

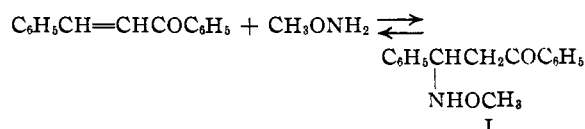
[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF HOWARD UNIVERSITY AND QUEENS COLLEGE]

## The Addition of Methoxyamine to $\alpha,\beta$ -Unsaturated Ketones and the Rearrangement of $\beta$ -Methoxyaminoketones<sup>1</sup>

BY A. H. BLATT

We have found from some experiments designed to determine the usefulness of methoxyamine<sup>2</sup> as a reagent for carbonyl compounds that, while methoxyamine hydrochloride reacts readily with both aldehydes and ketones to form oxime methyl ethers, the free base reacts in this fashion only with aldehydes and the more reactive ketones. This observation, which is in qualitative agreement with studies on the rate of oxime formation in relation to the *p*H of the reaction medium,<sup>3</sup> suggested that methoxyamine might, like numerous other basic nitrogen compounds,<sup>4</sup> add to the conjugated system present in  $\alpha,\beta$ -unsaturated ketones. Such addition, we have found, does take place and in the following paragraphs we report on one portion of a study of this addition reaction and the resulting addition products.

Methoxyamine adds readily and reversibly to benzalacetophenone and to a number of its analogs which contain a substituent in the *p* or *p'* position to furnish saturated  $\beta$ -methoxyamino ketones such as (I).



Methoxyamino-*bis*-propiophenones, such as VII, occasionally are formed also and from one unsaturated ketone, *p*-methylbenzalacetophenone, a *bis* compound of this type is the only product. The addition reaction is in itself unusual because it takes place in the absence of any added catalyst and because, when a strong base is added as a

(1) Presented in part at the Milwaukee meeting of the American Chemical Society, September, 1938.

(2) The name methoxyamine is both more concise and more clearly descriptive than the usual name,  $\alpha$ -methylhydroxylamine. Dr. E. J. Crane, Editor of *Chemical Abstracts*, to whom we are indebted for assistance in naming the methoxyamine addition products described in this paper, has also informed us that methoxyamine is the correct name. Compare Patterson, *THIS JOURNAL*, **55**, 3918 (1933).

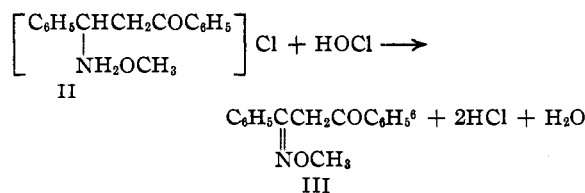
(3) Ölander, *Z. physik. Chem.*, **129**, 1 (1927); Huckel and Sachs, *Ann.*, **498**, 176 (1932).

(4) (a) Ammonia and amines: Tambor and Wildi, *Ber.*, **31**, 349 (1898); Kohn and Morgenstern, *Monatsh.*, **28**, 485 (1907); Smith and Adkins, *THIS JOURNAL*, **60**, 407 (1938). (b) Piperidine: Georgi and Schwyzer, *J. prakt. Chem.*, **86**, 273 (1912). (c) Piperazine and morpholine: Stewart and Pollard, *THIS JOURNAL*, **58**, 1980 (1936); **59**, 2006, 2702 (1937). (d) Hydroxylamine: Harries, *Ann.*, **330**, 191 (1904).

catalyst, the reaction does not stop with the formation of a  $\beta$ -methoxyamino ketone. Up to the present time the addition of methoxyamine to benzalacetophenone and eight substituted benzalacetophenones has been examined (see Table I). With every ketone, addition takes place. There are considerable variations in the yields of addition products obtained but differences in the solubilities of the products as well as in the position of equilibrium must be considered in order to account for the actual yields obtained, and there is no indication as yet of any regular influence on the addition reaction exerted by the substituent present in the unsaturated ketone.

In view of the large amount of information already available on the addition reactions of  $\alpha,\beta$ -unsaturated ketones, there can be little doubt but that the addition of methoxyamine to these unsaturated ketones is 1,4 and that the addition products are constituted like that from benzalacetophenone whose structure is shown in formula (I). However, the rearrangement which takes place on treatment of these addition products with strong bases, and which will be described shortly, makes it imperative to secure unequivocal evidence for the structures assigned to the addition products. This evidence was obtained for the addition product of methoxyamine to benzalacetophenone,  $\beta$ -phenyl- $\beta$ -methoxyaminopropiophenone (I), by oxidizing the material to a product whose structure was established by two independent syntheses.

