[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF WESTERN AUSTRALIA]

Imido Ester Formation in Aromatic Nitriles

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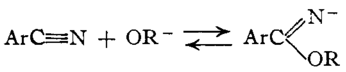
By titrimetric and infrared spectrophotometric procedures the reversible base-catalyzed formation of imido esters from certain aromatic nitriles has been shown,[1-4] and amounts of imido ester at equilibrium measured. The best titration procedure gives results with an accuracy of ±1%, while the accuracy of the infrared and a method involving plotting the curve of the direct titration of imido ester against standard acid is about ±3–4%. Evidence is given for the occurrence of both primary and secondary steric effects. The results confirm explanations given previously[5,6] for some anomalous kinetic results.

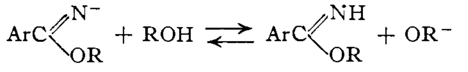
Although there has been comparatively little investigation of the reactions of nitriles with alcohols to form imido esters, the basic chemistry of these reactions was elucidated more than forty years ago by the work of Schlesinger,[1] and Acree and co-workers.[2-4]

The essential results of these authors are the demonstration of (i) preparation of imido esters as hydrochlorides by acid-catalyzed reaction of nitriles with alcohols; (ii) the faster *reversible* base-catalyzed formation of imido esters from alcohols and nitriles and *vice versa:* the equilibrium being unaffected by catalyst concentration; (iii) the amphoteric character of imido esters as weak bases and even weaker acids; (iv) the acid-catalyzed hydrolysis of imido esters to (ordinary) esters; (v) facilitation of imido ester formation from nitriles (R–CN) by electron attracting groups in R; for the base-catalyzed equilibria, the orders shown[3] are (a) $ClCH_2CN > CH_3CN$, (b) $CH_3CN > C_2H_5CN > C_3H_7CN$, (c) $C_6H_5CN > CH_3CN$, (d) *m*- and *p*-$NO_2C_6H_4CN >$ *m*- and *p*-$BrC_6H_4CN > C_6H_5CN >$ *p*-$CH_3C_6H_4CN$; (vi) complete inhibition of imido ester formation in the aromatic series by *ortho* groups, irrespective of polar character.

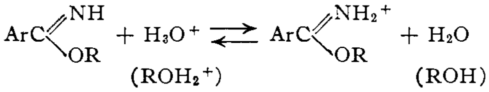
The general results are represented by the four equations



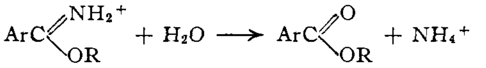
$$ArC{\equiv}N + OR^- \rightleftharpoons ArC\left\langle\begin{matrix}N^-\\ OR\end{matrix}\right. \qquad (1)$$



$$ArC\left\langle\begin{matrix}N^-\\ OR\end{matrix}\right. + ROH \rightleftharpoons ArC\left\langle\begin{matrix}NH\\ OR\end{matrix}\right. + OR^- \qquad (2)$$



$$ArC\left\langle\begin{matrix}NH\\ OR\end{matrix}\right. + \underset{(ROH_2^+)}{H_3O^+} \rightleftharpoons ArC\left\langle\begin{matrix}NH_2^+\\ OR\end{matrix}\right. + \underset{(ROH)}{H_2O} \qquad (3)$$



$$ArC\left\langle\begin{matrix}NH_2^+\\ OR\end{matrix}\right. + H_2O \longrightarrow ArC\left\langle\begin{matrix}O\\ OR\end{matrix}\right. + NH_4^+ \qquad (4)$$

Our interest in these reactions and the analogous hemiacetal formation from aldehydes arose during the course of some kinetic investigations[5,6] of the activating power of CO·X and CN groups in aromatic SN reactions. It was shown that 4-chloro-3-nitrobenzaldehyde, 4-chloro-3-nitrobenzonitrile and 2-chloro-5-nitrobenzaldehyde, but *not* 2-chloro-5-nitrobenzonitrile had abnormal Substituent Rate Factors (S.R.F.'s)[7] and Arrhenius parameters. For the three abnormal compounds, the anomalous results were explained[5,6] by nitrile–imido ester and aldehyde–hemiacetal equilibria (catalyzed by OMe^-) being set up more rapidly than the irreversible replacement of Cl by OMe^-. In the fourth compound, however, the nitrile–imido ester equilibrium being sterically inhibited, only the irreversible replacement of Cl by OMe^- occurs.

