Reactions of Sodium Borohydride in Acidic Media; VII. Reduction of Diaryl Ketones in Trifluoroacetic Acid[1]

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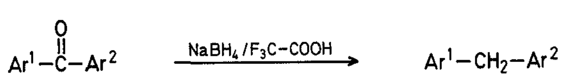
Sodium borohydride in trifluoroacetic acid reduces diarylmethanols to diarylmethanes in high yields[2]. We have now investigated the analogous reduction of diaryl ketones to diarylmethanes.

Diaryl ketones (**1**) are smoothly reduced by sodium borohydride in trifluoroacetic acid, with or without the addition of dichloromethane as a cosolvent, at 20–25° to afford diarylmethanes (**2**) in good to high yields.



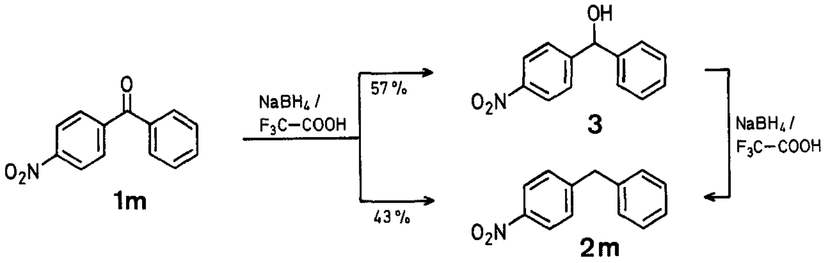
$$Ar^1-\overset{O}{\overset{\|}{C}}-Ar^2 \xrightarrow{NaBH_4/F_3C-COOH} Ar^1-CH_2-Ar^2$$

1 **2**

The reaction presumably involves initial reduction to the diarylmethanol, solvolysis to the carbocation, and reduction to the diarylmethane **2**[2]. The reduction **1**→**2** is general for a variety of substituted benzophenones and other diaryl ketones. The following substituents survive the reaction conditions and do not alter the course of the reduction: CH_3, OH, OCH_3, F, Br, $-N(CH_3)_2$, $-NO_2$, $-COOH$, $-NH-COC_6H_5$[3], $-CN$[4], and $COOCH_3$. However, the reaction fails with 4,4′-bis[dimethylamino]-benzophenone (Michler's ketone) and decafluorobenzophenone (starting material is largely recovered in both cases), and unidentified products form when fluorenone is subjected to the reduction. Reaction of 4-nitrobenzophenone (**1m**) under the standard conditions gives a mixture of 4-nitrodiphenylmethanol (**3**) and 4-nitrodiphenylmethane (**2m**). Not unexpectedly, solvolysis of **3** is retarded by the nitro group[5]. Further treatment of alcohol **3** affords **2m** in 84% yield.

The reduction is also retarded by steric effects. For example, mesityl phenyl ketone (**1p**), mesityl 1-naphthyl ketone (**1q**), and dimesityl ketone (**1r**) give little or no reduction product under the normal reaction conditions, and most of the ketone is recovered. Since we have shown[2] that the alcohols corresponding to **1p** and **1q** do undergo reduction to **2p** and **2q**, respectively, with sodium borohydride/trifluoroacetic acid, it is the ketone → alcohol step of the reaction that is not occurring with these hindered substrates. This lack of reduction is probably also a consequence of the hindered nature of the reducing agent (i.e., a trifluoroacetoxyborohydride species[3,4,6]), a fact which we have previously utilized[6].

Under the usual reaction conditions (Method A), anthrone (**4**) gives anthracene (**5**) as the major product. However, when sodium borohydride is added to a solution of **4** in trifluoroacetic acid (Method C), 9,10-dihydroanthracene (**6**) is the major product, resulting from reduction of the intermediate carbocation. These reaction products can be easily separated by column chromatography.



1m **3** **2m**

Table. Reduction of Diaryl Ketones (**1**) to Diarylmethanes (**2**) with Sodium Borohydride in Trifluoroacetic Acid

