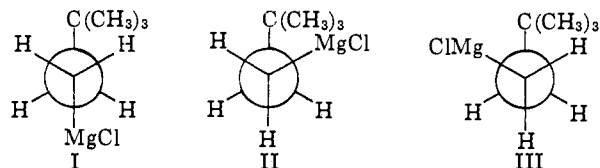
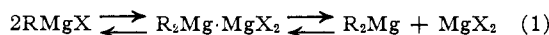


Fig. 2.—N.m.r. spectra of the $\text{CH}_2\text{-Mg}$ protons of 2-phenyl-3-methylbutyl Grignard reagent in tetrahydrofuran solution as a function of temperature. Only four of eight theoretical lines for the AB part of the spectrum have sufficient intensity to be observed.

solution changes from an A_2X_2 -type spectrum at $+33^\circ$ to an $\text{AA}'\text{XX}'$ -type at -50° ⁸ (Fig. 1). The observation of two distinct vicinal coupling constants at low temperatures indicates that inversion of configuration at the $-\text{CH}_2\text{-Mg}$ center is slow on the n.m.r. time scale, and strongly suggests that the populations of the three conformations (I-III) are not equal



The averaged vicinal coupling constants observed at room temperature might be the result of either rapid inversion of configuration at the carbon carrying the magnesium (such inversion interchanging the relative positions of the hydrogens at the α -carbon of I, II and III) or else a change in populations of the conformations. Incursion of a Schlenk equilibrium,⁴ eq. 1, at



the higher temperature clearly is not responsible for the variation in the spectra, because bis-(3,3-dimethylbutyl)-magnesium⁵ shows spectral behavior similar to that of the Grignard reagent (Fig. 1).

We have previously suggested⁸ that changes in the rate of inversion were responsible for the changes in the appearance of the spectrum; we now report further evidence supporting this suggestion.

Ten of the twelve theoretical lines for the A part of an $\text{AA}'\text{XX}'$ spectrum⁶ can be identified in the low-temperature spectra in Fig. 1. The 1,2 and 3,4 transitions are easily identified on the basis of intensity and position as the strong outer lines in these spectra; their separation is equal to the sum of the two vicinal coupling constants $J + J'$.⁶ On the reasonable assumption

magnesium chloride. For recent discussions of the structure of Grignard reagents, see E. C. Ashby and W. E. Becker, *J. Am. Chem. Soc.*, **85**, 118 (1963); G. E. Stucky and R. E. Rundle, *ibid.*, **85**, 1002 (1963), and references therein.

(3) J. D. Roberts, paper presented at the Symposium on High-Resolution Nuclear Magnetic Resonance, Boulder, Colorado, July 3, 1962.

(4) M. S. Kharasch and O. Reinmuth, "Grignard Reactions of Non-metallic Substances," Prentice-Hall Inc., New York, N. Y., 1954, pp. 104-109.

(5) Prepared from the Grignard reagent by precipitating the magnesium chloride with an excess of dioxan.⁴

(6) 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, Chapter 6.

that the *trans* and *gauche* coupling constants, J_t and J_g , have the same respective values for each conformation (I-III), the separation of the outer lines for I should be $(J_t + J_g)$, while the corresponding separation for a rapidly interconverting mixture of II and III would be $\frac{1}{2}(J_t + 3J_g)$. Therefore, if the averaging of coupling constants observed in the high-temperature spectra is a consequence of changes in conformational populations, the separation of the outer lines would be expected to change appreciably with temperature.⁷ Experimentally, no such temperature variation is observed—the separation of the outer lines of the Grignard reagent changes only from 18.2 to 18.4 c.p.s. over the temperature range of Fig. 1; the corresponding separation of the dialkylmagnesium compound remains unchanged at 18.0 c.p.s. We believe these data are incompatible with significant temperature-dependent variation in populations of the conformations.

The n.m.r. spectrum of the methylene group of 2-phenyl-3-methylbutylmagnesium chloride also shows a temperature variation suggesting changes in rate of inversion (Fig. 2). In this case, the inversion at the $-\text{CH}_2\text{-Mg}$ center is slow even at $+66^\circ$ and the two methylene protons are magnetically non-equivalent due to their proximity to a center of molecular asymmetry.⁸ As the temperature is increased, the rate of inversion increases until at about $+120^\circ$ the ABX spectrum collapses to an A_2X spectrum.⁹ The rates and thermodynamic parameters for the processes which result in the simplification of spectra of these Grignard reagents will be discussed in later papers.

(7) This would be true only, of course, if J_t is substantially different from J_g but this must be so in the present case because otherwise the low-temperature spectrum could only be of the A_2X_2 type.

(8) G. M. Whitesides, F. Kaplan, K. Nagarajan and J. D. Roberts, *Proc. Natl. Acad. Sci.*, **48**, 1112 (1962), and references therein.

