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Novel autoxidation and Michael addition of a butenolide-containing sugar leading to a C-branched-chain glucopyranosidulose, and X-ray structure of intermediates

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Abstract

A butenolide-containing sugar available from the aldol condensation of methyl 4,6-*O*-benzylidene-α-D-glucopyranosid-2-ulose with diethyl malonate is autoxidized at the C-3 position into the corresponding α,β-unsaturated γ-lactone sugar by air, which subsequently undergoes 1,4-conjugate (Michael) addition of hydroxide ion (or water) leading to a C-branched-chain glucopyranosidulose. The autoxidations are also performed in weakly basic, neutral and weakly acidic medium, respectively.

Keywords: Butenolide-containing sugar; 2-Oxoglucopyranoside; Autoxidation

1. Introduction

Since C-branched-chain glycopyranosiduloses are very efficient chiral building blocks for the synthesis of biologically active substances containing carbocyclic ring systems,[1–3] synthesis of such types of structural units has gained importance in recent years. Although the stereoselective addition of a nucleophile to a glycosidulose is an efficient method for synthesis of C-branched-chain sugars, previous studies on their syntheses were focused on the use of fully protected sugars,[4,5] because partially protected and unprotected glycosiduloses are very difficult to synthesize selectively, and are unstable.[6–9] A C-branched-chain sugar has never been synthesized from a partially protected or unprotected '2-oxoglycoside,' except for that which we reported on the synthesis of indole derivatives,[10] as well as a one-step synthesis of a 2-C-branched-chain glycopyranosid-3-ulose (**2**) (Scheme 1), by the reaction of '2-oxoglucopyranoside' (**1**) with diethyl malonate.[11] We were intrigued by the reaction mechanism, as well as by the structural features of **2**, which contains an active methylene at the 2-C-branched-chain and a carbonyl group at the C-3 position. These types of functionalities could be very useful for the construction of five- and six-membered carbocyclic ring carbohydrates by an intermolecular Claisen condensation and a Robinson annulation.

As a continuation of our studies, in this paper we report on the mechanism of this transformation by presenting evidence of autoxidation, followed by Michael addition, and report on the synthesis of two butenolide-containing intermediates. Butenolide-containing compounds are of interest as they are considered to be potential anticancer agents, cycooxygenase inhibitors, and phospholipase A_2 inhibitors, etc.[12–16]

2. Results and discussion

The reaction of compound **1**[8] with diethyl malonate in the presence of sodium methoxide for 3.5–4 h affords the 2-C-branched-chain sugar **2**. Reaction monitoring at different time intervals enabled the trapping of the reaction intermediates and gave evidence for the mechanism. Compound **1** in chloroform was added dropwise to a stirred solution of diethyl malonate and sodium methoxide in methanol, and stirring was continued for 30 min at 0 °C. The reaction was neutralized

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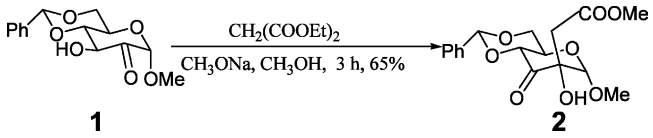


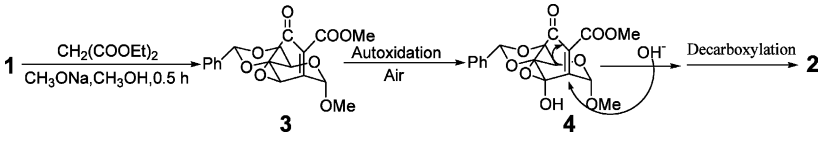
Scheme 1. Stereoselective synthesis of 2-C-branched-chain glycopyranosid-3-ulose **2** from **1.**

