Pergamon

Tetrahedron Vol. 51, No. 13, pp. 3841-3864, 1995

0040-4020/95 $9.50+0.00

0040-4020(95)00107-7

Synthesis and Structural Characterization of a Novel Pair of Rigid Diastereomeric Triads

James M. Lawson, Donald C. Craig, Anna M. Oliver, and Michael N. Paddon-Row*

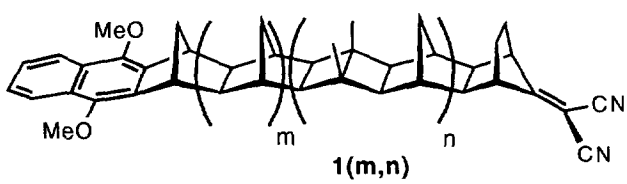
School of Chemistry, University of New South Wales, Sydney, 2052, Australia

Abstract: A method is described for constructing totally rigid triad (trichromophoric) systems, D_2–B_1–D_1–B_2–A, in which the chromophores D_2 (= dimethylaniline), D_1 (= 1,4-dimethoxynaphthalene), and A (= dicyanovinyl) are fused to rigid hydrocarbon bridges, B_1 and B_2, comprising linearly fused norbornane and bicyclo[2.2.0]hexane units.

INTRODUCTION

The central role played by electron transfer in a wide range of chemical and biological reactions ensures that it remains the focus of intense research activity.[1-9] In this respect, studies on intramolecular electron transfer in rigid, covalently linked Donor–Bridge–Acceptor dyads are playing a major role because the attachment of donor and acceptor groups to a fairly rigid bridge enables the dependence of electron transfer dynamics on donor–acceptor distance and orientation to be determined with minimum ambiguity.[4] Many types of bridge have been used, ranging from modified proteins and peptides,[1c,1e,1f] to hydrocarbon bridges of varying degrees of structural complexity.[5-7]

Studies on rigid dyads possessing saturated hydrocarbon bridges have amply demonstrated that rapid intramolecular electron transfer can take place over interchromophore separations exceeding 12 Å, by way of a through–bond coupling mechanism involving the bridge σ and σ* orbitals.[4,8]



1(m,n)

To date, our work has mainly focused on studying long–range intramolecular electron transfer in dyads, such as the series **1(m,n)**, in which the dimethoxynaphthalene (DMN) donor and the dicyanovinyl (DCV) acceptor are attached to a completely rigid norbornylogous bridge of variable length, comprising linearly fused norbornane and bicyclo[2.2.0]hexane units. The members of the **1(m,n)** series were found to

display extraordinarily rapid rates of intramolecular thermal electron transfer (in the corresponding anion radicals)[7a] and photoinduced electron transfer.[7b-e] For example, the rate of photoinduced intramolecular electron transfer, from locally excited DMN donor to DCV acceptor, was found to be *ca* 10^9 s^{-1} for the 12-bond sytem, **1(0,2)**, in which the interchromophore edge-to-edge separation is *ca* 13.5 Å.[7d]

The remarkable photoinduced electron transfer rates observed for the **1(m,n)** series demonstrate that the norbornylogous bridge is an efficient mediator of electron transfer over large distances. This type of bridge therefore offers promise in the construction of molecular electronic devices, such as photovoltaic systems,[1g] since it possesses the double advantage of fixing the spatial arrangement of the redox centres with respect to each other and controlling the dynamics and direction of electron transfer processes between the redox centres. However, the successful construction of such devices must simultaneously satisfy the dual criteria of efficient charge separation and longevity of the resulting charge-separated state towards charge recombination.[1g]

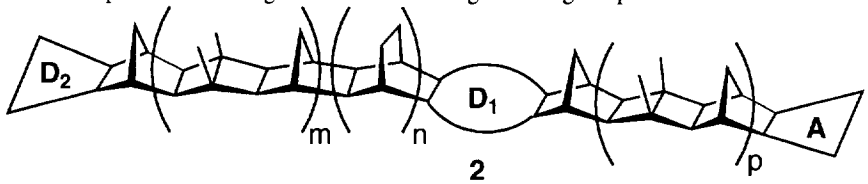
Covalently linked dyads are unsuitable for this purpose since, whereas the charge-recombination lifetime, τ_{cr}, increases with increasing bridge length, the quantum yield for the charge-separation step diminishes with increasing bridge length.[1g]

A solution to this problem is to use multichromophoric systems, *i.e.*, triads, tetrads, pentads, etc, that constitute a gradient of redox centres arranged within a spatially well-defined array.[1g,2e,9] The principle behind this strategy is illustrated in eq (1) for the case of the covalently linked triad, $\mathbf{D_2}$–$\mathbf{D_1}$–**A**, in which $\mathbf{D_1}$ is initially locally excited.

$$\mathbf{D_2—{}^*D_1—A} \longrightarrow \mathbf{D_2—D_1^+—A^-} \longrightarrow \mathbf{D_2^+—D_1—A^-} \qquad (1)$$

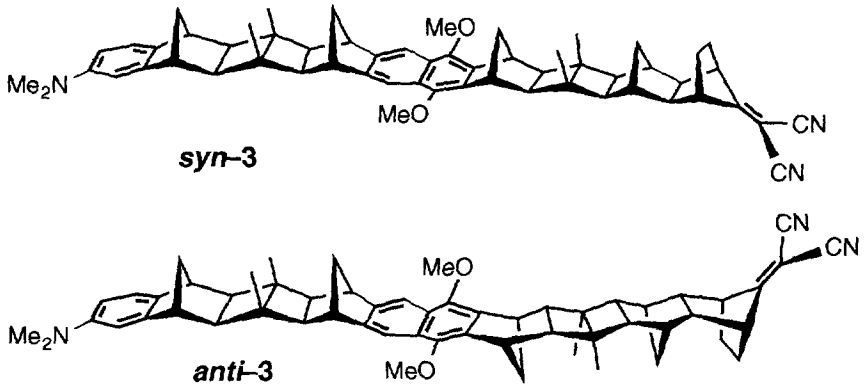
In this system, the electron transfer process takes place in a sequence of rapid "hops", between adjacent chromophores that are spanned by a bridge that is short enough to guarantee that the hop occurs with near unit efficiency. The final result is charge separation over a sufficiently large distance that the unwanted charge-recombination step becomes acceptably slow enough.

Our recent efforts in this area are focused on developing synthetic strategies for the construction of the general triad, **2** in which the primary donor group, $\mathbf{D_1}$, is connected to the other chromophores, $\mathbf{D_2}$ and **A** by a series of norbornylogous bridges. These systems offer several significant advantages over other polychromophoric systems studied to date.[1g,2e,9] In particular, the symmetry and complete rigidity of the norbornylogous framework, combined with our ability to append a wide range of chromophores to the bridge, and to alter systematically both the length and configuration of the bridge, confer upon **2** the potential for providing unprecedented insight into the factors governing the dynamics of photoinduced electron transfer processes leading to the formation of giant charge-separated states.[8]



2

In this paper, we describe the synthesis of the first representative, **3**, of this novel triad system.[10] In **3**, the N,N-dimethylaniline and DCV chromophores are connected to the central DMN group by respective bridges six and eight bonds in length. It is noteworthy that **3** possesses two rigid, noninterconverting diastereomeric forms, ***syn*–3** and ***anti*–3** which differ in the spatial disposition of the methylene bridges of the two central norbornane groups with respect to the DMN unit.

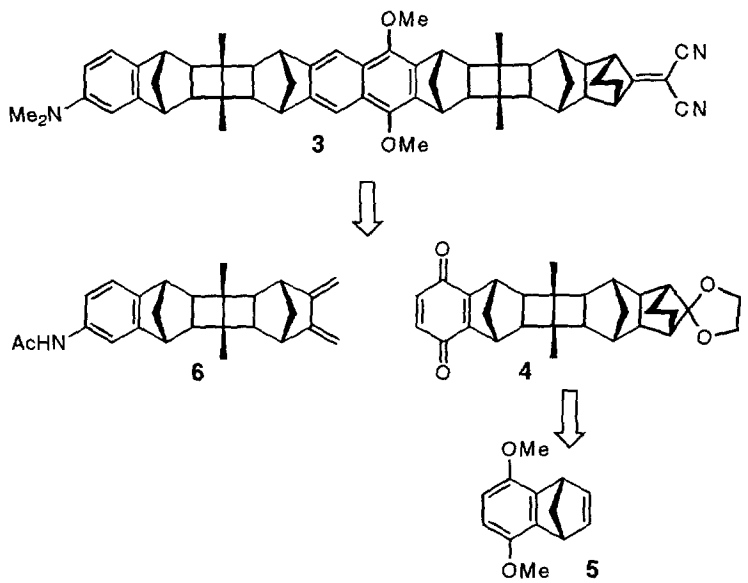


RESULTS AND DISCUSSION

Synthetic strategy

Triads of the type **3** have the important synthetic advantage of convergency (Scheme 1) in that disconnection of the DMN group produces two subunits, **4** and **6** of similar complexity. These units can be united to form the naphthalene ring through Diels–Alder methodology. The quinone bridge unit, **4**, should be readily accessible from 1,4-methano-5,8-dimethoxynaphthalene, **5**, onto which the polynorbornane-bicyclo[2.2.0]hexane bridge may be constructed in the usual way,[11] using the tandem Mitsudo–Smith reactions.[12,13]

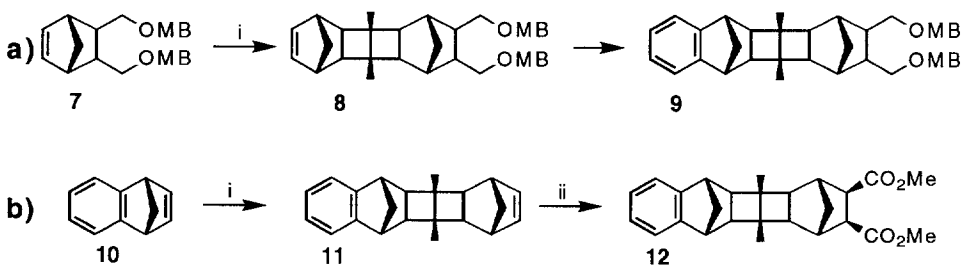
Scheme 1



Synthesis of the bridge unit **6**, containing the bismethylene group may be approached in two ways, as indicated in Scheme 2. In the first approach, (Scheme 2a), one begins with a suitably protected

2,3-bishydroxymethylnorbornene, **7**, from which **8** should be readily obtainable (using tandem Mitsudo–Smith reactions). Benzene annulation of **8** using well developed procedures[14] would give **9** which can be easily converted into the desired diene, **6**. In the second approach, benzonorbornadiene, **10**, is the starting point (Scheme 2b) from which **11** is obtainable using Mitsudo–Smith methodology. The success of this approach depends on the ability to effect bismethoxycarbonylation of the double bond of **11** to give **12**. This might be achievable using Stille–Vogel methodology.[15,16] Conversion of **12** into **6** should be straightforward. In this work, we decided to use the first approach (Scheme 2a) to synthesize the diene unit, although current studies indicate that the second approach is also viable.[17]

Scheme 2

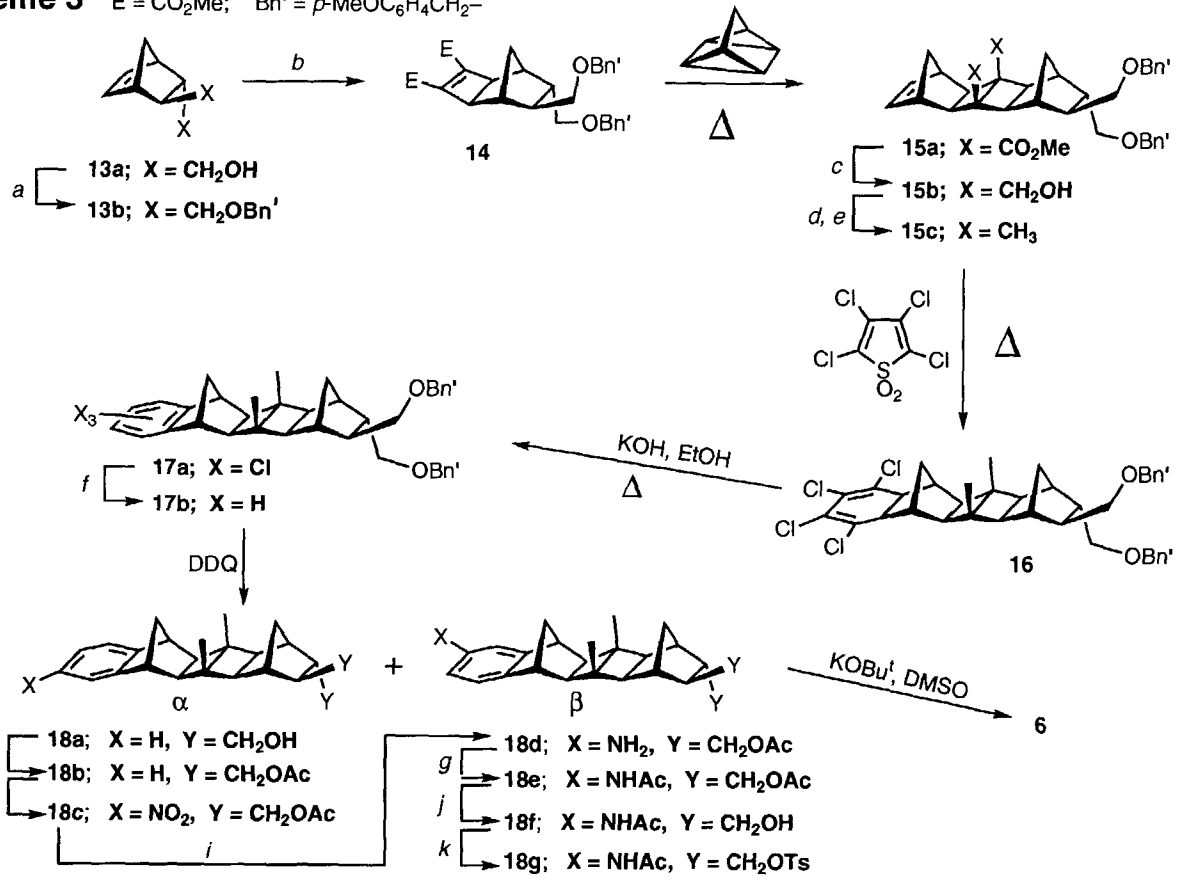


Diene unit, **6**

The synthesis of the diene, **6**, is outlined in Scheme 3. The hydroxyl groups of the known diol, **13a**, were protected through conversion to the bis–*p*–methoxybenzyl ether derivative, **13b**. The norbornylogous bridge was then constructed using the Mitsudo–Smith reactions in tandem, namely, the $RuH_2CO(PPh_3)_3$ catalyzed thermal [2 + 2] cycloaddition of dimethyacetylene dicarboxylate (DMAD) to **13b**, to form **14** (Mitsudo reaction[12]), and subsequent thermal [$\pi 2_S + \sigma 2_S + \sigma 2_S$] reaction of **14** with quadricyclane (Smith reaction[13]), to give **15a**. Conversion of **15a** into **15c**, by reduction (to the diol, **15b**), bismesylation, and finally, reductive bisdemesylation, proceeeded smoothly. The overall yield of **15c** from **13a** was 23%. Benzene annulation of the double bond of **15c** was carried out using the Raasch method.[14] This entails thermal reaction of **15c** with tetrachlorothiophene–1,1–dioxide which yields the dihydrobenzene adduct, **16**, by cheletropic loss of SO_2 from the initially formed Diels–Alder adduct. Aromatization of **16** to **17a**, followed by reductive dechlorination, employing standard procedures,[14a] gave **17b** in an acceptable yield of 55% from **15c**.

