(18) (a) A. A. Berchtold and G. F. Uhlig, *J. Org. Chem.*, **28**, 1459 (1963). (b) K. C. Brannock, R. D. Burpitt, V. W. Goodlett, and J. G. Thweatt, *ibid.*, **28**, 1464 (1963). (c) C. F. Huebner, L. Dorfman, M. M. Robison, E. Donoghue, W. G. Pierson, and P. Strachan, *ibid.*, **28**, 3134 (1963).
(19) Compound **16** was identical by TLC and NMR spectral comparison with a sample provided by Dr. R. A. Raphael. The position of the double bond has been assigned by Raphael.[4a]
(20) Catalytic hydrogenation of **16** in methyl acetate with W-2 Raney nickel (35 psi, 24 h) produced the keto ester **17a**, identical by TLC and NMR spectral comparison with an authentic sample provided by Drs. A. S. Kende and L. S. Liebeskind.[4b] Raphael[4a] reports hydrogenation of **16** occasionally results in the formation of a hydroxy compound, which upon oxidation with Jones reagent affords the saturated keto ester **17a**. We have also noted carbonyl reduction with some batches of Raney nickel. Keto ester **17a** has previously been converted by hydrolysis to **17b**, which reacts with formaldehyde in base to form isosteganone **18**. Thermally, **18** is converted quantitatively to steganone **4**.[4a,b]
(21) T. Shiori and K. Ninomiya, *J. Am. Chem. Soc.*, **94**, 6203 (1972).

Synthesis of *N,N*-Dialkylaminosulfenylcarbamate Insecticides via Carbamoyl Fluorides

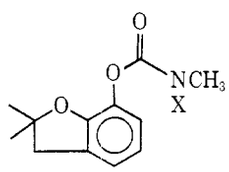
Charles E. Hatch III

Agricultural Chemicals Research Group, FMC Corporation, Princeton, New Jersey 08540

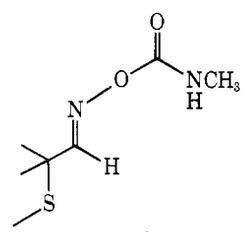
Received April 7, 1978

A facile and general process for the preparation of *N*-sulfenylated carbamates from carbamoyl fluorides and alcohols under phase-transfer conditions is described. Use of this method to prepare a series of 12 analogues of the carbamate insecticides carbofuran, methomyl, and carbaryl is discussed. The preparation and properties of the intermediate carbamoyl fluorides are also reported.

One of the major deficiencies of the widely used carbamate class of insecticides is their generally high mammalian toxicity. For example, carbofuran (**1a**) has an oral LD_{50} in rats of 11 mg/kg while for aldicarb (**2**) the value is only 1 mg/kg.[1]



1a, X = H
b, X = SR



2

With the goal of maintaining the insecticidal activity but decreasing the mammalian toxicity, a large number of analogues of carbamates have been synthesized. One group of analogues, which are considerably less toxic to mammals but which are cleaved by insects to the parent carbamate, is composed of *N*-sulfur compounds such as **1b**. Of particular interest to us were **1b** type compounds where R = N(alkyl)$_2$, which were originally prepared by Fukuto and Black.[2] Their preparation of these materials involved condensation of carbofuran with the appropriate sulfenyl chloride. Because of certain patent restrictions, we desired a general synthesis of dialkylaminosulfenylcarbamate analogues which did not utilize the parent carbamate either as a starting material or as an intermediate. Toward this goal we examine the approach outlined in Schemes I and II, which involves as a key intermediate an *N*-dialkylaminosulfenyl-*N*-alkylcarbamoyl fluoride. A related route, which had been previously reported for the preparation of SAr and SCX_3 (S = halogen or hydrogen) carbamate derivatives,[3] was found to work very poorly in our hands. Utilizing the process described herein, a series of dialkylaminosulfenyl derivatives of commercial carbamates was prepared in high yield and purity.[4,5]

Although *N*-methylcarbamoyl fluoride (**3**, see Scheme I) has been utilized in a number of patents,[3] a detailed report of its synthesis could not be found. There are several possible synthetic approaches to the material; however, only the reaction of methyl isocyanate (MIC) and anhydrous hydrogen fluoride (HF) was examined. All work with HF was carried out in polyethylene bottles equipped with polyethylene tubing and stopcocks.

Scheme I

$$CH_3NCO + HF \rightarrow \underset{\mathbf{3}}{CH_3NHCOF}$$

$$R^1R^2NH + S_2Cl_2 \rightarrow \underset{\mathbf{5}}{(R^1R^2NS)_2}$$
(**4**)

$$(R^1R^2NS)_2 + SO_2Cl_2 \rightarrow \underset{\mathbf{6}}{R^1R^2NSCl}$$
(**5**)

$$CH_3NHCOF + R^1R^2NSCl \rightarrow \underset{\mathbf{7}}{R^1R^2NSN(CH_3)COF}$$
(**3**, **6**)

	R^1	R^2
4a–7a	*n*-Bu	*n*-Bu
4b–7b	morpholino	
4c–7c	*n*-Pr	*n*-Pr
4d–7d	Me	$CH_2C_6H_5$
4e–7e	Et	$CH_2C_6H_5$
4f–7f	piperidino	
4g–7g	Et	Et

