Tautomerism

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Rediscovery, Isolation, and Asymmetric Reduction of 1,2,3,4-Tetrahydronaphthalene-1,4-dione and Studies of Its [Cr(CO)$_3$] Complex**

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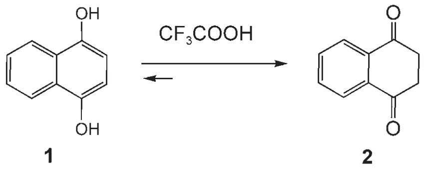
Melting 1,4-dihydroxynaphthalene (**1**) under vacuum generates a 2:1 equilibrium (1 h, 200 °C) with its tautomer 1,2,3,4-tetrahydronaphthalene-1,4-dione (**2**).[1] The conversion of **1** into **2** can also be effected in neat CF_3COOH.[2] The dione is kinetically stable at room temperature but rapidly converts into the phenolic form in the presence of a base. The keto form is implicated in the acid-catalyzed monoalkylation of **1**,[2] but surprisingly no chemistry of isolated **2** has ever been reported to our knowledge. We herein detail our results on a) an efficient access to pure diketone **2**, b) preliminary studies of the isomerization of **1** in solution, c) the asymmetric reduction of **2**, and d) the study of the corresponding [Cr(CO)$_3$] complexes.

As reported by Laatsch,[2] stirring **1** in trifluoroacetic acid afforded the tautomeric product **2** (Scheme 1). However, evaporation of this solvent from gram-amounts of **2** gave mixtures of **1** and **2.** As it is poorly soluble, **1** precipitates on concentration, which results in a displacement of the equilibrium. The addition of toluene to the reaction mixture before evaporation under vacuum solved this problem. The crude product consisted of a mixture of **1** and **2** in a ratio of 1:9, and recrystallization (*i*Pr$_2$O) afforded pure diketone **2** in 72% yield. The structure of **2** was confirmed by X-ray diffraction studies (Figure 1).[3]



Scheme 1. The equilibrium of the tautomers **1** and **2** in CF_3CO_2H overwhelmingly favors **2**. Tautomers **1** and **2** do not interconvert in apolar solvents at room temperature.

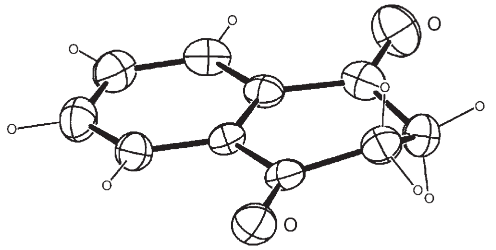
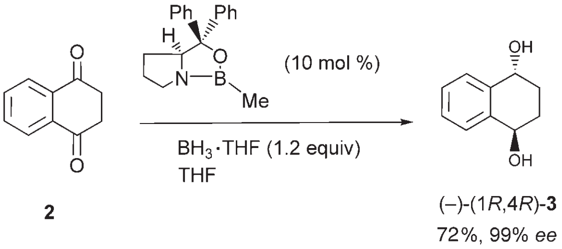


Figure 1. ORTEP view of the crystal structure of **2**. Ellipsoids are represented with 40% probability.

We also found that **1** equilibrates with **2** in degassed, dry benzene. This process requires heating to above 120 °C[6] and can be conveniently followed by ^{1}H NMR spectroscopic analysis at room temperature. Isomerization in benzene in a sealed NMR tube immersed in an oil bath at 150 °C exhibited first-order kinetics, and equilibrium was reached after 3 days (1:1 ratio).

Diketone **2** is an attractive and promising starting material for organic synthesis. Studies are ongoing, but a first example is shown in Scheme 2. The reduction of **2** with (*S*)-1-methyl-3,3-diphenyltetrahydropyrrolo[1,2-c][1,3,2]oxazaborole afforded the *trans*-diol (−)-(1*R*,4*R*)-**3** in 72% yield and with 99% *ee*.[7] To our knowledge, there is no viable alternative synthetic access to this C$_2$-chiral diol.[8]



Scheme 2. Reduction of dione **2** with CBS to give the *trans* diol **3**.

