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# FACILE SYNTHESIS OF QUINONE EPOXIDES AND 5,6-EPOXY-4-HYDROXY-2-CYCLOHEXENONES VIA THE RETRO-DIELS–ALDER REACTION[1]

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**Abstract**—From commercially available quinoes, quinone epoxides and 5,6-epoxy-4-hydroxy-2-cyclohexenones were easily prepared through the retro-Diels–Alder reactions under rather mild conditions.

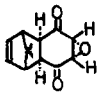
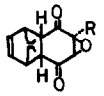
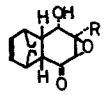
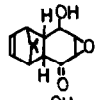
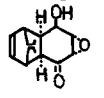
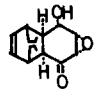
Recently highly oxygenated cyclohexane derivatives have been isolated from fungus and higher plants. It is known that some of these compounds are antibiotics, and others such as epoxydon[2] and crotepoxide[3] are cytotoxic natural products. Among them, epoxydon was also isolated from the culture filtrate of *Phyllosticta* sp., as a phytotoxic compound causing wilting and dark discoloration of the leafty stem cutting of red clover.[4a] Epoxydon has antibiotic activity. Among the organisms tested, Phycomycetes and Gram-negative bacteria appeared most susceptible to epoxydon. Epoxydon also promoted adventitious root formation.[4b] In order to investigate structure-activity relationship concerned with the structure of epoxydon and also prepare prominent intermediates for the synthesis of antitumor compounds, i.e. crotepoxide, it is needed to prepare quinone epoxides and 5,6-epoxy-4-hydroxy-2-cyclohexenones from easily available quinones. For the purpose, at first direct epoxidation of quinones using hydrogen peroxide in alkaline medium was taken into consideration. However, utilisation of this procedure was only limited to naphthoquinones, since, in the case of benzoquinones, resulting epoxides are labile in alkaline medium. Efficiency of t-butylhydroperoxide as an oxidant was reported in the preparation of alkylated quinone epoxides,[5] but the method would not be applicable for the synthesis of simple quinone epoxides. Versatile epoxidising reagent of simple quinone epoxides would be sodium perborate, which is used under mild alkaline conditions,[6] and the utility was demonstrated in the synthesis of terreic acid,[6] phyllostine, and epoxydon, though the yields were rather poor and no regioselectivity during the epoxidation was observed.[7] Alder *et al.* reported that quinone epoxides were prepared from the retro-Diels–Alder reaction of the epoxides of cyclopentakiene-quinone adducts.[8] However, in practice it involved decomposition and polymerisation of products because of drastic conditions (420°) during the retrodiene reaction. Therefore, our efforts were directed toward the improvement of conditions, and instead of cyclopentadiene, dimethylfulvene was used for the diene part, since the retro-Diels–Alder reaction of the adducts would proceed much easier than that of cyclopentadiene adducts. The advantages of the method through the retro-Diels–Alder reaction over those of others in the synthesis of quinone epoxides and $\alpha$-epoxycyclohexenones are summerized as follows: (1) epoxidation proceeds regioselectively to give an epoxide, in which only more substituted double bond in the starting quinone was epoxidised, (2) the adducts are stable, and appreciable modification in quinone moiety are possible, (3) stereoselectivities are expected in the modification of the *endo*-adducts.

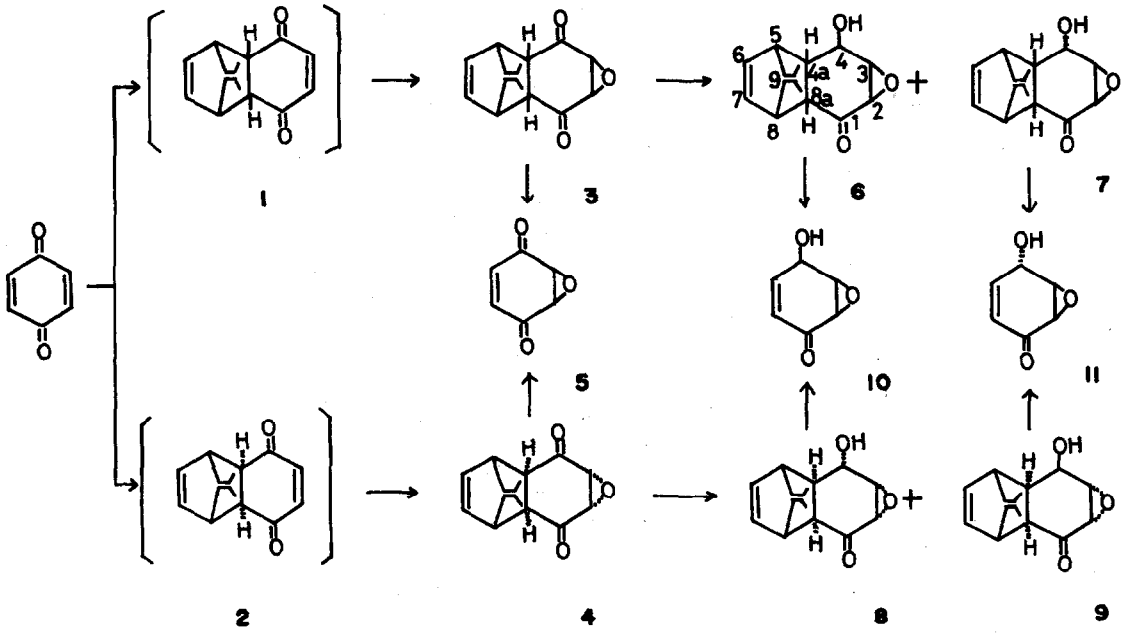
General procedure for the synthesis of the epoxides is outlined as follows. A solution of dimethylfulvene and 1,4-benzoquinones in ethanol was allowed to stand for 2 days. The adducts obtained were epoxidised with $H_2O_2$ in alkaline solution. The retro-Diels–Alder reaction of the epoxides without solvent are accompanied with decomposition and polymerisation. Therefore, two procedures using solvents were investigated. Thus, the epoxides were heated at 150–190° (A) in high boiling organic solvents like diglyme, diphenyl ether, or (B) in low boiling organic solvents such as benzene, toluene and THF in a sealed tube. Since both methods were carried out under rather mild conditions below 190° in organic solvents, most of the reaction proceeded quantitatively. The retro-Diels–Alder reactions according to the procedure A and B are summerised in Table 1.