Treatment of a solution of MIC in methylene chloride with 2–5 equiv of gaseous HF (bp 19 °C) at 0 °C over 1 h followed by removal of the solvent and excess HF under vacuum at 30

Scheme II

$$\underset{\mathbf{7}}{R^1R^2NSN(CH_3)COF} + \underset{\mathbf{8}}{R^3OH} \rightarrow \underset{\mathbf{9}}{R^1R^2NSN(CH_3)CO_2R^3}$$

	R^1	R^2	R^3
8h			2,2-dimethylbenzofuran-7-yl
i			$CH_3S(CH_3)C{=}N$
j			napth-1-yl
k			CH_3
9l	*n*-Bu	*n*-Bu	2,2-dimethylbenzofuran-7-yl
m	morphilino		2,2-dimethylbenzofuran-7-yl
n	Et	$CH_2C_6H_5$	2,2-dimethylbenzofuran-7-yl
o	*n*-Bu	*n*-Bu	$CH_3S(CH_3)C{=}N$
p	*n*-Pr	*n*-Pr	$CH_3S(CH_3)C{=}N$
q	CH_3	$CH_2C_6H_5$	$CH_3S(CH_3)C{=}N$
r	Et	Et	$CH_3S(CH_3)C{=}N$
s	*n*-Bu	*n*-Bu	napth-1-yl
t	*n*-Pr	*n*-Pr	napth-1-yl
u	Et	$CH_2C_6H_5$	napth-1-yl
v	piperidino		napth-1-yl
w	Et	Et	napth-1-yl
x	*n*-Bu	*n*-Bu	CH_3

0022-3263/78/1943-3953$01.00/0

Table I. Preparation of *N*-Dialkylaminosulfenyl-*N*-methylcarbamoyl Fluorides from *N*-methylcarbamoyl Fluoride

fluoride	registry no.	isolated[a] yield, %	Bp (pressure, mm) or mp, °C	elemental anal.[b] calcd (found) C	H	N	NMR (CCl_3D), δ
7a	62382-48-3	61	84–85 (0.2–0.3)	50.82 (51.15)	8.96 (8.84)	11.85 (11.99)	0.80–2.00 (m, 14), 3.15 (bt, 4, NCH_2), 3.30 (s, 3, $CONCH_3$)
7b	62382-41-6	38	49–50	37.12 (36.86)	5.79 (5.62)	14.43 (14.34)	3.10–3.40 (m, 4,), 3.40 (s, 3, $CONCH_3$), 3.60–3.80 (m, 4)
7c	67271-00-5	53	59–60 (0.2–0.3)	46.13 (46.60)	8.23 (8.10)	13.45 (13.92)	0.95 (t, 6, CH_2CH_3), 1.20–2.00 (m, 4, CH_2CH_3), 3.10 (bt, 4, NCH_2), 3.30 (s, 3, $CONCH_3$)
7d	67271-01-6	47	99–100 (0.2–0.3)	53.10 (52.49)	5.08 (5.62)	12.42 (12.09)	2.85 (s, 3, $SN[CH_3]CH_2$), 3.30 (s, 3 $CONCH_3$), 4.30 (bs, 2, NCH_2), 7.25 (s, 5, $CH_2C_6H_5$)
7e	67271-02-7	60	104–105 (0.2–0.3)	54.52 (55.19)	6.24 (6.89)	11.56 (12.10)	1.20 (t, 3, CH_2CH_3), 3.10 (q, 2, CH_2CH_3), 3.35 (s, 3, $CONCH_3$), 4.40 (bs, 2, NCH_2), 7.25 (s, 5, $CH_2C_6H_5$)
7f	62382-43-8	59	65–66 (0.2–0.3)	43.73 (44.24)	6.82 (6.78)	14.57 (14.84)	1.35–1.80 (m, 6), 3.25 (bt, 4 NCH_2), 3.35 (s, 3 $CONCH_3$)
7g	62382-46-1	45	43–44 (0.2–0.3)	39.98 (40.48)	7.27 (7.30)	15.54 (15.37)	1.20 (t, 6, CH_2CH_3), 3.15 (q, 4, CH_2CH_3), 3.30 (s, 3, $CONCH_3$)

[a] Either distilled or recrystallized from hexane. [b] Many of these materials which contain N–S–N bonding are unstable when analytically pure. As such, high accuracy combustion analyses were difficult to obtain.

°C gave a high yield of a crude liquid product. Attempts to transfer this product to glassware for analysis, storage, or distillation were unsuccessful, due to reaction of the material with any glass equipment. Substitution of pentane for the methylene chloride solvent resulted in a two-phase system after addition of the HF since both HF and the fluoride **3** are only slightly soluble in hydrocarbon solvents. In this case, removal of the solvent and excess HF as described above gave a crude liquid which could be handled and distilled in glassware. Distilled fluoride **3** (bp 30–35 °C at 0.5—1.0 mm), which was obtained in a 93% yield, could be stored in glassware at 0 °C for several months with no appreciable decomposition. On a routine basis, however, **3** was used as a residual product and handled only in polyethylene.

