Determination of the Configuration of Tricyclo[4.2.2.0^{2,5}]-7-decenes by Means of Vinyl Proton Nuclear Magnetic Resonance

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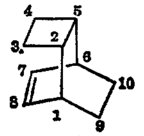
The configurations of the four-membered ring and its substituents in some derivatives of the title compound (*e.g.*, 2) have been established by an examination of the vinyl proton nmr.

The nmr shielding of protons situated above the plane of a double bond is a well-known phenomenon.[3,4] This effect has been exploited for structural studies,[5,6] conformational analysis,[7] and for the assignment of configuration in maleopimaric acid,[8,9] bicyclo[2.2.1]heptenes,[10-13] and bicyclo[2.2.2]octenes.[14] As a general rule the structural environment of a proton has been determined by comparing its nmr absorption in the presence of the double bond to that in a saturated analog.

The tricyclo[4.2.2.0^{2,5}]-7-decene system (**1**) is especially suited to an investigation of this type. The geometry of the ten-carbon framework requires *endo* substituents on the four-membered ring to be imbedded in the π cloud of the 7-double bond. We have made use of the resulting perturbation in the nmr spectrum to assign the configuration of the four-membered ring and the 3,4 substituents. In contrast to the earlier work, which concentrated on the fate of the proton immersed in the π cloud, we have made use of the changes induced in the vinyl proton resonance.[15]



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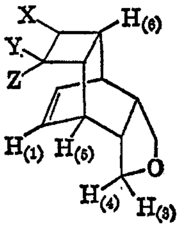
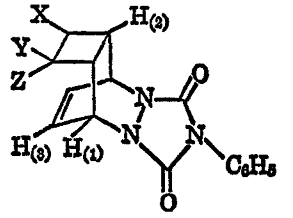
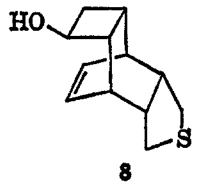
Compounds 2–16 are representative.[17] The spectra of the *cis* and *trans* tetrahydrofuran dibromides 2 and 3 are presented in Figure 1. The former possesses a fairly sharp triplet at τ 3.64 corresponding to the vinyl hydrogens H_1 split by each bridgehead proton, H_5. Because of the potential complexity of A_2X_2 spectra[18] and the inadequate resolution of those in hand, it is impossible to assign coupling constants. Nevertheless, it is clear that the nmr in the vinyl region for 2 is quite different from that for 3. The protons in 2 α to bromine, H_2, are registered as a sharp but unsymmetrical doublet at τ 5.81. The observed splitting is consistent with the expected coupling with the tertiary cyclobutane hydrogens, H_6. The methylene protons on the tetrahydrofuran ring give rise to a characteristic multiplet from τ 6.0 to 6.8; it is probable that the upfield multiplet corresponds to the inner protons, H_4, shielded by the double bond. The remaining hydrogens appear as a featureless smear from τ 7.0 to 8.0.



2, Z = $H_{(2)}$; X = Y = Br
3, Y = $H_{(2)}$; X = Z = Br
6, X = Z = H; Y = OH
7, X = Y = H; Z = OH



4, Z = $H_{(4)}$; X = Y = Cl
5, Y = H; X = Z = Br
13, X = Z = H; Y = OH
14, X = Y = H; Z = OH



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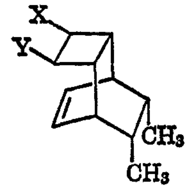
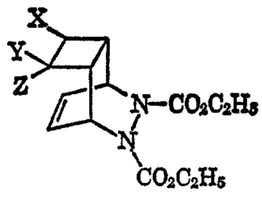
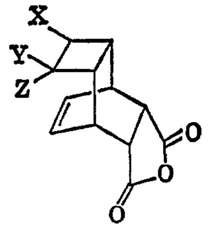


9, X = H; Y = OH
10, XY = –O–



11, Y = H; X = Z = Br
12, X = Y = H; Z = OH



15, X = Z = Br; Y = H
16, X = Y = Br; Z = H

The spectrum of *trans*-dibromide **3** is quite similar to that of the *cis* isomer **2** except for two significant features. The hydrogens α to bromine have now been separated. The *endo* hydrogen is observed as an unsymmetrical quartet at τ 5.82, a chemical

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[3] L. M. Jackman, "Applications of Nuclear Magnetic Resonance in Organic Chemistry," Pergamon Press Inc., New York, N. Y., 1961, p 112.

