Synthesis and Thermolysis of Aryl Hydroxyalkyl Carbonates

Kenneth F. Podraza

A variety of aryl hydroxyalkyl carbonates (1–7) have been synthesized and thermolyzed in the neat state at 150 and 250 °C. The aryl hydroxyalkyl carbonates 9 and 10 derived from glycerol and 11 derived from ethylene glycol decomposed at room temperature. Alkyl substitution in the diol moiety of the 1-[[(aryloxy)carbonyl]oxy]-3-propanol derivatives 4 and 5 enhanced the phenolic release as compared to the unsubstituted derivative 3. 2-[[(2-Methoxy-4-formylphenoxy)carbonyl]oxy]-4-pentanol (8) decomposed at room temperature while 2-[[(2-methoxyphenoxy)carbonyl]oxy]-4-pentanol (5) was stable, which was attributed to the effectiveness of the aryl moieties as leaving groups. Increasing the chain length between the hydroxyl group and carbonate moiety from three methylene units (3), to four (6), to five (7) decreased the phenolic release from 67% to 45% to 10%, respectively.

Alkyl- and alkoxy-substituted phenols such as 2-methoxyphenol have desirable flavor properties. These compounds have been detected in a wide variety of food products and have been used as flavoring agents (Fenaroli, 1975). However, their use as flavoring agents can be limited by their low odor threshold and high volatility. As a consequence, a limitation on the amount of the flavoring agent that can be utilized as well as losses on storage result.

To overcome these limitations, the use of a phenolic flavor precursor could be employed. The requirements of such a flavor precursor would include being nonvolatile, odorless, and stable in the product on storage. Then, when heat and/or water is applied to the product, the desired flavoring substance would be liberated.

In this study we prepared a number of aryl hydroxyalkyl carbonates and investigated their thermal behavior, with exclusion of water from the system, to directly examine the effect of the intramolecular hydroxyl group. The mechanism that would release the phenolic component was conceived to occur via an intramolecular or intermolecular nucleophilic substitution of the hydroxyl group on the carbonate as represented in Scheme I. We focused our investigation on the thermolysis of the aryl hydroxyalkyl carbonates at relatively low temperatures (150 and 250 °C) and in the neat state, in an attempt to obtain some basic thermolysis data and to correlate structure and reactivity.

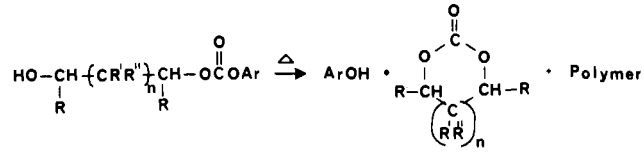
RESULTS AND DISCUSSION

The aryl hydroxyalkyl carbonates were prepared by reacting the appropriate alkyl diol with 1 equiv of a desired aryl chloroformate (Strain et al., 1950), in the presence of base (Scheme II). Compounds 1 and 2 and 3–7 were subjected to thermolysis in a sealed glass tube at 250 °C for 10 min and 150 °C for 5 min, respectively. The yield of the released phenolic component in each case was determined by GC quantitation with an authentic sample (Table I).

The aryl hydroxyalkyl carbonates 9 and 10 derived from glycerol and 11 derived from ethylene glycol were prepared but in each case were found to undergo rapid decomposition to release the phenolic component at room temperature. This high reactivity is attributed to the vicinal hydroxyl group participating in an intramolecular ring-closure reaction to eliminate the phenolic component. This observation is supported by literature data (Pfeiffer et al., 1970) where they noted that a glycerol-3-carbonate with a good leaving group, trichloroethoxy, underwent ring closure under mild conditions to yield glycerol-2,3-carbonate.

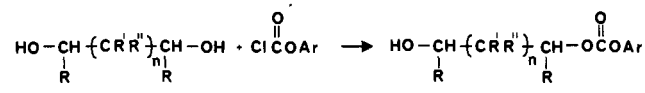
The reactivity of the carbonates derived from the 1,3-propanediol derivatives (1–5) was found to be dependent on the substitution pattern of the alkyl chain. The 1,3-propanediol derivative with alkyl substituents in the 1- and 3-positions (5) exhibited a slight increase in the phenolic release as compared to the unsubstituted derivative 3 (Table I). The presence of two alkyl substituents in the