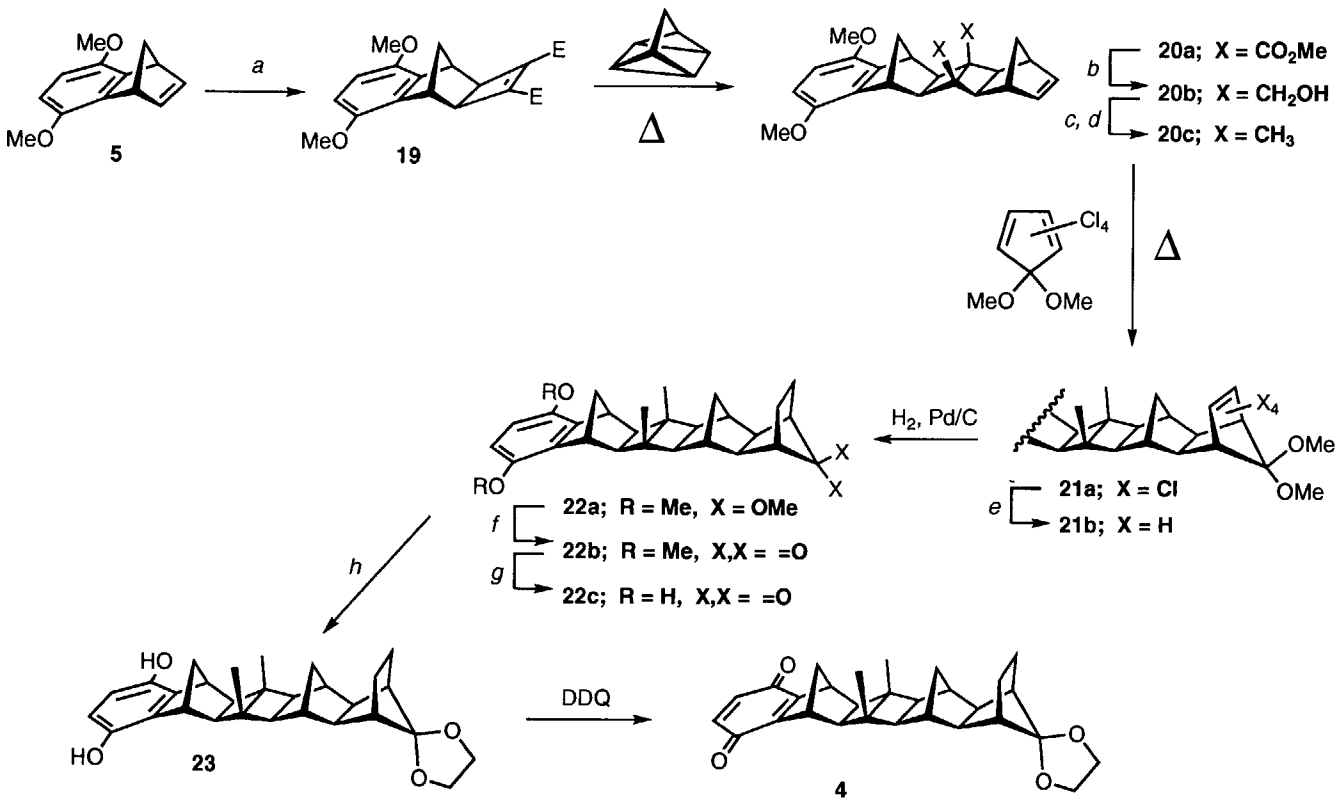
The next task was nitration of the aromatic ring. However, the *p*–methoxybenzyl group is extremely sensitive to oxidizing conditions and so it was necessary to replace this protecting group with the more robust acetyl group. Thus, **17b** was deprotected with DDQ to give the diol, **18a** which was immediately bisacetylated to produce **18b**. Nitration of this material, using the copper(II) nitrate/acetic anhydride system, gave a mixture consisting of approximately equal amounts of the two diastereomeric nitro compounds, **18c** (these diastereomers are designated α and β in Scheme 3). This mixture was not separated into diastereomerically pure forms since both isomers eventually yield the diene, **6**. Thus, the mixture of the nitro compounds, **18c** was converted into the diastereomeric amides **18e** using standard techniques. Treatment of **18e** with $LiBH_4$ gave the diol **18f**, through selective reduction of the ester groups. The desired diene, **6**, was readily obtained from **18f**, through bistosylation and subsequent bisdehydrotosylation. The overall yield of diene, **6** from **13a** was 1.3%.

Scheme 3 E = CO_2Me; Bn' = *p*-$MeOC_6H_4CH_2$–



Reagents: *a*, *p*–methoxybenzyl chloride, NaI, NaH; *b*, DMAD, $RuH_2CO(PPh_3)_3$; *c*, $LiAlH_4$; *d*, MsCl, py; *e*, $LiAlH_4$, THF, reflux; *f*, Na, Pr^iOH; *g*, Ac_2O, py; *h*, $Cu(NO_3)_2.3H_2O$, Ac_2O, CH_2Cl_2; *i*, H_2, 5% Pd/C; *j*, $LiBH_4$; *k*, TsCl, py.

Scheme 4 E = CO_2Me



Reagents: *a*, DMAD, $RuH_2CO(PPh_3)_3$; *b*, $LiAlH_4$; *c*, MsCl, py; *d*, $LiAlH_4$, THF, reflux; *e*, Na, Pr^iOH; *f*, HCO_2H; *g*, BBr_3; *h*, $HOCH_2CH_2OH$, TsOH.

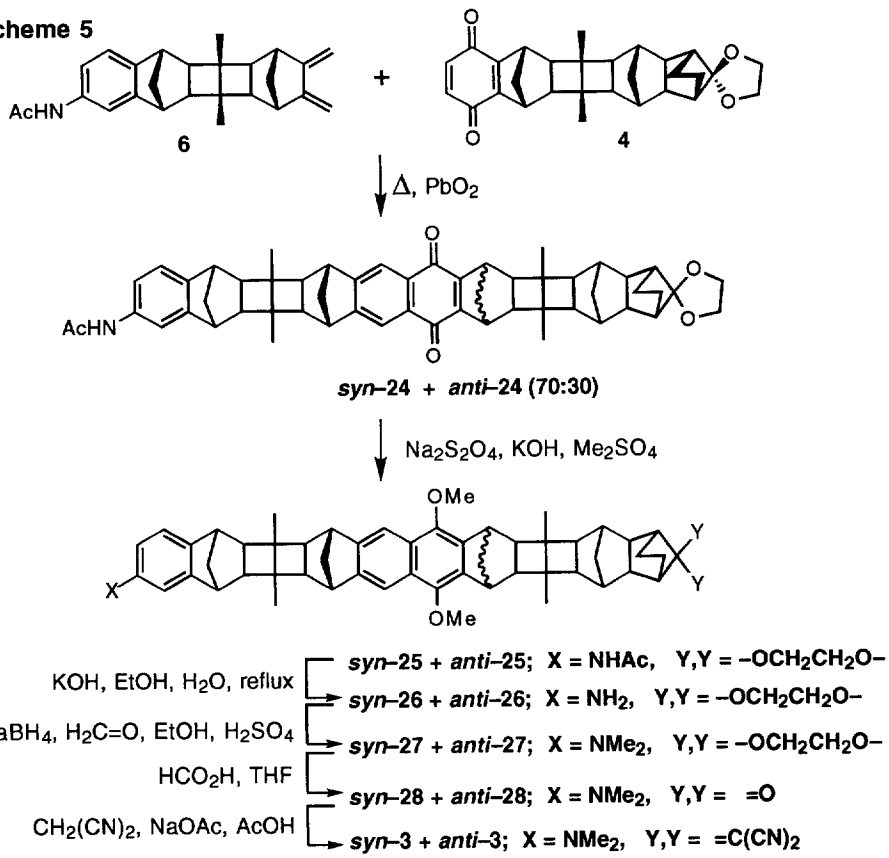
Quinone unit, **4**

The synthesis of the quinone, **4**, (Scheme 4) began with the dimethoxymethanonaphthalene, **5**, which was converted into the six–bond norbornylogous system, **20c**, using standard bridge building procedures, as described above. Diels–Alder reaction of **20c** with dimethoxytetrachlorocyclopentadiene readily gave the adduct, **21a**. Reductive dechlorination of this material (Na, Pr^iOH), followed by catalytic hydrogenation gave **22a**. Deacetalization of **22a** (formic acid in THF) and treatment of the resulting ketone, **22b**, with BBr_3 led to the formation of the hydroquinone, **22c**. In view of the nature of some of the later steps to be encountered in the synthesis, it was deemed prudent to protect the carbonyl function at this stage by converting it into the dioxolane, **23**. Treatment of this compound with DDQ produced the quinone, **4**, in 14% yield from **5**.

Synthesis of the triads, **3**

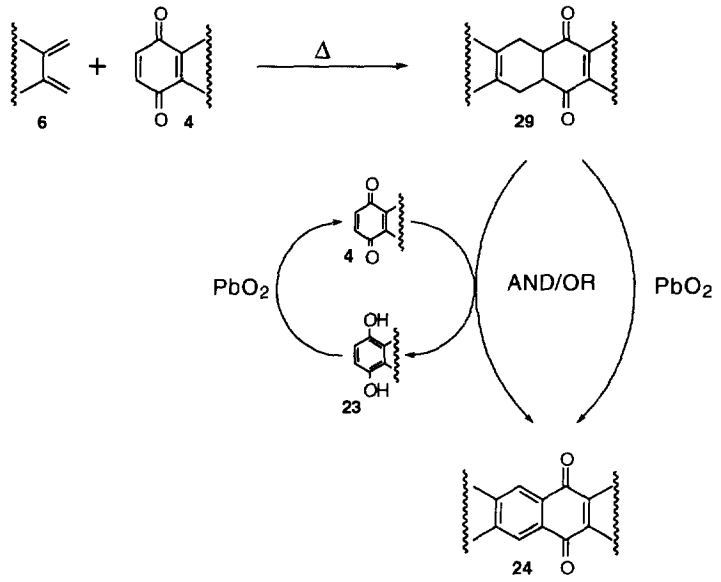
The final stage of the synthesis involves the Diels–Alder reaction between the bridge units **6** and **4**. It was found that this proceeded best in the presence of excess lead dioxide, the reaction then leading directly to the formation of the diastereomeric quinones, ***syn*–24** and ***anti*–24** (Scheme 5). In the absence of lead dioxide, the reaction did not go to completion; substantial quantities of unreacted diene, **6**, and hydroquinone, **23**, were also present in the product mixture. Presumably, the quinone reactant, **4**, is dehydrogenating the initially formed adduct, **29**, to give the product quinone, **24** and hydroquinone, **23**, as indicated in Scheme 6. Addition of lead dioxide prevents accumulation of unwanted hydroquinone, **23**, either by oxidizing **23** back to the quinone, **4**, or by directly dehydrogenating the adduct, **29** to **24**.

Scheme 5

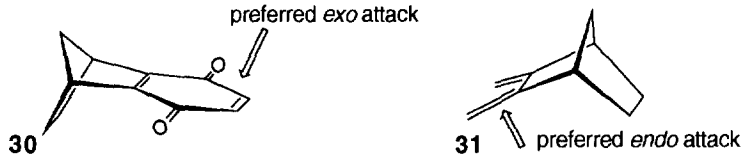


^{1}H nmr analysis of **24** showed it to comprise a 70:30 mixture of two diastereomeric quinones, presumably the *syn* and *anti* forms. However, the ^{1}H and ^{13}C nmr spectra of these isomers are barely distinguishable from each other, which is not surprising considering that the two methylene bridges that are responsible for the diastereoisomerism are distal (they are separated by the dimethoxynaphthalene ring).

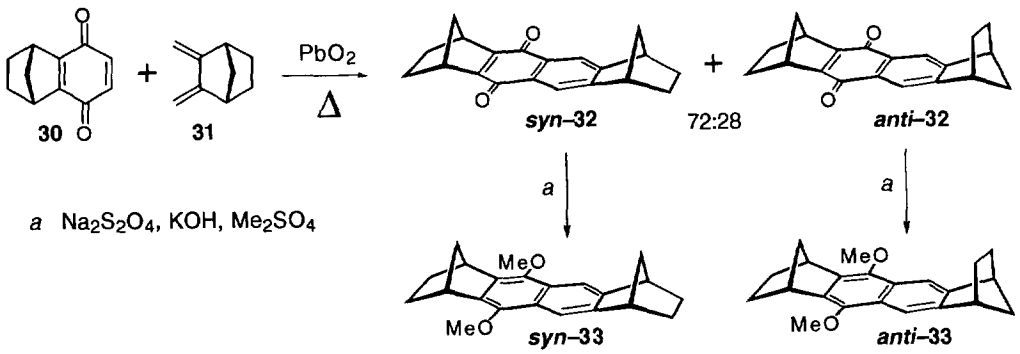
Scheme 6



Precedent, based on experimental studies of Diels–Alder reactions involving structurally more simple norbornanyl–fused *p*–benzoquinones and dimethylenenorbornanes,[18,19] suggests that the major quinone isomer **24**, arising from reaction between **4** and **6**, should have the *syn* configuration. This is because norbornanyl–fused *p*–benzoquinones and dimethylenenorbornanes are known to exhibit fairly strong *exo* and *endo* facial selectivities, respectively, as illustrated below:



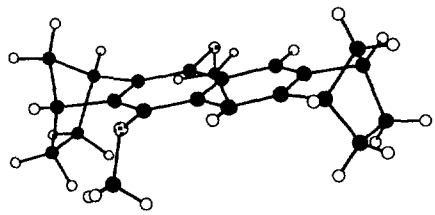
In the reaction between **4** and **6**, the reinforcing combination of these facial selectivities should result in the preferred formation of ***syn*–24**. Indeed, in a model reaction, we observed that the Diels–Alder reaction between quinone **30** and diene **31**, in the presence of PbO_2, led to the formation of a 72:28 mixture of the quinones, ***syn*–32** and ***anti*–32** respectively. The separated quinones were subjected to reductive methylation, to yield the respective dimethoxynaphthalenes, **33**. An X–ray crystal structure of the major isomer confirmed that it possesses the *syn* configuration (Figure 1).[20]



Unfortunately, the mixture of the diastereomeric quinones, **24**, resulting from the reaction between quinone **4** and diene **6**, was difficult to separate and so the entire product mixture was subjected to reductive methylation (Scheme 5), to yield a mixture of the dimethoxynaphthalene triads, **25**. This mixture could be separated (by TLC) into the two diastereomeric forms, ***syn*-25** and ***anti*-25**, the minor isomer having the higher R_f value and the major isomer having the lower R_f value.

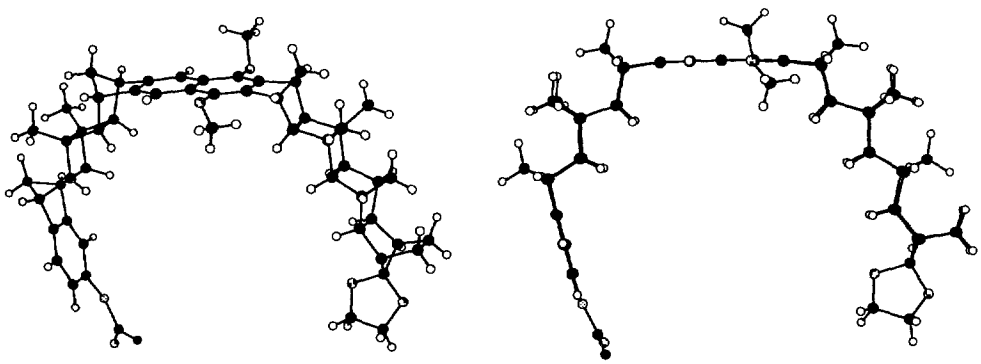
Figure 1

Single crystal X–ray structure of ***syn*–33**



Determination of the configurations of the isomers was secured by obtaining a single crystal X–ray structure of the major isomer (Figure 2).[20] This isomer clearly possesses the *syn* configuration. In summary, the major and minor diastereomers (70:30) of **25** (and **24**) have, respectively, the *syn* and *anti* configurations. The facial selectivity observed in the reaction between **4** and **6** (*syn*:*anti* = 70:30) is similar to that observed from the reaction between **30** and **31** (*syn*:*anti* = 72:28).

Figure 2 Single crystal X–ray structure of ***syn*–25**



Conversion of ***syn*–25** and ***anti*–25** into the respective triads, ***syn*–3** and ***anti*–3**, was achieved through hydrolysis to the anilines, **26**, methylation to the N,N–dimethylanilines, **27**, deacetalization to the ketones, **28**, followed by Knoevenagel condensation with malononitrile.

EXPERIMENTAL

Melting points were determined with a Mel-Temp (II) apparatus and are uncorrected. Microanalyses were performed by Dr H. P. Pham of the University of New South Wales.

^{1}H n.m.r. spectra were obtained on Bruker AC300F (300 MHz) and AM500 (500 MHz) spectrometers. ^{1}H data is reported as follows: chemical shifts (δ) measured in parts per million (ppm) down field from TMS; multiplicity; observed coupling constant (*J*) in Hertz (Hz); proton count; proton assignment. Multiplicities are reported as singlet (s), broad (br), doublet (d), triplet (t) and multiplet (m).

^{13}C spectra were obtained on a Bruker AC300F (75.47 MHz) spectrometer. ^{13}C chemical shifts (δ) are reported in parts per million (ppm) down field from TMS and identifiable signals are given. Assignment was determined with the aid of 90° DEPT and 135° DEPT experiments.

Chromatography was performed using gravity columns packed with Merck silica gel 7734 60 (70 - 230 mesh).

N,N-Dimethylformamide was dried over $MgSO_4$, distilled under reduced pressure and stored over 4Å molecular sieves. THF was dried using sodium benzophenone under argon.

