

# Application of Deuteron Nuclear Magnetic Resonance Spectroscopy to the Study of the Coupling Reactions of 1-Chlorocycloheptene and 1-Chlorocyclohexene with Phenyllithium

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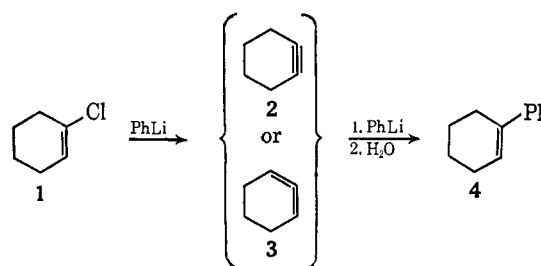
**Abstract:** Deuteron nuclear magnetic resonance spectroscopy has been employed to study the mechanism of two nucleophilic substitution reactions. In the first study it was found that 1-chlorocycloheptene-2,7,7-*d*<sub>3</sub> reacted with phenyllithium in ether at 150° to give deuterium-labeled 1-phenylcycloheptene. The distribution of deuterons in the cycloheptene ring was easily discerned from the deuteron nmr spectrum of the substitution product. From these data it was concluded that substitution occurred *via* an elimination-addition mechanism involving a cycloheptyne-3,3-*d*<sub>2</sub> intermediate. The mechanism of coupling of 1-chlorocyclohexene-2,6,6-*d*<sub>3</sub> with phenyllithium in the presence of lithium piperidide was also investigated. Lithium piperidide dramatically enhanced the rate of coupling, enabling the reaction to be carried out near room temperature. Deuteron nmr measurements provided evidence that the catalyzed substitution reaction proceeded by way of a cycloalkyne pathway.

In view of the widespread application of proton nmr spectroscopy to the elucidation of molecular structure and the investigation of chemical reactions, it is somewhat surprising that magnetic resonance phenomena of the remaining hydrogen nuclei, both of which have nuclear magnetic moments,<sup>8</sup> have not been studied more extensively. This is particularly true in the case of deuteron magnetic resonance (dmr), for deuterium-containing molecules can be synthesized with relative ease. To a first approximation the chemical shift parameters for deuterons are the same as for structurally equivalent protons.<sup>8</sup> In contrast, deuteron spin-spin coupling constants are substantially smaller than proton coupling constants. In systems differing only in terms of isotopic substitution,<sup>3</sup>  $J_{DD} = J_{HH}/(6.51)^2$  and  $J_{HD} = J_{HH}/6.51$ . These simple considerations alone suggest a host of possible applications of dmr spectroscopy. Among the conceivable factors that might limit the use of this tool are problems associated with line width (*e.g.*, deuterons have an electric quadrupole moment<sup>3</sup>) and sensitivity (listed as  $9.64 \times 10^{-3}$  the sensitivity of protons at constant field<sup>3</sup>). The work of Diehl and Leipert<sup>4</sup> indicates that these factors do not impose stifling limitations. Recently, we have been exploring the general utility of dmr spectroscopy. The organic reaction mechanism studies reported below represent two of our initial efforts in this area and serve to point out the considerable potential of dmr as well as some of its limitations.

Aryl halides react with aryllithium reagents to yield substitution products by way of an elimination-addition sequence involving aryne intermediates.<sup>5</sup> 1-Phenylcyclohexene and 1-phenylcyclopentene are

formed upon heating 1-chlorocyclohexene and 1-chlorocyclopentene with phenyllithium at elevated temperatures (100–150°).<sup>6,7</sup> Studies employing <sup>14</sup>C-labeled olefinic chlorides<sup>7</sup> have provided evidence that these coupling reactions, in a manner analogous to the aryl halide coupling reactions, take place *via* a two-step mechanism involving cyclohexyne and cyclopentyne intermediates.

One problem that arises in elucidating the mechanism of substitution of olefinic halides with strongly basic nucleophiles that is not encountered in comparable studies with aryl halides is that the olefinic halides have two elimination routes available to them, cycloalkyne formation (1 → 2) and cycloallene formation (1 → 3).



Both types of transient intermediates have been detected.<sup>8,9</sup> It has been shown<sup>10</sup> that the high-temperature 1-chlorocyclohexene- and 1-chlorocyclopentene-phenyllithium reactions do not proceed to an appreciable extent through cycloallenic intermediates.

