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# Behavior of Trifluoroacetohydrazonoyl Bromide in Basic Media

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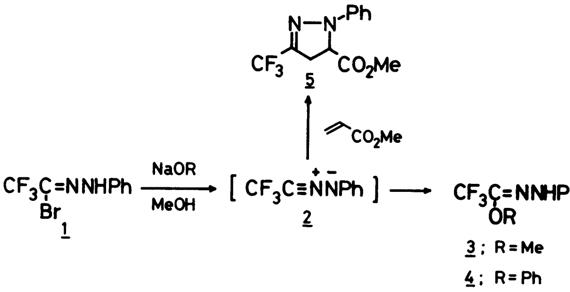
**Synopsis.** The bromide **1** was treated with sodium methoxide or phenoxide to give exclusively the corresponding substituted product. The predominant formation of the substituted products was also recognized with regard to various amines. However, the reaction with triethylamine proceeded more complicatedly to give the products *via* reduction process together with a trace amount of the dimer of *N*-phenyl-*C*-(trifluoromethyl)nitrilimine.

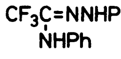
It is well known that hydrazonoyl halides, when treated with a base such as triethylamine or alkoxide, are converted into the corresponding nitrilimines which, in the absence of a reactive dipolarophile, result in the head-to-tail dimerizations to the corresponding tetrazines.[1] And only when treated with soft nucleophiles such as thiolates, hydrazonoyl halides are known to undergo the substitutions.[2–4] As a part of studies on the fluorinated nitrilimines,[5,6] we now wish to report the behavior of *N*-phenyltrifluoroacetohydrazonoyl bromide (**1**) toward bases such as alkoxides and amines.[7]

The bromide **1** was treated with sodium methoxide or phenoxide in methanol to give the corresponding substituted product **3** or **4** in 64 or 36% yield, respectively (Scheme 1). The reaction with sodium methoxide was next carried out in the presence of excess methyl acrylate to give a 56% yield of the 1,3-dipolar cycloadduct, 5-methoxycarbonyl-1-phenyl-3-trifluoromethyl-2-pyrazoline (**5**), as well as a 38% yield of **3**. These results indicate that the nitrilimine **2** is generated on treatment of **1** with sodium methoxide. Therefore, the substituted product **3** is thought to be formed entirely or partially *via* **2**. In this case, the usually observed dimerization of **2** was not detected at all.



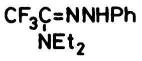
Scheme 1.

The predominant formation of the substituted products was also recognized with regard to amines. Aniline or diethylamine was allowed to react with **1** to afford *N*-phenyl- or *N*,*N*-diethyltrifluoroacetamide phenylhydrazone (**6** or **7**) in 49 or 89% yield, respectively. Similarly, the reaction with *N*-methylpyrrolidine proceeded smoothly to give the pyrrolidinium salt **8** in 79% yield. The IR spectrum of **8** shows the band at 1614 cm$^{-1}$ due to the C=N group, no absorption owing to the ammonium salt ($-\underset{|}{N}H^+$) being observed.[8] The salt is relatively unstable and gradually decomposes on storing for several weeks.



