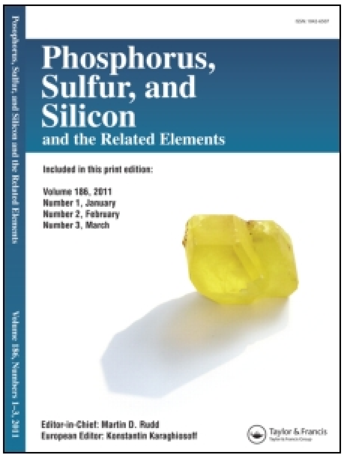

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STUDIES ON FLUORINE CONTAINING HETEROCYCLIC COMPOUNDS. 4. REACTIONS OF 3-NITRO-4-CHLOROBENZOTRIFLUORIDE AND 3,5-DINITRO-4-CHLOROBENZOTRIFLUORIDE WITH FIVE-MEMBERED HETEROCYCLES

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STUDIES ON FLUORINE CONTAINING HETEROCYCLIC COMPOUNDS.

4. REACTIONS OF 3-NITRO-4-CHLOROBENZOTRIFLUORIDE AND 3,5-DINITRO-4-CHLOROBENZOTRIFLUORIDE WITH FIVE-MEMBERED HETEROCYCLES

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The reactions of 3-nitro-4-chlorobenzotrifluoride (**1a**) and 3,5-dinitro-4-chlorobenzotrifluoride (**1b**) with heterocycles (**2–5**) are described. Six *S*-linked and *N*-substituted heterocycles (**6, 9–11, 13**), such as 2-(2-nitro-4-trifluoromethylphenylthio) benzothiazole (**9a**), were prepared from the reactions of **1a** with benzotriazole (**2**), 2-mercaptobenzothiazole (**5a**) and 2-mercaptobenzoxazole (**5b**) and from the reactions of **1b** with **2**, 1,2,4-triazole (**3**) and **5a** in DMF respectively. **1a** reacted with 2-mercaptothiazoline (**4**) to give desired product **7** and bis(2-nitro-4-trifluoromethylphenyl) thioether (**8**). 3-(2-Benzoxazolyl)-2-benzoazolinethione (**15**) was obtained from the reaction of **1b** with **5b**. The spectral data and elemental analyses were fully in accord with the proposed structures, and the possible mechanisms for these compounds and other by-products were discussed.

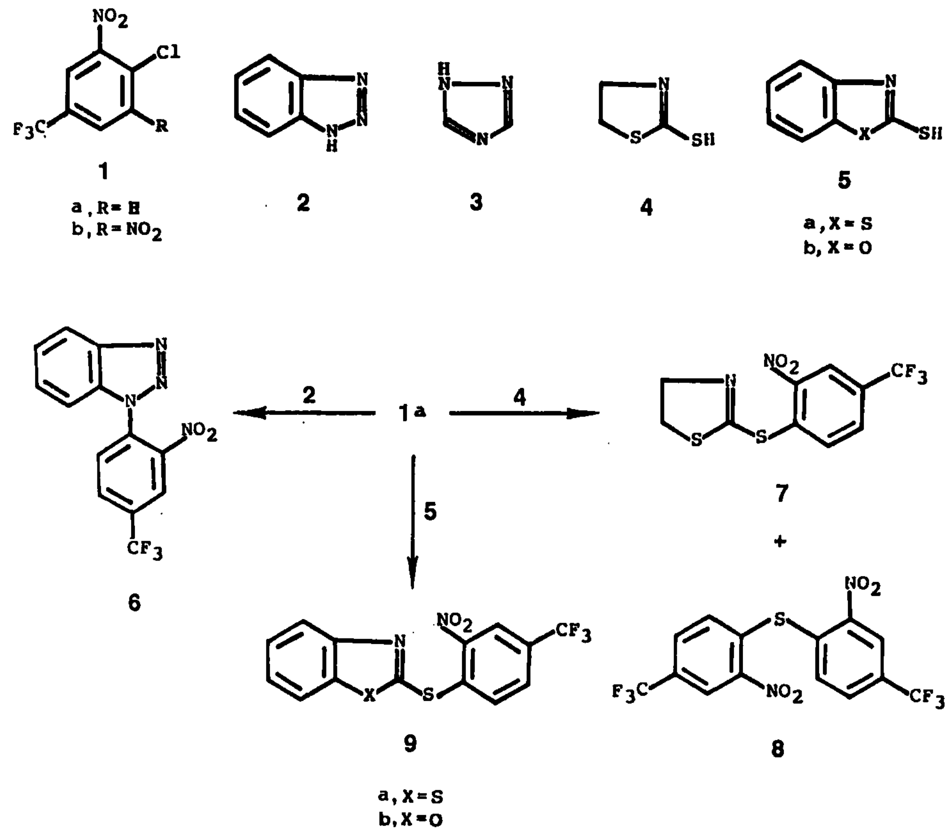
Key words: Heterocycles; organo-fluorine; benzotriazole; thiazole; displacement; *S*-linked compounds.