In the present work the reaction of a C<sub>7</sub> halide, 1-chlorocycloheptene-2,7,7-*d*<sub>3</sub>, and phenyllithium has been examined. This particular C<sub>7</sub> halide was chosen owing to its synthetic accessibility and the fact that its deu-

(1) National Science Foundation Trainee, 1966.  
 (2) National Institutes of Health Predoctoral Fellow, 1964–1967.  
 (3) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High-Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959.  
 (4) P. Diehl and T. Leipert, *Helv. Chim. Acta*, **47**, 545 (1964).  
 (5) (a) G. Wittig, G. Pieper, and G. Fuhrmann, *Ber.*, **73**, 1193 (1940); (b) G. Wittig, *Angew. Chem.*, **69**, 245 (1957); (c) R. Huisgen and H. Rist, *Naturwissenschaften*, **41**, 358 (1954); (d) R. Huisgen and H. Rist, *Ann.*, **594**, 137 (1955); (e) E. F. Jenny and J. D. Roberts, *Helv. Chim. Acta*, **38**, 1248 (1955).

(6) G. Wittig and G. Harborth, *Ber.*, **77**, 306 (1944).  
 (7) (a) F. Scardiglia and J. D. Roberts, *Tetrahedron*, **1**, 343 (1957); (b) L. K. Montgomery and J. D. Roberts, *J. Am. Chem. Soc.*, **82**, 4750 (1960); (c) L. K. Montgomery, F. Scardiglia, and J. D. Roberts, *ibid.*, **87**, 1917 (1965).  
 (8) A. T. Bottini and W. Schear, *ibid.*, **87**, 5802 (1965).  
 (9) G. Wittig and P. Fritze, *Angew. Chem. Intern. Ed. Engl.*, **5**, 856 (1966).  
 (10) L. K. Montgomery and L. E. Applegate, Abstracts, 149th National Meeting of the American Chemical Society, Detroit, Mich., April 1965, p 23N.

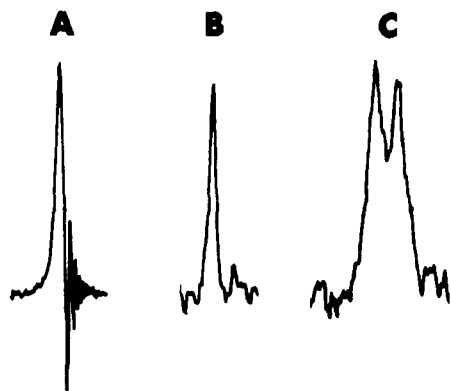


Figure 1. Deuteron resonance signals (5-mm insert, chloroform solvent) for 30% chloroform- $d_1$  (A), approximately 5% solution of chloroform- $d_1$  (B) from the same spectrum as C, and the saturated deuteron region of 1-phenylcycloheptene- $x-d_n$  (C, ~50% solution).

teriums function nicely as labels for distinguishing between conceivable coupling mechanisms, such as direct displacement and the cycloalkyne and cycloallene pathways. In a second investigation the mechanism of the lithium piperidide catalyzed coupling of 1-chlorocyclohexene-2,6,6- $d_3$  and phenyllithium has been explored. Lithium piperidide catalyzes the coupling reactions of five-, six, and seven-membered cyclic olefinic chlorides with organolithium compounds, enabling substitution to be carried out near room temperature.<sup>11</sup>

## Results and Discussion

**General.** Deuteron nmr spectra were, for the most part, taken at 9.201 Mc (14.098 kgauss) on a Varian Associates DP-60 spectrometer. In preliminary studies several different Varian inserts were used (15, 13, and 5 mm). Spinning was found to be beneficial for most applications. Wilmad spinning assemblies were used with the 15- and 13-mm inserts. Operating in the dispersion mode and utilizing the 15-mm insert (about 3-ml sample required), natural abundance ( $1.56 \times 10^{-2}\%$ ) deuteron resonance signals could be detected from water and acetone. In the absorption mode 0.1% solutions (15 mm) of chloroform- $d_1$ , acetone- $d_6$ , and deuterium oxide in protonic solvents gave detectable signals. Favorable signal-to-noise ratios were observed for fully deuterated molecules in moderately concentrated solutions. A typical chloroform- $d_1$  signal is shown in Figure 1 (A; 30% in chloroform, 5-mm insert). Partially deuterated molecules required more sample to give a comparable spectrum. In Table I deuteron chemical shifts are recorded for a number of partially deuterated molecules that were used in the coupling mechanism experiments. Satisfactory spectra could be obtained for all of the compounds using 5–50% solutions with the 5-mm insert. The four  $\alpha$ -deuterons of cycloheptanone-2,2,7,7- $d_4$  gave a strong signal even in 5% solution. The absorption line widths at half peak height for the compounds in Table I fell in the range 1–4 cps. Line widths for several completely deuterated molecules were 0.6–0.8 cps. Although the chemical shifts in Table I were not collected with the idea of precise chemical shift comparisons in mind, the deuteron chemical shifts generally differed from cor-

(11) L. K. Montgomery, Ph.D. Thesis, California Institute of Technology, 1961; (b) unpublished results this laboratory.

