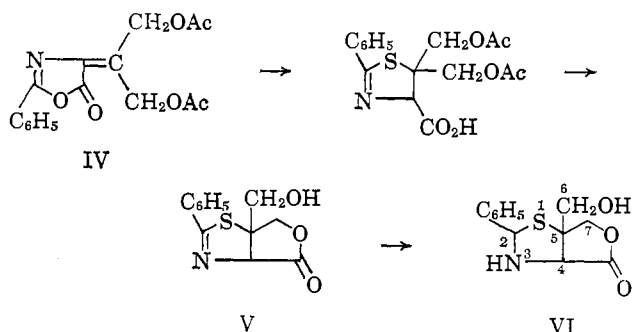


1600, 1580, 960, and 905 cm^{-1} . The mass spectrum showed, in addition to the molecular ion at 249, important peaks at 205, 174 (base peak), 121, 104, and 77. The n.m.r. spectrum in chloroform showed resonance at τ 4.55 (singlet, 1 H; C-4), 5.3 (2 H; C-7), and 6.05 (singlet, 2 H; C-6). The lactone ring of V is



undoubtedly *cis*-fused to the thiazolidine as shown.

Reduction of V with aluminum amalgam in moist ether⁷ for 45 min. at room temperature gave the hydroxymethylthiazolidine lactone VI as prisms melting at 159.5–160° from aqueous methanol. *Anal.* Found: C, 57.40; H, 5.15. The substance had end absorption at 215 $\text{m}\mu$ (ϵ 5,250) and $\nu_{\text{max}}^{\text{Nujol}}$ 3400, 3300, and 1770 cm^{-1} . The important features of the n.m.r. spectrum of VI (in acetone), compared to that of V, were the appearance of a singlet at τ 4.4 due to the hydrogen at C-2, while the C-4 hydrogen was moved upfield to τ 5.4 because of the increased shielding resulting from the saturation of the 2,3-double bond.

Acetylation of VI with acetic anhydride in benzene at room temperature gave large prisms of the N-acetyl derivative VII, m.p. 201–203°. *Anal.* Found: C, 57.08; H, 5.13. The ultraviolet spectrum showed only end absorption due to the benzene ring (ϵ 4650 at 220 $\text{m}\mu$). The substance had $\nu_{\text{max}}^{\text{Nujol}}$ 3300, 1790, and 1630 cm^{-1} , and its mass spectrum showed, in addition to the molecular ion at m/e 293, peaks at 250, 220, 218, 179 (base peak), 146, 122, and 121. The n.m.r. spectrum (in acetonitrile or acetone) showed the anticipated deshielding of the C-2 and C-4 hydrogens resulting from acetylation of the nitrogen; they now gave rise to resonance at τ 3.9 and 4.7, respectively.

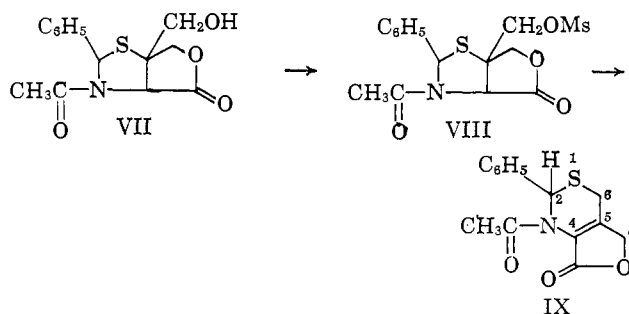
Treatment of VII with methanesulfonyl chloride in pyridine overnight at 5° gave an almost quantitative yield of the methanesulfonate VIII, m.p. 177–178° dec. The infrared spectrum showed $\nu_{\text{max}}^{\text{Nujol}}$ 1790, 1650, 1340, 1330, and 1170 cm^{-1} , while the n.m.r. spectrum (in dimethylformamide) showed the deshielding caused by the methanesulfonyl group on the hydrogens at C-4 and C-6 which now appear at τ 4.2 and 5.2 (compared with τ 4.7 and 6.2 for VII).

The stage was now set for the crucial step in the construction of the dihydrothiazine ring of cephalosporin C_c; when the mesylate VIII was refluxed for 5 hr. in dioxane with anhydrous sodium acetate, the desired substance IX appeared to be the only product formed, since the spectral properties of the crude reaction product were identical with those of pure IX. The latter was isolated in good yield on crystallization from petroleum ether–carbon tetrachloride as large prisms which melted at 77–78°⁸ after chromatography on alumina.

(7) A. H. Cook and I. M. Heilbron in ref. 5, p. 922.