Trans-5,6-bis[(4'-methoxyphenyl)methoxymethyl]bicyclo[2.2.1]hept-2-ene **13b:** NaI (8.3 g, 55 mmol) was added to a stirred solution of **13a**[21] (10.40 g, 67.4 mmol) and 4-methoxy benzyl chloride (22.4 g, 0.142 mol) in dry N,N–dimethyl formamide (60 ml) and dry monoglyme (30 ml) under argon atmosphere. The reaction mixture was stirred for 30 min and NaH (55% in paraffin oil) (7.30 g, 0.167 mol) was added in 2 portions. The first (3.5 g) was added over 2.5 h. The second (3.8 g) over 15 min. The reaction mixture was then heated to 60 °C for 15 h, then cooled to rt and the excess NaH was quenched by the cautious addition of water (10 ml). The reaction mixture was then poured onto ice (300 g) and the resulting mixture was extracted with diethyl ether (2 x 100 ml). The organic layers were combined and washed with saturated $NaHCO_3$ (2 x 200 ml) and brine (3 x 200 ml), and dried over anhyd Na_2SO_4. The solvent was evaporated under reduced pressure give a brown oil. This was subjected to column chromatography (silica, 60-80 light petroleum/ethyl acetate, 70:30) to give **13b** as a clear oil (21.3 g, 81%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.19 (m, 1H), 1.27 (br s, 2H), 1.80 (m, 1H), 2.72 (br s, 1H), 2.89 (br s, 1H), 3.24-3.57 (m, 4H), 3.75 (s, 6H, 2 x $ArOCH_3$), 4.28 (d, *J* = 11.5 Hz, 1H), 4.35 (d, *J* = 11.5 Hz, 1H), 4.37 (s, 2H), 5.92 (d of d, *J* = 3.3, 5.7 Hz, 1H, vinylic), 6.13 (d of d, *J* = 3.3, 5.7 Hz, 1H, vinylic), 6.77-6.82 (m, 4H), 7.15-7.20 (m, 4H).

Dimethyl-(1α,2β,5β,6α)-1,2,5,6,7,8-hexahydro-trans-7,8-bis[(4-methoxyphenyl)methoxymethyl]tricyclo[4.2.1.0^{2,5}]nonane-3,4-dicarboxylate **14.** A solution of **13b** (2.05 g, 5.20 mmol) dimethylacetylene dicarboxylate (1.00 g, 7.03 mmol) and $RuH_2CO(PPh_3)_3$[22] (0.20 g, 0.20 mmol) in benzene (15 ml) was heated at reflux under argon, for 5 d. The solvent was evaporated under reduced pressure to give a brown oil which was subjected to column chromatography (silica, 60-80 light petroleum/ethyl acetate, 70:30) to give **14** as a clear oil (2.44 g, 87%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.21 (m, 1H), 1.24 (d, *J* = 11.2 Hz, 1H), 1.34 (d, *J* = 11.2 Hz, 1H), 1.85 (m, 1H), 2.27 (s, 1H), 2.36 (d, *J* = 3.7 Hz, 1H), 2.65 (d, *J* = 3.4 Hz, 1H), 2.91 (d, *J* = 3.4 Hz, 1H), 3.26-3.46 (m, 4H), 3.76 (s, 3H, $ArOCH_3$), 3.78 (s, 3H, $ArOCH_3$), 3.80 (s, 6H, 2 x CO_2CH_3), 4.39 (d, *J* = 11.8 Hz, 1H), 4.42 (s, 2H), 4.48 (d, *J* = 11.8 Hz, 1H), 6.87 (m, 4H, ArH), 7.23 (m, 4H, ArH).

Dimethyl-(1α,4α,4aβ,4bα,4cβ,5α,8α,8aα,8bβ,8cα)-1,4,4a,4b,4c,5,6,7,8,8a,8b,8c-dodecahydro-trans-6,7-bis[(4-methoxyphenyl)-methoxymethyl]-1,4:5,8-dimethanobenzo[3',4']cyclobuta[1',2':3,4]cyclobuta[1,2]benzene-4b,8b-dicarboxylate **15a: 14** (10.00 g, 18.6 mmol) in quadricyclane (12.20 g, 130 mmol) was heated at 125 °C for 4 d. Excess quadricyclane was evaporated under reduced pressure to give a brown oil which was subjected to column chromatography

(silica, 60-80 light petroleum/ethyl acetate, 70:30) and crystallized with ethanol to give **15a** as a white powder (6.19 g, 53%) mp 114-116 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.07 (d, *J* = 11.1 Hz, 1H), 1.10 (m, 1H), 1.27 (d, *J* = 11.1 Hz, 1H), 1.68 (m, 1H), 1.80 (d, *J* = 9.7 Hz, 1H), 2.06 (s, 2H), 2.13 (s, 1H), 2.14 (d, *J* = 9.7 Hz, 1H), 2.22 (d, *J* = 5.3 Hz, 1H), 2.26 (br d, *J* = 3.6 Hz, 1H), 2.43 (d, *J* = 5.3 Hz, 1H), 2.79 (br s, 1H), 2.81 (br s, 1H), 3.20-3.26 (m, 3H), 3.38 (d of d, *J* = 6.3, 9.3 Hz, 1H), 3.68 (s, 3H, CO_2CH_3), 3.71 (s, 3H, CO_2CH_3), 3.78 (s, 3H, $ArOCH_3$), 3.79 (s, 3H, $ArOCH_3$), 4.33 (d, *J* = 11.8 Hz, 1H), 4.38 (s, 2H), 4.46 (d, *J* = 11.8 Hz, 1H), 6.04 (br t, *J* = 1.6 Hz, 2H), 6.83-6.89 (m, 4H), 7.18-7.23 (m, 4H). IR (KBr disc) υ 1755 (C=O), 1618, 1591, 1253 cm^{-1}. Anal. Calcd. for $C_{38}H_{44}O_8$: C, 72.59; H, 7.05. Found: C, 71.98; H, 7.13.

(1α,4α,4aβ,4bα,4cβ,5α,8α,8aα,8bβ,8cα)-1,4,4a,4b,4c,5,6,7,8,8a,8b,8c-dodecahydro-4b,8b-bis(hydroxymethyl)-trans-6,7-bis[(4-methoxyphenyl)-methoxymethyl]-1,4:5,8-dimethanobenzo[3',4']cyclobuta[1',2':3,4]cyclobuta[1,2]benzene **15b:** Lithium aluminium hydride (1.90 g, 50 mmol) was added portionwise to an ice cold, stirred solution of **15a** (6.11 g, 9.72 mmol) in dry THF (100 mL). After the addition was complete, the reaction mixture was heated at reflux for 3 d. The reaction mixture was cooled to 0 °C and the excess reagent was quenched by the sequential addition of water (1.9 mL), 15% NaOH (1.9 mL) and then water (5.7 mL). The reaction mixture was heated at reflux for 1 h, then the lithium and aluminium salts were removed by suction filtration. The solvent evaporated under reduced pressure to give **15b** as a white solid (5.34 g, 96%): ^{1}H NMR (60 MHz, $CDCl_3$) δ 1.10-2.50 (m, 14H), 2.90 (br s, 2H), 3.30-3.70 (m, 8H), 3.80 (s, 6H), 4.50 (br s, 4H), 6.10 (br s, 2H), 6.70-7.30 (m, 8H). IR (KBr disc) υ 3432 (OH), 1617, 1591, 1252, cm^{-1}.

(1α,4α,4aβ,4bα,4cβ,5α,8α,8aα,8bβ,8cα)-1,4,4a,4b,4c,5,6,7,8,8a,8b,8c-dodecahydro-trans-6,7-bis[(4-methoxyphenyl)-methoxymethyl]-4b,8b-dimethyl-1,4:5,8-dimethanobenzo[3',4']cyclobuta[1',2':3,4]cyclobuta[1,2]benzene **15c:** Methane sulfonyl chloride (4.7 g, 41 mmol) was added slowly to a solution of **15b** (5.34 g, 9.32 mmol) in dry pyridine (40 ml). The reaction mixture was left at -5 °C for 3 d. The reaction mixture then poured onto ice (150 g) and extracted with cold CH_2Cl_2 (2 x 100 ml). The organic layers were combined and washed with cold 1M HCl (5 x 200 ml), cold water (100 ml), cold saturated $NaHCO_3$ (2 x 200 ml), cold brine (200 ml) and dried over anhyd Na_2SO_4. The solvent was evaporated under reduced pressure to give crude dimesylate as a brown solid which was not purified further. T.L.C. analysis (silica, 60-80 light petroleum/ethyl acetate, 70:30) showed no starting material: IR (nujol) 1350, 1175 cm^{-1}.

The reduction of the crude dimesylate using lithium aluminium hydride (2.07 g, 54 mmol) in THF (120 ml) was performed according to the procedure for **15b** (see above). The crude product was recrystallized from 60-80 light petroleum to give **15c** as a white solid (3.20 g, 64%) mp 95-97 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.74 (s, 3H, CH_3), 0.75 (s, 3H, CH_3), 1.11 (m, 1H), 1.12 (d, *J* = 8.6 Hz, 1H), 1.31 (d, *J* = 8.6 Hz, 1H), 1.35 (d, *J* =10.3 Hz, 1H), 1.55 (d, *J* = 10.3 Hz, 1H), 1.66 (m, 1H), 1.70 (s, 2H), 1.83 (d, *J* = 5.7 Hz, 1H), 2.06 (d, *J* = 5.7 Hz, 1H), 2.11 (s, 1H), 2.20 (d, *J* = 5.8 Hz, 1H), 2.70 (br s, 2H), 3.24 (d, *J* = 6.7 Hz, 2H), 3.30 (d of d, *J* = 9.3, 9.3 Hz, 1H), 3.38 (d of d, *J* = 6.3, 9.3 Hz, 1H), 3.80 (s, 6H, 2 x $ArOCH_3$), 4.36 (d, *J* = 11.9 Hz, 1H), 4.41 (s, 2H), 4.44 (d, *J* = 11.9 Hz, 1H), 6.00 (br t, *J* = 1.7 Hz, 2H), 6.84-6.88 (m, 4H, ArH), 7.21-7.25 (m, 4H, ArH). Anal. Calcd. for $C_{36}H_{44}O_4$: C, 79.96; H, 8.20. Found: C, 79.98; H, 8.40.

(1α,4α,4aβ,4bα,4cβ,5α,5aβ,9aβ,10α,10aα,10bα,10cα)-6,7,8,9-Tetrachloro-1,2,3,4,4a,4b,4c,5,5a,9a,10,10a,10b,10c-tetradecahydro-trans-2,3-bis[(4-methoxyphenyl)-methoxymethyl]-4b,8b-dimethyl-1,4:5,8-dimethanobenzo[3',4']cyclobuta[1',2':3,4]cyclobuta[1,2-b]naphthalene **16:** A solution of **15c** (2.42 g, 4.48 mmol) and 2,3,4,5-tetrachlorothiophen-1,1-dioxide[14b] (1.80 g, 7.1 mmol) in toluene (10 ml), was heated at reflux for 4 d. The solvent was evaporated under reduced pressure to give a brown oil which was subjected to column chromatography (silica, 60-80 light petroleum/ethyl acetate, 70:30) to give **16** as a brown oil (3.08 g, 92%) which was not purified further: ^{1}H NMR (60 MHz, $CDCl_3$) δ 0.70 (br s, 6H, 2 x CH_3), 1.00-2.30 (m, 12H), 2.55 (br s, 2H), 2.70 (br s, 2H), 3.20-3.50 (m, 4H), 3.80 (br s, 6H, 2 x $ArOCH_3$), 4.40 (br s, 4H), 6.70-7.30 (m, 8H, ArH).

(1α,4α,4aβ,4bα,4cβ,5α,10α,10aα,10bα,10cα)-6,7,9-Triachloro-1,2,3,4,4a,4b,4c,5,10,10a,10b,10c-dodecahydro-trans-2,3-bis[(4-methoxyphenyl)-methoxymethyl]-4b,8b-dimethyl-1,4:5,8-dimethanobenzo[3',4']cyclobuta[1',2':3,4]cyclobuta[1,2-b]naphthalene **17a:** A solution of **16** (3.02 g, 4.13 mmol) and KOH (2.08 g, 37.1 mmol) in THF (10 ml) and ethanol (15 ml) was heated at reflux for 18 h. The solvent was evaporated under reduced pressure to give a thick brown oil which was washed into a separating funnel with H_2O (50 ml) and CH_2Cl_2 (50 ml), and the layers separated. The organic layer was washed with H_2O (2 x 50 ml), saturated $NaHCO_3$ (2 x 50 ml), brine (50 ml) and dried over anhyd $MgSO_4$. The solvent was evaporated under reduced pressure to give crude **17a** as a brown oil (2.18 g, 76%) which was not purified futher: ^{1}H NMR (60 MHz, $CDCl_3$) δ 0.80 (br s, 6H, 2 x CH_3), 1.00-2.30 (m, 12H), 3.10-3.40 (m, 4H), 3.50 (br s, 2H), 3.70 (br s, 6H, 2 x $ArOCH_3$), 4.40 (br s, 4H), 6.70-7.30 (m, 9H, ArH).

(1α,4α,4aβ,4bα,4cβ,5α,10α,10aα,10bα,10cα)-1,2,3,4,4a,4b,4c,5,10,10a,10b,10c-Dodecahydro-trans-2,3-bis[(4-methoxyphenyl)-methoxymethyl]-4b,8b-dimethyl-1,4:5,8-dimethanobenzo[3',4']cyclobuta[1',2':3,4]cyclobuta[1,2-b]naphthalene **17b:** Sodium metal (3.10 g, 0.135 mol) was added piecewise to a stirred, refluxing solution of **17a** (2.34 g, 3.37 mmol) in propan-2-ol (30 ml) and THF (20 ml) over 30 min. After the addition was completed, the resulting mixture was refluxed for a further 12 h then cooled to rt. The reaction was quenched by the addition of methanol (5 ml), then water (10 ml). The solvent was evaporated under reduced pressure to give an off white precipitate in an aqueous solution. Water (100 ml) was added and the resulting mixture was extracted with CH_2Cl_2 (3 x 50 ml). The organic layers were combined and washed with water (100 ml), saturated $NaHCO_3$ (2 x 100 ml) and brine (100 ml), and dried over anhyd Na_2SO_4. The solvent was evaporated under reduced pressure to give clear oil. The crude product was subjected to column chromatography (silica, 60-80 light petroleum/ethyl acetate, 60:40) and recrystallized from 60-80 light petroleum to give **17b** as a white solid (1.56 g, 78%) mp 126-128 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.85 (s, 3H, CH_3), 0.86 (s, 3H, CH_3), 1.02-1.09 (m, 1H), 1.37 (br d, J = 10.5 Hz, 1H), 1.60-1.69 (m, 2H), 1.78 (br d, J = 5.7 Hz, 1H), 1.84 (br d, J = 10.7 Hz, 1H), 1.93 (s, 2H), 2.09 (d, J = 5.6 Hz, 1H), 2.12 (s, 1H), 2.21 (br d, J = 3.8 Hz, 1H), 3.18-3.25 (m, 5H), 3.33 (d of d, J = 6.4, 9.2 Hz, 1H), 3.79 (s, 3H, $ArOCH_3$), 3.81 (s, 3H, $ArOCH_3$), 4.34 (d, J = 11.8 Hz, 1H), 4.40 (d, J = 11.8 Hz, 1H), 4.41 (s, 2H), 6.81-6.89 (m, 4H, ArH), 7.05-7.09 (m, 2H, ArH), 7.13-7.25 (m, 6H, ArH) Anal. Calcd. for $C_{40}H_{46}O_4$: C, 81.32; H, 7.85. Found: C, 81.12; H, 8.00.

