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KETONE EXCHANGE IN A SUGAR BISACETAL

RICHARD S. GLASS*, SHUAN KWOH, AND EUGENE P. OLIVETO
Chemical Research Department, Hoffmann-La Roche Inc., Nutley, N. J. 07110 (U. S. A.)
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ABSTRACT

An acid-catalyzed reaction of 2,3:4,6-di-*O*-isopropylidene-α-L-sorbofuranose with ketones resulted in replacement of the isopropylidene groups with alkylidene groups derived from the ketonic solvent. Kinetically controlled exchange occurs at the 4,6-position. Under equilibrium conditions exchange occurs at the 2,3- as well as the 4,6-position. Participation by the hydroxyl group at C-1 in the rate determining step of exchange at the 2,3-position could not be demonstrated.

INTRODUCTION

Selective formation, rearrangement, and hydrolysis of polyacetals is an area of much current interest[1,2]. Polyacetals derived from alcohols or glycols and polyketones, *e.g.* polyketo steroids, as well as those[1,3,4] from ketones and polyhydroxy compounds, *e.g.*, sugars[2,5,6], have been extensively investigated. Both kinetic and equilibrium approaches[1–6] have been used to study these reactions.

An important example of an equilibrium approach is the synthesis of L-ascorbic acid (vitamin C) reported by Reichstein and Grüssner[7]. Condensation of L-sorbose with acetone in the presence of sulfuric acid gave 2,3:4,6-di-*O*-isopropylidene-α-L-sorbofuranose (**1**).

This reaction apparently proceeds through a variety of mono- and bis-acetonides** which ultimately equilibrate to give a mixture consisting predominantly of the 2,3:4,6-bisacetal **1**. This isomer is the one required for the synthesis of L-ascorbic acid***.

This paper presents the reactions of **1** with ketones in the presence of catalytic amounts of acid. In these reactions the isopropylidene groups are replaced by alkylidene groups derived from the ketonic solvent. Conditions under which either kinetic control or thermodynamic control prevailed were investigated. The reactions under

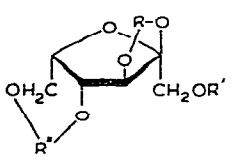
*Present address: University of Arizona, Tucson, Arizona 85721 (U. S. A.)
**The mechanism of the reaction of L-sorbose with acetone or dialkylacetals of acetone in the presence of acid has been studied[8].
***Oxidation of **1** to 2,3:4,6-di-*O*-isopropylidene-2-keto-L-gulonic acid followed by hydrolysis, lactonization, and enolization affords vitamin C[7].

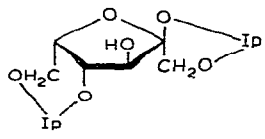
kinetic control may be mechanistically related to the selective* hydrolysis of **1** and those under thermodynamic control are related to the formation of this bisacetal under the conditions employed by Reichstein and Grüssner[7].

RESULTS AND DISCUSSION

Compound **1** dissolved in methyl ethyl ketone containing perchloric acid gave in 15 min at room temperature predominantly (93%) 4,6-*O*-isobutylidene-2,3-*O*-isopropylidene-α-L-sorbofuranose (**3**). Continued exposure gave mainly 2,3:4,6-di-*O*-isobutylidene-α-L-sorbofuranose (**5**) (79%) together with monoisobutylidene-monoisopropylidene-L-sorbose derivatives (17%). With diethyl ketone as the solvent, **1** in the presence of perchloric acid gave, after 10 min, a mixture in which 2,3-*O*-isopropylidene-4,6-*O*-(3-pentylidene)-α-L-sorbofuranose (**6**) predominates (80%). After 24 h the mixture consists of monoisopropylidene-mono-3′-pentylidene-L-sorbose derivatives (20%) and 2,3:4,6-di-*O*-(3-pentylidene)-α-L-sorbofuranose (**8**) (48%).

