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Reaction between *tert*-butyl isocyanide and 1,1,1-trifluoro-4-aryl-butane-2,4-diones Synthesis of new trifluoromethylated furan derivatives

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Abstract

The 2:1 adducts produced in the reaction between *tert*-butyl isocyanide and 1,1,1-trifluoro-4-arylbutan-2,4-diones were isolated and characterized as fluorinated aminoketenimines, which undergo enolization-cyclization reactions in boiling chloroform to produce new trifluoromethylated furan derivatives.

Keywords: CH-acid; Trifluoromethylated furans; Aminoketenimine; 1,3-Dicarbonyl compound

1. Introduction

The greatest reactivity observed for isocyanides is the reaction of the functional group with acidic reactants [1–10]. A general feature of isocyanide reactions is the formation of α,α-addition products, i.e. two new bonds are formed with the terminal isocyanide carbon atom. Typical examples include the reaction of isocyanides with protonic acids [4–6,10]. Here, we wish to report that CH-acids such as trifluoromethyl substituted 1,3-dicarbonyl compounds **1** react with *tert*-butyl isocyanide producing 1:2 adducts (acid:isocyanide).

2. Results and discussion

The reaction of 1,1,1-trifluoro-4-arylbutan-2,4-diones (**1**) with *tert*-butyl isocyanide leads to fluorinated aminoketenimines **2**, which were converted quantitatively to trifluoromethylated furan derivatives **3** (see Scheme 1). All the compounds are stable crystalline solids at room temperature whose structure is fully supported by elemental analyses, IR, ^{1}H, ^{13}C, and ^{19}F NMR spectroscopy and mass spectrometric data. Of interest are the strong ketenimine absorption bands at about 2090 cm^{-1} in the IR spectra of compounds **2a–c** and a broad N–H peak at about 3300 cm^{-1} for the alkylamino group. The mass spectra of these 1:2 adducts exhibited fairly weak molecular ion and/or MH^{+} ion peaks at appropriate *m/z* values for **2** and strong molecular ion peaks for **3**. Any initial fragmentations involve the loss of *t*-butylamino moieties and scission of the trifluoroacetyl bonds.

These trifluoromethylated aminoketenimines may be formulated as having been derived from initial α,α-addition of the CH-acid to the isocyanide and subsequent nucleophilic addition of another molecule of the isocyanide to yield intermediate **5**, which is converted into the aminoketenimine system **2** by proton transfer (Scheme 2).

Compounds **2a–c** can be converted quantitatively to the trifluoromethylated furan ring systems **3a–c** upon refluxing in chloroform for 2–5 h. However, compounds **2** do have two alternative ways to cyclize. Since the carbonyl signal of the arylketone moiety at about $\delta = 180$ ppm is present in the ^{13}C NMR spectra of compounds **3**, we conclude that the trifluoroacyl group undergoes cyclization. It seems that the electron-withdrawing trifluoromethy group enhances the nucleophilic addition to the adjacent carbonyl group. Further evidence is obtained from the mass spectra of compounds **3**, which exhibit strong peaks for the ArCO fragments. The IR spectra of **3a–c** are similar to those of the

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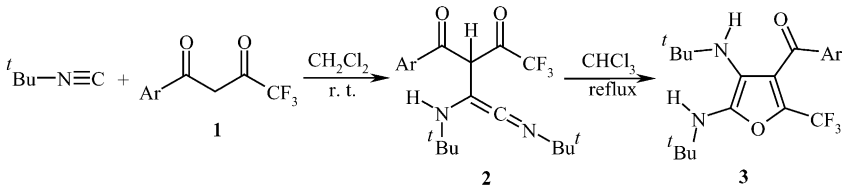
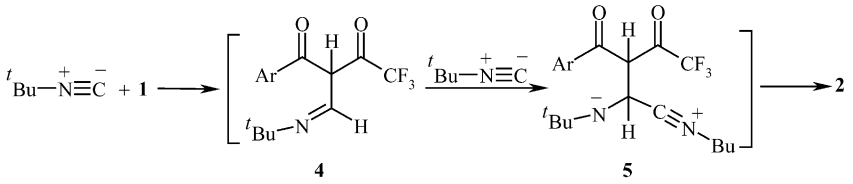


1-3	Ar	%Yield of 2
a	2-Thienyl	80
b	Phenyl	77
c	2-Naphthyl	72

Scheme 1.



Scheme 2.

corresponding aminoketenimines except for the strong absorption band at about 2090 cm^{-1} which is absent in compounds **3a–c**.

