Reactions of Sodium Borohydride in Acidic Media; XV[1]. A Convenient Synthesis of 1,1,1-Trifluoro-2,2-diarylethanes from Arenes and Sodium Borohydride/Trifluoroacetic Acid

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During our study of the reactions of indole with sodium borohydride in carboxylic acid media[2,3,4], we isolated[4] 1,1,1-trifluoro-2,2-bis{5-[*N*-(2,2,2-trifluoroethyl)-indolinyl]}-ethane as a major product when trifluoroacetic acid was used as the carboxylic acid in this reaction. We have since investigated this novel type of Friedel-Crafts alkylation (sometimes called[5] the Baeyer condensation[6]) with other aromatic compounds and now report our results.

Treatment of a solution of an arene **1** in trifluoroacetic acid with sodium borohydride (pellets), followed by refluxing the reaction mixture, affords the corresponding 1,1,1-trifluoro-2,2-diarylethane **2** in fair to good yields (Scheme **A** and Table).

Table. Compounds **2a**–**h**, **3i**, **3j**, and **4b** prepared

Compound	Yield [%][a]	m.p. [°C] (hexane/ether)	Molecular Formula[b]	^{1}H-N.M.R. ($CDCl_3$/TMS_{int})[c] δ [ppm]	^{13}C-N.M.R. ($CDCl_3$/TMS_{int})[d] δ [ppm]	^{19}F-N.M.R. ($CDCl_3$/CCl_3F_{ext})[e] δ [ppm]	Mass Spectra[f] m/e (rel. int. %)
2a	53	31.5–33°	$C_{26}H_{19}F_3O_2$ (420.4)	4.63 (q, J = 9 Hz, 1H); 6.9–7.4 (m, 18H)	53.6 (q, J = 27.3 Hz); 118.0; 118.8; 123.2; 129.3; 129.8; 156.0; 156.6	66.8 (d, J = 9.8 Hz)	420 (M^+, 39); 351 ($M - CF_3$, 100); 165 (44); 153 (16)
2b	36[g]	92–94°	$C_{26}H_{19}F_3S_2$ (452.5)	4.55 (q, J = 10 Hz, 1H); 7.25–7.4 (m, 18H)	54.5 (q, J = 9.8 Hz); 125.9 (q, J = 280.6 Hz); 127.6; 129.2; 129.6; 129.8; 132.1; 133.3; 134.1; 136.7	66.5 (d, J = 9.8 Hz)	452 (M^+, 33); 383 ($M - CF_3$, 32); 197 (12); 165 (100); 152 (13)
2c	65	220–222°	$C_{26}H_{19}F_3$ (388.4)	3.35 (s, 8H); 6.1 (q, J = 10 Hz, 1H); 7.1–7.3 (m, 10H)	29.8; 30.3; 44.9 (q, J = 7.3 Hz); 118.4; 118.8; 119.3; 126.9 (q, J = 281.2 Hz); 127.3; 128.1; 128.5; 130.3; 139.4; 146.3; 146.7	64.9 (d, J = 9.8 Hz)	388 (M^+, 54); 319 ($M - CF_3$, 100); 207 (40); 159 (66); 57 (CF_3, 96)
2d	29	72–74°	$C_{18}H_{19}F_3O_4$ (356.3)	3.7 (s, 12H); 5.85 (q, J = 11 Hz, 1H); 6.8 (m, 4H); 7.1 (br. s, 2H)	39.6 (q, J = 28.4 Hz); 55.6; 56.6; 112.4; 112.7; 116.0; 125.4; 126.4 (q, J = 279.6 Hz); 151.7; 153.3	54.1 (d, J = 9.8 Hz)	356 (M^+, 100); 336 (14); 241 (17); 176 (10); 151 (68)
2e	25	70°	$C_{18}H_{19}F_3O_4$ (356.3)	3.6 (s, 12H); 5.6 (q, J = 10 Hz, 1H); 6.2–6.4 (m, 4H); 7.25 (d, J = 9 Hz, 2H)	38.4 (q, J = 28.3 Hz); 55.2; 55.8; 93.0; 104.3; 117.4; 129.6; 150.3; 160.0	66.4 (d, J = 9.8 Hz)	356 (M^+, 14); 287 ($M - CF_3$, 40); 151 (100); 144 (21); 121 (40)
2f	30	88–90°	$C_{18}H_{19}F_3O_4$ (356.3)	3.9 (s, 12H); 4.55 (q, J = 9 Hz, 1H); 6.9 (s, 6H)	54.5 (q, J = 27.6 Hz); 55.7; 55.8; 111.1; 112.4; 121.3; 126.2 (q, J = 280.0 Hz); 127.9; 148.6; 148.9	66.6 (d, J = 9.8 Hz)	356 (M^+, 51); 287 ($M - CF_3$, 100); 257 (8); 138 (18); 123 (11)
2g	78	169–171°	$C_{24}H_{19}F_3O_2$ (396.4)	3.9 (s, 6H); 6.2 (q, J = 9 Hz, 1H); 6.7 (d, J = 8 Hz, 2H); 7.3–8.4 (m, 10H)	45.0 (q, J = 26.3 Hz); 55.4; 103.0; 122.5; 122.8; 123.7; 124.9; 126.0; 127.2; 132.5; 136.4; 155.2	64.5 (d, J = 9.8 Hz)	396 (M^+, 83); 327 ($M - CF_3$, 100); 295 (33); 239 (32); 156 (47)
2h	48	105–106°	$C_{18}H_{19}F_3$ (292.3)	2.3 (s, 6H); 4.95 (q, J = 10 Hz, 1H); 6.9–7.1 (m, 4H); 7.3 (d, J = 8 Hz, 2H)	19.6; 20.8; 46.6 (q, J = 27.0 Hz); 126.7; 126.8 (q, J = 281.1 Hz); 128.4; 130.8; 131.4; 136.5; 137.2	65.3 (d, J = 9.8 Hz)	292 (M^+, 39); 223 ($M - CF_3$, 100); 208 (21); 193 (27); 186 (94)
3i	34	52–54°	$C_{11}H_{13}F_3O$ (218.2)	2.2 (s, 3H); 2.4 (s, 6H); 5.5 (m, 1H); 6.8 (s, 2H)	20.7; 70.3 (q, J = 32.6 Hz); 125.4 (q, J = 283.5 Hz); 130.7 (br); 138.5	66.3 (d, J = 9.8 Hz)	218 (M^+, 42); 200 ($M - H_2O$, 34); 149 ($M - CF_3$, 100); 121 (39)
3j	15	58–60°	$C_{12}H_{15}F_3O$ (232.2)	2.2–2.3 (m, 12H); 5.7 (q, J = 8 Hz, 1H); 7.0 (s, 1H)	16.6 (br); 20.6; 70.5 (q, J = 32.4 Hz); 125.4 (q, J = 284.6 Hz); 129.9; 132.7; 133.7 (br.)	75.0 (d, J = 9.8 Hz)	232 (M^+, 90); 214 ($M - H_2O$, 46); 199 (18); 163 ($M - CF_3$, 69); 135 (100); 119 (45)
4b	11	oil	$C_{26}H_{19}F_3S_2$ (452.5)	5.6 (q, J = 10 Hz, 1H); 7.0–7.3 (m, 18H)	51.1 (q, J = 27.8 Hz); 125.9 (q, J = 280.9 Hz); 126.4; 127.5; 128.6; 128.7; 129.0; 129.2; 129.8; 130.1; 131.9; 133.0; 134.4; 134.6; 135.3; 136.17; 136.23; 137.4	65.6 (d, J = 9.8 Hz)	452 (M^+, 48); 343 (12); 305 (39); 197 (100); 183 (12); 165 (35)

