(ii) **With 75 Mole % Sodium Methoxide.**—A suspension of 13.05 g. (0.242 mole) of sodium methoxide in 50 g. (0.322 mole) of VIII was placed in a 200-ml. centrifuge bottle connected to a stillhead and arranged for stirring. The stillhead was connected to a Dry Ice–acetone cold trap so that any distillate would pass a water condenser and then into the cold trap. The stirrer was started and the reaction mixture was heated to 255–260° for one and three-quarter hours. At this time 7.11 g. (92%) of methanol had collected at the water condenser and 7.0 g. of material had collected in the cold trap. Distillation of this latter material to a second cold trap gave 6.5 g. (50%) of dimethyl ether, identified as its boron trifluoride complex.[13] The reaction mixture was cooled, 50 ml. of dry ether was added and the suspension was centrifuged. After the solid had been extracted with a total of 200 ml. of ether, the ether was evaporated and the residue distilled to give 21.0 g. (42%) of unchanged γ-cyanopropylketene dimethylacetal (VIII), b.p. 109–110° (9 mm.), $n^{25}\mathrm{D}$ 1.4488. The residue from the ether extraction was suspended in 100 ml. of ether and 14.5 g. (0.242 mole) of glacial acetic acid was added slowly with stirring. The resulting suspension was centrifuged and the sodium acetate was triturated with ether and centrifuged three times. Evaporation of the ether and distillation of the product gave 13.60 g. (61.4%) of 2-cyanocyclopentanone (XVIII), b.p. 135–136° (15 mm.), $n^{25}\mathrm{D}$ 1.4658. Redistillation of this product gave 12.3 g. of pure XVIII, b.p. 123–124° (8 mm.), $n^{25}\mathrm{D}$ 1.4672.

In the same apparatus used above a suspension of 11 g. (0.204 mole) of sodium methoxide in 42 g. (0.33 mole) of cyanomethylketene dimethylacetal (VI) was heated to 200° at which time a vigorous, exothermic reaction commenced. The reaction maintained itself for 10 minutes, during which time 7 g. (100%) of methanol had been collected. The reaction was then stopped by placing the flask in cold water. The reaction mixture had solidified and expanded to fill the centrifuge bottle. The cooled product was a hard black solid from which only 1 g. of methyl δ-cyanopropionate was extracted after acidification with acetic acid.

A suspension of 4.0 g. (0.075 mole) of sodium methoxide in 14.1 g. (0.10 mole) of β-cyanoethylketene dimethylacetal (VII) was heated to 240° as described above. After 40 minutes, during which time 2.1 g. (88%) of methanol and 1.6 g. (46%) of dimethyl ether were collected, the reaction was stopped. The reaction mixture was worked up in the usual way, except that ethyl acetate rather than ether was used for the extraction, to give a recovery of 4.05 g. (28.5%) of VII, b.p. 95–96° (8 mm.), $n^{25}\mathrm{D}$ 1.4446. The basic residue was neutralized with 4.45 g. (0.075 mole) of glacial acetic acid, but only a small amount of tar was obtained by extraction. More tar was obtained by dissolving the solid residues in 50 ml. of water acidified with 2 ml. of concentrated sulfuric acid.

Madison, Wisconsin Received October 1, 1951

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[13] A. W. Laubengayer and G. R. Findlay, This Journal, **65**, 884 (1943).

[Contribution from the Laboratory of Organic Chemistry of the University of Wisconsin]

Ketene Acetals. XXVII. The Bromination of Various Ketene Acetals

By S. M. McElvain and William R. Davie[1]

Monosubstituted ketene acetals (II, III and IV), when added to a solution of bromine, yield the corresponding bromoesters and alkyl halides (reaction 1). A reverse order of mixing of the reactants causes II and III to follow reaction 2 to a large extent; the resulting γ-bromo-β,β-dialkoxyesters (X and XI) are readily converted by pyrolysis to the tetronic acid enol ethers (XII and XIII). Under certain conditions dimethyl α,α'-diphenylsuccinate (XIV) may be formed during the bromination of the phenylketene acetal (III); possible reactions (4 and 5) to account for the formation of XIV are discussed. The cyanoketene acetal (IV) follows a different bromination course to yield a bromocyanoketene acetal (XVII) *via* reaction 6. The dimethylketene acetal (XVIII), which yields only methyl α-bromoisobutyrate regardless of the method of bromination, is converted in part to the corresponding bromo-orthoester XXII when brominated in the presence of an orthoester. A mechanism for this unusual reaction is shown in reactions 7 and 7a. Bromination of the unsubstituted ketene diethylacetal (XXIV) is complicated by the ease of polymerization of this compound; the only pure products that could be isolated were the mono- and dibromoesters XXV and XXVII. The structures and properties of the two products resulting from the action of diazomethane on 3,5-diphenyltetronic acid (XXIX) have been determined (reaction 10).

In the third paper[2] of this series the bromination of bromoketene diethylacetal (I) was described. At 0–5° this ketene acetal absorbed only 0.7 of an equivalent of bromine. This apparently incomplete absorption of bromine was shown to be the result of two concurrent reactions, in one of which the bromine added to an equivalent of the ketene acetal to give ethyl dibromoacetate (V) and ethyl bromide (reaction 1) while in the other (reaction 2) bromine reacted with two equivalents of the ketene acetal to yield the ketal of a tribromoacetoacetic ester (IX) and ethyl bromide.

The present paper reports the results of a study of the reaction of bromine with methylketene diethylacetal (II), phenylketene dimethylacetal (III), cyanoketene dimethylacetal (IV), dimethylketene dimethylacetal (XVIII) and ketene diethylacetal (XXIV).

With the exception of the unsubstituted ketene acetal XXIV, each of these acetals consumed practically the theoretical amount of bromine, when it was added to a solution of bromine in carbon tetrachloride at 0–5°, and yielded the corresponding bromoester VI, VII or VIII *via* reaction 1. The disubstituted ketene acetal XVIII gave similar results when the order of addition was reversed so that a high initial excess of the ketene acetal was present. However, under these latter reaction conditions, the monosubstituted ketene acetals II, III and IV showed significantly different behaviors.

