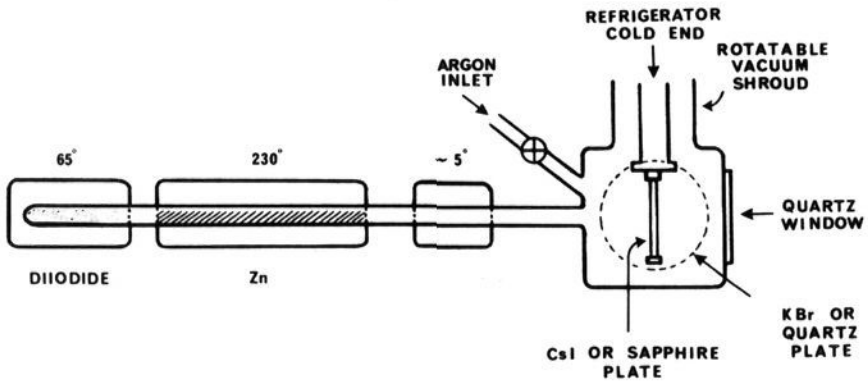


Figure 1. Apparatus for thermal generation and spectroscopic observation of benzocyclobutadiene. The system is evacuated to 10^{-6} mm during use.

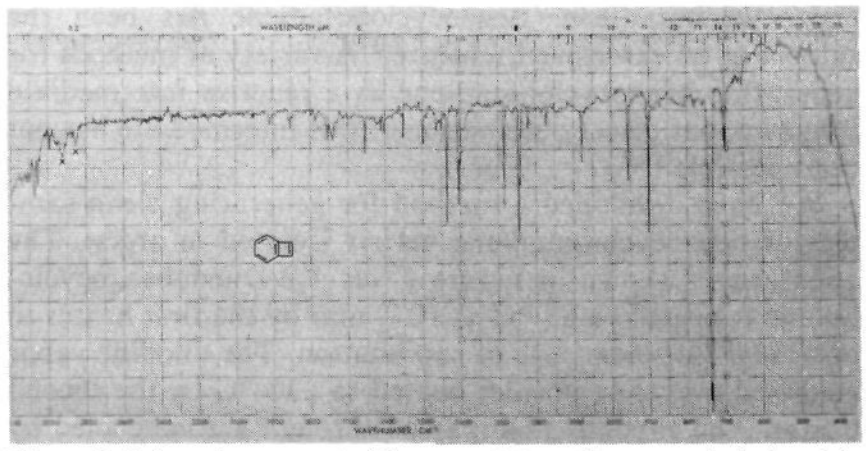


Figure 2. Infrared spectrum of benzocyclobutadiene matrix isolated in argon at 8 K. Bands marked × were in the spectrum of the cesium iodide plate before deposition.

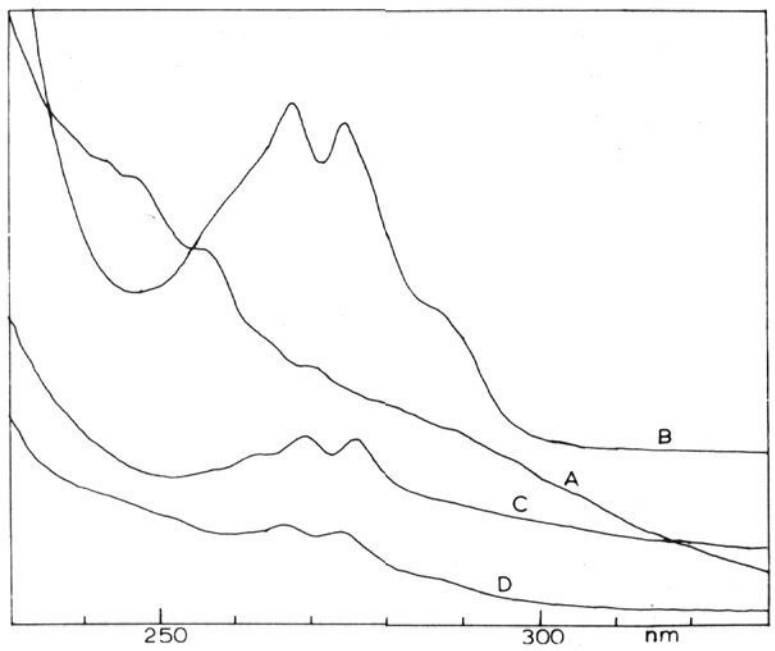
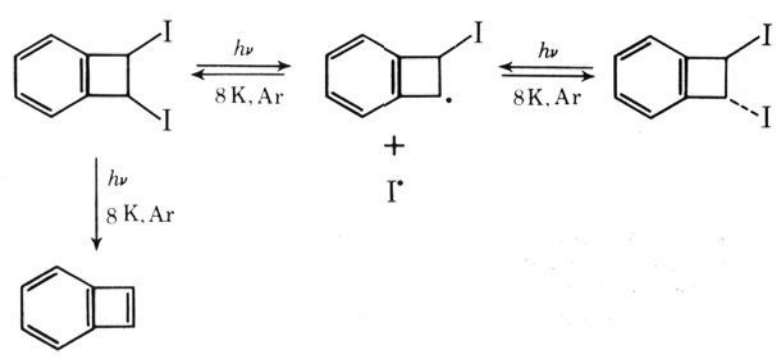
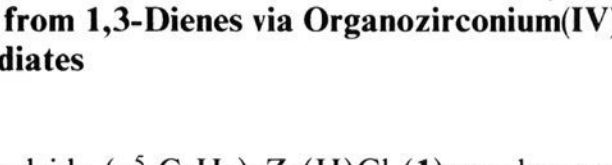