The facile isomerization of **1** into 1,4-tetralindione encouraged us to investigated the respective [Cr(CO)$_3$] complexes **4** and **5**. We recently reported a synthesis of [Cr(CO)$_3$(η^6-5,8-naphthoquinone)] (**6**), its reduction to the corresponding *meso syn*-diol complex, and efficient desymmetrization by using new chiral diamine acyl-transfer catalysts.[9,10] In a further study of this chemistry, we investigated access to [Cr(CO)$_3$(η^6-5,8-dihydroxynaphthalene)] (**4**) by demethylation of the readily accessible [Cr(CO)$_3$(η^6-5,8-dimethoxynaphthalene)] (**7**),[11] mild hydrolysis of [Cr(CO)$_3$(η^6-5,8-bis(trifluoroacetoxy)naphthalene]][9] (**8**), or catalytic hydrogenation or radical-transfer reduction of **6**.[9]

Both the reactions of **7** with BBr$_3$ and **8** with Et$_3$N/SiO$_2$[9] afforded red oils. The first reaction afforded the monodemethylated complex as the major product. Compound **4**

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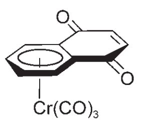

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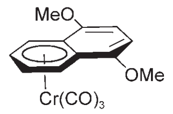

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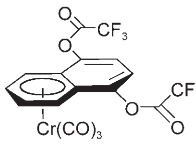

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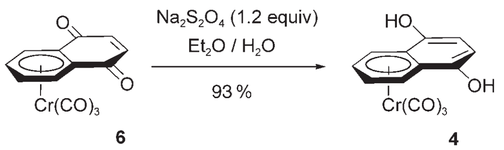
was the major product in the second reaction, which, however, proved difficult to isolate in pure form. Catalytic hydrogenation of **6** (benzene, Pd/C, H_2 50 bar),[12] also afforded **4** as the major product. The second, more soluble product, from these reactions proved to be the tautomer of **4**, $[Cr(CO)_3(\eta^6$-1,2,3,4-tetrahydronaphthalene-5,8-dione)] (**5**). Just as with **1** and **2**, the two tautomers appeared to be kinetically stable at ambient temperature (this point will be discussed later on). Finally, we found that the reduction[13] of **6** using sodium dithionite under biphasic conditions afforded **4** as the sole product in 93 % yield (Scheme 3).



Scheme 3. Reduction of the naphthoquinone complex **6** with sodium dithionite yields the dihydroxynaphthalene complex **4** as the sole product.

The X-ray structure of **4**, which forms orange crystals, is shown in Figure 2.[3] In accord with other naphthalene complexes, the projection of the metal atom onto the arene plane shows a displacement away from the central C–C bond, and the $[Cr(CO)_3]$ tripod adopts a staggered conformation with respect to the arene carbons.

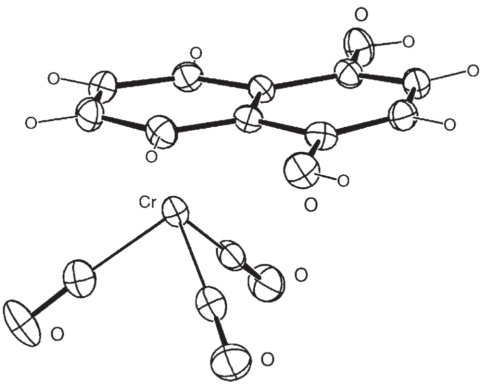
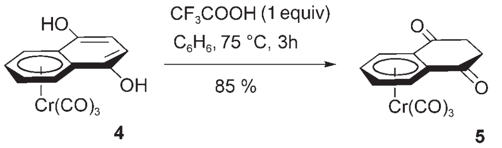


Figure 2. ORTEP view of the crystal structure of **4**. Ellipsoids are represented with 40% probability.

A solution of **4** in benzene at room temperature slowly changes from orange to red; this red color is characteristic of the diketone tautomer **5**. The tautomerization thus occurs far more readily than in uncomplexed **1**. Moreover, the equilibrium lies entirely on the side of the diketo form. Addition of a small amount of trifluoroacetic acid accelerates the tautomerization. The following protocol proved best for the synthesis of **5**: CF_3COOH (1 equiv) and **4** in degassed, dry benzene are stirred at 75 °C for 3 h to yield a mixture of **4** and **5** in a ratio of 8:92. Two successive recrystallizations from $i$$Pr_2O$ gave pure **5** in 85 % yield (Scheme 4). Longer reaction times give rise to the formation of small quantities of $[Cr(benzene)(CO)_3]$ by arene exchange in **4**, with concomitant appearance of free ligand **1**.



