1,2-Dihydroquinolin-2-one (carbostyril) anions as bidentate nucleophiles in their reactions with aryllead triacetates: synthesis of 1-aryl- and 3-aryl-tetrahydroquinoline-2,5,8-triones

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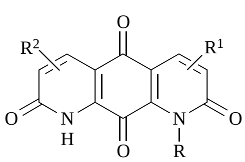
Arylation of 1,2-dihydroquinolin-2-one, 5-methoxy-, 8-methoxy- and 5,8-dimethoxy-1,2-dihydroquinolin-2-one anions with *p*-tolyllead triacetate has been studied. The reactions take place on nitrogen or on the C-3 position, depending on steric and electronic factors. The aryl derivatives thus obtained have been oxidized to the corresponding 3-aryltetrahydroquinoline-2,5,8-triones.

During the course of our research on the synthesis of antitumour 1,8-diazaanthracene-2,9,10-triones **1**,[1] designed as analogues of the natural antifolate diazaquinomycin A **2**,[2] we found that 5-aryl derivatives of **1** exhibit very potent and selective activity towards certain types of solid tumours. On this basis, the introduction of aryl substituents at other positions of **1** was planned. Since our main synthetic approach to structure **1** involves hetero Diels–Alder reactions between 1-dimethylamino-1-aza dienes[3] and tetrahydroquinoline-2,5,8-triones,[4] the preparation of compounds **3** became necessary. In this paper we examine their synthesis through direct arylation of carbostyrils (1,2-dihydroquinolin-2-ones) followed by oxidation.



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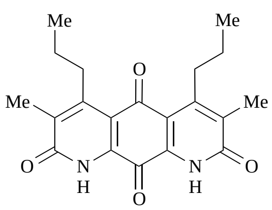

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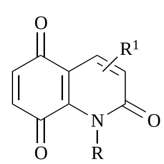


