Formation of Grignard Reagents from cis- and trans-β-Bromostyrenes

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Received June 16, 1964

Grignard solutions from cis- or trans-bromostyrene were found to contain cis- and trans-styrylmagnesium bromide, ω-phenylethynylmagnesium bromide, phenylacetylene, and styrene by inspecting the n.m.r. spectra of the D₂O addition products of the Grignard solutions. Dependence of both the ratio of styrylmagnesium bromide to the by-products and retention of the original cis or trans configuration on the various experimental conditions were examined. Possible mechanisms for the reaction are considered and it is concluded that (1) phenylacetylene and styrene are formed from an intermediate (or intermediates) leading to styrylmagnesium bromide, (2) phenylacetylene thus formed reacts with cis- or trans-styrylmagnesium bromide to give styrene and ω-phenylethynylmagnesium bromide, and (3) in this reaction the trans isomer has a larger reaction rate than the cis compound. High purity of cis- and trans-styrylmagnesium bromides (93 and 96%, respectively) was obtained by using ethyl bromide as additive and tetrahydrofuran as solvent, while the addition of iodine decreased retention of original cis or trans configuration.

In a previous paper[1] we have mentioned that in the formation of a Grignard solution from cis- or trans-β-bromostyrene, retention of the original cis or trans configuration is higher in tetrahydrofuran than in diethyl ether. We report here the effect on the formation of cis- and trans-styrylmagnesium bromides and other products of the reaction by solvent species and amount and addition of iodine or ethyl bromide to the reaction system.

The Grignard solution was prepared from cis- or trans-β-bromostyrene in tetrahydrofuran, diglyme, or diethyl ether in the dark with or without addition of iodine or ethyl bromide. Since quantitative measurement of the amount of various products in the Grignard solution is difficult and preparation of cis- and trans-styrene-β-d is one of the aims of the present investigation, the reaction products were examined after heavy water was added to the solution. The distillate at the boiling temperature of styrene from the ether extract of the D₂O addition product gave a chromatogram of only two peaks which corresponded to styrene and phenylacetylene.

The distillates obtained under different conditions of Grignard reagent formation, however, gave n.m.r. spectra different from each other. The proton and deuteron spectra of one of the distillates are shown in Fig. 1 as an example. The signal at the highest magnetic field (τ 7 p.p.m.) in each of the spectra is ascribed to the ethynyl proton (or deuteron) of phenylacetylene (or phenylacetylene-β-d) from its resonance frequency, and the presence of this compound was also confirmed by infrared inspection. For the purpose of identifying the chemical compounds contained in the distillates, the positions and intensities of the n.m.r. signals of the ethylenic protons and deuterons were calculated for all mono-, di-, and trideuteriostyrenes from the chemical shifts and spin-coupling constants of light styrene as shown in the Appendix. By comparing the observed and calculated spectra, it was confirmed that styrene and cis- and trans-styrene-β-d exist in all the distillates and small amounts of styrene-α,β-d₂ (the deuterium atoms are in cis configuration) in some of the distillates; any other deuteriostyrenes (including those with deuterated ring), except for styrene-β,β-d₂, are absent. As for styrene-β,β-d₂, it is rather difficult to conclude that even a trace of the compound is not present in the distillates because its n.m.r. spectral lines overlap those of other main products.

In Table I are listed the chemical compounds found in each of these distillates under different conditions and also their proportions in each of the distillates.

The compositions of the distillates depend upon the species or the amount of the solvent used in the preparation of the Grignard reagents. However, dilution of a Grignard solution by a solvent (tetrahydrofuran or diethyl ether), which may or may not be the same species as that used in the Grignard reagent formation, does not change the composition of the distillate obtained from the D₂O-treated product of the diluted Grignard solution except for a small change attributed to reaction of phenylacetylene with styrylmagnesium bromides described later. It may, therefore, be concluded that the D₂O addition only transforms the Grignard reagents to the corresponding deuterated compounds.