When bromine was added to methylketene acetal (II) at 0–5° only 58% of the theoretical amount was absorbed; similar results were obtained when the bromination was conducted at −78°. The only reaction products were the bromoester VI (20%) and the bromoketal X (77%) (reaction 2). This latter product could be distilled at 0.5 mm., but at higher pressures, *e.g.*, 15 mm., distillation converted X to the tetronic acid enol ether XII with the elimination of alcohol and ethyl bromide (reaction 3).

The phenylketene acetal IV absorbed 92% of the theoretical amount of bromine at 0–5° when a

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[1] Wisconsin Alumni Research Foundation Research Assistant, 1950–1951.

[2] A. Magnani and S. M. McElvain, This Journal, **60**, 2210 (1938).

$$\text{RCH}{=}\text{C(OR}')_2 + \text{Br}_2 \longrightarrow \text{RCHBrCOOR}' + \text{R}'\text{Br} \quad (1)$$

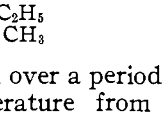
I, R is Br, R′ is C_2H_5 V, R is Br, R′ is C_2H_5
II, R is CH_3, R′ is C_2H_5 VI, R is CH_3, R′ is C_2H_5
III, R is C_6H_5, R′ is CH_3 VII, R is C_6H_5, R′ is CH_3
IV, R is CN, R′ is CH_3 VIII, R is CN, R′ is CH_3

$$2\text{RCH}{=}\text{C(OR}')_2 + \text{Br}_2 \longrightarrow$$

$$\text{I, II or III} \quad \text{R}'\text{Br} + \text{RCHBrC(OR}')_2\text{CHRCOOR}' \quad (2)$$

IX, R is Br, R′ is C_2H_5
X, R is CH_3, R′ is C_3H_5
XI, R is C_6H_5, R′ is CH_3

$$\text{X or XI} \xrightarrow{\Delta} \text{R}'\text{OH} + \text{R}'\text{Br} +$$



(3)

XII, R is CH_3, R′ is C_2H_5
XIII, R is C_6H_5, R′ is CH_3

solution of the latter was added over a period of 20 minutes; varying the temperature from −20 to 60° did not materially change the amount of bromine consumed. However, lengthening the time for addition of bromine to four hours at −20° decreased the absorption to 77% and from this reaction was isolated by distillation the bromoester VII, the enol ether XIII, *dl*-dimethyl α,α'-diphenylsuccinate (XIV) (6–12%), and a small amount of an unidentified high-melting (300–305°) solid. The enol ether XIII doubtless resulted from the pyrolysis of the bromoketal XI (reaction 3).

The origin of the succinic ester XIV is not as obvious. It may have resulted from an attack on III by bromine atoms (reaction 4) or by oxygen of the air; the latter seems more likely. Samples of III previously have been observed in this Laboratory to deposit crystals of XIV on exposure to air or on standing in partially filled bottles. Indeed, III was found to absorb oxygen rapidly, either on stirring or standing in an atmosphere of oxygen, with the formation of XIV (37%), together with similar amounts of benzaldehyde and dimethyl carbonate (reaction 5).

$$\text{III} + \text{Br}\cdot \longrightarrow \text{CH}_3\text{Br} + \text{C}_6\text{H}_5\text{CHCOOCH}_3 \xrightarrow{\text{dimerize}} \underset{\text{XIV}}{\begin{array}{c}\text{C}_6\text{H}_5\text{CHCOOCH}_3\\ |\\ \text{C}_6\text{H}_5\text{CHCOOCH}_3\end{array}} \quad (4)$$

$$\text{III} + \text{O}_2 \longrightarrow \text{C}_6\text{H}_5\text{CHO} + \text{O}{=}\text{C(OCH}_3)_2 + \text{XIV} \quad (5)$$

XIV is also formed by the interaction of III and the bromoester VII at 150–170°, and the occurrence of this reaction during the distillation of the bromination products of III could account for the formation of XIV, if any of the unreacted ketene acetal were available. This possibility is quite unlikely, as the bromination of III was continued to a permanent bromine color.

The addition of bromine to cyanoketene dimethylacetal (IV) stopped after 60% of one equivalent had been absorbed. The reaction products were relatively low boiling and consisted of VIII (8%), methyl cyanoacetate (XVI) (48%) and cyanobromoketene dimethylacetal (XVII) (43%). The small amount of VIII produced in this bromination indicated that reaction 1 was strongly suppressed by reaction 6, in which the initially formed carbonium ion (XV) is deprotonated by a second molecule of IV more rapidly than it reacts with the bromide anion to form VIII. Doubtless the negative bromo and cyano substituents are responsible for the facile loss of the proton of XV.

$$\text{IV} + \text{Br}_2 \longrightarrow \text{Br}^- + \underset{\text{XV}}{[\text{CNCHBr}\overset{+}{\text{C}}\text{(OCH}_3)_2]} \xrightarrow{\text{IV}}$$

$$\text{CH}_3\text{Br} + \underset{\text{XVI}}{\text{CNCH}_2\text{COOCH}_3} + \underset{\text{XVII}}{\text{CNCBr}{=}\text{C(OCH}_3)_2} \quad (6)$$

The disubstituted ketene acetal (XVIII), which yields only methyl α-bromoisobutyrate (XX) on treatment with bromine (reaction 7) regardless of the order of mixing of the reactants, shows an interesting reaction when it is brominated in the presence of an orthoester. This reaction was discovered when a sample of XVIII containing a small amount of unremoved orthoester (XXI) was used in a bromination experiment. The bromine absorption was correspondingly lower and, in addition to the expected bromoester XX, the bromo-orthoester XXII was isolated. Repetition of the experiment with equal amounts of XVIII and XXI gave a 42% yield of the bromo-orthoester XXII and a 47% yield of XX. This reaction doubtless involves the intermediate carbonium ion XIX, which preferentially removes a methoxyl group from the orthoester XXI to form XXII and XXIII *via* reaction 7a. The validity of this mechanism was shown by the bromination of XVIII at 0–5° in the presence of methyl orthopropionate. In this case 96% of the theoretical amount of bromine was absorbed and the reaction products were XX (43%), XXII (51%) and methyl propionate (39%); 46% of the methyl orthopropionate was recovered. This preparation of XXII is of particular interest in view of the uniformly unsuccessful attempts to prepare it by the direct bromination of methyl orthoisobutyrate[3] (XXI).

