sociates HA-100 spectrometer with a variable temperature accessory. The ambient-temperature spectra were recorded in the frequency-sweep mode using an internal lock. The low-temperature fmr spectra were recorded in HR mode and sweep widths were calibrated by the sideband technique using a Hewlett-Packard Model 200AB audio oscillator and Model 5512A frequency counter. At low temperature, the sample was thermostated with precooled nitrogen gas passing through a vacuum-jacketed Dewar into the probe. The temperatures were measured immediately after recording spectra by inserting a calibrated thermocouple to the bottom of a dummy nmr tube containing the solvents and measuring the potential relative to a second thermocouple in ice water. Temperatures were reproducible to better than 0.5° but systematic error[50] probably reduced the accuracy to ± 1–$2°$. In order to ensure that true Lorentzian lineshapes were actually observed in our lineshape analysis, precautions were made to avoid the saturation of the nmr signals, and to use minimum filtering of noise.

All computer calculations were performed on an IBM 360/65 computer equipped with a University Computing Co. (UCC) digital incremental plotter. The computer program, DNMR2, used for calculation of the theoretical curves for the intramolecular exchange process, was written by Binsch and Kleir.[29] The program simulates complex exchange-broadened nmr spectra from chemical shifts, coupling constants, effective relaxation times, rate constants, populations, and certain scaling parameters. The effective transverse relaxation time (in seconds) was obtained from the line width at half-height ($W_{1/2}$) of the internal fluorotrichloromethane reference signal by the relationship $T_2 = 1/(\pi W_{1/2})$. In most cases, only two nuclei (the fluorine and the C_2 proton) were included in the calculation, since no difference was observed for the two- and four-nuclei calculations for the range of rate constants reported. By placing the theoretical spectrum on top of the experimental spectrum, the lineshapes of the two spectra could be compared. The exchange rate constant at the particular sample temperature was obtained from the calculated spectrum considered to be in best agreement with the experimental spectrum. The rate constants so obtained were considered to have uncertainty less than 5%.

Activation parameters were calculated by a program ACTENG, written by DeTar.[30] The calculations are based on a weighted least squares treatment which allows the use of data of different precision.

Acknowledgments. Funds for purchase of the Varian HA-100 were provided through an institution grant from the National Science Foundation to the University of Southern California. Partial support of this research by a grant from the Research Corporation is gratefully acknowledged.

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Stereochemistry of 9,10-Dihydroanthracenes. Preferred Conformations in *cis*-9,10-Dialkyl Derivatives[1,2]

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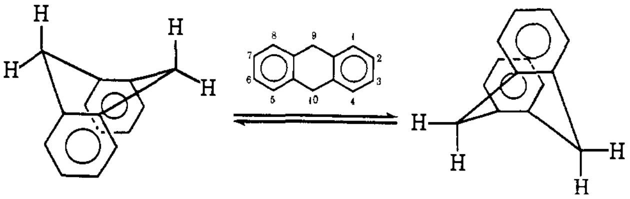
Contribution from the Department of Chemistry, Indiana-Purdue University at Indianapolis, Indianapolis, Indiana 46205. Received January 24, 1972

Abstract: The preferred orientation of alkyl groups in *cis*-1,4-dimethyl-9,10-dialkyl-9,10-dihydroanthracenes (and 1,4-dimethoxy) is shown to be diaxial with the alkyl groups rotated away from the 1 and 4 blocking groups. This produces some interesting nmr spectra as a result of diamagnetic anisotropy effects from the aromatic rings. For example, with diisopropyl derivatives, a methyl doublet appears upfield of the tetramethylsilane reference signal.

The conformational analysis of the 1,4-cyclohexadiene ring system has been the subject of a substantial number of investigations.[3-9] Unfortunately, the conformational preference of the parent 1,4-cyclohexadiene (planar *vs.* boat or equilibrating boats) remains a matter of controversy. On the other hand, 9,10-dihydroanthracene (**1**) has been shown by X-ray diffraction[10] to be nonplanar, and is presumed to undergo rapid ring inversion (nmr time scale) even at very low temperatures.[11] Only one report has appeared concerning the effect of aryl ring substitution on the ring inversion, and these authors[12] claimed that methoxy substituents inhibited this process. However, a reinvestigation of one of these compounds (2,3,6,7-tetramethoxy-9,10-dihydroanthracene) in our laboratories[13] suggests that this claim is untrue, and that substituents distant from the central ring do not affect the inversion process (as might be expected).



