



Synthesis and Crystal Structure of 2-(4-Chlorophenyl)-5-Ethyl-1,3-Dioxane-5-Carboxylic Acid

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Received: 18 September 2013;

Accepted: 20 February 2014;

Published online: 16 September 2014;

AJC-15926

A new synthetic intermediate 2-(4-chlorophenyl)-5-ethyl-1,3-dioxane-5-carboxylic acid, derived from the reaction of 2,2'-bis(hydroxymethyl)butyric acid with 4-chlorobenzaldehyde, has been prepared and characterized by IR spectra and ¹H NMR spectroscopy. The definitive molecular structure was determined by single-crystal X-ray analyses, which revealed that the title compound belongs to monoclinic system with space group P2(1)/n with a = 12.655(3) Å, b = 8.260(2) Å, c = 24.380(6) Å, β = 92.533(2)°, Mr = 270.70, V = 2545.89(11) Å³, Dc = 1.412 g/cm³, Z = 8, μ = 0.304 mm⁻¹, F(000) = 1136, R = 0.0336, wR = 0.0815. In the title compound, there are two independent molecules in the asymmetric unit. The 1,3-dioxane ring adopts a chair conformation and the 4-chlorophenyl substituent occupies an equatorial site. In the crystal, adjacent molecules are connected by O-H...O hydrogen bonding interactions into a dimer.

Keywords: 1,3-Dioxane, 2,2'-bis(Hydroxymethyl)butyric acid, 4-Chlorobenzaldehyde, Synthesis, Crystal structure.

INTRODUCTION

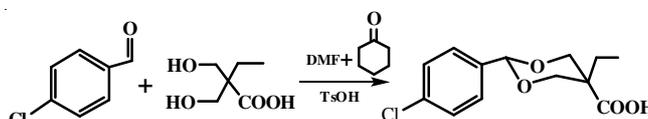
Acetal (ketal) compounds continue to be focus of much attention and have occupied a special place in organic chemistry because they are usually used as a protection of carbonyl or synthetic intermediate in organic syntheses¹ and have been widely applied in fragrance and flavors as well as a new type of spices. 2,2'-Dihydroxy methyl butyric acid, which has not only typical neoamyl group, but also polyfunctional group containing carboxyl and glycol, is a kind of common chemical products²⁻⁷. The neoamyl group display a good heat resistance, hydrolysis resistance and colour stability and the carboxyl and glycol groups makes it has some special purpose, such as the application in the synthesis of waterborne polyurethane and biodegradable surfactant using the carboxyl and glycol groups as hydrophilic group^{8,9}. Herein, a novel compound 2-(4-chlorophenyl)-5-ethyl-1,3-dioxane-5-carboxylic acid was synthesized by the reaction of 2,2-dihydroxy methyl butyric acid with *p*-chlorobenzaldehyde and *p*-toluene sulfonic acid as catalyst, DMF and cyclohexanone as solvent.

EXPERIMENTAL

Crystal structure was determined on a CrysAlis CCD, Gemini S Ultra (Oxford Diffraction Ltd.). All of the chemicals are commercially available and used without further purification. 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 Niconet 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 2-(4-chlorophenyl)-5-ethyl-1,3-dioxane-5-carboxylic acid: 2,2'-bis(Hydroxymethyl) butyric acid (0.5015 g, 3.38 mmol), 4-chlorobenzaldehyde (0.5740 g, 4.09 mmol), N,N-dimethylformamide (2 mL), cyclohexane (15 mL) and *p*-toluene sulfonic acid (0.03 g) were heated and stirred at 373 K for 6 h. Sodium bicarbonate (0.0350 g, 0.42 mmol) was added to dissolve the residue after the solvent was evaporated under reduced pressure. The organic solution was washed with water (20 mL) and dried with anhydrous sodium sulfate. The resulting solution was filtered and evaporated and the product was recrystallized from cyclohexane to afford colourless crystals (0.6 g; yield 65 %; m.p. 444.9 K) (**Scheme-I**). Anal. calcd for C₁₃H₁₅ClO₄: C, 57.67; H, 5.58 %. Found C, 57.22; H, 5.19 %. IR (KBr, ν_{max}, cm⁻¹): 2976, 2939, 2864, 2757.0, 26714, 25884, 1703, 1599, 1493, 1465, 1418, 1389, 1348, 1264, 1183, 1121, 1089, 1060, 1020, 934, 872, 829, 794, 725, 651, 579, 541, 467.