$$\underset{\text{XVIII}}{(\text{CH}_3)_2\text{C}{=}\text{C(OCH}_3)_2} + \text{Br}_2 \longrightarrow$$

$$\underset{\text{XIX}}{[(\text{CH}_3)_2\text{CBr}\overset{+}{\text{C}}\text{(OCH}_3)_2]} + \overset{-}{\text{Br}} \longrightarrow$$

$$\text{CH}_3\text{Br} + \underset{\text{XX}}{(\text{CH}_3)_2\text{CBrCOOCH}_3} \quad (7)$$

$$\text{XIX} + \underset{\text{XXI}}{(\text{CH}_3)_2\text{CHC(OCH}_3)_3} \longrightarrow$$

$$\underset{\text{XXII}}{(\text{CH}_3)_2\text{CBrC(OCH}_3)_3} + (\text{CH}_3)_2\text{CH}\overset{+}{\text{C}}\text{(OCH}_3)_2 \xrightarrow{\text{Br}^-}$$

$$\text{CH}_3\text{Br} + \underset{\text{XXIII}}{(\text{CH}_3)_2\text{CHCOOCH}_3} \quad (7a)$$

Ketene diethylacetal (XXIV) showed the most complex reaction pattern with bromine. When XXIV was added to bromine at 0–5°, approximately 85% of an equivalent of the latter was decolorized, but the only pure products that could be isolated were ethyl acetate, ethyl bromoacetate and a small amount of ethyl dibromoacetate (XXVII). When a few drops of a bromine solution was added to a chloroform solution of XXIV at −78°, the ketene acetal was converted to its polymer.[4] At 50–60° XXIV absorbed 79–86% of an equivalent of bromine and from this reaction was obtained the bromoesters XXV (28%) and XXVII

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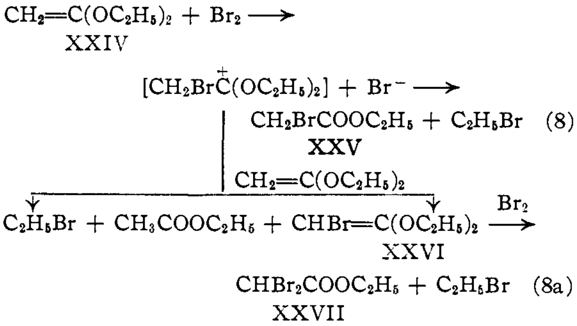
[3] R. E. Kent, Ph.D. Thesis, University of Wisconsin, 1944.

[4] P. R. Johnson, H. M. Barnes and S. M. McElvain, THIS JOURNAL, **62**, 964 (1940).

(9%), and ethyl acetate (29%), together with a mixture of higher boiling bromine-containing products which underwent continuous decomposition during distillation and could not be separated into any pure components. It would appear that the bromoesters are formed *via* reactions 8 and 8a and that the higher boiling products resulted from the various bromination–dimerization reactions involving the ketene acetals XXIV and XXVI, in the manner of reaction 2, followed by the incomplete pyrolysis of the resulting products as in reaction 3.



$$CH_2{=}C(OC_2H_5)_2 + Br_2 \longrightarrow$$

XXIV

$$[CH_2Br\overset{+}{C}(OC_2H_5)_2] + Br^- \longrightarrow$$

$$CH_2BrCOOC_2H_5 + C_2H_5Br \quad (8)$$

XXV

$$CH_2{=}C(OC_2H_5)_2$$

$$C_2H_5Br + CH_3COOC_2H_5 + CHBr{=}C(OC_2H_5)_2 \xrightarrow{Br_2}$$

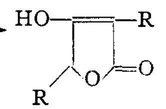
XXVI

$$CHBr_2COOC_2H_5 + C_2H_5Br \quad (8a)$$

XXVII

The Tetronic Acid Enol Ethers XII and XIII.—The tetronic acids, XXVIII and XXIX, were prepared from the corresponding bromoketoesters *via* reaction 9.[5] These acids were converted to enol ethers XII and XIII by reactions (10) and (11).

$$RCHBrCOCHRCOOC_2H_5 \xrightarrow{\Delta}$$

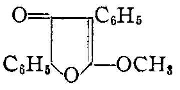


(9)

XXVIII, R is CH_3
XXIX, R is C_6H_5

$$XXVIII + CH_2{=}C(OC_2H_5)_2 \longrightarrow XII \quad (10)$$

$$XXIX + CH_2N_2 \longrightarrow XIII +$$



(11)

XXX

XII and XIII showed significantly different hydrolysis behavior in that the former was readily converted to XXVIII with aqueous acid while XIII is quite resistant to this reagent. However, XIII may be hydrolyzed to XXIX with aqueous alkali. Each of the tetronic acids XXVIII and XXIX gives a characteristic enol test with ferric chloride, decomposes sodium bicarbonate solution, and may be readily titrated with base against phenolphthalein.

Kohler and co-workers[6] reported the preparation of XXIX, m.p. 209°, by the action of alkali on α-phenyl-β-bromo-β-benzoylpropionic acid; the reaction of diazomethane with this product yielded two compounds, one of which, m.p. 105°, was assigned the structure XIII. Inasmuch as the sample of XXIX obtained in the present work melted at 203–206° and its enol ether XIII from reaction 3 melted at 84–86°, it seemed advisable to repeat this earlier work.[6] It was found that the action of diazomethane on XXIX did indeed yield a mixture of two compounds (reaction 11). With some difficulty this mixture was separated into two isomeric compounds, one of which melted at 84–86° and was identical with XIII obtained from reaction 3; the other compound, m.p. 117–118°, is assigned the isomeric cyclic ketene acetal structure XXX. After it was separated, XXX, in contrast to XIII, was found to be readily hydrolyzable to XXIX with aqueous acid. Utilizing this difference in properties, it was determined that the mixture resulting from the action of diazomethane on XXIX consisted of approximately 70% of XIII and 30% of XXX.