Light styrene found in the distillates as well as in the Grignard solutions was produced even when the Grignard solutions were prepared from sufficiently dry β-bromostyrene, magnesium, and solvent in a vessel connected to a vacuum system and the heavy water added to the Grignard solution was essentially free from hydrogen. This shows that the hydrogen is transferred to form light styrene from bromostyrene, its derivative, and/or the solvent used. The possibility of hydrogen transfer from the solvent was excluded by the fact that signals of deuteriostyrenes were not found but those of styrene were found in the n.m.r. spectra of the Grignard solutions prepared from cis- and trans-β-bromostyrene by using tetrahydrofuran-d₈ as solvent, and also in the spectra of their H₂O addition products.

When phenylacetylene-β-d was added to cis- or trans-β-bromostyrene in the preparation of a Grignard solution, or when phenylacetylene-β-d was added to a Grignard solution, the H₂O addition product of the Grignard solution contained cis- and trans-styrenes-β-d. This shows that light styrene found in the Grignard solutions prepared without addition of phenylacetylene-β-d is caused, at least in part, by the reaction

$$Ph—C\equiv CH + Ph—CH=CHMgBr \longrightarrow$$
$$Ph—CH=CH_2 + Ph—C\equiv CMgBr \quad (1)$$
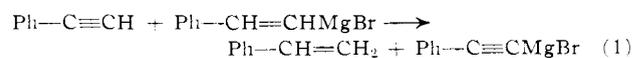
as is supposed from the hydrogen displacement method[2] of Grignard reagent preparation. Equation 1 shows that the total amount of phenylacetylene formed in the reaction of the Grignard reagent formation is the sum of the amounts of light and heavy phenylacetylenes in the D₂O

(1) T. Yoshino and Y. Manabe. J. Am. Chem. Soc., 85, 2860 (1963).

(2) M. S. Kharasch and O. Reinmuth. "Grignard Reaction of Nonmetallic Substances." Prentice-Hall, Inc., New York, N. Y., 1954, p. 66.

TABLE I

EXPERIMENTAL CONDITIONS AND REACTION PRODUCTS[a]

Br-St	Solvent	Concn.[b]	Additive	Temp., °C.	Ret., %	St-d, %	PA-d, %	PA, %	St, %	$\dfrac{St + PA}{PA\text{-}d + PA}$
trans	THF	1:6	None	26	85	87	5	0	8	1.6
	THF	1:15	None	26	91	95	2	0	3	1.5
	EE	1:6	None	26	59	44	15	7	34	1.9
	EE	1:15	None	26	55	62	10	7	21	1.6
	DG	1:6	None	50	75	39	7	35	19	1.3
	THF-EE	1:15	None	26	77	81	7	0	13	1.9
	THF	1:6	Iodine	26	78	70	12	0	18	1.5
	EE	1:6	Iodine	26	54	45	19	7	29	1.4
	THF	1:4.5	Iodine	26	72	64	15	0	21	1.4
	THF	1:9	Iodine	26	66	73	9	0	18	2.0
	THF	1:6	EtBr 150%[c]	26	96	100	0	0	Trace	
	EE	1:6	EtBr 150	26	52	100	Trace	0	Trace	
	THF	1:6	EtBr 30	26	87	88	5	0	7	1.4
	THF	1:6	EtBr 1000	26	95	100	0	0	0	
cis	THF	1:6	None	26	95 (85)	23 (53)	30 (0)	4 (34)	43 (13)	1.4
	THF	1:15	None	26	94 (82)	18 (46)	28 (0)	6 (34)	48 (20)	1.6
	THF-EE	1:6	None	26	91 (85)	24 (43)	19 (0)	12 (31)	45 (26)	1.8
	THF-EE	1:15	None	26	90 (86)	34 (54)	20 (0)	10 (30)	36 (10)	1.5
	THF	1:6	Iodine	26	65	30	21	6	43	1.8
	THF	1:6	EtBr 150%	26	93	100	0	0	Trace	
	THF-EE[d]	1:6	EtBr 150	26	85	87	6	0	7	1.2
	EE[d]	1:6	EtBr 150	26	68	67	12	4	15	1.2
	THF	1:6	EtBr 1000	26	93	100	0	0	0	

[a] Abbreviations used are: Br-St, bromostyrene; St-d, styrene-β-d; PA-d, phenylacetylene-β-d; PA, phenylacetylene; St, styrene; EE, ethyl ether; DG, diglyme; ret., retention. [b] Molar ratio (bromostyrene + ethyl bromide)/solvent. [c] Mole per cent relative to bromostyrene. [d] Styrene-α,β-d₂ was formed (2% when Grignard reagent was prepared in diethyl ether with addition of ethyl bromide, and trace for another marked with (d)).

addition product, and that the amount of styrylmagnesium bromides once formed is equal to the sum of the amounts of cis- and trans-styrene-β-d and phenylacetylene-β-d.

