# Reaction of Glyceraldehyde With Aryl and Alkyl Chloroformates Kenneth F. Podraza

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A number of 2,5-bis(aryl- and alkyloxycarbonyloxymethylene)-3,6-bis(aryl- and alkoxycarbonyloxy)-1,4-dioxanes 5a-d have been prepared by the reaction of glyceraldehyde with aryl and alkyl chloroformates. Bis aryl carbonates were also formed under certain conditions in this reaction. Nuclear magnetic resonance analysis of 5c indicated that it existed in a chair conformation with all the substituents in an equatorial position.

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Glyceraldehyde can exist in different structural forms in solution [1] depending on the solvent. It exists in a monomeric form in aqueous solution and in a dimeric form in organic solvents. Gardiner [2] and Hall [3] have shown that the reaction of glyceraldehyde with chlorotrimethylsilane or with acetic anhydride and pyridine yields 1,4-dioxane derivatives 1 and 2 respectively; i.e., the products originate from the dimeric form. We were interested in investigating the reaction of glyceraldehyde with aryl and alkyl chloroformates. Since the reaction of glyceraldehyde with chloroformates can only be conveniently carried out in aprotic organic solvents, we anticipated obtaining the 1,4-dioxane derivatives as products.

Matzner et al. [4] reported that chloroformates react with tertiary amines, such as pyridine, yielding unstable quaternary ammonium compounds. The latter react with alcohols and phenols to give the expected carbonates in good yield. It was also reported [5] that aryl chloroformates give bis-aryl carbonates directly when treated with pyridine at elevated temperatures. A later report [6] indicated that the presence of water was the reason for the formation of the bis aryl carbonate 6.

= 2-methoxy-4-formylphenyl

= 2-methoxy-4-methylpheny

Generally, in our hands, when the reaction of glyceraldehyde with aryl chloroformates was conducted at room temperature, a heterogeneous mixture was observed and maintained throughout the course of the reaction, with the isolation of 6 as the major product (Scheme 1, path B). When the reaction was carried out at an elevated temperature (40-60°) a homogeneous solution was observed with 5 as the major product obtained (Scheme 1, path A). However, in the case of alkyl chloroformates, the only product obtained was 5, regardless of the temperature (see Table I).

Table I Reaction of Glyceraldehyde with Aryl and Alkyl Chloroformates

Compound	Temperature (°C)	Yield (%) [a]	
1	• • • •	6	5
3a	40-60	- [b]	65
3b	25	- [b]	55
3b	40-60	- [b]	80
<b>3</b> c	40-60	- [c]	65
3d	25	53	35
3d	40-60	18	70
<b>3</b> e	25	20	- [b]
<b>3e</b>	40-60	20	- [b]

[a] Isolated yields. [b] These compounds were not detected in the reaction. [c] Compound 6c was not detected.

It may be assumed that at room temperature, the pyridine-chloroformate complex 4 would preferably react with the primary hydroxyl groups in the glyceraldehyde dimer, resulting in 7 (Scheme 2). Once the primary hydroxyl groups were substituted the vicinal secondary hydroxyl groups had two possible sites of nucleophilic attack. One would be an intermolecular nucleophilic attack on the pyridine-chloroformate complex 4 which would result in 5 being formed. The other alternative would be an intramolecular nucleophilic attack of the hydroxyl group on the carbonate. This would result in the formation of a cyclic carbonate 8 with the elimination of an alkoxy or aryloxy anion. The anion, in turn, could then attack the pyridinechloroformate complex, 4, which would result in the formation of the bis carbonate, 6.

For the intramolecular nucleophilic attack to occur, a good leaving group would have to have been present on the carbonate 7. Since alkoxy groups are poor leaving groups, the reaction of glyceraldehyde with alkyl chloroformates resulted in only 5 being isolated, regardless of the temperature at which the reaction was conducted (Table I).

