The desired **ethyl methallyloxypivalate** was obtained in only 17% yield, b.p. 91–94.5° (16 mm.); the later fraction, b.p. 94.5° (16 mm.), had $n^{25}D$ 1.4268, d^{25}_{25} 0.9203, MR 55.77 (calcd. 52.85).

Anal. Calcd. for $C_{11}H_{20}O_3$: C, 66.0; H, 10.0. Found: C, 65.9, 66.1; H, 10.2, 10.2.

The unsaturated ester was hydrogenated in methanol at atmospheric pressure over platinum oxide. The reduction was complete in 15 minutes. Most of the methanol was removed from the filtered solution, and the residue was refluxed with methanolic potassium hydroxide for 2.75 hours. The acid was isolated by evaporating the methanol, acidifying, and extracting with ether. **Isobutoxypivalic acid** was obtained in 55% yield, b.p. 78° (0.9 mm.), $n^{25}D$ 1.4200, d^{25}_{25} 0.9472.

Anal. Calcd. for $C_9H_{18}O_3$: C, 62.1; H, 10.3; neut. equiv., 174. Found: C, 62.2, 61.8; H, 10.3, 10.5; neut. equiv., 173, 174.

The amides were prepared from the two acids A and B; m.p. 35–36° and 36.5–38°, respectively, mixture m.p. 36–37°.

Anal. Calcd. for $C_9H_{19}NO_2$: N, 8.1. Found: amide A, N, 7.9, 7.9; amide B, N, 8.1, 8.0.

An attempt to alkylate ethyl hydroxypivalate with isobutyl iodide failed owing to competitive dehydroiodination. Since this technique had been used successfully to prepare ethoxypivalic acid[23] (the only previously known alkoxypivalic acid), this failure must be ascribed to the known low reactivity of isobutyl halides in S_N2 displacement reactions and to their pronounced tendency to undergo elimination of hydrogen halide.

Addition of Diethyl Formal to Ethyl Isobutenyl Ether.— Ethyl isobutenyl ether was prepared by the liquid-phase de-ethanolation of isobutyraldehyde diethyl acetal.[15] In our hands, the published directions yielded an ether heavily contaminated with unchanged acetal. Perhaps the head temperature limit given (72–84°) should have been 72–74°. A small distillation column did not achieve complete separation.[24] The ether was added dropwise to a 50% excess of diethyl formal containing a little boron fluoride etherate according to Brannock's method for addition of higher acetals to this ether. Crude 1,1,3-triethoxy-2,2-dimethylpropane was obtained in 60% yield. A higher-boiling frac-

tion is probably the 2:1 adduct resulting from addition of this new acetal to a second mole of vinyl ether, and if so, its formation could be suppressed by use of a larger excess of diethyl formal. The redistilled 1:1 adduct, b.p. 100° (33 mm.), $n^{25}D$ 1.4100, was analyzed.

Anal. Calcd. for $C_{11}H_{24}O_3$: C, 64.66; H, 11.84. Found: C, 64.8, 64.7; H, 11.6, 11.4.

A sample was exposed to the Johnson DNP reagent[19] and yielded ethoxypivalaldehyde 2,4-dinitrophenylhydrazone identical with that prepared from aldehyde obtained by pyrolysis of acetal 3. A second sample was hydrolyzed[15] to ethoxypivalaldehyde, the physical properties and infrared spectrum of which were identical with those of the pyrolysis product.

Addition of dimethyl formal to ethyl isobutenyl ether in the presence of boron fluoride etherate led to a complicated mixture of products because of the rapid interchange of methoxy and ethoxy groups, and because of poly-addition. The mixture of 1:1 adducts was separated by distillation, and hydrolysis gave an inseparable mixture of alkoxy aldehydes. The presence of methoxy- and ethoxy-pival-aldehyde was detected in the infrared spectrum. A dinitrophenylhydrazone prepared from the mixture could not be purified by crystallization; chromatography was not attempted. Methyl isobutenyl ether was no longer available; hence the addition of dimethyl formal was not attempted.

Isobutyl Isobutenyl Ether.—The pyrolyzate of acetal 35 was fractionated. After a large forerun of isobutyraldehyde the ether was collected at 129.0–130.5°, $n^{25}D$ 1.4139.[25] Continued distillation of the remainder yielded a small amount of a mixture boiling at 144–152° (135 mm.), $n^{25}D$ 1.4250, exhibiting the spectrum of the acetal plus a very strong band at 5.85 μ. There was only a faint absorption at 3.7 μ; hence the carbonyl compound is probably a ketone. An attempt to prepare a DNP yielded a mixture heavily contaminated with the derivative of isobutyraldehyde.

The isobutenyl ether was identified by its analysis (Calcd. for $C_8H_{16}O$: C, 75.0; H, 12.5. Found: C, 74.7, 74.8; H, 12.0, 12.1) and by hydrolysis in aqueous acid to isobutyraldehyde (DNP m.p. 183–184°, mixed m.p. 183–184°) and isobutyl alcohol (3,5-dinitrobenzoate m.p. 85.5–86.8°, mixed m.p. 86.5–87.5°).

Acknowledgment.—The author is indebted to James L. Chestnut and Wallace Buskirk for efficient and imaginative technical assistance.

(23) L. Marcilly, *Bull. soc. chim. France*, [3] **31**, 119 (1904).

(24) Preparation of methyl isobutenyl ether for another purpose was accomplished quantitatively by passing isobutyraldehyde dimethyl acetal through a bed of Grade 70 silica at 200°. It is believed that this procedure would be preferred for future preparation of the ethyl ether because of the simplicity and ease of operation; no attention is required once the drop rate has been set. This vapor phase method was not tried with the diethyl acetal since sufficient material was available from the other preparation.

(25) J. L. E. Erickson and M. Z. Woskow, *J. Org. Chem.*, **23**, 670 (1958), report b.p. 131–132°, $n^{25}D$ 1.4138. They state that their series of vinyl ethers shows C=C stretch frequencies at 5.9–6.1 μ and C–O–C stretch at 8.1–9.0 μ. Our product absorbs at 5.91, 8.4, 8.8 and 12.1 μ, all strong. The 12.1 μ band is curiously distorted on the short wave length side. The methyl and ethyl isobutenyl ethers have the same band patterns.

A New Rearrangement. Catalytic Isomerization of m-Dioxanes to β-Alkoxy Aldehydes. III. Reaction Mechanism and By-products

By Christian S. Rondestvedt, Jr.

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The rearrangement is portrayed by a four-stage process: 1. Adsorption on the catalyst; both oxygens of the acetal coördinate with acidic sites on the catalyst surface. 2. The oxygen–carbon bond is weakened to yield a carbonium ion center stabilized by the groups on C-2. 3. Hydrogen migrates from C-6 to C-2, assisted by the ring geometry. 4. Desorption. The by-products of the reaction are rationalized by ring cleavage to a carbonyl compound and a dipolar ion ^-O-CH_2-CMe_2-CH_2^+. Subsequent reactions of this dipolar ion can account for the wide variety of fragments produced.

