Stereochemical Aspects of Ether Oxygen Participation. VI. Acid-Promoted Reactions of Medium-Sized Cis [*n*.1.0] Oxabicyclics[1]

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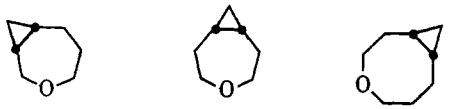
Abstract: The solvolysis of *cis*-3-oxabicyclo[5.1.0]octane (**1**) gave a mixture of three diformates (**14**, **15**, and **16**) which are the result of C_2–C_3 bond heterolysis of the protonated ether. For comparison purposes, **15** was synthesized unequivocally while **14** and **16** were converted to their dihydro derivatives. Suitable credence to the mechanism proposed above was gained by submitting diol **43** to the formolysis conditions. All three formates were similarly produced. The acid-catalyzed ring opening of *cis*-4-oxabicyclo[5.1.0]octane (**2**) gave formates **44** and **45** in approximately a 4:1 ratio. No transannular involvement of the ether oxygen was found. The enhanced proportion of internal cyclopropyl bond cleavage in **2** relative to *cis*-bicyclo[5.1.0]octane has been attributed to a reduction in steric constraints resulting from replacement of a methylene group by the heteroatom. Unequivocal syntheses of both **44** and **45** were achieved. Lastly, *cis*-4-oxabicyclo[6.1.0]nonane (**3**) in formic acid gives rise exclusively to formate **53**. The widely divergent behavior of **3** (internal bond cleavage only) and *cis*-bicyclo[6.1.0]-nonane (exclusive external bond cleavage) is taken as evidence that the solvolysis of **3** proceeds by concerted C_1–C_8 bond rupture and R_2O-5 bonding.

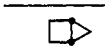
Previous and concurrent work from this laboratory has provided confirmatory evidence that ether oxygen situated in a medium-sized ring is intrinsically capable of interacting with transannularly disposed positive charge *via* R_2O-3[1c] and R_2O-5[1d,e,2] bonding modes. In contrast, the propensity of this polar functionality for direct R_2O-4 involvement appears negligible.[2-4] The present work is concerned with the behavior of medium-sized oxabicyclics **1**, **2**, and **3** under



1 **2** **3**

electrophilic conditions (98–100% formic acid at 50°). Because transannular dipolar and neighboring group effects on the acid-promoted opening of cyclopropane rings had not previously been examined, it was expected that the behavior of **1**–**3** would shed light on such phenomena. One immediate objective was to gain information on the ratio of internal to external bond cleavage and on the possible transannular involvement of ether oxygen and its effect on these processes. Previous experience with electrophilic additions to bicyclo[*n*.1.0]alkanes has revealed preferential *internal* bond cleavage in bicyclo[1.1.0]butanes[5] and bicyclo[2.1.0]pentane.[6,7] A gradual increase in *n* gives rise to proportionately larger amounts of *external* bond rupture until this process operates exclusively in the *cis*- and *trans*-bicyclo[6.1.0]nonanes (see Table I).

Table I. Ring Opening Modes in the Acid-Promoted Opening of Bicyclo[*n*.1.0]alkanes

Hydrocarbon	Internal/external bond cleavage	Conditions	Ref
	1.00	0.07 *M* TsOH in HOAc	*a*
	0.25	0.07 *M* TsOH in HOAc	*a*
	0.10	0.07 *M* TsOH in HOAc	*a*
	~0.01	0.07 *N* H_2SO_4 in HOAc	*b*
	0.00	HCOOH	*c*
	0.00	HCOOH	*d*

[a] Reference 4b. [b] R. T. LaLonde and L. S. Forney, *J. Org. Chem.*, **29**, 2911 (1964). [c] A. C. Cope and G. L. Woo, *J. Amer. Chem. Soc.*, **85**, 3601 (1963). [d] A. C. Cope and J. K. Hecht, *ibid.*, **85**, 1780 (1963).

It is to be specifically noted, however, that the ring opening of bicyclo[5.1.0]octane[8] is significantly slower

(1) (a) Part V: L. A. Paquette and P. C. Storm, *J. Org. Chem.*, **35**, 3390 (1970); (b) part IV: L. A. Paquette and P. C. Storm, *J. Amer. Chem. Soc.*, **92**, 4295 (1970); (c) part III: L. A. Paquette, R. W. Begland, and P. C. Storm, *ibid.*, **92**, 1971 (1970); (d) part II: L. A. Paquette, R. W. Begland, and P. C. Storm, *ibid.*, **90**, 6148 (1968); (e) part I: L. A. Paquette and R. W. Begland, *ibid.*, **87**, 3784 (1965).

(2) L. A. Paquette and M. K. Scott, *ibid.*, **94**, 6760 (1972).

(3) These observations parallel the earlier experience of Winstein in acyclic systems containing methyl ether oxygen [S. Winstein, E. Allred, R. Heck, and R. Glick, *Tetrahedron*, **3**, 1 (1958)] and agree in substance with the later work of Hazen on neighboring acetal participation [J. R. Hazen, *J. Org. Chem.*, **35**, 973 (1970)]. Backside MeO-4 participation has been invoked to account for methoxyl migration in the acetolysis of *endo*-7,7-dimethoxy-2-norbornyl tosylate [P. G. Gassman and J. L. Marshall, *Tetrahedron Lett.*, 2429, 2433 (1968)].

(4) *Bona fide* examples of R_2S-4 participation in carbonium ion reactions are known: (a) L. A. Paquette, G. V. Meehan, and L. D. Wise, *J. Amer. Chem. Soc.*, **91**, 3231 (1969); (b) R. E. Ireland and H. A. Smith, *Chem. Ind. (London)*, 1252 (1959).

(5) K. B. Wiberg and G. Szeimies, *J. Amer. Chem. Soc.*, **92**, 571 (1970); L. A. Paquette, G. R. Allen, Jr., and M. J. Broadhurst, *ibid.*, **93**, 4503 (1971); and relevant references cited in these papers.

(6) (a) R. Criegee and A. Rimmelin, *Chem. Ber.*, **90**, 414 (1957); (b) R. T. LaLonde and L. S. Forney, *J. Amer. Chem. Soc.*, **85**, 3767 (1963).

(7) In contrast, the reaction of bicyclopentane with HCl in the vapor phase and with concentrated hydrochloric acid in a two-phase system affords almost equal amounts of cyclopentene and cyclopentyl chloride (R. S. Boikess and M. Mackay, *J. Org. Chem.*, **36**, 901 (1971)). A changeover in mechanism has been proposed to account for this discrepancy.

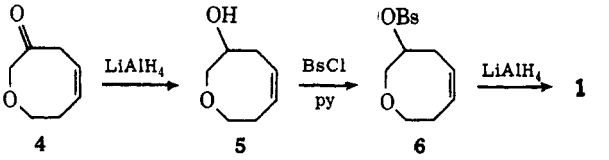
(8) Similar direct rate comparisons for the epimeric bicyclo[6.1.0]-nonanes are lacking.

than that of bicyclo[4.1.0]heptane. The principal causative factor underlying this rate retardation is presumably steric in origin.[9] Perhaps because backside (SN2) nucleophilic displacements in medium-sized rings are slow,[10] transannular hydride shifts attain kinetic significance. In any event, the tendency for transannular hydride shift is much greater in *cis*-bicyclo[6.1.0]nonane (97%)[11] than in *cis*-bicyclo[5.1.0]-octane (12%).[9]

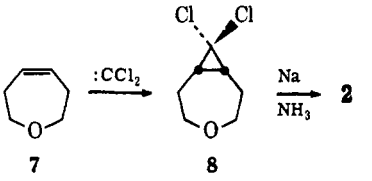
Hendrickson and Boeckman have recently published a detailed theoretical analysis of the stereochemical consequences of electrophilic σ-bond cleavage reactions in cyclopropanes.[12] Their intention was to provide a unified picture of electrophilic additions to three-membered rings which can account for the confusing variety of stereochemical results which have recently been described.[13] The current view is that either edge or corner protonation can initially transpire. Should the former operate, then retention at the electrophilic terminus will obtain; on the other hand, corner protonation can lead, because of the possibility of nucleophilic attack at either of the remaining two ring carbons, to retention or inversion with respect to electrophilic bonding. Although backside attack by the nucleophile is most commonly seen (with resulting inversion), the importance of carbonium ion stabilization at one or the other of the remaining carbon atoms must be reckoned with. It has been reasonably rationalized that the attainment of a high level of nucleophile retention probably takes place by collapse of an ion pair consisting of the complex cation and nucleophilic anion.[13a] Hendrickson has superimposed on this concept the need that the nucleophile be anionic in order to engage itself in an ion-pair situation for the ultimate attainment of stereochemical retention.[12] Clearly, ether oxygen as found in **1–3** is not such a species.

Accordingly, the presence of the oxygen atom in these oxabicyclics was expected at a minimum to: (a) enhance the conformational mobility of the system[14] with attendant reduction in the level of steric hindrance to rearside attack by nucleophile; (b) introduce a transannular dipolar effect which would be evident chiefly in those situations where the ether functionality is positioned four atoms from the center of electrophilic attack (R_2O-4 involvement); and (c) exert a significant changeover in preferential bond cleavage when R_2O-3 or R_2O-5 participation is feasible.

