Pergamon

Tetrahedron 57 (2001) 7755–7763

TETRAHEDRON

Dimerisations of cinnamates using acidic and acidic/oxidative conditions

Andrew Pelter,[a,*] Robert S. Ward,[a] Reveru Venkateswarlu,[b] Chakicherla Kamakshi,[b] Syed G. A. Moinuddin,[b] Pithani V. Subhash,[b] Michael B. Hursthouse,[c] Simon J. Coles[c] and Mark E. Light[c]

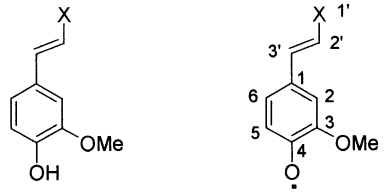
[a]*Department of Chemistry, University of Wales Swansea, Singleton Park, Swansea SA2 8PP, UK*
[b]*Department of Organic Chemistry, Andhra University, Visakhapatnam 530 003, India*
[c]*EPSRC X-ray Crystallography Service, Department of Chemistry, University of Southampton, Southampton SO17 1BJ, UK*

Received 20 April 2001; revised 5 July 2001; accepted 12 July 2001

Abstract—It is confirmed that the dimerisation of methyl dialkoxycinnamates in acidic conditions yields trisubstituted indanes. When the reactions are carried out for 1.5 h/0°C in acidic conditions in the presence of DDQ then a variety of lignan types result, two of which represent new classes of lignans. © 2001 Elsevier Science Ltd. All rights reserved.

1. Introduction

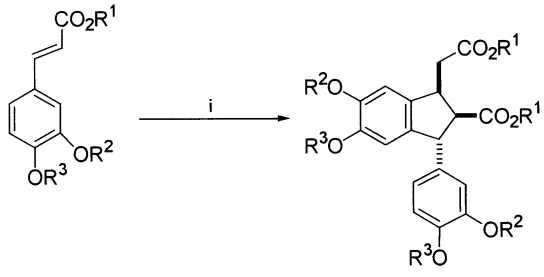
Products derived from the one-electron oxidation of C_6–C_3 phenols account for nearly 30% of the organic carbon in circulation in the biosphere.[1] The bulk materials are polymers such as lignin,[2] suberin[3] and algal cell walls.[4] An important sub-class consists of lignans, which are phenylpropenoid dimers[5] which are homochiral, possibly due to dirigent enzymes,[5] in contrast to the bulk polymers. Many lignans are bioactive and their presence, perhaps as chemical defence compounds[6,7] is ubiquitous in the plant kingdom.[1] The oxidative polymerisation involves units such as **1** and **2**[6–8] which on one-electron oxidation give rise to radicals **3** and **4** with radical activity at O-4, C-1, C3, C-5 and C-2′.



Thus many combinations can lead to dimers by reactions at any of the active positions of the neutral radicals both with themselves and their precursors **1** and **2**.[6,8] In turn there are many secondary reactions that complete the process and from this arises the wide structural diversity of lignans.[6–8]

In view of the bioactivity of many lignans[6–10] there is wide interest in their synthesis.[6,11,12] However biomimetic in vitro reactions using one-electron oxidation of phenols gives radicals which couple with little selectivity without the imposition of a variety of substituents and conditions.[1,6,12]

Dimerisation of a variety of methyl cinnamates can be induced by a Brönsted acid and the reactions proceed in each case to give one main product in good yields.[13,14]



Scheme 1. i TFA or $BF_3{\cdot}Et_2O$.

Keywords: cinnamates; coupling reactions; acidic-oxidative conditions; novel lignans.

* Corresponding author. Tel.: +44-1792-295258; fax: +44-1792-295747; e-mail: a.pelter@swansea.ac.uk

PII: S0040-4020(01)00742-6

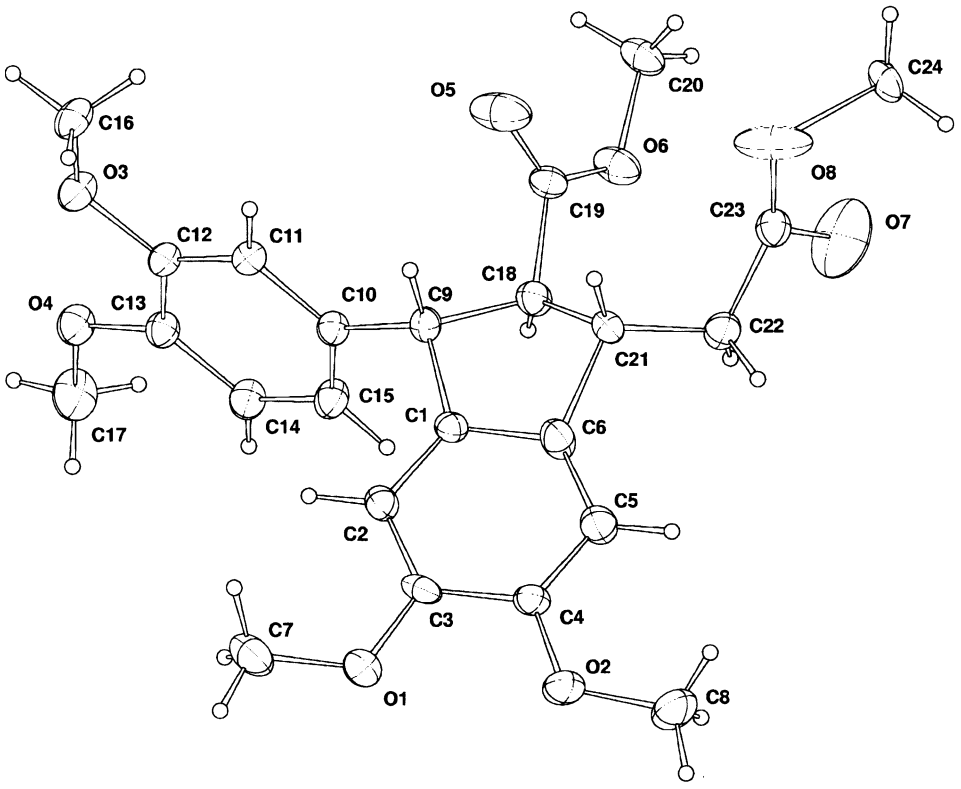


Figure 1. X-Ray structure for **7**.