(1α,4α,4aβ,4bα,4cβ,5α,10α,10aα,10bα,10cα)-1,2,3,4,4a,4b,4c,5,10,10a,10b,10c-Dodecahydro-trans-2,3-bis(hydroxymethyl)-4b,8b-dimethyl-1,4:5,8-dimethanobenzo[3',4']cyclobuta[1',2':3,4]cyclobuta[1,2-b]naphthalene **18a:** A solution of **17b** (18.2 g, 30.5 mmol) and DDQ (14.3 g, 63.0 mmol) in $CHCl_3$ (180 ml) and H_2O (20 ml) was stirred at rt for 2 h. The solvent was evaporated under reduced pressure to give a red oil. Methanol (50 ml) was added and the resulting precipitate was isolated by suction filtration. This was recrystallized from CH_2Cl_2 to give **18a** as an off white solid (7.30 g, 70%) mp 210 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.82 (s, 3H, CH_3), 0.83 (s, 3H, CH_3), 1.19 (m, 1H), 1.40 (d, J = 10.5 Hz, 1H), 1.56 (d, J = 9.5 Hz, 1H), 1.61 (d, J = 10.5 Hz, 1H), 1.73 (d, J = 9.5 Hz, 1H), 1.74 (m 1H), 1.92 (d, J = 3.5 Hz, 1H), 1.93 (s, 2H), 1.94 (d, J = 5.6 Hz, 1H), 2.07 (d, J = 5.6 Hz, 1H), 2.11 (br s, 2H, 2 x OH), 2.19 (d, J = 3.5 Hz, 1H), 3.19 (s, 2H), 3.27 (t, J = 10.0 Hz, 1H), 3.34 (t, J = 9.8 Hz, 1H), 3.60 (d of d, J = 4.6, 9.8 Hz, 1H), 3.64 (d of d, J = 5.4, 10.0 Hz, 1H), 7.04 (d of d, J = 3.3, 5.4 Hz, 2H, ArH), 7.12 (d of d, J = 3.3, 5.4 Hz, 2H, ArH). IR (Nujol) υ 3330 (OH), cm^{-1}. Anal. Calcd. for $C_{24}H_{30}O_2$: C, 82.24; H, 8.63. Found: C, 81.96; H, 8.48.

(1α,4α,4aβ,4bα,4cβ,5α,10α,10aα,10bα,10cα)-1,2,3,4,4a,4b,4c,5,10,10a,10b,10c-Dodecahydro-trans-2,3-bis(acetoxymethyl)-4b,8b-dimethyl-1,4:5,8-dimethanobenzo[3',4']cyclobuta[1',2':3,4]cyclobuta[1,2-b]naphthalene **18b:** A solution of **18a** (9.70 g, 28.4 mmol) in acetic anhydride (50 ml) and pyridine (100 ml) was stirred, under argon atmosphere, at rt for 22 h, then heated at 80 °C for 2 h. The reaction mixture was cooled to 0 °C and the excess acetic anhydride was quenched by the slow addition of methanol (30 ml) over 40 min. The solvent volume was reduced *in vacuo* to c.a. 50 ml and the resulting solution was poured onto ice (300 g) and 1M HCl (200 ml) and

extracted with CH_2Cl_2 (3 x 100 ml). The organic extracts were combined and washed with 1M HCl (6 x 200 ml), water (200 ml), saturated $NaHCO_3$ (2 x 200 ml), and dried over anhyd Na_2SO_4. The solvent was evaporated under reduced pressure to give a brown oil. The crude product was subjected to column chromatography (silica, 60-80 light petroleum/ethyl acetate, 70:30) and recrystallized from methanol to give **18b** as a white solid (9.45 g, 76%) mp 69-70 °C: ^1H NMR (300 MHz, $CDCl_3$) δ 0.87 (s, 3H, CH_3), 0.88 (s, 3H, CH_3), 1.20 (m, 1H), 1.44 (d, *J* = 9.6 Hz, 1H), 1.59 (d, *J* = 9.5 Hz, 1H), 1.67 (d, *J* = 9.6 Hz, 1H), 1.74 (m, 1H), 1.78 (d, *J* = 9.5 Hz, 1H), 1.92 (d, *J* = 5.6 Hz, 1H), 1.98 (s, 1H), 2.00 (s, 1H), 2.03 (s, 3H, OC(=O)CH_3), 2.06 (s, 3H, OC(=O)CH_3), 2.07 (s, 1H), 2.20 (s, 1H), 2.22 (s, 1H), 3.23 (s, 2H), 3.88 (d, *J* = 7.5 Hz, 2H), 3.89 (d of d, *J* = 8.8, 11.0 Hz, 1H), 4.02 (d of d, *J* = 7.2, 11.0 Hz, 1H), 7.06 (d of d, *J* = 3.4, 5.3 Hz, 2H, ArH), 7.14 (d of d, *J* = 3.4, 5.3 Hz, 2H, ArH). IR (Nujol) υ 1740 (C=O) cm^{-1}. Anal. Calcd. for $C_{28}H_{34}O_4$: C, 77.39; H, 7.89. Found: C, 77.70; H, 8.13.

(1α,4α,4aβ,4bα,4cβ,5α,10α,10aα,10bα,10cα)-1,2,3,4,4a,4b,4c,5,10,10a,10b,10c-Dodecahydro-trans-2,3-bis(acetoxymethyl)-4b,8b-dimethyl-6-nitro-1,4:5,8-dimethanobenzo[3',4']cyclobuta[1',2':3,4]cyclobuta[1,2-b]naphthalene **18c:** $Cu(NO_3)_2.2.5H_2O$ (7.00 g, 30.0 mmol) was added to an ice cold, stirred solution of **18b** (9.18 g, 21.6 mmol) in acetic anhydride (90 ml) and CH_2Cl_2 (20 ml). After 17 h, the reaction mixture was poured onto ice (300 g) and 15M NH_3 (150 ml) and left to stir for 30 min. The resulting solution was extracted with CH_2Cl_2 (3 x 100 ml). The organic layers were combined and washed with saturated $NaHCO_3$ (2 x 200 ml) and dried over anhyd Na_2SO_4. The solvent was evaporated under reduced pressure to give yellow oil. The crude product was subjected to column chromatography (silica, benzene/ethyl acetate, 90:10) and recrystallized from hexane/ CH_2Cl_2 to give a diastereometric mixture of **18c** as a white solid (9.31 g, 89%) mp 62-64 °C: ^1H NMR (300 MHz, $CDCl_3$) δ 0.88 (s, 3H, CH_3), 0.89 (s, 3H, CH_3), 1.20 (m, 1H), 1.46 (d, *J* = 10.7 Hz, 1H), 1.64-1.67 (m, 2H), 1.76 (m, 1H), 1.86 (d, *J* = 9.9 Hz, 1H), 1.94 (d, *J* = 5.9 Hz, 1H), 2.00 (s, 1H), 2.03 (s, 3H, OC(=O)CH_3), 2.06 (s, 3H, OC(=O)CH_3), 2.08 (br s, 2H), 2.21 (s, 1H), 2.22 (s, 1H), 3.35 (s, 2H), 3.88 (d, *J* = 7.7 Hz, 2H), 3.89 (m, 1H), 4.01 (m, 1H), 7.25 (m, 1H, ArH), 7.97-8.03 (m, 2H, ArH). IR (Nujol) υ 1740 (C=O), 1615, 1595, 1520 (NO_2), 1345 (NO_2), 1240 cm^{-1}. Anal. Calcd. for $C_{28}H_{33}NO_6$: C, 70.13; H, 6.96; N, 2.92. Found: C, 70.45; H, 7.24; N, 2.80.

(1α,4α,4aβ,4bα,4cβ,5α,10α,10aα,10bα,10cα)-1,2,3,4,4a,4b,4c,5,10,10a,10b,10c-Dodecahydro-6-amino-trans-2,3-bis(acetoxymethyl)-4b,8b-dimethyl-1,4:5,8-dimethanobenzo[3',4']cyclobuta[1',2':3,4]cyclobuta[1,2-b]naphthalene **18d:** A solution of **18c** (9.28 g, 19.4 mmol) in ethyl acetate (100 ml) and ethanol (25 ml) over 5% Pd/C (0.10 g), was stirred vigorously under hydrogen atmosphere until the uptake of hydrogen had ceased. The catalyst was removed by filtration and the filtrate was evaporated under reduced pressure to give a diastereometric mixture of **18d** as a brown oil (8.65 g, 99%). The crude product was used in the next reaction: ^1H NMR (300 MHz, $CDCl_3$) δ 0.84 (s, 3H, CH_3), 0.85 (s, 3H, CH_3), 1.18 (m, 1H), 1.42 (d, *J* = 10.8 Hz, 1H), 1.55 (d, *J* = 9.5 Hz, 1H), 1.65 (d, *J* = 10.5 Hz, 1H), 1.73 (d, *J* = 10.8 Hz, 1H), 1.74 (m, 1H), 1.90-1.99 (m, 4H), 2.02 (s, 3H, OC(=O)CH_3), 2.05 (s, 3H, OC(=O)CH_3), 2.18 (s, 1H), 2.20 (s, 1H), 3.00-3.40 (br s, 2H, NH_2), 3.12 (s, 2H), 3.87 (d, *J* = 7.4 Hz, 2H), 3.88 (m, 1H), 3.99 (d of d, *J* = 7.2, 11.0 Hz, 1H), 6.41 (d of d, *J* = 2.1, 7.7 Hz, 1H, ArH), 6.57 (m, 1H, ArH), 6.91 (m, 1H, ArH).

(1α,4α,4aβ,4bα,4cβ,5α,10α,10aα,10bα,10cα)-1,2,3,4,4a,4b,4c,5,10,10a,10b,10c-Dodecahydro-6-acetamido-trans-2,3-bis(acetoxymethyl)-4b,8b-dimethyl-1,4:5,8-dimethanobenzo[3',4']cyclobuta[1',2':3,4]cyclobuta[1,2-b]naphthalene **18e:** Acetic anhydride (3 ml, 32 mmol) was added to a stirred solution of **18d** (8.65 g, 19 2 mmol) in CH_2Cl_2 (50 ml) and stirring was continued for 30 m. Saturated $NaHCO_3$ (250 ml) was added and the resulting mixture was stirred for a further 2 h. The layers were separated and the aqueous layer was extracted with a further portion of CH_2Cl_2 (50 ml). The organic layers were combined and washed with brine (200 ml) and dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure to give a brown oil. The crude product was recrystallized from methanol to give a diastereometric mixture of **18e** as a white solid (8.20 g, 87%) mp 89-

92 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.85 (s, 3H, CH_3), 0.86 (s, 3H, CH_3), 1.18 (m, 1H), 1.43 (d, *J* = 10.5 Hz, 1H), 1.58 (d, *J* = 9.2 Hz, 1H), 1.65 (d, *J* = 10.5 Hz, 1H), 1.76 (d, *J* = 9.2 Hz, 1H), 1.89-2.00 (m, 4H), 2.02 (s, 3H, OC(=O)CH_3), 2.05 (s, 3H, OC(=O)CH_3), 2.14 (s, 3H, NC(=O)CH_3), 2.19 (s, 2H), 3.18 (s, 1H), 3.20 (s, 1H), 3.87 (d, *J* = 7.5 Hz ,2H), 3.88 (m, 1H), 4.00 (d of d, *J* = 7.2, 11.0 Hz, 1H), 7.02-7.06 (m, 2H, ArH), 7.21 (br s, 1H, NH), 7.42 (m, 1H, ArH). IR (Nujol) υ 1740 (C=O), 1660 (C=O), 1600, 1240 cm^{-1}. Anal. Calcd. for $C_{30}H_{37}NO_5.1/2H_2O$: C, 71.97; H, 7.65; N, 2.80. Found: C, 71.82; H, 7.84; N, 2.80.

(1α,4α,4aβ,4bα,4cβ,5α,10α,10aα,10bα,10cα)-1,2,3,4,4a,4b,4c,5,10,10a,10b,10c-Dodecahydro-6-acetamido-trans-2,3-bis(hydroxymethyl)-4b,8b-dimethyl-1,4:5,8-dimethanobenzo[3',4']cyclobuta[1',2':3,4]cyclobuta[1,2-b]naphthalene **18f:** Lithium borohydride (1.30 g, 59.7 mol) was added to a stirred solution of **18e** (7.80 g, 15.8 mmol) in dry THF (60 ml) at 0 °C. The reaction mixture was allowed to warm to rt and stirred for 156 h. 5% Acetic acid (20 ml) was added and the solvent was evaporated under reduced pressure to give a white viscous oil which was dried under high vacuum over phosphorus pentoxide. The dried solid was dissolved in dry THF (100 ml) and filtered through dry silica. The silica was washed with a further portion of dry THF (50 ml). The solutions were combined and evaporated under reduced pressure to give a diastereometric mixture of **18f** (6.00 g, 93%) as a white solid. This was dried over P_2O_5, under vacuum, then used in the next reaction: ^{1}H NMR (300 MHz, d_6-DMSO) δ 0.80 (s, 3H, CH_3), 0.81 (s, 3H, CH_3), 0.82 (m, 1H), 1.33 (d, *J* = 10.0 Hz, 1H), 1.37-1.48 (m, 3H), 1.69 (d, *J* = 9.2 Hz, 1H), 1.77 (m, 1H), 1.83 (s, 2H), 2.00 (s, 3H, NC(=O)CH_3), 2.02 (s, 1H), 2.09 (d, *J* = 3.3 Hz, 1H), 2.15 (m, 1H), 3.13-3.31 (m, 6H), 4.33 (t, *J* = 4.9 Hz, 1H, OH), 4.67 (t, *J* = 4.9 Hz, 1H, OH), 7.04 (m, 1H, ArH), 7.17 (m, 1H, ArH), 7.42 (m, 1H, ArH), 9.75 (s, 1H, NH). IR (Nujol) υ 3300 (OH), 1670 (C=O) cm^{-1}. .

(1α,4α,4aβ,4bα,4cβ,5α,10α,10aα,10bα,10cα)-1,2,3,4,4a,4b,4c,5,10,10a,10b,10c-Dodecahydro-6-acetamido-trans-2,3-bis(tosyloxymethyl)-4b,8b-dimethyl-1,4:5,8-dimethanobenzo[3',4']cyclobuta[1',2':3,4]cyclobuta[1,2-b]naphthalene **18g:** Toluene sulfonyl chloride (7.40 g, 43.0 mmol) was added to an ice cold solution of **18f** (5.70 g, 14.0 mmol) in pyridine (100 mL). The reaction mixture was left to stand at -5 °C for 36 h then poured onto ice (500 g). The resulting mixture was extracted with CH_2Cl_2 (3 x 150 mL). The extracts were combined and washed with 1M HCl (5 x 250 mL) and saturated $NaHCO_3$ (2 x 250 mL), and dried over anhyd Na_2SO_4. The solvent was evaporated under reduced pressure to give a diastereometric mixture of **18g** (8.20 g, 82%) as a pink solid. This was dried over P_2O_5, under vacuum, then used in the next reaction: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.74 (s, 3H, CH_3), 0.75 (s, 3H, CH_3), 1.02 (m, 1H), 1.25 (d, *J* = 11.0 Hz, 1H), 1.53-1.70 (m, 5H), 1.75-1.84 (m, 3H), 1.96 (d, *J* = 3.0 Hz, 1H), 2.13 (s, 1H), 2.14 (s, 3H, NC(=O)CH_3), 2.43 (s, 3H, ArCH_3), 2.45 (s, 3H, ArCH_3), 3.14 (s, 1H), 3.16 (s, 1H), 3.68-3.83 (m, 4H), 7.05-7.07 (m, 2H, ArH), 7.29-7.36 (m, 4H, ArH), 7.35 (s, 1H, NH), 7.42 (m, 1H, ArH), 7.68-7.77 (m, 4H).

(1α,4α,4aβ,4bα,4cβ,5α,10α,10aα,10bα,10cα)-1,2,3,4,4a,4b,4c,5,10,10a,10b,10c-Dodecahydro-6-acetamido-2,3-bismethylene-4b,8b-dimethyl-1,4:5,8-dimethanobenzo[3',4']cyclobuta[1',2':3,4]cyclobuta[1,2-b]naphthalene **6:** Potassium tertiary butoxide (4.20 g, 37.5 mmol) was added to a stirred solution of **18g** (8.20 g, 11.4 mmol) in dimethyl sulfoxide (100 ml). The reaction mixture was left to stir for 14 h then was poured onto ice (250 g) and brine (250 ml). The resulting precipitate was filtered, dissolved in CH_2Cl_2 (200 ml) and washed with saturated $NaHCO_3$ (2 x 200 ml). The solution was dried over anhyd Na_2SO_4 and evaporated under reduced pressure to give a brown solid. This was subjected to column chromatography (silica, ethyl acetate/benzene, 50:50) and recrystallized from CH_2Cl_2/ hexane to give **6** as a white solid (1.44 g, 34%) mp 175 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.89 (s, 6H, 2 x CH_3), 1.45 (d, *J* = 10.0 Hz, 1H), 1.58 (d, *J* = 9.8 Hz, 1H), 1.72 (d, *J* = 10.0 Hz, 2H), 1.76 (d, *J* = 9.8 Hz, 1H), 1.94 (s, 2H), 2.05 (s, 2H), 2.14 (s, 3H, NC(=O)CH_3), 2.73 (s, 2H), 3.19 (s, 1H), 3.21 (s, 1H), 4.744 (s, 1H, vinylic), 4.750 (s, 1H, vinylic), 5.08 (s, 2H, vinylic), 7.05 (br s, 2H, ArH), 7.13 (br s, 1H, NH), 7.39 (s, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 9.47 (CH_3), 24.59 (NC(=O)$\underline{C}H_3$), 35.06 (CH_2), 43.28 (CH), 43.75 (C), 43.96 (CH_2), 44.02 (CH), 45.54 (CH), 50.29 (CH), 51.23 (CH), 50.81 (CH), 100.05

(=CH_2), 100.09 (=CH_2), 113.66 (CH, aromatic), 117.09 (CH, aromatic), 120.83 (CH, aromatic), 135.32 (C, aromatic), 144.14 (C, aromatic), 148.72 (C, aromatic), 151.52 (=C), 151.54 (=C), 168.09 ($NC(=O)CH_3$). IR υ (KBr disc) 3280, 1650, 1595, 1540, 875, 820 cm^{-1}. Anal. Calcd. for $C_{26}H_{29}NO$: C, 84.06; H, 7.87; N, 3.77. Found: C, 83.86; H, 7.76; N, 3.75.