The effects of acetal structure upon the catalytic isomerization of m-dioxanes to β-alkoxy aldehydes were described in the preceding paper.[1] The present article discusses the mechanism of the rearrangement and attempts to account for some of the unexpected by-products of the reaction.

Acyclic acetals are dealcoholated by acid catalysts to vinyl ethers.[2] By analogy, conversion of

(1) C. S. Rondestvedt, Jr., and G. J. Mantell, *J. Am. Chem. Soc.*, **84**, 3307 (1962).

(2) A few examples of this reaction are found in the work of L. Claisen, *Ber.*, **31**, 1019 (1898); **29**, 1006 (1896); F. Sigmund, *Monatsh.*,
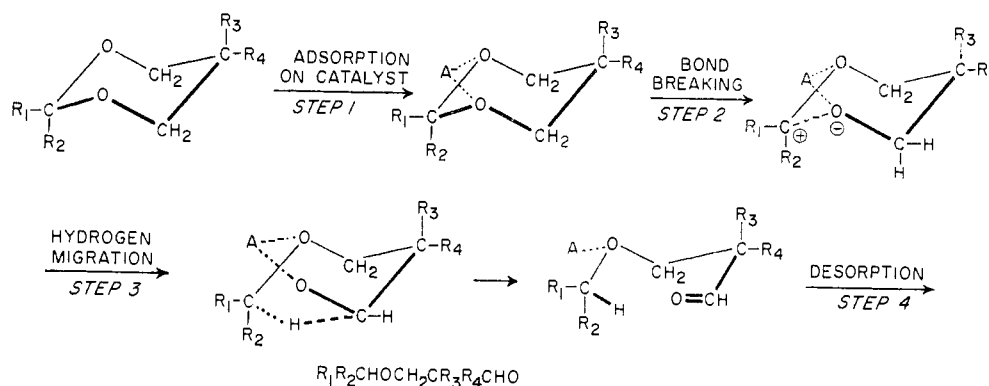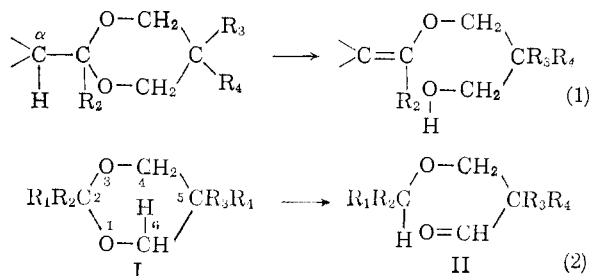
Fig. 1.

the *m*-dioxanes (I) to hydroxy vinyl ethers should be expected (eq. 1). Actually, vinyl ethers were formed only rarely, and the reaction instead followed eq. 2. These two paths differ only in the hydrogen atom which transfers its affiliation. The postulated mechanism of the reaction must account for the absence of vinyl ethers, as well as for the effects of acetal structure upon reactivity.

(1)

I   II   (2)

Mechanism of Rearrangement.—The formation of II is visualized through the following steps (Fig. 1): 1. The unshared electrons on the oxygen atoms coördinate with acidic sites A on the surface of the solid catalyst. 2. The electrons forming the bond between O-1 and C-2 are shifted toward the coördinated O-1, creating a positive center at C-2. This carbonium center is stabilized by electron-donating groups attached to C-2, especially the oxygen atom O-3. 3. The "axial"[3] hydrogen atom at C-6 is practically within

bonding distance of the positive C-2. As the O-1 to C-2 bond is broken, a bond is formed between H-6 and C-2. 4. The alkoxy aldehyde is desorbed from the catalyst surface. These steps are discussed in turn.

1. **Adsorption on the Catalyst.**—Acidic sites on the catalyst surface are believed to coördinate with *both* oxygen atoms of the *m*-dioxane ring. Fisher–Hirshfelder and Stuart–Briegleb models show that in a chair conformation of the ring, both oxygen atoms are simultaneously accessible to the surface atoms of a model of $(SiO_2)_x$. Dreiding models suggest that a slightly twisted boat form with R_1 equatorial and one methyl group at C-5 away from the oxygens would offer the least repulsion toward a catalyst surface. Two-point adsorption is impeded when both R_1 and R_2 are bulky groups, but this was not the case with the acetals studied. If R_1 is considerably bulkier than R_2, the acetal prior to adsorption should exist principally as the chair conformer in which R_1 is equatorial. In this conformation, however, R_1 is uncomfortably close to the catalyst surface, and repulsions should impede complex formation. The R_1–surface repulsions are eliminated if R_1 assumes an axial position.[5] The energy required for the equatorial to axial shift (1–4 kcal./mole, depending on the size difference between R_1 and R_2) would be compensated by the difference between the R_1–surface and R_2–surface repulsions.

In contrast, an equatorial 2-*aryl* group can lie flat over the catalyst surface. Not only is it unnecessary to force the aryl group into an axial position to minimize R_1–surface repulsion, adsorption can be enhanced by interaction between the π-electrons of the aromatic ring and additional acidic sites on the surface. The extent of this secondary adsorption would depend to a marked extent on the nature of substituents attached to the aromatic ring. It is well known that negative groups such as Cl, NO_2 and CF_3 reduce the π-basicity of aromatic rings drastically; in acetals containing these groups (16–20, 23[6]), ring complexing is probably prevented. Electron-releasing groups such as alkyl, methoxy and dimethylamino are known to increase the basicity, and therefore

51, 234 (1929); 58, 268 (1931); D. B. Killian, G. F. Hennion and J. A. Nieuwland, *J. Am. Chem. Soc.*, 57, 544 (1935); R. H. Hall, A. R. Philpotts, E. S. Stern and W. Thain, *J. Chem. Soc.*, 3341 (1951); W. H. Carothers, U. S. Patents 2.071,252 and 2,110,499; W. L. Howard and N. B. Lorette, *J. Org. Chem.*, 25, 521, 525 (1960); W. L. Howard and J. H. Brown, *ibid.*, 26, 1026 (1961).

(3) Throughout this paper, the conformations of the 1,3-dioxacyclohexane ring (*m*-dioxane) will be interpreted in terms of the conformational analysis used for cyclohexane derivatives. The literature records no X-ray or electron diffraction study of this ring system. In its absence, it will be assumed that the preferred conformation of *m*-dioxanes is the chair.[4] Since there are no hydrogen atoms on O-1 and O-3, an important 1,3-diaxial interaction is missing. It appears from models that a boat conformation in which one oxygen is at the bow is also reasonable, since bowsprit-flagpole interactions are absent. A further dimensional difference is that oxygen has a slightly smaller covalent radius than carbon.

