Research Article

Synthesis and Crystal Structure of 2-(Dichloromethyl)-2-(4-nitrophenyl)-1,3-dioxane

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A new compound, 2-dichloromethyl-2-*p*-nitrophenyl-1,3-dioxane, was synthesized and characterized. The crystal structure of the title compound ($C_{11}H_{11}Cl_2NO_4$, $M_r = 292.11$) has been determined by single-crystal X-ray diffraction. The crystal is of monoclinic, space group $P2_1/c$ with $a = 11.013(2)$ Å, $b = 14.653(3)$ Å, $c = 7.8693(16)$ Å, $\alpha = 90^\circ$, $\beta = 97.06(3)^\circ$, $\gamma = 90^\circ$, $V = 1260.3(4)$ Å³, $Z = 4$, $F(000) = 600$, $D_c = 1.540$ mg/cm³, the final $R_1 = 0.0508$, and $\omega R_2 = 0.1072$ for observed reflections with $I > 2\sigma(I)$. A total of 12162 reflections were collected, of which 2867 were unique ($R_{int} = 0.06999$).

1. Introduction

The 2-dichloromethyl-1,3-dioxacycloalkane compounds have received considerable attention due to safening activities against herbicidal injuries to crop plants [1]. 2-Dichloromethyl-1,3-dioxacycloalkane derivatives, such as MG-191 [2], have been investigated as herbicide safeners which protected crops from the injury by herbicides [3, 4]. Various substituents of the dioxacycloalkane have showed different activities, which encouraged us to synthesize novel 2-dichloromethyl-1,3-dioxane derivatives with enhanced biological activity.

Several synthetic procedures to obtain 1,3-dioxacycloalkanes have been reported [5–8], but most of these methods employ harsh reaction conditions, expensive catalysts, or poor yields. Microwave-assisted syntheses providing fast, clean, and high-yield transformations have been found several times more convenient and efficient methods to obtain organic compounds. In the view of these facts mentioned above, our objective was to find herbicide safeners with better bioactivity [9] and therefore the title compound was designed to prepare 1,3-dioxane derivative containing 4-nitrophenyl substituent at position 2. Synthesis of 2-dichloromethyl-(4-nitrophenyl)-1,3-dioxane (**4**) was planned by microwave-irradiated acetalization followed by insertion of dichlorocarbene using benzyl triethyl ammonium chloride (TEBA)

as phase transfer catalyst. In addition to the synthesis, molecular characterization of this novel compound by X-ray crystallography has been outlined.

2. Materials and Methods

2.1. Instruments. All chemicals and solvents were of reagent grade and were used as purchased without further purification. The melting point was determined on a Beijing Taike melting point apparatus (X-4) and was uncorrected. The ¹H NMR and ¹³C NMR spectra were run on a Bruker AVANCE 400 MHz spectrometer with CDCl₃ as the solvent and TMS as the internal standard. The mass spectrum was recorded on a Waters Xevo TQ mass spectrometer. The infrared (IR) spectra were recorded in KBr disks on a Bruker ALPHA-T. The X-ray data were collected on a Rigaku RAXIS-RAPID rapid X-ray diffraction measurement using graphite monochromated Mo K α radiation ($\lambda = 0.71073$ Å) at 293(2) K.

2.2. Synthesis. The title compound was synthesized according to the route shown in Scheme 1, and the yields were not optimized.

A mixture of *p*-nitrobenzaldehyde (**1**, 0.1 mol), 1,3-propanediol (**2**, 0.15 mol), CuSO₄ (1.5 g), and cyclohexane (50 mL) was exposed to microwave radiation for 15 min under reflux

SCHEME 1: Synthesis of the title compound 4.

TABLE 1: Crystal and structure refinement for title compound.