Scheme I



1: $n = 1$; R, R′, R″ = H; Ar = Ph
2: $n = 1$; R, R′, R″ = H; Ar = 2-(OCH_3)-4-$(CH_3)C_6H_3$
3: $n = 1$; R, R′, R″ = H; Ar = 2-$(OCH_3)C_6H_4$
4: $n = 1$; R = H; R′, R″ = CH_3; Ar = 2-$(OCH_3)C_6H_4$
5: $n = 1$; R = CH_3; R′, R″ = H; Ar = 2-$(OCH_3)C_6H_4$
6: $n = 2$; R, R′, R″ = H; Ar = 2-$(OCH_3)C_6H_4$
7: $n = 3$; R, R′, R″ = H; Ar = 2-$(OCH_3)C_6H_4$

Scheme II



1: $n = 1$; R, R′, R″ = H; Ar = Ph
2: $n = 1$; R, R′, R″ = H; Ar = 2-(OCH_3)-4-$(CH_3)C_6H_3$
3: $n = 1$; R, R′, R″ = H; Ar = 2-$(OCH_3)C_6H_4$
4: $n = 1$; R = H; R′, R″ = CH_3; Ar = 2-$(OCH_3)C_6H_4$
5: $n = 1$; R = CH_3; R′, R″ = H; Ar = 2-$(OCH_3)C_6H_4$
6: $n = 2$; R, R′, R″ = H; Ar = 2-$(OCH_3)C_6H_4$
7: $n = 3$; R, R′, R″ = H; Ar = 2-$(OCH_3)C_6H_4$

Table I. Thermolysis of the Aryl Hydroxyalkyl Carbonates

compd	conditions[a]	phenolic product	yield,[b] %
1	A	phenol	100
2	A	2-methoxy-4-methylphenol	95
3	B	2-methoxyphenol	67
4	B	2-methoxyphenol	95
5	B	2-methoxyphenol	75
6	B	2-methoxyphenol	45
7	B	2-methoxyphenol	10

[a] Conditions: (A) 250 °C/10 min; (B) 150 °C/5 min. [b] Determined by GC quantitation with an authentic sample of phenolic material.

Philip Morris Research Center, Richmond, Virginia 23261.

0021-8561/86/1434-0475$01.50/0

2-position (4) led to a significant increase in the phenolic release as compared to derivatives 3 and 5. Previous investigators (Sarel et al., 1959) examining the ester interchange of 1,3-propanediol derivatives with diethyl carbonate have found that alkyl substituents on the 1,3-propanediol backbone resulted in an increase in the intramolecular cyclization while reducing intermolecular condensation as measured by the yield of cyclic and acyclic carbonates obtained. The course of the reaction, intramolecular or intermolecular nucleophilic substitution, can be postulated to have a similar effect on aryl hydroxyalkyl carbonates comparable to Sarel's ethyl hydroxyalkyl carbonates. Thus, an increase in the intramolecular nucleophilic substitution is a possible explanation for the increase in the release of the phenolic components observed for compounds 4 and 5 as compared to the unsubstituted derivative 3.

The substituents on the aryl ring have also been observed to affect the phenolic release. 2-[[(2-Methoxy-4-formylphenoxy)carbonyl]oxy]-4-pentanol (8) was found to decompose at room temperature, while 2-[[(2-methoxyphenoxy)carbonyl]oxy]-4-pentanol (5) was stable. This observation can be explained by the better leaving group ability that the 2-methoxy-4-formylphenol exhibits as compared to 2-methoxyphenol.

The chain length between the hydroxyl group and carbonate moiety was shown to have a significant effect on the phenolic release. If the chain length had four methylene units, 6, or five methylene units, 7, the release was 45% or 10%, respectively. This represents a significant reduction in the phenolic release as compared to the 1,3-propanediol derivatives (1–5). In a previous study by Sarel, increasing the chain length was shown to favor intermolecular substitution while reducing intramolecular substitution in the ester interchange of alkyl diol derivatives with diethyl carbonate. Thus, increased intermolecular substitution is postulated to account for the reduction in the release of the phenolic components for 6 and 7.

In summary, we have observed that the reactivity of the aryl hydroxyalkyl carbonates is dependent on the number of methylene units between the hydroxyl group and the carbonate moiety, the substitution pattern on the alkyl backbone, and the particular phenolic component utilized.

EXPERIMENTAL SECTION

Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, TN. IR were recorded on a Perkin-Elmer 283B spectrophotometer. The chemical shifts and coupling constants (J) are reported in δ and Hertz, respectively, on a Bruker WP80 spectrometer, with Me_4Si as the internal standard. TLC was carried out on silica gel GF plates with the solvent compositions indicated for each application.

