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Intramolecular Diels–Alder Reactions of Silyl Acetal-tethered Trienes

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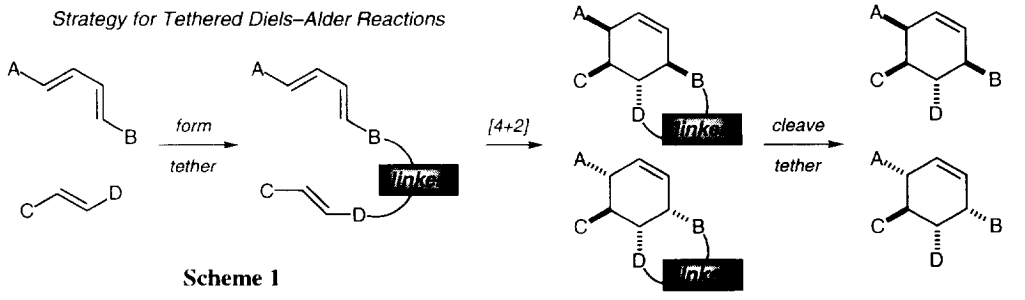
Abstract: The synthesis and intramolecular Diels–Alder reactions of a series of silyl acetal-tethered trienes **4-9** are described. The cycloadditions show complete regioselectivity, and in all but one case give exclusively cis-fused bicyclic products. The selectivities are rationalised in terms of stereoelectronic and steric effects.

INTRODUCTION

Intramolecular Diels–Alder (IMDA) reactions[1] frequently show enhanced selectivities when compared with their intermolecular counterparts. Firstly, unless the chain linking the diene and dienophile is long (typically greater than ten atoms) IMDA reactions are completely regioselective, even when there is no inherent regiochemical bias due to polarisation of the reacting π-systems. Thus, fused rather than bridged products are formed from type I trienes.[2] Secondly, the conformational preferences of the common unit linking the diene and dienophile impose stereochemical demands on the sense of their mutual approach. For example, steric interactions between diene substituents and groups in the linker may affect endo/exo selectivity, and stereocentres adjacent to or even several atoms removed from the diene or dienophile frequently exert a pronounced influence on the stereotopicity of the diene–dienophile interaction. Thirdly, intramolecular cycloadditions have a lower negative entropy of activation than comparable intermolecular variants because they are unimolecular, and this results in increased rates of reaction in many cases.

We have been pursuing a programme which seeks to harness the synthetic benefits of intramolecularity in the Diels–Alder reaction. We reasoned at the outset that temporary attachment of a diene and dienophile via a linking group, IMDA reaction of the resulting triene, and finally cleavage of the tether would give the products of a highly regio-and stereoselective in*ter*molecular transformation. The approach is depicted in Scheme 1.



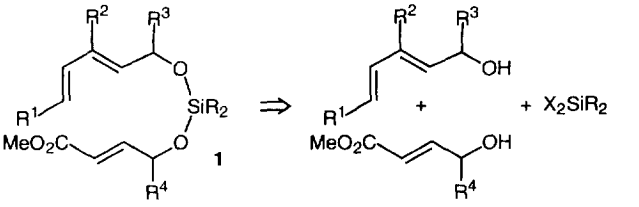
Scheme 1

There are several criteria for efficiency in this strategy. Firstly, the tether attachment and cleavage reactions must be efficient. Secondly, the nature of the linking chain must not disfavour the close approach of the diene and dienophile necessary for the cycloaddition to take place. Thirdly, the tether should be designed so as to allow the ready incorporation of stereocentres close to the reacting π-systems. We have investigated the use of benzylic and tertiary ethers,[3] diesters,[4] and carbon acetals[5] as tethering groups in Diels–Alder reactions. We now report in full[6] the results of our studies of IMDA reactions of trienes tethered with silyl acetals.[7,8]

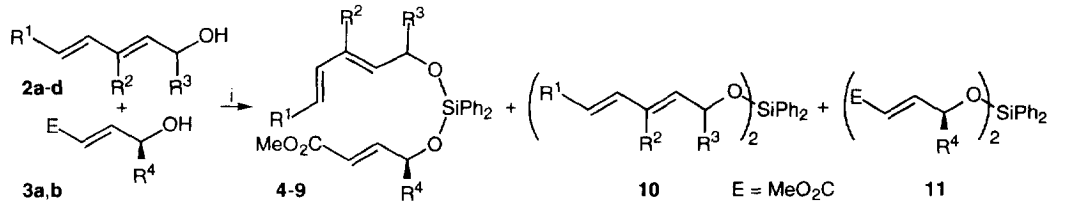
RESULTS AND DISCUSSION

Synthesis of trienes

Silyl acetals of the general structure **1** were chosen as IMDA substrates. It was felt that these materials would be readily accessible via a convergent approach involving the combination of a diene- and a dienophile-containing alcohol with a doubly electrophilic silylating reagent. This would allow the synthesis of a wide range of trienes, and would enable the assessment of the effect on reactivity and stereoselectivity of substitution at various positions in the substrates. Preliminary studies showed that trienes linked via a dimethylsilyl spacer were hydrolytically sensitive, undergoing desilylation to a significant extent during the cycloaddition reactions. The diphenylsilyl group combined ready availability of the required dichlorodiphenylsilane reagent with tolerance of the thermolysis conditions.



Trienes **4-9** were prepared according to the general procedure depicted in Scheme 2. Thus, addition of the appropriate alcohols **2** and **3** to a mixture of dichlorodiphenylsilane and triethylamine in dichloromethane gave the desired trienes, together with varying amounts of the tetraenes **10** derived from reaction of two molecules of the diene-containing alcohols with the silane, and the dienes **11** arising via similar reaction of the dienophilic alcohols (Table). For some of the trienes it was found that the best yields were obtained by sequential addition of the alcohols. The diene-alcohol **2a** was commercially available;[9] the remainder were prepared using for the most part Wittig-based strategies. Alcohol **2c** was synthesised via a reported[10] sequence involving Johnson–



Reagents and conditions: (i) Add **2** and **3** to Ph_2SiCl_2, Et_3N, CH_2Cl_2, then add petrol, filter, then Florisil® chromatography.

Scheme 2

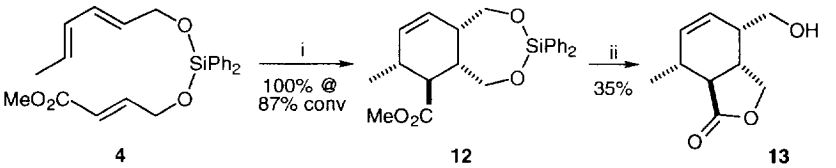
R^1	R^2	R^3	R^4	2	3	triene	% yield of triene	% yield of tetraene 10	% yield of diene 11
Me	H	H	H	**2a**	**3a**	**4**	32	10	5
Me	H	H	Me	**2a**	**3b**	**5**	47	12	7
Me	H	Me	H	**2b**	**3a**	**6**	37	18[11]	8
Me	H	Me	Me	**2b**	**3b**	**7**	26[11]	16[11]	10
H	Me	H	H	**2c**	**3a**	**8**	31	3	0
H	H	H	H	**2d**	**3a**	**9**	25	3	0

Table. Synthesis of Silyl Acetal-tethered Trienes

Claisen rearrangement of the in situ-generated ketene acetal derived from 2-butenol and triethyl orthoacetate to give ethyl 3-methyl-4-pentenoate, allylic bromination with double bond transposition, base-mediated elimination and reduction using alane. Full details are provided in the Experimental section.

Intramolecular Diels–Alder reactions

In order to establish reaction parameters for the IMDA reactions of trienes **4-9**, preliminary cyclisation reactions were carried out on degassed d_8-toluene solutions in sealed, base-washed nmr tubes prior to preparative-scale runs in similarly-treated Carius tubes. Product ratios were determined by 500 MHz ^{1}H nmr analysis of crude reaction mixtures. Prolonged thermolysis of **4** gave after evaporation of solvent an inseparable mixture comprising 87% (based on **4**) of a *single* bicyclic product, together with 13% of unreacted starting material. Filtration of the crude product mixture through Florisil®, followed by exposure to concentrated HCl in methanol gave in modest yield a single, crystalline hydroxylactone. X-Ray crystallographic analysis revealed the identity of the lactone as **13** (Figure 1), showing the structure of the cycloadduct to be **12** (Scheme 3).



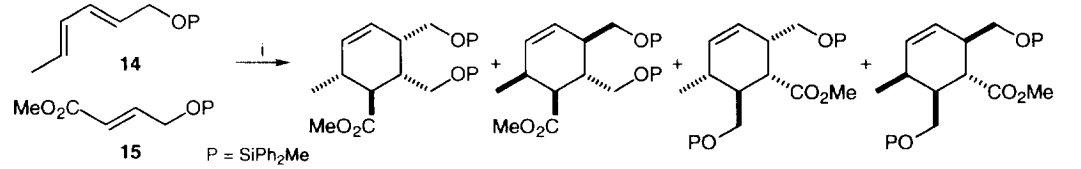
4 **12** **13**

Figure 1
X-ray structure
of **13**

Reagents and conditions: (i) PhMe (0.053M), 160°C, 168 h; Florisil® chromatography; (ii) conc. HCl, MeOH, rt, 5 h.

Scheme 3

The complete stereoselectivity of the IMDA reaction of **4** is remarkable. Lewis acid-catalysed IMDA reactions of substrates possessing enone dienophilic groups within an all-carbon tether have been reported to give good yields of cycloadducts with excellent selectivities in favour of the cis-fused isomers.[12] The stereochemical outcomes of these reactions have been explained in terms of endo transition-states, which at or below ambient temperature enjoy substantial extra stabilisation compared to the exo orientations due to secondary orbital overlap.[13] The sole formation of **12** in the reaction of **4** must proceed via an exo transition-state (see below); it is well-established that at the elevated temperatures employed for this cycloaddition endo preferences due to secondary orbital overlap become vanishingly small.[14] To discount the possibility that the Diels–Alder reaction of the diene–dienophile pairing present in **4** is inherently an exo-selective process, compounds **14** and **15** were prepared from alcohols **2a** and **3a** respectively, and their thermal cycloaddition behaviour examined. Prolonged heating of a concentrated, equimolar toluene solution of the two substrates gave a mixture of all four possible isomers (Scheme 4). This observation conclusively demonstrated the lack of regio- and stereoselectivity for the analogous intermolecular reaction, thereby vindicating the tethering strategy.



14

15 P = $SiPh_2Me$

Reagents and conditions: (i) PhMe (0.45M), 180°C, 168 h (ca. 60% conversion).

Scheme 4

The extremely high level of selectivity observed in the IMDA reaction of **4** presented ideal circumstances under which to assess the extent of asymmetric induction attainable from stereocentres positioned exo with respect to the pericyclic array. It was anticipated that the IMDA reactions of the methylated substrates **5** and **6** would be similarly exo-selective, and that analysis of the products would offer valuable insights concerning the

significant reactive conformations of this class of triene. IMDA Reaction of enantiomerically pure triene **5** was noticeably more rapid than that of **4**, and gave a single cycloadduct. Exposure of the cycloadduct to HF–acetonitrile gave in excellent overall yield a dihydroxyester **17** (Figure 2), showing the IMDA product to be **16** (Scheme 5). The formation of the monocyclic product **17** under the more weakly acidic conditions used for tether cleavage in **16** contrasts with the lactonisation of **12**, and may reflect destabilising 1,3-interactions between the hydroxymethyl substituent and the methyl group on the five-membered ring in the unobserved γ-lactone product.[6(ii)]

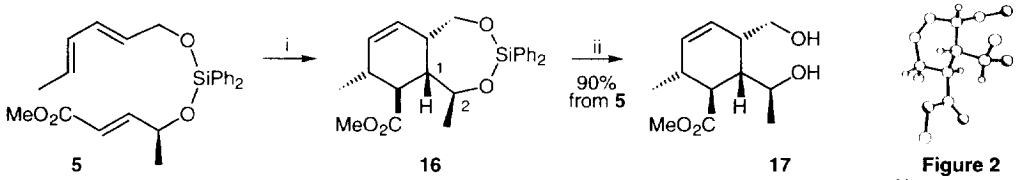
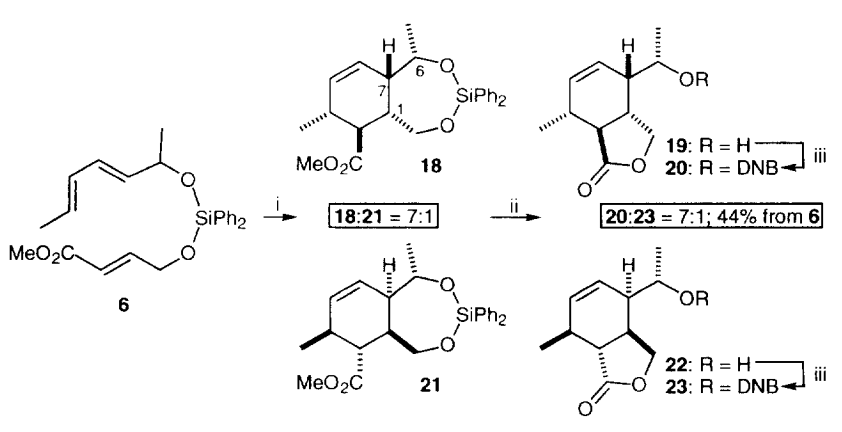


Figure 2
X-ray structure of **17**

Reagents and conditions: (i) PhMe (0.081M), 170°C, 112 h; (ii) HF (aq), MeCN, rt, 5 min.