It is desirable here to estimate the cis/trans molar ratio of styrylmagnesium bromides once formed and the relative magnitude of the reaction rates of cis- and trans-styrylmagnesium bromides in eq. 1.

We shall denote by y and yz the fractions of trans- and cis-styrylmagnesium bromides which disappear through the reaction of eq. 1, respectively, and by $(1 - x)/x$ the cis/trans molar ratio of styrylmagnesium bromides including those transformed to styrene. According to these notations, $(1 - x)(1 - yz)/x(1 - y)$ and $y[x + (1 - x)z]/[x(1 - y) + (1 - x)(1 - yz)]$, respectively, express the cis/trans molar ratio of styrene-β-d and the molar ratio of phenylacetylene-β-d to styrene-β-d observed for the D₂O addition product of a Grignard solution. For the second experiment of cis-bromostyrene in Table I, for example, these ratios are obtained as

$$(1 - x)(1 - yz)/x(1 - y) = 94/6 \qquad (2)$$

$$y[x + (1 - x)z]/[x(1 - y) + (1 - x)(1 - yz)] = 28/18 \qquad (3)$$

A Grignard solution was prepared from cis-β-bromostyrene containing a small amount of phenylacetylene-β-d which was one-tenth the molar quantity of bromostyrene used. The reaction was carried out under the same conditions as those of the experiment giving eq. 2 and 3 except for the addition of phenylacetylene-β-d. The cis/trans molar ratio of styrene-β-d in the H₂O addition product of the Grignard solution was found to be 75/25. Based on the reasonable assumption that the addition of phenylacetylene-β-d will scarcely affect the ratios yz/y and $(1 - x)/x$, we have the relation

$$(1 - x)z/x = 75/25 \qquad (4)$$

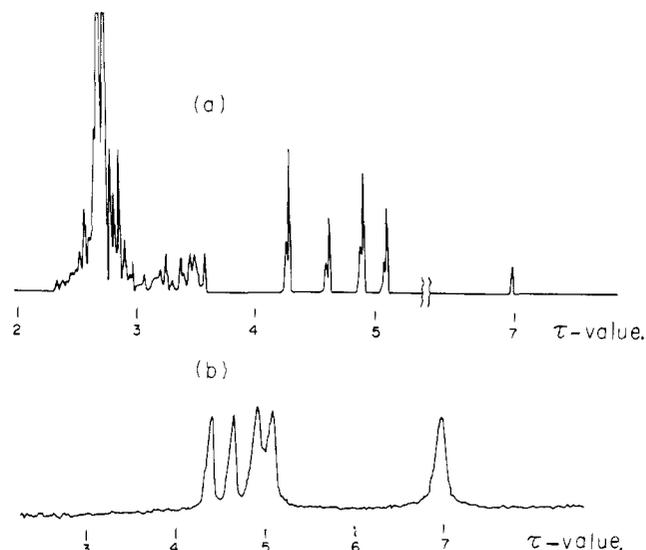From eq. 2, 3, and 4, z and $(1 - x)/x$ were obtained to be 0.6 and 82/18, respectively.

Fig. 1.—The n.m.r. spectra of a distillate from a Grignard solution prepared from trans-styrene-β-d in diethyl ether: (a), proton signals at 60 Mc.; (b), deuteron signals at 9.2 Mc.