1-[(Phenoxycarbonyl)oxy]-3-propanol (1). To a solution of 10.0 g of pyridine in 300 mL of methylene chloride was added with stirring 37.5 g (0.49 mol) of 1,3-propanediol. The resulting solution was chilled in an ice bath. A solution of 15.5 g (0.099 mol) of phenyl chloroformate in 30 mL of methylene chloride was added dropwise. Stirring was continued for approximately 15 min at 0 °C, then 18–24 h 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 $MgSO_4$, and evaporation of the solvent under reduced pressure yielded a residue, to which toluene was added and removed by evaporation under reduced pressure. The residue was purified by preparative TLC (chloroform), yielding 9.3 g (48.0%) of 1: mp 51–52 °C, IR (Nujol mull) 1756, 3400 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.58–7.03 (m, 5 H, Ph), 4.40 (t, J = 6.0 Hz, 2 H, CH_2), 3.78 (brt, J = 6.0 Hz, 2 H, CH_2), 2.28–1.78 (m, 3 H, CH_2, OH). Anal. Calcd for $C_{10}H_{12}O_4$: C, 61.22; H, 6.16. Found: C, 61.30; H, 6.20.

1-[[(2-Methoxy-4-methylphenoxy)carbonyl]oxy]-3-propanol (2). The synthesis of 2 was conducted on a 0.025-mol scale using the conditions described for 1, starting with the aryl chloroformate (derived from 2-methoxy-4-methylphenol) and 1,3-propanediol. The liquid was purified by preparative TLC (chloroform) to yield 3.3 g (55.0%) of 2 as an oil: IR (film) 1765, 3400 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.10–6.60 (m, 3 H, Ph), 4.40 (t, J = 6.0 Hz, 2 H, CH_2), 3.93–3.58 (m, 5 H, CH_3, CH_2), 2.33 (s, 3 H, CH_3), 2.15–1.63 (m, 3 H, CH_2, OH). Anal. Calcd for $C_{12}H_{16}O_5$: C, 59.99; H, 6.71. Found: C, 60.19; H, 6.85.

1-[[(2-Methoxyphenoxy)carbonyl]oxy]-3-propanol (3). The synthesis of 3 was conducted on a 0.01-mol scale using the conditions described for 1, starting with the aryl chloroformate (derived from 2-methoxyphenol) and 1,3-propanediol. The liquid was purified by preparative TLC (20% ethyl acetate/hexane) to yield 1.1 g (45.8%) of 3 as an oil: IR (film) 1765, 3400 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.38–6.77 (m, 4 H, Ph), 4.42 (t, J = 6.0 Hz, 2 H, CH_2), 3.92–3.60 (m, 5 H, CH_2, CH_3), 2.20–1.65 (m, 3 H, CH_2, OH). Anal. Calcd for $C_{11}H_{14}O_5$: C, 58.40; H, 6.24. Found: C, 58.31; H, 6.30.

1-[[(2-Methoxyphenoxy)carbonyl]oxy]-2,2-dimethyl-3-propanol (4). The synthesis of 4 was conducted on a 0.01-mol scale using the conditions described for 1, starting with the aryl chloroformate (derived from 2-methoxyphenol) and 2,2-dimethyl-1,3-propanediol, with the addition of the chloroformate solution conducted at room temperature. The liquid was purified by preparative TLC (20% ethyl acetate/hexane) to yield 1.4 g (51.3%) of 4 as an oil: IR (film) 1765, 3400 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.38–6.80 (m, 4 H, Ph), 4.10 (s, 2 H, CH_2), 3.85 (s, 3 H, CH_3), 3.40 (s, 2 H, CH_2), 2.25–1.88 (m, 1 H, OH), 0.98 (s, 6 H, $2CH_3$). Anal. Calcd for $C_{13}H_{18}O_5$: C, 61.41; H, 7.14. Found: C, 61.20; H, 7.34.

2-[[(2-Methoxyphenoxy)carbonyl]oxy]-4-pentanol (5). The synthesis of 5 was conducted on a 0.01-mol scale using the conditions described for 1, starting with the aryl chloroformate (derived from 2-methoxyphenol) and 2,4-pentanediol. The liquid was purified by preparative TLC (20% ethyl acetate/hexane) to yield 1.5 g (54.9%) of 5 as an oil: IR (film) 1765, 3400 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.38–6.77 (m, 4 H, Ph), 5.30–4.85 (m, 1 H, CH), 4.30–3.93 (m, 1 H, CH), 3.85 (s, 3 H, CH_3), 2.95–2.50 (m, 1 H, OH), 2.52–2.10 (m, 2 H, CH_2), 1.40 (d, J = 6.0 Hz, 3 H, CH_3), 1.22 (d, J = 6.0 Hz, 3 H, CH_3). Anal. Calcd for $C_{13}H_{18}O_5$: C, 61.41; H, 7.14. Found: C, 61.12; H, 7.10.