*Synthesis of the epoxides* (**5**, **10**, **11**) *starting from benzoquinone* (Scheme 1). Reaction of benzoquinone with dimethylfulvene in ethanol gave a mixture of adducts (*endo* **1**, *exo* **2**), which, without separation, were oxidised with $H_2O_2$ to give epoxides, **3** and **4** in a ratio of 1:1. The stereochemistry at ring juncture of **3** and **4** were deduced from the PMR spectra,[9] in which the signals due to the proton 4a-H and 8a-H appeared at $\delta$ 3.40 (multiplets) in *endo* compound **3**, but at $\delta$ 2.64 (singlet) in *exo* compound **4**. The shielding effect in *exo* compound **4** would be due to the C-6 double bond as analogously as norbornene.[10] The stereochemistry of other epoxides derived from toluquinone and 2-hydroxymethyl-1,4-benzoquinone are also confirmed by the PMR spectra as shown in Table 2. The relative configuration of the oxirane ring to the ring juncture protons in **3** and **4** was expected to be *cis*, since epoxidation occurred from less hindered side to the molecule, and this stereochemistry was further confirmed as described later.

The retro-Diels–Alder reaction of **3** and **4** in a sealed

Table 1. Retro-Diels–Alder reaction of epoxy derivatives of quinone-dimethylfulvene adducts

| starting material | | method | reaction temp(°C) | solvent | reaction time(min) | product | | yield(%) |
|---|---|---|---|---|---|---|---|---|
|  | **4** | B | 180 | toluene | 40 |  | **5** R=H | 100 |
|  | **3** R=H | B | 160 | toluene | 30 |  | **5** R=H | 95 |
| | **12** R=$CH_3$ | B | 150 | benzene | 30 | | **14** R=$CH_3$ | 100 |
| | **15** R=$CH_2OH$ | A | 165 | diglyme | 30 | | **17** R=$CH_2OH$ | 22 |
|  | **18** R=$CH_2OH$ | A | 190 | diglyme | 60 |  | **19** R=$CH_2OH$ | 43 |
| | **7** R=H | B | 160 | THF | 40 | | **11** R=H | 100 |
|  | **6** | B | 160 | THF | 30 |  | **10** | 100 |
|  | **9** | B | 180 | THF | 40 | | **11** | 100 |
|  | **8** | B | 180 | THF | 40 | | **10** | 100 |



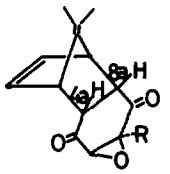
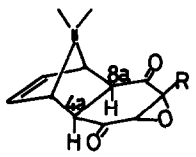
Scheme 1.

tube at 160–180° for 30–40 min yielded quantitatively 1,4-benzoquinone epoxide (**5**).

Reduction of each of the epoxides, **3** and **4** with $NaBH_4$ in THF afforded two stereoisomers, **6**, **7** and **8**, **9** respectively. The stereochemistry of each of these reduction products was determined by the analysis of the PMR spectra. For the examples, assuming O-axial conformation[11] with the oxirane ring in *endo* structure; a large coupling constant (9 Hz) with 4a-H in compound **6** indicates that the protons, 4a-H and 4-H, occupy *trans* diaxial disposition. The result is compatible with $\beta$-configuration of the oxirane ring in **3**, together with consideration of attack of hydroperoxide from less hindered side, and the stereochemistry of **6** must be depicted as shown and the other isomer as **7**.

