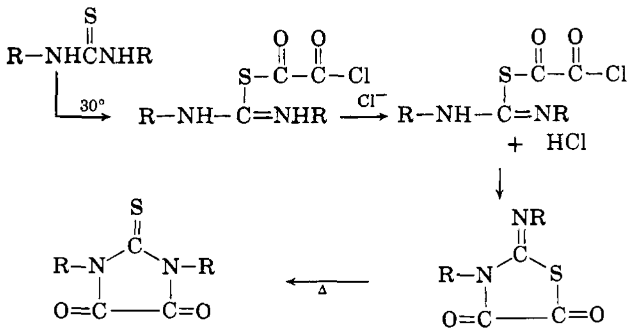
The synthesis provides a convenient route to 1,3-substituted parabanic acids using readily available 1,1,3-trisubstituted ureas. The alkyl groups are readily identified by n.m.r., leaving no doubt of the identity of the leaving group. Typical spectra for substituted parabanic acids show chemical shifts, a doublet (CH) at τ 5.65 and a quartet (CH_2) at 7.30 for the 2-propynyl group. The allyl group gives a septet (CH) at τ 4.50, a multiplet ($CH_2=$) at 5.00 and a quartet (CH_2) at 5.90. The isopropyl analog shows a septet (CH) at τ 5.65 and a doublet (CH_3) at 8.60. Spectra were measured on the Varian A-60 at 60 Mc./sec. using tetramethylsilane standard.

When 1,3-diisopropyl thiourea was treated with oxalyl chloride in refluxing benzene, the expected thioparabanic acid was obtained. When treated at 30–35°, an oil possessing a strong C=N band at 6.1 μ was obtained. The spectra strongly suggests that reaction occurred *via* attack of oxalyl chloride on sulfur to form the isomeric iminothiazolidine-4,5-dione (III).



The oil gradually formed on standing, or more rapidly on heating, a yellow solid, m.p. 128°, identified as the 2-thioparabanic acid (IV). Although an intermediate comparable to III was not observed in the reaction of ureas with oxalyl chloride, it seems likely that the reaction follows a similar course.

Experimental

3-(3,4-Dichlorophenyl)-1-(2-propynyl)parabanic Acid[5] (II).—A solution of 3-(3,4-dichlorophenyl)-3-isopropyl-3-(2-propynyl)-urea (28.5 g., 0.1 mole) and oxalyl chloride (13.0 g., 0.11 mole) in 100 ml. of benzene[6] was refluxed for 8 hr.[7]; HCl was evolved freely. The product separated on cooling. Recrystallization from methanol gave small colorless granules, m.p. 188.6–189.1°.

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[5] All compounds reported in Table I were prepared using this procedure with the appropriate urea.

[6] Benzene, toluene, or xylene can be used equally well.

[7] Heating time can be reduced; reaction can be followed and quenched when the evolution of HCl ceases.

The Preparation of Oxazolidinetriones. A Novel Cyclic Anhydride Derived from Carbamates and Oxalyl Chloride

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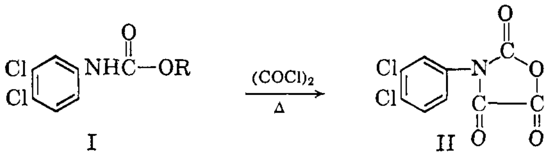
Received April 2, 1964

We have shown[1] that treatment of 1,1,3-trisubstituted alkyl ureas with oxalyl chloride gave parabanic acids *via* elimination of an alkyl group as olefin and/or halide. It seemed plausible that alkyl carbamates and carbanilates might react in an analogous manner under similar conditions. Isopropyl 3,4-dichlorocarbanilate (I) on refluxing in benzene with a slight excess of oxalyl chloride gave 3-(3,4-dichlorophenyl)oxazolidinetrione (II) with elimination of propylene (see Table I for physical constants). This ring system has not been reported.

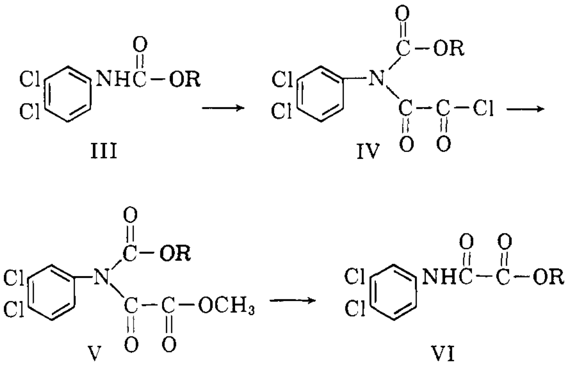


I II

a, R = i-C_3H_7; b, R = sec-C_4H_9; c, R = t-C_4H_9[2]; d, R = i-C_4H_9; e, R = C_6H_{11}

The same treatment of the *sec*-butyl, *t*-butyl, isobutyl, or cyclohexyl 3,4-dichlorocarbanilates gave II.