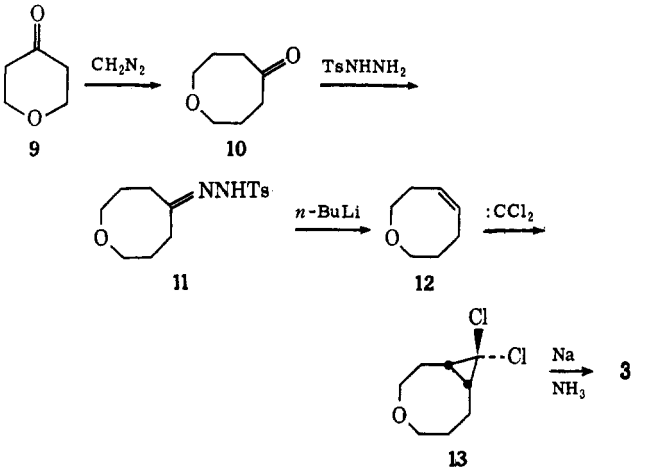
Synthesis of the Cis [*n*.1.0] Oxabicyclics. The preparation of **1** was accomplished by lithium aluminum hydride reduction of 7,8-dihydro-2*H*-oxocin-3(4*H*)-one (**4**), synthesized as described previously in 11 steps from chloroacetaldehyde dimethyl acetal,[1d] and subsequent functionalization of the derived alcohol **5** with *p*-bromobenzenesulfonyl chloride in pyridine.[1c] Treatment of **6** with lithium aluminum hydride resulted in homoallylic displacement of brosylate by hydride ion and formation of **1** in 70% yield.[15,16]



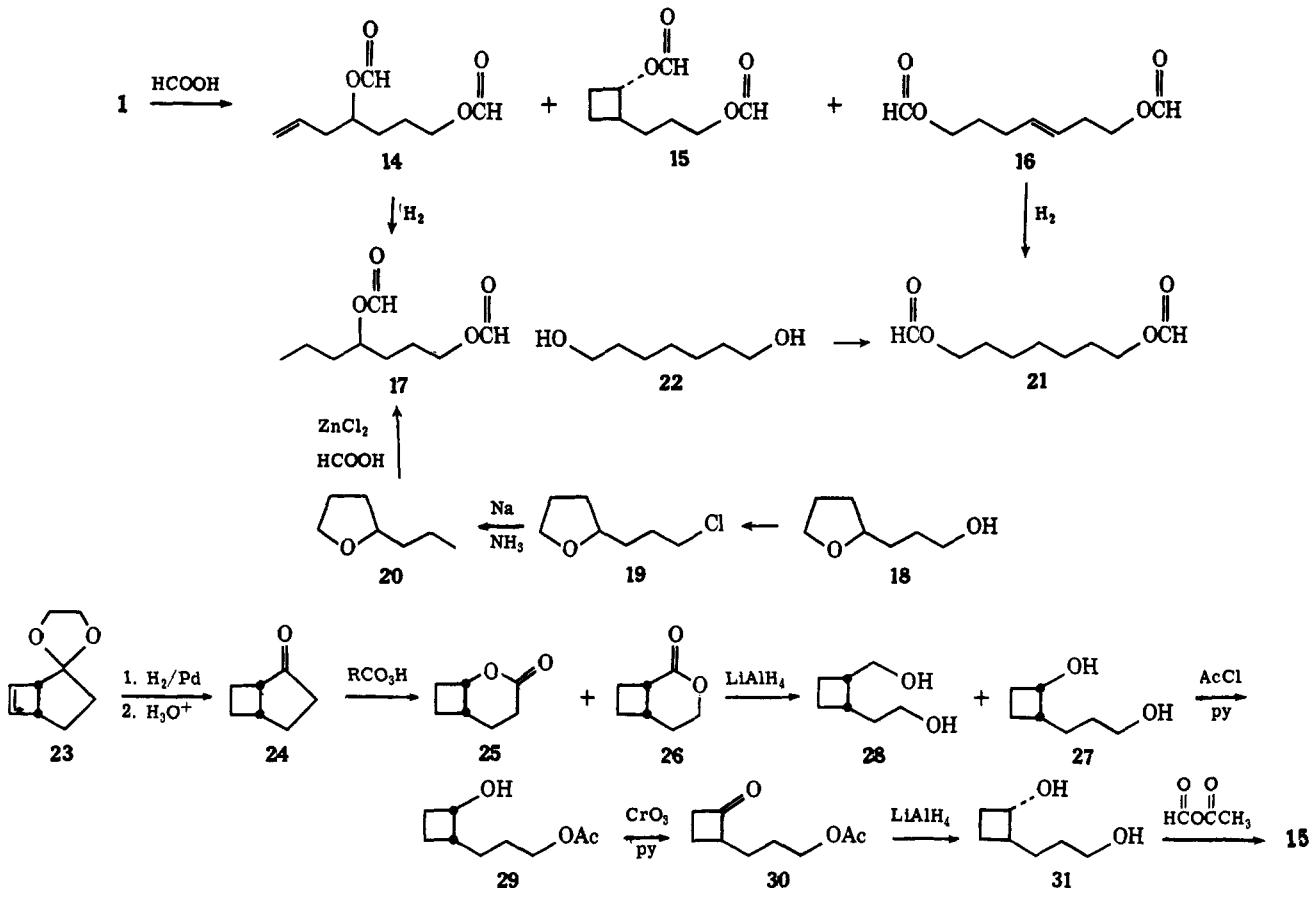
4-Oxabicyclo[5.1.0]octane (**2**) was obtained by addition of dichlorocarbene[17] to *cis*-2,3,6,7-tetrahydrooxepin (**7**)[18] and subsequent reduction of **8** with sodium in liquid ammonia.



The synthesis of **3** began with the addition of excess diazomethane to tetrahydro-4-pyrone (**9**).[19] Although a large quantity (79%) of epoxides and some oxocan-4-one (5%) were produced in this ring expansion, it proved possible to separate **10** rather well by distillation through a spinning band column. Although the isolated yield of oxocan-5-one (**10**) by this method was only 11%, the availability of **9** in relatively large quantities and the ease of the ring expansion step were more than sufficient to prompt the utilization of this sequence in preference to Leonard's more elaborate and tedious procedure.[20] Conversion of **10** to its tosylhydrazone **11** was followed by treatment with *n*-butyllithium to arrive at *cis*-3,6,7,8-tetrahydro-2*H*-



(9) R. T. LaLonde and L. S. Forney, *J. Org. Chem.*, **29**, 2911 (1964).
(10) (a) L. Schotsmans, P. J. C. Fierens, and T. Verlie, *Bull. Soc. Chem. Belg.*, **68**, 580 (1959); (b) P. J. C. Fierens and P. Verschelden, *ibid.*, **61**, 427, 609 (1952); (c) S. F. Van Straten, R. V. V. Nichols, and C. A. Winkler, *Can. J. Chem.*, **29**, 372 (1951).
(11) A. C. Cope and G. L. Woo, *J. Amer. Chem. Soc.*, **85**, 3601 (1963).
(12) J. B. Hendrickson and R. K. Boeckman, Jr., *ibid.*, **93**, 4491 (1971).
(13) For a listing of pertinent references, see: (a) S. J. Cristol, W. Y. Lim, and A. R. Dahl, *ibid.*, **92**, 4013 (1970); (b) S. J. Cristol, J. K. Harrington, T. C. Morrill, and B. E. Greenwald, *J. Org. Chem.*, **36**, 2773 (1971).
(14) L. A. Paquette and R. W. Begland, *ibid.*, **32**, 2723 (1967).
(15) This conversion was first realized by R. W. Begland, Ph.D. Thesis, The Ohio State University, 1968.
(16) Other examples of this phenomenon have been reported by: (a) P. R. Story, *J. Amer. Chem. Soc.*, **83**, 3347 (1961); (b) H. C. Brown and H. M. Bell, *ibid.*, **85**, 2324 (1963); (c) S. Winstein, A. H. Lewin, and K. C. Pande, *ibid.*, **85**, 2324 (1963).
(17) In our hands, the direct conversion of 7 to 2 by the Simmons–Smith procedure was not successfully realized.
(18) J. Meinwald and H. Nozaki, *J. Amer. Chem. Soc.*, **80**, 3132 (1958); see also L. A. Paquette and R. W. Begland, *ibid.*, **90**, 5159 (1968).
(19) S. Olsen and R. Bredock, *Chem. Ber.* 1589 (1958); F. Nerdel, J. Buddrus, W. Brodowski, and P. Weyerstahl, *Tetrahedron Lett.*, 5385 (1966).
(20) N. J. Leonard, T. W. Milligan, and T. L. Brown, *J. Amer. Chem. Soc.*, **82**, 4075 (1960).



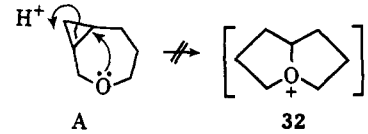
oxocin (**12**).[21] Reaction of **12** with dichlorocarbene gave **13** which afforded **3** on reduction with sodium in liquid ammonia. Spectral data on **1–3** are given in the Experimental Section.

Formolysis of 1. When **1** was heated in formic acid at 50° for 123 hr, there was produced a mixture of three diformates consisting of **14** (30.4%), **15** (19.5%), and **16** (45.4%). Further vpc analysis indicated the presence of three additional minor components (1.0, 1.6, and 2.1%) which were more rapidly eluted from the column than the diesters, but which were not identified because of severely limited quantities. The structure of **14** was established on the basis of its nmr spectrum and catalytic hydrogenation to 1,4-heptanediol diformate (**17**). The combined effect of zinc chloride and formic acid on 2-propyltetrahydrofuran (**20**), available from the reduction of chloride **19** with sodium in liquid ammonia, provided authentic **17**. Identification of **16** was likewise achieved by catalytic hydrogenation to **21** and ultimate comparison with the material prepared directly from 1,7-heptanediol (**22**). The olefinic proton region in the nmr spectrum of **16** exhibits a multiplicity pattern quite similar to that of *trans*-3-hexene but substantially different from that of *cis*-3-hexene. Accordingly, trans stereochemistry has been assigned to this diformate.

