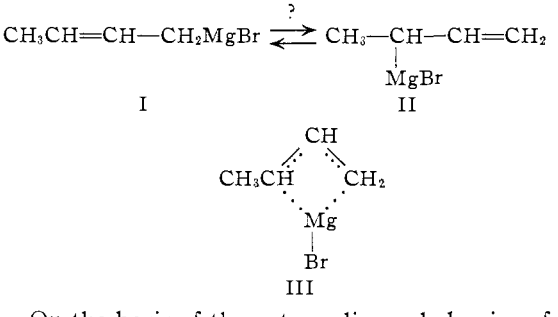
## NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY. THE STRUCTURE OF BUTENYLMAGNESIUM BROMIDE[1]

*Sir:*

Crotyl bromide and $\alpha$-methylallyl bromide each react with magnesium in ether to yield the same butenyl Grignard reagent, which conceivably could be crotylmagnesium bromide (I), $\alpha$-methylallylmagnesium bromide (II), a more or less mobile equilibrium mixture of I and II, or an intermediate, bridged structure such as III.[2,3]




On the basis of the extraordinary behavior of the butenyl Grignard reagent in a variety of chemical reactions, Young and Roberts[2a] inferred that the correct structure was crotylmagnesium bromide (I). This view was sharply criticized by Kharasch and Reinmuth,[4] who held that the problem could be solved only by physical means. The ultimate justice of the criticism is not to be denied; nonetheless, infrared evidence[5] and the nuclear magnetic resonance (n.m.r.) spectrum, as will be shown below, strongly support the inference that the butenyl Grignard reagent, at least largely and probably exclusively, is the crotyl isomer.

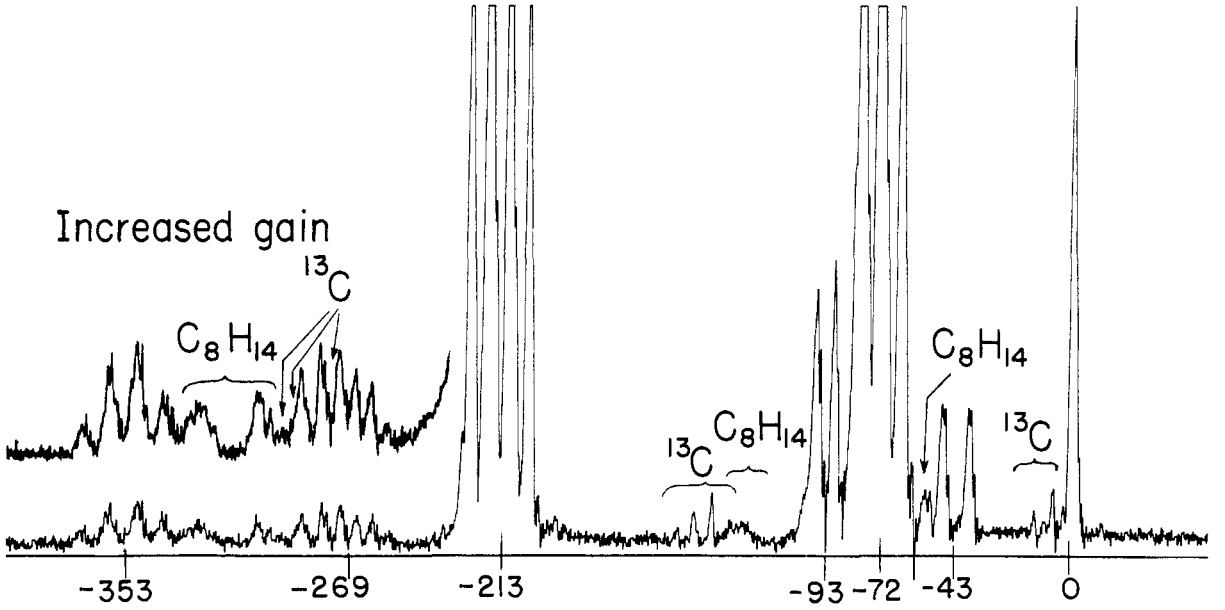



Fig. 1.—Nuclear magnetic resonance spectrum of butenylmagnesium bromide in diethyl ether at 25° and 60 Mc with tetramethylsilane (0 cps.) as internal standard. The intense triplet and quartet resonances centered on −72 and −213 cps. are the $CH_3$ and $CH_2$ of diethyl ether. The lines designated as $^{13}C$ are the proton satellite resonances produced by the $^{13}C$ in the solvent. The resonances arising from the octadienes formed by coupling in the preparation of the Grignard reagent are marked $C_8H_{14}$. The assignments of these were verified by addition of authentic material to the sample. The resonances of the Grignard protons were assigned as follows: $\alpha$-$CH_2$ doublet centered on −43 cps.; $\delta$-$CH_3$, doublet centered on −93 cps.; $\gamma$-CH, quintet centered on −269 cps.; and $\beta$-CH, quartet centered on −353 cps. The spin–spin splitting pattern is discussed in detail elsewhere.[8]

