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Synthesis of Diels-Alder *Bis*-Adducts of Methoxycarbonyl-1,4-benzoquinone

A. ASHNAGAR* and J.M. BRUCE†
Department of Nanobiotechnology, Pasteur Avenue,
Sq. No. 69, Post Code No. 13164, Pasteur Institute of Iran, Tehran, Iran
Fax: (98)(216)6465132; Tel.: (98)(216)6953311; E-mail: aashnagar2003@yahoo.com

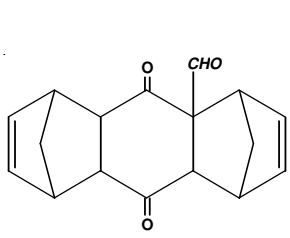
The feasibility of obtaining *bis*-adducts from a mono-substituted 1,4-benzoquinone with an electron withdrawing substituent, like methoxycarbonyl-1,4-benzoquinone with simple dienes such as 1,3-butadiene and cyclopentadiene were investigated and a procedure for the preparation of 9,10-anthraquinones was established. The *bis*-adducts were obtained in a moderate yield, around 35 %.

Key Words: Synthesis, Diels-Alder, *bis*-Adducts, Methoxycarbonyl-1,4-benzoquinone.

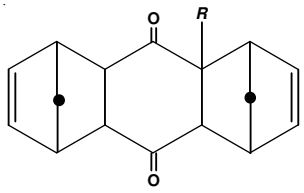
INTRODUCTION

In present studies, the Diels-Alder reactions of methoxycarbonyl-1,4-benzoquinone were discussed in detail[1]. In this work, the *bis*-adducts of methoxycarbonyl-1,4-benzoquinone is presented. First a brief introduction concerning these types of reactions is given. A mixture of two *bis*-adducts (4:1) has been isolated on addition of an excess of cyclopentadiene to formyl-1,4-benzoquinone[2]. Only the stereochemistry of the major component was assigned, *endo:exo* (**I**). The minor component decomposed during attempted separation. Addition of an excess of cyclopentadiene to acetyl-, propionyl-, isobutyryl-, phenylacetyl- and benzoyl-1,4-benzoquinone gave the corresponding *bis*-adducts (**II, a-e**). Brown *et al.*[3] assigned *endo-anti-endo* stereochemistry to the adducts (**II, a,b,d**). Coville[4] reported the *bis*-adducts of trifluoromethyl- and methoxycarbonyl-1,4-benzoquinones with cyclopentadiene and assigned structures (**IIIa**) and (**IIIb**), respectively and since he had obtained a mixture of two *bis*-adducts from trifluoro-methyl-1,4-benzoquinone, he suggested that the other isomer should have the *endo-anti-exo* configuration (**IV**). Pivaloyl-1,4-benzoquinone gives a mixture of two *bis*-adducts which were separated and identified as *endo-syn-exo* (**V**) and *endo-anti-endo* (**VI**) as major and minor components, respectively[5]. Reaction of quinone (**VII**), *mono*-adduct (**VIIIa**) and *mono*-adduct (**VIIIb**) with an excess of cyclopentadiene in acetonitrile gave the *endo-endo bis*-adduct (**IX**)[6]. Useful references are given for the reactions of simple alkyl- and chloro-substituted as well as more complex acyl-, cyano- and methoxycarbonyl-1,4-benzoquinones[7,8].

†Department of Chemistry, University of Manchester, Oxford Road, Manchester, M13 9PL, U.K.

