Cyclodimerization and Diels–Alder reaction of a spiroepoxycyclohexadienone with an *o*-quinodimethane structure

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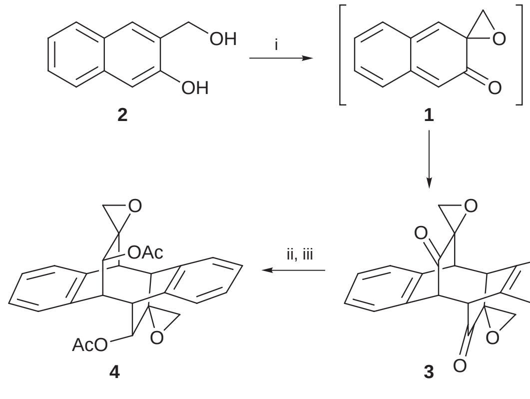
Oxidation of 3-hydroxymethyl-2-naphthol with periodate affords a single *exo-syn* dimer arising from the intermediate *ortho* quinonoid spiroepoxycyclohexadienone; the latter can also be trapped by reactive dienophiles.

Spiroepoxycyclohexadienones are easily obtained from the corresponding 2-hydroxymethylphenols upon $NaIO_4$ oxidation.[1] Like related *ortho*-quinones, quinols and quinol acetates, these dienones easily dimerize *via* a concerted $4\pi+2\pi$ process.[2] Indeed, cycloaddition with various dienophiles (dienes, alkenes, styrenes, enol ethers and esters, enamides) readily occurs to give highly functional adducts.[3] The preparation of similar, albeit stable, dienones in the naphthalene series has been also reported from 2-hydroxymethyl-1-naphthol[4] and 1-hydroxymethyl-2-naphthol.[5]

In this respect, we became interested in the preparation of spirodienone **1** possessing a reactive *ortho*-quinomethane structure which could lead to benzo-fused bicyclo[2.2.2] adducts with dienophiles. This material was prepared from the known 3-hydroxymethyl-2-naphthol[6] **2**, easily obtained in two steps from 3-hydroxy-2-naphthoic acid (MeOH, H^+, 90%; $LiAlH_4$, 86%) (Scheme 1). Upon $NaIO_4$ oxidation (MeOH, H_2O, 20 °C), a single dimeric compound, **3**, mp 201–203 °C, was isolated in 67% yield. This material is characterized, apart from signals of aromatic and CH_2O protons, by two sharp singlets at δ 3.52 and 4.23. This is consistent with only one of the four possible symmetrical head-to-head dimers resulting from *endo* or *exo* and *syn* or *anti* (with respect to the epoxide oxygen) approaches (two of these structures have C_2 symmetry and two are *meso*). The exclusive formation of the *exo-syn* dimer was secured by an X-ray analysis of **4**† (Fig. 1) obtained after $NaBH_4$ reduction and acetylation (Scheme 1). Such orbital symmetry forbidden dimerizations (a formal $\pi^4s + \pi^4s$ process) have already been observed with *ortho*-quinonoid species, usually under irradiation.[7] For example, *in situ* generated 2-benzopyran-3-one has been reported by Bleasdale[8] to give mainly photodimer **5** in unspecified low yield,‡ and Schlosser[9] has described the spontaneous dimerization to **6** (74%) of an *ortho*-quinomethane derived from MeOH elimination of a tetrahydroquinoline. As suggested by Trahanovsky to explain the dimerization of 2,3-dimethylene-2,3-dihydrofuran,[10] **3** probably results from the intermediate diradical **7**, arising from the less hindered *exo-syn* approach of two monomers **1.**



Scheme 1 *Reagents and conditions*: i, $NaIO_4$ (1.1 equiv.), MeOH, 90 min, rt; ii, $NaBH_4$ (1.1 equiv.), 0 °C, 10 min ; iii, Ac_2O, Py, 12 h, rt.

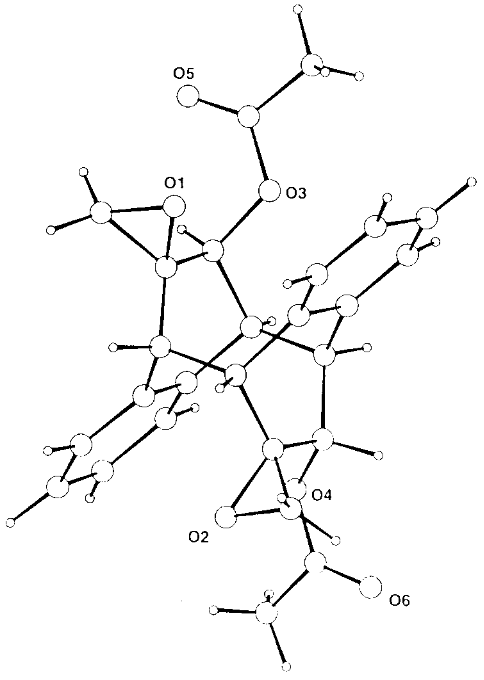
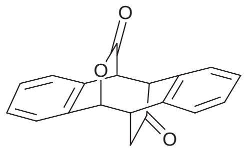


Fig. 1 Crystal structure of **4**.



