Likewise attempted methylation of 10 g. (0.024 mole) of VIIc gave 4.3 g. (80%), of VIc, m.p. 147-149° (m.m.p. with VIc 149-150° after recrystallization from acetone), and 4.5 g. (54%) of methyltributylphosphonium iodide. m.p. 132° .¹⁸

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ROCHESTER 4, N. Y.

[CONTRIBUTION NO. 979 FROM THE CHEMISTRY LABORATORY OF INDIANA UNIVERSITY]

Reduction of Schiff Bases. III. Reduction with Dimethylamine Borane

JOHN H. BILLMAN AND JOHN W. MCDOWELL

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A number of Schiff bases with various functional groups such as chloro, nitro, hydroxy, methoxy, carbethoxy, sulphonamido, and carboxy were prepared and reduced to the respective secondary amines by using dimethylamine borane in glacial acetic acid. The yields of the secondary amines generally ranged from 80-97%. None of the other functional groups were affected under the conditions used during the course of the reduction. The stoichiometry of the reaction was shown to be three moles of Schiff base to one mole of dimethylamine borane and indicated that borane was the probable reducing agent.

The reduction of Schiff bases to form secondary amines has been accomplished by catalytic hydrogenation¹ and by various chemical methods such

(1) C. R. Noller, *Chemistry of Organic Compounds*, 2nd Ed., W. B. Saunders Company, Philadelphia, Pa., 1958, p. 536.

as magnesium in methanol.² More recently it has been shown that lithium aluminum hydride³

(2) L. Zechmeister and J. Truka, Ber., 63B, 2883 (1930).
(3) Part II: J. H. Billman and K. N. Tai, J. Org. Chem., 23, 535 (1958).

TABLE I

Secondary Amines ArCH2NHAr' (I-XIV) ArCH2CH2NHCH2Ar' (XV-XVII)								
Ar	Ar'		M.P. (Corr.)	Yield, %	Method	Recryst. Solvent		
Phenyl	Phenyl	I	37.5-38.0ª	84.2 ^b				
Phenyl	<i>p</i> -Chlorophenyl	п	$47.5 - 48.0^{a}$	97.4	В	Ethanol		
p-Chlorophenvl	p-Chlorophenyl	III	70.0-70.5ª	89.5	Ā	Ethanol		
Phenyl	o-Chlorophenyl	IV	39.5-40.0ª	83.6°				
<i>p</i> -Nitrophenyl	p-Nitrophenyl	v	189.0-189.5 ^d	89.2	Α			
<i>m</i> -Nitrophenyl	<i>m</i> -Nitrophenyl	VI	136.5-137.0ª	94.5	Α	_		
<i>m</i> -Nitrophenyl	o-Nitrophenyl	VII	167.0-167.5	89.3	Α	Ethanol		
<i>p</i> -Methoxyphenyl	Phenyl	VIII	63.5 - 64.0'	90.9	В	Ethanol		
<i>m</i> -Hydroxyphenyl	Phenyl	IX	101.0-102.0ª	82.0	в	Ethanol		
Phenyl	<i>p</i> -Hydroxyphenyl	х	88.0-89.0"	94.0	в	Methanol		
Phenyl	<i>p</i> -Methoxyphenyl	XI	49.0-50.0ª	90.1	Α	Ethanol		
Phenyl	p-Carbethoxy- phenyl	XII	96.5–97.0 ^h	92.8	Α	Ethanol		
Phenyl	p-Sulfonamido- phenyl	XIII	170.0-171.04	79.5	Α			
p Methoxyphenyl	<i>p</i> -Phenylmercapto- acetic acid	XIV	131.5–133.0(d) ^{<i>i</i>}	84.5	в	Methanol		
<i>p</i> -Methoxyphenyl	p-Methoxyphenyl	XV	k	71.3	В			
p-Nitrophenyl	p-Nitrophenyl	XVI	78.0-78.5	71.0	в	Methanol		
<i>p</i> -Chlorophenyl	p-Chlorophenyl	XVII	l	84.0	В			

^a J. H. Billman and A. C. Diesing, J. Org. Chem., 22, 1069 (1957). ^b Amine purified by formation of the hydrochloride, m.p. 214-215°, yield based on hydrochloride, 90.0%. ^c Amine purified by formation of the hydrochloride. ^d C. Paal and C. Benker, Ber., 32, 1256, (1899) reported m.p. 192°. ^e Anal. Calcd. for N: 15.39; Found 15.55; also infrared spectra indicates reduction of the Schiff base. ^f O. J. Steingart, Ann., 241, 337, reported m.p. 64.5°. ^g M. Bakunin, Gazz. Chim. Ital., 36II, 213, 218. ^h Aladar Skita and Werner Stuhner, Ger. Patent No. 716,668, Dec. 24, 1941. ⁱ Schiff base m.p. 176°, reduction proven by infrared spectra and mixed m.p.; E. Miller, H. J. Rock, and M. L. Moore, J. Am. Chem. Soc., 61, 1199 (1939) m.p. 139-174°. ⁱ Anal. Calcd. for S: 10.56; Found 10.58. ^k Isolated as the dihydrochloride. ⁱ Isolated as the diacetate, m.p. 139-140°. ACETYL DERIVATIVES OF SECONDARY AMINES

$$\begin{array}{c} O \\ H \\ Ar - CH_2 - N - C - CH_3 (I - XIV) \\ Ar' \end{array}$$