[4] J. R. Dyer, "Applications of Absorption Spectroscopy of Organic Compounds," Prentice-Hall, Inc., Englewood Cliffs, N. J., 1965, pp 79–83.

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[6] G. Slomp, F. A. Mackellar, and L. A. Paquette, *ibid.*, **83**, 4472 (1961).

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[8] W. L. Meyer and R. W. Huffman, *Tetrahedron Letters*, 691 (1962).

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[10] F. A. L. Anet, *Tetrahedron Letters*, 1219 (1962).

[11] H. E. Simmons, *J. Am. Chem. Soc.*, **83**, 1657 (1961).

[12] R. R. Fraser, *Can. J. Chem.*, **40**, 78 (1962).

[13] K. Tori, Y. Hata, R. Muneyuki, Y. Takano, T. Tsuji, and H. Tanida, *ibid.*, **42**, 926 (1964).

[14] K. Tori, Y. Takano, and K. Kitahonoki, *Chem. Ber.*, **97**, 2798 (1964).

[15] Laszlo and Schleyer[16] have noted this effect in 5-*endo*-chloronorbornene and 5,5-dichloronorbornene. The response of the vinyl protons is smaller and more erratic than that reported in the current work, presumably because of the greater distance between the perturbing group and the double bond.

[16] P. Laszlo and P. von R. Schleyer, *J. Am. Chem. Soc.*, **86**, 1171 (1964).

[17] The syntheses and characterization of **2**, **3**, **5**, **15**, and **16** are described in D. G. Farnum and J. P. Snyder, *Tetrahedron Letters*, 3861 (1965). The syntheses and characterization of the remaining compounds will be reported in a subsequent paper.

[18] K. B. Wiberg and B. J. Nist, "The Interpretation of NMR Spectra," W. A. Benjamin, Inc., New York, N. Y., 1962, p 309 ff.

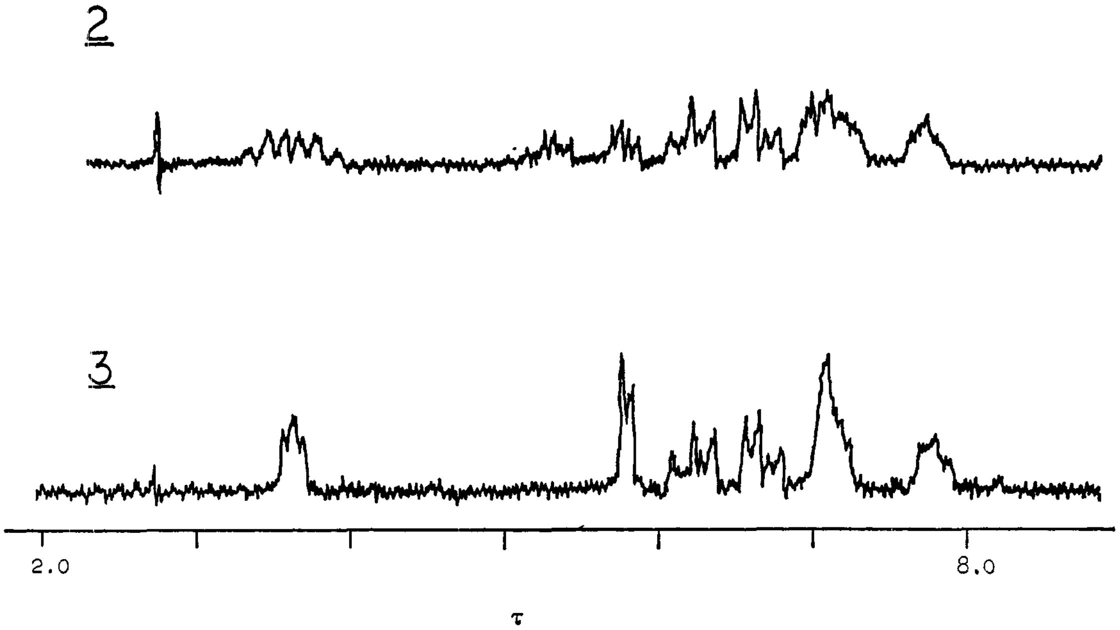

Figure 1.—Nmr spectra of *cis*-dibromide 2 and *trans*-dibromide 3.

