Registry No. 1, 935-00-2; 2, 824-90-8; $CH_3C(O)OCH(CH_3)CH{=}CH_2$, 6737-11-7; $CF_3C(O)OCH(CH_3)CH{=}CH_2$, 37729-50-3; $CH_3CH(OH)CH{=}CH_2$, 598-32-3; CF_3CO_2H, 76-05-1; benzene, 71-43-2.

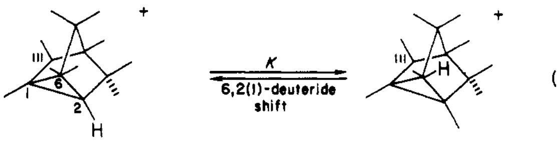
A Near Perfect Complementarity of Equilibrium Isotope Effects. A Corrected Value for a Recently Published Equilibrium Constant Derived for the 2-Norbornyl-$h_{10}d_1$ Cation

K. Ranganayakulu and T. S. Sorensen*

The Department of Chemistry, University of Calgary, Calgary, Alberta, Canada T2N 1N4

Received April 18, 1984

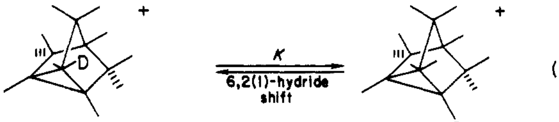
Several years ago, we initiated a study of the 2-norbornyl-h_1d_{10} cation (and others) in an attempt to measure primary isotope rate constant ratios (k_H/k_D) for typical intramolecular hydride shifts in carbocations.[1] This NMR line-broadening analysis required a prior knowledge of the equilibrium isotope effects, the one of major interest for a 6,2(1)-hydride(deuteride) shift being that shown in eq 1.



(1)

A (remaining atoms D) B

present work B/A=1.24 at -110 °C



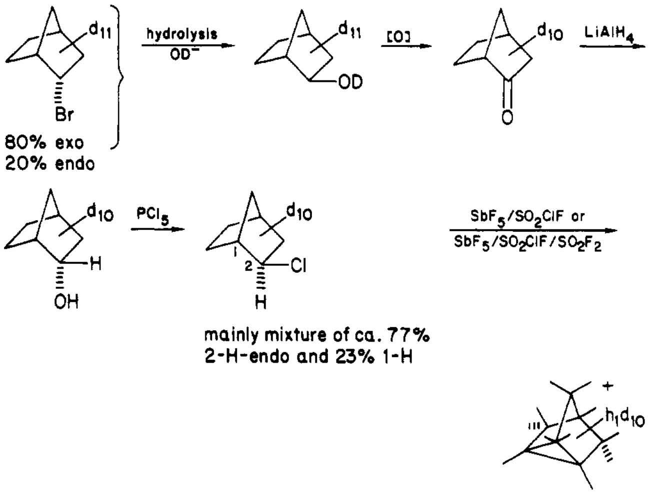
(2)

B' (remaining atoms H) A'

Saunders and Kates, A'/B'=2.14 at -105 °C

Recently, Saunders and Kates (S–K)[2] have reported equilibrium isotope data for the isotopically complementary system, the 2-norbornyl-$h_{10}d_1$ cation, as shown in eq 2, and one notes a large discrepancy in the two sets of data (compared to the "no effect" result of $K = 1$, our data are about 25% larger compared to over 100% for the S–K result). In discussion with S–K, it was apparent that neither of our data was subject to much experimental error and so it initially appeared to us that the expected isotopic complementarity[3] was being seriously violated in this case.[4] In any event, we have now undertaken a complete reinvestigation of the whole problem in order to try and resolve the matter.