With respect to the *exo* epoxides, **8** and **9**, there are four possible stereoisomers, a–d. From molecular model, the coupling constants, $J_{4\text{-}4a}$ and $J_{3\text{-}4}$, with these structures are calculated on two conformations, which have axial and equatorial OH group, and summerised in Table

Table 2. Chemical shifts ($\delta$) of ring juncture protons (4a-H, 8a-H) of quinone epoxidedimethylfulvene adducts

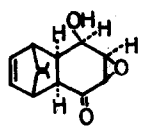
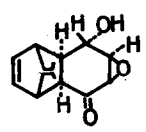
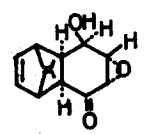
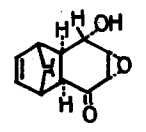
| Compound R | endo | exo |
|---|---|---|
| H (3,4) | 3.40 (m) | 2.64 (s) |
| $CH_3$ (12,13) | 3.40 (m) | 2.75 (s) |
| $CH_2OH$ (15,16) | 3.42 (m) | 2.80 (s) |
| |  |  |

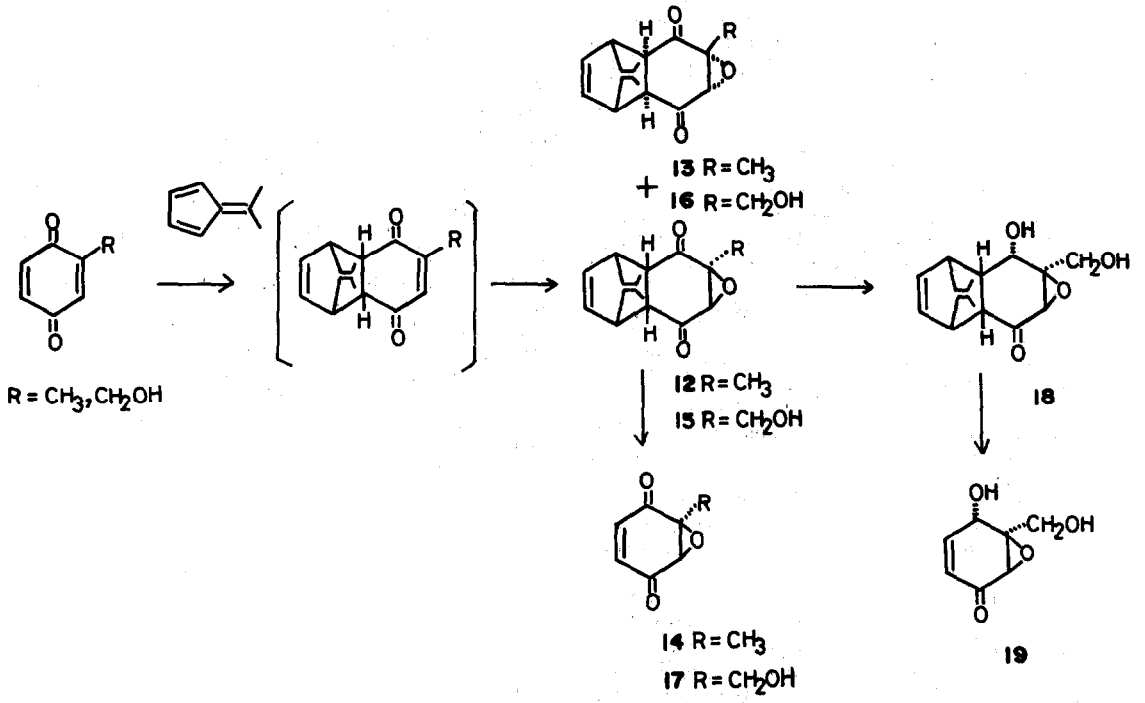
3. The observed coupling constants, $J_{4-4a} = 2$ Hz, $J_{3-4} = 4$ Hz, of the ketol **9** are adequate to the structure C, which has an axial OH group and an O-axial oxirane ring. In addition, in the IR spectra under high dilute conditions, a strong intramolecular H-bond (3550 $cm^{-1}$) between OH group and C-9 double bond in **9**(c), but none (3645 $cm^{-1}$, free OH) in **8**(d), was observed. These data demonstrate that the stereochemistry of the oxirane ring in **4** must be *cis* to the ring juncture protons (4a-H, 8a-H) and the ketols derived from **4** should be depicted as **9** and **8**. The retro-Diels–Alder reaction of the ketols **6** ~ **9** according to the procedure B afforded **10** from **6** and **8**, and **11** from **7** and **9**. The relative configuration of **11** was further confirmed to be *trans*, since a long range coupling due to W-configuration[11] between 2-H and 4-H was observed.

