excess of D_2O in dried dioxane solution. The infrared spectrum in carbon tetrachloride showed an N–D band at 2470 cm^{-1} and an N–H band at 3410 cm^{-1} which was absent in this compound. The compound was allowed to react with methyl iodide under high pressure as described above. The anilinium iodide produced was treated with aqueous Na_2CO_3 to yield the corresponding base. From the mass and nmr spectra, the compound was calculated to be 10–15% deuterated in the *ortho* position of 2,4-di-*t*-butyl-N,N-dimethylaniline. The peaks at mass 233 [$(t\text{-}C_4H_9)_2C_6H_3N(CH_3)_2$] and 218 (demethylated ion) were used for the analysis.

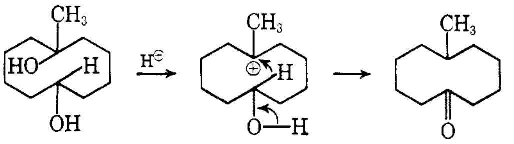
Acid-Promoted Rearrangements Involving Transannular Ether Oxygen Participation[1]

Leo A. Paquette, Robert W. Begland, and Paul C. Storm

Contribution from the Department of Chemistry, The Ohio State University, Columbus, Ohio 43210. Received April 24, 1968

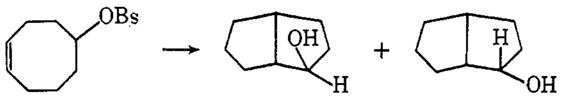
Abstract: When 7,8-dihydro-2H-oxocin-3(4H)-one (**14**) was heated with hydrochloric acid for several minutes, transannular rearrangement involving participation of ether oxygen was encountered and 5-(3-chloropropyl)dihydro-3(2H)-furanone (**13a**) was isolated in good yield. Exposure of **14** to hydrobromic acid gave rise to the corresponding bromide (**13b**). Under similar conditions, 7,8-dihydro-5-phenyl-2H-oxocin-3(4H)-one (**22**) and 5-phenyl-3,6,7,8-tetrahydro-2H-oxocin (**26**) were likewise converted to a dihydrofuranone and tetrahydrofuran, respectively. On the other hand, 5,6,7,8-tetrahydro-2H-oxocin-3(4H)-one (**15**) and 7,8-dihydro-4,4-dimethyl-2H-oxocin-3-one (**24**) were not acid labile and could be recovered unchanged from such treatment. The rearrangements are therefore the result of the generation of carbonium ion character at C-5, transannular oxygen participation, and solvolytic ring opening of the resulting oxonium ion. The various facets of this mechanism are discussed.

The phenomenon of transannular reaction is perhaps the most remarkable of a number of unique features exhibited by medium-sized rings. The origin of this characteristic is found in the existence of certain conformations wherein opposite sides of the ring are brought into close proximity. The pioneering work in this area, due to Prelog[2] and to Cope,[3] has centered predominantly upon transannular hydride shifts. These studies have shown that when substantial carbonium ion character develops in reaction intermediates involving mesocycles, transannular rearrangements are very likely to be of great importance. For example, the action of phosphoric acid on **1** results in the formation of 6-methylcyclodecanone (**2**) by a 1,6-hydride shift.[4]



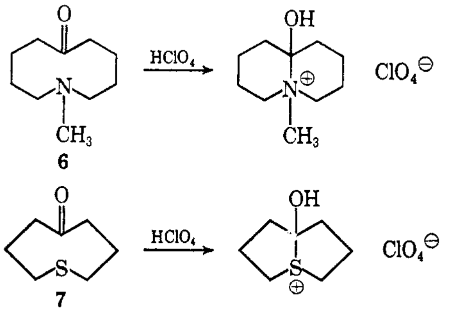
1 **2**

A further distinguishing feature of medium-sized rings is their tendency to go bicyclic to relieve existing nonbonded interactions. To illustrate, solvolysis of 4-cycloocten-1-yl brosylate (**3**) in acetic acid yields acetates of **4** and **5** in addition to 4-cyclooctenyl 1-acetate.[5]



3 **4** **5**

Leonard, in a broadening of such concepts to heterocyclic molecules, was able to detect transannular N–C_{CO} and S–C_{CO} interactions as revealed by the spectra of ketones such as **6** and **7**.[6,7] In addition, such ketones could be converted to their respective bicyclic salts when treated with strong acids. This effective electron-donating ability was found, however, to be restricted only to those molecules in which the interacting groups are diametrically opposed. Thus, treatment of **8** with acid does not lead to the formation of a



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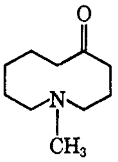

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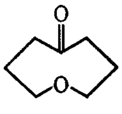

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[1] Unsaturated Heterocyclic Systems. XLV. For the previous paper, see L. A. Paquette and J. C. Philips, *J. Amer. Chem. Soc.*, **90**, 3898 (1968).

[2] V. Prelog and J. G. Traynham in "Molecular Rearrangements," Vol. I, P. de Mayo, Ed., Interscience Publishers, New York, N. Y., 1963, p 593.

[3] A. C. Cope, M. M. Martin, and M. A. McKervey, *Quart. Rev.* (London), **20**, 119 (1966).

[4] V. Prelog and W. Küng, *Helv. Chim. Acta*, **39**, 1394 (1956).

[5] A. C. Cope and P. E. Peterson, *J. Amer. Chem. Soc.*, **81**, 1643 (1959).

[6] N. J. Leonard, *Rec. Chem. Progr.*, **17**, 243 (1956).

[7] N. J. Leonard, T. W. Milligan, and T. L. Brown, *J. Amer. Chem. Soc.*, **82**, 4075 (1960).

product with a transannular bond across the ring.[6] By contrast, 1-oxacyclooctan-5-one (**9**) exhibited no such transannular effects in its spectra, a result which was attributed to its relatively low order of electron-donating ability.[7] Ketone **9** would also not form a salt; interestingly, however, reaction with aqueous hydrochloric acid gave 1,7-dichloro-4-heptanone in a process which may have passed through a bicyclic oxonium ion, although no proof was advanced in support of this postulate.