Controversy has also existed concerning the conformational preferences of 9-substituted 9,10-dihydroanthracenes (**2**). Earlier nmr results led some authors[14-16] to conclude that the conformation in which

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(1) This investigation was supported, in part, by a grant from the Eli Lilly Co., Indianapolis, Ind.

(2) A preliminary account of this work has been presented; P. W. Rabideau and J. W. Paschal, Abstracts of Papers, Third Central Regional Meeting of the American Chemical Society, Cincinnati, Ohio, 1971.

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(5) H. D. Stidham, *Spectrochim. Acta*, **21**, 23 (1965).

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(16) D. Nicholls and M. Szwarc, *Proc. Roy. Soc., Ser. A*, **301**, 231 (1967).

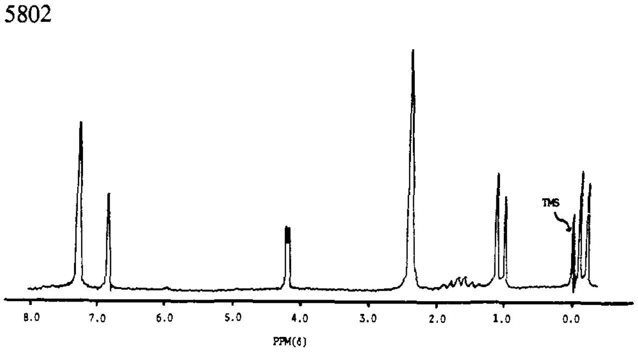
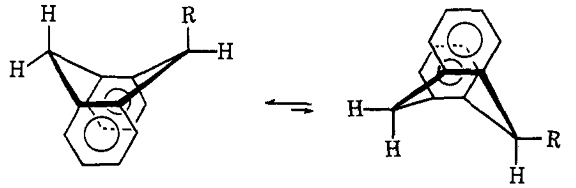


Figure 1. Nmr spectrum (CCl_4) of *cis*-1,4-dimethyl-9,10-diisopropyl-9,10-dihydroanthracene.



2 ⇌ 2′

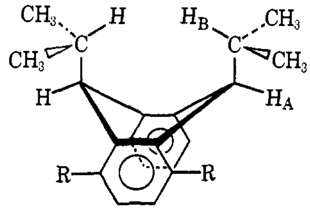
R is pseudoequatorial (**2′**) is favored over the pseudoaxial conformation **2**. However, their conclusions were based on chemical shift data using cyclohexane (chair form) as a model for the central ring in **1**, and a recent nmr study[17] involving long-range coupling constants and nuclear Overhauser effects, has shown that the preferred substituent position is actually psuedoaxial (**2**).

Less information is available concerning the effect of more than one substituent in the 9 and 10 positions. However, it appears as though *trans*-9,10-dialkyl-9,10-dihydroanthracenes also undergo rapid inversion, whereas the cis systems presumably exist in a fixed diaxial conformation.[18] It should be noted, however, that these studies have been concerned with the effect of substituents on the conformational preferences of the dihydroanthracene ring system. One might also consider the effect of this ring on any conformational preferences of the substituents. In fact, Zieger, *et al.*,[19] investigated the nmr spectrum of cis-9,10-diisopropyl-9,10-dihydroanthracene (**3**) and suggested that the relatively large constant for the coupling of the isopropyl methines with the 9 and 10 protons (J_{AB} = 9.5 Hz; see figure) indicated restricted rotation of the isopropyl groups leading to a large dihedral angle (H_AH_B near 180°). These results stimulated our interest in this type of study, and our results indicate that preferred conformations of substituents do exist and lead to some highly interesting nmr spectra.

Results

In an attempt to provide information regarding the possibility of preferred conformations in *cis*-9,10-dialkyl-9,10-dihydroanthracenes (cf. ref 19), we prepared *cis*-1,4-dimethyl-9,10-diisopropyl-9,10-dihydroanthracene (**4**). This is, of course, related to **3**, but the methyl groups on the 1 and 4 positions add an element of dissymmetry which in principle should lead to a more informative nmr spectrum.