When  $\beta$ -phenyl- $\beta$ -methoxyaminopropiophenone, as its hydrochloride (II), is oxidized by hypochlorous acid,<sup>5</sup> it furnishes the monoxime methyl ether of dibenzoylmethane (III).

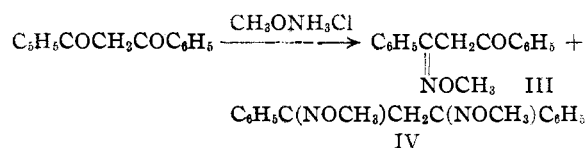


The structure of the oxime ether (III) is estab-

(5) Boese, Jones and Major, *THIS JOURNAL*, **53**, 3530 (1931).

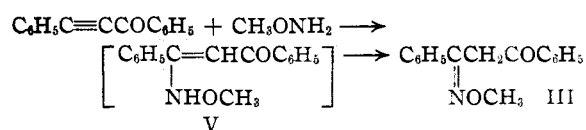
(6) The configuration assigned to this oxime ether is purely arbitrary.

lished by its preparation, accompanied by the dioxime dimethyl ether (IV), from methoxyamine hydrochloride and dibenzoylmethane (a synthesis which takes advantage of the fact mentioned previously that methoxyamine hydrochloride, in contrast with the free base, reacts with ketonic carbonyl groups).



This set of reactions, it should particularly be noted, establishes the location of the nitrogen atom in the addition product as attached to the carbon atom in the  $\beta$ -position to the carbonyl group.

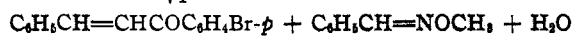
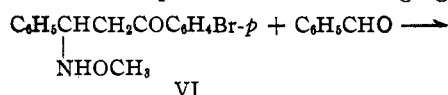
A second synthesis of the monoxime methyl ether of dibenzoylmethane, which establishes at the same time that methoxyamine adds also to acetylenic ketones, is furnished by the reaction between methoxyamine and benzoylphenylacetylene. The 1,4-addition of methoxyamine to this ketone would furnish a product (V) which, as the enamine tautomer of an oxime methyl ether, should rearrange to the same substance, (III), that was obtained by the oxidation of  $\beta$ -phenyl- $\beta$ -methoxyaminopropiophenone (I). This expectation is realized for the addition of methoxyamine to benzoylphenylacetylene furnishes directly the monoxime methyl ether of dibenzoylmethane (III).



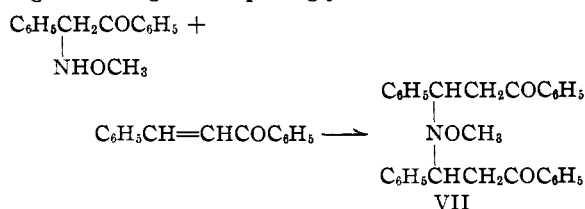
Finally, the fact may be mentioned, as corroborative negative evidence for 1,4-addition, that  $\beta$ -phenylbenzalacetophenone which does not undergo the customary 1,4-addition reactions<sup>7</sup> does not add methoxyamine.

It was stated earlier that the addition of methoxyamine to  $\alpha,\beta$ -unsaturated ketones is reversible. This is shown by the behavior of the addition products on heating, either alone or in the presence of a methoxyamine acceptor. Usually the addition products can be distilled in a high vacuum but when they are heated at only moderately reduced pressures they dissociate to regenerate methoxyamine and an  $\alpha,\beta$ -unsaturated

ketone. The equilibrium in the addition reactions usually is quite favorable to the formation of the addition products and this is true whether the addition is carried out at room temperature or near the boiling point of the solvent, alcohol. Consequently the addition products can be heated in alcoholic solution to the boiling point of the solution without appreciable change. If, however, a methoxyamine acceptor, for example, benzaldehyde which as an aldehyde will react with the free base, is present, then the addition reaction is reversed and the unsaturated ketone is regenerated. In effect, this process utilizes the addition products as oximating agents.



