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REACTIONS OF 2,2,2-TRIFLUOROETHOXY- AND 2,2,2-TRIFLUOROETHYLTHIOBENZENE WITH LITHIUM DIALKYLAMIDES. THE FORMATION OF PHENYLTHIOYNAMINES[1)]

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Reactions of 2,2,2-trifluoroethoxy-(2) and 2,2,2-trifluoroethylthiobenzene (3) with excess lithium dialkylamides afforded the difluorovinyl ether (4) and the phenylthioynamines (5), respectively. Thus the latter reaction provides a convenient method for preparing these particular ynamines. Such striking difference in reaction course between 2 and 3 is discussed in terms of the relative stability of carbanions involved.

Reactions involving carbanions stabilized by β-fluorine atoms have been the subject of many reports in organofluorine chemistry. Of particular interest are carbanions (1) derived from methylenes adjoining both trifluoromethyl group and a heterofunction (X) such as SR and OR, since the carbanions are greatly stabilized by the CF_3 group, and their reactivities (stabilities) vary with the nature of the heterofunction.

$CF_3\overset{\ominus}{C}H{-}X$ X=SR, OR, Halogens, etc.

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Our previous paper[2)] reported on the formation of the carbanion 1 (X=I) in the reaction of 2,2,2-trifluoroethyl iodide with phenolate ion. We now wish to report that the reaction of 2,2,2-trifluoroethoxybenzene (2) with an excess of lithium dialkylamides affords 2,2-difluoroethenyloxybenzene (4), whereas the similar reaction of 2,2,2-trifluoroethylthiobenzene (3) gives entirely different products, (N,N-dialkylaminoethynylthio)benzene (5); this points to the remarkable difference in stability between carbanions involved in these reactions of 2 and 3.

$CF_3CH_2{-}X$ $CF_2{=}CH{-}OPh$ $R_2N{-}C{\equiv}C{-}SPh$

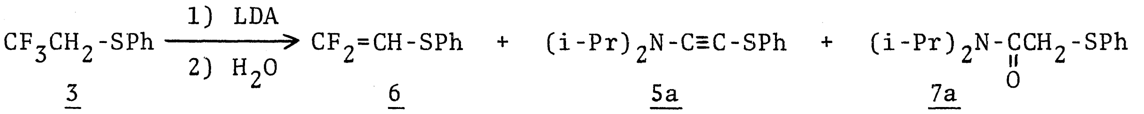
2, X=OPh; 3, X=SPh 4 5

The reaction of 2 with 3 equiv of lithium diisopropylamide (LDA) in diethyl ether at -75°C for 3 hr afforded, after quenching with water, the difluorovinyl ether 4 in 16% yield along with 52% recovery of 2. However, the use of THF in place of diethyl ether in the above reaction considerably increased the yield of 4 (80%). The product 4 was identified by its spectral data: bp 87-89°C/96mmHg; MS, m/e 156 (M^+); IR (neat), 1765 cm^{-1}(C=C); ^1H NMR[3] (CCl_4), δ6.02 (d of d, J_{HF}=14.5 and 3.3 Hz, 1H) and 6.8-7.5 (m, 5H); ^{19}F NMR[3] (neat), δ19.1 (d of d, J_{HF}=14.5 and J_{FF}=61.3 Hz) and 38.0 (d of d, J_{HF}=3.3 and J_{FF}=61.3 Hz).

$$\underset{2}{CF_3CH_2\text{-}OPh} \xrightarrow{LDA} \underset{4}{CF_2\text{=}CH\text{-}OPh} \xrightarrow{LDA} CF_2\text{=}CLi\text{-}OPh \xrightarrow{D_2O} \underset{4'}{CF_2\text{=}CD\text{-}OPh} \qquad (1)$$

Quenching of the reaction mixture with D_2O resulted in the formation of both the deuterated product 4' and 4 in the ratio of 8.6 : 1 (by ^{19}F NMR), indicating that 4 once formed is lithiated in the reaction mixture[4] (eq 1).