The preparation of **4** was achieved by reductive isopropylation[20] of 1,4-dimethylanthracene in liquid ammonia, which led to a single isomer. This cis assignment was made on the basis of the nmr spectrum (discussed below) and on the basis of previous studies[21] concerning the blocking effect of 1 and 4 substitution on the equatorial 9,10 positions in dihydroanthracenes.



3, R = H
4, R = CH_3
5, R = OCH_3

The nmr spectrum (Figure 1) showed aromatic signals as two singlets[22] at δ 7.12 (4 H) and 6.85 (2), the bridgehead protons as a doublet at 4.1 (2, J = 2 Hz), the benzylic methyls at 2.38 (s,6), and the isopropyl methine protons as a multiplet at 1.6 (2). Quite unexpectedly, however, the isopropyl methyls appeared as two doublets (J = 7 Hz), one at 1.07 and the other at −0.13, *upfield of TMS.* This apears to be a rather unusual high field shift for a methyl group shielded by a simple benzene ring,[23,24] and we offer the following explanation. Although one would expect a difference in chemical shifts between two pairs of isopropyl methyls[25] on the basis of a diastereotopic[26] relationship, the magnitude can be estimated at 15 Hz, the observed chemical shift difference in isopropyl methyls as a result of intrinsic assymetry in the monoisopropyl-1,4-dimethyl-9,10-dihydroanthracene.[21] The observed difference of 71 Hz in **4** is certainly not consistent with a simple diastereotopic relationship involving freely rotating isopropyl groups.[27] We feel that the most reasonable explanation involves a preferred conformation[28] with the isopropyl groups turned toward the unsubstituted ring (and away from the 1 and 4 methyls) producing the observed shielding.[29] This is also consistent with the relatively small bridgehead–isopropyl methine

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[17] A. W. Brinkman, M. Gordon, R. G. Harvey, P. W. Rabideau, J. B. Stothers, and A. L. Ternay, *J. Amer. Chem. Soc.*, **92**, 5912 (1970).

[18] (a) R. G. Harvey and L. Arzadon, *Tetrahedron*, **25**, 4887 (1969), and references therein; (b) R. B. Williams and H. R. Snyder, *J. Org. Chem.*, **36**, 2327 (1971).

[19] H. E. Zieger, D. J. Schaeffer, and R. M. Padronaggio, *Tetrahedron Lett.*, 57, 5027 (1969).

[20] R. G. Harvey, *Synthesis*, 161 (1970), and references therein.

[21] A. L. Ternay, Jr., A. W. Brinkman, S. Evans, and J. Hermann, *Chem. Commun.*, 654 (1969).

[22] Aromatic protons appearing as singlets are characteristic of *cis*-9,10-dialkyl-9,10-dihydroanthracenes, but not the trans isomers. D. A. Redford, Ph.D. Thesis, University of Saskatchewan, 1967.

[23] Albeit, a considerably greater shielding is observed from annulene systems, *e.g.*, V. Boekelheide and J. B. Phillips, *Proc. Nat. Acad. Sci. U. S.*, **51**, (1964).

[24] A similar example of methyl signals appearing upfield of TMS was recently reported: B. L. Shapiro, M. J. Gattusco, and G. R. Sullivan, *Tetrahedron Lett.*, 223 (1971).

[25] The possibility that the isomer assignment is incorrect and that the two doublets arise from an axial and an equatorial isopropyl in a trans isomer is ruled out since this presumably would lead to two different aryl methyl chemical shifts and two different bridgehead chemical shifts (since they would also consist of axial and equatorial).

[26] K. Mislow and M. Raban, *Top. Stereochem.*, **2**, 218 (1967).

[27] Differences in shifts due to diastereotopic relationships are normally small (*cf.* ref 9).

[28] The spectrum is essentially unchanged at 150° (in $CHCl_2CHCl_2$).

[29] C. E. Johnson, Jr., and F. A. Bovey, *J. Chem. Phys.*, **29**, 1012 (1958).