with acetic acid, and the butenolide-containing sugar **3** (Scheme 2) was isolated in 68% yield in another experiment. Alternatively, the mixture was stirred for 30 min, and then heated at 25–28 °C for 1 h while simultaneously bubbling air into the mixture. This mixture was then quenched with acetic acid to give a mixture of **3** and the corresponding oxidation intermediate product **4**, which was recrystallized from methanol to give mixed crystals in a ratio of about 2:3. Its ^{1}H NMR spectrum and X-ray structure are shown in Figs. 1 and 2, respectively. The mixed crystal was chromatographed on silica gel, affording **3** and **4**, respectively. Compound **4** was recrystallized from ethanol and acetone also to give a single crystal. Fig. 3 shows an ORTEP of its structure. However, when the silica gel was eluted with chloroform, **2** was obtained besides compound **3** and a small amount of **4**, indicating that **4** can be transformed into **2** in weakly acidic medium. When the reaction was continued for about 2.5 h, and a small amount of water was added, **2** was eventually obtained as the sole product.

Obviously, the reactants undergo an aldol condensation, with subsequent autoxidation, followed by 1,4-conjugate (Michael) addition as the three main steps in one pot, as described in Scheme 2. The reaction sequence starts with a base-catalyzed aldol condensation between '2-oxoglucopyranoside' **1** and diethyl malonate to form the five-membered ring butenolide-containing intermediate **3**, in which case, ester exchange and intramolecular cyclization are involved. This is followed by autoxidation of **3** at the C-3 position to give **4**. Both **3** and **4** bear α,β-unsaturated γ-lactone structures, which are considered as potentially biologically active compounds.[12–15] 1,4-Conjugate (Michael) addition of hydroxide ion to the α,β-unsaturated γ-lactone sugar (**4**), followed by decarboxylation, eventually generates **2**. In this procedure, **3** can be easily autoxidized into **4**, perhaps due to the fact that its five-membered lactone is very planar, with an r.m.s deviation of 0.0091 Å among the five atoms.[16] A possible mechanism for the autoxidation of **3** is as shown in Scheme 3. The radical intermediate **5**, generated from **3** by hydrogen abstraction, permits extensive delocalization of the unpaired electron into a five-membered ring conjugate system. It remains reactive toward oxygen to produce peroxy radical **6**, which then abstracts hydrogen from **3** or other substances to generate the hydroperoxy butenolide derivative **7**. This hydroperoxide is then reduced, resulting in the formation of **4**.

Further experiments were performed to investigate the autoxidation of **3** followed by Michael addition. Compound **3** or a mixture of **3** and **4** as starting material was treated under the same conditions as described above, resulting in the formation of **2** in both cases. In addition, we found that **3** can be autoxidized in weakly basic, neutral, and weakly acidic medium, even without added air. Table 1 depicts the results. In the presence of water, 2-C-branched-chain sugar **2** were obtained (entries 1–3). This is because **4**, which is formed in basic solution, was then subjected to Michael addition by hydroxide ion or water. Under anhydrous conditions, the terminal products were **4** (entries 4–6). Except for the hydroxide ion, oxygen nucleophiles such as alkoxide ions and carboxylate anions cannot effectively attack on **4** to generate the corresponding C-branched-chain sugars.

The intermediates **3**[16] and **4** and the mixed crystal of **3** and **4** were all characterized by spectroscopic data and X-ray crystallographic analysis. The high-resolution mass spectrum of compound **3** displayed an [M+1] peak at *m/z* 363.1065, indicating the formula to be $C_{18}H_{18}O_8$. ^{13}C NMR signals at δ 165.7 and 160.2, and absorptions at 1808 and 1735 cm^{-1} in the IR spectrum were assigned to carbonyl groups of the lactone and COOMe groups, respectively. In the ^{1}H NMR spectrum, the proton that appeared as a singlet at δ 6.15 was assigned to H-1. The proton at δ 5.25 (d, $J = 10.0$ Hz) was coupled with that at δ 4.08 (t, $J = 10.0$ Hz). They were ascribed to H-3 and H-4. The ^{13}C NMR peak at δ 94.6 was assigned to C-1. The two signals at δ 77.5 and 61.7 were ascribed to C-3 and C-4, respectively. The newly formed C=C exhibited two peaks at δ 166.6 (C-2) and δ 118.3. All the assignments were made on the basis of 2D NMR spectra. The X-ray analysis of **4** showed that crystalline structure has molecular stacking along a one-dimensional chain. Fig. 4 depicts the interaction among the molecules. In each parallel stacking, they are assembled in polymers through intermolecular hydrogen bonds between O-5 of one molecule and 3-OH of the