Scheme I



Results and Discussion

The h_1d_{10} cation was synthesized as shown in Scheme I. Mass spectrometric analysis shows 83% d_{11} and 17% h_1d_{10} compounds in the starting material, and this ratio is carried through in the synthesis without significant change (giving 83% h_1d_{10} and 17% h_2d_9 cations). The proton in the h_1d_{10} cation becomes rapidly and randomly scrambled into all positions, resulting in a set of either six or eleven different cations, depending on whether one views the cation as being symmetrical or not.[6] In the temperature range −40 to −100 °C, the 6,2(1)-deuteride shift is rapid but the 3,2-deuteride shift is slow, resulting in three observable ^1H NMR peaks, the same number found in the h_{11} cation. The lowest field ^1H peak in the spectrum is the averaged proton from structures A and B, and K can be calculated from a knowledge of the "frozen-out" positions for the hydrogen in the A and B structures. These in fact can be obtained at −140 °C, resulting in the K value given in eq 1. The averaged peak for A $\rightleftharpoons$ B is slightly temperature dependent, as expected, and shifts to higher fields at lower temperatures. This calculation of K is straightforward and there is very little possible error involved.

---

[1] The strategy for obtaining these ratios envisaged using 1:10 mixtures of the h_{11} and h_1d_{10} species in the same solution. Measurements in the same solution at the same instant and region of the NMR tube are needed in order that temperatures for k_H and k_D will be exactly the same. The need to use the h_1d_{10} species in our studies occurs because one cannot fix isotope labels in the 2-norbornyl cation, all hydrogen atoms being rapidly scrambled on a normal time scale over all possible positions, except at very low temperatures. However, when one observes ^1H NMR in an h_1d_{10} species, we can be positive that line-broadening phenomena will *only* be caused by deuterium migrations. Considering the low temperatures involved and the possibility of tunneling, values for $k_H/k_D > 10$ for a 6,2(1)-hydride(deuteride) shift would not have been surprising to us. Such rate differences would have allowed the slower rate system to clearly decoalesce under lowering temperature conditions whereas the faster rate system would still have given a single peak, thereby allowing both k's to be very accurately analyzed. In any event, these k_H/k_D ratios turned out to be much smaller than expected ($\lesssim 2$ at −130 °C) and not amenable to accurate analysis by our projected technique.

[2] Saunders, M.; Kates, M. R. *J. Am. Chem. Soc.* **1983**, *105*, 3571.

[3] Saunders and Kates[2] have argued, quite reasonably, that the preference for A' over B' is a consequence of a nonclassical structure for A'–B' (as indeed we have written these), i.e., that a hypervalent C_6–H bond is weaker than a "normal" C_1–H bond and therefore, using standard arguments, that the $h_{10}d_1$ cation, wishing to maximize bonding, will preferentially locate the deuterium in the stronger bond (C-1). An analogous argument applies to our data, i.e., the h_1d_{10} cation, also wishing to maximize bonding, will preferentially locate the proton in the weaker bond (C-6). There seems little reason why these preferences should not normally have been approximately equal and opposite; i.e., one might have expected similar K values for B/A and A'/B'.

[4] The divergent results suggested to us that the structures of A–B and A'–B' might be quite different, i.e., that the overall presence of ten proton or ten deuterium atoms makes a very significant *structural change* in the cation. The most recent ab initio calculations[5] on the 2-norbornyl cation substantiate the idea that, regardless of what the ground-state structure is, the potential energy surface is extremely "mushy". Thus it would not be entirely unreasonable for one to find such large structural changes in this particular case.

[5] Raghavachari, K.; Haddon, R. C.; Schleyer, P. v. R.; Schaefer, H. F., III. *J. Am. Chem. Soc.* **1983**, *105*, 5915.

[6] For simplicity of presentation only, we write a symmetrical structure for the 2-norbornyl cation. The alternate assumption of two "classical" structures interconverted by a very rapid Wagner–Meerwein shift leads to similar conclusions.