The dialkylamino disulfides (**5a–g,** see Scheme I) which were used in this work were prepared from the corresponding amines (**4a–g**) and sulfur monochloride. Initially they were obtained by reaction in carbon tetrachloride of 4 equiv of the amine with 1 equiv of sulfur monochloride; however, due to the problem of amine recover, better conditions were sought. It was found that addition of sulfur monochloride to a vigorously stirred two-phase mixture of 2 equiv of amine, hexane, sodium hydroxide, and water at 0 °C gave after 1 h the desired disulfide in high yield and good purity. In general the disulfides prepared in this manner were used without further purification. In the case of **5a,** samples of the corresponding monosulfide (**10**) and trisulfide (**11**) were prepared and shown by NMR and LC to be minor contaminants in the disulfide. Usually a small amount of solid, which was shown by LC to be elemental sulfur, precipitated out of the liquid disulfides on storage below room temperature.

Cleavage of the disulfides **5a–g** to the corresponding sulfenyl chlorides **6a–g** was examined both with chlorine gas in carbon tetrachloride solution and with sulfuryl chloride neat. Although the crude yields were good from both approaches, the latter was found preferable since it required the minimum amount of manipulation of the sulfenyl chlorides which generally, over several hours, darkened in color and formed amine hydrochloride salt precipitates. Some of the sulfenyl chloride **6a** was successfully flash distilled (bp 65–70 °C at 0.1–0.2 mm) although in low yield. Attempted batch distillation of similar material was unsuccessful. Routinely the appropriate disulfide was treated at 0–10 °C with 1 to 1.1 equiv of sulfuryl chloride for 1 h, followed by removal of any excess sulfuryl chloride and the sulfur dioxide by-product under vacuum. The thus obtained products were used immediately.

The reaction of di-*n*-butylaminosulfenyl chloride, **6a,** with *N*-methylcarbamoyl fluoride, **3,** to give the N,N-disubstituted carbamoyl fluoride **7a** was initially examined under literature conditions[3] for a similar transformation which involved reaction of equimolar quantities of the starting materials in a nonpolar organic solvent in the presence of a tertiary amine base for several hours. It was shown, however, that for the dialkylamino system these conditions resulted in both a very low yield and low purity of the desired product **7a.** As a result, other conditions were examined utilizing an n-$C_{13}H_{28}$ internal standard coupled with GLC analysis on a 10% OV17 Chromosorb W column. From these experiments it was found that use of a polar solvent such as pyridine at room temperature with 1.5 equiv of 1,4-diazabicyclo[2.2.2]octane base for several hours gave an 80–85% yield of crude **7a** (carbonyl IR at 1780 cm^{-1}) which was stable in glassware and could be purified by distillation to give a 75–80% yield of **7a** of >95% purity. The crude material was also purified by column chromatography; however, the recovery was only 25–30% indicating some reaction of **7a** with the silica packing. Although differential thermal analysis of **7a** indicated an exotherm of ~200 cal/g at 200 °C, no problems were encountered in its distillation. In methanol–triethylamine solution fluoride **7a** was converted to the corresponding methyl ester (**9x**) (carbonyl IR at 1740 cm^{-1}) which was also prepared from the sulfenyl chloride **6a** and the known methyl *N*-methylcarbamate.

Using conditions similar to those for the preparation of **7a,** the fluorides **7b–g** (see Table I) were prepared. All were liquids which were purified by distillation with the exception of the morpholino **7b** which was a solid (recrystallized from hexane) and the methylbenzylamino **7d** which slowly solidified after distillation. All of these fluorides could be analyzed by GLC on 10% OV17 on Chromosorb W except the ethylbenzyl **7e** which underwent partial decomposition.

The reaction of carbamoyl fluoride **7a** with the alcohol **8h** to give the carbamate **9l** was examined under various conditions. The reactions were followed by the loss of the fluoride peak on GLC against an n-$C_{13}H_{28}$ internal standard. Initially tried were conditions involving the reaction of equimolar amounts of the carbamoyl fluoride and alcohol in the presence of a tertiary amine base in a number of organic solvents at, or slightly above, room temperature. Thermal sensitivity of the final product prohibited utilizing higher reaction temperatures. However, it was found that for the carbamoyl fluoride **7a** and alcohol **8h,** these conditions resulted in reaction times of several days and product in low yield and purity (see Table II).

As a result of the apparent stability of the carbamoyl fluo-

Table II. Equimolar Reactions of *N*-(Di-*n*-butylaminosulfenyl)-*N*-methylcarbamoyl Fluoride (7a) with 7-Hydroxy-2,3-dihydro-2,2-dimethylbenzofuran (8h)

run	solvent	catalyst[a]	base	reaction time, (h)	reaction temp, °C	product (9l) % purity[b]	product (9l) % yield[c]
1	toluene		TEA[d]	20	ambient	26	11
				2	45		
2	acetonitrile		TEA	20	ambient	36	14
				2	45	36	14
3	toluene	tetrabutylammonium hydrogen sulfate	NaOH	2	ambient	86	73 (69[e])
4	methylene chloride	benzyltriethyl ammonium chloride	NaOH	6.5	ambient	66	80

[a] 10 mol %. [b] By LC on a C-18 reverse phase column against a purified standard. [c] Crude weight X LC determined purity. [d] TEA = triethylamine. [e] Isolated by silica gel column chromatography.