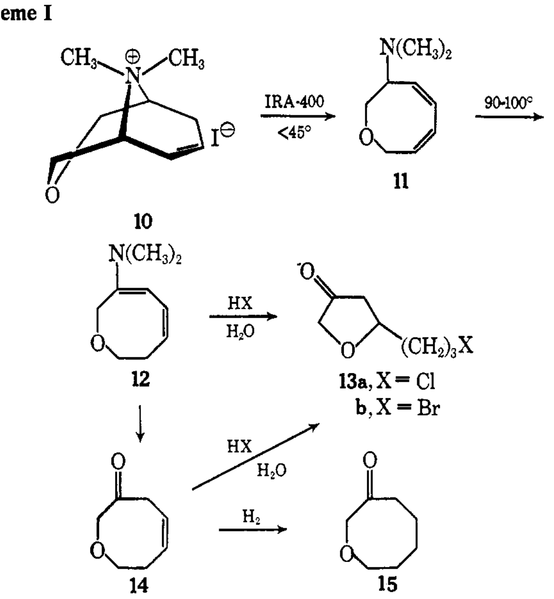
We were of the opinion that ether oxygen, despite its low order of nucleophilicity, should be entirely capable of transannular bonding in carbonium ion reactions. In actuality, many facts are available to support this theory. With particular regard to aliphatic and alicyclic ethers, the anomalously rapid rates of acetolysis of 4-methoxybutyl and 5-methoxypentyl brosylates have suggested that these reactions proceed through cyclic oxonium ions.[8] The enhanced solvolytic behavior of ω-(2-tetrahydrofuranyl)-3-propyl brosylate also pointed to anchimeric assistance by ether oxygen and formation of a bicyclic oxonium ion intermediate.[9] Additional evidence of such neighboring group participation has recently been reviewed[10] and summarized.[11]

In this paper, we wish to present evidence that ether oxygen, when suitably disposed in a mesocycle, will profoundly affect the course of reactions proceeding through carbonium ions.[12] Experimental verification of the intervention of oxonium ion intermediates was made by studying the microscopic reverse of one of the rearrangements. This transformation, as will become clear, provides an exceptionally facile synthetic entry to medium-sized heterocyclic systems.

Results and Discussion

Hofmann elimination of methiodide **10** under carefully controlled conditions resulted in the formation of 5-dimethylamino-7-oxa-1,3-cyclooctadiene (**11**) (Scheme I).[13] Heating of the aminodiene to 140–150° for a short period of time resulted in facile intramolecular dienyl 1,5-hydrogen transfer[14] and smooth conversion to dienamine **12**. Alternatively, **12** could be prepared directly from **10** in 87% yield. The ultraviolet spectrum of **12** [$\lambda_{\max}^{\text{isooctane}}$ 277.5 mμ (ϵ 8600)] is in excellent agreement with that of 1-dimethylamino-1,3-cyclooctadiene.[15] Hydrochloric acid hydrolysis of **12** gave rise in good yield to 5-(3-chloropropyl)dihydro-3(2H)-furanone (**13a**). This structural assignment followed from the elemental analysis, from the presence of an infrared carbonyl band at 1760 cm^{-1} which is typical of dihydro-3(2H)-furanones,[16] and from its nmr spectrum which, except for the resonance lines of the substituent at position 5, was superimposable upon that of 5-methyldihydro-3(2H)-furanone (see Experimental Section). In particular, it should be noted that this spectrum displayed no vinyl protons and that the ultraviolet spectrum of the 2,4-DNP derivative was that of a typical saturated ketone phenylhydrazone. Upon addition of warm 47% hydrobromic acid to **12**, there was obtained a 61.5% yield of the analogous bromide **13b**.

Scheme I



In contrast, unrearranged β,γ-unsaturated ketone **14**[17] was obtained in quantitative yield when hydrolysis was performed in refluxing 15% fluoroboric acid for short periods of time. The same result could be achieved in 10% aqueous acetic acid although the conversion was not as clean. The assignment of structure to **14** rests on spectroscopic criteria. The infrared absorptions for the carbonyl group and the *cis* double bond were located at 1720 and 1645 cm^{-1}, respectively. The ultraviolet spectrum in isooctane displayed peaks at 290 mμ (ϵ 146), 298 (185), 308 (161), and 318 (89), which can only be reconciled with the strengthened n → π* transition characteristic of β,γ-unsaturated ketones.[17] Further, the nmr spectrum provided definitive evidence for the various types of protons in **14** (see Experimental Section).

We deemed it imperative at this point to remove from consideration the possibility that such transformations were occurring because of the lability of α-alkoxy ketones in strongly acidic solution. Notwithstanding that the stability of a limited number of α-alkoxy ketones to acidic conditions had previously been demonstrated,[18] the point was further established in the present study by the observation that 5,6,7,8-tetrahydro-2H-oxocin-3-(4H)-one (**15**), prepared by catalytic hydrogenation of **14**, proved to be totally inert to the acidic reaction conditions utilized above. In view of these results, it would appear that the observed rearrangements can be explained in terms of the mechanism shown in Scheme

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(8) S. Winstein, E. Allred, R. Heck, and R. Glick, *Tetrahedron*, **3**, 1 (1958).

(9) G. T. Kwiatkowski, S. J. Kavarnos, and W. D. Closson, *J. Heterocycl. Chem.*, **2**, 11 (1965).

(10) B. Capon, *Quart. Rev.* (London), **18**, 45 (1964).

(11) L. A. Paquette and R. W. Begland, *J. Amer. Chem. Soc.*, **90**, 5159 (1968).

(12) A preliminary report on a portion of this work has appeared: L. A. Paquette and R. W. Begland, *ibid.*, **87**, 3784 (1965).

(13) L. A. Paquette and R. W. Begland, *J. Org. Chem.*, **32**, 2723 (1967).