Experimental

Ketene Acetals.—Cyanoketene dimethylacetal (IV) was prepared by the pyrolysis of methyl cyanoörthoacetate[7]; ketene diethylacetal (XXIV) was prepared from bromoacetal[8]; the other ketene acetals II, III and XVIII were prepared by dealcoholation of the corresponding orthoesters with aluminum alkoxides.[9]

The Tetronic Acids (XXVIII and XXIX).—A solution of 7.25 g. of ethyl α-methyl-β-ketovalerate[10] in absolute ether at 0° was treated with 7.5 g. of bromine by the procedure of Conrad and Schmidt.[11] After the bromine color had disappeared, the ether solution was washed with water and sodium bicarbonate solution and dried over anhydrous sodium sulfate. After removal of the ether, 8.8 g. of ethyl α-methyl-α-bromo-β-ketovalerate, b.p. 58–62° (0.2 mm.), $n^{25}D$ 1.4550, was distilled. A 7-g. sample of this compound was heated for two hours in refluxing 10% hydrobromic acid, after which the acid solution was neutralized with sodium bicarbonate and extracted with chloroform. The remaining aqueous solution was acidified, saturated with sodium chloride and extracted several times with ether. From the ether extract after evaporation 3 g. (80%) of 3,5-dimethyltetronic acid (XXVIII) was obtained. After recrystallization from benzene the product melted at 123–124° and gave a neutral equivalent of 128 (calcd. 128).

Anal. Calcd. for $C_6H_8O_3$: C, 56.24; H, 6.29. Found: C, 56.05; H, 6.59.

XXVIII formed a phenylhydrazone which melted at 188–191°.

Anal. Calcd. for $C_{12}H_{14}O_2N_2$: C, 66.03; H, 6.47; N, 12.84. Found: C, 65.91; H, 6.56; N, 12.76.

The 3,5-diphenyltetronic acid (XXIX), prepared by a similar procedure recently reported by Hey and Morris,[5] melted at 203–206°, gave a neutral equivalent of 258 (calcd. 252) and showed on analysis the correct carbon and hydrogen content.

Reaction of Diazomethane with XXIX.—To a solution of 3 g. of XXIX in 100 ml. of dioxane was added a solution of diazomethane in ether until a slight excess of the latter was present (yellow color). After the mixture had been allowed to stand at 5° for 30 minutes, the ether and dioxane were evaporated with a stream of air. Then 10 ml. of water, 10 ml. of ethanol and a small amount of sodium bicarbonate were added to the residue. The ethanol was evaporated off, and the aqueous mixture extracted with ether. The material obtained from the ether extraction, after recrystallization from an ether-petroleum ether mixture, melted at 65–100°. After four recrystallizations a small amount of product, which melted at 117–118°, was obtained. The more soluble fractions, after several recrystallizations melted at 65–75°; this material was subjected to distillation at 165° (0.1 mm.). After all the volatile material was removed at this temperature and pressure, the residue was recrystallized from ether and found to melt at 84–86°. It gave no depression in melting point when mixed with a sample of XIII obtained from the bromination of the ketene acetal III.

Analysis of the product m.p. 117–118° (XVII) showed

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[5] *Cf.* D. H. Hey and D. S. Morris, *J. Chem. Soc.*, 48 (1948).

[6] E. P. Kohler, W. D. Peterson and C. L. Bickel, This Journal, **56**, 2006 (1934).

[7] S. M. McElvain and J. P. Schroeder, *ibid.*, **71**, 47 (1949).

[8] S. M. McElvain and D. Kundiger, *Org. Syntheses*, **23**, 45 (1943).

[9] S. M. McElvain and W. R. Davie, This Journal, **73**, 1400 (1951).

[10] S. M. McElvain, *ibid.*, **51**, 3124 (1929).

[11] M. Conrad and L. Schmidt, *Ber.*, **29**, 1043 (1896).

that it was isomeric with XIV. Hydrolysis in either acidic or basic media readily converted this compound to 3,5-diphenyltetronic acid (XXIX). On this basis it was assigned the structure 2-methoxy-3,5-diphenyl-4-keto-4,5-dihydrofuran (XXX).

Anal. Calcd. for $C_{17}H_{14}O_3$: C, 76.7; H, 5.30. Found: C, 76.6; H, 5.58.

To determine the relative amount of XXX produced in the reaction of diazomethane with XXIX, 5 g. of the latter was treated with diazomethane as described above; after the ether and dioxane had been evaporated, practically all of the residue was soluble in ether. This ether solution was evaporated in a current of air and the residue boiled with a mixture of 5% hydrochloric acid and dioxane for 30 minutes. After the dioxane was distilled off, the cooled acidic mixture was extracted several times with chloroform. After evaporation of the chloroform, the residue was stirred with 50 cc. of ether and the insoluble tetronic acid XXIX, (0.9 g.), m.p. 200–206°, was filtered off. The ether solution when chilled and diluted with petroleum ether gave 0.9 g. of the enol ether XIII, which melted at 83–84° without recrystallization. By diluting the mother liquor further with petroleum ether an additional 0.6 g. of the tetronic acid XXIX, m.p. 190–200°, was obtained; the total yield of this acid from the hydrolysis of XXX was 1.5 g. As the material remaining in solution (2.6 g.) was found to be completely soluble in petroleum ether, it was presumed to be XIII. It would appear from this experiment that the isomers XIII and XXX are formed in the ratio of approximately 2.3:1 in the reaction of diazomethane with the tetronic acid XXIX.

The Addition of the Ketene Acetals to Bromine.—The general procedure for this reaction was to add a solution of the ketene acetal in carbon tetrachloride to a cooled (0–5°) solution of bromine in the same solvent until the bromine color was destroyed. The amount of bromine decolorized per mole of ketene acetal and the yields and properties of the resulting bromoesters are listed in Table I.