*Synthesis of the epoxide* (**14**) *starting from toluquinone* (Scheme 2). The Diels–Alder adduct from toluquinone and dimethylfulvene was, without isolation, oxidised with $H_2O_2$ to give two stereoisomers, *endo*-compound **12** and *exo*-compound **13** in a ratio of 19:1. The *endo*-structure of **12** was confirmed by the PMR spectrum which indicates a characteristic signal (3.40, multiplet) due to ring juncture protons (4a-H, 8a-H): in *exo*-compound **12**, the signal is shifted to higher field (Table 2) The *endo*-compound was heated at 150–160° in a sealed tube to yield **14** quantitatively.

*Synthesis of the epoxides* (**17**, **19**) *from 2-hydroxymethyl-1,4-benzoquinone* (Scheme 2). The epoxide isomers, **15** and **16** were prepared by the same way in a ratio of 20:1 starting from 2-hydroxymethyl-1,4-benzoquinone. Thus, the adduct derived from 2-hydroxymethyl-1,4-benzoquinone, without isolation, was epoxidised with hydrogen peroxide to yield *endo*-epoxide **15** and *exo*-epoxide **16** in a ratio of 20:1. The fulvene part of the *endo*-adduct plays an important role not only to control regio- and stereoselectivity but also to stabilize the adduct derivatives in the synthesis of senepoxyde[2] and crotepoxide[3] and could be easily removed in later stage. The stereochemistry of **15** was confirmed by the comparison of its PMR spectrum with that of **16**. Thus, the signals due to ring juncture protons (4a-H, 8a-H) of **15** and **16** were appeared at $\delta$ 3.42 as multiplet in the former and at $\delta$ 2.90 as singlet in the later.[9] These observations are in accord with structure **15a** and **16a** and in fact molecular model shows that the ring juncture protons in **16a** are effectively shielded by the double bond and the dihedral angle of the protons with vicinal

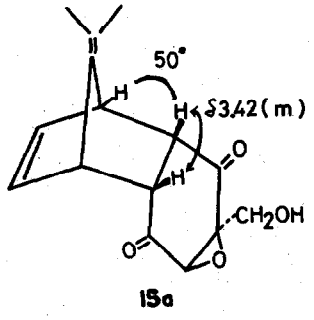
Table 3. Calculated coupling constants ($J_{4-H-4a-H}$, $J_{3-H-4-H}$) of **9**(c) and the stereoisomers (a, b, d)

| Stereoisomers | OH axial (Hz) | | OH equatorial (Hz) | |
|---|---|---|---|---|
| | $J_{4-H-4a-H}$ | $J_{3-H-4-H}$ | $J_{4-H-4a-H}$ | $J_{3-H-4-H}$ |
| a | 7 | 7 | <1 | 3 |
| b | 1 | 1 | 9 | 5 |
| c | 3 | 3 | 3 | 10 |
| d | 2 | 7 | 10 | 1 |
| |  |  |  |  |
| | a | b | c(9) | d(8) |

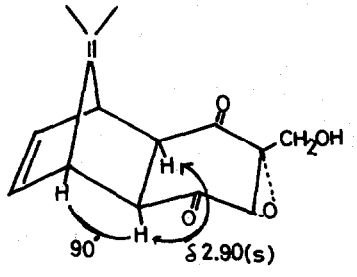



Scheme 2.

protons are *ca.* 90°. The configuration of epoxides in **15** and **16** was deduced as **15a** and **16a** respectively, *cis* to the ring juncture protons, since the epoxidation was occurred from less hindered side of the molecules. Validity of the stereochemistry **15a** was further proved by the PMR analysis on the derivatives in the synthesis of (±)-senepoxyde.[12]

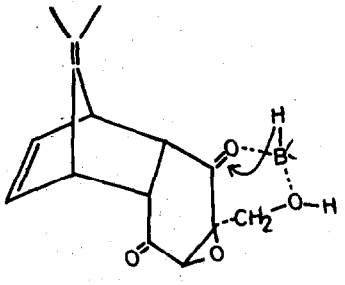



**15a**

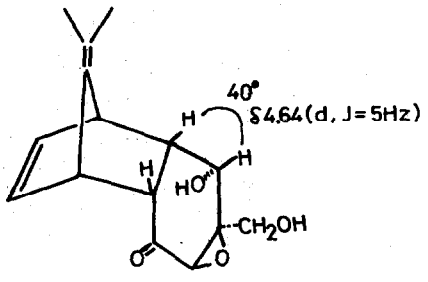



**16a**

Regioselective reduction of **15** with 1.1 equivalent of sodium borohydride in tetrahydrofuran gave a diol **18** in 73.5% yield. The structure and stereochemistry of **18** were confirmed by the facts that α-proton to the OH group appeared at δ 4.64 (d, J = 5 Hz), whose coupling constant is good agreement with the dihedral angle (50°) arising from O-oxial conformation of the epoxide.[11] The regio- and stereoselective reduction was explained by assuming a chelated intermediate **15b**, which results from neighboring group effect of the OH group.[13] In the intermediate, a hydride clearly attacks the CO group from less hindered side of the *endo*-structure to give the diol **18a**, whose stereochemistry was confirmed by the PMR spectrum. The retro-Diels–Alder reaction of the *endo*-isomer **15** was carried out in diglyme heating at 165° for 30 min to yield the epoxide **17**. The diol **18** derived from **15** was heated in diglyme to yield an epoxydiol **19**. Interestingly, the epoxydiol **19** exerted moderate