The n.m.r. spectrum of the butenyl Grignard reagent is independent of whether or not one starts from crotyl or $\alpha$-methylallyl bromide and is shown in Fig. 1. The spectrum is that expected for I since there are two vinyl proton resonances and an upfield two-proton resonance that is split into a doublet as expected for a —$CH_2$Mg— group connected to a carbon carrying a single proton.[6] The structural problem posed by the Grignard reagent might well be regarded as solved with this finding. However, allylmagnesium bromide has been found to give an n.m.r. spectrum that indicates the allylic isomers IV and V are interconverted faster than 1000 times per second.[7] A similarly rapid equilibrating mixture of I and II could lead to the spectrum of Fig. 1, provided only that the equilib-

(1) Supported in part by the Office of Naval Research.

(2) (a) W. G. Young and J. D. Roberts, *J. Am. Chem. Soc.*, **68**, 1472 (1946); (b) the chemistry of allylic Grignard reagents is summarized briefly by R. H. de Wolfe and W. G. Young, *Chem. Revs.*, **56**, 753 (1956).

(3) For the purposes of this paper, Grignard reagents will be expressed by the conventional formula RMgX, although there is good reason to believe that this formula is incorrect or, at least, incomplete; *cf.* R. E. Dessy, G. S. Handler, J. H. Wotiz and C. A. Hollingsworth, *J. Am. Chem. Soc.*, **79**, 3476 (1957); R. E. Dessy and G. S. Handler, *ibid.*, **80**, 5824 (1959).

(4) M. S. Kharasch and O. Reinmuth, "Grignard Reactions of Non-metallic Substances," Prentice-Hall, Inc., New York, N. Y., 1954, Chap. XVII, particularly pages 1154–1157.

(5) M. Gaudemar, *Bull. soc. chim. France*, 1475 (1958).

(6) J. D. Roberts, "Nuclear Magnetic Resonance Spectroscopy," McGraw-Hill Book Company, New York, N. Y., 1959, Chap. III.

(7) J. E. Nordlander and J. D. Roberts, *J. Am. Chem. Soc.*, **81**, 1769 (1959).

$$CH_2{=}CH{-}CH_2MgBr \rightleftharpoons BrMgCH_2{-}CH{=}CH_2$$
IV V

rium lies fairly far on the side of I. The extent of the contribution of II to the spectrum determines the chemical shift of the $-CH_2-$ resonance; if II were the dominant form this resonance would appear in the vinyl region. Since it actually appears in or near the $-CH_2-Mg$ region, we can safely infer that I is the dominant form. A comparison[8] of the effects of vinyl and methyl groups (as R) on the chemical shift of the methylene resonances in $RCH_2X$, X = Br, and MgBr suggests that the $-CH_2-$ resonance of the Grignard reagent in Fig. 1 may actually be some 50 cps. (at 60 Mc) downfield from the position it would have if the Grignard reagent were exclusively crotylmagnesium bromide. This figure corresponds to about 84% of I and 16% of II. A rather strong argument against the validity of the composition so calculated is provided by the fact that the position of the $-CH_2-$ resonance changes by only 1 cps. between $+30°$ and $-20°$, corresponding to an increase of but 0.3% in the proportion of the crotyl isomer. It could be argued that through coincidence $\Delta H$ is virtually zero for the equilibrium, but it seems more reasonable to conclude that I is more than 99% of the mixture. If so, then even a several-fold temperature effect on the concentration of II would give only a very small change in spectrum.

As with allylmagnesium bromide,[8] the spectrum of butenylmagnesium bromide shows no evidence of "freezing out"[9] of the separate allylic isomers at temperatures down to $-60°$. Interestingly, dibutenylmagnesium shows the same chemical shifts as does the ordinary Grignard reagent. This fact can be taken as an argument against the Grignard formula RMgBr since the bromine ought to have some influence on the chemical shift of $-CH_2-$ resonance. The n.m.r. evidence gives no support for structure III for the Grignard reagent. Bridged structures are favored for crotyl palladium chloride complex[10] and crotyl cobalt tricarbonyl,[11] which have very different n.m.r. spectra from the Grignard reagent.