(4) The chair conformation of *m*-dioxanes is preferred by B. Dobinson and A. B. Foster, *J. Chem. Soc.*, 2338 (1961), and previous papers, on the basis of studies of the hydrogen bonding of 5-hydroxy-*m*-dioxanes. These authors write a bifurcated hydrogen bond between the C-5 hydroxyl and both acetal oxygens. Models show that hydrogen bonding is also probable in some boat conformations.

(5) These repulsions may assist the hydrogen-transfer stage of the reaction; see section 3.

(6) The arabic numerals are the reference numbers assigned to the acetals in the previous papers.[1]

acetals 14–15, 21–22 should form complexes more readily. These predictions are confirmed in part by the experimental results. 2-*Phenyl*-5,5-dimethyl-*m*-dioxane is rearranged much more readily than 2-*alkyl*-5,5-dimethyl-*m*-dioxanes, while negatively substituted-phenyl-*m*-dioxanes are not rearranged at all on pumice. The positively substituted-phenyl compounds, surprisingly, are also difficult to rearrange; our experience suggests, however, that this anomaly results from desorption difficulties (see section 4).

"Extra" oxygen atoms or other basic centers outside the acetal ring reduce the reactivity of *m*-dioxanes in this rearrangement; compare the results from acetals 26–30, 47–49 with those from the simple acetals 1–8. It seems that adsorption at the "extra" oxygen atom reduces the probability of adsorption with the orientation required for rearrangement. Support for this interpretation is found in the normal rearrangement of acetal 33, in which the oxygen in the side-chain group $(CH_3)_2$-

$$CHCH_2OCH_2C(CH_3)_2\overset{\diagup}{\underset{\diagdown}{C}}H$$ is screened by fifteen

atoms (13 H and 2 O) in the "six" position.[7] Models also show the very thorough masking of this oxygen. Examination of a methoxyethyl-*m*-dioxane (I, $R_1 = CH_3OCH_2CH_2$, $R_2 = H$) would show whether this interpretation is valid.

Some other anomalies may also result from steric interference with proper adsorption on the catalyst surface. The long chain in acetal 34 can indeed assume conformations in which it does not interfere either with the catalyst surface or the acetal oxygen atoms, but only at the cost of increased activation entropy.

The two 4-isopropyl-*m*-dioxanes 35–36[10] do not undergo this rearrangement to any significant extent. The postulated two-point attachment to the catalyst ought to yield approximately equal quantities of aldehyde and ketone, since the probabilities of breaking the O-1 to C-2 and the O-3 to C-2 bonds should be equal. However, the 4-isopropyl-*m*-dioxanes have six more hydrogen atoms in the "six" position[7] with respect to the catalyst than 4-unsubstituted *m*-dioxanes. In the 2,4-diequatorial conformation, the 4-isopropyl substituent would be in contact with the catalyst surface if there were two-point adsorption. Though catalyst–substituent repulsions would be relieved by inversion of the molecule to 2,4-diaxial, the resulting inter-group non-bonded repulsions would

(7) Newman's "Rule of Six" is a convenient way of estimating the probable steric hindrance to a reaction.[8] The attacking reagent is numbered 1 and the atom undergoing attack is numbered 2; if the number of atoms in the "6" position exceeds seven or so, marked steric retardation will be observed at atom 1.

(8) M. S. Newman, ed., "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1956, especially p. 206. The rule was originally applied to compounds involving unsaturation between atoms 1 and 2, as in carbonyl additions, but it may be applied to substitution reactions if the attacking reagent is numbered 1, according to Gould.[9]

(9) E. S. Gould, "Mechanism and Structure in Organic Chemistry," Holt, Rinehart and Winston, New York, N. Y., 1959, p. 323 footnote.

(10) The *cis*-isomer (substituents at C-2 and C-4 both equatorial) is probably much more abundant than the *trans*-isomer (one substituent inevitably axial) in the samples of these acetals; this statement was not verified, however. Equations for the reactions discussed in this paragraph are given in the preceding paper.

cost a prohibitive amount of energy. On the other hand, though O-3 is screened, O-1 is not. If the alkoxy aldehyde rearrangement proceeded through single-point attachment at O-1, the rate with the 4-isopropyl acetals should be reduced only by the statistical factor of 2, and the product should be exclusively aldehyde, not ketone. It is neither; rather vinyl ether formation occurs according to eq. 1, followed by cleavage of the product.

Though our experiments support the two-point adsorption hypothesis, *m*-dioxanes with smaller substituents in the 4-position should be studied. The *cis* and *trans* isomers of 2,4,5,5-tetramethyl-*m*-dioxane are logical candidates. It is by no means certain that a 4-methyl group is small enough for two-point absorption, since it was found that a *gem*-dimethyl group next to the acetal oxygen prevented rearrangement (4,4-dimethyl-*m*-dioxane, 59). The failure to rearrange 2,4,4-trimethyl-1,3-dioxolane (51) may have resulted as much from hindrance to two-point adsorption as from the smaller ring size.

2. Bond Breaking and Carbonium Ion Stabilization.—When rupture of the O-1 to C-2 bond has advanced sufficiently, C-2 will acquire carbonium ion character. If effective catalyst coördination has already occurred, the energy required to break this bond will control the rate of rearrangement. This energy should be chiefly dependent on the ability of the groups at C-2 to delocalize (stabilize) the positive charge.[11] It should be possible to estimate the stabilizing ability of substituents at C-2 from consideration of other alkoxycarbonium ion reactions. Apparently there is no vapor-phase catalytic reaction of acetals or similar compounds which has received quantitative treatment. The closest parallel reaction is the acid-catalyzed hydrolysis of acetals in homogeneous liquid phase, and here the effects of structure on rate are generally well understood in terms of a simple mechanism. With the assumptions that mass transfer is not rate-controlling and that the adsorption process is similar for all simple acetals undergoing normal rearrangement, the effects of structure in liquid-phase hydrolysis can be compared to those obtained in this work.
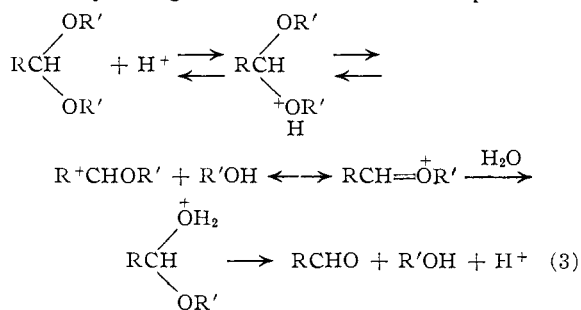
Acid-catalyzed hydrolysis proceeds *via* a carbonium ion in which the positive charge is delocalized through electron donation from the other oxygen atom (eq. 3).[12] The absence of a second oxygen accounts for the relatively slow hydrolysis of simple ethers. Kreevoy and Taft[13] determined the rates of hydrolysis of an extensive series of *diethyl* acetals in 50% aqueous dioxane at 25°. Their accurate measurements permitted correlation of reactivity with rather subtle structural changes. For comparison with the present results, their data

(11) To simplify the pictorial representation of the intermediates, they are drawn with unit charges. However, a full positive charge is probably never developed at C-2, so the charges imply only an electron deficiency (or surplus) at the atoms shown.