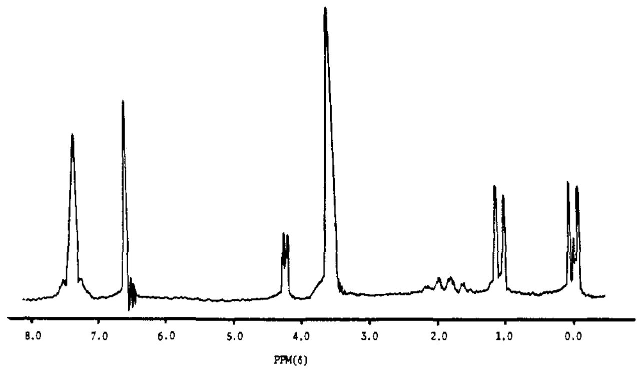
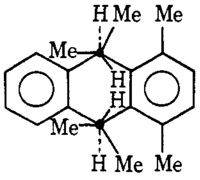


Figure 2. Nmr spectrum ($CDCl_3$) of *cis*-1,4-dimethoxy-9,10-diisopropyl-9,10-dihydroanthracene.



coupling constant which would be expected by the resulting dihedral angle.[30,31]

Even though the nmr spectrum was temperature independent,[28] we felt it would be of interest to investigate any changes related to solvation. We determined the nmr spectrum of **4** in several solvents, and the results are presented in Table I. Although it would be difficult to explain fully the effect of solvents, it is interesting to note the relatively large variations in $\Delta\nu$. For example, the two doublets are 15 Hz closer together in 1-bromonaphthalene than in acetone. Since the changes in chemical shifts are relatively large and in opposite directions, it can be assumed that the effect is not simply due to the diamagnetic anisotropy of the solvent. Hence, the effect may be due to transient collision complexes or possibly minor changes in the preferred conformation (or equilibrium) due to solvation.

Table I. Solvent Effects on the Nmr Spectrum of **4**[a]

	Isopropyl methyl doublets		
Solvent	High field[b]	Low field[b]	$\Delta\nu$, Hz
CCl_4	−0.13	1.07	71
Acetone-d_6	−0.15	1.08	74
DMSO-d_6	−0.22	1.01	64
Benzene-d_6	+0.07	1.01	58
Pyridine-d_5	−0.01	1.03	65
1-Bromonaphthalene	−0.05	0.95	59

[a] Concentrations of ~10%. [b] Parts per million.

In order to determine the generality of our observations, we sought a system with different blocking groups. Hence, we prepared *cis*-1,4-dimethoxy-9,10-diisopropyl-9,10-dihydroanthracene (**5**). The nmr spectrum (Figure 2) was analogous with that of **4** in that two doublets were observed for the isopropyl methyl groups, although the separation was not as large. This seems to indicate that the methoxy groups are exerting less steric interference in **5**, as compared with the methyls in **4**, which is consistent with known stereochemical results in the cyclohexane system (*i.e.*, *A* values).[32] It is also noted that **5** was less sensitive to solvent effects (Table II), and the addition of a rare earth shift reagent [Eu(fod)$_3$] produced no significant changes in chemical shift. The reason for this failure is unknown, but may be the result of steric interference of complex formation. Hence, the nmr spectrum of **5** suggests a preferred conformation similar to that postulated for **4**, although the isopropyl groups may not be rotated to quite the same extent.

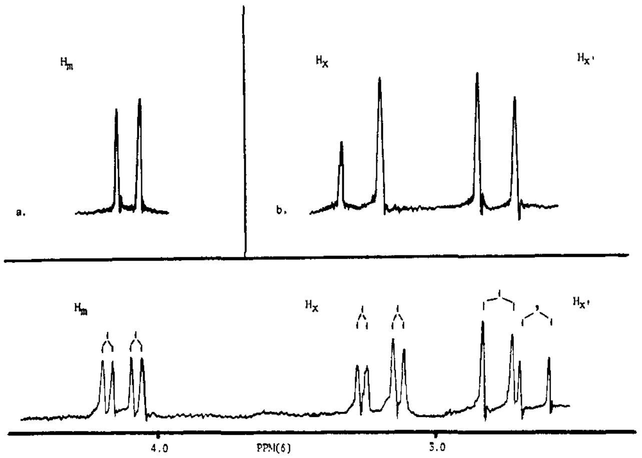


Figure 3. Partial nmr spectrum (CS_2) of *cis*-1,4-dimethyl-9,10-dibenzyl-9,10-dihydroanthracene; (a) H_m with double irradiation at H_x, (b) H_x,$H_{x'}$ with double irradiation at H_m.