TABLE I

BROMOESTERS FROM KETENE ACETALS AT 0–5°

Ketene acetal	Mole Br_2 used/ mole K.A.	Bromo-ester	Yield, %	B.p., °C.	Mm.	$n^{25}D$
II	0.97	VI	86	46–47	9	1.4430
III	.96	VII[a]	90	133–137	14	1.5502
IV	.99	VIII[b]	92	88–93	9	1.4712
XVIII	.98	XX[c]	92	41–45	11	1.4480
XXIV	.87	XXV	34[d]	45–50	9	1.4492

[a] *Cf.* Truitt, *et al.*, THIS JOURNAL, **70**, 4214 (1948). [b] *Anal.* Calcd. for $C_4H_4O_2BrN$: N, 7.88; CH_3O, 17.4. Found: N, 7.88; CH_3O, 15.9. [c] *Anal.* Calcd. for $C_5H_9O_2Br$: Br, 44.2; CH_3O, 17.1. Found: Br, 43.6; CH_3O, 17.0. Price and Coyner (THIS JOURNAL, **62**, 1306 (1940)) report that this bromoester, b.p. 52° (19 mm.), $n^{20}D$ 1.4410, readily loses hydrogen bromide and changes in physical properties on standing. In contrast, the bromo ester XX obtained from the ketene acetal (XVIII) gave no indication of such instability. [d] Plus a small amount of $Br_2CHCOOC_2H_5$, a mixture boiling at 65–125° (1 mm.), and a large residue of tar.

Bromination of Ketene Acetals (a) Methylketene Diethylacetal (II).—To 39 g. of II at 0° was added slowly, with stirring over an eight-hour period, 27 g. of bromine in 100 ml. of carbon tetrachloride solution; this amount of the bromine, which produced a permanent coloration corresponded to 58% of one equivalent. From the reaction mixture was isolated on distillation 26 g. (80%) of ethyl bromide, 11.2 g. (20.5%) of ethyl α-bromopropionate (VI), and 36 g. (77%) of **ethyl α-methyl-β,β-diethoxy-γ-bromovalerate** (X) b.p. 86–90° (0.2 mm.); $n^{25}D$ 1.4538.

Anal. Calcd. for $C_{12}H_{23}O_4Br$: Br, 25.7; C_2H_5O, 43.4. Found: Br, 26.0; C_2H_5O, 43.0.

Ethyl 3,5-Dimethyltetronate (2-Keto-3,5-dimethyl-4-ethoxy-2,5-dihydrofuran) (XII).—A 4-g. sample of X, in a flask equipped with a 10-cm. Vigreux column and still-head with a receiver placed in an ice-bath, was heated in an oil-bath at 200°. Within 5 minutes 1.6 g. of a mixture of ethyl alcohol and ethyl bromide, b.p. 60–70°, distilled out. The remaining material in the flask was distilled under reduced pressure to yield 1.8 g. (90%) of XII, b.p. 140–143° (15 mm.); $n^{25}D$ 1.4665. A purer sample of XII, obtained as a center cut from the refractionation of the products from a larger scale pyrolysis of X, had the following properties: b.p. 147–150° (15 mm.); $n^{25}D$ 1.4720; $d^{25}{}_4$ 1.074.

Anal. Calcd. for $C_8H_{12}O_3$: C, 61.52; H, 7.75; C_2H_5O, 28.8. Found: C, 61.67; H, 7.95; C_2H_5O, 28.3.

To 4.5 g. of XII in a flask equipped with a short distilling column was added 20 ml. of 10% hydrochloric acid. The mixture was heated gently for a few minutes and then the temperature was increased to distil out the alcohol. The material distilling 75–80° amounted to 0.8 g. (about 60% of the expected amount of ethyl alcohol). The solution was saturated with sodium chloride and extracted several times with ether. The material obtained by evaporation of the ether amounted to 2.3 g., and after recrystallization from benzene was identical with the synthetic sample of dimethyltetronic acid (XXVIII) described above.

The tetronic acid XXVIII was converted to XII in the following manner: To 4 g. of XXVIII in a flask equipped for distillation was added 5 g. of ketene diethylacetal. The solution immediately became quite warm and turned red. The reaction mixture was kept at 80° for half an hour and then distilled. After the distillation of ethyl acetate and a small amount of unchanged ketene acetal, 3 g. of XII, b.p. 155–157° (25 mm.); $n^{25}D$ 1.4740, was obtained.

(**b**) **Phenylketene Dimethylacetal** (III).—The bromine absorption of this ketene acetal was quite dependent on the temperature of the reaction and the rate of addition of the bromine as may be seen in Table II.

TABLE II

BROMINATION OF PHENYLKETENE DIMETHYLACETAL

Run	React. temp., °C.	Addition time	Solvent	Br_2 used, %
1	0–5	20 min.	CCl_4	92
2	0–5	4 hr.	CCl_4	85
3	30	20 min.	CCl_4	92
4	60	20 min.	CCl_4	92
5	−20	20 min.	CCl_4	89
6	−20	7 hr.	CCl_4	77
7	−50	9 hr.	CCl_4	65
8	−78	7 hr.	$CHCl_3$	55

It is apparent from Table II that lower reaction temperatures and slower addition of bromine to the ketene acetal favor the formation of dimeric products. When bromine absorption was high (runs 1, 2, 3, 4 and 5), methyl α-bromophenylacetate (VII) was the main reaction product. In run 6, 74 g. of the ketene acetal was treated with a solution of 55.5 g. of bromine in sufficient carbon tetrachloride to make 100 ml. Distillation of the reaction mixture under diminished pressure gave, after the removal of the carbon tetrachloride, 68.5 g. (66%) of VII, b.p. 100–140° (1–5 mm.) and left a semi-solid residue. This residue was placed in a two-bulb flask constructed from two 2.5 × 20 cm. test-tubes joined in the middle by 8 cm. of 1-cm. bore glass tubing. The tube containing the material to be distilled had large identations in the sides to prevent splashing. When this mixture was heated to 160–170° (0.05 to 0.1 mm.) a solid slowly sublimed out. It amounted to 4.3 g. (6.5%) and was identified as ***dl*-dimethyl α,α'-diphenylsuccinate** (XIV), contaminated with some of the *meso* form; it melted 165–170°.

