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β-ELIMINATION IN ALDONOLACTONES. THE CONVERSION OF L-RHAMNONO-1,5-LACTONE INTO 3-BENZOYLOXY-6-METHYLPYRAN-2-ONE

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ABSTRACT

Benzoylation of L-rhamnono-1,5-lactone (**1**) for 90 min at room temperature afforded 2,3,4-tri-*O*-benzoyl-L-rhamnono-1,5-lactone (**2**). When an excess of benzoyl chloride and pyridine was used for 20 h, with subsequent sublimation of benzoic acid from the mixture at 120° *in vacuo*, a double elimination took place and 3-benzoyloxy-6-methylpyran-2-one (**4**) was isolated as the main product. The conversion of **1**, **2**, and 2,4-di-*O*-benzoyl-3,6-dideoxy-L-*erythro*-hex-2-enono-1,5-lactone (**3**) into the pyran-4-one derivative **4** under different conditions was monitored chromatographically.

INTRODUCTION

In previous papers, we have reported the synthesis of unsaturated derivatives on benzoylation of aldonolactones[1–5]. Multiple elimination was observed with D-galactono-1,4-lactone[1] and D-*glycero*-D-*manno*-heptono-1,4-lactone[3], whereas aldono-1,5-lactones, under similar conditions, afforded a monounsaturated compound in excellent yield. Thus, 2,4,6-tri-*O*-benzoyl-3-deoxy-D-*erythro*-hex-2-enono-1,5-lactone was obtained from D-glucono-1,5-lactone[4], and 2,4-di-*O*-benzoyl-3,6-dideoxy-L-*erythro*-hex-2-enono-1,5-lactone (**3**) from L-rhamnono-1,5-lactone[5] (**1**).

Nelson and Gratzl[6] recently described the production of a diunsaturated derivative, namely 3-acetoxy-6-(acetoxymethyl)pyran-2-one, on prolonged reaction of D-glucono-1,5-lactone with acetic anhydride and pyridine. We now report the isolation of 3-benzoyloxy-6-methylpyran-2-one (**4**) when conditions of benzoylation more vigorous than those previously reported were used.

RESULTS AND DISCUSSION

Benzoylation of L-rhamnono-1,5-lactone (**1**) with benzoyl chloride and pyridine for 90 min at room temperature afforded 2,3,4-tri-*O*-benzoyl-L-rhamnono-1,5-lactone

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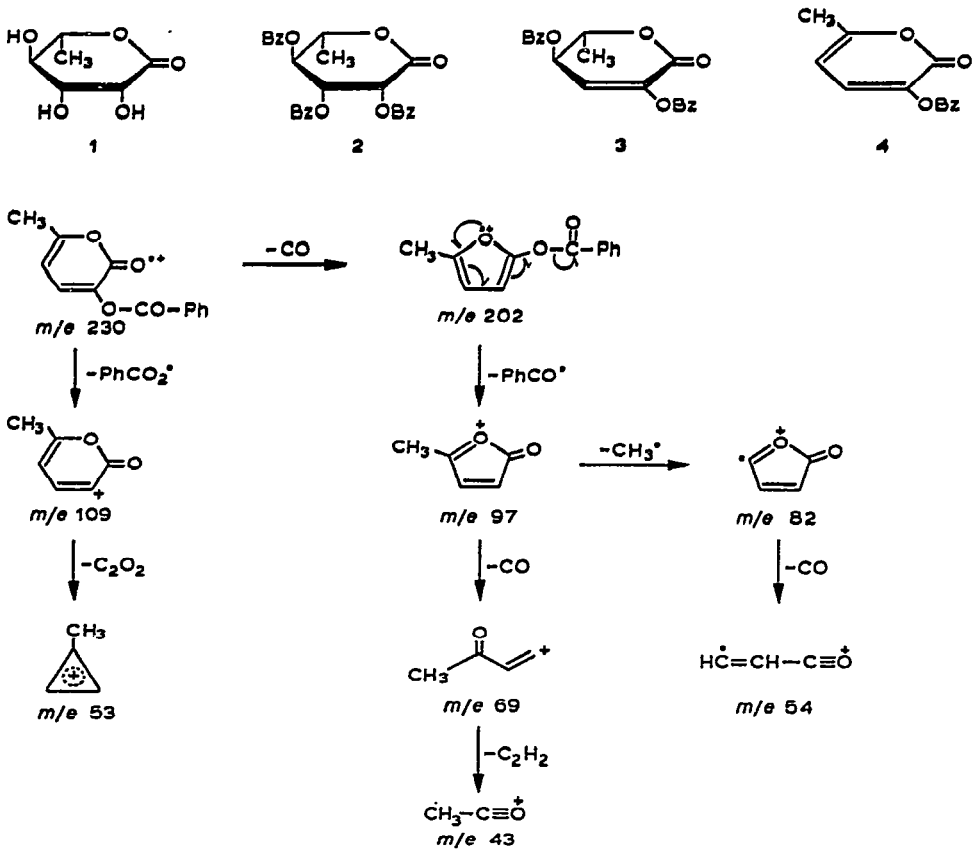