Scheme 2. A possible pathway for the formation of **2.**

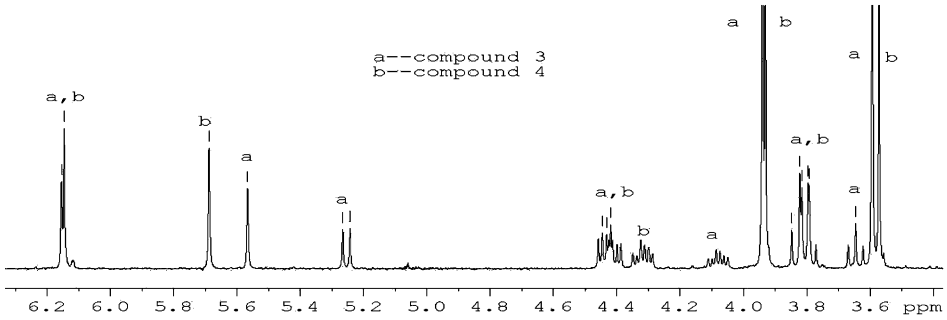


Fig. 1. ^{1}H NMR spectrum of the mixed crystal for **3** and **4** isolated in a ratio of $\sim$2:3.

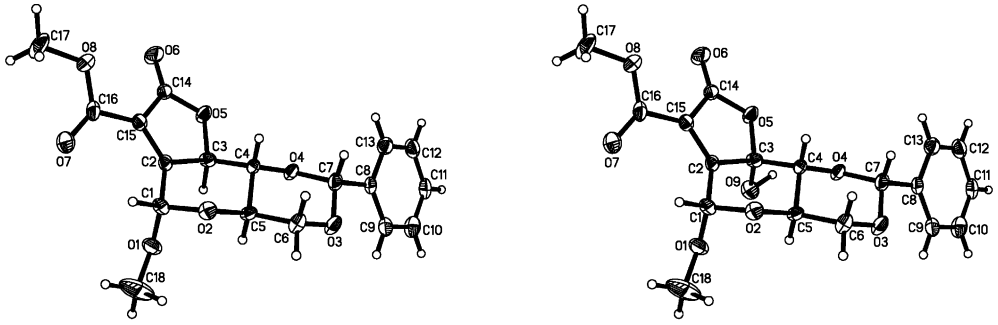


Fig. 2. X-ray crystal structure of the mixed crystal for **3** and **4** isolated in a ratio of about 2:3.

next one. The distance of 3-OH···O-5 is 2.858 Å and the angle of 3-OH···O-5 is 138.43°.

3. Experimental

3.1. General methods

TLC was performed on precoated plates of silica gel 60 F_{254}. Components were detected by UV light. Melting points were determined on a WC-1 melting-point apparatus and are uncorrected. Infrared spectra were recorded on a Shimadzu IR-435 instrument using KBr disks in the 400–4000 cm^{-1} region. NMR spectra were taken in $CDCl_3$ with Me_4Si as the internal standard on a Bruker DPX-400 spectrometer, and the chemical shifts are given in δ values. Liquid secondary-ion mass spectrometry spectra were taken with a ZAB-2SE double-focusing mass spectrometer (VG Analytical, Manchester, UK). Methyl 4,6-*O*-benzylidene-α-D-glucopyranosid-2-ulose was prepared as we reported previously.[8] Dry $CHCl_3$ was prepared by refluxing it with CaH_2. All organic solutions from workups were dried over anhyd sodium sulfate.