If the Grignard reagent is accepted to be crotylmagnesium bromide (I) with the possibility of very rapid equilibration with a small proportion of $\alpha$-methylallylmagnesium bromide (II), then the remaining problem is to account for the high yields of products in which it reacts, even with highly sterically-hindered carbonyl compounds, to insert $\alpha$-methylallyl groups. Presumably if equilibration were rapid, formation of the less-crowded crotyl addition products would be favored. This dilemma is resolved if we assume that coördination of the carbonyl oxygen with the magnesium of I diminishes the electrophilic character of the magnesium sufficiently to cause the rate of allylic isomerization to be much less than the rate of addition. In these circumstances, only the $\alpha$-methylallyl group would be inserted by the cyclic addition mechanism.[2a] If insertion of the $\alpha$-methylallyl group were very highly retarded by steric hindrance, as with di-*t*-butyl ketone,[12] then allylic isomerization could lead to the crotyl-addition product.

The n.m.r. spectra of other allylic Grignard reagents will be reported in later papers.

(8) J. E. Nordlander, Ph.D. Thesis, California Institute of Technology, 1960, pp. 41–43.

(9) Ref. 6, Chap. IV.

(10) H. C. Dehn and J. C. W. Chien, *J. Am. Chem. Soc.*, **82**, 4429 (1960).

(11) D. W. Moore, H. B. Jonassen, T. B. Joyner and A. J. Bertrand, *Chem. and Ind.*, 1304 (1960).

(12) K. W. Wilson, J. D. Roberts and W. G. Young, THIS JOURNAL, **72**, 218 (1950).

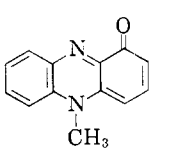
CONTRIBUTION NO. 2649 J. ERIC NORDLANDER
GATES AND CRELLIN LABORATORIES OF CHEMISTRY
CALIFORNIA INSTITUTE OF TECHNOLOGY
PASADENA, CALIFORNIA WILLIAM G. YOUNG
DEPARTMENT OF CHEMISTRY JOHN D. ROBERTS
UNIVERSITY OF CALIFORNIA AT LOS ANGELES
LOS ANGELES, CALIFORNIA

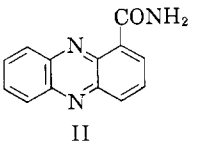
RECEIVED DECEMBER 12, 1960

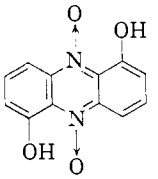
## THE BIOGENESIS OF PHENAZINE PIGMENTS[1]

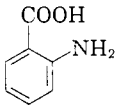
*Sir:*

Pigments that contain the aromatic phenazine nucleus such a spyocyanine (I),[1a] chlororaphin (a 3:1 molecular compound of phenazine-1-carboxamide (II) and its 9,10 dihydro derivative),[2] iodinin (III)[3] and phenazine-1-carboxylic acid[4] present an interesting biogenetic problem for which no definitive proposals have yet been made though a significant amount of work on the biosynthesis of pyocyanine (I) has been reported.[5,6,7,8]


I


II


III


IV

We were attacted by the possibility that natural products of this type may arise by an oxidative dimerization of anthranilic acid (IV) with loss of the carboxyl carbon where appropriate. A somewhat tenuously analogous mechanism apparently produces the phenoxazine ring system of the actinomycins.[9] We wish to report results which we interpret as indicating that one ring, at least, of phenazine-1-carboxamide (II) originates in anthranilic

(1) Supported in part by Grant E-2775 from the U. S. Public Health Service.

(1a) F. Wrede and E. Strack, *Z. physiol. Chem.*, **181**, 58 (1929).

(2) C. Dufraisse, A. Etienne and E. Toromanoff, *Compt. rend.*, **235**, 920 (1952).

(3) G. R. Clemo and A. F. Daglish, *J. Chem. Soc.*, 1481 (1950).

(4) W. C. Haynes, F. H. Stodola, J. M. Locke, T. G. Pridham, H. F. Conway, V. E. Sohns and R. W. Jackson, *J. Bact.*, **72**, 412 (1956).

(5) M. V. Burton, J. J. R. Campbell and B. A. Eagles, *Can. J. Res.*, **26C**, 15 (1948).

(6) A. C. Blackwood and A. C. Neish, *Can. J. Microbiol.*, **3**, 165 (1957).

(7) N. Grossowicz, P. Hayat and Y. S. Halpern, *J. Gen. Microbiol.*, **16**, 576 (1957).

(8) L. H. Frank and R. D. DeMoss, *J. Bact.*, **77**, 776 (1959).

(9) E. Bullock and A. W. Johnson, *J. Chem. Soc.*, 1602 (1957).