Scheme-I

¹HNMR (CDCl₃, 400 MHz) δ (ppm): 12.804 (1H, s, COOH); 7.394-7.415 (2H, d, J = 8.4 Hz, Cl-C-CH, Cl-C-CH); 7.308-7.329 (2H, d, J = 8.4 Hz, CH-CH-C, CH-CH-C); 5.444 (1H, s, O-CH-O); 4.650-4.679 (2H, d, J = 11.6 Hz, CO-CH₂-C, Heq); 3.688-3.717 (2H, d, J = 11.6 Hz, CO-CH₂-C, Hax); 1.485-1.542 (2H, q, J = 7.6 Hz, C-CH₂-CH₃); 0.907-0.945 (3H, t, J = 7.6 Hz, CH₃-CH₂).

X-Ray crystal structure determination: A colourless block crystal with dimensions of 0.43 mm \times 0.41 mm \times 0.38 mm was selected for measurement. Diffraction data of compound were collected at 153(2) K on a CrysAlis CCD area detector, with MoK α radiation (λ = 0.71073 Å). A total of 11447 reflections were collected in the range of 2.6 to 25.0° by using an ϕ - ω multiscan mode, of which 4465 were unique with R_{int} = 0.023 and 3673 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 = 0.0336, wR = 0.0815 ($w = 1/[\sigma^2(\text{Fo}^2) + (0.00442P)^2 + 0.54747P]$, where $P = (\text{Fo}^2 + 2\text{Fc}^2)/3$), S = 1.038, $(\Delta/\sigma)_{\text{max}}$ = 0.001, $(\Delta\rho)_{\text{max}}$ = 0.241 and $(\Delta\rho)_{\text{min}}$ = -0.343 e \cdot Å⁻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.

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

Parameter	Compound
Empirical formula	C ₁₃ H ₁₅ ClO ₄
Formula weight	270.70
Crystal size (nm)	0.43 \times 0.41 \times 0.38
Crystal system, Space group	Monoclinic, P2(1)/n
a, b, c (Å)	12.655(3), 8.260(2), 24.380(6)
α , β , γ (°)	β = 92.533(2)
$V/\text{Å}^3$	2545.89(11)
$D_c/\text{Mg cm}^{-3}$	1.412, 8
μ/mm^{-1}	0.304
$F_{(000)}$	1136
Index ranges (H, k, l)	-15 \leq h \leq 12, -9 \leq k \leq 9, -28 \leq l \leq 28
θ range for data collection	2.60–25.00
Reflections collected/unique	11447/4465(0.0231)
Completeness to θ	99.9 %
Goodness-of-fit on F^2	1.038
Final R indices [$I > 2\sigma(I)$]	0.0336, 0.0815
R indices (all data)	0.0448, 0.0882
Max. peak/hole (e \cdot Å ⁻³)	0.241/–0.343

RESULTS AND DISCUSSION

The aldol reaction of 2,2-bis(hydroxymethyl) butyric acid with 4-chlorobenzaldehyde in a 1:1.2 molar ratio was then conducted in DMF and cyclohexane with *p*-toluene sulfonic

TABLE-2
SELECTED BOND LENGTHS (Å) AND BOND ANGLES (°)