(14) This thermally induced sigmatropic change of order [1,5] is presumably concerted and suprafacial [R. B. Woodward and R. Hoffmann, *J. Amer. Chem. Soc.*, **87**, 2511 (1965)]. Evaluation of the stereochemical course of the proton transfer is, of course, not possible in this system.

(15) $\lambda_{\max}^{\text{isooctane}}$ 274.5 mμ (ϵ 8430): L. A. Paquette and R. W. Begland, *J. Amer. Chem. Soc.*, **88**, 4685 (1966).

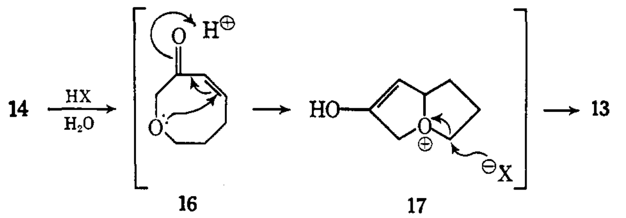
(16) J. H. S. Wieland, J. Dijkstra, and A. B. Pik, *Rec. Trav. Chim Pays Bas*, **82**, 651 (1963), and pertinent references cited therein.

(17) L. A. Paquette and R. F. Eizember, *J. Amer. Chem. Soc.*, **89**, 6205 (1967).

(18) See ref 16 and R. P. Mariella and J. L. Leech, *ibid.*, **71**, 3558 (1949); note also that the ultimate products **13a** and **13b** are members of this class of compounds.

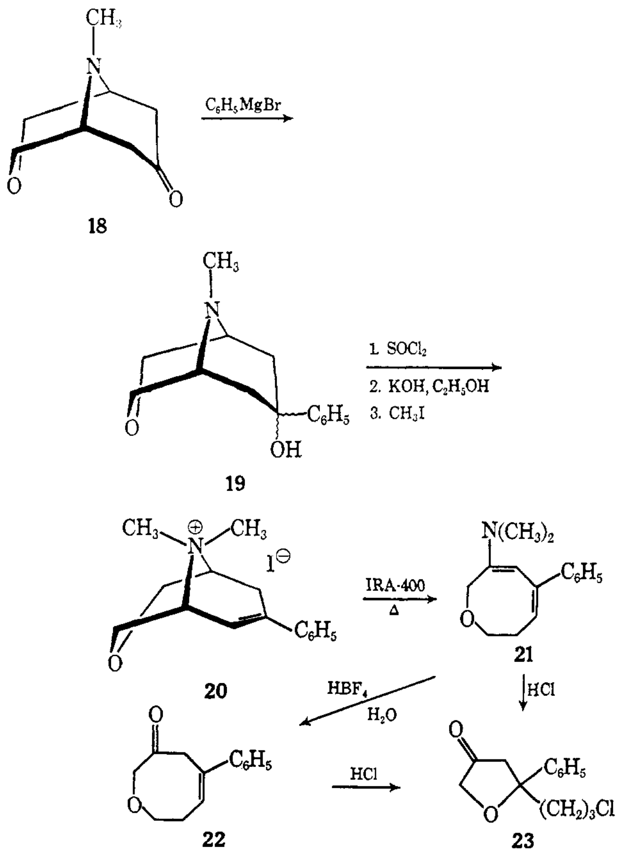
II. In the presence of strong acid, isomerization of **14** to the α,β isomer **16** can be expected to occur;[19] transannular nucleophilic attack by the remotely located divalent oxygen atom in a manner reminiscent of acid-catalyzed Michael additions leads to intermediate **17**.[20] This reactive oxonium salt (**17**) suffers nucleophilic attack by halide ion and ring cleavage in the indicated manner; ketonization eventuates in the formation of **13**.

Scheme II

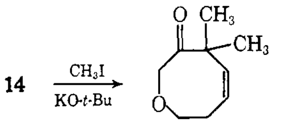


Two important features of this mechanism were subsequently established. First, attachment of a phenyl group at position 5 in **14** results in a diminished rate of rearrangement. 7,8-Dihydro-5-phenyl-2H-oxocin-3(4H)-one (**22**) was prepared in the unexceptional manner outlined in Scheme III. When 9-methyl-3-oxagranatanin-7-one (**18**) was treated with phenyllithium, a 36% yield of alcohol **19** was obtained; however, this conversion was increased to 71% when phenylmagnesium bromide was employed.[21] Tertiary alcohol **19** was transformed in the presence of thionyl chloride to the corresponding chloride, which without isolation was dehydrohalogenated with ethanolic potassium hydroxide to form 9-methyl-7-phenyl-3-oxagranatoline, isolated as its methiodide salt (**20**) in 90% over-all yield. Noncontrolled Hofmann elimination of **20** gave dienamine **21**, hydrolysis of which in fluoroboric acid produced the desired β,γ-unsaturated ketone **22** in 91% yield. The structure of **22** was immediately apparent from the spectroscopic data. Thus, its infrared (strong carbonyl absorption at 1720 cm^{-1}) and ultraviolet spectra [λ_{max}^{EtOH} 250 mμ (ε 11,000)] clearly indicated the β,γ orientation of the double bond. The observed wavelength is in good agreement with that of the isolated styrene chromophore found in 1-phenyl-1-cyclooctene [$\lambda_{max}^{cyclohexane}$ 248 mμ (ε 11,700)].[21] The detailed structure also follows from the intensity ratios of the various proton absorptions in the nmr spectrum (see Experimental Section). When either dienamine **21** or ketone **22** was heated with hydrochloric acid, the rearrangement observed earlier was virtually duplicated and furanone **23** was isolated in good yield. However, whereas the rearrangement of **14** was complete in less than 10 min, the half-life of **22**, under virtually identical conditions, was seen to be approximately 15 min. This retardation in the rate of transannular attack by oxygen in **22** cannot justifiably be attributed to an alteration in the nucleophilic character of the ether oxygen atom. Rather, the difference must lie either in the larger steric requirements of the phenyl substituent or in a diminution of electrophilicity at the site of oxygen attack. Although one might imagine some steric role played by the phenyl group that would account for the slower rate, it is more likely that the aromatic ring will choose to be coplanar with the sp^2-hybridized carbon atoms for maximum conjugative π orbital overlap; in view of the fact that conjugative π overlap in 2-cyclooctenone is known to be poor,[19] and since previous reviews[2,3] have suggested that a lobe of such p orbitals on cationic carbon is projected into the ring and toward the transannular center, minimal steric retardation should be experienced during the approach. It follows then that the diminished rate of rearrangement of **22** is likely due to a decrease in the electrophilicity of C-5, the seat of oxygen attack, brought about by delocalization of the positive charge developing at this site.