Item	Value
CCDC	928570
Empirical formula <i>t</i>	C ₁₁ H ₁₁ Cl ₂ NO ₄
Formula weigh	292.11
Temperature	293(2) K
Radiation λ	0.71073 Å
Crystal system, space group	Monoclinic, <i>P</i> 2 ₁ / <i>c</i>
Unit cell dimensions	$a = 11.013(2)$ Å, $\alpha = 90^\circ$ $b = 14.653(3)$ Å, $\beta = 97.06(3)^\circ$ $c = 7.8693(16)$ Å, $\gamma = 90^\circ$
Volume	1260.3(4) Å ³
<i>Z</i>	4
Calculated density	1.540 mg/m ³
Absorption coefficient	0.520 mm ⁻¹
<i>F</i> (000)	600
Item	Value
Crystal size	0.27 × 0.10 × 0.07 mm
Theta range for data collection	3.32 to 27.47 deg.
Range/indices (<i>h</i> , <i>k</i> , <i>l</i>)	−14, 14; −19, 19; −10, 9
Reflections collected/unique	12162 / 2867 (<i>R</i> _{int} = 0.0699)
Completeness to theta = 27.47	99.1%
Absorption correction <i>T</i> _{min} and <i>T</i> _{max}	0.9645 and 0.8736
Data/restraints/parameters	2867/0/163
Goodness-of-fit on <i>F</i> ²	1.032
<i>R</i> ₁ , <i>wR</i> ₂ [<i>I</i> > 2σ(<i>I</i>)]	0.0508, 0.1072
<i>R</i> ₁ , <i>wR</i> ₂ (all data)	0.1016, 0.1352
Largest diff. peak and hole (eÅ ⁻³)	0.268 and −0.232

removing the water formed. The reaction mixture was washed with water until the organic phase was colorless. The organic layer was extracted with ethyl acetate and dried over anhydrous MgSO₄. The crude product was purified by silica gel chromatography eluting with ethyl acetate-petroleum ether mixture (10:1). The yield of (3) was 50.9%; m.p. 112–113°C. IR (KBr): 3105–2856 (C–H), 1600–1519 (Ar, C=C), 1289–1036

(dioxane, C–O); ¹H NMR (CDCl₃, 400 MHz) δ : 7.28–8.25 (m, 4H, Ar–H), 5.59 (s, 1H, dioxane, C–H), 4.30–4.34, 4.00–4.07 (m, 4H, dioxane, 2×O–CH₂), 2.20–2.32, 1.56–1.61 (m, 2H, dioxane, CH₂); ¹³C NMR (CDCl₃, 100 MHz) δ : 148.12, 145.20, 127.18, 127.18, 123.44, 123.44, 99.90, 67.48, 67.48, 25.64. *Anal.* Calcd for C₁₀H₁₁NO₄: C 57.40, H 5.30, N 6.70. Found: C 57.46, H 5.38, N 6.65.

To a vigorously stirred solution of acetal (3, 0.025 mol) in CHCl₃ (40 mL), anhydrous Na₂SO₄ (30 g), and TEBA (0.3 g), 50% aq. NaOH (0.25 mol) was added at 0°C. The solution was stirred continuously for 48 h. Then water (100 mL) and diethyl ether (100 mL) were added into the mixture. After layers were separated, the aqueous layer was extracted with ether (50 mL) for three times. The organic layers were combined and washed with water until pH 7 and dried over anhydrous MgSO₄. The ether was removed by distillation and the residue was subjected to silica gel chromatography eluting with ethyl acetate-petroleum ether mixture (20:1). The yield of (4) was 51.4%; m.p. 164–165°C. IR (KBr): 3052 (Ar, C–H), 2999–2946 (dioxane, C–H), 2891 (–CHCl₂), 1600–1519 (Ar, C=C), 1289–1208 (dioxane, C–O); ¹H NMR (CDCl₃, 400 MHz) δ : 7.28–8.33 (m, 4H, Ar–H), 5.69 (s, 1H, –CHCl₂), 3.73–3.79, 4.09–4.13 (m, 4H, dioxane, 2×O–CH₂), 2.18–2.28, 1.36–1.40 (m, 2H, dioxane, CH₂); ¹³C NMR (CDCl₃, 100 MHz) δ : 148.66, 140.38, 131.00, 131.00, 123.37, 123.37, 100.17, 75.40, 62.34, 62.34, 24.62. *Anal.* Calcd for C₁₁H₁₁Cl₂NO₄: C 45.36, H 3.81, N 4.81. Found: C 45.42, H 3.88, N 4.76. Mass Spectrum: [M–1] = 290.