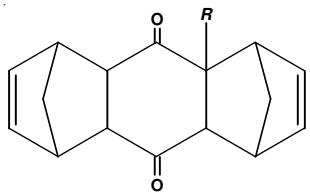


(I)

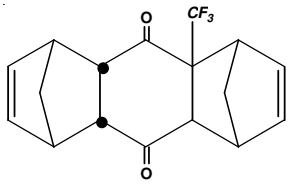


(II)

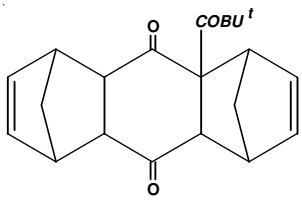
a. R=Me b. R=Et c. R=Pr^i
d. R=CH_2Ph e. R=Ph



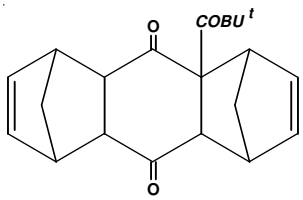
(III) a. R=CF_3 b. R=CO_2Me



(IV)



(V)



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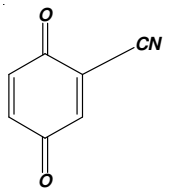

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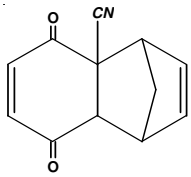
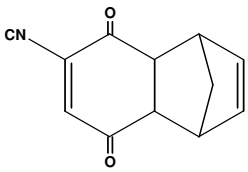
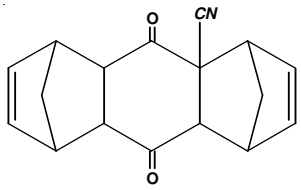


(VIIIa)



(VIIIb)



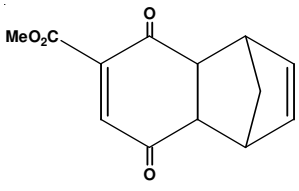
(IX)

EXPERIMENTAL

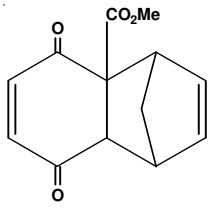
Nuclear magnetic resonance (NMR) spectra were recorded with Perkin-Elmer R12B (60 MHz), R32 (90 MHz) and R34 (220 MHz) spectrometers, respectively. Tetramethylsilane (TMS) was used as an internal standard and coupling constants (*J*) are expressed in Hz. Infrared spectra were measured using a Pye Unicam SP3-200 spectrophotometer. Low resolution electron impact mass spectra were recorded on A. Electron impact MS30 and Kratos MS25 instruments; mass measurements were made on the former and chemical ionization spectra were recorded on the latter using ammonia as the reagent gas. Sublimation and bulb-to-bulb distillation temperature are those of the Buchi Oven (heating bath). All solvents, liquid reagent and starting material were distilled prior to use. Irradiation with visible light was carried out at 15 °C, using tungsten-filament lamps. Analytical and preparative TLC were carried out with Merck silica gel plates (5 × 10 cm × 0.25 mm and 10 × 20 cm × 0.25 mm), type $60F_{254}$.