The structure of **3** was established by methylation to give the 1-*O*-methyl derivative **9**, which was further transformed into 2,3:4,6-di-*O*-isopropylidene-1-*O*-methyl-α-L-sorbofuranose (**10**), identical with an authentic sample[10], thus showing that the C-1 hydroxyl group was unprotected in the starting material. The conversion





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	R	R′	R″
1	Ip	H	Ip
2	Ip	H	H_2
3	Ip	H	CH_3–C–CH_2–CH_3
4	CH_3–C–CH_2–CH_3	H	Ip
5	CH_3–C–CH_2–CH_3	H	CH_3–C–CH_2–CH_3
6	Ip	H	CH_3–CH_2–C–CH_2–CH_3
7	CH_3–CH_2–C–CH_2–CH_3	H	Ip
8	CH_3–CH_2–C–CH_2–CH_3	H	CH_3–CH_2–C–CH_2–CH_3
9	Ip	Me	CH_3–C–CH_2–CH_3
10	Ip	Me	Ip
11	Ip	Me	H_2
12	Ip	Me	Ac_2
13	CH_3–C–CH_2–CH_3	H	H_2
14	CH_3–CH_2–C–CH_2–CH_3	H	H_2
15	CH_3–CH_2–C–CH_2–CH_3	*p*-NO_2–C_6H_4CO	(*p*-NO_2–$C_6H_4CO)_2$
16	Ip	*p*-NO_2–C_6H_4CO	(*p*-NO_2–$C_6H_4CO)_2$
17	CH_3–C–CH_2–CH_3	Me	CH_3–C–CH_2–CH_3

of **3** into **2** by selective hydrolysis afforded a compound identical with authentic[7,11] 2,3-*O*-isopropylidene-α-L-sorbofuranose (**2**), and the preparation of the diacetate **12** from either **9** or **10** demonstrates (if no rearrangement occured in the selective hydrolyses) that the isobutylidene group bridges the oxygens at C-4 and C-6 and the iso-

*An example of selective hydrolysis under presumably kinetically controlled conditions is the partial hydrolysis of **1** to give 2,3-*O*-isopropylidene-α-L-sorbofuranose (**2**). Formation of 4,6-*O*-isopropylidene-L-sorbose is not observed in this reaction[9].

propylidene group bridges the oxygens at C-2 and C-3. Furthermore, owing to the asymmetry of the isobutylidene group, compound **3** exists as a mixture of 2 stereomers which could be separated by preparative t.l.c.*.

The structure of **5** is supported by the spectral properties (i.r. and n.m.r.), elementary analysis, and hydrolysis which gave 2,3-isobutylidene-α-L-sorbofuranose (**13**). Compound **5** was prepared by Reichstein and Grüssner[7] by treating L-sorbose with methyl ethyl ketone in the presence of sulfuric acid. Repetition of this procedure afforded a product which gave the same spectra as that given by our material, but both products are mixtures of stereoisomers (four are possible since two new asymmetric centers are formed) and gave rise to two peaks in g.l.c. Partial separation of these compounds was achieved by column chromatography on silica gel.

Prolonged treatment of **1** in methyl ethyl ketone with perchloric acid gave a mixture containing both **3** and **4**. Although these compounds could not be separated from each other, the spectral properties of the mixture (particularly the n.m.r. spectrum), as well as those of their products of hydrolysis, support the structural assignments.

The structure of **6** is supported by the spectra, elementary analysis, and the spectra of the corresponding acetate (the n.m.r. spectrum in particular suggests an unprotected hydroxyl group at C-1). Selective hydrolysis afforded **2**, which is consistent with a 3′-pentylidene bridge between the oxygens at C-4 and C-6.

