mass which formed was pulverized and recrystallized from ethanol to give a white micro-crystalline powder.

1,1'-Tetramethylenebis-(3,4-dichlorophenylurea) (189).—Prepared following procedure A from 3,4-dichlorophenyl isocyanate and 1,4-butanediamine as a white micro-crystalline powder.

N,N'-Bis-(3,4-dichlorophenyl)-phthalamide[16] (190).—Phthaloyl chloride, 10.4 g. (0.05 mole), was added dropwise with stirring to 16.2 g. (0.1 mole), of 3,4-dichloroaniline in 75 ml. of pyridine. The temperature rose to 70° during the addition, the solution turning a brilliant red. The solution was held for 3 hours and quenched into 800 ml. of ice-water. The crude product which separated was filtered and recrystallized from acetone to give a fine white powder.

1,1'-*p*-Phenylenebis-[3-(3,4-dichlorophenyl)-urea] (191).—The compound was prepared following procedure A using 3,4-dichlorophenyl isocyanate and *p*-phenylenediamine as a white microcrystalline powder.

p-Phenylenebis-(3,4-dichlorocarbanilate) (194).—Prepared from 3,4-dichlorophenyl isocyanate and hydroquinone following procedure for compound 188; large, white flakes from ethanol.

N,N'-Sulfinylbis-(3,4-dichloroaniline) (195).—A solution of 65.0 g. (0.4 mole) of 3,4-dichloroaniline in 600 ml. of ether was stirred while adding dropwise 1.9 g. (0.1 mole) of thionyl chloride. After 1 hour, the heavy slurry was filtered and washed with 50 ml. of ether. The filtrate and wash were combined and the ether removed under vacuum. The residue was recrystallized from heptane to give fine, yellow needles. *Anal.* Calcd. for $C_{12}H_8Cl_4N_2OS$: Cl, 38.32; S, 8.64; N, 7.58. Found: Cl, 38.31; S, 8.60; N, 7.51.

2,2'-Thiodiethanolbis-(3,4-dichlorocarbanilate) (196).—Prepared from 3,4-dichlorophenyl isocyanate and thiodiethanol following the procedure for compound 188 in fine, white granules from ethanol.

1,3-Bis-(3,4-dichlorobenzoyl)-urea (197).—Prepared from 3,4-dichlorobenzoyl chloride and urea following procedure D in fine, white granules from ethanol.

1,6-Bis-(3,4-dichlorophenyl)-2,5-dithiobiurea (198).—Prepared from 3,4-dichlorophenyl isothiocyanate and 85% hydrazine hydrate following procedure A.

1,6-Bis-(3,4-dichlorophenyl)-biurea (199).—Prepared from 3,4-dichlorophenyl isocyanate and 85% hydrazine hydrate following procedure A as a white, micro-crystalline powder. The product is known to be contaminated with the symmetrical tetrachlorocarbanilide.

4-(3,4-Dichlorophenyl)-1-phenylsemicarbazide (200).—Prepared from 3,4-dichlorophenyl isocyanate and phenylhydrazine following procedure A in colorless, felted needles from ethanol.

1,4-Butanediolbis-(3,4-dichlorocarbanilate) (201).—On mixing 18.8 g. (0.1 mole) of 3,4-dichlorophenyl isocyanate and 4.5 g. (0.05 mole) of 1,4-butanediol, a vigorous reaction set in forming a hard, crystalline mass within 15 minutes. Recrystallization from acetone gave fine, colorless needles.

2,2,2-Trichloro-N,N'-bis-(3,4-dichlorophenyl)-ethylidenediamine (202).—A solution of 16.3 g. (0.1 mole) of 3,4-dichloroaniline and 7.4 g. (0.05 mole) of chloral in 50 ml. of benzene was refluxed for 3 hours. The benzene was removed under 60 mm. vacuum leaving a brown sirup which slowly crystallized on standing. The crude product was dissolved in 800 ml. of heptane, treated with 5 g. of decolorizing charcoal for 30 minutes, filtered and set aside to crystallize as fine, colorless needles.

1,3-Bis-(3,4-dichlorophenyl)-formamidine[23] (203).—A solution of 16.3 g. (0.1 mole) of 3,4-dichloroaniline and 7.4 g. (0.05 mole) of triethyl orthoformate in 250 ml. of ethanol was refluxed for 6 hours. On cooling, the product crystallized in fine, colorless needles.

