Tetrahedron Vol. 48, No. 22, pp. 4629-4640, 1992
Printed in Great Britain

0040-4020/92 $5.00+.00

Studies on Quinones. 24[1]. Rearrangement of Diels-Alder Adducts of Activated Quinones under Acidic Conditions

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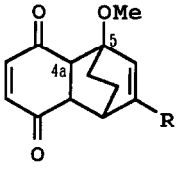
(*Received in UK* 13 *April* 1992)

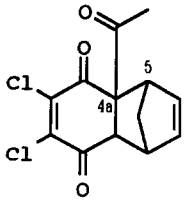
Abstract: *The Diels-Alder adducts* **5**, **19**, **9**, **10**, **8**, **11**, *of benzoquinones bearing activating groups (*$COCH_3$, $COCH{=}CHPh$, CO_2Me, NO_2, *CHO, CN) by treatment with 1.3 N hydrochloric acid are initially converted into the dihydrobenzofurans* **7**, **22**, *the corresponding alcohols* **12**, **13** *or the arylcrotonaldehydes* **14**, **15**, *respectively. By treatment with 8.5 N hydrochloric acid, adducts* **8-10** *are converted directly into the corresponding dihydrobenzofurans. In the presence of silica gel, adduct* **19** *is partially converted into the benzocyclooctatriene derivative* **21**. *The alcohol* **26**, *formed by hydrolysis of adduct* **25**, *rearranges to the benzodifuran derivatives* **28** *and* **29** *in the presence of silica gel and ethanol or methanol, respectively.*

INTRODUCTION

Among the broad structural variety of Diels-Alder adducts with quinones, compounds such as **1-4** are unique because of their propensity to undergo selective cleavage of one of the two carbon-carbon bonds generated in the cycloaddition reaction to afford rearranged products. Birch et al.[2] reported the



1, R=H
2, R=OMe



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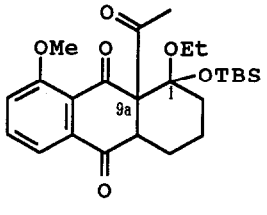

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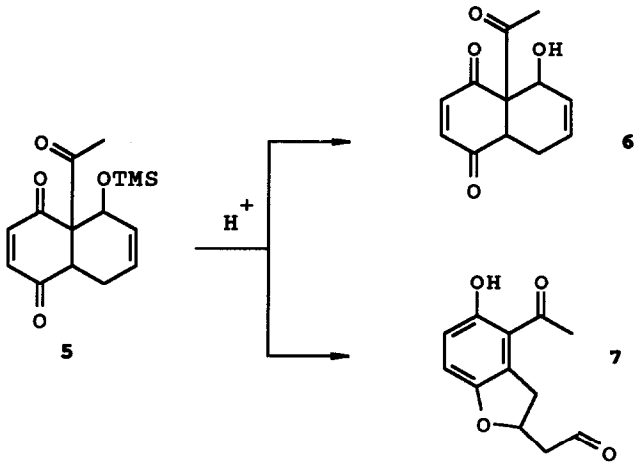
first example of this carbon-carbon fission in the adducts **1** and **2** which, under acidic conditions, afforded dibenzofuran derivatives through a 4a,5 bond cleavage. Bruce et al.[3] also reported that the adduct **3** undergoes the 4a,5 bond cleavage by thermolysis in benzene and acetic acid solutions to give dihydrobenzofurans. More recently Kraus[4] has described the 1,9a bond cleavage in the adduct **4** with tetrabutylammonium fluoride to give a naphthofuran derivative. According to the mechanism

proposed[2,3] for this carbon-carbon cleavage, the methoxy and acetyl substituents on these adducts favour the bond fission by stabilization of the incipient ionic intermediates.

In spite of its obvious potential, the above rearrangement has not been extensively utilized in organic synthesis and there are few examples reported in the literature. Thus, it has been successfully used in the synthesis of naturally occurring pyranoquinones,[4,5] for the construction of the skeleton of Amarylidaceae alkaloids,[6] and very recently in a novel synthesis of aromatic steroids.[7]

RESULTS AND DISCUSSION

Our interest in the synthesis of precursors of tetracyclic quinones related to rabelomycin[8] led us to explore the preparation of the alcohol **6** by mild acid hydrolysis of the adduct **5**. However, this treatment afforded the rearranged product **7** in nearly quantitative yield. On the basis of this result we decided to study the behaviour in acidic media of Diels-Alder adducts of several activated quinones with (*E*)-1-trimethylsilyloxybuta-1,3-diene. A preliminary communication of part of this work has been published previously.[9]

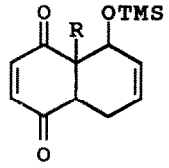


The adducts **8-11**, obtained as previously reported,[10] were reacted with 1.3 N hydrochloric acid in THF-water (9:1) under the same conditions as those under which the rearrangement of **5** into **7** was observed. The progress of the reaction was monitored by TLC and the reaction mixture was quenched with water immediately after the substrate had been consumed. The results of these experiments, including the one obtained in the reaction of the adduct **5**, indicated that under these acidic conditions three types of products can be generated: (i) dihydrobenzofurans such as **7**, (ii) the corresponding alcohols **12**, **13**, or (iii) arylcrotonaldehydes of type **14**, **15**. The reactions proceeded readily and the products were obtained in good to excellent yields. The results are summarised in Table 1.

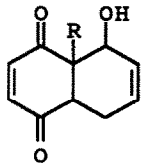
It is noteworthy that the arylcrotonaldehyde **14** isomerized smoothly to the dihydrobenzo[*b*]furan **18** under acidic conditions. In fact, when a solution of **14** in THF-water containing 1.3 N hydrochloric acid was kept at room temperature and the progress of the reaction was analysed by ^{1}H NMR, a mixture of

the arylcrotonaldehyde **14** and the dihydrobenzofuran **18** in nearly 1:1 ratio was observed. The compound **14** reacted gradually and, after 7 days, a 1:13 mixture of **14** and **18** was observed.