The method of Marshall and Acree[3] for determination of the amounts of imido ester in the base-catalyzed equilibria involves direct titration of formed imido ester against standard HCl; poor end-points were reported for all the aromatic compounds. Because of the weakly basic nature of the aromatic imido esters (similar to that of aromatic primary amines), the values obtainable by this method, though apparently capable of repetition with care, should depend on the *p*H range chosen for the end-point, and also to a lesser extent on the normality of the acid titrant, since the extent of the acid–base solvolysis (equation 3 above) of the (positive) conjugate acid of the imido ester should depend on the relative proportion of ROH to H_2O in the titration mixture.

These authors' investigation of *m*-nitrobenzonitrile and also its imido ester (0.0625 *M*), with NaOEt (0.5 and 0.25 *M*) and EtOH at 25°, titrating against 0.2 *N* HCl with methyl orange as indicator, gave the equilibrium concentration of imido ester as about 78%.

We investigated the titrimetric estimation of imido ester formed from *m*-nitrobenzonitrile by equilibration with OMe^- in MeOH (instead of OEt^- in EtOH). Titrations were (a) with brom cresol green–methyl red as indicator (end-point *p*H 5.1); (b) with methyl orange as indicator (end-point *p*H 3.2–4.4); (c) by following the complete titration curve (Fig. 1); both (a) and (b) were inaccurate.

From the earlier discussion (a) especially, but also (b), were expected to indicate less imido ester than is actually present, and this was found by experiment. Methods a and b indicated about 15% and 50% imido ester, respectively, while method c, showing a definite though small inflection at *p*H 2.5, gave an acceptable value for imido ester = 90 ± 4%.

We felt that the irreversible hydrolysis of imido ester to ester (equation 4 above) in aqueous acid should lead to a reliable method for estimating imido ester, since during the hydrolysis the strongly acid conjugate acid of the imido ester,

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(1) H. I. Schlesinger, *Am. Chem. J.*, **39**, 719 (1908).

(2) S. F. Acree, *ibid.*, **48**, 352 (1912).

(3) E. K. Marshall, Jr., and S. F. Acree, *ibid.*, **49**, 127 (1913).

(4) E. K. Marshall, Jr., J. P. Harrison and S. F. Acree, *ibid.*, **49**, 369 (1913).

(5) J. Miller, THIS JOURNAL, **76**, 448 (1954).

(6) R. L. Heppolette, J. Miller and V. A. Williams, *ibid.*, **78**, 1975 (1956).

(7) J. Miller, *J. Chem. Soc.*, 3550 (1952).

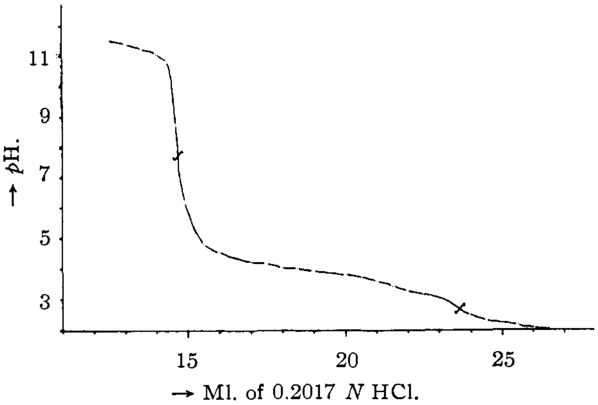

Fig. 1.—Titration of NaOMe and methyl *m*-nitroimido benzoate against aqueous HCl.

which behaves in usual acid–base titration conditions like H_3O^+, is converted to the very weakly acidic NH_4^+. By such a procedure (see Experimental section) we obtained the value for imido ester at equilibrium = 88 ± 1%.

It is relevant to note here that the kinetic runs[5,6] with 4-chloro-3-nitro- and 2-chloro-5-nitrobenzonitrile, in which Cl^- is replaced irreversibly by OMe^-, were followed by stopping the reaction by adding aliquots to standard HOAc, and back-titrating at once with phenolphthalein as indicator. These are conditions (and similarly if reaction were stopped by adding to standard HCl) in which imido ester formed by the 4-chloro-3-nitrobenzonitrile does not affect the change in titer due to replacement of OMe^- by Cl^- during runs. This has been confirmed, and the absence of side reactions, other than reversible imido ester formation shown, by carrying out parallel runs followed by the acid–base and Cl^- titrations, respectively; these gave identical results. Also, the amounts of OMe^- consumed and Cl^- liberated at 100% reaction are equal to those calculated for the reaction: $ClArCN + OMe^- \rightarrow OMeArCN + Cl^-$.