The structure of **8** is supported by the spectra and elementary analysis as well as those of the acetate. Further evidence was obtained by hydrolysis which afforded the mono-*O*-(3′-pentylidene) derivative **14** from which a high melting tri-*p*-nitrobenzoate **15** identical with that prepared from authentic **2** was obtained. This establishes that a 3′-pentylidene group bridges the oxygens at C-2 and C-3 in a furanose ring. Since the n.m.r. spectra of the starting material and its acetate are consistent with a free hydroxyl group at C-1, the other 3′-pentylidene group must bridge the oxygens at C-4 and C-6.

Prolonged exposure of **1** in diethyl ketone in the presence of perchloric acid gave a mixture containing both **6** and **7**. Although these two compounds could not be separated, hydrolysis gave a mixture of **2** and **14** which could be separated by chromatography on silica gel. The tri-*p*-nitrobenzoates of these compounds were shown to be the same as those just described.

To test whether the 1,2:4,6-bisacetal **18** is formed before or during the rate determining step in the ketone exchange at the 2,3-position**, the rate of acid-catalyzed exchange of **3** was compared with that of **9**, a compound which cannot form such an intermediate under these conditions. The rate of the exchange of **3** exceeds that of **9** by a small factor (*ca.* 2), which is too small to warrant the conclusion that **18** is a required intermediate in the exchange at the 2,3-position of compound **3**.

These results demonstrate that a kinetically controlled exchange of the iso-

*Stereoisomers were obtained in the ethylidenation of L-sorbose[12].

Rearrangement of **17 into **2** has been shown to occur rapidly in the presence of acids[13].

propylidene groups of **1** occurs preferentially at the 4,6-position. The initial steps in this reaction are undoubtedly the same as those for the hydrolysis of acetals[14], that is protonation of an acetal oxygen in an equilibrium step, followed by rate determining cleavage of the alkylidene carbon to the sugar-oxygen bond. Although examples are known in which partially rate-determining protonation of the acetal oxygen occurs[15–17], such a mechanism is unlikely in this case, because those examples have either good leaving groups with decreased basicity (aryloxy groups as opposed to alkoxy groups)[15] or form exceptionally stable carbonium ions, *e.g.* an ethoxytropylium cation[16,17]. Reversible C-O cleavage has also been found[18] but there is no evidence for its occurrence or absence in the exchange reactions of **1**. The concluding steps in the exchange reaction remain speculative.

Selective exchange of the 4,6-*O*-isopropylidene group of **1** is in accord with the results of other workers[8,19] who have studied the selective hydrolysis of this compound, if the initial steps of the exchange mechanism are the same as those for the hydrolysis. Also, the rate of hydrolysis of *m*-dioxanes is greater than that of dioxolanes[3–6,20]. Thus, the 4,6-*O*-isopropylidene group which is part of a *m*-dioxane ring would be expected to exchange more readily than the 2,3-*O*-isopropylidene group which is part of a dioxolane ring. Two additional factors decrease the rate of exchange of the 2,3-*O*-isopropylidene group. Fusion of a dioxolane *cis* to a five-membered ring lowers its rate of hydrolysis[3] and, therefore, presumably its rate of exchange. The electron-withdrawing inductive effect of the oxygen of the furanose ring decreases the basicity of the oxygens at C-2 and C-3 (the inductive effect on the oxygens at C-3, C-4, and C-6 would be similar but much less than the effect on the oxygen at C-2), perhaps without adequately compensating for this by increasing the rate of C-O bond cleavage[3]. A factor that increases the rate of reaction of the *m*-dioxane ring relative to the dioxolane ring is the destabilization, in the former case, by the methyl group (in the 4,6-*O*-isopropylidene moiety) which must necessarily be axial[3–6].

Prolonged exposure of **1** to ketones in the presence of acid results in a mixture consisting predominantly of 2,3:4,6-bisacetals. Interestingly, this mixture consists of both 2,3-*O*-isopropylidene-4,6-*O*-alkylidene- as well as 2,3-*O*-alkylidene-4,6-*O*-isopropylidene-α-L-sorbofuranoses. This may mean that the thermodynamic energy difference between these isomers is small under the conditions used. The selectivity for 2,3:4,6-bisacetals is in accord with the finding that the major product of the condensation of L-sorbose with acetone under thermodynamically controlled conditions is **1**.