4-Chlorophenyl-3,4-dichlorocarbanilate (204).—A mixture of 9.4 g. (0.05 mole) of 3,4-dichlorophenyl isocyanate and 6.5 g. (0.05 mole) of *p*-chlorophenol was heated to 90° in an Erlenmeyer flask, stoppered and held at 90° for 16 hours. On cooling, the hard crystalline mass was recrystallized from ethanol in glistening white plates.

3,4-Dichlorophenyl-3,4-dichlorocarbanilate (205).—Prepared as above from 3,4-dichlorophenyl isocyanate and 3,4-dichlorophenol as fine, white needles from ethanol.

Bacteriostatic Test Procedure.—In the preliminary bacteriostatic tests 1–100 stock solutions are prepared by dissolving 100 mg. of the test compound in 10 ml. of acetone, alcohol or other suitable solvent. The stock solutions are diluted serially by pipetting 2 ml. of the stock solution into 18 ml. of sterile nutrient agar to obtain a 1:1000 dilution, and continuing in the same manner for dilutions of 1:10,000, 1:100,000, and 1:1,000,000. The agar is poured in Petri dishes, allowed to harden, and spot inoculated with one drop of a cell suspension of *Micrococcus pyogenes* var. *aureus*, prepared by suspending the growth from a 24-hour nutrient agar slant culture in 10 ml. of distilled water. The plates are incubated at 37° for 48 hours, and examined for presence or absence of growth.

Those compounds found active in the range 1–10 p.p.m. are tested for their activity in the presence of soap. Additional stock solutions of the test compound are prepared and diluted in solutions of "neutral white high-grade toilet soap" sufficient to yield a ratio of 1:50 compound to soap dilutions; inoculation and incubation are carried out as in the preliminary screening.

Acknowledgment.—The authors are indebted to Mr. Andrew A. Bybell for the analyses and to Mr. Paul D. McDonald for the bacteriostatic screening.

(23) H. J. Backer and W. L. Wanmaker, *Rec. trav. chim.*, **67**, 257 (1948).

ST. LOUIS, MISSOURI

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

Allylmagnesium Bromide as a Selective Nucleophile toward Aza-aromatic Heterocycles

BY HENRY GILMAN, JOHN EISCH AND THEODORE SODDY

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In the interaction between allylmagnesium bromide and certain aza-aromatic heterocycles, the following reactivity series was observed: pyridine < quinoline ≃ isoquinoline < phenanthridine ≃ N-benzylideneaniline ≃ acridine < quinoxaline. Proof of structure of the resulting allyl derivatives was accomplished by synthesis, degradation and infrared analysis. The mechanism of the reaction is discussed as a nucleophilic attack of the Grignard reagent on the nitrogen heterocycle. The variation in reactivity of these heterocycles can be rationalized adequately in terms of the localization energies of the dihydro derivatives. In connection with the selectivity of allylmagnesium bromide, an explanation is advanced for the different behavior of butyllithium with these nitrogen heterocycles.

The interactions of Grignard reagents with aza-aromatic heterocycles such as pyridine, quinoline and acridine have been reported periodically, but the conditions employed have been so varied that the limitations of the reaction have not been drawn.[1]

(1) For an excellent survey of previous work see M. S. Kharasch and O. Reinmuth, "Grignard Reactions of Nonmetallic Substances," Prentice-Hall, Inc., New York, N. Y., 1954, pp. 1251–1259.