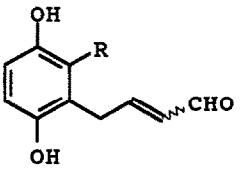
Additional experiments indicated that the treatment of the adducts **8**, **9**, and **10** with 8.5 N hydrochloric acid in THF-water solution afforded the corresponding dihydrobenzofurans **18**, **16**, and **17**, respectively. Interestingly, in an attempt to purify the alcohol **13** by filtering through silica gel, the rearrangement into the furan **17** was also observed.



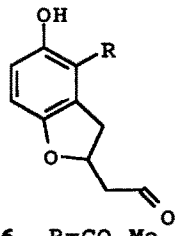
8, R=CHO
9, R=CO_2Me
10, R=NO_2
11, R=CN



12, R=CO_2Me
13, R=NO_2



14, R=CHO (*E*)
15, R=CN (*E*+*Z*)



16, R=CO_2Me
17, R=NO_2
18, R=CHO

Table 1. Reactions of Adducts **5**, **8-11** with 1.3 N Hydrochloric Acid

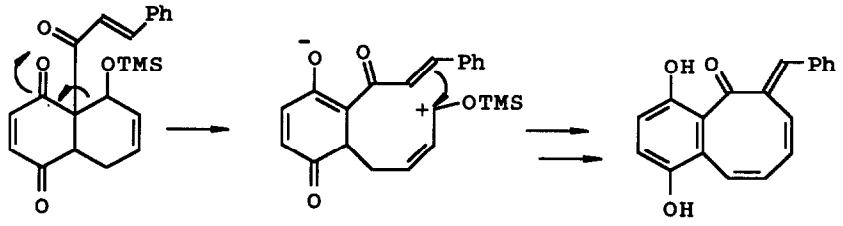
Substrate	Product	Time (h)	Yield (%)
5	**7**	2.5	99
8	**14**	3	96
9	**12**	2	92
10	**13**	3	97
11	**15***	6	72

* *E*+*Z* mixture

All these results suggest that the rearrangement of the Diels-Alder adducts **5**, **8-10** to the corresponding dihydrobenzofurans **7**, **16-18** in the presence of 8.5 N hydrochloric acid, is initiated by hydrolysis of the silyl ether to give the corresponding alcohol, which rearranges to the dihydrobenzofuran derivative *via* an arylcrotonaldehyde intermediate. Nevertheless, under these conditions, the formation of the dihydrobenzofurans by rearrangement of the corresponding alcohols of type **6** through a concerted mechanism cannot be disregarded.

To examine further the scope of the above rearrangement, we have also studied the reactivity of adduct **19** in acidic media. The adduct **19**, prepared as reported,[10] was subjected to purification by

filtering on a silica gel column. Elution with benzene afforded the adduct **19** as a pure substance. However, we have observed that **19** is in part transformed into a new compound, which was isolated as a red solid by further elution of the column with benzene.

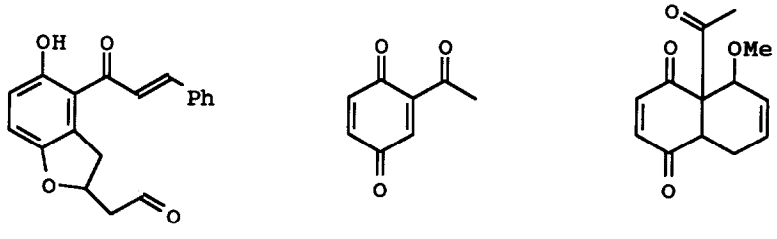


19 **20** **21**

The new compound, which was indeed generated on the supported silica gel, exhibited IR absorptions of hydroxy and carbonyl groups at 3260 and 1635 cm^{-1}, respectively. The ^1H NMR spectrum displayed a strong chelated hydroxyl proton at δ 14.80 ppm and a complex pattern of signals in the aromatic region. These properties along with the ^{13}C NMR data, the mass spectrum and combustion analysis are in accord with the benzocyclooctatriene structure **21**.

The formation of **21** can be rationalised by considering the participation of the zwitterionic intermediate **20** arising from the carbon-carbon bond cleavage of the adduct **19** or from the corresponding alcohol. This intermediate, by intramolecular attack of the carbon-carbon double bond of the cinnamoyl substituent on the allylic cation, undergoes cyclisation and after subsequent enolisation and elimination steps affords the bicyclic compound **21**.

When the adduct **19** was reacted with 1.3 N hydrochloric acid under the standard conditions, a complex product mixture was initially observed by TLC. Nevertheless, after two days at room temperature the dihydrobenzofuran **22** was detected as the sole product. The heterocyclic derivative **22** was isolated from the mixture in 92 % yield.



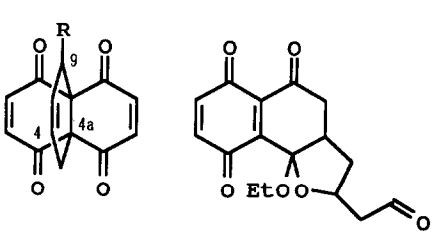
22 **23** **24**

In order to provide evidence to confirm that the silyl ether hydrolysis occurs prior to the cleavage of the 4a,5 carbon-carbon bond on the adducts **5**, **8-11**, the synthesis of the adduct **24** and its reactivity in

acidic media was studied. Cycloaddition of (*E*)-1-methoxybuta-1,3-diene with acetyl-1,4-benzoquinone (**23**) in dichloromethane at room temperature afforded the expected adduct **24** in 72% yield.

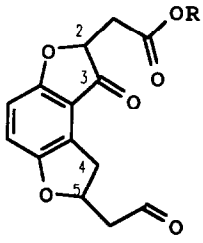
When the adduct **24** was treated for 4 days with 1.3 N hydrochloric acid under the usual conditions, no reaction was observed and the starting material was recovered. A similar result was obtained when the adduct **24** was treated with 8.5 N hydrochloric acid for 2 days at room temperature. These results are in accord with our assumption that in the rearrangement of the Diels-Alder adducts **5**, **8-11**, and **19** the silyl ether cleavage, to afford the corresponding alcohol, occurs prior to the 4a,5 carbon-carbon fission.