**15b**




**18a**

antileukemic activity (T/C 141) vs mouse leukemia P 388.[14] Further antibiotic and phytotoxic activities of the epoxides obtained by this procedure were examined.[15]

## EXPERIMENTAL

All m.ps are uncorrected and were determined on a Yanaco Micromelting Point Apparatus MP-3D. The IR spectra were recorded on a Hitachi IR Spectrophotometer Model 285 and PMR spectra on a Hitachi 90 MHz High Resolution Spectrometer Model R-22 and Japan Electrics JNM PS-100 High Resolution Spectrometers: The abreviations s, d, t, q and m signify singlet, doublet, triplet, quartet and multiplet. Mass spectra were determined on Hitachi RMU-4 Spectrometer.

Endo- *and* exo *adducts* (**3**, **4**) *of quinone-epoxide and dimethylfulvene.* To a soln of 2.0 g *p*-benzoquinone in 10 ml EtOH was added 4.0 g dimethylfulvene, and the mixture was allowed to stand for 2 days at 5°. The mixture was concentrated *in vacuo* below 20° and the concentrate was dissolved into 15 ml THF. To the soln, peroxide soln prepared from 1.05 g of $K_2CO_3$ in 20 ml water and 6 ml $H_2O_2$ (30%) was added dropwise under stirring. After allowing to stand for 30–40 min, the excess of $H_2O_2$ in the brown colored mixture was decomposed with $NaHSO_3$, and the mixture was extracted three times with benzene. The combined extracts were washed with satd brine and dried over $Na_2SO_4$, evaporated *in vacuo* to yield 2.8 g of a mixture of **3** and **4**. The mixture was chromatographed twice on silica gel column with benzene–$CHCl_3$–EtOAc (70:29.9:0.1) as eluent to give an *endo*-**3**: m.p. 128–129°; IR $\nu_{max}^{KBr}$ 1716 (C=O) $cm^{-1}$, PMR $\delta_{TMS}^{CDCl_3}$; 1.54 (6H, s, $CH_3$), 3.40 (2H, m, –CHCO), 3.50 (2H, s, –CHO), 3.75 (2H, m, –CH–), 6.23 (2H, m, =H), MS *m/e*: 230 ($M^+$) (Found: C, 73.04; H, 6.00. Calc. for $C_{14}H_{14}O_3$; C, 73.02; H, 6.13%) and *exo*-**4**: m.p. 116–117°; IR $\nu_{max}^{KBr}$ 1710 (C=O) $cm^{-1}$: PMR $\delta_{TMS}^{CDCl_3}$; 1.45 (6H, s, $CH_3$), 2.77 (2H, s, CHCO), 3.66 (2H, s, –CH–O), 3.92 (2H, m, –CH–), 6.34 (2H, m, =H), MS *m/e*: 230 ($M^+$) (Found: C, 73.05; H, 6.12. Calc. for $C_{14}H_{14}O_3$; C, 73.02; H, 6.13%).

*Reduction of the epoxide* **3**. A soln of 172 mg of the epoxide and 13 mg $NaBH_4$ in 3 ml THF was stirred for 2 hr at room temp. The mixture was extracted with EtOAc and the extract was washed with saturated brine and dried over $Na_2SO_4$. After removal of the solvent, the residue was fractionated on silica gel column using $CHCl_3$–MeOH (96:4) as eluent to give 30 mg of **6** and 33 mg of **7**, each of which was recrystallised from benzene to afford a white crystalline material **6**, m.p. 117–120°; IR $\nu_{max}^{KBr}$ 3430 (OH), 1707 (C=O) $cm^{-1}$; PMR $\delta_{TMS}^{CDCl_3}$; 1.51, 1.55 (each 3H, s, $CH_3$), 2.08 (1H, br.s, OH), 2.65 (1H, ddd, J = 11 Hz, 9 Hz, 3 Hz, –CH–), 3.02 (1H, q, J = 11 Hz, 3 Hz, –CHCO), 3.41 (2H, ABq, J = 5 Hz, –CHO–), 3.51, 3.70 (2H, m, –CH–), 3.77 (1H, d, J = 9 Hz, –CHO), 6.19, 6.43 (each 1 H, m, =H), MS *m/e*: 232 ($M^+$) (Found: C, 72.79; H, 7.37. Calc. for $C_{14}H_{16}O_3$; C, 72.39; H, 6.94%) and **7**, m.p. 131 ~ 132°; IR $\nu_{max}^{KBr}$ 3440 (OH), 1700 (C=O) $cm^{-1}$; PMR $\delta_{TMS}^{CDCl_3}$; 1.50, 1.51 (each 3H, s, $CH_3$), 2.92 (1H, ddd, J = 11 Hz, 5 Hz, 3 Hz, –CHO), 3.26 (1H, d, J = 5 Hz, –CHO), 3.40, 3.62 (3H, m, –CH–), 4.07 (1H, br.s, –CHO), 6.37 (2H, m, =H); MS *m/e* 232 ($M^+$) (Found: C, 72.49; H, 6.82. Calc. for $C_{14}H_{16}O_3$; C, 72.39; H, 6.94%).