Figure 3. *(A) Ultraviolet spectrum of benzocyclobutadiene matrix isolated in argon at 8 K. (B) Ultraviolet spectrum of authentic benzocyclobutadiene dimer in 95% ethanol solution. (C) Ultraviolet spectrum of sample A after warming above 75 K. (D) Ultraviolet spectrum of the product recovered from the cesium iodide window after warming the sample shown in Figure 2 to room temperature. Vertical axis is optical density. The relative positions of A, B, C, and D are arbitrary and do not show relative optical densities.*

289 nm) shows considerable structure over a broad range. The rapidly rising baseline in the ultraviolet spectrum is due to light scattering by the argon. On warming, the benzocyclobutadiene dimer absorption appears (Figure 3). In this process, the argon is pumped off, and light scattering is less serious.



Irradiation of *cis*-diiodide matrix isolated in argon at 8 K gives two primary products, *trans*-diiodide (major) and benzocyclobutadiene (minor). Similar irradiation of the *trans*-diiodide gives only *cis*-diiodide as a primary product. When the irradiations are monitored by ESR a free radical (presumably the 2-iodobenzocyclobutyl radical) signal is observed.



It is instructive to note that the zinc-induced elimination is much more facile with the *cis*- than with the *trans*-diiodide. This observation suggests the possibility of a cyclic elimination.

Acknowledgment. This research was supported by Grant MPS75-10939 from the National Science Foundation and by Grant HD9279 from the National Institute of Child Health and Human Development.

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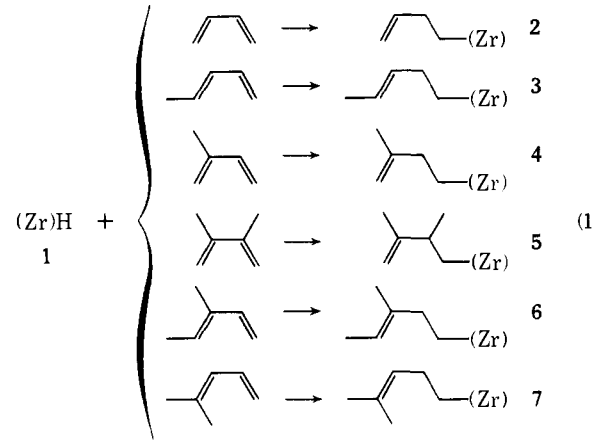
Hydrozirconation. V. γ,δ-Unsaturated Aldehydes and Halides from 1,3-Dienes via Organozirconium(IV) Intermediates

Sir:

The hydride $(\eta^5\text{-}C_5H_5)_2Zr(H)Cl$ (**1**) can be used to prepare reactive precursors of a variety of alkyl or alkenyl organic compounds from olefins or acetylenes, respectively. The overall mode of addition of **1** to these unsaturated hydrocarbons in many ways parallels reactions known for several main group or transition metal hydrides. We find now, however, that the course of addition of **1** to 1,3-dienes is significantly different from that observed for these other classes of hydrides. In contrast to boron[1] or aluminum[2] hydrides which often doubly metalate 1,3-dienes or give a mixture of products, or to most transition metal hydrides which add 1,4 or 1,2 to yield allylic complexes,[3,4] **1** reacts with a variety of 1,3-dienes via 1,2-addition to the sterically less hindered olefinic unit of the substrate to give γ,δ-unsaturated (homoallylic) complexes in high yield (80–90%, reaction 1). These compounds, in turn, can be used to prepare desirable organic products, γ,δ-unsaturated aldehydes or halides, under mild conditions.

