International Journal of ChemTech Research
CODEN(USA): IJCRGG ISSN : 0974-4290
Vol.2, No.1, pp 419-426, Jan-Mar 2010

Michael reactions with some of the Diels-Alder mono-adducts of 2,5-bismethoxycarbonyl-1,4-benzoquinone

Ashnagar, A.*[1] and Bruce, J.M.[2]

[1]Pasteur Institute of Iran, Nanobiotechnology department, Pasteur Avenue, SQ. NO. 69, Post Code No. 13164, Tehran, Iran.

[2]University of Manchester, Dept. of Chemistry, UK.

*Corres.author : aashnagar2003@yahoo.com
Tel. No. 00982166953311, Fax No. 00982166465132

Abstract: Michael additions between some of the Diels-Alder mono-adducts of 2,5-bismethoxycarbonyl-1,4-benzoquinone as acceptors and a few donor molecules such as malononitrile, thiophenol and p-cresol by using various bases (18-crown-6 ether +KF, 2-methoxypyridine, 4-dimethylaminopyridine, pyridine, sodium acetate) were investigated. In most cases a mixture was obtained which were separated and the desired product was characterized.
Keywords: Michael reactions, Diels-Alder, mono-adducts, 2,5-bismethoxycarbonyl-1,4-benzoquinone.

INTRODUCTION

The **Michael reaction** or **Michael addition** is the nucleophilic addition of a carbanion to an α,β-unsaturated carbonyl compound. It belongs to the larger class of conjugate additions. This is one of the most useful methods for the mild formation of C-C bonds. Many asymmetric variants exist.[1]

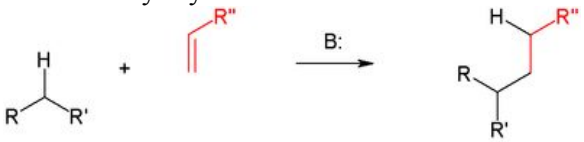


Figure 1

In this Fig. 1, the R and R' substituents on the nucleophile (a **Michael donor**) are electron-withdrawing groups such as acyl and cyano making the methylene hydrogen acidic forming the carbanion on reaction with base **B:**. The substituent on the activated alkene also called a **Michael acceptor** is usually a ketone making it an enone but it can also be a nitro group. As originally defined by Arthur Michael,[2,3] the reaction is the addition of an enolate of a ketone or aldehyde to an α,β-unsaturated carbonyl compound at the β carbon. A newer definition, proposed by Kohler,[4] is the 1,4-addition of a doubly stabilized carbon nucleophile to an α,β-unsaturated carbonyl compound. Some examples of nucleophiles include β-ketoesters, malonates, and β-cyanoesters. The resulting product contains a highly useful 1,5-dioxygenated pattern.

Further to the works published by the authors,[5-8] we decided to carry out the Michael addition reactions on some of the Diels-Alder mono-adducts of 2,5-bismethoxycarbonyl-1,4-benzoquinone; the results are presented in this article.

EXPERIMENTAL

Nuclear magnetic resonance (n.m.r.) 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 (EI) mass spectra were recorded on A.E.I. MS30 and Kratos MS25 instruments; mass measurements (M.M.) were made on the former, and

Chemical Ionization (CI) 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 $60F_{254}$.

Attempted reaction between 2,4a-bis methoxy carbonyl-4a,5,8,8a-tetrahydro-1,4-naphthoquinone and p-cresol: 2,4a-bismethoxy carbonyl-4a,5,8,8a-tetrahydro-1,4-naphthoquinone **(XI)** (55.6 mg, 0.2 mmol) in methylene chloride (2 mL) was added to a mixture of p-cresol (21.6 mg, 1 equ.) and the base [(i) 2-methoxypyridine(2.18 mg, 0.1 equ.), (ii) 4-dimethylaminopyridine (3 mg, 0.1 equ.)] in methylene chloride (1 mL) and refluxed for 18 hours. Removal of the solvent gave a yellow-brown mobile oil [(i) 72 mg, (ii) 80 mg]. NMR spectroscopy and mass spectrometry showed that no reaction had taken place, and that starting materials were recovered.

2,4a-Bismethoxycarbonyl-3-dicyanomethyl-2,3-4a,5,8,8a-hexahydro-1,4-naphthoquinone:

(a). Using 18-crown-6 + KF as base: 2,4a-bis methoxycarbonyl-4a,5,8,8a-tetrahydro-1,4-naphthoquinone **(XI)** (210 mg, 0.755 mmol) in methylene chloride (6 mL) was added to a solution of malononitrile (50 mg, 0.755 equ.), 18-crown-6 (6 mg, 0.03 equ.), and KF (9 mg, 0.3 equ.) in methylene chloride (2 mL) at room temperature and left for 4 hours while stirring. Removal of the solvent at 0 °C/20 mmHg, and pumping off the residue at 0.1 mmHg gave orange almost rectangular crystals (246 mg, 95%). Recrystallization from benzene-cyclohexane gave yellow-orange crystals (104 mg, 40%), m.p. 128-133 °C. (Found: C, 58; H, 4.7; N, 7.5; $C_{17}H_{16}O_6N_2$ requires: C, 59.3; H, 4.65; N, 8.74%). It had δ (5%, $CDCl_3$, 220 MHz) 12.75 (s, 1-OH), 5.70 (m, sharpened on irradiation at δ 2.95, 2.65, H-6+H-7), 4.73 [d, J=2.6, collapsed to a singlet on irradiation at δ 4.12, $CH(CN)_2$], 4.12 [d, J=2.3, collapsed to a singlet on irradiation at δ 4.73, H-3], 3.94 (s, CO_2Me), 3.80 (s, CO_2Me), 3.34 (dd, J_1=12.6, J_2=6.6, H-8a), 2.95 (dm, J_1=18.6, H-5α or H-5β), 2.65 (m, H-8β or H-8α), 2.19 (dm, J_1=18.6, H-5β or H-5a), 1.86 (m, H-8α or H-8β); δ (4%, C_6D_6, 220 MHz) 13.07 (s, OH), 5.35 (m, sharpened on irradiation at δ 2.27, H-6 or H-7), 5.22 (m, sharpened on irradiation at δ 2.30, H-7 or H-6),), 4.36 [d, J=2.2, collapsed to a singlet on irradiation at δ 4.06, $CH(CN)_2$ or H-3], 4.06 [d, J=2.2, collapsed to a singlet on irradiation at δ 4.36, H-3 or $CH(CN)_2$], 3.15-3.27 (H-8a), 3.20 (s, CO_2Me), 3.03 (s, CO_2Me), 2.27 (dm, J_1=19.6, H-5α or H-5β), 2.30 (s, 1.86 (m, H-8α or H-8β), 1.95 (m, H-8β or H-8α), 1.75 (dm, J_1=19.6, H-5β or H-5a); m/z (E.I.) 247 [$(M\text{-}CH_2(CN)_2 \text{–}MeO)^+$, 31], 219 [$(247 \text{–}CO)^+$, 73], 218 [$(247 \text{–}HCO)^+$, 55], 187 [$(219 \text{–}MeOH)^+$, 92], 186 [$(218 \text{–}MeOH)^{\cdot+}$, 81], 160 [$(219 \text{–}CO_2Me)^{\cdot+}$, 44], 159 [$(187 \text{–}CO)^+$, 70], 158 [$(186\text{–}CO)^{\cdot+}$, 18], 131 [$(159 \text{–}CO)^+$, 54], 105 [$(131 \text{–} C_2H_2)^+$, or $(159 - CH_2{=}CH\text{-}CH{=}CH_2)^+$, 81], 77 ($C_6H_5^+$, 90) 66 $[CH_2(CN)_2^+$, 100]; (C.I.) 362 $[(M+18)^+$, 1], 345 $[(M+H)^+$, 2], 247 (100). The NMR spectrum indicates that the adduct is in the enolic form.

(b). Using 2-methoxypyridine as base: Reaction (a) was repeated except that 2-methoxypyridine (0.1 equ.) was used instead of 18-crown-6 + KF, and the reaction mixture was left at 0 °C for 12 hours. NMR spectroscopy showed that a ca. 1:1 mixture of the starting material and the product had been formed. m/z (E.I.) .) 279 $[(M\text{-}CH(CN)_2)^+$, 10], 278 $[(M\text{-}CH_2(CN)_2)^{\cdot+}$, 7], 247 (65), 219 (40), 218 (36), 187 (44), 186 (44), 160 (25), 159 (44), 131 (36), 105 (100), 77 (84), 66 (44); (C.I.) 362 (2), 345 (7), 247 (74), 153 (100).

(c). Using DBU as base: Reaction (a) was repeated except that DBU (0.1 equ.) was used instead of 18-crown-6 + KF. NMR spectroscopy showed that a 1:1 mixture of the starting material and the product was formed.

(d). Using 4-dimethylaminopyridine as base: Reaction (a) was repeated except that 4-dimethylaminopyridine (0.5 equ.) was used instead of 18-crown-6 + KF, and the reaction mixture was refluxed for 3 hours. 2,4a-Bismethoxycarbonyl-3-dicyanomethyl-2,3-4a,5,8,8a-hexahydro-1,4-naphthoquinone was obtained as a red-orange glass (98%). It had δ (2%, $CDCl_3$, 60 MHz) 5.66 (m, H-6+H-7), 4.83 [m, $CH(CN)_2$], 4.12 [m, H-3], 4.0-3.70 (H-8a), 3.93(s, CO_2Me), 3.78 (s, CO_2Me), 3.63 (s, CO_2Me or $CH(CN)_2$), 1.90-3.40 (m, 2×H-5 + 2×H-8); m/z (E.I.) 344 $[(M\text{-}CO_2Me)^+$, 8], 278 $[(M - CH_2(CN)_2^{\cdot+}$, 9], 253 $[(285 \text{–}MeOH)^+$, 57], 247 $[(278 \text{–} MeO)^+$, 8], 245 (39), 244 (62), 226 $[(285\text{-}CO_2Me)^+$, 11], 187$[(246\text{-}CO_2Me)^+$, 10], 186 $[(246\text{-}HCO_2Me)^+$, 12], 159 $[(187\text{-}C)^+$, 8], 158 $[(186\text{-}CO)^+$, 9], 122 $[(MeN.C_5H_5N)^+$,67], 121(83), 105 (31), 66 $[(CH_2(CN)_2^+$, 100].