The unequivocal synthesis of **15** remained. To this end, ketal **23** was prepared by the method of House and Cronin[22] and subjected to sequential reduction and hydrolysis. Baeyer–Villiger oxidation[23] of **24**[24] gave a mixture of lactones **25** and **26** which upon treatment with lithium aluminum hydride gave diols **27** and **28**. At this point, alcohol **27** was separated by preparative scale vpc and converted to monoacetate **29**. Oxidation of this substance afforded cyclobutanone derivative **30** which was subsequently transformed to **15** by reduction and formylation. Microscale conversion of **27** to the cis isomer of **15** with formic acetic anhydride gave a diformate possessing substantially different nmr and ir spectra and vpc retention time. Consequently, **15** must be of trans stereochemistry.

Independent resubmission of **14–16** to the conditions of reaction led to the total recovery of **14** and **16**. However, diformate **15** was observed to undergo rearrangement exclusively to **14**. It would seem most plausible, therefore, that **14** is not a product of kinetic control, although this conclusion is not demanded by the data.

Although the solvolytic behavior of **1** might be explained by invoking a transannular participation mechanism in which the ether oxygen assists the acid-promoted ring opening (as in A) to produce initially bicyclo[3.3.0]octyloxonium ion **32**, this mechanism can



A 32

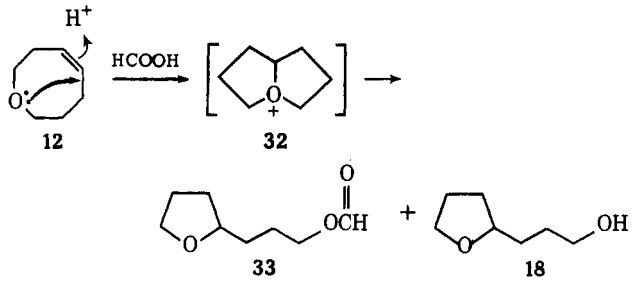
(21) A modification of the procedure of: (a) R. H. Shapiro and M. J. Heath, *ibid.*, **89**, 5734 (1967); (b) G. Kaufman, F. Cook, H. Shechter, J. Bayless and L. Friedman, *ibid.*, **89**, 5736 (1967); (c) W. G. Dauben, M. E. Lorber, N. D. Vietmeyer, R. H. Shapiro, J. H. Duncan, and K. Tomer, *ibid.*, **90**, 4762 (1968).

(22) H. O. House and T. H. Cronin, *J. Org. Chem.*, **30**, 1061 (1965).

(23) P. E. Eaton, *J. Amer. Chem. Soc.*, **84**, 2344 (1962).

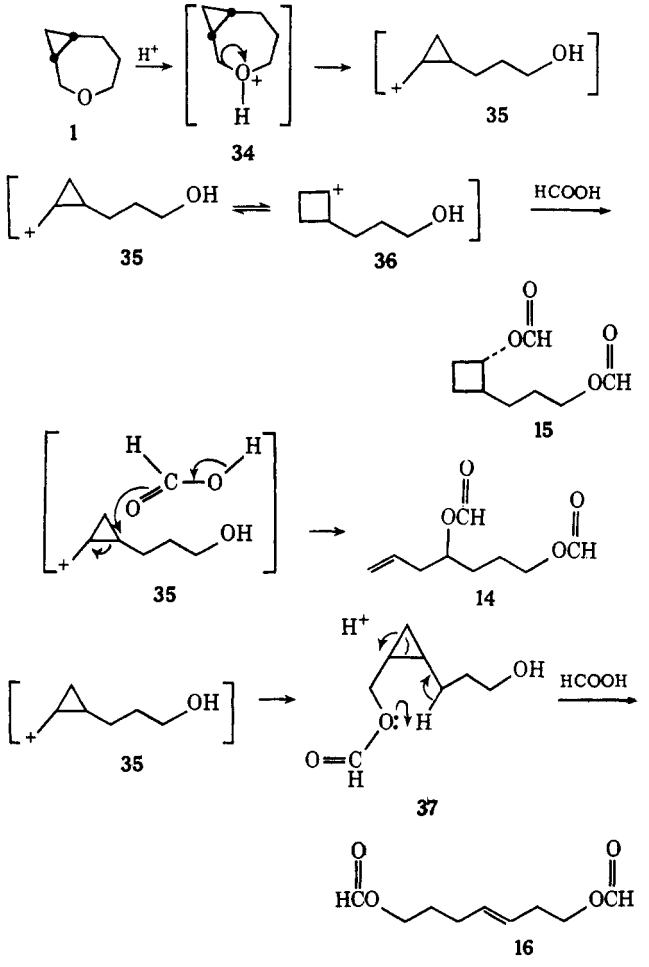
(24) Subsequent to our preparation of this ketone, an alternative synthesis appeared: T. S. Cantrell and J. S. Solomon, *ibid.*, **92**, 4656 (1970).

be readily dismissed. Thus, protonation of the double bond in tetrahydrooxocin **12** was expected on the basis of ample precedent[1c,d] to proceed unidirectionally (development of cationic character at C_5) with concomitant or subsequent R_2O-5 cyclization to furnish **32**. Under the operation of mechanism A, identical product compositions should result. However, formolysis of **12** afforded chiefly formate **33** together with lesser amounts of derived alcohol **18**. This behavior is fully expected of **32**.[1c-e]



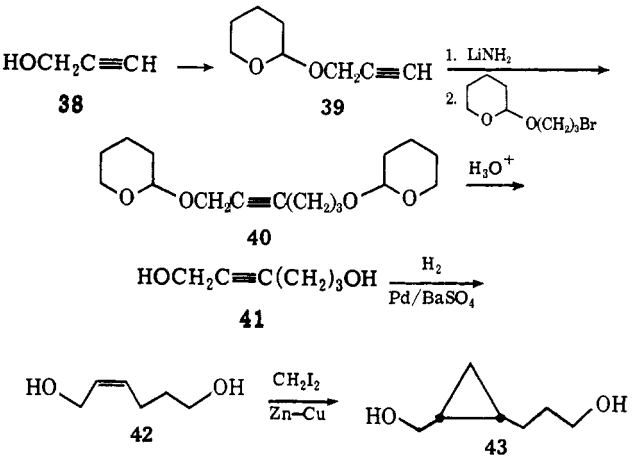
Scheme I outlines the details of a mechanism which is

Scheme I



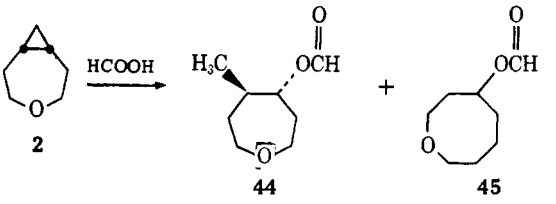
consistent with all the data. Evidently in the particular case of **1**, traditional protonation of the oxygen atom is followed by heterolysis of the C_2–C_3 bond (*cf.* **34**) due to the energetic advantage residing in cyclopropylcarbinyl cation **35**. This species can become equilibrated[25] with cyclobutyl cation **36**, the logical precursor to diformate **15**. Carbonium ion **35** is also anticipated to suffer solvent attack at the homoallylic center;[25] diformate **14** would then arise. Attachment of nucleophile at the primary cationic site in **35** would give *cis*-2-(3-hydroxypropyl)cyclopropylmethanol formate (**37**) which could rearrange *via* a six-center transition state to furnish **16**. Substantial credence was lent this mechanistic proposal by the observation that *cis*-2-(3-hydroxypropyl)cyclopropylmethanol (**43**), synthesized as shown in Scheme II, is converted in high

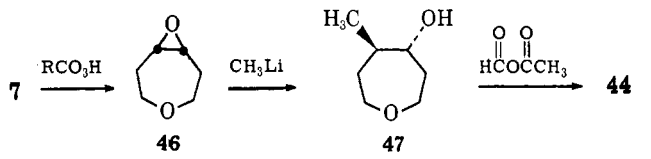
Scheme II



yield to **14**, **15**, and **16** under the formolysis conditions.

Formolysis of 2. The product mixture obtained from 115.5 hr of exposure of **2** to formic acid at 50° was shown by vpc to contain 81% of *trans*-4-hydroxy-5-methyltetrahydrooxepin formate (**44**) and 19% of oxocan-4-ol formate (**45**). An authentic sample of **44** was synthesized by treating alcohol **47**, available from stereospecific trans addition[26] of methyllithium to epoxide **46**, with formic acetic anhydride. At the outset of this work, 4-oxocanyl derivatives such as **45** were unknown. An





efficient route to such compounds, and particularly to **45**, is illustrated in Scheme III. Application of the elegant Whitham–Wright ring expansion procedure[27] to **7** led *via* dibromocyclopropane **48** to *exo*-bromocyclopropane **49**[28] and then to *trans*-3,4,7,8-tetrahydro-2*H*-oxocin-4-ol (**50**). Hydrogenation of **50** provided a 1:1 mixture of oxocan-4-ol (**51**) and oxocan-4-one (**52**), lithium aluminum hydride reduction of which cleanly

(25) J. D. Roberts and R. H. Mazur, *J. Amer. Chem. Soc.*, 73, 2509 (1951).