On the other hand, the reaction of the sulfide 3 with LDA proceeded more smoothly even in diethyl ether under the same conditions. When 1.5 equiv of LDA was used, we obtained, after extractive work-up, a complex mixture consisting of unreacted 3 (18%), 2,2-difluoroethenylthiobenzene (6) (15%), the phenylthioynamine 5a (16%), and N,N-diisopropylphenylthioacetamide (7a) (ca. 5%) (eq 2).



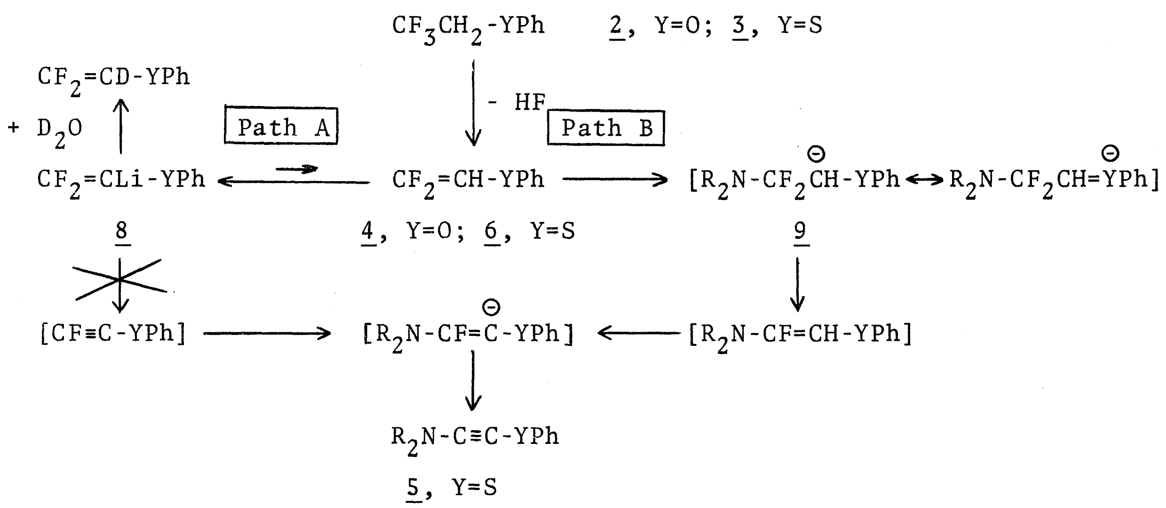
$$\underset{3}{CF_3CH_2\text{-}SPh} \xrightarrow[2)\ H_2O]{1)\ LDA} \underset{6}{CF_2\text{=}CH\text{-}SPh} + \underset{5a}{(i\text{-}Pr)_2N\text{-}C{\equiv}C\text{-}SPh} + \underset{7a}{(i\text{-}Pr)_2N\text{-}\underset{\overset{\Vert}{O}}{C}CH_2\text{-}SPh} \qquad (2)$$

These products were separated by fractional distillation and identified by their spectral data: 6, bp 68-69°C/11mmHg; IR (neat), 1705 cm^{-1}(C=C); ^1H NMR[3] (CCl_4), δ5.07 (d of d, J_{HF}=20.7 and 1.9 Hz, 1H) and 7.0-7.6 (m, 5H); ^{19}F NMR[3] (neat), δ-0.8 (d of d, J_{HF}=1.9 and J_{FF}=20.7 Hz) and 2.0 (d of d, J_{HF}=J_{FF}=20.7 Hz); 5a, bp 105-110°C/0.1mmHg; IR (neat), 2120 cm^{-1}(C≡C); ^1H NMR(CCl_4), δ1.20 (d, J=6.6 Hz, 12H), 3.13 (sep, J=6.6 Hz, 2H) and 6.9-7.4 (m, 5H); 7a, MS, m/e 251 (M^+); IR (neat), 1635 cm^{-1}(CON<); ^1H NMR(CCl_4), δ1.28 (d, 12H), 3.30 (m, 2H), 3.57 (s, 2H) and 7.0-7.5 (m, 5H).