(12) E. R. Alexander, "Principles of Ionic Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1950, p. 215; see also J. M. O'Gorman and H. J. Lucas, *J. Am. Chem. Soc.*, **72**, 5489 (1950); M. M. Kreevoy and R. W. Taft, *ibid.*, **77**, 3146 (1955); **82**, 3064 (1960).

(13) M. M. Kreevoy and R. W. Taft, *ibid.*, **77**, 5590 (1955).

have been grouped to show the following rate sequence: ketals $>$ α,β-unsaturated acetals $>$ benzal $>$ alkyl acetals $>>$ formal. The hydrolysis of both ketals and acetals is retarded by negative substituents on the carbon α- to the acetal carbon; this retarding effect in both series decreases in the order $Cl > Br > AcO > RO > HO > Ph > PhCH_2$. Comparable data for hydrolysis of *cyclic* acetals are not available. We assume that the difference in rate between cyclic and diethyl acetals of various aldehydes and ketones would be approximately constant; at least the differences should not vary enough to disturb the above sequences.

$$RCH\begin{array}{c}OR'\\ \\ OR'\end{array} + H^+ \rightleftarrows RCH\begin{array}{c}OR'\\ \\ {}^+OR'\\H\end{array} \rightleftarrows$$

$$R^+CHOR' + R'OH \longleftrightarrow RCH\overset{+}{=}OR' \xrightarrow{H_2O}$$

$$RCH\begin{array}{c}\overset{+}{O}H_2\\ \\ OR'\end{array} \longrightarrow RCHO + R'OH + H^+ \quad (3)$$

The reactivities of the cyclic acetals in rearrangement decrease in the order ketal $>$ alkyl acetal $>>$ formal, consistent with the idea that stabilization of the C-2 carbonium ion is rate controlling. But the benzal (13) is the most reactive and the α,β-unsaturated acetals (2-vinyl- (6) and 2-isopropenyl-5,5-dimethyl-m-dioxane[14]) are almost inert to pumice. These do not fit the Kreevoy–Taft sequence at all. Moreover, the substituted benzals appear not to fit a rational pattern. Numerous investigators have shown repeatedly that in reactions proceeding *via* a benzyl carbonium ion intermediate (*e.g.*, solvolysis of p-$YC_6H_4CH_2X$), the rate is markedly increased by electron-donating groups Y, such as alkyl and alkoxyl, and retarded by substituents of the opposite category such as nitro, halogen and trifluoromethyl. The p-tolyl- and p-cumyl-m-dioxanes (14–15) should yield more stable carbonium ions than the phenyl derivative 13; therefore 14–15 should rearrange more readily than 13. There were indications that *fresh* pumice rearranges 14–15 readily, but the catalyst was so rapidly deactivated, perhaps through failure of the desorption mechanism, that no firm conclusion on reactivity could be drawn. The inertness of the p-anisyl and p-dimethylaminophenyl compounds 21–22 is unmistakable, but here it is certain that desorption is difficult (see section 4).

3. **Hydrogen Transfer from C-6 to C-2.**—The first two steps just discussed are likewise involved in vinyl ether formation from acyclic acetals.[2,15] Why are the cyclic acetals not converted to vinyl ethers? We believe the answer is given by the ring geometry. First, compared to cyclohexane, the smaller size of oxygen relative to carbon tends
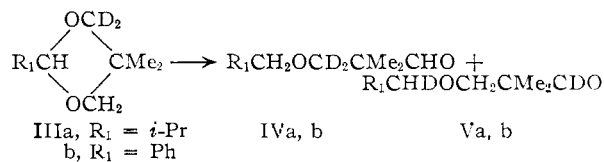
to shrink the ring somewhat and brings the axial hydrogen at C-6 closer to C-2. Simultaneously the α-hydrogen of R_1 (which must be removed for vinyl ether formation) will lie further from O-1. The detailed mechanism of vinyl ether formation on a catalyst surface is not known with certainty, but if the catalyst must assist in removal of this α-hydrogen, it cannot when R_1 is axial. If R_1 is equatorial, R_1–catalyst repulsions push C-2 closer to H-6. Second, the "geminal" effect of the two substituents R_3 and R_4 at C-5 also tends to compress the ring and force the axial H-6 close to C-2.[16]

When the O-1 to C-2 bond is stretched, H-6 can come within bonding distance of C-2 by a slight rotation of C-6 around the C-5 to C-6 bond. Dreiding models show that the C-2 to H-6 internuclear distance is about 15% shorter in the chair form than in the boat form. This proximity is undoubtedly one reason why H-6 migrates before the ends of the broken bond can fly apart; see the discussion of ring cleavage in the By-products section. A second reason is that the postulated two-point attachment to the catalyst would retard the separation of the two ends and allow more time for hydrogen transfer.

The deuterated acetals IIIa and IIIb were prepared and rearranged to answer the question whether hydrogen migration is synchronous with bond breaking or is a fast subsequent step. The results support the assertion that it is synchronous. Each acetal yielded a mixture of IV and V in about

$$R_1CH\begin{array}{c}OCD_2\\ \\ OCH_2\end{array}CMe_2 \longrightarrow \begin{array}{l}R_1CH_2OCD_2CMe_2CHO + \\ R_1CHDOCH_2CMe_2CDO\end{array}$$

IIIa, $R_1 = i$-Pr   IVa, b   Va, b
b, $R_1 = $ Ph

60:40 ratio; that is, protium migrates more readily than deuterium. The assumed intermediate is symmetrical, and the statistical probabilities of migration of protium and deuterium are equal.[19a,b]

(14) This acetal is formed during pyrolysis by loss of formaldehyde from acetal 28.[1]

(15) Isobutyraldehyde dimethyl acetal is quantitatively dealcoholated by the silica catalyst at 200° to methyl isobutenyl ether. Acetone dimethyl ketal is partially converted to methyl isopropenyl ether by pumice at 375°.[1]

(16) The "geminal" or "Thorpe-Ingold" effect of twinned alkyl groups has been invoked frequently to explain unusual differences in reactivity between unsubstituted and *gem*-disubstituted compounds. For example, 2,2-dialkyl-1,3-propanediols form cyclic acetals more rapidly and with a more favorable equilibrium than 1,3-propanediol itself.[17,18]

(17) M. S. Newman and R. J. Harper, *J. Am. Chem. Soc.*, **80**, 6350 (1958).

