

SHORT  
COMMUNICATIONS

## Synthesis of 2-Aryl-2,4,6-tris(trifluoromethyl)-1,2-dihydro-1,3,5-triazines by Reaction of Arylmagnesium Bromides with Trifluoroacetonitrile

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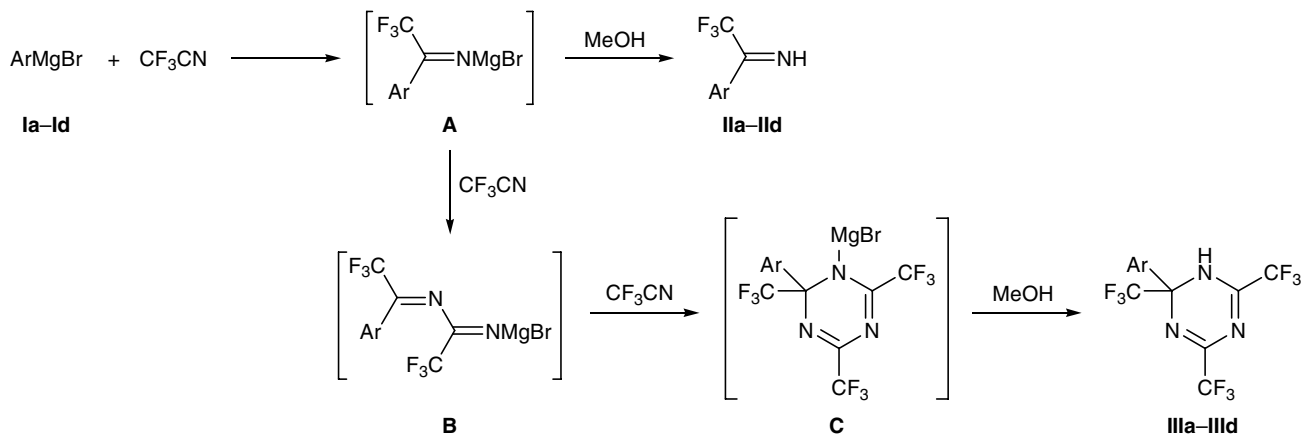
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Reaction of arylmagnesium bromides with trifluoroacetonitrile underlies a preparative procedure for the synthesis of aryl trifluoromethyl ketone imines [1, 2]. According to [1], the yields of the target products attain 50–60% at an arylmagnesium bromide–trifluoroacetamide (precursor of trifluoroacetonitrile) ratio of 1:1.2. The structure of minor products in this reaction remains unexplored; however, we believe it to be important from the viewpoint of development of optimal conditions for the synthesis of the corresponding ketone imines. While attempting to reproduce the procedure described in [1] we have found that, apart from aryl trifluoromethyl ketone imines **IIa–IIId**, 18–26% of 2-aryl-2,4,6-tris(trifluoromethyl)-1,2-dihydro-1,3,5-triazines **IIIa–IIIId** is formed in reactions of arylmagnesium bromides **Ia–Id** with trifluoroacetonitrile. Using the reaction with *p*-tolylmagnesium bromide

(**IIb**) as an example we have shown that the yields of compounds **IIb** and **IIIb** decrease by 6 and 4%, respectively, when an equimolar amount of trifluoroacetamide is used. Presumably, the reason is the reduced conversion of trifluoroacetamide into trifluoroacetonitrile. On the other hand, in the presence of 3 equiv of trifluoroacetamide the yield of triazine **IIIb** increases to 66%. These results led us to presume the following reaction scheme. Initially formed ketone imine salt **A** adds to trifluoroacetonitrile to give diaza diene intermediate **B** which undergoes intermolecular cyclization with another trifluoroacetonitrile molecule. Methanolysis of triazine derivative **C** thus formed yields compounds **IIIa–IIIId**.

**1-Aryl-2,2,2-trifluoroethanimines IIa–IIId and 2-aryl-2,4,6-tris(trifluoromethyl)-1,2-dihydro-1,3,5-triazines IIIa–IIIId (general procedure).** A stream of

Ar = Ph (**a**), 4-MeC<sub>6</sub>H<sub>4</sub> (**b**), 4-MeOC<sub>6</sub>H<sub>4</sub> (**c**), 2-Me-5-FC<sub>6</sub>H<sub>3</sub> (**d**).

trifluoroacetonitrile [prepared by heating a mixture of 81.36 g (0.72 mol) of trifluoroacetamide and 213 g (1.5 mol) of phosphoric anhydride to 140–150°C] was passed over a period of 4–5 h under stirring through a solution of arylmagnesium bromide **Ia–Id**, prepared from 0.6 mol of the corresponding aryl bromide and 14.4 g (0.6 mol) of metallic magnesium in 600 ml of diethyl ether. The mixture was left to stand for 12 h, and 60 ml of methanol was added over a period of 0.5 h under vigorous stirring. After cooling, the precipitate was filtered off, the filtrate was evaporated, and the residue was subjected to fractional distillation. Yields of compounds **IIa**, **IIb**, and **IIc** 53, 50, and 48%, respectively.