Table III. Reactions of *N*-Dialkylaminosulfenyl-*N*-methylcarbamoyl Fluorides with Alcohols

carbamate	registry no.	alcohol	isolated[a] yield, %	Mp, °C (or n^{20}_D)	elemental anal.[b] calcd (found) C	H	N	NMR (CCl_3D), δ
9l	55285-14-8	**8h**[c]	69	(1.5116)	63.13 (63.16)	8.48 (8.49)	7.36 (7.67)	0.80–2.00 (m, 14), 1.50 (s, 6, $C[CH_3]_2$), 3.00 (s, 2, ring CH_2), 3.20 (t, 4, NCH_2), 3.40 (s, 3, $CONCH_3$), 6.60–7.10 (m, 3, aromatic)
9m	55285-05-7	**8h**	75	80–81	56.79 (56.69)	6.55 (6.36)	8.28 (8.13)	1.45 (s, 6, $C[CH_3]_2$), 3.05 (s, 2, ring CH_2), 3.20–3.45 (m, 4), 3.45 (s, 3, $CONCH_3$), 3.60–3.80 (m, 4), 6.70–7.30 (m, 3, aromatic)
9n	55285-18-2	**8h**	65	(1.5606)	65.27 (65.13)	6.78 (6.78)	7.25 (6.96)	1.20 (t, 3, CH_2CH_3), 1.45 (s, 6, $C[CH_3]_2$), 3.05 (s, 2, ring CH_2), 3.20 (q, 2, CH_2CH_3), 3.45 (s, 3, $CONCH_3$), 4.60 (bs, 2, $CH_2C_6H_5$), 6.80–7.40 (m, 3, benzofuranyl aromatic), 7.35 (s, 5, C_6H_5)
9o	62382-35-8	**8i**[d]	69	(1.5080)	48.57 (49.07)	8.47 (8.44)	13.07 (13.63)	0.85–1.90 (m, 14), 2.25 (s, 3), 2.30 (s, 3), 3.20 (bt, 4, NCH_2), 3.30 (s, 3, $CONCH_3$)
9p	67271-03-8	**8i**	45	(1.5160)	45.04 (44.99)	7.90 (7.66)	14.33 (14.03)	0.90 (t, 6, CH_2CH_3), 1.40–2.00 (m, 4, CH_2CH_3) 2.25 (s, 3), 2.30 (s, 3), 3.15 (bs, 4, NCH_2), 3.35 (s, 3, $CONCH_3$)
9q	67271-04-9	**8i**	60	87–88	49.82 (49.69)	6.11 (6.08)	13.41 (13.18)	2.30 (s, 3), 2.35 (s, 3), 2.90 (s, 3, $SN[CH_3]CH_2$), 3.45 (s, 3, $CONCH_3$), 4.40 (s, 2, NCH_2), 7.35 (s, 5, C_6H_5)
9r	62382-32-5	**8i**	70	(1.5284)	40.73 (40.62)	7.22 (7.06)	15.83 (15.59)	1.20 (t, 6, CH_2CH_3), 2.30 (s, 3), 2.35 (s, 3), 3.25 (q, 4, CH_2CH_3), 3.40 (s, 3, $CONCH_3$)
9s	67316-53-4	**8j**[e]	67	(1.5486)	66.64 (66.31)	7.83 (7.74)	7.77 (7.70)	0.70–1.90 (m, 14), 3.25 (bt, 4, NCH_2), 3.50 (s, 3, $CONCH_3$), 7.30–8.10 (m, 7, napthyl)
9t	67271-05-0	**8j**	54	(1.5744)	65.04 (64.69)	7.28 (7.09)	8.43 (8.16)	0.85 (t, 6, CH_2CH_3), 1.40–2.05 (m, 4, CH_2CH_3), 3.25 (bt, 4, NCH_2), 3.50 (s, 3, $CONCH_3$), 7.20–8.20 (m, 7, napthyl)
9u	67271-06-1	**8j**	63	47–49	68.83 (69.20)	6.05 (6.33)	7.65 (8.15)	1.05 (t, 3, CH_2CH_3), 3.20 (q, 2, CH_2CH_3), 3.50 (s, 3, $CONCH_3$), 4.55 (bs, 2, $CH_2C_6H_5$), 7.20–8.10 (m, 7, napthyl), 7.25 (s, 5, C_6H_5)
9v	67271-07-2	**8j**	38	77–78	64.54 (64.89)	6.37 (6.30)	8.86 (8.93)	1.30–1.70 (m, 6), 3.20–3.50 (m, 4), 3.50 (s, 3, $CONCH_3$), 7.20–8.10 (m, 7, napthyl)
9w	67271-08-3	**8j**	45	(1.5801)	63.14 (63.39)	6.62 (6.80)	9.21 (8.95)	1.20 (t, 6, CH_2CH_3), 3.25 (q, 4, CH_2CH_3), 3.45 (s, 3, $CONCH_3$), 7.10–8.10 (m, 7, napthyl)

[a] Chromatographed on silica gel. [b] Many of these materials which contain N–S–N bonding are unstable when analytically pure. As such, high accuracy combustion analyses were difficult to obtain. [c] Registry no. 1563-38-8. [d] Registry no. 13749-94-5. [e] Registry no. 90-15-3.

