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Transformations of lignans. Part 4: Oxidative and reductive rearrangements of dibenzocyclooctadiene and spirodienone lignans☆

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Abstract—DDQ oxidation of a dibenzocyclooctadiene derived from a 2,3-dibenzylbutane-1,2,4-triol di-*O*-methyl ether gives an oxygen-bridged dibenzocyclooctadienone and an oxygen-bridged spirodienone. The same products may also be obtained directly from the dibenzylbutane derivative by treatment with excess DDQ. Acid treatment of the spirodienone leads to demethylation and rearrangement to an *ortho*-benzoquinone. Reductive rearrangement of the spirodienone produces an oxygen-bridged dibenzocyclooctadienone. These reactions yield unique cyclohexadienone lignans and illustrate readily achieved increases in complexity starting from a simple dibenzylbutane derivative. © 2001 Elsevier Science Ltd. All rights reserved.

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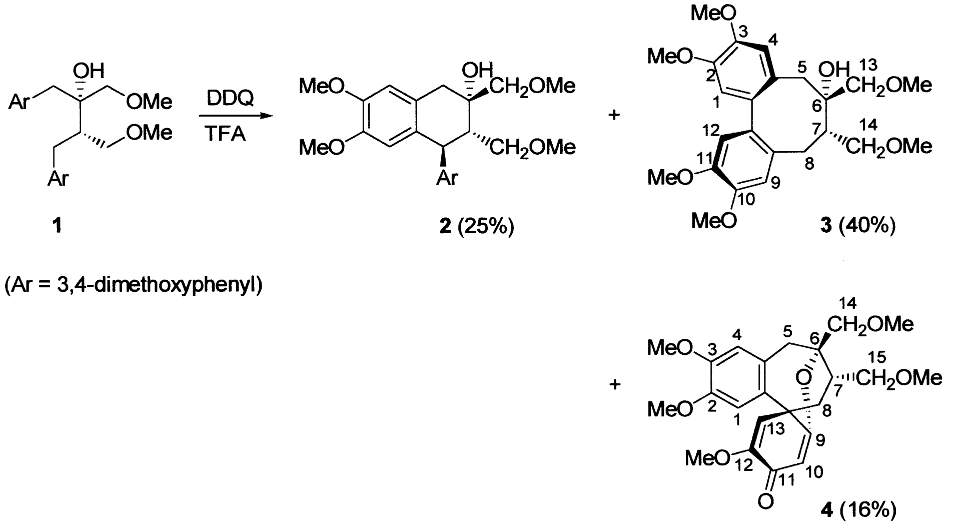
1. Introduction

In our earlier studies of lignan transformations,[1–7] we have shown that 2,3-dibenzyl-2-hydroxybutane-1,4-di-*O*-methyl ether **1** is converted into lignans such as **2** to **4**,[1] by reaction with DDQ (2,3-dichloro-5,6-dicyano-1,4-benzoquinone) in trifluoroacetic acid (TFA) (Scheme 1). Aryltetralin and dibenzocyclooctadiene lignans such as **2** and **3** are well



Scheme 1.

☆ See Ref. 1.

Keywords: lignans; oxidation; dienones; rearrangements; spiro compounds.

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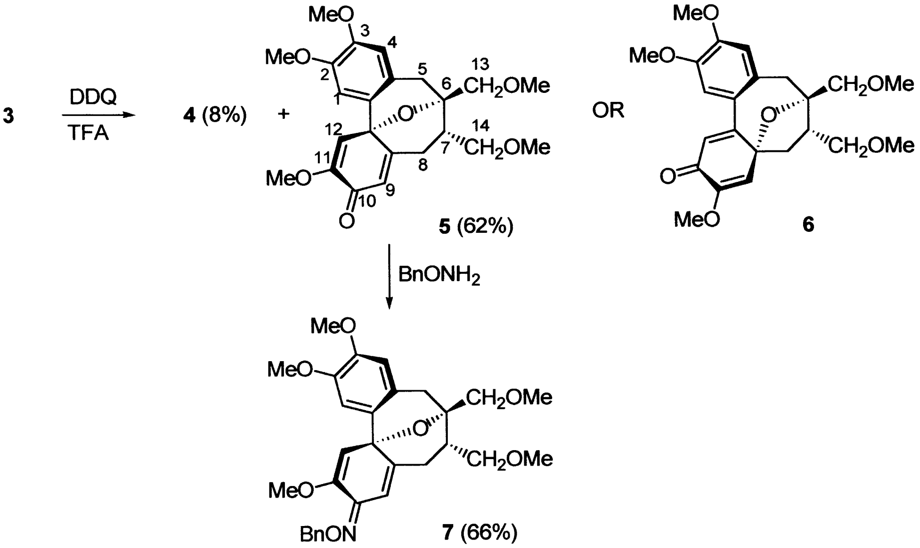


Scheme 2.

known and naturally occurring lignans containing a spirodienone moiety resembling **4** have been reported in the literature.[8–11] In this paper, we now report further interesting transformations of **3** and **4**.