2,4a-Bismethoxycarbonyl-3-phenylthio-2,3,4a,5,8,8a-hexahydro-1,4-naphthoquinone: 2,4a-Bismethoxycarbonyl-3-phenylthio-4a,5,8,8a-tetrahydro-1,4-naphthoquinone (351 mg, 1.263 mmol) in benzene (5 mL) was added to a solution of thiophenol (138.9 mg, 1.263 mmol) and 2-methoxypyridine (14.1 mg, 0.1 equ.) in benzene (2

mL) over 20 minutes at room temperature and left for 28 hours. Removal of the solvent and pumping off the residue at 0.1 mmHg gave a light brown sticky oil (439 mg, 90%). NMR spectroscopy showed that the product consisted of major and minor isomers. Soxhlet extraction (methylene chloride) gave the almost pure major isomer. (Found: C, 60.2; H, 4.95; S, 8.0; $C_{20}H_{20}O_6S$ requires: C, 61.86; H, 5.2; S, 8.2%). It had δ (4%, $CDCl_3$, 220 MHz) 12.93 (s, 1-OH), 7.20-7.80 (m, 5×H, aromatic), 5.67 (m, split to a dm, J_1=8, on irradiation at δ 2.56, 2.37, H-6+H-7), 4.63 (s, H-3), 3.80-4.0 (H-8a, buried under CO_2Me absorptions), 3.87 (s, CO_2Me), 3.84 (s, CO_2Me), 2.56 (dm, J_1=18, H-5+H-8), 2.37 (dm, J_1=18, H-5), 2.16 (dm, J_1=18, H-8); δ (3%, C_6D_6, 220 MHz) 13.36 (s, 1-OH), 7.54 (m, H-2'+H-6'), 7.06 (m, H-3'+H-4'+H-5'), 5.47 (m, sharpened on irradiation at δ 2.60, H-6 + H-7), 4.73 (S, H-3), 3.84 (ddm, H-8a), 3.42 (s, CO_2Me), 3.33 (s, CO_2Me), 2.60 (dm, J_1=19.6, H-5α or H-5β), 2.43 (dm, H-8α or H-8β), 2.25 (dm, H-8β or H-8α), 2.05 (dm, H-5β or H-5a); $\bar{\nu}$ (cm^{-1}) (CH_2Cl_2) 3030w, 2960m, 1760s, 1740s, 1660s, 1610m, 1580w, 1210s; m/z (E.I.) 388 [($M^{\cdot+}$, 1), 0.5], 279 [(M-PhS)$^+$, 7], 247 [(279-MeOH)$^+$, 23], 219 [(247 –CO)$^+$, 31], 218 [2×PhS or (247 –HCO)$^+$, 75], 187 [(219 –MeOH)$^+$, 29], 159 [(187 –CO)$^+$, 25], 131 [(159 –CO)$^+$, 18], 110 [PhSH, 100], 109 [(PhS)$^-$, 74], 103 [(131 -CO)$^+$, 81], 77 (109-S)$^-$?, 65]; (C.I.) 389 [(M+H)$^+$, 0.5], 296 [(M+18-PhS)$^+$, 25], 279 [(M-PhS)$^{\cdot+}$, 30], 247 [(279-MeOH)$^+$, 100], 219 [(247 –CO)$^+$, 24], 218 [2×PhS, 38], 110 [(PhSH)$^+$, 42], 109 [(PhS)$^-$, 20]. The NMR spectrum indicates that the adduct is in the enolic form.

Treatment of 2,4a-bismethoxycarbonyl-1-hydroxy-3-phenylthio-2,3,4a,5,8,8a-hexahydro-1,4-naphthoquinone with acetic anhydride:2,4a-Bismethoxycarbonyl-,4a,5,8,8a-hexahydro-1,4-naphthoquinone (265 mg, 0.953 mmol) in methylene chloride (2 mL) was added to a solution of thiophenol (104.9 mg, 0.953 mmol) and 2-methoxypyridine (10.4 mg, 0.1 equ.) in methylene chloride (1 mL) at room temperature and left for 4 hours (to prepare the mono-adduct in situ). The mixture was cooled to 0 °C. then pyridine (78.6 mg, 1 equ.) and freshly ditilled acetic anhydride (3 mL, excess) were added, and the mixture was maintained at this temperature for 1 hour. Removal of the solvents and excess of acetic anhydride gave a yellow-orange sticky oil (419 mg). NMR spectroscopy showed that a mixture of starting material and acetylated adduct had been formed. It had δ (5%, $CDCl_3$, 60 MHz) 7.35 (m, 5×H, aromatic), 6.90 (s, H-3, starting material), 5.74 (bs, H-6+H-7 adduct + H-6+H-7 starting material), 3.85, 3.75, 3.73 (all 's', 2× CO_2Me adduct + 2× CO_2Me starting material), 3.50-4.0 (H-8a adduct + H-8a starting material, buried under CO_2Me absorptions), 1.90-2.80 (m, 2× H-5+2× H-8 adduct + 2× H-5+2× H-8 starting material), 2.38 (s, AcO), 2.18 (s, AcO); m/z (E.I.) 430 [(M-CH_2=C=O)$^{\cdot+}$, or (monoacetylated adduct)$^{\cdot+}$, 21], 388 [(430- CH_2=C=O)$^{\cdot+}$, 51], 279 [(388-PhS)$^+$, 41], 247 [(279-MeOH)$^+$, 72], 219 [(247 –CO)$^+$, 44], 187 [(219 –MeOH)$^+$, 34], 159 [(187 –CO)$^+$, 29], 110 [PhSH, 100], 109 [(PhS)$^-$, 45], 77 (109-S)$^-$, 74]; (C.I.) 448 [(M+18 - CH_2=C=O)$^{\cdot+}$, or (monoacetylated adduct+18)$^{\cdot+}$, 4.3], 388[(448- CH_2=C=O)$^+$, 1.3], 298 [(388-MeO - CO_2Me)$^{\cdot+}$, 53], 296 [(388-MeOH - HCO_2Me)$^{\cdot+}$, 27], 126 [(C_5H_5N.OMe+18-H)$^+$?, 100].