When the methyl, ethyl, and *n*-propyl 3,4-dichlorocarbanilates were similarly treated, the anhydride (II) was not obtained, but instead 60–80% yields of the corresponding carboalkoxy-3,4-dichlorooxanilyl chlorides (IV) were obtained. The cyclization (IV to II) could not be forced by increasing the reaction time from 3 to 36 hr., increasing the temperature from 80 to 210°, or using more polar solvents.



III IV V VI

a, R = CH_3; b, R = C_2H_5; c, R = n-C_3H_7

Excess methanol and IV reacted exothermically giving the corresponding methyl carboalkoxyoxanilates (V). Ethanol and propanol gave the corresponding esters of V (see Table II for physical constants of the esters and chlorides). Refluxing IV with methanol, ethanol, or propanol, gave the corresponding oxanilates

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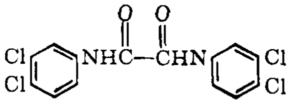
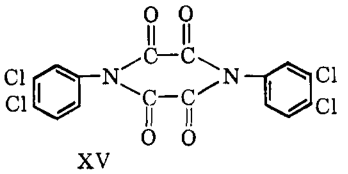
[1] P. J. Stoffel, **29**, *J. Org. Chem.*, 2794 (1964).

[2] The *t*-butyl ester, at reflux, gave two products identified as follows.



XIV

and

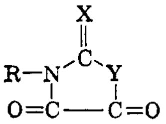


XV

This can be reasonably explained as a preferential acid hydrolysis of the *t*-butyl ester to the carbanilic acid with simultaneous decarboxylation to the aniline. The aniline then reacts with 1 or 2 moles of oxalyl chloride to give the two products. II was obtained by holding the reaction at 30–40°.

TABLE I

OXAZOLIDINETRIONES AND THIO ANALOGS

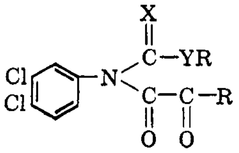


R	X	Y	Yield, %	M.p., °C.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found.	Nitrogen, % Calcd.	Nitrogen, % Found	Chlorine, % Calcd.	Chlorine, % Found
3,4-Dichlorophenyl	O	O	67.5	175[a]	41.55	41.62	1.15	1.85	5.38	5.39	27.15	27.24
Phenyl	O	O	65.5	137[a]	56.60	56.62	2.62	2.59	7.34	7.40	...	...
3,4-Dichlorophenyl	O	S	91.6	179.9–180.5	39.20	39.15	1.09	1.31	5.08	5.15	25.70	25.78
3,4-Dichlorophenyl	S	S	72.5	150.5–151.0	37.10	37.15	1.03	1.37	4.80	4.89	24.30	24.35
4-Nitrophenyl	O	O	78.3	155[a]	45.80	45.78	1.70	2.21	11.85	11.32	...	...
3-Nitrophenyl	O	O	95.5	177.6–178.4	45.80	45.88	1.70	1.85	11.85	11.77	...	...
4-Methylphenyl	O	O	93.0	148–149	58.60	58.65	3.42	3.84	6.83	6.87	...	...
4-Ethoxyphenyl	O	O	62.0	162[a]	56.20	56.23	3.80	4.12	5.90	5.95	...	...
3-Chlorophenyl	O	O	79.0	74[a]	48.00	47.50	1.78	2.20	6.23	6.43	...	...
3,4-Dichlorobenzyl	O	O	66.0	126–128	...	...	...	...	5.10	5.25	26.00	26.52
Methyl	O	O	79.0	114[a]	27.90	27.92	2.32	2.27	10.70	10.65		

[a] Decomposition point.