Table I. Deuteron Chemical Shifts

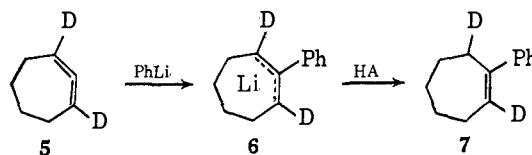
Compound	Chemical shift <sup>a</sup>	Concn (w/w), <sup>d</sup> %
Cycloheptanone-2,2,7,7- $d_4$	2.45	5
1-Chlorocycloheptene-2,7,7- $d_3$	5.88	~50
1-Phenylcycloheptene- $x-d_n$	2.51	~50
	<sup>c</sup>	
	2.80	
Cyclohexanone-2,2,6,6- $d_4$	2.50	10
	2.32 <sup>b</sup>	
1-Chlorocyclohexene-2,6,6- $d_3$	5.81 <sup>b</sup>	~35
	2.25	
1-Phenylcyclohexene- $x-d_n$	<sup>c</sup>	~50
	2.33	
1-Phenylcyclohexene-2,6,6- $d_3$	6.20	~50
	2.36	

<sup>a</sup> Expressed in ppm displacements downfield from *sym*-tetramethylsilane- $d_4$ . Calculated employing chloroform- $d_1$  (7.27 ppm assumed) as an internal standard. Chloroform solvent. <sup>b</sup> Carbon tetrachloride solvent (13-mm insert). Benzene- $d_6$  internal standard (7.37 ppm). <sup>c</sup> Too little vinyl deuteron for accurate measurement. <sup>d</sup> Measurement made in 5-mm tubes.

responding proton chemical shifts by no more than 0.1 ppm.

**Coupling of 1-Chlorocycloheptene-2,7,7- $d_3$  and Phenyllithium.** 1-Chlorocycloheptene-2,7,7- $d_3$  and phenyllithium were heated in ether in a stainless steel bomb at  $(150 \pm 10)^\circ$  for 1.3 hr. About 38% of the 1-chlorocycloheptene-2,7,7- $d_3$  did not react. Deuterium-labeled 1-phenylcycloheptene was obtained in 15% yield, which is quite respectable considering that a kinetic isotope effect of 7.2 ( $k_H/k_D$  for disappearance of starting material) is operative.<sup>12</sup> Unreacted olefinic chloride possessed proton nmr and infrared spectra which were very similar to those of the starting material. The proton nmr spectrum of the coupled product indicated that  $0.17 \pm 0.02$  deuteron and  $1.96 \pm 0.12$  deuterons were present in the olefinic and saturated ring positions, respectively. The exact locations of the saturated deuterons could not be determined owing to the fact that the saturated proton region consisted of complex absorption extending continuously from 1.1 to 2.9 ppm downfield from tetramethylsilane.

Direct displacement of the chlorine from 1-chlorocycloheptene-2,7,7- $d_3$  would give 1-phenylcycloheptene-2,7,7- $d_3$ . Therefore, either substitution did not follow such a route or the initial substitution product underwent further reaction. It is possible, though not likely, that exchange occurred at the olefinic position under the high-temperature, strongly basic reaction conditions.

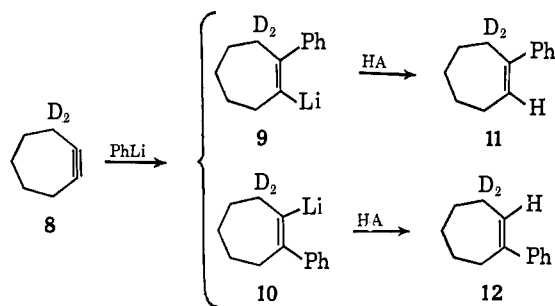


Allenic elimination from the deuterated chloride yields 1,2-cycloheptadiene-1,3- $d_2$  (5). If phenyllithium added to the center of the allenic system in 5, the two deuterons would be equally partitioned (6  $\rightarrow$  7) between the 2 and 7 positions of the product. This does not agree well with the observed distribution. Even poorer