(b). Using pyridine as base: The mono-adduct of thiophenol and 2,4a-bismethoxycarbonyl-4a,5,8,8a-tetrahydro-1,4-naphthoquinone (30 mg, 0.09 mmol) was dissolved in freshly distilled acetic anhydride (1 mL) and pyridine (2 drops) was added at room temperature. The solution was left for 1 hour. Removal of the excess of acetic anhydride gave a dark brown sticky oil (35 mg). NMR spectroscopy showed that the mono-adduct was partially decomposed to 2,5-bismethoxycarbonyl-1,4-benzoquinone and that a mixture was formed. The NMR spectrum was very complicated. The oil had m/z (E.I.) 430 [(M-CH_2=C=O)$^{\cdot+}$, or (monoacetylated adduct)$^{\cdot+}$, 14], 388 [(430- CH_2=C=O)$^+$, 35], 279 [(388-PhS)$^+$, 6], 278 [(388-PhSH)$^+$, 9], 276 (60), 247 [(279-MeOH)$^+$, 11], 244 (100), 219 [(247 –CO)$^+$, 35], 187 [(219 –MeOH)$^+$, 33], 159 [(187 –CO)$^+$, 21], 131 [(159 –CO)$^+$, 14], 105 [(131 –C_2H_2)$^+$, 38], 77 (105-CO)$^+$, 35]; 43 [(CH_3CO)$^+$, 71]; (C.I.) 448 [(M+18 - CH_2=C=O)$^{\cdot+}$, or (monoacetylated adduct+18)$^{\cdot+}$, 12], 388[(448-CH_2=C=O)$^+$, 18], 378 (100 ?), 298 [(388-MeO - CO_2Me)$^{\cdot+}$, 20], 296 [(388-MeOH - HCO_2Me)$^{\cdot+}$, 35], 126 (96 ?).

(c). Using acetic acid: Reaction (b) was repeated except acetic acid (10 drops) was used instead of pyridine. NMR spectroscopy showed that a similar mixture was formed. It had a very complicated NMR spectrum.

(d). Using sodium acetate: Reaction (b) was repeated except freshly fused sodium acetate (5 mg) was used instead of pyridine, and the mixture was left for 2 hours. A yellow oily solid was obtained. NMR spectroscopy showed that the mono-adduct was partially decomposed, and that a mixture was formed. The NMR spectrum was again very complicated; m/z (E.I.) 388 [(472- 2×CH_2=C=O)$^+$, or (430- CH_2=C=O)$^+$, 11], 279 (9), 247 (6), 219 (18), 187 (19), 159 (20), 131 (19), 105 (85), 77 (100), 35]; (C.I.) 448 [(diacetylated adduct+18)$^+$, 1.6], 473 [(diacetylated adduct+1)$^+$, 0.7], 430 (2), 388(33), 387 (100), 18], 298 (29), 296 (45)].

Treatment of 2,4a-Bismethoxycarbonyl-3-di cyanomethyl-2,3-4a,5,8,8a-hexahydro-1,4-naphthoquinone with acetic anhydride: 2,4a-Bismethoxycarbonyl-3-dicyanomethyl-2,3-4a,5,8,8a-hexahydro-1,4-naphthoquinone with acetic anhydride (25 mg, 0.073 mmol) was dissolved in a mixture of freshly fused sodium acetate (5 mg) and acetic anhydride (1 mL) at room temperature and left for 2 hours. Removal of the ecess of acetic anhydride and pumping off the residue at 0.1 mmHg gave a yellow-orange oil (30 mg). NMR spectroscopy showed that a mixture was formed. It had δ (3%, $CDCl_3$, 60 MHz) 5.67 (m, olefinic protons), 4.82 bs, $CH(CN)_2$], 3.91(s, CO_2Me), 3.77 (s, CO_2Me), 4.0 – 2.0 [m, partially buried under CO_2Me absorptions, H-5's + H-8's + H-8a's), 2.08 (s, 2×AcO); m/z (E.I.) 446 [(diacetylated adduct+18)$^+$, 1], 387 [(mono-acetylated adduct+H)$^+$, 2.3], 386 [(mono-acetylated adduc)$^+$, 4], 282 (68), 247 [(344 – $CH_2(CN)_2$ -MeO)$^+$, 100].

Treatment of 2,4a-Bismethoxycarbonyl-5,8-methano-4a,5,8,8a-tetrahydro-1,4-naphthoquinone with p-cresol: 2,4a-Bismethoxycarbonyl-5,8-methano-4a,5,8,8a-tetrahydro-1,4-naphthoquinone (30 mg, 0.103 mmol) in benzene (1 mL) was added to a mixture of p-cresol (11.2 mg, 1 equ.) and 2-methoxypyridine (11.3 mg, 0.103 mmol) in benzene (1 mL) and refluxed for 24 hours. Removal of the solvent gave a product (30 mg) which was not soluble in d-chloroform. It had δ (6%, $(CD_3)_2CO$, 90 MHz) 9.84 (bs, OH), 7.34 (s, H), 6.55-7.20 (m, overlapped with absorptions due to the unreacted p-cresol), 3.95 (s, CO_2Me), 1.26 (bs, CH_2 , due to cyclopentadiene); m/z 438 [(Me.C_6H_4.O. C_6 $(CO_2Me)_2(OH)_2$.O. C_6H_4O. Me)$^{\cdot+}$, 62], 406 [(438-MeOH), 31], 332 [(Me.C_6H_4.O. $C_6H(CO_2Me)_2(OH)_2)^{\cdot+}$, 65], 300 [(332 –MeOH)$^+$, 54], 290 [$(C_{15}H_{14}O_6)^{\cdot+}$, 7], 268 [(300 –MeOH)$^{\cdot+}$, 43], 240[(268 –CO)$^{\cdot+}$, 35], 226 [$(C_6H_2(OH)_2(CO_2Me)_2)^{\cdot+}$, 36], 194 [(226 –MeOH)$^+$, 62], 162 [(194 –MeOH)$^+$, 45], 119 (94), 108, [(Me.C_6H_4.OH)$^{\cdot+}$, 84], 107 [(108 – H)$^+$, 74], 66 [$(C_6H_5)^+$, 100].

