Tetrahedron Vol 47, No 25, pp 4287-4298, 1991
Printed in Great Britain

0040-4020/91 $3 00+ 00

Regiospecific α-Substitution of Crotonic Esters

Synthesis of Naturally Occurring Derivatives of 6-Ethyljuglone

Brigitte Caron and Paul Brassard

Département de chimie, Université Laval, Québec, Canada G1K 7P4

(*Received in USA* 27 *February* 1991)

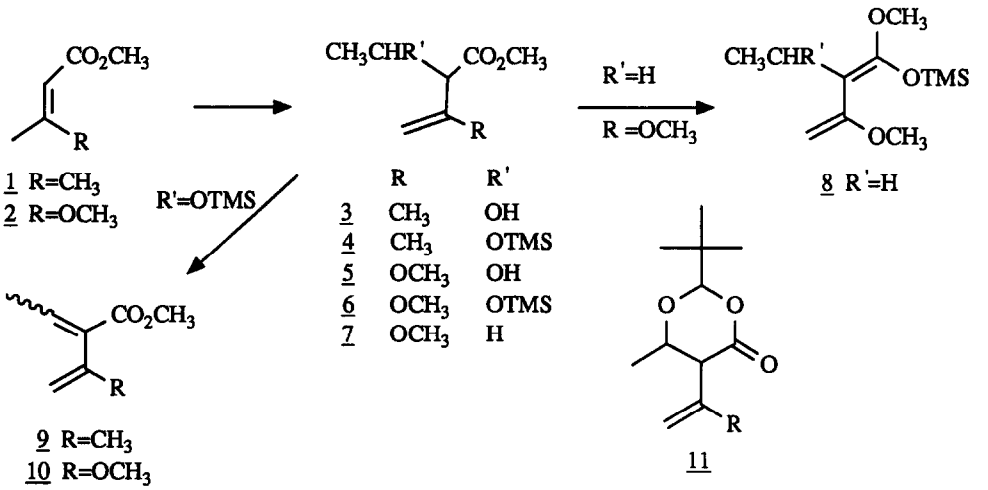
Summary - Methyl β-methoxycrotonate is alkylated regiospecifically, through the anion, in the α-position Enolsilylation of the resulting β,γ-unsaturated ester affords the corresponding 1,1,2,3-tetrasubstituted butadiene Cycloaddition of the latter to the appropriate halogenated benzoquinone, followed by various transformations, provides the first recorded syntheses of several natural products derived from 6-ethyl-7-methoxyjuglone

The synthesis of natural products through the Diels-Alder methodology involving electron-rich dienes and halogenated quinones can be envisaged systematically with the use of unsaturated esters as precursors[1] Nevertheless specific substitution patterns usually require a somewhat different approach in each case[1,2] A significant improvement of the overall strategy would be provided if a small number of substrates (butenoates) could be substituted regiospecifically by diverse reagents thus affording readier access to many different dienic materials

The substitution of unsaturated esters (less frequently acids) through the corresponding organometallic derivative, anion or dianion (in the case of acids) has been extensively studied and on occasion has shown a high degree of selectivity[3] In particular, reactions involving γ-bromocrotonate esters and zinc[4] or tin[5], tiglic acid and LDA in presence of cuprous ions[6] or crotonate, LDA and HMPA[7] are all claimed to provide excellent yields of the α-substituted products in alkylation or hydroxyalkylation procedures This result is generally favored by the use of low temperatures and conditions precluding reversibility, among others[7,8] Repetition of earlier methods gave low yields of complex mixtures in which however the γ-substituted products were absent. These approaches have frequently been applied to 3-methylcrotonates with varying results[9] but only linear products have been shown to occur in the few cases using the 3-methoxy analogues[10] (i e 2)

The ultimate objective of the present study consisted in the preparation, by simple and regiospecific means, of an unusual group of 6-ethylnaphthoquinones, the structures of which had not been confirmed by synthesis 6-Ethyl-7-methoxyjuglones in particular form a small group of fungal metabolites most of which present one of two unusual features oxidation at the 1'-C position or partial reduction of the quinonic moiety[11]

In the original project it was expected that hydroxyalkylation products 3 and 5, arising from reaction of acetaldehyde as electrophile and methyl 3-substituted crotonates (1 and 2), could be selectively enolsilylated to the desired diene (such as 8) since dehydration of an analogous substance (3, R=H) was reported to be difficult[7] However, in attempts with the dianions of hydroxy esters 3 and 5 or the anions of silyloxy esters 4 and 6 at different temperatures and using various bases, enolsilylation could not be induced to occur due to the competing rapid elimination An approach proposed by Seebach[12] which favors the required process (via an intermediate such as

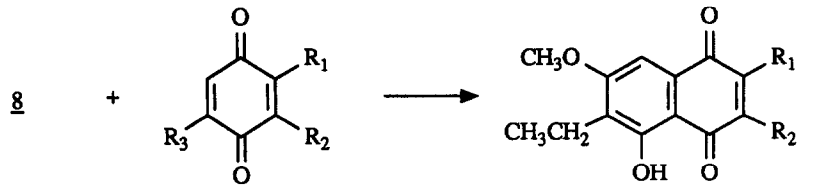


SCHEME I

11) would seem to involve more steps than a conventional functionalization of the side-chain (Scheme I)

2-Ethyl-3-methoxy-3-butenoate (7) obtained in essentially the same way as for hydroxyalkylation was converted to the mixed vinylketene acetal 8 by a standard procedure (LDA, ClTMS) From the 200 MHz nmr spectrum it appeared that the diene consists of only one diastereomer (probably the Z-configuration)[9], contains ~ 9% of the C-silylated compound but is otherwise quite pure It decomposes slowly at room temperature and so cannot be purified by distillation (even at -30 °C, one third of the reagent is converted to the C-silylated isomer within a month) Fortunately, diene 8 was found to be quite reactive and most cycloadditions could be conducted at 0-25 °C and were usually complete within a few hours Bromoquinones were the preferred dienophiles because of the ease with which the corresponding adducts aromatize since they contain sensitive enol ethers In contrast to earlier observations with other dienes, 2,5-disubstituted benzoquinones seemed to react more rapidly and efficiently than the 2,6-isomers and lowering reaction temperatures did not improve yields[1] Cycloadditions could be carried out in THF or benzene and sometimes better and more rapidly in dichloromethane In the case of benzoquinone 15, an increase in the reaction rate in dichloromethane was accompanied by an unusual if not surprising decrease in regioselectivity, with a 13% yield of the "wrong" isomer Finally aromatization of the adducts could be realized either by slow percolation through a column of silica gel or by treatment with HCl in THF

Among simpler natural products in this area, 6-ethyl-2,7-dimethoxyjuglone (22)[13-15] could be obtained directly, albeit in mediocre yield (44%) from diene 8 and benzoquinone 15 The substance is in all respects comparable to the authentic compound and to a synthetic material obtained earlier in extremely low yield and by a not unambiguous method[16] The synthesis of 6-ethyl-7-methoxyjuglone (19) should be possible by hydrogenolysis of the corresponding 2- or 3-bromojuglones (20) and (21) obtained respectively from benzoquinones 13 and 14 However, catalytic hydrogenation of 21 in the presence of palladium on charcoal and sodium acetate, afforded an array of products probably resulting from the action of base on the hydrogen bond-stabilized diketoform of the hydroquinone When the