Scheme III



The second point to be made arises from an examination of the behavior of ketone **24** toward hydrohalogen acids. Dimethylation of **14** was achieved with excess potassium *t*-butoxide and iodomethane according to established procedures.[22] Obviously, in ketone **24** double bond migration into conjugation with the carbonyl group is not possible unless a methyl substituent



24

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[19] A mixture of 2- and 3-cyclooctenones is known to achieve equilibrium under acidic conditions with a composition of 20% of the conjugated isomer and 80% of the β,γ-unsaturated ketone: N. Heap and G. H. Whitham, *J. Chem. Soc., B*, 164 (1966).

[20] Related acid-catalyzed transannular reactions have recently been described wherein α,β-unsaturated lactam chromophores were the Michael acceptors and tertiary nitrogen atoms were the nucleophilic centers: L. A. Paquette and L. D. Wise, *J. Amer. Chem. Soc.*, **87**, 1561 (1965); L. A. Paquette and M. K. Scott, *J. Org. Chem.*, **33**, 2379 (1968).

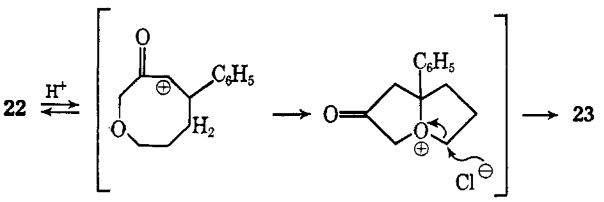
[21] A. C. Cope and A. A. D'Addieco [*J. Amer. Chem. Soc.*, **73**, 3419 (1951)] have observed the reverse order of effectiveness in the reactions of these organometallics with tropinone. In common with their observations, starting material was recovered in both cases.

[22] L. A. Paquette, R. F. Eizember, and O. Cox, *J. Amer. Chem. Soc.*, **90**, 5153 (1968), and pertinent references cited therein.

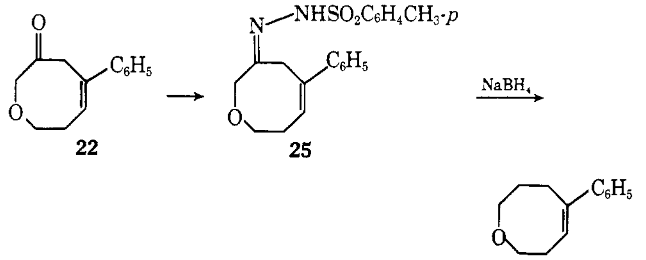
migrates. Therefore, should a furanone result, the conclusion could be reached that such a nonconjugated double bond is capable of transannular attack by oxygen. When **24** was refluxed with dilute hydrochloric acid for periods of time ranging from 15 min to 12 hr, no furanone was detected; only starting ketone and some polymer (in the prolonged runs) were obtained.

The observations so far permit utilization of the mechanism shown in Scheme II. However, a mechanism which does not require such isomerization prior to bonding can be written for ketone **22** (Scheme IV) in view of the stabilization provided the carbonium ion by the phenyl group. The possible validity of this proposal was next examined. To this end, our attention was directed to the synthesis of 5-phenyl-3,4,7,8-tetrahydro-2H-oxocin (**26**).

Scheme IV

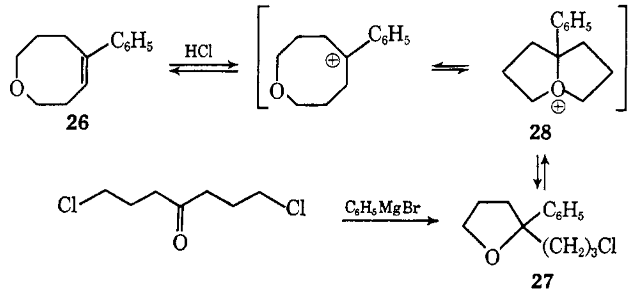


Preliminary attempts to reduce the carbonyl group in **22** by means of the Huang-Minlon modification[23] of the Wolff–Kishner procedure or by Raney nickel desulfurization of the corresponding ethylene dithioketal[24] failed to produce **26**. Ketone **22** was, however, convertible to its tosylhydrazone (**25**), sodium borohydride reduction[25] of which gave rise in low yield to **26**. When this olefin was treated with aqueous hydrochloric acid as above, a new compound was formed which exhibited an nmr spectrum compatible with the tetrahydrofuran formulation **27** (see Experimental Section). The identity of **27** was confirmed by independent synthesis from 1,7-dichloro-4-heptanone and phenylmagnesium bromide (Scheme V).



22 25 26

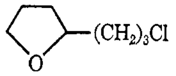
Scheme V



26 28 27

The genesis of **27** can be derived in mechanistically plausible fashion by invoking initial protonation of the styrene system. Conversion of the resulting benzylic cation to **27** can occur by transannular oxygen participation and formation of a bicyclic oxonium salt (**28**) which suffers attack by chloride ion. This successful conversion demonstrates that the transannular bonding process may proceed without the assistance of a carbonyl function and that a mechanistic alternative to Scheme II can in certain cases be operative (Scheme V).[26]

The ready availability of **27** provided the opportunity to examine the reversibility of the conversion of **26** to **27**. In principle, development of incipient carbonium ion character at the terminal carbon of the chloropropyl side chain in **27** should be anchimerically assisted by the tetrahydrofuranyl oxygen atom.[9] The consequence of C–O bond formation would be generation of bicyclic oxonium ion **28** which in the absence of efficient external nucleophiles could suffer concomitant proton loss and ring expansion to the eight-membered heterocycle **26**. Experimental support for this hypothesis was available from the reaction of **27** with an aqueous ethanolic solution of silver nitrate which gave rise to **26** in 48% yield. Thus the microscopic reversal of the transannular reaction was realized (Scheme V). In this connection, it appeared that reactions of the **27** → **26** variety could provide exceptionally easy synthetic entry to otherwise difficultly accessible medium-sized heterocycles. However, various similar reactions with **13b** and **29**[27] were observed not to afford products of ring expansion; rather, solvolysis of the halogen substituent was encountered.