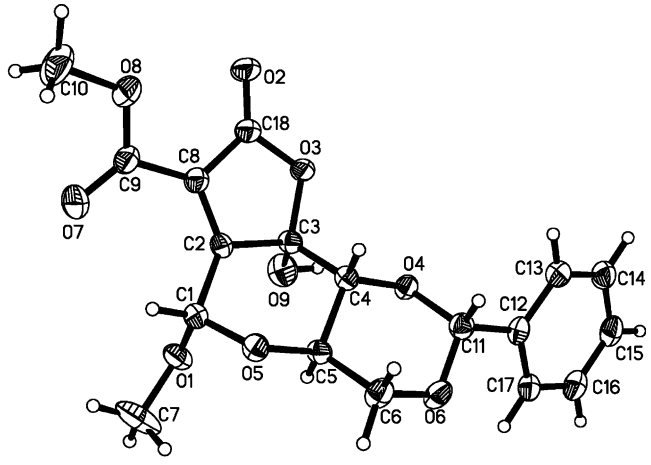
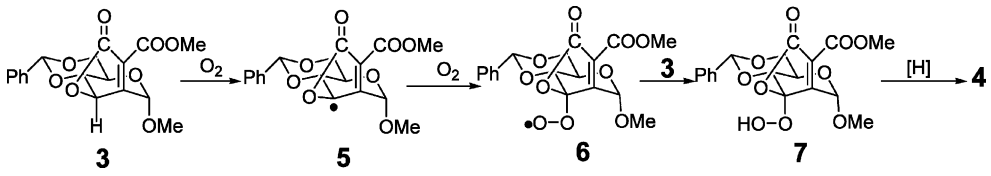


Fig. 3. X-ray crystal structure of intermediate **4**.

3.2. Methyl (2*R*,4a*R*,6*S*,9a*R*,9b*S*)-4,4a,6,8,9a,9b-hexahydro-6-methoxy-8-oxo-2-phenylfuro[2′,3′:4,5]pyrano[3,2-*d*]-1,3-dioxin-7-carboxylate (3)

Diethyl malonate (1.2 mL, 7.4 mmol) was added dropwise to a solution of Na (0.60 g, 26.1 mmol) in anhyd MeOH (20 mL) at 0 °C with stirring. After 10 min, a solution of methyl 4,6-*O*-benzylidene-α-D-glucopyranosid-2-ulose (**1**, 0.40 g, 1.43 mmol) in 20 mL of dry $CHCl_3$ was added. The mixture was stirred for another 30 min, made neutral with 50% HOAc, and evaporated. The residue was dissolved in water, extracted with EtOAc, then dried. The solvent was evaporated, and the residue was crystallized from MeOH to afford the title compound **3** (0.35 g, 68%), which was recrystallized



Scheme 3. A possible mechanism for the autoxidation of **3**.

from MeOH–acetone as colourless crystals: mp 170–172 °C; IR (KBr): 1808 (lactone C=O), 1735 (C=O), 965, 748, and 699 cm^{-1} (Ph); ^1H NMR (400 MHz, $CDCl_3$): δ 3.57 (s, 3 H, OMe), 3.62–3.69 (m, 1 H, H-5), 3.79 (t, 1 H, J 10.0 Hz, H-6a), 3.93 (s, 3 H, $COOCH_3$), 4.08 (t, 1 H, J 10.0 Hz, H-4), 4.41 (dd, 1 H, J 4.8, 10.0 Hz, H-6b), 5.25 (d, 1 H, J 10.0 Hz, H-3), 5.56 (s, 1 H, Ar–CH), 6.15 (s, 1 H, H-1), 7.37–7.41 (m, 3 H, Ar–H), 7.49–7.51 (m, 2 H, Ar–H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 52.8 (COOMe), 55.9 (OMe), 61.7 (C-4), 68.4 (C-6), 77.5 (C-3), 84.3 (C-5), 94.6 (C-1), 101.6 (Ar–C), 118.3 (=C<), 126.1, 128.3, 129.3, 136.3 (Ar), 160.2 (COOMe), 165.7 (lactone CO), 166.6 (C-2); HRLSIMS: Calcd for $C_{18}H_{19}O_8$, m/z 363.1080 (M+1), $C_{18}H_{17}O_8$ m/z 361.0923 (M−1). Found, 363.1062 (M+1), 361.0951 (M−1); Anal. Calcd for $C_{18}H_{18}O_8$ (362.33): C, 59.67; H, 5.01. Found: C, 59.76; H, 5.10.