	R_1	R_2	R_3
12	H	H	Br
13	Br	H	Br
14	H	Br	Br
15	OCH_3	H	Br
16	H	OCH_3	Br
17	OCH_3	OCH_3	Br
18	- benzo -		Cl

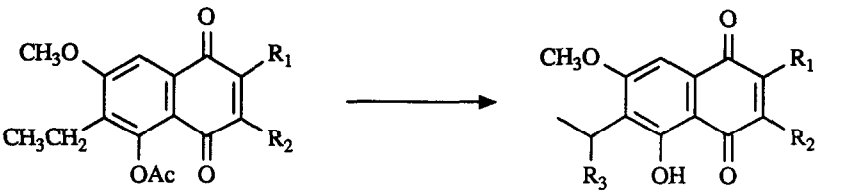
	R_1	R_2
19	H	H
20	Br	H
21	H	Br
22	OCH_3	H
23	H	OCH_3
24	OCH_3	OCH_3
25	OCH_3	OH
26	- benzo -	

SCHEME II

same procedure was applied to the acetate of 21 an excellent yield of the debrominated acetate of 19 was obtained However this ester could not be hydrolyzed to the parent compound, even under a variety of conditions, without extensive decomposition Finally, a cycloaddition with bromobenzoquinone (12) gave a 72% yield of the desired product 18 which was easily separated from a small amount of a bromo-derivative The only spinochrome in this series, 6-ethyl-2,3,7-trihydroxyjuglone was obtained similarly from benzoquinone 17 as the trimethyl ether (24)[18] However the m p was nearly 15 °C higher than that recorded for the same derivative, but selective demethylation gave the 2,7-dimethyl ether 25 having the same m p as the product obtained earlier in the same way (no spectral characteristics had been provided) (Scheme II)

Three cometabolites of juglone 22 (one conceivably an artefact) have been shown to be either hydroxylated, acetoxylated or ethoxylated in the 1'-C position of the parent compound [14,15] Syntheses of these antimicrobial[15] substances were explored on the less sensitive anthraquinone analogue 26 Reaction of the latter with NBS was unsatisfactory as expected but acetate 26a was readily converted to the acetate of bromide 28 and a similar result was observed with the acetate of juglone 22 When treated with $AgNO_3$ in aqueous acetone, this bromide 27 gave a 1 4 5 mixture of the 1'-nitrato derivative of 27 and juglone 29 in which the difficultly removed acetyl group had fortuitously migrated to the hydroxyl in position 1'-C Replacing $AgNO_3$ by $AgOCOCH_3$ afforded an excellent conversion to natural product 29 Subsequent treatment of this acetate with aqueous acetonitrile or ethanol containing 2% H_2SO_4 gave the required alcohol (31) and ethyl ester (33) respectively Another fungal metabolite showing partial reduction of the quinone ring, O-methylasparvenone (35) was obtained directly by reduction of juglone 19 with $LiAlH_4$[19] while various attempts to produce the natural acetone-adduct (36)[15] were unsuccessful[20] (Scheme III)

A number of useful or diagnostic correlations can readily be deduced from the numerous ^1H- and ^{13}C-NMR spectra recorded during this study In all 6-ethyl-7-methoxyjuglones, signals for 1'-and 8-protons fall within the



	R_1	R_2
22a	OCH_3	H
26a	- benzo -	

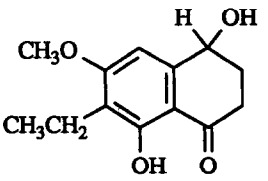
	R_1	R_2	R_3
27	OCH_3	H	Br
28	- benzo -		Br
29	OCH_3	H	OAc
30	- benzo -		OAc
31	OCH_3	H	OH
32	- benzo -		OH
33	OCH_3	H	OEt
34	- benzo -		OCH_3

SCHEME III

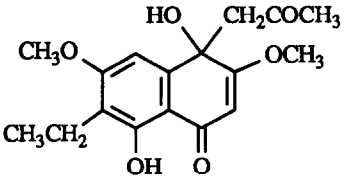
narrow margins of 2 69-2 74 and 7 20-7 29 p p m (~ 7 4 for anthraquinones) respectively (except of course if position 1' is substituted) These are modified to ~ 2 65 and ~ 7 5 p p m upon acetylation. In the case of ^{13}C-spectra, C-1 and C-4 resonances vary somewhat according to substitution at C-2 and C-3 However those at C-5, C-6 (except when C-1' is substituted) and those at C-7 and C-8 are markedly constant as are the corresponding signals for anthraquinones (i e C-1, C-2, C-3 and C-4) (After this work was completed, preparation of diene 10 was again attempted, care being taken to eliminate residual HMPA Under these conditions, elimination was suppressed and enolsilylation to diene 8 (R' = OTMS) finally carried out The new reagent, however, was not found to be very satisfactory in cycloadditions to benzoquinones)

EXPERIMENTAL

All melting points were taken for samples in capillary tubes with a Thomas-Hoover apparatus and are not corrected The UV spectra were determined on a Hewlett-Packard Model 8450A spectrophotometer, the IR spectra on a Beckman Model IR-4250 instrument and NMR spectra were recorded with a Varian XL-200 spectrometer using tetramethylsilane as internal standard Mass spectra were obtained with a Hewlett-Packard 5995A spectrometer Merck silica gel $60F_{254}$ for dry column chromatography and ICN SiliTech 32-63 60A for flash chromatography were used throughout in a



35



36

product-to-adsorbent ratio of 1 50-100 Elemental analyses were carried out by Galbraith Laboratories, Inc , Knoxville, TN

I Alkylation of Substituted Crotonic Esters.

General Procedure A To a solution of LDA (0 165 mol) at -78 °C, prepared in the usual way at O °C from diisopropylamine (0 165 mol) in THF (200 mL) and n-butyllithium (0 180 mol) in hexanes, was added, under nitrogen, crotonic ester 1 or 2 (0 150 mol) in THF (25 mL) (45 min) followed, after 90 min, by the freshly distilled electrophile (0 375 mol) in the same solvent (25 mL) and 2 h later by water (200 mL) The reaction mixture was then concentrated under vacuum and extracted with dichloromethane (3 x 200 mL) Finally the organic phase was washed several times with water, dried and evaporated

Methyl 2-(1-hydroxyethyl)-3-methyl-3-butenoate (3)

A reaction involving methyl 3-methyl-2-butenoate (1) (17 1 g, 0 150 mol) and acetaldehyde (16 5 g, 0 375 mol) according to the general procedure gave hydroxyalkylated ester 3 (23 5 g, 99%) as a quite pure 2 1 mixture of stereomers that could not be distilled without decomposition, IR ν_{max} (film) 3450, 1730 and 1640 cm^{-1}, ^{1}H-NMR (200 MHz, $CDCl_3$) δ (major isomer) 1 16 (3H, d, J = 6 2 Hz, 2'-H), 1 72 (3H, s, 3-CH_3), 2 97 (1H, d, J = 8 8 Hz, 2-H), ~ 3 4 (1H, br s, 1'-OH), 3 74 (3H, s, 1-OCH_3), 4 18 (1H, m, 1'-H), 4 92 and 4 94 (2 x 1H, 2d, J = 1 5 and 1 5 Hz, 4-H), (minor isomer) 1 20 (3H, d, J = 6 2 Hz, 2'-H), 1 81 (3H, s, 3-CH_3), 3,03 (1H, d, J = 7 3 Hz, 2-H) and 3 69 (3H, s, 1-OCH_3) (other signals superposed)

Methyl 2-(1-trimethylsiloxyethyl)-3-methyl-3-butenoate (4).