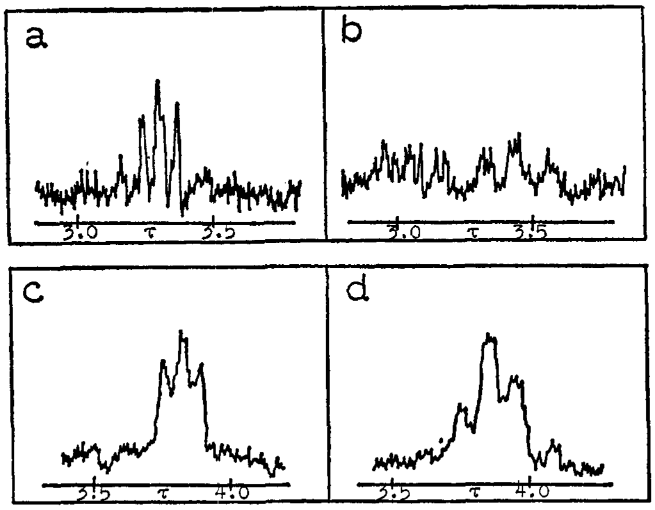

Figure 2.—Nmr spectra of the vinyl protons for several tricyclodecanes: (a) *cis*-dichloride 4, (b) *trans*-dibromide 5, (c) *exo*-alcohol 6, (d) *endo*-alcohol 7.

shift identical with that for the corresponding *endo* hydrogens of the *cis*-dibromide 2. The *exo* hydrogen, on the other hand, does not experience the shielding influence of the lower π-electron cloud and thus is detected as a skewed quartet at τ 5.31. The splitting of these hydrogens is consistent with an ABX pattern,[19] although, again, it would be fruitless to assign coupling constants. The second revealing difference is the absorption of the vinyl hydrogens H_1. Two broad, unsymmetrical, overlapping triplets are seen at τ 3.47 and 3.81, respectively. The *endo* bromine apparently alters the local magnetic environment about the double bond and destroys the vinyl hydrogen equivalency.

Identical behavior is observed for the urazole dihalo epimers 4 and 5. *cis*-Dichloride 4 exhibits five nmr signals with the appropriate area ratios. Peaks at τ 2.60, 4.79, and 6.58 are assignable to the phenyl hydrogens, the bridgehead hydrogens H_1, and to the cyclobutane pair H_2, respectively. Analogous to the *cis*-dibromide 2, *cis*-dichloride 4 affords a sharp triplet at τ 3.30 for the vinyl hydrogens, H_3 (see Figure 2a), and a well-defined doublet at τ 5.84 corresponding to the protons α to chlorine, H_4, respectively. In contrast the urazole *trans*-dibromide 5 continues the pattern observed with the furan *trans*-dibromide 3. The *endo* (τ 5.78) and *exo* (τ 5.26) hydrogens are again separated, and the nonequivalency of the vinyl protons results in the appearance of a pair of ragged triplets at τ 3.03 and 3.44 (see Figure 2b).

Two important structural details about compounds 2–5 are thus revealed by the observations made above. The configuration of the cyclobutane ring is without a doubt *syn* to the double bond. Likewise the epimeric nature and configuration of the vicinal dihalides is unequivocally established.

The relatively sharp triplet observed for the vinyl hydrogens in *cis*-*exo*-dihalides 2 and 4 arises from the equivalence of the vinyl hydrogens and the fortuitous near equivalence of the coupling constants. Equivalence of the vinyl hydrogens is a sufficient but not a necessary condition for the appearance of a triplet vinyl resonance. Thus, the secondary *exo*-alcohol 6 does not destroy the essential vinyl band multiplicity or shape even though it obscures the fine structure of the signal (Figure 2c). The broadened and skewed character of the vinyl proton multiplet for *endo*-alcohol 7 is depicted in Figure 2d.