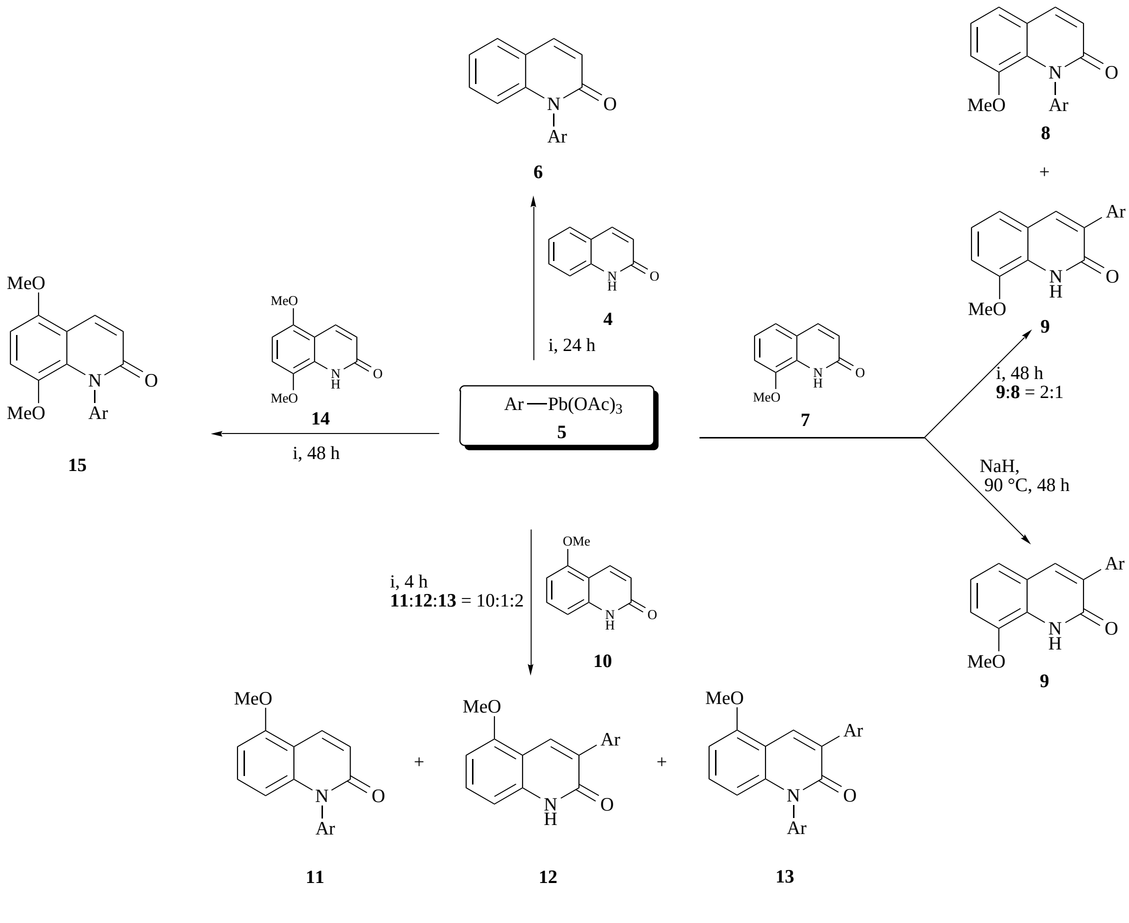
3 R, R^1 = H, Ar

Aryllead triacetates[5] behave as arylating reagents towards a variety of C-nucleophiles, including enamines,[6] phenols,[7] silyl enol ethers,[8] nitroalkane anions,[9] β-dicarbonyls[10] and other compounds with acidic methylene groups.[11] More recently, their ability to undergo copper-catalysed reactions with N-nucleophiles such as amines,[12] azoles[13] and amides[14] has been established. Therefore, we considered it of interest to study their reaction with carbostyrils as a means for the preparation of compounds **3**. In particular, and following our studies on the *N*-arylation of amide anions,[14] we were interested in ascertaining if the nitrogen atom in carbostyril reacts similarly to other amidic substrates.

Our first experiment seemed to confirm this behaviour, and thus treatment of carbostyril itself (compound **4**) with sodium hydride, *p*-tolyllead triacetate **5**[15] and copper(II) acetate afforded the corresponding *N*-arylation product **6** (62%). Since the preparation of quinones **3** required a final oxidation step that would benefit from the presence of oxygen functions at C-5 and C-8,[16] we studied the arylation of 8-methoxycarbostyril **7**.[17] In contrast to the result obtained for **4**, treatment of compound **7** with **5** in the presence of sodium hydride and copper(II) acetate gave the expected *N*-arylated compound **8**, but the major product was **9** from arylation at C-3 (**9**:**8** = 2:1). Suppression of the copper catalyst, which is essential for the *N*-arylation process, allowed the isolation of **9** as the only product, although the reaction could not be carried to completion. In the case of 5-methoxycarbostyril **10**,[18] three reaction products were obtained after 4 h at 90 °C, namely the 1-aryl- (**11**), 3-aryl- (**12**) and the 1,3-diaryl (**13**) derivatives, with **11** as the major product (**11**:**12**:**13** = 10:1:2). Longer reaction times led to an increase in the proportion of the diaryl derivative **13** at the expense of **11** but, again, complete conversion could not be achieved. Finally, 5,8-dimethoxycarbostyril **14**[19] was arylated only on nitrogen to yield compound **15** (Scheme 1).

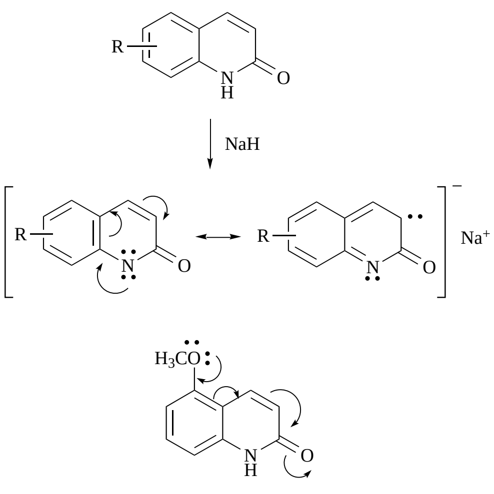
These results can be rationalized on the basis of a combination of electronic and steric effects. Arylation at C-3 is explained through delocalization of the nitrogen negative charge, allowing C-3 to compete with nitrogen for electrophiles, particularly if the latter position is hindered as in 8-methoxycarbostyril or 5,8-dimethoxycarbostyril.[20] The presence of a 5-OMe group inhibits the arylation of C-3 because its conjugation with the C-2 carbonyl prevents the above mentioned delocalization of the nitrogen negative charge onto C-3 (Scheme 2). Combination of this effect with steric hindrance explains the very low reactivity of 5,8-dimethoxycarbostyril. It is worth mentioning at this point that the reactivity described above has similarities with the one observed for carbostyrils in the presence of butyllithium, although in the latter case formation of a 1,3-dianion is needed for reactions with electrophiles to take place[21] because lithiation at C-3 requires assistance from the neighbouring C-2 oxygen.

