Transition Metal Catalyzed Oxidations; 4.[1] Improved Method for the Oxidation of 1- and 2-Naphthols to 1,2-Napthoquinones

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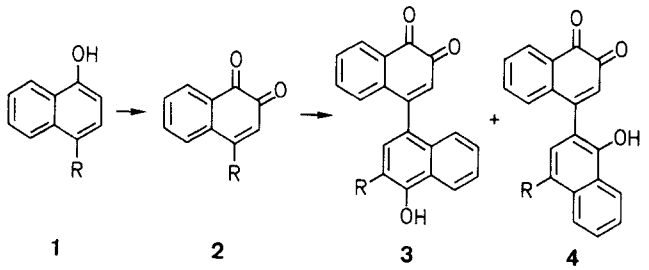
A specific oxidation of 1- and 2-naphthols to the corresponding 1,2-naphthoquinones can be achieved by slow addition of the preformed complex of the naphthols with titanium tetraisopropylate with a syringe pump to excess *tert*-butyl hydroperoxide (TBHP). A previously described method gave mainly coupling products from the Michael reaction.

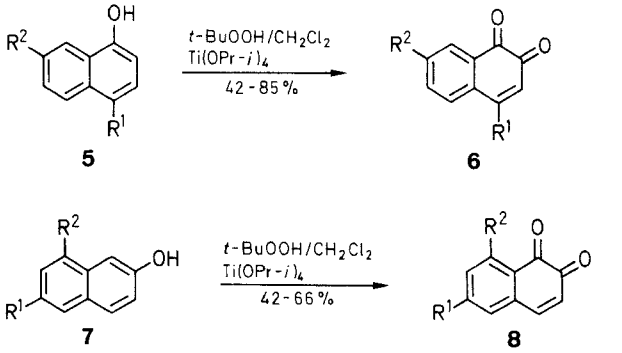
Recently we developed a new method for the specific oxidation of mono- and oligonuclear phenols to *ortho*-quinones using transition metal alcoholates such as titanium tetraisopropylate or zirconium tetraisopropylate and *tert*-butyl hydroperoxide (TBHP) or Mimoun's oxodiperoxo molybdenum complex, $[Mo(O_2)_2O] \cdot Py \cdot HMPT$.[2] The method produced exclusively the 1,2-oxidation products; a number of new and unstable donor- or acceptor-substituted *ortho*-quinones were prepared. However, in the naphthol series the method was limited to substrates sterically hindered by substituents at positions C-3, C-4 or C-5 to prevent the in situ Michael addition of the starting phenol **1** to the *ortho*-quinones **2**. This type of coupling reaction was also observed by other authors.[3-5] For instance, 1-naphthols of type **1** (R = H, Cl, Ac) mainly gave Michael adducts of type **3** and **4** (Scheme **A**). 2-Naphthols substituted at C-6 gave Michael adducts exclusively[2] (Table).



Scheme **A**

We now disclose a modified procedure in which four essential reaction parameters have been changed and the formation of coupling products, as the result of Michael additions, are almost completely suppressed. Our initial efforts were directed towards the replacement of the titanium catalyst by less active Lewis acids such as zirconium tetraisopropylate or $[Mo(O_2)_2O] \cdot Py \cdot HMPT$. This strategy was partially successful in some cases, increasing for instance the yield of 4-chloro-1,2-naphthoquinone (**6b**) from 4-chloro-1-naphthol (**5b**) from 5 to 21%[2] (Table). Titanium tetraisopropylate acetylacetonate also catalyzed the smooth oxygenation of naphthols to 1,2-naphthoquinones without formation of coupling products of structure **3** or **4**. However, side products resulted from the Michael addition of acetylacetonate to the *ortho*-quinone as observed earlier with the zirconium complex, zirconium diisopropylate diacetylacetonate.[2] The dropwise addition of a dilute solution of the naphthol to the oxidizing system transition metal/TBHP was tried next, but the coupling reaction of the highly reactive *ortho*-napthoquinone with the naphthol still occurred to a large extent. The decisive step was made by using a syringe pump to ensure the extremely slow and controlled addition of the naphthol to a solution of the transition metal and TBHP in dichloromethane. Further measures to decrease the concentration of the naphthols in solution by rapid conversion to the *ortho*-quinones, were the use of a threefold excess of TBHP, the replacement of the zirconium tetraisopropylate, or the molybdenum complex $[Mo(O_2)_2O] \cdot Py \cdot HMPT$ by the more reactive titanium tetraisopropylate catalyst, and running the reaction at room temperature and not at $-20\,^{\circ}C$. The best yields were obtained when a preformed complex of titanium tetraisopropylate and the corresponding naphthol in dilute dichloromethane solution was added to the TBHP solution over 5 to 20 hours. Any contact of this complex with steel needles must be strictly avoided.[6] Iron and chromium ions dissolved from the steel needle by metal exchange induced radical decomposition of the TBHP causing formation of some *para*-quinones and other side products.