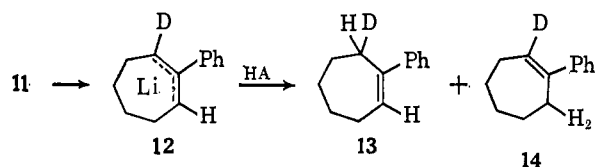
(12) L. K. Montgomery and L. E. Applegate, *J. Am. Chem. Soc.*, **89**, 2952 (1967).

agreement would result if part of the phenyllithium added to the ends of the allenic system.<sup>13</sup>

A cycloalkyne mechanism comes the closest to fitting the proton nmr data. Addition of phenyllithium to cycloheptyne-3,3-*d*<sub>2</sub> would give a 1:1 mixture of two isotopically isomeric organolithium compounds (**8** → **9** + **10**). Deuterated olefins **11** and **12** would ultimately be produced from **9** and **10**.<sup>14</sup> The 0.17 deu-



teron which was found in the olefinic position of the substitution product could have been picked up by **9** and **10** from 1-chlorocycloheptene-2,7,7-*d*<sub>3</sub>, or, alternatively, arisen from the prototropic rearrangement of **11** (**11** → **13** + **14**). Precedents exist for both types of processes.<sup>7,12</sup>



It can be seen that the proton nmr measurements prove to be fairly useful in evaluating hypothetical coupling mechanisms. Nevertheless, a much clearer indication of the mechanism of substitution was gained through an examination of the dmr spectrum of the coupled product. All of the information which was obtained from proton nmr measurements was contained in the dmr spectrum, and, in addition, it was possible to discern the specific locations of the saturated deuterons. The saturated deuteron region of the dmr spectrum consisted of a pair of overlapping peaks of roughly equal intensity at 2.50 and 2.80 ppm (Figure 1C). These peaks were assigned to the allylic deuterons in the 3 and 7 positions. Thus, the product possessed an average of one deuteron in each of the allylic positions. Such a distribution is in excellent agreement with a cycloheptyne-3,3-*d*<sub>2</sub> substitution pathway (**8** → **9** + **10**). Direct nucleophilic displacement is clearly ruled out.

Chloroform-*d*<sub>1</sub> was used as an internal standard in recording the dmr spectrum of the coupled product. Comparison of the 3 position and 7 position deuteron line widths of the product (Figure 1C) with that of chloroform-*d*<sub>1</sub> (Figure 1B; line width ~0.6 cps) shows that the product line widths are much broader. This increase must be due at least in part to H-D spin-spin

(13) This type of addition has been discussed in connection with related substitution reactions.<sup>7c,12</sup> If addition did occur to the ends of the multiple bond system in **5**, the double bond in the addition product would have to isomerize into conjugation with the phenyl ring.<sup>7c,12</sup>

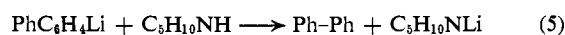
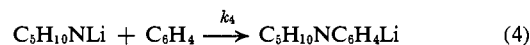
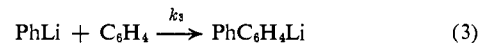
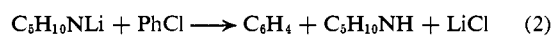
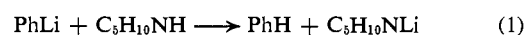
(14) Protonation of **9** and **10** could occur during reaction or in the process of quenching with water. In the coupling reaction of 1-chlorocyclopentene with phenyllithium, 60–80% of the organolithium intermediates like **9** and **10** were protonated during the 1.3-hr reaction period.<sup>12</sup>

coupling. Although electronic H-D decoupling was not tried with this system, an attempt was made to affect decoupling by adding paramagnetic species.<sup>4</sup> In principle such a decoupling procedure is possible because of the difference in proton and deuteron gyromagnetic ratios.<sup>3</sup> In order to achieve decoupling the protons would have to be relaxed rapidly and preferentially by the added paramagnetic reagent. Several brief attempts to carry out H-D decoupling by this method were not successful. Further evaluation of the technique is continuing, however, for its simplicity is most appealing.

**Catalyzed Coupling of 1-Chlorocyclohexene-2,6,6-*d*<sub>3</sub> and Phenyllithium.** Huisgen<sup>15</sup> has shown that the rate of coupling of aryl halides with aryllithium reagents is markedly enhanced by adding piperidine to the reaction mixture. Since piperidine reacts vigorously with phenyllithium, lithium piperidide is properly considered the catalytic reagent. Preliminary studies<sup>11</sup> indicated that the coupling reactions of 1-chlorocycloalkenes and phenyllithium could be catalyzed in a like manner. These findings were of considerable interest, for the higher temperature coupling reactions of olefinic chlorides are neither convenient experimentally nor particularly satisfactory from the synthetic point of view.