INTRODUCTION

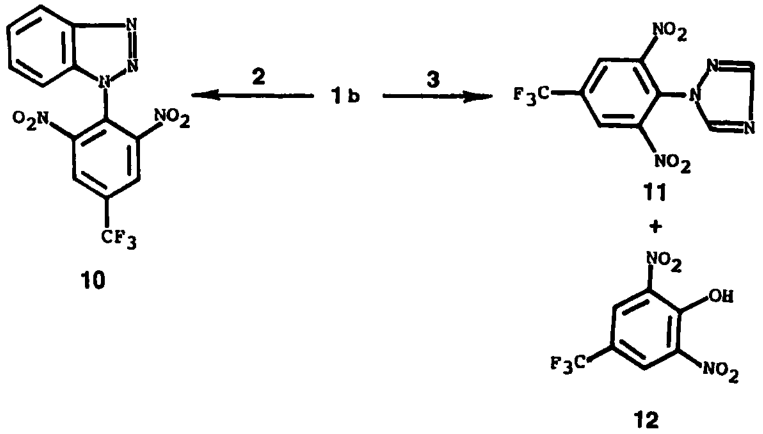
Five-membered heterocycles containing nitrogen and sulfur are often used as fungicides,[1] nematocides,[2] miticides[3] and herbicides.[4] They have received considerable attention in the last two decades and the results have been reviewed by Metzger.[5] Since organofluorine compounds provide great oxidative and thermal stabilities, the introduction of fluorine-containing groups to heterocycles is attractive.[6] Therefore, it seems useful to keep on our efforts in this area of research.

RESULTS AND DISCUSSION

Heterocycles **2–5** were employed to react with **1**. The reaction of 3-nitro-4-chlorobenzotrifluoride (**1a**) with benzotriazole (**2**) in DMF gave *N*-substituted benzotriazole (**6**) in a good yield (**Scheme 1**). The reaction of **1a** with an equimolar amount of 2-mercaptothiazoline (**4**) in DMF (80°C, 20 hrs) gave only 6.2% yield of *S*-linked thiazoline **7**, isolated by silica chromatography techniques. Instead, the diphenyl thioether derivative **8** was the main product,[7] isolated in 56% yield. Both 2-mercaptobenzothiazole (**5a**) and 2-mercaptobenzoxazole (**5b**) reacted analogously with **1a** (1.5–3 hrs) to generate *S*-substituted benzothiazole **9a** and *S*-linked benzoxazole **9b** in 95% and 89% yields respectively.