EXPERIMENTAL

All melting points are uncorrected and were taken on a Thomas–Hoover capillary melting-point apparatus. All i.r., u.v., n.m.r., and m.s. measurements were determined by our Physical Chemistry Laboratory. All elementary analyses and optical rotations were performed by our Microanalytical Laboratory on samples which were recrystallized.

*Preparation of 2,3:4,6-di-*O*-isobutylidene-α-*L*-sorbofuranose* (**5**) *by Reichstein's method*[7]. — A mixture consisting of L-sorbose (10.0 g, 56 mmoles), ethyl methyl ketone (220 ml), and conc. sulfuric acid (8.0 ml) was stirred for 20 h at room temperature. The mixture was then poured into an aqueous sodium hydroxide solution (200 ml containing 15.0 g, 0.375 mole of sodium hydroxide) and water (200 ml), shaken in a separatory funnel and then concentrated to about 100 ml. The mixture was extracted with toluene (3 × 150 ml), the extracts were combined, dried (sodium sulfate), and evaporated to dryness. The residue was distilled to give an oil (4.79 g, 30%), b.p. (0.04 mm) 121–126°, which crystallized. The material was recrystallized from hexane to give **5**, m.p. 96–99°, $[\alpha]_D^{25}$ −10.2° (*c* 0.39, ethanol); lit.[7]: m.p. 96–99°, $[\alpha]_D^{25}$ −16.6° (methyl ethyl ketone).

This mixture could be resolved into two peaks on preparative g.l.c. with the compound of longer retention time predominating.

*Ketone exchange of 2,3:4,6-di-*O*-isopropylidene-α-*L*-sorbofuranose* (**1**) *in methyl ethyl ketone.* — A solution of **1** (2.60 g, 10 mmoles), perchloric acid (71–72%, 0.05 ml), and methyl ethyl ketone (36 ml) was stirred at room temperature. Analysis by preparative g.l.c. indicated the presence, after 15 min, of 93% of **3** and **4**, 1.7% of **5**, and 4.7% of **1**, and after 26 h 17% of **3** and **4** and 79% of **5**. At this time the solution was neutralized, diluted with water, and extracted with a 1:1 benzene–ether mixture. The extracts were dried (sodium sulfate), concentrated to dryness, and a portion of the resulting solid (1.21 g) was chromatographed on silica gel (110 g). The sample was eluted with ether–hexane mixtures of increasing polarity. Two crystalline fractions (labeled 1 and 2 in order of their decreasing R_F on silica gel) were collected:

Fraction 1: 2,3:4,6-di-*O*-isobutylidene-α-L-sorbofuranose (**5**), m.p. 104–107°, $[\alpha]_D^{25}$ −14.5° (*c* 0.87, ethanol).

Fraction 2 (**3** and **4**): m.p. 85–95°.

Anal. Calc. for $C_{14}H_{24}O_6$: C, 58.31; H, 8.39. Found: C, 58.37; H, 8.57.

A sample of **5** (120 mg, 0.42 mmole) was hydrolyzed in the same way as the mixture of **6** and **7** (see following paragraphs). The reaction mixture, on workup, gave a solid (96 mg, 98%), m.p. 90–92°, $[\alpha]_D^{25}$ +13.4° (*c* 0.93, ethanol). This material, after silylation, had a different retention time on preparative g.l.c. than silylated **2**, although the melting point of a mixture of this material and **2** was 89–91°.

