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Oxidative cyclisation of *cis*- and *trans*-2,3-dibenzylbutyrolactones using phenyl iodonium bis(trifluoroacetate) and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone

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Abstract—A series of *cis*- and *trans*-2,3-dibenzylbutyrolactones have been subjected to oxidative cyclisation using phenyl iodonium bis(trifluoroacetate) and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone. The products obtained include two novel spirodienones **6** and **11**, which rearrange with acid to give the dibenzocyclo-octadienes **7**, and **12** and **13**, respectively. © 2001 Elsevier Science Ltd. All rights reserved.

1. Introduction

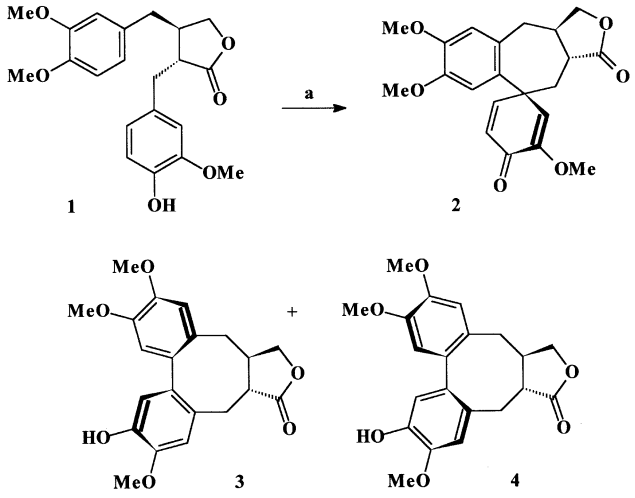
The biaryl unit is a key building block in the structure of a large number of important natural products.[1] For example, steganone, steganol, steganacin and steganangin are of particular interest due to their potential antitumour and antiviral properties.[2] An earlier paper describes the use of ruthenium tetra(trifluoroacetate) for the synthesis of compounds of this type.[3] Two other methods that have been reported for the construction of the biaryl bond in the dibenzocyclooctadiene skeleton involve the use of hypervalent iodine reagents and dehydrogenation by 'high potential' quinones.[4–7]

We have previously shown that *trans*-2,3-dibenzylbutyrolactones (**1**) having a hydroxyl group at the *para*-position of the 2-benzyl group react with hypervalent iodine reagents to afford the spirodienone (**2**) and the stegane and isostegane derivatives (**3**) and (**4**).[4] Compounds having a hydroxyl group at the *meta*-position of the 2-benzyl group on the other hand cyclise directly to give a dibenzocyclooctadiene without the intervention of a spirodienone intermediate. A number of unusual cyclisation and coupling reactions have also been reported using DDQ and some of these have been used in the synthesis of lignans.[5–7]

The aim of the work described in this paper was to study oxidative cyclisation of dibenzylbutyrolactones using phenyl iodonium bis(trifluoroacetate) (PIFA) and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ). In particular we report for the first time the cyclisation of *cis*-2,3-dibenzylbutyrolactones, and the cyclisation of *trans*-2,3-dibenzylbutyrolactones in which the phenolic OH group is located in the 3-benzyl group, using these reagents (Scheme 1).

2. Results and discussion

The *trans*-2,3-dibenzylbutyrolactone (**5**)[4,8] was treated with PIFA in TFE, and the reaction mixture stirred under an inert atmosphere for 24 h. After 1 h the starting material disappeared and a major polar product was formed, which was shown to be the spirodienone (**6**) (see below). When the reaction was allowed to continue for a longer time this intermediate disappeared and was replaced by the less polar product (**7**), which was isolated in 58% yield. When the



Scheme 1. *Reagents*: a, PIFA, TFE.

Keywords: lignans; oxidation; hypervalent iodine; quinones.

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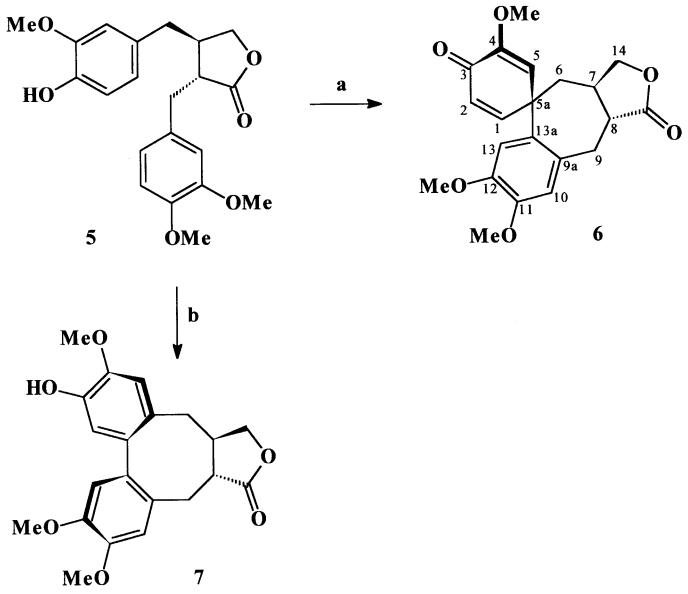


Scheme 2. *Reagents*: a, PIFA, TFE, 1 h (46%); b, PIFA, TFE, 24 h (58%).