TABLE II

CARBOALKOXYOXANILYL CHLORIDES AND ESTERS



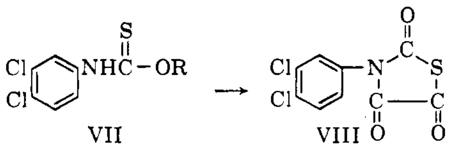
R	R′	Y	Y	Yield, %	M.p., °C.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found	Chlorine, % Calcd.	Chlorine, % Found
CH_3	Cl	O	O	69.0	101–102	38.85	38.90	2.05	2.29	4.55	4.55	34.40	34.73
C_2H_5	Cl	O	O	78.8	102–103	40.75	41.00	2.46	2.80	4.32	4.20	32.80	32.65
C_3H_7	Cl	O	O	88.7	56–57	42.50	42.65	2.95	3.20	4.12	4.23	31.50	31.40
C_2H_5	Cl	S	S	81.0	146[a]	37.00	37.11	2.24	2.41	3.93	3.87	29.90	30.02
CH_3	Cl	S	S	90.0	143[a]	35.10	35.18	1.75	2.02	...	...	31.10	30.95
i-C_3H_7	Cl	S	S	86.0	[b]	[c]							
CH_3	Cl	O	S	79.5	36–37	36.90	37.04	1.84	2.31	...	...	32.60	32.81
C_2H_5	Cl	O	S	66.5	35–36	38.90	38.72	2.36	2.51	...	...	31.40	31.23
i-C_3H_7	Cl	O	S	68.8	32–33	40.60	40.70	3.93	4.06	3.94	3.81	30.00	30.21
C_2H_5	CH_3	O	S	85.1	77.3–78.0	43.00	42.81	3.27	3.34	4.17	4.16	21.10	21.15
CH_3	CH_3	O	S	69.5	51.0–52.0	41.00	41.20	2.35	2.37	...	...	20.90	20.87
C_2H_5	CH_3	O	O	92.2	100.3–100.8	40.75	41.00	2.46	2.80	4.32	4.26	32.80	42.65

[a] Decomposition points. [b] Decomposes rapidly at 30°. [c] Too unstable for analysis, but gives expected methyl oxanilate with methanol. The oxanilyl chlorides and esters were all prepared following the procedures for IVa and Vb under Experimental.

VI. The structural assignments for III to VI are readily determined by proton nuclear magnetic resonance.

It was evident that the successful cyclization of alkyl carbanilates (I to II) was directly related to the ease of elimination of the alkyl group as a carbonium ion.

The investigation was extended to the thiono-, thiol-, and dithiocarbanilates. The thionocarbanilates (VII) reacted readily with oxalyl chloride in benzene under relatively mild conditions (30–80°) giving the thioazolidinetrione VIII. In contrast to our inability to cyclize primary alkyl carbanilates (III to II) at temperatures to 210°, the thionocarbanilates gave the cyclic product VIII eliminating any alkyl groups whether primary or secondary. It was apparent that additional and important factors were involved in the elimination reaction and the remaining thiol and dithiocarbanilates were examined.



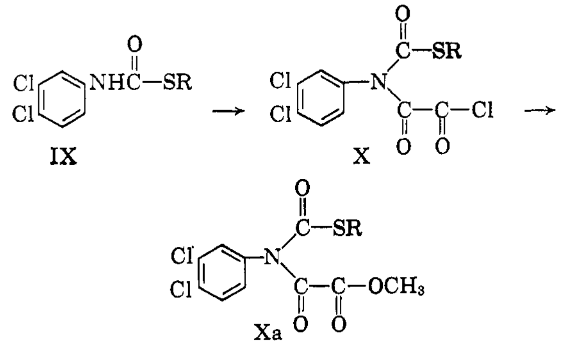
VII VIII

a, R = CH_3; b, R = C_2H_5; c, R = i-C_3H_7

Treatment of the alkyl thiolcarbanilates (IX) with oxalyl chloride at 170–180° did not give the corresponding cyclic oxazolidinedione-2-thione. The carbothioalkoxyoxanilyl chlorides (X) were obtained in all cases. More drastic treatment led to the complete destruction of X with no observable formation of the cyclic thione.

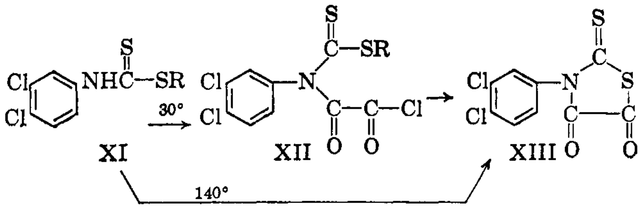
Treatment of X with excess methanol gave the methyl esters (Xa) and methyl oxanilate (VIa) at 25–30° and reflux, respectively.

