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The Preparation of 2,2-Bis(trifluoromethyl)-1,3-heterocycles from 2,2,4,4-Tetrakis(trifluoromethyl)-1,3-dithietane

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Synopsis. 2,2-Bis(trifluoromethyl)-1,3-heterocyclic compounds, **3**, **4**, **6**, **7**, and **8**, were prepared by the reaction of 2,2,4,4-tetrakis(trifluoromethyl)-1,3-dithietane (**1**) with bifunctional compounds such as amino alcohols, *o*-aminophenol, *o*-aminothiophenol and *o*-phenylenediamine.

In earlier communications we reported on several nucleophilic reactions of 2,2,4,4-tetrakis(trifluoromethyl)-1,3-dithietane (**1**), which can be obtained from hexafluoropropene and sulfur. Alkyl- and arylamines reacted with **1** to give *N*-substituted hexafluoroisopropylideneimines,[1)] while neither alcohol nor thiol reacted without the catalytic fluoride ion.[2)] In this paper, we wish to report on the reactions of aminoalcohols, *o*-aminophenol, *o*-aminothiophenol, or *o*-phenylenediamine with **1**. In these cases, we found that both functional groups in a molecule, an amino and a hydroxyl for example, reacted with the positive carbon atom of **1** to afford 2,2-bis(trifluoromethyl)-1,3-heterocyclic compounds.

2-Aminoethanol and **1** reacted at room temperature in methylene chloride with a liberation of sulfur, which is usual in the reactions between amines and **1**.[1)] The structure of the reaction product, 2,2-bis(trifluoromethyl)oxazolidine (**3**), was elucidated by means of its IR and NMR spectra.

In the IR spectrum, the presence of N–H and C–O–C was shown by the bands at 3370 and 1265 cm^{-1} respectively, but no O–H band was observed. In the ^{19}F NMR spectrum, only one singlet signal, at −2.1 ppm from external CF_3CO_2H in CCl_4, appeared. This is in contrast to the spectra of the hexafluoroisopropylidene imines, which have two ^{19}F signals corresponding to *syn* and *anti* CF_3. 3-Amino-1-propanol gave a similar compound, **4**.

Anilines with a functional group in the *ortho*-position reacted with **1** in dimethylformamide. *o*-Aminophenol, *o*-aminothiophenol, and *o*-phenylenediamine gave 2,2-bis(trifluoromethyl)benzoxazolidine (**6**), -benzothiazolidine (**7**), and -benzimidazolidine (**8**) respectively. The structures of these compounds were also elucidated by the IR, NMR, and mass spectra. The presence of the N–H group was proved by the band at 3200—3300 cm^{-1} in their IR spectra. In the ^{19}F NMR spectra, there was only one singlet signal each at about −3 ppm from external CF_3CO_2H in CCl_4. In the mass spectrum of **8**, for example, the strong molecular ion (M^+ 256) was observed, together with the appropriate fragment peaks,[3)] such as *m/e* 187 ($C_8H_6F_3N_2$), 167 ($C_8H_5F_2N_2$), 117 ($C_7H_5N_2$), 90 (C_6H_4N), and 69 (CF_3). When **6** was treated with methyl iodide, the *N*-methyl compound was obtained as expected.

Since alkyl- or arylamines are known to give hexafluoroisopropylideneimines by reacting with **1**,[1)] the ring formations mentioned above were estimated to proceed by the addition reaction of ZH across the neighboring >C=N double bond of **2** or **5**.