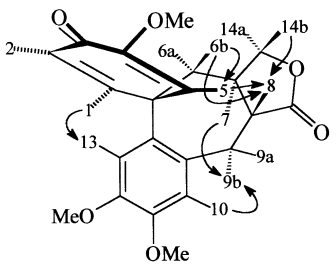
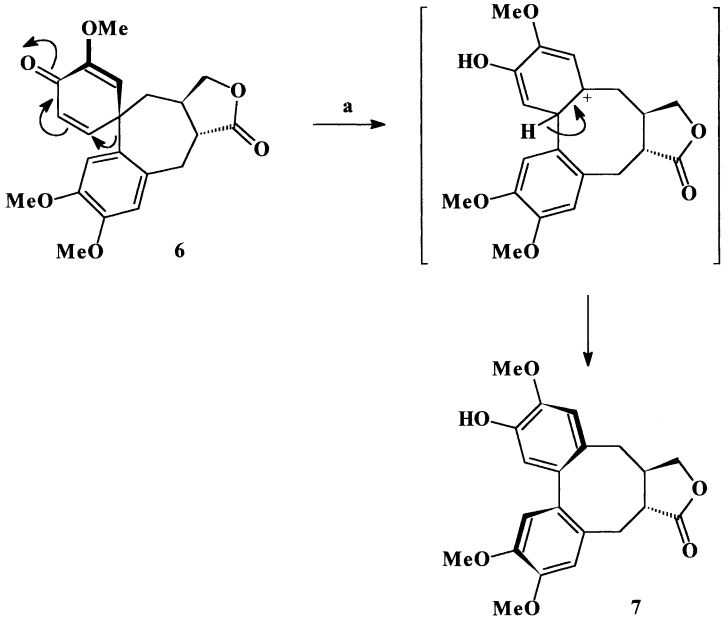


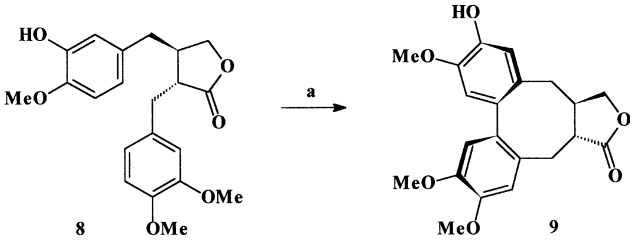
Figure 1. Spirodienone **6**.

reaction was repeated for only 1 h the spirodienone (**6**) was isolated in 46% yield (Scheme 2).

The structure assigned to the spirodienone (**6**) was based upon an analysis of its ^{1}H and ^{13}C NMR spectra and from nOe experiments. Thus, the observed nOe's between H-5 and H-8, H-5 and H-6b, H-6b and H-8, H-14b and H-8, H-7 and H-9b, H-13 and H-1 and H-10 and H-9b are only consistent with the configuration shown in Fig. 1. Other evidence came from the ^{1}H NMR spectrum, which showed two doublets and a double doublet, corresponding to H-2, H-5 and H-1, respectively, and 2 singlets, corresponding to H-10 and H-13, while the ^{13}C NMR spectrum indicated a single diastereoisomer and showed a quarternary, aliphatic carbon (C-5a) at 48.8 ppm. The IR spectrum showed the presence of the carbonyl group, as did the ^{13}C NMR spectrum. The coupling between H-7 and H-8 could not be measured, but it was assumed that the relative configuration of the lactone had been retained and that the lactone ring was *trans*-fused.



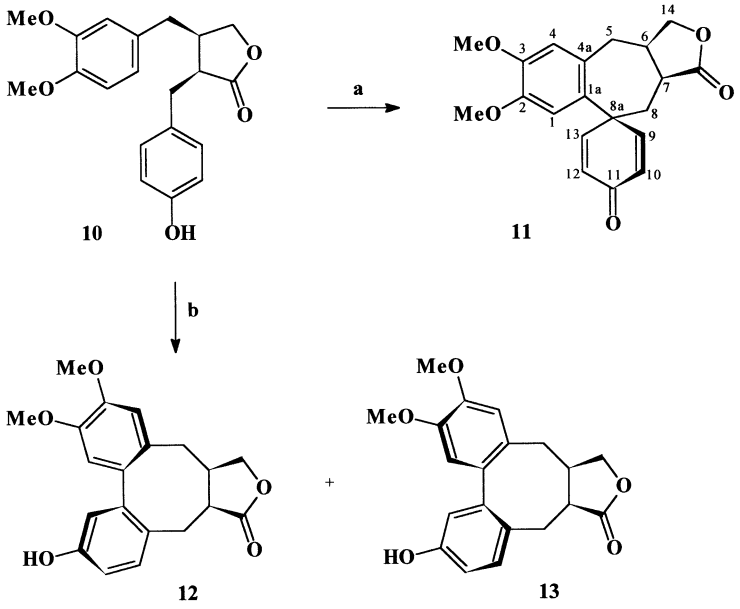
Scheme 3. *Reagents*: a, TFA, TFE (93%).