2. Results and discussion

When **3**[1] was treated with 2.5 equiv. of DDQ in TFA, it produced a mixture of two products (Scheme 2). The major product to which we assign structure **5** was obtained in 62% yield as a colourless crystalline solid and had molecular formula $C_{23}H_{28}O_7$. The ^{1}H and ^{13}C NMR spectra of **5** are compared with those of compound **3** in Tables 1 and 2. Its UV spectrum showed absorption maxima at λ_{max} ($CHCl_3$) 250, 280, 300 and 340 nm, and the IR spectrum had peaks at 1690, 1662, 1650 (C=O) and 1100 (CH_2OMe) cm^{-1}. The ^{13}C NMR spectrum revealed the presence of only three aromatic methoxyl groups at δ 55.3, 55.9 and 56.1 besides two aliphatic methoxyl groups at δ 58.9 and 59.5 and a carbonyl group at δ 181.3 (Table 2). The tertiary hydroxyl present in the starting compound **3** was absent in **5** as indicated by the absence of hydroxyl absorption in its IR spectrum. Instead the ^{13}C NMR spectrum showed two aliphatic quaternary carbon atoms with chemical shifts at δ 74.0 and 73.9. These indicate that the tertiary hydroxyl of the starting compound **3** may, in **5**, be involved in an oxygen bridge. The peak at δ 181.3 confirmed the presence of a cyclohexadienone carbonyl group. These facts can only be accounted for by an oxidative reaction leading to the formation of a cyclohexadienone moiety as shown in the two alternate structures **5** and **6**.

Table 1. ^{1}H NMR spectra of **3**, **5**, **7**, **10**, **11** and **12**

	3	**5**	**7**	**10**	**11**	**12**
H-1	6.77 s	6.42 s	6.47 s	6.44 s	6.66 s	6.37 s
H-4	6.78 s	6.68 s	6.64 s	6.68 s	6.84 s	6.68 s
H-5	2.84 d (13.9) 2.47 d (13.9)	3.53 d (17.7) 2.84 d (17.7)	3.51 d (17.7) 2.80 d (17.7)	3.49 d (17.8) 2.86 d (17.8)	3.50 d (17.8) 2.86 d (17.8)	3.53 d (17.8) 2.84 d (17.8)
H-7	1.86 m	2.26 m	2.17 m	2.30 m	2.21 m	2.24 m
H-8	2.50 m	2.48 ddd (1.4, 5.2, 14.2) 2.54 dd (2.4, 14.2)	2.46 ddd (1.6, 5.1, 14.0) 2.38 dd (1.9, 14.0)	2.57 dd (2.1, 14.1) 2.50 ddd (1.7, 5.4, 14.1)	3.27 m 2.53 m	2.51 br.s 2.52 br.s
H-9	6.81 s	5.96 d (1.4)	6.60 d (1.6)	6.04 d (1.5)	5.95 d (1.3)	5.94 d (1.8)
H-11	–	–	–	–	–	6.48 dd (1.8, 10.1)
H-12	6.82 s	5.84 s	5.33 s	6.09 s	6.52 s	6.88 d (10.1)
H-13	3.47 d (9.0) 3.37 m	3.46 d (9.4) 3.43 d (9.4)	3.40 d (9.3) 3.44 d (9.3)	3.45 d (9.3) 3.37 d (9.3)	3.46 d (11.3) 3.39 d (11.3)	3.45 d (9.4) 3.41 d (9.4)
H-14	3.52 dd (6.0, 9.5) 3.66 dd (3.4, 9.5)	3.55 dd (5.8, 9.1) 3.26 dd (8.5, 9.1)	3.55 dd (6.0, 9.3) 3.29 dd (7.8, 9.3)	3.51 dd (6.0, 9.2) 3.26 dd (8.6, 9.2)	3.54 dd (6.0, 9.3) 3.28 dd (8.7, 9.3)	3.51 dd (6.0, 9.1) 3.27 dd (8.5, 9.1)
OMe	3.87 s 3.88 s 3.90 s 3.91 s 3.36 s 3.38 s	3.86 s 3.72 s 3.76 s 3.42 s 3.32 s	3.86 s 3.81 s 3.73 s 3.42 s 3.32 s	3.86 s 3.75 s 3.42 s 3.32 s	3.85 s 3.78 s 3.42 s 3.32 s	3.86 s 3.73 s 3.42 s 3.32 s
PhCH_2	–	–	5.31 s	–	–	–
Ph	–	–	7.31–7.43 m	–	–	–
OH	1.86 m	–		6.46 br s	–	–
OAc	–	–	–	–	2.32 s	–

Table 2. ^{13}C NMR spectra of **3**, **5**, **7**, **10**, **11** and **12**

	3	**5**	**7**	**10**	**11**	**12**
C-1	111.6	107.3	106.3	107.3	107.4	106.9
C-1a	128.2	126.8	126.4	126.6	125.9	126.5
C-2	147.1	149.1	148.6	149.1	149.0	149.1
C-3	147.4	147.3	147.1	147.3	147.7	147.3
C-4	111.9	111.3	108.0	111.3	111.1	111.4
C-4a	132.5	126.7	129.2	126.3	122.1	125.2
C-5	41.0	35.6	35.6	35.8	35.3	35.5
C-6	71.7	74.0	74.5	73.7	74.1	72.4
C-7	46.2	43.6	43.8	43.7	43.2	43.4
C-8	31.6	29.2	29.1	29.5	28.9	29.3
C-8a	133.7	160.0	145.0	147.3	146.0	159.6
C-9	112.0	115.5	110.8	116.6	114.9	123.1
C-10	147.7	181.3	150.7	182.0	179.3	186.1
C-11	148.5	151.8	147.0	164.0	160.3	129.8
C-12	115.0	122.5	109.8	120.3	122.1	147.8
C-12a	133.9	73.9	73.8	120.3	125.1	74.1
C-13	75.8	77.4	77.7	77.4	77.4	77.2
C-14	80.1	70.7	71.2	70.5	70.7	70.7
OMe	56.0	55.3	55.4	56.1	56.1	56.0
	56.1	55.9	55.9	55.9	55.9	55.9
	58.9	56.1	56.0	58.9	58.9	58.8
	59.1	58.9	58.7	59.6	59.6	59.5
	59.4	59.5	59.5			
PhCH_2	–	–	77.1	–	–	–
OAc	–	–	–	–	169.1	–
					20.4	