0022-3263/84/1949-4310$01.50/0

The Saunders-Kates Result

In contrast to our data on A–B, Saunders and Kates have studied A′–B′ by looking at the multiple isotope nucleus (^{1}H). This leads to a fairly complex analysis in order to obtain the equilibrium constant shown in eq 2. In this treatment, the molecules of particular interest in the randomly scrambled $h_{10}d_1$ cation have three protons and one deuterium located on carbons 1,2 and 6,[6] i.e., cations A′–B′. Because of equilibrium isotope effects, i.e., unequal A′ and B′ populations, these *three* protons are assumed to average to a position slightly upfield of the position for "normal" averaging, taken in this case as the averaged four proton peak (H-1,2,6(two)) which results when the deuterium is at carbon 3, 4, 5, or 7.[7] The separation of these two peaks (labeled δ) is temperature dependent. If one arbitrarily labels these three protons on carbon 1, 2, and 6 in A′ or B′, then there are 24 ways (12 A′ cations and 12 B′ cations, consisting each of 6 *R* and 6 *S* enantiomers) to randomly arrange one deuterium (which introduces a chiral center) and three protons, at two separate double-occupancy sites. This leads to eq 3, Δ = the chemical shift separation (ppm) between the two sites and δ is defined as in the text. Substituting the experimental δ and Δ values leads to the K' value shown in eq 2.

$$K' = \mathrm{A}'/\mathrm{B}' = \frac{\Delta + 6\delta}{\Delta - 6\delta} \tag{3}$$

It was only when we looked *in detail* at the actual 6,2-(1)-hydride or deuteride shift in A′–B′ that we saw a possible explanation of the mutually conflicting data in eq 1 and 2. As mentioned, S–K assume completely random labeling. However, this need not be the case and in the present instance, if one assumes that the 6,2(1)-hydride-(deuteride) shift is *stereospecific*, only four of these structures (two A′ and two B′, having opposite chirality in each case) are accessible on the NMR time scale if one starts with any arbitrary labeling of the protons (there are of course 6 other sets of 4 or a total of three racemic sets of eight). It turns out that two of the protons never get to share the same site so that *regardless of the populations* of A′ and B′ they will always average to a position essentially identical with that found in the isotopically unperturbed case ("normal" position). The third proton has the same nonconjugal relationship with the deuterium; so in this case, the averaged position of this proton *or* of the deuterium would be a direct measure of K' (eq 4), where

$$K' = \mathrm{A}'/\mathrm{B}' = \frac{\Delta + 2\delta}{\Delta - 2\delta} \tag{4}$$

δ will be upfield (+ve) of the "normal" in the ^{1}H case and downfield (−ve) from a hypothetical averaged position with ^{2}H spectra). Equation 4 obviously leads to a very different K' value than the eq 3 used by S–K so that it becomes of paramount importance that the rearrangement mechanism be completely understood.

There are precisely three ways in which one could get random labeling, i.e., access to all 24 structures by a 6,2(1)-hydride shift rearrangement process: (1) the 6,2(1)-hydride shift is completely nonstereospecific; (2) the 6,2(1)-hydride shift is stereospecific but accompanied by an even faster rearrangement which specifically interchanges the two C-6 protons (or a proton and deuteron); or (3) as above, but accompanied instead by an even faster specific interchange of the protons on C-1 and C-2 (or proton and deuteron).

Based on previous work by ourselves and others,[8,9] where related 6,2(1)-H shifts have been shown to be highly stereospecific, none of the above possibilities seems even remotely likely. There are, however, two potentially straightforward experiments which should clearly distinguish between a random-label result and the more restrictive and stereospecific process which we have outlined: (a) The use of ^{2}H NMR to look at the single ^{2}H label in the $h_{10}d_1$ cation would be an identical methodology for obtaining K' to that used for the h_1d_{10} cation (^{1}H observe). Obtaining the averaged ^{2}H signal would be simple but it would be much more problematic to obtain the frozen-out positions for the deuterium sites at carbon 6 and carbons 1 and 2 since the latter measurement requires very low temperature, where ^{2}H lines usually become very broad. (b) The S–K treatment predicts an intensity ratio of about $(^7/_{11} \times 4\mathrm{H}):(^4/_{11} \times 3\mathrm{H}) = 1.00:0.43$, for the "normal" and "upfield" averaged signals of protons on carbons 1, 2, and 6, whereas the stereospecific process gives $(^7/_{11} \times 4\mathrm{H} + {}^2/_3(^4/_{11} \times 3\mathrm{H})):(^1/_3(^4/_{11} \times 3\mathrm{H})) = 9.00:1.00$. There will be unknown equilibrium isotope effects on these predicted population ratios, but there is an "uncorrected" factor of ca. 4 between the two mechanisms which should hopefully permit an unequivocal distinction to be made.