Treatment of 2,4a-Bismethoxycarbonyl-5,8-methano-4a,5,8,8a-tetrahydro-1,4-naphthoquinone with malononitrile: 2,4a-Bismethoxycarbonyl-5,8-methano-4a,5,8,8a-tetrahydro-1,4-naphthoquinone (145 mg, 0.5 mmol) in methylene chloride (2 mL) was added to a stirred mixture of malononitrile (33 mg, 1 equ.) 18-crown-6 (1.3 mh, 0.01 equ.) and KF (5.8 mg, 0.3 equ.) in methylene chloride (1 mL) at room temperature and left for 3 hours. Removal of the solvent and pumping off the residue at 0.1 mmHg gave a red-brown sticky oil which contained some small white particles (162 mg). NMR spectroscopy showed that the product was a 1:1 mixture of starting mono-adduct and the desired addition product. %). It had δ (8%, $CDCl_3$, 60 MHz) 12.75 (s, 1-OH), 6.89 (m, H-3 of starting material), 6.17 (m, H-6+H-7 of starting material, + H-6+H-7), 4.38 [bs, $CH(CN)_2$], 4.25 [bs, H-3], 4.05-3.60 (H-8a of starting material, + H-8a of product buried under CO_2Me absorptions), 3.87, 3. 83, 3.74 (all 's', 2×CO_2Me of starting material + 2×CO_2Me of product), 3.62 (bs, H-5+H-8), 3.52 (bs, H-5+H-8 of starting material), 1.68 (m, 2×H-9 of starting material + 2×H-9 of the product); m/z (E.I.) 291 [(M – $CH(CN)_2$$^+$, 5], 290 [(M – $CH_2(CN)_2$$^{\cdot+}$, 8], 259[(291 –MeOH)$^+$, 8], 258 [(290 –MeOH)$^{\cdot+}$, 15], 231 [(259-CO)$^+$, 6], 230 [(258-CO)$^+$, 3], 226 [(290+2H-$C_5H_6$)$^{\cdot+}$, 24], 225 [(291-$C_5H_6$)$^+$, 11], 194 [(226–MeOH)$^{\cdot+}$, 25], 193 [(225 –MeOH)$^{\cdot+}$, 9], 162 [(194 – MeOH)$^{\cdot+}$, 19], 134 [(162-CO)$^{\cdot+}$, 10], 66 [$(CH_2(CN)_2$$^+$ or $(C_5H_6)^{\cdot+}$, 100], 65 [$(CH(CN)_2$$^+$, 21]; (C.I.) 374 [(M+18)$^+$, 2], 357 [(M+H)$^+$, 0.3], 308 [(374 – $CH_2(CN)_2$$^{\cdot+}$, 17], 291 [(M – $CH_2(CN)_2$$^+$, 52], 242 [(308- C_5H_6)$^+$, 14], 227 [(226+H)$^+$, 100], 226(45), 66 (17).

2,4a-Bismethoxycarbonyl-3-phenylthio-5,8-methano-4a,5,8,8a-tetrahydro-1,4-naphthoquinone: (a). Using 18-crown-6+KF as base: 2,4a-Bismethoxycarbonyl-5,8-methano-4a,5,8,8a-tetrahydro-1,4-naphthoquinone **(XI)** (145 mg, 0.5 mmol) in methylene chloride (3 mL) was added to a mixture thiophenol (55 mg, 0.5 mmol), 18-crown-6 (4mg, 0.03 equ.), and KF (8.7 mg, 0.3 equ.) in methylene chloride (2 mL) over 10 minutes at room temperature and left for 4 hours while stirring. Removal of the solvent and pumping off the residue at 0.1 mmHg gave a yellow-brown sticky oil (190 mg, 95%) which solidified on standing at room temperature. It had δ (4%, $CDCl_3$, 220 MHz) 12.56 (s, OH), 7.26 (bs, 5×H, aromatic), 6.15 (m, H-6+H-7), 3.82 (s, CO_2Me), 3.60 (s, CO_2Me), 4.0-3.4 (H-8a, buried under CO_2Me), 1.65 (dm, J_1=12, 2×H-9); all of these absorptions are due to the addition product but resonance at δ 11.76 (bs, OH), 7.52 (m, H-3 + OH?), 7.31 (bs, 5×H, aromatic), 3.83 (s, CO_2Me), 3.82(s, CO_2Me) could be due to dimethyl 2,5-dihydroxy-3-phenylthioterephthalate; δ (4%, C_6D_6, 220 MHz) 13.0 (s, OH), 6.95 (bs, 5×H, aromatic), 5.98 (m, H-6+H-7), 3.22 (s, CO_2Me), 3.21 (s, CO_2Me), 3.60-3.10 (m, H-8a, buried under other absorptions), 1.35 (dm, J_1=12, 2×H-9); all of these absorptions are due to the addition product but resonance at δ 12.05 (m, OH), 7.70-6.95 (m, 5×H+ OH?), 3.87 (s, CO_2Me), 3.17 (s, CO_2Me) could be due to dimethyl 2,5-dihydroxy-3-phenylthioterephthalate. Absorptions due to H-3 of the addition product could not be assigned in either solvent, and could be buried under resonance in the region δ 4.0-3.0; $\bar{\nu}$ (cm^{-1}) (CH_2Cl_2) 3670w, 3050w, 2950w, 1750s, 1730s, 1655m, 1230s; m/z (E.I.) 402 [(M+2)$^{\cdot+}$, 17], 401 [(M+1)$^{\cdot+}$, 47], 400 [M$^{\cdot+}$, 89], 291