(18) The Thorpe-Ingold effect has recently been reviewed by P. R. Schleyer, *ibid.*, **83**, 1368 (1961). He concluded from the literature and from his own experiments that the "geminal" effect is real. See also ref. 6, pp. 117-120 and 460-470, and N. L. Allinger and V. Zalkow, *J. Org. Chem.*, **25**, 701 (1960).

(19) (a) It is unlikely that the observed isotope effect results from a "second-order" difference between the hyperconjugative abilities of deuterium and protium, of the type discussed by V. J. Shiner, *Tetrahedron*, **5**, 243 (1959), and E. S. Lewis, *ibid.*, **5**, 143 (1959). Such second-order effects are normally quite small and, moreover, a β-deuterium atom hyperconjugates with a positive center less effectively than β-protium. (b) The acetals III were synthesized from 2,2-dimethyl-1,3-propanediol-1,1-d_2 which was prepared by lithium aluminum deuteride reduction of methyl β-hydroxypivalate. The synthesis and pyrolysis of III was performed by Dr. Harold W. Pier. The isotopic purity of the acetals was established mass-spectroscopically by Prof. Kenneth B. Wiberg and his collaborators at the University of Washington. The mixtures of IV and V were analyzed by infrared spectroscopy by Dr. Robert K. Miller, and also by nuclear magnetic resonance by Mr. Thomas E. Beukelman, both in this Laboratory. I am greatly indebted to all of these chemists for their valuable contributions.

The ring geometry favoring hydrogen transfer can be modified by substituents elsewhere in the ring. The ring flexibility and the favorable geminal effect of the two alkyl groups at C-5 will be reduced by incorporating these alkyl groups into a *spiro* ring. Thus a four- or five-membered *spiro* ring (acetals 26–27) prevents rearrangement, although this result is partly explicable by the "extra oxygen" interference with proper adsorption. A six-membered carbocyclic ring allows normal rearrangement (acetals 37–38). It would be desirable to untangle adsorption and geometrical effects by studying acetals with four- and five-membered carbocyclic rings attached to C-5. A condensed ring system, as in 4,5-benzo-m-dioxane and its saturated relatives, would offer additional opportunities for the study of the geometrical factors influencing this rearrangement.
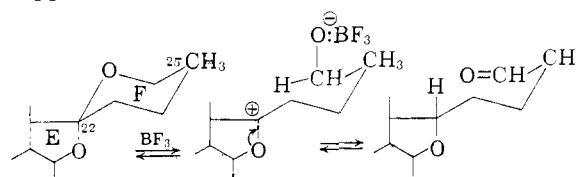
The stereochemical fate of C-2 could not be determined. When the O-1 to C-2 bond is broken, the migrating axial hydrogen could either take up the same position that the leaving oxygen occupied, or it could "invert" C-2. All the acetals which were rearranged successfully are symmetrical with respect to the perpendicular plane through C-2 and C-5; therefore, breaking the O-3 to C-2 bond with migration of H-4 is equally probable. As noted above, substitution of alkyl groups at C-4 to destroy this symmetry prevented normal rearrangement (35–36, 59). A possible approach to this problem is suggested by the partially selective rearrangement of the deuterated acetals III. The tritiated compounds III (T instead of D) should exhibit considerably greater selectivity; if they rearranged uni-directionally, the geometry of hydrogen transfer could be established.

The foregoing description of hydrogen transfer could also apply to the related rearrangement of 1,3-diols to aldehydes *via* a cyclic sulfite.[20]

Sapogenins are *spiro*-acetals in which the two oxygen atoms are in different rings, akin to acetal 57. They can be reversibly isomerized by Lewis acids under mild conditions to δ-alkoxy aldehydes which can be trapped with ethanedithiol.[21a,b] When these aldehydes are enolizable, stereochemical epimerization at C-25 can occur, and this forms the basis of the Marker–Rohrmann isomerization of sapogenins brought about by hot mineral acids. The δ-alkoxy aldehyde first formed recyclizes to the mixture of C-25 epimers, as recently demonstrated.[21c,d] The mechanism proposed[21b,d] is rather similar to that advanced above for the non-reversible m-dioxane isomerization. A key step is hydride transfer to the C-22 carbonium ion; Bartlett has recently discussed such hydride transfers.[21e]

The F-ring of sapogenins may also open in another sense to yield a vinyl ether-alcohol[21e];

(20) This was announced in a preliminary communication by J. H. Crowdle, J. E. Knipper, J. E. Schmidt and R. T. Conley, *J. Org. Chem.*, **25**, 1687 (1960). Details have not yet been published.

(21) (a) C. Djerassi, O. Halpern, G. R. Pettit and G. H. Thomas, *ibid.*, **24**, 1 (1959); (b) G. R. Pettit and W. J. Bowyer, *ibid.*, **25**, 84 (1960); (c) R. K. Callow and P. N. Massy-Beresford, *J. Chem. Soc.*, 2645 (1958); (d) R. B. Woodward, F. Sondheimer and Y. Mazur, *J. Am. Chem. Soc.*, **80**, 6693 (1958); (e) P. D. Bartlett and J. D. McCollum, *ibid.*, **78**, 1441 (1956); (f) J. A. Zderic, L. Cervantes and M. T. Galvan, *ibid.*, **84**, 102 (1962).

this process is reversible unless the alcohol is trapped.[21f]

4. **Desorption.**—Most of the simple alkoxy aldehydes encountered in this work are readily released from the catalyst surface. When isobutoxypivalaldehyde (4) was passed a second time through the same pumice bed at 400°, it was recovered almost quantitatively. The same treatment of benzyloxypivalaldehyde (13) caused some degradation to toluene and other fragments (see "By-Products section below"), the extent depending on temperature and contact time. The difficulties with p-alkylbenzals are probably in part related to slow desorption, for with the acetals 14–15 the initial facile rearrangement was rapidly retarded. The active sites apparently became saturated by products which were released slowly, after further alteration.

As already noted, an "extra" oxygen atom not only interferes with proper adsorption on the catalyst but also retards desorption, especially with the p-anisyl compound 21. The more basic nitrogen in 22 is retained even more strongly, and the high temperature required to force desorption completely degrades the acetal or its rearrangement product before it leaves the furnace.

The mechanism of rearrangement outlined above correlates most of our experimental observations. The assumptions made about adsorption on the catalyst surface should be tested and the entire adsorption process clarified by a detailed physical study of the interaction of m-dioxanes and solid catalysts. It should be possible to correlate catalytic activity of a solid with its crystal structure and chemical composition. The effect of acetal structure on reactivity is explained well by stabilization of a carbonium ion if the apparent exceptions—2-aryl- and 2-vinyl-m-dioxanes, and acetals with "extra" oxygen atoms—are blamed on an alteration of the mode of adsorption or desorption.

By-Products.—Even the most successful rearrangements yield small amounts of cracking fragments as well as II. In less favorable cases, fragmentation may predominate. Since most of the experiments were performed with acetals of neopentyl glycol (2,2-dimethyl-1,3-propanediol), the following discussion will deal chiefly with the specific acetal type VI.