It was noted that if the "quenched" aliquots of the 4-chloro-3-nitrobenzonitrile reaction mixture were allowed to stand, even at room temperature, then the hydrolysis to ester and NH_4^+ commenced, and that acid–base but *not* Cl^- titers were affected. The hydrolysis was visible, by precipitation of ester, in periods of the order of 15 minutes in aqueous HCl and 1 hour in aqueous HOAc (both about 0.05 *N*).

A relevant and supplementary infrared study of the interactions of benzonitrile, *m*-nitrobenzonitrile, 4-chloro-3-nitrobenzonitrile and 2-chloro-5-nitrobenzonitrile has been made, being also a preliminary investigation of the general problem of interactions of nitriles and similar compounds with nucleophilic reagents in solution.

The infrared spectra of solutions of the four nitriles in methanol, with and without added NaOMe, have been compared in the region of the C≡N stretching frequency[8]; both OMe^- and MeOH absorbed quite strongly in this region.

The results for *m*-nitrobenzonitrile are somewhat less accurate than for the other three nitriles, because in MeOH alone its solubility (the saturated solution is less than 0.05 *M*) is considerably below the concentration (0.19 *M*) used for the others. When NaOMe is added, however, 0.19 *M* solutions could be obtained in all cases.

Figures 2 and 3 show the spectra in MeOH and NaOMe–MeOH, respectively, of the three more soluble nitriles (the spectrum of the less soluble *m*-nitro compound is however almost identical with that of 4-chloro-3-nitrobenzonitrile). The intensities of nitrile absorption of benzonitrile and particularly 2-chloro-5-nitrobenzonitrile are scarcely affected by addition of NaOMe to the MeOH solution. The very small intensity reduction for the latter is well within the experimental error (±3–4%), but the 8% reduction for the former seems to

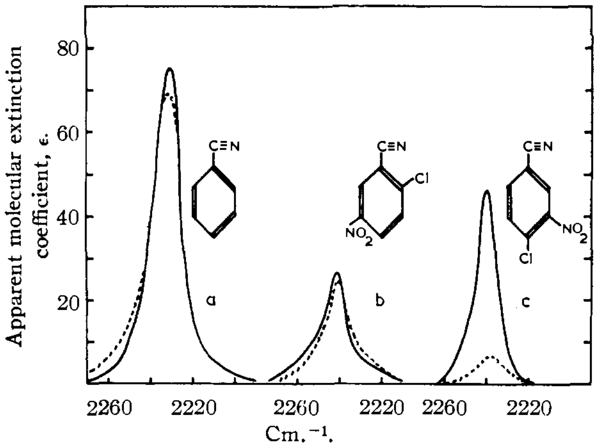

Fig. 2.—C≡N stretching of nitriles: (a) ————, benzonitrile (0.221 *M*) in methanol; — — — — —, benzonitrile (0.212 *M*) in sodium methoxide (0.190 *M*)-methanol; (b) ————, 2-chloro-5-nitrobenzonitrile (0.195 *M*) in methanol; — — — — —, 2-chloro-5-nitrobenzonitrile (0.189 *M*) in sodium methoxide (0.189 *M*)-methanol; (c) ————, 4-chloro-3-nitrobenzonitrile (0.213 *M*) in methanol; — — — — —, 4-chloro-3-nitrobenzonitrile (0.216 *M*) in sodium methoxide (0.189 *M*)-methanol.

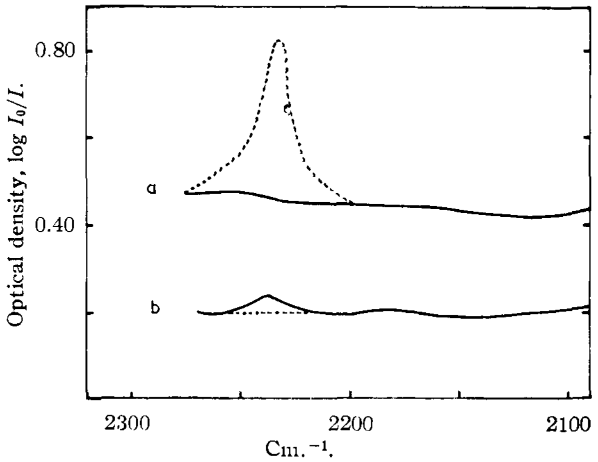

Fig. 3.—(a) ————, sodium methoxide (0.194 *M*) in methanol; — — — — —, benzonitrile (0.212 *M*), sodium methoxide (0.194 *M*) in methanol; (b) ————, 4-chloro-3-nitrobenzonitrile (0.216 *M*), sodium methoxide (0.189 *M*) in methanol.

