Journal of Fluorine Chemistry, 14 (1979) 289–297
© Elsevier Sequoia S.A., Lausanne – Printed in the Netherlands
Received: April 3, 1979

THE REACTION OF 2-TRIFLUOROMETHYL-3,3-DIFLUOROOXAZIRIDINE WITH NUCLEOPHILES.

AKIRA SEKIYA and DARRYL D. DESMARTEAU[1]

Department of Chemistry, Kansas State University, Manhattan, Kansas
66506, USA.

SUMMARY

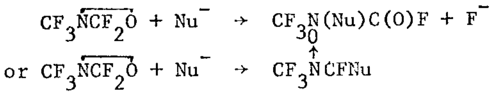
The facile reactions of $CF_3\overline{NCF_2O}$ with a variety of non-fluorinated nucleophiles are discussed.

$$CF_3\overline{NCF_2O} + Nu^- \rightarrow CF_3N(Nu)C(O)F + F^-$$

Reactions with alcohols, carboxylic acids, mercaptans, amines, KSCN, KCN, NaN_3 and NaOCN were carried out. All except NaN_3 and NaOCN were reactive and the expected compounds were isolated in most cases. Subsequent reaction of $CF_3N(Nu)C(O)F$ with additional nucleophile was observed in many cases forming $CF_3N(Nu)C(O)Nu$. With CH_3CO_2H, the latter reaction forms $CH_3C(O)F$ and the novel amine $CF_3N(H)OC(O)CH_3$[6]. Ten new compounds are reported with characterization by IR, NMR and physical properties.

INTRODUCTION

The novel oxaziridine,[2] $CF_3\overline{NCF_2O}$, has been shown to undergo reactions with fluorinated nucleophiles with attack occurring exclusively at nitrogen.[3,4] These reactions are analogous to those observed with hexafluoropropene epoxide,[5] $CF_3\overline{CFCF_2O}$, and thus reaction with fluoride forms $CF_3NFC(O)F$ and $CF_3CF_2C(O)F$, respectively. With CF_3O^-, $CF_3N(OCF_3)C(O)F$ and $CF_3CF(OCF_3)C(O)F$ are the products. In general, the reactivity of $CF_3\overline{NCF_2O}$ is lower than that of $CF_3\overline{CFCF_2O}$ with fluorinated nucleophiles. Because highly fluorinated nucleophiles are less nucleophilic than their hydrocarbon analogs, we expected that $CF_3\overline{NCF_2O}$ would show increased reactivity with the latter. In addition, attack at a site other than nitrogen might be observed.



$$
\begin{aligned}
&CF_3\overline{NCF_2O} + Nu^- \rightarrow CF_3N(Nu)C(O)F + F^- \\
\text{or } &CF_3\overline{NCF_2O} + Nu^- \rightarrow CF_3\overset{\overset{O}{\uparrow}}{N}CFNu
\end{aligned}
$$

Reaction of the oxaziridine with a variety of non-fluorinated nucleophiles leads to many interesting new compounds, but no evidence for attack at other than nitrogen. Ten new compounds are reported and chacterized.

EXPERIMENTAL

General. All volatile compounds were manipulated in glass and stainless steel vacuum systems as previously described. Characterization of new compounds was carried out in the usual way.[2]

All chemicals except $CF_3\overline{NCF_2O}$ were obtained from commercial sources. Liquids were distilled before use and solids were dried by warming under dynamic vacuum. The oxaziridine was prepared and purified by the literature method.[2]

Reactions of $CF_3\overline{NCF_2O}$

Reactions were carried out in 10ml Kel-F reactors fitted with a stainless steel valve. Solid reactants were added and pumped under dynamic vacuum for 8-12 hours. The reactor was then cooled to -193° and volatile reactants were condensed in by vacuum transfer. The reactor was then placed in a Dewar flask filled with ∿ 500 ml of $CFCl_3$ at -110° and allowed to warm slowly to 22° over a 16 hour period or warmed directly to 22° and allowed to stand for an appropriate time. The reactor was then cooled to -193° and non-condensable gases were checked. Volatile products were then separated by glc or distillation through traps cooled to appropriate temperatures. Details for all reactions are summarized in Table 1. Characterization for new compounds follows.

