[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF ROCHESTER, ROCHESTER 20, N. Y.]

An O^{18} Tracer Study of the Decomposition of Benzoic *sec*-Butylcarbonic Anhydride: the Absence of Alkyl–Oxygen Cleavage[1a]

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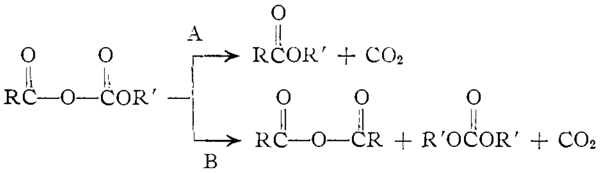
sec-Butyl chlorocarbonate and benzoic *sec*-butylcarbonic mixed anhydride have been prepared from O^{18}-labeled *sec*-butyl alcohol. Decomposition of the mixed anhydride at 150–160° leads to carbon dioxide (containing no O^{18}), *sec*-butyl benzoate and di-*sec*-butyl carbonate. Saponification of these esters separately gives, in each case, *sec*-butyl alcohol containing all of the O^{18} present in the mixed anhydride. The O^{18} content of the alcohol is determined by conversion to the chlorocarbonate, which is converted by heating with quinoline to CO_2 and *sec*-butyl chloride. There is thus no alkyl–oxygen cleavage in the decomposition of benzoic *sec*-butylcarbonic anhydride.

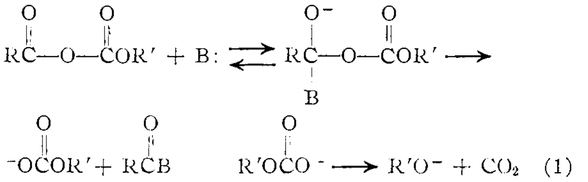
In earlier papers,[2,3] it has been shown that mixed carboxylic carbonic anhydrides decompose by two concurrent paths, A and B, yielding ester by path A, and the symmetrical anhydride and dialkyl carbonate by path B.



$$\mathrm{R\overset{\overset{O}{\|}}{C}{-}O{-}\overset{\overset{O}{\|}}{C}OR'}\ \left\{\begin{array}{l}\xrightarrow{\ A\ } \mathrm{R\overset{\overset{O}{\|}}{C}OR'} + \mathrm{CO_2}\\[2ex] \xrightarrow[\ B\ ]{} \mathrm{R\overset{\overset{O}{\|}}{C}{-}O{-}\overset{\overset{O}{\|}}{C}R} + \mathrm{R'O\overset{\overset{O}{\|}}{C}OR'} + \mathrm{CO_2}\end{array}\right.$$

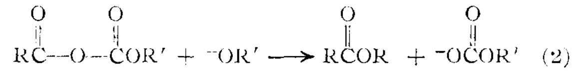
Studies on optically active benzoic *sec*-octylcarbonic anhydride showed that there was complete retention of configuration in both paths A and B, when the decomposition was carried out without solvent[2] or in pyridine solution.[3] The mesitoic *sec*-octylcarbonic anhydride also showed complete retention of configuration on decomposition.[2]

The stereochemical behavior was consistent with the proposed mechanism,[3] in which only acyl–oxygen cleavage occurs. For example, ester can be formed by base-catalyzed cleavage of the mixed anhydride (eq. 1), followed by attack of alkoxide ion on another molecule of mixed anhydride (eq. 2). The mechanism contains other steps in which ester is formed, but none of these involves alkyl-oxygen cleavage. Similarly, the alkyl carbonate is also predicted to be the result of acyl–oxygen cleavage processes.



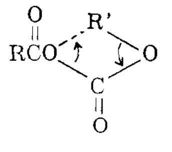
$$\mathrm{R\overset{\overset{O}{\|}}{C}{-}O{-}\overset{\overset{O}{\|}}{C}OR'} + \mathrm{B{:}} \rightleftarrows \mathrm{R\underset{\underset{B}{|}}{\overset{\overset{O^-}{|}}{C}}{-}O{-}\overset{\overset{O}{\|}}{C}OR'} \longrightarrow$$

$$\mathrm{^-O\overset{\overset{O}{\|}}{C}OR'} + \mathrm{R\overset{\overset{O}{\|}}{C}B} \qquad \mathrm{R'O\overset{\overset{O}{\|}}{C}O^-} \longrightarrow \mathrm{R'O^-} + \mathrm{CO_2} \quad (1)$$