The  $\beta$ -methoxyaminopropiophenones produced by the addition of methoxyamine to  $\alpha,\beta$ -unsaturated ketones are O,N-disubstituted hydroxylamines and as such are weak bases. They will add to a second molecule of unsaturated ketone, they can be readily acetylated, and they form easily hydrolyzed salts with the halogen acids. Addition to a second molecule of unsaturated ketone furnishes methoxyimino-*bis*-propiophenones such as (VII). These *bis* compounds or trimolecular products are relatively unreactive, high melting and sparingly soluble substances.



The acetyl derivatives of the  $\beta$ -methoxyaminopropiophenones (see Table II, p. 3498), which are formed in quantitative yield simply by dissolving the parent substances in acetic anhydride, are more sparingly soluble and crystallize better than do the addition products. The acetyl derivatives, like the parent compounds, regenerate  $\alpha,\beta$ -unsaturated ketones on heating; unlike the parent compounds they also regenerate  $\alpha,\beta$ -unsaturated compounds on treatment with sodium methylate. The salts formed by the addition compounds with the halogen acids can be hydrolyzed by solution in alcohol and dilution with water. If, however, these salts in alcoholic solution or the addition products in alcoholic acid are heated, the addition

(7) Kohler, *Am. Chem. J.*, **33**, 515 (1907).



TABLE I

Notes to Table I. All the products described are colorless solids; the  $\beta$ -methoxyaminopropiophenones are readily soluble in all the common solvents save petroleum ether. The letters in the column "Temperature" indicate that addition was made near the boiling point of the solution (H) or at room temperature (C). The yields reported refer to crude, washed addition products. No yields are reported for the *bis* compounds as they were obtained only in small amounts from reaction mixtures which had been allowed to stand for long periods of time. The addition product from anisalacetophenone could not be obtained solid; the oil left after evaporating the solvent and excess methoxyamine furnished a crystalline acetyl derivative, see Table II. The addition product from benzal-*p*-methylacetophenone was difficult to obtain as a solid and to handle once solid; the oil left after evaporating the solvent and excess methoxyamine was used to prepare the acetyl derivative, Table II, and the unsaturated amine, Table III.

Unsaturated ketone	Product	Temp., H C	Yield, % 78	M. p., °C.	Crystallized from	Formula	OCH <sub>3</sub> Anal., % Calcd. Found
C <sub>6</sub> H <sub>5</sub> CH=CHCOC <sub>6</sub> H <sub>5</sub>	C <sub>6</sub> H <sub>5</sub> CH(NHOCH <sub>3</sub> )CH <sub>2</sub> COC <sub>6</sub> H <sub>5</sub>	H	64	54-55	Ethanol	C <sub>16</sub> H <sub>17</sub> NO <sub>2</sub>	12.15 11.9
	C <sub>6</sub> H <sub>5</sub> CHCH <sub>2</sub> COC <sub>6</sub> H <sub>5</sub>   NOCH <sub>3</sub>	C	..	178-179	Ethanol	C <sub>21</sub> H <sub>23</sub> NO <sub>2</sub>	6.7 6.7
C <sub>6</sub> H <sub>5</sub> CH=CHCOC <sub>6</sub> H <sub>4</sub> CH <sub>3</sub> - <i>p</i>	C <sub>6</sub> H <sub>5</sub> CHCH <sub>2</sub> COC <sub>6</sub> H <sub>4</sub> CH <sub>3</sub> - <i>p</i>	C	60	43-44	Ether-pet. ether	C <sub>17</sub> H <sub>19</sub> NO <sub>2</sub>	11.5 11.45
	<i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> CHCH <sub>2</sub> COC <sub>6</sub> H <sub>5</sub>   NOCH <sub>3</sub>	C	..	185-186	Methanol	C <sub>22</sub> H <sub>23</sub> NO <sub>2</sub>	6.3 6.3
C <sub>6</sub> H <sub>5</sub> CH=CHCOC <sub>6</sub> H <sub>4</sub> Cl- <i>p</i>	<i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> CHCH <sub>2</sub> COC <sub>6</sub> H <sub>5</sub>	C	70	51-52	Ether-pet. ether	C <sub>16</sub> H <sub>16</sub> ClNO <sub>2</sub>	10.7 10.66
	C <sub>6</sub> H <sub>5</sub> CH(NHOCH <sub>3</sub> )CH <sub>2</sub> COC <sub>6</sub> H <sub>4</sub> Cl- <i>p</i>	H	86	67-68	Ethanol	C <sub>16</sub> H <sub>16</sub> ClNO <sub>2</sub>	10.7 10.7
<i>p</i> -ClC <sub>6</sub> H <sub>4</sub> CH=CHCOC <sub>6</sub> H <sub>5</sub>	<i>p</i> -ClC <sub>6</sub> H <sub>4</sub> CH(NHOCH <sub>3</sub> )CH <sub>2</sub> COC <sub>6</sub> H <sub>5</sub>	H	65	52-53	Ethanol	C <sub>17</sub> H <sub>19</sub> NO <sub>2</sub>	21.75 21.4
	C <sub>6</sub> H <sub>5</sub> CHCH <sub>2</sub> COC <sub>6</sub> H <sub>4</sub> OCH <sub>3</sub> - <i>p</i>	C	..	183-184	Ethanol	C <sub>22</sub> H <sub>23</sub> NO <sub>2</sub>	17.8 18.1
C <sub>6</sub> H <sub>5</sub> CH=CHCOC <sub>6</sub> H <sub>4</sub> Br- <i>p</i>	C <sub>6</sub> H <sub>5</sub> CH(NHOCH <sub>3</sub> )CH <sub>2</sub> COC <sub>6</sub> H <sub>4</sub> OCH <sub>3</sub> - <i>p</i>	C	83	66-67	Ethanol	C <sub>16</sub> H <sub>16</sub> BrNO <sub>2</sub>	9.3 8.9
	<i>p</i> -BrC <sub>6</sub> H <sub>4</sub> CH=CHCOC <sub>6</sub> H <sub>5</sub>	H	63	52-53	Ethanol	C <sub>16</sub> H <sub>16</sub> BrNO <sub>2</sub>	9.3 9.1