The phenomenon described above is general for the tricyclo$[4.2.2.0^{2,5}]$-7-decene system. Symmetrical *endo* substitution on the cyclobutane ring is evidenced by the appearance of a reasonably sharp symmetrical triplet for the vinyl hydrogen pair. Unsymmetrical *endo* substitution, and the resultant unsymmetrical magnetic environment, is reflected in increased multiplicity and broadening of the vinyl proton resonance. For example, symmetrical triplet absorption is observed for the *exo*-alcohols 8 and 9, and the dimethyl epoxide 10, while the *trans*-carbethoxy dibromide 11 exhibits a broad multiplet (Figure 3).

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(19) See ref 18, p 22.

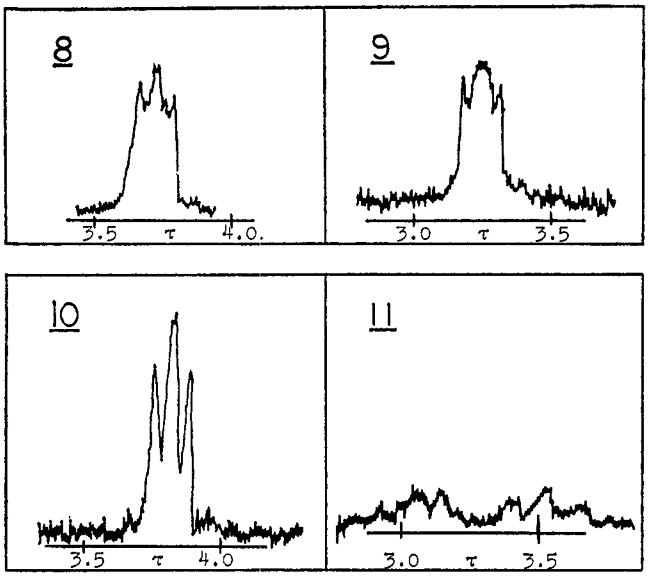


Figure 3.—Nmr spectra of the vinyl protons of *exo*-alcohols **8** and **9**, epoxide **10**, and *trans*-dibromide **11**.

The utility of the method is illustrated in two ways. Dicarbethoxy alcohol **12**, obtained by sodium borohydride reduction of the corresponding ketone, possesses an inordinately complex spectrum except in the olefinic region. Although the cyclobutane hydrogen resonances were buried in the saturated hydrogen resonance, the *endo* disposition of the hydroxyl group was assignable on the basis of the broad unsymmetrical multiplet for the vinyl protons centered at τ 3.28 (Figure 4). A different type of problem was encountered in the insolubility of the epimeric hydroxyl and dibromide pairs **13**,**14** and **15**,**16** in common nmr solvents. However, in tetrahydrofuran and dimethyl sulfoxide these systems portrayed their diagnostic olefinic hydrogens unobscured by solvent absorption (Figure 5). The configuration of both the four-membered ring and its substituents was thus easily determined. It should be mentioned that *trans*-dibromide **15** has received considerable attention with respect to the question of the disposition of the four-membered ring.[20]

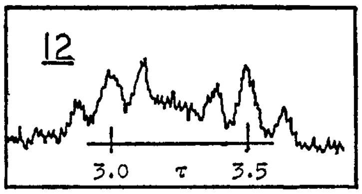


Figure 4.—Nmr spectrum of the vinyl protons of alcohol **12**.

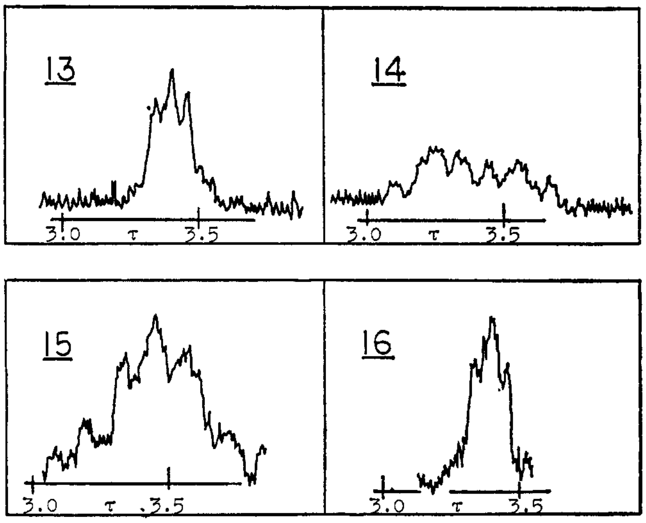
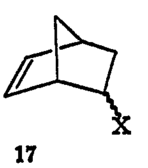
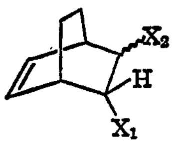