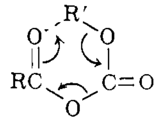


$$\mathrm{R\overset{\overset{O}{\|}}{C}{-}O{-}\overset{\overset{O}{\|}}{C}OR'} + \mathrm{^-OR'} \longrightarrow \mathrm{R\overset{\overset{O}{\|}}{C}OR} + \mathrm{^-O\overset{\overset{O}{\|}}{C}OR'} \quad (2)$$

The stereochemistry of the reaction can be explained on the basis of an SNi mechanism, which would proceed by a frontside attack on the asymmetric carbon at the alkyl–oxygen bond (I or II).



I



II

These transition states would be difficult to reconcile with kinetic data, which suggested that paths A and B were the result of a set of ionic chain reactions. Nevertheless it seemed desirable to make a tracer study of the possibility of alkyl–oxygen cleavage. This has now been done, and it has been found that there is no measurable alkyl–oxygen cleavage in either path A or B. The reactions employed are summarized in Fig. 1.

For convenience in separation, the reaction was carried out on the *sec*-butyl instead of the *sec*-octyl compound. O^{18}-Labeled *sec*-butyl alcohol[4] was converted to the chlorocarbonate III in the usual way.[2] The O^{18} label in this compound was determined quantitatively by conversion to CO_2 by heating with quinoline,[5] and the CO_2 was analyzed by mass spectrometry.

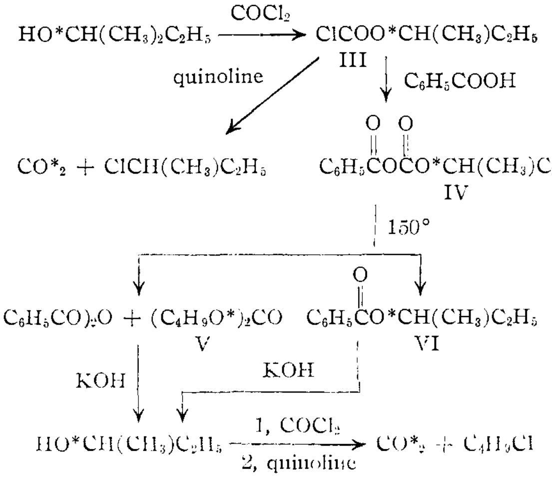


Fig. 1.

The chlorocarbonate was converted to the mixed anhydride IV in the usual way, and the latter was decomposed by heating at 150–160°; the CO_2 evolved showed no O^{18} above natural abundance, within limits of experimental error. The benzoic anhydride was partially removed from the reaction product by hydrolysis in aqueous acetone, and *sec*-butyl benzoate (VI) and di-*sec*-butyl carbonate (V) were separated by vacuum distillation. The esters were saponified separately, with potassium

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[1] (a) Aided by Grant NSF-G11240 from the National Science Foundation. (b) Esso Education Foundation Fellow, 1961–1962.

[2] D. S. Tarbell and E. J. Longosz, *J. Org. Chem.*, **24**, 774 (1959).

[3] E. J. Longosz and D. S. Tarbell, *ibid.*, **26**, 2161 (1961).

[4] C. A. Bunton, A. Konasiewicz and D. R. Llewellyn, *J. Chem. Soc.*, 604 (1955).

[5] P. Carré, *Bull. soc. chim. France*, **3**, 1061 (1936).

hydroxide in ethylene glycol; the *sec*-butyl alcohol samples were converted separately to the chlorocarbonates, and these were decomposed, as above, to CO_2 and *sec*-butyl chloride. The O^{18} in each of these CO_2 samples accounted for all of the isotope present in the original chlorocarbonate.

Table I summarizes the mass spectral data obtained. The O^{18} concentration is given by the ratio of peak 46 to peak 44 multiplied by one hundred.