Azidotrimethylsilane[21] (11 3 g, 0 10 mol) was added at 25 °C and under nitrogen to a solution of hydroxy ester 3 in dry THF (30 mL) The mixture was stirred for 2 h and evaporated Upon distillation, the residue gave silylated derivative 4 (50%), b p 48-51 °C/0 3 mmHg, as a 2 1 mixture of stereomers, IR ν_{max} (film) 1735, 1250 and 840 cm^{-1}, ^{1}H-NMR (200 MHz, $CDCl_3$) δ (major isomer) 0 08 (9H, s, 1'-OTMS), 1 08 (3H, d, J = 6 2 Hz, 2'-H), 1 74 (3H, s, 3-CH_3), 3 03 (1H, d, J = 7 7 Hz, 2-H), 3 64 (3H, s, 1-OCH_3), 4 20 (1H, dq, J = 7 7, 6 2 Hz, 1'-H), 4 89 and 4 91 (2 x 1H, 2d, J = 1 5 and 1 5 Hz, 4-H), (minor isomer) 0 06 (9H, s, 1'-OTMS), 1 15 (3H, d, J = 5 9 Hz, 2'-H), 1 79

(3H, s, 3-CH_3) and 2 99 (1H, d, J = 8 4 Hz, 2-H) (other peaks overlap) (Found C, 57 20, H, 9 73 Calc for $C_{11}H_{22}O_3Si$ C, 57 35, H, 9 63)

Methyl 2-(1-hydroxyethyl)-3-methoxy-3-butenoate (5).

To LDA (0 165 mol) obtained as per general method A, were added (60 min) at 0 °C a solution of HMPA (29 6 g, 0 165 mol) in THF (30 mL) and, after 45 min and upon cooling to -78 °C, methyl 3-methoxy-2-butenoate (2) (19 5 g, 0 150 mol) in THF (25 mL) (45 min) then, 90 min later, acetaldehyde (16 5 g, 0 375 mol) in the same solvent (25 mL) (60 min) and finally, after 2 h, water (200 mL) The crude product consisted essentially of hydroxy ester 5 as a 4 1 mixture of stereomers, IR ν_{max} (film) 3300, 1740 and 1620 cm^{-1}, ^{1}H-NMR (200 MHz, $CDCl_3$) δ (major isomer) 1 19 (3H, d, J = 6 2 Hz, 2'-H), 3 03 (1H, d, J = 8 8 Hz, 2-H), 3 17 (1H, s, 1'-OH), 3 54 (3H, s, 3-OCH_3), 3 74 (3H, s, 1-OCH_3), 4 09 (2H, s, 4-H) and 4 25 (1H, m, 1'-H)

Methyl 2-(1-trimethylsiloxyethyl)-3-methoxy-2-butenoate (6).

As in the formation of silylated ester 4, azidotrimethylsilane (8 1 g, 0 07 mol) and hydroxy ester 5 (8 7 g, 0 05 mol) in THF (20 mL) gave ester 6 (6 8 g, 55%), b p 63-66 °C/0 25 mmHg as a 4 1 mixture of isomers, IR ν_{max} (film) 1745, 1260 and 840 cm^{-1}, ^{1}H-NMR (200 MHz, $CDCl_3$) δ (major isomer) 0 06 (9H, s, 1'-OTMS), 1 09 (3H, d, J = 5 9 Hz, 2'-H), 3 02 (1H, d, J = 9 5 Hz, 2-H), 3 48 (3H, s, 3-OCH_3), 3 65 (3H, s, 1-OCH_3), 4 00 and 4 09 (2 x 1H, 2d, J = 2 6 and 2 6 Hz, 4-H) and 4 30 (1H, dq, J = 9 5, 5 9 Hz, 1'-H) (Found C, 53 38, H, 8 91 Calc for $C_{11}H_{22}O_4Si$ C, 53 62, H, 9 00)

Methyl 2-ethyl-3-methoxy-3-butenoate (7).

In a preparation analogous to that of ester 5, methyl 3-methoxy-2-butenoate (19 5 g, 0 150 mol) and ethyl iodide (58 5 g, 0 375 mol) gave 2-ethyl-3-butenoate 7 (19 2 g, 81%), b p 79-83 °C/19 mmHg, IR ν_{max} (film) 1740, 1655 and 1620 cm^{-1}, ^{1}H-NMR (200 MHz, $CDCl_3$) δ 0 90 (3H, t, J = 7 3 Hz, 2'-H), 1 80 (2H, m, 1'-H), 2 98 (1H, t, J = 7 7 Hz, 2-H), 3 54 (3H, s, 3-OCH_3), 3 70 (3H, s, 1-OCH_3) and 4 05 (2H, s, 4-H)

2-Ethyl-1,3-dimethoxy-1-trimethylsiloxy-1,3-butadiene (8).

To a solution of LDA (0 11 mol) in THF (100 mL) at -78 °C was added (45 min) ester 7 (15 8 g, 0 10 mol) in the same solvent (25 mL) After 30 min, the medium was warmed to 0 °C for 90 min and again cooled to -78 °C when chlorotrimethylsilane (16 3 g, 0 15 mol) in THF (25 mL) was added (1h) and stirring continued for an additional hour The reaction mixture was then allowed to come to room temperature, concentrated under vacuum, diluted with petroleum ether (b p 35-60 °C) (250 mL) and filtered (this procedure was repeated until salts no longer separated) The residue consisted of fairly pure but labile diene 8 as a single isomer; ^{1}H-NMR (200 MHz, $CDCl_3$) δ 0 18 (9H, s, 1-OTMS), 0 92 (3H, t, J = 7 4 Hz, 2'-H), 2 12 (2H, q, J = 7 4 Hz, 1'-H), 3 51 and 3 53 (2 x 3H, 2s, 1,3-OCH_3) and 4 08 (2H, s, 4-H)

II Cycloadditions with Diene 8.

General Method B A solution of diene 8 was added to the quinone (12-18) in the same solvent at 0 °C (10-30 min) The mixture was stirred at this temperature, raised to 25 °C and then evaporated under vacuum The crude adduct was then aromatized by slow percolation through a column of silica gel (25 g/mmol)

General Method C The cycloaddition was conducted as in method B however aromatization was carried out by adding 6N HCl (2 5 mL) in THF (5 mL) per mmol of quinone, stirring the mixture at 25 °C for 1 h, pouring it into water and extracting with dichloromethane

6-Ethyl-5-hydroxy-7-methoxynaphthoquinone (19).