1-[[(2-Methoxyphenoxy)carbonyl]oxy]-4-butanol (6). The synthesis of 6 was conducted on a 0.01-mol scale using the conditions described for 4, starting with the aryl chloroformate (derived from 2-methoxyphenol) and 1,4-butanediol. The liquid was purified by preparative TLC (20% ethyl acetate/hexane) to yield 1.5 g (58.2%) of 6 as an oil: IR (film) 1765, 3400 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.38–6.80 (m, 4 H, Ph), 4.30 (t, J = 6.0 Hz, 2 H, CH_2), 3.85 (s, 3 H, CH_3), 3.80–3.55 (m, 2 H, CH_2), 2.08–1.43 (m, 5 H, 2 CH_2, OH). Anal. Calcd for $C_{12}H_{16}O_5$: C, 59.99; H, 6.71. Found: C, 59.76; H, 5.89.

1-[[(2-Methoxyphenoxy)carbonyl]oxy]-5-pentanol (7). The synthesis of 7 was conducted on a 0.01-mol scale using the conditions described for 4, starting with the aryl chloroformate (derived from 2-methoxyphenol) and 1,5-pentanediol. The liquid was purified by preparative TLC (20% ethyl acetate/hexane) to yield 1.4 g (51.3%) of 7 as

an oil: IR (film) 1765, 3400 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.37–6.77 (m, 4 H, Ph), 4.28 (t, J = 6.0 Hz, 2 H, CH_2), 3.85 (s, 3 H, CH_3), 3.75–3.5 (m, 2 H, CH_2), 2.03–1.20 (m, 7 H, 3 CH_2, OH). Anal. Calcd for $C_{13}H_{18}O_5$: C, 61.41; H, 7.14. Found: C, 61.43; H, 7.15.

2-[[(2-Methoxy-4-formylphenoxy)carbonyl]oxy]-4-pentanol (8). The synthesis of 8 was conducted on a 0.02-mol scale using the conditions described for 1, starting with the aryl chloroformate (derived from 2-methoxy-4-formylphenol) and 2,4-pentanediol. NMR, IR, and TLC data indicate the product is formed. However, a pure sample could not be isolated due to contamination by the phenolic and cyclic carbonate components. The inability to isolate a pure sample indicates rapid decomposition during isolation.

1-[(Phenoxycarbonyl)oxy]glycerol (9). To 25 mL of 10% acetic acid was added 1.5 g (0.006 mol) of 1-*O*-(phenoxycarbonyl)-2,3-*O*-isopropylideneglycerol (Pfeiffer, 1970). The emulsion was stirred vigorously and heated to 60 °C for 2 h. The solution was cooled to room temperature and extracted several times with petroleum ether and then ethyl ether. The ethyl ether layer was washed with aqueous saturated sodium bicarbonate and dried over anhydrous $MgSO_4$, followed by evaporation of the solvent under reduced pressure to yield a liquid. NMR, IR, and TLC data indicate the product was formed, however, like 8, was unstable.

1-[[(2-Methoxy-4-methylphenoxy)carbonyl]oxy]-glycerol (10). The synthesis of 10 was conducted on a 5-mmol scale using the conditions described for 9, starting with 1-*O*-[(2-methoxy-4-methylphenoxy)carbonyl]-2,3-*O*-isopropylideneglycerol (Pfeiffer, 1970). NMR, IR, and TLC data indicate the product was formed, however, like 8, was unstable.

1-[[(2-Methoxyphenoxy)carbonyl]oxy]-2-ethanol (11). The synthesis of 11 was conducted on a 0.01-mol scale using the conditions described for 1, starting with the aryl chloroformate (derived from 2-methoxyphenol) and 1,2-ethanediol. NMR, IR, and TLC data indicate the product was formed, however, like 8, was unstable.

Thermolysis of the Aryl Hydroxyalkyl Carbonates (1–7). A 10–50-mg sample of each of the aryl hydroxyalkyl carbonates was thermolyzed in a sealed tube under the specific conditions listed in Table I. The yield of released phenolic component in each case was determined by GC quantitation with an authentic sample.