Scheme 4. *Reagents*: a, PIFA, TFE, 24 h (61%).

concluded that both the isostegane (**12**) and stegane (**13**) isomers had been formed (Scheme 5).

The structure assigned to the spirodienone (**11**) was based upon an analysis of its ^{1}H and ^{13}C NMR spectra, and nOe experiments. As with the *trans*-spirodienone (**2**), models indicated the possible existence of two distinct conformers of (**11**). Thus, the observed nOe's between H-6 and H-9, H-7 and H-9, H-8b and H-13, H-5b and H-9, and H-1 and H-13 are only consistent with the conformation shown in Fig. 2.



Scheme 5. *Reagents*: a, PIFA, TFE, 1 h (48%); b, PIFA, TFE, 24 h (63%, 1:1).

That dibenzocyclooctadiene (**7**) was formed by rearrangement of spirodienone (**6**) was confirmed by treating (**6**) with TFA in TFE, which gave (**7**) (Scheme 3). Evidence for the structure of (**7**) was based upon comparison of the spectral data with that of the product obtained from the reaction of (**5**) with ruthenium tetra(trifluoroacetate).[3]

When the *trans*-2,3-dibenzylbutyrolactone (**8**)[4,8] was treated with PIFA in TFE, and the mixture was stirred under an inert atmosphere for 24 h, compound (**9**) was obtained as the major product in 61% yield (Scheme 4). Evidence for the structure of (**9**) was based upon comparison of the spectral data with that of the product obtained from the reaction of (**8**) with ruthenium tetra(trifluoroacetate).[3]

The *cis*-2,3-dibenzylbutyrolactone (**10**)[8,9] was treated with PIFA, in TFE, and the mixture was stirred under an inert atmosphere. Regular monitoring of the reaction mixture showed that after approximately 1 h the starting material had disappeared and a polar product, which was identified as the spirodienone (**11**) (see below), was formed in 48% yield. When the reaction was repeated under the same conditions, and allowed to stir for 24 h, a mixture of two major products (approx. 1:1, 63% yield) was obtained, whose ^{1}H and ^{13}C NMR data were identical to those of the products obtained from the reaction of (**10**) with ruthenium tetra(trifluoroacetate).[3] It was therefore

Other evidence for the structure of (**11**) came from its ^{1}H NMR spectrum, which showed four double doublets, corresponding to H-9, 10, 12 and 13, and two singlets, corresponding to H-1 and H-4, while the ^{13}C NMR spectrum, indicated a single diastereoisomer and showed a quarternary, aliphatic carbon (C-8a) at 48.3 ppm. The IR spectrum showed the presence of the carbonyl group, as did the ^{13}C NMR spectrum. The coupling between H-6 and H-7 could not be measured. However, the corresponding signals in the ^{13}C NMR spectrum (39.2 and 40.0 ppm) were different from those of the *trans*-spirodienone (**2**) (45.6 and 47.4 ppm). Reaction of (**11**) with TFA gave a mixture of (**12**) and (**13**). A possible explanation for the formation of both isomers of the dibenzocyclooctadiene is shown in

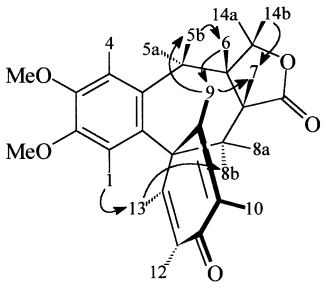
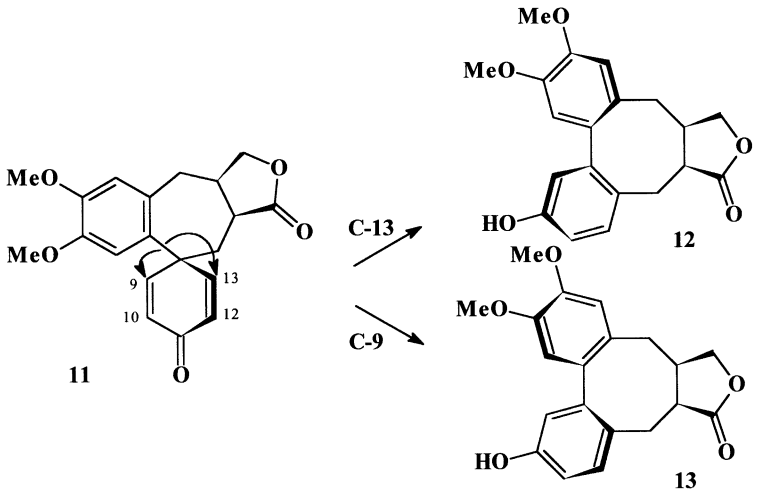


Figure 2. Spirodienone **11**.



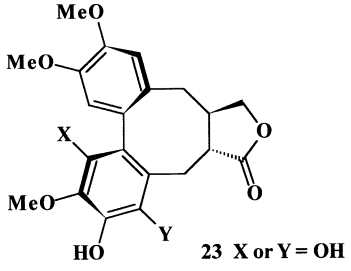
Scheme 6.