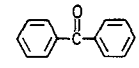
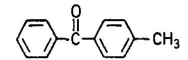
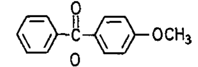
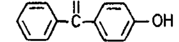
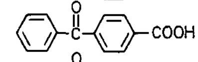
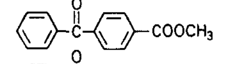
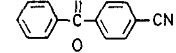
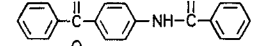
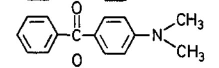
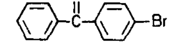
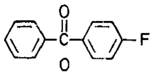
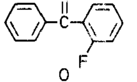
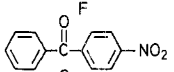
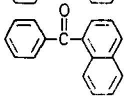
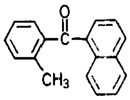
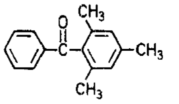
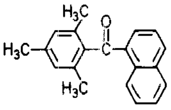
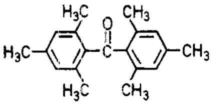
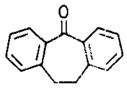
Substrate[a]		Method[b]	Yield[c] [%]	m.p. or b.p./torr[d]	Lit. m.p. or b.p./torr
1a		A	90	60–62°/0.35	85–86°/1[19]
1a		B	92		
1a		C	91		
1b		A	89	69–71°/0.25	110°/1[20]
1c[e]		A	88	89–91°/0.15	121–123°/1.5[21]
1d[f]		A	90[g]	81–82°[h]	83–84°[22]
1e		A	73	154–157°[i]	155–156°[23]
1f[j]		A	93	120–123°/0.15	149–150°/1[24]
1g[k]		A	90[g]	51–52°[l]	50–51°[25]
1h[m]		A	93	162–163°[n]	161°[26]
1i		A	82	33–34°[o]	31°[27]
1j[p]		A	94[g]	102–105°/0.1	128°/3[28]

Table. (Continued)

Substrate[a]		Method[b]	Yield[c] [%]	m.p. or b.p./torr[d]	Lit. m.p. or b.p./torr
1k		A	82	70–71°/0.01	132°/14[10]
1l		A	85	64–65°/0.1	74°/0.2[10]
1m		A	43[q]	139–140°/0.35	114–115°/0.05[15]
1n[r]		A	91	58–59°	57.5–59°[2]
1o[s]		A	91	147–148°/0.4[t]	139–140°/0.3[2]
1p[u]		A	5[v]		
1q[w]		A	0[x]		
1r[y]		A	0[z]		
4		A[aa]	78 (**5**)[bb]	210–211°	216.5°[29]
4		C	91 (**6**)[cc]	109–111°	107–108°[30]
		A	88	74–76°[dd]	77–78°[31]

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[a] Commercial materials unless otherwise specified.

[b] Method A: A solution of the ketone in dichloromethane is added to a premix of sodium borohydride pellets in trifluoroacetic acid at 15–20° under nitrogen.

Method B: The ketone is added neat to a premix of sodium borohydride pellets in trifluoroacetic acid at 15–20° under nitrogen.

Method C: Sodium borohydride pellets are added to a solution of ketone in trifluoroacetic acid at 15–20° under nitrogen.

[c] Yields of distilled or recrystallized material, in some cases with prior column chromatography. Products were identified by I.R. and ^{1}H-N.M.R. spectra and, where possible, by direct comparison with samples prepared earlier[2] or by comparison with literature data.

[d] Distillations were performed with a one-piece microware short-path distillation unit; a heat gun was used to drive over traces of product remaining in the distillation head and condenser.

[e] Prepared from benzoic acid and anisole in polyphosphoric acid at 90–100°; m.p. 60–61.5° (aqueous methanol); Ref. [32], m.p. 61–62°.

[f] Prepared from 4-aminobenzophenone by diazotization[33]; m.p. 130–133°; Ref. [34], m.p. 134°.

[g] Average of two reactions.

[h] This material was distilled: b.p. 115–120°/0.1 torr.

[i] Crystallized from aqueous ethanol.

[j] Prepared from **1e** by Fisher esterification; m.p. 105–106°; Ref. [35], 106–107°.

[k] Prepared from 4-aminobenzophenone by diazotization[36]; m.p. 105–106° (aqueous ethanol); Ref. [36], m.p. 107–108°.

[l] This material was distilled; b.p. 120–125°/0.1 torr.

[m] Prepared from 4-aminobenzophenone and benzoyl chloride; m.p. 151–152° (aqueous ethanol); Ref. [37], m.p. 152°.

[n] Crystallized from aqueous ethanol.

[o] b.p. 126–128°/0.3; Ref. [38], b.p. 180–181°/20–21 torr.

[p] Prepared from 4-aminobenzophenone by diazotization[39]; m.p. 80–81° (ethanol); Ref. [40] m.p. 82.5°.

[q] Accompanied by 57% of **3**: m.p. 73–75°; Ref. [41], m.p. 74.5–75°; separated by dry column chromatography (silica gel) using dichloromethane.

[r] This was a gift from Professor D. M. Bowen; recrystallized from 95% ethanol; m.p. 75.5–76°; Ref. [42], m.p. 75.5°.