[a] Yield of product isolated by flash chromatography.

[b] Satisfactory microanalyses obtained: C ±0.25, H ±0.20, S ±0.08.

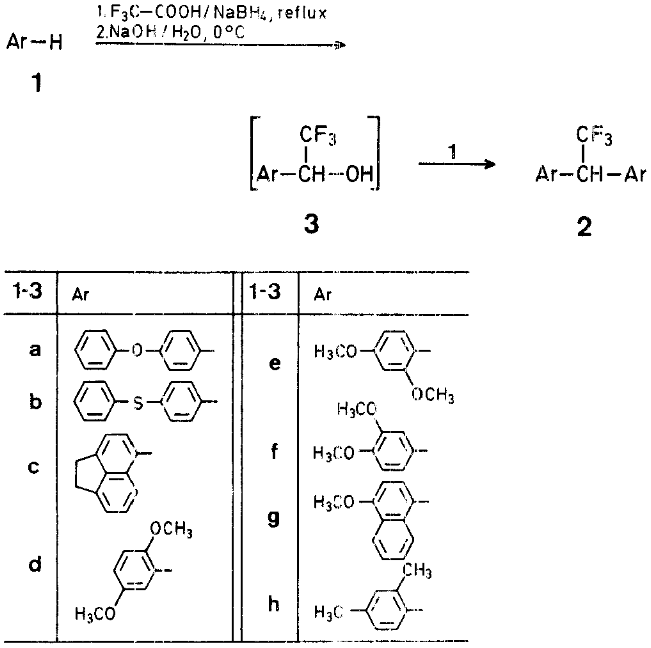
[c] Recorded on a Perkin-Elmer R-24.

[d] Recorded on a Varian XL-300.