Scheme 5

Triene **6** possesses a methyl group in an allylic position with respect to the diene. This racemic substrate showed similar reactivity to that of **5**; two cycloadducts were formed in a 7:1 ratio as shown by 500 MHz ^{1}H nmr analysis of the crude reaction product. Treatment of this crude material with HF–acetonitrile gave an inseparable 7:1 mixture of hydroxylactones, which was converted in good yield to a 7:1 mixture of 3,5-dinitrobenzoate esters which could be separated by flash chromatography. X-Ray crystallographic analysis enabled assignment of the esters as **20** and **23**, from which the structures **18**, **19**, **21** and **22** were inferred (Scheme 6, Figure 3, 4).



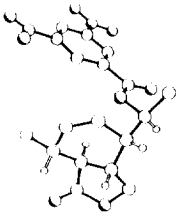


Figure 3
X-ray structure of **20**

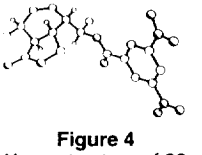
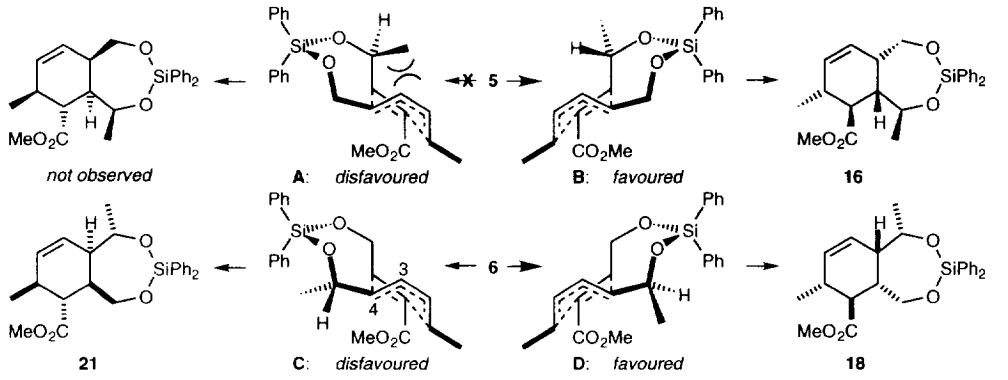


Figure 4
X-ray structure of **23**

Reagents and conditions: (i) PhMe (0.158M), 170°C, 112 h; (ii) HF (aq), MeCN, rt, 16 h; (iii) 3,5-$(O_2N)_2C_6H_3COCl$, Et_3N, DMAP, CH_2Cl_2, rt, 10 min.

Scheme 6

Inspection of the structures of the products of the IMDA reactions of **5** and **6** reveals an important difference. Compound **16**, the sole product formed from triene **5** has a syn relationship between H-1 and the C-2 methyl group which was allylic with respect to the dienophile unit in the substrate. In the reaction of **6**, the C-6 methyl group in the major cycloadduct **18** is oriented anti with respect to the proximal ring-junction hydrogen atom, H-7. Together with the complete cis-selectivity of all the the cycloadditions, this suggests that

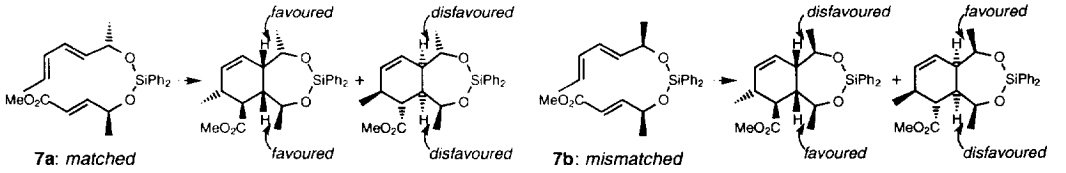


Scheme 7

in the most favourable IMDA transition-states the local conformations of the diene and dienophile are different. We propose the reacting geometries depicted in Scheme 7. The reactive conformations **A**-**D** are such that whilst the dienophile C=C bond is anti to the allylic C–O bond (the 'outside' conformation), in the 1,3-diene the C3-C4 bond is syn to the corresponding carbon–oxygen linkage (the 'inside' conformation). A consequence of this is that for **5** the favoured transition-state is **B**, because in the alternative **A** there would be serious non-bonded interactions between the allylic methyl group and the exo-oriented diene. For the isomer **6**, conformer **C** is disfavoured because of allylic methyl–dienophile interactions, but the effect is smaller because the methyl group is necessarily further away from the dienophilic moiety. Whilst lower than that induced by dienophile allylic substitution the latter selectivity is especially noteworthy. Formation of **18** (transition-state **D**) corresponds to attack of the dienophile on the *re* -face of C-4 of the *S*-configured diene, and as such is *unlike* attack.[15] Franck and co-workers demonstrated by analysing some twenty intermolecular Diels–Alder reactions of open-chain dienes possessing an allylic heteroatomic substituent that the normal preference was for *like* attack.[16] This contrast shows in the present work that intramolecularity additionally enables the generation of stereochemical motifs not accessible via the analogous intermolecular processes.

The analysis presented above raises the question of why the 'inside' and 'outside' conformations described above are favoured to such an extent, and why the IMDA reactions of this class of trienes are completely cis-selective. *Ab initio* studies[17] have suggested that during electrophilic attack on an allylic double bond, an ether linkage prefers the 'inside' conformation. This is because in this arrangement overlap between the diene HOMO and the allylic σ^*_{C-O} is minimised, thereby minimising the extent of electron withdrawal from the diene and maximising its nucleophilicity. Correspondingly, the 'outside' conformation is preferred for the dienophile allylic ether linkage, since electron withdrawal and therefore electrophilicity is maximised. Thus, the conformations leading to the observed cis-fused products are the most reactive ones, combining optimum diene nucleophilicity with maximum dienophile electron-deficiency.

The results described above demonstrate that the allylic methyl group in the silyl acetal-tethered triene **5** directs the approach of the diene with complete diastereofacial selectivity. In the isomeric substrate **6** the analogous methyl substituent induces selectivity to the extent of 7:1. It occurred to us that the trienes **7** offered the opportunity to study matching and mismatching effects. On the basis of the above results, diastereomer **7a** would be a matched substrate, and **7b** mismatched (Scheme 8).



Scheme 8

Enantiomerically pure trienes **7a** and **7b** had been synthesised as an inseparable mixture. Subjection of the mixture to the standard thermolysis procedure resulted in relatively rapid IMDA reaction to give a ca. 12:12:1 mixture of three bicyclic compounds as shown by high-field ^{1}H nmr analysis of the crude product. The observed increase in IMDA reactivity of increasingly substituted substrates presumably is a consequence of steric effects, which disfavour the unreactive distal triene conformations.[18] Treatment of the crude mixture with HF–acetonitrile as carried out previously gave a single, separable hydroxylactone together with an inseparable mixture of two dihydroxyesters. Subsequent exposure of this mixture to catalytic camphor-10-sulfonic acid in dichloromethane effected the conversion of one of the components to the hydroxylactone, enabling the separation of isomerically pure cycloadduct derivatives. X-Ray crystallographic analysis showed the structure of the lactone to be **25**, and that of the diol to be **27**, and therefore that the two major cycloadducts had the structures **24** and **26** (Scheme 9, Figure 5, 6). That matched triene **7a** gave only **24** was expected; in product

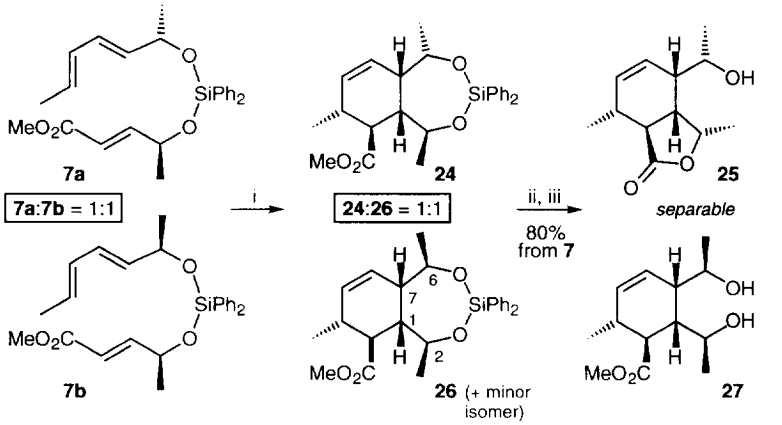


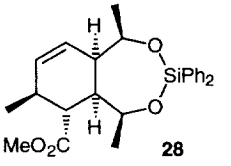
Figure 5
X-ray structure
of **25**

Figure 6
X-ray structure
of **27**

Reagents and conditions: (i) PhMe (0.1M), 172°C, 24 h; (ii) HF (aq), MeCN, rt, 1 h; (iii) camphor-10-sulfonic acid, CH_2Cl_2, rt, 13 h.

Scheme 9

26 however, the C1–C2 stereochemical relationship is inherently favoured as evidenced by the stereochemical outcome of the reaction of **5**, whereas the C6-C7 stereochemistry was shown to be unfavoured in the reaction of the singly-methylated triene **6**. This strongly suggests that the dienophile allylic methyl substituent exerts a more powerful stereodirecting effect than the diene methyl group, as would be expected on the basis of the selectivities of the IMDA reactions of **5** and **6**. We have not identified the minor cycloadduct formed in the reaction of **7b**, but we assign the structure **28** on the grounds that it arises from the matched$_{\text{diene}}$–mismatched$_{\text{dienophile}}$ pairing.



The final part of our study of silyl acetal-tethered IMDA reactions was concerned with attempting to evaluate the magnitude of the observed cis-selectivity. It was decided to design a substrate whose substitution pattern would be such as to promote the formation of a trans-fused product. Triene **8** was an attractive prospect, since it is well-established that the IMDA reactions of trienes possessing C-3 substituents show greatly enhanced trans-selectivities compared with the C-3 unsubstituted analogues, especially in the case of bicyclo[4.4.0] products.[19] Compound **8** was additionally suitable in that the alcohol precursor **2c** would be available by reduction of the known ester ethyl 3-methyl-2,4-pentadienoate.[10] Because of the absence of a terminal diene substituent in **8**, the unsubstituted triene **9** was synthesised for use in a control experiment to ascertain whether any observed change in selectivity was a consequence of this structural difference.

Thermolysis of **8** gave two cycloadducts **29** and **30** in a 1:1 ratio; the crude product was treated with HF–acetonitrile in the usual way to give directly an inseparable mixture of diastereomeric hydroxylactones **31** and

32 in excellent overall yield. IMDA Reaction of the control substrate **9** gave a single cycloadduct **33**. On sequential treatment with HF–acetonitrile and trifluoroacetic acid–dichloromethane this was converted via the dihydroxyester into the hydroxylactone **34**, whose structure was confirmed by X-ray crystallography (Scheme 10, Figure 7).

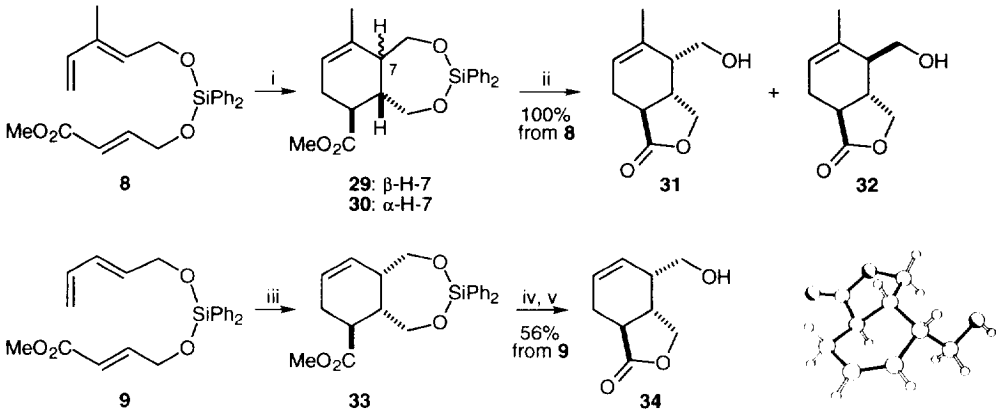


Figure 7
X-ray structure
of **34**

Reagents and conditions: (i) PhMe (0.070M), 165°C, 85 h; (ii) HF (aq), MeCN, rt, 1.5 h; (iii) PhMe (0.056M), 165°C, 36 h; (iv) HF (aq), MeCN, rt, 30 min; (v) CF_3CO_2H, CH_2Cl_2, rt, 5 h.

Scheme 10

The complete cis-selectivity of the IMDA reaction of **9** precludes the possibility that the non-selective reaction of **8** is a consequence of the absence of the diene C-1 methyl substituent. We rationalise the lack of selectivity in the cycloaddition of **8** in terms of the inherent cis-selectivity described above competing with repulsive interactions between the diene C-3 methyl group and the dienophile methylene unit (see Scheme 7). This experiment also ruled out the notion that steric repulsion between the diene C-3 hydrogen and the diene methylene unit in the putative trans transition-state is responsible for the cis-selectivity, since any such effect would be increased in the case of triene **8**.