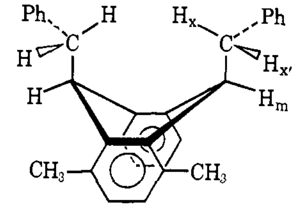
Table II. Solvent Effects on the Nmr Spectrum of **5**[a]

	Isopropyl methyl doublets		
Solvent	High field[b]	Low field[b]	$\Delta\nu$, Hz
CCl_4	−0.08	0.95	62
DMSO-d_6	−0.07	0.92	63
Acetone-d_6	−0.03	0.97	62
Benzene-d_6	0.20	1.10	56
Pyridine-d_5	0.10	1.05	58

[a] Concentration 10%. [b] Parts per million.

Thus far, chemical shift data have led us to propose preferred conformations as a result of blocking effects from the 1 and 4 positions. We became interested in synthesizing compounds that would exhibit these effects in a more quantitative manner, *e.g.*, coupling constants.

This led us to prepare *cis*-1,4-dimethyl-9,10-dibenzyl-9,10-dihydroanthracene (**6**),[33] and once again a conformational preference was indicated by the nmr spectrum (Figure 3). This was determined by the observa-



6

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[30] M. Karplus, *J. Amer. Chem. Soc.*, **85**, 2870 (1963).

[31] Nuclear Overhauser experiments were carried out on **4**, but significant enhancements were not observed. The reason for this was not investigated and subsequent use of this technique was not attempted.

[32] E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Wiley, New York, N. Y., 1965, p 44.

[33] Cis assignment based on arguments similar to those presented for **4**.

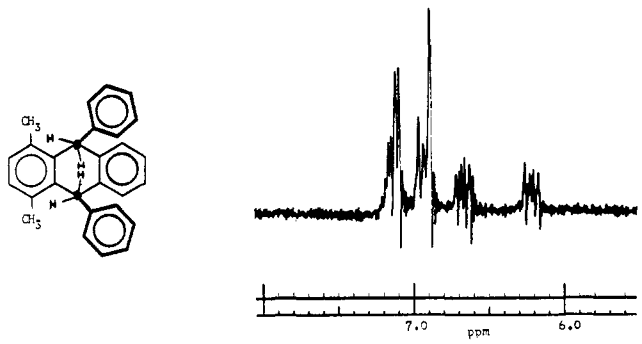

Figure 4. Partial nmr spectrum (aromatic region) of **6**.

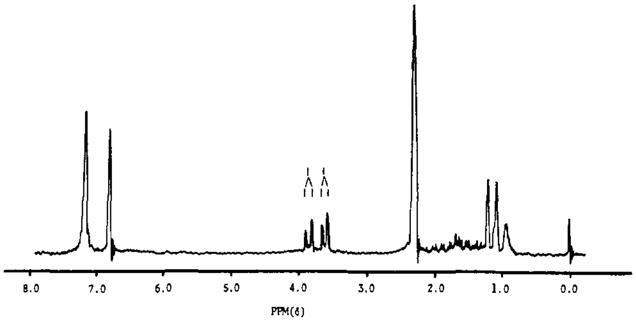

Figure 5. Nmr spectrum (CCl_4) of *cis*-1,4-dimethyl-9,10-diethyl-9,10-dihydroanthracene.

tion of different coupling constants between H_x and H_m (J_{xm} = 10.5 Hz), and $H_{x'}$ and H_m ($J_{x'm}$ = 4.0), confirmed by double irradiation experiments (Figure 3a and b). Since an equal population of rotameric conformations would lead to equivalent H_xH_m and $H_{x'}H_m$ dihedral angles as a result of averaging, the observed quite different coupling constants indicate significant differences for the two dihedral angles.[30,34] In addition, the 5, 6, 7, 8 aromatic protons were significantly shielded (an AA′ BB′ multiplet centered at δ 6.45 (4 H), and this seems to indicate a preferred conformation in which the benzyl groups are turned toward the unsubstituted ring (leading to the shielding[29]). This proposed preferred conformation, and its effect on the aromatic region of the nmr spectrum is shown in Figure 4.