(9) It has been suggested that the observation of an A_2 -type spectrum for the methylene protons of 2-phenylpropylmagnesium bromide indicates that this Grignard reagent is inverting rapidly at room temperature; cf. G. Fraenkel, D. G. Adams and J. Williams, Abstracts of Papers, 143rd National Meeting of the American Chemical Society, Los Angeles, Calif., April, 1963, p. 4 M. We have examined the spectrum of this compound and of bis-(2-phenylpropyl)-magnesium at -75° and find that the methylene protons are still magnetically equivalent, although inversion in the latter compound is very probably slow at this temperature. We believe, therefore that no conclusions can be drawn about the rate of inversion of this Grignard reagent from its n.m.r. spectrum.

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RECEIVED MAY 28, 1963

The Deamination of Tertiary Carbinamines

Sir:

We wish to report an oxygen-18 and stereochemical study of the nitrosoamide and nitrous acid deaminations of 2-phenyl-2-butylamine. Only one other example of the deamination of an optically active, acyclic, tertiary carbinamine has been reported in the literature; in that study, Arcus, Kenyon and Levin found that the nitrous acid deamination of optically active phenyl-tolylmethylcarbinylamine yielded inactive alcohol.¹

In the present work, 2-phenyl-2-butylamine was fully resolved *via* the tartrate salt,² and the salt was converted into optically pure N-(2-phenyl-2-butyl)-benzamide ($[\alpha]_D^{25} +19.2^\circ$ for one enantiomer and -19.2° for the other (c 7.0, CHCl_3)). The rotation of the free amine was determined (less accurately) to be $[\alpha]_D^{25} -15.7^\circ$ (neat, 1 dm.). (+)-2-Phenyl-2-methylbutanoic acid

(1) C. L. Arcus, J. Kenyon and S. Levin, *J. Chem. Soc.*, 407 (1951).

(2) We thank Professor C. H. DePuy for furnishing seed crystals of the partially resolved material.

Our results for the nitrous acid deamination of 2-phenyl-2-butylamine are less extensive, but they show that both 2-phenyl-2-butanol and 2-phenyl-2-butyl acetate are formed in the reaction with nitrous acid in acetic acid and that both compounds are formed with over-all retention of configuration (74% and 61%, respectively). The alcohol is of particular interest since it must be the product of an intramolecular reaction—the decomposition of a species such as VI or VIII (followed in the latter case by hydrolysis).⁶ The anion exchange illustrated appears to be a general reaction of diazonium ion pairs⁵; we propose that intermediates such as VII and VIII formed in the nitrous acid deamination are similar to those such as III formed in the nitrosoamide decomposition and that there is an overlap in the mechanisms of the two reactions.⁷

Acknowledgments.—We thank Dr. Robert R. Johnson for valuable assistance and the National Science Foundation for its support of this work (G 12311).

(6) In one case, that of sterically hindered amine, the alkyl nitrite itself has been isolated (A. Brodhag and C. R. Hauser, *J. Am. Chem. Soc.*, **77**, 3024 (1955)). A similar anion exchange of VI (or VII) with nitric acid (from the decomposition of nitrous acid) to yield $RN_2^+NO_3^-$ could account for the nitrate esters (and from these, the carbonyl compounds) that have been isolated from a number of deaminations (e.g., J. A. Berson and D. A. Ben-Efraim, *ibid.*, **81**, 4094 (1959); V. Prelog, H. J. Urech, A. A. Bothner-By and J. Würsch, *Helv. Chim. Acta*, **38**, 1095 (1955)).

(7) In this respect, one other comparison is available. The nitrous acid deamination of 1-phenylethylamine in acetic acid yielded 1-phenylethanol with 78.5% retention of configuration (R. Huisgen and C. Rüchardt, *Ann.*, **601**, 21 (1956)), whereas the nitrosoamide decomposition of the same amine in acetic acid proceeded with 81% retention of configuration.⁵

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RECEIVED MAY 6, 1963

Rates of Rotation of Asymmetric Diphenyls by Nuclear Magnetic Resonance Spectroscopy

Sir:

As a consequence of the steric requirements of *o*-substituents, the two aromatic rings of an *o*-substituted diphenyl are not coplanar. An *o*-substituent on one ring thus is located above the plane of the second, and if the second ring holds two different *o*- or *m*-groups, the substituent on the first ring is in an asymmetric environment. If that substituent contains a methylene group, its two protons thus are not necessarily magnetically equivalent even though the substituent rotates about the phenyl-substituent bond, for the conformers of the substituent about that bond (e.g., Ia-c or others¹) will not necessarily be equally populated and the environments of the two protons are different in each conformer.² That this can indeed be the case is clearly seen from the n.m.r. spectrum³ of *dl*-6,6'-diethyl-2,2'-bis-(hydroxymethyl)-diphenyl (IIa, prepared by lithium aluminum hydride reduction of the corresponding diphenic ester IIb; found: C, 80.0; H, 8.2) in which the methylol proton resonance appears as an AB quartet ($\tau_A = 5.80$; $\tau_B = 5.95$; $|J_{AB}| = 12$ c.p.s.). This appears to be the first reported example of such non-equivalence which results from diphenyl asymmetry,⁴