Anal. Calcd. for $C_{18}H_{18}O_4$: C, 72.5; H, 6.03; CH_3O, 20.8. Found: C, 72.6; H, 5.88; CH_3O, 19.6.

This ester on saponification yielded the corresponding acid[12] which melted 179–180°, and which on further heating solidified and remelted 226–228°.

By increasing the temperature of the oil-bath to 185–190° it was possible to distil 9.0 g. (14%) of a yellowish-red oil, which later crystallized on evaporation of its ether solution; after recrystallization from ether, the methyl 3,5-diphenyltetronate (2-keto-3,5-diphenyl-4-methoxy-2,5-dihydrofuran) (XIII) melted at 85–86°.

Anal. Calcd. for $C_{17}H_{14}O_3$: C, 76.7; H, 5.26; CH_3O, 11.6. Found: C, 76.4; H, 5.19; CH_3O, 11.3.

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[12] H. Wren and C. J. Still, *J. Chem. Soc.*, 444, 1449 (1915).

There remained as a residue in the flask, from which XIII and XIV were distilled, a white solid mixed with a small amount of tarry material. When washed with benzene the solid remained as a white flocculent residue that weighed 2.4 g. After recrystallization from chloroform, it melted at 300–305° dec. This material was quite inert; it remained insoluble and unchanged in an attempted methoxyl determination and showed no reaction with bromine in carbon tetrachloride or potassium permanganate in acetone. Analysis indicated that it contained C, 75.23; H, 4.85.

In run 8, 54 g. of the ketene acetal was used. After the bromination was completed, distillation of the reaction mixture yielded VII (18%) and XIII (80%); none of the other products obtained in run 6 could be isolated.

The succinic ester XIV was prepared in the following manner: A mixture of 33 g. (0.144 mole) of methyl α-bromophenylacetate (VII) and 23 g. (0.140 mole) of phenylketene dimethylacetal (III) was heated in a flask to which a cold trap was connected. Methyl bromide was evolved rapidly at 150° and after an hour the reaction mixture became solid. About 5 g. of unchanged bromoester and ketene acetal was removed by distillation. The remaining solid cake was crystallized from benzene–petroleum ether mixture to yield 31 g. (72%) of a mixture of *meso*- and *dl*-dimethyl α,α′-diphenylsuccinate (XIV), m.p. 173–203°.

When a sample of the enol ether XIII was boiled for three hours in a mixture of dioxane, water and concentrated hydrochloric acid, it was recovered unchanged after distilling off the dioxane and extracting the aqueous solution with chloroform. A mixture of 14 g. of XIII, 30 ml. of ethyl alcohol, 30 ml. of water, and 10 g. of potassium hydroxide was refluxed for one hour. After this time the ethyl alcohol was distilled off leaving a reddish-brown solution. This solution was acidified with 20 cc. of concentrated hydrochloric acid, whereupon a tacky solid separated. After two recrystallizations from a mixture of ethanol and water, the **3,5-diphenyltetronic acid** (XXIX) melted at 203–206° and gave a neutral equivalent of 258 (calcd. 252).

Anal. Calcd. for $C_{16}H_{12}O_3$: C, 76.19; H, 4.77. Found: C, 75.9; H, 4.88.

This acid decomposes bicarbonates and gives a pale greenish color with ferric chloride. It was found to be identical with a sample of 3,5-diphenyltetronic acid prepared by the method of Hey and Morris.[5]

(c) **Cyanoketene Dimethylacetal** (IV).—A solution of 43.2 g. (0.382 mole) of IV in 50 cc. of chloroform was cooled to −10 to −20° and with rapid stirring treated dropwise with a solution containing 61 g. (0.382 mole) of bromine in sufficient chloroform to make 100 ml. of solution. After 50 ml. of the bromine solution had been added the temperature of the reaction was permitted to rise to 0°. The bromine solution was then added in 1-ml. portions until the first semi-permanent bromine coloration was noted; at this point a total of 62 ml. of the bromine solution had been added. The solvent was removed under reduced pressure and the products fractionated into the following fractions: (a) 20.8 g., b.p. 49–52° (0.4 mm.), $n^{25}\mathrm{D}$ 1.4290; (b) 5.1 g., b.p. 53–63° (0.4 mm.), $n^{25}\mathrm{D}$ 1.4600; (c) 30.2 g., b.p. 63–67° (0.3 mm.), $n^{25}\mathrm{D}$ 1.5075. Fractions (a) and (b) were a mixture of methyl cyanoacetate (XVI), $n^{25}\mathrm{D}$ 1.4170, and methyl bromocyanoacetate (VIII), $n^{25}\mathrm{D}$ 1.4712. Fraction (c) was **cyanobromoketene dimethylacetal** (XVII) and corresponded to a 41% yield.

Anal. Calcd. for $C_5H_6O_2BrN$: N, 7.28; CH_3O, 32.2. Found: N, 7.28; CH_3O, 31.6.

A 15-g. sample of XVII was treated with a mixture of 5 ml. of water, 20 ml. of dioxane and 1 ml. of glacial acetic acid and allowed to stand at room temperature overnight. Then the water, dioxane and acetic acid were removed under reduced pressure and the product distilled to yield 11.5 g. of methyl cyanobromoacetate (VIII), b.p. 89–91° (9 mm.), $n^{25}\mathrm{D}$ 1.4718.

A solution of 15.5 g. (0.08 mole) of XVII in 10 ml. of chloroform was treated with a solution of 12.9 g. (0.08 mole) of bromine in 15 ml. of chloroform solution. The bromine solution, added dropwise with shaking and occasional cooling in an ice-bath, was rapidly decolorized to 87% of the theoretical amount. Distillation of the reaction mixture gave 17.8 g. (86%) of **methyl dibromocyanoacetate**, a colorless liquid, b.p. 58–62° (0.5 mm.), $n^{25}\mathrm{D}$ 1.5037. On standing a few hours it acquired an orange color.

Anal. Calcd. for $C_4H_3O_2Br_2N$: N, 5.45; CH_3O, 12.0. Found: N, 5.52; CH_3O, 12.6.