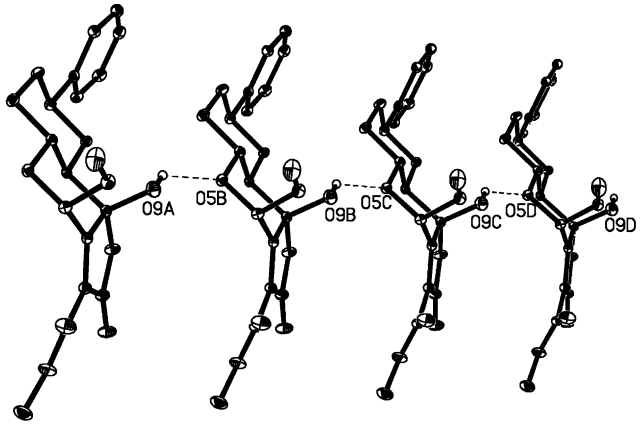


Fig. 4. Perspective ORTEP view of molecules of intermediate **4**, exhibiting the intermolecular hydrogen bonds. Hydrogen omitted.

3.3. Methyl (2*R*,4a*R*,6*S*,9a*R*,9b*S*)-4,4a,6,8,9a,9b-hexahydro-9a-hydroxy-6-methoxy-8-oxo-2-phenylfuro[2′,3′:4,5]pyrano[3,2-*d*]-1,3-dioxin-7-carboxylate (4)

3.3.1. Method 1. As for the procedure described above, after the mixture was stirred for another 30 min, instead of neutralization, it was heated at 25–28 °C while simultaneously bubbling air into the mixture. One hour later, the mixture was treated as described above to afford white powder, which was recrystallized from MeOH to give colourless crystals suitable for X-ray crystallograhpic analysis. The ^1H NMR spectrum of the colourless crystals were taken in $CDCl_3$, which is shown in Fig. 1. The mixed crystals were chromatographed on silica gel with petroleum ether–acetone as eluent to afford the title compound **4** (0.23 g, 42%) (4:1). Compound **4** was recrystallized from ethanol–acetone to afford colourless crystals, also suitable for X-ray crystallograhpic analysis: mp 208–210 °C; IR (KBr): 3446 (OH), 1791 (lactone C=O), 1728 (ester C=O), 753, and 707 cm^{-1} (Ph); ^1H NMR (400 MHz, $CDCl_3$): δ 3.59 (s, 3 H, OMe), 3.78–3.85 (m, 2 H, H-4, H-6), 3.94 (s, 3 H, COOMe), 4.32 (dt, 1 H, J = 4.8, 10.0 Hz, H-5), 4.44 (dd, 1 H, J 4.8, 10.0 Hz, H-6a), 5.69 (s, 1 H, Ar–CH), 6.16 (s, 1 H, H-1), 7.38-7.40 (m, 3 H, Ar–H), 7.49–7.51 (m, 2 H, Ar–H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 53.0 (COOMe), 56.6 (OMe), 61.5 (C-4), 68.5 (C-6), 82.9 (C-5), 95.2 (C-1), 99.4 (C-3), 101.7 (Ar–C), 121.6 (=C<), 126.2, 128.4, 129.4, 136.0 (Ar), 160.0 (COOMe), 160.8 (lactone C=O), 164.0 (C-2); HRLSIMS: Calcd for