The highly reactive *ortho*-naphthoquinones can easily be isolated in pure form by rapid filtration through a short column of silica gel. Longer contact with silica gel should be avoided particularly with the unstable 6-substituted 1,2-naphthoquinones **8a–c**. Three 1-naphthols **5a–c** and four 2-naphthols **7a–e** were converted by the new method to the corresponding 1,2-naphthoquinones **6a–c** and **8a–e**, respectively (Scheme **B**) (Table). The examples show that 1- and 2-naphthols that gave only Michael



5, 6	R^1	R^2	7, 8	R^1	R^2
a	H	H	a	PhCO	H
b	Cl	H	b	Ph_3C	H
c	H	OMe	c	Br	H
			d	H	OMe
			e	H	NHAc

Scheme **B**

adducts with the method published previously[2] can now be converted to pure *ortho*-naphthoquinones by direct oxygenation.

The ^{1}H-NMR spectra were measured at 400 MHz, the ^{13}C-NMR spectra at 100 MHz, and the coupling constants were determined by first order analysis.

Table. Oxidation of Naphthols to Naphthoquinones

Naphthol	Reaction Time (h)	Product	Yield (%)	mp (°C)	Molecular Formula[a] or Lit. mp (°C)	^{1}H-NMR ($CDCl_3$/TMS) δ, J(Hz)	^{13}C-NMR ($CDCl_3$/TMS) δ	MS *m/z* (%)
5a	18	**6a**	70	119	120–121[8]	–	–	–
5b	20	**6b**	85[b]	136	134–135[9]	–	–	–
5c	20	**6c**	42	151	165[10]	3.90 (s, 3H, OCH_3), 6.23 (d, 1H, $J_{3,4}$ = 10.1, H-3), 7.12 (dd, 1H, $J_{5,6}$ = 8.4, $J_{6,8}$ = 2.7, H-6), 7.28 (d, 1H, $J_{5,6}$ = 8.4, H-5), 7.38 (d, 1H, $J_{3,4}$ = 10.1, 1H, 4-H), 7.60 (d, 1H, $J_{6,8}$ = 2.7, H-8)	55.92 (q), 114.76 (d), 121.70 (d), 125.17 (d), 127.94 (s), 131.58 (d), 133.19 (s), 145.58 (d), 161.89 (s), 179.01 (s), 180.98 (s)	190 (M^+ + 2, 6), 188 (M^+, 20), 160 (M^+ − CO, 100), 145 (M^+ − CO, −CH_3, 33), 132 (M^+ − 2CO, 7)
7a[c]	20	**8a**	52	144	$C_{17}H_{10}O_3$ (262.3)	6.54 (d, 1H, $J_{3,4}$ = 10.1, H-3), 7.52–7.56 (m, 3H_{arom}), 7.67 (tt, 3H, 2H_{arom} + H-4 or H-5), 7.67 (tt, 1H_{arom}, J_o = 7.4, J_m = 1.3), 7.79–7.83 (m, 3H, 2H_{arom} + H-4 or H-5), 7.86 (dd, 1H, $J_{7,8}$ = 7.9, $J_{5,7}$ = 1.6, H-7), 8.22 (d, 1H, $J_{7,8}$ = 7.9, H-8)	128.76 (d), 128.83 (d), 130.07 (d), 130.08 (d), 130.67 (d), 133.45 (s), 133.57 (d), 134.91 (s), 136.15 (s), 143.86 (s), 144.51 (d), 178.48 (s), 180.28 (s), 194.80 (s)	264 (M^+ + 2, 13), 262 (M^+, 3), 234 (M^+ − CO, 100), 206 (M^+ − 2CO, 12), 187 (11), 178 (5), 157 (M^+ − PhCO, 52), 120 (11), 105 ($PhCO^+$, 73), 101 (17), 77 (34)
7b[d]	20	**8b**	66	181	$C_{29}H_{20}O_2$ (400.5)	6.37 (d, 1H, $J_{3,4}$ = 10.2, H-3), 7.20–7.32 (m, 17H, 15H_{arom} + H-4, 5), 7.43 (dd, 1H, $J_{7,8}$ = 8.2, $J_{5,7}$ = 1.9, H-7), 8.00 (d, 1H, $J_{7,8}$ = 8.2, H-8)	65.39 (s), 126.57 (d), 127.81 (d), 128.00 (d), 129.33 (s), 129.69 (d), 130.84 (d), 132.49 (d), 133.25 (d), 134.06 (s), 145.30 (s), 145.79 (d), 155.92 (s), 178.59 (s), 181.08 (s)	402 (M^+ + 2, 41), 400 (M^+, 5), 372 (M^+ − CO, 79), 344 (M^+ − 20, 34), 325 (M^+ + 2H, −Ph, 53), 295 (M^+ − Ph, −CO, 89), 265 (31), 263 (19), 243 (45), 239 (32), 217 (44), 189 (45), 165 (100), 134 (11), 107 (11), 91 (10), 77 (25)[e]
7c	5	**8c**	48	166	169–170[10]	6.49 (d, 1H, $J_{3,4}$ = 10.2, H-3), 7.39 (d, 1H, $J_{3,4}$ = 10.2, H-4), 7.55 (d, 1H, $J_{5,7}$ = 1.8, H-5), 7.67 (dd, 1H, $J_{7,8}$ = 8.2, $J_{5,7}$ = 1.8, H-7), 7.97 (d, 1H, $J_{7,8}$ = 8.2, H-8)	129.23 (d), 130.21 (s), 131.34 (s), 131.53 (d), 132.62 (d), 133.84 (d), 136.12 (s), 143.72 (d), 178.05 (s), 180.31 (s)	240 (M^+ + 2, 12), 238 (M^+ + 2, M^+, 19), 236 (M^+, 8), 210 (M^+ − CO, 99), 208 (M^+ − CO, 100), 182 (M^+ − 2CO, 39), 180 (M^+ − 2CO, 35), 101 (M^+ − 2CO, −Br, 34)[f]
7d	17	**8d**	42	156	153[11]	4.00 (s, 3H, OCH_3), 6.43 (br d, 1H, $J_{3,4}$ = 10, H-3), 6.96 (d, 1H, $J_{6,7}$ = 7.3, H-7), 7.11 (br d, 1H, $J_{5,6}$ = 8.5, H-5), 7.39 (d, 1H, $J_{3,4}$ = 10, H-4), 7.60 (dd, 1H, $J_{5,6}$ = 8.5, $J_{6,7}$ = 7.3, H-6)	56.39 (q), 115.40 (d), 119.28 (s), 123.05 (d), 127.88 (d), 136.75 (s), 137.07 (d), 145.86 (d), 162.99 (s), 177.68 (s), 180.85 (s)	190 (M^+ + 2, 24), 188 (M^+, 28), 160 (M^+ − CO, 87), 132 (M^+ − 2CO, 54), 131 (74), 102 (100)
7e	16	**8e**	58	162	162–165[12]	2.30 (s, 3H, OCH_3), 6.46 (d, 1H, J = 10, H-3), 7.05 (br d, 1H, $J_{6,7}$ = 7.2, H-7), 7.43 (d, 1H, J = 10, H-4), 7.62 (dd, 1H, $J_{5,6}$ = 8.8, $J_{6,7}$ = 7.2, H-6), 8.85 (br d, 1H, $J_{5,6}$ = 8.8, H-5), 11.87 (s, 1H, NH)	25.66 (q), 115.55 (s), 123.05 (d), 125.57 (d), 127.25 (d), 135.15 (s), 138.08 (d), 145.61 (s), 146.18 (d), 170.07 (s), 179.61 (s), 181.13 (s)	216 (M^+ + 1, 4), 215 (M^+, 20), 187 (M^+ − CO, 16)