Scheme 1

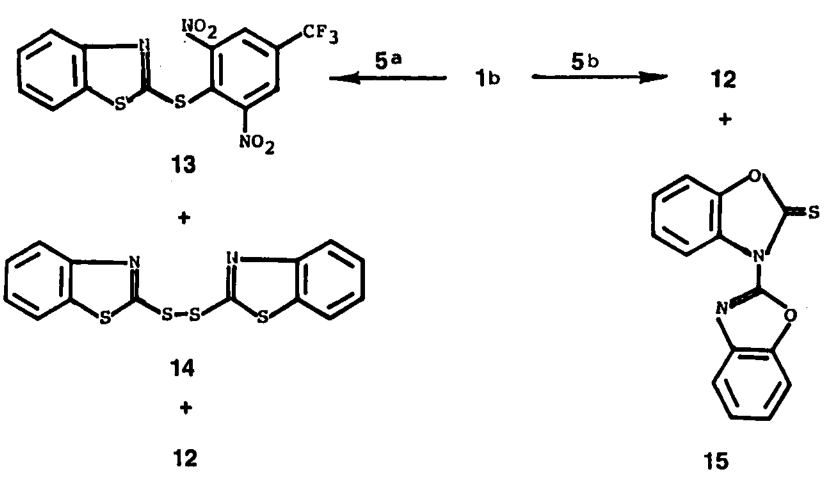


Scheme 2

The reactions of 3-nitro-4-chlorobenzotrifluoride (**1b**) with **2**, 1,2,4-triazole (**3**) (**Scheme 2**) were carried out in a system similar to **Scheme 1** in DMF solution with triethylamine as a base. When it was treated with **2**, **10** was obtained. Similarly, **1b** was treated with **3** in DMF to give 1-substituted 1,2,4-triazole **11**, and the phenol derivative **12**, in 57.8% and 40% yields respectively. The latter, which was often obtained as an oil and was difficult to recrystallize, resulted from **1b** and water added in aftertreatment.[8]

In a chlorine displacement process, compound **1b** underwent reaction with **5a** in DMF solution to give the desired product **13** and an unexpected product **14** plus a small amount of **12**. The reaction is described in **Scheme 3** and the results are summarized in **Table I**. In view of the unusual generation of **14** a further investigation was required. Oxygen in air, as oxidizing agent could lead to formation of **15**. This, in fact, had been shown to be true. The reaction, which was repeated under nitrogen atmosphere, did not give **14** at all. Instead, 78% yield of **13** was isolated, together with **12** being detected by TLC. An attempt to synthesize the *S*-substituted benzoxazole using compounds **1b** and **5b** as precursors proved unsuccessful. The reaction which did not proceed fully at R.T. for 34 hrs afforded mainly **12** (76%) and a 12.5% yield of the substituted benzoazolinethione **15**. The assigned structure of **15** seems to be reasonable on the basis of elemental analyses, NMR evidences and its mass spectrum which shows M^+ at *m/z* 268 (100%). The infrared spectrum which shows a band at 1620 cm^{-1} (C═N), a strong band at 1580 (or 1470) (N—C═S, thioureide), and a band at 1325 (or 1275) (C═S, st.) agrees with the assignment in the disputative report.[9]

Reaction of **1a** and **4** is thought to occur initially to yield **7**, followed by its attack towards **1a** producing an intermediate **16**,[8a,10] which may decompose by loss of chlorine leading to the isolated product **8**. In this regard, **7** was allowed to react with **1a** in DMF medium with triethylamine as base. When heated at 80°C for 10 hrs, the solution afforded a little amount of **8** as monitored by TLC. The conversion



Scheme 3

TABLE I
Reaction results of **1** with heterocycles **2–5** in DMF[a]

Substrates	Temperature (°C)	Time (hrs)	Product(s) (Yield (%))[b]
1a + **2**	100	17	**6** (87)
1a + **4**	80	20	**7** + **8** (6.2) (56)
1a + **5a**	70	1.5	**9a** (95)
1a + **5b**	R.T.	3	**9b** (89)
1b + **2**	R.T.	3.5	**10** (78.5)
1b + **3**	R.T.	2.5	**11** + **12** (57.8) (40)
1b + **5a**	R.T.	1.5	**12** + **13** + **14** (20) (52) (10.2)
1b + **5a** (N_2)	R.T.	1.5	**12**[c] + **13** – (78)
1b + **5b**	R.T.	34	**12** + **15**[d] (76) (12.5)

[a] Reactions carried out with equimolar amounts; Et$_3$N was used as base and water added in aftertreatment.

[b] Based on **1a** or **1b**.

[c] Detected by TLC, not isolated.