In the light of the above results, it was of interest to examine the acid-catalysed rearrangement on tricyclic adducts of type **25**, where the aromatisation by enolisation of the cyclohexenedione moiety was prevented due to the angular substitution on both the 4a and 8a positions. In this case the results were a little different.

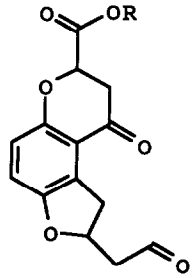


25, R=OTMS
26, R=OH

27



28, R=Et
29, R=Me



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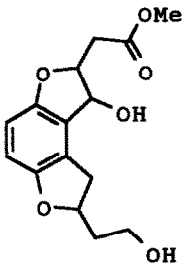
The acid-catalysed rearrangement was first attempted under conditions similar to those used for the adducts **5**, **8-11**. Thus, adduct **25** was allowed to react with 1.3 N hydrochloric acid at room temperature. After 20 h, the adduct was converted into a single product (68%), characterized as the alcohol **26** resulting from the hydrolysis of the trimethylsilyloxy group. Treatment of the alcohol **26** in acidic media, by using longer reaction periods or more concentrated acid, did not lead to any rearrangement product and resulted only in recovery of unchanged starting material.

In view of the fact that alcohol **13**, in the presence of silica gel, undergoes the rearrangement into the benzofuran derivative **17**, we have examined the reaction of the alcohol **26** under similar conditions. Thus, when the tricyclic alcohol **26** was filtered through a silica gel column using chloroform (stabilised with 1% ethanol) as the solvent, a rearrangement occurred to produce a new compound in moderate yield. The same compound can be obtained in 70% yield by stirring the tricyclic alcohol **26** with silica gel in chloroform-ethanol (3:1) for 24 h. Thus it appears that the presence of ethanol may be essential to effect the rearrangement of **26**. In fact, when compound **26** was adsorbed on silica gel and eluted with pure chloroform (HPLC grade, stabilised with *p*-cymene) only the unchanged alcohol **26** was recovered. Moreover, when the rearrangement of **26** was attempted with chloroform and methanol in the presence of silica gel, a similar compound was obtained, the ^{1}H NMR spectral pattern of which was almost completely identical with that of the former compound, except for the absence of EtO signals and the presence of a MeO singlet at δ 3.73.

In our preliminary communication[9], we have tentatively assigned the structure **27** to the former compound. However, on the basis of the spectral data and, especially, of a full analysis of the ^1H and ^{13}C NMR we have revised this assignment to the isomeric structure **28**. Therefore, we have also assigned the structure **29** to the rearrangement product obtained in the presence of methanol. In fact, the ^{13}C NMR chemical shifts are inconsistent with the quinonoid structure proposed previously. Thus, **29** shows two carbonyl carbon signals at δ 199.03 and 200.35 (CHO and CO groups) and one ester carbonyl carbon at δ 169.88. The presence of an ester carbonyl was also suggested by an IR carbonyl band at 1750 cm^{-1} and a MeOCO signal (δ 3.73) in the ^1H NMR spectrum. Moreover, the magnitude of the coupling constant $J_{H\text{-}7,H\text{-}8}$ 8.7 Hz was consistent with an *ortho* coupling between aromatic protons rather than quinonoid or enedione protons. Finally, on recording the ^1H NMR spectrum of compound **29** in benzene-d_6 we noticed the presence of separated signals for two diastereoisomers **29a+29b** in a ca. 1:1 ratio. This spectrum, complemented by extensive proton decoupling experiments, allowed to resolve the complex coupling pattern of the protons and provided additional support for the above assignment.



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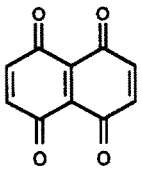

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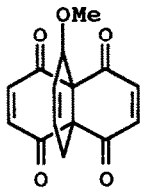

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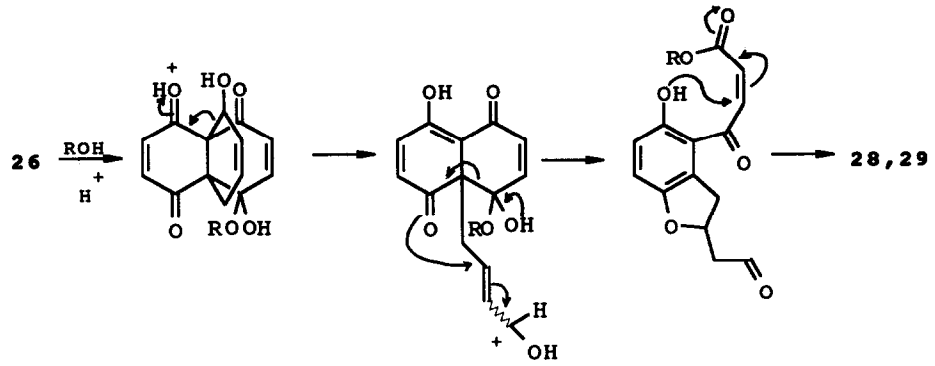
However, we could not from these data distinguish **29** (or **28**) from the isomeric structure of type **30**. The structure **29** has now been proved by reduction with sodium borohydride in methanol at 0 °C. to afford the dihydroxyester **31** and analysis of its ^1H NMR spectrum. The presence of a coupling constant J 4.12 Hz between H-2 and H-3, confirmed by spin-decoupling experiments, is only consistent with the structure **31** and we have, therefore, corroborated the benzodifuran structure **29** for its precursor.

