cis-3,5-Cyclohexadiene-1,2-diol derivatives: facial selectivity in their Diels–Alder reactions with ethylenic, acetylenic and azo dienophiles

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The Diels–Alder reactions of maleimide with the acetonide derivative (**6a**) of *cis*-3,5-cyclohexadiene-1,2-diol (**1a**) in various solvents showed facial selectivities ranging from 1 : 1 to 1 : 9. The same derivative **6a** reacted in benzene with ethylenic dienophiles with generally modest facial selectivity, but acetylenic dienophiles added exclusively *anti* to the oxygen functions of **6a**. Dimerization of cyclic acetals **6a** and **7** was mainly, but for **6a** not exclusively, by *anti* addition with respect to both the diene and the dienophile partners. Reactions of azo dienophiles with derivatives of **1a** were predominantly by *anti* addition, but the diol itself (**1a**) gave the *syn* adduct as the major product.

Introduction

cis-3,5-Cyclohexadiene-1,2-diol **1a** and its optically active variants **1b** (Fig. 1) are available directly from aromatic precursors by the action of mutant strains of *Pseudomonas putida*.[1,2] These *cis*-diols are now well established as compact, multifunctional starting materials,[3] and there are many recent examples of their use in synthesis.[4–10]

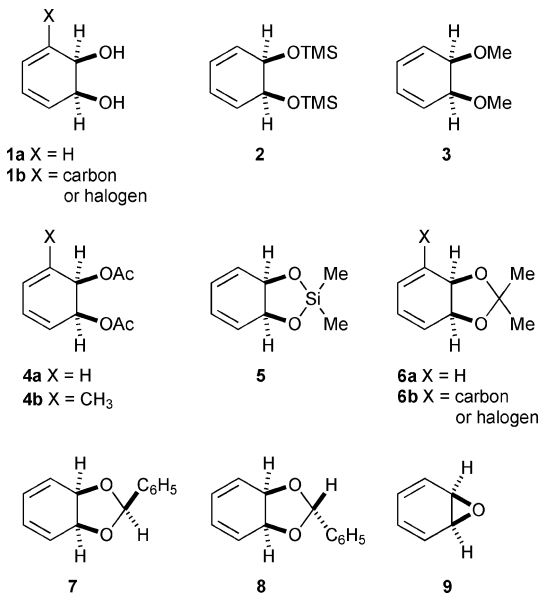

Fig. 1 The diene **1a** with its 3-substituted analogue **1b** and derivatives.

It is not surprising that the diols and their derivatives have served as Diels–Alder dienes in many instances. We assessed the facial selectivities of **1a** and a number of diol-protected derivatives **2–8** in Diels–Alder reactions in chloroform with *N*-phenylmaleimide as the dienophile.[11] What was most remarkable was that additions were very largely *syn* to the oxygen functions with **1a** and with the noncyclic derivatives **2**, **3** and **4a** (from 88 : 12 with **4a** up to exclusively *syn* with **2**). This was corroborated recently by the reaction of **1a** with a bromophenyl analog of *N*-phenylmaleimide,[9] and, under high pressure, cyclic enones added to **1b** (X = CH_3) to provide the *syn*-addition products with isolated yields of approximately 70%.[4,7,8] The reactions of 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD) with **1b** (X = carbon and halogen) took place with at least 97% *syn* selectivity.[12] Thus, the oxygen functions of **1a/b** appear to impart a significant bias toward *syn* addition, just as *syn* addition is the preferred mode of reaction of some 5-heteroatom-substituted 1,3-cyclopentadienes.[13–15] However, the structure of the adduct of a bromophenyl analog of PTAD with **4b** (X = CH_3) was determined by X-ray crystallography, and this was the *anti* adduct.[16]

The facial selectivities in the additions of *N*-phenylmaleimide to the cyclic derivatives **6a**, **7** and **8** ranged from 60 : 40, slightly favoring *syn* addition with **5** and **6a**, to 4 : 96, strongly favoring *anti* addition with **8**.[11] It was postulated that these cyclic derivatives present steric interactions in the *syn*-transition state that cannot be avoided by conformational mobility of the protecting groups, so the cyclic protecting groups in **6a**, **7** and **8** overcome the inherent tendency for *syn* addition. The result is that the *anti*-addition product either equals the amount of the *syn* adduct, or predominates.

