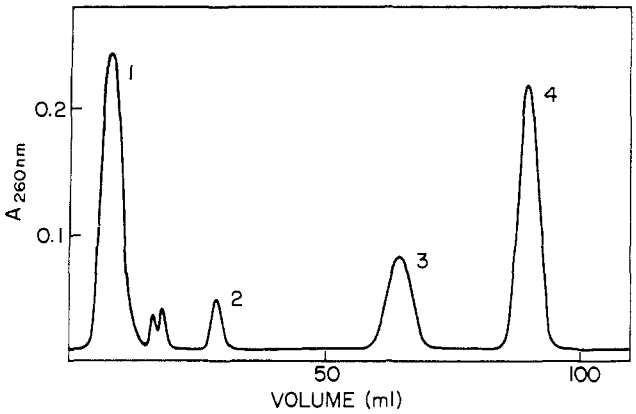

Figure 1. Elution pattern obtained from the chromatography of the reduced 30-min sample from the reaction of the dialdehyde Ib with 0.4 $M$ tetramethylglycinamide at 45°. The column (0.2 × 100 cm) contained Dowex 1-X4 (−400 mesh) ion-exchange resin and the elution was carried out at 10 ml/hr with 200 ml of 20% ethanol containing a linear gradient (0.01–0.5 $M$) of ammonium chloride adjusted to pH 9 with ammonia: peak 1, compound III; peak 2, adenine; peak 3, reduced form of Ib; peak 4, guanosine 3′-phosphate.

water solution whereas complete reaction was obtained after 2 hr in the tetramethylglycinamide solution.

Initial experiments with GpA showed that its oxidized form Ib was completely degraded to guanosine 3′-phosphate and II within 1 hr at 45° in the presence of 0.4 $M$ tetramethylglycinamide hydrochloride, pH 8.4. The course of this reaction was studied using a new chromatographic system[6] for the analysis of the products (Figure 1). The dinucleoside phosphate was treated with a tenfold excess of sodium periodate at 0°. The excess periodate was destroyed by the addition of excess rhamnose before the temperature was raised to 45° and the tetramethylglycinamide added. Samples were taken at various times and treated, as before, with sodium borohydride prior to analysis by column chromatography. After 1 hr the yield of guanosine 3′-phosphate was >95% and the other product was shown to be identical with III. Again, as before, a trace amount of adenine was formed early in the reaction; however, the amount of the base produced did not increase with time.

Similar $\beta$-elimination reactions have been carried out on the other nucleoside 5′-phosphates and on other dinucleoside phosphates such as ApA, CpA, UpA, and ApU. In each case the patterns of reaction and products were analogous to those discussed above.

The advantage of this method of $\beta$ elimination over previously developed methods is that it provides a means for selectively labeling the nucleoside fragment after it has been released from the polynucleotide chain. Using tritiated sodium borohydride it is possible to obtain the nucleoside residue labeled to a high specific activity for subsequent detection by either scintillation counting or by autoradiography. This procedure should increase the sensitivity of detection by a number of orders of magnitude over the usual spectrophotometric method.

It has also been found that both Ia and II readily form condensation products with primary amines and these products are presumed to be morpholine derivatives. In the case of the simple aliphatic amines the products formed are relatively insoluble in water, whereas reaction with glycine produces condensation products which can readily be chromatographed in aqueous systems. This observation provides another possible approach to the labeling of the nucleoside moieties from $\beta$-elimination reactions. The structural analysis and chromatographic characteristics of these condensation products will be reported in a forthcoming publication.

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*Received September 13, 1972*

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(6) G. T. Asteriadis and P. T. Gilham, unpublished experiments.

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## Electron–Electron Double Resonance Demonstration of Cross Saturation between Trapped Electrons and Radicals in $\gamma$-Irradiated 2-Methyltetrahydrofuran Glass

*Sir:*

Electrons generated by $\gamma$ radiation are trapped with high efficiency in a variety of aqueous and organic glasses near 77°K. 2-Methyltetrahydrofuran (MTHF) glass is one of the organic glasses in which the nature of trapped electrons has been most extensively studied.[1] After $\gamma$ irradiation of MTHF, the electron paramagnetic resonance (epr) signal is found to be a superposition of a sharp single-line spectrum due to trapped electrons and a seven-line spectrum due to free radicals formed from the MTHF molecule. A recent study of recombination luminescence suggests that the latter spectrum is due to a cationic entity.[2] Paramagnetic relaxation of the trapped electron in MTHF glass has been studied by epr saturation methods by Smith and Pieroni,[3] Williams and coworkers,[4] and Kevan and coworkers.[5] These studies reveal that the spatial distribution of the trapped electrons in MTHF glass is nonuniform, but the relaxation mechanism has not been completely delineated.

