The washings that were saved from above were chilled in an ice bath, causing colorless needles to crystallize. The needles were recrystallized three times from ethanol to yield 3.88 g (34.8%) of **2b:** mp 157–157.5 °C; IR (KBr) 3340 (=NH), 1680 (C=O), 1605 (C=N), cm^{-1}; NMR (Me_2SO-d_6) δ 3.32 (s, N_1-CH_3), 3.42 (s, N_3-CH_3), 6.78 (s, NH), 7.05–7.80 (m, 3 H, ArH). Anal. Calcd for $C_{10}H_{10}ClN_3O$: C, 53.70; H, 4.51; N, 18.79. Found: C, 53.45; H, 4.68; N, 18.49.

6-Nitro-1,3-dimethyl-2-imino-4(1*H*,3*H*)-quinazolinone (2c). To a slurry of 3.27 g (0.014 mol) of **1c** in 25 mL of ethanol was added a freshly prepared solution of 0.07 g (0.003 mol) of sodium in 25 mL of absolute ethanol. The slurry was heated to reflux, causing the solid to dissolve and the solution to turn a deep red color. The reflux was continued for 24 h and the solution was then cooled to room temperature. An olive-green solid crystallized from the cooled solution and was collected. Recrystallization from dioxane yielded 1.37 g (41.9%) of **2c** as golden-yellow crystals: mp 251–252 °C; IR (KBr) 3330 (=NH), 1680 (C=O), 1607 (C=N) cm^{-1}; NMR (TFA) δ 3.83 (s, N_1-CH_3), 4.00 (s, N_3-CH_3), 7.70–8.30 (m, 5 H, ArH, $=N^+H_2$). Anal. Calcd for $C_{10}H_{10}N_4O_3$: C, 51.28; H, 4.30; N, 23.92. Found: C, 51.18; H, 4.35; N, 23.70.

6-Nitro-1-methyl-2-(methylamino)-4(1*H*)-quinazolinone (3c). To 1.00 g (0.0043 mol) of **2c** was added 50 mL of absolute ethanol containing 0.10 g (0.0043 mol) of sodium. The solution was refluxed for 24 h and then allowed to stand overnight at room temperature. A solid crystallized in the reaction vessel and was filtered off. Analysis showed this solid to be starting material; 0.22 g (22%) was recovered. The reaction solution was then concentrated in vacuo to an oil which was induced to crystallize by scratching in a dioxane/ether solution. The crystals were collected and recrystallized from 50% ethanol to yield 0.30 g (30%) of **3c** as yellow crystals: mp >370 °C dec; IR (KBr) 3235 (NH), 1638 (C=O), 1603 (C=N) cm^{-1}; NMR (TFA) δ 3.45 (d, J = 4 Hz, $NHCH_3$), 3.95 (s, NCH_3), 7.85 (d, J = 10 Hz, H_8), 8.20 (br, NH_2^+), 8.84 (d, J = 10 Hz of d, J = 3 Hz, H_7), 9.23 (d, J = 3 Hz, H_5). Anal. Calcd for $C_{10}H_{10}N_4O_3$: C, 51.28; H, 4.30; N, 23.92. Found: C, 51.01; H, 4.52; N, 23.73.

Registry No.—**1a,** 59169-91-4; **1b,** 59169-92-5; **1c,** 59169-93-6; **2a,** 66809-70-9; **2a** HBr, 66809-71-0; **2b,** 66809-72-1; **2c,** 66809-73-2; **3a,** 5544-06-9; **3b,** 66809-74-3; **3c,** 66809-75-4.

References and Notes

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Communications

Deuterium Nuclear Magnetic Resonance. Evaluation of the Positional Distribution of Low Levels of Deuterium in the Presence of Eu(fod)$_3$

Summary: ^2H NMR spectroscopy, in conjunction with the shift reagent Eu(fod)$_3$, has been used to detect and quantify the positional incorporation of low levels of ^2H in catalytically deuterated saturated carboxylic acid esters.