Acid hydration of the ynamine 5a afforded the amide 7a quantitatively, indicating that 7a was formed by hydration during the work-up. Treatment of 3 with 3 equiv of LDA gave only the ynamine 5a which on hydration afforded the amide 7a in 62% yield. A similar reaction with excess lithium diethylamide followed by hydration produced the diethylamide 7b (bp 142-147°C/2mmHg) in 81% yield. Furthermore, pure ynamines were isolated in ca. 60% yields when the reaction mixture was distilled prior to hydration: 5b, bp 145-155°C/3mmHg (lit.5) 100-115°C/0.01mmHg). Consequently, this type of reaction provides a new, convenient method for preparing these particular ynamines.6)

Of the greatest mechanistic interest is the fact that the exclusive formation of the ynamine 5 in the reaction of the sulfide 3 with excess lithium amide is in direct contrast to the formation of the difluorovinyl ether 4 in the similar reaction of the ether 2. Such striking difference in the reaction course may be interpreted on mechanistic grounds as follows. Possible reaction paths are shown in Scheme 1.

Scheme 1



Both the reactions might be initiated by elimination of HF giving the difluorovinyl compounds (4 and 6) which are capable of further undergoing two discrete reactions; one is lithiation leading to the vinyllithiums 8 (Path A) and the other one is the addition process (Path B). In view of d-orbital carbanion stabilization by the phenylthio group, the vinyllithium 8(Y=S) should be more stable than the phenoxy analogue 8(Y=O) which was trapped as described above.7) Therefore, it appears very unlikely that the vinyllithium 8(Y=S) collapses into the fluoroacetylene under these conditions. Thus the ynamine 5 is formed favorably via Path B involving the addition-elimination sequence as shown in Scheme 1.

The question to be answered is why the vinyl sulfide 6 thus formed further undergoes the addition reaction with the amide anions whereas the vinyl ether 4 does not. Such striking difference in addition reactivity can be reasonably explained in terms of the difference in stability between the carbanions 9(Y=O and S) involved in the addition process; the carbanion 9(Y=S) should be much more stable than the carbanion 9(Y=O) apparently due to the involvement of d-orbitals of the sulfur atom. As a consequence, it can be said that the most important factor in determining the reaction course is the relative stability of the carbanions involved such as 9, which varied with the nature of the attached heterofunctions such as OPh and SPh.

REFERENCES AND NOTES

1) A part of this work was presented at the 8th International Symposium on Fluorine Chemistry, Kyoto, August 1976.

2) T. Nakai, K. Tanaka, and N. Ishikawa, J. Fluorine Chem., in press.

3) The chemical shifts for ^1H and ^{19}F NMR are given in δppm downfield from internal tetramethylsilane and upfield from external trifluoroacetic acid, respectively.

4) In support of this finding, we recently found that treatment of the reaction mixture with acetone followed by hydrolysis afforded an expected adduct, $CF_2=C(OPh)C(CH_3)_2OH$, in 60% yield. The synthetic utility of the phenoxyvinyllithium is now under study.

5) S. Y. Delevarenne and H. G. Viehe, Tetrahedron Lett., 1969, 4761.

6) For a recent review on the chemistry of ynamines, see H. G. Viehe, Angew. Chem., 79, 744 (1967).

7) Both 2,2-difluorovinyllithium and trifluorovinyllithium have been reported to be quite stable at -78°C: F. G. Drakesmith, R. D. Richardson, O. J. Stewart, and P. Tarrant, J. Org. Chem., 33, 286 (1968); P. Tarrant, P. Johncock, and J. Savory, ibid., 28, 839 (1963).

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