Application of method B to bromobenzoquinone (12) (764 mg, 4 09 mmol) in benzene (15 mL) and diene 8

(1 38 g, 6 00 mmol) in the same solvent (3 mL) at ~ 4 °C (90 min) and 25 °C (20 min) followed by aromatization (C_6H_6 then CH_2Cl_2) gave crude naphthoquinone 19, purified by flash chromatography (CH_2Cl_2-CCl_4 1 1), (679 mg, 72 %), m p 110-111 °C (hexane) (lit [17] m p 103-104 °C), UV λ_{max} (CH_3OH) (log ε) 220 (4 58), 260 (4 21), 267 (4 20) and 420 (3 70) nm, IR ν_{max} (KBr) 1670, 1635 and 1600 cm^{-1}, ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1 12 (3H, t, J = 7 5 Hz, 2'-H), 2 74 (2H, q, J = 7 5 Hz, 1'-H), 3 98 (3H, s, 7-OCH_3), 6 87 (2H, s, 2,3-H), 7 20 (1H, s, 8-H) and 12 21 (1H, s, 5-OH), ^{13}C-NMR (50 3 MHz, $CDCl_3$) δ 12 93 ($\underline{C}H_3CH_2$-6), 16 26 ($CH_3\underline{C}H_2$-6), 56 21 (CH_3O-7), 102 61 (C-8), 109 89 (C-4a), 126 51 (C-6), 130 63 (C-8a), 138 50 and 138 92 (C-2,3), 160 80 (C-5), 162 97 (C-7), 184 38 (C-1) and 188 78 (C-4), MS, m/z 232 (72) $(M)^+$, 217 (100) (Found C, 67 45, H, 5 27 Calc for $C_{13}H_{12}O_4$ C, 67 23, H, 5 21)

2-Bromo-6-ethyl-5-hydroxy-7-methoxynaphthoquinone (20).

According to method C, 2,5-dibromobenzoquinone[22] (13) (1 06 g, 4 00 mmol) in dichloromethane (10 mL) and diene 8 (1 38 g, 6 00 mmol) in the same solvent (2 mL) at 0 °C (2 h) and 25 °C (2 h), gave, after aromatization, quinone 20, purified by chromatography (CCl_4-$C_6H_5CH_3$ 2 1), (0 99 g, 80%), m p 135-136 °C (petroleum ether, b p 60-80 °C), UV λ_{max} (CH_3OH) (log ε) 223 (4 57), 268 (4 12), 299 (3 97) and 436 (3 71) nm, IR ν_{max} (KBr) 1670, 1625, 1580 and 1565 cm^{-1}, ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1 12 (3H, t, J = 7 5 Hz, 2'-H), 2 74 (2H, q, J = 7 5 Hz, 1'-H), 3 99 (3H, s, 7-OCH_3), 7 29 (1H, s, 8-H), 7 40 (1H, s, 3-H) and 12 06 (1H, s, 5-OH), ^{13}C-NMR (50 3 MHz, $CDCl_3$) δ 12 84 ($\underline{C}H_3CH_2$-6), 16 28 ($CH_3\underline{C}H_2$-6), 56 28 (CH_3O-7), 104 49 (C-8), 109 45 (C-4a), 127 24 (C-6), 129 52 (C-8a), 139 25 (C-2), 140 32 (C-3), 160 95 (C-5), 162 82 (C-7), 177 17 (C-1) and 186 05 (C-4), MS, m/z 310/312 (69/70) (M^+), 295 (100) (Found C, 50 09, H, 3 51; Br, 26 28 Calc for $C_{13}H_{11}BrO_4$ C, 50 18, H, 3 56, Br, 25 68)

3-Bromo-6-ethyl-5-hydroxy-7-methoxynaphthoquinone (21).

A mixture of 2,6-dibromobenzoquinone[23] (14) (1 06 g, 4 00 mmol) in dichloromethane (10 mL) and diene 8 (1 38 g, 6 00 mmol) in the same solvent (4 mL) at 0 °C (1 h) and 25 °C (1 h) was treated as in method B (toluene) and after chromatographic separation (CH_2Cl_2-CCl_4 1 1) gave quinone 21 (0 86 g, 69%), m p 157 5-158 5 °C (hexane), UV λ_{max} (CH_3OH) (log ε) 222 (4 57), 263 (4 12), 270 sh (4 13), 298 (4 00) and 430 (3 69) nm, IR ν_{max} (KBr) 1660, 1630, 1590 and 1570 cm^{-1}, ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1 12 (3H, t, J = 7 5 Hz, 2'-H), 2 74 (2H, q, J = 7 5 Hz, 1'-H), 3 99 (3H, s, 7-OCH_3), 7 22 (1H, s, 8-H), 7 40 (1H, s, 2-H) and 12 04 (1H, s, 5-OH), ^{13}C-NMR (50 3 MHz, $CDCl_3$) δ 12 83 ($\underline{C}H_3CH_2$-6), 16 35 ($CH_3\underline{C}H_2$-6), 56 28 (CH_3O-7), 103 45 (C-8), 108 80 (C-4a), 126 61 (C-6), 130 61 (C-8a), 139 88 (C-3), 140 08 (C-2), 161 46 (C-5), 163 37 (C-7), 181 21 (C-1) and 181 63 (C-4), MS, m/z 310/312 (84/88) $(M)^+$, 295 (100) (Found C 50 24, H, 3 46, Br, 25 66 Calc for $C_{13}H_{11}BrO_4$ C, 50 18, H, 3 56, Br, 25 68) Acetate (Ac_2O-H_2SO_4, 85%), m p 150 0-150 5 °C (ethanol), ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1 09 (3H, t, J = 7 5 Hz, 2'-H), 2 48 (3H, s, 5-OAc), 2 56-2 83 (2H, m, 1'-H), 4 00 (3H, s, 7-OCH_3), 7 42 and 7 47 (2H, 2s, 2,8-H)

Acetate of juglone 19 from bromonaphthoquinone 21

The acetate of juglone 21 (706 mg, 2 00 mmol), NaOAc (250 mg) and 10% palladized charcoal (200 mg) in acetic acid (50 mL) was hydrogenated at ~ 3 atm for 3 5 h After elimination of the catalyst, the reaction mixture, treated with CrO_3 (550 mg) in acetic acid (20 mL) at 25 °C (60 min), diluted with CH_2Cl_2 and washed several times with water afforded the acetate of juglone 19 (527 mg, 96%), m p 121 0-121 5 °C (ethanol), ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1 10 (3H, t, J = 7 5 Hz, 2'-H), 2 48 (3H, s, 5-OAc), 2 52-2 80 (2H, m, 1'-H), 4 01 (3H, s, 7-OCH_3), 6 81 (2H, AB pattern, J = 10 3 Hz, Δυ= 19 0 Hz, 2,3-H) and 7 48 (1H, s, 8-H), MS, m/z 274 (17) $(M)^+$, 217 (100)

6-Ethyl-5-hydroxy-2,7-dimethoxynaphthoquinone (22).

Diene 8 (1 38 g, 6 00 mmol) in THF (4 mL) was added to 2-bromo-5-methoxybenzoquinone[24] (15) (868 mg, 4 00 mmol) in the same solvent (15 mL) at O °C (45 min) and 25 °C (20 h) Two supplemental portions of the diene (691 mg, 3 00 mmol) in 2 mL of solvent were added after 20 and 40 h respectively Aromatization of the adduct as