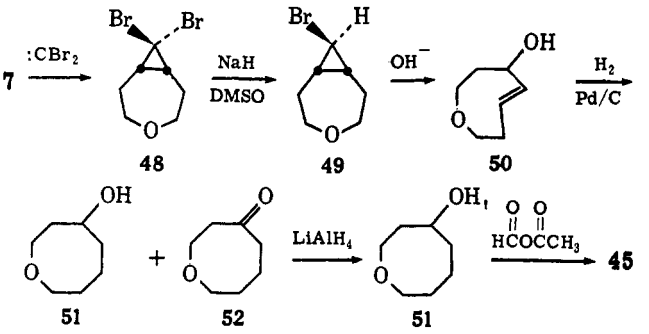
(26) See, for example, P. D. Bartlett and C. M. Berry, *ibid.*, **56**, 2683 (1934).

(27) G. H. Whitham and M. Wright, *Chem. Commun.*, 294 (1967).

(28) C. L. Osborn, T. C. Shields, B. A. Shoulders, C. G. Cardenas, and P. D. Gardner, *Chem. Ind. (London)*, 766 (1965).

furnished pure **51**. Formylation of this alcohol gave a formate (**45**) indistinguishable from that isolated above.

Scheme III

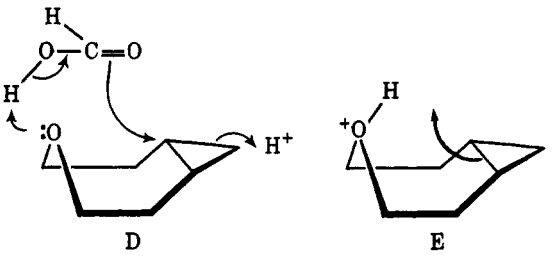


The isolation of **44** and **45** as the only formolysis products of **2** dramatically illustrates the reluctance of the oxygen atom in this ring system for R_2O-4 participation. If transannular involvement of ether oxygen were operative, bicyclic oxonium ion B (and probably also C) would result and several other formates of

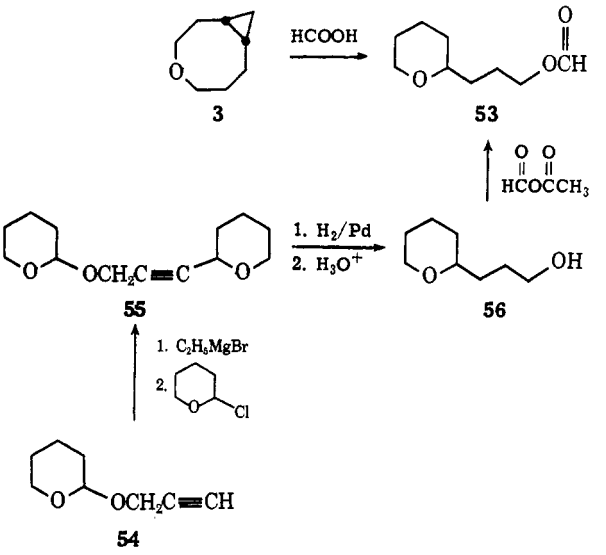
differing structure would be expected.[29] Rather, the product distribution warrants the conclusion that the cyclopropane ring in **2** is cleaved *without* participation of ether oxygen. Interestingly, the results with **2** deviate strikingly in two ways from the behavior of the closely related bicyclo[5.1.0]octane molecule. Although the conditions of ring opening are somewhat disparate,[9] **2** is seen to exhibit a very high level of stereoselectivity upon external bond cleavage whereas the hydrocarbon gives rise to both *cis*- and *trans*-2-methylcycloheptyl acetate with only a slight excess of the trans isomer. Additionally, the internal/external bond cleavage ratio exhibited by **2** is 0.23 whereas for bicyclo[5.1.0]octane the value approaches zero (Table I). Although a number of causes may underlie these marked changes, the principal factors would appear to be diminution of steric hindrance to backside collinear attack of nucleophile (compare the behavior of bicyclo[4.1.0]heptane, Table I) and possible direct proton transfer from ether oxygen to the internal cyclopropyl bond. Molecular models suggest that the boat configuration of **2** allows relatively unhindered access of the nucleophile to C_1 and C_7 (*cf.* D). Furthermore, this same conformation could allow for the incursion of "assisted" proton transfer from oxygen to the C_1–C_7 bond as depicted in E. Deuterium labeling experiments were not performed with **2** because the major product **44** lacks stereochemical consequence and the experimental difficulties involved in assigning stereochemistry to the minor product **45** were deemed excessive.

Formolysis of 3. Cleavage of **3** with formic acid (50°, 167 hr) proceeded exclusively by a transannular path to afford only 3-(2-tetrahydropyranyl)propyl formate (**53**).

(29) The acetolysis of oxocan-4-yl brosylate, a reaction which very likely proceeds through B, gives rise uniquely to 2-(2-tetrahydropyranyl)-ethyl acetate as a result of exclusive cleavage of the four-membered ring in B.[2]

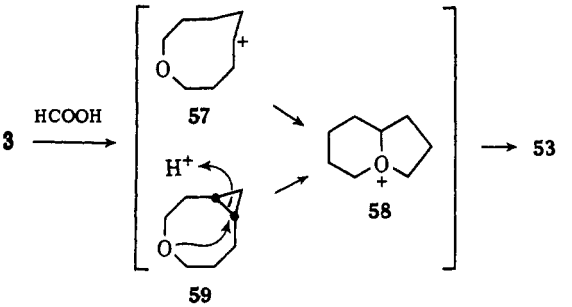


The structural assignment to **53** was founded on nmr studies and confirmed by independent synthesis of an authentic sample. The latter was achieved by coupling of the Grignard reagent of acetylene **54** with 2-chlorotetrahydropyran, catalytic reduction, removal of the blocking group, and formylation. The formation of **53** points to a mechanism involving either the stepwise



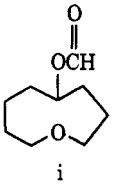
formation of secondary carbonium ion **57** and subsequent transannular interception by the ether oxygen to produce oxonium ion **58** or direct anchimeric assistance by the heteroatom during the electrophilic ring opening as in **59** (Scheme IV). Bicyclic oxonium ion **58** then

Scheme IV



suffers nucleophilic attack at C_9.[30] The widely di-

(30) Due to the unavailability of i, we have not been able to demon-



i

strate the stability or lability of this formate to the reaction conditions. As a result, it is within the realm of possibility that attack at C_6 in **58** also operates under conditions of kinetic control and that i transmutes rapidly to **53**. When the solvolysis of **3** in formic acid was conducted for shorter time periods, no extraneous product was seen.

vergent behavior of *cis*-bicyclo[6.1.0]nonane (external bond cleavage only)[11] and **3** (exclusive internal bond rupture) would appear to support that solvolysis mechanism in which bond cleavage operates in concert with R_2O-5 participation.

Concluding Remarks

Structural modification of the *cis*-bicyclo[5.1.0]octyl and *cis*-bicyclo[6.1.0]nonyl ring systems by introduction of ether oxygen into the larger bridge is seen to exert a profound influence on the intrinsic solvolytic behavior of these hydrocarbons. The reactivity of **1** is unique among the trio of heterocycles examined in that a marked kinetic preference for acid-promoted C–O bond cleavage is manifested. In **2** and **3** there is a return to the "normal" pattern of kinetically controlled strained ring cleavage. However, in **2** the oxygen atom exhibits a complete inability to intercept the cationic center which is developing transannularly to it. Such behavior is necessarily a consequence of the need for unfavorable R_2O-4 participation. In this particular instance, the avoidance of such neighboring group participation is more compelling than usual due to the sizable amount of added ring strain which must be overcome in proceeding to the hypothetical (at least with **2**) oxonium ions **B** and **C**. In **3**, the added flexibility of the molecule which no longer deters approach of the oxygen atom to the internal bond and the well-recognized anchimeric assistance which attends R_2O-5 participation combine to promote exclusive cleavage of the internal bond. Since this behavior is entirely contradictory to the adequately studied reactivity pattern of the related hydrocarbons (Table I), the capability of the heteroatom to promote mechanistic changeover is impressively demonstrated by **3**.

Experimental Section

Melting points are corrected. Proton magnetic resonance spectra were obtained with a Varian A-60A spectrometer and apparent coupling constants are cited. Elemental analyses were performed by the Scandinavian Microanalytical Laboratory, Herlev, Denmark.

***cis*-3-Oxabicyclo[5.1.0]octane (1).** A solution of 5.3 g (0.015 mol) of brosylate **6**[1c] in 20 ml of anhydrous ether was added dropwise to a stirred slurry of 1.4 g (0.037 mol) of lithium aluminum hydride in 55 ml of anhydrous ether and the resulting mixture was refluxed for 19 hr. The mixture was cooled, treated with 1.5 ml of water, 1.5 ml of 30% sodium hydroxide solution, and 6.0 ml of water, and filtered with the residue being washed thoroughly with ether. The combined ether solutions were dried over magnesium sulfate and evaporated at atmospheric pressure through a Vigreux column. The residue was distilled to give 1.2 g (70%) of **1**: bp 79–83° (75 mm); $\delta_{TMS}^{CCl_4}$ 2.9–4.25 (m, 4, CH_2O), 1.3–2.4 (m, 4, CH_2), and 0.1–1.3 (m, 4, cyclopropyl); near-ir band at 1.644 μ.

Anal. Calcd for $C_7H_{12}O$: C, 74.95; H, 10.78. Found: C, 74.78; H, 10.77.

8,8-Dichloro-4-oxabicyclo[5.1.0]octane (8). To a slurry of 40 ml of olefin-free petroleum ether (bp 30–60°), 3.90 g (0.072 mol) of freshly prepared sodium methoxide, and 2.0 g (0.2 mol) of **7**[18] was added dropwise with stirring during 30 min 13.3 g (0.070 mol) of ethyl trichloroacetate. The mixture was stirred at 0° for 4 hr and then at room temperature for 24 hr. Water (60 ml) was added and the petroleum ether layer was separated. The water layer was washed with two 20-ml portions of ether and the organic layers were combined, dried, and evaporated at atmospheric pressure through a Vigreux column. Distillation of the residue afforded 2.97 g (82%) of **8** as a colorless liquid: bp 55–60° (0.9 mm); ν_{max}^{neat} 1100, 820, and 875 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 3.10–4.10 (m, 4, CH_2O) and 1.50–2.50 (m, 6, CH_2).