Finally, the arylated carbostyrils were oxidized to the corresponding quinones (Scheme 3). Thus, 1-(*p*-tolyl)tetrahydroquinoline-2,5,8-trione **3a** was obtained either by direct oxidative demethylation of the 5,8-dimethoxy derivative **15** with cerium ammonium nitrate (CAN) or (in better yield) by demethylation of compound **8** with boron tribromide to **16** followed by oxidation with potassium nitrosodisulfonate (Fremy's salt). An attempt to prepare **3a** through a similar oxidation of compound **11** led only to a low yield of the *o*-quinone **18**, probably owing to steric hindrance on the C-8 position of the intermediate demethylated derivative **17**. Assignment of the *o*- and *p*-quinone structures was based on ^{13}C NMR data; the *o*-quinone gave two very close carbonyl resonances at $\delta = 179.01$ and



Ar = C_6H_4Me-*p*

Scheme 1 *Reagents and conditions:* i, NaH, $Cu(OAc)_2$, 90 °C



Scheme 2

178.32 ppm, while in the *p*-quinone the C-8 signal was more deshielded, appearing at 182.58 ppm, and C-5 resonating at 179.56 ppm.[22]

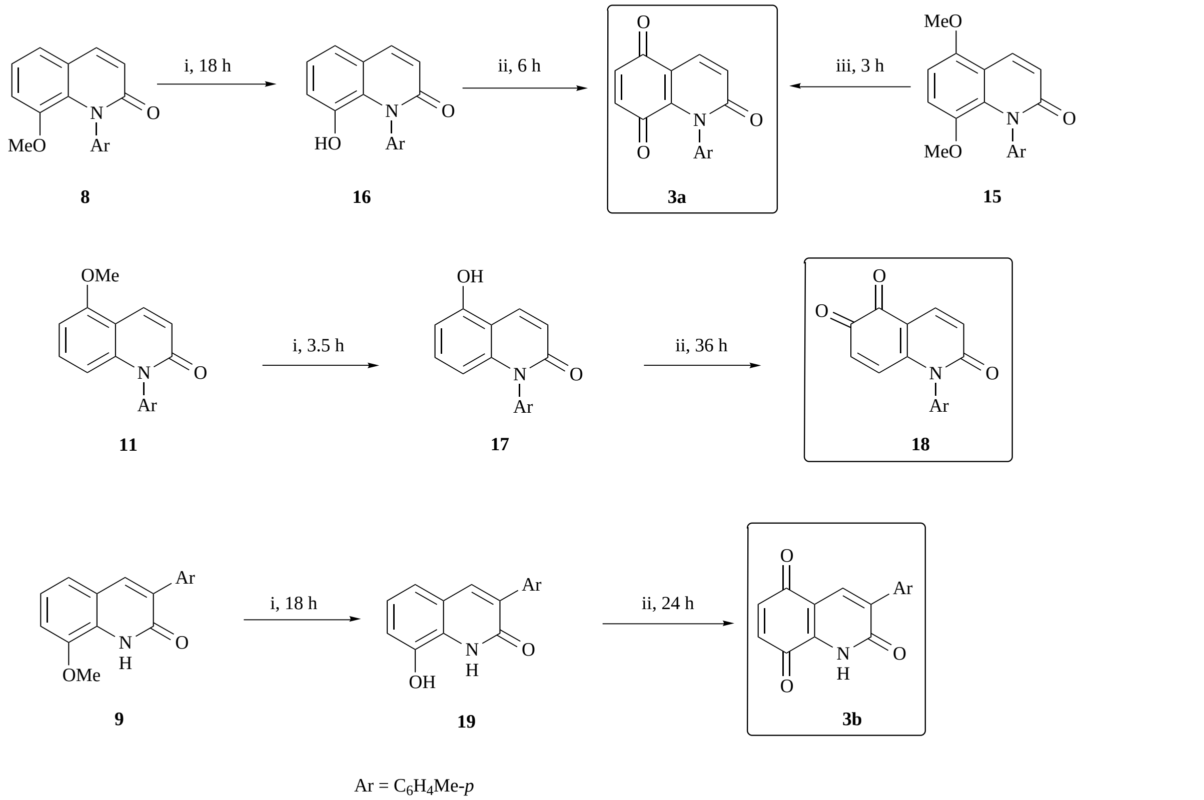
A similar demethylation–oxidation sequence allowed preparation of 3-(*p*-tolyl)tetrahydroquinoline-2,5,8-trione **3b** from compound **9** through the intermediacy of **19**.

