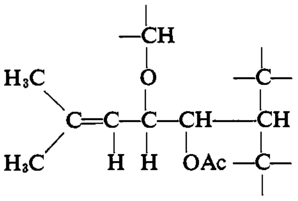
The nmr of diketone Ie shows the ether O–C–*H* protons as a *doublet* and multiplet, shifted downfield from the triplet and multiplet in previous compounds. Clearly the former proton must be on a carbon adjacent to the acetate bearing carbon. In addition, this same proton in Ie is coupled to the downfield vinyl hydrogen, and indeed returns to a triplet when Ie is catalytically reduced. The evidence thus far presented indicates the presence of the following group in Ia



This arrangement is most satisfactorily explained by formula Ia, the stereochemical assignments in the tetrahydropyran ring neatly explaining the noted diaxial coupling.[9] Chemical confirmation was obtained by saponification of Id to If, $C_{30}H_{46}O_3$, mp 186–187°, which was dehydrated ($POCl_3$–pyridine, room temperature) in high yield to vinyl ether III, $C_{30}H_{44}O_2$, mp 189–190°, λ_{max}^{alc} 233 mμ (ϵ 12,450), $\lambda_{max}^{CHCl_3}$ 1610 cm^{-1}. The conjugated diene III was then opened (6 *N* H_2SO_4 in THF) albeit in low yield to give hydroxyenone IV, $C_{30}H_{46}O_3$, mp 185–188°, λ_{max}^{alc} 238 mμ (ϵ 11,800), $\lambda_{max}^{CHCl_3}$ 1698, 1680, and 1615 cm^{-1}. Final confirmation of the ether attachment to a five-membered ring D was obtained by micro-Jones oxidation of IV to an oil which in the infrared showed one additional carbonyl band at 1741 cm^{-1}.

Wolff–Kishner reduction of this triketone under forcing conditions[10] gave a mixture of dienes,[11] mp 73–79°. Chromatography of this mixture on a silver nitrate impregnated silica gel column afforded the major diene, mp 80.5–81°, in 46% yield. This material was identical in all respects with an authentic sample of lanosta-8,24-diene.[12]

We are currently investigating the nature of other components of the crude extract as well as degradation of echinodol to trimethylprogestane derivatives. The interesting biogenetic features of this unusually highly oxygenated lanosterol derivative are also under study.

Acknowledgments. We acknowledge the generous financial support of the U. S. Public Health Service through Grant GM 10963. The nmr spectra were run on an instrument purchased with the assistance of the National Science Foundation. We wish to thank Professors W. G. Dauben and B. Weinstein for assistance in obtaining spectral data.

(9) With the exception of C-16 where the stereochemistry is assigned solely on the basis of analogy with other triterpenes.

(10) J. F. McGhie, M. K. Pradham, and J. F. Cavalla, *J. Chem. Soc.*, 3176 (1952).

(11) Tlc on SiO_2–Ag^+ plates showed three components, with the major corresponding in retention time and color to authentic lanosta-8,24-diene.[12]

(12) Kindly provided by Professor J. F. McGhie.

(13) National Science Foundation Undergraduate Research Participant.

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Mass Spectrometry in Structural and Stereochemical Problems. CXIX.[1] Interaction of Remote[2] Functional Groups in Mass Spectrometry

Sir:

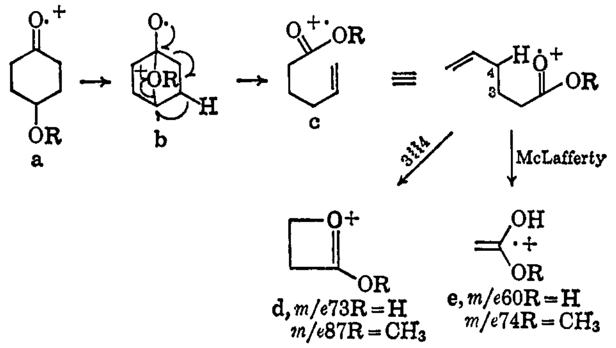
In connection with work under way in our laboratory[3] on the rearrangement of groups other than hydrogen in mass spectral fragmentations, we have encountered a case of electron-impact-induced oxygen rearrangement which is of considerable mechanistic interest and may be the prototype of other remote[2] functional group interactions in mass spectrometry.

One of the most abundant ions (relative abundance 78%, Σ_{20} 6.2%) in the mass spectrum of 4-hydroxycyclohexanone (I) corresponds to $C_2H_4O_2$ (*m/e* 60).[4] Analogously the base peak (Σ_{20} 9.1%) in the spectrum of 4-methoxycyclohexanone (II) corresponds to $C_3H_6O_2$ (*m/e* 74).[4] The presence of two oxygen atoms in a two-carbon fragment from I and a three-carbon fragment from II requires the intervention of an oxygen rearrangement in each case. The mass spectra of the three deuterated analogs III–V have shed some light on the most probable fragmentation pathway.