This results from the production of cationic intermediates that cannot readily react with themselves but only with neutral molecules thus greatly reducing the variety of possible combinations.

To further our studies on the synthesis[15] and transformations of lignans[16] we decided to look further into the dimerisations of simple C_6–C_3 precursors.

2. Dimerisations of methyl 3,4-dimethoxycinnamate 5 and methyl 3,4-methylenedioxycinnamate 6 in acidic conditions

When **5** and **6** were subjected to trifluoroacetic acid (TFA) treatment the products were characterised as trisubstituted indanes,[14] in contradiction to an earlier report[13] which had assigned aryltetralin structures (Scheme 1).

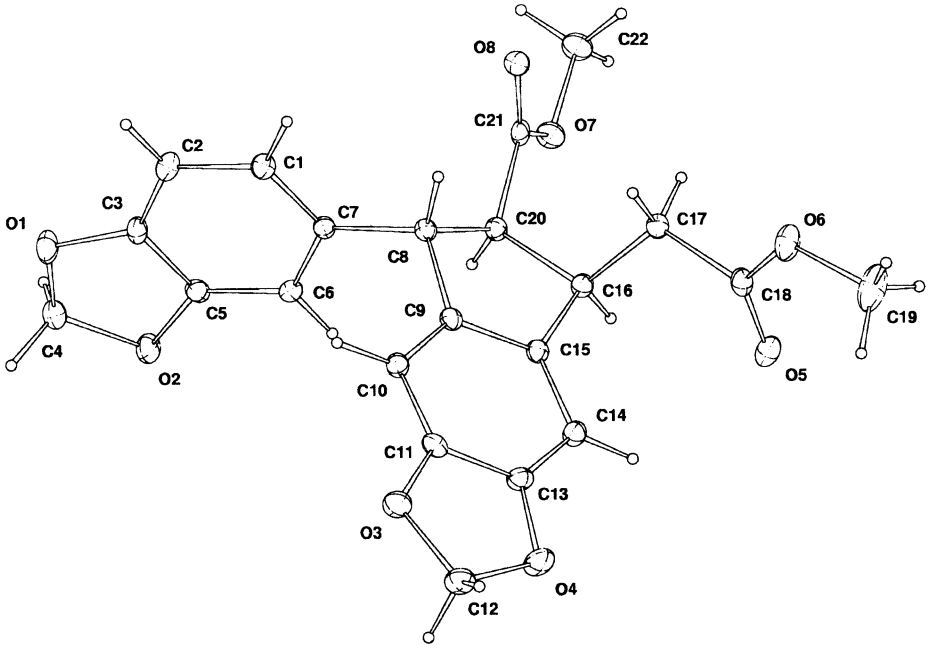
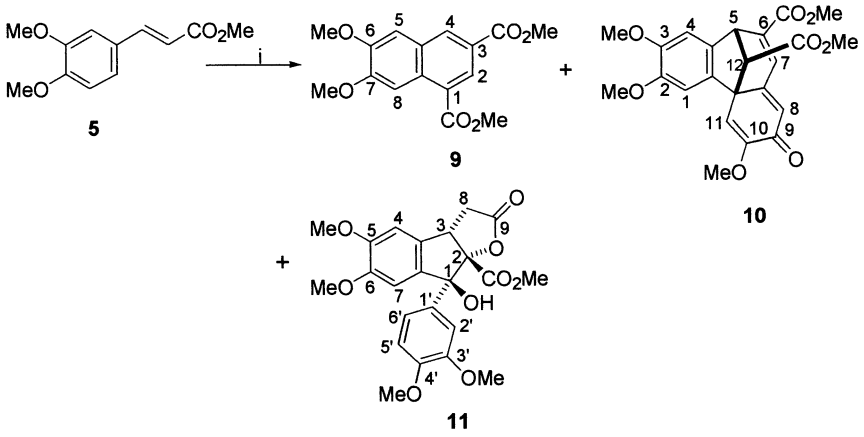


Figure 2. X-Ray structure for **8**.



Scheme 2. i, DDQ, $Et_2O{\cdot}BF_3$, TFA, 1.5h, 0°C.

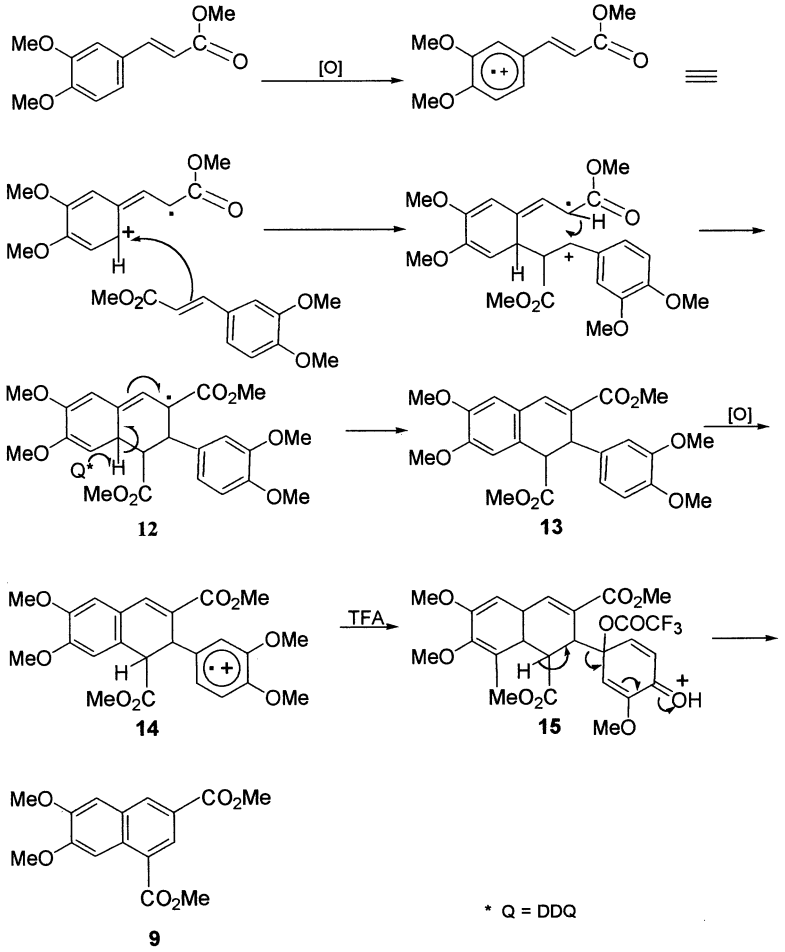
In our hands whether using TFA or a Lewis acid ($Et_2O{\cdot}BF_3$) the only isolated products from **5** and **6** were **7** and **8** in high yields. Our NMR data corresponded closely to those previously reported[14] and X-ray analyses (Figs. 1 and 2) confirm the indane structures **7** and **8**.