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[8] M. W. Skinner and H. W. Thompson, *J. Chem. Soc.*, 487 (1955).

be real, and is consistent with the value 8–9% imido ester reported by Marshall and Acree[3] for catalysis by NaOEt in EtOH. In contrast the nitrile absorption of 4-chloro-3-nitrobenzonitrile is reduced by addition of NaOMe to about 15% of its value in MeOH alone, and that of *m*-nitrobenzonitrile (not illustrated) to about 10%.

The decreases in intensity for the two latter compounds are far greater than any known solvent-induced intensity changes,[9] including those known to occur with nitriles,[10] and must be due to large decreases in the concentration of free $C\equiv N$ when NaOMe is added; this result is fully consistent with the discussion already given, including the results of Schlesinger[1] and Acree and co-workers[2–4] and the explanations advanced for the anomalous kinetic results.[5,6]

This is understandably due to a considerable conversion of nitrile to imido ester, but could not be directly demonstrated by the infrared measurements, since the disappearance of the $C\equiv N$ band should be accompanied by the appearance of $C=N$ and $N-H$ bands, which unfortunately occur in regions of intense MeOH absorption.

Comparison of the results for the three substituted nitriles indicates both primary and secondary steric effects. The results of Marshall and Acree[3] lead to the expectation that the introduction of a Cl *para* to the CN of *m*-nitrobenzonitrile will cause an increase of imido ester concentration at equilibrium, relative to the *m*-nitro compound. The slight decrease found experimentally presumably is due to the effect of the Cl on the NO_2 group *ortho* to it in preventing coplanarity of the NO_2 group and the ring,[11] thus reducing the favorable effect of the NO_2 group on imido ester formation. This is a secondary steric effect.

On the other hand, introducing the Cl *ortho* to the CN group itself appears to inhibit imido ester formation completely[3] (Fig. 2) because the $C(=NH)OR$ group cannot be coplanar with the ring as required for conjugation, whereas the $C\equiv N$ group can. The inhibiting effect is then regarded as due to the loss of delocalization energy and this is a primary steric effect.

Figure 3 shows the unusual contour of the sodium methoxide absorption in the nitrile region, relative to that of methanol. Due to the strong absorption of methanol it was not possible to follow the methoxide absorption beyond these limits with the path length used. This absorption, which we attribute to the free methoxide ion, is proportional to the concentration of the reagent.

In the case of benzonitrile and 2-chloro-5-nitrobenzonitrile dissolved with NaOMe in MeOH the nitrile absorption is superimposed on the sodium methoxide absorption (Fig. 3, curve a). However, for the corresponding solutions of 4-chloro-3-nitrobenzonitrile there is a marked decrease (Fig. 3, curve b) of the absorption of the NaOMe itself together with the decrease in the $C\equiv N$ intensity. If the optical density of the absorption of methoxide ion can be taken as proportional to the concentration of this reagent in the free state, this means that in the comparatively high concentrations used for the infrared measurements, about 50% of the methoxide ion has been removed, as in equation 1. Allowing for the 15% free nitrile, the concentrations of imido ester and its conjugate base are about the same.

While the imido ester equilibrium is established rapidly (within 10 minutes) in the conditions of the experiment (about 20°) the reaction involving replacement of Cl in both the chloronitrobenzonitriles is proceeding more slowly. In the concentrations used it may be estimated[5,6] that the half-life of Cl replacement at 20° is several hours for the 4-chloro-3-nitro compound, and about half an hour for the 2-chloro-5-nitro compound. Accordingly, it was found that on standing for short periods there is no further decrease in methoxide absorption in the 4-chloro-3-nitrobenzonitrile solution, while the methoxide absorption in the 2-chloro-5-nitrobenzonitrile absorption decreases quite rapidly, although there is *no* decrease in nitrile absorption in this case.