CONCLUSIONS

In conclusion, tethering of dienes and dienophiles via a silyl acetal linkage is an extremely effective strategy for the imposition of profound regio-and stereochemical directing effects on [4+2] cycloaddition reactions. In addition to complete cis-selectivity, complete asymmetric induction was observed for certain substrates possessing methyl substituents next to the diene or dienophile groups. Cleavage of the tethers post-cycloaddition provided in good overall yields the highly oxygenated products of formal intermolecular cycloaddition reactions.

ACKNOWLEDGEMENTS

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EXPERIMENTAL

General procedures

^{1}H nmr spectra were recorded in $CDCl_3$ on either Bruker AM-500, Jeol GX-270Q or Bruker WM-250 spectrometers, using residual isotopic solvent ($CHCl_3$, δ_H 7.26 ppm) as internal reference. Infrared spectra were recorded on a Perkin-Elmer 881 spectrophotometer. Mass spectra were obtained using Jeol SX-102, VG-7070B, VG 12-253 and VG ZAB-E instruments. Elemental combustion analyses were performed in the Imperial College Chemistry Department microanalytical laboratory. Melting points were measured on a Reichert hot stage apparatus and are uncorrected. Optical rotation measurements were carried out using an Optical Activity AA-100 polarimeter. Air- and moisture-sensitive reagents were transferred via syringe or cannula, and reactions involving these materials were carried out in oven-dried flasks under a positive pressure of argon or nitrogen. Liquid reagents were transferred via syringe. Chromatography refers to column chromatography on Merck Kieselgel 60 (230-400 mesh) or Matrex Silica 60 (35-70 micron) under pressure unless otherwise stated. Tlc refers to analytical thin-layer chromatography performed using pre-coated glass-backed plates (Merck Kieselgel 60 F_{254}) and visualised with ultraviolet light, iodine and acidic ammonium molybdate(IV), vanillin or potassium permanganate solutions as appropriate. Petrol refers to redistilled 40°–60° petroleum ether, and ether to diethyl ether. Ether and tetrahydrofuran were distilled from sodium–benzophenone ketyl, dichloromethane from phosphorus pentoxide, and toluene from sodium. Other solvents and reagents were purified according to standard procedures.[20]

Preparation of trienes

Preparation of (±)-(*E*,*E*)-3,5-heptadien-2-ol (2b).

To a solution of (*E*,*E*)-2,4-hexadienoic acid[9] (3.03 g, 27.022 mmol, 1.0 eq) in THF (300 ml) stirring at 0°C, was added methyllithium (38.60 ml of a 1.4M solution in ether, 54.04 mmol, 2.0 eq). After stirring for 10 min examination by tlc showed that all of the acid had been converted to ketone. The reaction was quenched by pouring the mixture into a rapidly stirring iced solution of acetic acid (100 ml) and water (250 ml). This was extracted with ether (4 x 300 ml), and washed with water (250 ml), saturated aqueous sodium hydrogencarbonate (500 ml), aqueous sodium hydroxide (500 ml, 0.1 M), water (250 ml) and brine (250 ml). The combined organic layers were then dried ($MgSO_4$) and the volume of the solvent reduced by approximately half by evaporation. The solution was then cooled to -78°C and DIBAL-H (54.0 ml of a 1M solution in CH_2Cl_2, 54.0 mmol, 2.0 eq) was added via cannula. Examination by tlc showed that the reaction was incomplete, so additional DIBAL-H (54.0 ml of a 1M solution in CH_2Cl_2, 54.0 mmol, 2.0 eq) was added. The solution was stirred at -78°C for 1 h, and was then worked up by cautious addition of water (108 ml) and slow warming to room temperature. Removal of the resultant white precipitate by filtration, drying ($MgSO_4$) and removal of the solvents by evaporation with cooling of the flask afforded a pale yellow oil. Purification by chromatography on silica gel (20% ether–petrol) yielded the desired secondary alcohol **2b** (2.216 g, 73%) as a colourless oil; υ_{max} (film) 3371, 2972, 2921, 2358, 1666, 1538, 1452, 1373, 1136, 1061, 989, 945, 862 cm^{-1}; δ_H (270 MHz) 6.23-5.98 (2H, m, H-4, H-5), 5.79-5.56 (2H, m, H-3, H-6), 4.34 (1H, quint, J 6.0 Hz, H-2), 1.75 (3H, d, J 6.5 Hz, H-7), 1.28 (3H, d, J 6.0 Hz, H-1); *m/z* (EI) 112 (M^+), 97 (M^+-CH_3), 94 (M^+-H_2O), 84 (M^+-CH_3CH), 79, 69, 67, 58, 55, 43.

Preparation of ethyl 3-methyl-4-pentenoate.[10]

A solution of 2-butenol[9] (5.0 g, 69 mmol) and propionic acid (308 mg, 4.2 mmol) in triethyl orthoacetate (64 ml) was heated at 140°C with distillative removal of EtOH for 1.5 h. The mixture was allowed to cool to room temperature. Aqueous oxalic acid (50 ml of a 1M solution) was added carefully and stirred for 2 h at rt and the mixture then extracted with ether (3 x 40 ml). The combined extracts were washed with aqueous $NaHCO_3$ (2 x 50 ml) and water (2 x 50 ml), dried ($MgSO_4$) and concentrated under reduced pressure to give a

pale yellow oil. This oil was purified by distillation under reduced pressure to give ethyl 3-methyl-4-pentenoate (6.71 g, 68%) as a colourless oil, bp_{15} 45°C; υ_{max} (film) 3082, 2979, 2936, 1738, 1641, 1461, 1419, 1372, 1278, 1247, 1184, 1149, 1098, 1032, 916 cm^{-1}; δ_H (270 MHz) 5.75 (1H, ddd, J 17.0, 10.0, 7.0 Hz, H-4), 5.01 (1H, d, J 17.0 Hz, H-5_{trans}), 4.95 (1H, J 7.0 Hz, H-5_{cis}), 4.12 (2H, q, J 7.0 Hz, OCH_2CH_3), 2.73-2.59 (1H, m, H-3), 2.39-2.16 (2H, m, H-2), 1.24 (3H, t, J 7.0 Hz, OCH_2CH_3), 1.05 (3H, d, J 7.0 Hz, $CHCH_3$); *m/z* (EI) 142 (M^+), 127 (M^+-Me), 114 (MH^+-Et), 96 (M^+-EtOH), 69 (M^+ -CO_2Et), 55, 41, 29.

Preparation of ethyl 5-bromo-3-methyl-3-pentenoate.[10]

A mixture of ethyl 3-methyl-4-pentenoate (6.0 g, 42.2 mmol, 1 eq), *N*-bromosuccinimide (7.5 g, 42.2 mmol, 1 eq) and AIBN (200 mg) in CCl_4 (140 ml) was heated under reflux for 2 h under N_2. The resulting mixture was cooled to 0°C and filtered, washing the residue with ice-cold CCl_4. The filtrate was washed with aqueous $Na_2S_2O_3$ (100 ml of a 1M solution) and water (100 ml), dried ($MgSO_4$) and concentrated under reduced pressure to give the crude product. This was purified by chromatography (10% ether–petrol) to give a 4:3 mixture of geometric isomers of ethyl 5-bromo-3-methyl-3-pentenoate (6.06 g, 65%) as a pale yellow oil; υ_{max} (film) 2981, 2940, 1736, 1447, 1368, 1319, 1299, 1257, 1235, 1203,1174, 1162, 1033 cm^{-1}; δ_H (270 MHz) 5.68 (1H, m, H-4), 4.14 (2H, q, J 7.0 Hz, OCH_2CH_3), 4.00 (2H, d, J 8.0 Hz, H-5), 3.12 and 3.04 (total 2H, both s, H-2), 1.86 and 1.80 (total 3H, both d, J 1.0 Hz, vinylic Me), 1.26 (3H, t, J 7.0 Hz, OCH_2CH_3); *m/z* (EI) 222, 220 (M^+), 194, 192 (MH^+-Et), 141 (M^+-Br), 113, 71, 67, 41, 29.

Preparation of ethyl 3-methyl-2,4-pentadienoate.[10]

Ethyl 5-bromo-3-methyl-3-pentenoate (6.0 g, 27.1 mmol, 1 eq) was added to a solution of NaOEt (2.76 g, 40.7 mmol, 1.5 eq) in EtOH (90 ml) under N_2. The resulting solution was allowed to stir for 2 h, poured into ice-cold water and extracted with CH_2Cl_2 (3 x 50 ml). The combined organic extracts were washed with water (2 x 50 ml), dried ($MgSO_4$) and concentrated under reduced pressure. The resulting oil was purified by chromatography (5% EtOAc–petrol), to give a 2:1 *E*:*Z* mixture of ethyl 3-methyl-2,4-pentadienoate (2.69 g, 71%) as a colourless oil; υ_{max} (film) 2982, 2907, 1713, 1633, 1604, 1369, 1353, 1274, 1247, 1235, 1159, 1071, 1036, 923, 872 cm^{-1}; δ_H (270 MHz): (major, trans-isomer) 6.43 (1H, dd, J 18.0, 10.0 Hz, H-4), 5.75 (1H, s, H-2), 5.53 (1H, d, J 18.0 Hz, H-5_{trans}), 5.32 (1H, d, J 10.0 Hz, H-5_{cis}), 4.12 (2H, q, J 7.0 Hz, OCH_2CH_3), 2.23 (3H, d, J 1.0 Hz, vinylic Me), 1.22 (3H, t, J 7.0 Hz, OCH_2CH_3); (minor, cis-isomer) 7.89 (1H, dd, J 18.0, 10.0 Hz, H-4), 5.68 (1H, s, H-2), 5.51 (1H, br d, J 18.0 Hz, H-5_{trans}), 5.43 (1H, br d, J 10.0 Hz, H-5_{cis}), 4.12 (2H, q, J 7.0 Hz, OCH_2CH_3), 1.96 (3H, d, J 1.0 Hz, vinylic Me), 1.22 (3H, d, J 7.0 Hz, OCH_2CH_3); *m/z* (EI) 140 (M^+), 111 (M^+-Et), 95 (M^+-OEt), 67, 41.

Preparation of (*E*)-3-methyl-2,4-pentadienol (2c).

To a solution of ethyl 3-methyl-2,4-pentadienoate (5.7 g, 40.7 mmol, 1 eq) in THF (40 ml) at 0°C was added a solution of AlH_3 (101.7 ml of a 0.5M solution in THF, 1.25 eq) over a period of 15 min. The mixture was allowed to stir for a further 30 min when tlc showed complete disappearance of starting material. Water (3 ml) was added cautiously, followed by NaOH (3 ml of a 3M aqueous solution), and water (7.5 ml). The layers were separated and the aqueous phase salted out with solid Na_2CO_3 and extracted with ether (3 x 10 ml). The combined organic layers were washed with water (100 ml), brine (100 ml), dried ($MgSO_4$) and evaporated to give a pale yellow oil. This was purified by chromatography (30% ether–petrol), to give the desired alcohols (2.47 g, 63%) as a colourless oil. The alcohols were dissolved in CH_2Cl_2 (35 ml) and the solution added to a solution of 3,5-dinitrobenzoyl chloride (6.4 g, 27.8 mmol, 1.1 eq) and DMAP (61 mg, 0.02 eq) in CH_2Cl_2 (20 ml). To the mixture was added Et_3N (5.27 ml, 37.8 mmol, 1.5 eq) dropwise over 10 min, giving an orange solution. After 15 min tlc indicated complete reaction. The mixture was poured into saturated aqueous $NaHCO_3$ (50 ml), the layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 x 15 ml).

The combined organic layers were washed with water (100 ml), dried ($MgSO_4$), and concentrated under reduced pressure to leave an orange oil. The oil was purified by chromatography (10% ether–petrol), to give the benzoate ester as a pale yellow solid. Fractional recrystallisation (EtOAc–petrol) gave the desired isomerically pure ester (0.92 g, 17%), as pale yellow crystals, mp 45°C. A sample (807 mg, 2.76 mmol, 1 eq) was dissolved in THF (9.2 ml) and treated with KOH (16 ml of a 10% aqueous solution, 10 eq), to give a deep red solution. The mixture was allowed to stir for 10 min and then poured into water (20 ml), the layers were separated and the aqueous phase was extracted with ether (3 x 10 ml). The combined organic layers were dried ($MgSO_4$) and concentrated under reduced pressure to give a pale red oil. This was purified by chromatography (20% ether–petrol) to give the desired dienol **2c** (213 mg, 82%) as a colourless oil; υ_{max} (film) 3338, 3091, 2982, 2926, 2872, 1608, 1441, 1415, 1386, 1328, 1301, 1246, 1064, 993, 900 cm^{-1}; δ_H (270 MHz) 6.39 (1H, dd, J 17.5, 10.0 Hz, H-4), 5.67 (1H, tq, J 7.0, 1.0 Hz, H-2), 5.21 (1H, d, J 17.5 Hz, H-5_{trans}), 5.06 (1H, d, J 10.0 Hz, H-5_{cis}), 4.30 (2H, d, J 7.0 Hz, H-1), 1.79 (3H, br s, vinylic Me), 1.44 (1H, br s, OH); *m/z* (EI) 98 (M^+), 83 (M^+-Me), 79, 69, 55 (Found: (M^+), 98.0729. $C_6H_{10}O$ requires (M^+), 98.0732).

Preparation of (*E*)-1-(*tert*-butyldiphenylsilyloxy)-2,4-pentadiene.