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The above results demonstrate unequivocally that the formation of transannular products can result from participation of ether oxygen. Thus virtually complete transannular reaction was observed in the acid-promoted rearrangements of **14**, **22**, and **26**. What is equally significant about the experimental findings is the apparent dependence of the propensity for rearrangement upon the intensity of electron deficiency at the developing carbonium ion center. Such observations may be compared, for example, with the results of the solvolysis of *cis*-cyclooctene oxide where the extent to which transannular reaction occurred was correlatable with the acid strength of the solvent.[28]

There remains to be established the relative efficiencies at which ether oxygen can participate in a wider variety of carbonium ion reactions in medium-sized rings. A systematic study of this question is now in progress and will be reported at a later date.

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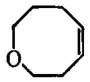
(23) Huang-Minlon, *J. Amer. Chem. Soc.*, **68**, 2487 (1946).

(24) L. F. Fieser, *ibid.*, **76**, 1945 (1954).

(25) A. C. Cope, D. L. Nealy, P. Scheiner, and G. Wood, *ibid.*, **87**, 3130 (1965).

(26) It is conceivable that tetrahydro-2H-oxocin (i) would also be subject to acid-promoted rearrangement despite the absence of a stabilizing group at C-5. To date, however, we have been unable to prepare i from a number of precursors and a wide variety of reactions [R. W. Begland, Ph.D. Thesis, The Ohio State University, 1968]. This problem remains under investigation.



i

(27) H. Gilman and A. P. Hewlett, *Rec. Trav. Chim.*, **51**, 93 (1932).

(28) A. C. Cope, J. M. Grisar, and P. E. Peterson, *J. Amer. Chem. Soc.*, **81**, 1640 (1959).

Experimental Section[29]

7,8-Dihydro-N,N-dimethyl-2H-oxocin-3-amine (12). A solution of 30 g (0.096 mol) of **10**[13] in water was passed through a column of Amberlite IRA-400 (hydroxide form). The eluate was collected until it was no longer alkaline, at which point the major portion of the water was evaporated under reduced pressure. The residue was rapidly distilled at approximately 15–60 mm and 90–150°. The organic product was rapidly separated from the liberated water by extraction with ether and the ether layer was dried. The recovered oil was redistilled at 123° (20 mm) to give 12.8 g (87%) of dienamine **12**: $n^{25}\mathrm{D}$ 1.5240; $\nu_{\max}^{\mathrm{CCl_4}}$ 1590 cm^{-1} (dienamine); $\lambda_{\max}^{\mathrm{isooctane}}$ 277.5 mμ (ε 8600); $\delta_{\mathrm{TMS}}^{\mathrm{CCl_4}}$ *ca.* 5.7 (multiplet, 2 H, vinyl protons), 4.78 (doublet, J = 4.5 Hz, vinyl proton at C-4), 3.95 (singlet, 2 H, protons at C-2), *ca.* 3.4 (multiplet, 2 H, protons at C-8), and *ca.* 2.2 (multiplet, 2 H, allylic protons).

Anal. Calcd for $C_9H_{15}NO$: C, 70.55; H, 9.87; N, 9.14. Found: C, 70.44; H, 9.87; N, 9.16.

5-(3-Chloropropyl)dihydro-3(2H)-furanone (13a). A. Hydrolysis of 12. To a warm solution of 1.5 g of **12** in 6 ml of concentrated hydrochloric acid was added 6 ml of water. The resulting solution was heated on a steam bath for 15 min, cooled, and extracted with ether. The combined organic layers were dried and evaporated and the residue was distilled to give 0.71 g (45%) of **13a** as a colorless liquid: bp 100–101° (2.2 mm); $n^{25}\mathrm{D}$ 1.4722; $\nu_{\max}^{\mathrm{CCl_4}}$ 1760 cm^{-1} (>C=O); $\delta_{\mathrm{TMS}}^{\mathrm{CCl_4}}$ *ca.* 4.2 (complex multiplet, 1 H, proton at C-5), 3.80 and 3.87 (singlets, 1 H each, protons at C-2), *ca.* 3.6 (multiplet, 2 H, $-CH_2Cl$), 2.0–2.7 (series of six peaks, 2 H, protons at C- 4), and *ca.* 1.9 (multiplet, 4 H, remaining methylene protons).[30]

The 2,4-dinitrophenylhydrazone of **13a**, prepared in the customary fashion, was obtained as orange crystals from ethanol: mp 94–95°; $\lambda_{\max}^{\mathrm{EtOH}}$ 228 mμ (ε 15,200), 255 sh (11,000), and 356 (20,800).

Anal. Calcd for $C_{13}H_{15}ClN_4O_5$: C, 45.55; H, 4.41; Cl, 10.35; N, 16.35. Found: C, 45.77; H, 4.69; Cl, 10.41; N, 16.33.

B. Rearrangement of 14. To a warm solution of 0.418 g (3.3 mmol) of **14** in 2 ml of concentrated hydrochloric acid was added 2 ml of water. The resulting solution was heated on a steam bath for 10 min, cooled, and extracted with ether. The ether was removed and the product was collected by preparative scale gas chromatography.[31] The clear liquid thus obtained (0.226 g) afforded an infrared spectrum and vpc retention time superimposable upon those of the sample obtained in A.