Dimethyl-(2aα,3β,8β,8aα)-2a,3,8,8a-tetrahydro-1,4-dimethoxy-5,8-methanocyclobuta[b]naphthalene-1,2-dicarboxylate **19:** The cycloaddition of **5**[23] (19.7 g, 97.4 mmol) and dimethylacetylene dicarboxylate (15.3 g, 0.108 mol) using $RuH_2CO(PPh_3)_3$[22] (0.80 g, 0.87 mmol) in benzene (150 ml) was performed according to the procedure for **14** (see above). The reaction mixture was poured into hot ethanol (400 ml) and cooled to 0 °C. The product, **19**, was isolated as a yellow solid (30.6 g, 91%) mp 168-169 °C: ^1H NMR (300 MHz, $CDCl_3$) δ 1.73 (s, 2H), 2.76 (s, 2H), 3.50 (s, 2H), 3.79 (s, 6H, 2 x $ArOCH_3$), 3.83 (s, 6H, 2 x CO_2CH_3), 6.62 (s, 2H, ArH). IR (Nujol) υ 1730 and 1705(C=O), 1630, 1250 cm^{-1}. Anal. Calcd. for $C_{19}H_{20}O_6$: C, 66.27; H, 5.85. Found: C, 66.15; H, 6.03.

Dimethyl-(1α,4α,4aβ,4bα,4cβ,5α,10α,10aβ,10bα,10cβ)-1,4,4a,4b,4c,5,10,10a,10c,10c-decahydro-6,9-dimethoxy-1,4:5,10-dimethanobenzo[3',4']cyclobuta[1',2':3,4]cyclobuta[1,2-b]naphthalene-4b,10b-dicarboxylate **20a:** The cycloaddition of **19** (30.6 g, 88.9 mmol) and quadricyclane (30 g, 0.32 mol) was performed according to the procedure for **15a** (see above). The product was crystallized with acetone to give **20a** as a white solid (33.8 g, 84%) mp 176-179 °C: ^1H NMR (300 MHz, $CDCl_3$) δ 1.14 (d, J = 10.3 Hz, 1H), 1.51 (d, J = 10.2 Hz, 1H), 1.88 (d, J = 9.7 Hz, 1H), 2.07 (s, 2H), 2.30 (s, 2H), 2.32 (d, J = 9.5 Hz, 1H), 2.86 (s, 2H), 3.56 (s, 2H,), 3.77 (s, 6H, 2 x CO_2CH_3), 3.79 (s, 6H, 2 x $ArOCH_3$), 6.04 (t, J = 1.6 Hz, 2H, vinylic), 6.60 (s, 2H, ArH). IR (Nujol) υ 1750 (C=O), 1605, 1250 cm^{-1}. Anal. Calcd for $C_{26}H_{28}O_6$: C, 71.54; H, 6.46. Found: C, 71.76; H, 6.72.

(1α,4α,4aβ,4bα,4cβ,5α,10α,10aβ,10bα,10cβ)-1,4,4a,4b,4c,5,10,10a,10c,10c-decahydro-4b,10b-bis(hydroxymethyl)-6,9-dimethoxy-1,4:5,10-dimethanobenzo[3',4']cyclobuta[1',2':3,4]cyclobuta[1,2-b]naphthalene **20b:** The reduction of **20a** (30.0 g, 68.7 mmol) using lithium aluminium hydride (11.5 g, 0.30 mol) in THF (300 ml) was performed according to the procedure for **15b** (see above). The crude product **20b** was isolated as a white solid (33.8 g, 84%): ^1H NMR (60 MHz, $CDCl_3$) δ 1.30 (d, J = 10.0 Hz, 1H), 1.45 (d, J = 11.0 Hz, 1H), 1.66 (d, J = 11.0 Hz, 1H), 1.83 (s, 2H), 1.85 (d, J = 10.0 Hz, 1H), 2.02 (s, 2H), 2.50 (br s, 2H, 2 x OH), 2.94 (s, 2H), 3.53 (s, 2H), 3.66-3.75 (br s, 4H), 3.78 (s, 6H, 2 x $ArOCH_3$), 6.03 (br s, 2H, vinylic), 6.60 (s, 2H, ArH).

(1α,4α,4aβ,4bα,4cβ,5α,10α,10aβ,10bα,10cβ)-1,4,4a,4b,4c,5,10,10a,10c,10c-decahydro-6,9-dimethoxy-4b,10b-dimethyl-1,4:5,10-dimethanobenzo[3',4']cyclobuta[1',2':3,4]cyclobuta[1,2-b]naphthalene **20c:** The bis mesylation of **20b** (24.3 g, 63.9 mmol) with methane sulfonyl chloride (19 ml, 0.25 mol) in pyridine (160 ml) was performed according to the procedure for **(D-7)** (see above). The crude dimesylate was isolated as a pink solid. This material was dried over P_2O_5 and not purified any further:

The reduction of the crude dimesylate using lithium aluminium hydride (20.0 g, 0.31 mol) in THF (400 ml) was performed according to the procedure for **15b** (see above). The crude product was recrystallized from ethanol to give **20c** as a white solid (15.2 g, 68%): ^1H NMR (300 MHz, $CDCl_3$) δ 0.90 (s, 6H, 2 x CH_3), 1.17 (d, J = 8.7 Hz, 1H), 1.38 (d, J = 8.7 Hz, 1H), 1.57 (d, J = 9.6 Hz, 1H), 1.67 (s, 2H), 1.77 (d, J = 9.4 Hz, 1H), 1.91 (s, 2H), 2.74 (s, 2H), 3.52 (s, 2H), 3.79 (s, 6H, 2 x $ArOCH_3$), 5.98 (t, J = 1.8 Hz, 2H, vinylic), 6.60 (s, 2H, ArH). Anal. Calcd. for $C_{24}H_{28}O_2$: C, 82.72; H, 8.10. Found: C, 82.44; H, 8.29.

(1α,4α,4aβ,5α,5aβ,5bα,5cβ,6α,11α,11aβ,11bα,11cβ,12α,12aβ)-1,2,3,4-Tetrachloro-1,4,4a,5,5a,5b,5c,6,11,11a,11b,11c,12,12a-tetradecahydro-5b,11b-dimethyl-7,10,15,15-tetramethoxy-1,4:5,12:6,11-trimethanonaphtho[2'',3'':3',4']cyclobuta[1',2':3,4]cyclobuta[1,2-b]naphthalene **21a:** A stirred solution of **20c** (10.24 g, 29.4 mmol) and 1,2,3,4-tetrachloro-5,5-dimethoxycyclopentadiene (8.20 g,

31.1 mmol) in xylenes (50 ml) was heated at reflux for 20 h under an argon atmosphere. The solvent was evaporated under reduced pressure to give a brown oil. The crude product was recrystallized from ethanol to give **21a** as an off white solid (17.2 g, 95%): ^{1}H NMR (60 MHz, $CDCl_3$) δ 0.90 (s, 6H, 2 x CH_3), 1.27-1.77 (m, 4H), 2.00 (br s, 4H), 2.32 (br s, 2H), 2.34 (s, 2H), 3.53 (br s, 5H, OCH_3 and 2H), 3.65 (s, 3H, OCH_3), 3.82 (s, 6H, 2 x $ArOCH_3$), 6.63 (s, 2H, ArH).

(1α,4α,4aα,5β,5aα,5bβ,5cα,6β,11β,11aα,11bβ,11cα,12β,12aα)-1,4,4a,5,5a,5b,5c,6,11,11a,11b,11c,12,12a-Tetradecahydro-5b,11b-dimethyl-7,10,15,15-tetramethoxy-1,4:5,12:6,11-trimethanonaphtho[2",3":3',4']cyclobuta[1',2':3,4]cyclobuta[1,2-b]naphthalene **21b:** The reductive dechlorination of **21a** (17.2 g, 28.1 mmol) with sodium (33.2 g, 1.44 mol) in THF (100 ml) and propan-2-ol (180 ml) was performed according to the procedure for **17b** (see above). The crude product was recrystallized from ethanol to give **21b** as a white solid (10.31 g, 77%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.79 (s, 6H, 2 x CH_3), 1.00 (d, J = 10.9 Hz, 1H), 1.49 (d, J = 9.5 Hz, 1H), 1.67 (d, J = 9.4 Hz, 1H), 1.86 (s, 2H), 1.93 (br s, 4H), 1.99 (s, 2H), 2.28 (d, J = 11.0 Hz, 1H), 3,06 (s, 3H, OCH_3), 3.13 (s, 3H, OCH_3), 3.45 (s, 2H), 3.79 (s, 6H, 2 x $ArOCH_3$), 6.03 (t, J = 2.3 Hz, 2H, vinylic), 6.58 (s, 2H, ArH).

(1α,4α,4aα,5β,5aα,5bβ,5cα,6β,11β,11aα,11bβ,11cα,12β,12aα)-1,2,3,4,4a,5,5a,5b,5c,6,11,11a,11b,11c,12,12a-Hexadecahydro-5b,11b-dimethyl-7,10,15,15-tetramethoxy-1,4:5,12:6,11-trimethanonaphtho[2",3":3',4']cyclobuta[1',2':3,4]cyclobuta[1,2-b]naphthalene **22a:** A solution of **21b** (10.31 g, 21.7 mmol) in ethyl acetate (600 mL) over 10% Pd/C (0.10 g) was stirred vigorously under hydrogen atmosphere until the uptake of hydrogen had ceased. The catalyst was removed by filtration and the solvent was evaporated under reduced pressure to give **22a** as a white solid (9.97 g, 97%) mp 213-214 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.88 (s, 6H, 2 x CH_3), 1.44 (d, J = 11.5 Hz, 1H), 1.51 (d, J = 9.2Hz, 1H), 1.60 (s, 4H), 1.70-1.73 (m, 3H), 1.87 (s, 2H), 1.91-1.93 (m, 3H), 2.01 (br s, 2H), 2.04 (s, 2H), 3.21 (s, 3H, OCH_3), 3.22 (s, 3H, OCH_3), 3.46 (s, 2H), 3.79 (s, 6H, 2 x $ArOCH_3$), 6.58 (s, 2H, ArH). Anal. Calcd. for $C_{31}H_{40}O_4$: C, 78.12; H, 8.46. Found: C, 78.01; H, 8.58.

(1α,4α,4aα,5β,5aα,5bβ,5cα,6β,11β,11aα,11bβ,11cα,12β,12aα)-1,2,3,4,4a,5,5a,5b,5c,6,11,11a,11b,11c,12,12a-Hexadecahydro-7,10-dimethoxy-5b,11b-dimethyl-1,4:5,12:6,11-trimethanonaphtho[2",3":3',4']cyclobuta[1',2':3,4]cyclobuta[1,2-b]naphthalen-15-one **22b:** **22a** (9.97 g, 20.9 mmol) was dissolved in THF (100 ml) and formic acid (80 ml), and stirred for 18 h at rt. The resulting solution was poured onto water (100 ml) and extracted with CH_2Cl_2 (2 x 100 ml). The organic layers were combined and washed with water (2 x 200 ml), saturated $NaHCO_3$ (2 x 200 ml), brine (200 ml) and dried over anhyd Na_2SO_4. The solvent was evaporated under reduced pressure to give an off white oil. The crude product was recrystallized from ethanol to give **22b** as a white solid (7.45 g, 83%) mp 218-219 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.91 (s, 6H, 2 x CH_3), 1.52 (d, J = 9.5 Hz, 1H), 1.65 (d, J = 11.8 Hz, 1H), 1.71 (br d, J = 9.4 Hz, 2H), 1.72 (d, J = 9.5 Hz, 1H), 1.78 (br s, 2H), 1.92 (s, 4H), 1.95 (s, 2H), 1.97 (br d, J = 9.4 Hz, 2H), 2.07 (d, J = 11.8 Hz, 1H), 2.26 (s, 2H), 3.48 (s, 2H), 3.78 (s, 6H, 2 x $ArOCH_3$), 6.59 (s, 2H, ArH). IR (Nujol) υ 1775 (C=O), 1635, 1265 cm^{-1}. Anal. Calcd. for $C_{29}H_{34}O_3$: C, 80.89; H, 7.96. Found: C, 81.16; H, 8.08.

(1α,4α,4aα,5β,5aα,5bβ,5cα,6β,11β,11aα,11bβ,11cα,12β,12aα)-1,2,3,4,4a,5,5a,5b,5c,6,11,11a,11b,11c,12,12a-Hexadecahydro-7,10-dihydroxy-5b,11b-dimethyl-1,4:5,12:6,11-trimethanonaphtho[2",3":3',4']cyclobuta[1',2':3,4]cyclobuta[1,2-b]naphthalen-15-one **22c:** A solution of boron tribromide (1.5 ml, 16 mmol) in dry CH_2Cl_2 (20 ml) was added dropwise to a stirring solution of **22b** (1.95 g, 4.53 mmol) in dry CH_2Cl_2 (100 ml) under argon atmosphere, at 0 °C. The reaction mixture was allowed to warm to rt and stirred for 15 h. H_2O (10 ml) was added dropwise to the reaction mixture resulting in the formation of a grey precipitate and the liberation of gas. After the addition was complete, the reaction mixture was heated at reflux for 5 min. The solvent was removed under reduced pressure and the resulting grey precipitate was dried under high vacuum. This was then dissolved in hot ethyl acetate (~500 ml) and filtered through a pad of silica. The silica was washed with a further portion of

hot ethyl acetate (500 ml). The organic solutions were combined and the volume reduced to c.a. 20 ml resulting in an off white precipitate.This was collected by suction filtration to give **22c** as an off white solid (1.46 g, 80%) mp 274 °C dec: ^{1}H NMR (300 MHz, d_6-DMSO) δ 0.85 (s, 6H, 2 x CH_3), 1.33 (d, J = 8.9 Hz, 1H), 1.57 (d, J = 11.4 Hz, 1H), 1.58 (d, J = 8.9 Hz, 1H), 1.65 (br d, J = 9.5 Hz, 2H), 1.73 (br s, 2H), 1.79 (s, 2H), 1.86 (br s, 2H), 1.89 (s, 2H), 1.91 (br d, J = 9.5 Hz, 2H), 2.06 (br d, J = 11.4 Hz, 1H), 2.24 (s, 2H), 3.35 (s, 2H), 6.29 (s, 2H, ArH), 8.31 (br s, 2H, 2 x ArOH). IR (nujol mull) 3370, 1730 cm^{-1}. IR (Nujol) υ 3380 (OH), 1735 (C=O), 1640 cm^{-1}. Anal. Calcd. for $C_{27}H_{30}O_3$: C, 80.56; H, 7.51. Found: C, 80.18; H, 7.84.

(1α,4α,4aα,5β,5aα,5bβ,5cα,6β,11β,11aα,11bβ,11cα,12β,12aα)-1,2,3,4,4a,5,5a,5b,5c,6,11,11a,11b,11c,12,12a-Hexadecahydro-7,10-dihydroxy-5b,11b-dimethyl-1,4:5,12:6,11-trimethanonaphtho[2",3":3',4']cyclobuta[1',2':3,4]cyclobuta[1,2-b]naphthalen-15-spiro-2'-(1',3'-dioxalane) **23:** A stirred solution of p-toluene sulfonic acid (100 mg, 0.58 mmol) and 1,2-ethandiol (0.4 ml, 8 mmol) in toluene (50 ml), containing a suspension of **22c** (1.71 g, 4.25 mmol), was heated to reflux under a Dean-Stark trap, under argon atmosphere, for 15 h. The reaction mixture was allowed to cool to rt. The grey suspension was removed by suction filtration, washed with water (5 x 10 ml) and dried over P_2O_5 to give **23** as a light grey powder (1.53 g, 80%) mp 200 °C dec: ^{1}H NMR (300 MHz, d_6-DMSO) δ 0.82 (s, 6H, 2 x CH_3), 1.33 (d, J = 9.1 Hz, 1H), 1.39 (d, J = 10.7 Hz, 1H), 1.54-1.60 (m, 5H), 1.66 (br s, 2H), 1.76 (m, 2H), 1.78 (s, 2H), 1.81 (s, 2H), 1.84 (d, J = 10.7 Hz, 1H), 2.04 (s, 2H), 3.34 (s, 2H), 3.78 (br s, 4H, $C(OCH_2)_2$), 6.29 (s, 2H, ArH), 8.31 (br s, 2H, 2 x ArOH). IR (Nujol) υ 3350 (OH), 1635, 1230 cm^{-1}. Anal. Calcd. for $C_{29}H_{34}O_4$: C, 78.00; H, 7.67. Found: C, 78.28; H, 7.90.