Scheme 4. High-yield conversion of **4** into its stable tautomer **5**.

The crystal structure of **5**, like that of **6**,[9] shows a displacement of the vertical projection of the metal onto the arene plane towards the ring junction. The Cr–C(5a) and Cr–C(8a) bonds are 0.04 Å shorter than the Cr–C(6) and Cr–C(7) bonds. Comparison of the structure of the metal-bound arene ligand in **5** with that of the free ligand **2** shows conformational change to be insignificant (Figure 3).[3]

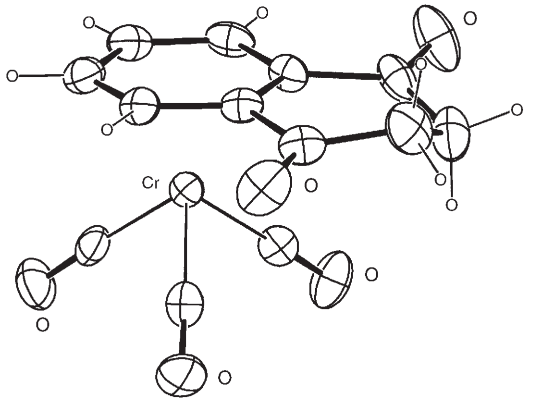
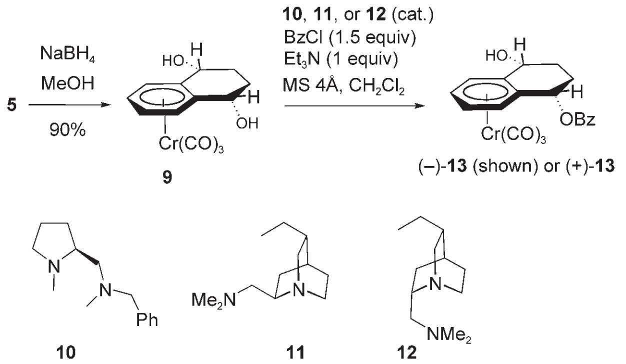


Figure 3. ORTEP view of the crystal structure of **5**. Ellipsoids are represented with 40% probability.

Reduction of the diketone complex **5** cleanly afforded the *cis* diol **9** (Scheme 5, Table 1).[3,9] Chiral-diamine-catalyzed acyl transfer efficiently desymmetrized the *meso* complex **9**. As in a previous report,[9] both the Oriyama catalyst **10**[15] and the readily synthesized quincorine- and quincoridine-derived diamines **11** and **12** performed well in this reaction. The 5*S*,8*R* configuration of (−)-**13** was assigned based on a comparison of its CD spectrum with that of (−)-$[Cr(CO)_3\{$(5*S*,8*R*)-(5,8-dihydro-5-benzoyloxy-8-hydroxy-naphthalene)}].[9,16]

The chemistry described herein is based on the known fact that the two tautomers 1,4-dihydroxynaphthalene and tetrahydronaphthalene-1,4-dione are not in equilibrium at room



Scheme 5. Highly asymmetric acyl-transfer reaction catalyzed by chiral diamines **10**–**12**.

Table 1: Asymmetric acylation of **9**.

Entry	Chiral diamine catalyst (10 mol%)	*T* [°C]	*t* [h]	**13** [%]	*ee* [%] (major prod)
1	**10**[15]	−60	22	78	95 (−)
2	**11**[9]	−60	23	80	94 (+)
3	**12**[9]	−60	22	76	99 (−)

temperature in apolar solvents. The rediscovery of this fact opens up new opportunities in organic synthesis and metal-mediated reactions. Future studies will delineate the scope of the transformations as well as the origin of the milder conditions for the conversion of the dihydroxynaphthalene system into the diketone tautomer in the case of the [Cr(CO)$_3$] complex compared with the free ligand.