*Reduction of the epoxide* **4**. A soln of 940 mg **4** and 70 mg $NaBH_4$ in 15 ml THF was stirred for 2 hr at room temp. The mixture was extracted with EtOAc, and the extract was washed with saturated brine and dried over $Na_2SO_4$. After removal of the solvent, the residue was chromatographed on silica gel with EtOAc-benzene–$CHCl_3$ (1:3:6) as eluent to yield 430 mg of **9** and 251 mg of **8**:**9**, m.p. 192–193°; IR $\nu_{max}^{KBr}$ 3490 (OH), 1698 (C=O) $cm^{-1}$; $\nu_{max}^{CDCl_3}$ (0.003 M/l) 3550 $cm^{-1}$ (bonded OH---$\pi$); PMR $\delta_{TMS}^{CDCl_3}$ 1.60, 1.55 (each 3H, s, $CH_3$), 2.34 (1H, d, J = 2 Hz, –CH–), 2.37 (1H, s, –CHCO–), 3.36 (2H, m, –CH–), 3.67 (1H, t, J = 4 Hz, –CHO), 3.78 (1H, m, –CH–), 4.64 (1H, m, –CHO), 6.38 (2H, m, =H): MS *m/e* 232 ($M^+$) (Found: C, 72.53; H, 6.95. Calc. for $C_{14}H_{16}O_3$; C, 72.39; H, 6.94%). **8**, m.p. 136–139; IR $\nu_{max}^{KBr}$ 3450 (OH), 1698 (C=O) $cm^{-1}$, $\nu_{max}^{CCl_4}$ 3645 $cm^{-1}$ (free OH); PMR $\delta_{TMS}^{CDCl_3}$ 1.51, 1.53 (each 3H, s, $CH_3$), 1.89, 2.35 (2H, m, –CH–), 3.36, 3.79 (5H, m, –CH–), 6.28 (2H, m. =H); MS *m/e* 232 ($M^+$). (Found: C, 72.32; H, 7.59. Calc. for $C_{14}H_{16}O_3$; C, 72.39; H, 6.94%).

*Retro-Diels–Alder reaction of* **3**. A soln of 52 mg **3** in 3 ml toluene was heated at 150–160° for 3 min in a sealed tube. The mixture was concentrated *in vacuo* to give 26 mg of **5**, which was recrystallised from benzene to afford pale yellow crystalline material, m.p. 83°; IR $\nu_{max}^{KBr}$ 1690 (C=O), 1597 (C=C) $cm^{-1}$; PMR $\delta_{TMS}^{CDCl_3}$ 3.80 (2H, d, J = 1 Hz, –CHO), 6.60 (2H, d, J = 2 Hz, =H); MS *m/e* 124 ($M^+$).

*Retro-Diels–Alder reaction of* **4**. A soln of 70 mg **4** in 7 ml toluene was heated at 180° for 40 min in a sealed tube. The mixture was concentrated to give 40 mg of the epoxyquinone which was identical with previously obtained **5** in all respects.

*Retro-Diels–Alder reaction of* **6**. A soln of 33 mg **6** in 0.5 ml THF was heated at 160° for 40 min in a sealed tube. The mixture was concentrated to give 15 mg of oily residue **10**, IR $\nu_{max}^{film}$ 3360 (OH), 1668 (C=O) $cm^{-1}$; PMR $\delta_{TMS}^{CDCl_3}$ 3.44 (1H, dd, J = 5 Hz, 2 Hz, –CHO), 3.87 (1H, m, –CHO), 4.75 (1H, br.s, –CHO), 5.89 (1H, td, J = 11 Hz, 2 Hz, =H), 6.57 (1H, td, J = 11 Hz, 2 Hz, =H); MS *m/e* 126 ($M^+$).

*Retro-Diels–Alder reaction of* **8**. A soln of 251 mg **8** in 5 ml THF was heated at 180° for 40 min in a sealed tube. The mixture was concentrated *in vacuo* to give a residue which was chromatographed on silica gel column using $CHCl_3$–MeOH (95:5) as eluent to yield, together with 78 mg of the unchanged **8**, 94 mg of **10** which was identical with authentic sample in spectroscopic data.