Experimental

All reagents were of commercial quality (Aldrich, Fluka, SDS, Probus) and were used as received. Solvents (SDS, Scharlau) were dried and purified using standard techniques; the expression 'light petroleum' refers to the fraction boiling at 40–60 °C. *p*-Tolyllead triacetate was prepared according to reference 15 (**CAUTION:** organolead reagents are very toxic and must be handled with care). Reactions were monitored by thin layer chromatography, on aluminium plates coated with silica gel with a fluorescent indicator (Scharlau Cf 530 and Alugram Sil G/UV_{254}). Separations by flash chromatography were performed on silica gel (SDS 60 ACC, 230–400 mesh). Melting points were measured on a Reichert 723 hot-stage microscope or in open capillary tubes using a Büchi immersion apparatus, and are uncorrected. IR spectra were recorded on Perkin-Elmer 577 and Perkin-Elmer Paragon 1000 spectrophotometers, with solid compounds compressed into KBr pellets. NMR spectra were obtained on Bruker AC-250 (250 MHz for ^{1}H, 63 MHz for ^{13}C) and Varian VXR-300 (300 MHz for ^{1}H, 75 MHz for ^{13}C) spectrometers with $CDCl_3$ or [$^2H_6$]-DMSO as solvents. Exchangeable assignments are marked with the symbols * and **. *J* Values are given in Hz. NMR data of compounds **4**–**19** are summarized in Tables 1 and 2. Elemental analyses were determined by the Servicio de Microanálisis, Universidad Complutense, on a Perkin-Elmer 2400 CHN microanalyzer.

Arylation of carbostyril derivatives

General procedure. A solution of the appropriate carbostyril (77–400 mg, 0.38–2.286 mmol) in dry dichloromethane (2–3 ml) was added to a heated (90 °C) suspension of sodium hydride (16–100 mg, 0.41–2.51 mmol, 1.1 equiv.), from a 60% commercial dispersion in paraffins, pre-washed with 2 × 10 ml of dry light petroleum, in dry dichloromethane (3 ml). After the suspension had been heated at 90 °C for 15 min it was treated with a solution of *p*-tolyllead triacetate **5**[15] (0.20–1.20 g,



Scheme 3 *Reagents and conditions:* i, BBr_3, CH_2Cl_2, 35 °C; ii, Fremy's salt [$^{\bullet}ON(SO_3K)_2$], HSO_4NBu_4, $CHCl_3$–H_2O; iii, CAN, MeCN–H_2O, room temp.

0.41–2.51 mmol) and copper(II) acetate (10–15 mg) in dry dichloromethane (3–5 ml). The reaction mixture was heated at 90 °C for 4–48 h, during which time it slowly evaporated; the reaction mixtures, were however, never allowed to evaporate completely. The reaction mixture was then poured onto a stirred mixture of dilute aqueous hydrogen sulfide (20 ml) and chloroform (30 ml). The biphasic system was vigorously stirred at room temperature for 30 min and then filtered through a layer of Celite, which was washed with chloroform (3 × 25 ml). The combined chloroform layers were dried (Na_2SO_4) and evaporated, and the residue was purified by column chromatography eluting with a gradient from neat dichloromethane to neat diethyl ether. NMR data of compounds thus obtained are in Tables 1 and 2. Other data are given below.

1-(*p*-Tolyl)-1,2-dihydroquinolin-2-one 6. Starting from the quinolinone **4** (100 mg, 0.689 mmol), **6** (100 mg, 62%) was obtained after 24 h; mp 139–141 °C (from diethyl ether); ν_{max}/cm^{-1} 1656 (C=O) (Found: C, 81.4; H, 5.3; N, 5.7. $C_{16}H_{13}NO$ requires C, 81.7; H, 5.6; N, 5.95%).

Arylation of 8-methoxy-1,2-dihydroquinolin-2-one 7. Starting from the quinolinone **7** (400 mg, 2.286 mmol) and with a reaction time of 48 h, the following compounds were obtained: recovered **7** (285 mg), **8** (45 mg, 7%, 27% based on unrecovered starting material) and **9** (95 mg, 16%, 58% based on unrecovered starting material).

The same conditions when employed in the absence of copper acetate, starting from the quinolinone **7** (50 mg, 0.286 mmol), of which 40 mg was recovered, gave only compound **8** (10 mg, 13%, 66% based on unrecovered starting material).

8-Methoxy-1-(*p*-tolyl)-1,2-dihydroquinolin-2-one **8**. Mp 163–165 °C (from diethyl ether); ν_{max}/cm^{-1} 1600 (C=O) and 1256 (OMe) (Found: C, 75.3; H, 6.45; N, 4.5. $C_{17}H_{15}NO_2\cdot\frac{1}{2}C_4H_9O$ requires C, 75.5; H, 6.7; N, 4.6%).

8-Methoxy-3-(*p*-tolyl)-1,2-dihydroquinolin-2-one **9**. Mp 171–173 °C (from diethyl ether); ν_{max}/cm^{-1} 3460 (NH), 1648 (C=O) and 1268 (OMe) (Found: C, 75.3; H, 6.4; N, 4.5. $C_{17}H_{15}NO_2\cdot\frac{1}{2}C_4H_9O$ requires C, 75.5; H, 6.7; N, 4.6%).