Anal. Calcd for $C_7H_{10}Cl_2O$: C, 46.43; H, 5.57. Found: C, 46.80; H, 5.78.

***cis*-4-Oxabicyclo[5.1.0]octane (2).** A solution of 2.85 g (0.158 mol) of **8** in 20 ml of anhydrous ether was added dropwise during 30 min to a solution of 2.45 g (0.107 mol) of sodium in liquid ammonia. The mixture was stirred for 2 hr and 20 ml of ether together with 2.0 ml of water were added slowly. After the ammonia had evaporated the ether layer was separated, dried, and evaporated to give a residue, distillation of which afforded 0.55 g (30%) of **3**: bp 80–83° (75 mm); $\delta_{TMS}^{CDCl_3}$ *ca.* 3.75 (m, 4, CH_2O) and 0.00–2.50 (br m, 8).

Anal. Calcd for $C_7H_{12}O$: C, 74.95; H, 10.78. Found: C, 74.72; H, 10.67.

Oxocan-5-one (10). A room temperature solution of diazomethane (prepared from 2.5 g (0.223 mol) of *N*-nitroso-*N*-methylurea, 200 ml of ether, and 68 ml of 50% potassium hydroxide solution) was added in two portions during 15 min to a solution of 5.0 g (0.5 mol) of **9**[19] in 95 ml of methanol. After standing overnight, the solution was evaporated to give 5.5 g of yellow liquid which was shown (vpc analysis and ir) to contain large amounts of epoxides (79%), oxocan-4-one (5%), and oxocan-5-one (16%). A total of 35 g of a mixture of ketones and epoxides was amassed and distilled through a spinning band column to give 5.0 g (11%) of **10**, bp 119–121° (19 mm), the ir and nmr spectra of which were identical with those of an authentic sample:[2] ν_{max}^{neat} 1696 and 1100 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 3.60 (t, J = 5.0 Hz, 4, CH_2O), 2.38 (m, 4, CH_2CO), and 2.05 (m, 4, CH_2).

Oxocan-5-one Tosylhydrazone (11). To a hot solution of 1.80 g (9.6 mmol) of *p*-toluenesulfonylhydrazide in 30 ml of alcohol was added 0.964 g (7.55 mmol) of **10**. The solution was distilled until the volume was reduced to 10 ml and then it was cooled. White crystals formed which were collected and dried to give 2.15 g (96%) of **11**, mp 170–171.5° dec, after two recrystallizations from the same solvent: $\delta_{TMS}^{(CD_3)_2SO}$ 7.50 (q, J = 8.0 Hz, 4, aromatic), 3.42 (s, 4, CH_2O), 2.33 (s, 3 H, CH_3), 2.25 (m, 4, $CH_2(C{=}N)$), and 1.80 (m, 4, CH_2).

Anal. Calcd for $C_{14}H_{20}N_2O_3S$: C, 56.74; H, 6.80; N, 9.45. Found: C, 56.69; H, 6.74; N, 9.47.

***cis*-3,6,7-Tetrahydro-2*H*-oxocin (12).** To a slurry of 2.00 g (6.75 mmol) of tosylhydrazone **11** and 30 ml of anhydrous ether was added slowly (2–3 min) 15 ml of 1.6 *M* *n*-butyllithium in pentane at 0°. The resulting mixture was stirred at 0° for 7.5 hr and allowed to stand overnight at room temperature. Water (5.0 ml) was added and the ether layer was separated, dried, filtered, and evaporated at atmospheric pressure to afford a liquid which by vpc analysis was shown to be approximately 30% ether, 10% toluene, and 60% olefin, corresponding to 0.62 g (83%) of **12**. A pure sample of **12** was obtained by preparative vpc: $\delta_{TMS}^{CDCl_3}$ 3.75 (m, 2, olefinic), 3.62 (m, 4, CH_2O), 2.25 (m, 4, allylic), and 1.62 (m, 2, remaining methylene).

The vinyl proton signals of *cis*-cyclooctene which appear at δ 5.60 have the same multiplicity pattern as the vinyl protons shown above, whereas the pattern for those of *trans*-cyclooctene are distinctly different. On this basis, cis stereochemistry is assigned to **12**.

Anal. Calcd for $C_7H_{12}O$: C, 74.95; H, 10.78. Found: C, 75.13; H, 10.84.

9,9-Dichloro-4-oxabicyclo[6.1.0]nonane (13). To a mixture of 0.3 g (2.68 mol) of **12**, 0.97 g (18.0 mmol) of freshly prepared sodium methoxide, and 7.0 ml of dry olefin-free petroleum ether (bp 30–60°) was added with cooling 2.0 g (10.5 mmol) of ethyl trichloroacetate during 0.5 hr. After stirring the mixture overnight at room temperature, water was added and the organic layer was separated. The aqueous layer was extracted several times with ether and the ether layers were combined, dried, and evaporated at atmospheric pressure. Preparative vpc[31] of the residue afforded a pure sample of **13**: ν_{max}^{neat} 1150 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 3.69 (m, 4, CH_2O) and 1.00–2.20 (m, 8, remaining methylene).

Anal. Calcd for $C_8H_{12}Cl_2O$: C, 49.25; H, 6.20; Cl, 36.35. Found: C, 49.31; H, 6.42; Cl, 35.73.

***cis*-4-Oxobicyclo[6.1.0]nonane (3).** To a solution of 0.5 g of sodium in 20 ml of liquid ammonia was added 0.300 g (1.5 mmol) of **13** in 3.0 ml of anhydrous ether. The mixture was stirred for 8 hr, water and ether were added slowly, and the ammonia was allowed to evaporate. The ether layer was separated and the aqueous layer was washed twice with 10-ml portions of ether. The ether layers were combined, dried, and evaporated at atmospheric pressure to give a liquid residue which was purified by preparative vpc[31] to give 11 mg (6%) of **3**: $\nu_{max}^{CCl_4}$ 1120 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 3.70 (m, 4, CH_2O), 0.60–2.40 (complex m, 9), and −0.20 (m, 1, cyclopropyl).

Anal. Calcd for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 76.10; H, 11.34.

Formolysis of 3-Oxabicyclo[5.1.0]octane (1). Following the procedure of Cope,[11] 0.30 g (2.68 mmol) of **1** was dissolved in 1.50

(31) A 5.5 ft × 0.25 in. aluminum column packed with 10% FFAP on 60–80 mesh Chromosorb G was employed.

ml of 98–100% formic acid and this solution was sealed in a Pyrex tube and maintained at 50° for 123 hr. The tube was cooled in ice and opened, and the contents were dissolved in 40.0 ml of ether. The ether solution was washed with three 30-ml portions of saturated sodium bicarbonate solution and the combined aqueous layers were extracted with 20 ml of ether. Drying of the combined organic layers and careful evaporation of the ether through a Vigreux column at atmospheric pressure afforded a liquid residue. Analysis of this material by vpc[32] revealed the presence of six components: A (1.56%), B (2.14%), C (1.08%), D (30.35%), E (19.48%), and F (45.39%) in order of retention time.

This product mixture and that of another identical (0.20 g, 1.79 mmol) run were combined to give 0.54 g of material from which was obtained by preparative vpc[32] the pure D component, hept-6-ene-1,4-diol formate (**14**): $\nu_{TMS}^{CDCl_3}$ 1720, 1180, 1645, 1420, and 995 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 8.10 (s, 2, C(=O)*H*), 5.70 (m, 1, olefinic), 5.25 (m, 2, olefinic), 5.05 (m, 1, *H*CO), 4.20 (m, 2, CH_2O), 2.40 (t, J = 5.0 Hz, 2, allylic), and 1.8 (q, J = 6.0 Hz, 4, remaining methylenes).

Anal. Calcd for $C_9H_{14}O_4$: C, 58.05; H, 7.58. Found: C, 58.05; H, 7.63.

The major component (E) of medium retention time, *trans*-2-(3-hydroxypropyl)cyclobutanol diformate (**15**), was also obtained by preparative vpc: $\nu_{max}^{CHCl_3}$ 1720, 1180, and 820 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 8.10 and 8.00 (two s, 2, C(=O)H), 4.80 (q, J = 6.5 Hz, 1, *H*CO), 4.20 (m, 2, CH_2O), and 1.00–2.60 (br m, 9, remaining methylenes).

Anal. Calcd for $C_9H_{14}O_4$: C, 58.05; H, 7.58. Found: C, 58.43; H, 7.26.

The component of greatest retention time (F) was similarly isolated and identified as *trans*-hept-3-ene-1,7-diol diformate (**16**): $\nu_{max}^{CHCl_3}$ 1720 and 1180 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 8.10 (s, 2, C(=O)*H*), 5.55 (d, J = 0.6 Hz, 2, olefinic), 4.20 (t, J = 6.5 Hz, 4, CH_2O), and 2.10 (m, 6, remaining methylenes). The olefinic proton region of **16** exhibits a multiplicity pattern quite similar to that of *trans*-3-hexene but different from that of *cis*-3-hexene. Accordingly, trans stereochemistry has been assigned to this diformate.

Anal. Calcd for $C_9H_{14}O_4$: C, 58.05; H, 7.58. Found: C, 58.09; H, 7.53.