[(M-PhS)$^+$, 77], 259 [(291-MeOH)$^+$, 36], 231 [(259 – CO)$^+$, 29], 226 [(291-C_6H_5)$^{\cdot+}$, 40)], 218 [(PhSSPh)$^+$, 48], 199 [(231 –MeOH)$^+$, 23], 174 (37), 171 [(199–CO)$^{\cdot+}$, 18], 110 [PhSH$^+$, 100], 109 [(PhS)$^-$, 59], 66 ($C_5H_6^+$, 57), 65 ($C_5H_5^-$, 39); (C.I.) 420 [(M+2+18)$^+$, 12], 419 [(M+1+18)$^+$, 24], 418 [(M+18)$^+$, 100], 401 [(M+H)$^+$, 54], 400 [M$^{\cdot+}$, 25], 308 [(418- PhSH)$^+$, 78], 291 [(M-PhS)$^{\cdot+}$, 45], 282 [(18-crown-6 +18)$^+$, 69], 227 [(291- C_5H_5+H)$^+$, 37], 231 [(259 –CO)$^+$, 29], 218 (30), 110 (28), 109 (36), 66 (8), 65 (15).

(b). Using 2-methoxypyridine as base: Reaction (a) was repeated except that 2-methoxypyridine (0.1 equ.) was used instead of 18-crown-6 + KF, as base. NMR spectroscopy showed that almost the pure desired addition product (98%) had been formed. m/z (E.I.) .) 400(M$^{\cdot+}$, 42), 291 (71), 259 (47), 226 (100), 231 (46), 218 (95), 110 (95), 109 (84), 66 (88); (C.I.) 420 (47), 418 (42), 401 (24), 308 (91), 291 (99.8), 227 999), 126 (100), 110 (34).

RESULTS AND DISCUSSION

Treatment of p-cresol with 2,4a-bismethoxy carbonyl-4a,5,8,8a-tetrahydro-1,4-naphthoquinone (I) using 2-methoxypyridine and 4-dimethylaminopyridine as bases failed to give any product; only starting materials were recovered.

Malononitrile reacted with 2,4-bismethoxy carbonyl-4a,5,8,8a-tetrahydro-1,4-naphthoquinone (I) in methylene chloride using 18-crown-6 + KF as base. Recrystallization of the crude product from benzene-cyclohexane gave yellow-orange crystals whose NMR spectra in both $CDCl_3$ and C_6D_6 confirmed that the addition took place at the 3-position giving (II). The NMR spectrum in $CDCl_3$ had a resonance at δ 12.75 (s, 1-OH) indicating that the adduct exists in the enolic form (III). The reaction was repeated with other bases like 2-methoxypyridine and 4-dimethylaminopyridine, DBU, and DBN; all resulted in a mixture of (I) and (II) except for 4-dimethylaminopyridine which gave results almost identical to those described for 18-crown-6 + KF.

Addition of thiophenol to 2,4-bismethoxycarbonyl-4a,5,8,8a-tetrahydro-1,4-naphthoquinone (I) in benzene using 2-methoxypyridine as base gave a light brown sticky oil whose NMR spectrum showed it to be a mixture of major and minor isomers. Separation was unsuccessful due to decomposition on TLC and column chromatography and on fractional sublimation. However, NMR spectra in both $CDCl_3$ and C_6D_6 were consistent with structures (IV) and (V), but it was not possible to assign the stereochemistry. The NMR spectrum in $CDCl_3$ showed resonances at δ 12.93 (s, 1-OH) confirming that the adducts are in enolic form.

Treatment of the mono-adduct mixture (IV) and (V) with pyridine and acetic anhydride gave a yellow-orange sticky oil whose NMR spectrum showed it to be a ca. 1:1 mixture of (I), formed by the loss of thiophenol, and acetylated adduct(s).

Repetition of the reaction using pyridine-acetic anhydride without solvent, and with sodium acetate-acetic anhydride or acetic acid-acetic anhydride gave mixtures whose NMR spectra were complicated and showed that some decomposition to 2,5-bismethoxycarbonyl-1,4-benzoquinone (VIII) had occurred. It appears that mono-adducts, such as (IV) and (V) were relatively unstable, and readily eliminate thiophenol.

Treatment of 2,4a-bismethoxycarbonyl-3-dicyano methyl-2,3,4a,5,8,8a-hexahydro-1,4-naphthoquinone (II) or its enolic form (III) with sodium acetate-acetic anhydride at room temperatures gave a yellow-orange oil whose NMR spectrum showed it to be a mixture. On the bases of NMR and mass spectra, structures (IX) and (X) were assigned to the mono- and di-acetylated adducts, respectively. Separation was unsuccessful.

Treatment of the cyclopentadiene adduct 2,4a-bismethoxycarbonyl-5,8-methano-4a,5,8,8a-tetrahydro-1,4-naphthoquinone (XI) with p-cresol and 2-methoxypyridine in benzene at 80 °C gave a compound which was insoluble in d-chloroform. Its NMR and mass spectra showed a mixture, suggesting thermal decomposition to cyclopentadiene and to 2,5-bismethoxycarbonyl-1,4-benzoquinone (VIII) which had then reacted with p-cresol to give (XII) and (XIII), respectively. Alternatively, it can be assumed that the Michael reaction occurred and gave (XIV), which then decomposed to give (XII), but this does not explain the formation of (XIII) Fig. 2; free quinone would be necessary for this.

