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Synthesis of 2-Acetyl-5,8-dihydro-1,4-dihydroxy-3-methyl Naphthalene: A Product from the Isomerisation of Diels-Alder Adducts of Both 5-Methyl- and 6-Methyl-2-acetyl-1,4-benzoquinone with 1,3-Butadiene

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SYNTHESIS OF 2-ACETYL-5,8-DIHYDRO-1,4-DIHYDROXY-3-METHYL NAPHTHALENE: A PRODUCT FROM THE ISOMERISATION OF DIELS-ALDER ADDUCTS OF BOTH 5-METHYL- AND 6-METHYL-2-ACETYL-1,4-BENZOQUINONE WITH 1,3-BUTADIENE.

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ABSTRACT. 2-Acetyl-5,8-dihydro-1,4-dihydroxy-3-methyl-naphthalene was synthesised via Diels-Alder addition of 2-acetyl-3-methyl-1,4-benzoquinone to buta-1,3-diene followed by enolisation. It was identical with material obtained by pyridine-induced acetyl migration from the 1,3-butadiene adducts of both 3- and 6-methyl-2-acetyl-1,4-benzoquinone.

We have reported[1] that treatment of the Diels-Alder adduct (2)' from 1,3-butadiene and 2-acetyl-6-methyl-1,4-benzoquinone (1), with 1:1 pyridine-methanol at 22°C causes a [1,5]-acetyl shift and gives a good yield of the triketone (3) which, in the same medium at 65°C, smoothly isomerises to 5,8-dihydro-3-methyl

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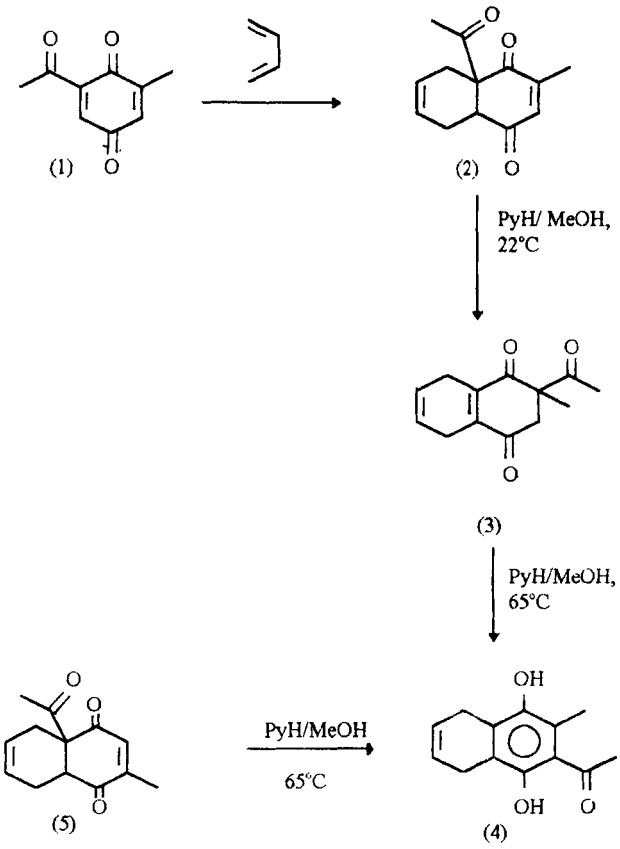
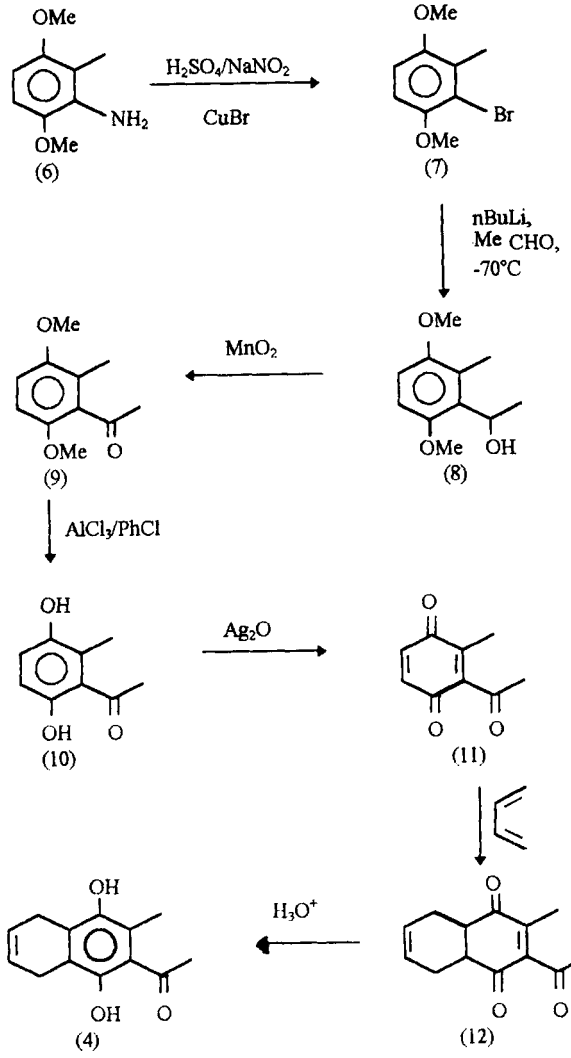