A catalyzed coupling of 1-chlorocyclohexene and phenyllithium was attempted under reaction conditions similar to those employed by Huisgen with aryl halides.<sup>15</sup> An ether solution which was 1.03 *M* in 1-chlorocyclohexene, 1.52 *M* in salt-free phenyllithium, and 0.18 *M* in lithium piperidide was heated at 35° for 66 hr. 1-Phenylcyclohexene was obtained in 30% yield, which is comparable to typical yields from the high-temperature reaction.<sup>7</sup> Little reaction was noted in the absence of lithium piperidide.

Huisgen has proposed a mechanism for the piperidine-catalyzed coupling of aryl halides with aryllithium reagents.<sup>15</sup> The mechanism is presented in eq 1–5 using the reaction of chlorobenzene with phenyllithium as an example. Substitution takes place through a



benzyne intermediate. The catalytic action of lithium piperidide has been attributed to two factors. First, the nitrogen base is a better dehydrohalogenating agent than phenyllithium, despite the fact that the latter compound is a stronger base thermodynamically.<sup>16</sup> Secondly, lithium piperidide does not compete well with phenyllithium for benzyne<sup>17</sup> ( $k_3/k_4$  is 4.4<sup>17</sup>). Thus, lithium piperidide can act as a base several times (eq 2 followed by eq 1 or 5) before being taken out (eq 4) of the catalytic cycle.

In view of the many parallels between the nucleophilic substitution reactions of nonactivated aryl halides and cyclic olefinic halides, it would not be at all sur-

(15) R. Huisgen, J. Sauer, and A. Hauser: (a) *Angew. Chem.*, **69**, 267 (1957); (b) *Ber.*, **91**, 2366 (1958).

(16) R. Huisgen and J. Sauer, *ibid.*, **92**, 192 (1959).

(17) R. Huisgen, W. Mack, and L. Mobius, *Tetrahedron*, **9**, 29 (1960).

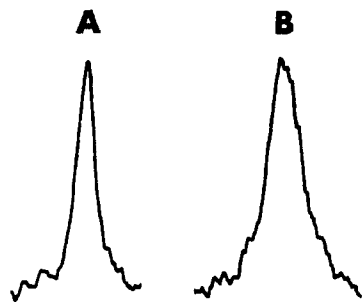


Figure 2. Deuterium resonance signals (5-mm insert) for the saturated deuterium regions of 1-phenylcyclohexene-2,6,6- $d_3$  (A, ~50% solution) and 1-phenylcyclohexene- $x-d_n$  (B, ~50% solution).

prising if the catalyzed coupling of 1-chlorocyclohexene and phenyllithium followed a course similar to the one in eq 1-5. As an experimental test of this possibility, the reaction of 1-chlorocyclohexene-2,6,6- $d_3$  with phenyllithium was studied. The reaction conditions were nearly the same as with the nondeuterated chloride, the major difference being that the reaction was heated for 155 hr. Even with the increased reaction time, the yield was only 10%, presumably because of a kinetic isotope effect. From both the deuterium and proton nmr spectra of the product, it was inferred that 0.1 deuterium and 2.0 deuteriums resided in the olefinic and saturated ring positions, respectively. In contrast to the  $C_7$  case, the saturated deuterium region of the dmr spectrum showed only a single absorption signal at 2.33 ppm (Figure 2B). The line width of this peak was abnormally large, however, being about 7 cps. 1-Phenylcyclohexene-2,6,6- $d_3$  was synthesized from cyclohexanone-2,2,6,6- $d_4$  for comparison purposes. The 6,6-deuteriums in this molecule absorbed at 2.36 ppm and possessed a line width of only 4 cps (Figure 2A). Accordingly, it is clear that if there are deuteriums in the 6 position of the substitution product, then there must also be deuteriums in a position at slightly different field. These observations are, in the very least, compatible with an elimination-addition mechanism involving a cyclohexyne-3,3- $d_2$  intermediate.

In conclusion, it would seem that there are a host of problems that could be effectively and profitably investigated employing dmr spectroscopy. The limitation which is pointed out most forcefully by the present studies is that associated with line width. Under the best of circumstances line widths are in the neighborhood of 0.6 cps, meaning that it will be difficult or impossible to resolve peaks which are separated by less than 0.1 ppm (14 kgauss). Nevertheless, there are many things that can be done working within this limitation.