in method C followed by purification of the crude product by chromatography ($C_6H_5CH_3$-AcOEt 10 1) gave quinone 22 (462 mg, 44%), m p 186-187 °C (toluene-ligroine) (lit [15] m p 186-188 °C), UV λ_{max} (CH_3OH) (log ε) 221 (4 52), 263 (4 30), 306 (4 07) and 424 (3 70) nm, IR ν_{max} (KBr) 1675, 1640 and 1595 cm^{-1}, ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1 12 (3H, t, J = 7 5 Hz, 2'-H), 2 73 (2H, q, J = 7 5 Hz, 1'-H), 3 90 and 3 97 (2 x 3H, 2 s, 2,7-OCH_3), 6 01 (1H, s, 3-H), 7 24 (1H, s, 8-H) and 12 49 (1H, s, 5-OH), ^{13}C-NMR (50 3 MHz, $CDCl_3$) δ 12 88 ($\underline{C}H_3CH_2$-6), 16 32 ($CH_3\underline{C}H_2$-6), 56 10 and 56 48 (CH_3O-2,7), 102 74 (C-8), 108 80 (C-4a), 109 14 (C-3), 127 41 (C-6), 129 66 (C-8a), 160 24 and 160 33 (C-2,5), 162 11 (C-7), 179 30 (C-1) and 189 69 (C-4), MS, m/z 262 (100) $(M)^+$ (Found C, 64 15, H, 5 41 Calc for $C_{14}H_{14}O_5$ C, 64 12, H, 5 38) Acetate (22a) (Ac_2O-H_2SO_4, 94%), m p 195 0-195 5 °C (ethanol), ^{1}H-NMR (200 MHz, $CDCl_3$) 1 10 (3H, t, J = 7 4 Hz, 2'-H), 2 47 (3H, s, 5-OAc), 2 52-2 79 (2H, m, 1'-H), 3 85 (3H, s, 2-OCH_3), 4 00 (3H, s, 7-OCH_3), 5 95 (1H, s, 3-H) and 7 53 (1H, s, 8-H), MS, m/z 304 (8) $(M)^+$, 69 (100)

6-Ethyl-5-hydroxy-3,7-dimethoxynaphthoquinone (23)

A similar reaction mixture obtained from 2-bromo-6-methoxybenzoquinone[24] (16) (434 mg, 2 00 mmol) in THF (18 mL) and diene 8 (691 mg, 3 00 mmol) also in THF (6 mL) at 0 °C (45 min) and 25 °C (3 h) was treated according to method B (C_6H_6 then C_6H_6-CH_2Cl_2 1 1) and provided quinone 23 (388 mg, 74%), m p 183 0-183 5 °C (benzene-petroleum ether b p 60-80 °C), UV λ_{max} (CH_3OH) (log ε) 222 (4 42), 260 (4 22), 265 (4 23), 306 (4 16) and 416 (3 68) nm, IR ν_{max} (KBr) 1650, 1635 and 1600 cm^{-1}, ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1 11 (3H, t, J = 7 3 Hz, 2'-H) 2 71 (2H, q, J = 7 3 Hz, 1'-H), 3 89 and 3 97 (2 x 3H, 2s, 3,7-OCH_3), 6 05 (1H, s, 2-H), 7 22 (1H, s, 8-H) and 12 08 (1H, s, 5-OH), ^{13}C-NMR (50 3 MHz, $CDCl_3$) δ 12 92 ($\underline{C}H_3CH_2$-6), 16 19 ($CH_3\underline{C}H_2$-6), 56 23 and 56 54 (CH_3O-3,7), 102 70 (C-8), 109 11 (C-4a), 109 32 (C-2), 125 44 (C-6), 131 17 (C-8a), 160 44 (C-3), 161 37 (C-5), 163 55 (C-7), 183 30 (C-1) and 184 00 (C-4), MS, m/z 262 (100) $(M)^+$ (Found C, 64 08, H, 5 52 Calc for $C_{14}H_{14}O_5$ C, 64 12, H, 5 38)

6-Ethyl-5-hydroxy-2,3,7-trimethoxynaphthoquinone (24).

When applied to 5-bromo-2,3-dimethoxybenzoquinone[25] (17) (494 mg, 2 00 mmol) in THF (18 mL) and diene 8 (691 mg, 3 00 mmol) in the same solvent (6 mL) at 0 °C (45 min) and 25 °C (2 h), method B (C_6H_6 then C_6H_6-CH_2Cl_2 1 1), after chromatography (CH_2Cl_2), gave quinone 24 (477 mg, 82%), m p 126 5-127 5 °C (petroleum ether, b p 60-80 °C) lit [18] m p 113-114 °C, UV λ_{max} (CH_3OH) (log ε) 217 (4 47), 266 (4 37), 318 (4 08) and 416 (3 63) nm, IR ν_{max} (KBr) 1660, 1635 and 1605 cm^{-1}, ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1 11 (3H, t, J = 7 5 Hz, 2'-H), 2 71 (2H, q, J = 7 5 Hz, 1'-H), 3 96 (3H, s, 7-OCH_3), 4 08 and 4 10 (2 x 3H, 2s, 2,3-OCH_3), 7 20 (1H, s, 8-H) and 12 20 (1H, s, 5-OH), ^{13}C-NMR (50 3 MHz, $CDCl_3$) δ 12 92 ($\underline{C}H_3CH_2$-6), 16 23 ($CH_3\underline{C}H_2$-6), 56 14 (CH_3O-7), 61 34 and 61 58 (CH_3O-2,3), 102 72 (C-8), 107 96 (C-4a), 125 28 (C-6), 129 73 (C-8a), 146 71 and 147 03 (C-2,3), 160 55 (C-5), 162 64 (C-7), 181 16 (C-1) and 185 89 (C-4), MS, m/z 292 (76) $(M)^+$, 277 (100) (Found C, 61 59, H, 5 40 Calc for $C_{15}H_{16}O_6$ C, 61 64, H, 5 52)

6-Ethyl-3,5-dihydroxy-2,7-dimethoxynaphthoquinone (25).

To a solution of naphthoquinone 24 (292 mg, 1 00 mmol) in acetic acid (20 mL) at 90 °C was added conc HCl (20 mL) The mixture was kept at the same temperature for 30 min, poured into water and extracted with ethyl acetate (2 x 200 mL) The organic extract, after repeated washing with water (10 x 300 mL) afforded quinone 25 (264 mg, 95%), m p 182 0-182 5 °C (benzene-petroleum ether, b p 60-80 °C) (lit [18] m p 183-184 °C), UV λ_{max} (CH_3OH) (log ε) 267 (4 48), 324 (4 22) and 410 (3 72) nm, IR ν_{max} (KBr) 3330, 1665, 1645 and 1600 (br) cm^{-1}, ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1 10 (3H, t, J = 7 5 Hz, 2'-H), 2 69 (2H, q, J = 7 5 Hz, 1'-H), 3 97 (3H, s, 7-OCH_3), 4 14 (3H, s, 2-OCH_3), 6 84 (1H, s, 3-OH), 7 24 (1H, s, 8-H) and 11 39 (1H, s, 5-OH), ^{13}C-NMR (50 3 MHz, $CDCl_3$) δ 12 92 ($\underline{C}H_3CH_2$-6), 16 19 ($CH_3\underline{C}H_2$-6), 56 32 (CH_3O-7), 60 61 (CH_3O-2), 103 96 (C-8), 106 65 (C-4a), 125 51 (C-6), 130 26 (C-8a), 140 01 and 142 14 (C-2,3), 160 24 (C-5), 163 59 (C-7), 180 28 (C-1) and 184 12 (C-4), MS, m/z 278 (100)

$(M)^+$ (Found C, 60 69, H, 5 02 Calc for $C_{14}H_{14}O_6$ C, 60.43, H, 5 07)

2-Ethyl-1-hydroxy-3-methoxyanthraquinone (26).