$CF_3N(OCH_3)C(O)F$: b.p. 60.4°; mol. wt. 165.1, calcd. 161.06
$\log P(\text{torr}) = 5.126 - \frac{45.50}{T} - \frac{2346 \times 10^2}{T^2}$; $\Delta H_{vap} = 6.64$ kcal/mol;
$\Delta S_{vap} = 19.9$ eu; IR 3030 (vw), 3000(w), 2968(m), 1871(vs), 1788(vw), 1468(w), 1449(w), 1395(vw), 1310(m), 1275(vs), 1253(vs), 1205(vs), 1155(vw), 1097(s), 1022(m), 1001(s), 979(m), 789(w), 757(m), 693(s) cm^{-1}; NMR ϕ^* 65.4, d, CF_3; 11.5, q, C(O)F; δ 4.7, s, CH_3; $J_{FF} = 14.4$ Hz.

$CF_3NFC(O)OCH_3$: m.p. -71.5 to -70.8°; mol. wt. 157.0, calcd. 161.06; IR 2963(m), 2860(vw), 1852(vw), 1818(m), 1803(s), 1555(vw), 1445(m), 1307(vs), 1280(vs), 1245(vw), 1214(vs), 1192(sh), 1098(sh), 1070(m), 1041(m), 1009(w), 932(w), 823(m), 813(m), 781(w), 719(m) cm^{-1}; NMR ϕ^* 68.1, d, CF_3; 75.0, q, NF; δ 4.2, s, CH_3; $J_{FF} = 11.2$ Hz.

$CF_3N(OCH_3)C(O)OCH_3$; b.p. 97.5°; mol. wt. 173.0, calcd. 173.09; $\log P(\text{torr}) = 3.338 + \frac{1697}{T} - \frac{6919 \times 10^2}{T^2}$;
$\Delta H_{vap} = 9.32$ kcal/mole; $\Delta S_{vap} = 25.1$ e.u.; IR 3040(vw), 3001(w), 2997(m), 2915(w), 2860(vw), 2835(vw), 1850(vw), 1788(vs), 1510(w), 1460(vw), 1442(m), 1318(vs), 1298(vs), 1057(vs), 1197(vs), 1113(m), 1062(s), 997(m), 932(m), 901(vw), 862(vw), 814(m), 773(m), 722(m), 642(m), 601(m) cm^{-1}; NMR ϕ^* 65.4, s, CF_3; δ 4.2, br, $NOCH_3$; 4.3, s, $COCH_3$.

$CF_3N(OC_2H_5)C(O)F$: m.p. -58.5 to -58.0°; mol. wt. 170.0, calcd. 175.08; IR 2992(m) 2957(w), 2910(w), 1860(vs), 1395(w), 1309(s), 1283(s), 1255(vs), 1206(vs), 1120(vw), 1110(vw), 1084(s), 1017(s), 987(s), 876(w), 795(w), 754(m), 606(w) cm^{-1}; NMR ϕ^* 65.1, d, CF_3; 11.25, q, C(O)F; δ 4.4, q, CH_2; 1.5, t, CH_3; $J_{FF} = 15.0$, $J_{HH} = 7.3$ Hz.

$CF_3N[OCH(CH_3)_2]C(O)F$: m.p. - 72.3 to -71.6°, mol. wt. 190.3, calcd. 189.11; IR 2997(m), 2951(w), 2278(vw), 1968(vw), 1867(vs), 1845(sh), 1500(vw), 1473(w), 1388(w), 1339(sh), 1310(s), 1264(vs), 1208(vs), 1150(m), 1113(m), 1082(s), 1043(w), 1018(m), 985(s), 950(vw), 911(m), 830(w), 794(w), 745(m), 698(m), 612(w) cm^{-1}; NMR ϕ^* 64.3, d, CF_3; 9.65, q, C(O)F; δ 4.5, sept., CH; 1.5, d, CH_3; J_{FF} = 15.3, J_{HH} = 6.2 Hz.

$CF_3N[OC(CH_3)_3]C(O)F$: m.p. -55.3 to -54.5°; mol. wt. 204.0, calcd. 203.14; IR 2982(m), 1877(vs), 1857(s), 1836(sh), 1495(m), 1368(w), 1346(w), 1303(s), 1252(s), 1209(vs), 1145(vw), 1070(m), 1009(m), 977(m), 949(w), 892(vw), 851(w), 805(w), 733(vw), 698(w), 600(w) cm^{-1}; NMR ϕ^* 62.4, d, CF_3; 7.90, q, C(O)F; δ 1.54, s, CH_3; J_{FF} = 16.4 Hz.