Arylation of 5-methoxy-1,2-dihydroquinolin-2-one 10. Starting from the quinolinone **10** (150 mg, 0.86 mmol) and with a reaction time of 4 h, the following compounds were obtained: recovered **10** (80 mg), **11** (85 mg, 37%, 80% based on unrecovered starting material), **12** (8 mg, 4%, 7% based on unrecovered starting material) and **13** (20 mg, 7%, 13% based on unrecovered starting material).

5-Methoxy-1-(*p*-tolyl)-1,2-dihydroquinolin-2-one **11**. Mp 198–200 °C (from diethyl ether); ν_{max}/cm^{-1} 1653 (C=O) and 1265 (OCH_3) (Found: C, 76.9; H, 5.5; N, 5.1. $C_{17}H_{15}NO_2$ requires C, 77.0; H, 5.7; N, 5.3%).

5-Methoxy-3-(*p*-tolyl)-1,2-dihydroquinolin-2-one **12**. Mp 240–242 °C (from diethyl ether); ν_{max}/cm^{-1} 3429 (NH), 1646 (C=O) and 1262 (OCH_3) (Found: C, 76.75; H, 5.6; N, 5.0. $C_{17}H_{15}NO_2$ requires C, 77.0; H, 5.7; N, 5.3%).

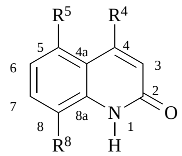
5-Methoxy-1,3-bis(*p*-tolyl)-1,2-dihydroquinolin-2-one **13**. Mp 214–216 °C (from diethyl ether); ν_{max}/cm^{-1} 1650 (C=O) and 1281 (OCH_3) (Found: C, 81.2; H, 5.9; N, 4.0. $C_{24}H_{21}NO_2$ requires C, 81.1; H, 5.95; N, 3.9%).

5,8-Dimethoxy-1-(*p*-tolyl)-1,2-dihydroquinolin-2-one 15. Starting from the quinolinone **14** (77 mg, 0.38 mmol), of which 53 mg was recovered, gave compound **15** (20 mg, 18%, 59% based on unrecovered starting material) after 48 h; mp 173–175 °C (from diethyl ether); ν_{max}/cm^{-1} 1663 (C=O) and 1266 (OCH_3) (Found: C, 72.95; H, 5.9; N, 4.7. $C_{18}H_{17}NO_3$ requires C, 73.2; H, 5.8; N, 4.7%).

Demethylation of 5- and 8-methoxy-carbostyril derivatives

General procedure. A 1 M solution of boron tribromide (3.2 equiv.) in dichloromethane was added to a solution of the appropriate methoxycarbostyril (0.11–0.23 mmol) in dichloromethane (5–15 ml) at 0 °C. The solution was allowed to warm to room temperature over 30 min after which it was stirred at 35–40 °C for 3.5–18 h. The reaction mixture was evaporated and the residue was suspended in chloroform (20 ml) and the solution washed with water (2 × 10 ml). The aqueous phase was extracted with ethyl acetate (2 × 15 ml) and the combined

Table 1 ^{1}H NMR data (250 MHz, $CDCl_3$) of methoxy- and hydroxycarbostyril derivatives