2.3. Crystal Structure Determination. The cube-shaped single crystal of the title compound was grown by slow cooling from a hot saturated solution in ethanol. The crystal with dimensions of 0.27 × 0.10 × 0.07 mm was mounted on a Bruker AXSII CCD area-detector diffractometer with a graphite-monochromated Mo K α radiation ($\lambda = 0.71073$ Å) at 293(2) K in the range of $3.32 < \theta < 27.47^\circ$. A total of 12162 reflections were collected, of which 2867 were independent (*R*_{int} = 0.0699) and 1676 were observed with *I* > 2σ(*I*). The structure was solved by direct methods using SHELXS-97 program and the multi-scan absorption corrections were applied to all intensity data. All nonhydrogen atoms were refined isotropically by the full-matrix least square method on *F*² using SHELXL-97 [10]. The hydrogen atoms were determined with theoretical calculations and refined isotropically. The final full-matrix least squares refinement gave *R* = 0.0508 eÅ⁻¹

FIGURE 1: Molecular diagram of compound 4 showing 30% probability ellipsoids.

and $\omega R = 0.1072$, $w = 1/[\sigma^2(F_o^2) + (0.0537P)^2 + 0.4327P]$ where $P = (F_o^2 + 2F_c^2)/3$, $S = 1.032$, $(\Delta/\sigma_{\max} = 0.000)$ $\Delta\rho_{\max} = 0.268 \text{ e}\text{\AA}^{-1}$, and $\Delta\rho_{\min} = -0.232 \text{ e}\text{\AA}^{-1}$. Crystallographic data (excluding structure factors) for the structure in this paper has been deposited with the Cambridge Crystallographic Date Center as supplementary publication number CCDC 928570. Table 1 summarized the crystal data, intensity data collection, and refinement detail for the title compound. The molecular structure and the packing view of the compound were shown in Figures 1 and 2, respectively.

3. Results and Discussion

3.1. Synthesis and Structure Identification. The synthesis of the compound 4 was carried out in two separate steps. In the first step, a microwave-assisted acetal formation resulted in the 2-(4-nitrophenyl)-1,3-dioxane (3) from which insertion of the dichlorocarbene moiety provided the target molecule 4 (Scheme 1) in a poor overall yield (25%). The measured data of elemental analytical results is in accord with the theoretical values.

3.2. Crystal Structure. The selected bond lengths and bond angles are shown in Table 2. The atomic coordinates of the nonhydrogen atoms with their equivalent temperature factors were presented in Table 3.

According to X-ray analysis, the structure, the title compound, $\text{C}_{11}\text{H}_{11}\text{Cl}_2\text{NO}_4$, contained a 1,3-dioxane and a benzene ring. The phenyl ring is almost vertical with the 1,3-dioxane ring, with the dihedral angles of 100.4° . The torsion angle of $\text{C}(7)\text{--O}(1)\text{--C}(8)\text{--C}(9)$ was $56.6(3)^\circ$. The torsion angle of $\text{C}(7)\text{--O}(2)\text{--C}(10)\text{--C}(9)$ was -54.0° , which made the 1,3-dioxane similar to chair conformation.

Generally, the average bond lengths and bond angles of ring system (phenyl and 1,3-dioxane) are normal. The bond lengths of C–N and C–O were close to the typical bond length. In the plane benzene ring, the C–C bond lengths range from $1.369(4)$ Å to $1.396(4)$ Å, almost equal to the values

TABLE 2: Selected bond lengths (Å) and angles ($^\circ$) for the title compound.