(d) **Dimethylketene Dimethylacetal** (XVIII).—The addition of a bromine solution in carbon tetrachloride to a solution of XVIII in the same solvent at 0° resulted in the absorption of 0.96 equivalent of bromine. Distillation of the reaction mixture yielded 89% of methyl α-bromoisobutyrate (XX) with the properties listed in Table I.

Bromination of XVIII in Presence of an Orthoester (i) **Methyl Orthopropionate**.—A mixture of 24 g. (0.207 mole) of dimethylketene dimethylacetal and 27.3 g. (0.207 mole) of methyl orthopropionate at 0° was treated with a solution of 33 g. (0.207 mole) of bromine in sufficient chloroform to make 50 ml. The bromine was added dropwise over a period of one hour; 48 ml. (96%) of the bromine solution was required to give a permanent bromine coloration. When this reaction mixture was distilled, 12.5 g. (46%) of unchanged methyl orthopropionate, 16.1 g. (43%) of methyl α-bromoisobutyrate (XX), and 24.2 g. (51.5%) of **methyl ortho-α-bromoisobutyrate** (XXII), b.p. 77–79° (18 mm.), $n^{25}\mathrm{D}$ 1.4510, m.p. *ca.* 25°, were obtained. The chloroform distillate contained 7 g. (39%) of methyl propionate, as determined by extraction with sulfuric acid.

Anal. Calcd. for $C_7H_{15}O_3Br$: Br, 35.2; CH_3O, 40.9. Found: Br, 35.1; CH_3O, 36.8.

(ii) **Methyl Orthoisobutyrate**.—To a mixture of 8.4 g. (0.072 mole) of dimethylketene dimethylacetal and 8.4 g. (0.057 mole) of methyl orthoisobutyrate in 10 ml. of chloroform at 0–5° was added a solution of 11.6 g. (0.072 mole) of bromine in sufficient chloroform to make 25 ml. of solution. The bromine solution was added slowly with rapid stirring; 23 ml. was required to produce a permanent bromine coloration. When the reaction mixture was distilled, there were obtained 1.6 g. (19%) of unchanged orthoester, 2.4 g. (18%) of methyl α-bromoisobutyrate (XX) and 9.9 g. of a mixture XX and the bromo-orthoester XXII; the $n^{25}\mathrm{D}$ 1.4500 of this mixture indicated that it contained 3.3 g. (29%) of XX and 6.6 g. (42%) of XXII.

The structure of the bromo-orthoester XXII was shown by hydrolysis to the normal ester, methyl α-bromoisobutyrate, in the following manner. To 5.4 g. of XXII was added 10 ml. of 10% hydrobromic acid; the mixture was allowed to stand at room temperature with occasional shaking for one hour. The solution was then extracted with ether; the ether extract was dried over anhydrous sodium sulfate and distilled through a 30-cm. Podbielniak column to yield 3.6 g. (84%) of methyl α-bromoisobutyrate (XX), b.p. 34–38° (8 mm.), $n^{25}\mathrm{D}$ 1.4478.

(e) **Ketene Diethylacetal** (XXIV).—To 15 g. of XXIV in 10 ml. of chloroform at −78° and under an atmosphere of nitrogen was added 3 drops of a 30% solution of bromine in chloroform while the solution was rapidly stirred. Within one minute the mixture solidified and stopped the stirrer. The white solid that separated remained solid at room temperature. By heating this reaction mixture for one hour at 150° (8 mm.) it was possible to remove the chloroform and some unchanged ketene acetal to leave as a residue 4.5 g. of a yellowish-white polymer, which gradually darkened on exposure to air.

In a bromination of 50 g. (0.43 mole) of XXIV in 10 ml. of carbon tetrachloride with slow stirring at 50–60°, 55 g. (0.34 mole) of bromine was absorbed. This mixture after removal of the carbon tetrachloride was distilled to yield the following fractions: (a) 20 g. (27.8%) of ethyl bromoacetate, b.p. 43–47° (9 mm.), $n^{25}\mathrm{D}$ 1.4493; (b) 3 g., b.p. 52–69° (9 mm.), $n^{25}\mathrm{D}$ 1.4681; (c) 9.9 g. (9.2%) of ethyl dibromoacetate, b.p. 69–72° (9 mm.), $n^{25}\mathrm{D}$ 1.4910; (d) 2.6 g., b.p. 79–108° (9 mm.), $n^{25}\mathrm{D}$ 1.4800; (e) 3.2 g., b.p. 108–115° (9 mm.), $n^{25}\mathrm{D}$ 1.4640; (f) 4 g., b.p. 74–78° (0.3 mm.), $n^{25}\mathrm{D}$ 1.4635; (g) 1.2 g., b.p. 83–88° (0.4 mm.), $n^{25}\mathrm{D}$ 1.4740; (h) 5.4 g., b.p. 91–100° (0.4 mm.), $n^{25}\mathrm{D}$ 1.4965. In spite of the narrowness of the boiling ranges and similarities of the refractive indices of certain of the higher boiling fractions (e) to (h), analytical data (Br and C_2H_5O) did not correspond to any single compound and indicated that each of these fractions was an inseparable mixture.

The ethyl acetate produced in the above reaction was separated from the carbon tetrachloride in the following manner: 75 g. of the 165 g. of the distillate containing ethyl bromide, carbon tetrachloride and ethyl acetate was extracted with 10 ml. of concentrated sulfuric acid. This extract, after separation from the carbon tetrachloride was poured onto 100 g. of crushed ice and this acid mixture made slightly basic to phenolphthalein with 5 molar sodium hydroxide. Distillation yielded a fraction (6.4 g.), b.p. 60–97°, which, after drying over calcium chloride, amounted to 4.6 g. The refractive index of this mixture of ethyl acetate and carbon tetrachloride indicated that it contained 3.8 g. of the ester. The same procedure carried out on a known mixture of 5 g. of ethyl acetate and 55 g. of carbon tetrachloride gave a recovery of 3.9 g. of ethyl acetate. On this basis it was concluded that the original 175 g. of the first distillate contained *ca.* 11 g. (29%) of ethyl acetate.