Scheme 1

1,4-dihydroxynaphthalene (4), identical with material obtained by similar rearrangement of the isomeric adduct (5) at 22°C (Scheme 1). Recently, we reported[2] that analogous [1,5]-benzoyl migration provides an approach to the anthracylinone ring system. Since the structure of the dihydroxynaphthalene (4) was previously established only by spectroscopic data, we now report on an unambiguous synthesis (Scheme 2) of (4), confirming its structure.



Scheme 2

2,5-Dimethoxy-6-methylaniline (6)[3], obtained by reduction of 2,5-dimethoxy-6-nitrobenzaldehyde,[4] was converted to the bromo-compound (7) by the Sandmeyer reaction. Cross-metallation with n-butyl-lithium followed by treatment with acetyldehyde gave the alcohol (8) which was oxidised with manganese dioxide to the ketone (9). Demethylation with aluminium chloride in chlorobenzene followed by oxidation with silver oxide in benzene gave 2-acetyl-3-methyl-1,4-benzoquinone (11). Treatment of this with 1,3-butadiene afforded the Diels-Alder adduct (12), which on enolisation with aqueous ethanolic sulfuric acid gave 2-acetyl-5, 8-dihydro-1,4-dihydroxy-3-methylnaphthalene (4), identical with material obtained previously[1] by isomerisation of the adducts (2) and (5) with pyridine - methanol.

EXPERIMENTAL

^{1}H n.m.r. spectra were recorded at 60 and 90 MHz on Perkin-Elmer R12 and R32 instruments. Infrared spectra were measured on a Perkin-Elmer 1710 FTIR spectrometer, and melting points were obtained using a Kofler block.

6-Bromo-2,5-dimethoxytoluene (7). 2,5-Dimethoxy-6-methylaniline (2 g, 0.01 mol) was dissolved in aqueous 5% sulphuric acid (25 ml) and diazotized with sodium nitrite (0.95 g, 0.01 mol) in water (9 ml) at less than 10°C (ice-salt). The cooled diazonium solution was then added below the surface of a hot (about 100°C) solution of potassium bromide (3.9g, 0.22 mol), hydrobromic acid (13.5 ml, 60% w/w in water) and freshly prepared cuprous bromide (2.42g, 0.22 mol) in water (25 ml) during 0.5h, under reflux, while the reaction mixture was shaken gently and the temperature of the reaction mixture was mantained at 90 - 100°C. The dark brown solution was then cooled and extracted with ether (2 x 50 ml, 5 x 25 ml). The combined ethereal extracts were washed with water (3 x 30 ml),

aqueous 5% sulphuric acid (2 x 30 ml), aqueous 5% sodium hydroxide (30 ml), water (3 x 30 ml), and dried ($CaCl_2$).

Removal of the solvent gave a brownish yellow solid (1.6 g, 57%), which on sublimation at 80-86°/0.05 mmHg. gave a white solid, m.p 97-98.5°C (Found: C, 46.8 ; H, 4.8; Br, 34.7. $C_9H_{11}BrO_2$ requires C, 46.8; H, 4.8; Br, 34.6%). It had δ (5%, $CDCl_3$, 90 MHz), 2.71 (s, ArH_2), 3.82 (s, OMe), 3.77 (s, OMe), 2.85 (s, Me); m/z 232, 230 ($M^{\cdot+}$,^{81}Br, ^{79}Br, 100, 100%), 217(91), 215(83); υ_{max} (Nujol) 1370s, 1255s, 1245s, 1030s, 1035s cm^{-1}.