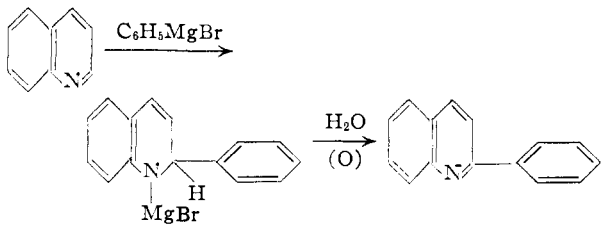
TABLE I

REACTION OF ALLYLMAGNESIUM BROMIDE WITH AZA-AROMATIC HETEROCYCLES

Reactant	Product	Formula	Yield, %	B.p., °C.	Mm.	d^{20}_4	$n^{20}D$	MRD Calcd.	MRD Found	Nitrogen, % Calcd.	Nitrogen, % Found[d]	Picrate, m.p., °C.
Pyridine	4-Allyl-	C_8H_9N	9[a]	84–89	11	....	1.5170	...		16.09	16.21[e]	167.5–168.5
				186–188	730							
Quinoline	2-Allyl-	$C_{12}H_{11}N$	56	119–121	4	1.0385	1.5920	56.20	55 90	8.30	8.49	150–151
Isoquinoline	1-Allyl-	$C_{12}H_{11}N$	57	95–100	0.5	1.0308	1.5701	55.30	55.78	8.30	8.11	215–216
Phenanthridine	6-Allyl-5,6-dihydro-	$C_{16}H_{13}N$	78	174–177[b]	3.6	....	....	...	...	6.33	6.36	Red solid
N-Benzylideneaniline	α-Allylbenzylaniline	$C_{16}H_{17}N$	80	146–148	2.9	1.0224	1.5920	73.12	73.90	6.24	6.07	.....
Acridine	9-Allylacridan	$C_{16}H_{15}N$	81	.....[c]	...	....				6.33	6.36	Red solid
Quinoxaline	2,3-Diallyl-1,2,3,4-tetrahydro-	$C_{14}H_{18}N_2$	80[f]	142–143	1.8	1.0301	1.5855	69.51	69.80	13.08	13.32	

[a] 70% recovery of pyridine; some tar was left in distillation flask. [b] Upon standing it solidified to white solid, m.p. 64.5–66°, from petroleum ether (b.p. 60–70°). [c] Pale yellow solid, m.p. 115–116° from petroleum ether (b.p. 60–70°). [d] Average of duplicate analyses, neither of which deviated more than 0.25% from calculated value. [e] Analyzed as the picrate. [f] The infrared spectra of the partially purified allyl derivatives of pyridine, quinoline and isoquinoline gave weak –NH bands which disappeared upon further purification. Any residual dihydro product was certainly oxidized in picrate formation. 5-Allyl-5,6-dihydrophenanthridine was extremely air-sensitive. A white sample became chartreuse when allowed to stand. Such dihydrophenanthridines are susceptible to oxidation. 2,3-Diallyl-1,2,3,4-tetrahydroquinoxaline turned a reddish-brown upon standing.

The products isolated have been considered to result from the addition of the Grignard reagent to the azomethine linkage and the subsequent oxidation of the adduct, either spontaneously or in the course of hydrolysis. The preparation of 2-phenylquinoline from quinoline and phenylmagnesium bromide has been represented thus[2]



The formation of the γ-substituted product as in the cases of pyridine[3] and acridine[4] would be regarded as arising through 1,4-addition to the azomethine linkage.

The conditions necessary for reaction, however, have been generally of a "forcing" nature. Oddo[5] ran the reaction in benzene–toluene mixtures; Bergstrom and McAllister[2] employed an autoclave; others[4,6] used dioxane mixtures. The yields ranged from 7 to 70% in no regular manner.

As part of a program to correlate the variation in reactivity of aza-aromatic heterocycles, the action of organometallic compounds on such systems has been reinvestigated. The use of butyllithium in this comparative study appeared to be unsatisfactory, since this reagent reacts rapidly with all the aza-aromatic heterocycles to give the dihydrobutyl derivative in high yield.[7] In our search for a more selective reagent, we observed that allylmagnesium bromide reacted with a series of nitrogen heterocycles with a marked difference in facility and without the necessity of stringent conditions.

(2) F. W. Bergstrom and S. H. McAllister, THIS JOURNAL, **52**, 2845 (1930).

(3) W. L. C. Veer and St. Goldschmidt, *Rec. trav. chim.*, **65**, 793 (1946), found that pyridine and benzylmagnesium chloride gave 4-benzylpyridine in small yield.

(4) E. Bergmann and W. Rosenthal, *J. prakt. Chem.*, [2] **135**, 267 (1932).

(5) B. Oddo, *Gazz. chim. ital.*, **37** [1], 568 (1907).

(6) H. Gilman and G. Gainer, THIS JOURNAL, **71**, 2327 (1949).