Reduction of *trans*-Hept-3-ene-1,7-diol Diformate (16). A small sample of **16** was dissolved in 20 ml of hexane and hydrogenated at atmospheric pressure over 5% Pd/C as catalyst. The mixture was filtered and the hexane was removed at atmospheric pressure. The residue was purified by means of preparative vpc[32] to give a pure liquid. The ir and nmr spectra and vpc retention time of this compound were identical with those of authentic **21**.

1,7-Heptanediol Diformate (21). Compound **22** (1.1 g, 0.008 mol) and 6.0 ml of 97–100% formic acid were mixed and allowed to react in a sealed tube at 50° for 2 days. The resulting clear solution was dissolved in 50 ml of ether and treated with 180 ml of saturated sodium bicarbonate solution. The ether layer was separated, dried, and evaporated. The residue was distilled to give 0.8 g (39%) of **21** as a clear liquid: bp 141–144° (10.0 mm); ν_{max}^{neat} 1725 and 1190 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 8.10 (s, 2, C(=O)*H*), 4.20 (t, $|J|$ = 6.0 Hz, 4, CH_2O), and 1.10–2.00 (m, 10, remaining methylenes).

Anal. Calcd for $C_9H_{16}O_4$: C, 57.43; H, 8.57. Found: C, 57.30; H, 8.62.

2-Propyltetrahydrofuran (20). A solution of 50 ml of dry benzene and 13.0 g (0.1 mol) of 2-tetrahydrofuranpropanol (**18**) was brought to reflux and 11.9 g (0.1 mol) of thionyl chloride was added dropwise. The mixture which became very dark was refluxed for 20 min. The benzene was evaporated on a rotary evaporator and the residue was distilled to give 5.8 g (40%) of **19**: bp 67–72° (6.0 mm) [lit.[33] bp 75° (4.0 mm)].

Chloride **19** was dissolved in 20 ml of ether and added dropwise to a solution of 1.50 g (0.065 g-atom) of sodium in liquid ammonia. After 2 hr, 50 ml of ether and 10.0 ml of water were slowly added to the mixture and the ammonia was allowed to evaporate. The ether layer was separated, dried, and evaporated at atmospheric pressure to give a residue, distillation of which afforded 1.01 g (87%) of **20** as a clear liquid: bp 70–72° (100 mm) [lit.[34] bp 70° (100 mm)].

1,4-Heptanediol Diformate (17). To a solution of 7.0 ml of 99% formic acid and 0.24 g of zinc chloride was added 1.0 g of 2-propyltetrahydrofuran (**20**) and the resulting solution was refluxed under anhydrous conditions for 4 days. The solution was dissolved in ether and treated with saturated sodium bicarbonate solution until all acid was neutralized. The ether layer was separated, dried, filtered, and evaporated at room temperature. The residue was separated into its two major components by preparative gas chromatography.[35] The component of shorter retention time (43%) was identical with the hydrogenation product of **14**: ν_{max}^{neat} 1725 and 1185 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 8.10 and 8.18 (two s, 2, C(=O)H), 5.10 (m, 1, *H*CO), 4.20 (m, 2, CH_2O), 1.1–1.90 (m, 6), and 0.90 (m, 3, methyl).

Anal. Calcd for $C_9H_{16}O_4$: C, 57.43; H, 8.57. Found: C, 57.51; H, 8.28.

Reduction of Hept-6-ene-1,4-diol Diformate (14). Catalytic hydrogenation of **14** as above afforded a single product which was identical in all respects with the authentic diformate **17** prepared previously.

Bicyclo[3.2.0]heptan-2-one (24). A solution of 6.83 g (0.045 mol) of ketal **23**[22] in 30 ml of ethanol was hydrogenated at 30 psig in the presence of 0.7 g of platinum oxide on a Paar apparatus. The mixture was filtered through Celite and evaporated at atmospheric pressure. The resulting liquid residue was distilled to give 6.2 g (91%) of saturated ketal as a clear liquid: bp 56–58° (2.7 mm); $n^{28}D$ 1.4742; ν_{max}^{neat} 1100 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 3.80 (m, 4, OCH_2CH_2O), and 1.20–3.00 (br m, 10).

A mixture of 6.0 g (0.039 mol) of this dihydro compound, 13 ml of 3 *N* hydrochloric acid, and 26 ml of ether was stirred at room temperature for 3 hr. The ether layer was separated, dried, and evaporated to give a liquid residue which was distilled to give 3.58 g (84%) of bicyclo[3.2.0]heptan-2-one (**24**): bp 71–80° (18 mm); ν_{max}^{neat} 1730 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 1.50–3.30 (br m).[24]

***cis*-2-(3-Hydroxypropyl)cyclobutanol (27).** To a solution of 1.10 g (0.01 mol) of **24** in 30 ml of ether at 0° was added 15.1 ml of ethereal 0.704 *N* monoperphthalic acid solution. After stirring at room temperature for 24 hr, a white precipitate had formed. The mixture was filtered, the precipitate was washed with chloroform, and the washing was combined with the ethereal filtrate. Evaporation of the solvents afforded a semisolid which was washed several times with chloroform. The chloroform washings were again evaporated to give a liquid which was distilled to afford 1.1 g of a mixture of lactones **25** and **26**, bp 115–120° (5.0 mm).

A solution of 0.47 g (3.73 mmol) of this liquid in 5.0 ml of ether was added slowly to a slurry of 0.15 g (3.95 mmol) of lithium aluminum hydride in 30 ml of ether. The mixture was stirred overnight at room temperature and after the usual work-up there was obtained 0.38 g (74%) of crude liquid. Purification of this material by preparative vpc[31] gave **27** as a pure colorless liquid: ν_{max}^{neat} 3220 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 4.35 (m, 4, CH_2O and *H*CO), 3.60 (m, 2, O*H*), and 1.80 (m, 9, remaining methylenes).

Anal. Calcd for $C_7H_{14}O_2$: C, 64.58; H, 10.84. Found: C, 64.62; H, 10.92.

Unequivocal Synthesis of *trans*-2-(3-Hydroxypropyl)cyclobutanol Diformate (15). **A.** To a solution of 0.249 g (1.92 mmol) of **27** in 1.25 ml of chloroform and 0.14 ml of pyridine at 0° was added 0.14 ml of acetyl chloride during 30 min. The solution was stirred for 3 hr at room temperature, washed with two 2.0-ml portions of water, dried, and evaporated to give a liquid residue. Preparative vpc[31] afforded 0.084 g (26%) of **29**: ν_{max}^{neat} 3300 and 1725 cm^{-1}.

B. Chromium trioxide (0.13 g) was added slowly to 1.25 ml of pyridine at 0° during 1 hr. The resulting yellow-orange suspension was treated with 0.084 g (0.49 mmol) of **29** and the mixture was stirred at room temperature for 48 hr. The sample was poured into 10 ml of ice water and was extracted with four 10-ml portions of ether. The ether layers were combined, dried, and evaporated to provide a liquid residue. Pure 2-(3-acetoxypropyl)cyclobutanone (**30**) (0.042 g, 32%) was isolated by preparative vpc:[31] ν_{max}^{neat} 1738 and 1779 cm^{-1}.

C. After reduction of 0.042 g (0.244 mmol) of keto acetate **30** with lithium aluminum hydride,[36] the crude *trans*-diol **31** was treated with 0.05 ml (0.57 mmol) of acetic formic anhydride and was allowed to react overnight.[37] The reaction mixture was dissolved in ether and washed with saturated sodium bicarbonate solution until neutral. After drying and careful evaporation of the ether solution, the residue was separated into three components by preparative vpc.[32] The major component (lowest retention time) had nmr and ir spectra identical with those of **15**: ν_{max}^{neat} 1720 and 1180 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 8.05 and 8.10 (two s, 2, C(=O)*H*), 4.80 (q, $|J|$ = 6.5 Hz, 1,

(32) A 6 ft × 0.25 in. aluminum column packed with 10% SE-30 on 60–80 mesh on Chromosorb G was employed.

(33) H. Gilman and A. P. Hewlett, *Recl. Trav. Chim. Pays-Bas*, **51**, 93 (1932).

(34) K. Thewalt and W. Rudolph, *J. Prakt. Chem.*, **26**, 233 (1964).

(35) A 6 ft × 0.25 in. aluminum column packed with 10% Carbowax 20M on 60–80 mesh Chromosorb G was employed.

(36) H. C. Brown and V. Varma, *J. Amer. Chem. Soc.*, **88**, 2871 (1966).

(37) W. Stevens and A. Van Es, *Recl. Trav. Chim. Pays-Bas*, **83**, 1287 (1964).

*H*CO), 4.20 (m, 2, CH_2O), and 1.00–2.60 (m, 9, remaining methylenes).

Attempted Formolysis of *trans*-Hept-3-ene-1,7-diol Diformate (16). A solution of 0.1864 g (0.1 mmol) of **16** in 1.5 ml of formic acid was sealed in a tube and heated at 50° for 120 hr. The tube was opened and the contents were worked up as previously described to give a liquid which had ir and nmr spectra identical with those of the starting material **16**.

Attempted Formolysis of Hept-6-ene-1,4-diol Diformate (14). A solution of 0.0890 g (0.04 mmol) of **14** in 0.75 ml of formic acid was subjected to the same conditions as above. Upon work-up, a liquid identical with the starting material (ir and nmr studies) was quantitatively recovered.

Formoylsis of *trans*-2-(3-Hydroxypropyl)cyclobutanol Diformate (15). A solution of 0.0413 g (0.22 mmol) of **15** in 0.1 ml of 97% formic acid was placed in a sealed tube and heated at 50° for 71 hr. The contents were dissolved in ether and extracted with 5% sodium bicarbonate solution. After drying, the ether solution was evaporated and the liquid residue was separated into its two components by preparative vpc.[31] On the basis of nmr and ir spectral comparisons the components were identified as diformates **14** (major) and recovered **15** (minor).