Proportions of styrene, phenylacetylene, styrene-β-d, and phenylacetylene-β-d corrected for the reaction of eq. 1 are listed in parentheses in Table I, together with corrected values obtained by applying $z = 0.6$ to the other D₂O addition products of some of the Grignard solutions in Table I, which contain fairly large amounts of phenylacetylene-β-d. We see that the molar
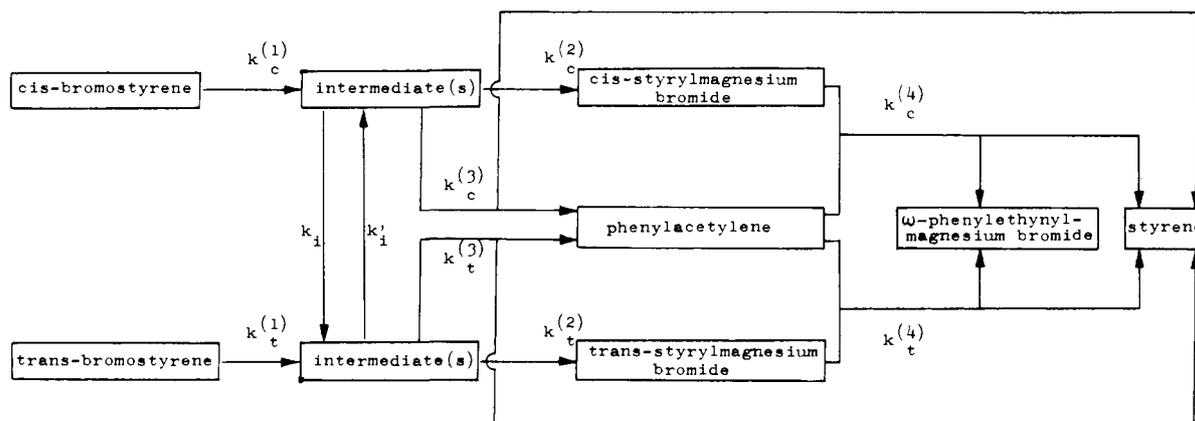
Fig. 2.—Diagram of reaction routes.

ratio of *cis-* to *trans*-styrylmagnesium bromide appears larger than the ratio in their formation owing to the fact that *trans*-styrylmagnesium bromide has a larger reaction rate than the *cis* compound in the reaction of eq. 1; that is, $k_t^{(4)}$ is greater than $k_c^{(4)}$ in Fig. 2.

The molar ratio (styrene + phenylacetylene)/(phenylacetylene + phenylacetylene-β-d) was observed to be 1.3–2.0 as shown in Table I independent of large variation of the total amount of these by-products owing to change in the condition of the preparation, except for the cases with addition of ethyl bromide, where a small value of the ratio is reasonable because of the reaction of phenylacetylene with ethylmagnesium bromide. The observed value larger than unity shows that styrene is also produced through a route other than eq. 1, because the ratio should be unity (or less than unity owing to polymerization of styrene) if styrene in the Grignard solution were derived solely through the reaction of eq. 1. Furthermore, the small variation of the observed ratio, in spite of the wide change in the total amount of the by-products, indicates that the route may also be related with formation of phenylacetylene.

It is seen in Table I that the amount of light and heavy phenylacetylenes and light styrene in the D_2O addition product derived from *trans*-β-bromostyrene is far less than that from *cis*-β-bromostyrene treated in the same condition, regardless of solvent species used and independent of addition of ethyl bromide or iodine. The α-protons of these compounds liberated in the formation of phenylacetylene must be used in the formation of light styrene, because hydrogen evolution was not observed in the course of Grignard reagent formation.

The following two experiments show that the formation of styrene (not attributed to eq. 1) and phenylacetylene and also the *cis–trans* isomerization take place only through an intermediate (or intermediates) in the reaction of bromostyrene with magnesium metal. In the first experiment an ethereal solution of *cis*-β-bromostyrene was kept in contact with magnesium metal. The combination of the *cis* compound and ether was selected because of very sluggish formation of the Grignard reagent for this combination. Infrared inspection of the solution shows that neither phenylacetylene, styrene, nor *trans*-β-bromostyrene is formed. In the second experiment a Grignard solution was prepared from an ethereal solution of *trans*-β-bromostyrene and separated from remaining magnesium metal. The Grignard solution was divided into two parts and an-

other ethereal solution of *trans*-β-bromostyrene was added to one of them. The amounts of phenylacetylene-β-d and styrene and the *cis/trans* molar ratios of styrene-β-d and β-bromostyrene were found to be the same for both the D_2O addition products from the original Grignard solution and from the mixture of the Grignard solution and the ethereal solution. The foregoing discussions on the reaction mechanisms are summarized in Fig. 2.