The same reaction was repeated on 52 g of **1** for 30 min and the resulting mixture was evaporated to give a dry solid (44.5 g) showing on preparative g.l.c. one major and two minor peaks. The solid was chromatographed on silica gel (750 g), and the material was eluted with mixtures of ether and hexane of increasing polarity. The first 14.0 g eluted was a mixture of **3** and **5**; the next 14.5 g eluted was pure **3**; the last 11.1 g eluted was a mixture of **3** and **1**.

The pure 4,6-*O*-isobutylidene-2,3-*O*-isopropylidene-α-L-sorbofuranose (**3**) so obtained was a 1:1 mixture of diastereomers (g.l.c.) which could be separated on a silica gel plate.

Anal. Calc. for $C_{13}H_{22}O_6$: C, 56.92; H, 8.08. Found: C, 56.63; H, 7.81.

A sample of **3** was hydrolyzed with dilute acetic acid as just described to give an oil which solidified on being kept. The solid, after recrystallization from benzene, gave **2**, m.p. 88–90°, identical with authentic material.

Ketone exchange of **1** *in diethyl ketone.* — A solution of **1** (2.60 g, 10 mmoles), perchloric acid (71–72%, 0.05 ml), and diethyl ketone (36 ml) was stirred for 6.5 h at 23°. The solution was neutralized with 4M aqueous sodium hydroxide solution (0.7 ml), filtered, and concentrated to an oil. A portion (1.89 g) of this oil was chromatographed on silica gel (150 g). The sample was eluted with ether–hexane mixtures of increasing polarity. The first pure fraction eluted consisted of 2,3:4,6-di-*O*-(3-pentylidene)-α-L-sorbofuranose (**8**), m.p. 58–60°, $[\alpha]_D^{25}$ −12.2° (*c* 1.09, ethanol).

Anal. Calc. for $C_{16}H_{28}O_6$: C, 60.74; H, 8.92. Found: C, 60.74; H, 8.91.

A solution of **8** (20 mg, 0.063 mmole), acetic anhydride (2 ml), and pyridine (1 ml) was stirred for 24 h at room temperature. On workup, an oil was obtained which was homogeneous on g.l.c.

A sample of **8** (20 mg, 0.063 mmole), prepared from L-sorbose, was hydrolyzed in the same way as the mixture of **6** and **7**. It gave a compound which on t.l.c. had the same R_F as that of the product, formed by the hydrolysis of a mixture of **6** and **7**, that had the highest R_F.

The next fraction eluted was a mixture of **6** and **7** which was used in the subsequent hydrolysis experiments.

The same reaction with diethyl ketone was performed for 13 min. The slurry obtained by addition of water (25 ml) to the residue was extracted with a 1:1 ether–benzene mixture (5 × 50 ml). The extracts were combined, dried (magnesium sulfate), filtered, concentrated, and recrystallized from pentane. The resulting solid (m.p. 77–78°) was purified by chromatography on silica gel (27.8 g) to give crystalline **6** (1.2 g, 42%, m.p. 84–86°) which gave one spot on t.l.c. and one peak on g.l.c.

Anal. Calc. for $C_{14}H_{24}O_6$: C, 58.31; H, 8.39. Found: C, 58.42; H, 8.26.

The reaction was repeated and aliquots (3 ml) were withdrawn after 5 min, 20 min, and overnight, and analyzed by g.l.c. After 5 min, **6** and **7** represented 73% of the reaction mixture, with none of **8**; at 20 min, **6** and **7** represented 79% and <1% of **8**. After overnight reaction, **6** and **7** were reduced to 20% and **8** had increased to 48%.

A solution of **6** (100 mg, 0.35 mmole), acetic anhydride (1.0 ml), and pyridine (0.8 ml) was stirred for 4 h at room temperature. The reaction mixture was evaporated to yield an oil which gave one spot on silica gel t.l.c., $[\alpha]_D^{25}$ −11.8° (*c* 0.98, ethanol).