$CF_3N[OC(O)CH_3]C(O)F$: m.p. -58.0 to -57.1°; mol. wt. 186.5, calcd. 189.07; IR 1878(vs), 1843(vs), 1795(w), 1442(w), 1370(w), 1340(vs), 1313(s), 1272(vs), 1211(vs), 1170(vs), 1100(vs), 1033(s), 1000(s), 895(vw), 832(m), 801(vw), 740(vw), 722(m), 688(m), 645(w), 585(m), 521(m) cm^{-1}; NMR ϕ^* 63.0, d, CF_3; 14.5, q, C(O)F; δ 2.6, s, CH_3; J_{FF} = 14.0 Hz.

$CF_3N(H)OC(O)CH_3$: m.p. 35.8 to 36.0°; mol. wt. 145.4, calcd. 143.07; IR 3250(m) 3223(m), 1876(w), 1856(m), 1788(vs), 1732(vw), 1692(vw), 1512(w), 1500(w), 1447(s), 1374(m), 1358(w), 1312(vs), 1215(vs), 1172(vs), 1103(w), 1044(s), 994(w), 954(s), 870(m), 823(m), 769(vw), 714(w), 680(sh), 664(m), 600(w), 568(w) cm^{-1}; NMR ϕ^* 70.5, d, CF_3; δ 8.5, br, NH; 2.4, s, CH_3; J_{HF} = 8.8 Hz.

$CF_3N(SC_2H_5)C(O)F$: m.p., glass -193°, mol. wt. 195.0, calcd. 191.48; IR 2985(w), 2953(w), 1695(vs), 1250(vs), 1223(vs), 1184(s), 1116(m), 1060(vw), 976(vw), 915(vw), 884(m), 842(w) 674(s), 620(w), 464(m) cm^{-1}; NMR ϕ^* 53.9, d, CF_3; 2.60, q, C(O)F; δ 2.93, q, CH_2; 1.60, t, CH_3; J_{FF} = 10.9, J_{HH} = 7.2 Hz.

$CF_3N(CN)C(O)F$: b.p. 42°; mol. wt. 156.5, calcd. 156.04; IR 2237(m), 1902(s), 1881(vs), 1872(s), 1810(w), 1794(m), 1767(s), 1616(vw), 1435(vs), 1290(vs), 1223(vs), 1208(sh), 1069(m), 1012(w), 995(w), 988(m), 937(vw), 912(m), 860(w), 844(w), 788(vw), 755(w), 705(sh), 674(m), 601(m), 501(w) cm^{-1}; NMR ϕ^* 68.1, m, CF_3; 14.0, br, C(O)F.

Table 1 Reactions of $CF_3\overline{NCF_2O}$ with Nucleophiles

Nu^- $(Nu/CF_3\overline{NCF_2O})$[a]	Conditions		Product(s)(Yield %)
	°C	Hr.	
CH_3OH (1/1)	-111 to 22°	16	$CF_3N(OCH_3)C(O)F$ (80)[d]
CH_3OH (2/1)	-111 to 22°	16	$CF_3N(OCH_3)C(O)OCH_3$ (90)[e]
CH_3OH (1/1)[b]	-111 to 22°	16	$CF_3NFC(O)OCH_3$ (99)[d]
C_2H_5OH (1/1)	-111 to 22°	16	$CF_3N(OC_2H_5)C(O)F$ (81)[d]
$(CH_3)_2CHOH$ (1/1)	-111 to 22°	16	$CF_3N[OCH(CH_3)_2C(O)F$ (88)[e]
$(CH_3)_3COH$ (1/1)	-111 to 22°	16	$CF_3N[OC(CH_3)_3]C(O)F$ (93)[e]
CH_3CO_2H (1/1)	22°	4.5	$CF_3N[OC(O)CH_3]C(O)F$ (32)[d]
			$CF_3N(H)OC(O)CH_3$ (21)[d]
			$CH_3C(O)F$ (46)[h]
CH_3CO_2H (2/1)	22°	4.5	$CF_3N[OC(O)CH_3]C(O)F$ (11)[d]
			$CF_3N(H)OC(O)CH_3$ (75)[d]
			$CH_3C(O)F$ (64)[h]
CH_3CH_2SH (1/1)	-111 to 22°	16	$CF_3N(SC_2H_5)C(O)F$ (30)[f]
KCN (100/1)[c]	22°	48	$CF_3N(CN)C(O)F$ (40)[d]
KSCN (10/1)[c]	22°	22	CF_3NCO (90)[g]

a. All reactions with 1.0 mmol of $CF_3\overline{NCF_2O}$ and 5.0 mmol of NaF except where noted.

b. 1.0 mmol of $CF_3NFC(O)F$

c. No NaF.

d. Isolated by glc.

e. -111° trap after a -35° trap.

f. -74° trap.

g. -193° trap after a -111° trap.

h. -111° trap after -78° trap.