Experimental Section

2: 1,4-Dihydroxynaphthalene (**1**; 10.00 g, 62.43 mmol) was placed in a round-bottomed flask with CF_3CO_2H (200 mL). Stirring of the reaction mixture for 30 min at room temperature resulted in a clear solution. Toluene (800 mL) was added followed by removal of the solvents under vacuum at 35 °C. Recrystallization from hot *i*Pr$_2$O (400 mL) afforded **2** (7.19 g, 72%) as a colorless crystalline solid. M.p. 94–95 °C; IR (solid): $\nu = 3352, 2971, 2910, 1683, 1585, 1425, 1282, 1200\ \text{cm}^{-1}$; ^{1}H NMR (300 MHz, CDCl$_3$, 25 °C, TMS): $\delta = 8.05$–8.01 (m, 2H), 7.76–7.71 (m, 2H), 3.08 ppm (s, 4H); ^{13}C NMR (75 MHz, CDCl$_3$, 25 °C, TMS): $\delta = 196.2$, 135.5, 134.5, 126.9, 37.7 ppm; TLC: $R_F = 0.26$ (ether/pentane = 1:6); ESI MS: *m/z* 161 (67) ([$M+1$]), 150 (100), 118 (66), 106 (82), 84 (34), 72 (18); HRMS: *m/z* calcd for $C_{10}H_9O_2$: 161.0603; found 161.0597.

3: Dione **2** (2.48 g, 15.5 mmol) in dry THF (124 mL) was added over a period of 2 h (syringe pump) to a solution of $BH_3{\cdot}THF$ (18.6 mL (1 M solution in THF), 18.6 mmol) and (*S*)-1-methyl-3,3-diphenyltetrahydro-3H-pyrrolo[1,2-c][1,2,3]oxazaborole (1.56 mL (1 M solution in toluene), 0.156 mmol) in dry THF (95 mL) at −10 °C. TLC analysis showed complete conversion of **2** after stirring of the reaction mixture for an additional hour. The volatiles were removed under vacuum after addition of MeOH (50 mL) and the reaction mixture had been warmed up to room temperature. Two successive recrystallizations from *i*Pr$_2$O afforded **3** (1.825 g, 72%; 99% *ee*) as a colorless solid. M.p. 141–142 °C; $[\alpha]_D^{20} = -73$ ($c = 0.305$, MeOH); IR (solid): $\nu = 3278, 2866, 1507, 1050, 761\ \text{cm}^{-1}$; ^{1}H NMR (400 MHz, CDCl$_3$, 25 °C, TMS): $\delta = 7.45$–7.43 (m, 2H), 7.35–7.31 (m, 2H), 4.80–4.84 (m, 2H), 2.33–2.27 (m, 2H), 1.86–1.79 (m, 2H), 1.55 ppm (brs, 2H); ^{13}C NMR (125 MHz, CDCl$_3$, 25 °C, TMS): $\delta = 138.5$, 128.4, 128.3, 67.9, 28.3 ppm; TLC: $R_F = 0.13$ (diethyl ether); EI MS: *m/z* 164 (1) ([M^+]), 146 (100) ([$M-H_2O$]), 131 (38), 120 (45), 105 (30), 77 (28); enantiomeric excess was determined by HPLC analysis on a Daicel Chiracel OJ-H column at $\lambda = 254$ nm; flow rate: 1 mL min^{-1}; eluent: hexane/*i*PrOH (99:1), $t_1 = 5.3$ min, $t_2 = 5.7$ min.

4: Complex **6**[9] (700 mg, 2.38 mmol) was placed in an schlenk tube with Et$_2$O (24.5 mL) under N$_2$ followed by the addition of an N$_2$-saturated aqueous solution of $Na_2S_2O_4$ (24 mL)). The reaction mixture was stirred at room temperature, and the color of the reaction mixture changed from deep violet to orange after 10 min. The organic phase was transferred by a cannula to another schlenk tube containing MgSO$_4$ and the aqueous phase was extracted three times with small portions of Et$_2$O. Filtration and evaporation under vacuum afforded a solid that was washed with pentane and then dried under vacuum to give **4** (651 mg, 93%) as an orange solid. M.p. 137–138 °C (under N$_2$); IR (CH$_2$Cl$_2$): $\nu = 3569, 3055, 1965, 1889, 1227{,}1232\ \text{cm}^{-1}$; ^{1}H NMR (500 MHz, C$_6D_6$, 25 °C, TMS): $\delta = 6.10$–6.07 (m, 2H), 5.59 (s, 2H), 4.59–4.57 (m, 2H), 4.27 ppm (s, 2H); ^{13}C NMR (125 MHz, C$_6$D$_6$, 25 °C, TMS): $\delta = 233.0$, 145.4, 108.1, 98.4, 91.9, 86.0 ppm; EI MS: *m/z* 296 (11) ([M^+]), 240 (7), 212 (42), 160 (26), 131 (9), 104 (9), 77 (6), 52 (100); HRMS: *m/z* calcd for $C_{13}H_8CrO_5$: 295.9777; found: 295.9759.