Sir: While ^1H NMR can be used effectively to determine the extent of ^2H incorporation in organic molecules, it has severe limitations. First, ^1H NMR requires that the molecule under study contain high concentrations of ^2H, since this technique can evaluate ^2H only by difference. Secondly, when ^2H is largely dispersed throughout a molecule even in relatively high total concentration, analysis becomes very difficult because of insignificant changes observed in the area of each of the dispersed ^1H resonances. As an alternate method, mass spectrometry can furnish information concerning the total level of isotopic incorporation; however, in most instances it cannot define the positional distribution of ^2H owing to ^2H–^1H scrambling during the fragmentation process.

Although two orders of magnitude less sensitive in response to a magnetic field than ^1H, the ^2H nucleus is more amenable to Fourier transform methods.[1] Under complete proton decoupling conditions, ^2H resonances are normally observed as single resonances (no ^2H–^2H spin coupling is observed), having chemical shifts closely corresponding to their ^1H counterparts.[2] Also, because of their relatively short longitudinal relaxation time, T_1, multiple transients may be rapidly accumulated with short repetition times.[1] For example, a 100-mg sample of molecular weight of 200–300, containing 5% ^2H, which in magnetic response is equivalent to 0.05% ^1H, can yield an excellent quantitative spectrum within 0.5 h from 300 transients (repetition time only 5 s and a pulse angle of 60°).

^2H NMR in the presence[2,3] and absence[4,5] of lanthanide shift reagents can be used to examine positional substitution patterns in both static and rapidly exchanging ^1H, ^2H systems. Such a technique seemed amenable to our studies concerning the catalytic incorporation of ^2H into the saturated alkyl chains of carboxylic acids, since no other approach could quantify and evaluate the positional distribution of the low levels of widely dispersed ^2H. Typically, not more than a total of 29%, and in some cases as little as 2%, ^2H was incorporated into our representative samples. All ^2H spectra were obtained by use of a ^{31}P 10-mm probe of a JEOL FX-60Q NMR spectrometer,[6] which normally operates at 24 MHz with a ^2H lock channel of 9.2 MHz. By reversing the offset/rf power modules and exchanging the lock and observation lines, we could lock

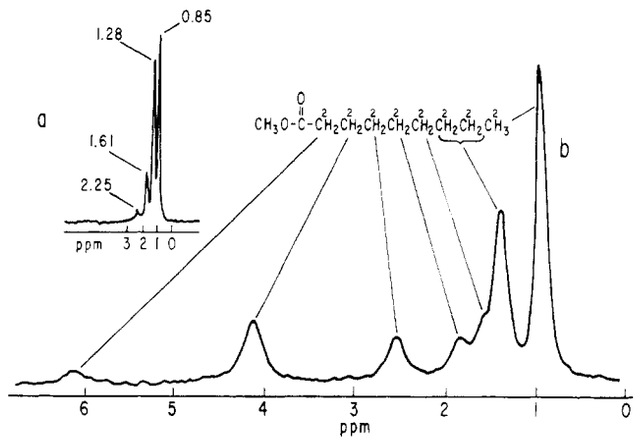

Figure 1. ^2H spectrum of: (a) methyl nonanoate, 255 transients, 4.4-s repetition rate, displayed spectral width = 500 Hz, 4K data points; (b) methyl nonanoate in the presence of Eu(fod)$_3$ shift reagent, molar ratio of Eu(fod)$_3$/substrate = 0.7, 200 transients, 4.4-s repetition rate, displayed spectral width = 62.5 Hz. Total ^2H content = 29%.

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Table I. Observed ^1H and ^2H Shifts (ppm) and ^2H Positional Distribution and Content[a]

$CH_3O\overset{O}{\overset{\|}{C}}\underset{R}{\underset{|}{C}}H—\underset{R'}{\underset{|}{C}}H(CH_2)_xR''$