Repeat of the S-K Experiment

Proton spectra of the randomly scrambled $h_{10}d_1$ cation were measured at 500 MHz in order to provide near base-line separation of the "normal" and "upfield" peaks described above. At −80 °C, δ = 0.195 ppm; at −70 °C, δ is 0.181 ppm, these values being virtually identical with those reported by S–K. However, integration of the two peaks at both temperatures gives, in each case, a ratio of (10 ± 0.5):1.00 for the "normal":"upfield" ratio, very close to the "uncorrected" value deduced for the stereospecific rearrangement mechanism (9.00:1.00).[10]

The ^{2}H spectra were run at 76.8 MHz. However, even at −140 °C, we were unable to "freeze out" the 6,2(1)-hydride shift. At this temperature even the nonexchanging deuterium at carbon 4 was quite broad and it was clear that going to even lower temperatures would be counterproductive. One can however make the assumption that the "frozen out" ^{2}H-6 and ^{2}H-1,2 positions will not differ much from the corresponding proton values.[11] This leads to a K' value of 1.14 at −70 °C. Using the proton data given above, together with eq 4, we find K' = 1.22 at −70 °C, in relatively good agreement. Using the published data of S–K at −65 °C, one obtains K' = 1.22.

---

[7] One can rigorously show that when the deuterium is located on carbons 3, 5, or 7, there is a 12-step rearrangement sequence involving sequential 6,2(1)-hydride shifts which obviates any equilibrium isotope effects between these sites and which averages the four protons on carbons 1, 2, and 6 to a "normal" position, i.e., as in the h_{11} cation (ignoring "intrinsic" isotope effects). However, if there are equilibrium isotope effects involving deuterium on C-5 vs. C-3, C-7 etc., then one will get several "averaged" H-3, -5, and -7 peaks. At 500 MHz, with cations A′–B′, we see evidence for this but the magnitude of the effect is much smaller than that observed for the protons on carbons 1, 2, and 6. When the deuterium in A–B is on carbon 4, the symmetry properties of the cation and the averaging process are identical with the h_{11} species.

[8] Huang, E.; Ranganayakulu, K.; Sorensen, T. S. *J. Am. Chem. Soc.* **1972** *94*, 1780.

[9] (a) Berson, J. A.; Grubb, P. W. *J. Am. Chem. Soc.* **1965**, *87*, 4016. (b) Benjamin, B. M.; Collins, C. J. *Ibid.* **1966**, *88*, 1556.

[10] This slight preference (above the statistical) of the deuterium for the "back end" of the cation (carbons 3, 4, 5, and 7) is also shown up in two other measurements: (a) integration of the ^{2}H peaks in A′–B′ shows that deuterium is slightly preferred at carbons 3, 5, and 7 as opposed to carbons 1, 2, and 6 and (b) integration of the ^{1}H peaks in A–B shows that proton is slightly preferred at carbons 1, 2, and 6 as opposed to carbons 3, 5, and 7.

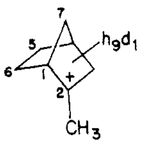
[11] Olah, G. A.; Prakash, G. K. S.; Arvanaghi, M.; Anet, F. A. L. *J. Am. Chem. Soc.* **1982**, *104*, 7105.

Our complementary isotope data for A–B at −70 °C gives $K = B/A = 1.23$. Thus, within experimental error, there is in fact no discrepancy between our data for the h_1d_{10} cation and the corrected data for the $h_{10}d_1$ cation. The data also prove that the 6,2(1)-hydride shift in the 2-norbornyl cation is highly stereospecific, a result one expects but one which is not available from an analysis of the h_{11} cation.