Preparation of *endo-anti-endo*-4a-methoxycarbonyl-1,4:5,8-dimethano-1,4,4a,5,8,8a,,9a,10a,-octahydro-9,10-anthraquinone: An excess of cyclopentadiene (5 mL) was added to methoxycarbonyl-1,4-benzoquinone (220 mg, 1.325 mmol) at room temperature and the resulting yellow solution was left for 14 h. Removal of the excess of cyclopentadiene at 20 °C/20 mmHg gave a yellow oil which was triturated with pentane (2 mL) to give a white-yellow crystalline compound. Crystallization from petroleum ether (b. 60-80 °C) gave almost white crystals (276 mg, 70 %), m.p. 86-88 °C (lit.[4] 91.5-92.5 °C). (Found (%): C, 72.5, H, 6.0; calculated (%) for $C_{18}H_{18}O_4$: C, 72.5, H, 6.0). It had δ (8 %, $CDCl_3$, 220 MHz) 6.36 (dd, J_{-1} = 5.6, J_{-2} = 3.1, H-2), 6.27 (dd, J_{-1} = 5.6, J_{-2} = 3.1, H-3), 6.15 (dd, J_{-1} = 5.7, J_{-2} = 2.9, H-6 or H-7), 6.0 (dd, J_{-1} = 5.7, J_{-2} = 2.9, H-7 or H-6), 3.67 (s, CO_2Me), 3.66 (partially buried under CO_2Me, H-4), 3.39 (bs, split to fine structure on irradiation at δ 6.15, 6.0 and to a dm, J_{-1} = 7.8 and sharpened on irradiation at δ 1.40, H-5 + H-8), 3.27 (m, split to fine structure on irradiation at δ 6.36, 6.27 and sharpened on irradiation at δ 3.13, H-1), 3.13 (d, J = 3.9, collapsed to a singlet on irradiation at δ 3.27, H-9a), 2.83 (dd, J_{-1} = 10.2, J_{-1} = 3.6, H-8a or H-10a), 2.84 (dd, J_{-1} = 10.6, J_{-2} = 3.6, H-10a or H-8a), 1.58 (dt, J_{-1} = 9.4, J_{-2} = 1.6, H-11 syn), 1.48 (bd, J = 9.4, H-11 anti), 1.40 (dt, J_{-1} = 8.6, J_{-2} = 1.9, H-12 syn), 1.23 (bd, J = 9.4, H-12 anti); δ (7 %, C_6D_6, 220 MHz) 6.22 (bd, J_{-1} = 5.2, J_{-2} = 2.4, H-6 or H-7), 6.06 (bd, J_{-1} = 5.2, J_{-2} = 2.4, H-7 or H-6), 5.60-6.0 (m, sharpened on irradiation at δ 3.63, 2.90, H-2 + H-3), 3.20-3.40 (buried under CO_2Me, H-5 + H-8), 3.28 (s, CO_2Me), 3.10 (d, J = 3.7, H-9a), 2.90 (m, split to fine structure on irradiation at δ 5.80, H-1), 2.50 (dd, J_{-1} = 10, J_{-1} =3.7, H-8a or H-10a), 2.41 (dd, J_{-1} = 10, J_{-1} = 4, H-10a or H-8a), 1.25-1.45 (m, sharpened on irradiation at δ 5.80, 3.63, 2.90, 2× H-11), 1.18 (dt, J_{-1} = 8.9, J_{-2} = 1.7, H-12 syn), 0.8 (bd, J = 8.9, H-12 anti); ν^- (cm^{-1}) (Nujol) 1750 s, 1685 s, 1235 s; m/z (Electron impact) 298 (M^+, 2), 270 [$(M-CO)^+$, 2], 266 [$(M-HCO_2Me)^+$, 1], 233 [$(M+1-C_5H_6)^+$, 23], 232 [$(M-C_5H_6)^+$, 11], 201 [$(M-MeOH)^+$, 7], 200 [$(232-MeOH)^+$, 7], 173 [$(201-CO)^+$, 3], 172 [$(200-CO)^+$, 3], 167 [$(M+1-2\times C_5H_6)^+$, 10], 144 [$(172-CO)^+$, 2], 116 [$(144-CO)^+$, 3], 107[$(173-C_5H_6)^+$, 2], 66 [$(C_5H_6)^+$, 100], 65 [$(C_5H_5)^+$, 19]; (Chemical ionization) 316 [$(M+18)^+$, 3], 299 [$(M+H)^+$, 1], 184 [$(M+18-2\times C_5H_6)^+$, 21], 66 ($C_5H_6^+$, 27).