Scheme 6. Aryl migration to C-13 would be expected to give the isostegane isomer (**12**), whereas aryl migration to C-9 would give the stegane isomer (**13**).

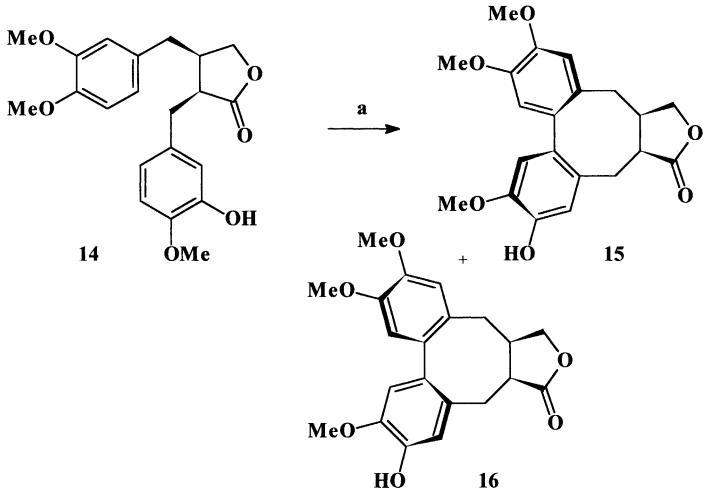
When the *cis*-2,3-dibenzylbutyrolactone (**14**)[8,9] was treated with PIFA in TFE, and the mixture stirred under an inert atmosphere for 24 h, the dibenzocyclooctadienes (**15**) and (**16**) were formed directly, in an approx. 1:1 ratio and in 60% yield (Scheme 7). The products were identified by comparison of their spectral data with those of the products obtained from the reaction of (**14**) with ruthenium tetra(trifluoroacetate).[3]

The *trans*-2,3-dibenzylbutyrolactones (**17**), (**18**) and (**19**)[4,8] were treated with DDQ in TFA and stirred under an inert atmosphere at room temperature for 24 h, yielding the dibenzocyclooctadienes (**20**), (**21**) and (**22**) in 52, 38 and 32% yield, respectively (Scheme 8). Evidence for the structures of the products came from comparison of the spectral data with those of the products obtained from the reaction of (**17**), (**18**) and (**19**) with ruthenium tetra(trifluoroacetate) and PIFA.[3,4]

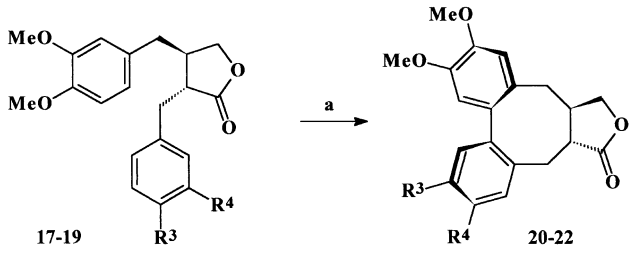
From the reaction of (**18**), a second, polar product was isolated in 14% yield. Analysis of its ^{1}H NMR spectrum showed that only three singlets were present in the aromatic region, each integrating for one proton, while the aliphatic region was quite similar to the corresponding cyclised product (**21**). The presence of the aromatic singlets indicated that this product was the result of a cyclisation reaction, and the fact that there were only three singlets indicated that an additional reaction had occurred, possibly leading to the insertion of a hydroxyl group. Indeed, the molecular ion had molecular formula $C_{21}H_{22}O_7$, and this product was therefore tentatively assigned structure **23**.



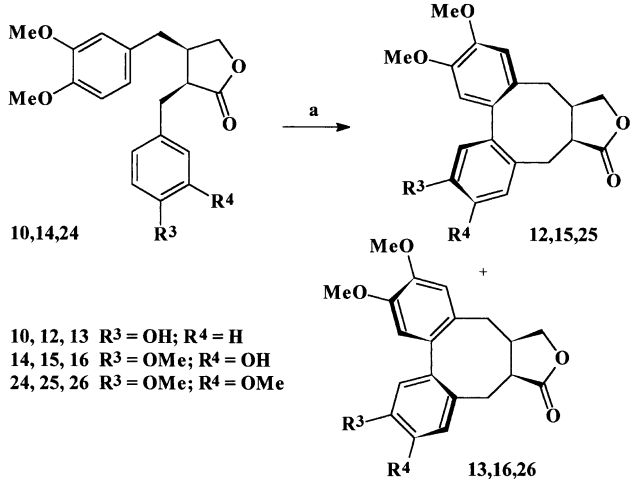
The *cis*-2,3-dibenzylbutyrolactones (**10**), (**14**) and (**24**)[8,9] were treated with DDQ in TFA and stirred under an inert



Scheme 7. *Reagents*: a, PIFA, TFE, 24 h (60%, 1:1).