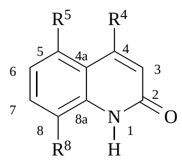


R^4 = H, Me
R^5, R^8 = H, OH, OMe

Cmpd.	NH	3-H	4-H	5-H	6-H	7-H	8-H	$OR^{5,8}$	N^1-Ar 2′6′-H	3′5′-H	CH_3-Ar
6	*a*	6.79 (d, *J* 9.6)	7.78 (d, *J* 9.6)	7.59 (dd, *J* 7.7, 1.3)	7.23–7.15 (m)	7.34 (td, *J* 8.6, 1.5)	6.70 (d, *J* 8.3)	—	7.17 (d, *J* 8.2)	7.40 (d, *J* 8.1)	2.47 (s)
8	*a*	6.73 (d, *J* 9.4)	7.69 (d, *J* 9.4)	7.19 (dd, *J* 10.2, 2.1)	7.13 (t, *J* 7.6)	6.92 (dd, *J* 7.5, 1.9)	—	3.28 (s)	7.08 (d, *J* 8.2)	7.22 (d, *J* 9.7)	2.40 (s)
9	9.30 (br s)	—	7.81 (s)	7.18 (dd, *J* 8.0, 1.4)	7.12 (t, *J* 7.8)	6.94 (dd, *J* 7.6, 1.4)	—	3.97 (s)	7.24 (d, *J* 7.9)	7.63 (d, *J* 8.1)	2.38 (s)
11	—	6.72 (d, *J* 9.8)	8.23 (d, *J* 9.8)	—	6.62 (d, *J* 8.1)	7.23 (t, *J* 8.3)	6.25 (d, *J* 8.5)	3.96 (s)	7.14 (d, *J* 8.2)	7.38 (d, *J* 8.1)	2.45 (s)
12	11.60 (br s)	—	8.24 (s)	—	6.55 (d, *J* 8.1)	7.31 (t, *J* 8.2)	6.87 (d, *J* 8.2)	3.88 (s)	7.21 (d, *J* 8.0)	7.66 (d, *J* 8.0)	2.34 (s)
13[b]	*a*	—	8.38 (s)	—	6.62 (d, *J* 8.1)	7.29–7.15 (m)	6.25 (d, *J* 8.6)	3.96 (s)	7.22* (d, *J* 8.0)	7.36 (d, *J* 8.0)	2.44 (s)
15	*a*	6.68 (d, *J* 9.8)	8.19 (d, *J* 9.8)	—	6.49 (d, *J* 8.8)	6.89 (d, *J* 8.8)	—	3.89 (s) 3.19 (s)	7.08 (d, *J* 8.3)	7.22 (d, *J* 9.1)	2.39 (s)
16	*a*	7.04 (d, *J* 9.5)	7.95 (d, *J* 9.5)	7.43–7.31 (m)	7.28 (t, *J* 7.5)	7.43–7.31 (m)	—	10.17 (br s)	7.61 (d, *J* 8.1)	7.43–7.31 (m)	2.36 (s)
17	*a*	6.56 (d, *J* 9.7)	8.27 (d, *J* 9.7)	—	6.58 (d, *J* 7.4)	6.53–6.89 (m)	5.97 (d, *J* 8.4)	*a*	6.96 (d, *J* 8.0)	7.08 (d, *J* 8.0)	2.11 (s)
19	9.27 (br s)	—	8.12 (s)	7.49 (dd, *J* 7.6, 1.1)	7.23 (t, *J* 7.8)	7.38* (d, *J* 8.0)	—	9.27 (br s)	7.39* (d, *J* 8.0)	8.13 (d, *J* 8.0)	2.38 (s)

[a] Not detected. [b] Signals due to the 3-(*p*-tolyl) group: 7.72 (d, *J* 7.9, 3″,5″-H), 7.17 (d, *J* 7.9, 2″,6″-H), 2.36 (s, CH_3).

Table 2 ^{13}C NMR data (63 MHz, $CDCl_3$) of methoxy- and hydroxycarbostyril derivatives



R^4 = H, Me
R^5, R^8 = H, OH, OMe

Compd.	OCH_3	C-2	C-3	C-4	C-4a	C-5	C-6	C-7	C-8	C-8a	C(4′)-CH_3	C-1′	C-2′,6′	C-3′,5′	C-4′
4[a]	—	162.1	121.9*	140.3	119.1	127.9	121.8*	130.4	115.2	138.9	—	—	—	—	—
6	—	162.6	122.4*	139.8	120.4	128.4	122.3*	130.2	116.2	141.4	21.4	139.0	128.5	131.0	135.0
7	56.1 (C-8)	162.2	122.2*	140.5	120.0	119.6	122.7*	110.2	145.6	128.6	—	—	—	—	—
8	56.8 (C-8)	163.3	122.3*	140.0	116.9	121.4	122.8*	115.0	147.8	128.6	21.2	139.4	127.2	128.9	136.8
9	55.9 (C-8)	162.2	133.0	137.2	120.3	119.5	122.0	109.4	146.0	133.4	21.2	127.9	128.5*	128.9*	138.0
10[b]	56.0 (C-5)	162.1	120.7	134.3	109.5	155.7	102.8	131.6	108.0	140.3	—	—	—	—	—
11	56.0 (C-5)	162.6	120.4	134.0	111.0	156.1	102.6	130.5	108.7	142.4	21.4	138.6	128.3	130.7	135.2
12	55.8 (C-5)	163.2	133.6	132.7	111.3	156.0	102.6	130.8	108.1	139.0*	21.4	128.9	128.8**	128.9**	137.7*
13[c]	55.8 (C-5)	161.8	133.8	131.1	111.3	156.2	102.6	130.1	108.6	141.8	21.2	138.5	128.5	130.6	135.9
14	56.3 (C-5) 55.9 (C-8)	162.3	121.0	135.6	111.1	149.9	101.4	110.5	139.7	129.6	—	—	—	—	—
15	58.2 (C-5) 55.9 (C-8)	163.4	120.7	134.2	112.8	150.6	102.9	117.2	141.8	132.4	21.2	139.2	127.1	128.9	136.9
16	—	163.0	123.0	140.6	117.1	146.5	123.2	119.8	*d*	130.2	20.7	140.2	128.6*	128.7*	136.3
17	—	162.4	119.4	135.0	110.8	155.8	106.8	131.1	107.5	143.0	21.9	138.2	128.8	130.5	135.9
19	—	161.4	134.0	137.1	120.9	118.1	121.7	114.1	144.3	132.4	20.5	128.5	128.4*	128.8*	135.4

