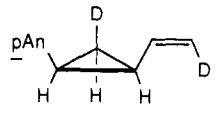
If cyclopropane cation radicals are intermediates in the isomerization, how do they interconvert? We consider three stereomutation mechanisms, called "two-center rotation", "deprotonation/reprotonation", and "one-center rotation" (Figure 1). The first of these has ample analogy in neutral cyclopropane chemistry.[12] It nonetheless suffers from one weakness. It does not readily accommodate an important experimental observation: the consistent failure to form 4-*p*-anisylcyclopentene under any of the experimental conditions explored. The other two mechanisms do. The second mechanism is additionally recommended by the high acidity estimated for arene cation radicals.[13] The last mechanism recognizes that reactivity may be controlled by the bonding changes that occur upon one-electron oxidation, If the singly occupied MO in the cation radical shares sufficient character with the antisymmetric ($^2B_2$) Walsh[14] MO, then the *two* cyclopropane bonds adjacent to the most electron-donating substituent (*p*-anisyl in this case) will be weakened.

The specifically deuteriated cyclopropane **5**[15] was synthesized to distinguish between these possibilities. The one-center rotation and the deprotonation/reprotonation mechanisms predict that isomerization will produce a single trans isotopomer, **6**. In contrast, the two-center rotation mechanism predicts that a mixture of the two trans isotopomers **6** and **7** will be formed.



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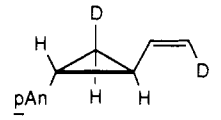

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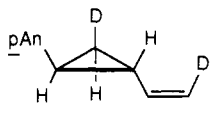

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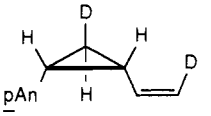

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In practice, partial isomerization (15–80%) of **5** with **3** or **4**, in either CH_3CN or CH_2Cl_2, resulted in the formation of nearly equal amounts of the two deuteriated *trans*-cyclopropanes **6** (48 ± 6%) and **7** (52 ± 6%). The near random distribution of deuterium did *not* result from prior automerization of **5** nor from a rapid automerization of **6** or **7** under the isomerization conditions. The former was excluded by ^1H and ^2H NMR analysis of recovered *cis*-cyclopropane, after 67% cis → trans conversion, which revealed a mixture consisting of 85% of **5** and 15% of **8**. The latter was excluded by the results of a similar control experiment. ^1H and ^2H NMR analysis of recovered *trans*-cyclopropane, after 57% cis → trans isomerization of an initial 63:37 mixture of **5** and **6**, revealed a nonequilibrium composition of the trans isotopomers **6** (62%) and **7** (38%).

The combined labeling results exclude the deprotonation/reprotonation and the one-center rotation mechanisms.[16] Correlated two-center rotation,[17] a subset of the two-center rotation mechanism, is similarly excluded; it would only permit the interconversion of the two cis isotopomers **5** and **8**. Only the two-center *uncorrelated* rotation mechanism remains.[18] The fact that the rotations must be uncorrelated, i.e., random, further suggests that the ring-opened cyclopropane cation radical is an intermediate on the potential energy surface for isomerization, rather than a transition state.

It is now apparent that the isomerization mechanism for cyclopropanes using one-electron chemical oxidants can differ from that using photochemical oxidants, The inability of the 1,2-diphenylcyclopropane cation radicals produced by photooxidation[2] to isomerize is likely dictated by the relative rates of back electron transfer to isomerization. This conclusion may be general and suggests opportunities for the discovery of other cation radical reactions.

Acknowledgment. We are grateful to the DAAD for the award of a NATO postdoctoral fellowship to M.S. and to R. S. Eisenberg and C. M. O'Connell for assistance in recording cyclic voltammograms. Support was provided by the Research Corporation and the Camille and Henry Dreyfus Foundation for research and by the National Science Foundation for an instrumentation grant (CHE78-03089).

(11) Amine cation radical–arene complexes are plausible isomerization intermediates when **3** is used as the initiator. The fact that **4** is also an initiator permits these complexes but does not require them.