Bonds	d	Bonds	d	Bonds	d
Cl(1)–C(1)	1.746(17)	Cl(2)–C(14)	1.747(17)	O(2)–C(7)	1.419(18)
O(1)–C(7)	1.414(19)	O(1)–C(8)	1.434(18)	O(2)–C(9)	1.431(19)
O(3)–C(13)	1.314(18)	O(4)–C(13)	1.222(19)	O(5)–C(20)	1.408(2)
O(6)–C(20)	1.414(18)	O(7)–C(26)	1.317(18)	O(5)–C(21)	1.426(19)
O(6)–C(22)	1.430(19)	O(8)–C(26)	1.219(19)	C(2)–C(3)	1.386(2)
C(1)–C(6)	1.381(2)	C(2)–C(1)	1.382(2)	C(5)–C(6)	1.377(2)
C(4)–C(3)	1.386(2)	C(7)–C(4)	1.501(2)	C(10)–C(9)	1.530(2)
C(4)–C(5)	1.390(2)	C(8)–C(10)	1.530(2)	C(10)–C(11)	1.546(2)
C(11)–C(12)	1.520(3)	C(13)–C(10)	1.517(2)	C(17)–C(16)	1.394(2)
C(14)–C(15)	1.380(2)	C(16)–C(15)	1.383(2)	C(17)–C(18)	1.388(2)
C(18)–C(19)	1.382(2)	C(19)–C(14)	1.383(2)	C(20)–C(17)	1.500(2)
C(23)–C(26)	1.519(2)	C(23)–C(21)	1.535(2)	C(24)–C(25)	1.518(3)
C(23)–C(22)	1.529(2)	C(23)–C(24)	1.539(2)		
Angles	ω	Angles	ω	Angles	ω
C(7)–O(1)–C(8)	110.88(12)	C(8)–C(10)–C(11)	111.11(13)	O(8)–C(26)–O(7)	123.00(14)
C(20)–O(6)–C(22)	109.46(12)	C(18)–C(17)–C(16)	118.77(16)	O(8)–C(26)–C(23)	123.57(14)
C(20)–O(5)–C(21)	109.78(12)	C(18)–C(17)–C(20)	120.91(14)	O(7)–C(26)–C(23)	113.34(14)
C(7)–O(2)–C(9)	110.48(12)	C(16)–C(17)–C(20)	120.15(15)	C(1)–C(2)–C(3)	118.84(15)
O(4)–C(13)–O(3)	123.12(14)	C(26)–C(23)–C(22)	110.65(13)	C(15)–C(16)–C(17)	120.62(16)
O(4)–C(13)–C(10)	123.86(13)	C(26)–C(23)–C(21)	110.36(13)	C(19)–C(18)–C(17)	121.27(15)
O(3)–C(13)–C(10)	112.95(13)	C(22)–C(23)–C(21)	107.71(13)	O(5)–C(21)–C(23)	111.50(13)
O(5)–C(20)–O(6)	111.11(12)	C(26)–C(23)–C(24)	107.84(13)	C(14)–C(19)–C(18)	118.63(16)
O(5)–C(20)–C(17)	109.57(13)	C(22)–C(23)–C(24)	110.23(14)	O(2)–C(9)–C(10)	111.28(13)
O(6)–C(20)–C(17)	110.00(13)	C(21)–C(23)–C(24)	110.07(13)	C(3)–C(4)–C(5)	119.16(15)
O(1)–C(8)–C(10)	111.47(12)	O(1)–C(7)–O(2)	110.28(11)	C(3)–C(4)–C(7)	120.13(14)
C(13)–C(10)–C(9)	111.14(13)	O(1)–C(7)–C(4)	109.53(13)	C(5)–C(4)–C(7)	120.66(14)
C(13)–C(10)–C(8)	110.42(13)	O(2)–C(7)–C(4)	108.09(12)	O(6)–C(22)–C(23)	110.97(13)
C(9)–C(10)–C(8)	107.32(12)	C(6)–C(1)–Cl(1)	119.00(13)	C(6)–C(5)–C(4)	120.71(15)
C(13)–C(10)–C(11)	107.87(12)	C(2)–C(1)–Cl(1)	119.66(13)	C(15)–C(14)–C(19)	121.54(16)
C(9)–C(10)–C(11)	109.00(13)	C(12)–C(11)–C(10)	115.11(15)	C(6)–C(1)–C(2)	121.33(16)
C(15)–C(14)–Cl(2)	119.55(13)	C(14)–C(15)–C(16)	119.11(15)	C(4)–C(3)–C(2)	120.72(15)
C(19)–C(14)–Cl(2)	118.90(14)	C(25)–C(24)–C(23)	114.85(15)		

acid as catalyst. Upon recrystallization colourless crystals were isolated to be the title compound, as shown in **Scheme-I**.

The compound gave satisfactory elemental analyses and the IR spectra exhibit the strong absorption in the range 1030-1183 cm^{-1} , which are consistent with O-C-O acetal bond character. The compound was also characterized by NMR spectroscopy, the ^1H NMR spectra show two sets of split signals corresponding to the $-\text{CH}_2-$ protons of 1,3-dioxane ring. These results indicated that the equatorial bond protons He_q and straight bond protons Hax of $-\text{CH}_2-$ in 1,3-dioxane ring produce coupling.