### Experimental Section

Boiling points are uncorrected. Nmr and infrared spectra were routinely recorded and are assumed to be in satisfactory agreement with authentic or predicted spectra when they are not explicitly discussed. The proton nmr spectra were obtained from dilute chloroform- $d_1$  solutions using a Varian Associates A-60 spectrometer. Deuterium nmr spectra were taken at 9.201 Mc (14.098 kgauss) on a Varian Associates V4300B (DP-60) spectrometer equipped with a Model V3521 integrator. A Model V4311 transmitter-receiver and a V4331-A probe which were tuned to 15 Mc were converted to the designated frequency employing crystals purchased from the International Crystal Co. Several different Var-

ian inserts (15, 13, and 5 mm) were utilized. Wilmad spinning assemblies were used with the 15- and 13-mm inserts. Infrared spectra were generally recorded on both Perkin-Elmer Model 137 and Model 137-G (near-infrared) Infracord spectrometers. Quantitative glpc determinations were carried out on an F & M Scientific Model 609 flame ionization gas chromatograph equipped with a Minneapolis-Honeywell recorder (Model Y153-999) fitted with a Disc Instruments integrator. All of the columns used with the Model 609 were stainless steel and 8 ft in length ( $1/4$  in. o.d.). The columns and their designations are: 20% silicone gum GE XE-60 on 60-80 mesh Chromosorb P (XEA), 20% Carbowax 20M on 60-80 mesh Chromosorb P (CWA). Preparative glpc was conducted on an F & M Model 720 gas chromatograph fitted with 8 ft ( $3/8$  in. o.d.) stainless steel columns. The columns were: 20% silicone gum GE XE-60 on 60-80 mesh Chromosorb P (XEP), 20% Carbowax 20 M on 60-80 mesh Chromosorb P (CWP).

Cycloheptanone-2,2,7,7- $d_4$  was prepared using a procedure similar to that employed by Streitwieser<sup>18</sup> for the preparation of cyclopentanone-2,2,5,5- $d_4$ . About 34 g (1.68 moles) of deuterium oxide (99.8%), 47.5 g (0.424 mole) of cycloheptanone, 0.5 g of potassium carbonate, and 2 g of sodium chloride were heated at the mixture's reflux temperature for 24 hr. The aqueous and organic layers were separated. Five additional exchanges were performed. The deuterated cycloheptanone was distilled, bp 173-177°, affording 33.7 g (69%).

Cyclohexanone-2,2,6,6- $d_4$ . A solution consisting of 67.5 g (0.69 mole) of cyclohexanone, 150 g (7.5 moles) of deuterium oxide (99.8%), 8 ml of triethylamine, and 475 ml of anhydrous dioxane was refluxed for 22 hr. Deuterium oxide, water, triethylamine, and dioxane were removed by distillation. The exchange procedure was repeated four more times using approximately 80-g portions of deuterium oxide in combination with 10 ml of triethylamine and 500 ml of dioxane. Final distillation afforded 34.7 g (52%) of cyclohexanone-2,2,6,6- $d_4$ , bp 153-154°. Proton nmr analysis of the deuterated ketone showed that exchange of the four  $\alpha$ -hydrogens had taken place to an extent greater than 99%.

1-Chlorocycloheptene-2,7,7- $d_3$ . A solution of 23.2 g (0.207 mole) of cyclohexanone-2,2,6,6- $d_4$  in 20 ml of methylene chloride was added slowly to 52 g (0.25 mole) of phosphorus pentachloride in 530 ml of methylene chloride (4-5°). The mixture was stirred for 1 hr at this temperature, allowed to warm to 20° over a 1-hr period, and poured onto crushed ice. The methylene chloride layer was washed thoroughly with 40% sodium hydroxide solution and water and dried over anhydrous calcium chloride. The solvent was removed yielding a mixture of 1-chlorocycloheptene-2,7,7- $d_3$  and 1,1-dichlorocycloheptane-2,2,7,7- $d_4$ .