3. Dimerisations of 5 and 6 in acidic/oxidative conditions

We wondered what would be the results of a combination of acidic and oxidative conditions upon lignan precursors and again chose **5** and **6** as our initial substrates.

3.1. Dimerisations of methyl 3,4-dimethoxycinnamate 5

Under very mild conditions (0°C/1.5 h) from the combined action of $Et_2O{\cdot}BF_3$, TFA and DDQ on **5** we were able to isolate several products to which we have assigned structures **9** (10%), **10** (35%) and **11** (6%) (Scheme 2).



Scheme 3.

Compound **9**, $C_{16}H_{12}O_6$ was obtained as colourless crystals mp 134–136°C. Most surprisingly, given the gentle conditions used, *one aromatic group has been lost in the dimerisation*. In the ^{1}H NMR, the aromatic protons showed as two *m*-coupled signals and two singlets. One of the singlets at δ 7.2 was well removed from the other three at δ 8.7–8.5 and is assigned to H-5 which is not α or γ to a carbomethoxy group. In the ^{13}C NMR there were four methoxy groups, two at 56.0, 55.9 (Ar–O*C*H$_3$) and two at 52.3 and 52.1 (CO$_2$*C*H$_3$). The other ^{13}C NMR data (see Section 5) were fully consistent with structure **9**.

Naphthalene **9**, *on first inspection, does not appear to be a lignan*. Yet it readily arises in mild conditions from lignan precursors and, despite its deceptively simple structure, it is a new class of lignan from which an aromatic group has been removed, probably as a quinol. A possible abbreviated pathway for its production is shown in Scheme 3. This envisages initial oxidation of **5** to give a cation radical which reacts with a neutral molecule of **5** to give **12**. Further oxidation yields the dihydronaphthalene **13** which in turn is oxidised to cation radical **14** which reacts with TFA to give **15**. Dienone **15** then undergoes acid induced elimination of an aryl group to yield **9**.

The major product, $C_{23}H_{22}O_8$, had lost one carbon atom overall but retained the carbon atoms of both benzene rings. The IR spectrum showed that no hydroxyl groups were present whilst the UV spectrum with λ_{max} 250, 280, 319 nm indicated the presence of a dienone system. In the ^{1}H NMR there were five methoxyl signals at δ 3.60, 3.77, 3.85, 3.86 and 3.87 confirming the loss of one methoxyl group during the dimerisation. There were five singlets at 6.03, 6.30, 6.52, 6.90 and 6.92 ppm as well as two methine protons showing at 4.62 d and 3.78 d. There were two particularly striking features of the ^{13}C NMR spectrum. The first was a signal at 181.2, assigned as the carbonyl group of a cyclohexadienone. The second was the presence of a quarternary aliphatic signal at δ 53.1 which we have assigned to a fully substituted C-1 of a cyclohexa-2,5-dien-4-one system. Additionally two methine carbon atoms gave signals at δ 43.9 and 65.1. Two sp^2 CH groups show at δ 131.6 and 128.0 and are assigned as the β-carbon atoms of two $\alpha\beta$-unsaturated carbonyl groups. Two signals due to carbomethoxy groups showed at 168.9 and 165.4. This evidence together with mechanistic considerations led us to propose structure **10** for this compound and that assignment was fully confirmed by X-ray analysis (Fig. 3).

Compound **10** is, to our knowledge, the first of a completely new class of unrearranged lignan the presence of which from natural sources can now be explored.

The large increase in complexity in passing from **5** to **10** is striking and requires a complex multistage pathway. A possible process is shown in Scheme 4 which requires both an acid and an oxidant. It uses the same intermediate **13** as in Scheme 3. In this case however the intermediate cation-radical **14**, produced on oxidation, suffers intramolecular attack leading on to **10**.

A further product $C_{23}H_{24}O_9$ (6%) had, like **10**, lost a methyl group and in the ^{1}H NMR there were indeed only five methoxy group signals. The aliphatic region was very simple showing well separated signals for a CH_2–CH grouping at 4.64 (d, J=2.1 Hz), 3.10 (dd, J_1=2.1 Hz, J_2=14 Hz) and 2.78 (d, J=14 Hz). The extreme clarity of this aliphatic system suggested that it was incorporated into