Bond Length (Å)		Bond Angle ($^\circ$)	
C(1)–C(6)	1.379(4)	C(6)–C(1)–C(2)	120.20(3)
C(1)–C(2)	1.382(4)	C(6)–C(1)–C(7)	119.80(2)
C(1)–C(7)	1.543(4)	C(2)–C(1)–C(7)	119.90(3)
C(2)–C(3)	1.391(4)	C(1)–C(2)–C(3)	120.50(3)
C(3)–C(4)	1.369(4)	C(4)–C(3)–C(2)	117.90(3)
C(4)–C(5)	1.372(4)	C(3)–C(4)–C(5)	123.30(3)
C(4)–N(1)	1.489(4)	C(3)–C(4)–N(1)	118.20(3)
C(5)–C(6)	1.396(4)	C(5)–C(4)–N(1)	118.50(3)
C(7)–O(1)	1.409(3)	C(4)–C(5)–C(6)	118.00(3)
C(7)–O(2)	1.411(3)	C(1)–C(6)–C(5)	120.10(3)
C(7)–C(11)	1.541(4)	O(1)–C(7)–O(2)	111.50(2)
C(8)–O(1)	1.454(3)	O(1)–C(7)–C(11)	103.60(2)
C(8)–C(9)	1.511(5)	O(2)–C(7)–C(11)	103.10(2)
C(9)–C(10)	1.498(5)	O(1)–C(7)–C(1)	111.90(2)
C(10)–O(2)	1.450(4)	O(2)–C(7)–C(1)	112.20(2)
C(11)–Cl(2)	1.764(3)	C(11)–C(7)–C(1)	113.90(2)
C(11)–Cl(1)	1.772(3)	O(1)–C(8)–C(9)	109.60(3)
N(1)–O(3)	1.204(4)	C(10)–C(9)–C(8)	109.50(3)
N(1)–O(4)	1.207(4)	O(2)–C(10)–C(9)	111.10(3)
		C(7)–C(11)–Cl(2)	112.10(2)
		C(7)–C(11)–Cl(1)	111.30(2)
		Cl(2)–C(11)–Cl(1)	109.30(16)
		O(3)–N(1)–O(4)	123.80(3)
		O(4)–N(1)–C(4)	117.90(3)
		C(7)–O(1)–C(8)	113.40(2)
		C(7)–O(2)–C(10)	113.70(2)

of typical bonds of aromatic structure. And the bond angles of the benzene ring change from $117.9(3)^\circ$ to $123.3(3)^\circ$, also with the average of 120° . The bond angles of 1,3-dioxane are between $109.50(3)$ and $113.70(2)$, close to 109.5 , which also confirm the chair conformation of 1,3-dioxane.

FIGURE 2: The packing view of compound 4.

TABLE 3: Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameter ($\times 10^3$) nonhydrogen atoms.

	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{eq}
C(1)	7449(3)	5587(2)	2026(3)	39(1)
C(2)	7093(3)	5514(2)	286(4)	43(1)
C(3)	7860(3)	5811(2)	−879(4)	45(1)
C(4)	8963(3)	6185(2)	−242(4)	46(1)
C(5)	9336(3)	6287(3)	1476(4)	56(1)
C(6)	8561(3)	5974(3)	2626(4)	53(1)
C(7)	6584(3)	5263(2)	3305(3)	41(1)
C(8)	6429(3)	3703(2)	2402(4)	52(1)
C(9)	7107(3)	3407(3)	4099(5)	62(1)
C(10)	7912(3)	4169(3)	4840(5)	65(1)
C(11)	5699(3)	6005(2)	3794(4)	44(1)
Cl(1)	4673(1)	6351(1)	1997(1)	56(1)
Cl(2)	6481(1)	6970(1)	4717(1)	69(1)
N(1)	9794(3)	6497(2)	−1481(4)	62(1)
O(1)	5800(2)	4560(1)	2618(2)	43(1)
O(2)	7226(2)	5011(2)	4898(2)	50(1)
O(3)	9484(3)	6373(3)	−2984(3)	93(1)
O(4)	10734(3)	6871(3)	−917(4)	98(1)

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