[a] Satisfactory microanalyses obtained: C ±0.1, H ±0.28.

[b] Reported[2] yield using a) $Ti(OPr\text{-}i)_4$ as catalyst: 5%; b) using $Zn(OPr\text{-}i)_4$ as catalyst: 21%.

[c] IR(KBr): ν = 3063, 3038, 1704, 1674, 1656, 1594, 1577, 1447, 1421, 1320, 1291, 1278, 1244, 1198, 979, 957, 861, 790, 725, 696 cm^{-1}.
UV(MeOH): $\lambda_{max}(\log\varepsilon)$ = 208 (4.37), 266 (4.52), 312 (sh), 400 nm (sh).

[d] IR(KBr): ν = 3059, 3030, 1699, 1678, 1670, 1587, 1491, 1442, 1281, 1253, 862, 765, 742, 704 cm^{-1}.
UV(MeOH): $\lambda_{max}(\log\varepsilon)$ = 210 (4.67), 258 (4.42), 263 (sh), 355 nm (3.70).

[e] Inlet temperature: 120°C.

[f] Inlet temperature: 40°C.

Oxidation of Naphthols to Naphthoquinones, General Procedure:
A solution of TBHP (6.0 mmol) in dry CH_2Cl_2 (60 mL) and 3 Å molecular sieves (1 g) are placed in a three-necked 250 mL flask equipped with N_2 inlet and a septum through which a thin Teflon tube is introduced. The end of the tube is inserted into the solution. A solution of naphthol **5** or **7** (1 mmol) and Ti(OPr-*i*)$_4$ (0.31 mL, 1 mmol) in anhydrous CH_2Cl_2 (20 mL) is prepared under N_2 in a 50 mL flask. The mixture is then sucked into a 50 mL syringe and the vessel is rinsed with CH_2Cl_2 (3 × 10 mL). The Ti(OPr-*i*)$_4$ naphthol complex in CH_2Cl_2 (50 mL) is then continuously pressed into the vigorously stirred TBHP solution over a period of 5 to 20 h (Table) with the aid of the syringe pump (Perfusor secura FT, B. Braun, Melsungen FRG). The mixture is then rapidly filtered through a short column of silica gel (30 g) to remove the catalyst and polar products. The solvent is removed under reduced pressure and the residue is crystallized from Et_2O (Table).

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