prepared according to the literature method⁹. All the starting materials and solvents were commercially available and used without further purification. acetophenone and ethyl acetate were obtained commercially from Tianjin Damao

Chemical Plant. 2,2-bis(Hydroxymethyl)butanol was the product of Aladin. Crystal structure was determined on a Bruker Smart Apex II diffractometer. Elemental analyses were performed by direct combustion with a PE2400 instrument. The IR spectra were recorded in the 4000-400 cm⁻¹ region using KBr pellets and a Nicolet AVATAR-360 spectrometer. ¹H NMR spectra were recorded in a CDCl₃ solution with a Bruker AV-400 spectrometer. Melting point data were recorded in a Buchi B545 spectrometer.

Synthesis of (5-ethyl-2-methyl-2-phenyl-1,3-dioxan-5-yl)methanol: 2,2-bis(Hydroxymethyl) butanol (1.3400 g, 10 mmol) and acetophenone (1.3215 g, 11 mmol) were added into 50 mL round-bottom flask provided with a stirrer and a reflux condenser. Both a solution of *N,N*-dimethylformamide (5 mL), cyclohexane (8 mL) and 1-acetyl-3-methylimidazole hydrogen sulfate (0.1 g) were simultaneously added dropwise to the flask and the reacting solution was kept at 378 K under reflux for 4 h. After the reaction completion, the reaction mixture was poured into separator funnel and separated. The organic layer was washed with water (10 × 3 mL), dried with MgSO₄. Once more filtered and evaporated to dryness. Then the white solid powder was obtained 1.3 g (yield: 53 %). The melting point of purified product was 357.3-358.1 K. The product was recrystallized from cyclohexane to afford colourless crystals (**Scheme-I**). Anal. Calcd. for C₁₄H₂₀O₃: C, 71.19; H, 8.47 %. Found C, 71.10; H, 8.29 %. IR (KBr, ν_{max}, cm⁻¹): 3327, 2954, 2870, 1461, 1377, 1242, 1087, 1021, 878, 767, 703.



^1H NMR (CDCl_3 , 400 MHz) δ (ppm): 7.314-7.413 (5H, m, ArH); 3.970-3.982 (2H, d, $J = 4.8$ Hz, $\text{CH}_2\text{-OH}$); 3.683-3.712 (2H, d, $J = 11.6$ Hz, $2\text{CO-CH}_2\text{-C}$, Heq); 3.443-3.472 (2H, d, $J = 11.6$ Hz, $2\text{CO-CH}_2\text{-C}$, Hax); 1.645 (1H, s, -OH); 1.510 (3H, s, $\text{CH}_3\text{-C}$); 1.002-1.040 (2H, q, $J = 7.6$ Hz, $\text{C-CH}_2\text{-CH}_3$); 0.726-0.888 (3H, t, $J = 7.6$ Hz, $\text{CH}_3\text{-CH}_2$).

X-ray crystal structure determination: A colourless block crystal with dimensions of $0.46 \text{ mm} \times 0.42 \text{ mm} \times 0.36 \text{ mm}$ was selected for measurement. Diffraction data of compound were collected at 296(2) K on a Bruker Smart CCD area detector, with $\text{MoK}\alpha$ radiation ($\lambda = 0.71073 \text{ \AA}$). A total of 21212 reflections were collected in the range of 1.36 to 27.34° by using an ϕ - ω multiscan mode, of which 3003 were unique with $R_{\text{int}} = 0.0228$ and 2354 were observed with $I > 2\sigma(I)$. The structure was solved by direct methods and refined on F^2 by full-matrix least-squares procedures using the SHELX-97 program package¹⁰. All non-hydrogen atoms were refined anisotropically. The hydrogen atoms attached to carbon atoms were fixed at their ideal positions. The final $R = 0.0595$, $wR = 0.1645$ ($w = 1/[\sigma^2(\text{Fo}^2) + (0.0979\text{P})^2 + 3.0971\text{P}]$, where $\text{P} = (\text{Fo}^2 + 2\text{Fc}^2)/3$), $S = 1.082$, $(\Delta/\sigma)_{\text{max}} = 0.001$, $(\Delta\rho)_{\text{max}} = 0.349$ and $(\Delta\rho)_{\text{min}} = -0.287 \text{ e \AA}^{-3}$. The crystallographic data for the title compound is summarized in Table-1. Selected bond lengths and angles are listed in Table-2. Hydrogen bond parameters are given in Table-3.