(1α,4α,4aα,5β,5aα,5bβ,5cα,6β,11β,11aα,11bβ,11cα,12β,12aα)-1,2,3,4,4a,5,5a,5b,5c,6,11,11a,11b,11c,12,12a-Hexadecahydro-7,10-dihydroxy-5b,11b-dimethyl-1,4:5,12:6,11-trimethanonaphtho[2",3":3',4']cyclobuta[1',2':3,4]cyclobuta[1,2-b]naphthalen-7,10-dione-15-spiro-2'-(1',3'-dioxalane) **4:** 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (1.0 g, 4.4 mmol) was added to a stirred suspension of **23** (1.87 g, 4.19 mmol) in CH_2Cl_2 (50 ml) and the stirring was continued for 30 min. The precipitate was removed by suction filtration and the filtrate evaporated under reduced pressure to give a brown solid. This was subjected to column chromatography (silica, 60-80 light petroleum/ ethyl acetate, 60:40) and recrystallized from ethanol to give **4** as a yellow solid (1.52 g, 84%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.83 (s, 6H, 2 x CH_3), 1.37-1.43 (m, 2H), 1.58 (t of d, J = 1.5, 9.8 Hz, 1H), 1.63-1.68 (m, 2H), 1.71-1.74 (m, 3H), 1.82 (m, 2H), 1.87 (s, 2H), 1.88 (s, 2H), 1.89 (s, 2H), 2.10 (s, 2H), 3.37 (t, J = 1.5 Hz, 2H), 3.88 (m, 4H, $C(OCH_2)_2$), 6.56 (s, 2H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 9.54 (CH_3), 22.00 (CH_2), 31.96 (CH_2), 36.82 (CH), 41.05 (CH), 41.65 (CH_2), 42.57 (CH), 43.73 (C), 45.38 (CH), 48.45 (CH), 54.13 (CH), 64.18 ($C(O\underline{C}H_2)_2$), 64.51 ($C(O\underline{C}H_2)_2$), 122.01 ($\underline{C}(OCH_2)_2$), 136.21 (=CH), 151.53 (=C), 184.32 (C=O). IR (Nujol) υ 1655 (C=O), 1575 cm^{-1}. Anal. Calcd. for $C_{29}H_{32}O_4$: C, 78.35; H, 7.25. Found: C, 78.54; H, 7.42.

(1α,4α,4aα,5β,5aα,5bβ,5cα,6β,9β,9aα,9bβ,9cα,10β,15β,15aα,15bβ,15cα,16β,19β,19aα,19bβ,19cα,20β,20aα)-1,2,3,4,4a,5,5a,5b,5c,6,9,9a,9b,9c,10,15,15a,15b,15c,16,19,19a,19b,19c,20,20a-Hexacosahydro-12-acetamido-5b,9b,15b,19b-tetramethyl-1,4:5,20:6,19:9,16:10,15-pentamethanobisnaphtho[2",3":3',4']cyclobuta[1',2':3,4]cyclobuta[1,2-b:1',2'-k]naphthacen-25-spiro-2'-(1',3'-dioxalane)-7-18-dione ***syn*-24** *and (1α,4α,4aα,5β,5aα,5bβ,5cα,6β,9α,9aβ,9bα,9cβ,10α,15α,15aβ,15bα,15cβ,16α,19β,19aα,19bβ,19cα,20β,20aα)-1,2,3,4,4a,5,5a,5b,5c,6,9,9a,9b,9c,10,15,15a,15b,15c,16,19,19a,19b,19c,20,20a-Hexacosahydro-12-acetamido-5b,9b,15b,19b-tetramethyl-1,4:5,20:6,19:9,16:10,15-pentamethanobisnaphtho[2",3":3',4']cyclobuta[1',2':3,4]cyclobuta[1,2-b:1',2'-k]naphthacen-25-spiro-2'-(1',3'-dioxalane)-7-18-dione* ***anti*-24:** A solution of **4** (1.00 g, 2.25 mmol) and **6** (0.800 g, 2.15 mmol) in THF (3 ml) over PbO_2 (5.0 g, 21 mmol) was heated at reflux, under argon atmosphere, for 5 d. The reaction was cooled to rt, the lead salts were removed by suction filtration and the solvent evaporated under reduced pressure to give a brown solid. ^{1}H NMR revealed that there were 2 products in a 72:28 ratio. The crude

product was subjected to column chromatography (alumina, benzene/ethyl acetate, 50:50) and recrystallized from CH_2Cl_2/ hexane to give a lime green solid which was a mixture of ***syn*-24** and ***anti*-24** (1.53 g, 87%) mp >270 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.85 (s, 6H, 2 x CH_3), 0.99 (s, 6H, 2 x CH_3), 1.39-1.43 (m, 2H), 1.57-1.65 (m, 7H), 1.73 (s, 2H), 1.82-1.91 (m, 13H), 1.95 (s, 2H), 2.10 (s, 2H), 2.13 (s, 3H, NC(=O)CH_3), 3.24 (s, 1H), 3.26 (s, 1H), 3.39 (s, 2H), 3.47 (s, 2H), 3.88 (br s, 4H, $C(OCH_2)_2$), 7.04 (br s, 2H, ArH), 7.13 (br s, 1H, NH), 7.39 (br s, 2H, ArH), 7.77-7.78 (m, 2H, ArH). IR (Nujol) υ 3290 (NH), 1660 (C=O), 1605 cm^{-1}. Anal. Calcd. for $C_{55}H_{57}NO_5.H_2O$: C, 79.58; H, 7.16; N, 1.68. Found: C, 79.90; H, 7.28; N, 1.60.

(1α,4α,4aα,5β,5aα,5bβ,5cα,6β,9β,9aα,9bβ,9cα,10β,15β,15aα,15bβ,15cα,16β,19β,19aα,19bβ,19cα, 20β,20aα)-1,2,3,4,4a,5,5a,5b,5c,6,9,9a,9b,9c,10,15,15a,15b,15c,16,19,19a,19b,19c,20,20a-Hexacosahydro-12-acetamido-7,18-dimethoxy-5b,9b,15b,19b-tetramethyl-1,4:5,20:6,19:9,16:10,15-pentamethanobisnaphtho[2",3":3',4']cyclobuta[1',2':3,4]cyclobuta[1,2-b:1',2'-k]naphthacen-25-spiro-2'-(1',3'-dioxalane) ***syn*-25** *and (1α,4α,4aα,5β,5aα,5bβ,5cα,6β,9α,9aβ,9bα,9cβ, 10α,15α,15aβ,15bα,15cβ,16α,19β,19aα,19bβ,19cα,20β,20aα)-1,2,3,4,4a,5,5a,5b,5c,6,9,9a,9b,9c,10,15,15a,15b,15c,16,19,19a,19b,19c,20,20a-Hexacosahydro-12-acetamido-7,18-dimethoxy-5b,9b,15b,19b-tetramethyl-1,4:5,20:6,19:9,16:10,15-pentamethanobisnaphtho[2",3":3',4']cyclobuta[1',2':3,4]cyclobuta[1,2-b:1',2'-k]naphthacen-25-spiro-2'-(1',3'-dioxalane)* ***anti*-25:** $Na_2S_2O_4$ (5.8 g, 33 mmol) was added to a stirred suspension of **(25)** (1.53 g, 1.88 mmol) in a 2 phase mixture of THF (15 mL) and water (30 mL) containing $NaHCO_3$ (1.5 g, 18 mmol) and triethyl benzylammonium chloride (TEBAC) (30 mg, 130 μmol). The reaction mixture was allowed to stir until the yellow colour had dissipated. KOH (9.1 g, 144 mmol) was added and the reaction mixture was left to stir for 15 min, resulting in a brown mixture. Dimethyl sulfate (12.5 ml, 131 mmol) was added and the reaction mixture was left to stir for 14 h. 15M NH_3 (80 mL) was added and the reaction mixture was left to stir for 30 min. Water (100 mL) was added and the resulting mixture was extracted with CH_2Cl_2 (2 x 50 mL). The organic layers were combined and washed with saturated $NaHCO_3$ (2 x 100 mL) and dried over anhyd Na_2SO_4. The solvent was evaporated under reduced pressure to give a brown solid. The products were separated by preparative thin layer chromatography (silica, benzene/ethyl acetate, 95:5) (5 developments). The higher R_f fraction was recrystallized from CH_2Cl_2/hexane to give ***anti*-25** as a white solid (0.301 g, 19%) mp 321 °C dec: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.92 (s, 6H, 2 x CH_3), 1.01 (s, 6H, 2 x CH_3), 1.46 (d, J = 10.5 Hz, 1H), 1.59-1.67 (m, 9H), 1.78-1.91 (m, 11H), 1.96 (s, 2H), 2.10 (s, 4H), 2.11 (s, 3H, NC(=O)CH_3), 3.22 (s, 1H), 3.24 (s, 1H), 3.38 (s, 2H), 3.59 (s, 2H), 3.87 (br s, 4H, $C(OCH_2)_2$), 3.94 (s, 6H, 2 x $ArOCH_3$), 7.03 (br s, 2H, ArH), 7.19 (br s, 1H, NH), 7.37 (s, 1H, ArH), 7.780 (s, 1H, ArH), 7.785 (s, 1H, ArH). IR (Nujol) υ 3300 (NH), 1660 (C=O) cm^{-1}. Anal. Calcd. for $C_{57}H_{63}NO_5.1/2H_2O$: C, 80.43; H, 7.57; N, 1.64. Found: C, 80.23; H, 7.65; N, 1.60.

The lower R_f fraction was recrystallized from CH_2Cl_2/hexane to give ***syn*-25** as a white solid (0.757 g, 48%) mp 260 °C dec: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.91 (s, 6H, 2 x CH_3), 1.01 (s, 6H, 2 x CH_3), 1.46 (d, J = 10.5 Hz, 1H), 1.59-1.67 (m, 9H), 1.78-1.88 (m, 9H), 1.91 (br d, J = 8.2 Hz, 2H), 1.96 (s, 2H), 2.06 (s, 2H), 2.08 (s, 2H), 2.11 (s, 3H, NC(=O)CH_3), 3.21 (s, 1H), 3.24 (s, 1H), 3.38 (s, 2H), 3.59 (s, 2H), 3.86 (br s, 4H, $C(OCH_2)_2$), 3.94 (s, 6H, 2 x $ArOCH_3$), 7.02 (br s, 2H, ArH), 7.14 (br s, 1H, NH), 7.37 (s, 1H, ArH), 7.774 (s, 1H, ArH), 7.780 (s, 1H, ArH). IR (Nujol) υ 3300 (NH), 1660 (C=O) cm^{-1}. Anal. Calcd. for $C_{57}H_{63}NO_5.1/2H_2O$: C, 80.43; H, 7.57; N, 1.64. Found: C, 80.47; H, 7.73; N, 1.62.

(1α,4α,4aα,5β,5aα,5bβ,5cα,6β,9α,9aβ,9bα,9cβ,10α,15α,15aβ,15bα,15cβ,16α,19β,19aα,19bβ,19cα ,20β,20aα)-1,2,3,4,4a,5,5a,5b,5c,6,9,9a,9b,9c,10,15,15a,15b,15c,16,19,19a,19b,19c,20,20a-Hexacosahydro-12-amino-7,18-dimethoxy-5b,9b,15b,19b-tetramethyl-1,4:5,20:6,19:9,16:10,15-pentamethanobisnaphtho[2",3":3',4']cyclobuta[1',2':3,4]cyclobuta[1,2-b:1',2'-k]naphthacen-25-spiro-2'-(1',3'-dioxalane) ***anti*-26:** A suspension of ***anti*-25** (0.276 g, 0.328 mmol) in a solution of KOH (5.5 g, 98 mmol) in ethanol (50 ml) and water (3 ml) was heated to reflux under argon atmosphere for 96 h. The reaction mixture was cooled to rt and the solvent was evaporated under reduced pressure to give a brown

solid. Water (50 ml) was added and the resulting suspension was extracted with CH_2Cl_2 (2 x 50 ml). The organic extracts were combined and washed with saturated $NaHCO_3$ (2 x 100 ml) and dried over anhyd Na_2SO_4. The solvent was evaporated under reduced pressure to give ***anti*-26** as a brown solid (0.259 g, 99%). The crude product was used in the next reaction: ^1H NMR (300 MHz, $CDCl_3$) δ 0.93 (s, 6H, 2 x CH_3), 1.02 (s, 6H, 2 x CH_3), 1.47 (d, J = 10.5 Hz, 1H), 1.59-1.72 (m, 9H), 1.81-1.96 (m, 11H), 1.98 (s, 2H), 2.10 (s, 4H), 3.19 (s, 1H), 3.21 (s, 1H), 3.38 (s, 2H), 3.45 (br s, 2H, NH_2), 3.59 (s, 2H), 3.87 (br s, 4H, $C(OCH_2)_2$), 3.94 (s, 6H, 2 x $ArOCH_3$), 6.35 (d of d, J = 2.1, 7.6 Hz, 1H, ArH), 6.53 (d, J = 2.1 Hz, 1H, ArH), 6.90 (d, J = 7.6 Hz, 1H, ArH), 7.78 (s, 2H, ArH).

(1α,4α,4aα,5β,5aα,5bβ,5cα,6β,9β,9aα,9bβ,9cα,10β,15β,15aα,15bβ,15cα,16β,19β,19aα,19bβ,19cα, 20β,20aα)-1,2,3,4,4a,5,5a,5b,5c,6,9,9a,9b,9c,10,15,15a,15b,15c,16,19,19a,19b,19c,20,20a-Hexacosahydro-12-amino-7,18-dimethoxy-5b,9b,15b,19b-tetramethyl-1,4:5,20:6,19:9,16:10,15-pentamethanobisnaphtho[2",3":3',4']cyclobuta[1',2':3,4]cyclobuta[1,2-b:1',2'-k]naphthacen-25-spiro-2'-(1',3'-dioxalane) **syn-26:** The hydrolysis of ***syn*-25** (0.730 g, 0.867 mmol) using KOH (5.4 g, 96 mmol) in ethanol (50 ml) and water (3 ml) was performed according to the procedure for ***anti*-26** (see above). The crude product ***syn*-26** (0.690 g, 99%) was isolated as a brown solid and not purified further: ^1H NMR (300 MHz, $CDCl_3$) δ 0.93 (s, 6H, 2 x CH_3), 1.03 (s, 6H, 2 x CH_3), 1.47 (d, J = 10.5 Hz, 1H), 1.61-1.72 (m, 9H), 1.83-1.96 (m, 11H), 1.98 (s, 2H), 2.11 (s, 4H), 3.19 (s, 1H), 3.22 (s, 1H), 3.40 (s, 2H), 3.60 (s, 2H), 3.72 (br s, 2H, NH_2), 3.86 (br s, 4H, $C(OCH_2)_2$), 3.95 (s, 6H, 2 x $ArOCH_3$), 6.36 (d of d, J = 2.1, 7.6 Hz, 1H, ArH), 6.54 (d, J = 2.1 Hz, 1H, ArH), 6.91 (d, J = 7.6 Hz, 1H, ArH), 7.78 (s, 2H, ArH).