Ethyl bromide is known as an "entrainer" to Grignard reagent formation and is supposed to cleanse continuously the magnesium surface.[3] In the present case, as is seen in Table I, addition of ethyl bromide favored the formation of styrylmagnesium bromide with original *cis* or *trans* configuration when tetrahydrofuran was used as solvent, while it reduced yields of styrene and phenylacetylene in a Grignard solution prepared from *cis*- or *trans*-β-bromostyrene in tetrahydrofuran or diethyl ether. The latter means increase of the ratio $k^{(2)}/k^{(3)}$ in Fig. 2. These "ethyl bromide effects" were found to be independent of whether a mixture of β-bromostyrene and ethyl bromide was added to magnesium metal, or β-bromostyrene was added to a system of magnesium metal and ethyl Grignard which was found to be free from ethyl bromide. This result shows that the "ethyl bromide effects" are caused neither by existence of ethyl bromide nor its reaction with magnesium metal to cleanse *continuously* the magnesium surface. However, the addition of ethyl bromide was found to be effective only when magnesium metal treated by ethyl bromide coexists with ethyl Grignard, because the "ethyl bromide effects" were not observed in the following experiments. (1) A Grignard solution prepared from a tetrahydrofuran solution of ethyl bromide was separated from the remaining magnesium metal, and new pieces of magnesium metal and a tetrahydrofuran solution of *trans*-β-bromostyrene were added to the ethyl Grignard. (2) Another tetrahydrofuran solution of *trans*-β-bromostyrene was added to the magnesium metal separated from the ethyl Grignard.

Iodine is also known to accelerate formation of a Grignard solution by shortening the induction period and this is also true in the case of β-bromostyrenes. In this case, however, a trace of iodine added to magnesium (1 mg. for 5 g. of β-bromostyrene) lowered retention of the original *cis* or *trans* configuration in a Grignard solution prepared from a tetrahydrofuran solution of *cis*- or *trans*-β-bromostyrene. This means that the

(3) Ref. 2, p. 44.

addition of iodine increases the ratio of k_1 (or k_1') to ($k^{(2)}$ + $k^{(3)}$) in Fig. 2. The isomerization and the formation of the by-products were hardly affected by increase of the amount of iodine by forty times.

Experimental

trans-β-Bromostyrene.—*trans-β*-Bromostyrene in commercial β-bromostyrene was recrystallized 2–4 times from methanol at −30° in the dark until the infrared absorption at 770 cm.⁻¹ of *cis-β*-bromostyrene showed *cis* content less than 1%. The *trans* compound separated from *cis* isomer was vacuum distilled below 70°, dried with calcium chloride, vacuum distilled, and then dried with phosphorus pentoxide. The dry *trans-β*-bromostyrene was vacuum distilled and stored in a dark place.

cis-β-Bromostyrene.—β-Bromostyrene rich in *cis* isomer was synthesized from commercial *trans*-cinnamic acid and bromine by means of Grovenstein's method.[4] The β-bromostyrene obtained was crystallized 2–4 times from *n*-pentane at −45° in the dark until the infrared absorption at 740 cm.⁻¹ of *trans-β*-bromostyrene showed *trans* content less than 1%. The *cis-β*-bromostyrene separated from *trans* isomer was distilled, dried, and stored in the same way as described above for the *trans* compound.

Preparation of Grignard Solutions and D₂O Addition.—In each run 3.5 g. of bromostyrene mixed with a solvent (and ethyl bromide, when mentioned) was added to 1.3 g. of polished magnesium with stirring during 60 min. in the dark. Stirring was continued for 30 min. after the addition was completed. The Grignard solution thus obtained was diluted with a solvent and then hydrolyzed with heavy water. The reaction products were vacuum distilled after extraction with diethyl ether. The yields of the distillates were about 80–90%.

Throughout the experiment great care was taken to maintain the temperature below 70° even during distillation, and to exclude any acid or base in order to avoid isomerization of the bromostyrenes and their derivatives. To eliminate the effect of moisture in the air, each procedure was carried out in an apparatus equipped with several break seals through which solvents and heavy water were added, and the apparatus was evacuated before hand or flushed with dry, oxygen-free nitrogen.