To a slurry of allyltriphenylphosphonium bromide (24.0 g, 62.63 mmol, 1.5 eq) in THF (134 ml) at 0°C was added *n*-BuLi (23.38 ml of 2.5M solution in hexanes, 58.45 mmol, 1.4 eq) to give a dark red solution. The mixture was allowed to stir for 10 min and then stirred for a further 30 min at room temperature, followed by cooling to -78°C. 2-(*tert*-Butyldiphenylsilyloxy)ethanal[21] (12.44 g, 41.75 mmol, 1 eq) in THF (25 ml) was added via cannula and the solution stirred for 10 min and then allowed to warm to room temperature. The solution was poured into saturated aqueous NH_4Cl (150 ml), extracted with ether (3 x 75 ml), and the combined organic phases were washed with water (200 ml), brine (200 ml) and dried ($MgSO_4$). Solvent was evaporated under reduced pressure and the resulting oil was purified by chromatography (10% ether–petrol) to yield a 6:1 mixture of the *Z*- and *E*-dienes (8.05 g, 63%) as a colourless oil. A solution of this mixture (7.55 g, 23.45 mmol) in CH_2Cl_2 (100 ml) was stirred for 3 h with I_2 (20 crystals) in sunlight. The solution was poured into saturated aqueous $Na_2S_2O_3$ (100 ml), and extracted with CH_2Cl_2 (2 x 30 ml). The combined organic layers were dried ($MgSO_4$) and concentrated under reduced pressure, and the resulting oil purified by chromatography (5% ether–petrol) to yield the desired *diene* (6.95 g, 92%) as a colourless oil; υ_{max} (film) 3071, 3048, 2958, 2931, 2892, 2857, 1472, 1428, 1112, 1056, 1005, 823, 740, 703, 612 cm^{-1}; δ_H (270 MHz) 7.76-7.63 (4H, m, ortho C_6H_5), 7.48-7.32 (6H, m, meta and para C_6H_5), 6.34 (2H, m, H-3 and H-4), 5.78 (1H, dt, J 14.5, 6.5 Hz, H-2), 5.17 (1H, d, J 15.0 Hz, H-5_{trans}), 5.04 (1H, d, J 9.0 Hz, H-5_{cis}), 4.23 (2H, d, J 6.5 Hz), 1.04 (9H, s, *t*-Bu); *m/z* (CI) 340 ($M+NH_4^+$), 323 (MH^+), 282 ($CHCH_2OTBDPS^+$), 265 (M^+-*t*-Bu), 196, 187, 179 ($HSi(O)(t\text{-}Bu)(Ph)^+$), 155, 138 ($CH_2CHCHCHCH_2OSiCCH_3^+$), 105 ($SiPh^+$), 84 ($CH_2CHCHCHCH_2OH^+$), 67 (Found: ($M+NH_4^+$), 340.2102. $C_{21}H_{26}OSi$ requires ($M+NH_4^+$), 340.2097).

Preparation of (*E*)-2,4-pentadienol (2d).

To a solution of (*E*)-1-(*tert*-butyldiphenylsilyloxy)-2,4-pentadiene (4.05 g, 12.58 mmol, 1 eq) in THF (10 ml) was added TBAF (25.15 ml of a 1M solution in THF, 25.15 mmol, 2 eq). Deprotection was shown to be complete by tlc after 45 min. Brine (20 ml) was added, the mixture extracted with ether (3 x 20 ml), and the combined organic layers were dried ($MgSO_4$) and concentrated under reduced pressure. The resulting oil was purified by chromatography (40% ether–petrol) to yield the desired alcohol **2d** (750 mg, 71%) as a colourless oil; υ_{max} (film) 3331, 3019, 2960, 2932, 2915, 2872, 2856, 1447, 1438, 1378, 1097, 1071, 988, 926 cm^{-1}; δ_H (270 MHz) 6.43-6.21 (2H, m, H-3 and H-4), 5.86 (1H, dt, J 14.5, 6.5 Hz, H-2), 5.22 (1H, dd, J 15.0, 1.5 Hz, H-5_{trans}), 5.10 (1H, dd, J 9.0, 1.0 Hz, H-5_{cis}), 4.19 (2H, d, J 6.5 Hz, H-1), 1.52 (1H, br s, OH); *m/z* (EI) 84 (M^+), 67 (M^+-OH), 66 (M^+-H_2O), 57 ($HOCH_2CHCH^+$), 53 ($CH_2CHCHCH^+$), 40 (CH_2CHCH^+).

Preparation of methyl (*E*)-4-hydroxy-2-butenoate (3a).

To a solution/suspension of glycolaldehyde dimer[9] (0.5 g, 4.16 mmol, 1.0 eq) in benzene (75 ml) under reflux was added, via dropping funnel, a solution of methoxycarbonylmethylenetriphenylphosphorane (2.78 g, 8.33 mmol, 2.0 eq) in cold benzene (50 ml). As the product formed, the undissolved glycol aldehyde dimer was taken into solution. After addition of the phosphorane was complete, the mixture was heated under reflux for 4 h before removal of the solvent by evaporation to yield an oily white solid. Chromatography on silica gel (75% ether–petrol) afforded the alcohol **3a** (0.88 g, 91%) as a clear oil; υ_{max} (film) 3426, 2954, 1723, 1663, 1439, 1281, 1173, 1099, 1014, 959, 928, 835 cm^{-1}; δ_H (270 MHz) 7.04 (1H, dt, J 14.5, 9.5 Hz, H-2), 6.10 (1H, dt, J 14.5, 2.0 Hz, H-3), 4.33 (2H, br s, H-4), 3.72 (3H, s, OCH_3), 2.17 (1H, br s, OH); *m/z* (EI) 116 (M^+), 101 (M^+-CH_3), 99 (M^+-OH), 85 (M^+-CH_3O_2), 73 (M^+-CH_3OCO), 31 (CH_3O).

Preparation of (-)-(2*S*)-methyl 2-(*tert*-butyldiphenylsilyloxy)propanoate.

A solution of (*S*)-methyl lactate (9.20 ml, 10.00 g, 96.00 mmol, 1.0 eq) in THF (100 ml) was stirred at room temperature overnight with *tert*-butylchlorodiphenylsilane (32.50 ml, 34.30 g, 125.00 mmol, 1.3 eq), DMAP (1.17 g, 10 mmol, 0.1 eq) and Et_3N (24.30 g, 33.40 ml, 240.00 mmol, 2.5 eq). The solvent was removed by evaporation and the residue triturated with ether (250 ml). The solids were removed by filtration and the filtrate washed with acetic acid (15% v/v in water; 250 ml), water (200 ml), saturated aqueous sodium hydrogencarbonate (150 ml) and water (150 ml). The dried ($MgSO_4$) solvents were removed by evaporation and the residue purified by chromatography on silica gel (50% CH_2Cl_2–petrol) to yield the desired protected alcohol (29.14 g, 89%) as a colourless oil, $[\alpha]_D^{20}$ -51.8 (*c* 0.78, 95% ethanol); υ_{max} (film) 1762, 1429, 1281, 1137, 1113 cm^{-1}; δH (270 MHz) 7.69-7.64 (4H, m, ortho C_6H_5), 7.43-7.33 (6H, m, meta and para C_6H_5), 4.28 (1H, q, J 7.0 Hz, H-2), 3.56 (3H, s, OCH_3), 1.37 (3H, J 7.0 Hz, H-3), 1.09 (9H, s, *t*-Bu); *m/z* (EI) 285 (M^+-*t*-Bu), 213 ($CH_3Si(O)Ph_2$) 183 ($HSiPh_2$), 91, 77, 59, 43, 28 (Found: C, 70.30; H, 7.70. $C_{20}H_{26}O_3Si$ requires C, 70.14; H, 7.65%).

Preparation of (-)-(2*S*)-2-(*tert*-butyldiphenylsilyloxy)propanal.

To a solution of (-)-(2*S*)-methyl 2-(*tert*-butyldiphenylsilyloxy)propanoate (6.66 g, 19.44 mmol, 1.0 eq) in hexane (25 ml) at -78° C, was added DIBAL-H (16.20 ml of a 1.5M solution in toluene, 24.31 mmol, 1.25 eq) over a period of 15 min. The mixture was stirred at -78°C for 1 h. Water (16.20 ml) was added cautiously to the reaction which was then allowed to warm slowly to room temperature. Solid sodium hydrogencarbonate was added to bind the resultant precipitate and to absorb excess water. The precipitate was removed by filtration and the residues washed with ether. The organic layers were dried ($MgSO_4$) before removing the solvents by evaporation, and purification of the residue by chromatography on silica gel (50% CH_2Cl_2–petrol) to yield the desired aldehyde (4.426 g, 72%) as a colourless oil, $[\alpha]_D^{20}$ -10.2 (*c* 1.2, 95% ethanol); υ_{max} (film) 2862, 2811, 1743, 1697, 1457, 1429, 1376, 741, 702 cm^{-1}; δ_H (270 MHz) 9.65 (1H, d, J 1.0 Hz, H-1), 7.70-7.63 (4H, m, ortho C_6H_5), 7.48-7.35 (6H, m, meta and para C_6H_5), 4.09 (1H, dq, J 7.0, 1.0 Hz, H-2), 1.22 (3H, d, J 7.0 Hz, H-3), 1.11 (9H, s, *t*-Bu); *m/z* (EI) 283 (M^+-CHO), 255 (M^+-*t*-Bu), 197, 181, 177 ($OCC(CH_3)(OSiC_6H_5)$, 135, 105.

Preparation of (-)-(4*S*)-methyl (*E*)-4-(*tert*-butyldiphenylsilyloxy)-2-pentenoate.

To a solution of (-)-(2*S*)-2-(*tert*-butyldiphenylsilyloxy)propanal (4.43 g, 14.16 mmol, 1.0 eq) in CH_2Cl_2 (14 ml) was added, portionwise, methoxycarbonylmethylidenetriphenylphosphorane (4.74 g, 14.16 mmol, 1.0 eq) over three minutes. Heat was liberated in the reaction and it was left to stir overnight. The solvent was removed by evaporation to yield an oily white precipitate. The solids were removed by filtration and the residue washed extensively with ether. Removal of the solvents by evaporation caused further precipitation, but the

products were dissolved in toluene and purified by chromatography on silica gel (10% ether–petrol) to yield the desired *ester* (4.36 g, 84%) as a colourless oil; $[\alpha]_D^{20}$ -52.3 (*c* 0.94, $CHCl_3$); υ_{max} (film) 2365, 2355, 1733, 1591, 1540, 1392, 1113, 940, 892, 862, 770 cm^{-1}; δ_H (270 MHz) 7.70-7.61 (4H, m, ortho C_6H_5), 7.48-7.32 (6H, m, meta and para C_6H_5), 6.92 (1H, dd, J 15.5, 4.5 Hz, H-3), 6.04 (1H, br d, J 15.5 Hz, H-2), 4.48 (1H, m, H-4), 3.74 (3H, s, OCH_3), 1.13 (3H, d, J 6.5 Hz, H-5), 1.09 (9H, s, *t*-Bu); *m/z* (EI) 353 (M^+-CH_3), 311 (M^+-*t*-Bu), 255 ($OSi(C_6H_5)_2t$-Bu^+), 183 ($Si(C_6H_5)_2H$), 91, 77 (Found: C, 71.40; H, 7.70. $C_{22}H_{28}O_3Si$ requires C, 71.70; H, 7.66%).

Preparation of (+)-(4*S*)-methyl (*E*)-4-hydroxy-2-pentenoate (3b).

To a solution of (-)-(4*S*)-methyl (*E*)-4-(*tert*-butyldiphenylsilyloxy)-2-pentenoate (22.17 g, 60.154 mmol) in methanol (200 ml) stirring at room temperature, was added concentrated hydrochloric acid (4 ml). The mixture was stirred for 5 h when tlc showed the deprotection to be complete. Solid sodium hydrogencarbonate was added until effervescence had ceased, and the solids removed by filtration. The solvents were removed by evaporation with cooling of the flask, and the residue purified by chromatography on silica gel (40-50% ether–petrol) to yield the *alcohol* **3b** (5.56 g, 71%) as a colourless oil, $[\alpha]_D^{20}$ +27.7 (*c* 1.48, $CHCl_3$); υ_{max} (film) 3417, 2976, 2353, 1719, 1653, 1538, 1437, 1275, 1174, 1047, 979, 923, 864 cm^{-1}; δ_H (270 MHz) 6.96 (1H, dd, J 15.5, 4.5 Hz, H-3), 6.03 (1H, dd, J 15.5, 1.5 Hz, H-2), 4.49 (1H, m, H-4), 3.74 (3H, s, OCH_3), 1.34 (3H, d, J 6.5 Hz, $CHCH_3$); *m/z* (EI) 130 (M^+), 115 (M^+-CH_3), 113 (M^+-OH), 99 (M^+-CH_3O), 87, 55, 43 (Found: C, 55.11; H, 7.39. $C_6H_{10}O_3$ requires C, 55.37; H, 7.74%).

Preparation of methyl (*E*,*E*,*E*)-6,6-diphenyl-5,7,6-dioxasila-2,9,11-tridecatrienoate (4).