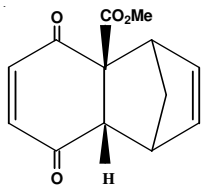
Thermolysis of *endo-anti-endo*-4a-methoxycarbonyl-1,4:5,8-dimethano-1,4,4a,5,8,8a,9a,10a-octahydro-9,10-anthraquinone: The following reactions were qualitative. (a). Sublimation of the *bis*-adduct at 135-140 °C/0.05-0.1 mmHg gave a pale yellow oil. ^{1}H NMR spectroscopy showed that a mixture of three mono-adducts was formed: (i) 2-methoxycarbonyl-5,8-methano-4a,5,8,8a-tetrahydro-1,4-naphthoquinone (**X**). (ii) *exo*-4a-methoxycarbonyl-5,8-methano-4a,5,8,8a-tetrahydro-1,4-naphthoquinone (**XI**). (iii) *endo*-4a-methoxycarbonyl-5,8-methano-4a,5,8,8a-tetrahydro-1,4-naphthoquinone (**XII**), in 1:2:3 ratio, respectively. It had δ (8 %, $CDCl_3$, 60 MHz) 6.98 (s, H-3, i), 6.80 (m, H-2+H-3, ii), 6.61 (s, H-2+H-3, iii), 2.50-4.0 (m, partially buried under CO_2Me absorptions, H-4a+H-8a+H-5+H-8, I, + H-5+H-8+H-8a, ii, +H-5+H-8+H-8a, iii), 3.88 (s, CO2Me, i), 3.84 (s, CO_2Me,



(X)



(XI)



(XII)

ii), 3.72 (s, CO_2Me, iii), 1.64 (m, 2×H-9, iii), 1.52 (m, 2×H-9, ii), 1.37 (m, 2×H-9, i); the spectrum in d_6-benzene had too many overlapping and could not be interpreted; m/z (Electron impact) 233 [$(M+1)^+$, 1], 200 [$(M-MeOH)^+$, 8], 173 [$(M-CO_2Me)^+$, 3], 172 [$(200-CO)^+$, 3], 167 [$(M+1-C_5H_6)^+$, 6], 136 [(167-MeO)+, 9], 135 [$(167-MeOH)^+$, 6], 107[$(135-CO)^+$ or $(172-C_5H_6)^+$, 3], 66 [$(C_5H_6)^+$, 100]; (Chemical ionization) 250 [$(M+18)^+$, 82], 233 [$(M+H)^+$, 100], 184 [$(250-C_5H_6)^+$, 64], 169 (97).

(b) *Bis*-adducts (40 mg) was dissolved in chlorobenzene (2 mL) and refluxed at 130 °C in oil bath for 3 h. A dark material was obtained. ^{1}H NMR spectroscopy showed that the product was a 2:1 *exo:endo mono*-adducts mixture. It had δ (3 %, $CDCl_3$, 60 MHz) 6.78 (AB-q, H-2+H-3, *exo*), 6.59 (s, H-2+H-3, *endo*), 6.09 (m, H-6+H-7, *exo*, +H-6+H-7, *endo*), 2.50-4.0 (m, partially buried under CO_2Me absorptions, H-8a+H-5+H-8, *exo*, +H-8a+H-5+H-8, *endo*), 3.90 (s, CO_2Me), 3.73 (s, CO_2Me), 1.64 (m, 2×H-9, *exo*, +2×H-9, *endo*); m/z (Electron impact) 232 (2), 200 (2), 173 (1), 172 (1), 167 (2), 136 (7), 135 (4), 107 (3), 66 (100); (Chemical ionization) 250 (44), 233 (57), 184 (37), 169 (100).

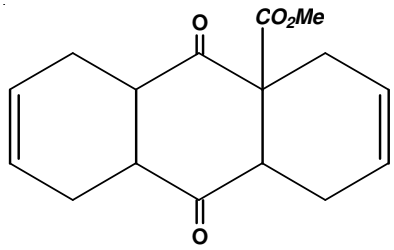
(c). Reaction (b) was repeated under a nitrogen atmosphere; less *exo*-isomer was obtained in comparison with (b).

(d). Reaction (b) was carried out in benzene; a pale yellow sticky oil was obtained which had a very complicated NMR spectrum.

