Carbanion Character at the α-Position of Tertiary Amines in the Direct Alkylation Reaction
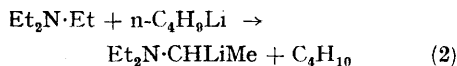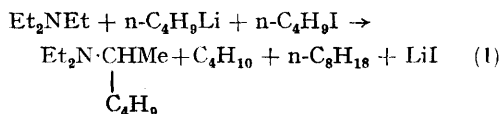
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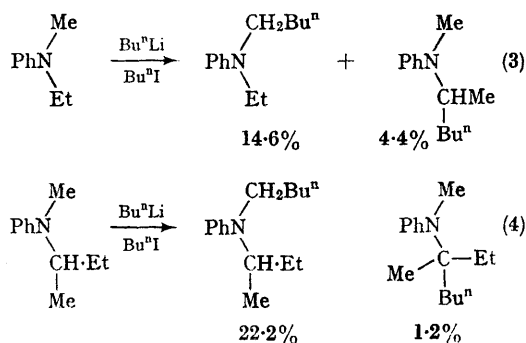(Department of Chemistry, Marshall University, Huntington, West Virginia 25701)

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In recent papers, the direct α-alkylation of tertiary amines has been described.[1-3] The reaction, which occurs on a tertiary amine such as triethylamine[2] with n-butyl-lithium and 1-iodobutane (equation 1), apparently does not involve a metalation, i.e., anionic amine, intermediate (equation 2).[3,4]

$$Et_2NEt + n\text{-}C_4H_9Li + n\text{-}C_4H_9I \rightarrow$$
$$\underset{\underset{C_4H_9}{|}}{Et_2N \cdot CHMe} + C_4H_{10} + n\text{-}C_8H_{18} + LiI \quad (1)$$

$$Et_2N \cdot Et + n\text{-}C_4H_9Li \rightarrow$$
$$Et_2N \cdot CHLiMe + C_4H_{10} \quad (2)$$

However, we have now found evidence for considerable carbanionic character in the reaction transition state at the α-position of the tertiary amine which undergoes alkylation. These observations are based on intramolecular competitive reactions.

N-Ethyl-N-methylaniline or N-(2-butyl)-N-methylaniline was treated with n-butyl-lithium and 1-iodobutane with initial cooling. Each of these anilines led to two products as shown in equations 3 and 4, respectively.

$$\underset{\underset{Et}{\diagdown}}{\overset{\overset{Me}{\diagup}}{PhN}} \xrightarrow[Bu^nI]{Bu^nLi} \underset{\underset{\underset{14\cdot6\%}{Et}}{\diagdown}}{\overset{\overset{CH_2Bu^n}{\diagup}}{PhN}} + \underset{\underset{\underset{4\cdot4\%}{CHMe}}{\diagdown} Bu^n}{\overset{\overset{Me}{\diagup}}{PhN}} \quad (3)$$

$$\underset{\underset{\underset{Me}{|}}{CH\cdot Et}}{\overset{\overset{Me}{\diagup}}{PhN}} \xrightarrow[Bu^nI]{Bu^nLi} \underset{\underset{\underset{\underset{22\cdot2\%}{Me}}{|}}{CH\cdot Et}}{\overset{\overset{CH_2Bu^n}{\diagup}}{PhN}} + \underset{\underset{\underset{1\cdot2\%}{Bu^n}}{|}}{\overset{\overset{Me}{\diagup}}{PhN}} \quad (4)$$

Although separation of the two isomeric materials in each reaction was not achieved by gas chromatography, it was possible to obtain structure confirmations and quantitative analyses by [1]H n.m.r. spectra on preparative g.l.c. samples. In particular, the N-Me chemical shifts for the isomer with highest chain branching, δ 2·58 p.p.m. (equation 3) and 2·65 p.p.m. (equation 4), characterized the less abundant isomers. Independent synthesis of all but the N-[(3-methyl)-3-heptyl] isomer aided the interpretation process.

The immediately apparent $CH_3 > CH_2 > CH$ reactivity is confirmed by the statistical results, based on reduction of the values to ratios per

α-hydrogen. These relative rates† of attack normalized to Me, are in the general order[5] of α-alkyl proton acidities in alkylbenzenes. Comparison with the results of relative rates, using lithium[6-8] and cæsium[9] cyclohexylamide (cha) on the arenes, shows a remarkable similarity with the latter results (Table). Since the cæsium base is less discriminating in proton exchange, it would appear that considerable anionic character must exist in some stage of the α-alkylation reaction. However, metallation of NN-dimethylaniline with n-butyl-lithium is much slower than alkylation and takes place on the aromatic ring.[4] This eliminates the participation of a characteristic α-anionic amine intermediate as a participating thermodynamic state. Thus carbanionic character at the α-position in tertiary amines, while enhanced over alkanes,[5] is negligible when compared to α-proton acidities in the alkylbenzenes and must only predominate in an unstable transition state for the α-amine alkylation process.

The parallel observed between σ^* and log $k/k°$ is in good agreement with an inductive effect on acidities,[9] and seems to confirm a transition state with carbanionic character as the rate-controlling activation step in α-alkylation. Since no distinct intermediate is involved, the importance of structure participation in the tertiary amine appears as a fundamental feature of a kinetic rather than a thermodynamic state in the reaction control process.

TABLE

Relative rates of α-proton exchange in alkylbenzenes and reaction in tertiary anilines
$$k/k°$$

Group	Alkylbenzenes		N-Alkylanilines	$-\sigma^{*a}$
	Li cha	Cs cha[b]		
CH$_3$	1·0[c]	1·0	1·0	0·00
CH$_2$	0·11[d]	0·49	0·45	0·10
CH	0·008[e,f]	0·13[e]	<0·16	0·20[e,g]

[a] Calculated by additivity of inductive effects neglecting NPh as a constant, ref. 10; [b] ref. 9; [c] ref 6; [d] ref. 7; [e] value for isopropyl; [f] s-butyl value may be calculated as 0·003 from the data of ref. 8 assuming the same primary effect as in ref. 7; [g] s-butyl value is 0·215 by this method, *cf.*, ref. 10.

† Since the reactions were not carried on at constant temperature, this is a composite value rather than being equivalent to the ratios of absolute rates.

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