A plausible rationalisation for the formation of the rearrangement products **28, 29** is shown in the following Scheme. The transformation presented can be explained by a sequence of reactions involving: (i) acid-catalysed 8a,9 carbon-carbon bond cleavage; (ii) hemiacetal formation of C-5 carbonyl in the presence of the alcohol; (iii) 4a,5 carbon-carbon bond fission which allows the aromatisation by enolisation to afford a dihydrobenzofuran intermediate[11]; and (iv) cyclisation to the benzodifuran derivative **28** (or **29**).



It is noteworthy that the present acid-catalysed rearrangement occurs only in the tricyclic compound **26**, bearing an OH substituent at the C-9. In fact, we have also attempted the rearrangement on the adduct **33**, MeO substituted at C-9, readily prepared by cycloaddition of (*E*)-1-methoxybuta-1,3-diene with the diquinone **32**. In contrast to **26**, treatment of adduct **33** with hydrochloric acid, for several days under the usual conditions, resulted only in recovery of the starting material.

In summary, the alcohols obtained by hydrolysis of the adducts of (*E*)-1-trimethylsilyloxybuta-1,3-diene with benzoquinones activated by electron attracting groups undergo rearrangements initiated by selective cleavage of one of the two C-C bonds originated in the cycloaddition reaction. Although the rearrangements may give different initial products according to the conditions and to the nature of the activating groups, the reactions described here provide a versatile entry to benzofuran and benzodifuran derivatives.

EXPERIMENTAL

M.p.s were determined on a Kofler hot-stage apparatus and are uncorrected. UV-vis spectra were recorded on a Perkin-Elmer model 402 spectrophotometer. Unless otherwise stated, IR spectra were recorded on a Perkin-Elmer model 257 spectrophotometer as KBr discs, ν values in cm^{-1}. ^1H NMR spectra were determined on either a Varian EM-390 or a XL-300 spectrometer. ^{13}C NMR were determined on either a Varian XL-300 or a Bruker AM-200 in $CDCl_3$ solution, unless otherwise stated. Chemical shifts are reported in p.p.m. (δ) downfield from Me_4Si. Mass spectra were determined on a VG-12-250 spectrometer. Silica gel Merck 60 (70-230 mesh) and DC-Alufolien $60F_{254}$ were normally used for preparative column and analytical TLC, respectively.

The adducts **5**, **8-11**, **19**, and **25** were prepared according to the method previously reported.[10]

Reactions of the Adducts 5, 8-11 with 1.3 N Hydrochloric Acid. General Procedure

A solution of the adduct in THF-water (9:1) and 5-20 drops of 1.3 N hydrochloric acid was kept at room temperature for 2-6 h until no susbstrate was detected by TLC. The mixture was poured into water (30 ml) and the solution was extracted with chloroform (30 ml). The organic layer was successively washed with water, aq. sodium hydrogen carbonate, water, and dried ($MgSO_4$). The solvent was removed and the crude product was purified as stated below.

4-Acetyl-5-hydroxy-2-(2-oxoethyl)-2,3-dihydrobenzo[*b*]furan (7)

From adduct **5** (740 mg, 2.53 mmol) in THF-water (9:1, 15 ml) and 1.3 N hydrochloric acid (6 drops); reaction time 2.5 h (TLC eluant $CHCl_3$). Removal of the solvent afforded **7** (550 mg, 99 %) as a yellow solid, m.p. 82-84 °C (from n-hexane). Anal. Calcd. for $C_{12}H_{12}O_4$: C, 65.44; H, 5.49. Found : C, 65.84; H, 5.76%. ν_{max} 3400, 1730, 1635 ; δ_H (90 MHz) 2.56 (3H, s, MeCO), 2.70-3.30 (3H, m, 1'-H, 3-H), 3.75 (1H, dd, *J* 18, 10 Hz, 3-H'), 5.00-5.50 (1H, m, 2-H), 6.80 (1H, d, B of AB, *J* 9 Hz, 6-H), 6.96 (1H, d, A of AB, *J* 9 Hz, 7-H), 9.90 (1H, br s with fine coupling, CHO), 12.20 (1H, s, OH).

(*E*)-2,5-Dihydroxy-6-(4-oxobut-2-enyl)benzaldehyde (14)

Obtained from adduct **8** (512 mg, 1.84 mmol), THF-water (9:1, 15 ml), 5 drops of hydrochloric acid, reaction time 3 h (TLC eluant 40:1 $CHCl_3$-MeOH). The residue was triturated with hot petroleum ether (40-60 °C) to give **14** (365 mg, 96%), m.p. 85-87 °C (from diethyl ether). Anal. Calcd. for $C_{11}H_{10}O_4$: C, 64.07; H, 4.85. Found: C, 63.71; H, 5.16%. ν_{max} 3210, 1660; δ_H ($CDCl_3$ + drops DMSO-d_6, 90 MHz) 3.96 (2H, d, *J* 6 Hz, 1'-H), 5.90 (1H, dd, *J* 16.5, 7.5 Hz, 3'-H), 6.50-7.35 (3H, m, 2'-H, 3-H, and 4-H), 7.7-8.3 (1H, br s, OH), 9.42 (1H, d, *J* 7.5 Hz, CHO), 10.14 (1H, s, CHO), 11.20 (1H, br s, OH).

5-Hydroxy-4a-methoxycarbonyl-4a,5,8,8a-tetrahydro-1,4-naphthoquinone (12)

From adduct **9** (155 mg, 0.50 mmol) in THF-water (9:1, 10 ml) and 1.3 N hydrochloric acid (8 drops), reaction time 2 h (TLC eluant $CHCl_3$). Removal of the solvent gave **12** (109 mg, 92%) as an oily liquid; ν_{max} 3460, 1730, 1690, 1670, 1600; δ_H (90 MHz) 2.04 (1H, dd, *J* 18, 9 Hz, 8-H), 2.60-3.04 (2H, m, 8-H', OH), 3.70 (1H, dd, *J* 6, 3 Hz, 8a-H), 3.72 (3H, s, CO_2Me), 4.70 (1H, m, 5-H), 5.65-6.10 (2H, m, 6-H, 7-H), 6.74 (1H, d, B of AB, *J* 10 Hz, 2-H), 6.86 (1H,d, A of AB, *J* 10 Hz, 3-H). *m/z* 236 (M^+), 204, 176, 160 (100).