product by a molecular weight determination (calcd. for C<sub>21</sub>H<sub>23</sub>NO<sub>2</sub>: mol. wt., 463. Found: mol. wt. (camphor), 458) and by a synthesis from  $\beta$ -phenyl- $\beta$ -methoxyaminopropiophenone (I) and benzalacetophenone. For this purpose 1.0 g. of the unsaturated ketone and 1.2 g. of the methoxyamino ketone were dissolved in 15 cc. of alcohol and left for sixty-seven days at room temperature. During this time, 0.6 g. of the sparingly soluble *bis* compound precipitated. On high vacuum distillation this material furnished benzalacetophenone.

The effect of acids on the  $\beta$ -methoxyaminopropiophenones and the reversal of the addition reaction which leads to their formation were examined using  $\beta$ -phenyl- $\beta$ -methoxyamino-*p*-bromopropiophenone (VI), since the products obtained from the compound were easily handled. When a solution of 1.0 g. of the propiophenone (VI) in 16 cc. of alcohol, 1 cc. of concd. hydrochloric acid and 3 cc. of water was boiled for three hours then chilled, it deposited 0.35 g. of benzal-*p*-bromoacetophenone (mixed m. p.). The filtrate, after removal of the unsaturated ketone, left on slow evaporation benzal-*p*-bromoacetophenoneoxime methyl ether (VIII). This material was identified by comparison with a sample prepared by boiling for three hours an alcoholic solution containing benzal-*p*-bromoacetophenone and an equivalent amount of methoxyamine hydrochloride. The oxime ether (VIII), obtained by evaporating an ether extract of the reaction mixture, crystallizes from alcohol in long silky needles which melt at 77-78°.

Anal. Calcd. for C<sub>16</sub>H<sub>14</sub>BrNO<sub>2</sub>: OCH<sub>3</sub>, 9.8. Found: OCH<sub>3</sub>, 9.6.

When 1.65 g. of  $\beta$ -phenyl- $\beta$ -methoxyamino-*p*-bromo-

propiophenone in 5 cc. of methyl alcohol was boiled for forty-eight hours with two equivalents of benzaldehyde, the solution on cooling set to a paste. Filtration furnished 0.5 g. of benzal-*p*-bromoacetophenone, identified by comparison with an authentic sample.

**Oxidation of  $\beta$ -Phenyl- $\beta$ -methoxyaminopropiophenone (I).**—One-half gram of the hydrochloride (II) was stirred into 50 cc. of cold water, and 20 cc. of cold sodium hypochlorite solution ("Oxol") was added. Dilute hydrochloric acid in excess was next added and the reaction mixture was stirred for an hour. The precipitated solid, which was slightly sticky and weighed 0.5 g., was crystallized from alcohol. It then melted at 114-115° and was shown to be the monoxime methyl ether of dibenzoylmethane (III) by a mixed melting point with a synthetic sample of that material.