(7) (a) K. Ziegler and R. Zeiser, *Ber.*, **63**, 1847 (1930); (b) *Ann.*, **485**, 174 (1931); (c) H. Gilman and S. Spatz, THIS JOURNAL, **63**, 1553 (1941); (d) we have realized a 90% yield of 6-butyl-5,6-dihydrophenanthridine by the reaction of butyllithium and phenanthridine at −50° for 10 minutes and subsequent work-up.

Experimental[8]

Starting Materials.—The heterocycles employed in this study were of the purest grade commercially available. The liquids, pyridine, quinoline and isoquinoline, were distilled over pellet sodium hydroxide before use. The solid quinoxaline also was distilled (b.p. 99–100° at 12 mm.), since it darkened upon storage. The acridine (m.p. 107–108°), phenanthridine (m.p. 105–106°) and N-benzylideneaniline (m.p. 55–56°) were used without further purification.

The allylmagnesium bromide was prepared in yields ranging from 79 to 88% (according to the quality of the allyl bromide) by following a published procedure.[9] The reagent was analyzed by titrating a hydrolyzed aliquot with standard acid.[10]

General Procedure for the Reaction of the Heterocycle with Allylmagnesium Bromide.—In order that the yields would be as indicative as possible of the heterocycle's activity, an arbitrarily chosen general set of directions was rigidly adhered to. Thus, in an addition funnel flushed with oxygen-free nitrogen were placed 0.175 mole of the heterocycle and 100 ml. of dry ether. (A solution was obtained except with acridine and phenanthridine.) To the stirred mixture was added dropwise 0.230 mole of filtered allylmagnesium bromide in ether (*ca.* 1 *M*). In the case of quinoxaline 0.460 mole of the Grignard reagent was employed. Gentle reflux and the formation of a yellow to red precipitate characterized the 40-minute addition period. Thereafter, a complete solution was obtained, except for the pyridine and acridine runs in which a yellow suspension persisted. The mixture was refluxed under nitrogen for 18 hr. and then hydrolyzed with 500 ml. of saturated ammonium chloride solution. In all cases except acridine the product was ether soluble. Hence, after separating the ether layer and extracting the aqueous layer with ether, the combined ether extracts were dried over anhydrous sodium sulfate and the ether subsequently removed. The residue was distilled under reduced pressure.

Since the product from acridine was only slightly soluble in ether, the hydrolyzed mixture was filtered to obtain the crude product. An additional amount was obtained by removing the solvent from the dried ether layer. The crude solid was recrystallized from petroleum ether (b.p. 60–70°).

The yields of the products together with other pertinent data are given in Table I. The yields are computed for the product after one purification (either distillation or recrystallization) and the physical constants after this purification were within two to three degrees of those given in the table.

Proof of Structure of the Products. a. 2-Allylpyridine.—The procedure employed to prepare this unreported com-

(8) All melting points are corrected.

(9) H. Gilman and J. H. McGlumphy, *Bull. soc. chim. France*, **43**, 1325 (1928).

(10) H. Gilman, P. D. Wilkinson, W. P. Fishel and C. H. Meyers, THIS JOURNAL, **45**, 150 (1923).

pound was essentially the same as that detailed above for the interaction of allylmagnesium bromide and the nitrogen heterocycles. To minimize bipyridine formation, however, the 2-bromopyridine was added to the cooled Grignard reagent. To 0.230 mole of allylmagnesium bromide in 225 ml. of dry ether was added 34.8 g. (0.220 mole) of 2-bromopyridine in 125 ml. of dry ether. During the 45-minute addition period the flask was cooled in an ice–salt–bath. The resulting mixture became blood-red, but this color darkened somewhat upon stirring overnight. The reaction mixture, upon usual work-up and subsequent distillation, gave 10.7 g. (41%) of water-white liquid, b.p. 59–65° (12 mm.). The product was redistilled and collected at 63–65° (12 mm.), $n^{20}D$ 1.5190.

Anal. Calcd. for C_8H_9N: N, 11.75. Found: N, 11.42.

The picrate was prepared and recrystallized from 95% ethanol as golden yellow needles, m.p. 118.5–120°.