The Reaction of Oxygen with Phenylketene Dimethylacetal.—In an apparatus used for hydrogenation at atmospheric pressure, 20.5 g. of phenylketene dimethylacetal was placed under an atmosphere of oxygen. When stirred the ketene acetal began to absorb oxygen and the reaction soon was sufficiently exothermic that the flask had to be cooled with a water-bath occasionally in order to keep the temperature below 60°. At the end of three hours the oxygen absorption had practically stopped; the reaction flask was warmed to 60° and some additional oxygen was absorbed, but after an hour at 60° the rate of absorption of oxygen was negligible. A total of 2240 ml. (740 mm., 28°) of oxygen was absorbed.

The reaction mixture was then heated at 70° under 8 mm. pressure; 4.5 g. (40%) of dimethyl carbonate, m.p. −1°, $n^{25}D$ 1.3761 collected in the cold trap. As the temperature was increased, 5.1 g. (38%) of benzaldehyde distilled at 53° (10 mm.); $n^{25}D$ 1.5212. The next fraction (4.9 g.) boiled up to 90° (0.4 mm.) and was shown to be a mixture of methyl benzoate and methyl phenylacetate by preparation of the amides after partial separation of the esters by fractional distillation. Finally, 7 g. (37%) of dimethyl α,α'-diphenylsuccinate (XIV) was sublimed from the remaining material; only 1.5 g. of a tarry residue remained.

MADISON, WISCONSIN RECEIVED OCTOBER 11, 1951

[CONTRIBUTION FROM THE VENABLE CHEMICAL LABORATORY OF THE UNIVERSITY OF NORTH CAROLINA]

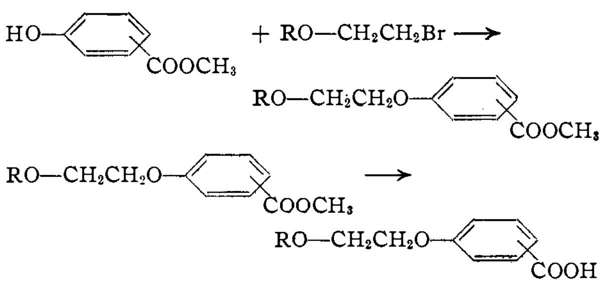
The Preparation of Some Polyalkoxy Ethers of the Isomeric Hydroxybenzoic Acids[1]

BY R. W. BOST[2] AND MELDRUM B. WINSTEAD, JR.[3]

A number of new compounds have been synthesized in connection with a study of the relationship of position isomerism with surface activity. These compounds are of the type consisting of various polyalkoxy ethers of the isomeric hydroxybenzoic acids, and have been prepared by the Williamson synthesis of mixed ethers.

In connection with the investigation of the relationship of position isomerism with the surface activity of various compounds—a study which has been under observation in this Laboratory for the past ten years—a number of new compounds have been prepared by the present investigators. Due to the availability of various Cellosolves and Carbitols from the Carbide and Carbon Chemicals Corporation, a method was sought which would most conveniently enable one to introduce the polyalkoxy ether linkage into the benzene ring. This was accomplished, first, by converting the various Cellosolves and Carbitols into the corresponding β-bromoethers by the action of phosphorous tribromide, and, second, by employing the Williamson synthesis of ethers for the reaction between the various β-bromoethers and the particular substituted phenol desired. The series of reactions followed can be outlined in this manner:

$$3RO{-}CH_2CH_2OH + PBr_3 \longrightarrow 3RO{-}CH_2CH_2Br + H_3PO_3$$



$R = CH_3, C_2H_5, n\text{-}C_4H_9, C_2H_5OCH_2CH_2, C_4H_9OCH_2CH_2$ and C_6H_5

Of the compounds reported in this article, only one was found to have been previously reported.[4] The phosphorus tribromide employed in this series of reactions, as well as β-bromoethyl ethyl ether, was obtained in a good degree of purity from Eastman Kodak Company. Methyl cellosolve, butyl cellosolve, ethyl carbitol and butyl carbitol were obtained from Carbide and Carbon Chemicals Corporation and were redistilled before use. β-Phenoxyethyl bromide was prepared according to the procedure outlined in "Organic Syntheses" for γ-phenoxypropyl bromide.[5] The procedures involved in the preparation of β-bromoethyl methyl ether, β-bromoethyl *n*-butyl ether, 2-(2′-ethoxyethoxy)-ethyl bromide and 2-(2′-butoxyethoxy)-ethyl bromide are described in the experimental section. The yields obtained in these reactions varied from 26% for 2-(2′-ethoxyethoxy)-ethyl bromide and 36% for β-bromoethyl methyl ether to 52% for β-bromoethyl *n*-butyl ether and 64% for 2-(2′-butoxyethoxy)-ethyl bromide. In all cases the reaction was considered to involve merely a replacement of the hydroxy group by a bromine atom. However, the reaction appears to be of a more complex nature than one of simple substitution, and this would tend to account in some respects for the low yields obtained in several cases. In connection with this the reader is referred to the work of Gerrard[6] concerning the mechanism of the reaction between hydroxy compounds and phosphorus tribromide.

Methyl *p*-hydroxybenzoate and methyl *m*-hydroxybenzoate were prepared from *p*-hydroxybenzoic acid and *m*-hydroxybenzoic acid, re-

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[1] This paper represents a portion of a thesis submitted by Meldrum B. Winstead, Jr., in partial fulfillment of the requirements for the degree of Doctor of Philosophy, University of North Carolina, June, 1952.

[2] Deceased.

[3] du Pont Fellow in Chemistry, 1951–1952.

[4] W. G. Christiansen and S. E. Harris (to E. R. Squibb and Sons) U. S. 2,404,691, July 23, 1946.

[5] H. Gilman and A. H. Blatt, "Organic Syntheses," Coll. Vol. I 2nd. Edition, 4th Printing, John Wiley and Sons, Inc., New York N. Y., 1947, p. 436 (Note 6).

[6] W. Gerrard, *J. Chem. Soc.*, 848 (1945).