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(15) Prepared as a separable mixture with **6** by cyclopropanation[4b] of (*Z*,*Z*)-1,3-butadiene-*1,4-d*$_2$ (Stephenson, L. M.; Gemmer, R. V.; Current, S. P. *J. Org. Chem.* **1977**, *42*, 212).

(16) Also consistent with the labeling data are competing one-center rotations at any two of the three cyclopropane carbon atoms or similarly competing deprotonations. Both of these hypotheses are unlikely since they would each require two heterotopic processes with essentially identical activation barriers over a wide range of temperature (−90 to −40 °C) and in two different solvents (CH_2Cl_2 and CH_3CN).

(17) Correlated rotation may occur in a conrotatory or a disrotatory fashion. These experimentally indistinguishable processes are not considered separately.

(18) Not considered here are two-center rotations which involve cleavage of either of the two less substituted cyclopropane bonds (C1–C3 or C2–C3). Experiments are in progress to test these possibilities.

Dehydration of Silica–Aluminas Monitored by High-Resolution Solid-State Proton NMR

Charles E, Bronnimann, I-Ssuer Chuang, Bruce L. Hawkins, and Gary E. Maciel*

Department of Chemistry, Colorado State University Fort Collins, Colorado 80523

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Knowledge of the acid sites on silica–aluminas and zeolites has been addressed by various techniques,[1-9] With a combination of multiple-pulse techniques[10,11] and magic-angle spinning (MAS)[10-13] one can obtain high-resolution ^1H NMR spectra of solid samples.[14] In this paper we report the initial results of a study of the dehydration of silica–alumina, silica gel, and γ-alumina by the ^1H CRAMPS (combined rotation and multiple-pulse spectroscopy)[14] NMR technique.

Silica–alumina samples SA-14 (containing 14% Al_2O_3 and 86% SiO_2 by weight) and SA-25 (containing 25% Al_2O_3 and 75% SiO_2

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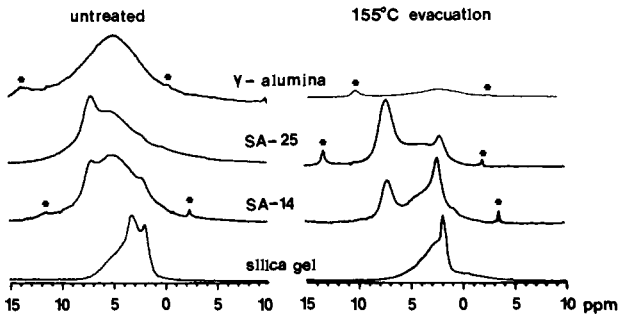


Figure 1. ^{1}H CRAMPS spectra, 187 MHz, of untreated samples (left) and samples evacuated at 155 °C and 10^{-2} torr (right). Rotor frequency lines[16,17] are indicated with asterisks. Chemical shifts are given relative to tetramethylsilane (Me_4Si).

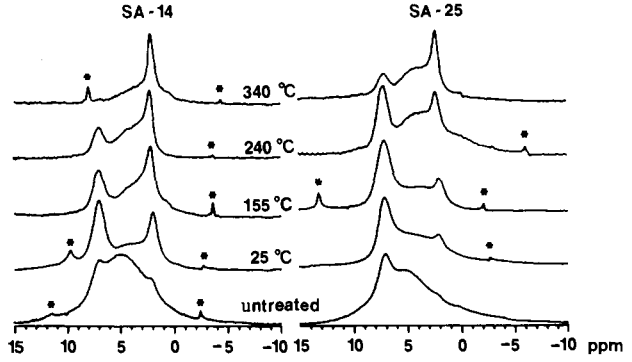


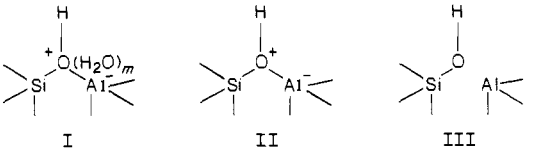
Figure 2. ^{1}H CRAMPS spectra, 187 MHz, of silica–aluminas, SA-14 (left) and SA-25 (right), untreated (bottom) or evacuated at 10^{-2} torr at the indicated temperature. Rotor frequency lines[16,17] are indicated with asterisks. Chemical shifts are given relative to Me_4Si.