Measurement of the Amounts of Compounds in a Hydrolysis Product of a Grignard Solution.—The amounts of light and heavy phenylacetylene were estimated from the intensities of the n.m.r. signals of ethynyl proton and deuteron, respectively. The amount of styrene was estimated from the ratio of the highest-field signal of the α-proton quartet by using the area ratio of the highest-field signal of the α-proton to the β-proton signals in pure light styrene. Since the β-proton signals of styrene overlap with those of *cis-* and *trans*-styrene-β-*d*, contribution of styrene to the observed total area of the β-proton signals was subtracted and the ratio of the area of the *trans*-proton signals to that of the *cis*-proton signals was used as *cis/trans* molar ratio of styrene-β-*d*. The *cis/trans* molar ratio was also obtained from the area ratio of the *cis/trans* deuteron signals.

Miscellaneous.—The n.m.r. spectra were obtained by the use of a Varian DP 60 n.m.r. spectrometer and infrared spectra by a Perkin–Elmer 125 spectrometer. The gas chromatogram was obtained by using a column packed with Carbowax (polyethylene glycol) on firebrick.

The deuterium content of the heavy water used (Showa Denko) was 99.75% and deuterium content of the tetrahydrofuran-*d₈* (Merck Sharp and Dohme) was 98%.

Appendix

The transition energies and relative intensities of spectral lines were calculated for monodeuteriostyrenes

(4) E. Grovenstein, *J. Am. Chem. Soc.*, **75**, 2639 (1953).
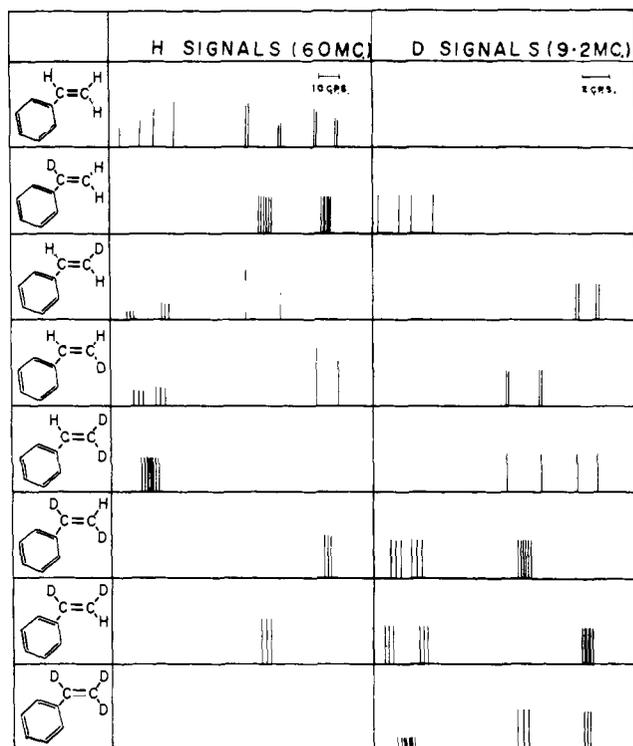

Fig. 3.—Calculated signal patterns of styrene and deuterated styrenes (field strength increases from left to right).

by means of the second-order perturbation method and for di- and trideuteriostyrenes on the approximation that the ratio of the spin-coupling constant to the chemical shift is equal to zero.

From the spectrum of styrene,[5] the chemical shifts, σ, and the spin-coupling constants, J, were determined as
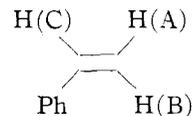
$$\sigma_A - \sigma_B = 1.50 \text{ p.p.m.}$$

$$\sigma_B - \sigma_C = 0.98 \text{ p.p.m.}$$

$$J_{AB} = 1.3 \text{ c.p.s.}$$

$$J_{AC} = 10.7 \text{ c.p.s.}$$

$$J_{BC} = 17.5 \text{ c.p.s.}$$

$$\begin{array}{cc} \text{H(C)} & \text{H(A)} \\ \diagdown\!\!\!\diagup \\ \diagup\!\!\!\diagdown \\ \text{Ph} & \text{H(B)} \end{array}$$

The spectral patterns of deuterated styrenes shown in Fig. 3 were calculated by assuming (1) that $J^{HD} = (\gamma_D/\gamma_H)J^{HH}$, and $J^{DD} = (\gamma_D/\gamma_H)^2 J^{HH}$ and (2) that the chemical shifts are not affected by deuterium substitution.

(5) As for assignments of styrene signals, see 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, p. 238.