The molecular structure of complex was further confirmed by X-ray crystallography (Fig. 1). Selected bond distances and angles are given in Table-2. There are two crystallographically independent molecules of the title compound in an asymmetric unit labeled as molecule I (Fig. 1a) and molecule II (Fig. 1b) containing 1,3-dioxane rings (O1-O2/C7-C10) and (O5-O6/C20-C23), respectively and the 4-chlorophenyl substituent occupies an equatorial site. The 1,3-dioxane rings in both molecules adopt chair conformation with torsion angles deviations for C7-O2-C9-C10 and C20-O6-C22-C23 being 0.01(16) and for C7-O1-C8-C10 and C20-O5-C21-C23 being 0.25(16). There are some differences between the two molecules in the torsion angles deviations for C3-C4-C7-O2 and C18-C17-C20-O6 being 154.20(15). In the crystal, adjacent molecules are connected by O-H...O (O3-H...O8 2.639(15) Å and O7-H...O4 2.657(15) Å) hydrogen bonding interactions between the oxygen atoms into a dimer (Fig. 2 and Table-3). The crystal structures of some similar 1,3-dioxanes have been reported¹¹⁻¹³.

TABLE-3
HYDROGEN BOND PARAMETERS (Å, °)
FOR THE TITLE COMPOUND

D-H...A	d(D-H)	d(H...A)	d(D...A)	$\angle(\text{DHA})$
O(7)-H(7)...O(4)	0.84	1.82	2.657(15)	176.6
O(3)-H(3)...O(8)	0.84	1.80	2.639(15)	174.9

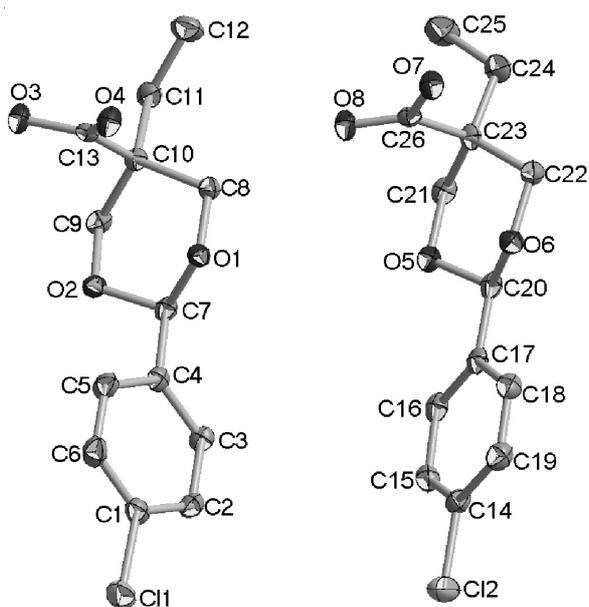


Fig. 1. Molecular structure of the title compound with the atom numbering scheme. Displacement ellipsoids are drawn at the 50% probability level for non-H atoms ((a) for molecule I, (b) for molecule II)

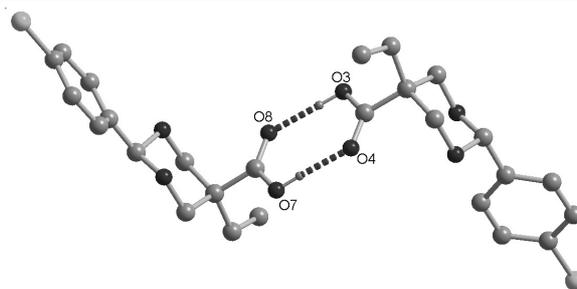


Fig. 2. Two monomers are connected by hydrogen bonding interactions into a dimer. H atoms non-participating in hydrogen-bonding were omitted for clarity

Conclusion

In conclusion, 2-(4-chlorophenyl)-5-ethyl-1,3-dioxane-5-carboxylic acid was synthesized by using 2,2-bis(hydroxy-methyl)butyric acid with 4-chlorobenzaldehyde as raw material, *p*-toluene sulfonic acid as catalyst, DMF and cyclohexanone as solvent. In the title compound, the 1,3-dioxane ring adopts a chair conformation and the 4-chlorophenyl substituent occupies an equatorial site and adjacent molecules are connected by O-H...O hydrogen bonding interactions into a dimer.

Supplementary data

Crystallographic data for the structural analysis have been deposited with the Cambridge Crystallographic Data Centre: CCDC 961200. Copies of the data can be obtained free of charge via <http://www.ccdc.cam.ac.uk>

ACKNOWLEDGEMENTS

This work was financially supported by the Construct Program of the Key Discipline in Hunan Province (2011-76), the Science and Technology Planning Project of Hunan Province (2013FJ3004), the Scientific Research Fund of Hunan Provincial Education Department (13A030, 13B029, 13C350), the Key Laboratory of Functional Organometallic Materials of Hunan Province College (13K09, 13K10), the Science and Technology Innovative Research Team in Higher Educational Institutions of Hunan Province (2012-318).

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