Treatment of the alkyl dithiocarbanilates (XI) with oxalyl chloride in benzene at 30° gave the carbodithio-



a, R = CH_3; b, R = C_2H_5; c, R = n-C_3H_7; d, R = i-C_3H_7

alkoxyoxanilyl chlorides (XII) in all cases. Refluxing XI or XII in xylene with oxalyl chloride gave thiazolidinedione-2-thione (XIII) in all cases.



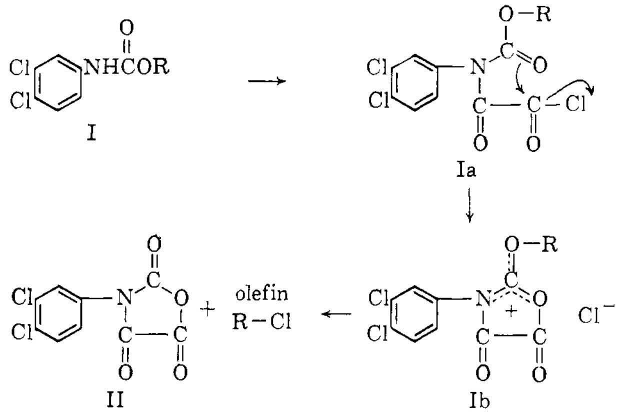
a, R = CH_3; b, R = C_2H_5; c, R = i-C_3H_7

Treatment of XIII with alcohol gave the corresponding oxanilates (VI). We have not been able to isolate the esters corresponding to V or Xa.

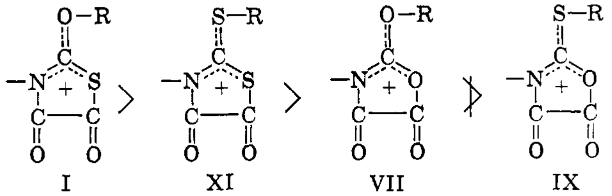
It has been clearly demonstrated that a marked delineation exists in the treatment of normal *vs.* branched alkyl carbanilates with oxalyl chloride; that *sec*-, iso-, and *t*-alkyl carbanilates cyclized readily to the anhydride (II) with the elimination of the alkyl group as olefin and/or halide. In contrast, the normal alkyl carbanilates gave only the noncyclized N-carboalkoxyoxanilyl chlorides (IV) and did not cyclize under drastic heating.

The mechanism for cyclization can be visualized as proceeding *via* the oxanilyl chloride (Ia).[3] Nucleophilic attack by carbonyl oxygen with elimination of chloride ion would give the carbonium ion Ib which would be stabilized by the distribution of charge among four atoms.

Attack by chloride ion on the carbonyl carbon of Ib would lead to regeneration of the oxanilyl chloride (Ia). When R = CH_3, C_2H_5, and n-C_3H_6, this pathway is more favorable than the second route to anhydride II. However, when R is capable of forming a relatively stable carbonium ion (*sec*- and *i*-C_3H_7, *t*-C_4H_9, and C_6H_{11}), anhydride II formation is favored. Addition of chloride or abstraction of a proton would give both olefin and alkyl halide observed experimentally.



The apparent anomaly of the thiocarbanilates can be explained by the known greater nucleophilicity of sulfur over oxygen. The observed order of ease of cyclization is the following.



Data would indicate that the ease of cyclization and alkyl elimination is intrinsically dependent upon the initial nucleophilic attack and the relative ease of formation of the incipient carbonyl and thiocarbonyl bond. The greater nucleophilicity of sulfur would place I and XI > VII and IX. The relative ease of formation of $=\overset{+}{O}R$ *vs.* $=\overset{+}{S}R$ would correctly place I > XI and VII > IX. Experimentally, the thiocarbanilates leading to I and XI cyclize irrespective of the ester group but XI requires stronger heating. The carbanilates leading to VII undergo cyclization only when a relatively stable carbonium ion can be formed, while the carbanilates leading to IX do not cyclize under any condition regardless of the nature of the ester function.

Experimental

3-(3,4-Dichlorophenyl)oxazolidinetrione (II).—A slurry of isopropyl 3,4-dichlorocarbanilate (49.6 g., 0.2 mole) and oxalyl chloride (25.4 g., 0.2 mole) in 50 ml. of toluene was refluxed for 6 hr. After cooling, the addition of 300 ml. of hexane precipitated the product. The crude product was dissolved in the minimum amount of acetone and stirred into 300 ml. of boiling carbon tetrachloride. On cooling the product crystallized in small white granules, m.p. 175° dec., 43.0 g., 52.5%.