A solution of diene alcohol **2a** (0.116 g, 1.18 mmol, 1.0 eq) and dienophile alcohol **3a** (0.159 g, 1.37 mmol, 1.2 eq) in CH_2Cl_2 (1 ml) was added, with stirring, to a flask containing dichlorodiphenylsilane (0.249 ml, 0.299 g, 1.18 mmol, 1.0 eq) and Et_3N (0.346 ml, 0.251 g, 2.48 mmol, 2.1 eq). The mixture was stirred for 1 h before adding petrol to ensure complete precipitation of triethylammonium chloride, which was removed by filtration. The solvents were removed from the filtrate by evaporation to yield a pale yellow oil. Chromatography on Florisil® (1-8% ether–petrol) afforded, in order of elution, the symmetrical tetraene *bis[(*E,E*)-2,4-hexadienyloxy]diphenylsilane* **10a** (0.044 g, 10%), the desired *triene* **4** (0.147 g, 32%) and the symmetrical diene *bis[(*E*)-3-methoxycarbonyl-2-propenyloxy]diphenylsilane* **11a** (0.024 g, 5%) all as colourless oils; **10a**: υ_{max} (film) 3069, 3022, 2931, 2854, 2730, 1962, 1891, 1828, 1662, 1631, 1591, 1430, 1380, 1262, 1222, 1117, 1078, 1048, 988, 926, 857, 827, 797, 740, 719, 700, 676, 665 cm^{-1}; δ_H (270 MHz) 7.72-7.61 (4H, m, ortho C_6H_5), 7.59 -7.28 (6H, m, meta and para C_6H_5), 6.26-6.00 (4H, m, H-3, H-4), 5.74-5.61 (4H, m, H-2, H-5), 4.34 (4H, d, J 5.5 Hz, H-1), 1.75 (6H, d, J 6.5 Hz, H-6); *m/z* (EI) 376 (M^+), 295 (M^+-C_6H_9), 279 (M^+-OC_6H_9), 221, 199, 139, 91, 77 (Found: (M^+), 376.1859. $C_{24}H_{28}O_2Si$ requires (M^+), 376.1859); **4**: υ_{max} (film) 3025, 2919, 1727, 1666, 1593, 1281, 1127, 990, 966, 720, 701, 625 cm^{-1}; δ_H (270 MHz) 7.64-7.72 (4H, m, ortho C_6H_5), 7.32-7.50 (6H, m, meta and para C_6H_5), 7.05 (1H, dt, J 15.0, 3.5 Hz, H-3), 6.25 (1H, dt, J 15.0, 2.0 Hz, H-2), 6.25-5.95 (2H, m, H-10, H-11), 5.75-5.60 (2H, m, H-9, H-12), 4.49 (2H, dd, J 3.0, 2.0 Hz, H-4), 4.33 (2H, br d, J 5.5 Hz, H-8), 3.75 (3H, s, OCH_3), 1.75 (3H, br d, J 6.5 Hz, H-6); *m/z* (EI) 394 (M^+), 297 (M^+-$CH_3(CH)_4CH_2O$), 279 (M^+-$OCH_2(CH)_2CO_2CH_3$), 115 ($OCH_2(CH)_2CO_2CH_3$), 91, 77 (Found: C, 70.04; H, 6.51. $C_{23}H_{26}O_4Si$ requires C, 70.02; H, 6.64%); **11a**: υ_{max} (film) 3071, 2950, 2848, 1725, 1664, 1592, 1432, 1380, 1301, 1118, 1021, 964, 837, 792, 721, 701, 666 cm^{-1}; δ_H (270 MHz) 7.68-7.65 (4H, m, ortho C_6H_5), 7.60-7.37 (6H, m, meta and para C_6H_5), 6.99 (2H, dt, J 15.5, 3.5 Hz, H-2), 6.22 (2H, dt, J 15.5, 2.0 Hz, H-3), 4.48 (4H, dd, J 3.5, 2.0 Hz, H-1), 3.75 (6H, s, OCH_3); *m/z* (EI) 412 (M^+), 397 (M^+-CH_3), 381 (M^+-CH_3O), 353 (M^+-CH_3OCO), 297 (M^+-$CH_3OCOCH{=}CHCH_2O$), 250, 213, 115 ($CH_3OCOCH{=}CHCH_2O^+$), 91, 77 (Found: C, 64.12; H, 6.00. $C_{22}H_{24}O_6Si$ requires C, 64.06; H, 5.86%).

Preparation of (-)-(4*S*)-methyl (*E*,*E*,*E*)-4-methyl-6,6-diphenyl-5,7,6-dioxasila-2,9,11-tridecatrienoate (5).

To a stirred solution of dichlorodiphenylsilane (0.176 ml, 0.211 g, 0.835 mmol, 1.0 eq) and Et_3N (0.256 ml, 0.186 g, 1.836 mmol, 2.2 eq) in CH_2Cl_2 (1 ml) at 0°C, was added slowly a solution of alcohol **3b** (0.109 g, 0.835 mmol, 1.0 eq) in CH_2Cl_2 (1 ml). A white precipitate formed over ca. 2 min, and stirring was continued for 10 min before the addition of a solution of the second alcohol **2a** (0.082 g, 0.835 mmol, 1.0 eq), in CH_2Cl_2 (1 ml). The reaction was stirred at 0°C for a further 10 min, before the addition of extra CH_2Cl_2 (5 ml) in order to dissolve the precipitate of triethylammonium chloride. The solution was filtered quickly through a short column of Florisil®, the column being rinsed with ether. Removal of the solvents by evaporation, followed by purification of the residue by chromatography on Florisil® (3% ether–petrol) afforded, in order of elution, the symmetrical tetraene **10a** (0.038 g, 12%), the desired *triene* **5** (0.159 g, 47%), and *(-)-bis[(3S)-(E)-1-methoxycarbonyl-1-buten-3-yloxy]diphenylsilane* **11b** (0.026 g, 7%) all as colourless oils; **10a**: spectroscopic data were in agreement with those listed above; **5**: $[\alpha]_D^{20}$ -21.9 (*c* 1.34, $CHCl_3$); υ_{max} (film) 3370, 2948, 2321, 1729, 1653, 1539, 1432, 1373, 1299, 1275, 1166, 1117, 1055, 989, 742, 719, 701 cm^{-1}; δ_H (500 MHz) 7.69-7.65 (4H, m, ortho C_6H_5), 7.46-7.35 (6H, m, meta and para C_6H_5), 6.94 (1H, dd, J 15.5, 4.5 Hz, H-3), 6.18 (1H, br dd, J 15.0, 10.5 Hz, H-10), 6.09 (1H, dd, J 15.5, 1.5 Hz, H-2), 6.04 (1H, br dd, J 15.0, 10.5 Hz, H-11), 5.69-5.61 (2H, m, H-9, H-12), 4.67 (1H, qdd, J 6.5, 4.5, 1.5 Hz, H-4), 4.31 (2H, br d, J 5.5 Hz, H-8), 3.74 (3H, s, OCH_3), 1.75 (3H, d, J 6.5 Hz, H-13), 1.30 (3H, d, J 6.5 Hz, C-4 CH_3); *m/z* (EI) 408 (M^+), 393 (M^+-CH_3), 377 (M^+-CH_3O), 365 (M^+-CH_3OC), 311 (M^+-$OCH_2(CH)_4CH_3$), 279 (M^+-$OCH(CH_3)CHCHCO_2CH_3$) 199 ($Si(C_6H_5)_2OH$), 153, 139, 91, 77, 53, 41, 27 (Found: C, 70.23; H, 6.96. $C_{24}H_{28}O_4Si$ requires C, 70.55; H, 6.91%); **11b**: $[\alpha]_D^{20}$ -25.8 (*c* 1.06, $CHCl_3$); υ_{max} (film) 3578, 3424, 3060, 2981, 1725, 1661, 1593, 1436, 1363, 1273, 1159, 1118, 1087, 1060, 978, 788, 710, 658 cm^{-1}; δ_H (270 MHz) 7.70-7.62 (4H, m, ortho C_6H_5), 7.48-7.34 (6H, m, meta and para C_6H_5), 6.90 (2H, dd, J 15.5, 4.5 Hz, H-2), 6.03 (2H, dd, J 15.5, 1.5 Hz, H-1), 4.63 (2H, m, H-3), 3.73 (6H, s, OCH_3), 1.27 (6H, d, J 6.5 Hz, H-4); *m/z* (EI) 440 (M^+), 425 (M^+-CH_3), 409 (M^+-OCH_3), 311 (M^+-$OCH(CH_3)CHCHCO_2CH_3$), 214, 213, 199, 91, 77, 53, 45, 28 (Found: C, 65.70; H, 6.64. $C_{24}H_{28}O_6Si$ requires C, 65.43; H, 6.41%).

Preparation of (±)-methyl (*E*,*E*,*E*)-8-methyl-6,6-diphenyl-5,7,6-dioxasila-2,9,11-trideca-trienoate (6).

To a solution of dichlorodiphenylsilane (0.958 ml, 1.153 g, 4.555 mmol, 1.0 eq) and Et_3N (1.40 ml, 1.014 g, 10.020 mmol, 2.2 eq) in CH_2Cl_2 (25 ml) stirring at -78°C, was added slowly a solution of the racemic secondary alcohol **2b** (0.511 g, 4.555 mmol, 1.0 eq) in CH_2Cl_2 (5 ml). After the addition was complete the solution was allowed to stir at -78°C for 1 h, when a solution of alcohol **3a** (0.529 g, 4.612 mmol, 1.01 eq) in CH_2Cl_2 (5 ml) was added and the solution allowed to warm slowly to room temperature. The reaction mixture was poured into saturated aqueous sodium hydrogencarbonate (50 ml) which had been pre-cooled to 0°C. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (4 x 30 ml). The combined organic layers were dried ($MgSO_4$) before removal of the solvent by evaporation. The residue was purified by chromatography on Florisil® (3% ether–petrol) to yield, in order of elution, the symmetrical tetraene, *bis[(*E,E*)-3,5-heptadien-2-yloxy]diphenylsilane* **10b** (0.166 g, 9%), as a 1:1 mixture of inseparable diastereoisomers, the *triene* **6** (0.687 g, 37%) and the symmetrical diene **11a** (0.150 g, 8%), all as colourless oils; **10b**: υ_{max} 3070, 3019, 2972, 2928, 1831, 1662, 1592, 1486, 1430, 1370, 1323, 1223, 1124, 1058, 987, 942, 901, 796, 740, 717, 700 cm^{-1}; δ_H (270 MHz) 7.68-7.63 (4H, m, ortho C_6H_5), 7.44-7.27 (6H, m, meta and para C_6H_5), 6.09-5.93 (4H, m, H-4, H-5), 5.68-5.55 (4H, m, H-3, H-6), 4.56-4.49 (2H, m, H-2), 1.75 and 1.74 (3H, d, J 6.0 Hz, H-1), 1.24 and 1.23 (3H, J, 6.5 Hz, H-7); *m/z* (EI) 404 (M^+), 389 (M^+-CH_3), 309 (M^+-C_7H_{11}), 293 (M^+-$C_7H_{11}O$), 277, 199, 139, 94, 79, 39 (Found: C, 77.39; H, 8.00. $C_{26}H_{32}O_2Si$ requires C 77.18; H, 7.97%); **6**: υ_{max} (film) 3021, 2973, 2734, 1726, 1665, 1592, 1486, 1431, 1378, 1301, 1124, 1059, 990,

908, 836, 720, 701 cm^{-1}; δ_H (500 MHz) 7.72-7.59 (4H, m, ortho C_6H_5), 7.47-7.31 (6H, m, meta and para C_6H_5), 7.00 (1H, dt, J 15.0, 3.5 Hz, H-3), 6.25 (1H, dt, J 15.0, 2.5 Hz, H-2), 6.11-5.96 (2H, m, H-10, H-11), 5.68-5.56 (2H, m, H-9, H-12), 4.51 (1H, q, J 6.0 Hz, H-8), 4.45 (2H, dd, J 3.0, 3.0 Hz, H-4), 3.76 (3H, s, OCH_3), 1.74 (3H, d, J 6.5 Hz, H-13), 1.27 (3H, d, J 6.5 Hz, C-8 CH_3); *m/z* (EI) 408 (M^+), 309 (M^+-$CH_3O_2C(CH)_2CH_2$), 296 (M^+-$CH_3(CH)_4CH(O)CH_3$), 213, 183, 153, 139, 91, 77, 43 (Found: (M^+), 408.1757. $C_{24}H_{28}O_4Si$ requires (M^+), 408.1757); **11a**: spectroscopic data were in agreement with those listed above.

Preparation of (4*S*,8*S*)-methyl (*E*,*E*,*E*)-4,8-dimethyl-6,6-diphenyl-3,7,6-dioxasila-2,9,11-trideca-trienoate (7a) and (4*S*,8*R*)-methyl (*E*,*E*,*E*)-4,8-dimethyl-6,6-diphenyl-3,7,6-dioxasila-2,9,11-tridecatrienoate (7b).