 $\begin{array}{c} \operatorname{Ar-CH_2-N-CH_2-CH_2-N-CH_2-Ar'}(XV-XVII) \\ \downarrow \\ O = C \\ O = C \\ \end{array}$

 \backslash

Sec- ondary	Acetamide M.P.	Analysis			
Amine	(Corr.)		Calcd.	Found	
I	57.5-58.0 ^a				
II	91.0-91.5	Cl	13.68	13.52	
III	104.5 - 105.0	Cl	24.15	24.43	
IV	b				
v	$148.5 - 149.0^{\circ}$				
VI	102.0 - 102.5	Ν	13.32	13.36	
VII	127.5 - 128.0	Ν	13.32	13.14	
VIII	53.0-53.5	Ν	5.49	5.38	
IX	99.0-100.0	Ν	5.82	5.77	
х	169.0 - 169.5	Ν	5.81	5.73^{d}	
XI	e	Ν	5.49	5.44	
XII	58.0	N	4.72	4.66	
XIII	155.5 - 156.5	Ν	8.10 ^f	8.12	
XIV	112.0 - 113.0	\mathbf{S}	9.28	9.11	
XV	$150.0 - 150.5^{g}$				
XVI	185.0 - 186.0	Ν	13.49	13.17	
XVII	135.5-136.0 ^h				

^a Yu. V. Svetkin, Zhur. Obshchei Khim., 26, 1261 (1956). ^b Benzoyl derivative; m.p. 111.0-111.5°. J. H. Billman and A. C. Diesing, J. Org. Chem., 22, 1069 (1957). ^c C. Paal and C. Benker, Ber., 32, 1257 (1899) reported m.p. 145°. ^d Analysis indicated monoacetylated derivative and infrared spectra indicated an amide rather than an ester. ^e Acetamide was a high-boiling oil. ^f Calculated for the diacetyl derivative. ^g J. Th. L. B. Rameau, Rec. trav. chim., 57, 194 (1938) reported m.p. 151-152°. ^h J. H. Billman, J. Y. C. Ho, and L. R. Caswell, J. Org. Chem., 22, 538 (1957) reported m.p. 135.0-135.5°.

and sodium borohydride⁴ are excellent reagents for effecting this reduction.

Since it has been shown that dimethylamine borane will reduce a carbonyl group to an alcohol,⁵ it was thought that the affect of this reagent on the imine linkage and various other substituent groups such as chloro, nitro, hydroxy, methoxy, carboxy, carbalkoxy, and sulfonamido would be interesting to investigate.

The Schiff bases used in this study were, in general, derivatives of the parent compound N-benzylidenaniline. These were found to be easily converted to the corresponding amines according to the following equation:

 $Ar-CH=N-Ar' + (CH_3)_2NH \rightarrow BH_3 \xrightarrow[acetic]{acetic} acetic acid} Ar-CH_2-NH-Ar,$

(5) The Amine Borane, Technical Bulletin C-200, Callery Chemical Co. (1957).

Table I contains a list of the secondary amines and diamines produced by the procedure. The diamines which were made from the respective di-Schiff bases and which illustrate the versatility of this method, were oils or low-melting solids and were conveniently isolated as the dihydrochlorides or diacetates. Table II lists the acetyl derivatives of the secondary amines.

The yields of the secondary amines were generally good, most being in the neighborhood of 90%. One notable exception is the *N*-benzylidensulfanilamide which is reduced in a 79.5% yield. According to the literature this Schiff base is very easily hydrolyzed in the presence of water.⁶ Thus the lower yield is probably due to some hydrolysis by the acetic acid. However, the yield obtained by this method is comparable to any reported in the literature.

The ease and speed with which this reduction occurs is worthy of mention, since it is comparable to or better than the reductions using sodium borohydride or lithium aluminum hydride. The entire reaction seems to occur within a matter of a few minutes and, although in most of the cases the reaction mixture was refluxed an additional fifteen minutes, it was found that this was not necessary and indeed in one case, that of N-benzylidene-paminophenol, it was even detrimental to obtaining a good yield of the secondary amine. It is not necessary for the Schiff base to be completely dissolved in the glacial acetic acid for reduction to take place. Since the dimethylamine borane is very soluble in glacial acetic acid, generally only enough acid was used to dissolve it and to make a good suspension of the Schiff base. Due to the loss of some of the active hydrogen when dimethylamine borane is dissolved in glacial acetic acid a 25%excess of the calculated amount was used in all cases.