RESULTS AND DISCUSSION

The aldol reaction of 2,2-bis(hydroxymethyl)butanol reacted with acetophenone in 1:1.1 molar ratio was then conducted in DMF and cyclohexane with ionic liquid of 1-acetyl-3-methylimidazole hydrogen sulfate as catalyst. Upon recrystallization colourless crystals were isolated and characterized to be the target products (**Scheme-I**).

The compound gave satisfactory elemental analyses and the IR spectra exhibits the strong absorption in the range 1088-

TABLE-1
CRYSTAL DATA AND STRUCTURE
REFINEMENT FOR THE TITLE COMPOUND

Parameter	Compound
Empirical formula	$\text{C}_{14}\text{H}_{20}\text{O}_3$
Formula weight	236.30
Crystal size (nm)	$0.46 \times 0.42 \times 0.36$
Crystal system, space group	Tetragonal, $I4(1)/a$
a, b, c ($\text{\AA}$)	29.921(2), 29.921(2), 5.9629 (9)
α, β, γ ($^\circ$)	$\alpha = 90, \beta = 90, \gamma = 90$
$V/\text{\AA}^3$	5338.1(10)
$D_c/\text{mg cm}^{-3} Z$	1.176, 16
μ/mm^{-1}	0.081
$F_{(000)}$	2048
Index ranges (H, k, l)	$-38 \leq h \leq 33, -38 \leq k \leq 38, -7 \leq l \leq 7$
θ range for data collection	$1.36\text{--}27.34$
Reflections collected/unique	21212/3003(0.0228)
Completeness to θ	98.9 %
Goodness-of-fit on F^2	1.082
Final R indices [$I > 2\sigma(I)$]	0.0595, 0.1645
R indices (all data)	0.0743, 0.1838
Max. peak/hole ($\text{e \AA}^{-3}$)	0.349/−0.287

TABLE-3
HYDROGEN BOND PARAMETERS
($\text{\AA}, ^\circ$) FOR THE TITLE COMPOUND

D-H...A	d(D-H)	d(H...A)	d(D...A)	$\angle(\text{DHA})$
$\text{O}(3)\text{--H}(3)\cdots\text{O}(3)^{\#1}$	0.82	1.93	2.739(2)	171.6
Symmetry codes: #1 $y + 3/4, -x + 5/4, -z + 5/4$				

1021 cm^{-1} , which are associated with O-C-O acetal bond character. The compound was also characterized by NMR spectroscopy, the ^1H NMR spectra shows two sets of split signals corresponding to the $-\text{CH}_2-$ protons of 1,3-dioxane ring. These results indicate that the equatorial bond protons Heq and straight bond protons Hax of $-\text{CH}_2-$ in 1,3-dioxane ring produce coupling. The hydroxyl group displays a single signal at $\delta = 1.654 \text{ ppm}$ and the methyl group of the $\text{CH}_3\text{-C}$ fragment has a single signal at $\delta = 1.510 \text{ ppm}$, these results demonstrates the formation of the desired compound.

The molecular structure of compound was further confirmed by X-ray crystallography (Fig. 1). X-ray diffraction analyses indicated that the title compound contains 1,3-dioxane

TABLE-2
SELECTED BOND LENGTHS ($\text{\AA}$) AND BOND ANGLES ($^\circ$)