A mixture obtained from 2-chloronaphthoquinone (18) (385 mg; 2 00 mmol) in benzene (6 mL) and diene 8 (691 mg, 3 00 mmol) in the same solvent (2 mL) at ~ 4 °C (2 h) and 25 °C (3 h) was treated according to method B (C_6H_6-CCl_4 1 1) Purification of the crude material by flash chromatography (CH_2Cl_2-CCl_4 1 2) gave pure anthraquinone 26 (458 mg, 81%), m p 158 5-159 0 °C (ethanol), IR ν_{max} (KBr) 1665, 1630 and 1590 cm^{-1}, ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1 16 (3H, t, J = 7 4 Hz, 2'-H), 2 78 (2H, q, J = 7 4 Hz, 1'-H), 4 02 (3H, s, 3-OCH_3), 7 42 (1H, s, 4-H), 7 68-7 86 (2H, m, 6,7-H), 8 19-8 37 (2H, m, 5,8-H) and 12 97 (1H, s, 1-OH), ^{13}C-NMR (50 3 MHz, $CDCl_3$) δ 12 95 ($\underline{C}H_3CH_2$-2), 16 37 ($CH_3\underline{C}H_2$-2) 56 21 (CH_3O-3), 102 68 (C-4), 111 03 (C-9a), 126 55 (C-2), 126 66 and 127 10 (C-5,8), 132 35, 133 32 and 133 44 (C-4a, 8a, 10a), 133 88 and 133 97 (C-6,7), 161 82 (C-1), 163 20 (C-3), 182 43 (C-10) and 187 09 (C-9), MS, m/z 282 (59) $(M)^+$, 77 (100) (Found C, 72 32, H, 5 19 Calc for $C_{17}H_{14}O_4$ C, 72 33, H, 5 00) Acetate (26a) (Ac_2O-H_2SO_4, 93%), m p 190 0-190 5 °C (ethanol), ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1 13 (3H, t, J = 7 5 Hz, 2'-H), 2 54 (3H, s, 1-OAc), 2 58-2 84 (2H, m, 1'-H), 4 05 (3H, s, 3-OCH_3), 7 73 (1H, s, 4-H), 7 66-7 81 (2H, m, 6,7-H) and 8 16-8 29 (2H, m, 5,8-H), MS, m/z 324 (15) $(M)^+$, 267 (100)

III Sidechain-substituted Products.

(±)-5-(Acetoxy)-6-(1-bromoethyl)-2,7-dimethoxynaphthoquinone (27).

A mixture of naphthoquinone 22a (913 mg; 3 00 mmol), NBS (587 mg, 3 30 mmol), benzoylperoxide (100 mg) and CCl_4 (45 mL) was refluxed for 18 h. Purification of the crude product by flash chromatography (CH_2Cl_2 then CH_2Cl_2-$(C_2H_5)_2O$ 1 1) gave bromoquinone 27 (1 03 g, 90%), m p 153 5-155 °C (1,2-dichloroethane-petroleum ether, b p 65-110 °C), IR ν_{max} (KBr) 1770, 1680, 1640 and 1620 cm^{-1}, ^{1}H-NMR (200 MHz, $CDCl_3$) δ 2 05 (3H, d, J = 6 7 Hz, 2'-H), 2 51 (3H, s, 5-OAc), 3 86 (3H, s, 2-OCH_3), 4 07 (3H, s, 7-OCH_3), 5 54-5 80 (1H, m, 1'-H), 5 99 (1H, s, 3-H) and 7 57 (1H, s, 8-H), MS, m/z 382/384 (<1) $(M)^+$, 261 (100) (Found C, 50 43, H, 4 06, Br, 20 56 Calc for $C_{16}H_{15}BrO_6$ C, 50 15, H, 3 95, Br, 20 85)

(±)-1-Acetoxy-2-(1-bromoethyl)-3-methoxyanthraquinone (28).

A reaction, similar to the foregoing, with anthraquinone 26a (324 mg, 1 00 mmol), NBS (196 mg, 1 1 mmol), benzoylperoxide (50 mg) and CCl_4 (15 mL) (16 h), after separation by flash chromatography (CH_2Cl_2-CCl_4 25 1), gave bromoquinone 28 (365 mg, 91%), m p 190-191 5 °C (ethanol), IR ν_{max} (KBr) 1770, 1670 and 1570 cm^{-1}, ^{1}H-NMR (200 MHz, $CDCl_3$) δ 2 09 (3H, d, J = 7 0 Hz, 2'-H), 2 58 (3H, s, 1-OAc), 4 12 (3H, s, 3-OCH_3), 5 62-5 79 (1H, m, 1'-H), 7 76 (1H, s, 4-H), 7 68-7 83 (2H, m, 6,7-H), 8 16-8 31 (2H, m, 5,8-H), MS, m/z 402/404 (<1) $(M)^+$, 281 (100) (Found C, 57 06, H, 4 19, Br, 19 65 Calc for $C_{19}H_{15}BrO_5$ C, 56 59, H, 3 75, Br, 19 82)

(±)-6-(1-Acetoxyethyl)-5-hydroxy-2,7-dimethoxynaphthoquinone (29).

A suspension of bromoquinone 27 (945 mg, 2 47 mmol), silver (I) acetate (1 25 g, 7 50 mmol) in 50% aqueous acetone (50 mL) was stirred for 48 h at 25 °C, diluted with water and extracted with CH_2Cl_2 (3x) The organic extracts, washed several times with water, gave acetoxy-derivative 29 (597 mg, 76%), m p 165-166 5 °C dec (ethanol) (lit.[14] (-)-isomer, m p 160-163 °C dec), UV λ_{max} (CH_3OH) (log ε) 218 (4 62), 263 (4 25), 305 (4 08) and 426 (3 66) nm, IR ν_{max} (KBr) 1725, 1680, 1630 and 1590 cm^{-1}, ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1 63 (3H, d, J = 7 0 Hz, 2'-H), 2 06 (3H, s, 1-OAc), 3 90 and 4 00 (2 x 3H, 2s, 2,7-OCH_3), 6 03 (1H, s, 3-H), 6 36 (1H, q, J = 7 0 Hz, 1'-H), 7 25 (1H, s, 8-H) and 12 78 (1H, s, 5-OH), ^{13}C-NMR (50 3 MHz, $CDCl_3$) δ 18 30 ($\underline{C}H_3CH$-6), 21 21 ($\underline{C}H_3CO_2$-1'), 56 50 and 56 63 (CH_3O-2,7), 64 78 ($CH_3\underline{C}H$-6), 103 01 (C-8), 109 00 (C-4a), 109 45 (C-3), 122 49 (C-6), 131 39 (C-8a), 160 55 and 160 95 (C-2,5), 162 37 (C-7), 170 41 ($CH_3\underline{C}O_2$-1'), 179.21 (C-1) and 189 65 (C-4), MS, m/z 320 (16)

$(M)^+$, 69 (100) (Found C, 60,03, H, 5 14 Calc for $C_{16}H_{16}O_7$ C, 60 00, H, 5 04)

(±)-2-(1-Acetoxyethyl)-1-hydroxy-3-methoxyanthraquinone (30).