4a-Methoxycarbonyl-1,4,4a,5,8,8a,9a,10a-octahydro-9,10-anthraquinone: 2-Methoxycarbonyl-1-benzoquinone (166 mg, 1 mmol) was introduced in a drawn-out test tube and cooled in solid carbon dioxide. Butadiene gas was passed in until liquid butadiene (*ca.* 2 mL) had condensed. The tube was partially evacuated, sealed and left in a Carius furnace at 80°C for 48 h. The initial orange colour faded to pale yellow. The tube was cooled in solid carbon dioxide and opened, then warmed up to room temperature to allow the excess of butadiene to evaporate. A pale yellow oil (315 mg) remained. Sublimation at 110 °C/0.1 mmHg gave a very sticky colourless oil (200 mg, 73 %). (Found (%): C, 69.8, H, 6.8; calculated (%) for $C_{16}H_{18}O_4$: C, 70.0, H,6.6). It had δ (5 %, $CDCl_3$, 220 MHz) 5.66 (m, H-2+H-3+H-6+H-7), 3.78 (s, CO_2Me), 3.57 (dt, J_{-1} = 6.7, J_{-2} = 1.6, collapsed to a doublet, J = 6.7, on irradiation at δ 2.95, 2.85, 2.70 and collapsed almost to a singlet on irradiation at δ 1.95, H-8a+H-9a+H-10a), 1.60-3.35 (m, 2×H-1 + 2×H-5+2×H-8); δ (5 %, C_6 D_6, 220 MHz) 5.46 (m, H-2+H-3+H-6+H-7), 3.34 (s, CO_2Me), 1.50-2.95 (m, H-8a+H-9a+H-10+2×H-1 + 2×H-4+2×H-5+2×H-8), a second order spectrum; m/z

(Electron impact) 274 (M^+, 72), 242 [(M-MeOH)$^+$, 43], 215 [(M-CO_2Me)$^+$, 74], 214 [(242-CO)$^+$, 58], 186 [(214-CO)$^+$, 37], 160 [(186-C_2 H^2)$^+$, 33], 107 [(214-C_7H_7O)$^+$, 57], 105 [(107-2H)$^+$, 82], 79 [(107-CO)$^+$, 100], 91 (30), 77 [(105-CO)$^+$, 91]; (Chemical ionization) 292 [(M+18)$^+$, 44], 275 [(M+H)$^+$, 100], 242 [(M+H-MeOH)$^+$, 8], 215 [(M+H- CO_2Me)$^+$, 35].

Preparation of 9,10-anthraquinone: (a) Using manganese dioxide: 4a-Methoxycarbonyl-1,4,4a,5,8,8a,9a,10a-octahydro-9,10-anthraquinone (**XIII**) (55 mg, 0.201 mmol) in benzene (15 mL) was treated with freshly prepared manganese dioxide[9] (660 mg, 12 equ.), was refluxed for 48 h. Filtration through Celite, washing the cake with benzene and removal of the solvent gave a pale brown crystalline compound (32 mg, 0.154 mmol, 77 %), sublimation point 253-288 (lit.[10], m.p. 273 °C). Sublimation at 110 °C/0.1 mmHg gave 9,10-anthraquinone as cream crystals (30 mg, 72 %), m.p. (sealed tube) 285-288 °C. (Found (%): C, 80.4; H, 3.8. Calcd. (%) for $C_{14}H_8O_2$, C,80.8; H, 3.8 %). It had δ (2 %, $CDCl_3$, 90 MHz) 8.35 (dd, J_{-1} = 6, J_{-2} = 3, H-1+H-4+H-5+H-8), 7.75-7.95 (m, H-1+H-4+H-5+H-8); δ (3 %, C_6 D_6, 90 MHz) 8.22 (dd, J_{-1} = 6, J_{-1} = 3.6, H-1+H-4+H-5+H-8), 7.08-7.28 (m, partially buried under benzene absorption, H-2+H-3+H-5+H-6); ν$^-$ (cm^{-1}) (Nujol) 1680 s, 1595 s, 1580 s; m/z (Electron impact) 209 [(M+1)$^+$, 17], 208 (M^+, 95), 180 [(M-CO)$^+$, 100], 152 [(180-CO)$^+$, 99], 126 [(152-C_2H_2)$^+$, 13], 76 [(152-CH)$^+$, 38], 50 [(176-C_2H_2)$^+$, 30]; (Chemical ionization) 226 [(M+18)$^+$, 53], 209 [(M+H)$^+$, 100], 180 [(M+H-CO)$^+$, 68], 152[(180-CO)$^+$, 67].