	sample size, g	CH_3	2-CH_3	3-CH_3	$(CH_2)_x$	2-CH_2	3-CH_2	2-CH	3-CH	total % ^2H content
					^1H shifts (δ)[b]					
methyl nonanoate R = R′ = H; R″ = CH_3; x = 5		0.86			1.25	2.30	1.6[c]			
methyl 2-methyloctanoate R = R″ = CH_3; R′ = H; x = 4		0.90	1.16		1.30			2.42		
methyl 3-methylpentanoate R = R″ = H; R′ = CH_3; x = 1		0.86		0.90	1.28	2.10			1.90	
dimethyl 1,7-heptanedioate R = R′ = H; R″ = CO_2CH_3; x = 5					1.30	2.30	1.50			
					^2H Shifts (δ)[d]					
methyl nonanoate	0.085	0.85 (0.35)			1.28 (0.10)[e] (0.39)[f]	2.25 (0.03)	1.61 (0.13)			29
methyl 2-methyloctanoate	0.128	0.85 (0.61)	1.08 (0.24)		1.26 (0.15)			nf		8.7
methyl 3-methylpentanoate	0.103	0.90 (0.68)		0.90 (0.32)	nf	nf			nf	12.6
dimethyl 1,7-heptanedioate	0.096				1.30[g] (0.39)	2.25[h] (0.15)	1.50[i] (0.46)			8.1

[a] Content given as total percent deuterium incorporation determined by mass spectrometry. Numbers in parentheses represent the fractional distribution of ^2H found from the Eu(fod)$_3$ spectrum. All proton shift assignments were in agreement with those reported in the Aldrich Catalog of proton NMR spectra. [b] Shifts were recorded in CCl_4 relative to internal Me_4Si. [c] Not clearly resolved at 60 MHz. [d] Shifts were recorded in CCl_4 and reported relative to 2% internal $CDCl_3$ referenced as 7.25 ppm. nf = no deuterium found at these positions. [e] Represents the 4-CH_2 position. [f] Represents 5- through 8-CH_2 positions. [g] Represents only the 5-CH_2 position. [h] Represents 2- and 8-CH_2 positions. [i] Represents 3-, 4-, 6-, and 7-CH_2 positions.

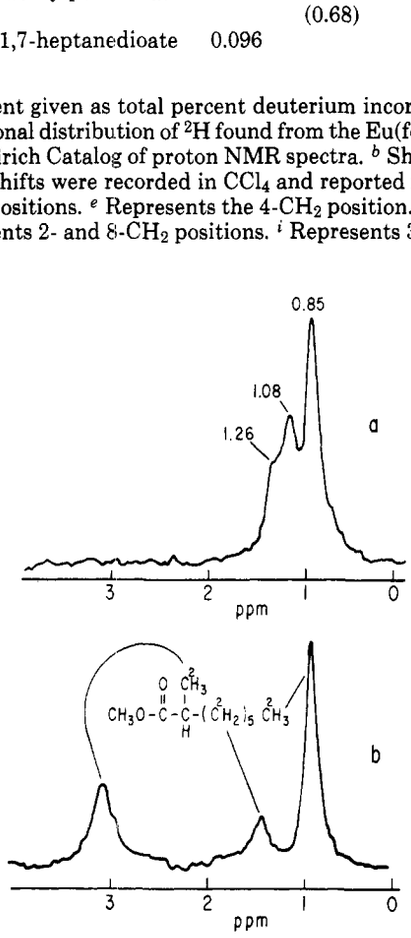

Figure 2. ^2H spectrum of: (a) methyl 2-methyloctanoate, 200 transients, 4.4-s repetition rate, displayed spectral width = 125 Hz, 8K data points; (b) methyl 2-methyloctanoate in the presence of Eu(fod)$_3$ shift reagent, molar ratio of Eu(fod)$_3$/substrate = 0.25, 208 transients, 4.4-s repetition rate, displayed spectral width = 125 Hz. Total ^2H content = 8.7%.

onto the ^{31}P resonance of H_3PO_4 in a 1.8-mm capillary tube secured in the center of the 10-mm tube with a drilled out vortex plug and observe ^2H at 9.2 MHz.[7]