Formolysis of *cis*-3,6,7,8-Tetrahydro-2*H*-oxocin (12). A solution of 0.065 g (0.58 mmol) of **12** in 0.25 ml of 97% formic acid was heated at 50° for 115 hr. The contents were dissolved in ether and extracted with 5% sodium bicarbonate solution. After drying, the ether solution was evaporated and the residue was separated into its three components by preparative vpc.[31] The components were identified, in the order of their retention time, as starting material (33.4%), 3-(2-tetrahydrofuranyl)propyl formate (**33**, 48.8%), and 3-(2-tetrahydrofuranyl)propanol (**18**, 17.8%) by comparison of their nmr and ir spectra with those of the known compounds.

3-(2-Tetrahydrofuranyl)propyl Formate (33). To 1.4 g (0.0159 mol) of formic acetic anhydride at 0–10° was added dropwise 1.37 g (0.0105 mol) of 2-tetrahydrofuranpropanol (**18**). After standing overnight at room temperature, the mixture was taken up in ether, washed with saturated sodium bicarbonate solution until neutral, dried, filtered, and evaporated to give 1.00 (68%) g of liquid. Preparative vpc[32] of this material afforded pure **33**: ν_{max}^{neat} 1740 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 8.08 (s, 1, C(=O)*H*), 4.20 (t, $|J|$ = 6.0 Hz, 2, side-chain CH_2O), 3.78 (m, 3, ring CH_2OCH<), and 1.20–2.30 (m, 8, remaining methylenes).

Anal. Calcd for $C_8H_{14}O_3$: C, 60.74; H, 8.92. Found: C, 60.34; H, 9.20.

Tetrahydropyranyl Derivative of Propargyl Alcohol (39). A solution of 41.7 g (0.745 mol) of propargyl alcohol (**38**), 25.0 g (0.30 mol) of dihydropyran, 1.3 g of *p*-toluenesulfonic acid, and 100 ml of ether was stirred at 0° for 0.5 hr and then refluxed overnight. Anhydrous sodium acetate (1.3 g) was added and the mixture was refluxed for 0.5 hr, cooled, and filtered. The filtrate was extracted with 10% sodium carbonate solution, dried, filtered, and evaporated. The liquid residue was distilled to give 30.5 g (73%) of **39**: bp 80–82° (18 mm) [lit.[38] bp 78–82° (18 mm)].

Tetrahydropyranyl Derivative of 1-Bromopropanol. To 5.15 g (0.037 mol) of 3-bromopropanol at 0° was added 3.1 g (0.037 mol) of dihydropyran, followed by three drops of concentrated hydrochloric acid. After stirring at room temperature for 3 hr, the mixture was dissolved in ether and extracted with 10% sodium hydroxide solution. The organic phase was dried and evaporated and the resulting oil was distilled to give 5.95 g (72%) of product: bp 110–115° (12 mm) [lit.[39] bp 111–112° (12 mm)].

Hex-2-yne-1,6-diol (41). **A.** A mixture of 1.58 g (0.228 g-atom) of lithium wire, 900 ml of liquid ammonia, and a catalytic amount of ferric nitrate was allowed to react until gray-colored. Acetylene **39** was added during 10 min, after which the reaction was stirred for 45 min. A solution of 59.5 g (0.267 mol) of the preceding bromide was added and the mixture was stirred for 6 hr and allowed to evaporate overnight. To the residue was added 45 ml of saturated ammonium chloride solution, 180 ml of water, and 225 ml of ether. The aqueous layer was extracted twice with ether and the combined organic layers were dried and evaporated. Distillation of the residual liquid afforded 36.3 g (57%) of the bistetrahydropyranyl derivative of hex-2-yne-1,6-diol (**40**): bp 157–163° (0.4 mm); ν_{max}^{neat} 1050 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 4.75 (m, 2, OCH_2C≡C), 4.20 (m, 2, OC*H*O), 3.65 (m, 6, CH_2O), 2.30 (m, 2, C≡CCH_2), and 1.60 (m, 14, remaining methylenes).

B. To a solution of 36.3 g (0.129 mol) of **40**, 70 ml of water, and 210 ml of methanol at 0° was added dropwise with stirring 16.8 ml of concentrated sulfuric acid. After stirring overnight at room temperature, the mixture was neutralized with 31.5 g of sodium carbonate. The solution was evaporated to a sludge which was extracted with methylene chloride and chloroform. The organic layers were combined, dried, and evaporated to a clear liquid residue which was distilled to give 6.48 g (44%) of hex-2-yne-1,6-diol (**41**): bp 103° (0.3 mm) [lit.[40] bp 145–147° (4.0 mm)].

***cis*-Hex-2-ene-1,6-diol (42).** Hydrogenation of 3.42 g (0.03 mol) of **41** in 60 ml of ethyl acetate over 5% Pd on barium sulfate at atmospheric pressure afforded 2.3 g (67%) of **42**: bp 96° (0.3 mm); ν_{max}^{neat} 3340 and 1090 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 5.60 (m, 2, olefinic), 4.42 (s, 2, OCH_2), 4.18 (d, $|J|$ = 5.0 Hz, 2, O*H*), 3.60 (t, $|J|$ = 6.0 Hz, 2, CH_2O), 2.20 (m, 2, CH_2C=), and 1.60 (m, 2, remaining methylenes).

The diacetate of diol **42** was prepared and a pure sample was obtained by preparative vpc[31] for analysis: ν_{max}^{neat} 1740 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 5.65 (m, 2, olefinic), 4.65 (d, $|J|$ = 5.0 Hz, 2, OCH_2C=), 4.10 (t, $|J|$ = 6.0 Hz, 2, CH_2O), 2.00 (s, 6, CH_3), and 1.20–2.40 (br m, 4, remaining methylenes).

Anal. Calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05. Found: C, 59.59; H, 8.00.

***cis*-2-(3-Hydroxypropyl)cyclopropanemethanol (43).** To zinc–copper couple prepared by LeGoff's method[41] (3.5 g, 0.054 g-atom) was added 15.0 ml of anhydrous ether followed by a few drops of methylene iodide. The mixture was heated to initiate the reaction and the remainder (9.4 g, 0.035 mol) of the methylene iodide was added during 20 min with stirring. A mixture of 2.01 g (0.017 mol) of **42** and 10 ml of ether was added slowly, causing a slight exothermic reaction to take place. The mixture was refluxed overnight, 10% sodium hydroxide solution was added, the ether layer was separated, and the aqueous layer was extracted with ether and chloroform. The organic layers were combined, dried, and evaporated. The residual oil was distilled to afford 0.7 g of liquid: bp 95–100° (0.3 mm). Preparative vpc[31] of this material gave pure **43**: $\delta_{TMS}^{CDCl_3}$ 4.21 (s, 2, O*H*), 3.65 (m, 4, CH_2O), 1.25 (m, 6), and −0.05 (m, 2, cyclopropyl).

The diacetate of **43** was prepared for analytical purposes: ν_{max}^{neat} 1735 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 4.08 (m, 4, CH_2O), 2.00 (s, 6, CH_3), 0.80–2.10 (br, m, 7), and 0.00 (m, 1, cyclopropyl).

Anal. Calcd for $C_{11}H_{18}O_4$: C, 61.66; H, 8.47. Found: C, 61.67; H, 8.36.

Reaction of 43 with Formic Acid. A solution of 0.1 g (0.77 mmol) of **43** in 0.3 ml of formic acid was heated at 50° in a sealed tube for 99 hr and worked up in the previously described manner. Preparative vpc[31] of the reaction mixture afforded three diformates: **15** (23.7%), **16** (23.5%), and **14** (52.8%) in the order of their elution. Identification of each component was achieved by spectral comparisons.

Formolysis of 4-Oxabicyclo[5.1.0]octane (2). A solution of 0.558 g (4.96 mmol) of **2** and 1.0 ml of 99% formic acid was maintained at 50° in a sealed Pyrex tube for 115.5 hr, cooled, dissolved in ether, and washed with saturated sodium bicarbonate solution until neutral. The ether solution was dried, filtered, and evaporated to give 0.950 g of liquid which was separated into five components by preparative vpc: A (1.6%), B (3.5%), C (30.9%), D (51.5%), and E (12.5%).

Component C was identified as recovered bicyclic ether (**2**). Component D was identified as the formate of *trans*-4-hydroxy-5-methyl-2,3,4,5,6,7-hexahydrooxepin (**44**) on the basis of comparison with an authentic sample: ν_{max}^{neat} 1725 and 1190 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 8.10 (s, 1, *H*C(=O)), 4.90 (q, $|J|$ = 6.5 Hz, 1, >C*H*O), 3.75 (m, 4, CH_2O), 2.00 (m, 6), and 1.00 (d, $|J|$ = 6.5 Hz, 3, CH_3).

Anal. Calcd for $C_8H_{14}O_3$: C, 60.74; H, 8.92. Found: C, 60.60; H, 8.84.

Component E was identified as oxocan-4-ol formate (**45**) by comparison with an authentic sample: ν_{max}^{neat} 1725 and 1190 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 8.10 (s, 2, *H*C(=O)), 5.20 (m, 1, >C*H*O), 3.70 (m, 4, CH_2O), and 1.10–2.30 (m, 8, remaining methylenes).

Anal. Calcd for $C_{18}H_{14}O_3$: C, 60.74; H, 8.92. Found: C, 60.54; H, 8.90.