On the other hand, the reaction of **3e** with glyceraldehyde resulted in **6e** as the only product obtained, regardless of the temperature at which the reaction was conducted. Thus, the intramolecular nucleophilic attack occurred when a good leaving group was present. The cyclic carbonate **8**, which is assumed to be formed in addition to the bis carbonate **6**, was never detected. However, literature data [7] indicate similar six membered cyclic carbonates to be unstable.

The reaction of 3d with glyceraldehyde was affected by the temperature at which the reaction was conducted (Table I). When the reaction was conducted at room temperature the heterogeneous mixture afforded 6d as the major product. When the reaction was conducted at the elevated temperature (40-60°), the solid suspension dissolved. The resulting homogeneous solution yielded 5d as the major product. An attempt was made to isolate and characterize the solid suspension, assumed to be an intermediate in the reaction, however the solid decomposed before it could be characterized. Presumably the change in the physical state of the reaction effected the rate of the intramolecular and intermolecular reactions. The major products obtained suggest that the rate of the intramolecular reaction was greater than the intermolecular reaction in the heterogeneous mixture, while in the case of the homogeneous solution, the rate of the intramolecular reaction was less than the intermolecular reaction.

The nmr data for 1 and 2, generated by Gardiner [2] and Hall [3], showed that the 1,4-dioxane structure existed in a chair conformation in which all the substituents were in an equatorial position. These results were obtained by a comparison of the vicinal coupling constants of the anomeric hydrogens of 1 and 2 with the penta-O-trimethylsilyl

and penta-O-acetyl- $\alpha$ - and  $\beta$ -D-glucopyranoses respectively.

A similar nmr analysis was conducted on **5c**. The coupling constant observed for the anomeric hydrogen of **5c** was 7.5 Hz. This value was similar to the coupling constant of **1** and **2** (i.e. 7.4 and 7.6 Hz respectively).

### **EXPERIMENTAL**

Melting points were determined with a Thomas Hoover capillary melting point apparatus and are uncorrected. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tennessee. Infrared spectra were recorded on a Perkin-Elmer 283B Spectrophotometer. The chemical shifts and coupling constants (J) are reported in  $\delta$  and Hertz respectively, using a Varian XL-100 or Bruker WP80 spectrometer, with TMS as the internal standard.

Reaction of Glyceraldehyde With Aryl and Alkyl Chloroformates.

Method A.

To a solution of 5 ml of pyridine in 50 ml of chloroform was added with stirring 1.0 g (11.1 mmoles) of glyceraldehyde. The resulting suspension was chilled in an ice bath. A solution of 22.2 mmoles of an aryl (alkyl) chloroformate [9] in 10 ml of chloroform was added dropwise. Stirring was continued for approximately 15 minutes while maintaining the temperature at 0°, then 18-24 hours at room temperature. The mixture was heated with stirring at 40° for 1.5 hours, then for 1 hour at 60°, after which time the solution was cooled to room temperature. The reaction mixture was washed with water, followed by aqueous saturated sodium bicarbonate solution. The organic layer was dried over anhydrous sodium sulfate. Evaporation of the solvent under reduced pressure yielded a residue, to which toluene was added and subsequently removed by evaporation under reduced pressure. The semi-solid obtained was then purified according to the procedure indicated for each compound.

Method B.

To a solution of 5 ml of pyridine in 50 ml of chloroform was added with stirring 1.0 g (11.1 mmoles) of glyceraldehyde. The resulting suspension was chilled in an ice bath. A solution of 22.2 mmoles of an aryl (alkyl) chloroformate in 10 ml of chloroform was added dropwise. Stirring was continued for approximately 15 minutes while maintaining the temperature at 0°, then 18-24 hours at room temperature. The reaction mixture was washed with water, followed by saturated sodium bicarbonate solution. The organic layer was dried over anhydrous sodium sulfate. Evaporation of the solvent under reduced pressure yielded a residue, to which toluene was added and then subsequently removed by evaporation under reduced pressure. The semi-solid obtained was then purified according to the procedure indicated for each compound.

2,5-bis(3-Hexenoxycarbonyloxymethylene)-3,6-bis(3-hexenoxycarbonyloxy)-1,4-dioxane (5a).