Scheme 1. Mass-spectral fragmentation pattern of 3-benzoyloxy-6-methylpyran-2-one.

(2), which showed i.r.-spectral absorption characteristic for 1,5-lactones. The ^{1}H-n.m.r. spectrum of 2 showed $J_{3,4}$ 1.8 and $J_{4,5}$ 8.3 Hz, which suggests a half-boat conformation for this compound. The small coupling-value requires a dihedral angle of H-3 and H-4 near 90°. Both half-boat and half-chair conformations are compatible with the planar, lactone group and have been proposed for 1,5-lactones[7].

When benzoylation was conducted with a fourfold excess of reactants for 16 h, elimination of the benzoyloxy group β to the carbonyl group of the lactone took place, and 2,4-di-*O*-benzoyl-3,6-dideoxy-L-*erythro*-hex-2-enono-1,5-lactone (3) was obtained crystalline in 87% yield[5].

In order to obtain the α-pyrone derivative, the reaction was conducted for longer periods, but the main product continued to be the 2-enono-lactone 3 (as shown by t.l.c.). When benzoic acid was sublimed from the mixture at temperatures >100°, formation of a compound having lower mobility was observed by t.l.c. It crystallized from ethanol in 54% yield. The assigned structure of 3-benzoyloxy-6-methylpyran-2-one (4) was confirmed by spectroscopic methods.

The u.v. spectrum of 4 showed an absorption maximum (300 nm, ε 7900)

consistent with that expected for the α-pyrone chromophore. Thus, 3-acetoxy-6-(acetoxymethyl)pyran-2-one exhibits λ_{max} 292 nm (ε 5760)[6] and 3-bromopyran-2-one, λ_{max} 300 nm (ε 5750)[8]. Its i.r. spectrum showed absorption in the carbonyl zone at 1740 (carbonyl of vinyl benzoate) and 1720 cm^{-1} (conjugated 1,5-lactone carbonyl).

The ^{1}H-n.m.r. spectrum was in accord with the postulated structure. It showed two doublets, at δ 7.15 and 6.02 having *J* 7.0 Hz, assigned to H-4 and H-5, respectively; these signals are characteristic of 3,6-disubstituted α-pyrone derivatives[6,9]. Allylic coupling between H-5 and the methyl protons was observed.

The mass-spectral fragmentation pattern of compound **4** is shown in Scheme 1.

Similar mass-spectral results have been reported for other 2-pyrone structures[10]. Examples are cited in which substituted 2-pyrones initially lose the 6-substituent[11], but we did not observe an ion at *m/e* M-15. A similar stability of the 6-methyl group has been reported for 3-bromo-4,6-dimethyl-2-pyrone[10,12].

The mass spectrum of 2,4-di-*O*-benzoyl-3,6-dideoxy-L-*erythro*-hex-2-enono-1,5-lactone (**3**) showed elimination of 122 mass units ($C_6H_5CO_2H$) from its molecular ion to give *m/e* 230, corresponding to the 2-pyrone derivative, which shows the same fragmentation pattern as compound **4**. Similar behavior was described for 2,4,6-tri-*O*-acetyl-3-deoxy-D-*erythro*-hex-2-enono-1,5-lactone[6].

The ion at *m/e* 231 corresponds to the loss of 121 mass units ($C_6H_5CO_2$), and undergoes successive eliminations of benzoyl and methyl groups (*m/e* 111). This fragment can lose either carbon monoxide (*m/e* 83) or carbon dioxide (*m/e* 67).