RESULTS AND DISCUSSION

The reaction of $CF_3\overline{NCF_2O}$ with oxygen-containing nucleophiles was expected to occur readily. Methanol was chosen as a typical source of an alkoxy nucleophile and reaction with $CF_3\overline{NCF_2O}$ produced two CH_3O containing products, $CF_3N(OCH_3)C(O)F$ [1] (35%) and $CF_3N(OCH_3)C(O)OCH_3$ [2] (30%) along with HF and several low molecular wt. products. Four products are possible from this reaction and could arise in several ways as shown by the following reaction scheme.

$$\begin{tikzcd}
HF + [1] \arrow[d, "II"', "CH_3OH"] & CF_3\overline{NCF_2O} \arrow[l, "CH_3OH"', "I"] \arrow[r, "CH_3OH", "IV"'] \arrow[d, "III"', "CH_3OH"] & CF_3NFC(O)F\ [3] \arrow[d, "V"', "CH_3OH"] \\
HF + [2] & CF_3NFC(O)OCH_3\ [4] \arrow[l, "CH_3OH"', "VI"] & \text{or } [1] + HF
\end{tikzcd}$$

We believe that [1] and [2] arise from reactions I and II. To eliminate reactions III-VI, reaction of [3] with CH_3OH was carried out in the presence of NaF to absorb HF and [4] (99%) was observed. Assuming NaF does not inhibit reactions III-VI, these potential reaction paths are clearly unimportant for the formation of [1] and [2]. Reaction of $CF_3\overline{NCF_2O}$ with CH_3OH in the presence of NaF yields [1] in very high yield and subsequent reaction of [1] with CH_3OH under the same conditions forms [2] in very high yield. These results suggest that reaction I is catalyzed by NaF and that the nucleophilic attack first occurs at nitrogen to form [1] and that [2] is formed via path II. The increased yield of [1] follows from base catalysis by NaF and the fact that side reactions of HF with $CF_3\overline{NCF_2O}$ are effectively eliminated. Reaction of HF with the oxaziridine leads to several low molecular weight products and thus in the uncatalyzed reaction, $CF_3\overline{NCF_2O}$ is consumed by both CH_3OH and HF. The latter results in an effective increase in CH_3OH relative to the oxaziridine and favors the formation of [2] via II.

Other alcohols react similarly to CH_3OH in the presence of NaF to form $CF_3N(OR)C(O)F$. The selectivity for the formation of the latter increases in the order 1° < 2° < 3° alcohols. Thus reaction path II is less favorable as the size of OR increases. Most probably, reactions I and II are general for a wide variety of alcohols, but additional examples were not tried.

Reaction of $CF_3\overline{NCF_2O}$ with acetic acid in the presence of NaF led to the expected product, $CF_3N[OC(O)CH_3]C(O)F$ [5], but a significant amount of an unexpected product, $CF_3N(H)OC(O)CH_3$ [6], was observed along with CO_2, $CH_3C(O)F$ and unreacted oxaziridine. Reaction of CH_3CO_2H under the same conditions on a 2:1 scale gave [6] as the major product with CO_2 and $CH_3C(O)F$ in equal amounts. These results can be explained by the following reaction scheme.

$$\begin{tikzcd}
CF_3\overline{NCF_2O} + CH_3CO_2H \arrow[r, "NaF"] & {[5] + HF} \arrow[d, "CH_3CO_2H/NaF"] \\
{[6] + CO_2} & \{CF_3N[OC(O)CH_3]C(O)OH\} + CH_3C(O)F \arrow[l]
\end{tikzcd}$$

In support of this, reaction of [5] with H_2O in the presence of NaF forms [6] and CO_2 in excellent yield.

$$\begin{tikzcd}
{[5] + H_2O} \arrow[r, "NaF"] & \{CF_3N[OC(O)CH_3]C(O)OH\} + HF \arrow[d] \\
 & {[6]}
\end{tikzcd}$$

A related reaction of $C_2F_5C(O)F$ with RCO_2H is also supportive of this scheme. In this case, reaction occurs to give RC(O)F and the stable acid $C_2F_5CO_2H$.[7]

Two sulfur nucleophiles, C_2H_5SH and KSCN, were tried with $CF_3\overline{NCF_2O}$. With ethanethiol, the expected product $CF_3N(SC_2H_5)C(O)F$ [7] could be isolated in moderate yield. With KSCN, none of the expected product was found. Instea the reaction provided a high yield synthesis of CF_3NCO from the oxaziridine.