The presented reaction of *t*-butyl isocyanide with fluorinated 1,3-diketones provides a simple entry into the synthesis of trifluoromethylated ketenimine derivatives of potential synthetic interest. The procedure described here may be useful as a method for the preparation of 2,3-diaminofurans which are difficult to prepare [11].

3. Experimental

Melting points were measured with an Electrothermal 9100 apparatus. Elemental analyses were performed using a Heraeus CHN-O-Rapid analyzer. Mass spectra were recorded with a FINNIGAN-MAT 8430 mass spectrometer operating at an ionization potential of 70 eV. IR spectra were recorded with a Shimadzu IR-470 spectrometer. ^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded with a JEOL EX-90A spectrometer at 90, 22.6 and 84.7 MHz, respectively. ^{1}H, ^{13}C and ^{19}F NMR spectra were obtained on solution in $CDCl_3$ using TMS or $CFCl_3$ as internal standard. The triflouromethylated 1,3-dicarbonyl compounds used in this work were purchased from Fluka (Buchs, Switzerland) and used without further purifications.

*3.1. Preparation of 2-[1-(tert-butylamino)-2-(tert-butylimino)vinyl]-4,4,4-trifluoro-1-(2-thienyl)-butane-1,3-dione (**2a**): typical procedure*

To a magnetically stirred solution of 1,1,1-trifluoro-4-(2-thienyl)-butane-2,4-dione (0.44 g, 2 mmol) in CH_2Cl_2 (3 mL) was added dropwise a solution of *t*-butyl isocyanide (0.33 g, 4 mmol) in CH_2Cl_2 (3 mL) at −5 °C over 10 min. The reaction mixture was then allowed to warm up to room temperature and stirred for 24 h. The solvent was removed under reduced pressure and the residue was purified by silica gel (Merck silica gel 60, 230–400 mesh) column chromatography using *n*-hexane-ethyl acetate as eluent. The solvent was removed under reduced pressure to afford the product which was recrystallized from ethyl acetate to yield **2a** as colorless crystals, 0.62 g, yield 80%, mp 147–149 °C.

IR (KBr) (ν_{max}, cm^{-1}) = 3340 (NH), 2070 (C=C=N), 1683 (C=O).

^{1}H NMR ($CDCl_3$) $\delta = 1.4$ (9H, s, CMe_3), 1.5 (9H, s, CMe_3), 4.4 (1H, q, $^{4}J_{HF} = 9$ Hz, CH), 7.2 (1H, m, CH), 7.6 (1H, br s, NH), 7.7–7.8 (2H, m, 2 CH) ppm.

^{13}C NMR ($CDCl_3$) $\delta = 28.5$ (CMe_3), 30.1 (CMe_3), 51.9 (CMe_3), 53.5 (CMe_3), 116.0 (C), 123.6 (q, $^{1}J_{FC} = 264$ Hz, CF_3), 124.4 (CH), 125.1 (CH), 127.5 (CH), 131.2 (C), 139.4 (C), 153.9 (C), 171.0 (q, $^{2}J_{FC} = 28$ Hz, CF_3–*C*=O), 182.8 (C=O) ppm.

^{19}F NMR ($CDCl_3$) $\delta = -66.74$ (CF_3) ppm.

MS (EI, 70 eV): *m/z* (ion, %) = 389 (MH^+, 1), 333 (MH^+ − $Me_2C{=}CH_2$, 11), 157 (31), 111 ($C_5H_3SO^+$, 46), 57 ($C_4H_9^+$, 100), 41 ($C_3H_5^+$, 48).

Analytically calculated for $C_{18}H_{23}F_3N_2O_2S$ (388.5): C, 55.7; H, 6.0; N, 7.2%. Found: C, 55.4; H, 5.9; N, 7.2%.

*3.2. 2-[1-(tert-Butylamino)-2-(tert-butylimino)vinyl]-4,4,4-trifluoro-1-phenyl-butane-1,3-dione (**2b**)*

Colorless crystals; yield: 0.59 g (77%), mp 150–152 °C.

IR (KBr) (ν_{max}, cm^{-1}) = 3315 (NH), 2085 (C=C=N), 1684 (C=O).

^{1}H NMR ($CDCl_3$) $\delta = 1.2$ (9H, s, CMe_3), 1.4 (9H, s, CMe_3), 4.3 (1H, q, $^4J_{HF} = 9$ Hz, CH), 5.9 (1H, br s, NH), 7.3–7.7 (5H, m, Ph) ppm.