Depending on the nature of R_1 and R_2, the following by-products were identified: the carbonyl compound R_1R_2CO from the left-hand side of VI, and formaldehyde, isobutylene, isobutyraldehyde, methyl isopropyl ketone, pivalaldehyde, methanol, 3,3-dimethyloxetane, ethylene, propylene and hydrocarbons with *more* carbons than the building blocks of VI. These fragments were found in the distillation foreruns and for the most part were isolated and identified by conventional means such as physical properties, infrared spectrum
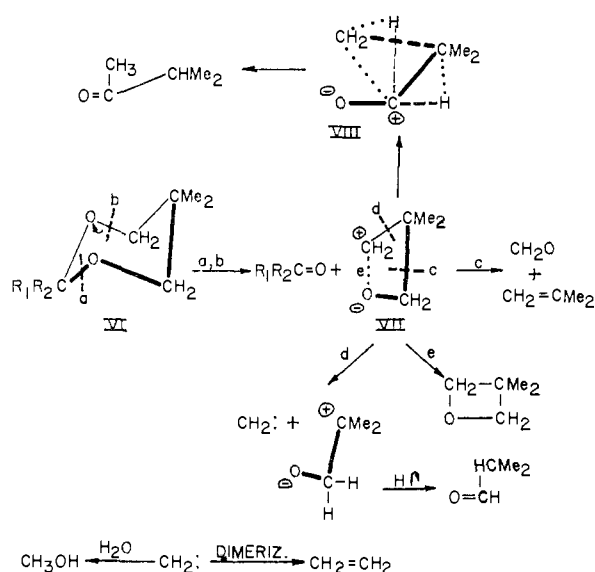
Fig. 2.

and preparation of known derivatives. Some trace components were separated by vapor-phase chromatography (V.P.C.) and identified by time-of-flight mass spectrometry (T.O.F.).[22] The compounds VI, R_1 = aryl, R_2 = H, also furnished $ArCH_3$ as a further by-product. Only rarely were vinyl ethers detected. It should be stated that the by-products from every acetal were studied to identify the major components, but only a few were examined in enough detail to identify all the minor constituents.

These by-products may be rationalized by the scheme given in Fig. 2.[23]

The electron shift b occurring after weakening or breaking of bond a liberates the carbonyl compound $R_1R_2C=O$ and requires no further comment. It is proposed that the remainder of the molecule resembles the dipolar ion VII. Cleavage at c would yield formaldehyde and isobutylene. Fragmentation of 1,3-diol derivatives to olefin and carbonyl compound is well known[24] and these two products might be expected to predominate. They do not. Instead, the major by-product in most examples is isobutyraldehyde, and its formation is depicted via route d; alternatively, the migrating H atom could displace methylene without formation of a new dipolar ion.

Brown and Dougherty[24d] obtained isobutyraldehyde (70% yield) and methanol from neopentyl glycol by heating it with alumina at 200° in the

(22) I am indebted to Mr. Fulton G. Kitson and Dr. Alfred A. Ebert for their expert assistance with the V.P.C. and T.O.F. analyses, respectively.

(23) Undoubtedly most of the reactions take place on the catalyst surface and are influenced by it. The catalyst is not shown explicitly since it is not understood how it participates. In the structures written, dashed lines indicate bonds being broken, dotted lines, bonds being formed.

(24) Some examples of this type of fragmentation are found in the work of: (a) H. E. Zimmerman and J. English, J. Am. Chem. Soc., 76, 2294 (1954), and preceding papers; (b) S. Searles, E. K. Ives and S. Nukina, J. Org. Chem., 24, 1770 (1959); (c) V. J. Traynelis and J. G. Dadura, ibid., 26, 686 (1961); (d) R. W. Brown and G. Dougherty, ibid., 13, 173 (1948); (e) These and other cleavages have been correlated by C. A. Grob, Experientia, 13, 126 (1957), and expressed in a general principle of "complex fragmentation."

liquid phase; this result was confirmed by Searles, et al.,[24b] who also showed that base cleaves this glycol to isobutyl alcohol and formaldehyde. It is of course possible that water from the catalyst surface[25] could hydrolyze the acetal to neopentyl glycol, and such hydrolysis could explain the fact that a fresh catalyst causes much more cleavage than used catalyst. However, susceptible acetals continue to crack long after the surface water would have been exhausted.

Cleavage is not the only fate of VII. It may isomerize by a 1,3-hydride shift (or two 1,2-shifts or by a push-pull mechanism involving surface OH groups) to pivalaldehyde. Traces of pivalaldehyde were always found among the by-products investigated in detail, though it was never a major product. Methyl migration in VII apparently does not occur, for α-methylbutyraldehyde was never observed, even though sought. The formation of methyl isopropyl ketone could be rationalized through two hydride shifts and a methyl migration, but a less labored explanation is presented below.

The dipolar ion VII could also ring-close to 3,3-dimethyloxetane by path e. Close examination of the infrared spectra of crude by-product fractions indicates that traces of dimethyloxetane are probably formed in the pyrolysis of all acetals VI. One ketal, that from cyclohexanone (12), produced about 10% of dimethyloxetane, accompanied by smaller amounts of isobutylene, isobutyraldehyde and formaldehyde.[26] The cyclopentanone ketal (11) gave no more than a trace of oxetane. Apparently the cyclohexyl ring forces O-1 and C-4 to lie closer together than they do in most m-dioxanes, thus facilitating ring closure. Ring closure is also the only significant reaction of the seven-membered 1,3-dioxepanes (52, 54), which are transformed to isobutyraldehyde (or benzaldehyde) and tetrahydrofuran with almost quantitative yield; the conversion increases as the temperature is raised.

Methylene (carbene) is postulated as a cleavage product for several reasons. First, it is the stoichiometric residue remaining after separation of isobutyraldehyde from VII. Second, its reaction with surface hydroxyl groups[25] would yield the methanol which is observed, and the depletion of the surface hydroxyls would explain why methanol production decreases rapidly during a run even though isobutyraldehyde formation continues. Third, carbene could react with surface hydroxyl groups to

(25) The catalysts were baked at 400° for an hour in a stream of nitrogen, and prolongation of this treatment yielded no more water. However, silica and aluminosilicates have surface hydroxyl groups which are not removed except by very drastic heat treatment.

(26) This observation may form the basis of a new method for dehydrating 1,3-diols to oxetanes. Since with ketals, the amount of cracking increases rapidly as the temperature is raised, at around 450–500° cracking should be the chief reaction. The more potent catalyst silica should be even more effective. Provided the other modes of degradation do not predominate, a substantial yield of oxetane could be anticipated.