5-(3-Bromopropyl)dihydro-3(2H)-furanone (13b). A 2.0-g (13.0 mmol) sample of **12** was hydrolyzed with 47% hydrobromic acid in the manner described above. There was obtained 1.66 g (61. 5%) of **13b**: bp 89–90° (0.18 mm); $n^{29}\mathrm{D}$ 1.4944; $\nu_{\max}^{\mathrm{CCl_4}}$ 1765 cm^{-1} (>C=O). The nmr spectrum was very similar to that of **13a**. The 2,4-dinitrophenylhydrazone melted at 107–108°.

Anal. Calcd for $C_7H_{11}BrO_2$: C, 40.32; H, 3.90; N, 14.47; Br, 20.64. Found: C, 40.28; H, 4.02; N, 14.24; Br, 20.50.

7,8-Dihydro-2H-oxocin-3(4H)-one (14). A. Acetic Acid Hydrolysis. A solution of 3.1 g (0.020 mol) of **12** in 20 ml of 10% aqueous acetic acid was refluxed for 2.5 hr. The solution was cooled and extracted three times with ether. The ether solution was dried and evaporated, and the remaining oil was distilled to give 1.55 g (60.9%) of colorless liquid consisting of **14** (93%) and **12** (7%). Preparative scale gas chromatography[31] at 165° gave pure **14**: $\nu_{\max}^{\mathrm{CCl_4}}$ 1720 cm^{-1} (>C=O); $\lambda_{\max}^{\mathrm{isooctane}}$ 290 mμ (ε 146), 298 (185), 308 (161), and 318 (89); $\delta_{\mathrm{TMS}}^{\mathrm{CCl_4}}$ 5.73 (complex multiplet, 2 H, vinyl protons), 3.92 (singlet, 2 H, protons at C-2), 3.28 (doublet, J = 6.5 Hz, 2 H, protons at C-4), and *ca.* 2.3 (multiplet, 2 H, allylic protons).

Anal. Calcd for $C_7H_{10}O_2$: C, 66.64; H, 7.99. Found: C, 66.34; H, 8.01.

The 2,4-dinitrophenylhydrazone of **14**, prepared in the customary fashion, was obtained as orange crystals from ethanol: mp 114–116°; $\lambda_{\max}^{\mathrm{EtOH}}$ 228 mμ (ε 14,600), 255 sh (11,400), and 356 (21,600).

Anal. Calcd for $C_{13}H_{14}N_4O_5$: C, 50.98; H, 4.61; N, 18.29. Found: C, 51.06; H, 4.77; N, 18.50.

B. Fluoroboric Acid Hydrolysis. A solution of 3.0 g (19.6 mmol) of **12**, 6 ml of 50% fluoroboric acid, and 15 ml of water was refluxed for 15 min, cooled, neutralized with sodium bicarbonate, and extracted with three 100-ml portions of ether. The ether layer was dried, the ether removed, and the remaining solution distilled to give 2.46 g (99%) of **14** as a colorless liquid, bp 85–87° (15 mm), $n^{25}\mathrm{D}$ 1.4838.

Oxocan-3-one (15). A solution of 2.0 g (15.9 mmol) of **14** in 50 ml of diethyl ether was hydrogenated over palladium-on-charcoal catalyst for 1.5 hr at 45 psi. The catalyst was removed by filtration, and the filtrate was carefully distilled to give 1.95 g (96%) of **15** as a colorless liquid: bp 77–78° (11 mm); $n^{27}\mathrm{D}$ 1.4588; $\nu_{\max}^{\mathrm{CCl_4}}$ 1720 cm^{-1} (>C=O). The ketone was characterized as its 2,4-dinitrophenylhydrazone, mp 174–175°, from ethanol.

Anal. Calcd for $C_{13}H_{16}N_4O_5$: C, 50.64; H, 5.23; N, 18.18. Found: C, 50.34; H, 5.34; N, 18.10.

9-Methyl-7-phenyl-3-oxagranatanin-7-ol (19). To a solution of approximately 0.15 mol of phenylmagnesium bromide in ether was added 10.0 g (0.06 mol) of **18**[32] dissolved in 80 ml of dry benzene. The solution was stirred overnight, heated at reflux for 1 hr, and then cooled. A solution of 24 g of ammonium chloride in 160 ml of water was added dropwise and the mixture was extracted with three 200-ml portions of ether and subsequently with dichloromethane. The combined dichloromethane extracts were dried and concentrated to give 2.0 g of recovered **18**. The combined ether extracts were dried and evaporated to give 11.5 g (96% based upon recovered starting material) of **19**, colorless crystals from hexane, mp 129–130°, $\nu_{\max}^{\mathrm{Nujol}}$ 3400 cm^{-1} (-OH).

Anal. Calcd for $C_{14}H_{19}NO_2$: C, 72.07; H, 8.21; N, 6.00. Found: C, 71.81; H, 8.21; N, 6.03.

The methiodide of **19** was prepared with excess iodomethane in ethanol, mp 274–277°.

9,9-Dimethyl-7-phenyl-3-oxa-9-azoniabicyclo[3.3.1]non-6-ene Iodide (20). A solution of 12.0 g (0.05 mol) of **19** dissolved in 10 ml of dry benzene was added to a solution of 18 g (0.15 mol) of thionyl chloride in 50 ml of the same solvent. The resulting solution was heated at 45–55° for 1 hr. After cooling, the mixture was evaporated under reduced pressure and the solid residue was dissolved in 40 ml of absolute ethanol. The dehydrohalogenation was effected by adding to this solution a mixture of 8 g of potassium hydroxide, 14 ml of water, and 20 ml of ethanol. The mixture was stirred at room temperature for 30 min, treated with a solution of 8 g of potassium hydroxide in 32 ml of water, and finally extracted with ether. The combined organic layers were dried and concentrated to give a viscous oil which was dissolved in 100 ml of absolute ethanol containing 20 ml of iodomethane. After standing overnight, the mixture was cooled and filtered to give 16.0 g (90%) of **20** as pale brown crystals. Recrystallization from ethanol–water afforded white crystals, mp 298–299°.

Anal. Calcd for $C_{15}H_{20}INO$: C, 50.43; H, 5.64; N, 3.92. Found: C, 50.32; H, 5.71; N, 3.82.