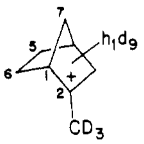
Note Added in Proof. At one time, Roberts' nortricyclonium ion (Roberts, J. D.; Lee, C. C. *J. Am. Chem. Soc.* **1951**, *73*, 5009) was seriously considered as a structure for the 2-norbornyl cation and this would have yielded a completely nonstereospecific 6,2(1)-hydride shift. The low-temperature NMR work of Olah (Olah, G. A.; White, A. M.; DeMember, J. R.; Commeyras, A.; Lui, C. Y. *J. Am. Chem. Soc.* **1970**, *92*, 4627) unequivocally ruled out nortricyclonium as the ground-state structure of 2-norbornyl) but did not exclude such a structure as a higher energy intermediate (note also the Berson–Roberts controversy of the early 1960's described in ref 9a). The present results unequivocally rule out the involvement of the nortricyclonium ion as a high-energy intermediate in the 6,2-(1)-hydride shift. As a referee points out, "that geometry is not achieved probably to an extent greater than one in a million rearrangement steps".

Comparison of K' for A′/B′ with the Equilibrium Isotope Effects Found for the 2-Methyl-2-norbornyl Cation. Although we have written the 2-norbornyl structure, for convenience, in a symmetrical fashion, the intent of the S–K work was to use the equilibrium isotope effect to probe the structure of this ion. It is within this context that one should ask whether a much smaller value for K' can still be interpreted as they have. The original K' values of 1.66–2.14 (−43 to −105 °C) reported by S–K probably were large enough to interpret in terms of pentacoordinate bonding at C-6 of the 2-norbornyl cation.[3] Our corrected values are still 20–25% larger than the "no effect" result, in the same direction, and could still be interpreted as supporting a symmetrical structure using the arguments presented in the S–K paper.

In order to assess the significance of an equilibrium isotope effect of 1.20–1.25, we have turned to the 2-methyl-2-norbornyl cation, which is certainly not symmetrical, even though partial bridging is thought to be involved.[12,13] This cation was prepared in two forms, the h_9d_1 CH_3 cation C and the h_1d_9 CD_3 species C′.



C



C′

At low temperature, the proton in C′ is positioned only between H-6-endo and H-1. Integration of these signals at from −80 °C to −100 °C gives K = H-6-endo/H-1 = 1.05 ± 0.05. In the case of cation C, one can get a more accurate value by using the averaged position of these peaks,[14] D-1/D-6-endo = 1.02 at −5 °C (deuterium NMR). These results look consistent and indicate virtually *no* equilibrium isotope effect. If one warms these cations to −5 °C, the deuterium (or proton) is randomly scrambled over all ring positions.[15] Examination of C′ shows that H-6-exo, H-6-endo, and H-1 have areas within ±10% of each other.

Surprisingly, the largest equilibrium isotope effects are observed between the H-5 and H-7 protons (or D-5 and D-7), these data being obtained under temperature conditions where one gets averaged signals. For example, one H-7/H-5 pair[16] has $K = 1.3$ at −5 °C (the D-5/D-7 result is ca. 1.2 at −20 °C). The other pair appears to have an even larger K but the data are not as accurate because the "frozen-out" positions are much closer together.

On the basis of these results, there are two ways to look at the 2-norbornyl cation data: 1. Compared to the 2-methyl analogue, there appears to be a modest increase in the K value for positioning a proton at C-6 vs. C-1. 2. Since there are no very obvious structural or electronic reasons for favoring a proton at carbon 7 vs. 5, and since *the effect* is at least as large as that found for the 2-norbornyl cation (carbon 6 vs. 1), one might hesitate to interpret the results for the latter.