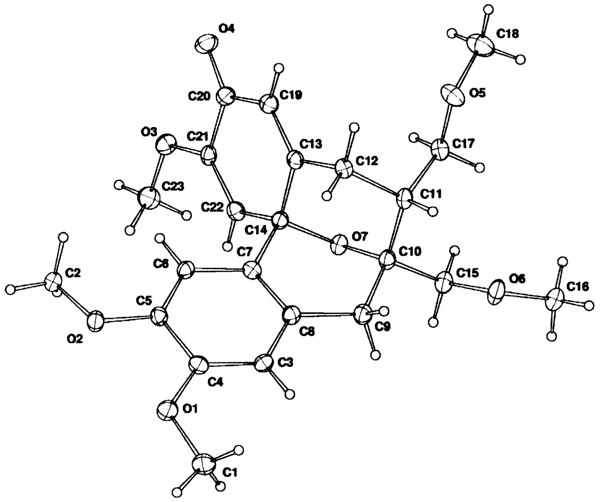


Figure 1. X-Ray structure of **5**.

HMBC studies (Table 3) proved inconclusive in distinguishing between **5** and **6** and finally the structure was settled by X-ray analysis as **5**, containing a spirodienone moiety with an oxygen bridge between C-6 and C-12a of the cyclooctene skeleton (Fig. 1).

Table 3. HMBC correlation spectra of **5**

Position	^{1}H NMR	^{13}C NMR	Correlated carbons
1	6.42 (1H, s)	107.3 (CH)	126.8 or 126.7 (C-4a or C-1a) 149.1 (C-2)
1a	–	126.8[a]	–
2	–	149.1	–
3	–	147.3	–
4	6.68 (1H, s)	111.3 (CH)	147.3 (C-3) 126.7 or 126.8 (C-1a or C-4a)
4a	–	126.7[a]	–
5	2.84 (1H, d, 18.8)	35.6 (CH_2)	126.8 or 126.7 (C-4a or C-1a) 111.3 (C-4)
	3.55 (1H, m)[a]		126.8 or 126.7 (C-4a or C-1a) 111.3 (C-4) 35.5 (C-5) 74.0 (C-6) 43.6 (C-7)
6	–	74.0	–
7	2.29 (1H, m)	43.6 (CH)	–
8	2.51–2.55 (2H, m)	29.2 (CH_2)	74.0 or 73.4 (C-6 or C-12a)
8a	–	160	–
9	5.84 (1H, s)	115.5 (CH)	181.3 (C-10) 151.8 (C-11) 160.0 (C-8a)
10	–	181.3	–
11	–	151.8	–
12	5.96 (1H, d, 1.3)	122.5 (CH)	151.8 (C-11) 73.9 or 74.0 (C-12a or C-6)
12a	–	73.9	–
13	3.43 (1H, d, 9.3) 3.46 (1H, d, 9.3)	77.4 (CH_2)	–
14	3.55 (1H, m)[a] 3.22 (1H, t, 8.8)	70.7 (CH_2)	43.6 (C-7) 74.0 (C-6)
–OMe	3.86	56.1	–
	3.76	55.9	
	3.72	55.3	
	3.42	59.5	
	3.32	58.9	

[a] Merged signals.

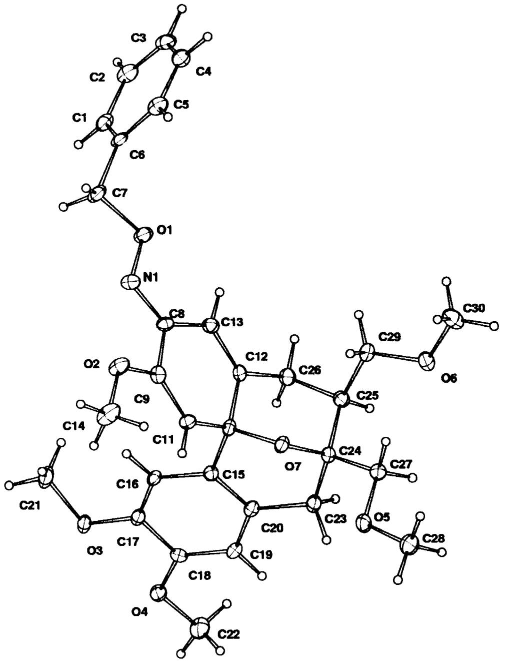


Figure 2. X-Ray structure of **7**.

With benzyloxyamine hydrochloride compound **5** yielded the simple oxime derivative **7** thus fulfilling our aim of introducing nitrogen into the lignan skeleton. The structure of **7** was assigned on the basis of ^{1}H and ^{13}C NMR spectra (Tables 1 and 2) and confirmed by X-ray analysis (Fig. 2).