The synthesis of **5a** was conducted on a 11.1 mmole scale using the conditions desribed in Method A. The product was recrystallized from methanol and yielded 2.0 g (65%) of the pure product, mp 68-69°; ir (nujol mull): 1756 cm<sup>-1</sup> (carbonate); nmr (deuteriochloroform):  $\delta$  5.75-5.08 (10H, m, CH=CH, and C<sub>3</sub>), 4.5-3.8 (14H, m, CH<sub>2</sub>CH<sub>2</sub>CH, CO<sub>2</sub>CH<sub>2</sub>, and C<sub>2</sub>), 2.6-1.8 (16H, m, -CH<sub>2</sub>CH=CHCH<sub>2</sub>CH<sub>3</sub>), 0.95 (12H, t, J = 7.0 Hz, CH<sub>2</sub>CH<sub>3</sub>).

Anal. Calcd. for C<sub>34</sub>H<sub>52</sub>O<sub>14</sub>: C, 59.64; H, 7.65. Found: C, 59.40; H, 7.65.

2,5-bis(Menthoxycarbonyloxymethylene)-3,6-bis(menthoxycarbonyloxy)-1,4-dioxane (5b).

Method A.

The synthesis of **5b** was conducted on a 11.1 mmole scale using the conditions described in Method A. The product was recrystallized from

2-propanol to yield 4.0 g (80%) of the pure product, mp 139-140°; ir (nujol mull): 1748 cm<sup>-1</sup> (carbonate); nmr (deuteriochloroform):  $\delta$  5.7 (2H, d, J = 7.0 Hz, C<sub>3</sub>), 4.75-4.25 (8H, m, CO<sub>2</sub>CH<sub>2</sub>, and OCH<sub>2</sub>CH), 3.9 (2H, m, C<sub>2</sub>), 2.25-0.65 (72H, m, menthyl protons).

Anal. Calcd. for C<sub>50</sub>H<sub>84</sub>O<sub>14</sub>: C, 66.05; H, 9.31. Found: C, 65.85; H, 9.46.

## Method B.

The synthesis of **5b** was conducted on a 11.1 mmole scale using the conditions described in Method B. The product was recrystallized from isopropanol and yielded 2.7 g (55%) of the pure product, mp 139-140°. Its spectral data were identical to that obtained by Method A.

2,5-bis(Phenoxycarbonyloxymethylene)-3,6-bis(phenoxycarbonyloxy)-1,4-dioxane (5c).

The synthesis of 5c was conducted on a 11.1 mmole scale using the conditions described in Method A. The product was recrystallized from ethanol to yield 2.4 g (65%) of the pure product, mp 155°; ir (nujol mull): 1768 cm<sup>-1</sup> (carbonate); nmr (deuteriochloroform):  $\delta$  7.55-7.05 (20H, m, aromatic protons), 5.95 (2H, d, J = 7.5 Hz, C<sub>3</sub>), 4.6 (4H, m, CO<sub>2</sub>CH<sub>2</sub>), 4.23 (2H, m, C<sub>2</sub>).

Anal. Calcd. for C<sub>34</sub>H<sub>28</sub>O<sub>14</sub>: C, 61.82; H, 4.27. Found: C, 61.64; H, 4.49.

2,5-bis(2-Methoxy-4-methylphenoxycarbonyloxymethylene)-3,6-bis(2-methoxy-4-methylphenoxycarbonyloxy)-1,4-dioxane (5d).

#### Method A.

The synthesis of **5d** was conducted on a 11.1 mmole scale using the condition described in Method A. The product was recrystallized from chloroform:isooctane and yielded 3.2 g (70%) of the pure product, mp 191-192°; ir (nujol mull): 1766 cm<sup>-1</sup> (carbonate); nmr (deuteriochloroform):  $\delta$  7.1-6.6 (12H, m, aromatic protons), 5.9 (2H, d, J = 6.0 Hz, C<sub>3</sub>), 5.05 (4H, m, CO<sub>2</sub>CH<sub>2</sub>), 4.28 (2H, m, C<sub>2</sub>), 3.8 (12H, s, OCH<sub>3</sub>), 2.3 (12H, s, CH<sub>3</sub>).