There is probably some merit in both arguments. We continue to believe (based on other evidence) that the 2-norbornyl cation is either symmetrical or a pair of nearly symmetrical cations separated by an extremely small barrier. Interestingly there is another equilibrium isotope effect which could arise if the 2-norbornyl cation were unsymmetrical and which is relevent in our results with cations A–B. At −140 °C, we find the "frozen-out" positions of the *single* proton on carbon 6 or carbon 1 and 2 to be nearly identical with those for the h_{11} cation. This indicates that were the cation unsymmetrical, there would have to be virtually no equilibrium isotope effects *between* H-6-exo and H-6-endo or between H-1 and H-2 (this assumes that, like the 2-methyl-2-norbornyl cation, there would be a substantial chemical shift difference between these pairs).

Experimental Section

All compounds prepared are known in their undeuterated form.

***exo*-2-Chlorobicyclo[2.2.1]heptane-d_{10}.** 2-Bromobicyclo-[2.2.1]heptane-d_{11} (exo and endo) was obtained from Merck, Sharp and Dohme (≳98% deuterium content). This was hydrolyzed to the exo alcohol by refluxing in D_2O–dioxane–Na_2CO_3. Oxidation with Jones reagent (D_2O–D_2SO_4–CrO_3) gave the d_{10} ketone, which was reduced with $LiAlH_4$ to the $d_{10}h_1$ endo alcohol. This was converted to the exo chloride by using the procedure of Brown.[17] Products along this route were checked by MS and NMR for isotope content.

***exo*-2-Chloro-*endo*-2-methyl-d_3-bicyclo[2.2.1]heptane-d_9.** This synthesis followed literature procedures for the corresponding proton compounds. Methyl-d_3-magnesium iodide was added to 2-norbornanone-d_{10} and the resulting alcohol then rearranged to the 1-methyl-d_3, 2-formate derivative.[18] Saponification and Jones oxidation gave the corresponding 1-methyl-d_3-2-bicyclo[2.2.1]-heptan-2-one-d_9. Reduction with $LiAlH_4$ gave the corresponding endo alcohol, which was converted to the chloride by using the method of Brown.[17] The final chloride was a ca. 1:1 mixture of 1-methyl-d_3- and the 2-methyl-d_3-2-chlorobicyclo[2.2.1]heptanes. Products along this route were checked by NMR for isotope content.

The monodeuterio compounds were prepared in a similar way, the d_1h_{10} endo alcohol (≳98% D by NMR) from $LiAlD_4$ reduction of the ketone and conversion to the chloride and the methyl analogue by $LiAlD_4$ reduction of 1-methylbicyclo[2.2.1]heptan-

---

[12] Olah, G. A.; White, A. M.; DeMember, J. R.; Commeyras, A.; Lui, C. Y. *J. Am. Chem. Soc.* **1970**, *92*, 4627.

[13] Haseltine, R.; Wong, N.; Sorensen, T. S.; Jones, A. J. *Can. J. Chem.* **1975**, *53*, 1891.

[14] The rearrangement is a Wagner–Meerwein shift–6,2-hydride shift–Wagner–Meerwein Shift, see ref 8.

[15] Kelly, D. P.; Underwood, G. R.; Barron, P. F. *J. Am. Chem. Soc.* **1976**, *98*, 3106. These authors have observed scrambling starting with a 3,3-dideuterio cation.

[16] Although one can readily identify the separate H-7 and H-5 protons and in fact to correlate these, it is not possible to make an absolute assignment.

[17] Brown, H. C.; Kawakami, J. H.; Misumi, S. *J. Org. Chem.* **1970**, *35*, 1360.

[18] Beckmann, S.; Eder, G. *Chem. Ber.* **1958**, *91*, 2878.

2-one followed by conversion to the chloride. In this case, a ca. 1:2 mixture of the 1-methyl and 2-methyl compounds were formed.

