Nucleophilic Aromatic Substitution on Tricarbonyl(halogenoarene)chromium Complexes: A New Synthesis of *O*-Arylhydroxylamines

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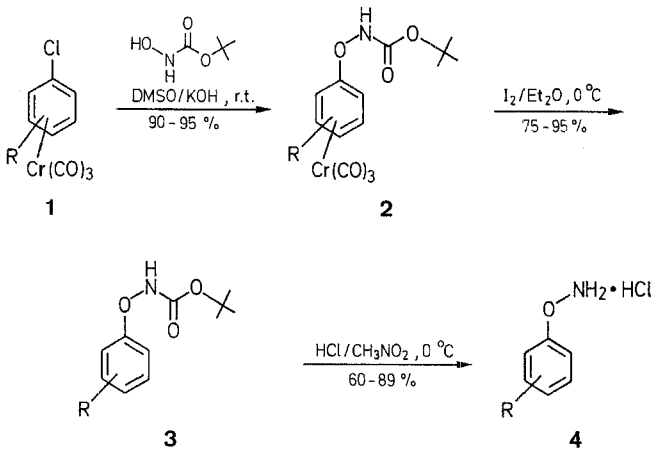
A series of *O*-arylhydroxylamines **4** have been synthesized under mild conditions and in good yields by the reaction of tricarbonyl(halogenoarene)chromium complexes **1** with *N*-(*tert*-butyloxycarbonyl)hydroxylamine (*tert*-butyl *N*-hydroxycarbamate), followed by decomplexation and acidic hydrolysis of the *tert*-butyl *N*-(aryloxy)carbamates **3**.

O-Arylhydroxylamines are an interesting class of compounds due to their widespread use in organic synthesis, particularly as intermediates in the preparation of benzofurans,[1,2] hydroxybiphenyls[3] and catechols.[4]

O-Arylhydroxylamines themselves have found some applications as growth factors for vegetables;[5] however, not many convenient methods for their synthesis are reported and most of them allow only the preparation of a narrow range of derivatives in low yields.[6,7] Only recently, two methods have been proposed to synthesize some previously unavailable substituted phenoxyamines, by *O*-amination of a range of phenols with 2,4-dinitrophenoxyamine or with mesitylene sulfonylhydroxylamine.[4,8]

In a previous work, we reported the synthesis of a number of *O*-aryloximes[9] with a large substitution pattern on the aromatic ring; the reaction was performed on tricarbonyl(halogenoarene)chromium complexes with the potassium salts of ketoximes. These results prompted us to extend our *O*-aryloxime synthesis to the preparation of *O*-arylhydroxylamines, by reacting the tricarbonylchromium activated halogenoarenes with an appropriate nucleophilic reagent. In the present paper, we wish to report our findings, which have led to an easy and efficient synthesis of the title compounds, carrying both electron withdrawing and electron donating substituents on the aryl ring. The aromatic nucleophilic substitution on tricarbonyl(halogenoarene)chromium complexes **1** with the *in situ* generated oxygen anion of *N*-*tert*-butyloxycarbonylhydroxylamine leads to the tricarbonyl [(*tert*-butyloxycarbonylaminoxy)arene]chromium complexes **2**. Iodine decomplexation of **2** followed by acid hydrolysis of the *tert*-butyl *N*-(aryloxy)carbamates **3** gives the hydrochlorides of the *O*-arylhydroxylamines **4** in overall high yields. Among the tricarbonylchromium complexes, **2b, d, e, g** could not be isolated due to their instability.



1–4	R	1–4	R	1–4	R
a	H	**d**	4-Cl	**f**	2,5-CH_3
b	2-Cl	**e**	3-OCH_3	**g**	2-CH_3
c	3-Cl				

The present reaction scheme provides a convenient access to a large number of *O*-arylhydroxylamines, of which **4b, f** were hitherto unknown. Furthermore, the intermediate *tert*-butyl *N*-(aryloxy)carbamates **3a–g** are rather stable and can be stored at 25 °C for an extended period. They therefore constitute useful and easily-handled precursors of *O*-arylhydroxylamines.