5-Hydroxy-4a-nitro-4a,5,8,8a-tetrahydro-1,4-naphthoquinone (13)

From adduct **10** (284 mg, 0.96 mmol) in THF-water (9:1, 10 ml) and 1.3 N hydrochloric acid (7 drops); reaction time 3 h at room temperature (TLC eluant $CHCl_3$). The crude product **13** (208 mg, 97%) was obtained as an oily liquid, ν_{max} 3500, 1710, 1690, 1615; δ_H (acetone-d_6, 300 MHz) 3.05 (1H, dd, *J* 20, 5 Hz, 8-H), 4.36 (1H, d, *J* 6.5 Hz, 8a-H), 5.00 (1H, t, *J* 5 Hz, 5-H), 5.21 (1H, d, *J* 5 Hz, OH), 5.80-5.90 (2H, m, 6-H, 7-H), 6.92, (1H, d, B of AB, *J* 10 Hz, 2-H), 7.09 (1H, d, A of AB , *J* 10 Hz, 3-H). The signals of the 8-H are overlapped by the solvent signals. *m/z* 223 (M^+), 179 (100), 162, 149, 131, 119, 103, 91, 82, 65, 55, 39.

(*E*)- and (*Z*)-2,5-Dihydroxy-6-(4-oxobut-2-enyl)-benzonitrile (15 + 15')

From adduct **11** (100 mg, 0.41 mmol) in THF-water (9:1, 10 ml) and 1.3 N hydrochloric acid (7 drops), reaction time 6 h (TLC eluant 40:1 $CHCl_3$-MeOH). After the usual work-up, the crude product was washed with hot n-hexane to afford 60 mg (72%) of a 4:1 mixture (^1H NMR) of stereoisomers **15** and **15'** as a pale yellow solid. Anal. Calcd. for $C_{11}H_9O_3N$: C, 65.03; H, 4.43; N, 6.89. Found: C, 65.32; H, 4.64; N, 6.95% . ν_{max} 3340, 2230, 1680, 1665; δ_H (300 MHz, acetone-d_6) (*E*-isomer): 3.82 (1.6H, dd, *J* 6.5 , 1.7 Hz, 1'-H), 6.01 (0.8H, tdd, *J* 15.5, 7.8, 1.6 Hz, 3'-H), 6.68 (0.8H, d, B of AB, *J* 9 Hz, 3-H), 7.07 (0.8H,

d, A of AB, *J* 9 Hz, 4-H), 7.07 (0.8H, td, *J* 15.5, 6.5 Hz, 2'-H), 8.5-9.5 (1.6H, br s, OH), 9.56 (0.8H, d, *J* 6.5 Hz, CHO) ; (*Z*-isomer): 4.12 (0.4H, dd, *J* 8.5, 1.7 Hz, 1'-H), 5.94 (0.2H, tdd, *J* 11, 7.8, 1.6 Hz, 3'-H), 6.68 (0.2H, td, *J* 11, 8.5 Hz, 2'-H), 6.85 (0.2H, d, B of AB, *J* 9 Hz, 3-H), 7.07 (0.2H, d, A of AB, *J* 9 Hz, 4-H), 8.5-9.4 (0.4H, br s, OH), 10.40 (0.2H, d, *J* 8.5 Hz, CHO).

5-Hydroxy-4-methoxycarbonyl-2-(2-oxoethyl)-2,3-dihydrobenzo[*b*]furan (16)

A solution of the adduct **9** (262 mg, 0.86 mmol) in THF-water (9:1, 10 ml) and 8.5 N hydrochloric acid (10 drops) was kept at room temperature for 48 h. The crude product obtained after the usual work-up was purified by column chromatography ($CHCl_3$) to give the benzofuran **16** (142 mg, 70%), m.p. 71-74 °C. Anal. Calcd. for $C_{12}H_{12}O_5$: C, 61.02; H, 5.09. Found: C, 61.00; H, 5.40%. ν_{max} 3150, 1710, 1660, 1610; δ_H (90 MHz) 2.60-3.25 (3H, m, 1'-H, 1'-H', 3-H), 3.66 (1H, dd, *J* 18, 10 Hz, 3-H'), 3.96 (3H, s, OMe), 5.20 (1H, m, 2-H), 6.75 (1H, B of AB, *J* 9 Hz, 6-H), 6.89 (1H, A of AB, *J* 9 Hz, 7-H), 9.90 (1H, t with fine coupling, CHO), 10.50 (1H, s, OH).

5-Hydroxy-4-nitro-2-(2-oxoethyl)-2,3-dihydrobenzo[*b*]furan (17)

A solution of the adduct **10** (156 mg, 0.53 mmol) in THF-water (9:1, 10 ml) and 8.5 N hydrochloric acid (5 drops) was kept at room temperature for one hour. After the usual work-up, the benzofuran **17** was isolated (104 mg, 88%); an analytical sample was obtained by column chromatography ($CHCl_3$), m.p. 88-90 °C. Anal. Calcd. for $C_{10}H_9O_5N$: C, 53.81; H,4.00; N, 6.27. Found C, 54.55; H, 4.52; N, 5.80%. ν_{max} 3290, 1720, 1620, 1600 ; δ_H (90 MHz, acetone-d_6) 2.96 (2H, d with fine coupling, *J* 6 Hz, 1'-H), 3.30 (1H, dd, *J* 18, 9 Hz, 3-H), 3.86 (1H,dd, *J* 19, 9 Hz, 3-H'), 5.32 (1H, m, 2-H), 6.91 (1H, B of AB, *J* 9 Hz, 6-H), 7.01 (1H, A of AB, *J* 9 Hz, 7-H), 9.77 (1H, t, with fine coupling, CHO), 9.9 (1H, s, OH); *m/z* 223(M^+), 203, 179 (100), 149, 105, 91, 77.