Bonds	d	Bonds	d	Bonds	d
O(1)–C(7)	1.414(2)	O(1)–C(9)	1.424(2)	O(2)–C(7)	1.407(2)
C(1)–C(2)	1.379(3)	C(12)–C(13)	1.501(3)	C(5)–C(4)	1.361(4)
O(2)–C(10)	1.433(2)	C(1)–C(6)	1.382(3)	C(3)–C(4)	1.365(4)
C(11)–C(10)	1.524(2)	C(2)–C(3)	1.396(3)	C(11)–C(14)	1.532(2)
C(11)–C(9)	1.520(2)	C(1)–C(7)	1.525(2)	O(3)–C(14)	1.416(3)
C(11)–C(12)	1.523(2)	C(7)–C(8)	1.512(2)	O(3)–C(14)	1.416(3)
Angles	ω	Angles	ω	Angles	ω
C(7)–O(1)–C(9)	114.16(12)	C(4)–C(5)–C(6)	120.6(3)	C(13)–C(12)–C(11)	115.6(2)
C(7)–O(2)–C(10)	113.77(12)	C(2)–C(1)–C(6)	118.55(18)	C(4)–C(3)–C(2)	120.6(3)
C(9)–C(11)–C(12)	110.12(15)	O(2)–C(7)–C(8)	106.72(15)	C(6)–C(1)–C(7)	120.49(17)
C(9)–C(11)–C(10)	105.99(13)	C(2)–C(1)–C(7)	120.76(17)	O(2)–C(7)–O(1)	111.05(13)
C(12)–C(11)–C(10)	109.12(15)	C(9)–C(11)–C(14)	110.02(15)	C(12)–C(11)–C(14)	111.55(15)
C(10)–C(11)–C(14)	109.89(15)	O(1)–C(7)–C(8)	105.32(15)	O(2)–C(7)–C(1)	111.68(13)
O(2)–C(10)–C(11)	111.50(14)	O(1)–C(7)–C(1)	111.54(14)	C(5)–C(4)–C(3)	119.5(2)
C(8)–C(7)–C(1)	110.24(15)	O(3)–C(14)–C(11)	112.84(17)	O(1)–C(9)–C(11)	111.97(14)
C(1)–C(2)–C(3)	119.9(2)	C(5)–C(6)–C(1)	120.8(2)	—	—

rings and the phenyl substituent occupies an equatorial site. The 1,3-dioxane ring displays chair conformation with torsion angles for C7-O2-C10-C11 and C7-O1-C9-C11 being 57.07(18) and -55.99(19), respectively. In this crystal, adjacent four molecules are connected by O-H...O ($O_3-H\cdots O_3^{\#1}$ 2.739(2) Å, $\#1 y + 3/4, -x + 5/4, -z + 5/4$) hydrogen bonding interactions between the oxygen atoms into a tetramer (Fig. 2). The similar crystal structures have been described in previous report^{1,11-13}.

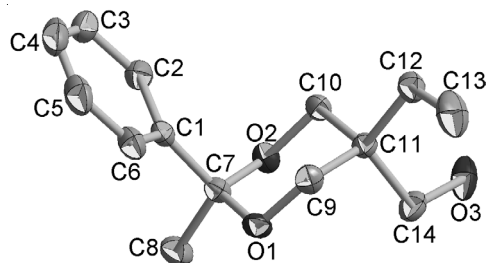


Fig. 1. Molecular structure of the title compound with atom numbering scheme. Displacement ellipsoids are drawn at 30 % probability level for non-H atoms

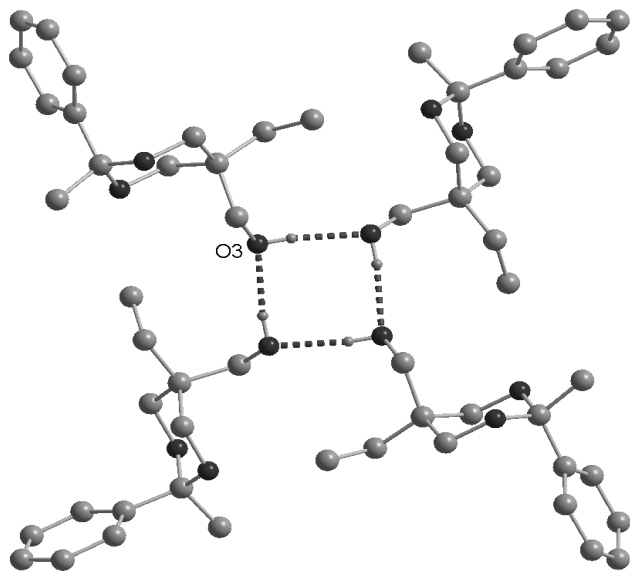


Fig. 2. Four monomers are connected by hydrogen bonding interactions into a tetramer. H atoms non-participating in hydrogen-bonding were omitted for clarity

Conclusion

In conclusion, the title compound (5-ethyl-2-methyl-2-phenyl-1,3-dioxan-5-yl)methanol was synthesized by the reaction of 2,2-bis(hydroxymethyl)butanol with acetophenone, DMF and cyclohexane as solvent, ionic liquid of 1-acetyl-3-methylimidazole hydrogen sulfate as catalyst, heating reflux 4 h. The yield was 53 % (1.3 g). The product was characterized by ¹H NMR, IR and single crystal X-ray diffraction, which was confirmed to be in good agreement with the title compound.

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