^{1}H-NMR spectra were recorded on a Varian EM 390 spectrometer. All melting points are uncorrected. The microanalyses were performed on Perkin-Elmer 240 Elemental Analyzer. *N*-tert-Butyloxycarbonyl)hydroxylamine was purchased from Fluka. Reagents and quality solvents were used without further purification. The tricarbonyl(halogenoarene)chromium complexes **1a–g** were prepared according to literature procedures.[11]

Table 1. Tricarbonyl[(*tert*-butyloxycarbonyl)aminoxyarene]chromium Complexes **2a, c, f**

Product	Yield (%)	mp (°C)	Molecular Formula[a]	^{1}H-NMR ($CDCl_3$/TMS) δ
2a	96	85–86 (dec)	$C_{14}H_{15}CrNO_6$ (345.3)	1.5 (s, 9H, *t*-C_4H_9); 4.8–5.1 (m, 1H_{arom}); 5.3–5.7 (m, 4H_{arom}); 7.6 (s, 1H, NH)
2c	95	98–99 (dec)	$C_{14}H_{14}ClCrNO_6$ (379.7)	1.6 (s, 9H, *t*-C_4H_9); 5.1–5.7 (m, 4H_{arom}); 7.7 (s, 1H, NH)
2f	89	90–91 (dec)	$C_{16}H_{19}CrNO_6$ (373.3)	1.5 (s, 9H, *t*-C_4H_9); 2.1 (s, 6H, 2 × CH_3); 4.8–5.6 (m, 3H_{arom}); 7.6 (s, 1H, NH)

[a] Satisfactory microanalyses obtained: C ±0.17, H ±0.03, N ±0.09.

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Table 2. *tert*-Butyl *N*-(Aryloxy)carbamates **3a–g** Prepared

Product	Yield (%)	mp (°C) (solvent) or bp (°C)/mbar	Molecular Formula[a]	^{1}H-NMR ($CDCl_3$/TMS) δ
3a	90	68–69 (i-Pr_2O)	$C_{11}H_{15}NO_3$ (209.2)	1.5 (s, 9H, t-C_4H_9); 6.7–7.3 (m, 5H_{arom}); 7.8 (s, 1H, NH)
3b	75	78–79 (n-pentane)	$C_{11}H_{14}ClNO_3$ (243.7)	1.5 (s, 9H, t-C_4H_9); 6.8–7.4 (m, 4H_{arom}); 7.8 (s, 1H, NH)
3c	82	130–135/0.3	$C_{11}H_{14}ClNO_3$ (243.7)	1.5 (s, 9H, t-C_4H_9); 6.8–7.3 (m, 4H_{arom}); 7.9 (s, 1H, NH)
3d	90	82–85/0.13	$C_{11}H_{14}ClNO_3$ (243.7)	1.5 (s, 9H, t-C_4H_9); 6.8–7.2 (m, 4H_{arom}); 7.8 (s, 1H, NH)
3e	95	100–110/0.4	$C_{12}H_{17}NO_4$ (239.3)	1.5 (s, 9H, t-C_4H_9); 3.7 (s, 3H, OCH_3); 6.3–7.0 (m, 4H_{arom}); 8.3 (s, 1H, NH)
3f	80	135–140/0.5	$C_{13}H_{19}NO_3$ (237.3)	1.5 (s, 9H, t-C_4H_9); 2.2 (s, 3H, CH_3); 2.4 (s, 3H, CH_3); 6.6–7.0 (m, 3H_{arom}); 7.7 (s, 1H, NH)
3g	88	125–130/0.3	$C_{12}H_{17}NO_3$ (223.3)	1.5 (s, 9H, t-C_4H_9); 2.3 (s, 3H, CH_3); 6.7–7.2 (m, 4H_{arom}); 8.1 (1, 1H, NH)

[a] Satisfactory microanalyses obtained: C ±0.33, H ±0.30, N ±0.23.