ride **7a** to attack at the acyl carbon, more severe reaction conditions were sought. It was found that under phase transfer conditions[6] involving an organic solvent–water mixture utilizing a quarternary ammonium salt catalyst and sodium hydroxide base, the desired transformation occurred rapidly and gave product of high purity in good yield. Both tetrabutylammonium hydrogen sulfate and benzyltriethylammonium chloride were examined as catalyst in several solvents. For the preparation of **9l**, a 10 mol % quanitity of the tetrabutylammonium hydrogen sulfate in toluene solvent was the best combination. The use of an excess of base increased the reaction rate considerably. The best conditions (see Table II) gave in 2 h an 85% yield of crude **9l** which was 86% pure as determined by quantitative LC analysis on a μ-particle C-18 reverse phase column using acetonitrile–water eluant. A 69% yield of high purity **9l** was isolated by column chromatography on silica gel.

The reactions of **7a** with the alcohols **8i** and **8j**, to give respectively **9o** and **9s**, were also examined under phase-transfer conditions with several different catalysts and organic solvents. In a manner similar to **8h**, the aromatic alcohol **8j** was found to react best with **7a** using toluene solvent and a 10 mol % quantity of tetrabutylammonium hydrogen sulfate catalyst for 2–3 h. In contrast to **8h** and **8j**, the nonaromatic alcohol **8i** was found to react best with **7a** in methylene chloride using a 10 mol % quantity of benzyltriethylammonium chloride catalyst. This latter reaction was significantly slower, requiring 22 h for completion.

Using the specific conditions worked out for each of the three alcohols, **8h–j**, described above, the 12 carbamate de-

rivatives in Table III were prepared. In all cases the NMR spectra were consistent with the desired product containing small amounts of impurities. Reactions involving alcohol **8j** had a strong propensity to turn black upon exposure to air, in contrast to the reactions of the other alcohols.

The carbamate products were all found to be active insecticides with lower mammalian toxicity than the corresponding parent compound. For example, the parent compound carbofuran, **1a,** has an oral LD_{50} in rats of 11 mg/kg and causes death at 0.1 mg/eye in a rabbit eye irritation test while the di-*n*-butylaminosulfenyl analogue of carbofuran, **9l,** in the same tests, had values of 105 mg/kg for the rat LD_{50} and no reaction in the rabbit eye test.

Experimental Section

Melting points were taken on a Thomas-Hoover melting point apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 735B spectrometer. NMR spectra were recorded either on a Varian T-60 or XL-100 instrument using $CDCl_3$ solvent and tetramethyl silane reference. Mass spectra (70 eV) were recorded on a DuPont 21-490B instrument. Microanalyses were determined by the Analytical Department of FMC Corp., Princeton, N.J. LC work was performed on a Waters Associates instrument equipped with a 254 nm fixed wavelength UV photometer detector and a 30 cm × 4 mm i.d. SS u-Bondapak C-18 reverse phase partition column. GLC work was carried out on a Hewlett-Packard 5840A instrument equipped with a thermal conductivity detector and a 6 ft. × ⅛ in. i.d. stainless steel column packed with 10% OV 17 on Chromosorb W. In all cases hexane and pentane were mixtures of isomers.

***N*-Methylcarbamoyl Fluoride (3).** Through the cap of a 2 oz. polyethylene bottle were run two ¼ in. i.d. polyethylene tubes, one of which extended to the bottom of the vessel (inlet tube) and one which went only through the cap (vent tube). After sealing the two tubes in place with epoxy, polyethylene stopcocks were attached to the ends of both tubes. A length of polyethylene tubing was run from the stopcock on the "inlet tube" to a cylinder of anhydrous hydrogen fluoride (HF), while another piece was run from the stopcock on the "vent tube" to an aqueous sodium hydroxide trap. To the reaction vessel was charged methyl isocyanate (10.0 g, 0.175 mol) and pentane (30 mL). To the resulting solution stirred and cooled to 0 °C was added a slow stream of HF (2–5 equiv) over 1 h. The HF (bp 19 °C) liquidified in the reactor during the addition and at the end of the addition two phases were present in the reactor. The HF flow was replaced by a nitrogen flow and the solution was warmed to 30 °C. After the pentane (upper layer) and any excess HF had distilled into the trap, the reaction mixture was transferred to a 1 oz. polyethylene bottle and placed under a vacuum of 2–5 mm for 30 min to give 13.40 g (99% yield by weight of a colorless liquid). This was transferred to glassware and distilled to give 12.51 g (93%) of colorless **3:** bp 30–35 °C (0.5–1.0 mm); NMR (CCl_3D) δ 2.85 (d, 3, NCH_3), 6.00 (broad s, 1, NH); mass spectrum (70 eV) *m/e* 77 (M+).

The material, if totally free of HF, could be stored at least several months in glassware; however, it was best stored in polyethylene containers. For most of our work the crude material was placed under high vacuum but not distilled.

Anal. Calcd for C_2H_4NOF: C, 31.17; H, 5.23; N, 18.18; F, 24.65. Found: C, 31.24; H, 5.27; N, 18.17; F, 24.41.