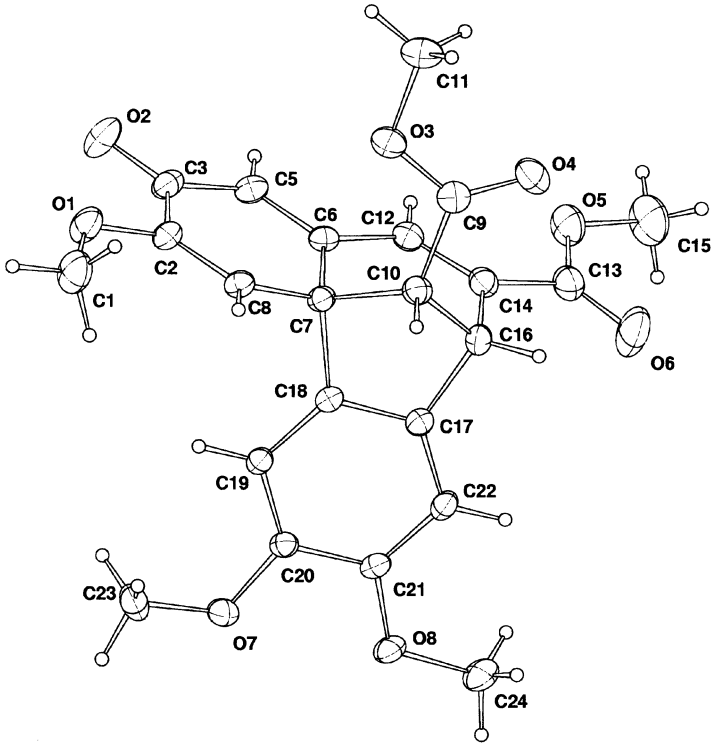
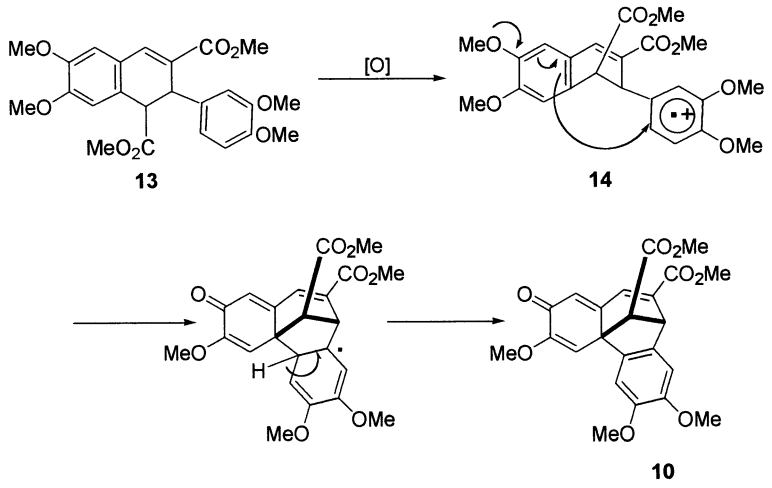


Figure 3. X-Ray structure for **10**.



Scheme 4.

a rigid ring. In the IR spectrum there were two carbonyl stretching frequencies at 1783 and 1740 cm^{-1} indicating the presence of γ-lactone and ester groupings. In the ^{13}C NMR two signals at 173.7 and 169.2 confirmed that there were two carbonyl groups present and showed that a dienone group was not present. The methoxyl signals were at δ 56.2, 55.9, 55.8, 55.6 and 52.9, and this suggests that all four $ArOCH_3$ groups are present but that only one carbomethoxyl group is left. Unlike **10** there are two quarternary sp^3 atoms that give signals at δ 87.1 and 96.2 suggesting that one oxygen atom is attached to each of the quarternary aliphatic carbon atoms. The CH_2 group gives a signal at 35.0 with the associated CH group at 46.1. There are 10 quarternary sp^2 atoms (including both C=O groups) and five sp^2 CH atoms present. The NMR spectra of **11** had much in common with previously prepared indanes (see Section 2).

An X-ray structure of this compound (Fig. 4) showed that it had structure **11** and was thus an oxidised indane belonging to the same series as **7** and **8**. The ^1H NMR was a little anomalous as the signals for H-12 and H-13 coincided and so gave a deceptive simplicity to the aromatic region. Happily its analogue **18** (vide infra) did not suffer such a coincidence of chemical shifts though similar in other fashions.

3.2. Dimerisations of methyl 3,4-methylenedioxycinnamate, 6

The results of the dimerisation of cinnamate **6** are summarised in Scheme 5. As expected there are similarities but also deviations from the dimerisation of **5**.

The first product (7%), mp 154–156°C, had the formula

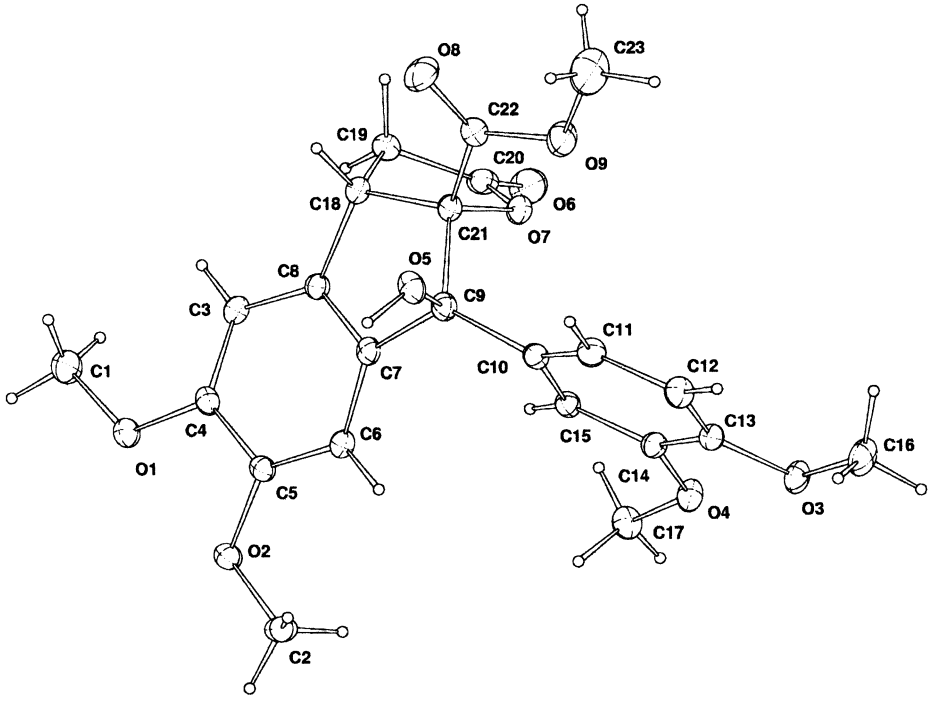
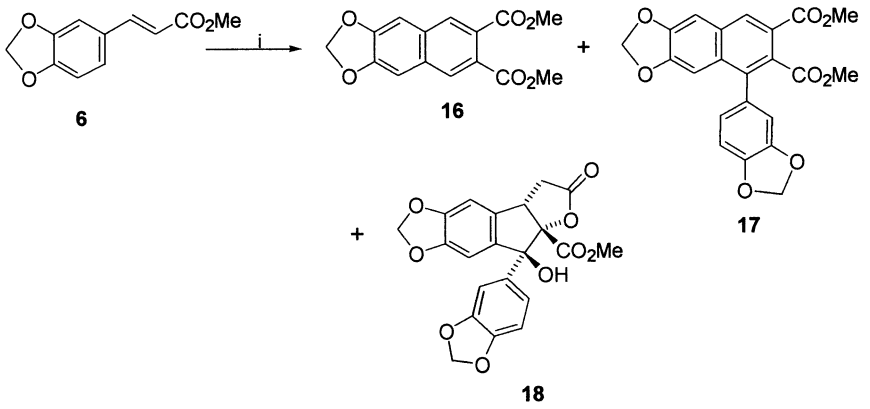