*Retro-Diels–Alder reaction of* **7**. A soln of 15 mg **7** in 0.3 ml THF was heated at 160° for 30 min in a sealed tube. The mixture was concentrated *in vacuo* to give 9 mg of oily product **11**, IR $\nu_{max}^{film}$ 3450 (OH), 1659 (C=O) $cm^{-1}$; PMR $\delta_{TMS}^{CDCl_3}$ 3.43 (1H, m, –CHO), 3.77 (1H, m, –CHO), 4.58 (1H, m, –CH–), 5.99 (1H, td, J = 1 Hz, 11 Hz, =H), 6.70 (1H, ddd, J=2 Hz, 4Hz, 11 Hz, =H); MS *m/e* 126 ($M^+$).

*Retro-Diels–Alder reaction of* **9**. A soln of 420 mg **9** in 5 ml THF was heated for 40 min at 170–180° in a sealed tube. The mixture was concentrated to dryness to yield quantitatively almost pure **11**, which was further purified on silica gel column using $CHCl_3$–MeOH (95:5) as eluent to give 194 mg of purified **11**.

Endo- *and* exo *adducts of toluquinone epoxide and dimethylfulvene.* A soln of 5 g toluquinone and 4.46 g dimethylfulvene in 20 ml EtOH was allowed to stand for 2 days at 4°. The mixture was concentrated *in vacuo* below 20° to give a residue, which was dissolved into 30 ml THF and epoxidised with 150 ml peroxide soln prepared from 5.8 g $K_2CO_3$ and 33 ml $H_2O_2$(30%) in 110 ml water under stirring and ice-cooling. After 40 min, the resultant crystals (3.1 g) were collected, and the mother liquor was extracted twice with EtOAc. The combined extracts were dried over $Na_2SO_4$ and concentrated *in vacuo* to give additional crystalline material (1.3 g), which contained 5% of *exo*-isomer, and was chromatographed on silica gel column with benzene–$CHCl_3$–EtOAc (70:29.9:0.1) or benzene as eluent to give *endo*-**12**, m.p. 157°, and minor amount of *exo*-**13**, m.p. 84–85°; spectral data, **12**, IR $\nu_{max}^{KBr}$ 1710 (C=O) $cm^{-1}$; PMR $\delta_{TMS}^{CDCl_3}$ 1.44 (3H, s, $CH_3$), 1.54 (6H, s, $CH_3$), 3.30 (2H, s, –CHO), 3.40 (2H, m, –CHC=O), 3.70 (2H, m, –CH–), 6.20 (1H, t, J = 2 Hz, =H); MS *m/e* 244 ($M^+$). (Found: C, 73.62; H, 6.63. Calc. for $C_{15}H_{16}O_3$, C, 73.75; H, 6.60%), and *exo*-**13**, IR $\nu_{max}^{KBr}$ 1710 (C=O) $cm^{-1}$; PMR $\delta_{TMS}^{CDCl_3}$ 1.46 (6H, s, $CH_3$), 1.50 (3H, s, $CH_3$), 2.79 (2H, s, –CHO), 2.77 (2H, s, –CHCO), 3.49 (1H, s, –CHO), 3.90 (2H, m, –CH–), 6.32 (2H, t, J = 2 Hz, =H); MS *m/e* 244 ($M^+$). (Found: C, 73.73; H, 6.66. Calc. for $C_{15}H_{16}O_3$, C, 73.75; H, 6.60%).

*Retro-Diels–Alder reaction of* **12**. A soln of 58 mg **12** in 3 ml benzene was heated for 30 min at 150° in a sealed tube. The mixture was concentrated to give 33 mg of a product, which was recrystallised from benzene to yield pure **14**, m.p. 68–69°, IR $\nu_{max}^{KBr}$ 1690 (C=O) $cm^{-1}$; PMR $\delta_{TMS}^{CDCl_3}$ 1.58 (3H, s, $CH_3$), 3.54 (1H, d, J = 2 Hz, –CHO), 6.56 (1H, d, J = 2 Hz, =H), 6.57 (1H, s, =H); MS *m/e* 138 ($M^+$).

*Epoxides* **15** *and* **16**. A mixture of 4.11 g 2 - hydroxymethyl - 1,4 - benzoquinone and 3.2 g dimethylfulvene in 15 ml EtOH was allowed to stand for 24 hr at 5°. To the mixture was added EtOH and ice and then peroxide soln which made up from 1.6 g