TABLE I

O^{18} ANALYSES[a]

Source of CO_2	$\frac{\text{Mass 46}}{\text{Mass 44}} \times 100$
Tank (Ohio Chemical)	0.38
Chlorocarbonate III	1.40
Mixed anhydride IV[b]	0.36
Carbonate V	1.37
Ester VI	1.38

[a] The values for O^{18} concentration in Table I are the averages of two or more runs at 100μ sample pressure in the mass spectrometer. [b] Only one run at 100 mμ sample pressure.

These results show conclusively that there is no alkyl–oxygen cleavage in the decomposition of benzoic *sec*-butylcarbonic anhydride, and hence presumably none in the decomposition of other mixed anhydrides, where *R'* is primary or secondary. Transition states such as I or II are therefore not involved in the decomposition of the mixed anhydride under our conditions.[6]

It is quite possible that alkyl–oxygen cleavage may occur in mixed anhydrides where R' is a group capable of forming a relatively stable carbonium ion, such as benzyl or *tert*-butyl. We are currently studying this problem.

Experimental

Equilibration of Methyl Ethyl Ketone with Water-O^{18}.—Redistilled methyl ethyl ketone (Eastman Kodak Co. White label; 17.0 g., 0.246 mole) was mixed with 30 ml. of water-O^{18} (Isomet Corp., O^{18} = 1.575%) in a 100-ml. round-bottom flask equipped with a condenser. Three drops of concentrated sulfuric acid was added and the mixture was kept under reflux for 4 hr. The mixture was cooled in ice and a little potassium carbonate was added to neutralize the sulfuric acid. The water layer was saturated with sodium chloride to yield upon separation 15.0 g. (89%) of methyl ethyl ketone-O^{18}. The ketone was taken up in 30 ml. of ether and dried over anhydrous magnesium sulfate.

Reduction of Methyl Ethyl Ketone-O^{18}.—The ether solution of the butanone-O^{18} was added dropwise, with vigorous stirring, to 3.5 g. of lithium aluminum hydride in 250 ml. of dry ether. The reaction mixture was contained in a 500-ml. flask equipped with an addition funnel, a stirrer and a condenser protected by a drying tube. The reaction was allowed to stir for 5 hr. at room temperature. Water was then added carefully to decompose the excess lithium aluminum hydride, followed by 50 ml. of 3 *N* sulfuric acid. The ether layer was separated and dried over anhydrous magnesium sulfate.

Preparation of *sec*-Butyl Chlorocarbonate-O^{18}.—The same procedure was used in all chlorocarbonate preparations. The ether solution of 2-butanol-O^{18} was concentrated and added with stirring to 17 ml. (0.24 mole) of phosgene condensed in a 50-ml. flask and cooled with an ice-bath. After the addition was complete the reaction mixture was allowed to stand at room temperature overnight.

The mixture then was cooled to −15° with an acetone-ice-bath and kept under aspirator pressure for 1.5 hr., to remove excess phosgene. The residue was distilled *in vacuo* (17 mm.) through a 10-cm. Vigreux column. The fraction boiling at 50° was collected to yield 16.8 g. of *sec*-butyl chlorocarbonate. The yield was 62% based on the butanone. The infrared spectrum, containing a sharp absorption at 1770 cm.$^{-1}$ and no hydroxyl absorption (nothing above 3100 cm.$^{-1}$), was identical in every respect with spectra of previously prepared samples of the compound.

Benzoic *sec*-Butylcarbonic Anhydride.[2]—In a 500-ml. flask equipped with a stirrer and an addition funnel was placed 13.3 g. (0.11 mole) of benzoic acid and 11.0 g. (0.11 mole) of triethylamine in 200 ml. of dry ether. The solution was cooled in an ice-bath and 14.9 g. (0.11 mole) of *sec*-butyl chlorocarbonate-O^{18} was added dropwise with stirring. Immediately a copious precipitate of the amine hydrochloride formed. The mixture was allowed to stir for 5 hr. after the addition was complete. The precipitate of the hydrochloride was filtered off (92%) and the filtrate was washed successively with water, dilute hydrochloric acid, dilute sodium bicarbonate solution and again with water, and then was dried over magnesium sulfate. Removal of the ether left a residue of 20.7 g. (85.5%) of benzoic *sec*-butylcarbonic anhydride-O^{18}. The infrared spectrum was identical with those of previously obtained samples. *Anal.* Calcd. for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35. Found: C, 64.69; H, 6.14.