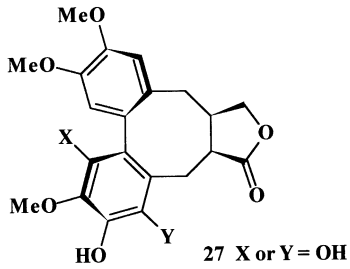
Scheme 8. *Reagents*: a, DDQ, TFA (32–52%).



Scheme 9. *Reagents*: a, DDQ, TFA (37–51%).

atmosphere at room temperature for 24 h. Analysis of the ^{1}H and ^{13}C NMR spectra of the products indicated that, as in the reactions of (**10**), (**14**) and (**24**) with ruthenium tetra(trifluoroacetate),[3] and (**10**) and (**14**) with PIFA, the reactions afforded the corresponding dibenzocyclooctadienes as a mixture of isomers, in a 1:1, 1:1 and 1.5:1 ratio, and in 37, 42 and 51% yield, respectively (Scheme 9).

From the reaction of **14** with DDQ, a third, polar product was isolated in 9% yield. Analysis of the ^{1}H NMR spectrum showed that only three singlets were present in the aromatic region, each integrating for one proton, while the aliphatic region was very similar to that of compound **23**. The molecular ion had molecular formula $C_{21}H_{22}O_7$, and this product was therefore tentatively assumed to be a *cis*-lactone, containing an additional hydroxyl group, and having structure **27**.



3. Conclusion

In conclusion, we have shown that *trans*-2,3-dibenzylbutyrolactones in which a phenolic OH group is located in the 3-benzyl unit undergo oxidative coupling with PIFA to afford either a spirodienone or a dibenzocyclooctadiene derivative, depending upon the position of the OH group. In the case where a spirodienone is the first-formed product, this rearranges with acid or on longer exposure to the reaction medium to afford a dibenzocyclooctadiene. We have also shown that *cis*-2,3-dibenzylbutyrolactones can be cyclised using PIFA to give either a spirodienone or a mixture of two dibenzocyclooctadienes, corresponding to both the stegane and isostegane series. Finally, we have shown that cyclisation of these compounds can also be accomplished using DDQ in TFA, when the eight-membered ring products are again obtained.

4. Experimental

4.1. General procedure

^{1}H and ^{13}CNMR spectra were recorded on a Bruker AC 400 instrument and were run in $CDCl_3$ unless otherwise stated. Mass spectra were recorded on a VG 12-250 low-resolution 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. IR spectra were recorded on a Perkin–Elmer FT 1725X spectrometer and were measured using KBr discs unless otherwise stated. Melting points were recorded on an Electrothermal 9100 apparatus and are uncorrected.

Flash chromatography was performed on silica gel (Fisons Matrex, 35–70μm). Dichloromethane was dried by passing it down an alumina column and distillation from calcium hydride. Ethyl acetate was dried over anhydrous potassium carbonate and distilled from calcium hydride. TFA was dried by refluxing and distillation from P_2O_5.

4.1.1. Preparation of spirodienone (6). To the dibenzylbutyrolactone (**5**)[4,8] (0.116 g, 0.312 mmol) dissolved in dry TFE (5 ml) under an inert atmosphere was added PIFA (0.161 g, 0.374 mmol) in dry TFE (5 ml), and stirring continued for 1 h at rt. After this time the reaction mixture was neutralised by addition of powdered $NaHCO_3$ and concentrated in vacuo. The residue was dissolved in EtOAc, filtered, and the filtrate evaporated. The residue was purified by chromatography on silica using gradient elution with CH_2Cl_2/EtOAc. An 80:20 mixture afforded (**6**) as a gum (0.053 g, 46%); IR (film): 1780 cm^{-1} (γ-lactone), 1670 cm^{-1} (C=O); ^{1}H NMR (400 MHz, $CDCl_3$): 1.84 (1H, dd, *J*=2.8, 13.1 Hz, H-6a), 2.24 (1H, m, H-6b), 2.45 (1H, m, H-7), 2.57 (1H, m, H-9a), 2.73 (1H, m, H-8), 3.02 (1H, dd, *J*=11.6, 15.5 Hz, H-9b), 3.58 (3H, s, OMe), 3.72 (3H, s, OMe), 3.81 (3H, s, OMe), 4.04 (1H, dd, *J*=8.6, 11.2 Hz, H-14a), 4.34 (1H, dd, *J*=8.6, 7.0 Hz, H-14b), 6.07 (1H, d, *J*=2.6 Hz, H-5), 6.42 (1H, d, *J*=10.0 Hz, H-2), 6.66 (1H, s, H-13), 6.75 (1H, s, H-10), 7.24 (1H, dd, *J*=2.6, 10.0 Hz, H-1); ^{13}C NMR (100.6 MHz, $CDCl_3$): 180.6 (C-3), 176.4 (C-15), 156.8 (C-1), 152.6

(C-4), 147.7 (C-12), 146.3 (C-11), 133.0 (C-13a), 130.9 (C-9a), 128.8 (C-5), 115.9 (C-10), 114.8 (C-13), 112.6 (C-2), 71.2 (C-14), 55.9 (2×OMe), 54.8 (OMe), 48.8 (C-5a), 47.4 (C-8), 45.6 (C-7), 35.9 (C-6), 34.1 (C-9); *m/z*: (EI) 370 (M^+, 30%), 281 (20), 207 (38), 165 (22), 151 (32); *m/z* (CI) 388 ($M+NH_4^+$, 100%), 358 (31), 279 (41), 151 (45); [Found: $(M+NH_4)^+$ 388.1763, $C_{21}H_{22}O_6$ requires 388.1760].