4,5-Epoxy-2,3,4,5,6,7-hexahydrooxepin (46). A solution of 7.4 g (0.0382 mol) of 89.5% *m*-chloroperbenzoic acid in 150 ml of chloroform was added slowly with cooling to a solution of 2.5 g (0.0255 mol) of **7** in 10 ml of chloroform. After standing for 3 days, the solution was extracted with 10% sodium bicarbonate solution and dried. Evaporation of the solvent afforded a liquid which was

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distilled to give 1.52 g (52%) of **46**: bp 77–80° (30 mm) [lit.[42] bp 77.5–78° (30 mm)]; $\delta_{TMS}^{CDCl_3}$ 4.00–3.00 (m, 6, C*H*O) and 2.19 (m, 4, remaining methylenes).

Formate of 4-Hydroxy-5-methyl-2,3,4,5,6,7-hexahydrooxepin (44). To 1.14 g (0.01 mol) of **46** under nitrogen was added slowly with stirring 5.43 ml (0.01 mol) of a 5.26% solution of methyllithium in ether. After the slight exothermic reaction had subsided the mixture was stirred for 48 hr at room temperature, poured into 50 ml of ice, and extracted with three 20-ml portions of ether and three 20-ml portions of chloroform. The organic layers were combined, dried, and evaporated. Vpc analysis[31] of the resulting yellow liquid afforded as a single peak two inseparable components (nmr methods). This material was treated with 0.15 ml of formic acetic anhydride and after standing overnight the reaction was worked up in the usual manner. The liquid which was isolated was now readily separable into the two components by preparative vpc.[32] The minor component was formate **44** and the major component was identified as the formate of 3-hydroxy-2,3,4,7-tetrahydrooxepin: ν_{max}^{neat} 1720 and 1180 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 8.10 (s, 1, *H*C(=O)), 5.78 (s, 3, C*H*CH=C*H*), 4.20 (m, 2, OCH_2CH=), 3.90 (t, $|J|$ = 5.5 Hz, 2, OCH_2), and 2.19 (q, $|J|$ = 5.5 Hz, 2, methylene).

No attempt was made to obtain analysis for this compound.

8,8-Dibromo-4-oxabicyclo[5.1.0]octane (48). To a stirred mixture of 3.0 g of potassium *tert*-butoxide, 2.0 g (0.02 mol) of **7**, and 18 ml of pentane at 0° was added 4.95 g (0.0196 mol) of bromoform during 1 hr. The mixture was stirred for 3 hr at 0° and then overnight at room temperature. Water was added dropwise and the mixture was extracted with ether, dried, and evaporated. Distillation of the liquid residue afforded 1.1 g of recovered **7** and 1.53 g (28%) of **48**: bp 87° (0.4 mm); ν_{max}^{neat} 1120 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 3.20–4.20 (m, 4, CH_2O), and 1.30–2.70 (m, 6).

Anal. Calcd for $C_7H_{10}Br_2O$: C, 31.14; H, 3.73; Br, 59.20. Found: C, 31.27; H, 3.80; Br, 59.06.

***exo*-8-Bromo-4-oxabicyclo[5.1.0]octane (49).** To 11.1 ml of dry distilled dimethyl sulfoxide under nitrogen was added 0.555 g of 57% sodium hydride which had been washed three times with pentane. The mixture was stirred at 75° for 45 min and cooled to 15–20°, and **48** was added during 2 min. After stirring for 6 hr at room temperature and standing overnight, 37 ml of water was added while keeping the temperature at 20° with an ice bath. The mixture was extracted with ether and the combined ether layers were extracted with water and saturated sodium chloride solution. After drying, the ether solution was evaporated and the orange brown liquid was molecularly distilled to give 0.465 g (44%) of **49**: bp 95° (20 mm); ν_{max}^{neat} 1120 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 3.60 (m, 4, CH_2O), 2.85 (m, 1, C*H*Br), 1.90–2.50 (m, 2), and 1.54 (m, 4).

Anal. Calcd for $C_7H_{11}BrO$: C, 44.00; H, 5.80. Found: C, 44.01; J, 5.94.

***trans*-3,4,7,8-Tetrahydro-2*H*-oxocin-4-ol (50).** A solution of 0.465 g (2.44 mmol) of **49**, 0.2 g of sodium bicarbonate, 11.1 ml of dioxane, and 5.7 ml of water was refluxed for 20 hr, cooled, and distilled at 90° (pot temperature) and 35 mm. The liquid residue was dissolved in 5 ml of water and extracted with ether. The ether solution was dried and evaporated to give 0.14 g of crude liquid. Preparative vpc of this liquid afforded two minor components and a major component identified as **50**: ν_{max}^{neat} 3450 and 1040 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 5.63 (m, 2, olefinic), 3.50–4.60 (m, 4, CH_2O), 2.50–3.40 (m, 2, >C*H*O*H*), and 1.40–2.40 (m, 4, CH_2 and CH_2CH=).

The corresponding 3,5-dinitrobenzoate, mp 145–190°, was prepared in the usual fashion. The broad melting point range attests to the presence of the epimeric mixture.

Anal. Calcd for $C_{14}H_{14}N_2O_7$: C, 52.17; H, 4.38; N, 8.69. Found: C, 52.47; H, 4.54; N, 8.42.

Oxocan-4-ol (51). A solution of 0.12 g (0.94 mmol) of **50** in 7 ml of ethyl acetate was hydrogenated over 10% Pd on carbon at atmospheric pressure. The solution was filtered and the filtrate was evaporated. Preparative vpc[31] of the residue afforded two components in the ratio of 1:1. The component of lesser retention time was ketone **52**: ν_{max}^{neat} 1700 and 1090 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 3.70 (d of t, $|J|$ = 6.0 Hz and 18 Hz, 4, CH_2O), 2.52 (m, 4, CH_2C(=O)), and 1.82 (m, 4).

Alcohol **51** was the component of greater retention time: ν_{max}^{neat} 3350 and 1105 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 3.58 (m, 5, >C*H*O and CH_2O), 3.20 (m, 1, O*H*), and 1.72 (m, 8, remaining methylenes).

A mixture (1.3 g, 0.01 mol) of the ketone and alcohol was reduced with 0.735 g (0.02 mol) of lithium aluminum hydride. The usual work-up afforded 1.100 g (85%) of **51**.

Anal. Calcd for $C_7H_{14}O_2$: C, 64.58; H, 10.84. Found: C, 64.20; H, 10.81.

Oxocan-4-yl Formate (45). A mixture of 0.03 g (2.3 mmol) of **51** and 0.35 ml of formic acetic anhydride was allowed to stand overnight. The solution was dissolved in ether, extracted with 5% sodium bicarbonate solution, dried, and evaporated. Preparative vpc of the residual oil afforded formate **45**, a colorless liquid identical in all respects with the material previously isolated.

Formolysis of 4-Oxabicyclo[6.1.0]nonane (3). A solution of 5.5 mg (0.044 mol) of **3** in 0.032 ml of 99% formic acid sealed in a small Pyrex tube was heated at 50° for 167 hr, dissolved in ether, and treated with saturated sodium bicarbonate solution until neutral. The ether was evaporated at atmospheric pressure and the lone product was separated from a small amount of unreacted **3** by preparative vpc.[31] This substance was identified as the formate of 3-(2-tetrahydropyranyl)propanol (**53**): $\nu_{max}^{CCl_4}$ 1725 and 1175 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 8.09 (s, 1, *H*C(=O)), 4.20 (t, $|J|$ = 7.0 Hz, 2, CH_2O), 3.90 (m, 1, >C*H*O), 3.34 (m, 2, CH_2O), and 1.54 (m, 10, remaining methylenes).

Anal. Calcd for $C_8H_{16}O_3$: C, 62.76; H, 9.36. Found: C, 62.64; H, 9.51.

3-(2-Tetrahydropyranyl)propanol (56). A solution of 7.0 g (0.05 mol) of **54**[43] in 12.5 ml of tetrahydrofuran was added slowly to a solution of ethylmagnesium bromide (from 8.17 g of ethyl bromide and 1.82 g of magnesium turnings) in 38 ml of anhydrous tetrahydrofuran. Gas was evolved. The mixture was stirred at reflux for 1 hr and then treated with 11.7 g (0.075 mol) of 2-chlorotetrahydropyran (from anhydrous HCl and dihydropyran). After stirring of this solution overnight, 100 ml of saturated ammonium chloride was added. The aqueous layer was extracted with ether and the organic layers were combined, dried, and evaporated. Distillation of the residue at 117–122° (0.4 mm) afforded 5.0 g of liquid. This material (1.4 g) was hydrogenated at atmospheric pressure over 5% Pd/C as catalyst in ethyl acetate. After removal of the solvent, the oily residue was refluxed overnight in a solution of 6.0 ml of methanol, 6.0 ml of water, and 0.55 ml of concentrated sulfuric acid. The mixture was neutralized with sodium carbonate, evaporated, and extracted with dichloromethane. After drying and evaporation of the dichloromethane solution, a liquid residue was isolated which was purified by preparative vpc[31] to give 0.1 g (1.5%) of **56**: ν_{max}^{neat} 3325 and 1090 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 3.10–4.25 (m, 5, CH_2O-C*H*<), 2.90 (s, 1, O*H*), 1.60 (m, 10, remaining methylenes).

3-(2-Tetrahydropyranyl)propyl Formate (53). Alcohol **56** (0.10 g, 0.69 mmol) was treated with 0.60 g (0.69 mmol) of formic acetic anhydride and allowed to stand overnight. The solution was taken up in ether and treated with 5% sodium bicarbonate solution until neutral. Drying of the ether layer with magnesium sulfate and evaporation afforded a liquid residue which was purified by preparative vpc to give a formate identical in all respects with that isolated earlier.

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