Table I lists the ^1H and the corresponding ^2H shifts observed for the methyl esters derived from catalytically deuterated carboxylic acids. Total percent ^2H incorporation into the esters was determined by mass spectrometry and the positional distribution by ^2H NMR. Figure 1a shows the ^2H spectrum of methyl nonanoate with 29% ^2H incorporation in the alkyl chain. In this spectrum the 2- and 3-methylene and terminal methyl ^2H resonances were clearly defined, whereas the remaining ^2H in the chain are seen as a single resonance. Although this spectrum was obtained at only 9.2 MHz, it illustrates the separation which is achievable from single line resonances in the absence of couplings. Note that the 3-position ^2H is readily distinguished, whereas the corresponding ^1H spectrum yields only a broad shoulder. A predominance of incorporation is apparent in the terminal methyl group, while the 2 position appears to have a low concentration. In the presence of shift reagent [Eu(fod)$_3$] (Figure 1b), the distribution of ^2H throughout the chain is easily ascertained (Table I). While such a separation was obtained for a ^1H spectrum of this ester in the presence of a shift reagent,[8] it was not posssible to quantify the low levels of ^1H depleted in each resonance peak. Figure 2a shows the ^2H spectrum of methyl 2-methyloctanoate, Figure 2b the corresponding spectrum in the presence of Eu(fod)$_3$ shift reagent. The latter spectrum clearly demonstrates the presence of ^2H in positions 3 to 7 and the terminal and 2-position methyl groups of this carboxylic ester. No resonance corresponding to the 2-methine ^2H was observed. A predominance of incorporation is seen in the terminal methyl group resonances, which separate from the 2-methyl group under the influence of shift reagent (Figure 2b). Figures 3a and 3b illustrate the exclusive substitution of ^2H in the 3-methyl and terminal methyl groups of methyl 3-methylpentanoate and the dramatic resolution obtainable with the shift reagent. Dimethyl 1,7-heptanedioate exhibits

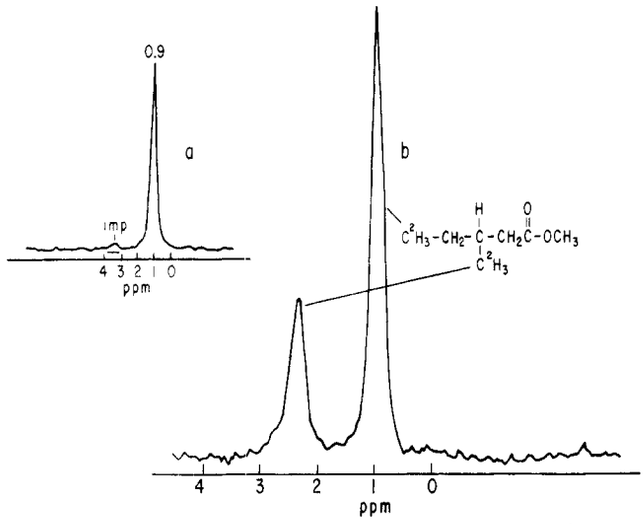

Figure 3. ^2H spectrum of: (a) methyl 3-methylpentanoate, 428 transients, 4.4-s repetition rate, displayed spectral width = 500 Hz, 8K data points; (b) methyl 3-methylpentanoate in the presence of $Eu(fod)_3$ shift reagent, molar ratio of $Eu(fod)_3$/substrate = 0.25, 400 transients, 4.4-s repetition rate, displayed spectral width = 125 Hz. Total ^2H content = 12.6%.

a somewhat broadened spectrum in the presence of $Eu(fod)_3$ because of the increased molecular weight and longer T_1 values of the double coordination site complex. However, the ^2H distribution for three distinct regions along the chain was still evident (Table I).

A full report concerning the catalytic procedures used for the ^2H exchange reactions into various compounds and their analyses by mass spectrometry and ^2H NMR spectroscopy will be the subject of future publications.

References and Notes

(1) For a comprehensive review of the most recent work in ^2H NMR spectroscopy see: H. H. Mantsch, H. Saito, and I. C. P. Smith in "Progress in Nuclear Magnetic Resonance Spectroscopy", J. W. Emsley, J. Feeney, and L. H. Sutcliffe, Ed., Pergamon Press, London, 1977.
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Cuprates Derived from *endo*-(*n* + 3)-Bromobicyclo[*n*.1.0]alkanes and Related Compounds and Their Reaction with β-Iodo Enones. Facile Homo-[1,5]-sigmatropic Hydrogen Migrations Involving *endo*-(*n* + 3)-(3-Keto-1-cycloalkenyl)bicyclo[*n*.1.0]alkanes

Summary: The tricyclic compounds **6, 7, 13, 15, 21,** and **26,** efficiently obtained by reaction of the appropriate β-iodo enone (**4** or **5**) with cuprate reagents derived from *endo*-(*n* + 3)-bromobicyclo[*n*.1.0]alkanes and related compounds, undergo facile and, in the case of compounds **21** and **26,** completely site-selective homo-[1,5]-sigmatropic hydrogen migrations to afford, respectively, products **28–33,** inclusive.