Carbocation Preparations. These were prepared at ca. −120 °C by using previously described procedures.[19]

NMR Spectra. ^{1}H spectra of A–B and the 2-methyl analogue were obtained on a Varian XL-200 spectrometer, either locked ($Me_4Si/(CD_3)_2O$) or unlocked). Peaks were referenced internally to the H-4 proton (this peak is inexplicably a 4-Hz doublet with good resolution). ^{1}H spectra of A′–B′ were obtained unlocked on a Bruker AM-500 instrument. ^{2}H spectra of the 2-methyl-d_1 cation were obtained unlocked at 30.7 MHz on the XL-200, while ^{2}H spectra of A′–B′ were obtained at 76.8 MHz on the Bruker instrument. These latter spectra were internally referenced to the 4-^{2}H peak, this assumed to be the same as that of the corresponding proton compound.

Acknowledgment. We thank the Natural Sciences and Engineering Research Council of Canada for generous financial support. We also thank Bruker Canada for the use of the 500-MHz NMR instrument and Professor R. Childs of McMaster University for laboratory facilities.

Registry No. C, 92314-77-7; C′, 92314-78-8; h_1d_{10} cation, 92456-12-7; $h_{10}d_1$ cation, 92456-13-8; D_2, 7782-39-0; 2-norbornyl cation, 24321-81-1; 2-methyl-2-norbornyl cation, 3197-78-2; *exo*-2-chlorobicyclo[2.2.1]heptane-1,3,3,4,5,5,6,6,7,7-d_{10}, 92314-79-9; *exo*-2-chloro-*endo*-2-methyl-d_3-bicyclo[2.2.1]heptane-3,3,4,5,5,6,6,7,7-d_9, 92314-80-2.

[19] Kirchen, R. P.; Sorensen, T. S. *J. Am. Chem. Soc.* **1978**, *100*, 1487.

Malonic Ester Derivatives. 2[1]

Andrew A. Chiu,[2] R. Russel Gorby,[3a] John E. H. Hancock,* and Eric J. Hustedt[3b]

Department of Chemistry, Reed College, Portland, Oregon 97202

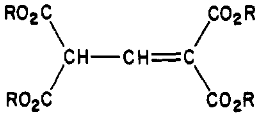
Received April 23, 1984

The reactivity, ready availability, and low cost of malonic esters combine to make them attractive starting materials in many synthetic schemes. This paper continues some initial investigations originally designed to produce precursors to dodecahedrane; in the work reported here, methyl esters were used rather than ethyl esters because melting points are generally higher.[4,12]

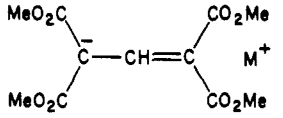
This paper furnishes data on the pK_a of **1a**, the alkylation of its sodium and tetra-*n*-butylammonium salts **2b** and **2a** by methyl bromoacetate, and an attempted Michael reaction on the alkylation product **3**: this last reaction produced an unexpected result.

Indications that **1a** might be unusually acidic may be gleaned from the fact that its sodium salt is both stable to water and recoverable in good yield after crystallization from suitable alcohols.[5] Acetic acid is strong enough to convert **2b** to **1a**, and sodium bicarbonate is basic enough for the reverse process.[6] The parent ester **1a** is easily purified as a solid, mp 50–51 °C[12] (the ethyl ester **1b** is a liquid at room temperature), and it may be titrated with sodium hydroxide or with tetraalkylammonium hydroxide[7] in methanol–water mixtures to give the corresponding salts. A determination of the pK_a of **1** does not appear to have been reported: we were pleasantly surprised to find a pH of 5.8 for the half-neutralization point in a titration of **1a** with tetra-*n*-butylammonium hydroxide solution. Similar titration of **1a** with sodium hydroxide solution showed a pH at half-neutralization of 5.6, in a medium containing a greater proportion of water to methanol.[10b] The sodium salt **2b** has been known for about a hundred years,[8] but the tetraalkylammonium salts have not been previously described.[16]

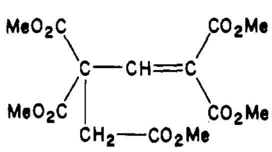
The alkylation[9] of salts of **1a** by methyl bromoacetate proceeded smoothly, once suitable conditions had been established (see Experimental Section); the optimum yield of **3** was 94%.