The preceding method applied to bromoquinone 28 (81 mg, 0 20 mmol), silver (I) acetate (100 mg, 0 60 mmol) and 50% acetone (4 mL) afforded corresponding anthraquinone 30 (50 mg, 73%), m p 163-164 °C (ethanol), IR ν_{max} (KBr) 1730, 1670, 1620, 1590, and 1570 cm^{-1}, ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1 68 (3H, d, J = 6 8 Hz, 2'-H), 2 09 (3H, s, 1'-OAc), 4 05 (3H, s, 3-OCH_3), 6 43 (1H, q, J = 6 8 Hz, 1'-H), 7 37 (1H, s, 4-H), 7 73-7.86 (2H, m, 6,7-H), 8 22-8 36 (2H, m, 5,8-H) and 13 24 (1H, s, 1-OH), MS, m/z 340 (19) $(M)^+$, 265 (100) (Found C, 67 43, H, 4 98 Calc for $C_{19}H_{16}O_6$ C, 67 05, H, 4 74)

(±)-5-Hydroxy-6-(1-hydroxyethyl)-2,7-dimethoxynaphthoquinone (31).

Treatment of acetoxynaphthoquinone 29 (160 mg, 0 500 mmol) in CH_3CN (7 mL) with 20% H_2SO_4 (2 mL) at reflux temperature for 90 min followed by dilution of the reaction mixture with water and extraction with CH_2Cl_2 (3 x) gave a residue which by purification by dry-column chromatography (CH_2Cl_2-AcOEt 4 1) provided hydroxyquinone 31 (85 mg, 61%), m p 196 5-197 °C dec (chloroform-hexane) (lit.[14] m p 202-204 °C,[15] 201-204 °C), UV (CH_3OH) λ_{max} (log ε) 218 (4 57), 262 (4 23), 305 (4 04) and 424 (3 61) nm, IR ν_{max} (KBr) 3560, 1680, 1630 and 1590 cm^{-1}, ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1 56 (3H, d, J = 6 7 Hz, 2'-H), 3 74 (1H, d, J = 11 8 Hz, 1'-OH), 3 91 (3H, s, 2-OCH_3), 4 00 (3H, s, 7-OCH_3), 5 33 (1H, dq, J = 6 7, 11 8 Hz, 1'-H), 6 04 (1H, s, 3-H), 7 25 (1H, s, 8-H) and 12 85 (1H, s, 5-OH), ^{13}C-NMR (50 3 MHz, $CDCl_3$) δ 22 83 ($\underline{C}H_3CH$-6), 56 41 and 56 66 (CH_3O-2,7), 63 72 ($CH_3\underline{C}H_2$-6), 103 12 (C-8), 109 14 (C-4a), 109 27 (C-3), 126 73 (C-6), 130 72 (C-8a), 159 93 and 160 51 (C-2,5), 161 29 (C-7), 179 10 (C-1) and 184 91 (C-4), MS, m/z 278 (8) $(M)^+$, 263 (100) (Found C, 60 18, H, 5 07 Calc for $C_{14}H_{14}O_6$ C, 60 43, H, 5 07)

(±)-1-Hydroxy-2-(1-hydroxyethyl)-3-methoxyanthraquinone (32).

By a procedure analogous to the preceding one, acetoxyquinone 30 (17 mg, 0 05 mmol) and 20% H_2SO_4 (0 2 mL) in CH_3CN (0 7 mL) (120 min), gave, after dry column chromatography (CH_2Cl_2 then $(C_2H_5)_2O$) hydroxyquinone 32, (8 mg, 54%), m p 139 5-141 5 °C (ethanol), ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1 58 (3H, d, J = 6 8 Hz, 2'-H), 3 78 (1H, d, J = 11 8 Hz, 1'-OH), 4 03 (3H, s, 3-OCH_3), 5 35-5 42 (1H, m, 1'-H), 7 41 (1H, s, 4-H), 7 73-7 88 (2H, m, 6,7-H), 8 22-8 36 (2H, m, 5,8-H) and 13 31 (1H, s, 1-OH), MS, m/z 298 (4) $(M)^+$, 283 (100)

(±)-6-(1-Ethoxyethyl)-5-hydroxy-2,7-dimethoxynaphthoquinone (33).

A mixture of acetoxynaphthoquinone 29 (163 mg, 0 509 mmol), conc H_2SO_4 (0 4 mL) in water (3 ml) and ethanol (6 mL) was heated to reflux for 100 min, diluted with water and extracted with CH_2Cl_2 (3 x) Purification of the crude product by dry-column chromatography (CH_2Cl_2) afforded ethoxyquinone 33 (71 mg, 46%), m p 135 0-135 5 °C (chloroform-hexane) (lit [15] m p 136-137 °C, UV λ_{max} (CH_3OH) (log ε) 219 (4 71), 263 (4 38), 306 (4 21) and 4 24 (3 86) nm, IR ν_{max} (KBr) 1680, 1630 and 1590 cm^{-1}, ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1 17 (3H, t, J = 7 1 Hz, 1'-$OCH_2\underline{CH_3}$), 1 58 (3H, d, J = 6 6 Hz, 2'-H), 3 37 (1H, m, 1'-H), 3 89 (3H, s, 2-OCH_3), 3 98 (3H, s, 7-OCH_3), 5 17 (2H, q, J = 6 6 Hz, 1'-$O\underline{CH_2}CH_3$), 6 02 (1H, s, 3-H), 7 24 (1H, s, 8-H) and 12 72 (1H, s, 5-OH), ^{13}C-NMR (50 3 MHz, $CDCl_3$) δ 15 52 ($\underline{C}H_3CH_2O$-1'), 19 34 (C-2'), 56 36 and 56 61 (CH_3O-2,7), 64 32 (C-1'), 68 51 ($CH_3\underline{C}H_2O$-1'), 103 07 (C-8), 108 83 (C-4a), 109 47 (C-3), 124 35 (C-6), 131 19 (C-8a), 160 29 and 161 33 (C-2,5), 163 24 (C-7), 173 54 (C-1) and 189 72 (C-4), MS, m/z 306 (<1) $(M)^+$, 69 (100) (Found, C, 62 97, H, 6 09 Calc for $C_{16}H_{18}O_6$, C, 62 74, H, 5 92)

(±)-1-Hydroxy-3-methoxy-2-(1-methoxyethyl)anthraquinone (34).

As in the preceding case, acetoxyanthraquinone 30 (21 mg, 0 061 mmol), conc H_2SO_4 (0 05 mL), in water (0 3 mL) and methanol (0 6 mL) (70 min at reflux and 16 h at room temperature) gave methyl ether 34 (9 mg, 48%), m p 142 5-144 5 (ethanol), ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1 62 (3H, d, J = 6 8 Hz, 2'-H), 3 29 (3H, s, 1'-OCH_3), 4 03

(3H, s, 3-OCH_3), 5 12 (1H, q, J = 6 8 Hz, 1'-H), 7 43 (1H, s, 4-H), 7 73-7 86 (2H, m, H-6,7), 8 23-8 35 (2H, m, 5,8-H) and 13 26 (1H, s, 1-OH), MS, m/z 312 (10) $(M)^+$, 297 (100)

IV Reduction of 6-ethyl-7-methoxyjuglone.

(±)-6-Ethyl-1,5-dihydroxy-7-methoxy-4-oxo-1,2,3-trihydronaphthalene (35).