Figure 5.—Nmr spectrum of the vinyl protons of *exo*-alcohol **13**, *endo*-alcohol **14**, *trans*-dibromide **15**, and *cis*-dibromide **16**.



17

19, X=NO$_2$



18

20, X$_1$=X$_2$=*endo*-CO$_2$CH$_3$

21, X$_1$=CO$_2$CH$_3$;
X$_2$=*exo*-CO$_2$CH$_3$

2,3-Substituted bicycloheptenes (**17**) and bicyclooctenes (**18**) also fall within the scope of the above described method.[15] Thus, the published spectrum of *endo*-2-nitrobicyclo[2.2.1]-5-heptene (**19**) exhibits a pair of unsymmetrical well-separated doublets centered at τ 3.87.[12] While hydrogen shifts on the 1 and 2 hydrogens were employed for a configurational assignment of the nitro group, the olefinic region displays at a glance the characteristic pattern for *endo* substitution. Furthermore, while our work was in progress, Dinwiddie and McManus reported the observation of similar splitting of vinyl resonances in a number of *endo*-substituted bicycloheptenes.[21] Likewise, the stereochemistry of dicarbomethoxybicyclooctenes **20** and **21** was elucidated by comparing the nmr shifts of hydrogens buried in the olefinic π cloud.[14] Use of the criterion established in this work confirms the assignment with the appearance of a sharp symmetrical sextet at τ 3.67 for the diester **20** and a very much broadened multiplet also centered at τ 3.67 for its epimer **21**.

Experimental Section

The synthesis of the compounds used in this work will be described elsewhere.[17] The melting points are given in Table I as

TABLE I

Compd	Mp, °C	Nmr solvent
2	104.5–105.5	CDCl$_3$
3	174.5–176.0	CDCl$_3$
4	258–258	CDCl$_3$
5	254–258	CDCl$_3$
6	104–105	CDCl$_3$
7	86–88	CDCl$_3$
8	91–95	CDCl$_3$
9	55–60	CDCl$_3$
10	60–61.5	CDCl$_3$
11	121–122	CDCl$_3$
12	93–94	Acetone-d_6
13	178–180	THF
14	219–220.5	THF
15	209.5–211	CDCl$_3$
16	255–260	DMSO

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[20] M. Avram, G. Mateescu, and C. D. Nenitzescu, *Ann.*, **636**, 184 (1960), and references contained therein.

[21] J. G. Dinwiddie, Jr., and S. P. McManus, *J. Org. Chem.*, **30**, 766 (1965).

a means of characterization. All new compounds were characterized by elemental analyses within 0.5% of the calculated values.

Nmr spectra were determined on a Varian A-60 instrument at its operating temperature (*ca.* 35°) on samples of 5% w/v in the solvent indicated in Table I. They were referenced against internal chloroform (τ 2.73), tetramethylsilane (τ 10.0), or both. Reported spectra were determined at 500 cps full scale width.

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The Reduction of *gem*-Dibromocyclopropanes to Monobromocyclopropanes with Methylmagnesium Bromide

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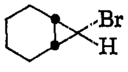
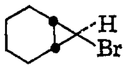
Methylmagnesium bromide in tetrahydrofuran solution reduces *gem*-dibromocyclopropanes to monobromocyclopropanes in good yields. Evidence is presented which suggests that this reaction occurs by a radical process with the hydrogen atom introduced into the product deriving from the solvent.