by weight) were provided by W.R. Grace. Silica gel (100–200 mesh S-679) was obtained from Fisher Scientific Co. and γ-alumina was provided by Gulf. Sets of all four samples were evacuated for 16 h at 10^{-2} torr at four different temperatures, 25, 155, 240, and 340 °C. Samples were sealed off in short 5-mm NMR tubes and spectra were obtained at 187 MHz on a modified NT-200 spectrometer by using the BR-24 sequence.[15]

Figure 1 shows ^{1}H CRAMPS spectra of the four untreated samples and of those four samples after evacuation at 155 °C. Figure 2 shows the ^{1}H CRAMPS spectra of the two silica–aluminas evacuated at four different temperatures and also untreated. Examination of these figures reveals in at least some of the spectra prominent, sharp peaks at about 7.0, 3.1, and 2.0 ppm and broad peaks or shoulders in the range of about 5–3 ppm. The sharp peak at 1.8–2.1 ppm, which is evident in all of the samples except the untreated γ-alumina, is enhanced in relative intensity as the evacuation temperature is increased for a given sample and its relative intensity is seen to increase with the formal percentage of silica in the samples. This peak is identified with SiOH moieties of either silica gel or silica-like regions of a silica–alumina. The 3.1-ppm peak is dominant only for untreated silica gel, for which it is strongly attenuated by 155 °C evacuation. This peak is identified with H_2O physisorbed on silica gel or (as a broad shoulder) in silica-like regions of a silica–alumina sample. The broad 4.8-ppm peak that dominates the spectrum of untreated γ-alumina and is dramatically eliminated by 155 °C evacuation of γ-alumina is assigned to H_2O physisorbed on γ-alumina or alumina-like regions of silica–aluminas.[18-21] The 7.0-peak is present only in spectra of silica–aluminas and is seen to decrease in relative intensity as the evacuation temperature is increased (compare the peaks at 7.0 and 2.1 ppm). Peaks at 6–8 ppm have previously[9,21] been assigned to Brønsted sites in regions of zeolites or silica–aluminas in which there is an "interface" of silica and alumina structures.

In a previous study,[9] the intensity of the 7-ppm peak in samples prepared at fixed temperature has been compared between samples of differing SiO_2/Al_2O_3 ratios. As the Si/Al atomic ratio was increased the intensity at 7 ppm was also found to increase and the increase was found to correlate with increased catalytic activity.[9] We see a similar pattern in our data in comparing SA-14 with SA-25 at the same activation temperature, but we also see a *decrease* in intensity at 7 ppm as the temperature is increased for either sample. Thus, the correlation between 7-ppm intensity and catalytic activity is not as direct or simple as previously described.[9]

According to the interpretation[9,21] that the 7-ppm peak is due to a catalytically active Brønsted site, the observed temperature effect on this peak would seem to indicate the loss of Brønsted acidity at 340 °C. In order to reconcile these observations with customary activation at high temperature, ostensibly to generate Brønsted sites,[22] we propose an interpretation of the behavior of silica–alumina under evacuation below 340 °C, in which the 7-ppm peak is assigned to a hydrated Brønsted site (I), whereas catalytic activity for most processes is identified with "bare" Brønsted sites (II), for which a chemical shift outside the range of peaks observed in this study can be expected.[21]



According to this interpretation, the "bare" Brønsted acid site (II) is, under most conditions, the least populated of the three forms shown. For untreated silica–alumina, species of type I are important. Upon evacuation, especially at higher temperature, the concentrations of II and unhydrated ≥Si–OH structures (III) increase at the expense of I and hydrated ≥Si–OH moieties. For SA-14 evacuated at 340 °C the unhydrated ≥Si–OH (III) species become more important, even though II reaches its maximum concentration (still small and undetected by ^{1}H CRAMPS), accounting for the maximum catalytic activity for most processes at that temperature.[22] The hydrated Brønsted acid form I, which is too weak an acid to be catalytically effective for many reactions, gives a peak at 7.0 ppm, which appears to be the weighted average chemical shift of the formal Brønsted acid proton and the hydrogen-bonded water associated with it. The hydrogen-bonded water present in various structures that are unspecified here has ^{1}H chemical shifts that are as yet undetermined and may contribute to the broad peaks in the 5–3-ppm regions. For activation temperatures above 340 °C, even species II and other unhydrated structures are depleted by dehydroxylation (dehydration) mechanism(s) not well understood.[23-25]