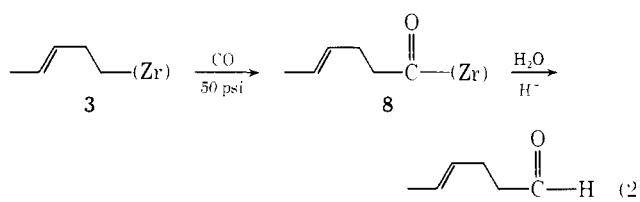
1,3-Dienes react more slowly with **1** than do terminal olefins (relative rate ca. 1:50); the γ,δ-unsaturated zirconium



(1)

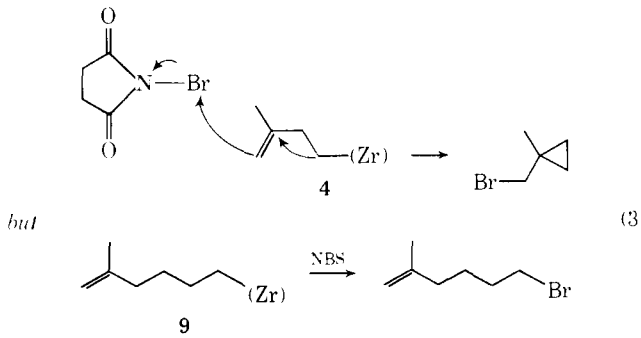
(Zr) = (η^5 – C_5H_5)$_2$Zr(Cl)–

complexes thus produced insert CO faster than do their alkyl analogues.[5] One such diene was converted to a γ,δ-unsaturated aldehyde as follows. An excess amount (2 ml, ca. 50% excess) of 1,3-pentadiene was stirred with a suspension of **1** (5.6 g, 21.8 mmol) in benzene[6] for 12 hr at room temperature. Solvent and excess diene were removed from the red reaction mixture by evaporative distillation at 20°. The soluble zirconium complex[7] **3** was redissolved in benzene and was treated with CO (50 psi) in a Fischer-Porter apparatus for 2 hr at 20°. Hydrolysis (20°, dilute HCl) of the resulting acyl species **8**[7] (reaction 2) gave 4-hexenal (81% based on **3**). Other γ,δ-unsaturated aldehydes were produced in similar fashion (Table I). In only one case (arising from **6**) was a by-product aldehyde (2,3-dimethyl-3-pentenal, 9%) observable by VPC or NMR analysis.[10] No products attributable to dimetalation or to double bond migration could be observed by either of these techniques.



(2)

γ,δ-Unsaturated zirconium complexes can also be converted to the corresponding bromides. However, here the path of reaction can be less straightforward than was observed in aldehyde synthesis. Whereas **2**, **3**, and **7** reacted with NBS[11] to give the expected γ,δ-unsaturated compound as the only bromide observed, **4**, **5**, and **6**, with NBS, gave mixtures of γ,δ-unsaturated and cyclopropylcarbinyl bromides[12] (Table II). Methods exist,[14] though, for the high yield conversion of these cyclic products to γ,δ-unsaturated halides. The mechanism proposed to account for cyclopropylcarbinyl bromide formation from certain γ,δ-unsaturated zirconium species is illustrated for **4** as shown in reaction 3. Noteworthy in this context is the observation that

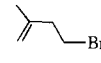
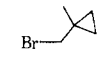
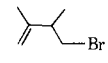
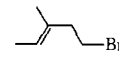
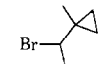


(3)

Table I

Zr(IV) complex	1. CO, 2. H_2O–H^+ Product[8]	Yield (%)[9]
3	(E)-4-Hexenal	81
4	4-Methyl-4-pentenal	98
5	3,4-Dimethyl-4-pentenal	59
6	(E)-4-Methyl-4-hexenal	91
7	5-Methyl-4-hexenal	98

Table II

Complex	Products (relative amounts)[12,13]			
4		(56)		(44)
5		(56)		(44)
6		(75)		(25)

only properly alkyl-substituted γ,δ-unsaturated zirconium precursors undergo this cyclization reaction. For example, treatment of **9** (prepared from 2-methyl-1,5-hexadiene) with NBS yields only the acyclic olefinic bromide (reaction 3).[12]

Hydrozirconation thus enables the direct and selective conversion, under mild reaction conditions, of 1,3-dienes[15] to reactive precursors of γ,δ-unsaturated organic products. Because of the availability of 1,3-dienes,[16] this technique, in combination with known synthetic procedures,[14] provides a facile means for the straightforward elaboration of small, accessible starting materials into larger organic molecules of continuing interest.