Different reaction conditions (Table I) were examined in order to obtain better yields of 3-benzoyloxy-6-methylpyran-2-one (**4**). L-Rhamnono-1,5-lactone (**1**) was

TABLE I

RELATIVE AMOUNT OF 3-BENZOYLOXY-6-METHYLPYRAN-2-ONE (**4**) OBTAINED UNDER DIFFERENT REACTION CONDITIONS

Starting material	*Reaction conditions*[a]	*Reaction time (h)*	*Temperature (degrees)*	*Products (%)*[b]		
				2	3	4
1	A	1.5	25	100		
	B	16	25		100	
	C	10	100		18	82
2	D	16	25		100	
	E	8	100	100[c]		
	F	8	100		80	20
3	E	8	100		100[c]	
	D	8	60		100[c]	
	F	8	100		40	60

[a]A: BzCl–C_5H_5N (1:1, v/v); B: BzCl–C_5H_5N (1:2, v/v); C: BzCl–triethylamine–$HCONMe_2$ (1:1.3:2.5); D: 20% triethylamine in chloroform; E: acetic acid was added to a 0.6% solution of the lactone in *N,N*-dimethylformamide until the pH reached 5; and F: benzoic acid (30 mg) and triethylamine (1 mL) were added to a 0.6% solution of the lactone in *N,N*-dimethylformamide (1.5 mL). [b]Expressed as percent of the reaction product. [c]No reaction, starting material recovered.

first converted into the tribenzoate **2**, which undergoes elimination of the benzoyloxy group β to the carbonyl group. This elimination step is base-catalyzed and should take place by an E1cB mechanism, with the intermediate formation of a carbanion on C-2, stabilized by resonance. A similar reaction pathway for the conversion of the 2-enono-lactone **3** into the 2-pyrone derivative **4** is ruled out, as it would require a non-stabilized intermediate negatively charged at C-5. Experimentally, it was observed that base alone does not catalyze the second elimination. Both acid and base are required, suggesting a concerted process in which the 4-benzoate group is removed by acid with the formation of an incipient allylic cation, and H-5 is abstracted by the base. Nelson and Gratzl[6] postulated a similar mechanism for the formation of 3-acetoxy-6-(acetoxymethyl)pyran-2-one from D-glucono-1,5-lactone.

EXPERIMENTAL

General methods. — Melting points were determined with a Fisher–Johns apparatus and are uncorrected. Optical rotations were recorded with a Perkin–Elmer 141 polarimeter and i.r. spectra with a Perkin–Elmer Model 421 spectrophotometer. U.v. absorption was determined with a Beckman DK-2A spectrophotometer. ^{1}H-N.m.r. spectra were determined in chloroform-*d* with a Varian A-60 spectrometer, with tetramethylsilane as internal reference; the apparent coupling contants (Hz) reported are the directly observed line-spacings. T.l.c. was performed on Silica Gel G (Merck) with 19:1 benzene–ethyl acetate, and detection was effected with iodine vapor. G.l.c. was effected with a Hewlett–Packard 5830 A gas chromatograph equipped with glass columns (180 × 0.2 cm) packed with 3% SE-30 on Chromosorb WAW-DMCS (80–100 mesh), with nitrogen at a flow rate of 30 mL.min^{-1}; T_i 280°; T_d 280°; T_c was 2 min at 230° and was then programmed from 230 to 270° (10°/min). Mass spectra were obtained with a Varian MAT CH 7 spectrometer coupled to a Varian MAT data-system 166. L-Rhamnono-1,5-lactone (**1**) was obtained as already described[13] by oxidation of L-rhamnose with bromine.