Electron–electron double resonance (eldor) is a powerful new technique for studying paramagnetic relaxation processes.[6] Eldor is the change in an epr signal, as monitored by an observing microwave frequency, which is caused by a different pump microwave frequency. In the present experiment the pumping microwave frequency and the observing microwave frequency are separated by a fixed amount and the magnetic field is swept to produce an epr spectrum as shown in Figure 1. When the pumping microwave

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frequency irradiates a hyperfine line of the MTHF radical, an effect on the epr signal of the trapped electron is detected by the observing microwave frequency. This demonstrates cross saturation between these two different spin systems and is the first demonstration of this effect involving trapped electrons in glassy systems. This also shows that relaxation of trapped electrons in irradiated systems cannot be considered solely in terms of the trapped electron spin system.

2-Methyltetrahydrofuran, purified and dried as described elsewhere,[7] was sealed in a quartz epr tube under vacuum, $\gamma$ irradiated with $^{60}$Co to a dose of 2.6 Mrads at 77°K in the dark, and measured at 73°K with a Varian Model E-800 eldor spectrometer attached to a conventional X-band epr spectrometer. The trapped electron concentration is $2.5 \times 10^{18}$ spins g$^{-1}$ and the MTHF radical concentration is $3.2 \times 10^{18}$ spins g$^{-1}$.

Figure 1a shows an epr signal recorded from the sample in the dual mode (observing mode and pumping mode) eldor cavity with no pumping microwave frequency applied. The observing microwave power ($H_1$ = 0.063 G) is high enough to slightly saturate the trapped electron spectrum. However, in order to obtain a good signal to noise ratio, all measurements were carried out at this level of the observing microwave power. When the higher power pumping microwave frequency ($H_1$ = 0.63 G) is greater than the observing microwave frequency by 230, 120, and 45 MHz, the recorded signals change in shape and intensity as shown in Figure 1b–d, respectively. The pumping microwave frequency is applied to the seven-line spectrum at the positions indicated by arrows when the observing microwave frequency is detecting the trapped electron spectrum. When the pumping position is beyond the low-field limit of the seven-line spectrum, no change is observed in the intensity of the trapped electron spectrum, as shown in Figure 1b. However, if the pumping microwave frequency is applied to the seven-line spectrum when the trapped electron line is observed, the trapped electron spectrum decreases appreciably in intensity as in Figure 1c and 1d even though the observing microwave power is unchanged.

The effect of the pumping microwave frequency on the trapped electron spectrum is more pronounced as the difference between pumping and observing microwave frequencies is decreased (see Figure 1c and 1d). These results clearly indicate that energy is transferred from the free-radical spin system to the trapped electron spin system to partially saturate it. This implies that paramagnetic relaxation of the trapped electron involves cross saturation with the radical.

There are at least two possible mechanisms for this cross saturation. One mechanism is cross relaxation[8] in which direct spin–spin interaction between the two spin systems causes simultaneous spin flips in both systems with any excess energy conserved by dipolar interactions. The efficiency of this mechanism depends on the degree of overlap between the tails of the epr lines of the two species involved. A second mechanism involves hot phonon production.[9] In this mechanism one relaxing species (in our case the radical) creates sufficient microwave phonons at the resonance frequency of a second species (in our case the trapped electron) to effectively raise the lattice temperature and to increase saturation of the second species.