Figure 4. X-Ray structure for **11**.



Scheme 5. i, DDQ, TFA, $BF_3{\cdot}OEt_2$, 1.5h, 0°C.

$C_{15}H_{12}O_6$, and so, as in the case of **9**, an aromatic group had been lost in the dimerisation. However the ^{1}H NMR of this product was extremely simple as compared with **9** and consisted of four singlets at δ 8.05 (2H), 7.17 (2H), 6.11 (2H, OCH_2O) and 3.94 (6H, $2\times OCH_3$). The molecule therefore has a high degree of symmetry and is assigned structure **16**. The ^{13}C NMR was in complete accord with this having $2\times sp^2$ CH at 128.8 and 104.5 as well as peaks at 101.8 (OCH_2O) and 168.3 (CO_2Me) and 36.6 (OCH_3).

This product, like **9**, is a profoundly modified lignan that has lost an aromatic group as compared with the sum of the two precursor cinnamates. The different orientation of the carbomethoxy groups in **16** as compared with **9** must be due to a different orientation in the presumed dihydronaphthalene precursor (see Scheme 3) and thus to the two methylenedioxycinnamate units aligning themselves in a different fashion from the two dimethoxycinnamate units when forming the initial linkage.

Another product (6%), $C_{22}H_{16}O_8$, was isolated as crystals, mp 188–190°C. It had retained all the functionality of the precursor **6** and its physical characteristics indicated that it was a 4-arylnaphthalene lignan.[1] In the ^{1}H NMR there was only one low field proton at δ 8.39 as a singlet. By contrast there are three such signals in **9** and two in **16** due to the proximity of carbomethoxy groups. To this compound we therefore assign structure **17** rather than **19**.

A third product $C_{21}H_{16}O_9$ (6%) had, like **11**, lost a methyl group as compared with the sum of two units of **6**. The similarity of the new compound to **11** was emphasised in the IR spectrum as the new product was also a γ-lactone containing an ester group with two absorptions at 1783 and 1740 cm^{-1}. Leaving aside the methylenedioxy and methoxyl groups, the ^{13}C NMR spectra of **11** and the new compound were so similar (see Section 5) as to leave no doubt as to their close relationship. The same holds for the aliphatic region of the ^{1}H NMR spectra but the new compound exhibited a normal set of signals for the pendant aryl group with peaks at 6.67 d (J=1.2 Hz), 6.60 d (J=8.0 Hz) and 6.59 dd (J=1.2, 8.0 Hz). It was therefore

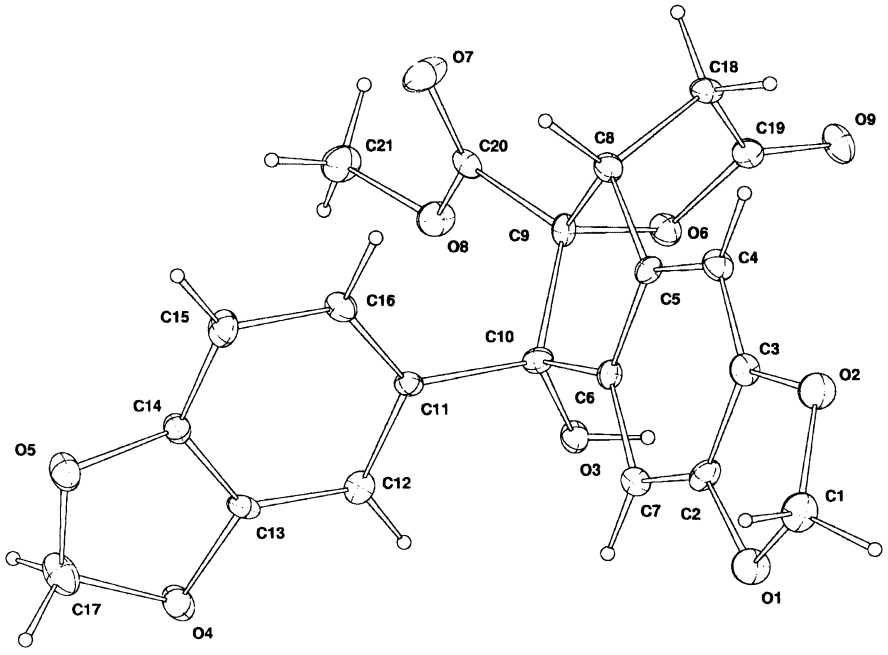
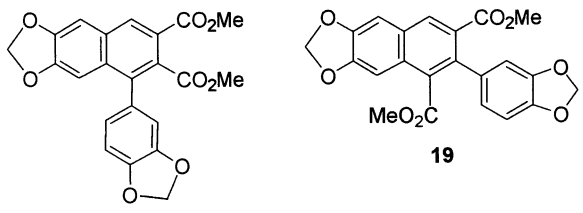
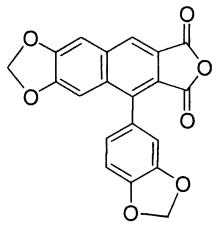


Figure 5. X-Ray structure for **18**.





no surprise that X-ray analysis (Fig. 5) gave structure **18** for this product.

