5.75 μ (broad), nmr ($CDCl_3$): α-H_aH_e and γ-H_aH_e τ ~7–9 (4 H), β-H_a at τ 4.72 (1 H; half-band width ~15 cps), δ-H_a at τ 5.53 (1 H; half-band width ~20 cps), β-OAc at τ 7.93 (3 H; sharp), and δ-CH_3 at τ 8.56 (3 H; J = 6.0 cps).

Provisional Specifications from Biogenetic Considerations. 1*R*′:1′′*R*:6*R*:8*R*:12*R*:13*S*:15*R* (substantiated) and 3*R*:4*S*:5*S* (untested). The workings of a macrolide configuration model,[22] in dictating biogenetically expected specifications (Fischer projections) for asymmetric centers in various macrolide[14] macrocycles, are summarized in Chart II. Provisional specifications for Ia were gained as follows (*cf.* Charts I and II). Straightforward matchings with the model leads to 3*R*:5*S*:6*R*:8*R*:13*S* and 15*R*; 4*S* is in accord with an "extra"[6] oxygen proviso;[23] 12*R* follows 13*S* from after-the-fact knowledge of C-12:C-13 relative configuration (which happens to be consistent with the assumption that C-12 of carbomycin-A is comparable with C-10 of the model); 1′*R*:1′′*R* stem from a corollary[1c] applicable to pyranosyloxy constituents of macrolides.

Acknowledgment. Special thanks are extended to Mr. M. Jefferson for technical assistance and to Dr. I. A. Solomons and many research colleagues for their helpful interest.

(22) See ref 1c, 11, and 12 for development and applications of the model in the face of some six confrontations, all of which have been dispatched in favor of the model (*cf.* ref 1b, 13f, and this report).

(23) The proviso now states that a branched or unbranched asymmetric center containing an "extra" oxygen, either as a ligand or on the branch, remains configurationally subservient to the model; *cf.* ref 1c, 11, and K. R. Hanson, *J. Am. Chem. Soc.*, **88**, 2731 (1966).

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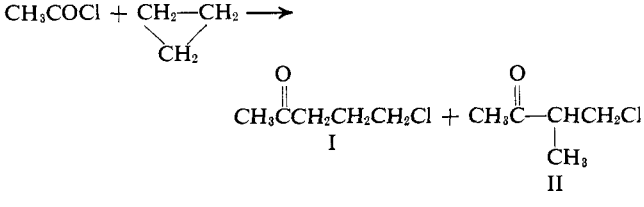
Bridged Ionic Intermediates in the Acylation of Cyclopropane

Sir:

Some years ago we observed that addition of cyclopropane to a 1:1 acetyl chloride–aluminum chloride complex in chloroform gave not only the expected 5-chloro-2-pentanone (I) but also, and as the major product, the β-chloro ketone II.[1] The rearrangement was also observed with several substituted cyclopropanes;[2] indeed, with some cyclopropanes, only the "abnormal" product was isolated. These results have been described[3] as "curious...difficult to account for," and have remained in the literature for some years as an enigma. We have recently reinvestigated this reaction with the help of vpc and nmr. The earlier work has been confirmed and extended, with the result that a plausible mechanism can now be suggested.



(1) H. Hart and O. E. Curtis, Jr., *J. Am. Chem. Soc.*, **79**, 931 (1957).
(2) H. Hart and G. Levitt, *J. Org. Chem.*, **24**, 2161 (1959).
(3) R. Breslow in "Molecular Rearrangements," P. deMayo, Ed., John Wiley and Sons, Inc., New York, N. Y., 1963, p 256.

Cyclopropane was acetylated as previously described,[1] and the products separated by vpc (5-ft SE-30 column, 50 cc of He/min, 115°). Four peaks were observed, two of which were due to I (6.6 min, 23 ± 2%) and II (4.8 min, 42 ± 3%); their nmr spectra were consistent with the previously assigned structures. The two additional products were shown to be III (0.7 min, 31 ± 3%) and IV (3.2 min, 4 ± 1%). The nmr spectrum and other properties of III agreed with the previously assigned structure.[4]

The structure of IV was clear from its infrared spectrum ($\nu_{C=O}$ at 1718 cm^{-1}, ν_{CCl} at 758 cm^{-1}), nmr spectrum (τ 7.75 (singlet, 3H), 5.96 (two doublets, J = 7.4 cps, 1 H), 8.12 (multiplet, 2 H), 8.97 (triplet, J = 7.1 cps, 3 H assigned to the protons on C-1, -3, -4, and -5, respectively)), and mass spectrum,[5] which in addition to the parent peak (*m/e* 120, 122) had prominent peaks at *m/e* 92, 94 ($CH_3C(OH)=CHCl^+$) and 43 (CH_3CO^+). IV synthesized from 2-pentanone and sulfuryl chloride[6] was found to be identical (retention time, infrared, nmr) with the acylation product.

All four products were also formed using CH_2Cl_2, CS_2, or nitrobenzene as solvent; the highest yield of IV was 10% (in CS_2).

Direct nmr examination of the homogeneous reaction mixture (in CCl_4) showed that all four products were present before work-up. Integration of the $-CH_2Cl$ peak of I *vs.* the $CH_3CH<$ peak of II gave (after statistical correction) a ratio of II:I of 1.20; the vpc ratio after work-up was 1.17. This not only verifies the reliability of the vpc method, but establishes that III is formed directly, and not by dehydrohalogenation of II during work-up.[7]

The data in Table I show that the chloro ketones are not interconverted during the reaction and that acetylcyclopropane (V) does not suffer ring opening in the acylating medium. Indeed, treatment of V with HCl and $AlCl_3$ in CH_2Cl_2 at 5° for 1 hr led only to recovered starting material. Thus acetylcyclopropane cannot be a reaction intermediate.