A sample of **6** (120 mg, 0.42 mmole) was hydrolyzed in the same way as the mixture of **6** and **7** to give a solid (90 mg, 97%), m.p. 89–90°, which showed one spot on t.l.c. This material, recrystallized from benzene, gave crystals, m.p. 90–92°, identical with an authentic sample of **2**.

A solution* of a mixture of **6** and **7** (122 mg, 0.42 mole) in aqueous acetic acid (5 ml of a solution of 0.1 ml of glacial acetic acid and 500 ml of water) was heated for

*This procedure is based on that for selectively hydrolyzing **9**.

4 h at 70°. The solution was cooled, evaporated, and the residue purified by preparative t.l.c. on silica gel (elution with 1:2:2 methanol–dichloromethane–hexane). Four fractions were obtained (2, 19, 15, and 5 mg, respectively). The R_F on silica gel of fraction 3 was the same as that of authentic **2**.

A solution of fraction 2 (40 mg, 0.16 mmole), *p*-nitrobenzoyl chloride (118 mg, 0.64 mmole), and pyridine (2 ml) was stirred for 5 days at room temperature. The mixture was filtered, the filtrate evaporated, and the residue purified by preparative t.l.c. and recrystallized from chloroform–ethanol to give a tri-*p*-nitrobenzoate, m.p. 139–141°, identical with 2,3-*O*-isopropylidene-1,4,6-tri-*O*-*p*-nitrobenzoyl-α-L-sorbofuranose (**16**) described in the next paragraph.

2,3-O-Isopropylidene-1,4,6-tri-O-p-nitrobenzoyl-α-L-sorbofuranose (**16**). — A mixture consisting of **2** (220 mg, 1.0 mmole), *p*-nitrobenzoyl chloride (557 mg, 3.0 mmoles), and pyridine (5.2 ml) was stirred overnight at room temperature. Water (1 ml) was then added to the reaction mixture. An additional amount of water was added and then ether, giving a precipitate (635 mg) which was separated by filtration. The precipitate was recrystallized from acetonitrile to give 136 mg, m.p. 191.5–191.9°. An additional 33 mg was obtained on cooling the mother liquors from the first recrystallization (m.p. 190.1–191.5°; total yield 169 mg, 25%).

1,4,6-Tri-O-p-nitrobenzoyl-2,3-O-(3-pentylidene)-α-L-sorbofuranose (**15**) *from* **16**. — A mixture of **16** (133 mg, 0.20 mmole), perchloric acid (71–72%, 0.01 ml), tetrahydrofuran (3 ml), and diethyl ketone was stirred for 19 h at room temperature. Analysis by t.l.c. showed the presence only of starting material. An additional portion (0.01 ml) of perchloric acid was added and the mixture was heated at 70° for 2 days, after which time no starting material was present. The reaction mixture was then cooled, poured into saturated aqueous sodium hydrogen carbonate, and extracted with chloroform (6 × 25 ml). The extracts were combined, dried, evaporated, and the residue was recrystallized from aqueous acetone to give crystals, m.p. 135–138°.

Anal. Calc. for $C_{32}H_{29}N_3O_{15}$: C, 55.26; H, 4.20; N, 6.04. Found: C, 54.96; H, 4.05; N, 5.95.

4,6-O-Isobutylidene-2,3-O-isopropylidene-1-O-methyl-α-L-sorbofuranose (**9**) *from* **3**. — To a stirred solution of **3** (6.0 g, 22 mmoles) dissolved in acetone (37.5 ml) and heated to 40° was added dimethyl sulfate (12.5 ml) and 37.5 ml of a 30% aqueous sodium hydroxide solution. Portions (1/10) of each reagent were added every 10 min until the addition was completed. The mixture was then stirred for an additional 1 h at 40°. Hot water (50 ml) was added and the solution was heated at 100° for 2 h (at which time all the methanol and acetone had been distilled). The reaction mixture was allowed to cool and extracted with three portions of ether. The extracts were combined, washed with water, dried (sodium sulfate), and evaporated. The resulting oil was diluted with water (100 ml) and extracted with pentane (6 × 100 ml). The pentane extracts were dried and evaporated to an oil (4.2 g) which was purified by chromatography on silica gel (250 g). The fractions of 4,6-*O*-isobutylidene-2,3-*O*-isopropylidene-1-*O*-methyl-α-L-sorbofuranose (**9**) giving rise to one spot on t.l.c. were combined (3.7 g, 58%).