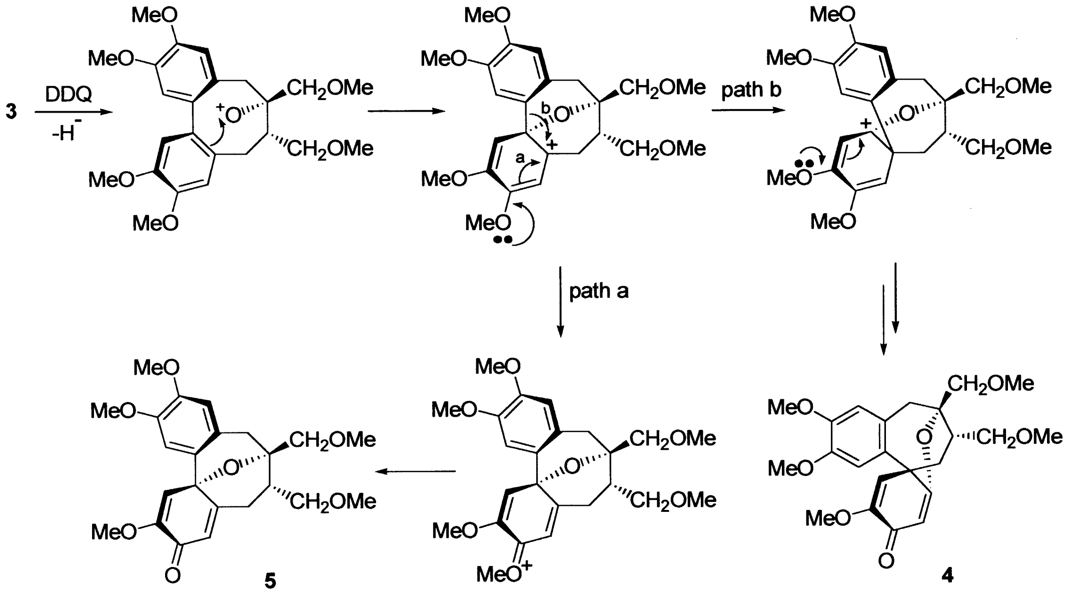
The minor product (8%) of oxidation of **3** was obtained as a colourless crystalline solid having molecular formula $C_{23}H_{28}O_7$. By direct comparison it was readily identified as the seven-membered spirodienone **4**, produced earlier by the DDQ oxidation of **1**.[1]

Possible mechanisms for the formation of an eight-membered spirodienone **5** and the isomeric seven-membered spirodienone **4** from **3** are shown in Scheme 3.

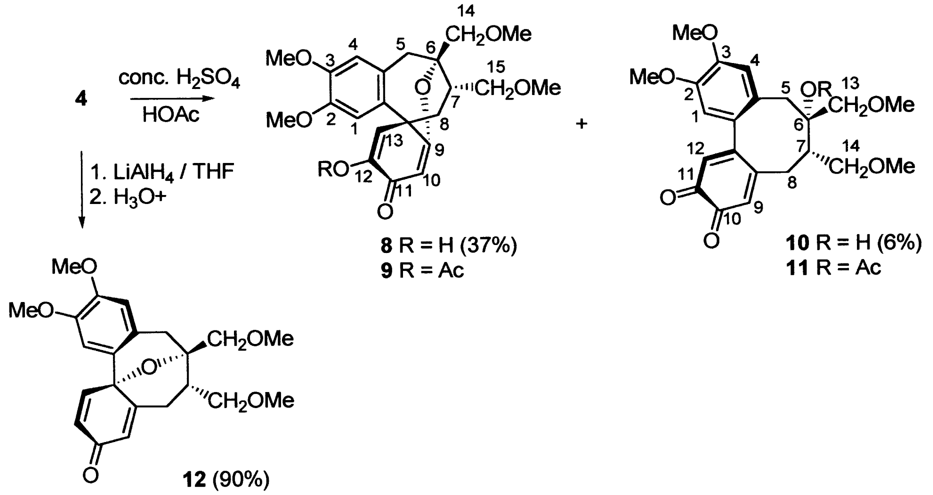
Later we showed that **5** and **4** could also be prepared directly from **1** by the action of excess DDQ (6 equiv.) in TFA. This reaction is a striking example of an increase in complexity brought about by simple reagents and may provide analogies for the biogenetic formation of novel lignans of the spirocyclohexadienone type containing an oxygen-bridge.[8]

When **4** was treated with conc. H_2SO_4 in acetic acid it produced two products (Scheme 4). The major product (37%), to which we assign structure **8**, was obtained as a colourless crystalline solid which had molecular formula $C_{22}H_{26}O_7$, and very similar ^{1}H and ^{13}C NMR spectra to those of the starting compound **4** except for the presence of a hydroxyl instead of a vinylic methoxyl group (Tables 4 and 5). Its IR spectrum revealed peaks at 3570 (OH), 1655 (C=O), 1600 (arom.) and 1100 (CH_2OMe) cm^{-1}, whilst the ^{1}H NMR spectrum contained a broad singlet at δ 3.87 that disappeared on D_2O exchange. Compound **8** gave a monoacetate **9** with acetic anhydride in pyridine. The ^{1}H NMR spectrum of **9** indicated that H-10 had moved downfield from δ 6.06 in **8** to 6.58. The ^{1}H and ^{13}C NMR spectra of **8** and **9** showed only four methoxyl groups, of which two are aromatic and two are aliphatic in nature (Tables 4 and 5). With this evidence structure **8** was assigned to the main product and was confirmed by X-ray analysis (Fig. 3).

A minor product **10** (6%) had molecular formula $C_{22}H_{20}O_7$. Its IR spectrum showed peaks at 3560 (OH), 1720 (C=O), 1600 (arom.) and 1100 (CH_2OMe) cm^{-1}. Its ^{1}H NMR spectrum (Table 1) showed only 3 singlets and a narrow doublet at δ 6.68, 6.44, 6.09 and 6.04 and its ^{13}C NMR spectrum (Table 2) indicated the presence of two carbonyls at δ 182.0 and 164.6. Hence the two signals at δ 6.09 and 6.04 could be due to the protons of an *ortho*-quinone system. Acetylation of **10** yielded a monoacetate **11** in 40% yield, which suggested that a tertiary hydroxyl is present in **10**. The



Scheme 3.



Scheme 4.

formation of a tertiary hydroxyl and *ortho*-quinone could have happened by the cleavage of the vinylic ether bridge, and migration of an alkyl group leading to the rearrangement of the seven-membered spirodienone **4** to the eight-membered *ortho*-quinone **10**. A possible mechanism for this transformation is shown in Scheme 5.