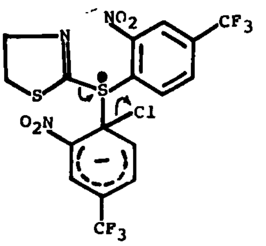
[d] 10% of **5b** recovered.

of **5b** into **15** can be explained in terms of the mechanism outlined in **Scheme 4**. The proposed mechanism includes the generation of **17** and **18**, which, however would not be isolated. Suggestion of **18** as an intermediate is on the fact[9] that it can readily undergo rearrangement to afford **15**. In order to gain some insight into the formation of **18**, the reaction of **5b** with triethylamine or sodium hydride in DMF was carried out (80°C, 10 hrs), emphasis being placed on whether **15** can be obtained in the absence of **1b**, and the experiment showed that in the formation of **15** compound **1b** must be present.

EXPERIMENTAL

Melting points were taken in open capillaries and are uncorrected. Infrared spectra were measured on Shimadzu IR-440 spectrophotometer (KCl pellets). ^{1}H and ^{19}F NMR spectra were performed on a Varian EM-360L and FX-90Q spectrometers using tetramethylsilicane (TMS) and trifluoroacetic acid (TFA) as external standards for ^{1}H and ^{19}F respectively. Mass spectral data were recorded on a Finnigan-402 spectrometer. Chemical shifts and wave numbers are reported in ppm and cm^{-1} respectively.

1-(2'-Nitro-4'-trifluoromethylphenyl)benzotriazole (**6**). To a stirred solution of 10 ml DMF containing 1.19 g (10 mmol) of benzotriazole (**2**) and 1.1 g (11 mmol) of triethylamine, was added 2.25 g (10 mmol) of **1a** dissolved in 10 ml DMF. The mixture was continuously stirred at 100°C for 17 hrs. The white solid was collected by filtration, washed with water and air-dried at R.T. Recrystallization from alcohol and alcohol-acetone (1:1) afforded 2.68 g (87% yield) of **6** m.p. 127–128°C. IR:1140: (s, C—F), 1320 (s, NO$_2$), 1550 (s, N=N), 3050 (w, ArH). NMR: δ ^{1}H (CDCl$_3$): 7.95 (3H, m, ArH), 8.45 (3H,



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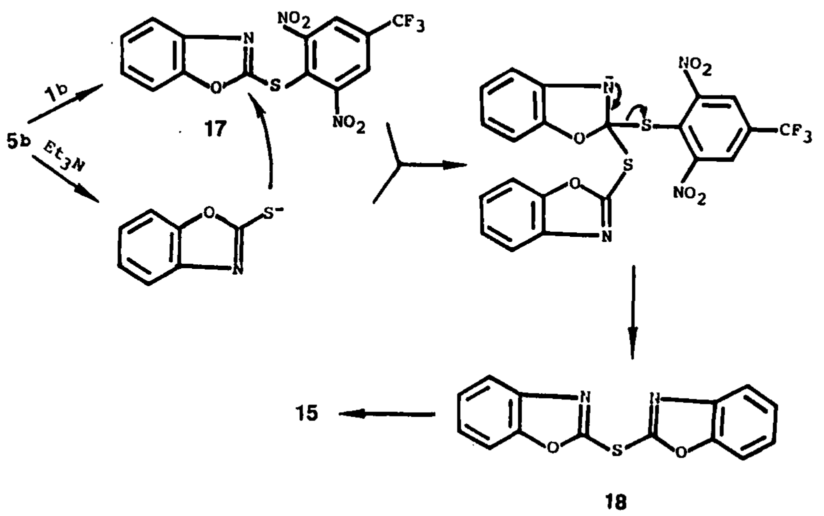

Scheme 4

m, ArH), 8.85 (1H, s, ArH, *ortho*- to NO$_2$). δ ^{19}F(CDCl$_3$): −14.3. MS: 308 (M$^+$), 309 (M$^+$ + 1). *Anal.* Calcd for C$_{13}$H$_7$N$_4$F$_3$O$_2$: C, 50.65; H, 2.27; N, 18.18; F, 18.51; Found: C, 50.10; H, 2.03; N, 18.18; F, 18.68%.