It is of interest that Stevenson[17] found that reaction of 3,4-methylenedioxydioxypropiolic acid with acetic anhydride yielded the 4-arylnaphthalene **20**. In that case no further oxidation was required due to the precursor being an alkyne rather than an alkene. Having the oxidant in situ however leads to a much greater variety of products.

4. Conclusions

Treatment of methyl dialkoxycinnamates with a combination of Brönsted acid, Lewis acid and an oxidant yielded three classes of lignans, two of them previously unknown. The cooperative action of each component of the reagent mixture was vital for the final results which offer leads into the search for new lignans of natural origin, as well as making the products available for biological evaluation.

5. Experimental

5.1. General

^{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. Infrared 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 it down on alumina column followed by distillation from 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 **7**, **8**, **10**, **11** and **18** 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(MoKα)=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,[18] DENZO[19] and maXus[20] and an empirical absorption correction was applied using SORTAV.[21,22]

The structures were solved via direct methods[23] and refined by full matrix least squares[23] on F^2. Non-hydrogen atoms were refined anisotropically and hydrogen atoms were treated using a riding model. In the case of 013 disorder over two equally occupied conformations was modelled for the CH_2COOCH_3 group branching from the five membered ring. 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 161481 (1), 161482 (2), 161483 (3), 165947 (4), 165948 (5). 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).

5.2. The reaction of methyl 3,4-dimethoxycinnamate 5 with DDQ in TFA and $Et_2O{\cdot}BF_3$

To a solution of DDQ (2.0 g, 9.0 mmol) in TFA (10 ml) was added methyl 3,4-dimethoxycinnamate **5**. (1.0 g, 4.5 mmol) and the mixture was stirred for 0.5 h at 0°C. Freshly distilled $Et_2O{\cdot}BF_3$ (0.18 g, 1.32 mmol) was then added and the solution was stirred for 1.5 h at 0°C, when the colour slowly changed from greenish-yellow to bluish-pink. The reaction mixture was then poured onto crushed ice and extracted with EtOAc (3×50 ml). The combined organic extracts were washed successively with sodium metabisulphite (3×30 ml), $NaHCO_3$ (3×30 ml) and brine (3×30 ml), then dried ($MgSO_4$). Removal of the solvent under reduced pressure gave a reddish-brown residue (1.0 g) which on column chromatography on silica gel (hexane–EtOAc 3:2) yielded three products.

5.2.1. Compound 9. Yield: 70 mg, 10% crystallised from methanol as colourless crystals, mp 134–136°C. δ_H (400 MHz, $CDCl_3$): 8.66 (1H, d, J=1.6 Hz, H-2), 8.55 (1H, br.s, H-4), 8.51 (1H, s, H-8), 7.19 (1H, s, H-5), 4.07 (3H, s), 4.01 (3H, s), 4.00 (3H, s), 3.97 (3H, s). δ_C (100.6 MHz, $CDCl_3$): 167.6 (CO_2Me), 166.6 (CO_2Me), 152.8 (C-6), 149.9 (C-7), 133.9 (C-2), 130.4 (C-1), 129.4 (C-3), 128.5 (C-4), 124.7 (C-4a), 124.4 (C-8a), 107.7 (C-5), 104.8 (C-8), 56.0 (OMe), 55.8 (OMe), 52.2 (CO_2Me), 52.1 (CO_2Me). m/z (e.i.) 304 (M^+, 100%), 273 (65), 245 (13), 231 (17), 230 (22), 215 (12). m/z (c.i.) 322 ($M+NH_4^+$, 100%), 305 ($M+H^+$, 8%), 292 (7), 264 (8). Found: $M+NH_4^+$, 322.1285. $C_{16}H_{16}O_6+NH_4^+$ requires 322.1291.

5.2.2. Compound 10. Yield: 250 mg, 27% crystallised from methanol as yellow crystals, mp 210°C. ν_{max} (Nujol) 1750 (CO_2Me), 1700 (CO), 1610 (arom.) cm^{-1}. λ_{max} ($CHCl_3$) (log ϵ) 250 (3.5), 280 (3.5), 319 (4.3) nm. δ_H (400 MHz, $CDCl_3$): 6.92 (1H, s, H-1), 6.90 (1H, s, H-4), 6.52 (1H, s, H-7), 6.30 (1H, s, H-8), 6.03 (1H, s, H-11), 4.62 (1H, d,

J=4.1 Hz, H-12), 3.78 (1H, d, J=4.1 Hz, H-5), 3.87 (3H, s, OMe), 3.86 (3H, s, OMe), 3.85 (3H, s, OMe), 3.77 (3H, s, CO_2Me), 3.60 (3H, s, CO_2Me). δ_C (100.6 MHz, $CDCl_3$): 181.2 (C-9), 168.9 (CO_2Me), 165.4 (CO_2Me), 153.8 (C-10), 151.4 (C-3), 149.3 (C-7a), 148.6 (C-2), 139.2 (C-6), 136.5 (C-1a), 134.8 (C-4a), 131.6 (C-7), 128.0 (C-11), 117.1 (C-8), 106.9 (C-1), 106.6 (C-4), 65.1 (C-5), 56.3 (OMe), 56.2 (OMe), 55.5 (OMe), 53.1 (C-11a), 52.5 (CO_2Me), 52.1 (CO_2Me), 43.9 (C-12). m/z (e.i.) 426 (M^+, 100%), 398 (10), 395 (10), 367 (25), 339 (20), 335 (28), 307 (35). m/z (c.i.) 427 ($M+H^+$, 75%), 176 (23). Found: $M+H^+$, 427.1395. $C_{23}H_{23}O_8$ requires 427.1393.