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(2) For example, see L. I. Zakharkin and L. A. Savina, *Izv. Akad. Nauk SSSR, Ser. Khim., Engl. Ed.*, 72 (1967); or K. Ziegler, *Angew. Chem.*, **68**, 721 (1956).
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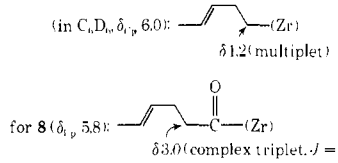
(6) All reactions were performed under argon or nitrogen. The solvent was distilled from sodium benzophenone ketyl under argon.[5]
(7) The structure of each γ,δ-unsaturated zirconium alkyl was determined by NMR. For example, for **3**



(8) Products were identified by NMR and by comparison with authentic material.
(9) Yields were determined by VPC and are based on the γ,δ-unsaturated zirconium(IV) complex.
(10) In general, the desired aldehyde was the only high-boiling volatile product formed. Occasionally, small amounts of residual diene, olefin (from incomplete CO insertion and hydrolysis), or cyclopentadiene (from slow subsequent hydrolysis of the organometallic product) were also observed by VPC.

(11) D. W. Hart, T. F. Blackburn, and J. Schwartz, *J. Am. Chem. Soc.*, **97**, 679 (1975).
(12) In each case, the yield[9] of bromide (or of both bromides combined) was ca. 85%.
(13) These bromides were readily separated on an 8 ft × ¼ in. column packed with 5% Carbowax 20M on Chromosorb P (NAW).
(14) S. F. Brady, M. A. Ilton, and W. S. Johnson, *J. Am. Chem. Soc.*, **90**, 2882 (1968).
(15) Preliminary results indicate that the reactivity of 2,4-dienes is not analogous. Deuterium labeling studies show that these species react with *3* equiv of **1** to yield *saturated*, terminally functionalized alkyl complexes.
(16) For example, see H. O. House, "Modern Synthetic Reactions", 2nd ed, W. A. Benjamin, New York, N.Y., 1972, Chapter 10.

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Nonexponential Methyl Proton Spin–Lattice Relaxation in the C-Terminal Tetrapeptide of Gastrin

Sir:

In this communication we report the observation of nonexponential spin–lattice relaxation for the methyl protons of the C-terminal tetrapeptide of gastrin. The most likely source of this nonexponentiality is cross-correlations between the methyl proton spin pairs. This observation is important in view of the recent increasing interest in the effects of cross-correlations in NMR relaxation. Cross-correlations have been discussed by a number of authors and have been shown to result in a slower nonexponential relaxation mechanism.[1-4] With few exceptions,[5,6] the observations of these effects have been in solid systems. In physiologically active molecules the effects have not been observed.

The C-terminal tetrapeptide of gastrin has the primary structure TRP-MET-ASP-PHE-NH_2 and has the same physiological range of activity as gastrin itself. The material[7] used in this study was synthesized by the method of Davey et al.[8] and isolated as the gastrin tetrapeptide amide trifluoroacetate, purity ≥95%. The material was dissolved in 100% DMSO-d_6, deoxygenated via at least three freeze–pump–thaw cycles, and sealed with pressure caps under nitrogen in 5-mm NMR tubes.

Spin–lattice relaxation measurements at 30 ± 1°C were performed in the Fourier transform mode at 100 MHz on a JEOL-PFT-100 spectrometer with a disk storage system. The conventional inversion recovery method (180°-τ-90°-t) was used with the phase of the 90° pulse changed by 180° on every scan.[9] The value of t was 17.0 sec for all measurements and was intentionally kept long relative to the time scale of the relaxation. A bandwidth of 2.0 kHz was employed with 8192 data points. Peak heights were taken to be proportional to magnetization. Resonance assignments are available in the literature.[10,11] It should be noted that we use "aromatic" to designate the partially overlapping resonances of the aromatic protons of phenylalanine and tryptophan.