To a stirred solution of dichlorodiphenylsilane (0.517 ml, 0.622 g, 2.458 mmol, 1.0 eq) and Et_3N (0.754 ml, 0.547 g, 5.407 mmol, 2.2 eq) in CH_2Cl_2 (2 ml) at 0°C, was added slowly a solution of racemic alcohol **2b** (0.276 g, 2.458 mmol, 1.0 eq) in CH_2Cl_2 (1 ml). A white precipitate formed rapidly, and the mixture was allowed to stir for 10 min before the addition of a solution of alcohol **3b** (0.320 g, 2.458 mmol, 1.0 eq) in CH_2Cl_2 (1 ml). After stirring for 5 min, tlc indicated that the reaction had reached completion. Further CH_2Cl_2 (5 ml) was added to the reaction mixture to dissolve all of the triethylammonium chloride, and the solution was filtered through a pad of Florisil®, which was washed thoroughly with CH_2Cl_2. Removal of the solvent by evaporation, followed by purification of the residue by chromatography on Florisil® (3% ether–petrol) afforded, in order of elution, an inseparable 1:1 diastereomeric mixture of **10b** (0.159 g, 16%), an inseparable 1:1 diastereomeric mixture of *trienes* **7a** and **7b** (0.273 g, 26%), and the symmetrical diene **11b** (0.108 g, 10%), all as colourless oils; **10b**: spectroscopic data were in agreement with those listed above; **7a,b**: υ_{max} (film) 2978, 1728, 1664, 1537, 1434, 1299, 1272, 1147, 1121, 1057, 989, 701 cm^{-1}; δ_H (500 MHz) 7.67-7.63 (4H, m, ortho C_6H_5), 7.44-7.33 (6H, m, meta and para C_6H_5), 6.932 and 6.929 (1H, dd, J 15.5, 4.0 Hz, H-2), 6.08 and 6.07 (1H, dd, J 15.5, 1.5 Hz, H-1), 6.03-5.94 (2H, m, H-10, H-11), 5.65-5.54 (2H, m, H-9, H-12), 4.66 (1H, m, H-4), 4.49 and 4.48 (1H, quintet, J 6.5 Hz, H-2), 3.74 and 3.73 (3H, s, OCH_3), 1.74 (3H, d, J 6.5 Hz, H-13), 1.27, 1.25, 1.24 and 1.23 (6H, d, J 6.5 Hz, C-4 CH_3 and C-8 CH_3); *m/z* (EI) 422 (M^+), 407 (M^+-CH_3), 328 (M^+-$CH(CH_3)(CH)_4CH_3$), 309 (M^+-$CH(CH_3)CHCHCO_2CH_3$), 213, 199, 113, 91, 77, 43 (Found: C, 71.21; H, 7.05. $C_{25}H_{30}O_4Si$ requires C, 71.06; H, 7.16%); **11b**: spectroscopic data were in agreement with those listed above.

Preparation of methyl (*E*,*E*)-10-methyl-6,6-diphenyl-5,7,6-dioxasila-2,9,11-dodecatrienoate (8).

To a solution of diphenyldichlorosilane (453 µl, 546 mg, 2.16 mmol, 1.18 eq) and Et_3N (535 µl, 388 mg, 3.84 mmol, 2.1 eq) in CH_2Cl_2 (2.5 ml) at 0°C was added a mixture of diene alcohol **2c** (179 mg, 1.83 mmol, 1 eq) and dienophile alcohol **3a** (254 mg, 2.19 mmol, 1.2 eq) in CH_2Cl_2 (2 ml). There was immediate precipitation of a white solid, and this mixture was allowed to stir for a further 30 min. Petrol was added, and the mixture filtered, and concentrated under reduced pressure. The resulting oil was purified by chromatography (Florisil®, 1-4% ether–petrol) to yield, in order of elution the symmetrical tetraene *bis[(2E,4E)-3-methyl-2,4-pentadienyloxy]diphenylsilane* **10c** (14 mg, 3%) and the desired *triene* **8** (223 mg, 31%) as colourless oils; **10c**: υ_{max} (film) 3091, 3072, 3042, 3026, 3003, 1603, 1425, 1375, 1164, 1113, 1057, 1008, 990 cm^{-1}; δ_H (270 MHz) 7.71-7.63 (4H, m, ortho C_6H_5), 7.47-7.32 (6H, m, meta and para C_6H_5), 6.37 (2H, dd, J 17.0, 11.0 Hz, H-4), 5.69 (2H, tq, J 6.5, 0.5 Hz, H-2), 5.16 (2H, d, J 17.0 Hz, H-5_{trans}), 5.03 (2H, d, J 11.0 Hz, H-5_{cis}), 4.47 (4H, d, J 6.5 Hz, H-1), 1.66 (6H, br s, vinylic Me); *m/z* (CI) 394 ($M+NH_4^+$), 377 (MH^+), 295, 216, 199, 161, 98 ($C_6H_9OH^+$), 81 (Found: (MH^+), 377.1923. $C_{24}H_{29}O_2Si$ requires (MH^+), 377.1937); **8**: υ_{max} (film) 3071, 3050, 2949, 2852, 1725, 1665, 1608, 1431, 1301, 1278, 1125, 1051, 964, 835, 720 cm^{-1}; δ_H (270 MHz) 7.71-7.63 (4H, m, ortho C_6H_5), 7.49-7.35 (6H, m, meta and para C_6H_5), 7.03

(1H, dt, J 15.5, 3.5 Hz, H-3), 6.36 (1H, dd, J 17.0, 11.0 Hz, H-11), 6.27 (1H, dt, J 17.0, 2.5 Hz, H-2), 5.67 (1H, tq, J 6.5, 0.5 Hz, H-9), 5.17 (1H, d, J 17.0 Hz, H-12_{trans}), 5.04 (1H, d, J 11.0 Hz, H-12_{cis}), 4.20 (4H, m, H-4 and H-8), 3.76 (3H, s, OCH_3), 1.65 (3H, s, vinylic Me); *m/z* (CI) 412 ($M+NH_4^+$), 394 (M^+), 332 (M^+-Me_2O_2), 237 (MH^+-Ph-C_6H_9), 98 ($C_6H_9OH^+$), 81 (Found: C, 70.01; H, 6.68%. $C_{23}H_{26}O_4Si$ requires C, 70.02; H, 6.64%).

Preparation of methyl (*E,E,E*)-6,6-diphenyl-5,7,6-dioxasila-2,9,11-dodecatrienoate (9).

To a solution of diphenyldichlorosilane (602 µl, 724.8 mg, 2.86 mmol, 1.18 eq) and Et_3N (710 µl, 516 mg, 5.09 mmol, 2.1 eq) in CH_2Cl_2 (2.5 ml) at 0°C was added a mixture of diene alcohol **2d** (204 mg, 2.43 mmol, 1 eq) and dienophile alcohol **3a** (338 mg, 2.92 mmol, 1.2 eq) in CH_2Cl_2 (2 ml). There was immediate precipitation of a white solid, and the mixture was allowed to stir for a further 30 min. Petrol was added, the mixture filtered, and the filtrate concentrated under reduced pressure. The resulting oil was purified by chromatography (Florisil®, 1-4% ether–petrol) to yield, in order of elution the symmetrical tetraene *bis[(*E,E*)-2,4-pentadienyloxy]diphenylsilane* **10d** (25 mg, 3%) and the desired *triene* **9** (233 mg, 25%), both as colourless oils; **10d**: υ_{max} (film) 3086, 3047, 3005, 2921, 2859, 1604, 1592, 1430, 1373, 1300, 1168, 1117, 1051, 1004, 981 cm^{-1}; δ_H (270 MHz) 7.73-7.65 (4H, m, ortho C_6H_5), 7.49-7.34 (6H, m, meta and para C_6H_5), 6.38 (4H, m, H-3 and H-4), 5.79 (2H, dt, J 14.5, 5.0 Hz, H-2), 5.21 (2H, d, J 16.0 Hz, H-5_{trans}), 5.08 (2H, d, J 8.5 Hz, H-5_{cis}), 4.39 (4H, d, J 5.0 Hz, H-1); *m/z* (EI) 348 (M^+), 281 (M^+-C_5H_7), 265 (M^+-C_5H_7O), 244, 237, 199 (Ph_2SiOH^+), 187, 183, 139, 77 (Ph^+), 67 ($C_5H_7^+$), 45, 41 (Found: (M^+), 348.1552. $C_{22}H_{24}O_2Si$ requires (M^+), 348.1546); **9**: υ_{max} (film) 3071, 3004, 2852, 1724, 1664, 1431, 1301, 1279, 1125, 1050, 1007, 965, 837, 720, 701 cm^{-1}; δ_H (270 MHz) 7.72-7.61 (2H, m, ortho C_6H_5), 7.49-7.30 (3H, m, meta and para C_6H_5), 7.01 (1H, dt, J 15.5, 3.5 Hz, H-3), 6.27 (3H, m, H-2, H-10 and H-11), 5.80 (1H, dt, J 14.5, 5.0 Hz, H-9), 5.18 (1H, d, J 16.0 Hz, H-5_{trans}), 5.08 (1H, d, J 8.5 Hz, H-5_{cis}), 4.48 (2H, dd, J 3.5, 2.0 Hz, H-4), 4.07 (2H, d, J 5.0 Hz, H-8), 3.75 (3H, s, OCH_3); *m/z* (EI) 380 (M^+), 296 (M^+-C_5H_7OH), 237 (M^+-C_5H_7OH-CO_2Me), 213, 199 (Ph_2SiOH^+), 183, 153, 139, 77 (Ph^+), 67 ($C_5H_7^+$), 45, 41 (Found: C, 69.23; H, 6.08%. $C_{22}H_{24}O_4Si$ requires C, 69.44; H, 6.36%).

Intramolecular Diels–Alder reactions

IMDA Reaction of triene (4).

A resealable pressure tube was base-washed by heating with HMDS under reflux overnight . The tube was then washed thoroughly with dry acetone, and dried by purging with a stream of argon while being heated in a Wood's metal bath at a temperature of 150°C. The tube was then removed from the heat and cooled by the continuing stream of argon. A solution of triene **4** (azeotropically dried with toluene (3 x 15 ml); 0.250 g, 0.634 mmol) in dry toluene (12 ml) was rigorously degassed by alternate sonication for 5 min, followed by degassing with argon, the whole procedure being repeated three times. The solution was transferred via cannula to the pressure tube which was sealed. The tube was then heated (Wood's metal bath) at 160°C for 168 h. After cooling the toluene was removed by evaporation to yield a pale yellow oil which was shown by ^1H nmr to consist of unreacted triene (13%) together with a single stereoisomer of *[1R*,7R*,10S*,11R*]-11-methoxycarbonyl-10-methyl-4,4-diphenyl-3,5,4-dioxasilabicyclo[5.4.0]-8-undec-ene* **12** (87%; overall mass recovery = 100%); δ_H (500 MHz) 7.75 (2H, m, ortho C_6H_5), 7.68 (2H, m, ortho C_6H_5), 7.49-7.36 (6H, m, meta and para C_6H_5), 5.57-5.50 (2H, m, H-8, H-9), 4.12 (1H, dd, J 12.5, 2.0 Hz, CH_2O), 3.93 (1H, dd, J 12.5, 4.0 Hz, CH_2O), 3.83 (3H, s, OCH_3), 3.77-3.73 (2H, m, CH_2O), 2.68 (1H, m), 2.53 (1H, m), 2.22 (1H, m) (H-1, H-7 H-10, H-11), 1.00 (3H, br d, J 6.5 Hz, C-10 CH_3). The crude mixture was purified on Florisil® (6% ether–petrol) to remove polar impurities. The mixture of product and starting material (0.163 g) was dissolved in methanol (12 ml) and to this solution was added concentrated hydrochloric acid (ca. 5 ml). The solution was stirred for 5 h and then solid sodium hydrogencarbonate added until effervescence had ceased. Removal of the solids by filtration and concentration under reduced pressure followed by chromatography on

silica gel (50-75% ether–petrol) afforded *[1R*,5R*,6R*,9S*]-6-(hydroxymethyl)-9-methyl-2-oxo-3-oxabicyclo[3.4.0]-7-nonene* **13** (41 mg, 35%) as a colourless crystalline solid, mp 78-81°C; υ_{max} (Nujol) 3453, 2913, 1742, 1461, 1378, 1062, 997, 722 cm^{-1}; δ_H (500 MHz) 5.68 (1H, dt, J 10.0, 2.0 Hz, H-8), 5.58 (1H, ddd, J 10.0, 4.5, 2.5 Hz, H-7), 4.41 (1H, dd, J 9.0, 7.0 Hz) and 4.32 (1H, dd, J 12.5, 9.0 Hz, H-4 AB_{SYS}), 3.73 (1H, br dt, J 11.5, 4.0 Hz, CH_2OH), 3.65 (1H, m, CH_2OH), 2.58 (1H, m, H-6), 2.54-2.46 (1H, m, H-5), 2.39 (1H, m, H-9), 2.10 (1H, dd, J 14.0, 10.0 Hz, H-1), 1.43 (1H, br t, J 4.0 Hz, OH), 1.28 (3H, d, J 7.0 Hz, CH_3); *m/z* (EI) 182 (M^+), 164 (M^+-H_2O), 151 (M^+-CH_2OH), 107 (M^+-H_2O-CO_2CH_2), 91, 77 (Found; C, 66.05; H, 7.44. $C_{10}H_{14}O_3$ requires C, 65.90; H, 7.75%).

IMDA Reaction of triene (5).