Anal. Calcd. for $C_{14}H_{12}N_4O_7$: N, 16.09. Found: N, 16.14, 16.25.

b. **4-Allylpyridine.**—The compound formed from the interaction of pyridine and allylmagnesium bromide was shown to be the 4-isomer in the following manner. The compound (1.1 g.) in ethanol was reduced with hydrogen and prereduced platinum catalyst at room temperature. The volume of hydrogen was monitored to reduce the allyl group selectively to the propyl side chain. The filtered solution was concentrated and an ethanolic solution of picric acid was added. The precipitated crude picrate melted over the range 112–120° and after successive recrystallizations from water and ethyl acetate, yellow needles, m.p. 128.0–129.5°, were obtained. Admixed with an authentic sample of 4-propylpyridine picrate[11] the picrate melted at 128.0–129.5°. The infrared spectrum of the unknown propylpyridine picrate was identical with that of the 4-isomer.

c. **2-Allylquinoline.**—Similar to the above procedure the product from quinoline and allylmagnesium bromide subsequent to hydrolysis was reduced with hydrogen and prereduced platinum catalyst. The picrate of the propylquinoline thus obtained melted at 162–163°. According to published directions for 2-butylquinoline,[7] authentic 2-propylquinoline was prepared from quinoline and propyllithium. The picrate of the product melted at 162–163° and melted undepressed admixed with the propylquinoline picrate obtained by hydrogenation. Infrared spectra indicated that the solids were identical.

d. **Dichromate Oxidation.** (1) **6-Allyl-5,6-dihydrophenanthridine.**—This compound (1.0 g.) was oxidized by heating it in glacial acetic acid solution with 3.9 g. of potassium dichromate for 90 minutes and then pouring into cold water. The crude 6(5H)-phenanthridinone (0.9 g.) melted over the range 265–275°. Recrystallized from acetic acid it melted at 291–293°.

(2) **9-Allylacridan.**—Similar dichromate oxidation of this compound gave yellow platelets of 9-acridanone which melted at 356–358° after recrystallization from 95% ethanol.

e. **Picrate Formation.**—The picrates listed in Table I were prepared in the usual manner. The significant observation is that the allyl derivatives of acridine and phenanthridine formed distinctly red picrates. Attempted recrystallization changed them to brownish-yellow solids. Since Ziegler and Zeiser[7] have noted that dihydro derivatives of pyridine-type bases form red picrates, this indicates that the products from acridine and phenanthridine are dihydro types. Presumably, the red dihydro picrate is slowly oxidized by the picric acid complexed with it.

f. **Infrared Analysis.**—The infrared spectra of the products were obtained to check for expected bands. The most indicative bands were those for –N–H, –C–H and $-C{=}CH_2$ (terminal vinyl).

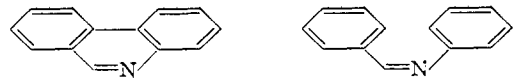
The –N–H stretching band established an excellent criterion of whether a dihydro adduct was obtained subsequent to hydrolysis. The band occurred at 2.9 μ for the products from N-benzylideneaniline and quinoxaline, but was shifted slightly (3.00 μ) for the allyl derivatives of acridine and phenanthridine.[12]

The –CH band occurred at 3.18 μ for allyl derivatives of acridine and phenanthridine. When run in bromoform, however, the compounds from N-benzylideneaniline and quinoxaline gave two sharp bands at 3.30 and 3.45 μ.

The bands correlated with the terminal vinyl group appeared at 10.1 and at 11.0 μ when the sample was run in bromoform.[13]

Results

Table I shows that, under the same conditions, the reactivity of the heterocycles toward allylmagnesium bromide increases in the series: pyridine $<<$ quinoline $\simeq$ isoquinoline $<$ phenanthridine $\simeq$ acridine. Quinoxaline, included as an example of a diaza-aromatic heterocycle, shows greater reactivity than any of the monaza-aromatic types. In order to compare an open-chain model of an aza-aromatic system with these heterocycles, N-benzylideneaniline was tested as the open model of phenanthridine. The reactivity of the two compounds seems about of the same order.



It should also be stressed that the stability of the dihydro derivative of the product seems to parallel the reactivity of the original heterocycle. All the more reactive heterocycles gave the product in the dihydro form, whereas the less reactive heterocycles yielded the product in the oxidized form. Infrared analysis and the colors of the picrates were used to detect the dihydro derivatives.