Bis(di-*n*-butylamino) Disulfide (5a). To a rapidly stirred and cooled to 0 °C two-phase system composed of water (1800 mL), hexane (750 mL), di-*n*-butylamine (516.0 g, 4.00 mol, 1.00 equiv), and sodium hydroxide (211.6 g, 5.29 mol, 1.32 equiv) was added over 10 min a solution of sulfur monochloride (310.0 g, 2.30 mol, 1.14 equiv) in hexane (500 mL) which was protected from moisture until the addition. The cooling bath was removed and the mixture stirred an additional 45 min. The water layer (pH ~11) was washed with hexane (500 mL) after which the combined organics were washed with 1 N HCl then water until a pH of 6–7 had been reached. Drying over Na_2SO_4 followed by concentration at <40 °C gave 592 g (92.5%) of light-yellow liquid **5a:** NMR (CCl_3D) δ 0.80–2.00 (m, 28), 2.72 (t, 8, NCH_2); mass spectrum (70 eV) *m/e* 320 (M^+).

Anal. Calcd for $C_{16}H_{36}N_2S_2$: C, 59.94; H, 11.32; N, 8.74; S, 20.00. Found: C, 59.79; H, 11.08; N, 8.62; S, 20.19.

In a manner similar to that for the preparation of **5a,** compounds **5b–g** were synthesized.

Di-*n*-butylaminosulfenyl Chloride (6a). To bis(di-*n*-butylamino) disulfide (**5a,** 40.0 g, 125 mmol, 1 equiv) cooled to −78 °C under a nitrogen atmosphere was added all at once sulfuryl chloride (25.1 g, 188 mmol, 1.5 equiv). The flask was transferred to an ice water bath and allowed to stir at 0–5 °C for 2–3 h after which it was placed under aspirator vacuum followed by high vacuum to give 58.1 g (99%) of foul smelling yellow liquid **6a:** NMR (CCl_3D) δ 0.80–2.00 (m, 14), 3.25 (t, 4, NCH_2). Batch distillation of a sample of the crude product was unsuccessful. The material could be flash distilled (bp 70 °C at 0.4 mm); however, the recovery of product was low.

In a manner similar to that for the preparation of **6a,** compounds **6b–g** were synthesized.

***N*-(di-*n*-butylaminosulfenyl)-*N*-methylcarbamoyl Fluoride (7a) and Methyl Ester 9x.** To a solution of *N*-methylcarbamoyl fluoride (10.0 g, 130 mmol, 1.0 equiv) and di-*n*-butylaminosulfenyl chloride (25.4 g, 130 mmol, 1 equiv) in pyridine (80 mL) at room temperature under a nitrogen atmosphere was added dropwise over 30 min 1,4-diazabicyclo[2.2.2]octane (21.8 g, 195 mmol, 1.5 equiv). Salts began forming as soon as the base was added. The resulting mixture was stirred 4 h beyond the addition time, after which it was poured into a cold (10 °C) mixture of water (160 mL) and hexane (160 mL). The layers were separated and the water (pH ~11) back extracted with cold hexane (80 mL). The combined organics were then washed twice with 1 N HCl (80 mL) and twice with water (80 mL), dried over Na_2SO_4, and concentrated on a rotary evaporator followed by high vacuum to give 22.7 g (74%) of yellow liquid **7a** which had an 82% purity by GLC area percent on 10% OV 17 on Chromosorb W. Distillation of this material gave 18.9 g (61%) of high purity colorless **7a:** bp 84–85 °C (0.20–0.33 mm); $n^{20}D$ 1.4578; IR (thin film) 1780 cm^{-1} (C=O); NMR (CCl_3D) δ 0.80–2.00 (m, 14), 3.15 (bt, 4, NCH_2), 3.30 (s, 3, $CONCH_3$).

Anal. Calcd for $C_{10}H_{21}N_2OSF$: C, 50.82; H, 8.96; N, 11.85. Found: C, 51.15; H, 8.84; N, 11.99.

The material could be converted rapidly (1 h) to the corresponding methyl ester (**9x**) in methanol with triethylamine at room temperature. Compound **9x** was also prepared from methyl *N*-methylcarbamate and di-*n*-butylaminosulfenyl chloride. For **9x:** IR (thin film) 1740 cm^{-1} (C=O); NMR (CCl_3D) δ 0.80–2.00 (m, 14), 3.10 (t, 4, NCH_2), 3.30 (s, 3, $CONCH_3$), 3.70 (s, 3, CH_3); mass spectrum (70 eV) *m/e* 248 (M^+).

In a manner similar to the preparation of **7a,** compounds **7b–g** were prepared (see Table I).