2-(2′-Nitro-4′-trifluoromethylphenylthio)thiazoline (**7**) *and Bis(2-nitro-4-trifluoromethylphenyl) thioether* (**8**). 1.18 g (5.3 mmol) of **1a** was added to a stirred solution of 2-mercaptothiazoline (0.6 g, 5.0 mmol) and triethylamine (0.51 g, 5.0 mmol) dissolved in 15 ml DMF. The reaction mixture was stirred at 80°C for 20 hrs. It was then washed with water and extracted with ethyl acetate. The organic layer was dried (sodium sulfate), filtered and the solvent was removed under reduced pressure yielding a yellow oil. It was left overnight to give a yellow crystal of **8** (0.6 g, 56%). The mother liquor was isolated chromatographically on silica gel with toluene as eluant to afford **7** (0.1 g, 6.2%). (**7**): m.p. 55.0–55.5°C. IR: 1095 (m, C—S), 1150 (s, C—F), 1330 (s, NO$_2$), 1530 (m, C=N). NMR: δ ^{1}H(CCl$_4$): 3.7 (2H, t, J = 7.8 Hz, SCH$_2$), 4.56 (2H, t, J = 7.8 Hz, NCH$_2$), 8.15 (1H, d, J = 9 Hz, ArH, *ortho*- to S), 8.63 (2H, m, ArH, *ortho*- to CF$_3$). δ ^{19}F(CCl$_4$): −14.5. MS: 307 (M$^+$ − 1), 308 (M$^+$), 309 (M$^+$ + 1). *Anal.* Calcd for C$_{10}$H$_7$N$_2$F$_3$O$_2$S$_2$: C, 38.96; H, 2.27; N, 9.09; F, 18.51; S, 20.78; Found: C, 38.94; H, 2.15; N, 9.23; F, 18.96; S, 20.99%. (**8**): m.p. 140.5–141.0°C. IR: 1327 (s, C—F), 1541 (s, NO$_2$). NMR: δ ^{1}H(acetone-d$_6$): 7.53–7.60 (2H, d, ArH, *ortho*- to S), 7.70–7.85 (2H, d, ArH, *para*- to NO$_2$), 8.26 (2H, s, ArH, *ortho*- to NO$_2$); δ ^{19}F(acetone-d$_6$): −13.5. MS: 412 (M$^+$), 366 (M$^+$ − NO$_2$). *Anal.* Calcd for C$_{14}$H$_6$N$_2$F$_6$O$_4$S: C, 40.78; H, 1.46; N, 6.80; F, 27.67; S, 7.77; Found: C, 40.70; H, 1.24; N, 6.79; F, 28.97; S, 7.85%.

2-(2′-Nitro-4′-trifluoromethylphenylthio)benzothiazole (**9a**) *and 2-(2′-Nitro-4′-trifluoromethylphenylthio) benzoxazole* (**9b**). To a stirred solution of 10 ml DMF containing 1.1 g (11 mmol) of triethylamine and 1.67 g (10 mmol) of **5a** or 1.0 g (6.6 mmol) of **5b**, was added 2.25 g (10 mmol) of **1a**. The reaction mixture was continuously stirred at 70°C for 1.5 hrs (for **9a**) or at R.T. for 3 hrs (for **9b**). After the addition of water and extraction with ethyl acetate, the combined extracts were washed with a saturated solution of NaCl and were dried over sodium sulfate. Then, the solvent was evaporated and a yellow oil was obtained. The oil from **5a** solidified slowly to give 3.38 g of **9a** in 95% of yield, whereas the oil from **5b** was subjected to a chromatography (silica gel) with toluene-petroleum ether (6:4) as eluant to afford 2.0 g of **9b** in 89% of yield. Samples for analysis were recrystallized from ethanol. (**9a**): m.p. 118–119°C. IR: 1150 (s, C—F), 1310 (s, NO_2), 1520 (s, C=N), 1620 (w, C=C). NMR: δ ^{1}H(DMSO-d_6): 7.66, 8.16 (3H, m, 3H, m, ArH), 8.50 (1H, s, ArH, *ortho*- to NO_2). δ ^{19}F(DMSO-d_6): −15.0. MS: 310 (M^+ − NO_2), 356 (M^+), 357 (M^+ + 1). *Anal.* Calcd for $C_{14}H_7N_2F_3O_2S_2$: C, 47.19; H, 1.97; N, 7.87; F, 16.01; S, 17.98; Found: C, 47.29; H, 1.69; N, 7.87; F, 16.53; S, 18.13%. (**9b**): m.p. 76–77 C. IR: 1120 (s, C—F), 1320 (s, NO_2), 1340 (m, C—O), 1530 (m, C=N). NMR: δ ^{1}H(acetone-d_6): 7.20 (4H, m, ArH), 7.66 (2H, m, ArH, *meta*- and *para*- to NO_2), 8.33 (1H, s, ArH, *ortho*- to NO_2). δ ^{19}F(acetone-d_6): −13.0. MS; 294 (M^+ − NO_2), 340 (M^+). *Anal.* Calcd for $C_{14}H_7N_2F_3O_3S$: C, 49.41; H, 2.06; N, 8.24; F, 16.76; S, 9.41; Found: C, 49.36; H, 1.62; N, 8.10; F, 16.84; S, 9.79%.