Replacement of the hydrogen atoms α to the carbonyl group in II by deuterium (V) resulted in a 2 mass unit shift of *m/e* 74 to 76, thus indicating that only one of the α-carbon atoms is retained in the rearrangement ion. Of crucial importance is the observation that approximately one-half of the *m/e* 60 peak is shifted to *m/e* 61 in III and IV, since this leads to the conclusion that one of the hydrogen atoms at C-3 or C-5 becomes equivalent to the C-4 hydrogen atom.

Another significant oxygen rearrangement ion occurs at *m/e* 73 ($C_3H_5O_2$;[4] relative abundance 28%, Σ_{20} 2.2%) in the mass spectrum of I and analogously at *m/e* 87 ($C_4H_7O_2$;[4] relative abundance 12%, Σ_{20} 1.1%) in that of II. The *m/e* 87 ion is shifted to *m/e* 89 in V while the *m/e* 73 ion remains unchanged in the mass spectrum of IV and is moved to *m/e* 75 in III. A plausible rationalization[5] consistent with these data is shown in Scheme I.

Scheme I



At the present time, no information is available on the details of the proposed rearrangement step (*i.e.*, bridged

(1) For paper CXVIII see P. Brown, J. Kossanyi, and C. Djerassi, *Tetrahedron*, in press.

(2) "Remote" is meant to designate numbers of bonds rather than spatial relationships.

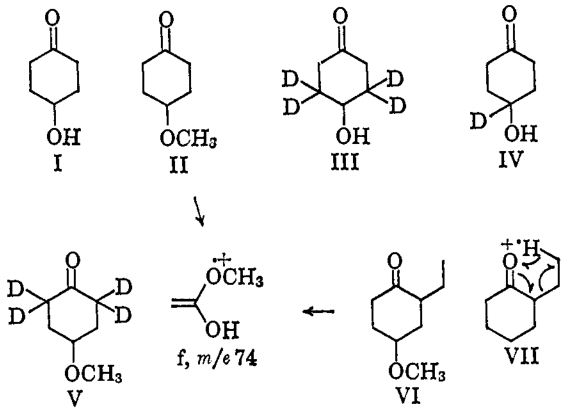
(3) C. Djerassi, A. M. Duffield, F. Komitsky, Jr., and L. Tökés, *J. Am. Chem. Soc.*, **88**, 860 (1966); M. Fischer and C. Djerassi, *Chem. Ber.*, **99**, 750 (1966), and references cited therein.

(4) High-resolution measurements were performed on all relevant ions in the labeled as well as unlabeled compounds.

(5) Two-electron transfers could equally well be used.

intermediate[6] or one-step transfer) and the subsequent hydrogen transfer. Further studies are currently under way to settle these questions and especially to delineate the scope[7] of this novel rearrangement.

In order to compare this process with other energetically favorable rearrangements, such as the McLafferty rearrangement[8] of ketones, we examined the mass spectrum of 2-ethyl-4-methoxycyclohexanone (VI). In the parent ketone, 2-ethylcyclohexanone (VII), the M − 28 ion resulting from McLafferty rearrangement (see arrows in VII) is responsible for the second most intense peak (relative abundance 95%, Σ_{40} 13.4%) in the mass spectrum. However, in the 4-methoxy analog VI, the McLafferty rearrangement (*m/e* 128) is greatly repressed[9] (relative abundance 22%, Σ_{40} 2.1%) while the methoxyl rearrangement ion f (*m/e* 74, $C_3H_6O_2$)[4] is responsible for the base peak (Σ_{40} 9.3%) of the spectrum. It is also interesting to note that almost all of the α fission (analogous to b → c) in 2-ethyl-4-methoxycyclohexanone (VI) occurs between C-1 and C-2, since very little *m/e* 102 (Σ_{40} 1.1%) fragment is produced. The latter peak would result from alternate α cleavage in VI between carbon atoms 1 and 6.



Acknowledgment. Grateful acknowledgment is made to Dr. A. M. Duffield and Mr. R. Ross for the mass spectral measurements and to the National Institutes of Health of the U. S. Public Health Service (Grant No. AM-04257) for financial assistance.

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[6] The unusual strength of the molecular ion in the spectra of I and II (relative abundance 71%, Σ_{20} 5.6% in I) is noteworthy and may have a bearing on this question. The driving force for the migration step could be envisioned as the alleviation of the electron deficiency at C-1. One need not go much further to connect this phenomenon with the long-range assisted solvolyses observed in ground-state reactions (see, for example: D. S. Noyce and B. N. Bastian, *J. Am. Chem. Soc.*, **82**, 1246 (1960)). We are currently investigating a possible parallelism between such assisted solvolyses and similar electron-impact-induced processes.

[7] Methoxyl rearrangements have recently been postulated in the mass spectra of some permethylated methyl glycosides: (a) K. Heyns and D. Müller, *Tetrahedron*, **21**, 55 (1965); *Tetrahedron Letters*, **4**, 449 (1966); (b) N. K. Kochetkov and O. S. Chizhov, *Tetrahedron*, **21**, 2029 (1965).

[8] For leading references and most recent study see H. Budzikiewicz, C. Fenselau, and C. Djerassi, *ibid.*, **22**, 1391 (1966).