2,3,4-Tri-O-benzoyl-L-rhamnono-1,5-lactone (**2**). — To a suspension of L-rhamnono-1,5-lactone (**1**, 0.4 g) in anhydrous pyridine (2 mL), cooled to 0°, was added benzoyl chloride (1.8 mL) with stirring. The mixture was shaken for 90 min at ~25° and then poured into ice–water. The oil formed was extracted with chloroform (3 × 30 mL), and the organic layer was repeatedly washed with saturated aqueous sodium hydrogencarbonate and water to neutrality, dried (magnesium sulfate), and evaporated to a syrup that was purified by dissolution in ether and reprecipitation with light petroleum. The product could not be crystallized. The chromatographically pure compound, yield 0.96 g (83%) had $[\alpha]_D^{20}$ −15.3° (*c* 0.9, chloroform); R_F 0.43; ν_{max}^{Nujol} 1750 (1,5-lactone C=O), 1710 (benzoate C=O), and 1600 cm^{-1} (aromatic C=C), no hydroxyl peak; ^{1}H-n.m.r.: δ 8.2–7.2 (m, 15 H, 3 Bz), 6.25 (d, 1 H, $J_{2,3}$ 3.8 Hz, H-2), 6.02 (q, $J_{3,4}$ 1.8 Hz, H-3), 5.36 (q, $J_{4,5}$ 8.3 Hz, H-4), 4.86 (m, H-5), and 1.61 (d, $J_{5,6}$ 6.2 Hz, CH_3).

Anal. Calc. for $C_{27}H_{22}O_8$: C, 68.35; H, 4.64. Found: C, 68.55; H, 4.88.

3-Benzoyloxy-6-methylpyran-2-one (**4**). — L-Rhamnono-1,5-lactone (**1**, 1.6 g) was suspended in anhydrous pyridine (20 mL) and benzoyl chloride (10 mL) was added with external cooling. The mixture was shaken for 20 h at room temperature and poured into ice–water. After 2 h, it was extracted with chloroform and the organic layer washed conventionally, dried (magnesium sulfate), and evaporated. Benzoic acid was sublimed during 10 h from the resulting syrup at 0.01 mmHg and 120°. A yellow precipitate obtained upon addition of ethanol (1.53 g) showed (t.l.c.) a main compound having R_F 0.33, together with 2,4-di-*O*-benzoyl-3,6-dideoxy-L-*erythro*-hex-2-enono-1,5-lactone (**3**, R_F 0.46). G.l.c. of the mixture showed two peaks, having T 1.6 and 8.8, respectively, in 4:1 ratio. The main product was purified by column chromatography on Silica Gel G, with benzene containing increasing concentrations of ethyl acetate as eluant. Upon recrystallization from ethanol, 3-benzoyloxy-6-methylpyran-2-one (**4**) was obtained in 54% yield; m.p. 112–114°, $[\alpha]_D$ 0° (*c* 1.1, chloroform); λ_{max}^{MeOH} 300 (ε 7900) and 234 nm (16000); ν_{max}^{Nujol} 1740 (enoiic benzoate C=O), 1720 (unsaturated lactone C=O), 1640 (conjugated C=C), and 1580 cm^{-1} (aromatic C=C); ^{1}H-n.m.r.: δ 7.4–8.3 (m, 5 H, Bz), 7.15 (d, $J_{4,5}$ 7.0 Hz, H-4), 6.02 (m, J_{5,CH_3} 0.8 Hz), and 2.28 (d, 3 H, CH_3); *m/e* 230 (M^+, 10), 202 (0.2), 109 (0.4), 105 (100), 97 (3.5), 82 (1.5), 77 (100), 69 (2.2), 54 (2.3), 53 (0.5), 51 (28.4), and 43 (20.2).

Anal. Calc. for $C_{13}H_{10}O_4$: C, 67.83; H, 4.35. Found: C, 67.76; H, 4.49.

*2,4-Di-*O*-benzoyl-3,6-dideoxy-*L-erythro-*hex-2-enono-1,5-lactone* (**3**). — Compound **3** was obtained from L-rhamnono-1,5-lactone as already described[5]; *m/e* 352 (M^+, 1.2), 231 (1.2), 230 (1.6), 202 (9.6), 111 (1.6), 105 (100), 97 (2.8), 83 (2.8), 82 (6.8), 77 (100), 67 (4.4), 54 (5.2), 51 (40), and 43 (4).

Determination of the relative amount of 3-benzoyloxy-6-methylpyran-2-one (**4**) *obtained under different conditions.* — Monitoring of the reaction upon treatment of **1**, **2**, and **3** with various reagents was made by t.l.c. and g.l.c. under the conditions described in General Methods. The relative proportion of compounds **3** and **4** was determined by electronic integration of the areas under the corresponding peaks in g.l.c. The results are shown in Table I. In all instances, the reaction was stopped by pouring the mixture into ice–water, followed by extraction with chloroform. The organic layer was washed conventionally to neutrality, and dried (magnesium sulfate).

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