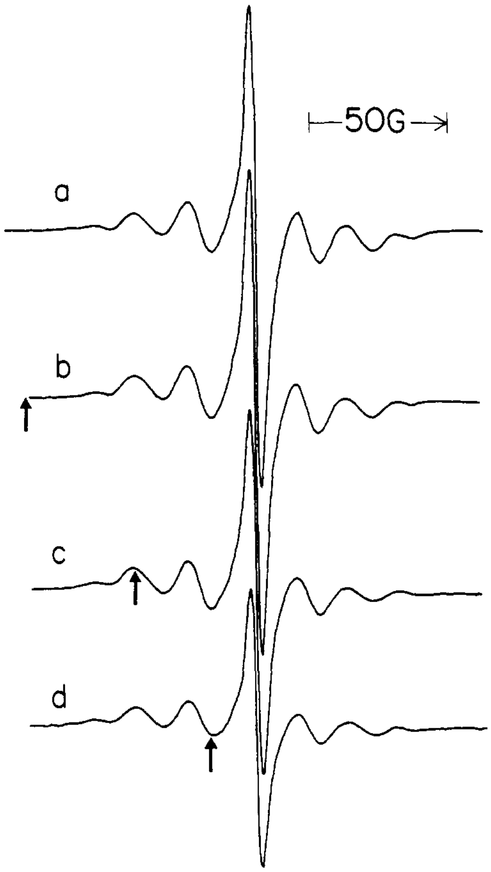

Figure 1. Epr spectra of 2-methyltetrahydrofuran glass $\gamma$ irradiated to a dose of 2.6 Mrads at 77°K and measured at 73°K in a dual mode eldor cavity (a) with no pumping microwaves applied and (b–d) with pumping microwaves applied with a frequency higher than that of the observing microwaves by (b) 230 MHz, (c) 120 MHz, and (d) 45 MHz. The arrows indicate the pumping microwave positions when the trapped electron line in the center is observed. Relative peak-to-peak heights of the third ($x$) and fifth ($y$) hyperfine lines from the low-field limit of the seven-line spectrum and the trapped electron line ($z$) are as follows: (a) $x = 1.0$, $y = 1.0$, $z = 9.6$; (b) $x = 1.07$, $y = 0.91$, $z = 9.6$; (c) $x = 0.93$, $y = 0.73$, $z = 7.3$; (d) $x = 0.67$, $y = 0.57$, $z = 5.5$.

These two mechanisms may possibly be distinguished by the effect of temperature and concentration on the cross saturation effects. Such experiments are in progress. The increased cross saturation effect, as the difference between the pumping and observing frequencies decreases (compare Figure 1c and 1d), does not distinguish between the two mechanisms. The spin-lattice relaxation mechanism of the trapped radicals and electrons is not yet well characterized. But, if Raman processes predominate at 77°K, as seems likely, then phonons of all frequencies participate in the relaxation process and a hot phonon mechanism does not seem probable.

The radical spectrum itself shows some eldor effects in Figure 1b–d. When the field is swept with the pumping microwave frequency greater than the observing microwave frequency, the low-field part of the radical spectrum is being pumped when the high-field

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[7] M. Irie, K. Hayashi, S. Okamura, and H. Yoshida, *J. Phys. Chem.*, **75**, 476 (1971).

[8] N. Bloembergen, S. Shapiro, P. S. Pershan, and J. O. Artman, *Phys. Rev.*, **114**, 445 (1959).

[9] J. A. Giordmaine, L. E. Alsop, F. R. Nash, and C. H. Townes, *ibid.*, **109**, 302 (1958).

part of the radical spectrum is being observed. Figure 1 shows that the high-field lines of the radical are somewhat decreased in intensity relative to the low-field lines of the radical. This communication between the hyperfine levels of the radicals probably arises from nuclear relaxation and will be discussed in a subsequent publication.

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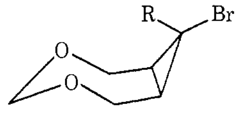
## Carbenoids with Neighboring Heteroatoms. IV. Electrophilic Reactions of Epimeric α-Chlorocyclopropyllithium Compounds[1]

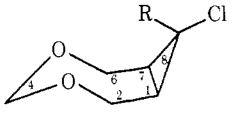
*Sir:*

We wish to report, in preliminary form, our observations on the thermally induced electrophilic reactions of carbenoids which are epimeric at the carbenoid center. Earlier studies on α-haloalkyllithium compounds have provided kinetic[2] and other evidence[3] which implicates these reagents as the reacting species in the addition of certain "chlorocarbenes" to carbon–carbon double bonds. More pertinent to the present work was the observation, by Goldstein and Dolbier,[4] of a halogen-dependent primary deuterium isotope effect in the intramolecular C–H insertion reaction of α-haloneopentyllithium compounds, a result which implicated carbenoids as key intermediates in this electrophilic reaction, as well. In this communication we demonstrate the dependence of the course of the C–H insertion reaction on the stereochemistry of the substituents at the carbenoid carbon atom.