A blank experiment showed that 3,3-diethyloxetane was almost unchanged by silica at 325°; a little 2-ethyl-1-butene and water were formed by the fresh catalyst, but later portions of the pyrolyzate were essentially pure oxetane. This experiment incidentally shows that the cleavage fragments from other pyrolyses do not result from further degradations of initially formed oxetanes.

yield carbon and water. In pyrolyses where substantial cleavage occurred, water was indeed formed, and the catalyst darkened and gained in weight. Fourth, its dimerization would yield ethylene which could react subsequently by insertion to yield propylene. Fifth, a carbene insertion at the aldehyde C–H bond offers an easy route to methyl isopropyl ketone; this could even occur intramolecularly via a cyclopropane-like intermediate VIII. But the sixth, and most compelling reason is that methylene insertion reactions permit the simplest explanation of the formation of the unexpected products described in the next paragraph.

2 - Isopropyl - 5,5 - dimethyl - m - dioxane is constructed of a four- and a five-carbon block connected by oxygen atoms. Astonishingly, small amounts of six-carbon olefins and paraffins were found by V.P.C.–T.O.F. in the pyrolyzate of a carefully processed large run. The amounts were too small for complete identification, but Dr. Ebert stated that the mass-spectral patterns were unmistakable. Acetal 44 from glutaraldehyde and two moles of neopentyl glycol has three five-carbon blocks. Carefully purified acetal was pyrolyzed in a large run and the by-products were analyzed by distillation, V.P.C. and T.O.F. In addition to the usual major by-products, 1,4-pentadiene and the same six-carbon olefin and paraffin were present in trace amounts. It is unprofitable to speculate further on the mechanism of formation of these unexpected products without knowledge of their structure.

Pyrolysis of 2-aryl-m-dioxanes yielded the usual by-products, and in addition appreciable quantities of the substituted toluene ArCH₃. The amount of ArCH₃ varies from slight to nearly quantitative, depending upon catalyst activity, temperature and particularly ring substitution. The formation of ArCH₃ and ArCHO is most pronounced with rings holding electron-releasing substituents, increasing in the order p-Cl < p-H < p-alkyl < p-CH₃O < p-(CH₃)₂N. Thus the p-dimethylaminophenyl-m-dioxane (22) yielded 90% of p-dimethylaminotoluene on passage through copper chromite. Undoubtedly much of the cleavage takes place directly upon the acetal. The product itself is also attacked. Benzyloxypivalaldehyde was passed through silica at 335°. The effluent contained 23% of the starting material, 56% of benzaldehyde, 12% of toluene, 4% of benzene (together accounting for 97% of the aromatic portion of the molecule), 30% of isobutyraldehyde and 16% of isobutylene. The other aliphatic fragments were not examined in this experiment.

As shown in eq. 4, the hydrogen atom required for toluene formation could come from the other ether carbon. In this case, the stoichiometric residue is dimethylmalonaldehyde. The available information about this little-known compound suggests that it would decarbonylate promptly to isobutyraldehyde under the influence of the acidic catalyst[27a]; alternatively, the complexed ether could

(27) (a) R. K. Miller, in unpublished results in this Laboratory, has prepared (EtO)₂CHCMe₂CHO. His attempts to convert it to the free dialdehyde by mild acid hydrolysis led to ethyl formate, isobutyraldehyde, and ethanol. Hydrolysis in the presence of dinitrophenyl-

disproportionate to benzaldehyde and toluene.[27b] It is also possible to write radical mechanisms for this degradation, but since the reaction takes place on an acidic catalyst, a radical process seems improbable.

$$CO + Me_2CHCHO \quad (4)$$
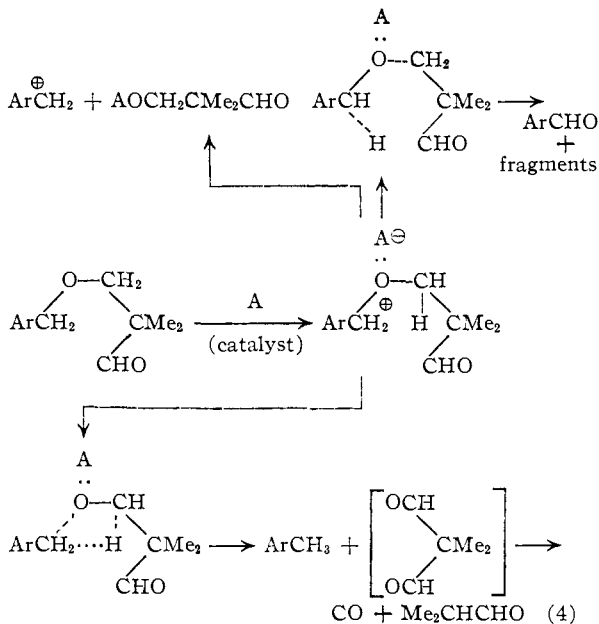
In summary, formation and decomposition of the dipolar ion VII can account for all of the identified by-products. Other mechanisms can of course be written to explain individual products, but the one discussed is simpler and more general. It suggests further experimentation to establish its validity.

Experimental

Preparation of Deuterated Acetals.—Hydroxypivalic acid[28] was esterified with diazomethane to minimize self-esterification. Reduction of the ester with lithium aluminum hydride in ether alone did not go to completion because a large amount of solid complex separated. Addition of about 20 volume % of tetrahydrofuran dissolved the complex and allowed complete reduction (absence of carbonyl in the infrared). This procedure was used with lithium aluminum deuteride, Metal Hydrides, 96.4% pure. The solution was hydrolyzed, dried, and evaporated to leave the solid deuterated diol, which was used directly.

The diol was converted to acetals as described previously.[29]

2-Isopropyl-5,5-dimethyl-m-dioxane-4,4-d₂ (IIIa) boiled at 72° (30 mm.), n^{25}D 1.4217; the undeuterated analog boiled at 70° (30 mm.), n^{25}D 1.4227.[26] A vapor-phase chromatogram showed 99.6% purity. Mass spectral analysis showed the material to be at least 97% dideuterio and no more than 3% monodeuterio.

Anal. Calcd. for C₉H₁₆D₂O₂: C, 67.5; H + D, 11.5. Found (by micro-combustion): C, 67.4; H + D, 11.2.

2-Phenyl-5,5-dimethyl-m-dioxane-4,4-d₂ (IIIb) was recrystallized from hexane, m.p. 35.5–36.0°; the undeuterated analog melts at 35–36°.[26] It was 99.7% pure by

hydrazine led to a high yield of dimethylmalonaldehyde bis-dinitrophenylhydrazone. K. C. Brannock, *J. Org. Chem.*, **25**, 258 (1960), observed a similar cleavage with the bis-acetal (EtO)₂CHCMe₂CH(OEt)₂. (b) A. Rieche, H. Seeboth and G. Rohs, *J. prakt. Chem.*, [4] **15**, 139 (1962), obtained benzaldehyde and toluene by passing benzyl ethers or benzyl alcohol over alumina at 340°. They assume that benzyl cations are formed and abstract hydride from the carbon next to the oxygen.