**2,2,2-Trifluoro-1-(5-fluoro-2-methylphenyl)ethanimine (IIc)** (a mixture of *Z* and *E* isomers). Yield 49%, bp 93–95°C (12 mm). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 1.67 s, 2.05 s (3H, CH<sub>3</sub>), 6.48–6.72 m (4H, H<sub>arom</sub>), 9.76 s and 10.84 s (1H, NH). <sup>19</sup>F NMR spectrum,  $\delta_F$ , ppm: –71.51 s and –72.85 s (3F, CF<sub>3</sub>), –116.1 s and –116.5 s (1F). Found, %: F 37.21; N 6.99. C<sub>9</sub>H<sub>10</sub>F<sub>4</sub>N. Calculated, %: F 37.04; N 6.83.

**2-Phenyl-2,4,6-tris(trifluoromethyl)-1,2-dihydro-1,3,5-triazine (IIIa)**. Yield 18%, bp 52°C (0.045 mm). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 7.43 m (3H, H<sub>arom</sub>), 7.67 m (2H, H<sub>arom</sub>), 8.31 br.s (1H, NH). <sup>13</sup>C NMR spectrum,  $\delta_C$ , ppm: 78.76 q (C<sup>2</sup>, <sup>2</sup>J<sub>CF</sub> = 30 Hz), 116.49 q (CF<sub>3</sub>, <sup>1</sup>J<sub>CF</sub> = 277 Hz), 122.35 q (CF<sub>3</sub>, <sup>1</sup>J<sub>CF</sub> = 284 Hz), 125.41 (C<sup>4'</sup>), 127.74 (C<sup>2'</sup>, C<sup>6'</sup>), 128.68 (C<sup>3'</sup>, C<sup>5'</sup>), 136.91 (C<sup>1'</sup>), 142.31 q (C<sup>4</sup>, C<sup>6</sup>, <sup>2</sup>J<sub>CF</sub> = 42 Hz). <sup>19</sup>F NMR spectrum,  $\delta_F$ , ppm: –82.32 s (CF<sub>3</sub>), –74.41 s (2CF<sub>3</sub>). Found, %: F 47.24; N 11.79. C<sub>12</sub>H<sub>6</sub>F<sub>9</sub>N<sub>3</sub>. Calculated, %: F 47.08; N 11.57.

**2-(4-Methylphenyl)-2,4,6-tris(trifluoromethyl)-1,2-dihydro-1,3,5-triazine (IIIb)**. Yield 21%, bp 120–123°C (12 mm), mp 42–43°C. <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 2.38 s (3H, CH<sub>3</sub>), 7.24 d (2H, H<sub>arom</sub>), 7.55 d (2H, H<sub>arom</sub>), 8.35 br.s (1H, NH). <sup>13</sup>C NMR spectrum,  $\delta_C$ , ppm: 2.13 (CH<sub>3</sub>), 78.50 q (C<sup>2</sup>, <sup>2</sup>J<sub>CF</sub> = 30 Hz), 116.51 q (4-CF<sub>3</sub>, <sup>1</sup>J<sub>CF</sub> = 275 Hz), 122.42 q (6-CF<sub>3</sub>, <sup>1</sup>J<sub>CF</sub> = 284 Hz), 126.52 (C<sup>2'</sup>, C<sup>6'</sup>), 129.27 (C<sup>3'</sup>, C<sup>5'</sup>), 133.85 (C<sup>1'</sup>), 140.11 (C<sup>4'</sup>), 142.09 q (C<sup>4</sup>, C<sup>6</sup>, <sup>2</sup>J<sub>CF</sub> = 40 Hz).

<sup>19</sup>F NMR spectrum,  $\delta_F$ , ppm: –82.68 s (CF<sub>3</sub>), –74.21 s (2CF<sub>3</sub>). Found, %: F 45.55; N 11.03. C<sub>13</sub>H<sub>8</sub>F<sub>9</sub>N<sub>3</sub>. Calculated, %: F 45.33; N 11.14.