When **4** was treated with lithium aluminium hydride in THF, a new compound shown to have structure **12** was obtained in 90% yield. This was a colourless crystalline solid having molecular formula $C_{22}H_{26}O_6$ (Scheme 4). Its IR spectrum showed peaks at 1700 (C=O), 1610 (arom.) and 1100 (CH_2OMe) cm^{-1}. Its ^{13}C NMR spectrum indicated a single carbonyl function at δ 186.1 and only four methoxyl groups at δ 56.0, 55.9, 58.8 and 59.5, of which two are aromatic and two are aliphatic in nature (Table 2). Together with the fact that there was no OH stretching frequency and that it could not be acetylated, this indicates that the remaining oxygen must be present as an ether bridge. Its ^1H NMR spectrum indicated the presence of three protons at δ 6.48 dd (1.8, 10.1 Hz), 6.88 d (10.1 Hz) and 5.94 d (1.8 Hz) as required for a disubstituted dienone (Table 1).

Table 4. ^1H NMR spectra of **4**, **8** and **9**

	4	8	9
H-1	6.74 s	6.72 s	6.98 s
H-4	6.63 s	6.61 s	6.62 s
H-5	3.50 dd (5.0, 9.2)	3.51 dd (5.4, 9.3)	3.51 dd (5.4. 9.4)
	3.22 dd (7.7, 9.2)	3.19 dd (7.7, 9.3)	3.20 dd (8.2, 9.4)
H-7	2.53 m	2.51 m	2.50 m
H-8	2.66 dd (9.6, 13.9)	2.67 dd (9.6, 14.1)	2.64 dd (9.4, 14.0)
	2.21 dd (2.4, 13.9)	2.20 dd (2.5, 14.1)	2.27 dd (2.0, 14.0)
H-10	5.77 s	6.06 s	6.58 s
H-13	5.65 s	5.68 s	5.63 s
H-14	3.64 d (9.5)	3.65 d (9.5)	3.65 d (9.5)
	3.55 d (9.5)	3.57 d (9.5)	3.55 d (9.5)
H-15	3.48 d (17.9)	3.52 d (17.7)	3.45 d (17.7)
	3.41 d (17.9)	3.39 d (17.7)	3.42 d (17.7)
OMe	3.82 s	3.82 s	3.83 s
	3.82 s	3.79 s	3.82 s
	3.77 s	3.47 s	3.46 s
	3.46 s	3.30 s	3.31 s
	3.30 s		
OH	–	3.87 br s	–
OAc	–	–	2.34 s

Table 5. ^{13}C NMR spectra of **4**, **8** and **9**

	4	8	9
C-1	113.8	113.7	113.7
C-1a	127.2	127.0	126.5
C-2	149.9	148.4	148.4
C-3	148.3	146.9	147.3
C-4	114.7	114.8	134.0
C-4a	133.0	132.9	132.2
C-5	36.8	36.3	37.8
C-6	80.9	81.4	81.1
C-7	37.6	41.9	42.1
C-8	42.3	37.4	35.1
C-8a	42.9	43.3	43.8
C-9	176.5	179.3	176.2
C-10	104.5	102.1	104.1
C-11	182.5	182.9	180.6
C-12	146.8	145.2	143.5
C-13	109.6	109.6	109.6
C-14	76.9	76.8	76.8
C-15	72.5	72.5	72.3
OMe	55.3	56.1	56.1
	55.9	55.9	55.9
	56.0	59.5	58.9
	58.9	59.0	59.6
	59.6		
OAc	–	–	169.0
			20.6

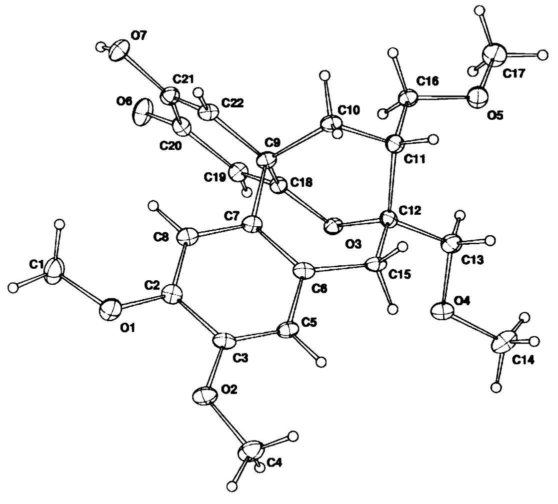
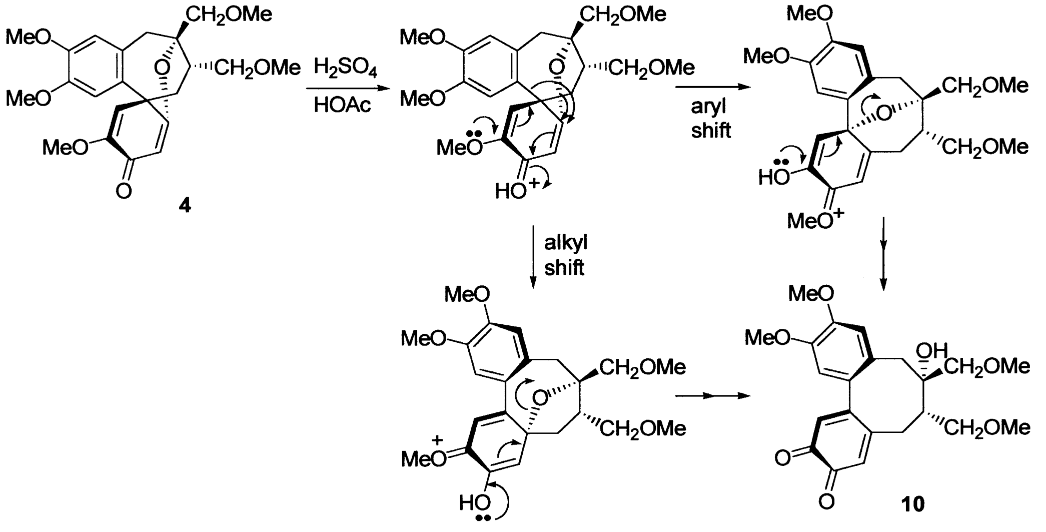


Figure 3. X-Ray structure of **8**.