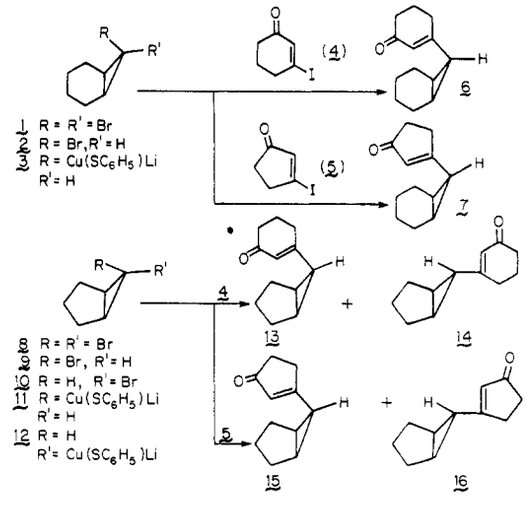
Sir: Recent reports[1–4] have indicated that various lithium cyclopropylcuprates may have considerable potential as reagents in organic synthesis. Our initial work in this area was concerned with the reactions of lithium phenylthio(cyclopropyl)cuprate and lithium phenylthio(2-vinylcyclopropyl)cuprate with β-iodo enones to produce intermediates which could be employed in cyclopentane-[2a] and cycloheptane-type[2b] annelation processes. More recently, we have been engaged in studies concerning the preparation and reactivity of more highly substituted cyclopropylcuprate reagents. We report herein some preliminary results regarding (a) the preparation of cuprate reagents derived from *endo*-(*n* + 3)-bromobicyclo[*n*.1.0]alkanes and related compounds, (b) the reaction of these reagents with β-iodo enones, and (c) the thermal sigmatropic rearrangement of the resultant intermediates to produce 2-cycloalken-1-ones which are uniquely functionalized on the β carbon of the α,β-unsaturated ketone system. Apart from the intrinsic interest in this work from a methodological point of view, we feel that the final rearrangement products possess considerable potential as intermediates in projected natural product syntheses.

Reduction of 7,7-dibromonorcarane (**1**) with Zn–HOAc[5] afforded a mixture of monobromo derivatives in which the endo isomer **2**[6,7] predominated (ratio of endo/exo ≈ 10:1). Treatment of **2** with 2 equiv of *t*-BuLi (ether, −78 °C), dilution of the resultant solution with THF, addition of 1 equiv of C_6H_5SCu,[8] and warming the mixture to −20 °C gave a solution of the cuprate reagent **3.** When the latter was allowed to react (−20 °C, 2 h; 0 °C, 2 h) with each of the β-iodo enones **4**[9] and **5**,[2a] the corresponding endo enones **6** and **7** were obtained in excellent yields (93 and 83%, respectively, Scheme I).

Treatment of 6,6-dibromobicyclo[3.1.0]hexane (**8**)[10] with *n*-Bu_3SnH[11] afforded a 1:1 mixture of the corresponding monobromo derivatives **9** and **10**[12] (Scheme I). Conversion of this material into a mixture of the corresponding cuprate reagents **11** and **12,** followed by reaction of the latter with 3-iodo-2-cyclohexen-1-one (**4**),[9] gave a mixture of compounds **13** (46%) and **14** (48%), which could be separated readily by column chromatography on silica gel. In similar fashion, reaction of the mixture of **11** and **12** with the β-iodo enone **5**[2a] produced the epimeric derivatives **15** and **16** (isolated yields 35 and 41%, respectively).

Conversion of the MEM ethers[13] of 2-cyclohexen-1-ol (**17**) and 2-cyclopenten-1-ol (**22**) into the corresponding dibro-

Scheme I



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