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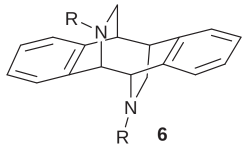

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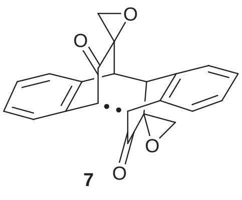

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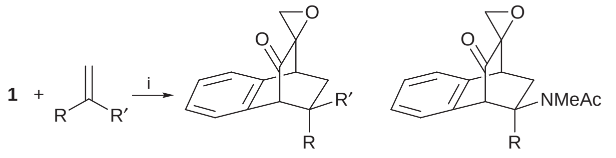
The high facial selectivity observed in the reduction of **3** with $NaBH_4$ is also noteworthy since reduction of α,β-epoxy ketones with hydrides predominantly occurs *syn* to the oxygen epoxide.[11,12] On the other hand, Okada[13] has shown that $NaBH_4$ reduction of 2,3-benzo-fused norbornen-7-one proceeds *syn* to the phenyl ring, while *anti* reduction of 5,6-benzo-fused bicyclo[2.2.2]octan-2-one has been reported[12b] with $LiAlH_4$.



8 R = OEt, R′ = H
9a R = H, R′ NMeAc
9b R = NMeAc, R′ = H
10 R = *p*-MeOC$_6$H$_4$, R′ = H
11a R = OMe, R′ = Me
11b R = Me, R′ = OMe

9c

Scheme 2 *Reagents and conditions*: i, NaIO$_4$ (1.1 equiv.), dienophile (5 equiv.), MeOH–H$_2$O, 2–12 h, rt.

The π-facial selectivity of the reduction observed here is not controlled by the epoxide group, but this may be due to steric hindrance from the remote phenylene group rather than stereoelectronic control by the nearest phenyl ring.

Then, *in situ* cycloaddition of dienone **1** was attempted by carrying out the oxidation step in presence of 5 equiv. of dienophile (Scheme 2). Ethoxyethene and *N*-methyl-*N*-vinylacetamide add to **1** to give **8** (82%) and **9a–c** (70%) without notable dimer formation, unlike the less reactive 4-methoxystyrene, which gave **10** (42%) together with **3** (30%), and 2-methoxyprop-2-ene, which gave **11a** (25%), **11b** (4%) and **3** (44%). As expected, *syn-endo* cycloadition is observed in most cases, except for the enamide which exhibits low selectivity, giving *syn-exo* (**9a**), *syn-endo* (**9b**) and *anti-exo* (**9c**)§ adducts in a 2 : 1 : 1 ratio (a high *syn-exo* selectivity has been observed with enamides for a related spirocyclohexadienone[3d] and for a pyrone[14]).

In summary, oxidation of 3-hydroxymethyl-2-naphthol affords chiral dimer **3** possessing C_2 symmetry in a rigid framework, and trapping of the unstable dienone **1** is possible at room temperature with electron-rich dienophiles. Such adducts may serve as useful templates for the preparation of rigid phenethylamine derivatives[15] or of tetrahydronaphthalene derivatives after cleavage of the α,β-epoxy ketone moiety.[16]

Notes and references

† *Selected data* for **4**: mp 190 °C; δ_H(300 MHz, CDCl$_3$) 1.81 (s, 6 H, Ac), 2.50 (AB q, *J* 6, 4 H, CH$_2$O), 3.14 (s, 2 H, ArC*H*), 3.89 (d, *J* 2, 2 H, ArC*H*), 5.12 (d, *J* 2, 2 H, C*H*OAc), 7.30 (m, 8 H); δ_C 20.4, 46.0, 51.4, 55.0, 58.7, 70.4, 127.0, 127.4, 129.1, 130.1, 138.9, 139.1, 170.2.

Crystal data for **4**: C$_{28}$H$_{24}$O$_6$, M_r = 1729.89, monoclinic, a = 16.578(7), b = 25.37(1), c = 20.826(8) Å, β = 105.99(7)°, V = 8420(2) Å^3, space group $P2_1/n$, Z = 16, D_c = 1.36 g cm^{-3}, $F(000)$ = 3659.166, colourless prismatic crystal stable in air, μ(Cu-Kα) = 0.754 mm^{-1}, 3030 independent reflections with $I \geq 3\sigma(I)$ were used in the structural analysis. The structure was solved using direct methods (ref. 17) and refined using least-squares calculations (ref. 18). Positional and anisotropic thermal parameters of all atoms except hydrogen were refined. Hydrogen atom positions were calculated, an equivalent isotropic thermal parameter was given for hydrogen atom groups. Finally R = 9.39%, R_w = 10.53% and S = 1.53 for 1250 refined parameters and 3030 reflections. A Chebychev polynomial with three coefficients was used in the weighting scheme. There are four independent molecules in the asymmetric unit and, although this is rather rare, no significant difference between these molecules was evidenced. CCDC 182/1253. See http://www.rsc.org/suppdata/cc/1999/1143/ for crystallographic data in .cif format.

‡ The analoguous isoquinolin-3-ol is reported to give a head-to-tail *exo* photodimer (ref. 19).

§ All new compounds were fully characterized by ^{1}H, ^{13}C NMR and HRMS except for adducts **9a** and **9b** which could not be separated by chromatography. *Selected data* for **9a**: δ_H 1.70 (ddd, *J* 14.2, 5.1 and 2.7, 1H), 2.03 (s, 3H), 2.18 (s, 3 H), 2.72 (ddd, *J* 14.2, 10.6 and 2.8), 5.58 (ddd, *J* 10.6, 5.1 and 2.5). For **9b**: δ_H 1.85 (ddd, *J* 14.2, 5.4 and 2.5), 2.14 (s, 3 H), 2.22 (s, 3 H), 2.76 (ddd, *J* 14.2, 10 and 2.5), 4.67 (ddd, *J* 10, 5.4 and 2.5). For **9c**: δ_H 2.13 (s, 3 H), 2.24 (m, 2 H), 2.90 (s, 3 H), 5.17 (ddd, *J* 9.6, 7.9 and 2.5).

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