(8) The dihydrothiazine IX crystallized well only as a carbon tetra-

The structure of the dihydrothiazine IX was confirmed by analytical and spectral data⁸: molecular weight (mass spectrum) 275 (other peaks at 233 (base peak), 215, 200, 122, 121, and 105). The presence of the unsaturated lactone and of the N-acetyl group was confirmed by the infrared spectrum ($\nu_{\text{max}}^{\text{CHCl}_3}$ 1775, 1690, and 1660 cm^{-1}),⁹ while the n.m.r. spectrum in carbon tetrachloride was entirely in agreement with structure IX: τ 2.6–2.9 (5 H; phenyl), 3.05 (singlet, 1 H; C-2), 5.4 (quartet, $J = 17$ c.p.s., 2 H; C-7), 6.7 (singlet, broad, 2 H; C-6), and 7.7 (singlet, 3 H; N-acetyl). The absence of resonance corresponding to a hydrogen at C-4 and the characteristic position of the maximum in the ultraviolet ($\lambda_{\text{max}}^{\text{MeOH}}$ 268 $\text{m}\mu$ (3.65)¹⁰) were further evidence of the correctness of structure IX.¹¹



chloride solvate which seemed to contain 4 molecules of CCl_4 for 9 molecules of IX. *Anal.* Calcd. for $\text{C}_{14}\text{H}_{13}\text{O}_3\text{NS}\cdot 0.44\text{CCl}_4$: C, 50.55; H, 3.82; S, 9.35; Cl, 18.20. Found: C, 50.73; H, 3.79; S, 9.29; Cl, 18.39. Correct analytical figures for solvent-free IX were obtained after heating under reduced pressure for 2 hr. at 100°. *Anal.* Found: C, 61.27; H, 4.79.

(9) Cf. infrared spectrum of 4-benzylthiomethyl-3-aminofuran-2(5H)-one: Green *et al.*, ref. 3.

(10) Cf. the spectrum of cephalosporin C_c (II), ref. 1.

(11) We wish to thank the National Institutes of Health for their support of this work.

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Transannular Participation of Ether Oxygen in the Hydrolysis of a Mesocyclic Dienamine¹

Sir:

Leonard's extensive study^{2,3} of transannular interactions between heteroatoms and ketone carbonyls in mesocycles⁴ has demonstrated the existence of transannular bonding of the N–C_{CO} and S–C_{CO} type, but the absence of O–C_{CO} interactions. This effective electron-donating ability was found, however, to be restricted only to those molecules in which the interacting groups were diametrically opposed.

We wish to present evidence that ether oxygen, despite its low order of nucleophilicity, can indeed profoundly affect the course of a reaction by transannular bonding and that the participating groups need not be diametrically opposed.

(1) Unsaturated Heterocyclic Systems, part XIX. For part XVIII, see L. A. Paquette, J. H. Barrett, R. P. Spitz, and R. Pitcher, *J. Am. Chem. Soc.*, **87**, 3417 (1965).

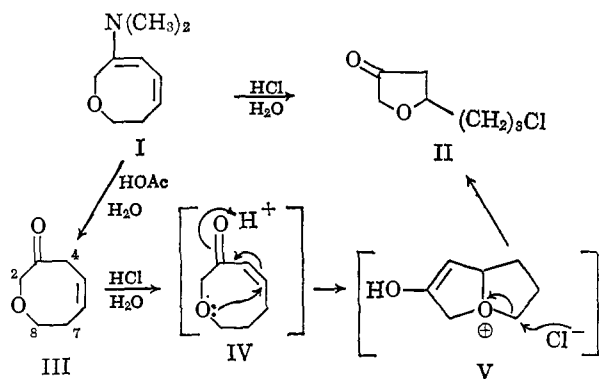
(2) N. J. Leonard, *Record Chem. Progr.* (Kresge-Hooker Sci. Lib.) **17**, 243 (1956).

(3) N. J. Leonard, T. W. Milligan, and T. L. Brown, *J. Am. Chem. Soc.*, **82**, 4075 (1960).

(4) "Mesocycle" is herein employed as an alternative to "medium-sized ring," as suggested in footnote 4 of ref. 3.

Thus, hydrochloric acid hydrolysis of the dienamine I⁵ gave rise in good yield to 5-(3-chloropropyl)dihydro-3(2H)-furanone (II), b.p. 100–101° (2.2 mm.); 2,4-dinitrophenylhydrazone, m.p. 94–95°. *Anal.* Found: C, 45.55; H, 4.41; Cl, 10.41; N, 16.35. Structure II follows from the elemental analysis, from the presence of an infrared carbonyl band at 1760 cm.⁻¹, which is typical of dihydro-3(2H)-furanones,⁶ and from the n.m.r. spectrum, which, except for the resonance lines of the substituent at position 5, was superimposable upon that of 5-methyldihydro-3(2H)-furanone.⁷ It should be noted that no vinyl proton was present in this spectrum and that the ultraviolet absorption of the 2,4-DNP derivative was that of a typical saturated ketone derivative.⁸