4.1.2. Preparation of *trans*-2-hydroxy-6-(hydroxymethyl)-3,10,11-trimethoxydibenzo[1a,4a/8a,12a]cyclooctadiene-7-carboxylic acid lactone (7) using PIFA. The above experimental procedure was employed using as starting material the dibenzylbutyrolactone (**5**)[4,8] (0.078 g, 0.210 mmol), and the reaction mixture was stirred for 24 h. Purification by chromatography on silica and elution with CH_2Cl_2/EtOAc (95:5), followed by crystallisation from EtOAc, afforded (**7**) as a white solid (0.045 g, 58%), mp 232–4°C (lit. 3 232–4°C). ^1H and ^{13}C NMR spectra were identical to those reported for the method employing ruthenium tetra(trifluoroacetate).[3]

4.1.3. Preparation of *trans*-2-hydroxy-6-(hydroxymethyl)-3,10,11-trimethoxydibenzo[1a,4a/8a,12a]cyclooctadiene-7-carboxylic acid lactone (7) from (6). TFA (2 ml) was added to a stirred solution of **6** (0.045 g, 0.122 mmol) in TFE (10 ml). Stirring was continued for 1 h, when the solution was neutralised by addition of saturated aq. $NaHCO_3$ and extracted with $CHCl_3$ (3×20 ml). The combined organic extracts were washed with water (2×20 ml), dried ($MgSO_4$), filtered and evaporated to give **7** (0.042 g, 93%) as a hard white gum. The NMR spectra and other physical characteristics were identical to those of the sample prepared in the above experiment.

4.1.4. Preparation of *trans*-3-hydroxy-6-(hydroxymethyl)-2,10,11-trimethoxydibenzo[1a,4a/8a,12a]cyclooctadiene-7-carboxylic acid lactone (9) using PIFA. The above experimental procedure was employed using as starting material the dibenzylbutyrolactone (**8**)[4,8] (0.114 g, 0.306 mmol), and the reaction mixture was stirred for 24 h. Purification by chromatography on silica and elution with CH_2Cl_2/EtOAc (98:2), followed by crystallisation from EtOAc, afforded (**9**) as a white solid (0.069 g, 61%). ^1H and ^{13}C NMR spectra were identical to those reported for the method employing ruthenium tetra(trifluoroacetate).[3]

4.1.5. Preparation of spirodienone (11). The above experimental procedure was employed using as starting material the dibenzylbutyrolactone (**10**)[8,9] (0.149 g, 0.436 mmol), and the reaction mixture was stirred for 1 h. The residue was purified by chromatography on silica using gradient elution with CH_2Cl_2/EtOAc. An 85:15 mixture afforded (**11**) as white crystals, mp 171–3°C (0.071 g, 48%); IR (film): 1778 cm^{-1} (γ-lactone), 1669 cm^{-1} (C=O); [Found: C, 69.83; H, 5.71. $C_{20}H_{20}O_5$ requires C, 70.58; H, 5.92%]; ^1H NMR (400 MHz, $CDCl_3$): 2.11 (1H, dd, *J*=3.4, 14.6 Hz, H-8a), 2.58 (2H, d, *J*=14.6 Hz, H-5a, H-8b), 2.98 (2H, m, H-6, H-7), 3.33 (1H, dd, *J*=11.9, 14.6 Hz, H-5b), 3.64 (3H, s, OMe), 3.78 (3H, s, OMe), 4.08 (1H, dd, *J*=2.5, 9.5 Hz, H-14a), 4.45 (1H, dd, *J*=6.7, 9.5 Hz, H-14b), 6.20 (1H, dd, *J*=1.8, 9.8 Hz, H-12), 6.25 (1H, dd, *J*=1.8, 9.8 Hz, H-10), 6.39 (1H, s, H-1), 6.52 (1H, s, H-4), 6.92 (1H, dd, *J*=3.0, 9.8 Hz, H-13), 7.04 (1H, dd, *J*=3.0, 9.8 Hz, H-9); ^{13}C NMR (100.6 MHz, $CDCl_3$): 185.4 (C-11), 178.2 (C-15), 155.5 (C-13), 152.9 (C-9), 148.2 (C-2), 148.1 (C-3), 129.9 (C-4a), 127.5 (C-1a), 127.4 (C-12), 125.8 (C-10), 115.0 (C-4), 113.4 (C-1), 72.5 (C-14), 56.0 (2×OMe), 49.2 (C-6), 48.3 (C-8a), 40.0 (C-7), 36.5 (C-5), 34.2 (C-8); *m/z*: (EI) 340 (M^+, 100%), 243 (19), 212 (40), 165 (33), 151 (45); *m/z* (CI) 358 ($M+NH_4^+$, 100%), 341 ($M+H^+$, 8%), 262 (6), 116 (17); [Found: $M+H^+$ 341.1393, $C_{20}H_{20}O_5$ requires 341.1389].