The relaxation of the aromatic and methionine methyl protons is shown in Figure 1. It is evident from the curvature exhibited in Figure 1A that the methyl relaxation cannot be characterized by a single exponential. The linearity exhibited in Figure 1B establishes that the curvature in Figure 1A does not result from nonlinearities in our detection system. Furthermore, since Figure 1 is a composite (without scaling of the vertical axis) of three separate data runs, the scatter depicted therein is indicative of the reproducibility of the results. One of these runs was taken with 40 accumulated transients and the other two with ten accumulated transients per spectrum. Two of the runs were made using a

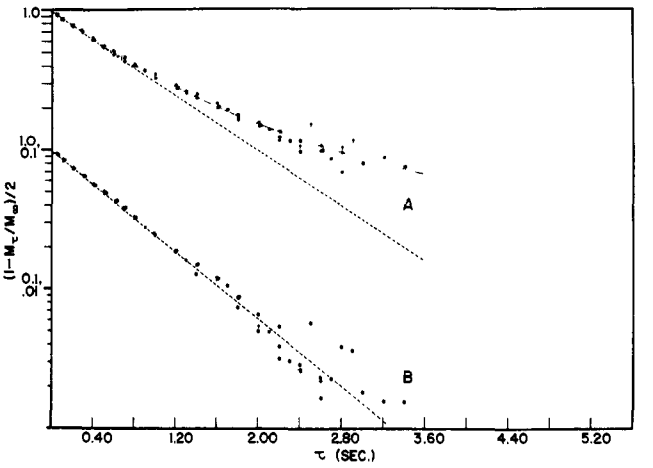

Figure 1. Spin–lattice relaxation in the C-terminal tetrapeptide of gastrin (0.03 *M* in DMSO-d_6, 30 ± 1°C): A, methionine methyl proton relaxation (dotted line denotes results of nonlinear regression analysis using the weighted sum of two exponentials, dashed line denotes initial slope calculated from the results of the double exponential fit); B, aromatic proton relaxation (dashed line denotes results of nonlinear regression analysis using a single exponential).

computer program which sequentially increments the time interval τ in the inversion recovery method. The third run was performed manually with τ values chosen at random and the equilibrium spectrum at effectively infinite pulse separation measured before and after each measurement at finite τ. This procedure ensures that any instrument drift appears as scatter and not as curvature in Figure 1.

There are alternative reasons, in addition to cross-correlations, why the methyl protons might relax nonexponentially. One alternative is that of slow exchange between various molecular conformations which are characterized by different spin–lattice relaxation rates. We reject this alternative on the grounds that although the protons all have T_1's in the same time domain, nonexponentiality is not reflected in both plots in Figure 1. Another possibility is that there is cross-relaxation[12] between the methyl protons and other protons on the same or neighboring molecules. We reject the alternative of intermolecular cross-relaxation between solute molecules on the grounds that results for a 0.015 *M* solution are identical with those shown in Figure 1 for a 0.03 *M* solution. The possibility remains that intramolecular cross-relaxation contributes to the curvature depicted in Figure 1A. We consider this possibility unlikely (but not rigorously excludable in view of the absence of accurate and complete structural information) on the basis of internuclear separations between nearest proton neighbors as seen in a space filling model of the tetrapeptide arranged to minimize steric interactions.

We are thus led to the conclusion that the observed nonexponential methyl relaxation is most likely due to cross-correlations. Theory predicts[3] in general that the magnetization M relaxes nonexponentially to its equilibrium value M_0, and the quantity $(M_0 - M)/2M_0$ is given by the sum of three decaying exponentials, each with its own rate constant λ_i and preexponential weighting factor A_i. We note that the scatter in our data prevents the determination of reliable values of six parameters. The values of the four parameters determined via nonlinear regression analysis using the weighted sum of two exponentials are $A_1 = 0.817 \pm 0.162$, $\lambda_1^{-1} = 0.762 \pm 0.126$ sec, $A_2 = 0.155 \pm 0.168$, and $\lambda_2^{-1} = 3.77 \pm 4.65$ sec. For comparison a fit of the aromatic data to a single exponential yields $A_1 = 0.969 \pm 0.008$ and $\lambda_1^{-1} = 0.724 \pm 0.010$ sec. The ± figures denote approximate *95% confidence limits* (approximately two standard deviations) provided by the computer analysis. The