It should be emphasized that the ability of NMR to distinguish individual species is unlike the information obtained by classical base titration. The classical determination of acidic sites by base titration has shown that strong acid sites are converted to weak acid sites upon rehydration, while the total number of acid sites is conserved.[3] ^{1}H CRAMPS experiments show that rehydration of the 340 °C evacuated silica–aluminas reestablishes the 7.0-ppm

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intensity (spectra not shown), demonstrating the population shift from unhydrated ≥Si–OH species (at about 2 ppm) to I (at 7 ppm). Detailed investigations of this type and analogous experiments with other bases are in progress.

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Iterative Butenolide Construction of Polypropionate Chains

Gilbert Stork* and Scott D, Rychnovsky†

Department of Chemistry, Columbia University
New York, New York 10027

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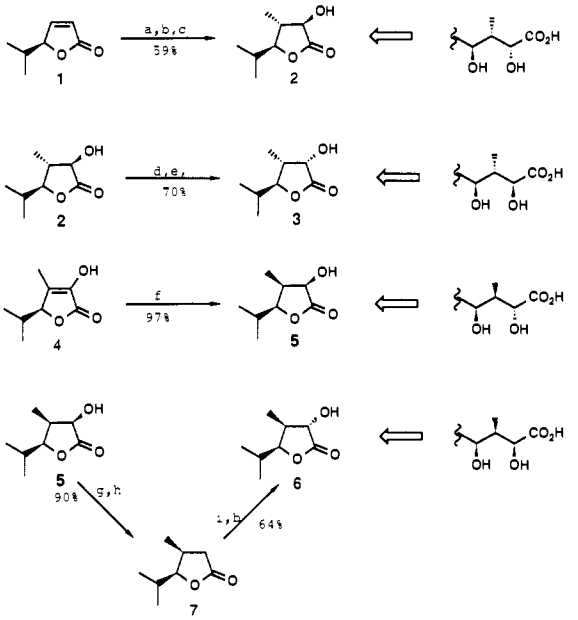
Sequences of alternating secondary methyl and hydroxyl groups are typical of the polypropionate-derived chains found, for example, in many macrolide antibiotics. Although much fascinating chemistry has been brought to bear on the stereochemical problems which these structures pose, this has not yet led to a reliable and generally applicable method.[1]

We now wish to report such a method[2] and demonstrate its usefulness by the synthesis of the C_7–C_{13} fragment of erythronolide A,

The method proceeds through two stages: First, stereoselective addition of a methyl and of a hydroxyl group to a 5-substituted butenolide leads to 3-hydroxy-4-methyl-2-furanones (e.g., **1** and **2**). Second, elaboration to the next butenolide (e.g., **5** to **11**) once again sets the stage for the introduction of methyl and hydroxyl groups. Stereoselective synthesis of each of the four possible 5-alkyl-3-hydroxy-4-methylfuranone diastereomers (e.g., **2**, **3**, **5**, and **6**), coupled with the appropriate butenolide elaborations, allows any regular polypropionate stereoisomer to be constructed.[2]

We now illustrate the first stage below using a model with a 5-isopropyl group. Butenolide **1**[3] served as the starting material for construction of two of the four possible 3-hydroxy-4-methyl-2-furanone diastereomers. The 3β,4α,5β-furanone **2** was obtained, starting with the conjugate addition of tris(thiophenyl)methyllithium.[4] The bulky 4-tris(thiophenyl)methyl substituent now directed the in situ MoOPH[5] oxidation of the resulting enolate to the β-face, so that removal of the thiophenyl substituents (Raney nickel) gave the desired 3β-hydroxy-4α-methyl-2-furanone **2**.[6] Simply inverting the secondary hydroxyl group[7] of furanone **2** led to the 3α,4α,5β-furanone **3**.[8]



(a) LiC(SPh)$_3$, THF, −78 °C; (b) MoOPH 0 °C; (c) Raney nickel, EtOH; (d) DEAD, PPh$_3$, PhCOOH, THF; (e) K_2CO_3, MeOH; (f) 5% Rh/alumina, H_2, MeOH; (g) MsCl, Et_3N; (h) 2% Na(Hg), NaH_2PO_4, MeOH, 0 °C; (i) LDA, THF, −78 °C.