(XIII)

(b) Air and aqueous sodium hydroxide: A suspension of 4a-Methoxycarbonyl-1,4,4a,5,8,8a,9a,10a-octahydro-9,10-anthraquinone (**XIII**) (53 mg, 0.193 mmol) in aqueous sodium hydroxide (10 %, 2 mL) and dioxane (8 mL) was prepared. Air was passed through the suspension whilst it was refluxed for 7 h. Addition of water (6 mL) and filtration gave a solid (16.2 mg, 40 %), sublimation point 208-212 °C. Sublimation at 104 °C/0.1 mmHg gave 9,10-anthraquinone as cream crystals (16 mg, 37 %), sub. P. 220-230 °C.(lit.[10], m.p. 273 °C). The NMR spectrum showed the complete removal of the methoxycarbonyl group but the product was a mixture. The major component had δ (2 %, $CDCl_3$, 90 MHz) 8.32 (dd, J_{-1} = 6, J_{-2} = 3, H-1 + H-4+H-5+H-8), 7.68-7.90 (m, H-2+H-3+H-6+H-7); m/z (Electron impact) 208 (M^+, 30), 180 [(M-CO)$^+$, 91], 152 [(180-CO)$^+$, 20], 79 (100).

RESULTS AND DISCUSSION

The aim of this research is to investigate the feasibility of obtaining *bis*-adducts from a mono-substitued 1,4-benzoquinone with simple dienes such as 1,3-butadiene and cyclopentadiene and establish a procedure for the preparation of 9,10-anthraquinones. Addition of an excess of cyclopentadiene to methoxycarbonyl-1,4-benzo-quinone at room temperature eventually resulted in a white crystalline compound (70 %), whose spectroscopic and microanalysis results indicated it to be 4a-methoxycarbonyl-1,4:5,8-dimethano-1,4,4a,5,8,8a,9a,10a-octahydro-9,10-anthraquinone (**XIV**) as the *endo-endo* isomer, probably the *endo-anti-endo* one as indicated in Fig. 1. Approach for the anti-configuration is preferred. If compound (**XIV**) is the *endo-syn-endo* isomer, as shown in Fig. 2 all four olefinic protons have a similar environment and therefore are expected to have similar chemical shifts. This is not observed, thus supporting the anti configuration. Pyrolysis of (**XIV**) at 135-140 °C/0.1 mmHg gave a pale yellow oil whose NMR spectrum showed a mixture of three materials. Comparison of this spectrum with that of the product obtained from addition of one equivalent of cyclopentadine to methoxy-carbonyl-1,4-benzoquinone in the absence of trifluoroacetic acid showed that these three materials are: (i) *endo*-2-methoxycarbonyl-5,8-methano-4a,5,8,8a-tetrahydro-1,4-naphthoquinone (**X**). (ii) *exo*-4a-methoxycarbonyl-5,8-methano-4a,5,8,8a-tetrahydro-1,4-naphthoquinone (**XI**). (iii) *endo*-4a-methoxycarbonyl-5,8-methano-4a,5,8,8a-tetrahydro-1,4-naphthoquinone (**XII**) in 1:2:3 ratio, respectively.