[s] This was a gift from Professor D. M. Bowen; recrystallized from 95% ethanol; m.p. 58–59°; Ref. [43], m.p. 59–61°.

[t] m.p. 34–36°.

[u] This was a gift from Professor D. M. Bowen; b.p. 113–114°/0.1; Ref. [44], b.p. 174°/12 torr; m.p. 35.5–36°; Ref. [40], m.p. 35°.

[v] Analysis by G.L.C. showed a **1p**:**2p** ratio of 94:6; a second reaction product showed 96:4 (1.5% OV-101 on 100/120 Chromosorb G; 5′ × 1/8″; 200°), by comparison with known[2] material.

[w] This was a gift from Professor D. M. Bowen; recrystallized from 95% ethanol; m.p. 158–159°; Ref. [45], m.p. 159°.

[x] There was recovered 87% **1q** (4 crops from hexane); m.p. 155–157°, homogeneous by T.L.C. (benzene).

[y] Prepared from mesitylmagnesium bromide and mesitoyl chloride[46]; m.p. 138–140° (95% ethanol); Ref. [46], m.p. 136–137°.

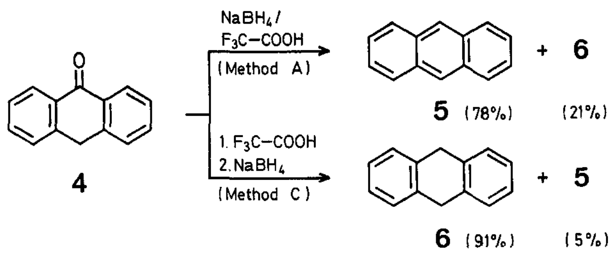
[z] There was recovered 94% **1r** (3 crops from 95% ethanol); m.p. 137°. Analysis by G.L.C. showed 99% **1r** (1.5% OV-101 on 100/120 Chromosorb G; 5′ × 1/8″; 200°).

[aa] When the premix was made at 20° there was isolated **5** (72%) and recovered **4** (23%); m.p. 155–157°.

[bb] There was also isolated by column chromatography (benzene) **6** (21%); m.p. 108–110°; Ref. [30], 107–108°.

[cc] There was also isolated by column chromatography (1:1 hexane/benzene) **5** (5%); m.p. 214–216° Ref. [29], 216.5°.

[dd] This material was first distilled; b.p. 109–111°/0.02 torr.



The reaction **1**→**2** is performed by adding the ketone **1** neat (Method B) or, more conveniently, as a dichloromethane solution (Method A) to a mixture of sodium borohydride pellets and trifluoroacetic acid at 15–20° under nitrogen. Alternatively, the pellets can be added to a solution of the ketone in trifluoroacetic acid (Method C). The pellets are preferred in all three methods to the powdered sodium borohydride because of the danger of ignition of the evolved hydrogen with the latter[2]. We have never experienced hydrogen ignition using sodium borohydride pellets. After the pellets have dissolved, the mixture is worked up and the product isolated.

The sodium borohydride/trifluoroacetic acid reduction of diaryl ketones to diarylmethanes is an excellent alternative to other methods that have been reported for this specific transformation: Wolff-Kishner[7], Clemmensen[8], lithium aluminum hydride/aluminum chloride[9,10], catalytic hydrogenation[11], diphenylsilane[12], trialkylsilanes/trifluoroacetic acid[13,14,15], trichlorosilane/trialkylamine[16], lithium/ammonia[17], and hydrogen sulfide/molybdenum sulfide[18].

Diarylmethanes (2) from Diaryl Ketones (1); General Procedure (Method A):

To magnetically stirred trifluoroacetic acid (redistilled; 50 ml) at 0–5° under nitrogen in a hood are added sodium borohydride pellets (Ventron; 60 mmol, 10 pellets, oven dried at 110°) over 30 min. To this mixture at 15° is added dropwise over 30 min a solution of diaryl ketone **1** (10 mmol) in dry dichloromethane (30 ml). The mixture is stirred under nitrogen at 20–25° for 15–30 h (to complete dissolution of the pellets). Additional sodium borohydride pellets can be added at this point if necessary (T.L.C. analysis). The mixture is diluted with water, cooled in an ice bath, made basic with sodium hydroxide pellets, and extracted with ether. The ether extract is washed (water, brine), dried (anhydrous sodium sulfate), and concentrated in vacuo. The crude product is analyzed by T.L.C. or G.L.C. and, depending on the purity, either distilled in vacuo or subjected to column chromatography (silica gel or neutral alumina) and then distilled in vacuo to give the yields shown in the Table. Solid products can be purified by crystallization. In either case, the purified products are homogeneous by T.L.C. or >95% by G.L.C.

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