The two remaining 3-hydroxy-4-methyl-2-furanone diastereomers were prepared from 3-hydroxybutenolide **4**.[9] Hydrogenation of **4** with rhodium on alumina[10] gave the 3β,4β,5β-furanone **5**.[11] The final diastereomer, 3α,4β,5β-furanone **6**, was formed by inversion of the secondary hydroxyl group in furanone **5** or, alternatively, by deoxygenation of furanone **5** to furanone **7**, followed by reoxidation of the corresponding enolate with MoOPH reagent.[12]

These highly effective routes (stereoselectivity ≥40:1) to the four possible -hydroxy-4-methyl diastereomers of a 5-substituted 2-furanone complete the first stage of the method. The second stage, which makes the method iterative, requires elaboration of any given 3-hydroxyfuranone to the next butenolide or 3-hydroxybutenolide (cf. **1** and **4**). Note that every new cycle incorporates the two centers created on the furanone template into the growing C5 substituent at the same time as it sets the stage for creation of the next two centers.

Conversion of **5** to **11** illustrates the "butenolide elaboration". In situ protection of **5** as the trimethylsilyl ether,[13] addition of ethyl acetate anion, and basic methanolysis gave bicyclic hemiketal **8**. Hemiketal **8** is in equilibrium with the corresponding monocyclic tetronic acid and could be transformed to **9** by phase-transfer benzylation, followed by acylation of the secondary alcohol. Hydrogenation of **9** with rhodium on alumina removed the benzyl group and saturated the double bond to give **10**. Elimination of

† National Science Foundation predoctoral fellow, 1981–1984.

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(6) (a) Analysis of the product by gas chromatography showed less than 1% of any other of the stereoisomers of **2**. (b) ^{1}H NMR of **2** ($CDCl_3$) δ 4.03 (d, J = 10.5 Hz, 1 H), 3.83 (dd, J = 4.4, 9.6 Hz, 1 H), 2.8 (s, 1 H), 2.25 (m, 1 H), 1.98 (m, 1 H), 1.24 (d, J = 6.5 Hz, 3 H), 1.04 (d, J = 6.9 Hz, 3 H), 0.97 (d, J = 6.8 Hz, 3 H).

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(8) ^{1}H NMR of **3** ($CDCl_3$) δ 4.47 (d, J = 8.0 Hz, 1 H), 3.93 (dd, J = 3.2, 7.6 Hz, 1 H), 2.7? (s, 1 H), 2.56 (m, 1 H), 1.86 (m, 1 H), 1.12 (d, J = 7.1 Hz, 3 H), 0.99 (d, J = 6.7 Hz, 3 H), 0.98 (d, J = 6.7 Hz, 3 H).

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(11) (a) Analysis of the product by gas chromatography showed a 40:1 mixture of **5** and **3**. (b) ^{1}H NMR of **5** ($CDCl_3$) δ 4.55 (d, J = 6.7 Hz, 1 H), 3.84 (dd, J = 3.8, 10.5 Hz, 1 H), 2.96 (s, 1 H), 2.73 (m, 1 H), 1.88 (m, 1 H), 1.07 (d, J = 6.4 Hz, 3 H), 0.91 (d, J = 7.0 Hz, 3 H), 0.89 (d, J = 6.6 Hz, 3 H).

(12) (a) Analysis of the product from MoOPH oxidation of **7** by gas chromatography showed less than 1% of lactone **5**. (b) ^{1}H NMR of **6** ($CDCl_3$) δ 4.38 (t, J = 6.8 Hz, 1 H), 4.09 (d, J = 6.1 Hz, 1 H), 3.62 (s, 1 H), 2.55 (m, 1 H), 1.93 (m, 1 H), 1.10 (d, J = 7.3 Hz, 3 H), 0.98 (d, J = 6.6 Hz, 3 H), 0.97 (d, J = 6.7 Hz, 3 H).

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