The crude chloride mixture was treated with potassium *t*-butoxide (10 g of potassium, 0.26 g-atom) in 350 ml of *t*-butyl alcohol (reflux 3 hr). The dehydrohalogenation products were poured into water and taken up in methylene chloride. The solution was washed extensively with water and dried over anhydrous calcium chloride. Distillation gave 20.1 g of product, bp 50-81° (13-16 mm). Chromatographed (CWP, 140°), redistilled, bp 52-53° (11 mm), lit.<sup>19</sup> (1-chlorocycloheptene) bp 54-58° (14 mm), 1-chlorocycloheptene-2,7,7- $d_3$ ,  $n_D^{25}$  1.4859, contained 2.89  $\pm$  0.06 deuterons per molecule, as assessed by proton nmr (biphenyl, quantitative internal standard). There was no visually discernible absorption in the olefinic proton region.

1-Chlorocyclohexene-2,6,6- $d_3$  was prepared following a synthetic procedure like that outlined for the preparation of 1-chlorocycloheptene-2,7,7- $d_3$ . Cyclohexanone-2,2,6,6- $d_4$  (31.6 g, 0.312 mole), phosphorus pentachloride (80.7 g, 0.392 mole), and potassium *t*-butoxide (14 g of potassium, 0.36 equiv, in 365 ml of *t*-butyl alcohol) afforded 18.6 g of crude 1-chlorocyclohexene-2,6,6- $d_3$ , bp 146-150°. The material was chromatographed (XEP, 100°) immediately prior to being used. No olefinic proton absorption was noticeable in the proton nmr spectrum of the chloride.

1-Chlorocyclohexene was prepared in a similar manner.

Reaction of 1-Chlorocycloheptene-2,7,7- $d_3$  and Phenyllithium. Into a 500-ml stainless steel bomb was placed 5.13 g (0.0384 mole) of 1-chlorocycloheptene-2,7,7- $d_3$  and 110 ml (0.113 mole) of 1.03 *M* phenyllithium solution.<sup>20</sup> The solution was heated at 150  $\pm$  10° for 1.3 hr. The bomb was cooled in air (30 min), ice water (30 min), and a Dry Ice-acetone bath (10 min). The reaction products

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were washed out of the bomb with water and ether. The ether layer was washed several times with water and dried over anhydrous calcium chloride. The solution was reduced to 50.0 ml and analyzed employing glpc. The reaction products included 1.83 g (35.8%; CWA, 110°) of 1-chlorocycloheptene-2,7,7-*d*<sub>3</sub> and 0.97 g (14.6%; CWA, 170°) of deuterated 1-phenylcycloheptene. Both compounds were isolated utilizing preparative glpc (CWP, 140; CWA, 170°). The nmr and infrared spectra of the recovered chloride were virtually identical with those of the starting material. Proton nmr analysis of the deuterated 1-phenylcycloheptene indicated the presence of  $0.17 \pm 0.02$  deuteron and  $1.96 \pm 0.12$  deuterons in the olefinic and saturated ring positions, respectively. The results of dmr measurements are reported in Table I and Figure 1.

**Salt-Free Phenyllithium.** About 220 ml (0.44 mole) of 2 *M* *n*-butyllithium in *n*-hexane (Alfa Inorganics) was maintained at 0° under an argon atmosphere. Iodobenzene (41.6 g, 0.204 mole) was added dropwise to the solution over a 20-min period. Stirring was continued at 0° for an additional 20 min. The phenyllithium precipitated out as a fine white solid. The solvent was filtered off and the precipitate washed successively with 200 ml of pentane, 150 ml of benzene, and two 150-ml portions of pentane. All manipulations were carried out under argon. The solvents had been distilled and stored over 4A Molecular Sieves. About 60 ml of anhydrous ether was added dropwise with stirring to the phenyllithium (0°). Double titration<sup>20b</sup> indicated that the solution was 1.43 *M* in phenyllithium.

**Catalyzed Coupling of 1-Chlorocyclohexene and Phenyllithium.** A solution of 6.01 g (51.7 mmoles) of 1-chlorocyclohexene, 0.747 g (8.79 mmoles) of piperidine, and 50 ml (85.0 mmoles) of 1.70 *M* salt-free phenyllithium solution in ether was heated in a sealed

ampoule at 35° for 66.5 hr. *t*-Butyl alcohol was added to the products. The solution was made up to 100 ml with ether. The products were analyzed employing glpc. The reaction products included 2.10 g (34.9%; XEA, 90°) of 1-chlorocyclohexene and 2.39 g (29.3%; XEA, 160°) of 1-phenylcyclohexene.