A solution of juglone 19 (464 mg, 2 00 mmol) in THF (55 mL) was added slowly (2 h) to $LiAlH_4$ (900 mg, 24 0 mmol) in ether (75 mL) at room temperature and after stirring was continued for 1 h, the mixture was carefully poured into 5% aqueous HCl at 0 °C The crude product, obtained by extraction with ether (3 x), was stirred at 25 °C in 2,2-dimethoxypropane (25 mL) containing camphorsulfonic acid (32 mg) for 75 min and evaporated Purification of the residue by dry column flash chromatography $(C_2H_5)_2O$ afforded trihydronaphthalene 35 (312 mg, 66%), m p 109-111 °C (benzene-petroleum ether, b p 35-60 °C) (lit [19] (+)-isomer, m p 132-133 °C), UV λ_{max} (CH_3OH) (log ε) 223 (4 27), 287 (4 23), 650 (1 58) and 656 (1 75) nm, IR ν_{max} (KBr) 3590-3010, 1620 and 1570 cm^{-1}, ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1 07 (3H, t, J = 7 5 Hz, 2'-H), 1 97 (1H, m, 1-OH), 2 00-2 40 (2H, m, 2-H), 2 46-3 00 (2H, m, 3-H), 2 63 (2H, q, J = 7 5 Hz, 2'-H), 3 90 (3H, s, 7-OCH_3), 4 84 (1H, m, 1-H), 6 63 (1H, s, 8-H) and 12 81 (1H, s, 5-OH), ^{13}C-NMR[26] (50 3 MHz, $CDCl_3$) δ 13 19 (C-2'), 15 64 (C-1'), 31 74 (C-2), 34 65 (C-3), 55 77 (CH_3O-7), 68 18 (C-1), 100 41 (C-8), 109 80 (C-4a), 118 91 (C-6), 145 36 (C-8a), 161 80 (C-5), 163 49 (C-7) and 202 09 (C-4), MS, m/z 236 (47) $(M)^+$, 221 (100)

Acknowledgment

We gratefully acknowledge financial support and bursaries (to B C) from the Natural Sciences and Engineering Research Council of Canada and the Fonds F C A R (Gouv du Québec) We also wish to thank Dr G W van Eijk for the generous provision of samples

REFERENCES

1 J SAVARD and P BRASSARD, Tetrahedron Lett., 1979, 4911, Tetrahedron, 1984, 40, 3455

2 G ROBERGE and P BRASSARD, J Org Chem , 1981, 46, 4161, J -P GESSON, J -C JAQUESY, and M MONDON, Tetrahedron Lett , 1981, 22, 1337, B A PEARLMAN, J M McNAMARA, I HASAN, S HATAKEYAMA, H SEKIZAKI, and Y KISHI, J Am Chem Soc , 1981, 103, 4248, D W CAMERON, G I FEUTRILL, A F PATTI, P PERLMUTTER, and M A SEFTON, Aust. J Chem , 1983, 35, 1501, T R. Kelly, M BEHFOROUZ, A ECHAVARREN, and J VAYA, Tetrahedron Lett , 1983, 24, 2331, V GUAY and P BRASSARD, Tetrahedron, 1984, 40, 5039, Y TAMURA, M SASHO, K. NAKAGAWA, T TSUGOSHI, and Y KITA, J Org Chem , 1984, 49, 473, B SIMONEAU and P BRASSARD, Tetrahedron, 1986, 42, 3767, V GUAY and P BRASSARD, Synthesis, 1987, 294, B SIMONEAU and P BRASSARD, J Nat Prod , 1987, 50, 1080, Tetrahedron, 1988, 44, 1015, M BLOUIN, M -C BELAND, and P BRASSARD, J Org Chem , 1990, 55, 1466, etc

3 For some recent examples, see M BELLASSOUED, F HABBACHI, and M GAUDEMAR, Tetrahedron, 1987, 43, 1785, Y YAMAMOTO, S HATSUYA, and J YAMADA, J Chem Soc Chem Commun , 1987, 561, S TSUBOI, H WADA, K MURANAKA, and A TAKEDA, Bull Chem Soc , Jpn , 1987, 60, 2917, M PARA, R MESTRES, D APARICIO, N DURANA, and G RUBIALES, J Chem Soc Perkin Trans I, 1989, 327, T IBUKA, W TANAKA, S NISHII, and Y YAMAMOTO, J Am Chem Soc , 1989, 111, 4864, T HUDLICKY, A FLEMING, and L RADESKA, J Am Chem Soc , 1989, 111, 6691, etc

4 L E RICE, M C BOSTON, H O FINKLEA, B J SUDER, J O FRAZIER, and T. HUDLICKY, J Org Chem, 1984, 49, 1845
5 T HARADA and T MUKAIYAMA, Chem Lett, 1982, 161
6 P M SAVU and J A KATZENELLENBOGEN, J Org Chem, 1981, 46, 239
7 A S KENDE and B H TODER, J Org Chem, 1982, 47, 163
8 Y YAMAMOTO, S HATSUYA, and J YAMADA, J Chem Soc Chem Commun, 1988, 1639, P ALBAUGH-ROBERTSON and J A KATZENELLENBOGEN, J Org Chem, 1983, 48, 5288, I CASINOS and R MESTRES, J Chem Soc Perkin Trans I, 1978, 1651, etc
9 P BALLESTER, A COSTA, A GARCIA-RASO and R MESTRES, J Chem Soc Perkin Trans I, 1989, 21, F L HARRIS and L WEILER, Tetrahedron Lett., 1985, 26, 1939, J A KATZENELLENBOGEN and A L CRUMRINE, J Am Chem Soc, 1976, 98, 4925, etc
10 R W DUGGER and C H HEATHCOCK, J Org Chem, 1980, 45, 1181, M T AYOUB, M.Y SHANDALA, and A W JAFAR, Synthesis, 1987, 653
11 R H THOMSON, Naturally Occurring Quinones III, Chapman and Hall London, 1987, pp 214, 228
12 D SEEBACH and J ZIMMERMANN, Helv Chim Acta, 1986, 69, 1147
13 R HOWE and R H MOORE, Experientia, 1969, 25, 474
14 G W van EIJK and H J ROEYMANS, Experientia, 1978, 34, 1257, ibid 1983, 39, 513
15 N OTOMO, H SATO, and S SAKAMURA, Agric Biol Chem, 1983 47, 1115
16 R E MOORE, H SINGH, C W J CHANG, and P J SCHEUER, J Org Chem, 1966, 31, 3638
17 P-D CHAO, P L SCHIFF, jr, D J SLATKIN and J E KNAPP, J Chem Res, 1979, 236
18 R E MOORE, H SINGH, C W J CHANG, and P J SCHEUER, Tetrahedron, 1967, 23, 3271
19 P D CHAO, P L SCHIFF, Jr, D J SLATKIN, J E KNAPP, M CHAO, and R D ROSENSTEIN, Lloydia, 1975, 38, 213
20 Y FUJIMOTO and M SATOH, Chem Pharm Bull, 1986, 34, 4540
21 M G SARNGADHARAN and T R SESHADRI, Tetrahedron, 1966, 22, 739
22 D SINOU and M EUZIANE, Synthesis, 1986, 1045
23 J Y SAVOIE and P BRASSARD, Can J Chem, 1966, 44, 2867, R K NORRIS and S STERNHELL, Aust J Chem, 1973, 26, 333, J F BAGLI and Ph L'ECUYER, Can J Chem, 1961, 39, 1037
24 J M BLATCHLY, R J S GREEN, J F W McOMIE, and J B SEARLE, J Chem Soc (C), 1969, 1353
25 J C CATLIN, G D DAVES, jr, and K FOLKERS, J Med Chem, 1971, 14, 45, M MATSUMOTO and H KOBAYASHI, J Org Chem, 1985, 50, 1766
26 T J SIMPSON and D J STENZEL, J Chem Soc, Chem Commun, 1982, 1074