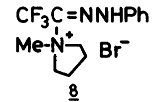
$CF_3\underset{NHPh}{C}=NNHPh$

**6**



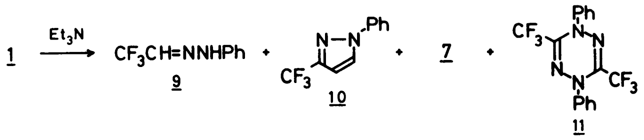
$CF_3\underset{NEt_2}{C}=NNHPh$

**7**



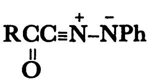
**8**

On the other hand, the reaction with triethylamine was found to be more complicated to give trifluoroacetaldehyde phenylhydrazone (**9**) (16%), 1-phenyl-3-(trifluoromethyl)pyrazole (**10**) (16%), and the acetamide **7** (7%) together with a trace amount of 1,4-diphenyl-3,6-bis(trifluoromethyl)-1,4-dihydro-1,2,4,5-tetrazine (**11**) (Scheme 2). The products **7**, **9**, and **10** were identified by comparing their physical and spectral data with those of the authentic samples. Regarding the structure of **11**, the MS spectrum and elemental analysis indicate the dimer of **2** and the UV spectrum ($\lambda_{max}$ 267 nm, log $\varepsilon$=4.23; 275 nm(sh), log $\varepsilon$=4.22) supports the 1,2,4,5-tetrazine ring.[9] The formation of **7**, **9**, and **10** is quite curious. However, a similar reduction is reported by Knunyants and his co-workers in the reaction of trifluoroacetyl chloride with triethylamine which affords trifluoroacetaldehyde and 4-diethylamino-1,1,1-trifluoro-3-buten-2-one derived from once formed *N*,*N*-diethylvinylamine.[10] The products **7**, **9**, and **10** may be formed through a similar reduction. That is, **1** is reduced with triethylamine to give **9** and *N*,*N*-diethylvinylamine. *N*,*N*-Diethylvinylamine is trapped with **2** to produce the unstable 5-diethylamino-1-phenyl-3-trifluoromethyl-2-pyrazoline which undergoes breakdown to **10** and diethylamine.[11] Diethylamine thus formed reacts with **1** to give **7**, as shown above.



Scheme 2.

In summary, it is found that the nucleophilic substitution of the bromide **1** is predominant over the dimerization of the nitrilimine **2** *in situ* formed. It should be also noted that the nitrilimine **2** dimerizing with great difficulty is in sharp contrast to the nitrilimine **12** with a similar electron-withdrawing group such as benzoyl[12] or ethoxycarbonyl group[9] which easily dimerize to the corresponding tetrazines.



$R\underset{\underset{O}{\|}}{C}C\equiv\overset{+}{N}-\overset{-}{N}Ph$

**12**

## Experimental

The IR spectra were recorded on a JASCO IRA-1 spectrometer and $^1$H NMR spectra were measured with a JEOL JNM-PMX 60 spectrometer using tetramethylsilane as an internal standard, the chemical shifts being given in $\delta$ ppm downfield. The MS spectra were obtained on a Finnigan 4023 GC-MS DS spectrometer. The UV spectra were observed with a Hitachi 340 spectrometer. The bromide **1** was prepared by the method reported in our previous papers.[5,7]

*Reaction of 1 with Sodium Methoxide.* A solution of 1.00 g (3.7 mmol) of **1** in 10 cm$^3$ of methanol was added dropwise to a solution of 0.61 g (11.3 mmol) of sodium methoxide in 20 cm$^3$ of methanol. After stirring at room temperature for 0.5 h, the solvent was removed. To the residue was added 100 cm$^3$ of ethyl ether and the mixture was washed with water and brine, dried over magnesium sulfate, and evaporated to leave crude **3** which was purified by distillation to give 0.52g (64%) of pure **3**, bp 80°C/2mmHg (1mmHg=133.322 Pa), $^1$H NMR (CCl$_4$) $\delta$=3.96 (q, $J$=2 Hz, 3H), 6.6—7.4 (m, 5H), and 7.6 (br.s, 1H), IR (neat) 1643 (C=N) and 1115 cm$^{-1}$ (CF$_3$).

Found: C, 49.37; H, 3.98; N, 12.75%. Calcd for $C_9H_9F_3N_2O$: C, 49.55; H, 4.16; N, 12.84%.

In a similar manner, the reaction of **1** (1.00 g) with sodium phenoxide (1.30 g, 11.2 mmol) in methanol (30 cm$^3$) was carried out to give a mixture of **4** and **3**. The mixture was submitted to column chromatography (silica gel, hexane–chloroform; 8:1) to give 0.38 g (36%) of **4** and 40 mg (5%) of **3**. The hydrazonate **4** was further purified by bulb-to-bulb distillation (bath temperature 123—125 °C, 1 mmHg), $^1$H NMR (CCl$_4$) $\delta$=6.6—7.5 (m, 10H) and 7.6 (br.s, 1H), IR (neat) 3330 (NH), 1638 (C=N), and 1159, 1125 cm$^{-1}$ (CF$_3$).

Found: C, 60.11; H, 3.71; N, 9.77%. Calcd for $C_{14}H_{11}F_3N_2O$: C, 60.00; H, 3.96; N, 10.00%.

*Reaction of 1 with Sodium Methoxide in the Presence of Methyl Acrylate.* A solution of **1** (1.00 g, 3.7 mmol) in 10 cm$^3$ of methanol was added dropwise to a mixture of methyl acrylate (0.97 g, 11.3 mmol) and sodium methoxide (0.40 g, 7.4 mmol) in 20 cm$^3$ of methanol and the mixture was stirred at room temperature for 24 h. The usual workup gave 0.57 g (56%) of **5** and 0.31 g (38%) of **3**. **5**, mp 60—61 °C (lit,[5] mp 60—61.5 °C). Spectral data are consistent with those of our authentic sample.