A sample (250 mg, 0.87 mmole) was hydrolyzed in the same way as the mixture of **6** and **7**. After the same workup, a hygroscopic solid (184 mg) m.p. 75–80° was obtained. This material was acetylated with acetic anhydride (0.8 ml) and pyridine (1.5 ml) for 6 h at room temperature. The reaction mixture was diluted with water (5 ml) and extracted with ether (6 × 50 ml). The extracts were dried (magnesium sulfate) and concentrated to give 93 mg as an oil, $[\alpha]_D^{25}$ +1.8 (*c* 1.3, ethanol).

Anal. Calc. for $C_{14}H_{22}O_8$: C, 52.83; H, 6.97. Found: C, 53.07; H, 6.99.

4,6-O-Isobutylidene-2,3-O-isopropylidene-1-O-methyl-α-L-sorbofuranose (**9**) *from* **10**. — A solution of **10** (500 mg, 1.82 mmole), prepared according to Sowden and Mao[10], was hydrolyzed in the same way as the mixture of **6** and **7**. Part (208 mg) of the oil obtained on workup was acetylated with acetic anhydride (0.8 ml) in pyridine (1.5 ml) for 3 days at room temperature. The acetylation mixture was diluted with water (10 ml), and extracted with ether (6 × 50 ml). The extracts were combined, dried (magnesium sulfate), and evaporated to yield an oil, $[\alpha]_D^{25}$ +1.95° (*c* 2.1, ethanol). The i.r. and n.m.r. spectra of this compound were superimposable with those of the diacetate obtained by hydrolysis and acetylation of **9**.

Ketone exchange of **9** *in acetone*. — A solution of **9** (279 mg, 0.97 mmole) and perchloric acid (71–72%, 0.05 ml) in acetone (36 ml) was stirred and heated for 72 h at 40°. A portion of the solution was neutralized, concentrated to dryness, and purified by chromatography on silica gel. A solid was obtained which was recrystallized from pentane to give crystals, m.p. 53–56°, identical with an authentic sample of **10**.

Rate of ketone exchange of **3**. — A solution of **3** (2.74 g, 10 mmoles), perchloric acid (71–72%, 0.05 ml), and methyl ethyl ketone (36 ml) was stirred at room temperature (21.5°). Aliquots (3 ml) were taken after every h from 1–8 h, after 24 and 30 h, then neutralized, filtered, diluted to 10 ml, and analyzed by g.l.c.

Time (h)	1	2	3	4	5	6	7	8	24	30
3 (%)	83.7	70.5	65.0	57.6	51.7	45.0	43.0	38.7	15.4	13.6
5 (%)	16.3	29.5	35.0	42.4	48.3	55.0	57.0	61.3	84.6	86.4

Rate of ketone exchange of **9**. — A solution of **9** (2.88 g, 10 mmoles), perchloric acid (71–72%, 0.05 ml), and methyl ethyl ketone (36 ml) was stirred at 23°. Aliquots (3 ml) were removed every h from after 1–8, after 24, and 30 h, neutralized, diluted to 10 ml, and analyzed by g.l.c.

Time (h)	1	2	3	4	5	6	7	8	24	30
9 (%)	89.3	80.8	76.1	70.0	64.9	60.9	57.9	55.2	29.1	26.7
17 (%)	10.7	19.0	23.9	30.0	35.1	39.1	46.1	44.8	70.9	73.3

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