2,3-Dihydro-2,2-dimethyl-7-benzofuranyl *N*-(Di-*n*-butylaminosulfenyl)-*N*-methylcarbamate (9l) (Run No. 3 in Table II). To a vigorously stirred two-phase mixture of 2,3-dihydro-7-hydroxy-2,2-dimethylbenzofuran (1.39 g, 8.47 mmol, 1.0 equiv), sodium hydroxide (0.51 g, 12.71 mmol, 1.5 equiv), tetrabutylammonium hydrogen sulfate (0.29 g, 0.85 mmol, 1.0 equiv), toluene (5 mL), and water (10 mL) was added over 15 min at room temperature a mixture of *N*-(di-*n*-butylaminosulfenyl)-*N*-methylcarbamoyl fluoride (2.00 g, 8.47 mmol, 1.0 equiv) in toluene (5 mL). Analysis of the reaction mixture by GLC after an additional 2 h of stirring indicated none of the fluoride was remaining so the mixture was poured into a separatory funnel containing toluene (10 mL) and water (10 mL). The layers were separated after which the water layer (pH ~11) was washed with toluene (10 mL). The combined organics were washed twice with water (pH of last wash ~6), dried over Na_2SO_4, and concentrated to give 2.75 g (85%) of light-yellow oil which was chromatographed on silica gel to give 2.23 g (69%) of colorless oily **9l:** $n^{20}D$ 1.5116; IR (thin film) 1740 cm^{-1} (C=O); NMR (CCl_3D) δ 0.80–2.00 (m, 14), 1.50 (s, 6, $C[CH_3]_2$), 3.00 (s, 2, ring CH_2), 3.20 (t, 4, NCH_2), 3.40 (s, 3, $CONCH_3$), 6.60–7.10 (m, 3); mass spectrum (70 eV) *m/e* 380 (M^+).

Anal. Calcd for $C_{20}H_{32}N_2O_3S$: C, 63.12; H, 8.48; N, 7.36. Found C, 63.10; H, 8.48; N, 7.05.

Utilizing reactions similar to **9l** above, compounds **9m–w** were prepared (see Table III).

Bis(di-*n*-butylamino) Sulfide (10). To a stirred solution of di-*n*-butylaminosulfenyl chloride (**6a**) (8.00 g, 41 mmol, 1.0 equiv) in diethyl ether (75 mL) under a nitrogen atmosphere at 10 °C was added over 30 min a solution of di-*n*-butylamine (12.14 g, 94 mmol, 2.3 equiv) in ether (25 mL). The resultant mixture was stirred an additional hour, filtered, and concentrated at <40 °C to give 7.83 g (84%) of yellow oily **10:** NMR (CCl_3D) δ 0.80–2.00 (m, 28), 3.00 (t, 8, NCH_2); mass spectrum (70 eV) *m/e* 288 (M^+).

Anal. Calcd for $C_{16}H_{36}N_2S$: C, 66.60; H, 12.58; N, 9.71; S, 11.11. Found: C, 66.85; H, 12.39; N, 9.91; S, 11.36.

Bis(di-*n*-butylamino) Trisulfide (11). To a solution of bis(di-*n*-butylamino) disulfide (**5a**) (16.00 g, 0.05 mol, 1.0 equiv) in hexane (100 mL) at 0 °C under a nitrogen atmosphere was added sulfuryl chloride (6.70 g, 0.05 mol, 1.0 equiv) dropwise over 15 min. The mixture was stirred for 30 min at 0 °C then used below as "solution A".

To a vigorously stirred mixture of hexane (50 mL), water (75 mL), sodium sulfide nonahydrate (14.40 g, 0.06 mol, 1.2 equiv), and sodium hydroxide (1.60 g, 0.04 mol, 0.8 equiv) at 0 °C under a nitrogen at-

mosphere was added dropwise over 30 min "solution A". After the feed, the cooling bath was removed and the mixture was stirred for 1 h. At the end of the reaction period the layers were separated (pH of water ~7) after which the organic layer was washed once with water (50 mL), dried over Na_2SO_4, and concentrated to give 14.75 g (70%) of yellow liquid **11**: NMR (CCl_3D) δ 0.80–2.00 (m, 28), 2.95 (t, 8, NCH_2).

Anal. Calcd for $C_{16}H_{36}N_2S_3$: C, 54.59; H, 10.29; N, 7.94; S, 27.27. Found: C, 53.78; H, 9.52; N, 7.70; S, 28.35.

Acknowledgment. The author wishes to acknowledge FMC for permission to publish this material and the FMC Princeton Analytical Group for analyses and spectra.

Registry No.—**3**, 51229-17-5; **4a**, 111-92-2; **4b**, 110-91-8; **4c**, 142-84-7; **4d**, 103-67-3; **4e**, 14321-27-8; **4f**, 110-89-4; **4g**, 109-89-7; **5a**, 67271-09-4; **5b**, 103-34-4; **5c**, 38126-23-7; **5d**, 62158-05-8; **5e**, 67271-10-7; **5f**, 10220-20-9; **5g**, 15575-30-1; **6a**, 6541-82-8; **6b**, 2958-89-6; **6c**, 34695-15-3; **6d**, 53370-27-7; **6e**, 55285-27-3; **6f**, 16005-90-6; **6g**, 14274-26-1; **9x**, 67271-11-8; **10**, 67271-12-9; **11**, 67271-13-0; HF, 7664-39-3; S_2Cl_2, 10025-67-9; SO_2Cl_2, 7791-25-5; methyl isocyanate, 624-83-9; methyl *N*-methylcarbamate, 6642-30-4.