ACKNOWLEDGMENT

I thank Dr. Geoffrey Chan and Dr. Yoram Houminer for helpful discussions, Dot Seal for secretarial assistance, and Ronald C. Bassfield for NMR spectral analysis.

Registry No. 1, 100899-45-4; 2, 100899-46-5; 3, 100899-47-6; 4, 100899-48-7; 5, 100899-49-8; 6, 100899-50-1; 7, 100899-51-2; 8, 100899-52-3; 9, 100899-53-4; 10, 100899-54-5; 11, 100899-55-6; *o*-$MeOC_6H_4OH$, 90-05-1; PhOH, 108-95-2; $HOCH_2CH(OH)CH_2OH$, 56-81-5; $HOCH_2CMe_2CH_2OH$, 126-30-7; $HOCH(Me)CH_2CH(Me)OH$, 625-69-4; $HO(CH_2)_4OH$, 110-63-4; $HO(CH_2)_5OH$, 111-29-5; $HO(CH_2)_2OH$, 107-21-1; $HO(CH_2)_3OH$, 504-63-2; 2-methoxy-4-methylphenol, 93-51-6; phenyl chloroformate, 1885-14-9; 2-methoxy-4-methylphenyl chloroformate, 94192-20-8; 2-methoxyphenyl chloroformate, 2293-75-6; 2-methoxy-4-formylphenyl chloroformate, 94192-21-9; 2-methoxy-4-formylphenol, 121-33-5; 1-*O*-[(2-methoxy-4-methylphenoxy)carbonyl]-2,3-*O*-isopropylideneglycerol, 100899-57-8; 1-*O*-(phenoxycarbonyl)-2,3-*O*-isopropylideneglycerol, 100899-56-7.

LITERATURE CITED

Fenaroli, G. *Fenaroli Handbook of Flavor Ingredients*; Furia, T. E., Bellanea, N., Eds.; CRC Press: Cleveland, OH, 1975.

Pfeiffer, F. R.; Miao, C. K.; Weisbach, J. A. *J. Org. Chem.* **1970**, *35*, 221.

Sarel, S.; Pohoryles, L. A.; Ben-shoshan, R. *J. Am. Chem. Soc.* **1959**, *24*, 1873.

Strain, F.; Bissinger, W. E.; Dial, W. R.; Rudoff, M.; DeWitt, B. J.; Stevens, H. C.; Langston, J. H. *J. Am. Chem. Soc.* **1950**, *72*, 1254.

Received for review October 4, 1985. Accepted January 2, 1986.

Pungent Compounds of Ginger (*Zingiber officinale* Roscoe) Extracted by Liquid Carbon Dioxide

Chu-Chin Chen,* May-Chien Kuo, Chung-May Wu, and Chi-Tang Ho

The pungent principles of ginger (*Zingiber officinale* Roscoe) were extracted by liquid carbon dioxide (600–700 psi). Individual pungent component was isolated by thin-layer chromatography (TLC) followed by preparative high-performance liquid chromatography (HPLC). Identification of pungent compounds was conducted by analytical HPLC and mass spectrometry (MS). 6-Gingerol (11.88%, w/w) was the most abundant pungent compound identified in the liquid carbon dioxide extract (CO_2(l) extract); other homologues of gingerols identified were 8-gingerol (1.67%) and 10-gingerol (2.38%). Only a trace amount of 6-shogaol was identified in the CO_2(l) extract.

INTRODUCTION

The pungent principle of ginger (*Zingiber officinale* Roscoe) has long been recognized as an important character related to the quality. To extract the pungent compounds, organic solvents such as acetone and dichloromethane can be used; the final product is dark and viscous oleoresin (Krukonis, 1984).

The knowledge of using carbon dioxide to extract plant materials has been known for 50 years; however, only recently has it been received with incresaing attentions (Moyler, 1984). It has been tried to extract the flavoring materials of vegetable or fruit juices (Schultz and Randall, 1970) and many other natural products (Caragay, 1981; Moyler 1984). This method shows great potential in replacing the conventional methods such as solvent extraction and steam distillation (Gardner, 1982; Meyer-Warnod, 1984).

Department of Food Science, Cook College, New Jersey Agricultural Experiment Station, Rutgers, The State University of New Jersey, New Brunswick, New Jersey 08903 (C.-C.C., C.-T.H.), and Food Industry Research and Development Institute (FIRDI), Hsinchu 30099, Taiwan, Republic of China (M.-C.K., C.-M.W.).

0021-8561/86/1434-0477$01.50/0