Experimental

Infrared spectra were recorded on a Grubb Parsons infrared spectrophotometer model S3A[12] using a calcium fluoride prism. Frequency calibrations were made from the spectra of hydrogen bromide[13] and carbon monoxide.[14] The cell windows were mica plates or microscope cover glasses, and were cemented to 0.2 mm. lead washers with an adhesive (Seccotine). The cell lengths were measured by focusing a microscope in turn on the two inner surfaces of the windows.

The titrimetric procedures were used quantitatively on *m*-nitrobenzonitrile only.

Procedure 1.—Equimolar concentrations (0.0509 *M*) of nitrile and NaOMe in MeOH were left for several hours at 25° and then titrated directly and rapidly against standard HCl (0.0565 *N*) using brom cresol green–methyl red as indicator (end point *p*H 5.1). In duplicate titrations values 9.95 and 10.05 were obtained as against 8.93 for OMe^- alone. This corresponds to 12.0% imido ester. A similar experiment using 0.0509 *M* nitrile and 0.0754 *N* OMe^- gave titers 14.50 and 14.50 as against 13.22 for OMe^- alone. This corresponds to 15.5% imido ester. The end-points in these titrations were very poor despite the reproducibility.

Procedure 2.—Similar experiments in which methyl orange was the indicator had worse end-points and could not be reproduced satisfactorily but led to the value about 50% imido ester.

Procedure 3.—One of the reaction mixtures as in procedure 1 (that with excess OMe^-) was titrated against 0.202 *N* HCl after equilibration and the whole titration curve plotted (Fig. 1) using a Beckman automatic titrimeter model K. A small but definite inflection at *p*H 2.5 enables imido ester to be estimated as 90 ± 4%.

Procedure 4.—The same two reaction mixtures as in procedure 1 were used. The equilibrated solutions were poured into excess 0.102 *N* HCl. Although hydrolysis is seen to proceed within 15 minutes by the precipitation of methyl *m*-nitrobenzoate (isolated in separate experiments and compared with an authentic sample), aliquots were withdrawn between 6 and 24 hours after acidification and titrated against 0.0155 *N* baryta using the automatic titrimeter. It was clear from these results that any middle *p*H range indicator could have been used.

In one case titers 1.85, 1.90, 1.87 were obtained corresponding to 88.5% imido ester; in the other titers were 12.39 and 12.34 corresponding to 88.2% imido ester. The estimated maximum error in this procedure is ±1%.

The two chloronitrobenzonitriles were investigated only qualitatively by procedure 4. With 4-chloro-3-nitrobenzonitrile "quenched" aliquots from runs allowed to stand

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(9) N. S. Bayliss, A. R. H. Cole and L. H. Little, *Aust. J. Chem.*, **8**, 26 (1955).

(10) N. S. Bayliss, A. R. H. Cole and L. H. Little, unpublished work.

(11) A. L. Beckwith, J. Miller and (in part) G. D. Leahy, *J. Chem. Soc.*, 3552 (1952).

(12) A. R. H. Cole, *ibid.*, 3807 (1954).

(13) H. W. Thompson, R. L. Williams and H. J. Callomon, *Spectrochim. Acta*, **5**, 313 (1952).

(14) K. N. Rao, *J. Chem. Phys.*, **18**, 213 (1950).

about 2 hours at room temperature, had precipitated (ordinary) ester, which gave acid–base titers very markedly less than those of similar aliquots titrated at once. With 2-chloro-5-nitrobenzonitrile, on the other hand, there was no difference, even when allowed to stand overnight, thus demonstrating the presence of imido ester in the former reaction mixture only.

Duplicate kinetic runs using equimolar concentrations (0.0509 M) of 4-chloro-3-nitrobenzonitrile and OMe^- in MeOH were carried out at 44.9°. In one the progress of the run was followed by a standard procedure involving "quenching" aliquots with standard HOAc and back-titrating against baryta to pH 7.75 with the automatic titrimeter. In the other the procedure involved "quenching" aliquots with standard chloride-free HNO_3 and estimating Cl^- by titration against $AgNO_3$ with the automatic titrimeter. Both runs, followed to about 60% completion for calculation of k_2, gave identical results: $k_2 = 3.14 \times 10^{-3}$ l. mole^{-1} sec.$^{-1}$. The amount of OMe^- consumed and Cl^- liberated for 100% reaction is that calculated for replacement of Cl^- by OMe^- without any irreversible side-reaction.