Any mechanism which begins with the formation of a classical carbonium ion (*i.e.*, VI, with or without stabilization by the carbonyl oxygen) seems doomed to a series of irrational subsequent steps to account for the observed products. We suggest instead that an

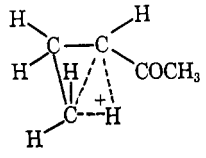
acetyl group displaces a proton from cyclopropane, but that the proton remains associated with the cyclo-

(4) In the previous work[1] the reaction mixture was dehydrohalogenated with Na_2CO_3 before product isolation; III was identified, and the initial formation of II was inferred. With other acyl halides, however, the β-chloro ketones were isolated and identified.
(5) We are indebted to S. Meyerson, American Oil Company, Whiting, Ind., for the mass spectrum.
(6) E. R. Buchman and E. M. Richardson, *J. Am. Chem. Soc.*, **67**, 395 (1945).
(7) Separate experiments showed that II was not dehydrohalogenated under the vpc conditions used.

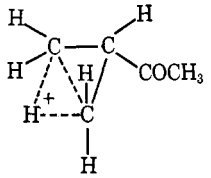
Table I. Cyclopropane Acylation with Added Chloro Ketones or Acetycyclopropane

Cyclopropane, mole	Solvent	Added reactant, mole	Products	Normal acylation, %	Expected, %	Obsd, %
0.010	CCl_4	I, 0.0044	I	35	55	57
			II	41	28	24
			III	20	14	16
			IV	4	3	3
0.005	CCl_4	II, 0.0017	I	35	26	28
			II	41	56	48
			III	20	15	20
			IV	4	3	4
0.010	CH_2Cl_2	IV, 0.0077	I	24	14	16
			II	56	32	28
			III	16	9	11
			IV	4	46	45
0.05	CH_2Cl_2	V, 0.05	I	24	12	11
			II	56	28	32
			III	16	8	7
			IV	4	2	2
			V		50	48

propane ring, as in VII. VII may react with a nucleophile (*i.e.*, $AlCl_4^-$) to give I or IV or may, by a process similar to those described by Baird and Aboderin,[8] isomerize to VIII. VIII should be more stable than VII, since the positive charge is further from the carbonyl group. VIII may react with nucleophile to give II or may lose the proton α to the carbonyl group, giving III.



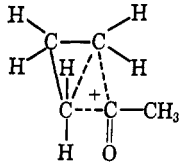
VII



VIII

One might expect that if the nucleophile concentration were kept low to allow time for the conversion VII → VIII, most of the product would be derived from VIII. Inverse addition gave results in accord with this hypothesis. The yields of II and III were increased at the expense of I and IV. For example, in CH_2Cl_2 the yields of I–IV were changed from 24, 56, 16, and 4% to 4, 74, 20, and 2%, respectively, by inverse addition.

Acetylcyclopropane does not give the observed chloro ketones because it is probably first protonated on oxygen.[9] Because of the retarding effect of electron-withdrawing substituents on the rate of cyclopropane acylation,[2] we regard the formation of VII or its probable immediate precursor IX as rate determining, and subsequent steps as fast.



IX

We believe intermediates similar to VII–IX will be important in the attack of other electrophiles on cyclopropanes[10] and are continuing our studies.[11]

(8) R. L. Baird and A. A. Aboderin, *J. Am. Chem. Soc.*, **86**, 252 (1964); A. A. Aboderin and R. L. Baird, *ibid.*, **86**, 2300 (1964).

(9) VII or VIII might possibly lose the bridged proton. Experiments using various nonnucleophilic bases in the acylating mixture have thus far not yielded any acetylcyclopropane.

(10) N. C. Deno and D. N. Lincoln have obtained similar results in the addition of bromine to cyclopropane (private communication from Professor Deno).

(11) We are grateful to the National Science Foundation (GP-71) and the National Institutes of Health (GM 11775) for partial financial support of this work.

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A Large Enhancement of Solvation Enthalpy by the Reduction of Temperature[1,2]

Sir:

Recently we reported[3] a very large (about 17 kcal/mole) change in the partial molal heat of solution, $\Delta\bar{H}_s$, of sodium tetraphenylboride produced on going from pure water to water containing 0.04 mole fraction of *t*-butyl alcohol. That experiment was tried because a variety of evidence[3] suggested that very large changes in thermodynamic properties related to the structuredness of water would be found using that binary solvent system and that solute.[4] One test of our interpretation of these phenomena[3,5] would be to see if the inflection in $\Delta\bar{H}_s$ would be further amplified by cooling since the structuredness of water is very sensitive to temperature change. The results displayed in Table I[6] and Figure 1 indicate that, in fact, there is a considerable increase in the endothermic maximum so that *the change in* $\Delta\bar{H}_s$ *on going from*

(1) Solvent Effects in Organic Chemistry. XI.

(2) This work was made possible by grants from the National Science Foundation (NSF-GP-2014) and the Health Research and Services Foundation of Pittsburgh.

(3) E. M. Arnett and D. R. McKelvey, *J. Am. Chem. Soc.*, **87**, 1393 (1965).

(4) See the recent ultrasonic studies of M. J. Blandamer, M. J. Foster, N. J. Hidden, and M. C. R. Symons, *Chem. Commun.*, 62 (1966), for support of this interpretation.

(5) E. M. Arnett, W. G. Bentrude, J. J. Burke, and P. M. Duggleby, *J. Am. Chem. Soc.*, **87**, 1541 (1965).

(6) A preliminary, and less accurate, examination of this phenomenon was made in our laboratory by Dr. George Mach and reported at the Symposium on Physico-Chemical Process in Aqueous Solvents held at Bradford, England, in May 1966, which is to be published.