4.1.6. Preparation of *cis*-11-hydroxy-6-(hydroxymethyl)-2,3-dimethoxydibenzo [1a,4a/8a,12a]cyclooctadiene-7-carboxylic acid lactone (12) and *cis*-11-hydroxy-6-(hydroxymethyl)-2,3-dimethoxydibenzo [1a,4a/8a,12a]-cyclooctadiene-7-carboxylic acid lactone (13) using PIFA. The above experimental procedure was employed using as starting material the dibenzylbutyrolactone (**10**)[8,9] (0.118 g, 0.345 mmol), and the reaction mixture was stirred for 24 h. Purification by chromatography on silica and elution with CH_2Cl_2/EtOAc (95:5) afforded a mixture of (**12**) and (**13**), in a 1:1 ratio, as a gum (0.074 g, 63%). ^1H and ^{13}C NMR spectra were identical to those reported for the method employing ruthenium tetra(trifluoroacetate).[3]

4.1.7. Preparation of *cis*-10-hydroxy-6-(hydroxymethyl)-2,3,11-trimethoxydibenzo[1a,4a/8a,12a]cycloocta-diene-7-carboxylic acid lactone (15) and *cis*-10-hydroxy-6-(hydroxymethyl)-2,3,11-trimethoxydibenzo [1a,4a/8a,12a]cyclooctadiene-7-carboxylic acid lactone (16) using PIFA. The above experimental procedure was employed using as starting material the dibenzylbutyrolactone (**14**)[8,9] (0.116 g, 0.312 mmol), and the reaction mixture was stirred for 24 h. Purification by chromatography on silica and elution with CH_2Cl_2/EtOAc (95:5) afforded a mixture of (**15**) and (**16**), in a 1:1 ratio, as a gum (0.069 g, 60%). ^1H and ^{13}C NMR spectra were identical to those reported for the method employing ruthenium tetra(trifluoroacetate).[3]

4.1.8. Preparation of *trans*-6-(hydroxymethyl)-2,3,10,11-tetramethoxydibenzo[1a,4a/8a,12a]cyclooctadiene-7-carboxylic acid lactone (20) using DDQ. To a mixture of the dibenzylbutyrolactone (**17**)[8] (0.080 g, 0.207 mmol) and DDQ (0.094 g, 0.414 mmol) was added TFA (8 ml) and the mixture was stirred at rt for 24 h. The dark purple reaction mixture was then poured onto crushed ice and extracted with toluene (3×40 ml). The combined organic extracts were washed with aq. $NaHCO_3$ (2×40 ml), water (2×30 ml), aq. NaOH (2×30 ml), aq.NaCl (2×30 ml), dried ($MgSO_4$), filtered and evaporated in vacuo to afford a reddish brown foam. Purification by chromatography on silica and elution with CH_2Cl_2/EtOAc (90:10) afforded (**20**) as a white solid (0.041 g, 52%), mp 208–210°C (lit. 10 212–3°C). ^1H and ^{13}C NMR spectra were identical to those reported for the method employing ruthenium tetra-(trifluoroacetate).[3]

4.1.9. Preparation of *trans*-10-hydroxy-6-(hydroxymethyl)-2,3,11-trimethoxydibenzo[1a,4a/8a,12a]cyclooctadiene-7-carboxylic acid lactone (21) and compound (23) using DDQ. The above experimental procedure was employed using as starting material the dibenzylbutyrolactone

(**18**)[4,8] (0.130 g, 0.349 mmol). Purification by chromatography on silica and elution with CH_2Cl_2/EtOAc (95:5) afforded (**21**) as a white solid (0.049 g, 38%), mp 194–5°C (lit. 4 190–2°C). ^1H and ^{13}C NMR spectra were identical to those reported for the method employing ruthenium tetra(trifluoroacetate) and PIFA.[3,4] Further elution with CH_2Cl_2/EtOac (95:5) afforded **23** as an orange foam (0.018 g, 14%). ^1H NMR (400 MHz, $CDCl_3$): 1.93 (1H, t, J=12.6 Hz), 2.58 (1H, m), 2.73 (2H, d, J=3.6 Hz), 2.88 (1H, m), 3.03 (1H, dd, J=12.1, 2.4 Hz), 3.79 (3H, s, OMe), 3.81 (3H, s, OMe), 3.83 (3H, s, OMe), 3.97 (1H, dd, J=8.5, 11.7 Hz), 4.38 (1H, d, J=8.5 Hz), 6.01 (1H, s), 6.49 (1H, s), 6.62 (1H, s); ^{13}C NMR (100.6 MHz, $CDCl_3$): 181.9, 177.9, 158.5, 149.8, 147.6, 141.4, 141.3, 128.4, 124.3, 113.8, 112.8, 107.7, 68.7, 56.4, 56.1, 55.9, 53.4, 39.8, 36.5, 30.4, 25.1; *m/z*: (EI) 387 (21), 386 (100), 384 (18), 371 (8), 165 (7), 108 (31%); *m/z* (CI) 404 (22), 387 (26), 230 (21), 213 (24), 170 (25), 116 (46%); [Found: $M+H^+$ 387.1443, $C_{21}H_{22}O_7$ requires 387.1444].