References and Notes

(1) R. J. Kuhr and H. W. Dorough, "Carbamate Insecticides: Chemistry, Biochemistry and Toxicology", Chemical Rubber Publishing Company, Cleveland, Ohio, 1976.
(2) L. Black and T. Fukuto, German Patent 2 433 680 (January 1975).
(3) For example, see: (a) E. Kuehle and I. Hammann, German Patent 2 106 300 (August 1972); (b) E. Kuehle, E. Klauke, W. Behren, P. Frahberger, and E. Paul, German Patent 2 041 322 (February 1972); (c) E. Kuehle, E. Klauke, B. Hamburger, and H. Scheinpflug, German Patent 2 243 626 (March 1974).
(4) Shortly after completion of our investigation, Belgian patent applications 843 415 and 843 416 were published which parallel portions of this work.
(5) It is interesting to note that we were unable to carry out the corresponding carbamoyl chloride chemistry. In our hands, *N*-methylcarbamoyl chloride decomposed upon the slightest provocation.
(6) (a) J. Dockx, *Synthesis*, 441 (1973); (b) E. Dehmlow, *Angew. Chem., Int. Ed. Engl.*, **13**, 170 (1974).
(7) (a) D. Armitage and C. Tso, *J. Chem. Soc., Chem. Commun.*, 1413 (1971); (b) M. Raban, D. Noyd, and L. Bermann, *J. Org. Chem.*, **40**, 752 (1975).

Notes

Heterocycles in Organic Synthesis. 11.[1] Reactions of Heteroaromatic *N*-Oxides with Pyridine and Diazoles

Alan R. Katritzky,* George H. Millet, Rehan bt. H. M. Noor, and Frank S. Yates

School of Chemical Sciences, University of East Anglia, Norwich, NR4 7TJ, England

Received February 24, 1978

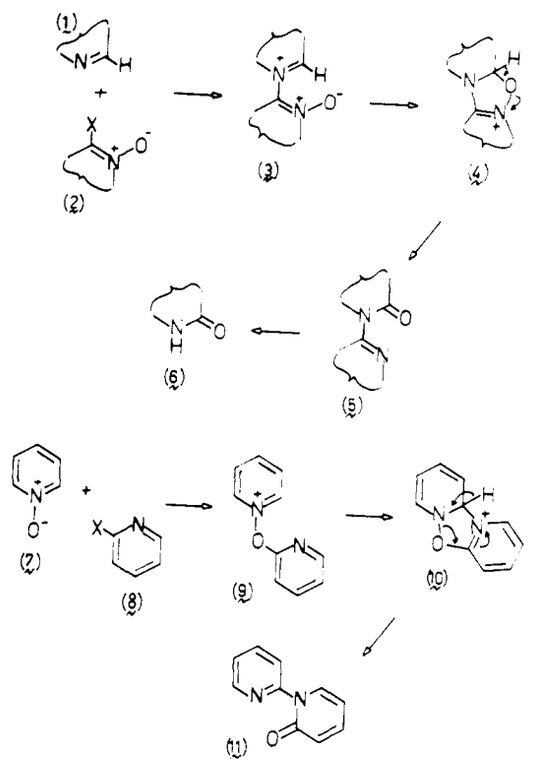
The aim of the present work was to develop a synthetic sequence for the oxidation of heterocyclic nitrogen compounds **1** to the corresponding α-oxo derivatives **6**. Previous methods are inconvenient and/or not general. Direct conversion of pyridine to 2-pyridone requires extreme conditions[2] or conversion to *N*-oxide.[3] Benzimidazole is attacked by most oxidizing agents at the benzene ring,[4] although imidazole itself slowly gives 2-imidazolone with singlet oxygen.[5] Pyrazole is resistant to oxidation.[6]

The reported[7] conversion of pyridine 1-oxide (**7**) to the pyridylpyridone **11** by condensation with a suitably 2-substituted pyridine **8** and intermediates **9** and **10**, led us to consider the reaction sequence **1** + **2** → **6** via intermediates **3**, **4**, and **5** (Scheme I).

Experiments with 2-Chloro-5-nitropyridine 1-Oxide (12) as Compound 2. This oxide possesses a reactive chlorine atom and readily formed substitution products with aniline (**13**, R = NHPh) and piperidine [**13**, R = $N(CH_2)_5$] (Scheme II). Pyrazole also gave the expected product **14**, but this was stable to heat and sublimed unchanged: with acetic anhydride an acetoxy group was introduced into the 6 position of the pyridine ring to give **15** by a known[8] reaction, leaving the pyrazole ring unaffected.

Imidazole readily formed **16**, which was again stable to heat and also sublimed unchanged. It was converted by acetic anhydride to **17**, which was also obtained directly from **12** by Ac_2O treatment. The structure of **17** was confirmed by hydrolysis to the known[9] 1-hydroxy-2-pyridone **18**. Methyl tosylate with **16** gave **19** (X = OTs), whereas **19** (X = Cl) was

Scheme I



obtained by direct reaction of **12** and methylimidazole. The salts **19** (X = Cl or OTs) gave an inseparable mixture after prolonged heating in the presence of a hindered base.

Attempted reaction of **12** with pyridine did not succeed. With pyridine 1-oxide, the product was **20** (Scheme II), apparently formed by the reaction of **12** with itself followed by reduction and hydrolysis. This structure of **20** was based on analytical, mass spectral, IR, and NMR data; attempts to synthesize **20** by reaction of 2-chloro-5-nitropyridine with **18**, or the sodium salt of **18**, failed.

0022-3263/78/1943-3957$01.00/0