[a] In [$^2H_6$]-DMSO. [b] Data from reference 18*b*. [c] Signals due to the 3-(*p*-tolyl) group: 21.2 [C(4′)-Me], 128.8 (C-1″), 128.6 (C-2″,6″), 128.9 (C-3″,5″), 137.7 (C-4″). [d] Not detected.

organic layers were dried (Na_2SO_4) and evaporated. The residue was purified by column chromatography on silica gel, eluting with ethyl acetate. NMR data of the hydroxycarbostyrils **16**, **17** and **19** are given in Tables 1 and 2. Other data are given below.

8-Hydroxy-1-(*p*-tolyl)-1,2-dihydroquinolin-2-one **16**. Starting from compound **8** (40 mg, 0.15 mmol) and with a reaction time of 3.5 h, compound **16** (34 mg, 92%) was obtained; mp 301–303 °C (from ethyl acetate); ν_{max}/cm^{-1} 3277 (OH) and 1637 (C=O) (Found: C, 76.6; H, 5.0; N, 5.35. $C_{16}H_{13}NO_2$ requires C, 76.5; H, 5.2; N, 5.6%).

5-Hydroxy-1-(*p*-tolyl)-1,2-dihydroquinolin-2-one **17**. Starting from compound **11** (30 mg, 0.11 mmol) and with a reaction time of 18 h, compound **17** (28 mg, 99%) was obtained; mp >300 °C (from ethyl acetate); ν_{max}/cm^{-1} 3421 (OH, NH) and 1624 (C=O) (Found: C, 76.7; H, 4.9; N, 5.4. $C_{16}H_{13}NO_2$ requires C, 76.5; H, 5.2; N, 5.6%).

8-Hydroxy-3-(*p*-tolyl)-1,2-dihydroquinolin-2-one **19**. Starting from compound **9** (60 mg, 0.23 mmol) and with a reaction time of 18 h, compound **19** (55 mg, 97%) was obtained; mp 285–286 °C (from ethyl acetate); ν_{max}/cm^{-1} 3446 (OH, NH) and 1641 (C=O) (Found: C, 76.7; H, 5.4; N, 5.4. $C_{16}H_{13}NO_2$ requires C, 76.5; H, 5.2; N, 5.6%).

Fremy's salt oxidation of hydroxycarbostyrils

General procedure. To a magnetically stirred solution of each of compounds **16**, **17** or **19** (32–47 mg, 0.12–0.19 mmol) in chloroform (10–20 ml) and methanol (0–1 ml) at 0 °C was dropwise added a solution containing potassium nitrosodisulfonate (Fremy's salt; 1.4–6.2 equiv.), trihydrated sodium acetate (28–51 mg, 2 equiv.) and tetrabutylammonium hydrogen sulfate (21–48 mg, 0.6–1.25 equiv.) in water (8–13 ml). After completion of the addition, the system was allowed to reach room temperature; it was then heated at 35–40 °C for 24–36 h, whilst being vigorously stirred. After this, the organic layer was separated and the aqueous phase was extracted with chloroform (20 ml). The combined organic layers were dried (Na_2SO_4) and evaporated. The residue was dissolved in chloroform (20 ml) and this solution was washed with water (2 × 10 ml), dried (Na_2SO_4) and evaporated to yield the pure quinones **3a**, **18** and **3b**, respectively.

1-(*p*-Tolyl)-1,2,5,8-tetrahydroquinoline-2,5,8-trione 3a. Starting from compound **16** (28 mg, 0.11 mmol), Fremy's salt (1.4 equiv.) and tetrabutylammonium hydrogen sulfate (0.6 equiv.) with a reaction time of 6 h, compound **3a** (19 mg, 64%) was obtained; mp 199–201 °C (from ethyl acetate); ν_{max}/cm^{-1} 1685 (C=O, *p*-quinone), 1654 [C(2)=O]; δ_H($CDCl_3$; 250 MHz) 8.05 (1 H, d, *J* 9.6, 4-H), 7.30 (2 H, d, *J* 8.2, 3′,5′-H), 7.00 (2 H, d, *J* 8.3, 2′,6′-H), 6.93 (1 H, d, *J* 9.6, 3-H), 6.82 (1 H, d, *J* 10.2, 7-H), 6.64 (1 H, d, *J* 10.2, 6-H) and 2.43 (3 H, s, 4′-Me); δ_C($CDCl_3$; 63 MHz) 182.58 (C-8), 179.56 (C-5), 162.26 (C-2), 139.09 (C-1′), 138.74 (C-8a), 137.03 (C-4), 135.41* (C-6), 135.34 (C-4′), 134.86* (C-7), 130.08 (C-3′,5′), 126.62 (C-2′,6′), 126.37 (C-3), 117.15 (C-4a) and 21.28 [C(4′)-Me] (Found: C, 69.7; H, 4.8; N, 4.3. $C_{16}H_{11}NO_3 \cdot \frac{1}{2}C_4H_8O_2$ requires C, 69.9; H, 4.9; N, 4.5%).