A resealable pressure tube was base-washed with HMDS and dried as previously described. A solution of triene **5** (0.398 g, 0.974 mmol) in toluene (12 ml) was thoroughly degassed by alternate sonication and argon purge, as described previously. The solution was transferred to the argon-filled tube *via* cannula, and the tube heated (170°C) in a Wood's metal bath for 112 h. Removal of the toluene by evaporation at reduced pressure yielded a yellow oil (0.398 g, 100% mass recovery), which was shown by ^1H nmr to consist of a single stereoisomer. The crude cycloaddition product was dissolved in acetonitrile (15 ml) and treated with hydrofluoric acid (150 µl of a 48% aqueous solution), and the reaction mixture stirred at room temperature for 5 min. The reaction was quenched by the addition of solid sodium hydrogencarbonate until all effervescence had stopped. The mixture was then added to a saturated aqueous sodium hydrogencarbonate–CH_2Cl_2 bilayer (50 ml of each). The layers were separated and the aqueous layer extracted with CH_2Cl_2 (2 x 50 ml). The combined organic layers were washed with water (100 ml) before drying ($MgSO_4$) and removal of the solvents by evaporation. The residue was purified by chromatography on silica gel (40-100% ether–petrol) to yield *(+)-[1S,2S,3S,6R,1'S]-methyl 2-(1-hydroxyethyl)-3-hydroxymethyl-6-methyl-4-cyclohexene-1-carboxylate* **17** (0.199 g, 90%) as a colourless, crystalline solid, mp 94-96°C, $[\alpha]_D^{20}$ +41.0 (*c* 0.71, $CHCl_3$); υ_{max} (Nujol) 3280, 2923, 1727, 1457, 1285, 1038 cm^{-1}; δ_H (500 MHz) 5.57 (1H, ddd, J 10.0, 5.5, 2.5 Hz, H-4), 5.52 (1H, dt, J 10.0, 1.5 Hz, H-5), 3.86 (1H, qd, J 6.5, 2.5 Hz, *CH*OH), 3.78 (3H, s, OCH_3), 3.53 (2H, d, J 5.5 Hz, CH_2OH), 2.71 (1H, br quintet, J 5.5 Hz, H-3), 2.64 (1H, m, H-6), 2.53 (1H, dd, J 11.5, 10.5 Hz, H-1), 1.97 (1H, ddd, J 11.5, 4.0, 2.5 Hz, H-2), 1.35 (3H, d, J 6.5 Hz, C-1' CH_3), 0.97 (3H, d, J 7.0 Hz, C-6 CH_3); *m/z* (EI) 198 (M^+-CH_2O), 180 (M^+-CH_2O-H_2O), 151, 121, 93, 43 (CH_3OC^+) (Found: C, 63.30; H, 8.90. $C_{12}H_{20}O_4$ requires C, 63.14; H, 8.83%).

IMDA Reaction of triene (6).

A resealable pressure tube was base-washed with HMDS and dried as previously described. A solution of the triene **6** (0.775 g, 1.89 mmol) in toluene (12 ml) was thoroughly degassed by alternate sonication and argon purge, as described previously. The solution was transferred to the argon-filled tube *via* cannula, and the tube heated (170°C) in a Wood's metal bath for 112 h. Removal of the toluene by evaporation at reduced pressure yielded a yellow oil (0.775 g, 100% mass recovery) which was shown by ^1H nmr to consist of two stereoisomers in a ratio of 7:1. The crude reaction product (0.775 g) was dissolved in CH_3CN (9.5 ml) was treated with aqueous hydrogen fluoride (0.5 ml; 48% aqueous solution). The mixture was stirred at room temperature for 16 h. It was then poured into a chloroform–ether bilayer (10 ml of each) in a separating funnel, and the layers separated. The aqueous layer was extracted with chloroform (10 ml), and the combined organic layers dried ($MgSO_4$). Removal of the solvents by evaporation and purification of the residue by chromatography on silica gel (20% ether–petrol to 20% ethyl acetate–petrol to 30% ethyl acetate–petrol) yielded the inseparable hydroxylactones **19** and **22** (0.246 g, 66%) in a 7:1 ratio, as a colourless oil. A portion of this material (39.0 mg, 0.198 mmol) in CH_2Cl_2 (4 ml), was treated with Et_3N (40.0 mg, 55 ml, 0.398 mmol, 2.0 eq), DMAP (catalytic), and 3,5-dinitrobenzoyl chloride (91 mg, 0.398 mmol, 2.0 eq). The mixture was stirred at room temperature for 10 min. Additional 3,5-dinitrobenzoyl chloride (91.0 mg, 0.398 mmol, 2.0 eq) was

added, and the reaction allowed to stir until tlc indicated absence of starting material. The mixture was poured into a saturated aqueous sodium hydrogencarbonate–CH_2Cl_2 bilayer (8 ml of each), and the layers separated. The aqueous layer was extracted with CH_2Cl_2 (3 x 8 ml) and the combined CH_2Cl_2 layers were washed with water (8 ml) before drying ($MgSO_4$). Removal of the solvents by evaporation followed by purification of the residue by chromatography (30% EtOAc–petrol) yielded, in order of elution, *[1R*,5R*,6R*,9S*,1'S*]-6-[1-(3,5-dinitrobenzoyl-oxy)ethyl]-9-methyl-2-oxo-3-oxabicyclo[3.4.0]-7-nonene* **20** (6 mg, 8%) and its C-1' epimer *[1R*,5R*,6R*,9S*,1'R*]-6-[1-(3,5-dinitrobenzoyloxy)ethyl]-9-methyl-2-oxo-3-oxabicyclo[3.4.0]-7-nonene* **20** (41 mg, 58%), both as yellow crystalline solids; **20**: mp 134°C; υ_{max} (Nujol) 1773, 1731, 1548, 1466, 1345, 1283, 1180, 1077, 990, 804, 665 cm^{-1}; δ_H (270 MHz) 9.24 (1H, m, para $C_6H_3(NO_2)_2$), 9.10 (2H, m, ortho $C_6H_3(NO_2)_2$), 5.88 (2H, m, H-7, H-8), 5.45 (1H, dq, J 13.5, 5.5 Hz, H-1'), 4.45 (1H, dd, J 9.0, 7.0 Hz, H-4), 4.15 (1H, dd, J 12.0, 9.0 Hz, H-4), 2.74 (1H, m, H-6), 2.66-2.35 (2H, m, downfield H-5, upfield H-9), 2.10 (1H, dd, J 14.0, 10.0 Hz, H-1), 1.52 (3H, d, J 5.5 Hz, C-1' CH_3), 1.31 (3H, d, J 7.0 Hz, C-9 CH_3); *m/z* (EI) 390 (M^+), 346 (M^+-CO_2), 318 (M^+-CH_3CHOCO), 239 ($CH_3CHOCOC_6H_3(NO_2)_2^+$), 195 ($M^+$-$COC_6H_3(NO_2)_2$), 163, 106, 91, 75 (Found: (M^+), 390.1063. $C_{18}H_{18}N_2O_8$ requires (M^+), 390.1063); **23**: mp 150°C; υ_{max} (Nujol) 1783, 1732, 1547, 1467, 1349, 1279, 1170, 1158, 1078, 670 cm^{-1}; δ_H (270 MHz) 9.27 (1H, dd, J 3.0, 2.0 Hz, para $C_6H_3(NO_2)_2$), 9.12 (2H, d, J 2.5 Hz, ortho $C_6H_3(NO_2)_2$), 5.81 (1H, br d, J 10.0 Hz, H-8), 5.69 (1H, ddd, J 10.0, 5.0, 3.0 Hz, H-7), 5.22 (1H, dq, J 15.0, 7.5 Hz, H-1'), 4.32 (1H, dd, J 8.5, 6.5 Hz, H-4), 3.81 (1H, dd, J 12.0, 8.5 Hz, H-4), 2.92 (1H, m, H-6), 2.68-2.50 (1H, m, H-5), 2.50-2.37 (1H, m, H-9), 1.98 (1H, dd, J 15.0, 10.5 Hz, H-1), 1.49 (3H, d, J 7.5 Hz, C-1' CH_3), 1.33 (3H, d, J 8.0 Hz, C-9 CH_3); *m/z* (EI) 390 (M^+), 346 (M^+-CO_2), 318 (M^+-CH_3CHOCO), 239 ($CH_3CHOCOC_6H_3(NO_2)_2^+$), 195 ($M^+$-$COC_6H_3(NO_2)_2$), 165, 106, 91, 75 (Found: (M^+), 390.1063. $C_{18}H_{18}N_2O_8$ requires (M^+), 390.1063).

IMDA Reaction of trienes (7).

A resealable pressure tube was base-washed with HMDS and dried as previously described. A solution of the trienes **7a** and **7b** (0.473 g, 1.120 mmol) in toluene (12 ml) was thoroughly degassed by alternate sonication and argon purge, as described previously. The solution was transferred to the argon-filled tube via cannula, and the tube heated (170°C) in a Wood's metal bath for 24 h. Removal of the toluene by evaporation under reduced pressure yielded a yellow oil (0.473 g, 100% mass recovery). Examination of the crude reaction mixture by ^1H nmr showed it to consist of two major products and a minor cycloadduct in a ratio of ca. 12:12:1. The crude reaction mixture (0.473 g) was dissolved in acetonitrile (10 ml) and treated with aqueous hydrofluoric acid (50 ml of a 48% aqueous solution). The reaction was stirred at room temperature for 30 min when examination by tlc indicated the absence of starting material. The reaction was worked up by the addition of solid sodium hydrogencarbonate until effervescence had ceased, and the mixture poured into a saturated aqueous sodium hydrogencarbonate–CH_2Cl_2 bilayer (60 ml of each) and the layers separated. The aqueous layer was extracted with CH_2Cl_2 (3 x 40 ml), and the combined organic layers washed with water (60 ml) and then dried ($MgSO_4$). Removal of the solvent by evaporation followed by purification of the residue by chromatography on silica gel (40-80% ethyl acetate–petrol) yielded, in order of elution, *(+)-[1S,4S,5S,6S,9R,1'S]-6-(1-hydroxyethyl)-4,9-dimethyl-2-oxo-3-oxabicyclo[3.4.0]-7-nonene* **25** (19 mg, 8%) as a colourless crystalline solid, and an inseparable mixture of *(+)-[1S,2S,3S,6R,1'S,1''R]-methyl 2,3-bis(1-hydroxyethyl)-6-methyl-4-cyclohexene-1-carboxylate* **27** and its C-1'' epimer *[1S,2S,3S,6R,1'S,1''S]-methyl 2,3-bis(1-hydroxyethyl)-6-methyl-4-cyclohexene-1-carboxylate* (195 mg, 72%) as a colourless oil. To the inseparable mixture of dihydroxyesters (194 mg, 0.801 mmol) in CH_2Cl_2 (2 ml) was added catalytic (±)-10-camphorsulfonic acid. The reaction mixture was stirred at room temperature for 13 h, and was then purified by chromatography on silica gel (30-50% ethyl acetate–petrol) to yield further hydroxylactone **25** (0.072 g, 43%), and the unaffected dihydroxyester **27** (0.111 g, 57%) as a clear crystalline solid; **25**: mp 130.5-132°C, $[\alpha]_D^{20}$ +30.0 (*c* 0.78, $CHCl_3$); υ_{max} (Nujol) 3582, 3456, 3028, 2854, 2727, 2346, 2277, 1749, 1410, 1319, 1264, 1188, 1084, 1059, 1035, 963, 935, 900, 865, 847, 804, 770 cm^{-1}; δ_H (500 MHz) 5.86 (1H, br dt, J 10.0, 1.5 Hz, H-7),

5.75 (1H, ddd, J 10.0, 5.0 Hz, H-8), 4.79 (1H, quintet, J 7.0 Hz, H-4), 4.29 (1H, dq, J 6.5, 2.0 Hz, H-1'); 2.92 (1H, dd, J 14.5, 10.0 Hz, H-1), 2.53 (1H, ddd, J 14.5, 7.0, 5.5 Hz, H-5), 2.46-2.43 (1H, m, H-6), 2.42-2.36 (1H, m, H-9), 1.55 (3H, d, J 7.0 Hz, C-4 CH_3), 1.30 (3H, d, J 7.0 Hz, C-9 CH_3), 1.28 (3H, d, J 6.5 Hz, C-1' CH_3); *m/z* (EI) 210 (M^+), 195 (M^+-CH_3), 192 (M^+-H_2O), 177 (M^+-CH_3-H_2O), 166 (M^+-CH_3CHO), 137, 121, 93, 45 (Found: C, 68.42; H, 8.91. $C_{12}H_{18}O_3$ requires C, 68.55; H, 8.63%); **27**: mp 123-125°C, $[\alpha]_D^{20}$ +25.5 (*c* 0.2, $CHCl_3$); υ_{max} (Nujol) 3164, 1726, 1314, 1284, 1174, 1093, 1045, 937, 907, 741 cm^{-1}; δ_H (500 MHz) 5.64 (1H, ddd, J 10.0, 6.0, 2.5 Hz, H-4), 5.49 (1H, ddd, J 10.0, 2.5, 1.0 Hz, H-5), 3.85 (1H, dq, J 6.5, 3.0 Hz, H-1'), 3.79 (3H, s, CH_3O), 3.70 (1H, dq, J 9.0, 6.0 Hz, H-1"), 2.69-2.64 (1H, m, H-6), 2.58 (1H, dd, J 11.5, 10.0 Hz, H-1), 2.43-2.38 (1H, m, H-3), 1.97 (1H, dt, J 11.5, 3.5 Hz, H-2), 1.36 (3H, d, J 6.5 Hz, C-1' CH_3), 1.25 (3H, d, J 6.0 Hz, C-1" CH_3), 0.98 (3H, d, J 7.0 Hz, C-6 CH_3); *m/z* (CI) 243 (MH^+), 225 (MH^+-H_2O), 207 (MH^+-$2H_2O$), 181, 121, 93 (Found: (MH^+), 243.1596. $C_{13}H_{22}O_4$ requires (MH^+), 243.1596).

IMDA Reaction of triene (8).