4-Formyl-5-hydroxy-2-(2-oxoethyl)-2,3-dihydrobenzo[*b*]furan (18)

A solution of the adduct **8** (160 mg, 0.57 mmol) in THF-water (9:1, 10 ml) and 8.5 N hydrochloric acid (20 drops) was kept at room temperature for 48 h. The reaction mixture was diluted with water and extracted with chloroform. The organic layer was washed with water and dried with magnesium sulfate. The solvent was evaporated off to afford the benzofuran **18** (86 mg, 73%), m.p. 78-79 °C. Anal. Calcd. for $C_{11}H_{10}O_4$: C, 64.08; H, 4.85. Found: C, 63.90; H, 4.96% . ν_{max} 3380, 1700, 1640; δ_H (90 MHz) 2.70-3.40 (3H, m, 1'-H, 1'-H', 3-H), 3.75 (1H, dd, *J* 17, 10 Hz, 3-H'), 5.33 (1H, m, 2-H), 6.79 (1H, d, B of AB, *J* 9 Hz, 6-H), 7.00 (1H, d, A of AB, *J* 9 Hz, 7-H), 9.90 (1H, t with fine coupling, CHO), 10.00 (1H, s, CHO), 11.6 (1H, s, OH).

Conversion of Adduct 19 into Benzocyclooctatriene 21

A solution of adduct **19** (475 mg, 1.25 mmol) was filtered through a silica gel column using benzene as the eluant. From the initial eluate (orange band) the pure adduct **19** (200 mg, 0.52 mmol) was isolated. Further elution (red band) gave the compound **21** as red crystals (80 mg, 22% based on recovered **19**), m.p. 179-180 °C (from ethanol). Anal. Calcd. for $C_{19}H_{14}O_3$: C, 78.60; H, 4.82. Found: C, 78.41; H, 5.09%. ν_{max} 3260, 1635, 1610 ; δ_H (300 MHz) 7.44-7.52 (5H, m, ArH), 7.61 (1H, ddd, *J* 7.7, 7.6, 1.3 Hz, 6-H), 7.72 (1H, ddd, *J* 7.7, 7.6, 1.3 Hz, 7-H), 7.82-7.86 (1H, m, 11-H), 7.87 (1H, d, B of AB, *J* 15.6

Hz, 2-H), 7.94 (1H, d, A of AB, *J* 15.6 Hz, 3-H), 8.23 (1H, ddd, *J* 7.6, 1.3, 0.8 Hz, 8-H), 8.42 (1H, ddd, *J* 7.7, 1.3, 0.8 Hz, 5-H), 8.75 (1H, s, OH), 14.50 (1H, s, OH); δ_C (75 MHz): 105.24, 113.66, 121.79, 123.06, 124.90, 126.78, 127.14, 129.62, 129.72, 129.78, 129.88, 130.38, 131.02, 131.67, 135.78, 145.48, 158.83, 193.99; *m/z* 290 (M^+), 213, 186 (100), 158, 130, 102, 77, 51.

4-Cinnamoyl-5-hydroxy-2-(2-oxoethyl)-2,3-dihydrobenzo[*b*]furan (22)

A solution of the adduct **19** (200 mg, 0.52 mmol) in THF-water (9:1, 10 ml) and 1.3 N hydrochloric acid (4 drops) was allowed to react at room temperature for 48 h (TLC eluant $CHCl_3$). After the usual work-up, the crude product was triturated with n-hexane-dichloromethane (4:1) to afford the benzofuran **22** (148 mg, 92%). An analytical sample of this compound was obtained by column chromatography on silica gel ($CHCl_3$), m.p. 136-138 °C. Anal. Calcd. for $C_{19}H_{16}O_4$: C, 72.54; H, 5.19. Found: C, 72.54 ; H, 5.35%. ν_{max} 1730, 1640, 1600; δ_H (300 MHz) 2.86 (1H, ddd, *J* 17.5, 5.8, 1.5 Hz, 1'-H), 3.06 (1H, ddd, *J* 17.5, 7.0 , 2 Hz, 1'-H'), 3.24 (1H, dd, *J* 15.6, 7.6 Hz , 3-H), 3.82 (1H, dd, *J* 15.6 , 9.1 Hz, 3-H'), 5.25 (1H, m, 2-H), 6.83 (1H, d, B of AB, *J* 8.5 Hz, 6-H), 6.96 (1H, d, A of AB, *J* 8.5 Hz, 7-H), 7.30 (1H, d, *J* 15 Hz, COCH=CH), 7.4-7.7 (5H, m, ArH), 7.83 (1H, d, *J* 15 Hz, COCH=CH), 9.86 (1H, t, *J* 1.8 Hz, CHO), 12.20 (1H, s, OH); *m/z* 205 (M^+- CH=CHPh), 158, 130, 104, 102, 76 (100), 50.

4a,5-*trans*-4a,8-*cis*-4a-Acetyl-5-methoxy-4a,5,8,8a-tetrahydro-1,4-naphthoquinone (24)

A solution of acetyl-1,4-benzoquinone (**23**)[12] (213 mg, 1.42 mmol) in dichloromethane (10 ml) was reacted with (*E*)-1-methoxybuta-1,3-diene (150 mg, 1.78 mmol) for 2.5 h at room temperature. The solvent was removed under reduced pressure and the residue was triturated with petroleum ether to give the adduct **24** (241 mg, 72%), m.p. 213-216 °C (from petroleum ether 40-60 °C). Anal. Calcd. for $C_{13}H_{14}O_4$: C, 66.66; H, 5.98. Found: C, 66.90; H, 5.98%. ν_{max} 1725, 1710, 1675, 1610; δ_H (300 MHz) 1.98 (1H, tdd, *J* 19, 7, 3 Hz, 8-H), 2.37 (3H, s, COMe), 3.06 (1H, m, 8-H'), 3.18 (3H, s, OMe), 3.76 (1H, d, *J* 7 Hz, 8a-H), 4.34 (1H, d, *J* 5 Hz, 5-H), 5.90-6.07 (2H, m, 6-H, 7-H), 6.62 (1H, d, B of AB, *J* 10 Hz, 2-H), 6.86 (1H, d, A of AB, *J* 10 Hz, 3-H).