Anal. Calcd. for $C_9H_3Cl_2NO_4$ (260.1): C, 41.55; H, 1.15; Cl, 27.15; N, 5.38. Found: C, 41.62; H, 1.85; Cl, 27.24; N, 5.39.

Methyl 3,4-Dichlorooxanilate (VIa).—3-(3,4-Dichlorophenyl)-oxazolidinetrione (13.0 g., 0.05 mole) was added to excess methanol (40 ml.). A vigorous reaction ensued, and CO_2 was evolved. On cooling, the product crystallized in small white plates, m.p. 163.6–164.2°, 11.1 g., 90.5%.

Anal. Calcd. for $C_9H_7Cl_2NO_3$ (248.1): Cl, 28.60; N, 5.65. Found: Cl, 28.77; N, 5.68.

N-(Carbomethoxy)-3,4-dichlorooxanilyl Chloride (IVa).—A solution of methyl 3,4-dichlorocarbanilate (22.0 g., 0.1 mole) and oxalyl chloride (12.7 g., 0.1 mole) in 50 ml. of benzene was refluxed for 6 hr. The crude product separated on adding 200 ml. of hexane to the cooled solution. Small white plates were formed upon recrystallization from toluene, m.p. 100.4–101.2°, 25.4 g., 82.0%.

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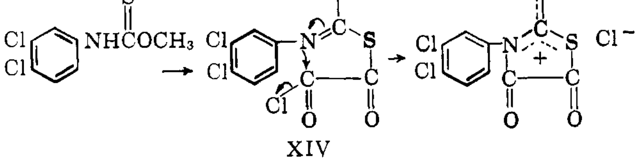
(3) Initial attack of oxalyl chloride by oxygen or sulfur would give the same intermediate corresponding to Ib. Whereas the carboalkoxyoxanilyl



chlorides (IV, X, and XII) have been isolated and characterized, we have no evidence for the existence of XIV.

Anal. Calcd. for $C_{10}H_6Cl_3NO_4$ (310.6): C, 38.85; H, 2.05; Cl, 34.40; N, 4.55. Found: C, 38.90; H, 2.29; Cl, 34.73; N, 4.55.

The product reacts exothermically with methanol to give methyl 3,4-dichlorooxanilate, identical with the product prepared from the cyclic anhydride II.

Methyl N-(Carboethoxy)-3,4-dichlorooxanilate (Vb).—A solution of N-carboethoxy-3,4-dichlorooxanilyl chloride (6.3 g., 0.02 mole) in a large excess of methanol (60 ml.) was allowed to react at 30-35° for 3 hr. Excess methanol was removed at 30–35° and the crude product was recrystallized from hexane as small white plates, m.p. 100.3–100.8°, 5.9 g., 92.2%.

Anal. Calcd. for $C_{12}H_{11}Cl_2NO_5$: C, 40.75; H, 2.46; Cl, 32.80; N, 4.32. Found: C, 41.00; H, 2.80; Cl, 32.65; N, 4.26.

3-(3,4-Dichlorophenyl)thiazolidinetrione (VIII).—Oxalyl chloride (12.7 g., 0.1 mole) was added dropwise to a solution of isopropyl 3,4-dichlorothionocarbanilate (26.4 g., 0.1 mole) in 50 ml. of toluene. The reaction was exothermic and HCl was evolved. After stirring for 1 hr., the solution was stirred into 250 ml. of hexane, precipitating the product. Fine white granules crystallized from toluene, m.p. 179.9–180.5°, 24.0 g., 91.6%.

Anal. Calcd. for $C_9H_3Cl_2NO_3S$ (276.1): C, 39.20; H, 1.09; Cl, 25.70; N, 5.08; S, 11.60. Found: C, 39.15; H, 1.25; Cl, 25.80; N, 5.15; S, 11.55.

The compound was also obtained on treating methyl or ethyl 3,4-dichlorothionocarbanilate with oxalyl chloride as above. Infrared and n.m.r. data are identical.

3-(3,4-Dichlorophenyl)thiazolidinedione-2-trione (XIII).—A solution of methyl 3,4-dichlorodithiocarbanilate (18.8 g., 0.075 mole) and oxalyl chloride (10.0 g., 0.08 mole) in 100 ml. of xylene was refluxed for 24 hr. HCl was evolved and a brilliant yellow color developed. Toluene was removed under vacuum at 50° leaving a gummy orange solid. Recrystallization from benzene gave bright orange needles, m.p. 150.5–151.2°, 16.0 g., 72.5%.

