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NUCLEOPHILIC NITROGEN-NITROGEN EXCHANGE REACTION AT AROMATIC CARBON ATOMS —— REACTION OF N,N-DIMETHYL-2,4-BISTRIFLUOROACETYL-1-NAPHTHYLAMINE WITH VARIOUS AMINES

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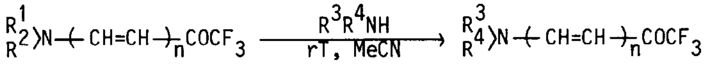
Summary : N,N-Dimethyl-1-naphthylamine reacted easily with trifluoroacetic anhydride to give the title compound 2 quantitatively. Aromatic nucleophilic substitution reaction of 2 with various amines proceeded readily under mild conditions to give the corresponding nitrogen-nitrogen exchanged products 6-14 in excellent yields.

In the course of our investigations on the nucleophilic substitution reactions at olefinic carbon atoms, it was found that vinylogs of trifluoroacetamide 1 undergo nitrogen-nitrogen exchange reaction very easily as shown by equation (1).[1,2]

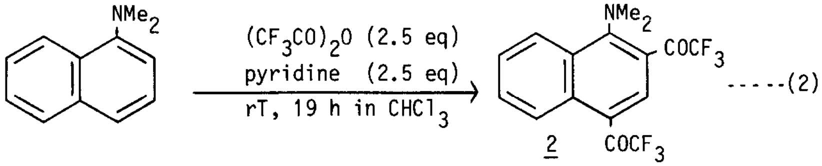


$$\overset{R^1}{\underset{R^2}{\,}}\rangle N\text{-}(CH{=}CH)_n\text{-}COCF_3 \xrightarrow[\text{rT, MeCN}]{R^3R^4NH} \overset{R^3}{\underset{R^4}{\,}}\rangle N\text{-}(CH{=}CH)_n\text{-}COCF_3 \qquad \text{-----(1)}$$

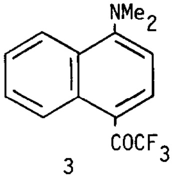
1 (n=1, 2)

Activated aromatic compounds bearing good leaving groups such as polynitrohalo- and polynitroalkoxybenzenes, etc., are wellknown to undergo aromatic nucleophilic substitution with various nucleophiles.[3] However, amino groups of polynitroanilines are seldom replaced by nucleophiles.[4,5] The nitrogen-nitrogen exchange shown by equation (1) prompted us to realize such an exchange reaction at aromatic carbon atoms. We have found that aromatic nucleophilic substitution of N,N-dimethyl-2,4-bistrifluoroacetyl-1-naphthylamine 2 with various amines occurred quite easily under mild conditions and we now wish to communicate the results.[6]

Synthesis of 2 was successfully performed by trifluoroacetylation of N,N-dimethyl-1-naphthylamine according to our method[7] as shown in equation (2). The reaction with the use of an equimolar amount of trifluoroacetic anhydride in the presence of pyridine occurred quite easily to give 3 in a quantitative yield without any formation of the positional isomers.



100%, mp 87-8 °C



3

Attempted N-N exchange reaction of 4-trifluoroacetyl- and 2,4-bistrifluoroacetyl-N,N-dimethylanilines (4 and 5) with amines such as pyrrolidine and methylamine did not proceed at all. Compared to the benzene system (4 and 5), naphthalene system (3 and 2) seemed promising because diene character would be enhanced and it becomes more akin to the vinylogs of trifluoroacetamide 1. While the N-N exchange reaction of monoacyl compound 3 did not take place, diacyl compound 2 underwent readily and cleanly aromatic nucleophilic substitution with 1-3 equivalents of various amines in acetonitrile to afford the corresponding N-N exchanged products in excellent yields. The results are shown by equation (3) and summarized in Table 1.

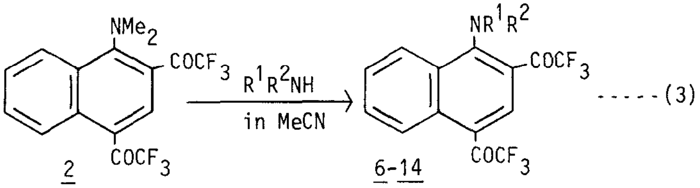
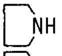
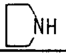


Table 1. Reaction of 2 with various amines

Entry	$R^1R^2NH^{a)}$	(°C)	(h)	Product$^{b)}$	Yield (%)$^{c)}$
1	NH_3aq.	rT	2	6	100
2	$MeNH_2$aq.	rT	2	7	100
3	$EtNH_2$aq.	rT	2	8	100
4	i-$PrNH_2$	rT	2	9	100
5	t-$BuNH_2$	rT	92	10	87 (13)
6	$PhCH_2NH_2$	rT	2	11	100
7	p-$AnisNH_2$	refl	24	12	91
8	Et_2NH	60	23	13	35 (65)
9		rT	5	14	78 (12)
10		refl	23	14	100

a) Molar ratio, [2]/[R^1R^2NH] : 1/3 for entries 1-5, 8 and 9 ; 1/1 for entries 6, 7 and 10. b) Products were characterized on the basis of combustion microanalysis (except for 13) and ^1H-NMR and IR (except for 13) spectroscopy. c) Yields of isolated products for entries 1-4, 6, 7 and 10. Values in parentheses are the recovery of 2. For entries 5, 8 and 9, yields were determined by ^1H-NMR integration of the mixtures.

Reactions of 2 with ammonia and primary amines gave 6-11 in 87-100 % yields. The reaction even with p-anisidine did proceed to afford 12 in 91 % yield by heating. Secondary amines showed lower reactivity, for example, diethylamine afforded 13 only in 35 % yield even at 60 °C and for 23 h. However, pyrrolidine revealed considerably enhanced reactivity to give 14.

In an attempt to evaluate ability of various amino groups as a leaving group in this N-N exchange reaction, compounds 2, 7 and 6 were allowed to react with 1.2 equivalents of pyrrolidine in refluxing acetonitrile for 4 h. The result obtained is as follows. substrate, % conversion into 14 : 2, 99 ; 7, 34 ; 6, 0. The decreasing order of ability, Me_2N- > MeNH- > NH_2-, is just reversed to the case of the corresponding N-N exchange reactions[1,2] of vinylogs 1, Me_2N- < MeNH- < NH_2-. It is not certain at present why Me_2N group is a much better leaving group than NH_2 group in the present reaction and further studies are now in progress to elucidate electronic and steric requirements.

The present reaction can be extended to use bifunctional reagents as nucleophiles and is applicable to the syntheses of various fluorine containing heterocycles. These results will be published elsewhere in our forthcoming papers.

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References and Notes

1. Hojo, M. ; Masuda, R. unpublished work. These results will be reported in our forthcoming papers.
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