The position assumed by the entering allyl group was always either alpha or gamma to the nitrogen atom. It might be expected that pyridine would form the 2-isomer by analogy with the reaction of butyllithium on this heterocycle.[7] However, that the 4-isomer results was demonstrated by hydrogenating the compound to the corresponding propylpyridine and comparing the picrate of the latter with authentic 4-propylpyridine picrate.[14] Moreover, 2-allylpyridine was unambiguously prepared from 2-bromopyridine and allylmagnesium bromide and was shown to differ from the hydrolyzed products of pyridine and allylmagnesium bromide. Additional support for these conclusions is derived from the report that benzylmagnesium chloride and pyridine also form the 4-isomer.[3]

The question as to whether the allylquinoline was the 2- or 4-isomer was satisfactorily resolved by similar hydrogenation studies. The reduction of the allylquinoline led to a propylquinoline whose picrate was shown to be identical with that of authentic 2-propylquinoline by infrared analysis and a mixed melting point determination.

In the cases of isoquinoline, phenanthridine and acridine only one mode of attack was considered possible, that is, on the available carbon, alpha or gamma to the nitrogen (isoquinoline is presumably not attacked at C_3 but only at C_1). However,

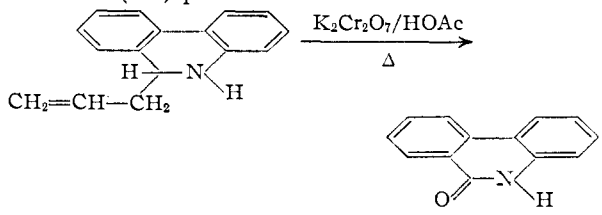
(11) Professor J. P. Wibaut generously furnished a sample of this compound. On our apparatus it melted at 127.5–129.0°; *cf.* J. F. Arens and J. P. Wibaut, *Rec. trav. chim.*, **61**, 59 (1942).

(12) Unless otherwise stated, the spectra were obtained as Nujol mulls.

(13) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1954, pp. 42–43.

(14) We are aware of the occasional unreliability of the mixed melting point determination in showing the identity of picrates (*cf.* L. Ruzicka and L. Ehmann, *Helv. Chim. Acta*, **15**, 140 (1932)). Our results, however, are never based solely on this criterion.

dichromate oxidation of the products from phenanthridine and acridine lent independent proof that the allyl group occupied the available position in the pyridinoid ring. If there is an alkyl group at the 6-position in phenanthridine, dichromate oxidation will produce 6(5H)-phenanthridinone.[15] Thus, 6-allyl-5,6-dihydrophenanthridine was oxidized to 6(5H)-phenanthridinone

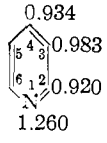


In a similar fashion 9-allylacridan gave 9-acridanone.

Discussion

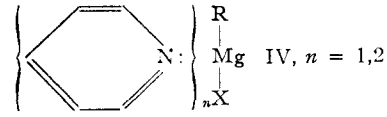
The addition of Grignard reagents to the azomethine linkage has been considered as analogous to their reaction with the carbonyl group. The justification for this view stems from the consideration of the –CH=N– linkage as an aldehyde (–CH=O) in the ammonia system of compounds.[16] Underlying such a parallelism is the assumption that the azomethine linkage may properly be called a genuine double bond. As applied to nitrogen heterocycles, this reasoning has led to the notion of bond fixation. Theoretical advances in molecular structure make such bond fixation untenable and account for the experimental results by saying that the azomethine linkage has double-bond character (resonance approach).

Alternately, the semi-quantitative method of molecular orbitals may be used to calculate the charge density distribution for the π-electrons in aza-aromatic heterocycles, and chemical behavior can be rationalized by assuming nucleophilic (electrophilic) attack to occur at centers of low (high) π-electron density.[17] Modified calculations for pyridine give the charge distribution noted in III.[18] If the interaction of allylmagnesium bromide and pyridine is considered to be a nucleophilic attack of the allyl carbanion upon the hetero-



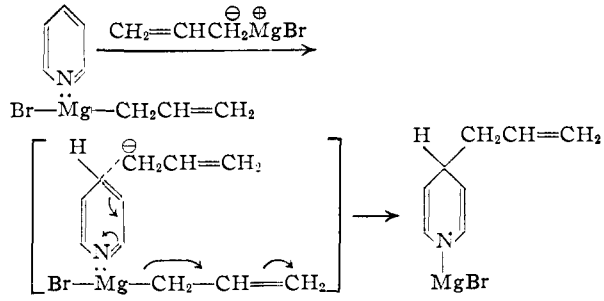
III

cycle, it is understandable why either the 2- or the 4-position is attacked.[19] The recognition of the fact that pyridine initially forms a complex[20] with the Grignard reagent (as in IV) complicates this simple view but does not change the results. Such complexation should enhance the electronegativity