Anal. Calcd. for $C_9H_3Cl_2NO_2S_2$ (292.1): C, 37.10; H, 1.03; Cl, 24.30; N, 4.80; S, 21.90. Found: C, 37.15; H, 1.37; Cl, 24.35; N, 4.89; S, 21.52.

The Synthesis of Oxetane-d_6

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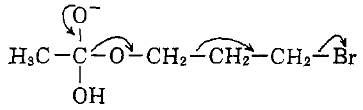
Received March 24, 1964

The far-infrared spectrum of oxetane (trimethylene oxide) is of value in connection with the structure of this and related four-membered ring molecules. To assist in the interpretation of the far-infrared results, it became necessary to prepare oxetane-d_6. We have synthesized this derivative and report its preparation here. The spectroscopic studies are reported elsewhere.[2]

Oxetane has been prepared previously by several routes, all starting with 1,3-propanediol.[3–9] Most of these involve three steps and give a low final yield. Further, impurities are formed in the final step which are difficult to remove from a small amount of volatile product. In this work a two-step synthesis has been used which is a modification of those of Derrick and Bissell[4] and Searles.[6] It consists of treatment of 1,3-propanediol with acetyl bromide to form γ-bromopropyl acetate, which is then converted to oxetane with strong base.

The starting material, 1,3-propane-d_6-diol, was prepared from diethyl malonate-d_2 and lithium aluminum deuteride. Deuteration of diethyl malonate with deuterium oxide containing sodium carbonate was more than 98% complete after 4 days at room temperature. The heavy glycol was converted to γ-bromopropyl-d_6 acetate by treatment with *freshly distilled* acetyl bromide. The acyl bromide was used because direct conversion to the acetate derivative[4] made unnecessary the isolation of the usual halohydrin intermediate,[5] and by employing the bromohydrin rather than the usual chlorohydrin, separation of allyl chloride (b.p. 47°, oxetane b.p. 48°) from oxetane-d_6 was avoided. The unsaturated chloride is formed as a dehydration by-product during the final step of the synthesis.

Ring closure was effected under conditions similar to those of Searles, *et al.*[7] In addition to the desired oxetane-d_6, however, a second volatile product was trapped from the reaction mixture and identified spectroscopically as ethylene-d_4. Ethylene has not been previously isolated during the preparation of oxetane and represents the simplest possible example of a 1–3 cleavage reaction. This type of elimination had been earlier observed to occur during formation of substituted oxetanes by the intramolecular Williamson reaction. Thus, during the preparation of 2,2-dimethyloxetane from 3-bromo-2,2-dimethyl-1-propanol[10] and during the preparation of 1-methyl-3-ethyloxetane from 2-chloro-4-hexanol,[11] considerable quantities of isobutylene and propylene respectively have been obtained.



$$\mathrm{H_3C{-}\underset{OH}{\overset{O^-}{C}}{-}O{-}CH_2{-}CH_2{-}CH_2{-}Br}$$

Complete separation of the olefin from the less volatile cyclic ether was accomplished by repeated low-temperature trap-to-trap distillations. The isotopic purity of the final product was 98.8% as determined by mass spectrometry, and by-product contamination was less than 0.1% as judged by vapor phase chromatographic analysis.

Experimental

Deuterium Exchange of Diethyl Malonate with Deuterium Oxide.—All operations were carried out under anhydrous atmospheric conditions and all glass apparatus was dried at 140° for at least 10 hr. before use. To 100 g. (0.63 mole) of diethyl malonate was added a solution of 3 g. (0.03 mole) of sodium carbonate (dried at 140°) dissolved in 100 g. (5 moles) of deuterium oxide. The flask was sealed and then stirred for a 24-hr. period. At the end of that time the flask was opened and the organic phase was separated from the aqueous phase. The above procedure was repeated three times with 100-g. portions of deuterium oxide containing 3 g. of sodium carbonate in each exchange. Following the fourth exchange the ester was washed with three 10-ml. portions of deuterium oxide and dried over anhydrous magnesium sulfate. The yield of diethyl malonate-d_2 was 51 g. (50%).

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[1] (a) National Bureau of Standards, Washington 25, D. C.; (b) Department of Chemistry, Bowdoin College, Brunswick, Maine.

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