Scheme 5.

Its ^{13}C NMR spectrum, in comparison with that of the starting compound **4**, indicated the absence of a vinylic methoxyl and a vinylic ether bridge. Instead peaks at δ 72.4 and 74.1 indicated an oxygen bridge between C-6 and C-12a, as in the case of eight-membered spirodienone **5**. The loss of one methoxyl group from the starting compound **4** is accounted for by the reduction of the carbonyl group to a hydroxyl group, and dehydration followed by alkyl migration resulting in the rearrangement of a seven-membered ring to give oxygen-bridged cyclohexadienone **12**. Structure **12** was confirmed by X-ray analysis (Fig. 4) and a possible mechanism for the reductive rearrangement is shown in Scheme 6.

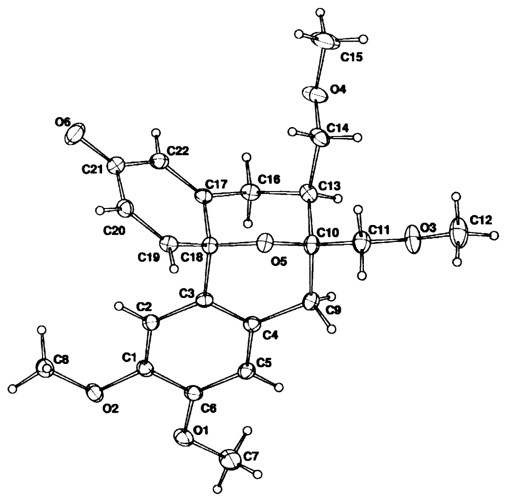
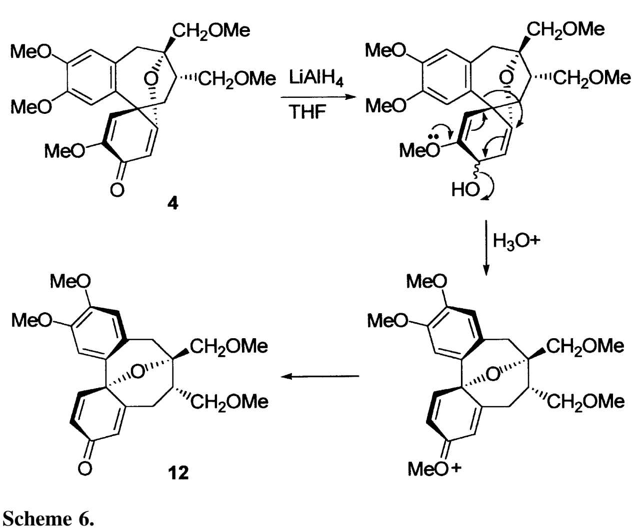


Figure 4. X-Ray structure of **12**.



Scheme 6.

3. Conclusion

We have shown that the dibenzocyclooctadiene **3** can be transformed into spirodienones **5** and **4** by oxidation with DDQ in TFA. Spirodienone **4** itself can be rearranged into oxygen-bridged spirodienone **8** and the *ortho*-quinone **10** by the action of conc. H_2SO_4 and acetic acid. Furthermore, the seven-membered spirodienone **4** can be transformed into an oxygen-bridged cyclohexadienone **12** by reductive rearrangement with LAH in THF. These reactions provide methods for the preparation of novel lignan spirodienone derivatives which have the potential for the introduction of an amino function into the lignan skeleton. They illustrate facile transformations which produce complex lignan spirodienones from a simple dibenzylbutane precursor. Such rearrangements were previously unknown and introduce novel lignan types, some of which have undergone rearrangement.

4. Experimental

4.1. General procedure

^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC 400 instrument at 400 and 100 MHz, respectively. All spectra used tetramethylsilane as internal standard and were run in $CDCl_3$. Mass spectra were recorded either on a VG 12-250 quadrupole instrument or on a VG Micromass Quattro II instrument. Accurate mass measurements were made using either a ZAB-E high-resolution double focussing instrument or a Finnigan Mat 900 instrument. Infra-red spectra were recorded either as a nujol mull or as films on NaCl plates using a Perkin–Elmer Fourier transform 1725X spectrometer. Dichloromethane was purified by passing down an alumina column followed by distillation over calcium hydride. Silica gel-G was used for column chromatography and for TLC. Melting points were recorded on an Electrothermal 9100 melting point apparatus and are uncorrected.

Suitable crystals of **5**, **7**, **8**, and **12** were selected for single crystal X-ray diffraction. Cell dimensions and intensity data were recorded at 150 K, using a Nonius KappaCCD area detector diffractometer mounted at the window of a rotating molybdenum anode (λ (Mo-Kα)=0.71073 Å). The crystal-to-detector distance was 30 mm and ϕ and Ω scans (2° increments, 10 s exposure time) were carried out to fill the Ewald sphere. Data collection and processing were carried out using the programs collect,[12] DENZO[13] and MAXUS[14] and an empirical absorption correction was applied using SORTAV.[15,16]

The structures were solved via direct methods[17] and refined by full matrix least squares[17] on F^2. Non-hydrogen atoms were refined anisotropically and hydrogen atoms were treated using a riding model. In the case of **5** two chemically identical molecules are in the asymmetric unit differing slightly in the positions of the methoxy groups. Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC 158,647 (**5**), 158,648 (**7**), 158,645 (**8**), 1,588,646 (**12**). Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