Prior to this time dimethylamine borane has been allowed to react in benzene or dioxane solution. However, it has now been found that it may be used in glacial acetic acid with very little loss of active hydrogen. The reduction of N-N-benzylidene-p-chlorobenzylidenaniline and aniline with dimethylamine borane was tried in benzene but was found to be very slow and gave poor yields. Thus benzene was abandoned as the solvent in favor of glacial acetic acid. The fact that glacial acetic acid can be used is interesting and important in that reductions may now be performed in an acid medium. This can not be done with any of the hydrides such as lithium aluminum hydride or sodium borohydride. This may also permit the reduction of compounds which are capable of undergoing tautomerization in a basic medium to a structure which would be difficult or impossible to reduce. Such a tautomeric shift to

⁽⁴⁾ J. H. Billman and A. C. Diesing, J. Org. Chem., 22, 1068 (1957).

⁽⁶⁾ H. G. Kolloff and J. H. Hunter, J. Am. Chem. Soc., 62, 159 (1940).

a quinoid-type structure has been postulated as the reason for the failure of N-benzylidene-paminophenol (A) to undergo reduction with sodium borohydride² which provides a basic environment. This same type of tautomerization has also been used to explain the failure of the imino derivatives of anthrone to be reduced to the corresponding amines.¹



In the case of the N-benzylidene-p-aminophenol (A) it was found that reduction occurred rapidly and smoothly when the dimethylamine borane was used in the acid medium thus giving strong support to the postulated basic tautomerization. This Schiff base was reduced to N-benzyl-p-aminophenol (XI) in 94% yield. However, in the case of N-phenyl-9-anthrylidenimine (B), no reduction could be effected even after prolonged heating in glacial acetic acid in order to shift the above tautomerization to the left. The failure of this latter reduction is not wholly unexpected in view of the presence in this Schiff base of an inherent quinoid-type structure which is normally not readily reduced.

Under the conditions used in these experiments dimethylamine borane had no apparent affect on the nitro, carboxy, carbalkoxy, or sulfonamido groups or did not remove the chloro, hydroxy, or methoxy groups. In this respect dimethylamine borane is remarkably similar to sodium borohydride.

The secondary amines were easily liberated from the reaction mixture by the addition of cold water or by neutralization of the acetic acid solution with sodium hydroxide. In the case of the high melting secondary amines the product usually precipitated upon cooling the reaction mixture or upon the addition of water. In most instances these products were sufficiently pure as to require no further recrystallization. In the case of the lowmelting secondary amines, the addition of sodium hydroxide and water caused the amine to form as an oil which was then crystallized from another solvent. The method used in each case is indicated in Table I.

A study of the stoichiometry of the reduction was made using N-(m-nitrobenzylidene)-m-nitroaniline as the Schiff base. The various molar ratios, yields, and melting points of the crude products are shown in Table III. It is evident from the yields obtained and the purity of the crude products that the stoichiometry of the reduction is three moles of Schiff base to each mole of dimethylamine borane and that borane is the probable reducing agent. The actual mechanism of reduction may involve either a coordination of the borane with the nitrogen of the Schiff base followed by an intramolecular hydride transfer from boron to carbon such as has been proposed by Brown⁷ for reduction of carbonyl with diborane in diglyme or tetrahydrofuran, or a direct intermolecular hydride trans-



fer from amine borane to the carbon atom of the Schiff base, such as postulated by Jones⁸ in the boron trifluoride catalyzed reduction of carbonyls with trimethylamine borane.



TABLE III

STOICHIOMETRY STUDY

Schiff Base (Moles)	Di- methyl- amine Borane (Moles)	Molar Ratio Schiff Base/Di- methyl- amine Borane	Acetic Acid, Ml.	Yield, % (Crude Prod- uct)	M.P. (Crude Prod- uct)
$\begin{array}{c} 0.074 \\ 0.010 \\ 0.010 \\ 0.010 \\ 0.010 \end{array}$	0.092 0.005 0.0033 0.0025	$1:1.25 \\ 1:0.5 \\ 1:0.33 \\ 1:0.25$	20 10 10 5	94.594.196.447.6a	138–139 139–140 142–143 139–142

^a Remainder of material obtained was Schiff base.

The role of the glacial acetic acid in the case of the first type of proposed mechanism may be to facilitate liberation of borane, as it is needed for coordination with the Schiff base, by means of some type of concerted effort in conjunction with the Schiff base itself. In the second possible mechanism the role of the acetic acid would be one of

(7) H. C. Brown and B. C. Subba Rao, J. Am. Chem. Soc., 82, 681 (1960).