Decomposition of the Mixed Anhydride.—A sample of the anhydride (*ca.* 4 g.) was placed in a flask equipped with a reflux condenser and a side arm for admission of a dry nitrogen stream. The top of the condenser was attached to a trap cooled with liquid nitrogen, for trapping carbon dioxide. The trap had two stopcocks, one at the inlet and the other at the outlet. The outlet of the trap was connected by a standard taper joint to a small manifold which could be evacuated with an oil-pump. The manifold was equipped with an inner standard taper joint (12/30) so that a sample tube could be connected to the system. During a decomposition the sample tube was replaced by an Ascarite-filled bulb to permit free passage of nitrogen through the system. The decomposition vessel was heated to 150–160° with an oil-bath, while a slow stream of nitrogen was passed over it. The condensed carbon dioxide was transferred to the sample tube by expanding it from the trap into the evacuated manifold from a Dry Ice-acetone-bath (−78°) and recondensing it in the sample tube cooled by a liquid nitrogen bath (−196°).

Separation of the Decomposition Products of the Mixed Anhydride.—The benzoic anhydride was partially removed by treatment of the decomposition residue (*ca.* 13 g.) with 3 ml. of pyridine and 3 ml. of water in enough acetone to make a homogeneous solution. The solution was left to stand for 26 hr. at room temperature. The mixture was taken up in 100 ml. of ether and was extracted with dilute hydrochloric acid, dilute sodium bicarbonate and water. The bicarbonate washings, upon acidification and extraction with ether, yielded 1.8 g. of benzoic acid, m.p. 122°.

The ether solution of the residue was dried and concentrated. The concentrate was distilled into two fractions with a 10-cm. vacuum jacketed Vigreux column equipped with a total reflux head. The first fraction, b.p. 35° (0.5 mm.), 1.98 g., n^{20}_D 1.4057 (authentic sample n^{20}_D 1.4024), was *sec*-butyl carbonate. Its infrared spectrum was identical in every detail with that of an authentic sample. The second fraction had the properties b.p. 55° (0.5 mm.), 4.89 g., n^{20}_D 1.4893 (authentic sample n^{20}_D 1.4897). Its infrared spectrum compared well with that of authentic *sec*-butyl benzoate.

Saponification of *sec*-Butyl Benzoate and *sec*-Butyl Carbonate.—The procedure was the same for both compounds, so only one will be described. The *sec*-butyl benzoate (4.8 g.) was mixed with 6.2 g. of potassium hydroxide in 25 ml. of ethylene glycol. The mixture was stirred magnetically and heated to 85°, until the two phases merged (*ca.* 5 hr.). After 7 ml. of water was added, the mixture was neutralized to *p*H 8 (universal indicator) by careful addition of concentrated hydrochloric acid. A distillation head was attached to the flask and the *sec*-butyl alcohol–water azeotrope, b.p. 87°, was collected. The distillate was saturated with sodium chloride and extracted with ether. The extracts were dried over magnesium sulfate. The ether solution of the alcohol was used directly for the preparation of the chlorocarbonates.

Decomposition of *sec*-Butyl Chlorocarbonates-O^{18}.—The chlorocarbonates were decomposed in the same system used for the decomposition of the mixed anhydride. Into the

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[6] *Cf.* R. Boschan, *J. Am. Chem. Soc.*, **81**, 3341 (1959), and T. B. Windholz, *J. Org. Chem.*, **25**, 1703 (1960).

decomposition vessel was placed *ca.* 0.2 g. of *sec*-butyl chlorocarbonate (identified by its infrared spectrum, and mixed melting point of its carbamate derivative, m.p. 94°, with an authentic sample) and an equal amount of redistilled quinoline. The mixture was heated to 70° under a slow nitrogen stream and the carbon dioxide was condensed by liquid nitrogen.

Mass Spectral Data.—The samples of carbon dioxide to be measured in the mass spectrometer were distilled and degassed on a standard high vacuum manifold.

The instrument used was a Consolidated Electrodynamics mass spectrometer, model 21-620. It was found that with this instrument the apparent mass ratios were slightly dependent on the sample pressure in the mass spectrometer. To nullify this effect all samples reported were run at 100-μ sample pressure.