IV, n = 1,2

of the nitrogen and further deplete the electron density at the 2- and 4-positions. In addition, the coördination of the nitrogen with the magnesium should facilitate the heterolysis of the magnesium–carbon bond. The over-all reaction may then occur thus



Although in qualitative agreement with the observed reactivity of the α- and γ-positions of aza-aromatic heterocycles toward nucleophilic reagents, this charge density approach does not enable us to explain the factors governing selection between α- and γ-positions in a given molecule. As previously indicated, it is puzzling why butyllithium should attack the 2-position, whereas allylmagnesium bromide attacks the 4-position in pyridine. Nor does the charge density approach readily rationalize the marked difference in reactivity among a series of nitrogen heterocycles.

Instead of considering the energy of the reagents before reaction, we may rationalize differences in reactivity by considering the variation of the energy of the transition state. This approach demands that we have a fair notion of the geometry of the transition state. At the carbon atom being attacked the hybridization is changed from sp^2 to sp^3 in the course of reaction. The activation energy of the reaction, therefore, should be related to the loss of π-electron delocalization in removing that carbon's p-orbital from conjugation.[21] Theoretically, one would expect the localization energy for a given α- or γ-carbon atom to increase in the series; acridine $\simeq$ phenanthridine $<$ quinoline $\simeq$ isoquinoline $<$ pyridine. (In this view the reactivity of a position should bear an inverse relationship to the localization energy of that position.) Then in the transition state the carbon atom attacked should have nearly a tetrahedral configuration; in other words, its geometry closely resembles that of the product. Employing the thermic postulate of Hammond,[22] one would expect the activation energy necessary to attain this transition state to vary with the energy of the product. Although the product is actually the dihydromagnesium bromide salt, this should closely resemble the dihydro compound obtained upon hydrolysis. In the light of this proposal, one might correlate the reactivity

(15) Unpublished studies of this Laboratory. By analogy the same observation may apply to 9-alkylacridines.

(16) (a) H. Decker and A. Kaufmann, *J. prakt. Chem.*, [2] **84**, 219 (1911); (b) E. C. Franklin, THIS JOURNAL, **46**, 2150 (1924).

(17) For further elaboration on this view see B. Pullman and A. Pullman, "Les Theories Electroniques de la Chimie Organique," Masson Co., Paris, France, 1952, pp. 615–620.

(18) C. Sandorfy, C. Vroelant, P. Yvan, O. Chalvet and R. Daudel, *Bull. soc. chim. France*, **17**, 304 (1950).

(19) The assumption of this reaction as a nucleophilic process accords well with experimental observations. However, in reactions carried out in the presence of dioxane or at elevated temperatures it is quite conceivable that radical processes may play a part.

(20) F. Sachs and L. Sachs, *Ber.*, **37**, 3088 (1904).

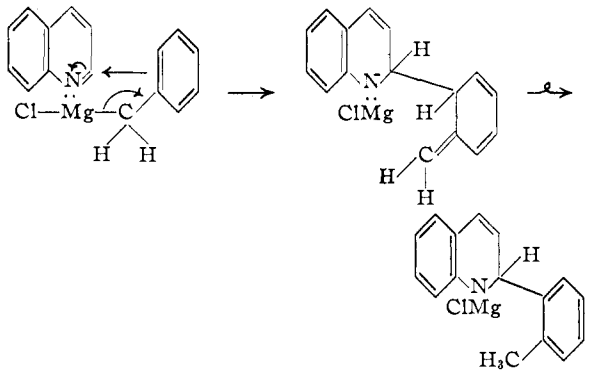
(21) G. W. Wheland, THIS JOURNAL, **64**, 900 (1942).