*Reaction of 1 with Diethylamine.* A mixture of diethylamine (3 cm$^3$) and **1** (1.00 g) in 10 cm$^3$ of toluene was stirred at room temperature for 4 h. The residue obtained by the usual workup was chromatographed over silica gel (hexane–chloroform; 4:1) to give 0.86 g (89%) of **7** which was further purified by distillation, bp 103—104 °C/4 mmHg, $^1$H NMR (CCl$_4$) $\delta$=1.13 (t, 6H), 2.96 (q, 4H), 6.6—7.4 (m, 5H), and 8.5 (br.s, 1H), IR (neat) 3290 (NH), 1602 (Ph and C=N), and 1139, 1109 cm$^{-1}$ (CF$_3$).

Found: C, 55.68; H, 6.26; N, 16.03%. Calcd for $C_{12}H_{16}F_3N_3$: C, 55.59; H, 6.22; N, 16.21%.

The reaction with aniline was similarly performed at 100 °C for 7 h to give **6** in 49% yield, mp 66.5—67.5 °C (hexane) (lit,[6] mp 66.5—67.5 °C).

*Reaction of 1 with N-Methylpyrrolidine.* *N*-Methylpyrrolidine (3 cm$^3$) was added dropwise to a solution of 2.00 g (7.5 mmol) of **1** in 10 cm$^3$ of toluene holding the temperature below 20°C. After stirring for 2 h, the deposited white crystals were collected on a filter, washed with hexane, and dried to give 2.09 g (79%) of **8**, mp 72°C (dec.), $^1$H NMR (CDCl$_3$) $\delta$=1.84 (m, 4H), 2.46 (s, 3H), 2.62 (m, 4H), 6.9—7.5 (m, 5H), and 8.0 (br.s, 1H), IR (KBr) 3355 (NH), 1614 (C=N), and 1179, 1129 cm$^{-1}$ (CF$_3$).

Found: C, 44.08; H, 4.66; N, 11.84%. Calcd for $C_{13}H_{17}BrF_3N_3$: C, 44.33; H, 4.86; N, 11.93%.

*Reaction of 1 with Triethylamine.* A mixture of 2.00 g (7.5 mmol) of **1** and 6 cm$^3$ of triethylamine in 10 cm$^3$ of toluene was stirred at room temperature for 23 h. To the reaction mixture was added 100 cm$^3$ of ethyl ether and the mixture was washed with water and brine, dried over magnesium sulfate, and evaporated. The residue was chromatographed over silica gel (hexane–chloroform; 7:1) to give 0.22 g (16%) of **9**, 0.25 g (16%) of **10**, 0.13 g (7%) of **7**, and 30 mg (2%) of **11**. Spectral data of **7** are consistent with those obtained above. **9**, mp 69—71 °C (lit,[5] mp 69—73 °C), $^1$H NMR (CCl$_4$) $\delta$=6.5—7.3 (m, 6H) and 7.6 (br.s, 1H).

**10**, $^1$H NMR (CCl$_4$) $\delta$=6.60 (d, $J$=2.5 Hz, 1H), 7.2—7.8 (m, 5H), and 7.83 (d, $J$=2.5 Hz, 1H), IR (neat) 3135 (=CH), 1605 (Ph and C=N), and 1166, 1130 cm$^{-1}$ (CF$_3$).

Found: C, 56.36; H, 3.27; N, 13.15%. Calcd for $C_{10}H_7F_3N_2$: C, 56.61; H, 3.33; N, 13.20%.

**11**, mp 118—120 °C (hexane), $^1$H NMR (CDCl$_3$) $\delta$=7.37 (s), IR (KBr) 1612 (C=N) and 1138, 1104 cm$^{-1}$ (CF$_3$), MS (CI, $m/z$) 372 (M)$^+$ and 401 (M+C$_2$H$_5$),$^+$ UV $\lambda_{\max}^{\mathrm{EtOH}}$ (log $\varepsilon$) 267 (4.23) and 275 nm (sh, 4.22).

Found: C, 51.47; H, 2.69; N, 15.25%. Calcd for $C_{16}H_{10}F_6N_4$: C, 51.62; H, 2.71; N, 15.05%.

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