4.1.1. Synthesis of compounds 4 and 5. To a mixture of **3** (0.27 g, 0.625 mmol) and DDQ (0.35 g, 1.56 mmol, 2.5 equiv.) was added freshly distilled TFA (8 mL) and the mixture was stirred for 1 h at rt. The mixture was then poured onto crushed ice and extracted with EtOAc (3×30 mL). The combined organic extracts were washed successively with aq. $NaHSO_3$ (3×20 mL), aq. $NaHCO_3$ (3×20 mL) and brine (3×20 mL), then dried ($MgSO_4$) and filtered. Removal of the solvent under reduced pressure gave a reddish-brown residue (0.27 g) which on column chromatography on silica gel (hexane–EtOAc 3:2) yielded 5 (0.17 g, 62%), which crystallised from MeOH/H_2O as colourless shining crystals, mp 148°C, $[\alpha]_D^{25}=+68.75$ (*c* 0.4, $CHCl_3$). λ_{max} ($CHCl_3$) (log ϵ) 250 (3.67), 300 (3.65), 340 (3.76) nm. ν_{max} (Nujol) 1690, 1662, 1650 (C=O) and 1100 (CH_2OMe) cm^{-1}. *m/z* (EI) 416 (M$^+$, 60%), 384 (25), 372 (11), 352 (75), 297 (35), 285 (100), 269 (32), 255 (55), 241 (42), 225 (38), 211 (37), 197 (43), 181 (60), 165 (92), 152 (92), 139 (65), 128 (60), 115 (93). *m/z* (CI) 417 (M+H$^+$, 100), 401 (30), 390 (26), 383 (10), 369 (64), 131 (14). Acc. Mass 416.1793. $C_{23}H_{28}O_7$ requires 416.1835. Also obtained was the spirodienone **4** (0.02 g, 8%), which crystallised from benzene as colourless shining crystals, mp 160°C. λ_{max} ($CHCl_3$) (log ϵ) 260 (3.6), 300 (3.68), 320 (3.5), 340 (4.0) nm, identical to the sample reported in our previous paper.[1] For NMR spectra of **5** see Tables 1 and 2, and for **4** see Tables 4 and 5.

4.1.2. Synthesis of the oxime 7. To a solution of **5** (0.15 g, 0.36 mmol) in ethanol (5 mL) was added *O*-benzyloxyamine hydrochloride (0.075 g, 0.6 mmol) and $NaHCO_3$ (0.03 g) and the mixture was refluxed for 4 h. The reaction mixture was then poured into ice-water and extracted with EtOAc (3×30 mL). The combined organic extracts were washed successively with dil. HCl (3×20 mL) and brine (3×20 mL), then dried ($MgSO_4$) and filtered. Removal of the solvent under reduced pressure gave a reddish-brown residue (0.13 g) which on column chromatography on silica gel (hexane–EtOAc 7:3), followed by crystallisation from methanol yielded the oxime **7** (0.1 g, 66%) as colourless shining crystals, mp 218–220°C, $[\alpha]_D^{25}=+209.0$ (*c* 0.1, CH_2Cl_2). ν_{max} (Nujol) 3430 (C–N), 1354 (Ar–N), 1190, 1020 (C–N) cm^{-1}. *m/z* (EI) 521 (M$^+$, 10%), 430 (5), 389 (5), 91 (100). *m/z* (CI) 522 (M+H$^+$, 80%), 435 (20), 418 (25), 416 (30), 400 (100), 389 (50), 372 (80). Acc. Mass (M+H$^+$) 522.2494. $C_{30}H_{35}NO_7$ requires 522.2492. For NMR spectra of **7** see Tables 1 and 2.

4.1.3. Synthesis of the spirodienone 8 and the *ortho*-quinone 10. To a solution of **4** (0.25 g, 0.6 mmol) in glacial acetic acid (6 mL) cooled to 0°C, was added conc. H_2SO_4 (0.32 g, 3.3 mmol) dropwise with gentle shaking. The mixture was left at rt for 1 h, during which time the yellow colour slowly changed to red. The reaction mixture was then poured onto crushed ice and extracted with EtOAc (3×30 mL). The combined organic extracts were washed successively with $NaHCO_3$ (3×20 mL) and brine (3×20 mL), then dried ($MgSO_4$) and filtered. Removal of the solvent under reduced pressure gave a reddish-brown residue (0.25 g) which on column chromatography on silica gel (hexane–EtOAc 3:2), followed by crystallisation from methanol yielded **8** (0.09 g, 37%) as colourless crystals mp 154°C, $[\alpha]_D^{25}=-197.50$ (*c* 0.2, $CHCl_3$). λ_{max} ($CHCl_3$) (log ϵ) 250 (3.56), 280 (3.55), 300 (3.56), 340 (4.57) nm. ν_{max} (Nujol) 3570 (chelated OH), 1655 (C=O), 1600 (arom.), 1100 (CH_2OMe) cm^{-1}. *m/z* (EI) 402 (M$^+$, 2%), 370 (1), 329 (2), 297 (4), 283 (2), 271 (3), 181 (4), 165 (7), 152 (6), 139 (5), 128 (8), 115 (15). *m/z* (CI) 420 (M+NH$_4^+$, 2%), 403 (M+H$^+$, 100%), 389 (13). Acc. Mass (M+H$^+$) 403.1757. $C_{22}H_{27}O_7$ requires 403.1757. Also obtained was the *ortho*-quinone **10** (0.015 g, 6%) as a pale yellow gum, $[\alpha]_D^{25}=+70.0$ (*c* 0.1, $CHCl_3$). λ_{max} ($CHCl_3$) (log ϵ) 240 (3.3), 300 (1.2) nm. ν_{max} (Nujol) 3560 (OH), 1720 (C=O), 1600 (arom.), 1100 (CH_2OMe) cm^{-1}. *m/z* (EI) 402 (M$^+$, 9%), 388 (3), 370 (4), 355 (2), 329 (11), 307 (9), 297 (12), 283 (6), 271 (10), 255 (6), 241 (4), 227 (3), 201 (5), 181 (4), 165 (6), 151 (8), 139 (7), 128 (9), 115 (18). *m/z* (CI) 403 (M+H$^+$, 100%), 106 (10). Acc. Mass (M+NH$_4^+$) 420.2024. $C_{22}H_{30}NO_7$ requires 420.2022. For NMR spectra of **8** see Tables 4 and 5, and for **10** see Tables 1 and 2.