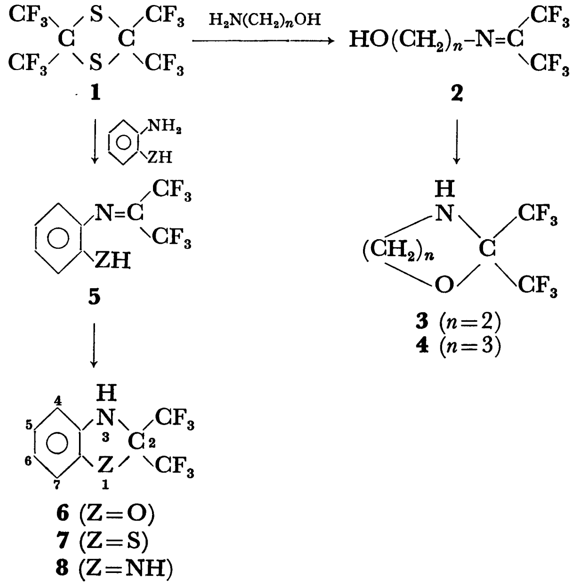

Table 1. Preparation and physical properties of compounds

Compound	Yield (%)	Bp (°C/mmHg)	IR (cm^{-1}) N–H	IR (cm^{-1}) C–O–C	NMR ^{19}F$^{a)}$ CF_3	NMR ^{1}H (τ) NH	F (%) Found	F (%) Calcd
3	23	48—51/760	3370	1265	−2.10	4.80	54.8	54.5
4	31	52—54/760	3440	1272	−2.30	4.75	50.4	51.1
6	61	91—93/21	3220	1265	−3.20	4.70	43.7	44.3
5-Me-**6**	54	97—98/25	3240	1260	−3.20	5.30	42.5	42.1
7	48	103—105/25	3370	——	−3.15	5.20	41.9	41.6
8	42	113—114/28	3360	——	−3.80	5.00	44.8	44.5
5-F-**8**	20	60—63/3	3385	——	−3.10	5.10	48.0	48.5

a) Given δ in ppm from ext. CF_3CO_2H in CCl_4.

Experimental

2,2-Bis(trifluoromethyl)oxazolidine (3). To a stirred mixture of 2-aminoethanol (5.0 g, 0.08 mol) and methylene chloride (30 ml), **1** (18.2 g, 0.05 mol) was added, drop by drop, at room temperature. The stirring was continued for 1 hr at that temperature, and then the liberated sulfur was removed by filtration. The filtrate was distilled to give **3** (n=2) (3.8 g); bp 48—51 °C.

2,2-Bis(trifluoromethyl)tetrahydro-1,3-oxazine (4). This compound was prepared by using 3-amino-1-propanol (6.0 g) instead of the 2-aminoethanol used in the preceding reaction.

2,2-Bis(trifluoromethyl)benzoxazolidine (6). A mixture of **1** (7.30 g, 0.02 mol), 2-aminophenol (2.18 g, 0.02 mol). and dimethylformamide (30 ml) was stirred for 4 hr at room temperature, and then filtered. The filtrate was poured into water, and the oily material thus separated was extracted with ethyl ether. The extract was dried over magnesium sulfate, and the solvent was removed. A fraction with a bp of 91—93 °C/21 mmHg was collected to give **6** (3.15 g, 61%).

5-Methyl-substituted **6** was prepared in a similar manner, using 4-methyl-2-aminophenol.

N-*Methyl Derivative of* ***6***. Into a mixture of **6** (2.57 g, 0.01 mol), potassium hydroxide (0.56 g, 0.01 mol) and ethyl alcohol (15 ml), methyl iodide (1.44 g, 0.01 mol) was added, drop by drop, after which the whole was stirred for 10 hr at room temperature. The reaction mixture was poured into water, and the oily material was extracted with ethyl ether. The extract was then dried over magnesium sulfate, and the solvent was removed. The vaccum distillation of the residue gave an *N*-methyl derivative (bp 109—110 °C/29 mmHg), in a yield of 63%. Found: F, 42.5%. Calcd for $C_{10}H_7F_6NO$: F, 42.1%.

2,2-Bis(trifluoromethyl)benzothiazolidine (7). A mixture of **1** (14.6 g, 0.04 mol), 2-aminothiophenol (6.00 g, 0.04 mol), and dimethylformamide (30 ml) was stirred for 4 hr at room temperature. The usual work-up process gave a product (**7**) (6.5 g).

2,2-Bis(trifluoromethyl)benzimidazolidine (8). *o*-Phenylenediamine (4.32 g, 0.04 mol), **1** (14.6 g, 0.04 mol), and dimethylformamide (30 ml) were used as in the preceding reaction, and then worked up similarly. Subsequent distillation gave **8** (4.3 g). 5-Fluoro-**8** was prepared similarly by using 4-fluoro-*o*-phenylenediamine.

References

1) N. Ishikawa and T. Kitazume, This Bulletin, **46**, 3260 (1973).

2) T. Kitazume and N. Ishikawa, *ibid.*, **46**, 3285 (1973).

3) Q. N. Porter and J. Baldas, "Mass Spectrometry of Heterocyclic Compounds," Wiley-Interscience (1971), Chap. 11—14.