The conversion of the easily accessible *gem*-dibromocyclopropanes to monobromocyclopropanes has been a subject of some interest in recent years. Reagents which serve for this purpose include zinc dust in glacial acetic acid,[3] hydrogen (using a platinum catalyst in methanolic potassium hydroxide),[3] tri-*n*-butyltin hydride,[4] and the sodium salt of dimethyl sulfoxide (DMSO) in DMSO solution.[5] We report here that this reduction can be effected simply and in good yield by reaction of *gem*-dibromocyclopropanes with methylmagnesium bromide in tetrahydrofuran (THF) solution at room temperature.

Addition of 7,7-dibromobicyclo[4.1.0]heptane (henceforth 7,7-dibromonorcarane) to an equimolar quantity of methylmagnesium bromide in THF resulted in an exothermic reaction with precipitation of solid after a short induction period. Hydrolysis with saturated ammonium chloride gave an organic layer which was distilled to give a mixture of *cis*- and *trans*-7-bromonorcarane (I) in 72.4% yield. Glpc analysis showed the *cis*/*trans* ratio to be 2.7. (In other experiments this ratio varied between this value and 2.2.) Similar reduction of 1,1-dibromo-2-*n*-amylcyclopropane was easily effected by this procedure, giving *trans*-1-bromo-2-*n*-amylcyclopropane (21%) and its *cis* isomer (54.2%). The monobromocyclopropanes thus produced were themselves unaffected by CH_3MgBr in THF at reflux.

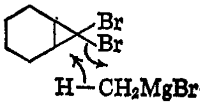

cis-I


trans-I

Further work was concerned with a study of the mechanism of this apparently general reaction. In view of the known RMgX–R′X exchange reactions, which appear to be facilitated by THF solvent,[6] a mechanism involving exchange of CH_3MgBr with the *gem*-dibromocyclopropane to give II in the case of 7,7-dibromonorcarane seemed a possibility that required consideration. Hydrolysis of II would then result in formation of the observed product. However, α-haloalkylmagnesium halides are, in general, not stable at room temperature,[7] and thus the survival of II until the hydrolysis step did not seem likely. That hydrolysis of II was not the reaction which produced product was shown by treatment of such a methylmagnesium bromide–7,7-dibromonorcarane reaction mixture with D_2O. The intervention of II as a *stable* intermediate in this reduction reaction would require formation in this case of 7-bromo-7-deuterionorcarane. However, the bromonorcarane obtained did not contain deuterium. Also, quenching of such a reaction mixture with trimethylchlorosilane gave only 7-bromonorcarane, not the trimethylsilyl derivative that might have been expected if II were a stable intermediate. Furthermore, nonhydrolytic work-up of such a CH_3MgBr + 7,7-dibromonorcarane reaction mixture gave 7-bromonorcarane.


II

Another possible mechanism, reduction of the dibromonorcarane directly by the Grignard reagent *via* a transition state such as III, was shown not to be operative by carrying out the reduction using CD_3MgI in THF. In this case also the 7-bromonorcarane isolated contained no deuterium.


III

Elimination of these possibilities leaves as possible alternatives (1) a route in which an α-bromocyclopropylmagnesium bromide such as II is only a transient intermediate which abstracts a hydrogen atom from a solvent molecule by a polar or a radical process, and (2) direct radical reduction of *gem*-dibromocyclopropanes by methylmagnesium bromide (eq 1 and 2), with the hydrogen atom introduced into the product being provided by the solvent as shown.

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(1) Alfred P. Sloan Fellow, 1962–1966.

(2) Postdoctoral Research Associate, 1964–1966.

(3) K. Hofmann, S. F. Orchena, S. M. Sax, and G. A. Jeffrey, *J. Am. Chem. Soc.*, **81**, 992 (1959).

(4) D. Seyferth, H. Yamazaki, and D. L. Alleston, *J. Org. Chem.*, **28**, 703 (1963).

(5) C. L. Osborn, T. C. Shields, B. A. Shoulders, C. G. Cardenas, and P. D. Gardner, *Chem. Ind.* (London), 766 (1965).

(6) L. I. Zakharkin, O. Yu. Okhlobystin, and K. A. Bilevich, *J. Organometal. Chem.* (Amsterdam), **2**, 309 (1964); *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 1347 (1964).

(7) H. Normant and J. Villieras, *Compt. Rend.*, **260**, 4535 (1965).