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# FLUORIDE INDUCED ALKYLATION OF α-SILOXYAMINES. A NEW METHOD FOR TRANSALKYLATION OF TERTIARY AMINES VIA THEIR N-OXIDES

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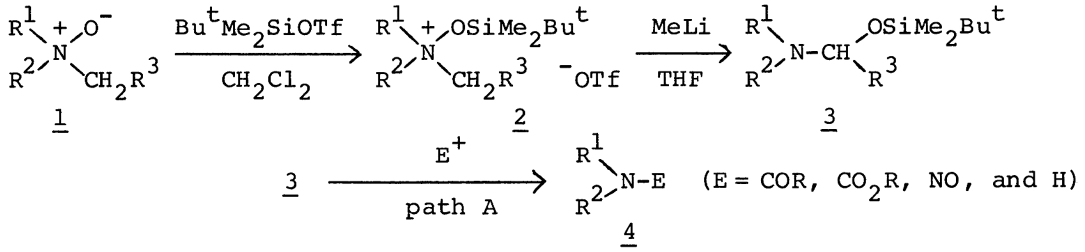
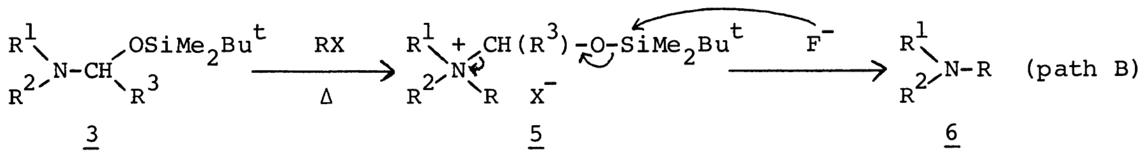
α-Siloxyamines obtained from tertiary amines via their N-oxides react with alkyl halides to give the corresponding α-siloxyammonium salts, which can be converted into new tertiary amines by fluoride induced desilylation reaction.

Structural modification in amines is one of the most important problems in the syntheses of N-containing natural products such as alkaloids. Among the structural modification is transalkylation (i.e., the replacement of a substituent on the nitrogen atom by other groups) which is useful in the introduction of a new functional group. However, there have been very few reports on direct transalkylation[1)] for tertiary amines and the conventional methods involve some steps, i.e., dealkylation to secondary amine derivatives, deprotection to free secondary amines, and their realkylation.[2)]

Recently we have reported a new general method for dealkylation of tertiary amines via their N-oxides (1).[3)] Thus, siloxyammonium salts (2) prepared from 1 and trialkylsilyl trifluoromethanesulfonate undergo rearrangement in the presence of alkyllithiums to give α-siloxyamines (3), which can be converted into various secondary amine derivatives (4) with appropriate electrophiles (path A).



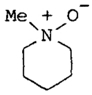
In this paper we wish to report the reaction of α-siloxyamines (3) with some alkyl halides in the presence of fluoride ion leading to direct N-transalkylation of tertiary amines (path B).



Thus, treatment of 3 obtained in situ from 1 with alkyl halides (formation of α-siloxyammonium salts (5)) followed by desilylation with fluoride ion ($Bu_4N^+F^-$/THF) afforded the corresponding transalkylation products (6) in moderate yields.

Results obtained from the reactions of N-methylpiperidine N-oxide ($\underline{1a}$) and triethylamine N-oxide ($\underline{1b}$) with several alkyl halides are summerized in Table 1.[4)]

Table 1. Transalkylation of Tertiary Amines via Their N-Oxides

| Entry | N-Oxide ($\underline{1}$) | RX | $F^-$ | Time/h | Product ($\underline{6}$) | Yield/%[a)] |
|---|---|---|---|---|---|---|
| 1 |  ($\underline{1a}$) | $PhCH_2Cl$ | $Bu_4N^+F^-$ | 10 | $R^1R^2 = (CH_2)_5$, $R = CH_2Ph$ | 58 |
| 2 | $\underline{1a}$ | n-AmBr | $Bu_4N^+F^-$ | 10 | $R^1R^2 = (CH_2)_5$, R = n-Am | 45 |
| 3 | $\underline{1a}$ | n-OcBr | $Bu_4N^+F^-$ | 6 | $R^1R^2 = (CH_2)_5$, R = n-Oc | 47 |
| 4 | $\underline{1a}$ | $BrCH_2CO_2Et$ | $Bu_4N^+F^-$ | 5 | $R^1R^2 = (CH_2)_5$, $R = CH_2CO_2Et$ | 38 |
| 5 | $\underline{1a}$ | $BrCH_2COPh$ | $Bu_4N^+F^-$ | 10 | $R^1R^2 = (CH_2)_5$, $R = CH_2COPh$ | 33 |
| 6 | $Et_3N^+-O^-$ ($\underline{1b}$) | $PhCH_2Cl$ | $Bu_4N^+F^-$ | 10 | $Et_2N-CH_2Ph$ | 65 |
| 7 | $\underline{1b}$ | n-OcBr | $Bu_4N^+F^-$ | 10 | $Et_2N$-n-Oc | 51 |
| 8 | $\underline{1b}$ | $BrCH_2CO_2Et$ | $Bu_4N^+F^-$ | 10 | $Et_2N-CH_2CO_2Et$ | 31 |

a) Isolated yield after alumina column chromatography.

In contrast to the dealkylation reaction by acyl halides or chloroformate,[3)] this transalkylation did not proceed without heating and in the absence of fluoride ion perhaps due to the rather lower reactivity of alkyl halides in quarternization. Of particular note among these results is the introduction of carbonyl functionality in new alkyl groups ( entries 4, 5, and 8 ), which provides a route to further functionalization. In view of ready availability of amine N-oxides and alkyl halides, and the achievement of the prolongation of N-alkyl groups, i.e., the formal functionalization of α-position of tertiary amines,[5)] we believe this direct transalkylation reaction without isolation of intermediates provides a new convenient synthetic method for nitrogen-containing natural products.

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## References

1) T. S. Manoharan, K. M. Madyastha, B. Bali Singh, S. P. Bhatnagar, and U. Weiss, Synthesis, 1983, 809.

2) J. von Braun, O. Kruber, and E. Aust, Ber. Dtsch. Chem. Ges., 47, 2312 (1914); R. A. Olofson, R. C. Schnur, L. Bunes, and J. P. Pepe, Tetrahedron Lett., 1977, 1567 and references cited therein.

3) Demethylation, deethylation, and debenzylation were achieved for either cyclic or acyclic tertiary amines via the corresponding α-siloxyamines: R. Okazaki and N. Tokitoh, J. Chem. Soc., Chem. Commun., 1984, 192.

4) A typical example is as follows. $\underline{1a}$ (1 mmol) was allowed to react with t-butyldimethylsilyl trifluoromethanesulfonate (1.1 mmol) in dichloromethane to give $\underline{2a}$. After replacement of solvent by tetrahydrofuran, $\underline{2a}$ was treated with methyllithium (1.2 mmol) at 0 °C and then with benzyl chloride (1.5 mmol) and tetrabutylammonium fluoride (1.1 mmol) in a sealed tube at 110 °C for 10 h to afford amine $\underline{6a}$ ($R = CH_2Ph$) in 58 % yield. All the products described in Table 1 gave the satisfactory spectral and/or analytical data ($^1H$-NMR, $^{13}C$-NMR, and exact mass analysis).

5) Nucleophilic α-substitution of tertiary amines can also be achieved via the α-siloxyamines described here with various organometallics: N. Tokitoh and R. Okazaki, Tetrahedron Lett., in press.

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