6-(1-Hydroxyethyl)-2,5-dimethoxytoluene (8). 6-Bromo-2,5-dimethoxy toluene (1.7 g, 7.32 mmol) was dissolved in dry ether (65 ml) in a three-necked flask fitted with a serum cap, nitrogen gas inlet, thermometer, drying tube, and magnetic stirrer. The reaction was carried out under nitrogen throughout. The solution was stirred and cooled to - 70° (acetone-solid CO_2) and n-butyl-lithium (6 ml, 15% excess, as 15% solution in hexane) was injected through the serum cap. [After 1.5 hrs. TLC (1:1 ether: petroleum ether (bp. 40-60°) of a hydrolysed sample, showed that only dimethoxytoluene was present]. Freshly distilled acetaldehyde (3 ml, 18 mmol) was then injected and the mixture was stirred at -70° for a further 2.5 h. The mixture was allowed to warm to room temperature, and was then poured into water (200 ml). Extraction with ether (1 x 75, 2 x 50 ml), washing with water (2 x 100 ml), drying ($MgSO_4$), and removal of the solvent gave a yellow oil which was distilled (bulb-to-bulb) at 94-100°/0.05 mmHg to give the alcohol as a colourless oil, which solidified (1.3 g, 88%), m.p 40.5 - 42.5°C (Found C, 67.0 ; H, 8.4. $C_{11}H_{16}O_3$ requires C, 67.3; H, 8.2%). It had δ (5%, $CDCl_3$, 90 MHz), 6.68 (s, ArH_2), 5.10 (sextet, became quartet, J 6 Hz, on

adding D_2O, Ar-CH), 4.05 (d, J = 7 Hz, OH, removed by D_2O), 3.82 (s, OMe), 3.77 (s, OMe), 2.20 (s,ArMe), 1.51 (d, J 6 Hz, Me); m/z 198 ($M^{+}\cdot$, 80%), 182(93), 181(100), 166(34); υ_{max} (film) 3560-3100s cm^{-1}.

2',5'-Dimethoxy-6'-methylacetophenone (9). 6-(1-Hydroxyethyl)-2,5-dimethoxytoluene (1.0 g, 5.0 mmol) in dry ether (250 ml) was refluxed with active[5] manganese dioxide (9.0 g) for 24 h. The oxidant was then removed by filtration through Celite. Removal of the solvent from the filtrate gave white crystals (930 mg, 94%) which were sublimed at 90-96°/0.1 mmHg to give the ketone as a white solid, m.p. 59-59.5°C (Found: C, 67.7; H, 7.1. $C_{11}H_{14}O_3$ requires C, 68.0; H, 7.1). It had δ (10%, $CDCl_3$, 90 MHz), 6.82 (d, J 9 Hz, ArH), 6.68 (d, J 9 Hz, ArH), 3.88 (s, OMe), 3.86 (s, OMe), 2.47 (s, COMe), 2.1 (s, ArMe); m/z, 194 ($M\cdot^{+}$, 57%), 181(10), 79(100), 164(16), 151(8), 121(10), 91(19), 77(12), 65(10), 43(47), 18(25); υ_{max} (Nujol) 1700s cm^{-1}.

2',5'-Dihydroxy-6'-methylacetophenone (10). A mixture of 2',5'-dimethoxy-6'-methylacetophenone (0.9 g, 4.6 mmol) and powdered freshly sublimed aluminium chloride (2.0 g) in dry redistilled chlorobenzene (45 ml) was refluxed for 4 h. The brown solution was then cooled and poured into 10% hydrochloric acid (150 ml). The aqueous solution was extracted with ether (5 x 50 ml) and the combined extracts washed with water (2 x 40 ml), and dried (Na_2SO_4).

Removal of the solvent gave a pale yellow solid (715 mg) which was sublimed at 86-90°/0.1 mmHg to gave the hydroquinone as a pale yellow solid (526 mg, 74%), m.p. 122.5-123.5°C (Found: C, 65.1; H, 6.2. $C_9H_{10}O_3$ requires C, 65.1; H, 6.1%). It had δ (10%, $CDCl_3$, 60 MHz), 10.70 (s, OH, removed by D_2O), 6.90 (d, J 9 Hz, ArH), 6.70 (d, J 9 Hz, ArH), 6.80 (b, OH,

removed by D_2O), 2.62 (s, COMe), 2.41 (s, Ar Me); m/z 166 ($M^{+}\cdot$, 79%), 151 (100), 43 (14); υ_{max} (Nujol), 3330b, 3200b cm^{-1}.

2-Acetyl-3-methyl-1,4-benzoquinone (11). A mixture of 2',5'-dihydroxy-6'- methylacetophenone (0.55 g, 3.3 mmol), silver oxide (4.0 g), and anhydrous sodium sulphate (3.6 g) in dry benzene (30 ml), was shaken for 2.5 h at room temperature, and then filtered through Celite. Removal of the solvent gave an orange oil which slowly solidified at room temperature (530 mg, 94%), m.p. 39-42°C. Sublimation at 38-42°/0.1 mmHg gave the qumone as orange rectangular prisms, m.p 42-43°C (Found: C, 65.5; H, 4.8 $C_9H_8O_3$ requires C, 65.8; H, 4.9%). It had δ (15%, $CDCl_3$, 60 MHz), 6.85 (d, J = 9 Hz, quinonoid H), 6.65 (d, J = 9 Hz, quinonoid H), 2.42 (s, COMe), 2.00 (s, Me), δ (15%, C_6D_6), 6.10 (s, quinonoid H_2), 2.17 (s, COMe), 1.82 (s, Me); m/z 166 [(M+2)$\cdot^{+}$ 11], 164 ($M\cdot^{+}$, 100), 149(28), 121(50); υ_{max} (Nujol) 1710b, 1650s, 1670s cm^{-1}.