(1α,4α,4aα,5β,5aα,5bβ,5cα,6β,9α,9aβ,9bα,9cβ,10α,15α,15aβ,15bα,15cβ,16α,19β,19aα,19bβ,19cα ,20β,20aα)-1,2,3,4,4a,5,5a,5b,5c,6,9,9a,9b,9c,10,15,15a,15b,15c,16,19,19a,19b,19c,20,20a-Hexacosahydro-7,18-dimethoxy-12-(N,N-dimethylamino)-5b,9b,15b,19b-tetramethyl-1,4:5,20:6,19:9,16:10,15-pentamethanobisnaphtho[2",3":3',4']cyclobuta[1',2':3,4]cyclobuta[1,2-b:1',2'-k]naphthacen-25-spiro-2'-(1',3'-dioxalane) **anti-27:** A slurry of ***anti*-26** (0.259 g, 0.325 mmol) and $NaBH_4$ (1.0 g, 26 mmol) in THF (8 ml) and ethanol (2 ml) was added dropwise to an ice cooled, stirring solution consisting of 35% formaldehyde (2.0 ml, 22 mmol), 3M H_2SO_4 (3 ml) and THF (4 ml). The dropping rate was controlled so that the reaction temperature remained between 15-20 °C. After the addition was complete, 2.5 M KOH (20 ml) was added and the solution allowed to stir for 30 min. Water (100 ml) was added and the resulting mixture was extracted with CH_2Cl_2 (3 x 50 ml). The organic layers were combined and washed with water (100 ml), saturated $NaHCO_3$ (100 ml), brine (100 ml) and dried over anhyd. Na_2SO_4. The solvent was evaporated under reduced pressure to give a brown solid which was subjected to column chromatography (silica, benzene/ethyl acetate, 90:10) and recrystallized from hexane to give ***anti*-27** as a white solid (0.210 g, 78%) mp >250 °C (dec): ^1H NMR (300 MHz, $CDCl_3$) δ 0.93 (s, 6H, 2 x CH_3), 1.02 (s, 6H, 2 x CH_3), 1.47 (d, J = 10.5 Hz, 1H), 1.59-1.72 (m, 9H), 1.81-1.96 (m, 11H), 1.98 (s, 2H), 2.10 (s, 4H), 2.88 (s, 6H, $N(CH_3)_2$), 3.19 (s, 1H), 3.21 (s, 1H), 3.38 (s, 2H), 3.59 (s, 2H), 3.87 (br s, 4H, $C(OCH_2)_2$), 3.94 (s, 6H, 2 x $ArOCH_3$), 6.42 (d of d, J = 2.1, 7.6 Hz, 1H, ArH), 6.68 (d, J = 2.1 Hz, 1H, ArH), 6.99 (d, J = 7.6 Hz, 1H, ArH), 7.78 (s, 2H, ArH). IR (Nujol) υ 1640, 1620, 1580 cm^{-1}. Anal. Calcd. for $C_{57}H_{65}NO_4.H_2O$: C, 80.90; H, 7.98; N, 1.65. Found: C, 80.63; H, 8.08; N, 1.64.

(1α,4α,4aα,5β,5aα,5bβ,5cα,6β,9β,9aα,9bβ,9cα,10β,15β,15aα,15bβ,15cα,16β,19β,19aα,19bβ,19cα, 20β,20aα)-1,2,3,4,4a,5,5a,5b,5c,6,9,9a,9b,9c,10,15,15a,15b,15c,16,19,19a,19b,19c,20,20a-Hexacosahydro-7,18-dimethoxy-12-(N,N-dimethylamino)-5b,9b,15b,19b-tetramethyl-1,4:5,20:6,19:9,16:10,15-pentamethanobisnaphtho[2",3":3',4']cyclobuta[1',2':3,4]cyclobuta[1,2-b:1',2'-k]naphthacen-25-spiro-2'-(1',3'-dioxalane) **syn-27:** The N,N-bis methylation of ***syn*-26** (0.690 g, 0.862 mmol) using a slurry of $NaBH_4$ (1.0 g, 26 mmol) in a solution of ***syn*-26** in THF (8 ml) and ethanol (2 ml) added to a solution of 35% formaldehyde (2 ml, 24 mmol), 3M H_2SO_4 (3 ml) and THF (4 ml) was performed according to the procedure for ***anti*-26** (see above). The crude product was subjected to column chromatography (silica, benzene/ethyl acetate, 90:10) and recrystallized from hexane to give ***syn*-27** as a white solid (0.510 g, 71%) mp >250 °C (dec): ^1H NMR (300 MHz, $CDCl_3$) δ 0.93 (s, 6H, 2 x CH_3), 1.03 (s,

6H, 2 x CH_3), 1.47 (d, J = 10.5 Hz, 1H), 1.61-1.72 (m, 9H), 1.83-1.96 (m, 11H), 1.98 (s, 2H), 2.11 (s, 4H), 2.89 (s, 6H, $N(CH_3)_2$), 3.19 (s, 1H), 3.22 (s, 1H), 3.40 (s, 2H), 3.60.(s, 2H), 3.86 (br s, 4H, $C(OCH_2)_2$), 3.95 (s, 6H, 2 x $ArOCH_3$), 6.43 (d of d, J = 2.1, 7.6 Hz, 1H, ArH), 6.69 (d, J = 2.1 Hz, 1H, ArH), 7.00 (d, J = 7.6 Hz, 1H, ArH), 7.78 (s, 2H, ArH). IR (Nujol) υ 1640, 1620, 1580 cm^{-1}. Anal. Calcd. for $C_{57}H_{65}NO_4$: C, 82.67; H, 7.91; N, 1.69. Found: C, 82.43; H, 8.20; N, 1.77.

(1α,4α,4aα,5β,5aα,5bβ,5cα,6β,9α,9aβ,9bα,9cβ,10α,15α,15aβ,15bα,15cβ,16α,19β,19aα,19bβ,19cα ,20β,20aα)-1,2,3,4,4a,5,5a,5b,5c,6,9,9a,9b,9c,10,15,15a,15b,15c,16,19,19a,19b,19c,20,20a-Hexacosahydro-7,18-dimethoxy-12-(N,N-dimethylamino)-5b,9b,15b,19b-tetramethyl-1,4:5,20:6,19:9,16:10,15-pentamethanobisnaphtho[2",3":3',4']cyclobuta[1',2':3,4]cyclobuta[1,2-b:1',2'-k]naphthacen-25-one ***anti*-28:** A stirred solution of ***anti*-27** (0.201 g, 0.243 mmol) in THF (25 ml) and formic acid (20 ml) was heated to 80° C for 12 h under argon atmosphere. The reaction mixture was cooled to rt and the solvent evaporated under reduced pressure to give a brown solid. This was dissolved in CH_2Cl_2 (50 ml) and washed with saturated $NaHCO_3$ (3 x 50 ml) and dried over anhyd Na_2SO_4. The solvent was evaporated under reduced pressure to give an off white solid. The crude product ***anti*-28** (0.170 g, 89%) was used in the next reaction: ^1H NMR (300 MHz, $CDCl_3$) δ 0.95 (s, 6H, 2 x CH_3), 1.02 (s, 6H, 2 x CH_3), 1.57-1.65 (m, 3H), 1.71 (d, J = 8.7 Hz, 2H), 1.74 (d, J = 9.8 Hz, 1H), 1.81 (s, 2H), 1.86 (d, J = 8.7 Hz, 2H), 1.88 (s, 2H), 1.93-2.00 (m, 9H), 2.06 (d, J = 9.8 Hz, 1H), 2.14 (s, 2H), 2.29 (s, 2H), 2.88 (s, 6H, $N(CH_3)_2$), 3.19 (s, 1H), 3.21 (s, 1H), 3.37 (s, 2H), 3.60 (s, 2H), 3.94 (s, 6H, 2 x $ArOCH_3$) 6.44 (d of d, J = 1.9, 8.0 Hz, 1H, ArH), 6.70 (d, J = 1.9 Hz, 1H, ArH), 7.00 (d, J = 8.0 Hz, 1H, ArH), 7.77 (s, 2H, ArH). IR (Nujol) υ 1770 (C=O), 1640, 1620, 1580 cm^{-1}.

(1α,4α,4aα,5β,5aα,5bβ,5cα,6β,9β,9aα,9bβ,9cα,10β,15β,15aα,15bβ,15cα,16β,19β,19aα,19bβ,19cα, 20β,20aα)-1,2,3,4,4a,5,5a,5b,5c,6,9,9a,9b,9c,10,15,15a,15b,15c,16,19,19a,19b,19c,20,20a-Hexacosahydro-7,18-dimethoxy-12-(N,N-dimethylamino)-5b,9b,15b,19b-tetramethyl-1,4:5,20:6,19:9,16:10,15-pentamethanobisnaphtho[2",3":3',4']cyclobuta[1',2':3,4]cyclobuta[1,2-b:1',2'-k]naphthacen-25-one ***syn*-28:** The deacetalisation of ***syn*-27** (0.492 g, 0.594 mmol) with formic acid (20 ml) in THF (25 ml) was performed according to the procedure for ***anti*-28** (see above). The crude product ***syn*-28** (0.420 g, 90%) was used in the next reaction: ^1H NMR (300 MHz, $CDCl_3$) δ 0.95 (s, 6H, 2 x CH_3), 1.02 (s, 6H, 2 x CH_3), 1.57-1.65 (m, 3H), 1.71 (d, J = 8.7 Hz, 2H), 1.74 (d, J = 9.8 Hz, 1H), 1.81 (s, 2H), 1.86 (d, J = 8.7 Hz, 2H), 1.88 (s, 2H), 1.93-2.00 (m, 9H), 2.06 (d, J = 9.8 Hz, 1H), 2.12 (s, 2H), 2.29 (s, 2H), 2.88 (s, 6H, $N(CH_3)_2$), 3.19 (s, 1H), 3.21 (s, 1H), 3.37 (s, 2H), 3.61 (s, 2H), 3.94 (s, 6H, 2 x $ArOCH_3$) 6.45 (d of d, J = 1.9, 8.0 Hz, 1H, ArH), 6.70 (d, J = 1.9 Hz, 1H, ArH), 7.00 (d, J = 8.0 Hz, 1H, ArH), 7.76 (s, 2H, ArH). IR (Nujol) υ 1770 (C=O), 1640, 1620, 1580 cm^{-1}.

[(1α,4α,4aα,5β,5aα,5bβ,5cα,6β,9α,9aβ,9bα,9cβ,10α,15α,15aβ,15bα,15cβ,16α,19β,19aα,19bβ,19c α,20β,20aα)-1,2,3,4,4a,5,5a,5b,5c,6,9,9a,9b,9c,10,15,15a,15b,15c,16,19,19a,19b,19c,20,20a-Hexacosahydro-7,18-dimethoxy-12-(N,N-dimethylamino)-5b,9b,15b,19b-tetramethyl-1,4:5,20:6,19:9,16:10,15-pentamethanobisnaphtho[2",3":3',4']cyclobuta[1',2':3,4]cyclobuta[1,2-b:1',2'-k]naphthacen-25-ylidine]-propanedinitrile ***anti*-3:** A solution of ***anti*-28** (0.170 g, 0.216 mmol), malanonitrile (0.51 g, 7.7 mmol) and NH_4OAc (0.61 g) in acetic acid (0.9 ml) and toluene (12 ml) was heated to reflux under a Dean Stark trap, under argon atmosphere, for 15 h. The reaction mixture was cooled and then poured onto saturated $NaHCO_3$ (100 ml) and the resulting mixture was extracted with CH_2Cl_2 (2 x 50 ml). The organic extracts were combined and washed with saturated $NaHCO_3$ (50 ml) and brine (50 ml), and dried over anhyd Na_2SO_4. The solvent was evaporated under reduced pressure and the crude product was subjected to column chromatography (silica, benzene/ethyl acetate, 95:5) and recrystallized from ethyl acetate/hexane to give ***anti*-3** as a white solid (67.8 mg, 38%) mp 250 °C dec: ^1H NMR (500 MHz, $CDCl_3$) δ 0.94 (s, 6H, 2 x CH_3), 1.02 (s, 6H, 2 x CH_3), 1.60 - 1.65 (m, 3H), 1.66 - 1.69 (m, 3H), 1.73 (s, 2H), 1.83 (d, J = 7.7 Hz, 1H), 1.85 (d, J = 8.8 Hz, 1H), 1.88 (s, 2H), 1.89 (s, 2H), 1.93 (d, J = 11.8 Hz, 1H), 1.97 (s, 2H), 1.97 (d, J = 8.0 Hz, 1H), 2.05 (d, J = 8.4 Hz, 2H), 2.11 (s, 2H), 2.31 (s, 2H), 2.89 (s, 6H, $N(CH_3)_2$), 2.98 (s,

2H), 3.20 (s, 1H), 3.22 (s, 1H), 3.38 (s, 2H), 3.60 (s, 2H), 3.94 (s, 6H, 2 x $ArOCH_3$), 6.44 (d of d, J = 1.9, 8.0 Hz, 1H, ArH), 6.70 (d, J = 1.9 Hz, 1H, ArH), 7.00 (d, J = 8.0 Hz, 1H, ArH), 7.77 (s, 2H, ArH). IR (KBr disc) υ 2930, 2236, 1642, 1620, 1580, 1323 cm^{-1}. Anal. Calcd. for $C_{58}H_{61}N_3O_2.H_2O$: C, 81.84; H, 7.47; N, 4.94. Found: C, 81.75; H, 7.59; N, 4.96.

[(1α,4α,4aα,5β,5aα,5bβ,5cα,6β,9β,9aα,9bβ,9cα,10β,15β,15aα,15bβ,15cα,16β,19β,19aα,19bβ,19cα,20β,20aα)-1,2,3,4,4a,5,5a,5b,5c,6,9,9a,9b,9c,10,15,15a,15b,15c,16,19,19a,19b,19c,20,20a-Hexacosahydro-7,18-dimethoxy-12-(N,N-dimethylamino)-5b,9b,15b,19b-tetramethyl-1,4:5,20:6,19:9,16:10,15-pentamethanobisnaphtho[2",3":3',4']cyclobuta[1',2':3,4]cyclobuta[1,2-b:1',2'-k]naphthacen-25-ylidine]-propanedinitrile ***syn*-3:** The condensation of ***syn*-28** (0.420 g, 0.536 mmol) and malanonitrile (0.51 g, 7.7 mmol) in a solution of NH_4OAc (0.61 g) in toluene (12 ml) and acetic acid (0.9 ml) was performed according to the procedure for ***anti*-3** (see above). The crude product was subjected to column chromatography (silica, benzene/ethyl acetate, 95:5) and recrystallized from hexane to give ***syn*-3** as a white solid (0.274 g, 61%) mp 250 °C (dec):^{1}H NMR (500 MHz, $CDCl_3$) δ 0.94 (s, 6H, 2 x CH_3), 1.02 (s, 6H, 2 x CH_3), 1.59-1.67 (m, 6H), 1.71 (s, 2H), 1.82-1.86 (m, 2H), 1.86 (s, 2H), 1.87 (s, 2H), 1.92 (d, J = 11.8 Hz, 1H), 1.94 (s, 2H), 1.97 (d, J = 9.4 Hz, 1H), 2.04 (d, J = 8.7 Hz, 2H), 2.10 (s, 2H), 2.30 (s, 2H), 2.89 (s, 6H, $N(CH_3)_2$), 2.98 (s, 2H), 3.20 (s, 1H), 3.21 (s, 1H), 3.38 (s, 2H), 3.61 (s, 2H), 3.94 (s, 6H, 2 x $ArOCH_3$), 6.42 (d of d, J = 1.9, 8.0 Hz, 1H, ArH), 6.68 (d, J = 1.9 Hz, 1H, ArH), 6.99 (d, J = 8.0 Hz, 1H, ArH), 7.77 (s, 2H). IR (KBr disc) υ 2930, 2236, 1642, 1620, 1580, 1323 cm^{-1}. Anal. Calcd. for $C_{58}H_{61}N_3O_2$: C, 83.72; H, 7.39; N, 5.05. Found: C, 83.35; H, 7.48; N, 5.08.

(1α,4α,7α,10α)-1,2,3,4,7,8,9,10-Octahydro-1,4:7,10-dimethano naphthacen-5,12-dione ***syn*-32** *and (1α,4α,7β,10β)-1,2,3,4,7,8,9,10-Octahydro-1,4:7,10-dimethanonaphthacen-5,12-dione* ***anti*-32:** The oxidative cycloaddition of **30**[24] (0.74 g, 4.25 mmol) and **31**[25] (0.51 g, 4.24 mmol) in THF (4 ml) over PbO_2 (4.30 g, 17.6 mmol) was performed according to the procedure for **(25)** (see above). ^{1}H NMR revealed that there were 2 products in a 72:28 ratio. The crude product was subjected to column chromatography (alumina, benzene) and crystallized with methanol to give lime green solid (1.02 g, 83%). A portion of the product (840 mg) was separated by fractional recrystallization (hexane) into a major component (530 mg) and a minor component (150 mg).

The major isomer ***syn*-32** mp 242 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.12-1.24 (m, 4H), 1.42 (d, J = 9.0 Hz, 1H), 1.59 (d, J = 9.0 Hz, 1H), 1.67 (br d, J = 9.0 Hz, 1H), 1.78 (br d, J = 9.0 Hz, 1H), 1.91-1.99 (m, 4H), 3.48 (br s, 2H), 3.61 (br s, 2H), 7.83 (s, 2H, ArH). Anal. Calcd. for $C_{20}H_{18}O_2$: C, 82.73; H, 6.23. Found: C, 82.54; H, 6.30.

The minor isomer ***anti*-32** mp 249 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.14-1.26 (m, 4H), 1.43 (d, J = 8.8 Hz, 1H), 1.59 (d, J = 9.0 Hz, 1H), 1.67 (br d, J = 8.8 Hz, 1H), 1.75 (br d, J = 9.0 Hz, 1H), 1.91-1.99 (m, 4H), 3.48 (br s, 2H), 3.60 (br s, 2H), 7.82 (s, 2H, ArH). Anal. Calcd. for $C_{20}H_{18}O_2$: C, 82.73; H, 6.23. Found: C, 82.66; H, 6.40.