Finally it was shown that the nitriles did not form imido ester with MeOH alone, nor was there any reaction of the CN group with MeOH/HCl aq., which could conceivably occur as side-reactions in procedure 4.

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[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Some Secondary Amines in the Sommelet Reaction

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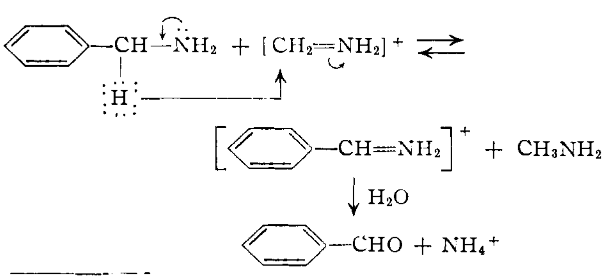
A number of secondary amines have been subjected to the Sommelet reaction, and the amounts of aromatic aldehydes produced from them have been determined. Most of the observations are better correlated on the assumption that the first step in the Angyal mechanism of reaction is the loss of a hydride ion from the nitrogen atom rather than from an adjacent carbon atom.

In the course of their investigation of the Sommelet reaction, Angyal and Rassack[1] found that in the hydrolysis of a hexaminium salt *via* the Sommelet procedure a primary amine is formed and converted to an aldehyde. Angyal and Rassack obtained a 79% yield of benzaldehyde by the hydrolysis of benzylhexaminium chloride in aqueous solution, and Graymore and Davies[2] reported a 66% yield of the aldehyde by allowing benzylamine, formaldehyde and hexamine to react in the same solvent. In this Laboratory, yields of benzaldehyde as high as 84% have been obtained from benzylamine when 50% acetic acid was used as the solvent.

The conversion of an amine to the aldehyde by the Sommelet procedure is visualized by Angyal and his associates[3] as being an oxidation–reduction process in which the amine is dehydrogenated by the conjugate acid of methyleneamine ($CH_2{=}NH$), a hydrolysis fragment of hexamine, to the corresponding benzylideneamine, which in turn is hydrolyzed to the aldehyde. The reaction scheme postulated by these investigators is shown as



The use of primary amines as precursors of aldehydes in the Sommelet reaction has not been thoroughly investigated, although Angyal and his associates have prepared a number of aldehydes from primary amines. The behavior of secondary amines, which are generally not as reactive as primary ones in the Sommelet reaction, has received even less attention; N-methylbenzylamine and dibenzylamine have been used in the reaction,[1] and one study of the behavior of a series of symmetrical, phenolic dibenzylamines has been made.[4] The present investigation was undertaken to study the fate of a number of other secondary amines in the Sommelet reaction.

N-Methylbenzylamine was reinvestigated and found to be converted to benzaldehyde in 15% yield, while N-isopropylbenzylamine was even less reactive, only 6% of the aromatic aldehyde being obtained from it. Dibenzylamines proved to be somewhat more reactive. Dibenzylamine itself gave benzaldehyde in yields of from 25–30%, and p,p'-dinitrodibenzylamine afforded the corresponding aldehyde in yields of 31–48%, while p,p'-dicarbomethoxydibenzylamine furnished p-carbomethoxybenzaldehyde in only 12.2% of the theoretical amount. These yields are calculated on the assumption that each molecule of a dibenzylamine would furnish two molecules of aldehyde. The relatively small amount of p-carbomethoxybenzaldehyde obtained from the secondary amine is difficult to understand, for p-carbomethoxybenzylhexaminium bromide is converted into the aldehyde in 74.7% yield by hydrolysis *via* the Sommelet procedure.

Six unsymmetrical dibenzylamines were subjected to the conditions of the reaction. The results are shown in Table I.

The behavior of some of the secondary amines in

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[1] S. J. Angyal and R. C. Rassack, *J. Chem. Soc.*, 2700 (1949); for an excellent discussion of the Sommelet reaction see S. J. Angyal, "Organic Reactions," Vol. VIII, John Wiley and Sons, Inc., New York, N. Y., 1954, p. 197.

[2] J. Graymore and D. R. Davies, *J. Chem. Soc.*, 293 (1945).

[3] S. J. Angyal, D. R. Penman and G. P. Warwick, *ibid.*, 1742 (1953).

[4] J. C. Duff and V. I. Furness, *ibid.*, 1512 (1951).