2-Acetyl-4a,5,8,8a-tetrahydro-3-methyl-1,4-naphthoquinone (12). A solution of 2-acetyl-3-methyl-1,4-benzoquinone (0.45g, 3.7 mmol) in dry benzene (6 ml), in a drawn-out a test tube was cooled in solid CO_2 until the solution was frozen, and then butadiene gas was passed in until liquid (6 ml) had condensed. The tube was partially evacuated (water-pump) until the butadiene began to boil, and then sealed. After 8 days at room temperature in the dark a pale yellow solution had been formed. The tube was then cooled (solid CO_2), opened and the excess of butadiene allowed to evaporate at room temperature. Removal of the benzene left brown-yellow crystals (662 mg), m.p. 98-101°C.

Recrystallisation from petroleum ether (b.p 40-60°), gave the Deels-Alder adduct as pale yellow crystals (485 mg, 82%), m.p 100-101°C (Found: C, 71.6;

H, 6.7. $C_{13}H_{14}O_3$ requires C, 71.5; H, 6.4%). It had δ (10%, $CDCl_3$, 60 MHz), 5.74 ('q', H-6+H-7), 3.30 (m, H-4a+H-8a), 3.00-2.00 (br 's', 2 x H - 5 + 2 x H-8), 2.40 (s, COMe), 1.96 (s, Me), δ (15%, C_6D_6, 60 MHz), 5.35 ('d' H-6 + H-7), 2.50 ('d', H-4a + H-8a), 2.30-1.75 (br s, 2 x H-5 + 2, 2 x H-8), 2.02 (s, COMe), 1.68 (s, Me); m/z 218($M^{\cdot+}$, 13), 203(13), 175(56), 77(34), 67(52); υ_{max} (Nujol) 1670s, 1690s cm^{-1}.

2-Acetyl-5,8-dihydro-1,4-dihydroxy-3-methylnaphthalene(4). The foregoing adduct (0.235 g, 1.07 mmol) was dissolved in 95% ethanol (13.0 ml), treated with 5% sulphuric acid (12.0 ml), and the yellow solution was then refluxed for 2 h. It became deep yellow. It was then cooled, concentrated to about half volume, and diluted with water (20 ml): the suspension was left to stand overnight in the dark. Filtration gave a yellow powder (165.5 mg), m.p. 135-145°C, which was sublimed at 120-124°/0.2 mmHg to give the hydroquinone as bright yellow crystals (150 mg, 64%) , m.p. 154-155°C (Found: C, 71.2; H, 6.5. $C_{13}H_{14}O_3$ requires C, 71.3; H, 6.5%). It had δ (5%, $CDCl_3$, 90 MHz), 11.75 (s, OH, removed by D_2O), 5.85 ('q', H-6+H-7), 4.25 (s, OH, removed by D_2O), 3.29 (s, 2 x H-5 + 2 x H-8), 2.65 (s, COMe), 2.45 (s, Me), δ (10%, 1:1 PyD_5: CD_3OD), 7.86 (s, H-6 + H-7), 3.41 (br s, 2 x H-5 + 2 x H-8), 2.60 (s, COMe), 2.39 (s, Me); m/z 218 ($M^{\cdot+}$, 100%), 203(93), 185(13), 175(25), 129(12), 105(14), 77(16), 58(29), 18(53); υ_{max} (Nujol) 3400b, 1600s cm^{-1}.

REFERENCES

1. Ahmad F.B.H, Bruce J.M, Khalafy J and Sabetian K., *J. Chem. Soc., Chem. Commun.*, 1981, 169.

2. Ahmad F.B.H and Bruce J.M. *Synth. Commun.*, 1994, *24*, 1639.

3. Ahmad F.B.H, *Pertanika*, 1989, *12*, 219.

4. Howe C.A, Howe A, Hamel C.R, Gibson H.W. and Flynn R.R., *J. Chem. Soc.*, 1965, 795.

5. Attenburrow, J., Cameron, A.F.B., Chapman, J.H., Evans, R.M., Hems, B.A., Jansen, A.B.A. and Walker, T., *J. Chem. Soc.*, 1952, 1094.

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