(1α,4α,7α,10α)-1,2,3,4,7,8,9,10-Octahydro-5,12-dimethoxy-1,4:7,10-dimethanonaphthacene ***syn*-33:** The reductive methylation of ***syn*-32** (0.51 g, 2.34 mmol) using $Na_2S_2O_4$ (3.8 g, 22 mmol), Me_2SO_4, (8.0 ml, 84 mmol), TEBAC (10 mg, 44 μmol), $NaHCO_3$ (1.0 g, 12 mmol),and KOH (5.4 g, 96 mmol) in THF (10 ml) and water (20 ml) was performed according to the procedure for ***syn*-25** (see above). The crude product was subjected to column chromatography (silica, benzene) and recrystallized from hexane to give ***syn*-33** as a clear crystalline solid (0.46 g, 82%) mp 163 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.25-1.29 (m, 2H), 1.33-1.38 (m, 2H), 1.61 (d, J = 8.9 Hz, 1H), 1.63 (d, J = 8.9 Hz, 1H), 1.79 (br d, J = 8.9 Hz, 1H), 1.81 (br d, J = 8.9 Hz, 1H), 1.95-2.03 (m, 4H), 3.48 (br s, 2H), 3,75 (br s, 2H), 3.98 (s, 6H, 2 x $ArOCH_3$), 7.81 (s, 2H, ArH). Anal. Calcd. for $C_{22}H_{24}O_2$: C, 82.46; H, 7.55. Found: C, 82.74; H, 7.60.

(1α,4α,7β,10β)-1,2,3,4,7,8,9,10-Octahydro-5,12-dimethoxy-1,4:7,10-dimethanonaphthacene ***anti*-33:** The reductive methylation of ***anti*-32** (0.110 g, 0.379 mmol) using $Na_2S_2O_4$ (1.9 g, mmol), Me_2SO_4, (4 ml,

42 mmol), TEBAC (15 mg, 66 μmol), $NaHCO_3$ (0.50 g, 6.0 mmol),and KOH (2.7 g, 48 mmol) in THF (15 ml) and water (10 ml) was performed according to the procedure for ***syn*-25** (see above). The crude product was subjected to column chromatography (silica, benzene) and recrystallized from hexane to give ***anti*-33** as a clear crystalline solid (0.116 g, 95%) mp 165 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.25-1.29 (m, 2H), 1.33-1.38 (m, 2H), 1.61 (d, J = 8.9 Hz, 1H), 1.63 (d, J = 8.9 Hz, 1H), 1.77 (br d, J = 8.9 Hz, 1H), 1.79 (br d, J = 8.9 Hz, 1H), 1.95-2.03 (m, 4H), 3.48 (br s, 2H), 3,75 (br s, 2H), 3.97 (s, 6H, 2 x $ArOCH_3$), 7.81 (s, 2H, ArH). Anal. Calcd. for $C_{22}H_{24}O_2$: C, 82.46; H, 7.55. Found: C, 82.60; H, 7.61.

Crystallography.

Crystal data for ***syn*-33**. $C22H_{24}O_2$, M 320.4, monoclinic, space group C2/c, a 52.716(8), b 11.830(1), c 11.451(2)Å, β 102.384(7)°, V 6975(2)Å^3, D_c 1.22 g cm^{-3}, Z 16, μ_{Cu} 5.63 cm^{-1}. Crystal size 0.09 by 0.21 by 0.26 mm, $2\theta_{max}$ 110°, min. and max.transmission factors 0.86 and 0.94. The number of reflexions was 2944 considered observed out of 4378 unique data, with R_{merge} 0.021 for 38 pairs of equivalent 0kl reflexions . Final residuals R, R_w were 0.058, 0.081 for the observed data.

Crystal data for ***syn*-25**. $C_{57}H_{59}NO_5.(CH_3OH)_{0.5}$, M 858.2, monoclinic, space group $P2_1/c$, a 19.181(3), b 18.074(2), c 13.043(2)Å, β 96.937(9)°, V 4489(1)Å^3, D_c 1.27 g cm^{-3}, Z 4, μ_{Cu} 5.93 cm^{-1}. Crystal size 0.08 by 0.26 by 0.41 mm, $2\theta_{max}$ 110°, min. and max. transmission factors 0.86 and 0.94. The number of reflexions was 3797 considered observed out of 5625 unique data, with R_{merge} 0.019 for 137 pairs of equivalent 0kl reflexions . Final residuals R, R_w were 0.078, 0.116 for the observed data.

Structure Determination. Reflexion data were measured with an Enraf-Nonius CAD-4 diffractometer in θ/2θ scan mode using nickel filtered copper radiation (λ 1.5418Å). Data were corrected for absorption using the method of de Meulenaer and Tompa.[26] Reflexions with $I > 3\sigma(I)$ were considered observed. The structures were determined by direct phasing and Fourier methods. Hydrogen atoms were included in calculated positions and were assigned thermal parameters equal to those of the atom to which they were bonded. For ***syn*-33** positional and anisotropic thermal parameters for the non-hydrogen atoms were refined using full matrix least squares (BLOCLKS). In the case of ***syn*-25**, a close approach of the amide oxygen to a centrosymmetrically related equivalent (*ca* 1Å) was avoided by disorder of the amide group over two positions related by an approximate 2-fold rotation about the C23-N bond. Refinement was accomplished using the program RAELS,[30] with the amide modelled as two identical planar groups, and the remainder of the atoms having individual positional and anisotropic thermal parameters. Slack constraints were used to make the C23-N distances approach equality, and to keep the bond lengths within the amide reasonable. Rigid body 12-parameter TL models with centres of libration at C23 were used to describe the thermal motions of the amides.

Reflexion weights used were $1/\sigma^2(F_o)$, with $\sigma(F_o)$ being derived from $\sigma(I_o) = [\sigma^2(I_o) + (0.04I_o)^2]^{1/2}$. The weighted residual is defined as $R_w=(\Sigma w\Delta^2/\Sigma wF_o^2)^{1/2}$. Atomic scattering factors and anomalous dispersion parameters were from International Tables for X-ray Crystallography.[27] Structure solutions were by MULTAN80[28] and refinement used BLOCKLS, a local version of ORFLS[29] for ***syn*-33** and RAELS[30] for ***syn*-25**. A DEC Alpha-AXP workstation was used for calculations.

Material deposited with this journal comprises all atom and thermal parameters, interatomic distances and angles, and observed and calculated structure factors.

ACKNOWLEDGEMENTS

The support of the Australian Research Council is gratefully acknowledged.

REFERENCES AND NOTES

1. (a) Fox, M. A.; Chanon, M. Eds.; *Photoinduced Electron Transfer*; Parts A–D; Elsevier: Amsterdam, 1988. (b) Closs, G. L.; Miller, J. R. *Science* **1988**, *240*, 440. (c) Isied, S. S, in: Bolton, J. R.; Mataga, N.; McLendon, G. Eds; *Electron Transfer in Inorganic, Organic, and Biological Systems*; Advances in Chemistry Series 228, American Chemical Society: Washington, DC, 1991; ch. 15. (d) Meyer, T. J. *Acc. Chem. Res.* **1989**, *22*, 163. (e) Winkler, J. R.; Gray, H. B. *Chem. Rev.* **1992**, *92*, 369. (f) Isied, S. S.; Ogawa, M. Y.; Wishart, J. F. *Chem. Rev.* **1992**, *92*, 381. (g) Gust, D.; Moore, T. A.; Moore, A. L. *Acc. Chem. Res.* **1993**, *26*, 198.
2. (a) Gust, D.; Moore, T. A. Eds.; *Covalently Linked Donor–Acceptor Species for Mimicry of Photosynthetic Electron and Energy Transfer*; Tetrahedron, Tetrahedron Symposium–in–Print No. 39, 1989, Vol. 49. (b) Paddon-Row, M. N.; Verhoeven, J. W. *New J. Chem.* **1991**, *15*, 107. (c) Moser, C. C.; Kesker, J. M.; Warncke, K.; Farid, R. S.; Dutton, P. L. *Nature (London)* **1992**, *355*, 796. (d) Balzani, V. *Tetrahedron* **1993**, *48*, 10443. (e) Wasielewski, M. R. *Chem. Rev.* **1992**, *92*, 435.
3. Marcus, R. A.; Sutin, N. *Biochim. Biophys. Acta* **1985**, *811*, 265.
4. Wasielewski, M. R. *Photoinduced Electron Transfer*; Part D, Fox, M. A.; Chanon, M. Eds.; Elsevier: Amsterdam, 1988; ch. 1.4.
5. (a) Wasielewski, M. R.; Niemczyk, M. P.; Svec, W. A.; Pewitt, E. B. *J. Am. Chem. Soc.* **1985**, *107*, 5562. (b) Wasielewski, M. R.; Niemczyk, M. P.; Johnson, D. G.; Svec, W. A.; Minsek, D. W. *Tetrahedron* **1989**, *45*, 4785. (c) Wasielewski, M. R.; Niemczyk, M. P.; Svec, W. A.; Pewitt, E. B. *J. Am. Chem. Soc.* **1985**, *107*, 1080.
6. (a) Perkins, T. A.; Hauser, B. T.; Eyler, J. R.; Schanze, K. S. *J. Phys. Chem.* **1990**, *94*, 8745. (b) Hermant, R. M.; Bakker, N. A.; Scherer, T.; Krijnen, B.; Verhoeven, J. W. *J. Am. Chem. Soc.* **1990**, *112*, 1214. (e) Verhoeven, J. W. *Pure Appl. Chem.* **1990**, *62*, 1585. (c) Leland, B. A.; Joran, A. D.; Felker, P. M.; Zewail, A. H.; Hopfield, J. J.; Dervan, P. B. *J. Phys. Chem.* **1985**, *89*, 557. (d) Stein, C. A.; Lewis, N. A.; Seitz, G. *J. Am. Chem. Soc.* **1982**, *104*, 2596.
7. (a) Penfield, K. W.; Miller, J. R.; Paddon–Row, M. N.; Cotsaris, E.; Oliver, A. M.; Hush, N. S. *J. Am. Chem. Soc.* **1987**, *109*, 5061. (b) Hush, N. S.; Paddon–Row, M. N.; Cotsaris, E.; Oevering, H.; Verhoeven, J. W.; Heppener, M. *Chem. Phys. Lett.* **1985**, *117*, 8. (c) Warman, J. M.; de Haas, M. P.; Paddon–Row, M. N.; Cotsaris, E.; Hush, N. S.; Oevering, H.; Verhoeven, J. W. *Nature (London)* **1986**, *320*, 615. (d) Oevering, H.; Paddon–Row, M. N.; Heppener, M.; Oliver, A. M.; Cotsaris, E.; Verhoeven, J. W.; Hush, N. S. *J. Am. Chem. Soc.*, **1987**, *109*, 3258. (e) Kroon, J.; Verhoeven, J. W.; Paddon-Row, M. N.; Oliver, A. M. *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 1358.
8. Paddon–Row, M. N. *Acc. Chem. Res.* **1994**, *27*, 18.
9. (a) Gust, D.; Moore, T. A.; Makings, L. R.; Liddell, P. A.; Nemeth, G. A.; Moore, A. L. *J. Am. Chem. Soc.* **1986**, *108*, 8028. (b) Sakata, Y.; Tatemitsu, H.; Bienvenue, E.; Seta, P. *Chem. Lett.* **1988**, 1625. (c) Collin, J. P.; Guillerez, S.; Sauvage, J.–P.; Barigelletti, F.; De Cola, L.; Flamigni, L.; Balzani, V. *Inorg. Chem.* **1991**, *30*, 4230. (d) Osuka, A.; Najata, T.; Maruyama, K.; Mataga, N.; Asahi, T.; Yamazaki, I.; Nishimura, Y. *Chem. Phys. Lett.* **1991**, *185*, 88. (e) Mecklenburg, S. L.; Peek, B. M.; Erickson, B. W.; Meyer, T. J. *J. Am. Chem. Soc.* **1991**, *113*, 8540. (f) Cooley, L. F.; Larson, S. L.; Elliott, C. M.; Kelley, D. F. *J. Phys. Chem.* **1991**, *95*, 10694. (g) Larson, S. L.; Cooley, L. F.; Elliott, C. M.; Kelley, D. F. *J. Am. Chem. Soc.* **1992**, *114*, 9504. (h) Brouwer, A. M.; Mout, R. D.; Maassen, P. H.; van den Brink, M.; van Ramesdonk, H. J.; Verhoeven, J. W.; Jonker, S. A.; Warman, J. M. *Chem. Phys. Lett.* **1991**, *186*, 481. (i) Brouwer, A. M.; Eijckelhoff, C.; Willemse, R. J.; Verhoeven, J. W.; Schuddeboom, W.; Warman, J. W. *J. Am. Chem. Soc.* **1993**, *115*, 2988.
10. For a preliminary report on the synthesis of this system see: Lawson, J. M.; Paddon-Row, M. N. *J. Chem. Soc., Chem. Commun.* **1993**, 1641.
11. (a) Golka, A.; Keyte, P. J.; Paddon–Row, M. N. *Tetrahedron* **1992**, *48*, 7663. (b) Antolovich, M.; Oliver, A. M.; Paddon–Row, M. N. *J. Chem. Soc., Perkin Trans. 2* **1989**, 783. (c) Khan, S. I.; Oliver,

A. M.; Paddon–Row, M. N.; Rubin, Y. *J. Am. Chem. Soc.* **1993**, *115*, 4919. (d) Warrener, R. N.; Pitt, I. G.; Butler, D. N. *J. Chem. Soc., Chem. Commun.* **1983**, 1340. (e) Paddon–Row, M. N.; Cotsaris, E.; Patney, H. K. *Tetrahedron* **1986**, *42*, 1779.

12. Mitsudo, T.; Kokuryo, K.; Shisugi, T.; Nakagawa, Y.; Watanabe, Y.; Takegami, Y. *J. Org. Chem.* **1979**, *44*, 4492.
13. Smith, C. D. *J. Am. Chem. Soc.* **1966**, *88*, 4273.
14. (a) Paddon–Row, M. N.; Patney, H. K.; Pasupuleti, L. *Aust. J. Chem.* **1982**, *35*, 307. (b) Raasch, M. S. *J. Org. Chem.* **1980**, *45*, 856.
15. (a) D. E. James, D. E.; Stille, J. K. *J. Am. Chem. Soc.*, **1976**, *98*, 1810. (b) Stille, J. K.; Divakaruni, R. *J. Org. Chem.*, **1979**, *44*, 3474.
16. Mahaim, C.; Carrupt, P.-A.; Hagenbuch, J.-P.; Florey, A.; Vogel, P. *Helv. Chim. Acta*, **1980**, *63*, 1149.
17. Jolliffe, K.; Paddon–Row, M. N. *Tetrahedron* submitted.
18. Mehta, G.; Padma, S.; Pattabhi, V.; Pramanik, A.; Chandrasekhar, J. *J. Am. Chem. Soc.* **1990**, *112*, 3642.
19. Paquette, L. A.; Schaefer, A. G.; Blount, J. F. *J. Am. Chem. Soc.* **1983**, *105*, 2942.
20. Lists of refined coordinates and bond distances with e.s.d.'s for ***syn*–25** and ***syn*–33** have been deposited with the Editor at the Cambridge Crystallographic Centre.
21. Alder, K.; Roth, W. *Chem. Ber.* **1954**, *87*, 161.
22. Ahmad, N.; Levison, J. J.; Robinson, S. D.; Uttley, M. F. *Inorg. Synth.* **1974**, *15*, 45.
23. Chang, D. S. C.; Filipescu, N. *J. Am. Chem. Soc.* **1972**, *94*, 4170.
24. Cookson, R. C.; Hill, R. R.; Hudec, J. *J. Chem. Soc.* **1964**, 3043.
25. Butler, D. N.; Snow, R. A. *Can. J. Chem.* **1972**, *50*, 795.
26. De Meulenaer, J.; Tompa, H. *Acta Cryst.*, **1965**, *19*, 1014.
27. Ibers, J.A.; Hamilton, W.C., (Eds) '*International Tables for X-Ray Crystallography*' Vol. 4 , Kynoch Press, Birmingham, 1974.
28. Main, P. 'MULTAN80', University of York, England, 1980.
29. Busing, W.R.; Martin, K.O.; Levy, H.A., 'ORFLS', Oak Ridge National Laboratory, Tennessee, U.S.A., 1962.
30. Rae, A.D. 'RAELS'. A comprehensive Constrained Least Squares Refinement Program, University of New South Wales, 1989.

(*Received in UK* 15 *December* 1994; *revised* 31 *January* 1995; *accepted* 3 *February* 1995)