**Synthesis of the Monoxime Methyl Ether of Dibenzoylmethane (III).**—A. When a solution of 4.5 g. of dibenzoylmethane and 1.7 g. of methoxyamine hydrochloride in 20 cc. of alcohol was boiled for two hours, then cooled, it deposited 3.4 g. of colorless solid which melted over the range 70-100°. Crystallization from alcohol furnished the pure monoxime ether (III) in fine silky needles which melted at 114-115°.

Anal. Calcd. for C<sub>16</sub>H<sub>16</sub>NO<sub>2</sub>: OCH<sub>3</sub>, 11.79. Found: OCH<sub>3</sub>, 11.85.

The impurity accompanying the monoxime ether (III) and responsible for the low melting point of the crude product is the dioxime dimethyl ether of dibenzoylmethane (IV). The dioxime dimethyl ether can be prepared directly from dibenzoylmethane and two equivalents of methoxyamine hydrochloride or from the monoxime

TABLE II

Substance	M. p., °C.	Crystallized from	Compn.	OCH <sub>3</sub> anal., % Calcd.	% Found
$C_6H_5CH\left(N\left\langle\begin{array}{l} COCH_3 \\ OCH_3 \end{array}\right\rangle\right)CH_2COC_6H_5$	94.5-95.5	EtOH-water	$C_{18}H_{19}NO_3$	10.44	10.2
$C_6H_5CH\left(N\left\langle\begin{array}{l} COCH_3 \\ OCH_3 \end{array}\right\rangle\right)CH_2COC_6H_4CH_3-p$	118-119	Methanol	$C_{19}H_{21}NO_3$	10.0	10.0
$C_6H_5CH\left(N\left\langle\begin{array}{l} COCH_3 \\ OCH_3 \end{array}\right\rangle\right)CH_2COC_6H_4Cl-p$	142-143	Methanol	$C_{18}H_{18}ClNO_3$	9.35	9.35
$p-ClC_6H_4CH\left(N\left\langle\begin{array}{l} COCH_3 \\ OCH_3 \end{array}\right\rangle\right)CH_2COC_6H_5$	91-92	Ethanol	$C_{18}H_{18}ClNO_3$	9.35	9.1
$C_6H_5CH\left(N\left\langle\begin{array}{l} COCH_3 \\ OCH_3 \end{array}\right\rangle\right)CH_2COC_6H_4OCH_3-p$	115-116	Ethanol	$C_{19}H_{21}NO_4$	19.3	19.75
$p-CH_3OC_6H_4CH\left(N\left\langle\begin{array}{l} COCH_3 \\ OCH_3 \end{array}\right\rangle\right)CH_2COC_6H_5$	130-131	Ethanol	$C_{19}H_{21}NO_4$	19.3	19.6
$C_6H_5CH\left(N\left\langle\begin{array}{l} COCH_3 \\ OCH_3 \end{array}\right\rangle\right)CH_2COC_6H_4Br-p$	157-158	Ethanol	$C_{18}H_{18}BrNO_3$	8.24	8.0
$p-BrC_6H_4CH\left(N\left\langle\begin{array}{l} COCH_3 \\ OCH_3 \end{array}\right\rangle\right)CH_2COC_6H_5$	91-92	Ethanol	$C_{18}H_{18}BrNO_3$	8.24	8.37

TABLE III

Substance	Yield, %	Crystallized from	M. p., °C.	Compn.	Analyses, %			
					Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
$C_6H_5CH=C(NH_2)COC_6H_5$	94	Methanol	100-101	$C_{16}H_{15}NO$	80.73	81.08	5.8	5.8
$C_6H_5CH=C(NH_2)COC_6H_4CH_3-p$	64	Methanol	92-93	$C_{16}H_{15}NO$	81.0	80.64	6.3	6.4
$C_6H_5CH=C(NH_2)COC_6H_4Cl-p$	66	Ethanol	81-82	$C_{15}H_{12}ClNO$	69.9	69.8	4.7	5.2
$p-ClC_6H_4CH=C(NH_2)COC_6H_5$	80	Ethanol	88-89	$C_{15}H_{12}ClNO$	69.9	70.1	4.7	4.8
$C_6H_5CH=C(NH_2)COC_6H_4Br-p$	83	Methanol	103-104	$C_{15}H_{12}BrNO$	59.6	60.0	4.0	4.2
$p-BrC_6H_4CH=C(NH_2)COC_6H_5$	90	Methanol	114-115	$C_{15}H_{12}BrNO$	59.6	59.7	4.0	4.4