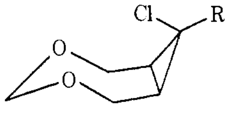
The precursors to the epimeric carbenoids used in this work, namely bromochlorocyclopropanes **2d** and **3a**, were synthesized as follows. The reaction of ethereal dibromocyclopropane **1a**[5] (mp 56–57.5°) with methyllithium–LiBr at −20 or −78° afforded carbenoid **1b** in high yield as evidenced by the 90% yield of **1c** (nmr H-8 at δ 3.23 (t, $J_{\text{trans}}$ = 4.7 Hz)) obtained upon water or $D_2O$ quench of the reaction. In a similar manner, dichlorocyclopropane **2a**[5] gave, upon reaction with butyllithium,[6] chlorocarbenoid **2b**, as evidenced by the 70% yield of **2c** (nmr H-8 at δ 3.44 (t, $J_{\text{trans}}$ = 4.0 Hz)) obtained after a water quench of the reaction. Chlorination of bromocarbenoid **1b** under narrowly controlled conditions (**1a** plus butyllithium at −78° in 20:80 ether–THF, followed by a rapid addition of excess $CCl_4$ and a quench 7 min after the addition) gave **3a** (mp 55–56.5°) in 40–50% yields. The bromination of chlorocarbenoid **2b** with $BrCCl_3$ was more easily accomplished to yield **2d** (mp 59–61.5°) in 48% yield. While several vpc columns gave identical retention times for **2d** and **3a**, the mixture melting point of **2d** with **3a** was depressed, and chemical-shift differences were apparent when spectra of the pure compounds were compared. The successive reactions at −78° of **2d** with methyllithium and methanol gave **2c** (98%) while the same reaction sequence with **3a** gave a new monochloro compound, **3c** (nmr H-8 at δ 3.58 (t, $J_{\text{cis}}$ = 7.5 Hz); mass spectrum $M\cdot^{+} - Cl$ at 113.0595; ~80% yield).[7] Thus, the bromochlorocyclopropanes **2d** and **3a** were shown to be isomers with their structures as indicated.



**1a**, R = Br
**b**, R = Li
**c**, R = H or D
**d**, R = $CH_3$

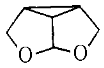


**2a**, R = Cl
**b**, R = Li
**c**, R = H
**d**, R = Br

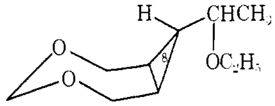


**3a**, R = Br
**b**, R = Li
**c**, R = H

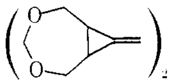
Carbenoids **1b** and **2b** were stable in ether below −20° while, in contrast, carbenoid **3b** yielded products of electrophilic reaction slowly even at −78°. The products of thermal decomposition in ether of the three carbenoids prepared from methyllithium (*without* lithium bromide) are given in Table I. As can be seen from the data those carbenoids with exo halogen gave high yields of intramolecular C–H insertion (**4**, mp 44.5–46°) while that carbenoid with endo halogen gave, almost exclusively, products of intermolecular reactions (**5**, H-8 $J_{\text{trans}}$ = 5.5 Hz determined using $Eu(DPM)_3$ with decoupling; *syn*-**6**, mp 209.5–211°; *anti*-**6**, mp 126.5–127.5°). Under more dilute conditions and at higher



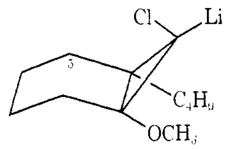
**4**



**5**



**6**, syn, anti



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(1) (a) The generous support of the National Science Foundation through Grants GP-9543 and 28381 is acknowledged with appreciation. (b) Paper III: K. G. Taylor, W. H. Hobbs, M. S. Clark, and J. Chaney, *J. Org. Chem.*, 37, 2436 (1972).

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(3) (a) G. L. Closs and R. A. Moss, *J. Amer. Chem. Soc.*, **86**, 4042 (1964); (b) W. T. Miller and D. M. Whalen, *ibid.*, **86**, 2089 (1964); (c) D. F. Hoeg, D. I. Lusk, and A. L. Crumbliss, *ibid.*, **87**, 4147 (1965).

(4) M. J. Goldstein and W. R. Dolbier, *ibid.*, **87**, 2293 (1965).

(5) *gem*-Dihalocyclopropanes were prepared by dihalocarbene addition to 1,3-dioxep-5-ene (K. C. Brannock and G. R. Lappin, *J. Org. Chem.*, 21, 1366 (1956)).

(6) In ether solvent at −78°, 2 equiv of butyllithium was required for complete reaction of **2a**. At −20°, or with small amounts of THF present at −78°, the exchange reaction stoichiometry was 1:1.

(7) With the exception of 3c and the carbenoids, all compounds gave elemental analyses, or displayed molecular ions, within the prescribed limits. Also, nmr, ir, and mass spectra were consistent with the proposed structures.