1-(*p*-Tolyl)-1,2,5,6-tetrahydroquinoline-2,5,6-trione 18. Starting from compound **17** (32 mg, 0.12 mmol), Fremy's salt (6.2 equiv.) and tetrabutylammonium hydrogen sulfate (1.25 equiv.) with a reaction time of 36 h, compound **18** (7 mg, 21%) was obtained; mp 172–174 °C; ν_{max}/cm^{-1} 1694 (C=O, *o*-quinone), 1648 [C(2)=O]; δ_H($CDCl_3$; 250 MHz) 8.06 (1 H, d, *J* 9.6, 4-H), 7.41 (2 H, d, *J* 8.2, 3′,5′-H), 7.16 (2 H, d, *J* 8.2, 2′,6′-H), 6.88 (1 H, d, *J* 10.8, 7-H), 6.72 (1 H, d, *J* 9.6, 3-H), 6.34 (1 H, d, *J* 10.8, 8-H) and 2.47 (3 H, s, 4′-Me); δ_C($CDCl_3$; 63 MHz) 179.01* (C-5), 178.32* (C-6), 162.07 (C-2), 147.00 (C-8a), 140.46 (C-1′), 136.26 (C-4), 134.95 (C-8), 132.84 (C-4′), 130.88 (C-3′,5′), 130.73 (C-7), 127.92 (C-2′,6′), 121.54 (C-3), 114.05 (C-4a) and 21.42 [C(4′)-Me] (Found: C, 72.7; H, 4.3; N, 5.0. $C_{16}H_{11}NO_3$ requires C, 72.4; H, 4.2; N, 5.3%).

3-(*p*-Tolyl)-1,2,5,8-tetrahydroquinoline-2,5,8-trione 3b. Starting from compound **19** (47 mg, 0.19 mmol), Fremy's salt (1.4 equiv.) and tetrabutylammonium hydrogen sulfate (0.6 equiv.) with a reaction time of 24 h, compound **3b** (30 mg, 61%) was obtained; mp 211 °C (decomp); ν_{max}/cm^{-1} 3447 (NH), 1654 (C=O, *p*-quinone) and 1636 [C(2)=O]; δ_H($CDCl_3$; 250 MHz) 9.36 (1 H, br s, NH), 8.03 (1 H, s, H-4), 7.66 (2 H, d, *J* 8.1, 3′,5′-H), 7.25 (2 H, d, *J* 7.0, 2′,6′-H), 6.90 (2 H, d, *J* 1.2, H-6,7) and 2.38 (3 H, s, 4′-Me); δ_C($CDCl_3$; 63 MHz) 182.27 (C-8), 178.94 (C-5), 160.60 (C-2), 139.58 (C-1′), 138.21 (C-8a), 138.09 (C-4), 135.41 (C-4′), 134.82 (C-6), 131.62 (C-7), 131.45 (C-3), 129.06 (C-3′,5′), 128.39 (C-2′,6′), 115.22 (C-4a) and 21.26 [C(4′)-Me] (Found: C, 72.6; H, 4.1; N, 5.1. $C_{16}H_{11}NO_3$ requires C, 72.4; H, 4.2; N, 5.3%).

Alternative synthesis of 3a by cerium ammonium nitrate oxidation of compound 15

A mixture of the dimethoxycarbostyril **15** (16 mg, 0.054 mmol) in acetonitrile (2 ml) and water (1 ml) was heated at 40 °C until complete dissolution. To the solution thus obtained was added cerium ammonium nitrate (44 mg, 0.081 mmol, 1.5 equiv.) in one portion. The reaction mixture was stirred at room temperature for 3 h after which it was diluted with water and extracted with chloroform (3 × 20 ml). The combined extracts were washed with water (2 × 20 ml), dried (Na_2SO_4) and evaporated. The residue was purified by rapid chromatography on silica gel, eluting with diethyl ether to yield quinone **3b** (14 mg, 97%).

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