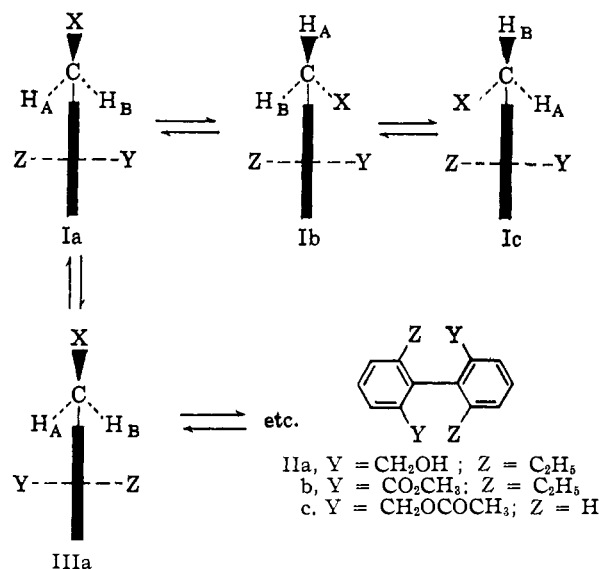
(1) Whether energy minima in fact correspond to Ia-c in which H or X eclipses the *m*-hydrogen, to structures in which H or X and H stagger the *m*-hydrogen, to both, or to intermediate ones is not clear, but is immaterial for the non-equivalence argument.

(2) In principle, the argument holds for a *m*-substituent as well, and of course for groups other than methylene which contain two similar magnetically active units, e.g., isopropyl or difluoromethylene.

(3) N.m.r. spectra were obtained from dilute solutions in carbon tetrachloride or deuteriochloroform using Varian A-60 and DP-60 spectrometers operating at 60 Mc./sec.

(4) K. Mislow and M. A. W. Glass, *J. Am. Chem. Soc.*, **83**, 2780 (1961), and K. Mislow, E. Simon and H. B. Hopps, *Tetrahedron Letters*, 1011 (1962), have observed non-equivalent *o*-methylene protons in several bridged di-

although the corresponding phenomenon when the asymmetric environment is provided by a tetrahedral carbon holding three dissimilar groups is well known.^{5,6}

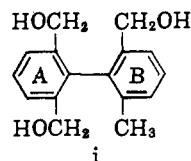


Non-equivalence of this type can only be observed provided rotation about the diphenyl bond is sufficiently slow, for such a rotation through 180° serves to exchange the environments of protons A and B of the AB system (compare Ia and IIIa). When such rotational exchange is rapid compared to the chemical shift difference between A and B, the same average environment is observed for both by the n.m.r. technique, producing a single line (A₂) spectrum. Indeed while the CH₂O resonance of *dl*-2,2'-bis-(acetoxymethyl)-diphenyl (IIc) is of the AB type at room temperature ($\delta_{AB} \cong 3.5$ c.p.s.; $|J_{AB}| \cong 12.6$ c.p.s.), at 127° the pattern has collapsed to a single line. Examination of the shape of the outer peaks of the AB system at intermediate temperatures,⁷ where they first broaden and then disappear, reveals that at 94° the average lifetime of a molecule between rotations is 4 sec., and that the Arrhenius activation energy for rotation is approximately 13 kcal./mole. Thus the n.m.r. technique provides a means for studying the process by which an optically active diphenyl would be racemized, without requiring a resolved sample. Further, it is applicable to systems, such as the *o,o'*-disubstituted case here reported, which are difficult to study by the

phenyls, but in these systems the methylene groups are part of a ring and thus not free to rotate. Professor Mislow has very recently informed us that he has also observed non-equivalent methylene protons in the unbridged systems II, Y = CH₂OH and Z = CH₃ ($\tau_A = 5.85$; $\tau_B = 6.02$; $|J_{AB}| = 11.6$ c.p.s.), and II, Y = CH₂OH and Z = CD₃ ($\tau_A = 5.83$; $\tau_B = 6.00$; $|J_{AB}| = 11.8$ c.p.s.). We are grateful to Prof. Mislow for communication of these results prior to publication and permission to cite them here.

(5) Early examples and a concise discussion of the principles involved are provided by P. M. Nair and J. D. Roberts, *J. Am. Chem. Soc.*, **79**, 4565 (1957). An elegant test of the commonly accepted theoretical explanation is reported by G. M. Whitesides, F. Kaplan, K. Nagarajan and J. D. Roberts, *Proc. Natl. Acad. Sci. U. S. A.*, **48**, 1112 (1962).

(6) It should be noted that the structural requirements which permit such non-equivalence are less restrictive than those which produce molecular dissymmetry and consequently permit optical activity, just as is the case for non-equivalence due to location near "asymmetric" carbon, ref. 5. In principle, a system such as i, although unresolvable, could have non-equivalent methylene protons on the methylol groups of the A but not the B ring.



(7) J. Kaplan, *J. Chem. Phys.*, **28**, 278 (1958).