9-Hydroxy-4a,8a-dihydro-4a,8a-(but-2-eno)naphthalene-1,4,5,8-tetraone (26)

A solution of the adduct **25** (1.32 g, 4 mmol) in THF-water (9:1, 80 ml) and 1.3 N hydrochloric acid (1 ml) was allowed to react for 20 h at room temperature. After the usual work-up the crude product was triturated with diethyl ether to afford **26** (0.7 g, 68%), m.p. 131.5-135 °C (from benzene-n-hexane). Anal. Calcd. for $C_{14}H_{10}O_5$: C, 65.11; H, 3.87. Found: C, 64.75; H, 4.04%. ν_{max} (Nujol) 3530, 3480, 1710, 1680, 1610; δ_H (300 MHz) 2.60-2.72 (3H, m, 12-H, 12-H', OH), 4.73 (1H, m, 9-H), 5.79-5.99 (2H, m, 10-H, 11-H), 6.79-6.92 (4H, m, 2-H, 3-H, 6-H, 7-H); δ_C (75 MHz) 27.36, 63.38, 65.17, 69.73, 126.38, 128.11, 138.93, 141.05, 143.01, 145.03, 191.25, 191.64, 194.92, 196.10; *m/z* 258 (M^+), 260, 242, 240, 229, 190 (100), 108.

2-(2-Ethoxycarbonylmethyl)-3-oxo-5-(2-oxoethyl)-2,3,4,5-tetrahydrobenzo[1,2-*b*;4,3-*b'*]difuran (28)

A mixture of compound **26** (190 mg, 0.7 mmol), silica gel (Merck 70-230 mesh, 6 g), 95% ethanol (20 ml) and chloroform (60 ml) was vigorously stirred at room temperature for 24 h. The resulting mixture was filtered and the solvent removed. The solid residue was triturated with diethyl ether to give

the benzodifuran **28** (154 mg, 70%), m.p. 90-93 °C. Anal. Calcd. for $C_{16}H_{16}O_6$: C, 63.16; H, 5.26. Found C, 62.97; H, 5.15%. λ_{max} ($CHCl_3$) 258, 383 nm (log ε 3.94, 3.60); ν_{max} (Nujol) 1740, 1720, 1710, 1630, 1610; δ_H (300 MHz) 1.19-1.24 (3H, m, CH_3), 2.77-2.87 (2H, m, 1'-H, 1"-H), 2.98-3.18 (3H, m, 1'-H', 4-H, and 1"-H'), 3.64-3.75 (1H, m, 4-H'), 4.12-4.19 (2H, m, OCH_2), 4.83-4.87 (1H, m, 2-H), 5.31-5.39 (1H, m, 5-H), 6.89, 7.04 (2H, AB syst., *J* 8.8 Hz, 7-H, 8-H), 9.87 (1H, t, *J* 1.2 Hz, CHO); δ_C (75 MHz): 14.02, 34.47, 36.10, 49.58, 61.22, 78.79, 81.39, 112.17, 117.75, 119.03, 122.23, 154.64, 167.61, 169.34, 199.07, 200.51; *m/z* 305 ($M^+ + 1$), 304 (M^+), 260, 231, 187 (100).

2-(2-Methoxycarbonylmethyl)-3-oxo-5-(2-oxoethyl)-2,3,4,5-tetrahydrobenzo[1,2-*b*;4,3-*b'*]difuran (29a+29b)

According to the above procedure but using methanol and chloroform stabilised with amylene, the alcohol **26** (190 mg, 0.7 mmol) was converted into the benzodifuran **29** (130 mg, 72%), m.p. 130-134 °C. Anal. Calcd. for $C_{15}H_{14}O_6$: C, 62.07; H, 4.83. Found C, 62.54; H, 4.94%. λ_{max} ($CHCl_3$) 255, 379 nm (log ε 3.99, 3.64); ν_{max} (Nujol) 1750, 1725, 1710, 1630, 1615; δ_H (200 MHz) 2.72-2.88 (2H, m, 1'-H, 1"-H), 2.95-3.19 (3H, m, 1'-H', 1"-H', 4-H), 3.61-3.76 (1H, m, 4-H'), 3.73 (3H, s, OCH_3), 4.83-4.89 (1H, m, 2-H), 5.27-5.42 (1H, m, 5-H), 6.88, 7.04 (2H, AB syst. *J* 8.7 Hz, 7-H, 8-H), 9.86 (1H, t, *J* 1.3 Hz, CHO); δ_H (300 MHz, benzene-d_6) 1.68-1.80 (1H, m, 1"-H), 2.09-2.22 (1H, m, 1"-H'), 2.55 (0.5H, dd, *J* 17.0, 6.9 Hz, 1'-H of **29a**), 2.57 (0.5H, dd, *J* 16.9, 6.7 Hz, 1'-H of **29b**), 2.61-2.67 (1H, m, 4-H), 2.73 (0.5H, dd, *J* 17.0, 4.05 Hz, 1'-H' of **29a**), 2.74 (0.5H, dd, *J* 16.9, 4.1 Hz, 1'-H' of **29b**), 3.15-3.26 (1H, m, 4-H'), 3.16, 3.17 (2s, 3H, OMe), 4.45 (0.5H, dd, *J* 6.7, 4.1, 2-H of **29b**), 4.49 (0.5H, dd, *J* 6.9, 4.05 Hz, 2-H of **29a**), 4.65 (0.5H, m, 5-H of **29b**), 4.72 (0.5H, m, 5-H of **29a**), 6.52, 6.63 and 6.52, 6.64 (2H, AB syst., *J* 8.7 Hz, 7-H, 8-H), 9.16 (0.5H, t, *J* 1.87 Hz, CHO of **29b**), 9.19 (0.5H, t, *J* 1.04 Hz of **29a**); δ_C (75 MHz) 34.42, 35.84, 49.52, 52.18, 78.78, 81.30, 112.15, 117.60, 119.06, 122.26, 154.85, 167.54, 169.88, 199.03, 200.35; *m/z* 291($M^+ + 1$), 290 (M^+), 246, 231, 187 (100).

