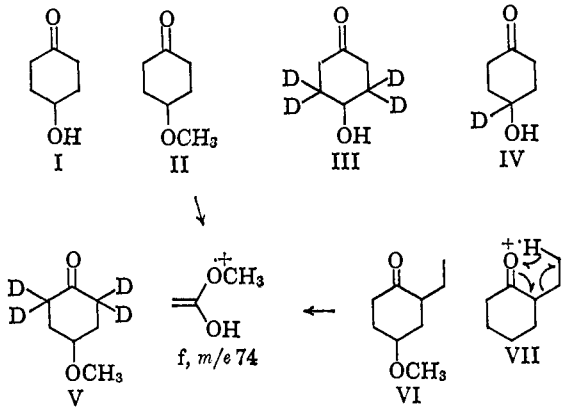
intermediate[6] or one-step transfer) and the subsequent hydrogen transfer. Further studies are currently under way to settle these questions and especially to delineate the scope[7] of this novel rearrangement.

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.

(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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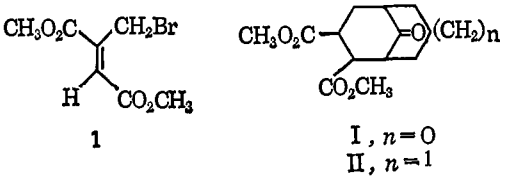
On the α,α' Annelation of Cyclic Ketones

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.

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); $\nu_{max}^{CHCl_3}$ (cm^{-1}) 1747, 1725, 1260, 1175, and 1025 (three peaks); τ_{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; $\nu_{max}^{CHCl_3}$ (cm^{-1}) 1785, 1730, 1310, 1150 (three peaks), and 1025; τ_{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** [$\nu_{max}^{CHCl_3}$ (cm^{-1}) 1780, 1730, 1150, and 1015 (three peaks); τ_{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°; $\nu_{max}^{CHCl_3}$ (cm^{-1}) 1745, 1730, 1320, and 1250; τ_{CDCl_3} (ppm) 6.30 (3 H, singlet), 6.31 (3 H, singlet), 6.71

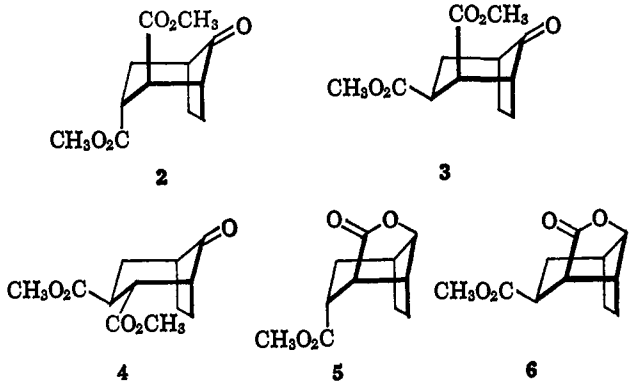
(1) G. Stork and H. K. Landesman, *J. Am. Chem. Soc.*, 78, 5129 (1956).

(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).

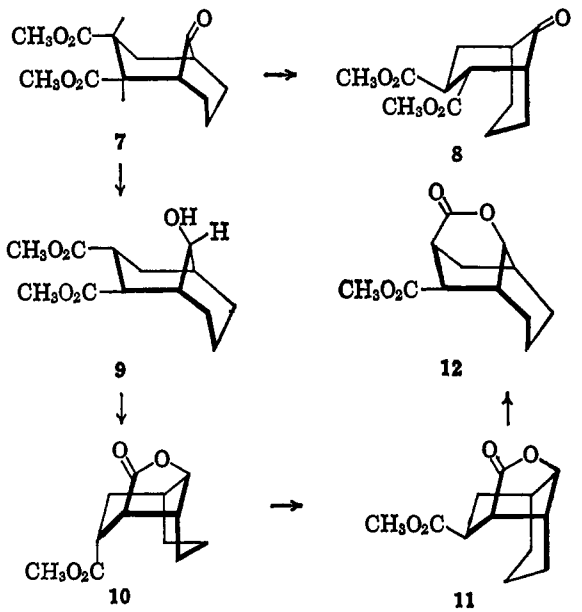
(4) G. Stork, A. Brizzolara, H. Landesman, J. Szmuszkovicz, and R. Terrell, *J. Am. Chem. Soc.*, 85, 207 (1963).

(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).



(quartet), 7.47 (multiplet), 7.77 (multiplet), and 8.10 (multiplet); dinitrophenylhydrazone, $C_{18}H_{20}N_4O_8$, mp 186.5–188°].