Table 1
Autoxidation of **3** into **4** under various conditions

Entry	Reagents	Time (h)	Temperature (°C)	Product (yield) (%)
1	Butenolide-containing intermediate **3**, $NaOCH_3$, MeOH, moist air	3	25–28	2 (47)
2	**3** and **4**, $NaOCH_3$, MeOH, moist air	3	25–28	2 (50)
3	**3**, $NaHCO_3$, H_2O, THF	21	rt	2 (55)
4	**3**, $H_2NNHCSNH_2$, NH_4Cl, $CHCl_3$, MeOH, 4 Å sieves	1	50	4 (55)
5	**3**, *p*-Anisidine, NH_4Cl, $CHCl_3$, 4 Å sieves	1.5	55–60	4 (54)
6	**3**, NBS, DMF, 4 Å sieves	70	rt	4 (64)

$C_{18}H_{19}O_9$, *m/z* 379.1029 (M+1), $C_{18}H_{17}O_9$ *m/z* 377.0873 (M−1). Found, 379.1052 (M+1), 377.0877 (M−1); Anal. Calcd for $C_{18}H_{18}O_8$ (378.33): C, 57.14; H, 4.80. Found: C, 57.01; H, 4.75.

3.3.2. Method 2. A mixture of **3** (0.30 g, 0.83 mmol), NH_4Cl (0.030 g, 0.56 mmol), 4 Å molecular sieves (5 g), and dry $CHCl_3$ (20 mL) was heated at 50 °C with stirring, to which $H_2NNHCSNH_2$ (0.075 g, 0.82 mmol) in anhyd MeOH (12 mL) was added. After 1 h, the molecular sieves were removed. The mixture was evaporated, dissolved in EtOAc, then washed twice with water, dried and evaporated. Some ethanol was added, and the residue was crystallized to afford the title compound **4** (0.17 g, 55%), identical in all respects with the sample obtained as described above.

3.3.3. Method 3. A mixture of **3** (0.21 g, 0.58 mmol), *p*-anisidine (0.071 g, 0.58 mmol), NH_4Cl (0.020 g, 0.37 mmol), 4 Å molecular sieves (4 g), and dry $CHCl_3$ (20 mL) was heated at 55–60 °C with stirring for 1.5 h, then the molecular sieves were removed. The solution was washed with water (2 × 4 mL), dried, and evaporated. The residue was treated as described in Method 2 to give the title compound **4** (0.12 g, 54%), identical in all respects with the sample obtained as described above.

3.3.4. Method 4. A solution of **3** (0.21 g, 0.58 mmol), NBS (0.10 g, 0.56 mmol) and 0.8 mL of anhyd DMF was stirred at room temperature (rt) (17–20 °C) for 70 h, then EtOAc (7 mL) was added. The solution was treated as described in Method 3 to give the title compound **4** (0.14 g, 64%), identical in all respects with the sample obtained as described above.

3.4. Methyl 4,6-*O*-benzylidene-2-*C*-methoxycarbonylmethyl-α-D-ribo-hexopyranosid-3-ulose (2)

3.4.1. Method 1. Na (0.30 g, 13.0 mmol) was dissolved in MeOH (18 mL), to which **3** (0.30 g, 0.83 mmol) in $CHCl_3$ (15 mL) was added. The mixture was stirred at 25–28 °C and moist air was bubbled through. The solvent was added at regular intervals to supplement the loss of its evaporation by air. After 3 h, the mixture was neutralised with 50% HOAc and evaporated. The residue was dissolved in water, extracted with EtOAc, and dried. The solvent was evaporated, and the residue was crystallized from MeOH to give **2** (0.14 g, 47%), identical in all respects with the sample we reported.[11]

3.4.2. Method 2. **3** (0.30 g, 0.83 mmol) was dissolved in THF (8 mL), to which $NaHCO_3$ (catalytic amount) and water (0.4 mL) was added. The mixture was stirred at rt (17–20 °C) for 21 h, then evaporated. The residue was dissolved in EtOAc, washed twice with satd NaCl solution, then dried. The solvent was evaporated to give the titled compound **2** as a white powder (0.16 g, 55%), identical in all respects with the sample obtained as described above.