[9] It is conceivable that the reduced intensity of this ion is due to its further decomposition which may be more favorable than that of the M − 28 species derived from VII.

[10] National Institutes of Health Postdoctoral Fellow.

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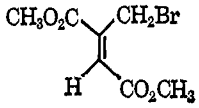
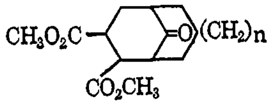
On the α,α′ Annelation of Cyclic Ketones

Sir:

The construction of bridged bicyclic systems from cyclic ketones has frequently been accomplished by the Stork enamine procedure[1] or by the closely related Michael aldol reaction.[2] We wish to report an alternate approach, based upon consecutive enamine alkylation and Michael reactions, which appears to offer considerable promise as a general synthetic tool. This new annelation process, developed with dimethyl γ-bromomesaconate (**1**)[3] and enamines of cyclic ketones, has provided some conformationally interesting and synthetically useful bridged bicyclic structures unobtainable by the former methods.


1


I, *n*=0
II, *n*=1

Reaction of **1** with the pyrrolidinenamine of cyclopentanone[4] in acetonitrile afforded, after acid hydrolysis of the imine salt, a 51% yield of a dimethyl bicyclo[3.2.1]octan-8-one-2,3-dicarboxylate [I, $C_{12}H_{16}O_5$; bp 161–164° (1.8 mm); $\nu_{\max}^{\mathrm{CHCl_3}}$ (cm^{-1}) 1747, 1725, 1260, 1175, and 1025 (three peaks); $\tau_{\mathrm{CDCl_3}}$ (ppm) 6.20 (3 H, singlet) and 6.27 (3 H, singlet), 8.10 (4 H, multiplet), 7.76 (1 H, multiplet), 7.38 (3 H, multiplet), and 6.88 (1 H, multiplet); dinitrophenylhydrazone, $C_{18}H_{20}N_4O_8$, mp 206–207°].[5] The product appeared to consist of a major isomer contaminated with about 2% of a second component as shown by glpc analysis. Upon borohydride reduction, the keto diesters I formed γ-lactone esters directly; these were separated by careful chromatography. The major γ-lactone ester **5** [$C_{11}H_{14}O_4$; liquid, bp 200° (1 mm), Kugelrohr; $\nu_{\max}^{\mathrm{CHCl_3}}$ (cm^{-1}) 1785, 1730, 1310, 1150 (three peaks), and 1025; $\tau_{\mathrm{CDCl_3}}$ (ppm) 6.21 (3 H, singlet), 5.22 (1 H, triplet), 6.82 (1 H, multiplet), 7.21 (2 H, multiplet), 7.67 (2 H, multiplet), and 8.25 (4 H, multiplet)] could be converted to the minor γ-lactone ester **6** [$\nu_{\max}^{\mathrm{CHCl_3}}$ (cm^{-1}) 1780, 1730, 1150, and 1015 (three peaks); $\tau_{\mathrm{CDCl_3}}$ (ppm) 6.25 (3 H, singlet), 5.22 (1 H, multiplet), 7.07 (multiplet), 7.65 (multiplet), and 8.17 (multiplet)] with *t*-butoxide in *t*-butyl alcohol making possible the assignment of the relative stereochemistry of the major and minor keto diesters as **2** and **3**, respectively. Further confirmation of these structural assignments was indicated by the facile isomerization of **2** and **3** to a crystalline isomer **4** [$C_{12}H_{16}O_5$; mp 92–94°; $\nu_{\max}^{\mathrm{CHCl_3}}$ (cm^{-1}) 1745, 1730, 1320, and 1250; $\tau_{\mathrm{CDCl_3}}$ (ppm) 6.30 (3 H, singlet), 6.31 (3 H, singlet), 6.71

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[1] G. Stork and H. K. Landesman, *J. Am. Chem. Soc.*, **78**, 5129 (1956).

[2] See, for example: (a) A. C. Cope, D. L. Nealy, P. Scheiner, and G. Wood, *ibid.*, **87**, 3130 (1965); (b) W. S. Johnson, J. J. Korst, R. A. Clement, and J. Dutta, *ibid.*, **82**, 614 (1960); (c) J. A. Marshall and D. J. Schaeffer, *J. Org. Chem.*, **30**, 3642 (1965); (d) J. Martin, W. Parker, and R. A. Raphael, *J. Chem. Soc.*, 289 (1964); (e) A. C. Cope and M. E. Sneyerholm, *J. Am. Chem. Soc.*, **72**, 5228 (1950).

[3] N. R. Campbell and J. H. Hunt, *J. Chem. Soc.*, 1176 (1947).

[4] G. Stork, A. Brizzolara, H. Landesman, J. Szmuszkovicz, and R. Terrell, *J. Am. Chem. Soc.*, **85**, 207 (1963).

[5] Satisfactory analytical results have been obtained for all compounds for which an empirical formula is given. Liquids were purified by chromatography on acid-washed silicic acid followed by distillation (Kugelrohr).