An analogous structural feature is found with *cis*-1,4-dimethyl-9,10-diethyl-9,10-dihydroanthracene (**7**). Unfortunately, the regions of greatest interest in the nmr spectrum are rather complex. However, we interpret the methine signal (Figure 5) to be indicative of the X portion of an ABX pattern with unequal coupling constants (J_{AX} and J_{BX}) of 10 and 4 H_z. This is once again consistent with a preferred conformation analogous to those described earlier.

Experimental Section

Nmr spectra were recorded on Varian HA-100, A60-A, and T60 spectrometers. Melting points were determined by a capillary method and are uncorrected.

1,4-Dimethylanthracene.[35] This was prepared in the normal manner by the acylation of *p*-xylene with phthalic anhydride followed by ring closure with fuming sulfuric acid to form 1,4-dimethylanthraquinone. The anthraquinone was reduced in high yield using activated ($CuSO_4$) zinc dust,[36] 2 *N* NaOH, and toluene with the mixture at reflux for 5 days.

Metal-Ammonia Reductive Alkylations. All of the compounds used in this study were prepared by metal-ammonia reductive alkylations.[20] In a typical experiment, the appropriate anthracene (5 mmol) dissolved in anhydrous ether (50 ml) was added to liquid ammonia (100 ml), followed by lithium wire (12.5 g-atoms). After 15 min, the alkyl halide (in an equal amount of ether) was added quickly until the dark color was discharged. Ammonium chloride and water were then added and the product was isolated in the usual manner. Yields were not maximized.

***cis*-1,4-Dimethyl-9,10-diisopropyl-9,10-dihydroanthracene (4).** This was prepared by the above method from 1,4-dimethylanthracene and isopropyl bromide. Recrystallization from ethanol gave white crystals in 50% yield, mp 105°. Nmr is described under results and in Figure 1.

Anal. Calcd for $C_{22}H_{28}$: C, 90.35; H, 9.65. Found: C, 90.48; H. 9.63.

***cis*-1,4-Dimethoxy-9,10-diisopropyl-9,10-dihydroanthracene (5).** This was prepared by the above method from 1,4-dimethoxyanthracene (Aldrich) and isopropyl bromide. Recrystallization from methanol gave white crystals in 40% yield, mp 104–106°. Nmr is given in Figure 2.

Anal. Calcd for $C_{22}H_{28}O_2$: C, 81.95; H, 8.63. Found: C, 81.55; H, 8.37.

***cis*-1,4-Dimethy-9,10-dibenzyl-9,10-dihydroanthracene (6).** This was prepared by the above method from 1,4-dimethylanthracene and benzyl chloride. Recrystallization from ethanol gave white crystals in 40% yield, mp 215–218°. Nmr is given in Figures 3 and 4.

Anal. Calcd for $C_{30}H_{28}$: C, 92.74; H, 7.26. Found: C, 92.49; H, 7.15.

***cis*-1,4-Dimethyl-9,10-diethyl-9,10-dihydroanthracene (7).** This was prepared by the above method from 1,4-dimethylanthracene and ethyl bromide.[37] Recrystallization from ethanol gave white crystals in 75% yield, mp 93–94°. Nmr is given in Figure 5.

Anal. Calcd for $C_{20}H_{24}$: C, 90.85; H, 9.15. Found: C, 91.19; H, 9.14.

Acknowledgment. We would like to thank the Eli Lilly Company for use of their 60- and 100-MHz nmr instruments, and Dr. P. Demarco for helpful comments.

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[34] For a recent application of this approach, see F. Schweinsberg and J. G. Traynham, *Tetrahedron Lett.*, 3809 (1970).

[35] S. V. Kessar, V. P. Kubba, and S. M. Mukherji, *J. Indian Chem. Soc.*, **32**, 697 (1955).

[36] L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis," Wiley, New York, N. Y., 1967, p 1282.

[37] This is identical with material prepared by addition of ethyllithium followed by ethyl bromide: R. G. Harvey, private communication.