5.2.3. Compound 11. Yield: 60 mg, 6% crystallised from EtOAc–benzene as colourless crystals, mp 238–240°C. δ_H (400 MHz, $CDCl_3$): 6.93 (1H, s), 6.86 (2H, s), 6.78 (1H, s) (H-2′, H-4, H-6′, H-7), 6.54 (1H, s, H-5′), 4.64 (1H, d, J=8.8 Hz, H-3), 3.93 (3H, s), 3.90 (3H, s), 3.83 (3H, s), 3.82 (3H, s) (4×ArOMe), 3.75 (3H, s, CO_2Me), 3.26 (1H, s, OH), 3.10 (1H, dd, J=9.0, 17.8 Hz, H-8a), 2.78 (1H, dd, J=1.4, 17.8 Hz, H-8b). δ_C (100.6 MHz, $CDCl_3$): 173.7 (C-9), 169.2 (CO_2Me), 151.6, 150.4 (C-5, C-6), 148.9, 148.0 (C-3′, C-4′), 136.1 (C-1′), 134.0 (C-3a), 130.8 (C-7a), 121.1 (C-6′), 111.7 (C-2′), 110.1 (C-5′), 107.5, 106.5 (C-4, C-7), 96.2 (C-1), 87.1 (C-2), 56.2, 55.9, 55.8, 55.6 (4×OCH_3), 52.9 (CO_2CH_3), 46.1 (C-3), 35.0 (C-8). ν_{max} (KBr) 1784, 1784 cm^1. m/z (e.i.) 444 (M^+, 63%), 398 (15), 385 (22), 353 (40), 327 (35), 314 (42), 165 (100). m/z (c.i.) 462 ($M+NH_4^+$, 64%), 427 (45), 385 (17), 383 (16), 156 (100). Found: M^+, 444.1417. $C_{23}H_{24}O_9$ requires 444.1420.

5.3. Reaction of methyl 3,4-methylenedioxycinnamate 6 with DDQ in TFA and $Et_2O{\cdot}BF_3$

To a solution of DDQ (2.6 g, 11.6 mmol) in TFA (12 ml) was added methyl 3,4-methylenedioxycinnamate **6** (1.2 g, 5.8 mmol) and the mixture stirred for 0.5 h at 0°C. Freshly distilled $Et_2O{\cdot}BF_3$ (0.2 g, 1.9 mmol) was then added and the solution was stirred for 1.5 h at 0°C, when the colour slowly changed from greenish-yellow to blue. The reaction mixture was then poured onto crushed ice and extracted with EtOAc (3×50 ml). The combined organic extracts were washed successively with sodium metabisulphite (3×30 ml), $NaHCO_3$ (3×30 ml) and brine (3×30 ml), then dried ($MgSO_4$). Removal of the solvent under reduced pressure gave a reddish-brown residue (1.2 g) which on column chromatography on silica gel (hexane–EtOAc 7:3) yielded three products.

5.3.1. Compound 16. Yield: 60 mg, 7% crystallised from methanol as yellow crystals, mp 154–156°C. δ_H (400 MHz, $CDCl_3$): 8.05 (2H, s, H-1, H-4), 7.17 (2H, s, H-5, H-8), 6.11 (2H, s, OCH_2O), 3.95 (6H, s, CO_2Me). δ_C (100.6 MHz, $CDCl_3$): 168.3 (CO_2Me), 149.8 (C-6, C-7), 131.0 (C-2, C-3), 128.8 (C-1, C-4), 127.1 (C-4a, C-8a), 104.5 (C-5, C-8), 101.8 (OCH_2O), 52.6 (CO_2Me). m/z (e.i.) 288 (M^+, 40%), 257 (100), 171 (17), 170 (17), 141 (22), 113 (30), 86 (25). m/z (c.i.) 289 ($M+H^+$, 100%). Found: M^+, 288.0647. $C_{15}H_{12}O_6$ requires 288.0633.

5.3.2. Compound 17.[24] The compound was crystallised from methanol as yellow crystals (70 mg, 6%), mp 188–190°C. δ_H (400 MHz, $CDCl_3$): 8.39 (1H, s, H-4), 7.22 (1H, s, H-5), 6.90 (1H, d, J=8.0 Hz, H-5′), 6.89 (1H, s, H-8), 6.76–6.81 (2H, m, H-2′, H-6′), 6.04–6.08 (4H, m, OCH_2O), 3.94 (3H, s, CO_2Me), 3.68 (3H, s, CO_2Me). δ_C (100.6 MHz, $CDCl_3$): 169.5 (CO_2Me), 166.3 (CO_2Me), 150.3 (C-6), 148.7 (C-7), 147.3 (C-3′, C-4′), 137.0 (C-2), 132.3 (C-3), 130.4 (C-1), 130.0 (C-4), 129.8 (C-8a), 123.7 (C-6′), 122.8 (C-4a), 110.7 (C-5), 108.1 (C-8), 104.8 (C-2′), 103.3 (C-5′), 101.8 (OCH_2O), 101.3 (OCH_2O), 52.5 (CO_2Me), 52.2 (CO_2Me). m/z (e.i.) 408 (M^+, 100%), 407 (40), 394 (33), 377 (73), 366 (60), 319 (30), 307 (40), 306 (95), 291 (30), 276 (50), 174 (70), 163 (73). m/z (c.i.) 426 ($M+NH_4^+$, 50%), 409 ($M+H^+$, 100%), 395 (23), 377 (35), 289 (55). Found: $M+H^+$, 409.0920. $C_{22}H_{17}O_8$ requires 409.0923.

5.3.3. Compound 18. The compound was isolated as crystals, mp 206–208°C, *ex* methanol. δ_H (400 MHz, $CDCl_3$): 6.70 (1H, s, H-4/H-7), 6.67 (1H, s, H-4/H-7), 6.60 (1H, d, J=8.0 Hz, H-6′), 6.59 (1H, dd, J=8.0, 1.2 Hz, H-5′), 6.67 (1H, d, J=1.2 Hz, H-2′), 4.63 (1H, d, J=8.8 Hz, H-3), 3.10 (1H, dd, J=8.8, 17.8 Hz, H-8a), 2.78 (1H, dd, J=1.4, 17.8 Hz, H-8b). δ_C (100.6 MHz, $CDCl_3$): 173.2 (C-9), 167.5 (CO_2Me), 149.8, 149.4 (C-5, C-6), 147.6, 147.5 (C-3′, C-4′), 137.6 (C-1′), 133.5, 132.2 (C-3a, C-7a), 120.3 (C-6′), 107.7, 107.2 (C-4, C-7), 105.0, 103.7 (C-2′, C-5′), 101.9, 101.2 (2×OCH_2O), 96.8 (C-1), 86.8 (C-2), 52.8 (CO_2CH_3), 44.9 (C-3), 35.9 (C-8). ν_{max} (KBr) 1787, 1736 cm^{-1}. m/z (e.i.) 412 (M^+, 22%), 282 (39), 149 (53). m/z (c.i. NH_3), 430 ($M+NH_4^+$, 22%), 412 (5), 395 (50). Found: M^+, 430.1138. $C_{21}H_{16}O_9+NH_4^+$ requires 430.1133.