Table 3. *O*-Arylhydroxylamine Hydrochlorides **4a–g** Prepared

Product	Yield[a] (%)	mp (°C)	Molecular Formula[b] or Lit. bp (°C)/mbar[c]	^{1}H-NMR ($CDCl_3$/TMS) δ
4a	80 (54)[4]	121–122	67/6[4]	7.0–7.5 (m, 5H_{arom}); 9.9–10.4 (br s, 3H, NH_3)
4b	60	90–92	$C_6H_7Cl_2NO$ (180.0)	6.7–7.4 (m, 4H_{arom}); 7.8–8.0 (br s, 3H, NH_3)
4c	89 (73)[4]	132–133	69/2[4]	7.1–7.4 (m, 4H_{arom}); 9.8–10.2 (br s, 3H, NH_3)
4d	80 (74)[4]	122–123	66/2[4]	7.2–7.6 (m, 4H_{arom}); 8.2–8.7 (br s, 3H, NH_3)
4e	75 (30)[2]	118–121	$C_7H_{10}ClNO_2$[d,2] (175.6)	3.75 (s, 3H, OCH_3); 6.6–7.4 (m, 4H_{arom}); 10.2–10.6 (br s, 3H, NH_3)
4f	65	154–156	$C_8H_{12}ClNO$ (173.6)	2.0 (s, 3H, CH_3); 2.35 (s, 3H, CH_3); 6.6–7.1 (m, 3H_{arom}); 8.1–8.6 (br s, 3H, NH)
4g	75 (15)[10]	85–86	$C_7H_{10}ClNO$[d,10] (159.6)	2.2 (s, 3H, CH_3); 7.0–7.4 (m, 4H_{arom}); 8.0–8.3 (br s, 3H, NH_3)

[a] Yields of *O*-Arylhydroxylamines reported in literature are shown in parenthesis.
[b] Satisfactory microanalyses obtained: C ±0.35, H ±0.09, N ±0.14.
[c] Boiling points of free bases.
[d] Boiling point not reported.

Tricarbonyl[(*tert*-butyloxycarbonyl)aminoxyarene]chromium Complexes 2a–g; General Procedure:

The appropriate tricarbonyl(halogenoarene)chromium complex **1**[11] (10.0 mmol) is added under nitrogen atmosphere to a stirred solution of *N*-*tert*-butyloxycarbonylhydroxylamine (1.46 g, 11.0 mmol) and powdered KOH (0.62 g, 11.0 mmol) in DMSO (50 mL). The yellow solution is stirred at room temperature for 2 h. The mixture is diluted with ice-cold water (50 mL), extracted with ether (3 × 20 mL), dried (Na_2SO_4), and filtered over celite. Evaporation of the solvent gives the crude product. Compounds **2a, c, f** are purified by crystallization from diisopropyl ether (Table 1). The ether solutions of **2b, d, e, g** are directly used for decomplexation.

Decomplexation of 2a–g to *tert*-Butyl *N*-(Aryloxy)carbamates 3a–g; General Procedure:

A solution of **2** (10 mmol) in ether (60 mL) is treated with iodine (3.8 g, 15 mmol) at 0 °C. After stirring for 5 h, the excess iodine is destroyed with a sat. aq. solution Na_2SO_3, the ether layer dried (Na_2SO_4), filtered with charcoal over celite and evaporated. The crude products **3a–g** are sufficiently pure for the subsequent reaction, but can be purified by distillation under reduced pressure in the case of **3c–g**, or by crystallization for **3a, b**. (Table 2)

***O*-Arylhydroxylamine Hydrochlorides 4a–g; General Procedure:**

tert-Butyl *N*-(aryloxy)carbamate **3** (1 mmol) is dissolved in nitromethane (3 mL), cooled to 0 °C, and treated with an excess of sat. ethereal solution of dry HCl (5 mL). The mixture is stirred at 0 °C for 1 h and filtered. The precipitate is washed with diisopropyl ether to give pure *O*-arylhydroxylamine hydrochlorides (Table 3).

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