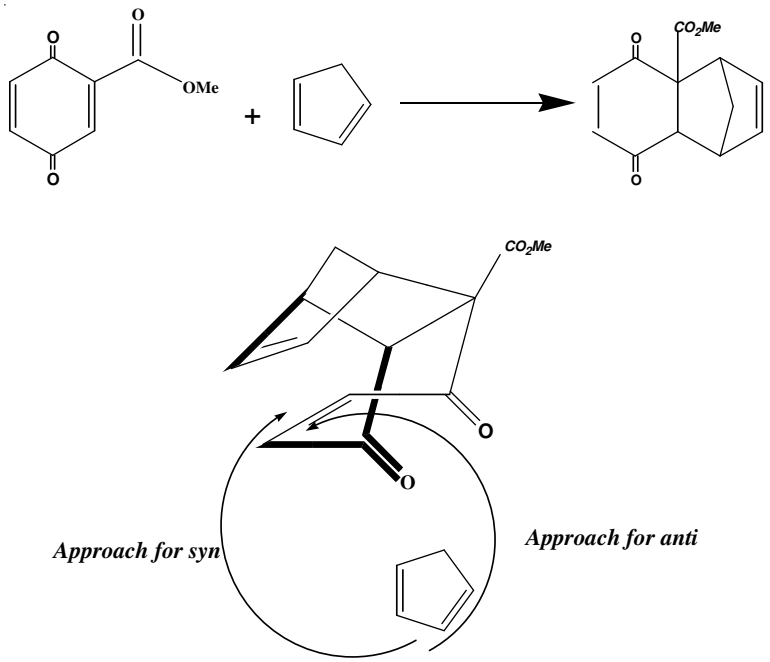
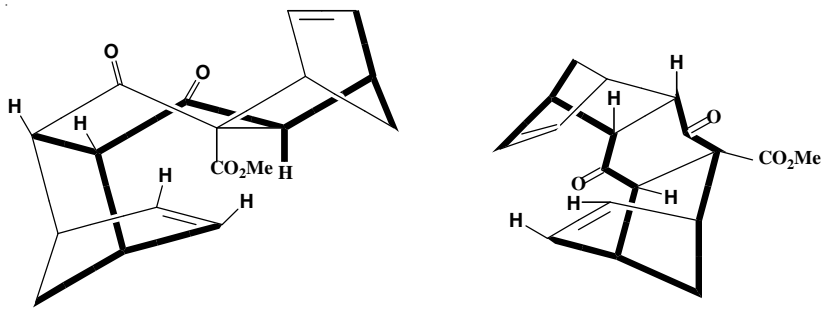


Fig. 1



Anti ***Syn***

Fig. 2

The formation of (**XI**) is due to the greater thermal stability of the *exo*-isomer than the *endo*-isomer and the formation of (**XII**) confirms the fact that the two newly formed σ-bonds at the substituted side are weaker than the two newly formed σ-bonds at the unsubstituted side of the quinone. Attempts were not made to separate these isomers.

Pyrolysis of the *bis*-adduct (**XIV**) in chlorobenzene at 130 °C for 3 h resulted in a 2:1 *exo:endo-mono*-adducts mixture. Again the more thermally stable and favoured *mono*-adducts (**XI**) was formed, indicating the thermal decomposition of the *bis*-adduct followed by re-addition of cyclopentadiene to the quinone and resulting in the formation of (**XI**) and (**XII**). The adduct (**X**) was not detected. The following mechanism is suggested given in Fig. 3. Since these pyrolyses did not give a sufficiently high proportion of (**X**) to make the method of preparative use for selective protection of the unsubstituted ethane linkage of methoxycarbonyl-1,4-benzoquinone, they were not investigated any further.