Reduction of **29a+29b** with sodium borohydride in methanol at 0 °C afforded **3-hydroxy-2-(2-methoxycarbonylmethyl)-5-(2-hydroxyethyl)-2,3,4,5-tetrahydrobenzo[1,2-*b*;4,3-*b'*]difuran(31)**, δ_H (300Mz) 1.80-2.16 (4H, m, 1"-H, 1"-H', OH), 2.69 (1H, dd, *J* 16.4, 7.5 Hz, 1'-H), 2.85 (1H, dd, *J* 16.4, 6.6 Hz, 1'-H'), 2.86, 3.03, 3.28, 3.45 (2H, 4dd, 4-H, 4-H'), 3.74, 3.75 (2s, 3H, OMe), 3.75-3.60 (2H, m, CH_2OH), 4.88 (1H, m, $J_{2,3}$ 4.12 Hz, 2-H), 4.94 (1H, m, 5-H), 5.14 (1H, m, 3-H), 6.55, 6.63 (2H, AB syst., *J* 8.5 Hz, 7-H, 8-H).

9-Methoxy-4a,8a-dihydro-4a,8a-(but-2-eno)naphthalene-1,4,5,8-tetraone (33)

A solution of naphthalene-1,4,5,8-tetraone[13] (**32**) (500 mg, 2.65 mmol) in dichloromethane (20 ml) was reacted with (*E*)-1-methoxybuta-1,3-diene (235 mg, 2.8 mmol) for 12 h at room temperature. The reaction mixture was evaporated and the residue was triturated with n-hexane and filtered to give the adduct **33** (685 mg, 95%), m.p. 198-202 °C (from n-hexane). Anal. Calcd. for $C_{15}H_{12}O_5$: C, 66.17; H, 4.41. Found: C, 66.20; H, 4.48. ν_{max} 1710, 1680, 1610; δ_H (300 MHz) 1.94 (1H, dd, *J* 20, 1.5 Hz, 12-H), 3.04 (3H, s, OMe), 3.06 (1H, ddd, *J* 20, 4.5, 2 Hz, 12-H'), 4.32 (1H, dd, *J* 4.8, 1.2, 9-H), 5.75-5.99 (2H, m, 10-H, 11-H), 6.71, 6.89 (AB system, 2H, *J* 10.5 Hz, 2-H, 3-H or 6-H, 7-H), 6.72, 7.02 (2H, AB system, *J* 10.5 Hz, 6-H, 7-H or 2-H, 3-H). δ_C (20 MHz, acetone-d_6): 27.53, 57.27, 63.26, 69.13, 73.77, 124.58, 128.60, 138.90, 140.78, 143.01, 145.23, 190.66, 190.81, 193.97, 196.08; *m/z* 272 (M^+), 245, 212, 190 (100), 175, 77.

Attempted Cleavage of Adducts 24 and 33

To a solution of the adduct (**24**, 55 mg; **33**, 80 mg, 0.25 mmol) in THF-water (9:1, 20 ml) was added 1.3 N hydrochloric acid (6 drops) and the solution was kept at room temperature for 4-6 days. After the usual work-up, the residue was shown to be recovered adduct (by ^{1}H NMR). Attempts of cleavage effected by using 8.5 N hydrochloric acid (3 drops) at room temperature for 3 days were unsuccessful.

ACKNOWLEDGMENTS

We thank the Programa de Cooperación Científica con Iberoamérica (M.E.C.), the Consejo Superior de Investigaciones Cientfficas (Spain), and the Fondo Nacional de Investigaciones Cientffica y Tecnológica de Chile (Grant 88/0316) for financial support.

REFERENCES AND NOTES

1. Part 23 of this series: Valderrama, J. A.; Pessoa-Mahana, H.; Tapia, R. submitted to *J. Het. Chem.*
2. Birch, A. J.; Butler, D. N.; Siddall, J. B. *J. Chem. Soc.* **1964**, 2932.
3. Beddoes, R. L.; Bruce, J. M.; Finch, H.; Heelamn, L. M. J.; Hunt, I. D.; Mills, O. S. *J. Chem. Soc. Perkin Trans. 1*, **1981**, 2670.
4. Kraus, G. A.; Molina, M. T.; Walling, J. A. *J. Org. Chem.*, **1987**, *52*, 1273.
5. Kraus, G. A.; Shi, J.; Reynolds, D. *J. Org. Chem.*, **1990**, *55*, 1105.
6. Bird, C. W.; Brown, A. L.; Chan, C. C.; Lewis, A. *Tetrahedron Lett.*, **1989**, *30*, 6223.
7. Rao, G. S. R. S.; Devi, L. U.; Sheriff, U. J. *J. Chem. Soc. Perkin Trans. 1*, **1991**, 964.
8. Valderrama, J.; Araya-Maturana, R.; González, M. F.; Tapia,R.; Fariña, F.; Paredes, M.C. *J. Chem. Soc. Perkin Trans. 1*, **1991**, 555.
9. Fariña, F.; Paredes, M. C.; Valderrama, J. A. *J. Chem. Soc. Perkin Trans. 1*, **1990**, 2345.
10. Valderrama, J.; Fariña, F.; Paredes, M. C. *Synth. Commun.*, **1989**, *19*, 3301.
11. In the present case, no direct evidence was obtained for the formation of the dihydrobenzofuran intermediate. However, concrete evidence for this type of intermediates has been obtained recently in our laboratory for the rearrangement products from similar adducts of anthradiquinone.
12. Cassis, R.; Valderrama, J. *Synth. Commun.*, **1983**, *13*, 347.
13. Zahn, K.; Ochwat, P. *Liebigs Ann. Chem.*, **1928**, *426*, 72.