(22) G. S. Hammond, *ibid.*, **77**, 334 (1955).

of aza-aromatic heterocycles toward allylmagnesium bromide with the stability of the dihydro derivatives formed upon hydrolysis. The dihydro derivatives of allyl-acridine and -phenanthridine were quite stable, and the parent heterocycles showed high reactivity. On the other hand, pyridine had a low activity and the instability of the dihydro derivatives is well known.[23] This view also helps to clarify why the 4-position, rather than the 2-position, of pyridine is attacked. The superior stability of 1,4-dihydropyridine over 1,2-dihydropyridine[23] means, in view of our explanation, that the activation energy (hence, the localization energy) may be lower for attack at the 4-position. This correlation might be placed on a quantitative basis for selective nucleophiles, in general, if the localization energies for the various dihydro derivatives were known.[24]

(23) J. A. Berson and E. Brown, THIS JOURNAL, **77**, 444 (1955).

(24) A referee has suggested reasonably that allylmagnesium bromide may initially attack the 2-position of pyridine *via* a cyclic mechanism analogous to the Claisen rearrangement and rearrange to the 4-position *via* a *para*-Claisen process. Indeed, such a possibility has been considered by the authors; however, they feel that such a view would be inconsistent with the behavior of unsymmetrical allylic systems in these processes. For example, benzylmagnesium chloride reacts with quinoline and isoquinoline to yield benzyl-substituted products. A cyclic mechanism would demand that *o*-tolyl derivatives result (*cf.* ref. 4)



In addition, *ortho* attack on acridine is extremely improbable and yet *para* attack occurs smoothly. Hence, it is not necessary to postulate an initial *ortho* attack. Another possibility considered by the authors is that the complex between pyridine and the Grignard reagent hinders attack at the 2-position. Although such steric factors may play a part, this view is weakened by the observation that quinoline which also forms a complex is readily attacked at the 2-position.

(25) H. C. Brown and K. L. Nelson, THIS JOURNAL, **75**, 6292 (1953).

Although we have offered an explanation for the attack of allylmagnesium bromide at the 4-position in pyridine, we must now consider why the similar butyllithium prefers the 2-position. For electrophilic attack on aromatic systems Brown[25] has noted an inverse relationship between the selectivity of an agent in choosing *meta*- or *para*-positions in toluene and its rate relative to benzene. This leads to the conclusion that the more reactive reagents react by way of looser transition states which are relatively insensitive to factors such as localization energy. Clearly, by applying this argument to nucleophilic attack on nitrogen heterocycles, this implies that the extremely reactive butyllithium in its reaction with pyridine will attain a transition shifted toward the reactants. Hence, factors such as charge density and autopolarizability of the initial pyridine molecule will become more important in determining the position attacked. Since both factors favor attack at the 2-position,[17] butyllithium readily gives the 2-butyl-1,2-dihydrolithium salt.

It also follows from Brown's correlation[24] that since allylmagnesium bromide is more selective than butyllithium, it is less reactive. Supposing that the two reagents have roughly the same ionic character, the greater reactivity of the butyl carbanion is understandable, since it cannot participate in the sort of π-electron stabilization available to the allyl carbanion, $\overset{\ominus}{C}H_2-CH=CH_2 \longleftrightarrow CH_2=CH-\overset{\ominus}{C}H_2$.

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AMES, IOWA

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF ILLINOIS INSTITUTE OF TECHNOLOGY]

The Reactions of Diazonium Salts with Some Substituted Hydrazines. II. 1,6-Bisaryl-3,4-diacetyl-1,5-hexazadienes[1,2]

BY JEROME P. HORWITZ AND VYTAUTAS A. GRAKAUSKAS[3]

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The addition of two moles of a negatively substituted benzenediazonium salt to an alkaline solution of 1,2-diacetylhydrazine affords a 1,6-bisaryl-3,4-diacetyl-1,5-hexazadiene (I). The structure of I is established from degradative evidence.

The sole claim to the successful preparation of a stable chain of six nitrogen atoms is contained in a report by Hofmann and Hock who obtained 1,6-bis-(5′-tetrazolyl)-1,5-hexazadiene from the interaction of hydrazine and excess tetrazolediazonium chloride.[4] Unfortunately, the evidence in support of this structure is not unequivocal, and hence the

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(2) Previous communication on this subject, *J. Org. Chem.*, **19**, 194 (1954).

(3) Abstracted in part from a dissertation submitted by Vytautas A. Grakauskas to the Graduate School of Illinois Institute of Technology in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(4) K. A. Hofmann and H. Hock, *Ber.*, **44**, 2946 (1911).