7,8-Dihydro-N,N-dimethyl-5-phenyl-2H-oxocin-3-amine (21). A solution of 5.0 g (14 mmol) of **20** in 800 ml of water was eluted through a column of Amberlite IRA-400 ion-exchange resin (hydroxide form). The alkaline eluate was concentrated under reduced pressure at 75–80°. After the water had been removed, the oily residue was heated at 80° for 2 hr, and the residue was extracted with boiling benzene. This extract was concentrated and distilled to give 2.0 g (62.3%) of **21** as a pale yellow, viscous liquid, bp 115–120° (0.05 mm); $\nu_{\max}^{\mathrm{neat}}$ 1600 cm^{-1} (dienamine). This material was employed without further purification.

7,8-Dihydro-5-phenyl-2H-oxocin-3(4H)-one (22). A solution composed of 3.3 ml of 48–50% fluoroboric acid and 8.2 ml of water was added to 2.0 g (8.7 mmol) of **21** and the solution was heated on a steam bath for 30 min. After cooling, the mixture was extracted with three 30-ml portions of ether. The combined ether layers were washed with saturated sodium bicarbonate solution, dried, concentrated, and distilled to give 1.6 g (91%) of **22** as a colorless liquid: bp 115–120° (0.1 mm); $\nu_{\max}^{\mathrm{neat}}$ 1720 (>C=O) and 1600 cm^{-1} (>C=C<); $\lambda_{\max}^{\mathrm{EtOH}}$ 250 mμ (ε 11,000); $\delta_{\mathrm{TMS}}^{\mathrm{CCl_4}}$ 2.38 (multiplet, 2 H, protons at C-7), 3.77 (multiplet, 6 H, protons at C-2, -4, and -8), 6.17 (triplet, J = 8 Hz, 1 H, vinyl proton), and 7.30 (multiplet, 5 H, phenyl group).

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(29) The microanalyses were performed by the Scandinavian Microanalytical Laboratory, Herlev, Denmark. Infrared spectra were determined with a Perkin-Elmer Model 237 spectrometer fitted with a sodium chloride prism. Ultraviolet spectra were determined with a Cary Model 14 spectrometer and the nmr spectra were recorded with a Varian A-60 spectrometer. Boiling points are uncorrected while melting points are corrected.

(30) Compare N. S. Bhacca, D. P. Hollis, L. F. Johnson, and E. A. Pier, "NMR Spectra Catalog," Vol. 2, Varian Associates, Palo Alto, Calif., 1963, Spectrum No. 439.

(31) A 20 ft × 3/8 in. stainless steel column packed with 20% SE-30 on 60–80 mesh Chromosorb W was employed in conjunction with an Aerograph A90-P3 gas chromatograph.

(32) C. L. Zirkle, F. R. Gerns, A. M. Pavloff, and A. Burger, *J. Org. Chem.*, **26**, 395 (1961).

The corresponding 2,4-dinitrophenylhydrazone was obtained as yellow crystals from ethanol–water, mp 206–207°, $\lambda_{\max}^{\mathrm{EtOH}}$ 240 mμ (ε 26,200) and 356 (25,400).

Anal. Calcd for $C_{19}H_{18}N_4O_5$: C, 59.68; H, 4.75; N, 14.65. Found: C, 59.58; H, 4.83; N, 14.84.

5-(3-Chloropropyl)-5-phenyldihydro-3(2H)-furanone (23). A. Hydrolysis of 21. A solution of 1.5 g (6.5 mmol) of **21** was dissolved in 6 ml of 12 *N* hydrochloric acid, heated to the boiling point, and treated with 6 ml of water. After heating on a steam bath for 20 min, the mixture was cooled and extracted with ether. The combined ether layers were dried and concentrated under reduced pressure to give an oil consisting of two components in the ratio of 84:16.[33] Separation of the components was accomplished by column chromatography on silica gel. Elution with hexane–ether (3:1) yielded the minor component which was shown to be **22** by all the usual criteria. The major component, eluted from the column with hexane–ether (1:1), was assigned structure **23**: $\nu_{\max}^{\mathrm{neat}}$ 1760 cm^{-1} (>C=O); $\delta_{\mathrm{TMS}}^{\mathrm{CCl_4}}$ 7.07 (multiplet, 5 H, phenyl group), 3.75 (multiplet, 2 H, protons at C-2), 3.22 (triplet, *J* = 6 Hz, 2 H, $-CH_2Cl$), 2.45 (multiplet, 2 H, protons at C-4), and *ca.* 1.8 (broad multiplet, 4 H, remaining methylene protons).

The semicarbazone of **23**, prepared in the customary fashion, was recrystallized from aqueous ethanol to give white crystals, mp 167–168°.

Anal. Calcd for $C_{14}H_{18}ClN_3O_2$: C, 56.85; H, 6.13; N, 14.21. Found: C, 56.84; H, 6.31; N, 14.11.

B. Rearrangement of 22. A mixture of 150 mg (0.74 mmol) of **22** and 10 ml of 6 *N* hydrochloric acid was heated on a steam bath for 5 min. The mixture was cooled quickly and extracted with dichloromethane. The combined extracts were concentrated and the product composition was determined by vpc.[33] The remaining oil was treated again for subsequent time periods and the above analysis was repeated. The conversion of **22** into **23** was essentially complete after 75 min. The ratio of **23**:**22** and the time in minutes (in parentheses) for the conversion are given as follows: 0:1 (0), 1:3 (5), 2:3 (10), 1:1 (15), 7:5 (20), 2:1 (25), 3:1 (30), 6:1 (40), 10:1 (50), 12:1 (60), 1:0 (70).