**Catalyzed Coupling of 1-Chlorocyclohexene-2,6,6-*d*<sub>3</sub> and Phenyllithium.** A solution of 8.87 g (74.4 mmoles) of 1-chlorocyclohexene-2,6,6-*d*<sub>3</sub>, 0.758 g (8.92 mmoles) of piperidine, and 50 ml (71.5 mmoles) of 1.42 *M* salt-free phenyllithium solution in ether was heated in a sealed ampoule at 35° for 155.5 hr. Water was used for quenching. Analysis of the reaction products by glpc indicated that 4.14 g (46.8%; XEA 60°) of 1-chlorocyclohexene-2,6,6-*d*<sub>3</sub> and 1.17 g (9.8%; XEA, 160°) of 1-phenylcyclohexene-*x-d*<sub>n</sub> were present. These compounds were isolated by glpc. The proton nmr and infrared spectra of the recovered 1-chlorocyclohexene-2,6,6-*d*<sub>3</sub> (XEP, 100°) were very similar to those of the starting material. The ratio of saturated to olefinic deuterons (dmr) was  $1.93 \pm 0.03$ . Both the proton and deuteron nmr spectra of the 1-phenylcyclohexene-*x-d*<sub>n</sub> (XEP, 160°) showed that 0.1 deuteron and 2.0 deuterons were present in the olefinic and saturated ring positions, respectively. The saturated deuteron absorption is shown in Figure 2B.

1-Phenylcyclohexene-2,6,6-*d*<sub>3</sub> was synthesized by way of a two-step sequence. Cyclohexanone-2,2,6,6-*d*<sub>4</sub> was converted to 1-phenylcyclohexanol-2,2,6,6-*d*<sub>4</sub> employing phenylmagnesium bromide. The recrystallized (pentane) carbinol, mp 61–65.5°, was dehydrated using formic acid.<sup>7c</sup> Chromatographed (XEP, 160°) 1-phenylcyclohexene-2,6,6-*d*<sub>3</sub> was deuterated to an extent greater than 99% (nmr). The ratio of saturated to olefinic deuterons as determined by dmr was  $2.1 \pm 0.1$ . Additional dmr data are provided in Table I and Figure 2.

## The Stereospecific Synthesis and Electronic Absorption Properties of *cis*- and *trans*-4-Acetoxyisopulegone

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**Abstract:** *trans*- (1a) and *cis*-4-acetoxyisopulegone (1e) have been synthesized stereospecifically from  $\alpha$ - and  $\beta$ -epoxyisopulegone, respectively. This chemical correlation supports the epoxide stereochemistry predicted by the "reverse octant rule." An unusual equilibrium between 1a and 1e is reported together with the thermal isomerization of these isomers to *cis*- and *trans*-2-acetoxypulegone. The optical rotatory dispersion and the absorption properties of 1a and 1e have been examined in detail and applied to the interpretation of the ultraviolet spectrum of 3-acetoxy-4-methyl-4-penten-2-one (3), a freely rotating system possessing the same chromophoric array.

The thermal elimination of acetic acid from both 4-acetoxyisopulegone (1)<sup>1a</sup> and 2-acetoxypulegone (2)<sup>1b</sup> to form menthofuran has been of special interest to us since we had observed an apparently analogous, although photochemical, cyclization in various desyl systems (Figure 1).<sup>1c</sup> Even though this comparison is somewhat tenuous in view of the fact that benzoin acetate is cleaved thermally to benzaldehyde and  $\alpha$ -ketopropiophenone,<sup>2</sup> the 4-acetoxyisopulegone molecule does offer the opportunity to restrict the orientation of the acetoxy and isopropenyl groups with respect to the ketone carbonyl. Since it has been shown in a number of instances that carbonyl  $n \rightarrow \pi^*$  transitions are influenced by the nature and relative orientation of  $\alpha$  substituents,<sup>3</sup> it was of interest to assess the effect of

these interactions upon the reactivity of the carbonyl  $n \rightarrow \pi^*$  state. In this accounting we relate the synthetic approach to and electronic absorption properties of the 4-acetoxyisopulegones as a foundation for future publications dealing with the photochemical behavior of these molecules.

The system selected for this investigation (1) may exist in two isomeric modifications which will be designated 1a for the isomer with an *axial* isopropenyl group and 1e for the isomer with an *equatorial* isopropenyl group. To date these isomers have not been separately characterized, and so the first objective was to remedy this deficiency by means of an independent stereospecific synthesis for each isomer.

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(3) C. Djerassi, "Optical Rotatory Dispersion: Applications to Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1960, pp 111–122; R. C. Cookson, *J. Chem. Soc.*, 282 (1954); H. Labhart and G. Wagniere, *Helv. Chim. Acta*, **42**, 2219 (1959); to mention only a few of the notable efforts in this area.