^{13}C NMR ($CDCl_3$) $\delta = 28.3$ (CMe_3), 30.1 (CMe_3), 51.8 (CMe_3), 53.3 (CMe_3), 92.2 (CH), 117.1 (C), 123.9 (q, $^1J_{FC} = 265$ Hz, CF_3), 127.6 and 129.0 (CH_{meta} and CH_{ortho}), 132.8 (C_{ipso}), 134.0 (CH_{para}), 154.2 (C), 177.2 (q, $^2J_{FC} = 37$ Hz, CF_3–C=O), 186.2 (C=O) ppm.

^{19}F NMR ($CDCl_3$) $\delta = -65.81$ (CF_3) ppm.

MS (EI, 70 eV): *m/z* (ion, %) = 383 (MH^+, 1), 382 (M^+, 0.5), 326 ($M^+ - Me_2C{=}CH_2$, 23), 253 (326 − Me_3CNH_2, 15), 227 (253 − CN, 44), 105 ($C_7H_5O^+$, 41), 77 ($C_6H_5^+$, 29), 57 ($C_4H_9^+$, 100), 41 ($C_3H_5^+$, 76).

Analytically calculated for $C_{20}H_{25}F_3N_2O_2$ (382.4): C, 62.8; H, 6.6; N, 7.3%. Found: C, 63.0; H, 6.5; N, 7.4%.

*3.3. 2-[1-(tert-Butylamino)-2-(tert-butylimino)vinyl]-4,4,4-trifluoro-1-(2-naphthyl)-butane-1,3-dione (**2c**)*

Colorless crystals; yield: 0.60 g (97%), mp 160–162 °C.

IR (KBr) (ν_{max}, cm^{-1}) = 3275 (NH), 2090 (C=C=N), 1684 and 1649 (C=O).

^{1}H NMR ($CDCl_3$) $\delta = 1.2$ (9H, s, CMe_3), 1.37 (9H, s, CMe_3), 4.6 (1H, q, $^4J_{HF} = 9$ Hz, CH), 6.7 (1H, br s, NH), 7.4–8.3 (7H, m, naphthyl) ppm.

^{13}C NMR ($CDCl_3$) $\delta = 28.4$ (CMe_3), 30.3 (CMe_3), 52.0 (CMe_3), 53.5 (CMe_3), 91.3 (CH), 117.9 (C), 122.5 (q, $^1J_{FC} = 263$ Hz, CF_3), 122.8, 124.4, 126.2, 126.6, 128.2, 128.3, 128.7, 132.6 and 133.3 (naphthyl), 142.2 (C), 154.5 (C), 178.1 (q, $^2J_{FC} = 35$ Hz, CF_3–C=O), 188.1 (C=O) ppm.

^{19}F NMR ($CDCl_3$) $\delta = -66.22$ (CF_3) ppm.

MS (EI, 70 eV): *m/z* (ion, %) = 432 (M^+, 0.5), 376 ($M^+ - Me_2C{=}CH_2$, 15), 303 (376 − Me_3CNH_2, 7), 277 (M^+ − 155, 30), 155 ($C_{11}H_7O^+$, 38), 127 ($C_{10}H_7^+$, 23), 57 ($C_4H_9^+$, 100), 41 ($C_3H_5^+$, 36).

Analytically calculated for $C_{24}H_{27}F_3N_2O_2$ (432.5): C, 66.7; H, 6.3; N, 6.5%. Found: C, 66.5; H, 6.2; N, 6.4%.

*3.4. Preparation of [4,5-bis(tert-butylamino)-2-(trifluoromethyl-3-furyl)]-(2-thienyl)-methanone (**3a**): typical procedure*

A magnetically stirred solution of **2a** (0.78 g, 2 mmol) in $CHCl_3$ (10 mL) was refluxed for 5 h. The solvent was removed under reduced pressure and the residue was obtained as pale yellow powder; yield: 0.75 g (98%), mp 141–143 °C.

IR (KBr) (ν_{max}, cm^{-1}) = 3435 and 3330 (2 NH), 1655 (C=O).

^{1}H NMR ($CDCl_3$) $\delta = 1.4$ (9 H, s, CMe_3), 1.5 (9H, s, CMe_3), 4.4 (H, br s, NH), 5.7 (H, br s, NH), 7.0–7.4 (3H, m, 3 CH) ppm.

^{13}C NMR ($CDCl_3$) $\delta = 28.4$ (CMe_3), 30.0 (CMe_3), 51.8 (CMe_3), 53.4 (CMe_3), 89.9 (q, $^3J_{FC} = 35$ Hz, C=C–CF_3), 115.9 (C), 123.7 (q, $^1J_{FC} = 263$ Hz, CF_3), 124.3 (CH), 125.0 (CH), 127.4 (CH), 130.7 (C), 139.2 (C), 153.8 (q, $^2J_{FC} = 4$ Hz, C–CF_3), 180.5 (C=O) ppm.