7,8-Dihydro-4,4-dimethyl-2H-oxocin-3-one (24). To a solution of 1.51 g (0.012 mol) of **14** in 40 ml of absolute *t*-butyl alcohol, to which 1.40 g (0.036 g-atom) of potassium had been added, was slowly added 10.2 g (0.072 mol) of iodomethane. The resulting solution was stirred overnight, poured into 100 ml of water, and extracted with ether. The ether layer was dried and evaporated, and the remaining liquid was distilled to give 1.35 g (73%) of clear liquid: bp 89–90° (11 mm); $n^{25}\mathrm{D}$ 1.4755; $\nu_{\max}^{\mathrm{CCl_4}}$ 1710 cm^{-1}; $\delta_{\mathrm{TMS}}^{\mathrm{CCl_4}}$ *ca.* 5.4 (multiplet, 2 H, vinyl protons), 4.06 (singlet, 2 H, $-OCH_2C-$), *ca.* 3.6 (multiplet, 2 H, $-OCH_2-$), *ca.* 2.1 (multiplet, 2 H, allylic protons), and 1.22 (singlet, 6 H, methyl groups).

The 2,4-dinitrophenylhydrazone of **24** was obtained as orange crystals from 95% ethanol, mp 152–153°.

Anal. Calcd for $C_{15}H_{18}N_4O_5$: C, 53.89; H, 5.43; N, 16.76. Found: C, 53.80; H, 5.48; N, 16.65.

7,8-Dihydro-5-phenyl-2H-oxocin-3(4H)-one *p*-Toluenesulfonylhydrazone (25). A mixture of 1.2 g (5.9 mmol) of **22**, 1.4 g (14 mmol) of *p*-toluenesulfonylhydrazide, and 30 ml of absolute ethanol was heated at reflux for 30 min. After cooling, the mixture was filtered to give 2.0 g (91.5%) of white crystalline **35**. Recrystallization from ethanol afforded white needles, mp 154–155°.

Anal. Calcd for $C_{20}H_{22}N_2O_3S$: C, 64.84; H, 5.99. Found: C, 64.43; H, 5.90.

5-Phenyl-3,4,7,8-tetrahydro-2H-oxocin (26). A mixture of 7.3 g (20 mmol) of **25**, 7.6 g (0.2 mol) of sodium borohydride, and 200 ml of *p*-dioxane was heated at reflux for 2 hr. After cooling, the solution was treated with 300 ml of water and extracted with ether. The combined ether extracts were dried, concentrated, and distilled to give 600 mg of a two-component pale-yellow liquid, bp 115–120° (0.1 mm). Preparative scale vpc[34] gave **26** as a colorless liquid: $\lambda_{\max}^{\mathrm{EtOH}}$ 248 mμ (ε 9000); $\delta_{\mathrm{TMS}}^{\mathrm{CCl_4}}$ 7.19 (multiplet, 5 H, phenyl group), 6.02 (triplet, *J* = 8 Hz, 1 H, vinyl proton), 3.54 (multiplet, 4 H, protons at C-2 and C-8), 2.60 (triplet, *J* = 6 Hz, 2 H, protons at C-6), 2.23 (multiplet, 2 H, protons at C-3), and *ca.* 1.72 (broad multiplet, 2 H, protons at C-7).

Anal. Calcd for $C_{13}H_{16}O$: C, 82.93; H, 8.57. Found: C, 82.02; H, 8.45.

2-(3-Chloropropyl)-2-phenyltetrahydrofuran (27). A. From 1,7-Dichloro-4-heptanone. A solution containing approximately 0.3 mol of phenylmagnesium bromide in 200 ml of ether was added dropwise to a solution of 43.0 g (0.24 mol) of 1,7-dichloro-4-heptanone[35] in 100 ml of the same solvent. The resulting solution was heated at reflux for 2 hr, cooled in an ice bath, and treated dropwise with 150 ml of water. The layers were separated and the aqueous layer was extracted with ether. The combined ether layers were dried, concentrated, and distilled to give 30.5 g (57%) of impure **27**, bp 142–145° (0.3 mm). Chromatography of this oil on silica gel (elution with benzene–hexane 1:1) and redistillation gave pure **27** as a colorless oil: $\delta_{\mathrm{TMS}}^{\mathrm{CCl_4}}$ 7.21 (multiplet, 5 H, phenyl group), 3.85 (triplet, *J* = 6 Hz, 2 H, $-OCH_2-$), 3.35 (triplet, *J* = 7 Hz, 2 H, $-CH_2Cl$), and *ca.* 1.9 (broad multiplet, 8 H, remaining CH_2 groups).

Anal. Calcd for $C_{13}H_{17}ClO$: C, 69.47; H, 7.63; Cl, 15.78. Found: C, 69.92; H, 7.58; Cl, 15.32.

B. From Rearrangement of 26. A mixture of 290 mg of **26** and 10 ml of 6 *N* hydrochloric acid was heated on a steam bath for 1 hr. After cooling, the mixture was extracted with three 25-ml portions of dichloromethane. The combined organic extracts were dried and concentrated and the residue was subjected to microdistillation. The colorless liquid thus obtained (136 mg, 40%) proved to be identical in all respects with **27**.

Silver Ion Assisted Rearrangement of 27 to 26. A solution containing 1.5 g (6.7 mmol) of **27**, 1.2 g (7.0 mmol) of silver nitrate, 10 ml of water, and 25 ml of 90% ethanol was stirred overnight at room temperature. The precipitated silver chloride was separated by filtration and the filtrate was concentrated under reduced pressure. The residual oil was taken up in ether, and the combined ether extracts were dried, concentrated, and distilled to give 0.6 g (48%) of **26**, bp 96–99° (0.2 mm), identical in all respects with the authentic sample.

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(33) Percentage composition was determined by vpc analysis on a 10 ft × 0.25 in. aluminum column packed with 20% SF-96 on 60–80 mesh Chromosorb W.

(34) A 10 ft × 0.25 in. column packed with 1% Carbowax 20M on 60–80 Chromosorb W was employed at 140°.

(35) (a) O. E. Curtis, Jr., J. M. Sandri, R. E. Crocker, and H. Hart, "Organic Syntheses," Coll. Vol. IV, John Wiley & Sons, Inc., New York, N. Y., 1962, p 278; (b) H. Hart and O. E. Curtis, *J. Amer. Chem. Soc.* 78, 112 (1956).