Table 2
Summary of crystallographic data for the mixed crystal of **3** and **4** in a ratio of 2:3, and **4**

	The mixed crystal of **3** and **4** in a ratio of 2:3, and **4**	
Chemical formula	$C_{18}H_{17.63}O_{8.63}$	$C_{18}H_{18}O_9$
Formula weight	371.95	378.32
Temperature (°C)	18	18
Wavelength (Mo K_α, Å)	0.71073	0.71073
Crystal system	Orthorhombic	Orthorhombic
Space group	$P2_12_12_1$	$P2_12_12_1$
Unit cell dimensions		
a (Å)	6.2914(13)	6.3659(13)
b (Å)	11.579(2)	11.591(2)
c (Å)	23.725(5)	23.782(5)
V (Å^3)	1728.3(6)	1754.8(6)
Z	4	4
D_{calc} (mg m^{-3})	1.429	1.432
μ (mm^{-1})	0.115	0.116
F(000)	779	792
Crystal size (mm^3)	0.30 × 0.20 × 0.20	0.30 × 0.20 × 0.20
Diffractometer	Rigaku RAXIS-IV	Rigaku RAXIS-IV
θ Range for data collection (°)	1.72–25.00	1.71–27.53
Index ranges	$-7 \le h \le 7$, $-13 \le k \le 0$, $-27 \le l \le 27$	$-8 \le h \le 8$, $-15 \le k \le 0$, $-30 \le l \le 30$
Reflections collected/unique	2574/2060 $R(\text{int}) = 0.0738$	5999/3520 $R(\text{int}) = 0.0412$
Structure solution	Direct method (SHELX-97)	Direct method (SHELX-97)
Refinement method	full-matrix least-squares on F^2	full-matrix least-squares on F^2
Data/restraints/parameters	2060/0/249	3520/0/244
Final *R* indices [$I > 2\sigma(I)$]	$R_1 = 0.0851$, $wR_2 = 0.1916$	$R_1 = 0.0557$, $wR_2 = 0.1064$
Goodness-of-fit on F^2	1.137	1.021

3.5. X-ray diffraction experiment

Crystal data and experimental details for the mixed crystal of **3** and **4** in ratio of 2:3, and the crystal **4** are contained in Table 2. All measurements were made on a Rigaku RAXIS-IV imaging plate with graphite monochromated Mo K_α radiation ($\lambda = 0.71073$ Å). Ortho-

Table 3
Fractional atomic coordinates and equivalent isotropic displacement factors for the mixed crystal of **3** and **4** in a ratio of 2:3, and **4**