(8) W. M. Jones, J. Am. Chem. Soc., 82, 2530 (1960).

providing a proton for initial coordination with the nitrogen of the Schiff base.

The results of this investigation seem to favor the second possible mechanism by analogy to reduction by means of sodium borohydride, since the reducing power of dimethylamine borane in glacial acetic acid is much more like that of sodium borohydride than to that of diborane in diethylene glycol dimethyl ether or tetrahydrofuran.

The stoichiometry study further supports the selectivity of this reduction since in all cases a three- to four-fold excess of the reducing agent was used.

EXPERIMENTAL

Reduction method A. Ten grams of the Schiff base were suspended in 20 ml. of glacial acetic acid in a three-necked flask fitted with a reflux condenser, magnetic stirrer, thermometer, and dropping funnel and placed in a cold water bath. An equimolar amount plus 25% excess of the dimethylamine borane was dissolved in 20 ml. of glacial acetic acid and this solution added slowly through the dropping funnel to the Schiff base suspension keeping the temperature approximately at 20° . After the addition was complete, the reaction mixture was heated under reflux for an additional 15 min. and allowed to cool. If precipitation had not occurred, cold water was added slowly until precipitation was complete. The precipitate was collected by suction filtration, washed with cold water, and dried.

Reduction method B. The reduction was performed as in Method A except that when water was added to the cool reaction mixture an oil resulted. The reaction mixture was then completely neutralized with sodium hydroxide and the oil was extracted with diethyl ether. The ether extracts were dried over anhydrous magnesium sulfate and the ether removed under reduced pressure. The remaining oil was crystallized from petroleum ether or an ethanol-water mixture.

Preparation of acetyl derivatives. The petyl derivatives were prepared from across anhydride and pyridine by the usual method and recrystallized from cycle becane, cyclohexane-benzene, or ethanol-water mixtures.

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BLOOMINGTON, IND.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, FACULTY OF SCIENCE, CAIRO UNIVERSITY]

Action of Organomagnesium Compounds, Piperidine, and Aromatic Thiols on 4-Arylazo-2-phenyloxazolin-5-ones

WAFIA ASKER AND ZIEN E. ELAGROUDI

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Treatment of 4-arylazo-2-phenyloxazoline-5-ones (Va-d) with organomagnesium compounds, followed by hydrolysis, effected the opening of the heterocyclic ring and cyclization to the corresponding 1-aryl-5-phenyl-3-diarylmethanol-1*H*-1,2,4-triazoles (VId-h). Similarly, Va-d are rapidly rearranged by the action of piperidine and by the action of aromatic thiols to give 1-aryl-5-phenyl-3-carbpiperide-1*H*-1,2,4-triazoles (VIIa-d) and 1-aryl-5-phenyl-3-arylthiocarboxy-1*H*-1,2,4-triazoles (VIIa-e).

Although the reaction of 2-phenyl-4-benzylidene-5-(4H)-oxazolone (I) with excess of phenylmagnesium bromide, yielding a mixture of 2,5,5triphenyl-4-benzylidene-2-oxazoline (IIa) and 1,1diphenyl-2-benzamidocinnamyl alcohol (IIb), has been widely studied,¹ little attention has been paid to the study of the behavior of the corresponding hydrazone derivatives (V) toward the same reagent.



Recently, it has been shown² that 4-phenylazo-2phenyloxazoline-5-one (Va) is rapidly rearranged by methanolic potassium hydroxide or methanolic ammonia with the formation of 1,5-diphenyl-3carboxy-1H-1,2,4-triazole (VIa) and 1,5-diphenyl-3-carbamido-1H-1,2,4-triazole (VIc) respectively.

A similar rearrangement was also reported³ when 4-benzylidene-2-thio-5-thiazolidone (III) was treated with potassium hydroxide, sodium alkoxides, or primary or secondary amines, giving respectively the 5-substituted 2-thiothiazolidone-4-carboxylic acid (IV), ester and or N-substituted amides.

We have now investigated the behavior of 4arylazo-2-phenyloxazoline-5-ones (Va-d) toward

⁽¹⁾ H. Pourrat, Bull. soc. chim. France, 828 (1955), A. Mustafa and A. H. E. S. Harhash, J. Org. Chem., 21, 575 (1956), R. Filler and J. D. Wismar, J. Org. Chem., 22, 853 (1957).

⁽²⁾ G. W. Sawdey, J. Am. Chem. Soc., 79, 1955 (1957).

⁽³⁾ I. M. H. Heilbron, J. Chem. Soc., 2102 (1949), J. D. Billmoria and A. H. Cook, J. Chem. Soc., 2323 (1949).