4.1.4. Preparation of the acetate 9. To a solution of **8** (0.075 g, 0.18 mmol) in pyridine (3 mL) was added acetic anhydride (3 mL) and DMAP (0.04 g) and the mixture was refluxed for 11/2 h. The reaction mixture was then poured onto crushed ice and extracted with EtOAc (3×30 mL). The combined organic extracts were washed successively with dil. HCl (3×20 mL) and brine (3×20 mL), then dried ($MgSO_4$) and filtered. Removal of the solvent under reduced pressure gave a reddish-brown residue (0.075 g) which on column chromatography on silica gel (hexane–EtOAc 3:2) yielded the acetate **9** (0.06 g, 80%) as a pale yellow gum, $[\alpha]_D^{25}=-197.50$ (*c* 0.2, $CHCl_3$). λ_{max} ($CHCl_3$) (log ϵ) 347.1 (4.5) nm. ν_{max} (Nujol) 1735 (OAc), 1655 (C=O), 1600 (arom.), 1100 (CH_2OMe) cm^{-1}. *m/z* (EI) 444 (M^+, 15%), 402 (4), 371 (9), 339 (5), 329 (8), 309 (7), 297 (11), 283 (6), 271 (14), 201 (6), 181 (6), 165 (8), 151 (6), 128 (7), 115 (12). *m/z* (CI) 462 ($M+NH_4^+$, 1%), 445 ($M+H^+$, 100%), 403 (13), 389 (12). Acc. Mass ($M+H^+$) 445.1856. $C_{24}H_{29}O_8$ requires 445.1855. For NMR spectra of **9** see Tables 4 and 5.

4.1.5. Preparation of the acetate 11. To a solution of **10** (0.025 g, 0.062 mmol) in pyridine (2 mL) was added acetic anhydride (2 mL) and DMAP (0.03 g) and the mixture was refluxed for 10 h. The reaction mixture was then poured onto crushed ice and extracted with EtOAc (3×30 mL). The combined organic extracts were washed successively with dil. HCl (3×15 mL) and brine (3×15 mL), then dried ($MgSO_4$) and filtered. Removal of the solvent under reduced pressure gave a reddish-brown residue (0.025 g) which on column chromatography on silica (hexane–EtOAc 3:2) yielded the acetate **11** (0.023 g, 92%) as a pale yellow gum, $[\alpha]_D^{25}=+80.0$ (*c* 0.025, $CHCl_3$). λ_{max} ($CHCl_3$) (log ϵ) 250 (4.0), 280 (4.5), 310 (4.55) nm. ν_{max} (Nujol) 1735 (OAc), 1720 (C=O), 1600 (arom.), 1100 (CH_2OMe) cm^{-1}. *m/z* (EI) 444 (M^+, 37%), 402 (11), 371 (21), 339 (20), 325 (30), 307 (31), 297 (48), 283 (33), 271 (58), 255 (28), 241 (26), 227 (25), 211 (29), 197 (39), 181 (55), 165 (86), 152 (76), 128 (60), 115 (100). *m/z* (CI) 462 ($M+NH_4^+$, 21%), 445 ($M+H^+$, 32%), 167 (100), 150 (10), 124 (12), 110 (10). Acc. Mass ($M+H^+$) 445.1852. $C_{24}H_{29}O_8$ requires 445.1855. For NMR spectra of **11** see Tables 1 and 2.

4.1.6. Synthesis of the cyclohexadienone 12. To a solution of spirodienone **4** (0.1 g, 0.24 mmol) in THF (5 mL) was added LAH (0.15 g, 3.8 mmol) and the mixture was stirred for 1/2 h at rt. The excess LAH was decomposed with EtOAc (10 mL), then poured into ice-water and extracted with EtOAc (3×30 mL). The combined organic extracts were washed with brine (3×10 mL), then dried ($MgSO_4$) and filtered. Removal of the solvent under reduced pressure gave a reddish-brown residue (0.1 g) which on column chromatography on silica gel (hexane–EtOAc 4:1), followed by crystallisation from methanol yielded **12** (0.09 g, 90%) as colourless shining crystals, mp 171°C, $[\alpha]_D^{25}=+234.0$ (*c* 0.15, $CHCl_3$). λ_{max} ($CHCl_3$) (log ϵ) 250 (3.6), 310 (1.8) nm. ν_{max} (Nujol) 1700 (C=O), 1610 (arom.), 1100 (CH_2OMe) cm^{-1}. *m/z* (EI) 386 (M^+, 88%), 354 (34), 342 (18), 322 (12), 313 (100), 291 (18), 281 (78), 267 (35), 255 (82), 241 (22), 225 (19), 211 (13), 195 (14), 181 (17), 165 (28), 152 (23), 139 (14), 128 (9), 115 (21). *m/z* (CI) 387 ($M+H^+$, 100%). Acc. Mass (M^+) 386.1728. $C_{22}H_{26}O_6$ requires 386.1729. Acc. Mass ($M+H^+$) 387.1806. $C_{22}H_{27}O_6$ requires 387.1807. For NMR spectra of **12** see Tables 1 and 2.

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