1-(2',6'-Dinitro-4'-trifluoromethylphenyl)benzotriazole (**10**). The procedure was the same as in the preparation of **6** except **1b** was used instead of **1a** as substrate and except the reaction mixture was stirred at R.T. for 3.5 hrs instead of at 100°C for 17 hrs. 2.77 g (78.5%) of **10** was obtained. m.p. 216–216.5°C. IR: 1160 (s, C—F), 1310 (s, NO_2), 1550 (s, N=N), 1560 (s, C=C), 3100 (w, ArH). NMR: δ ^{1}H(acetone-d_6): 7.54 (s, 3H, ArH), 8.03 (s, 1H, ArH), 8.93 (s, 2H, ArH, *ortho*- to CF_3). δ ^{19}F(acetone-d_6): −13.0. MS: 353 (M^+), 354 (M^+ + 1). *Anal.* Calcd for $C_{13}H_6N_5F_3O_4$: C, 44.19; H, 1.70; N, 19.83; F, 16.15; Found: C, 44.17; H, 1.46; N, 20.07; F, 16.27%.

3,5-Dinitro-4-(1H-1,2,4-triazol-1-yl)benzotrifluoride (**11**). **1b** (2.70 g, 10 mmol) dissolved in 10 ml DMF was added to 1,2,4-triazole (0.69 g, 10 mmol) and an excess of triethylamine (in 10 ml DMF). The reaction mixture was stirred at R.T. for 2.5 hrs. It was washed with water, extracted with ethyl acetate and dried over sodium sulfate. Removal of solvent gave an oil which was isolated chromatographically (on silica gel) with ethyl acetate-petroleum ether (1:2) as eluant to give **11** (1.75 g, 57.8%) and subsequently with methanol as eluant to furnish **12** (1.0 g, 40%). (**11**): m.p. 153–154°C. IR: 1140 (s, C—F), 1320 (s, NO_2), 1550 (s, C=N), 3050 (w, ArH), 3120 (w, N=CH). NMR: δ ^{1}H(acetone-d_6): 7.83 (1H, s, Het-H), 8.60 (3H, d, ArH and Het-H). δ ^{19}F(acetone-d_6): −13.3. MS: 303 (M^+), 304 (M^+ + 1). *Anal.* Calcd for $C_9H_4N_5F_3O_4$: C, 35.64; H, 1.32; N, 23.10; F, 18.81; Found: C, 35.57; H, 1.03; N; 23.34; F, 19.20%.