Atom	*x*	*y*	*z*	U_{eq} (Å^2 × 10^3)
The mixed crystal of **3** and **4** in a ratio of 2:3				
O(3)	−1769(5)	6700(3)	1707(1)	45(1)
O(4)	697(4)	8202(3)	1660(1)	35(1)
O(5)	1423(5)	10727(3)	1311(1)	43(1)
O(6)	1392(6)	12654(3)	1352(2)	59(1)
O(2)	−4105(5)	9019(3)	879(1)	37(1)
O(1)	−2497(6)	9229(3)	−3(1)	48(1)
O(7)	−3869(6)	12374(3)	195(2)	63(1)
O(8)	−2736(6)	13438(3)	916(1)	56(1)
O(9)	1573(9)	9327(5)	653(2)	47(2)
C(1)	−3302(6)	9798(4)	460(2)	31(1)
C(2)	−1518(7)	10475(4)	729(2)	31(1)
C(3)	196(7)	9828(4)	1029(2)	35(1)
C(4)	−813(7)	8979(4)	1437(2)	30(1)
C(5)	−2462(7)	8277(4)	1107(2)	32(1)
C(6)	−3455(8)	7405(4)	1499(2)	44(1)
C(7)	−304(8)	7352(4)	2013(2)	40(1)
C(8)	1449(7)	6593(4)	2237(2)	36(1)
C(9)	1911(8)	5511(4)	2012(2)	42(1)
C(10)	3624(8)	4891(5)	2203(2)	51(2)
C(11)	4915(9)	5315(5)	2623(2)	49(1)
C(12)	4444(8)	6384(5)	2858(2)	51(2)
C(13)	2754(8)	7011(4)	2662(2)	42(1)
C(14)	596(7)	11791(4)	1183(2)	37(1)
C(15)	−1286(7)	11613(4)	817(2)	35(1)
C(16)	−2795(8)	12510(4)	603(2)	41(1)
C(17)	−4215(11)	14348(5)	752(3)	73(2)
C(18)	−4006(11)	8759(7)	−361(3)	97(3)
Crystal **4**				
O(1)	7481(4)	5759(2)	−2(1)	50(1)
O(2)	3673(4)	2320(2)	1361(1)	63(1)
O(3)	3613(4)	4258(2)	1327(1)	47(1)
O(4)	4249(3)	6782(2)	1663(1)	37(1)
O(5)	9037(3)	5980(2)	892(1)	40(1)
O(6)	6697(3)	8298(2)	1713(1)	49(1)
O(7)	8799(4)	2629(2)	184(1)	74(1)
O(8)	7749(4)	1562(2)	920(1)	64(1)
O(9)	3404(4)	5677(2)	656(1)	65(1)
C(1)	8268(5)	5189(2)	469(1)	40(1)
C(2)	6483(5)	4520(2)	731(1)	34(1)
C(3)	4760(5)	5152(2)	1040(1)	35(1)
C(4)	5782(5)	6008(2)	1438(1)	33(1)
C(5)	7403(4)	6713(2)	1110(1)	36(1)
C(6)	8379(5)	7595(2)	1503(1)	49(1)
C(7)	9043(8)	6204(4)	−355(2)	98(2)
C(8)	6288(5)	3394(2)	819(1)	40(1)
C(9)	7755(5)	2489(2)	604(1)	46(1)
C(10)	9248(7)	667(3)	757(2)	82(1)
C(11)	5244(5)	7642(3)	2023(1)	42(1)
C(12)	3503(5)	8399(2)	2242(1)	40(1)
C(13)	2227(6)	7980(2)	2668(1)	48(1)
C(14)	533(6)	8597(3)	2857(1)	55(1)
C(15)	92(6)	9675(3)	2628(1)	54(1)
C(16)	1368(6)	10104(3)	2213(1)	52(1)
C(17)	3076(5)	9480(2)	2020(1)	45(1)
C(18)	4429(5)	3191(2)	1190(1)	45(1)

U_{eq} is defined as one-third of the trace of the orthogonalized *U*ij tensor.

rhombic mixed crystal of **3** and **4** ($0.30 \times 0.20 \times 0.20$ mm) and single crystal of **4** ($0.30 \times 0.20 \times 0.20$ mm) were selected and mounted on a glass fiber. All data were collected at a temperature of 291(2) K and corrected for Lorentz-polarization effects. A correction for secondary extinction was applied.

3.6. Structure solution and refinement

The two structures were solved by direct methods and expanded using the Fourier technique. The non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were included but not refined. The final cycle of full-matrix least-squares refinement was based on 2060 reflections and 249 variable parameters for the mixed crystal of **3** and **4**, and 3520 reflections and 244 variable parameters for **4**. All calculations were performed using the SHELX-97 crystallographic software package.[17]

The final fractional atomic coordinates and equivalent isotropic thermal displacement factors are listed in Table 3.

4. Supplementary material

The crystal structure data have been deposited with the Cambridge Crystallographic Data Centre. These data may be obtained upon request from The Directory, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK. (Fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk; WEB: www: http://www.csdc.cam.ac.uk. Deposition numbers CCDC 200167 and CCDC 200166.

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