$\alpha$ -Aminobenzalacetophenone can also be prepared, less satisfactorily, in a single reaction using benzalacetophenone, methoxyamine and alcoholic potassium hydroxide.  $\alpha$ -Aminobenzal-*p*-methylacetophenone was prepared from the crude oily product obtained from benzal-*p*-methylacetophenone and methoxyamine. The yield of this amino ketone is, therefore, based on the unsaturated ketone used and is the over-all yield of two reactions. The amino ketone from  $\beta$ -phenyl- $\beta$ -methoxyamino-*p*-methoxypropiofenone was an intractable oil.

methyl ether with the same reagent. The pure dioxime ether, crystallized from alcohol, melts at 57.5-58.5°.

*Anal.* Calcd. for  $C_{17}H_{18}N_2O_2$ : OCH<sub>3</sub>, 21.98. Found: OCH<sub>3</sub>, 21.4.

B. One gram of benzoylphenylacetylene<sup>9</sup> was dissolved in 5 cc. of warm methanol and 0.3 g. of methoxyamine was added. After eighteen hours at room temperature the solution set solid when rubbed with a stirring rod. On chilling and filtering, 1.0 g. of crude oxime ether, identified by comparison with a sample prepared from dibenzoyl-methane, was obtained.

**Acetylation of the  $\beta$ -methoxyaminopropiofenones** takes place on dissolving them in excess acetic anhydride. In some cases, solution occurs at room temperature while in other cases gentle warming on the steam-bath for a minute or two is required. The acetyl derivatives crystallize when the reaction mixtures, after cooling to room temperature, are stirred with water to destroy the excess anhydride. The yields are quantitative and the products are all colorless solids. Detailed information about the acetylation products is summarized in Table II.

When the acetyl derivative of  $\beta$ -phenyl- $\beta$ -methoxyamino-*p*-bromopropiofenone was distilled at 15 mm., it furnished benzal-*p*-bromoacetophenone. The same product, in

quantitative yield, was obtained when this acetyl derivative suspended in methyl alcohol was treated in the cold with one equivalent of sodium methylate.

**Rearrangement of the  $\beta$ -Methoxyaminopropiofenones to  $\alpha$ -Aminobenzalacetophenones.**—Although the conversion of the  $\beta$ -methoxyaminopropiofenones to unsaturated  $\alpha$ -amino ketones can be effected using a rather wide range of concentrations, temperatures and reaction times, we have found it most convenient to dissolve one equivalent of the methoxyamino ketone in two equivalents of 2 *N* sodium methylate solution at about 60°, adding absolute methyl alcohol when necessary to bring about complete solution. The reaction mixture is kept warm until it develops a yellow to orange color, usually about ten minutes is required, then left to stand overnight. Next day on chilling, the  $\alpha$ -amino ketone crystallizes. The transformation is probably finished in less time but this procedure ensures completeness of reaction. Estimates of the amounts of  $\alpha$ -amino ketones which remain dissolved in the reaction mixture, based on rough determinations of the solubility of the  $\alpha$ -amino ketones, indicate that the rearrangement is essentially quantitative. We shall describe in detail the conversion of two  $\beta$ -methoxyamino ketones to  $\alpha$ -amino ketones for illustrative purposes. Other data on the rearrangements and products are given in Table III.

When 2.55 g. (0.01 mole) of  $\beta$ -phenyl- $\beta$ -methoxyamino-

(9) We are indebted to Dr. R. C. Fuson for a sample of this ketone.

propiophenone (I) was dissolved by warming to 60° for ten minutes in 10 cc. of sodium methylate solution containing 0.46 g. (0.02 mole) of sodium and the orange-yellow solution was left for eighteen hours, it deposited on chilling 2.19 of  $\alpha$ -aminobenzalacetophenone (IX); yield, 94%. The product, after crystallization from methyl alcohol, melted at 100–101°. This amino ketone, which had previously been prepared by a different method,<sup>3</sup> was identified by analysis, by the formation of a hydrochloride melting with decomposition at 180° (instantaneous melting point, 185°), and by hydrolysis on warming with dilute hydrochloric acid to phenylbenzylglyoxal which was isolated and characterized as the antimony derivative, m. p. and mixed m. p. 174–175°.