Further insight into the mechanism of the above transformation was obtained in the following manner. Hydrolysis of I in 10% aqueous acetic acid afforded the β,γ -unsaturated ketone III,⁵ b.p. 84–85° (15 mm.); 2,4-dinitrophenylhydrazone, m.p. 114–116°. The structure of III was readily established on the basis of spec-



tral evidence. The infrared absorptions for the carbonyl group and the *cis* double bond were located at 1720 and 1645 cm.⁻¹, respectively. The ultraviolet spectrum of III in isooctane displayed peaks at 290 m μ (ϵ 146), 298 (185), 308 (161), and 318 (89), which can only be reconciled with the strengthened $n \rightarrow \pi^*$ transition characteristic of β,γ -unsaturated ketones⁹ (the ultraviolet spectrum of the 2,4-DNP derivative was also typical of a nonconjugated ketone¹⁰). The presence of the various protons in III was obvious from the following chemical shifts and multiplicities: δ ca. 5.73 (complex multiplet, vinyl protons), 3.92 (singlet, H-2), ca. 3.75 (multiplet, H-8), 3.28 (doublet, H-4), and ca. 2.3 (multiplet, H-7).

The stability of α -alkoxyketones to acidic conditions in the absence of oxidizing agents has previously been demonstrated in a limited number of instances.¹¹ The point was further established in the present study by the observation that 5,6,7,8-tetrahydro-2H-oxocin-

(5) Satisfactory elemental analyses were obtained for all new compounds reported herein.

(6) J. H. S. Wieland, H. Dijkstra, and A. B. Pik, *Rec. trav. chim.*, **82**, 651 (1963), and references cited therein.

(7) 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.

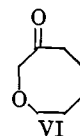
(8) $\lambda_{\text{max}}^{\text{EtOH}}$ 228 m μ (ϵ 15,200), 255 sh (11,000), and 356 (20,800).

(9) A. Moscovitz, K. Mislow, M. A. W. Glass, and C. Djerassi, *J. Am. Chem. Soc.*, **84**, 1945 (1962).

(10) $\lambda_{\text{max}}^{\text{EtOH}}$ 228 m μ (ϵ 14,600), 255 sh (11,400), and 356 (21,600).

(11) See ref. 6 and R. P. Mariella and J. L. Leech, *J. Am. Chem. Soc.*, **71**, 3558 (1949); note also that the ultimate product (II) is a member of this class of compounds.

3(4H)-one (VI),⁵ prepared by catalytic hydrogenation of III, proved to be totally inert to the acidic reaction



conditions utilized above. In view of these results, it would appear that the observed rearrangement can only be explained in terms of the ensuing mechanism. In the presence of hydrochloric acid, isomerization of III to the α,β -unsaturated isomer IV would be quite rapid; transannular nucleophilic attack by the remotely located divalent oxygen atom in a manner reminiscent of acid-catalyzed Michael additions leads to intermediate V. This oxonium salt (V) is expected to be extremely sensitive to nucleophilic attack by chloride ion¹²; ring cleavage (as shown) and ketonization eventuate in the formation of II.¹³

The facility with which divalent oxygen participates in this unusual transannular process is remarkable and suggests that the effect of substituting sulfur and nitrogen for this heteroatom can only be favorable. Furthermore, the replacement of nitrogen for oxygen should permit the isolation of the corresponding bicyclic intermediate V. Work to elucidate these points is presently in progress.

Acknowledgment. This work was supported in part by the Petroleum Research Fund, administered by the American Chemical Society. The authors are indebted to the donors of this fund. We also wish to thank the Elanco Products Co. for a generous gift of chloroacetaldehyde dimethyl acetal which was used in the preparation of I.

(12) H. Meerwein, *Angew. Chem.*, **70**, 630 (1958).

(13) These data lend strong support to the proposal that the hydrolysis of 1-oxacyclooctan-5-one to 1,7-dichloro-4-heptanone in aqueous hydrochloric acid proceeds through an intermediate bicyclic oxonium salt.³

(14) Alfred P. Sloan Foundation Research Fellow.

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Sulfonium Salts. I. Fragmentations of Chlorosulfonium Chlorides. A Route to 1,4-Oxathienes¹

Sir:

Scission of the sulfur heteroatom bond is a common step in the reactions of acyloxy-,² halo-,³ and hydroxy-

(1) Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research.

(2) For examples, see (a) R. Pummerer, *Chem. Ber.*, **43**, 1401 (1910); (b) W. E. Parham and M. D. Bhavsar, *J. Org. Chem.*, **28**, 2686 (1963); (c) L. Horner and P. Kaiser, *Ann.*, **626**, 19 (1959); (d) L. Horner and E. Jürgens, *ibid.*, **602**, 135 (1957).

(3) For lead references, see (a) W. E. Lawson and T. P. Dawson, *J. Am. Chem. Soc.*, **49**, 3119 (1927); (b) H. Böhme, H. Fischer, and R. Frank, *Ann.*, **563**, 54 (1949); (c) F. G. Bordwell and B. M. Pitt, *J. Am. Chem. Soc.*, **77**, 572 (1955); (d) H. Böhme and H. Gran, *Ann.*, **581**, 133 (1953); (e) H. Richtzenhain and B. Alfredsson, *Chem. Ber.*, **86**, 142 (1953).