$Na_2CO_3$, 40 ml water and 8 ml aqueous 30% $H_2O_2$ under stirring. The resulting crystals were collected by filtered and washed with water and n-hexane to yield 2.91 g of **15**. Recrystallisation from benzene afforded pure **15**, m.p. 101–102°, IR $\nu_{max}^{KBr}$: 3350 (OH), 1710 (C=O) $cm^{-1}$, PMR $\delta_{TMS}^{CDCl_3}$ 1.53 (6H, s, $CH_3$), 3.42 (2H, m, CH), 3.56 (1H, s,  ), 3.72 (2H, m, $=CH_2$), 3.85, 4.00 (2H, ABq, J = 14 Hz, $-CH_2-$), 6.19 (2H, m, =H). MS *m/e*: 260 ($M^+$), 245 ($M^+$, $-CH_2$). (Found: C, 68.81, H, 6.14. Calc. for $C_{15}H_{16}O_4$; C, 69.21; H, 6.20%). The filtrate and washing solvents, water and n-hexane, were combined and extracted with ether. The combined extracts were dried over $NaSO_4$ and evaporated *in vacuo* to give 1.98 g of residue, which contains **15** and **16** in a ratio of 3:1. The residue was chromatographed on silicic acid eluted with benzene-EtOAc–MeOH (90:8:2, v/v) to yield **16**. Recrystallisation from benzene gave pure **16**, m.p. 127 ~ 128°, IR $\nu_{max}^{KBr}$; 3500 (OH), 1700 (C=O) $cm^{-1}$, PMR $\delta_{TMS}^{CDCl_3}$ 1.54 (6H, s, $CH_3$), 2.80 (2H, s, CH), 3.71 (1H, s,  ), 3.89 (2H, m,$-CH_2-$), 3.90, 4.12 (2H, ABq, J = 13 Hz, $CH_2O$), 6.34 (2H, m, =H), MS *m/e*; 2.60 ($M^+$), 245 ($M^+$, $-CH_3$). (Found: C, 69.26; H, 6.06. Calc. for $C_{15}H_{16}O_4$; C, 69.21; H, 6.20%).

*Reduction of* **15**. A soln of 953 mg **15** and 43 mg $NaBH_4$ (1.1 eq) in 15 ml anhydrous THF was allowed stand for 3 hr at room temp. under stirring. After adding EtOAc the mixture was washed with brine, and the brine layer was extracted twice with EtOAc.

The combined organic layers were dried over $NaSO_4$ and then concentrated under reduced pressure to leave a residue, which was recrystallised from EtOAc, to yield 564 mg of pure **18**, m.p. 149.5–150°. Additional diol **18** (141 mg) was obtained by the column chromatography of the mother liquor. IR $\nu_{max}^{KBr}$; 3500, 3300 (OH), 1705 (C=O) $cm^{-1}$, PMR $\delta_{TMS}^{d_6\text{-acetone}}$; 1.48 (6H, s, $CH_3$), 2.74 (1H, ddd, J = 12 Hz, 5 Hz, 3 Hz, CH), 3.00 (1H, dd, J = 12 Hz, 3 Hz, –CH–), 3.16 (1H, s,  ), 3.39 (2H, m, CH), 3.54, 3.98 (2H, ABq, J = 13 Hz, $CH_2O$), 4.64 (1H, d, J = 5 Hz, –CHO), 6.05 (1H, m, =H), 6.23 (1H, m, =H); MS *m/e* 262 ($M^+$), 247 ($M^+$, $-CH_3$), 231 ($M^+$, $-CH_2OH$). (Found: C, 68.79; H, 7.00. Calc. for $C_{15}H_{18}O_4$; C, 68.68; H, 6.92%).

*Retro-Diels–Alder reaction of* **15**. A soln of 599 mg **15** in 5 ml diglyme was heated at 165° under $N_2$. After 30 min, the mixture was evaporated with toluene and obtained residue was chromatographed on silica gel using $CHCl_3$: MeOH (9:1) to yield 89 mg of yellow oil, **17**, IR $\nu_{max}^{film}$ 3410, 3510 (OH), 1690 (C=O) $cm^{-1}$; PMR $\delta_{TMS}^{CD_3COCD_3}$ 3.92 (1H, br.s, –CHO), 4.07 (2H, br.s, $-CH_2O$), 6.68 (2H, s, =H); MS *m/e* 138 ($M^+$).

*Retro-Diels–Alder reaction of* **18**. A soln of 182 mg **18** in 5 ml diglyme was heated at 190° for 1 hr under $N_2$. The mixture was evaporated with toluene and the residue was chromatographed on silica gel using EtOAc as eluent. Resultant crystalline material (47 mg) was recrystallised from $CHCl_3$ to give pure **19**, m.p. 98–100°, IR $\nu_{max}^{KBr}$ 3350 (OH), 1675 (C=O) $cm^{-1}$; PMR $\delta_{TMS}^{CD_3COCD_3}$ 3.36 (1H, m, –CHO), 3.99 (3H, m, $CH_2OH$), 4.77 (2H, br.m, –CH–O), 5.87 (1H, dd, J = 10 Hz, 1 Hz, =H), 6.76 (1H, dd, J = 10 Hz, 5 Hz, =H); MS *m/e* 154 ($M^+$). (Found: C, 53.68; H, 5.19. Calc. for $C_7H_8O_4$; C, 53.84; H, 65.16%).

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