^{19}F NMR ($CDCl_3$) $\delta = -76.52$ (CF_3) ppm.

MS (EI, 70 eV): *m/z* (ion, %) = 388 (M^+, 43), 332 ($M^+ - Me_2C{=}CH_2$, 84), 276 (45), 260 (53), 111 ($C_5H_3SO^+$, 67), 83 (24), 57 ($C_4H_9^+$, 100), 41 ($C_3H_5^+$, 81).

Analytically calculated for $C_{18}H_{23}F_3N_2O_2S$ (388.5): C, 55.7; H, 6.0; N, 7.2%. Found: C, 55.5; H, 5.8; N, 7.2%.

*3.5. [4,5-bis(tert-Butylamino)-2-(trifluoromethyl-3-furyl)]-phenyl-methanone (**3b**)*

Pale yellow powder; yield: 0.59 g (95%), mp 145–146 °C.

IR (KBr) (ν_{max}, cm^{-1}) = 3320 and 3253 (2 NH), 1664 (C=O).

^{1}H NMR ($CDCl_3$) $\delta = 1.4$ (9H, s, CMe_3), 1.5 (9H, s, CMe_3), 4.4 (H, br s, NH), 5.7 (H, br s, NH), 7.2–7.7 (5H, m, Ph) ppm.

^{13}C NMR ($CDCl_3$) $\delta = 28.4$ and 30.2 (CMe_3), 52.0 and 53.5 (CMe_3), 89.7 (q, $^3J_{FC} = 36$ Hz, C=C–CF_3), 117.4 (C), 123.5 (q, $^1J_{FC} = 265$ Hz, CF_3), 124.9 and 128.6 (CH_{ortho} and CH_{meta}), 127.7 (CH_{para}), 129.2 (C_{ipso}), 142.1 (C), 154.32(q, $^2J_{FC} = 4$ Hz, C–CF_3), 182.4 (C=O) ppm.

^{19}F NMR ($CDCl_3$) $\delta = -75.91$ (CF_3) ppm.

MS (EI, 70 eV): *m/z* (ion, %) = 382 (M^+, 25), 326 (27), 227 (51), 105 ($C_7H_5O^+$, 49), 57 (100).

Analytically calculated For $C_{20}H_{25}F_3N_2O_5$ (382.4): C, 62.8; H, 6.6; N, 7.3%. Found: C, 62.7; H, 6.6; N, 7.2%.

*3.6. [4,5-bis(tert-Butylamino)-2-(trifluoromethyl-3-furyl)]-(2-naphthyl)-methanone (**3c**)*

Pale yellow powder; yield: 0.86 g (100%), mp 151–153 °C.

IR (KBr) (ν_{max}, cm^{-1}) = 3315 and 3235 (2 NH), 1669 (C=O).

^{1}H NMR ($CDCl_3$) $\delta = 1.4$ (9H, s, CMe_3), 1.5 (9H, s, CMe_3), 4.4 (H, br s, NH), 5.7 (H, br s, NH), 7.3–8.2 (7H, m, naphthyl) ppm.

^{13}C NMR ($CDCl_3$) $\delta = 28.4$ (CMe_3), 30.3 (CMe_3), 52.0 (CMe_3), 53.5 (CMe_3), 91.1 (q, $^3J_{FC} = 36$ Hz, C=C–CF_3), 123.5 (q, $^1J_{FC} = 264$ Hz, CF_3), 123.8, 124.2, 126.3, 126.6, 127.7, 128.2, 128.35, 129.9, 132.6 and 133.3 (naphthyl), 142.2 (C), 154.5 (q, $^2J_{FC} = 4$ Hz, C–CF_3), 182.6 (C=O) ppm.

^{19}F NMR ($CDCl_3$) $\delta = -76.33$ (CF_3) ppm.

MS (EI, 70 eV): *m/z* (ion, %) = 432 (M^+, 25), 376 ($M^+ - Me_2C{=}CH_2$, 17), 303 (376 − Me_3CNH_2, 5), 277 (M^+ − 155, 33) 155 ($C_{11}H_7O^+$, 34), 127 ($C_{10}H_7^+$, 23), 57 ($C_4H_9^+$, 100), 41 ($C_3H_5^+$, 46).

Analytically calculated for $C_{24}H_{27}F_3N_2O_2$ (432.5): C, 66.7; H, 6.3; N, 6.5%. Found: C, 66.6; H, 6.2; N, 6.6%.

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