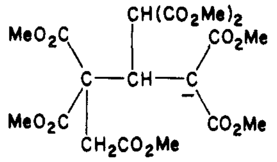
1a, R = Me
1b, R = Et



2a, M = $N(CH_2CH_2CH_2CH_3)_4$
2b, M = Na



3



4

An attempted Michael reaction on **3** by the sodio derivative of dimethyl malonate in methanol did not yield the expected **4**; an immediate yellow color in the system (an indication of formation of the sodium salt **2b**) suggested that a substitution had occurred (eq 1).

Triester **5** was identified by NMR analysis and by comparison with an authentic sample; acidification of the nonneutral fraction from the reaction furnished **1a**.

---

[1] Part 1 of this series is considered to be the paper by Galakatos et al. (Galakatos, N. G.; Hancock, J. E. H.; Morgan, O. M.; Roberts, M. R.; Wallace, J. K. *Synthesis* **1978**, 472.

[2] From the B.A. Thesis of Andrew Alex Chiu, Reed College, May 1983.

[3] Research assistant, (a) summer 1980; (b) summer 1979.

[4] That a methyl ester of a given acid has a melting point higher than that of the corresponding ethyl ester is exemplified by data in several sources: see, for example: (a) Palomaa, M. H.; Mikkilä, I. *Ber. Dtsch. Chem. Ges.* **1942**, *75*, 1659. (b) [The experimental section of] Crombie, L.; Hancock, J. E. H.; Linstead, R. P. *J. Chem. Soc.* **1953**, 3496. (c) Reference 12 and similar entries in "Beilstein".

[5] See, for example: ref 1 and literature cited therein.

[6] Compare: Bateman, L.; Koch, H. P. *J. Chem. Soc.* **1945**, 221. Sodium bicarbonate and sodium carbonate are unsatisfactory because they are soluble in water but insoluble in methanol; **1a** has the reverse solubility properties. An initial reluctance to use hydroxide bases because of possible hydrolysis proved groundless.

[7] Preliminary work by M. Bossé (summer research assistant, 1980) with tetraalkylammonium salts of **1b** suggested that the tetra-*n*-butylammonium salt would be the optimum choice. We were interested in such salts because of anticipated greater solubilities in organic solvents, compared to the sodium salts such as **2b**, which is sparingly soluble in cold common organic solvents. Salt **2a** is very soluble in cold acetonitrile and is easily crystallized from ethyl acetate.

[8] See ref 1 and literature cited therein.

[9] Few alkylations of salts of **1** appear in the literature; indeed, alkylations of only the sodium salt of **1b** have been reported. (a) Methylation: the highest yields in a methylation appear to be those obtained by F. B. Thole and J. F. Thorpe (*J. Chem. Soc.* **1911**, *99*, 2196), who obtained a yield of 83% with methyl iodide in ethanol on the steam bath for 5 h. Earlier workers (ref 13) had conducted their experiments at 150–160 °C in sealed tubes and reported that the presence of ethanol led to unsatisfactory results under those conditions. (b) Ethylation. (i) With ethyl iodide in 80% yield: Thole, F. B.; Thorpe, J. F. *J. Chem. Soc.* **1911**, *99*, 2196. (ii) With ethyl iodide in 53% yield; Lukeš, R.; Heřmánková, V.; Heřmánek, S. *Collect. Czech. Chem. Commun.* **1959**, *24*, 1699. (c) Propylation. (i) With 1-iodopropane in 50% yield; see Lukeš et al. (ii) With 2-bromopropane (ref 14) and 2-iodopropane (ref 15) the reaction furnished triethyl trimesate, and much gas, thought to be propene. (d) Butylation with 1-bromobutane in 30% yield, see Lukeš et al. These alkylations are generally not reported in "Beilstein" under reactions of propene-1,1,3,3-tetracarboxylic esters or of its salts; they were found by a thorough search of "Beilstein" in the complete section on monounsaturated tetracarboxylic esters.