**2-(4-Methoxyphenyl)-2,4,6-tris(trifluoromethyl)-1,2-dihydro-1,3,5-triazine (IIIc)**. Yield 26%, bp 80–81°C (0.045 mm), mp 94–95°C. <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 3.82 s (3H, OCH<sub>3</sub>), 6.93 d (2H, H<sub>arom</sub>), 7.58 d (2H, H<sub>arom</sub>), 7.99 br.s (1H, NH). <sup>13</sup>C NMR spectrum,  $\delta_C$ , ppm: 55.33 (OCH<sub>3</sub>), 77.12 q (C<sup>2</sup>, <sup>2</sup>J<sub>CF</sub> = 31 Hz), 114.02 (C<sup>3'</sup>, C<sup>5'</sup>), 116.52 q (CF<sub>3</sub>, <sup>1</sup>J<sub>CF</sub> = 277 Hz), 122.42 q (CF<sub>3</sub>, <sup>1</sup>J<sub>CF</sub> = 284 Hz), 126.78 (C<sup>2'</sup>, C<sup>6'</sup>), 128.10 (C<sup>1'</sup>), 142.18 q (C<sup>4</sup>, C<sup>6</sup>, <sup>2</sup>J<sub>CF</sub> = 39 Hz), 160.64 (C<sup>4'</sup>). <sup>19</sup>F NMR spectrum,  $\delta_F$ , ppm: –81.31 s (CF<sub>3</sub>), –73.20 s (2CF<sub>3</sub>). Found, %: F 43.65; N 10.47. C<sub>13</sub>H<sub>8</sub>F<sub>9</sub>N<sub>3</sub>O. Calculated, %: F 43.48; N 10.69.

**2-(5-Fluoro-2-methylphenyl)-2,4,6-tris(trifluoromethyl)-1,2-dihydro-1,3,5-triazine (IIIc)**. Yield 23%, bp 133–135°C (12 mm), mp 94–95°C. <sup>1</sup>H NMR spectrum (CDCl<sub>3</sub>),  $\delta$ , ppm: 2.54 s (3H, CH<sub>3</sub>), 6.92–6.98 m (1H, H<sub>arom</sub>), 7.26 t (1H, H<sub>arom</sub>), 7.34 d (1H, H<sub>arom</sub>), 8.03 br.s (1H, NH). <sup>13</sup>C NMR spectrum,  $\delta_C$ , ppm: 21.19 (CH<sub>3</sub>), 79.50 q (C<sup>2</sup>, <sup>2</sup>J<sub>CF</sub> = 32 Hz), 115.33 d (C<sup>4'</sup>, <sup>2</sup>J<sub>CF</sub> = 26 Hz), 118.49 q (4-CF<sub>3</sub>, <sup>1</sup>J<sub>CF</sub> = 212 Hz), 116.61 d (C<sup>6'</sup>, <sup>2</sup>J<sub>CF</sub> = 21 Hz), 122.73 q (6-CF<sub>3</sub>, <sup>1</sup>J<sub>CF</sub> = 284 Hz), 133.83 d (C<sup>2'</sup>, <sup>4</sup>J<sub>CF</sub> = 2.5 Hz), 134.60 d (C<sup>3'</sup>, <sup>3</sup>J<sub>CF</sub> = 7.5 Hz), 135.89 d (C<sup>1'</sup>, <sup>3</sup>J<sub>CF</sub> = 3.7 Hz), 142.10 q (C<sup>4</sup>, C<sup>6</sup>, <sup>2</sup>J<sub>CF</sub> = 39 Hz), 160.51 d (C<sup>5'</sup>, <sup>1</sup>J<sub>CF</sub> = 244 Hz). <sup>19</sup>F NMR spectrum,  $\delta_F$ , ppm: –74.04 s (2CF<sub>3</sub>), –81.29 s (CF<sub>3</sub>), –117.43 s (F). Found, %: F 47.98; N 10.57. C<sub>13</sub>H<sub>7</sub>F<sub>10</sub>N<sub>3</sub>. Calculated, %: F 48.07; N 10.63.

The <sup>1</sup>H, <sup>13</sup>C, and <sup>19</sup>F NMR spectra were recorded from solutions in CDCl<sub>3</sub> on a Varian-Gemini spectrometer at 299.95, 75.4, and 282.2 MHz, respectively; the chemical shifts were measured relative to tetramethylsilane (<sup>1</sup>H, <sup>13</sup>C) and trichlorofluoromethane (<sup>19</sup>F) as internal references.

## REFERENCES

1. Fetyukhin, V.N., Koretskii, A.S., Gorbatenko, V.I., and Samarai, L.I., *Zh. Org. Khim.*, 1977, vol. 13, p. 271.
2. Koos, M. and Mosher, H.S., *Tetrahedron*, 1993, vol. 49, p. 1541.