Anal. Calcd. for C<sub>42</sub>H<sub>44</sub>O<sub>18</sub>: C, 60.28; H, 5.30. Found: C, 60.13; H, 5.37. The mother liquor was evaporated under reduced pressure to yield a solid which was recrystallized from chloroform:hexane to yield 0.6 g (18%) of **6d**. Its spectral data was identical to that obtained for an authentic sample of **6d**.

#### Method B.

The synthesis of 5d was conducted on a 11.1 mmole scale using the conditions described in Method B. The product was recrystallized from chloroform:isooctane to yield 1.6 g (35%) of the pure product, mp 191-192°. Its spectral data was identical to that obtained by Method A.

The mother liquor was evaporated under reduced pressure to yield a solid which was recrystallized from chloroform:hexane to yield 1.8 g (53%) of 6d. Its spectral data were identical to the authentic sample of 6d.

Reaction of Glyceraldehyde With 2-Methoxy-4-formylphenyl Chloroformate (3e).

#### Method A.

The reaction was conducted on a 11.1 mmole scale using the conditions described in Method A. The product was washed with ethanol yielding 0.7 g (20%) of bis(2-methoxy-4-formylphenyl)carbonate (6e). Its spectral data were identical to the authentic sample of 6e.

#### Method B.

The reaction was conducted on a 11.1 mmole scale using the conditions described in Method B. The product was washed with ethanol which yielded 0.7 g (20%) of bis(2-methoxy-4-formylphenyl) carbonate (6e). Its spectral data was identical to the authentic sample of 6e.

#### bis(2-Methoxy-4-formylphenyl) Carbonate (6e).

To a solution of 4 ml of pyridine in 50 ml of methylene chloride was added 0.7 g (4.7 mmoles) of 2-methoxy-4-formylphenol. The solution was chilled in an ice bath. A solution of 1.0 g (4.7 mmoles) of 2-methoxy-4-formylphenyl chloroformate in 10 ml of methylene chloride was added dropwise. Stirring was continued for approximately 15 minutes, while maintaining the temperature at 0°, then 18-24 hours at room temperature. Ether was added and the reaction mixture was washed with water, followed by aqueous saturated sodium bicarbonate. The organic layer was dried over anhydrous sodium sulfate. Evaporation of the solvent under reduced pressure yielded a solid. It was washed with ethanol to remove any 2-methoxy-4-formylphenol yielding 1.3 g (85%) of **6e**, mp 149-150°; ir (nujol mull); 1700 cm<sup>-1</sup> (aldehyde), 1770 cm<sup>-1</sup> (carbonate); nmr (deuteriochloroform):  $\delta$  9.97 (2H, s, CHO), 7.63-7.25 (6H, m, aromatic protons), 4.0 (6H, s, OCH<sub>3</sub>).

Anal. Calcd. for C<sub>17</sub>H<sub>14</sub>O<sub>7</sub>: C, 61.82; H, 4.27. Found: C, 62.01; H, 4.47.

### bis(2-Methoxy-4-methylphenyl) Carbonate (6d).

The synthesis of **6d** was conducted on a 5 mmole scale by using the conditions described for **6e**. The product was recrystallized from chloroform:hexane to yield 1.2 g (87%) of the pure product, mp 145-147°; ir (nujol mull): 1780 cm<sup>-1</sup> (carbonate), nmr (deuteriochloroform):  $\delta$  7.3-6.63 (6H, m, aromatic protons), 3.88 (6H, s, OCH<sub>3</sub>), 2.35 (6H, s, OCH<sub>3</sub>).

Anal. Calcd. for C<sub>17</sub>H<sub>18</sub>O<sub>5</sub>: C, 67.54; H, 6.00. Found: C, 67.30; H, 5.91.

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