In a similar condensation of bromomesaconic ester **1** with the pyrrolidinenamine of cyclohexanone,[4] there was produced a 76% yield of a bicyclononanone diester [II; $C_{13}H_{18}O_5$; bp 175–179° (2.5 mm); $\nu_{max}^{CHCl_3}$ (cm^{-1}) 1735, 1175, 1040; τ_{CDCl_3} (ppm) 6.29 (3 H, singlet), 6.30 (3 H, singlet), 7.40 (5 H, multiplet), and 8.08 (7 H, multiplet); dinitrophenylhydrazone, $C_{19}H_{22}O_8N_4$, mp 201.5–202.5°]. In contrast to the initially formed major bicyclooctanone diester **2**, the nonanone exhibited nearly identical ester OCH_3 absorptions in the nmr which suggested a different stereochemistry or conformation or both. Treatment of the keto diester with sodium methoxide–methanol afforded a crystalline isomer [$C_{13}H_{18}O_5$; mp 96–97.5°; $\nu_{max}^{CHCl_3}$ (cm^{-1}) 1735, 1280, and 1173; τ_{CDCl_3} (ppm) 6.27 (3 H, singlet), 6.31 (3 H, singlet), 6.62 (multiplet), 7.22 (multiplet), 7.50 (multiplet), and 7.96 (multiplet); dinitrophenylhydrazone, $C_{19}H_{22}N_4O_8$, mp 149–150.5°] assumed to have the most stable configuration (**8**). Borohydride reduction of the first formed keto diester (II) afforded a



hydroxy diester, **9**, which did not undergo lactonization until heated to 170° for 2 hr. Since the γ-lactone ester **10**[6] [$C_{12}H_{16}O_4$; mp 106–107°; $\nu_{max}^{CHCl_3}$ (cm^{-1}) 1770, 1725, 1160, and 995; τ_{CDCl_3} (ppm) 6.20 (3 H, singlet), 5.55 (1 H, triplet), 6.85 (multiplet), 7.27 (multiplet), 7.45 (multiplet), 7.75 (multiplet), 8.05–8.60 (multiplet)] produced by this treatment was converted to an epimeric γ-lactone ester [**11**; $\nu_{max}^{CHCl_3}$ (cm^{-1}) 1775, 1730, 1155, and 1005; τ_{CDCl_3} 6.28 (3 H, singlet), 5.60 (1 H, multiplet), 7.10 (multiplet), 7.50 (multiplet), 7.20 (multiplet), 8.43 (multiplet)] with *t*-butoxide–*t*-butyl alcohol, we conclude that II has a *trans* orientation of the ester functions as did I, but has at least the substituted ring in a boat conformation (**7**).[7] Additional justification for the above assignments was obtained from the observed facile transformation of the γ-lactone ester **10** to a δ-lactone ester (**12**) [$C_{12}H_{16}O_4$; liquid; $\nu_{max}^{CHCl_3}$ (cm^{-1}) 1755, 1735, 1265, 1135, and 1050 (three peaks); τ_{CDCl_3} (ppm) 6.27 (3 H, singlet), 5.75 (1 H, triplet), 7.10 (1 H, multiplet), 7.33 (2 H, multiplet), 7.69 (1 H, multiplet), and 8.45 (8 H, multiplet)] with sodium methoxide–methanol at room temperature. Undoubtedly the resistance to γ-lactone formation is a consequence of the interaction of the 3-carbomethoxy group with the methylenes of the unsubstituted cyclohexane ring which develops as a result of the conformational inversion prior to lactone formation (**9** → **10**). δ-Lactone formation must occur by epimerization at position 3, opening of the γ-lactone, conformational inversion to a boat form, and formation of δ-lactone (**12**).

Since both the enamine and α-(1-haloalkyl)-unsaturated ester would seem able to include many diverse features, this synthesis provides a general method for the construction of a wide variety of structures. The scope, limitations, and logical extensions of this reaction are under active investigation as are the further uses of the products in synthetic and conformational studies.[8]

(6) The unsubstituted ring must reside in a boat conformation so as to relieve the 3-carbomethoxy–7-H interaction.

(7) The substituted ring might assume a very flat chair conformation; however, this would bring the 3-carbomethoxy group much closer to the methylenes of the unsubstituted ring. Thus, these compounds appear to be the first examples of the bicyclo[3.3.1]nonane system having a boat form. *Cf.* G. Eglinton, J. Martin, and W. Parker, *J. Chem. Soc.*, 1243 (1965); W. A. C. Brown, G. Eglinton, J. Martin, W. Parker, and G. A. Sim, *Proc. Chem. Soc.*, 57 (1964).

(8) Preliminary studies on the mechanism indicate that of the available pathways, the C-alkylation followed by proton transfer and Michael addition process is that preferred over the Michael–elimination–Michael or N-alkylation–rearrangement–Michael routes.

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9-[β-DL-2α,3α-Dihydroxy-4β-(hydroxymethyl)-cyclopentyl]adenine, the Carbocyclic Analog of Adenosine[1,2]

Sir:

During recent years much interest has been manifested in analogs of the ribofuranosyl- and deoxyribofuranosylpurines and -pyrimidines that occur in nucleic acids. Investigations of such analogs are exemplified

(1) This investigation was supported by the C. F. Kettering Foundation and by the Cancer Chemotherapy National Service Center, National Cancer Institute, National Institutes of Health, Contract No. PH43-64-51.

(2) Analytical data for compounds II, III, III-diacetate, IV, IV-anhydride, V, VI, VII (R_1 = $COCH_3$, R_2 = H or $COCH_3$), VIII, IX, XI, II-isopropylidene derivative, and XII were satisfactory.