Acknowledgements

The authors express their gratitude to DST, New Delhi for financial assistance.

References

1. Orlandi, M.; Rindone, B.; Molteni, G.; Rummakko, P.; Brunow, G. *Tetrahedron* **2001**, *57*, 371.
2. Higuchi, T. In *Biosynthesis and Biodegradation of Wood Components*; Higuchi, T., Ed.; Academic: New York, 1986; pp 141–148.
3. Bernards, M. A.; Lopez, M. L.; Zajicek, J.; Lewis, N. G. *J. Biol. Chem.* **1995**, *270*, 7382.
4. Ragan, M. A. *Phytochemistry* **1984**, *23*, 2029.
5. Wang, C-Z.; Davin, L. B.; Lewis, N. G. *Chem. Commun.* **2001**, 113.
6. Ayres, D. C.; Loike, J. D. *Lignans: Chemical, Biological and Clinical Properties*; Cambridge University: Cambridge, 1990.
7. Lewis, N. G.; Davin, L. B. *Lignans: Biosynthesis and Function in Comprehensive Natural Product Chemistry*; Barton, D. R. H., Nakanishi, K., Meth-Cohn, O., Eds.; Elsevier: London, 1999; Vol. 1, pp 639–712.
8. Ward, R. S. *Natl. Prod. Rep.* **1999**, *16*, 75.
9. Eickhoff, H.; Jung, G.; Rieker, A. *Tetrahedron* **2001**, *57*, 353.
10. MacRae, W. D.; Towers, G. H. N. *Phytochemistry* **1984**, *23*, 1207.
11. Ward, R. S. *Tetrahedron* **1990**, *46*, 5029.
12. Syrjänen, K.; Brunow, G. *Tetrahedron* **2001**, *57*, 365.

13. Botta, B.; Jacomacci, P.; Vinciguerra, V.; Monache, G. D.; Gacs-Baitz, E.; Botta, M.; Misiti, D. *Chem. Pharm. Bull.* **1990**, *38*, 3238.
14. Al-Farhan, E.; Keehn, P. M.; Stevenson, R. *Synthesis* **1992**, 959.
15. (a) Venkateswarlu, R.; Kamakshi, C.; Moinuddin, S. G. A.; Subhash, P. V.; Ward, R. S.; Pelter, A.; Hursthouse, M. B.; Light, M. E. *Tetrahedron* **1999**, *55*, 13087. (b) Ward, R. S.; Pelter, A.; Venkateswarlu, R.; Kamakshi, C.; Subhash, P. V.; Moinuddin, S. G. A.; Hursthouse, M. B.; Coles, S. J.; Hibbs, D. E. *Tetrahedron* **1999**, *55*, 13071. (c) Ward, R. S.; Pelter, A.; Venkateswarlu, R.; Kamakshi, C.; Lakshmi, A. *Tetrahedron* **1996**, *52*, 14349. (d) Pelter, A.; Ward, R. S.; Venkateswarlu, R.; Kamakshi, C. *Tetrahedron* **1992**, *48*, 7209. (e) Pelter, A.; Ward, R. S.; Venkateswarlu, R.; Kamakshi, C. *Tetrahedron* **1991**, *47*, 1275.
16. (a) Ward, R. S.; Pelter, A.; Edwards, M. I. *Tetrahedron* **1996**, *52*, 12799. (b) Pelter, A.; Ward, R. S.; El-Ghani, A. *J. Chem. Soc., Perkin Trans. 1* **1996**, 1353. (c) Pelter, A.; Ward, R. S.; El-Ghani, A. *Tetrahedron* **1996**, *52*, 1303. (d) Pelter, A.; Satchwell, P.; Ward, R. S.; Baker, K. *J. Chem. Soc., Perkin Trans. 1* **1995**, *18*, 2201. (e) Pelter, A.; Ward, R. S.; Ma, W.-Y. *J. Natl. Prod.* **1994**, *57*, 1598.
17. (a) Block, E.; Stevenson, R. *J. Org. Chem.* **1971**, *36*, 3450. (b) Brown, D.; Stevenson, R. *J. Org. Chem.* **1965**, *30*, 1795.
18. Collect data collection software, Nonius, B.V., **1998**.
19. Otwinowski, Z.; Minor, W. Processing of X-ray diffraction data collected in oscillation mode. In *Methods in Enzymology, Macromolecular Crystallography, Part A*; Carter, Jr., C. W., Sweet, R. M., Eds.; Academic Press: New York, 1997; Vol. 276, pp 307–326.
20. Mackay, S.; Gilmore, C. J.; Edwards, C.; Tremayne, M.; Stuart, N.; Shankland, K. maXus: a computer program for the solution and refinement of crystal structures from diffraction data; University of Glasgow, Scotland, UK, Nonius, B.V., Delft, The Netherlands and MacScience Co. Ltd., Yokohama, Japan, **1998**.
21. Blessing, R. H. *Acta Crystallogr.* **1995**, *A51*, 33.
22. Blessing, R. H. *J. Appl. Crystallogr.* **1997**, *30*, 421.
23. Sheldrick, G. M.; SHELX97: Programs for Crystal Structure Analysis (Release 97-2); Institüt für Anorganische Chemie der Universität, Tammanstrasse 4, D-3400 Göttingen, Germany, **1998**.
24. Arnold, B. J.; Mellors, S. M.; Sammes, P. G. *J. Chem. Soc., Perkin Trans. 1* **1973**, 1266.