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N, N'-DISUBSTITUTED TRIFLUOROACETAMIDINES FOR TRIFLUOROMETHYLATED POLYNITROGEN HETEROCYCLES.

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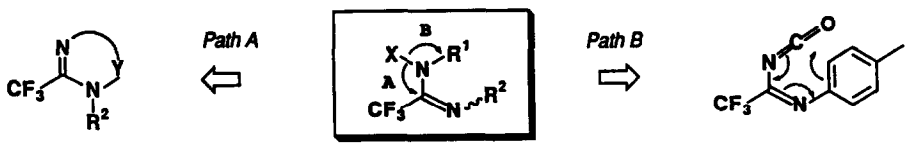
Summary; N, N'-Disubstituted trifluoroacetamidines have been prepared and transformed to the trifluoromethylated polynitrogen heterocycles.

Preparations of trifluoromethylated compounds are in great demand because of their unique nature for biological activities and high performance material science.[1] Therefore, trifluoromethylated building blocks have been accepting an increasing attention.[2] The unsymmetrically N, N'-disubstituted trifluoroacetamidines **1** would become multifunctional key-compounds for trifluoromethylated heterocycles by changing substituents X, R^1 and R^2, but their chemistries have not yet studied in detail. Here, we describe a preliminary study on preparations and transformations of **1** to the trifluoromethylated polynitrogen heterocycles.



3 R^2=p-Tolyl

1a ; X=H, R^1=N(C_6H_5)$CO_2C_2H_5$
1b ; X=H, R^1=$C_6H_4CO_2C_2H_5$
1c ; X=Lone Pair Electron, R^1=N_2
1d ; X=H, R^1=CO_2CH_3

4

5 **6** **7** **8**

N-p-Tolyl trifluoroacetimidoyl chloride (**2**)[3] reacts with various nitrogen nucleophiles. For example, to a benzene solution of phenylhydrazine was added **2** dissolved in benzene and the mixture was allowed to react at room temperature for 4 h. Then, the products were treated with ethyl chloroformate and pyridine in benzene at room temperature for 5 h, providing **1a** (60%) from **2**. Similarly, reactions of **2** with

methyl urethane (NaH/THF at room temperature for 5 h) afforded **1d** (93%).

The amidines **1** cyclize via two path ways (A and B). The path A involves deprotonation (X=H) and intramolecular amidation for **5** (84%, heated at 200°C for 20 min.)[4] and **6** (65%, heated at 200°C for 3 h)[4,5]. Similarly, cyclization of **1c** (X=lone pair electron) to **7** (87%)[4,6] proceeds spontaneously on treating **2** with NaN_3 in acetone-water at room temperature.

On the other hand, N-methoxycarbonyl compound **1d** undergoes dehydromethoxylation at first, on heating at 250°C for 30 min., leading to ketenimide **4**, which then cyclizes by electrocyclic reaction and subsequently aromatizes by prototropy, affording **8** (71%)[4,7] (path B). By changing the functionalities of N-substituents, **1** would become potentional building blocks for functionally and skeletally variable polynitrogen heterocycles. Investigation along this synthetic strategy and examination of the biological activities of these heterocycles are in progress.

References and Notes

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4) ^{19}F, ^{13}C, and ^{1}H-NMR(∂, C_6F_6 for ^{19}F and TMS for ^{13}C and ^{1}H in $CDCl_3$) and MS; **5**=93.33: 21.3, 117.2(q, J=271 Hz), 119.2, 126.6, 127.2, 128.5, 129.2, 130.4, 135.9(q, J=41 Hz), 137.0, 140.5, 151.1: 2.44(s, 3H), 7.28(d, J=8.4 Hz, 2H), 7.30(m, 1H), 7.34(d, 8.4 Hz, 2H), 7.47(m, 2H), 8.00(m, 2H): m/e=319(M^+, 85); **6**=97.66: 21.3, 118.0(q, J=277 Hz), 122.2, 127.4, 128.6, 128.7, 129.5, 130.0, 132.0, 135.2, 140.1, 142.4(q, J=35 Hz), 145.2, 161.8: 2.45(s, 3H), 7.18(d, J=8.3 Hz, 2H), 7.34(d, J=8.3 Hz, 2H), 7.65(m, 1H), 7.88(m, 1H), 7.89(m, 1H), 8.34(m, 1H): m/e=304(M^+, 100); **7**=101.73: 21.2, 117.8(q, J=271 Hz), 124.8, 130.0, 130.4, 142.2, 146.1(q, J=43 Hz): 2.49(s, 3H), 7.39(d, J=8.7 Hz, 2H), 7.42(d, J=8.7 Hz, 2H): m/e=228(M^+, 10); **8** =93.27: 20.9, 117.8(q, J=275 Hz), 122.2, 125.5, 127.9, 136.2, 139.0, 141.8, 144.3, 161.1: 2.55(s, 3H), 7.70(dd, J=8.1 Hz, J=2.0 Hz, 1H), 7.78(d, J=8.1 Hz, 1H), 8.16(d, J=2.0 Hz, 1H): m/e=228(M^+, 100).

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