When 6.7 g. (0.02 mole) of  $\beta$ -phenyl- $\beta$ -methoxyamino- $p$ -bromopropiophenone (VI) was dissolved in 20 cc. of warm sodium methylate, containing 0.92 g. of sodium (0.04 mole), plus 20 cc. of absolute methyl alcohol and warmed for fifteen minutes the orange reaction mixture set solid

on cooling. Chilling and filtering furnished 5.0 g. of  $\alpha$ -aminobenzal- $p$ -bromoacetophenone, a yield of 83%.

### Summary

Methoxyamine adds to benzalacetophenone and its  $p$  or  $p'$  substituted analogs to furnish  $\beta$ -methoxyaminopropiophenones and  $\beta, \beta'$ -methoxyimino-*bis*-propiophenones. The same reagent adds also to benzoylphenylacetylene. The addition reaction has been shown to be reversible and the structures of the addition products have been established. The chemical behavior of the addition products has been described and it has been shown that the  $\beta$ -methoxyaminopropiophenones on treatment with strong bases lose a molecule of alcohol and rearrange to form  $\alpha$ -amino unsaturated ketones.

FLUSHING, N. Y.

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[A COMMUNICATION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

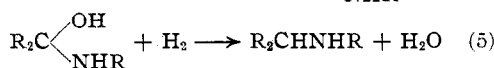
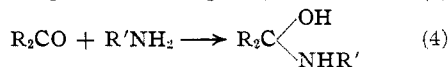
## Preparation of Certain Amines

BY EDWARD J. SCHWUEGLER AND HOMER ADKINS

Alcohols react with primary and secondary amines under the influence of such hydrogenating and dehydrogenating catalysts as nickel,<sup>1,2</sup> palladium<sup>3</sup> and copper chromite<sup>4,5</sup> with the formation of secondary and tertiary amines.



Since tertiary alcohols do not show this type of reaction it is plausible to assume that the primary function of the catalyst is to dehydrogenate the alcohol to an aldehyde or ketone. The latter would then react with an amine to give a product which is readily hydrogenated to an amine.



An alternative series of reactions depending upon the dehydrogenation of the original amine instead of the alcohol is not plausible for the product of reactions similar to (3), (4) and (5) would be an ether:

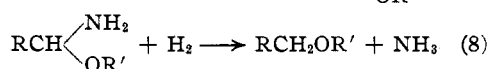
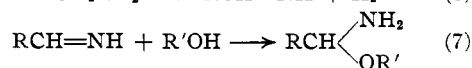
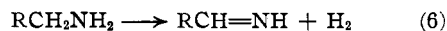
(1) Adkins and Cramer, *THIS JOURNAL*, **52**, 4350 (1930).

(2) Winans and Adkins, *ibid.*, **54**, 306 (1932).

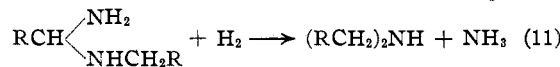
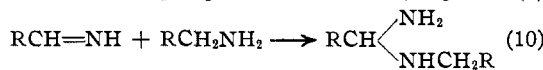
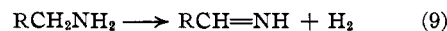
(3) Kindler, *Ann.*, **488**, 113 (1931).

(4) Paden and Adkins, *THIS JOURNAL*, **56**, 2487 (1936).

(5) Hill and Adkins, *ibid.*, **60**, 1033 (1938).



However, a dehydrogenation as shown in (6) probably occurs, for secondary amines having the same alkyl groups as the primary amine are readily formed over palladium,<sup>3</sup> nickel<sup>2</sup> and copper chromite.<sup>4</sup> In fact this reaction constitutes an important side reaction when it is desired to combine an alcohol and an amine according to the type reactions (1) and (2). The series of probable reactions is



Reactions of the type shown in (1) and (2) go smoothly and almost quantitatively in certain cases, but this is by no means always true. It seemed desirable therefore to ascertain the optimum conditions for the reaction of representative alcohols and aliphatic amines. The data given in Table I indicate the yields which have been obtained under the specified conditions. A consid-