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[Contribution from the Department of Chemistry of the University of Rochester, Rochester 20, N. Y.]

The Chemistry of Some Derivatives of the 7-Oxabicyclo[2.2.1]heptene System, Especially the Epoxy Derivatives (3,8-Dioxatricyclo[3.2.1.0^{2,4}]octanes)[1]

By Martin P. Kunstmann,[2] D. Stanley Tarbell and Robert L. Autrey

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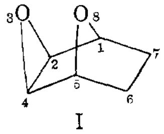
The Diels–Alder addition of ethyl acrylate to furan yields a mixture of the *exo* and *endo* isomers of 2-carbethoxy-7-oxabicyclo[2.2.1]hept-5-ene; variation of the ester function leads to several other derivatives of the 7-oxabicyclo[2.2.1]heptene system. The two epimeric 2-carboxy and 2-carbinyl derivatives have been separated and the configurations established. Epoxidation yields the epoxy compounds, (3,8-dioxatricyclo[3.2.1.0^{2,4}]octanes, or derivatives thereof, formed without Wagner–Meerwein rearrangement. The epoxidation is accompanied by some isomerization of the 2-*endo*-carboxyl group to the 2-*exo* configuration; epoxidation of the 2-carbethoxy and 2-carbinol derivatives is accompanied by some isomerization of the 2-*exo* substituent to the 2-*endo* configuration. Treatment of the dioxatricyclooctanes with various nucleophiles results in products derived from intramolecular nucleophilic displacement; products derived from Wagner-Meerwein rearrangement have not been isolated.

Introduction

In connection with studies on the antibiotic fumagillin,[3,4] information was needed concerning the behavior of compounds containing a 1,2-epoxide as well as a 1,4-epoxide grouping. The 3,8-dioxatricyclooctane system I is accessible by the Diels–Alder reaction of furan with some appropriate dienophile, followed by epoxidation of the unsaturated bicyclic compound. Some compounds derived from this system have been prepared from the adduct of furan and trifluorocrotonic acid,[5] and from the furan–maleic anhydride adduct.[6,7] The present paper describes the preparation, stereochemistry and properties of a series of 2-substituted 7-oxabicyclo[2.2.1]hept-5-enes (II), and their corresponding saturated derivatives (III). From the bicycloheptenes, members of the dioxatricyclooctane series have been obtained. The results may have some interest in connection with the chemistry of the intensively investigated norbornane-type compounds.



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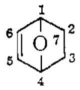

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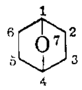
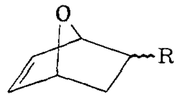


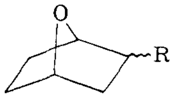
III

Preparation of the 2-Substituted-7-oxabicyclo[2.2.1]hept-5-enes.—Earlier work[8,9] on the furan–maleic anhydride adduct indicated that the equilibrium is unfavorable to the adduct and that a mixture of *endo* and *exo* products is formed. The *endo* is formed more rapidly, but the *exo* adduct is slightly more stable thermodynamically. The same relations were indicated in the present work with the furan–ethyl acrylate adduct; the equilibrium is unfavorable, both *endo* and *exo* forms result, and the latter is favored at elevated temperatures.

Treatment of furan with ethyl acrylate leads to a small yield of the adduct, a mixture of *endo*- and *exo*-2-carbethoxy-7-oxabicyclohept-5-ene (IVa). This mixture was converted into a series of related compounds (IVb to IVf) by standard procedures. The saturated bicycloheptanes (Va to Ve) were obtained by catalytic reduction. The *endo-exo* ratio in the reduced compounds could be determined by vapor phase chromatography (v.p.c.); this technique could not be applied to the unsatu-



IVa, R = $CO_2C_2H_5$
b, R = CO_2H
c, R = CH_2OH
d, R = CH_2OTos
e, R = CH_3
f, R = $C(CH_3)_2OH$



Va, R = $CO_2C_2H_5$
b, R = CO_2H
c, R = CH_2OH
d, R = CH_3
e, R = $C(CH_3)_2OH$

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[1] Aided by Grant E-1138 of the U. S. Public Health Service.

[2] Esso Fellow, 1960-1961; Summer Fellow of the National Science Foundation.

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