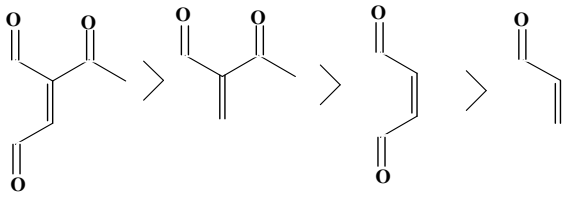
Treatment of malononitrile with ((XII) resulted in a 1:1 mixture of (XI) and 2,4a-bismethoxycarbonyl-1-hydroxy-3-dicyanomethyl-5,8-methano-2,3,4a,5,8,8a-hexahydro-1,4-naphthoquinone (XV). Separation was unsuccessful.

Thiophenol reacted with (XII) in methylene chloride, using 18-crown-6 + KF as base giving a mixture, but two components were characterized, i.e. 2,4a-bismethoxycarbonyl-1-hydroxy-3-phenylthio-5,8-methano-2,3,4a,5,8,8a-hexahydro-1,4-naphthoquinone (XVI) and dimethyl-2,5-dihydroxy-3-phenyl thio terephthalate (XVII) resulting from the formation of a very unstable intermediate (XVIII), followed by rapid retrodiene decomposition to cyclopentadiene (XVII), Fig. 3. The reaction was repeated by using 2-methoxypyridine as base, the NMR spectrum now showing the desired adduct (XVI) almost pure, and thiophenol. The reason why 2-methoxypyridine was better than 18-crown-6 + KF could be due to fluoride ion in the latter abstracting H-3 in (XVI) and causing enolization followed by decomposition to cyclopentadiene and (XVII), whereas the former base is too weak to do this.

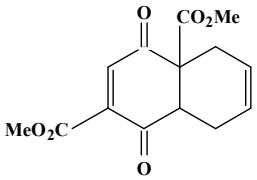
From the results obtained in this work it can be concluded that malononitrile adducts are fairly stable, but they are not good starting materials for further synthetic purposes. Thiophenols are rather unstable and readily lose thiophenol. Therefore, retro-Diels-Alder reactions designed to yield phenylthiophyroquinones are difficult to achieve. p-Cresol did not give satisfactory adducts. A further problem is that of separation. Most of the adducts decomposed on TLC or on column chromatography, and on bulb-to-bulb sublimation.

Therefor, there is a fine balance between the ease of formation of the Michael adduct, its stability relative to removal of the 'cyclopentadiene' protecting group, and the synthetical usefulness of the group which can be introduced in the initial Diels-Alder adduct.

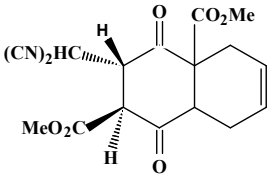
Michael reactivity for some functional groups is in the order:



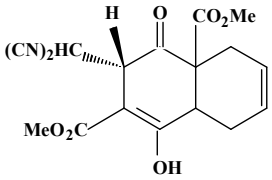
As observed, methoxycarbonyl-1,4-benzoquinone and 2,5-bismethoxycarbonyl-1,4-benzoquinone (VIII) are very reactive Michael acceptor, but their mono-adducts with cyclopentadiene are of lower reactivity, probably because the enedione rings are not planar and therefore there is poor C=C-C=O conjugation.



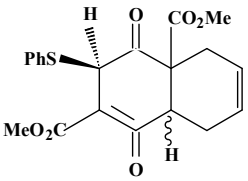
(I)



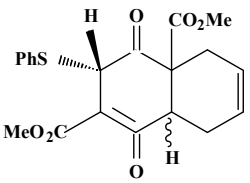
(II)



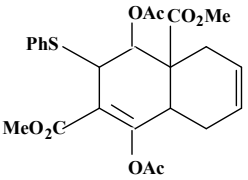
(III)



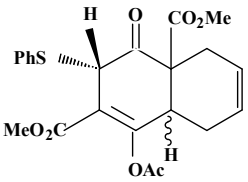
(IV)



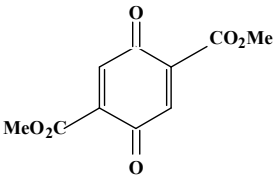
(V)



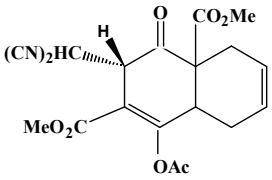
(VI)



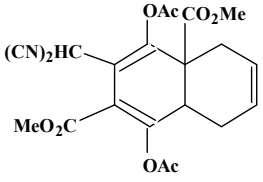
(VII)



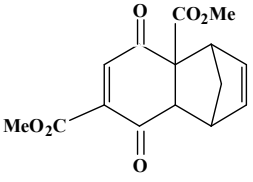
(VIII)



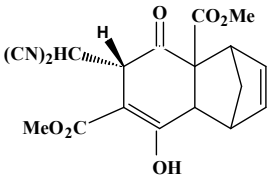
(IX)



(X)



(XI)



(XV)