4.1.10. Preparation of *trans*-11-hydroxy-6-(hydroxymethyl)-2,3-dimethoxydibenzo[1a,4a/8a,12a]cyclooctadiene-7-carboxylic acid lactone (22) using DDQ. The above experimental procedure was employed using as starting material the dibenzylbutyrolactone (**19**)[4,8] (0.157 g, 0.459 mmol). Purification by chromatography on silica and elution with CH_2Cl_2/EtOAc (95:5) afforded (**22**) as a white solid (0.050 g, 32%), mp 213–5°C (lit. 4 210–5°C). ^1H and ^{13}C NMR spectra were identical to those reported for the method employing ruthenium tetra(trifluoroacetate) and PIFA.[3,4]

4.1.11. Preparation of *cis*-11-hydroxy-6-(hydroxymethyl)-2,3-dimethoxydibenzo[1a,4a/8a,12a]cyclooctadiene-7-carboxylic acid lactone (12) and *cis*-11-hydroxy-6-(hydroxymethyl)-2,3-dimethoxydibenzo [1a,4a/8a,12a]-cyclooctadiene-7-carboxylic acid lactone (13) using DDQ. The above experimental procedure was employed using as starting material the dibenzylbutyrolactone (**10**)[8,9] (0.193 g, 0.564 mmol). Purification by chromatography on silica and elution with CH_2Cl_2/EtOAc (90:10) afforded a mixture of (**12**) and (**13**), in an approx. 1:1 ratio, as a gum (0.071 g, 37%). ^1H and ^{13}C NMR spectra were identical to those reported for the method employing ruthenium tetra-(trifluoroacetate).[3]

4.1.12. Preparation of *cis*-10-hydroxy-6-(hydroxymethyl)-2,3,11-trimethoxydibenzo[1a,4a/8a,12a]cyclooctadiene-7-carboxylic acid lactone (15) and *cis*-10-hydroxy-6-(hydroxymethyl)-2,3,11-trimethoxydibenzo [1a,4a/8a,12a]cyclooctadiene-7-carboxylic acid lactone (16) using DDQ. The above experimental procedure was employed using as starting material the dibenzylbutyrolactone (**14**)[8,9] (0.160 g, 0.430 mmol). Purification by chromatography on silica and elution with CH_2Cl_2/EtOAc (90:10) afforded a mixture of (**15**) and (**16**), in an approx. 1:1 ratio, as a gum (0.067 g, 42%). ^1H and ^{13}C NMR spectra were identical to those reported for the method employing ruthenium tetra(trifluoroacetate).[3] Further elution with CH_2Cl_2/EtOAc (90:10) afforded a third minor product 27, as an orange foam (0.014 g, 9%). ^1H NMR (400 MHz, $CDCl_3$): 1.93 (1H, t, J=12.7 Hz), 2.58 (1H, m), 2.74 (2H, d, J=3.7 Hz), 2.89 (1H, m), 3.02 (1H, dd, J=12.1, 2.4 Hz), 3.80 (3H, s, OMe), 3.81 (3H, s, OMe), 3.84 (3H, s, OMe), 3.97 (1H, dd, J=8.5, 11.7 Hz), 4.38 (1H, d, J=8.5 Hz), 6.01 (1H, s), 6.49 (1H, s), 6.62 (1H, s); ^{13}C NMR (100.6 MHz, $CDCl_3$): 181.4, 177.9, 158.5, 149.8, 147.6, 141.4, 141.2, 128.2, 124.3, 113.8, 112.6, 107.7, 68.7, 60.4, 56.5, 56.1, 56.0, 39.9, 36.5, 30.4, 25.1; *m/z*: (EI) 387 (24), 386 (100), 384 (18), 371 (7), 165 (8), 108 (28%); *m/z* (CI) 404 (82), 387 (93), 279 (33), 214 (35), 194 (47), 152 (47%); [Found: $M+H^+$ 387.1449, $C_{21}H_{22}O_7$ requires 387.1444].

4.1.13. Preparation of *cis*-6-(hydroxymethyl)-2,3,10,11-tetramethoxydibenzo[1a,4a/8a,12a]cyclooctadiene-7-carboxylic acid lactone (25) and *cis*-6-(hydroxymethyl)-2,3,10,11-tetramethoxydibenzo[1a,4a/8a,12a] cyclooctadiene-7-carboxylic acid lactone (26) using DDQ. The above experimental procedure was employed using as starting material the dibenzylbutyrolactone (**24**)[8,9] (0.160 g, 0.415 mmol). Purification by chromatography on silica and elution with CH_2Cl_2/EtOAc (90:10) afforded a mixture of (**25**) and (**26**), in an approx. 1.5:1 ratio, as a gum (0.081 g, 51%). ^1H and ^{13}C NMR spectra were identical to those reported for the method employing ruthenium tetra(trifluoroacetate).[3]

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