(28) I am indebted to Dr. F. W. Knobloch for supplying this material.

(29) C. S. Rondestvedt, Jr., *J. Org. Chem.*, **25**, 2247 (1961).

V.P.C. analysis. Mass spectral analysis was complicated by cracking at the lowest convenient voltage. Prof. Wiberg estimated a *minimum* of 88% dideuterio derivative was present, and stated that this figure was probably considerably low. The value of 97%, as obtained for IIIa, is probably more realistic, since both acetals were prepared from the same diol.

The infrared spectrum of IIIa shows strong C–D stretching at 4.5 and 4.8 μ. Additional bands not in the non-deuterated analog appear at 9.33m, 10.55s, 11.34s, 11.70m, 12.40m and 13.28mμ. The bands of the non-deuterated analog at 8.20, 10.78, 11.52 and 12.62 μ disappear completely, while those at 10.2 and 10.4 μ are attenuated to shoulders. The bands at 4.5, 4.8 and 12.4 μ are suitable for analysis. The spectrum of IIIb differs from that of its undeuterated analog in a similar way.

Pyrolysis of Deuterated Acetals.—The standard procedure used previously[1] was modified by using a 12 mm. o.d. tube with 12–20 mesh pumice. At 400°, conversion of IIIa to isobutoxypivalaldehyde was 70%, with 6% fragmentation. At 430°, only a trace of acetal remained but almost 30% was fragmented. The optimum temperature appeared to be about 425°, since for analysis of the mixture of IV and V it was desirable to have a minimum of unchanged acetal. The phenyl derivative IIIb was pyrolyzed at 355°.

The crude pyrolyzate of IIIa was collected in a receiver cooled in Dry Ice. It contained 57.2% of mixed IVa and Va, 2.5% of unchanged IIIa, 18.7% of isobutyraldehyde, 18.0% of other low-boiling fragments and 2.6% of high boiling products (V.P.C.). It was pumped at room temperature (1 mm.) to remove volatile products, and the residue was analyzed directly by n.m.r. The composition was 60% IV and 40% Va, calculated from the areas of the aldehyde C–H peak and the CH₂ and CHD peaks. Infrared analysis showed a composition of 57% IV and 43% V. In another run, 25% of the acetal IIIa survived. Because of the substantial correction required for this, the n.m.r. values of 54% IVa and 46% Va (corrected) are probably less reliable.

The crude pyrolyzate of IIIb contained 5.6% of isobutyraldehyde, 3.5% of benzaldehyde, 1.8% of other volatiles and 88.7% of product (V.P.C.; no column was found which would resolve a mixture of acetal and benzyloxypivalaldehyde). It was evacuated at 50–80° (30 mm.), and the residue then contained 1.6% of isobutyraldehyde, 3.6% of benzaldehyde, 0.87% of other volatiles and 94% product; n.m.r. showed 60% IVb, 35% Vb and 5% IIIb. Correcting for the unchanged acetal, the ratio of IVb to Vb was 61:39.

By-products in Acetal Pyrolysis.—Pyrolysis of a large sample of 2-isopropyl-5,5-dimethyl-*m*-dioxane (acetal 4) at 435° caused considerably more than normal fragmentation. V.P.C. analysis of the pyrolyzate showed 68.5% of isobutoxypivalaldehyde, 2.3% of acetal, 10.6% of isobutyraldehyde, 16.5% of other low-boiling materials and 2% of higher-boiling impurities. The volatile components were separated by distillation at bath temperature 60–80° (50 mm.) into a Dry Ice-cooled receiver. V.P.C.–T.O.F. analysis showed isobutylene (3%), acetone (trace), a pentadiene (1%), a pentene or dimethylcyclopropane (0.46%), pivalaldehyde (5%), methyl isopropyl ketone (6.9%) and two six-carbon hydrocarbons (traces), in addition to the 10.6% of isobutyraldehyde already determined. (The percentages are based on starting acetal.)

Examination of the by-products from other acetals was conducted similarly, but since the compositions were not determined quantitatively, the qualitative description given in the Discussion section will suffice.

Positive Halogen Compounds. IV. Radical Reactions of Chlorine and *t*-Butyl Hypochlorite with Some Small Ring Compounds[1]

BY CHEVES WALLING AND P. S. FREDRICKS

The liquid phase photoreaction of cyclopropane with chlorine has been reinvestigated and found to give much 1,3-dichloropropane as well as cyclopropyl chloride. On this basis earlier results[2] on C–H bond reactivities in small rings have been reevaluated. In contrast, little ring opening occurs with *t*-butyl hypochlorite and competitive reactions show decreasing C–H bond reactivities with decreasing ring size for C₆–C₃-cycloparaffins. *t*-Butyl hypochlorite chlorination of methyl- and 1,1-dimethylcyclopropanes occurs chiefly by attack on methyl to give chloromethylcyclopropanes and products arising from ring opening of the intermediate cyclopropylmethyl radicals. Competitive experiments show enhanced methyl reactivity compared with open chain compounds, interpreted as arising from homoallylic conjugation of cyclopropylmethyl radicals. *t*-Butyl hypochlorite reacts with ethylene and propylene oxides to give the corresponding chloroepoxides with little ring opening, and this reagent thus appears to be an excellent mild radical chlorinating agent for a variety of small ring compounds.

In 1959, some results on the liquid-phase photochlorination of C₃–C₆-cycloparaffins were reported in a paper from this Laboratory.[2] The data indicated a continuous decrease in reactivity with decreasing ring size, without the unusual reactivity of cyclopentane predicted by Brown on the basis of "I-strain."[3] However, the results had two anomalous features. First, differences in reactivity were much less than those reported by Knox and Nelson[4] for gas-phase chlorination; second, relative reactivity differences decreased at lower temperatures. Tentatively, our results were ascribed to complex formation between small ring cycloparaffins (particularly cyclopropane) and chlorine atoms, analogous to that proposed by Russell[5] to account for the large solvent effects on selectivity observed in radical chlorinations employing molecular chlorine.[2,5]

We have now repeated the experiments with chlorine, and extended them to similar chlorinations using *t*-butyl hypochlorite. While we confirm the earlier results with C₄–C₆-cycloparaffins,

(1) Support of this work by a Grant from the National Science Foundation is gratefully acknowledged.

(2) C. Walling and M. F. Mayahi, *J. Am. Chem. Soc.*, **81**, 1485 (1959).

(3) H. C. Brown, R. S. Fletcher and R. B. Johannesen, *ibid.*, **73**, 212 (1951).

(4) J. H. Knox and R. L. Nelson, *Trans. Faraday Soc.*, **55**, 937 (1959).

(5) G. A. Russell, *J. Am. Chem. Soc.*, **80**, 4997 (1958).