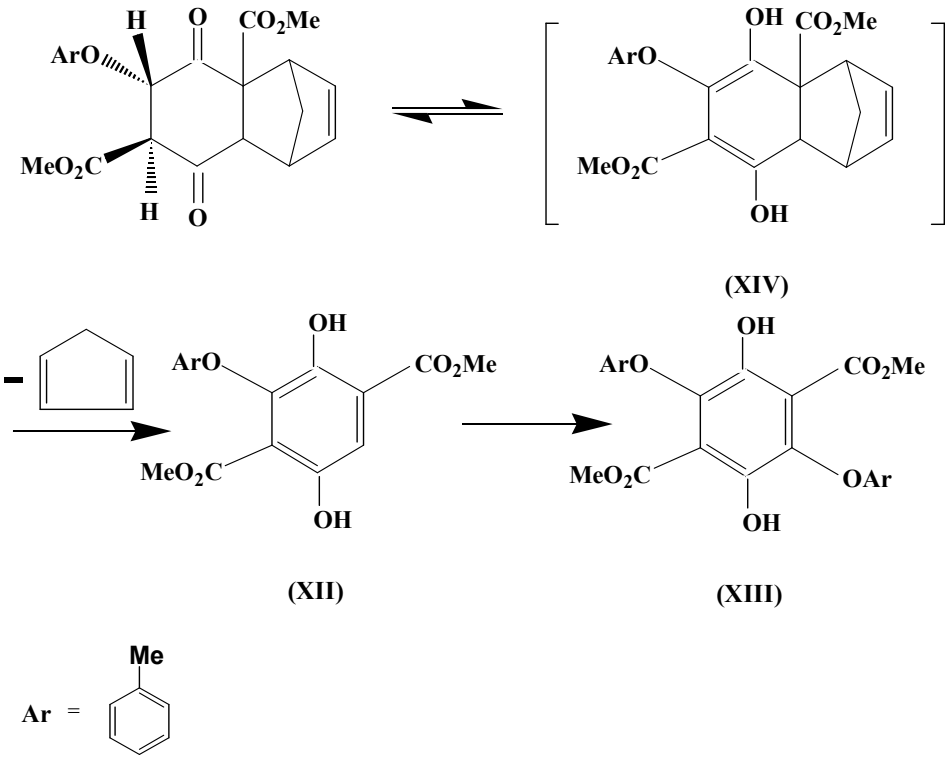


Figure 2

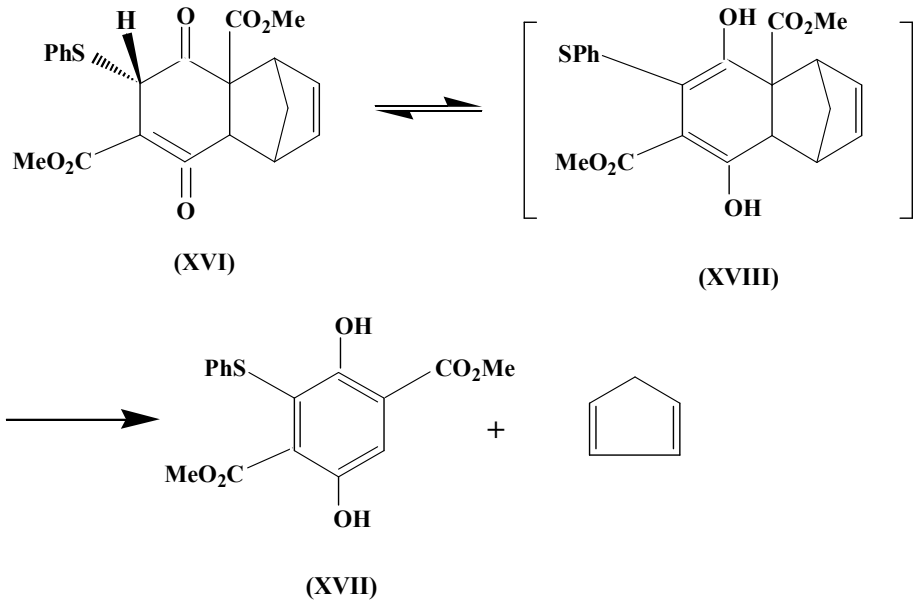


Figure 3

REFERENCES

1. Hunt I,"Chapter 18: Enols and Enolates — The Michael Addition reaction", University of Calgary, http://www.chem.ucalgary.ca/courses/351/Carey5th/Ch18/ch18-4-3.html
2. Michael A, "Ueber die Addition von Natriumacetessig- und Natriummalonsäureäthern zu den Aethern ungesättigter Säuren". Journal für Praktische Chemie 1887, **35** (1): 349–356. doi:10.1002/prac.18870350136. http://gallica.bnf.fr/ark:/12148/bpt6k907989/f356.chemindefer.
3. Michael A, "Ueber die Addition von Natriumacetessig- und Natriummalonsäureäther zu den Aethern ungesättigter Säuren". Journal für Praktische Chemie **49** (1): 20–29. doi:10.1002/prac.18940490103. http://gallica.bnf.fr/ark:/12148/bpt6k90814q/f29.table.
4. Kohler, J. Am. Chem. Soc., 1907, **37**, 385; ibid., 1935, **57**, 1316.
5. Ashnagar A, and Bruce JM, "Michael adducts of 2,5-bismethoxycarbonyl-1,4-benzoquinone with several different donor molecules", International J. of Chem. Tech., 2010, (in print).
6. Ashnagar A, and Bruce JM, "Michael Adducts of 2-Methoxycarbonyl-1,4-benzoquinone with Several Different Donor Molecules", Asian J. of Chem., 2010, 22 (10), (in print).
7. Ashnagar A, and Bruce JM, "Synthesis of Diels-Alder mono-adducts of methoxycarbonyl-1,4-benzoquinone", ", International J. of Chem. Tech., 2010, (in print).
8. Ashnagar A, and Bruce JM, "Synthesis of Diels-Alder bis-adducts of methoxycarbonyl-1,4-benzoquinone", Asian J. of Chem., 2010, (in print).

*****