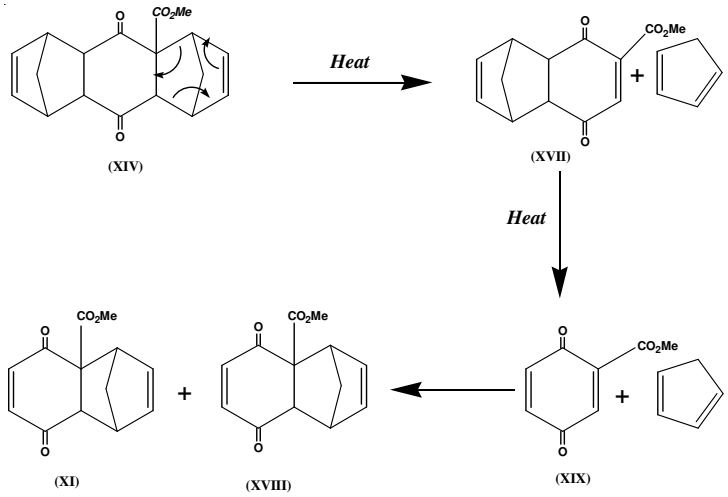
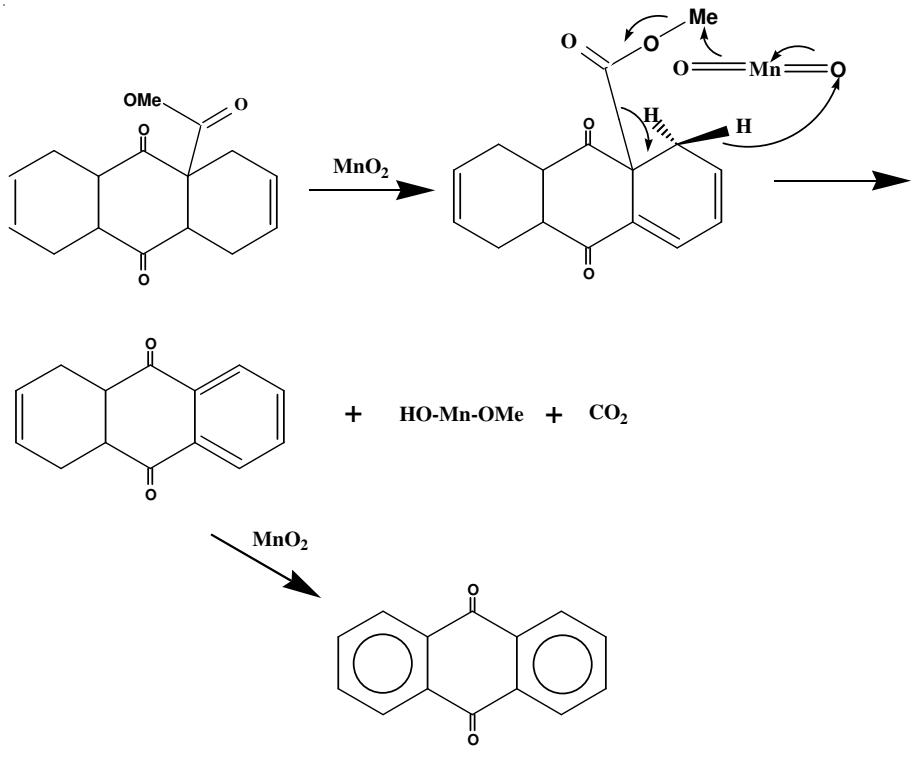


Fig. 3

Methoxycarbonyl-1,4-benzoquinone and an excess of butadiene heated at 80 °C for 48 h and the product then sublimed at 110 °C/0.1 mmHg gave a viscous colourless oil in 73 % yield. Its 220 MHz ^{1}H NMR in both d-$CDCl_3$ and C_6D_6 solvents were complex but showed only one absorption due to the methoxycarbonyl group and identification was correct for the formation of the *bis*-adduct (**XIII**). The mass spectra also indicated the formation of a *bis*-adduct.

It was decided to convert this *bis*-adduct to the corresponding 9,10-antrhaquinone. Therefore, treatment of 4a-methoxycarbonyl-1,4,4a,5,8,8a,9a,10a-octahydro-9,10-anthraquinone (**XIII**) with manganese dioxide in benzene at 80 °C for 48 h gave, after purification by sublimation and crystallization, a 72 % yield of 9,10-anthraquinone (**XVI**). The mechanism is given in Fig. 4. In an alternative procedure, adduct (**XIII**) was treated with aqueous 10 % sodium hydroxide in dioxane under reflux whilst a current of air was passed through the mixture for 7 h. Sublimation of the product afforded crude 9,10-anthraquinone (**XVI**) in *ca.* 35 % yield. Therefore, the methoxycarbonyl group located at an angular position can be removed and 9,10-anthraquinone can be obtained in a reasonable yield. This is a general procedure which can be used for the preparation of other substituted 9,10-anthraquinones.



(XVI)

Fig. 4

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