A thoroughly degassed solution of triene **8** (109 mg, 0.28 mmol) in toluene (4 ml) was heated in a base-washed resealable pressure tube under N_2 at 165°C for 85 h, after which the toluene was removed by evaporation under reduced pressure to yield a pale yellow oil. This was shown by ^1H nmr to consist of a 1:1 mixture of diastereomeric cycloadducts. The crude mixture (59 mg) was dissolved in MeCN (4 ml) and to this solution was added aqueous HF (10 ml of a 48% solution in water). The reaction mixture was allowed to stir at room temperature for 1.5 h, after which solid $NaHCO_3$ was added portionwise until effervescence had ceased. The mixture was poured into saturated aqueous $NaHCO_3$ (30 ml) and extracted with DCM (3 x 30 ml), and the combined organic extracts were washed with water (30 ml), dried ($MgSO_4$) and evaporated under reduced pressure. The resulting brown oil was purified by chromatography (EtOAc–petrol), to yield an inseparable mixture of *[1R*,5R*,6S*]-6-(hydroxymethyl)-7-methyl-2-oxo-3-oxabicyclo[3.4.0]-7-nonene* **31** and its C-6 epimer *[1R*,5R*,6R*]-6-(hydroxymethyl)-7-methyl-2-oxo-3-oxabicyclo[3.4.0]-7-nonene* **32** (51 mg, 100%) as a colourless crystalline solid; υ_{max} (film) 3477, 3451, 3429, 2930, 1763, 1187, 1159, 1139, 1109, 1054, 1032, 989, 961, 944, 911 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 5.64-5.63 (1H, m, H-8 one isomer), 5.61-5.59 (1H, m, H-8 one isomer), 4.69 (1H, dd, J 9.0, 6.5 Hz, H-4 one isomer), 4.46 (2H, m, H-4 one isomer), 4.02 (1H, dd, J 11.0, 9.0 Hz, H-4 one isomer), 3.95 (1H, dd, J 10.5, 3.5 Hz, C*H*$_2$OH one isomer), 3.82 (1H, dd, J 11.5, 2.5 Hz, C*H*$_2$OH one isomer), 3.74 (1H, dd, J 11.5, 11.0 Hz, C*H*$_2$OH one isomer), 3.59 (1H, dd, J 10.0, 8.0 Hz, C*H*$_2$OH one isomer), 2.60 (1H, ddd, J 17.5, 9.5, 5.5 Hz, H-1 one isomer), 2.46-2.03 (9H, m, H-1 one isomer, and H-5, H-6 and H-9 both isomers) 1.78 (3H, s, CH_3 one isomer), 1.71 (3H, s, CH_3 one isomer); *m/z* (CI) 200 (M+NH_4^+), 183 (MH^+), 164 (M^+-H_2O), 153, 137, 119, 107, 91 (Found: (M+NH_4^+), 200.1288. $C_{10}H_{14}O_3$ requires (M+NH_4^+), 200.1287).

IMDA reaction of triene (9).

A solution of triene **9** (170 mg, 0.45 mmol) in toluene (8 ml) was thoroughly degassed, and then transferred to a base-washed resealable pressure tube under N_2. The tube was heated at 165°C for 36 h, and the toluene was then removed by evaporation under reduced pressure to yield a pale yellow oil. This was shown by ^1H nmr to consist of a single cycloadduct. The crude mixture (170 mg) was dissolved in MeCN (7 ml) and to this solution was added aqueous HF (25 ml of a 48% solution in water). The reaction mixture was allowed to stir at room temperature for 30 min when solid $NaHCO_3$ was added portionwise until effervescence had ceased. The mixture was poured into saturated aqueous $NaHCO_3$ (30 ml) and extracted with CH_2Cl_2 (3 x 30 ml), and the combined organic layers were washed with water (30 ml), dried ($MgSO_4$) and concentrated under reduced pressure. The resulting brown oil was purified by chromatography (50% EtOAc–petrol), to yield a colourless oil (51 mg). A portion of this material (25 mg, 0.125 mmol) was dissolved in CH_2Cl_2, TFA (2 drops) was added and the mixture allowed to stir for 5 h at room temperature. Solid $NaHCO_3$ was added until

effervescence ceased, the mixture was filtered and the residue washed with CH_2Cl_2 (10 ml). The filtrate was concentrated under reduced pressure and the resulting pale yellow solid purified by chromatography (50% EtOAc–petrol) to give *[1R*,5R*,6R*]-6-(hydroxymethyl)-2-oxo-3-oxabicyclo[3.4.0]-7-nonene* **34** (22 mg, 98%; 56% from **9**) as a colourless crystalline solid, mp 76-78°C (EtOAc–petrol); υ_{max} ($CHCl_3$) 3362, 2921, 2898, 2885, 1772, 1187, 1145, 1110, 1071, 1042, 995, 798, 783, 724, 706 cm-1; δ_H (500 MHz) 5.95-5.91 (1H, m, H-8), 5.67-5.63 (1H, m, H-7), 4.46 (1H, dd, J 9.0, 7.0 Hz, H-4), 4.38 (1H, dd, J 11.0, 9.0 Hz, H-4), 3.75 (1H, dd, J 11.0, 3.5 Hz, H-1'), 3.68 (1H, dd, J 11.0, 7.5 Hz, H-1'), 2.63-2.59 (1H, m, H-6), 2.57-2.41 (4H, m, H-1, H-5 and H-9); *m/z* (CI) 186 ($M+NH_4^+$), 169 (MH+), 150 (M^+-H_2O), 123, 105, 93, 78 (Found: ($M+NH_4^+$), 186.1124. $C_9H_{12}O_3$ requires ($M+NH_4^+$), 186.1130).

X-Ray crystal data[22]

All data were corrected for Lorentz and polarisation factors; the non-hydrogen atoms were refined anisotropically. Unless stated otherwise, the positions of all hydrogen atoms were idealised, C–H = 0.96Å, assigned isotropic thermal parameters, $U(H) = 1.2U_{eq}(C)$, and allowed to ride on their parent carbon atoms. All methyl groups were refined as rigid bodies. All computations were carried out using the SHELXTL programme system.[23]

Compound **13**: data were measured using a Nicolet R3m diffractometer, using Cu-K_α radiation (λ = 1.54178Å, graphite monochromator), using ω-scans, with $0° \le 2\theta \le 116°$. $C_{10}H_{10}O_3$, M = 182.2, monoclinic, a = 12.276(7), b = 5.664(3), c = 15.041(11) Å, β = 112.11(5)°, V = 969 Å^3, space group $P2_1/c$, Z = 4, D_c = 1.25 g cm^{-3}, μ(Cu-K_α) = 7 cm^{-1}, $F(000)$ = 392. 1306 Independent reflections were measured of which 1183 had $|F_o| > 3\sigma(|F_o|)$, and were considered to be observed. Refinement was by full-matrix least squares to give R = 0.044, R_w = 0.052 [$w^{-1} = \sigma^2(F) + 0.0002F^2$]. The maximum and minimum residual electron densities in the final ΔF map were 0.19 and -0.17 eÅ^{-3} respectively. The maximum and mean shift/error ratios in the final refinement cycle were 0.018 and 0.005 respectively.

Compound **17**: data were measured using a Siemens P3/PC diffractometer, using Mo-K_α radiation (λ = 0.71073Å, graphite monochromator), using ω-scans, with $3° \le 2\theta \le 45°$. $C_{12}H_{20}O_4$, M = 228.3, orthorhombic, a = 11.799(3), b = 14.665(3), c = 15.003(3) Å, V = 2596 Å^3, space group $P2_12_12_1$, Z = 8, D_c = 1.17 g cm^{-3}, μ(Mo-K_α) = 0.86 cm^{-1}, $F(000)$ = 992. 1941 Independent reflections were measured of which 1423 had $|F_o| > 4\sigma(|F_o|)$, and were considered to be observed. Refinement was by full-matrix least squares to give R = 0.039, R_w = 0.040 [$w^{-1} = \sigma^2(F) + 0.0007F^2$]. The maximum and minimum residual electron densities in the final ΔF map were 0.12 and -0.12 eÅ^{-3} respectively. The maximum and mean shift/error ratios in the final refinement cycle were 0.001 and 0.000 respectively.

Compound **20**: data were measured using a Siemens P4/PC diffractometer, using Cu-K_α radiation (λ = 1.54178Å, graphite monochromator), using ω-scans, with $3° \le 2\theta \le 110°$. $C_{18}H_{18}N_2O_8$, M = 390.3, triclinic, a = 8.215(3), b = 14.377(4), c = 17.097(5) Å, α = 112.31(2)°, β = 97.90(3)°, γ = 91.04(3)°, V = 1845 Å^3, space group $P\bar{1}$, Z = 4, D_c = 1.41 g cm^{-3}, μ(Cu-K_α) = 9.56 cm^{-1}, $F(000)$ = 816. 4253 Independent reflections were measured of which 2820 had $|F_o| > 4\sigma(|F_o|)$, and were considered to be observed. Refinement was by full-matrix least squares to give R = 0.077, R_w = 0.076 [$w^{-1} = \sigma^2(F) + 0.0005F^2$]. The maximum and minimum residual electron densities in the final ΔF map were 0.28 and -0.27 eÅ^{-3} respectively. The maximum and mean shift/error ratios in the final refinement cycle were 0.001 and 0.000 respectively.

Compound **23**: data were measured using a Siemens P3/PC diffractometer, using Mo-K_α radiation (λ = 0.71073Å, graphite monochromator), using ω-scans, with $3° \le 2\theta \le 47°$. $C_{18}H_{18}N_2O_8 \cdot C_6H_6$, M = 468.5, monoclinic, a = 7.249(6), b = 28.99(2), c = 11.175(12) Å, β = 97.84(2)°, V = 2327 Å^3, space group $P2_1/a$, Z = 4, D_c = 1.34 g cm^{-3}, μ(Mo-K_α) = 1.01 cm^{-1}, $F(000)$ = 984. 3438 Independent reflections were measured of

which 1796 had $|F_o| > 4\sigma(|F_o|)$, and were considered to be observed. Refinement was by full-matrix least squares to give $R = 0.048$, $R_w = 0.047$ [$w^{-1} = \sigma^2(F) + 0.0007F^2$]. The maximum and minimum residual electron densities in the final ΔF map were 0.18 and -0.15 eÅ^{-3} respectively. The maximum and mean shift/error ratios in the final refinement cycle were 0.000 and 0.000 respectively.

Compound **25**: data were measured using a Siemens P3/PC diffractometer, using Cu-K$_\alpha$ radiation (λ = 1.54178Å, graphite monochromator), using ω-scans, with $0° \leq 2\theta \leq 116°$. $C_{12}H_{18}O_3$, M = 210.3, orthorhombic, a = 7.917(3), b = 10.776(4), c = 13.455(4) Å, V = 1148 Å^3, space group $P2_12_12_1$, Z = 4, D_c = 1.22 g cm^{-3}, μ(Cu-K$_\alpha$) = 6.98 cm^{-1}, $F(000)$ = 456. 922 Independent reflections were measured of which 894 had $|F_o| > 4\sigma(|F_o|)$, and were considered to be observed. Refinement was by full-matrix least squares to give R = 0.048, R_w = 0.056 [$w^{-1} = \sigma^2(F) + 0.0005F^2$]. The maximum and minimum residual electron densities in the final ΔF map were 0.19 and -0.17 eÅ^{-3} respectively. The maximum and mean shift/error ratios in the final refinement cycle were 0.004 and 0.000 respectively.

Compound **27**: data were measured using a Siemens P3/PC diffractometer, using Cu-K$_\alpha$ radiation (λ = 1.54178Å, graphite monochromator), using ω-scans, with $0° \leq 2\theta \leq 116°$. $C_{13}H_{22}O_4$, M = 242.3, monoclinic, a = 5.873(5), b = 8.548(7), c = 14.158(11) Å, β = 94.56(2)°, V = 709 Å^3, space group $P2_1$, Z = 2, D_c = 1.14 g cm^{-3}, μ(Cu-K$_\alpha$) = 6.77 cm^{-1}, $F(000)$ = 264. 1012 Independent reflections were measured of which 988 had $|F_o| > 4\sigma(|F_o|)$, and were considered to be observed. Refinement was by full-matrix least squares to give R = 0.035, R_w = 0.041 [$w^{-1} = \sigma^2(F) + 0.0005F^2$]. The maximum and minimum residual electron densities in the final ΔF map were 0.13 and -0.12 eÅ^{-3} respectively. The maximum and mean shift/error ratios in the final refinement cycle were 0.002 and 0.001 respectively.

Compound **34**: data were measured using a Siemens P4/PC diffractometer, using Cu-K$_\alpha$ radiation (λ = 1.54178Å, graphite monochromator), using ω-scans, with $3° \leq 2\theta \leq 120°$. $C_9H_{12}O_3$, M = 168.2, monoclinic, a = 5.525(2), b = 9.796(3), c = 15.518(6) Å, β = 95.63(2)°, V = 836 Å^3, space group $P2_1/n$, Z = 4, D_c = 1.34 g cm^{-3}, μ(Cu-K$_\alpha$) = 8.27 cm^{-1}, $F(000)$ = 360. 1236 Independent reflections were measured of which 1091 had $|F_o| > 4\sigma(|F_o|)$, and were considered to be observed. Refinement was by full-matrix least squares to give R = 0.042, R_w = 0.051 [$w^{-1} = \sigma^2(F) + 0.0005F^2$]. The maximum and minimum residual electron densities in the final ΔF map were 0.20 and -0.16 eÅ^{-3} respectively. The maximum and mean shift/error ratios in the final refinement cycle were 0.000 and 0.000 respectively.

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