5: Complex **4** (735 mg, 2.48 mmol) and degassed, dry benzene (37 mL) were placed in a schlenk tube under N$_2$. CF_3COOH (190 μL, 2.48 mmol) was added and the mixture was subjected to three freeze/pump/thaw cycles prior to heating to 75 °C for 3 h. On cooling to room temperature, the solvent was removed under vacuum, and two recrystallizations from hot *i*Pr$_2$O (44 mL) yielded red complex **5** (624 mg, 85%). M.p. 100–101 °C (under N$_2$); IR (CH$_2$Cl$_2$): $\nu = 3569, 3055, 1965, 1889, 1630\ \text{cm}^{-1}$; ^{1}H NMR (400 MHz, C$_6D_6$, 25 °C, TMS): $\delta = 5.44$–5.40 (m, 2H), 4.36–4.32 (m, 2H), 2.32–2.22 (m, 2H), 2.01–1.91 ppm (m, 2H); ^{13}C NMR (100 MHz, C$_6$D$_6$, 25 °C, TMS): $\delta = 229.8$, 193.8, 95.8, 92.5, 89.0, 35.6 ppm; ESI MS: *m/z* 297 (8) ([$M+1$]), 296 (24), 295 (100), 173 (88), 113 (68), 63 (8); HRMS: *m/z* calcd for $C_{13}H_8CrO_5$: 295.9777; found: 295.9777.

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[3] Crystallographic data: Cell dimensions and intensities were measured at 200 K on a Stoe IPDS diffractometer with graphite-monochromated $Mo_{K\alpha}$ radiation ($\lambda = 0.71073$ Å). Data were corrected for Lorentz and polarization effects and for absorption. The structures were solved by direct methods (SIR97),[4] all other calculations were performed with XTAL system.[5] **2**: $C_{10}H_8O_2$, $M_r = 160.2$, monoclinic, $P2_1$, $a = 4.7167(8)$, $b = 7.4607(10)$, $c = 11.285(3)$ Å, $\beta = 96.95(3)°$,$V = 394.18(12)$ Å^3, $Z = 2$, $\mu = 0.094\ \text{mm}^{-1}$, $d_x = 1.349\ \text{g cm}^{-3}$, $R = 0.033$, $\omega R = 0.031$. **4**: $C_{13}H_8CrO_5{\cdot}1/2\,C_6H_6$, $M_r = 335.3$, monoclinic, $P2_1/c$, $a = 14.2611(9)$, $b = 7.2120(4)$, $c = 14.5831(9)$ Å, $\beta = 109.885(7)°$, $V = 1410.46(16)$ Å^3, $Z = 4$, $\mu = 0.83\ \text{mm}^{-1}$, $d_x = 1.579\ \text{g cm}^{-3}$, $R = \omega R = 0.032$. **5**: $C_{13}H_8CrO_5$, $M_r = 296.2$, orthorhombic, $Pna2_1$, $a = 11.2836(9)$, $b = 10.3052(10)$, $c = 10.3366(7)$ Å, $V = 1201.94(18)$ Å^3, $Z = 4$, $\mu = 0.96\ \text{mm}^{-1}$, $d_x = 1.637\ \text{g cm}^{-3}$, Flack parameter $x = -0.02(4)$, $R = \omega R = 0.027$. **9**: $C_{13}H_{12}CrO_5$, $M_r = 300.3$, triclinic, $P\bar{1}$, $a = 7.3157(7)$, $b = 13.3798(11)$, $c = 13.6957(11)$ Å, $\alpha = 101.996(9)$, $\beta = 105.332(10)$, $\gamma = 97.332(10)°$,

$V=1240.7(3)$ Å^3, $Z=4$, $\mu=0.935$ mm^{-1}, $d_x=1.607$ g·cm^{-3}, $R=\omega R=0.030$. CCDC 277444–277447 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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