[e] Recorded on a JEOL FX-60.

[f] Recorded on a Finnigan 4023 GC/MS.

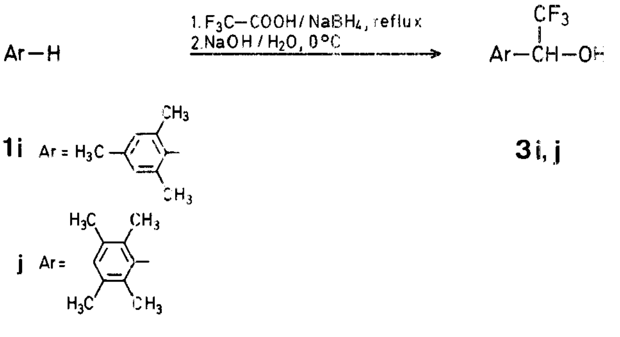
[g] The *ortho,para*-isomer **4b** is also formed.



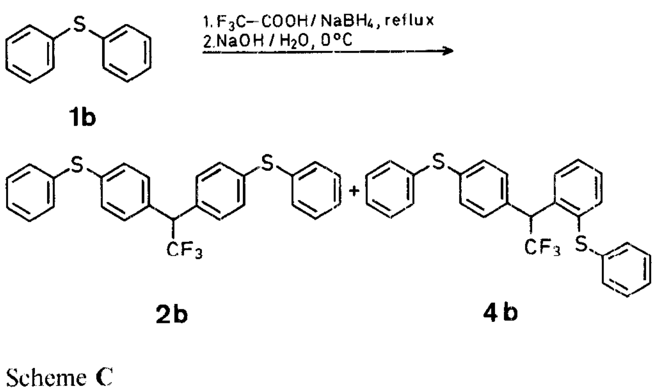
Scheme A

This conversion presumably involves generation of trifluoroacetaldehyde, or its synthetic equivalent, and acid-promoted Friedel-Crafts (Baeyer) condensation with **1** to give an intermediate 2,2,2-trifluoro-1-arylethanol **3**, which undergoes another condensation with **1** to afford **2**. Although this reaction is well-known for trichloroacetaldehyde (chloral) and other aldehydes[5,6], it is not well-documented for trifluoroacetaldehyde (fluoral)[7]. Recently, Briody and Marshall[8] described a synthesis of 1,1,1-trifluoro-2,2,2-triarylethanes and 2,2,2-trifluoro-1,1-diarylethanols from the reaction of arenes with tris[trifluoroacetoxy]borane in trifluoroacetic acid.

The reaction of the sterically congested arenes mesitylene (**1i**) and durene (**1j**) with sodium borohydride/trifluoroacetic acid stops at the carbinol stage and **3i** and **3j** are isolated as the major products, respectively (Scheme **B**). With all but one of the other arenes the expected[5] *para, para*-isomer **2** is the only product isolated. The exception is diphenyl sulfide (**1b**) which gives some of the *ortho, para*-isomer **4b** (Scheme **C**).



Scheme **B**



Scheme **C**

Although most of the reactions required heating for completion, the reaction of 1,3-dimethoxybenzene (**1e**) proceeded at 0 °C and that of 1-methoxynaphthalene (**1g**) occurred readily at 25 °C to give **2e** and **2g**, respectively. Little or no reaction is observed with the less nucleophilic arenes, benzene, toluene, and *p*-xylene.

In summary, the reaction of nucleophilic arenes **1** with sodium borohydride/trifluoroacetic acid gives 1,1,1-trifluoro-2,2-diarylethanes **2** in fair to good yields. This synthesis is convenient and obviates the need for using trifluoroacetaldehyde (or its hydrate, acetal, or hemiacetal) since this highly reactive aldehyde, or its equivalent, is generated *in situ*.

1,1,1-Trifluoro-2,2-diarylethanes 2 from Arenes 1; General Procedure: To a magnetically stirred solution of arene **1** (6–7 mmol) in trifluoroacetic acid (redistilled; 50 ml) at 25 °C under nitrogen in a hood are added sodium borohydride pellets (Ventron; 80 mmol, 10 pellets) over 5 min. The mixture is then heated to reflux and treated with additional sodium borohydride (80 mmol, 10 pellets) over 2 h. The mixture is refluxed for an additional 1 h, allowed to cool, poured slowly into a mixture of ice chips and 25% aqueous sodium hydroxide (pH 11), and extracted with dichloromethane (3 × 75 ml). The organic extract is dried with anhydrous sodium sulfate and concentrated in vacuo. The resulting crude product is flash chromatographed over silica gel (230–400 mesh; 1 : 1 hexane/ether) to give **2** in the yields shown in the Table. Recrystallization from hexane/ether gives the analytically pure products.

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