We believe that further reaction of $CF_3N(Nu)C(O)F$ with the sulfur nucleophile is especially facile in these cases and the products can be explained by the following reactions.

$$\begin{tikzcd}
CF_3\overline{NCF_2O} + C_2H_5SH \arrow[r, "NaF"] & {[7] + HF} \arrow[d, "C_2H_5SH/NaF"] \\
CF_3NCO + (C_2H_5S)_2 & \{CF_3N(SC_2H_5)C(O)SC_2H_5\} + HF \arrow[l]
\end{tikzcd}$$

$$\begin{tikzcd}
CF_3\overline{NCF_2O} + KSCN \arrow[r] & \{CF_3N(SCN)C(O)F\} + KF \arrow[d, "KSCN"] \\
(SCN)_n + CF_3NCO & \{CF_3N(SCN)C(O)SCN\} + KF \arrow[l]
\end{tikzcd}$$

Neither $(C_2H_5S)_2$ nor $(SCN)_2$ was unequivocally identified but a low volatile oil and non-volatile yellow solid were observed in the respective reactions, consistent with the proposed products. Similar results were previously observed with CF_3SH and in this case, $(CF_3S)_2$ was clearly identified.[4] Apparently, the observed disproportionation with sulfur nucleophiles simply reflects the low oxidation potential of sulfur in these compounds.

Attempts to react $CF_3\overline{NCF_2O}$ with nitrogen nucleophiles were unsuccessful. Azide from NaN_3 was unreactive and $(C_2H_5)_2NH$ in the presence of the NaF gave a variety of products but no $CF_3N[N(C_2H_5)_2]C(O)F$ was observed. Previously, reaction with the very acidic amine $(CF_3)_2NH$ was similarly unsuccessful.[4]

As an example of a carbon nucleophile, excess KCN was allowed to react with $CF_3\overline{NCF_2O}$. The reaction was slow but a significant yield of $CF_3N(CN)C(O)F$ [8] (40%) could be isolated after two days at 22°. The other product, $CF_3N(F)C(O)F$, results from isomerization of the oxaziridine by KF formed in the reaction.

$$\begin{tikzcd}
CF_3\overline{NCF_2O} + KCN \arrow[r] \arrow[dr, "KF"'] & CF_3N(CN)C(O)F + KF \\
& CF_3N(F)C(O)F
\end{tikzcd}$$

Attempts to prepare $CF_3N(OH)C(O)F$ from NaOH and the oxaziridine were unsuccessful. It was hoped that this compound might yield $CF_3\overline{NC(O)O}$ by loss of HF. However, the reaction was very fast to yield CO_2 as the main identifiable product.

Characterization of all new compounds by ^{1}H and ^{19}F NMR, IR and physical properties was straightforward. The new materials formed from $CF_3\overline{NCF_2O}$ further illustrate the utility of this novel oxaziridine in synthesis. We are not aware of any analogous N-trifluoromethyl derivatives, nor do any alternate methods of synthesis come readily to mind. The synthesis of $CF_3N(H)OC(O)CH_3$ described in this work suggests that many analogous amines can be obtained from $CF_3N(R)C(O)F$ by hydrolysis. A study of this reaction with variety of such compounds obtained from the nucleophilic attack on $CF_3\overline{NCF_2O}$ is underway.

ACKNOWLEDGEMENT

The support of this work by the Army Research Office-Durham (Grant No. DAAG29-77-G-0071) is gratefully acknowledged.

REFERENCES

1 Alfred P. Sloan Fellow, 1975-77.

2 E. R. Falardeau and D. D. DesMarteau, J. Am. Chem. Soc., 98, 3529 (1976).

3 A. Sekiya and D. D. DesMarteau, Inorg. Chem., 18, 919 (1979).

4 A. Sekiya and D. D. DesMarteau, J. Org. Chem., 44, 1131 (1979).

5 P. Tarrant, C. G. Allison, K. P. Barthold and E. C. Stump, Fluorine Chem. Rev., 5, 177 (1971).

6 A. Yu. Yakubovich, S. P. Markarov, V. A. Ginsburg, N. F. Privezentseva and L. L. Margnova, Doklady Akad. Nauk S.S.S.R., 14, 125 (1961).

7 S. Sasaki and N. Ishikawa, Chem. Lett. (Japan), 12, 1407 (1976).