2-(2',6'-Dinitro-4'-trifluoromethylphenylthio)benzothiazole (**13**). 1.67 g (10 mmol) of **5a** was dissolved in 10 ml DMF and added to a solution of 1.01 g (10 mmol) of triethylamine and 2.70 g (10 mmole) of **1b** dissolved in 10 ml DMF. The reaction mixture was stirred at R.T. for 1.5 hrs and then water and ethyl acetate were added to. 0.17 g of **14** (10.2% of yield), a suspension was filtered and washed with water. The extracts of ethyl acetate were dried (sodium sulfate) and condensed to give an oil, which was subjected to a chromatography (silica gel) with ethyl acetate-petroleum ether (1:3) and subsequent acetone as eluants to afford 2.1 g of **13** and 0.5 g of **12** in 52% and 20% of yields respectively. The repeated reaction under nitrogen atmosphere furnished 3.13 g of **13** (78%). (**13**): m.p. 162–163°C. IR: 1150 (s, C—F), 1305 (s, NO_2), 1545 (s, C=N), 3050 (w, ArH). NMR: δ ^{1}H(DMSO-d_6): 7.7, 8.0 (4H, dd, ArH), 8.8 (2H, s, ArH, *ortho*- to CF_3). δ ^{19}F(DMSO-d_6): −15.0. MS: 309 (M^+ − $2NO_2$), 355 (M^+ − NO_2), 401 (M^+). *Anal.* Calcd for $C_{14}H_6N_3F_3O_4S_2$: C, 41.90; H, 1.51; N, 10.47; F, 14.21; S, 15.96; Found: C, 42.00; H, 1.31; N, 10.52; F, 13.73; S, 16.48%. (**15**): m.p. 179–180°C. Lit.[11] m.p. 178°C.

3-(2-Benzoxazolyl)-2-benzoazolinethione (**15**). The procedure was the same as in the preparation of **13** except **5b** was used instead of **5a** as substrate and except the reaction mixture was stirred for 34 hrs instead of for 1.5 hrs. It was isolated by chromatography techniques to give **5b** (10% recovered), **15** (12.5% yield) (ethyl acetate-petroleum ether, 1:3, as eluant) and **12** (76% yield) (ethanol as eluant). **15** was recrystallized from ethanol. m.p. 170–171°C. IR: 1275 or 1325 (s, C=S), 1470 or 1580 (s, N—C=S), 1620 (s, C=N). NMR: δ ^{1}H(DMSO-d_6): 7.50 (4H, m, ArH), 7.90 (4H, ArH). MS: 268 (M^+), 269 (M^+ + 1). *Anal.* Calcd for $C_{14}H_{18}N_2O_2S$: C, 62.69; H, 2.99; N, 10.45; S, 11.94; Found: C, 62.62; H, 2.84; N, 10.36; S, 12.38%. Lit.[9] m.p. 160°C (ethyl acetate).

REFERENCES

1. (a) P. G. Hughes, J. P. Verge, Brit. Pat. 1 379 754/1975 cited in *Chem. Abstr.*, **83,** 10053x (1975).
   (b) S. Isamu, T. Shuntaro, Japan. Pat. 7 208 162/1970 cited in *Chem. Abstr.*, **74,** 3608t (1971).
2. M. E. Brokke, U.S. Pat. 3 697 536/1972 cited in *Chem. Abstr.*, **78,** 43464g (1973).

3. J. J. D'Amico, U.S. Pat. 3 002 977/1961 cited in *Chem. Abstr.*, **56,** 12905 (1962).
4. R. E. Diehl, R. V. Kendall, U.S. Pat. 4 240 822/1980 cited in *Chem. Abstr.*, **94,** 134160b (1981).
5. C. Roussel, M. Chanon and R. Barone, '*Thiazole and Its Derivatives,*' Ed. J. V. Metzger, 1979, part 2, p. 369.
6. (a) R. Filler, Y. Kobayashi, '*Biomedicinal Aspects of Fluorine Chemistry,*' Kodansha Ltd., Tokyo, 1982. (b) Huang Wei Yuan, *YouJi HauXue,* **1,** 16 (1985).
7. (a) P. G. Ruminski, L. A. Suba, J. J. D'Amico, *Phosphorus Sulfur,* **19,** 335 (1984). (b) Ching-Sung Chi and Mei-Jin Chen, unpublished work.
8. (a) Ching-Sung Chi, Mei-Jin Chen and Qi-Wen Wang, unpublished work. (b) R. L. Jacobs, *J. Org. Chem.*, **36,** 242 (1971).
9. J. J. D'Amico, R. H. Campbell, *J. Org. Chem.*, **32,** 3196 (1967).
10. M. J. Strauss, *Chem. Rev.*, **70,** 667 (1970).
11. TCI Catalog, **28,** 342 (1986).