The acetonide (**6a/b**) has been the derivative of **1a/b** that has been utilized far more than any other. Experiments with **6a** and **6b** (X = alkyl, 7-norbornadienyl, CF_3, and halogens) and *N*-phenyl- and *N*-ethylmaleimide resulted in additions with low facial selectivities,[11,17–20] with the ratios being somewhat dependent on the solvent.[19,20] However, for the reactions of **6b** (X = carbon) with maleic anhydride, a dienophile that with 5-alkyl- and 5-halogen-substituted 1,3-cyclopentadienes was closely related to the maleimides in terms of reactivity and facial selectivity,[14,21] only *anti*-addition products were reported,[22,23] and the additions of substituted maleic anhydride derivatives to **6a** gave the *anti*-addition products in roughly 75% yield.[5] Quinones are also closely related to maleimides in terms of their Diels–Alder behavior,[14,21] so it is curious that the reactions of benzoquinone

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and naphthoquinone with **6b** (X = Cl, Br) gave only the *anti* adducts, although the yields were reported to be modest.[23–25] All other reactions of **6b** (X = carbon, halogens) with carbon-based dienophiles provided *anti*-addition products only.[6,8,17–20,24,26] Reactions of **6a** and **6b** (X = CF_3, 7-norbornadieneyl, halogen) with PTAD and with nitroso compounds gave the *anti* adducts exclusively.[17,18,20,24,26,27] Also, addition of singlet oxygen to **6b** (X = Cl) was only *via anti* addition.[28]

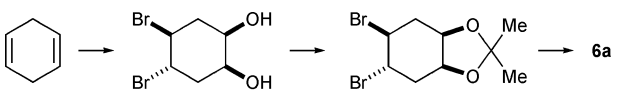
The epoxide compound **9** has some similarity to **1a**, and its Diels–Alder reaction with *N*-phenylmaleimide took place exclusively *anti* to the oxygen.[29] The same facial preference was reported for the addition of PTAD to **9**.[30] Calculations pointed to steric hindrance as the controlling factor.[31]

In spite of the number of examples of Diels–Alder reactions of **1a** and **1b** in the literature, explanations for the facial selectivities are still lacking. The major drawback of using the published data for the development of hypotheses is that in most instances it appears that only the major adduct was isolated and characterized. Yields of less than 70% are not uncommon—some are even less than 50%—and so it is not known if the reactions of **1a/b** are really highly facially selective with some important dienophiles. Therefore we undertook a reexamination of the facial selectivity in the Diels–Alder reactions of diol **1a** and some of its derivatives. First, the acetonide **6a** was reacted with a series of carbon-based dienophiles to determine if the maleimides are truly different from other dienophiles in that only they have been reported to have low facial selectivities. Second, **1a** and a number of derivatives were reacted with azo-dienophiles in order to confirm whether large differences exist in facial selectivity between **1a** and the derivatives. Our results are presented here.

Results and discussion

The acetonide 6a with carbon-based dienophiles

The acetonide **6a** was prepared from **10** by acetonization and double-elimination with base. The diol **10** had been synthesized from 1,4-cyclohexadiene (Scheme 1) by a previously described method.[11]



Scheme 1 Preparation of acetonide **6a**.

The reactant pair of diene **6a** and maleimide provided an opportunity to assess the influence of the solvent on facial selectivity, because both addends might be expected to associate significantly with polar solvents. To the best of our knowledge, only three similar studies have been reported.[11,19,32] The reactions of **6a** with maleimide were carried out at room temperature in a variety of solvents (Table 1). In every instance two adducts (**11** and **12**, in Fig. 2) were obtained, in combined yields of over 80%. As in all of the work described here, the relative amounts of the adducts were determined by careful integration of the well-dispersed signals for the olefinic hydrogens in the ^{1}H NMR spectra of the reaction mixtures. (In this, and most subsequent reactions, the adducts were separable by flash chromatography, and the stereochemistry of each adduct was determined by measurement of NOE enhancements.)

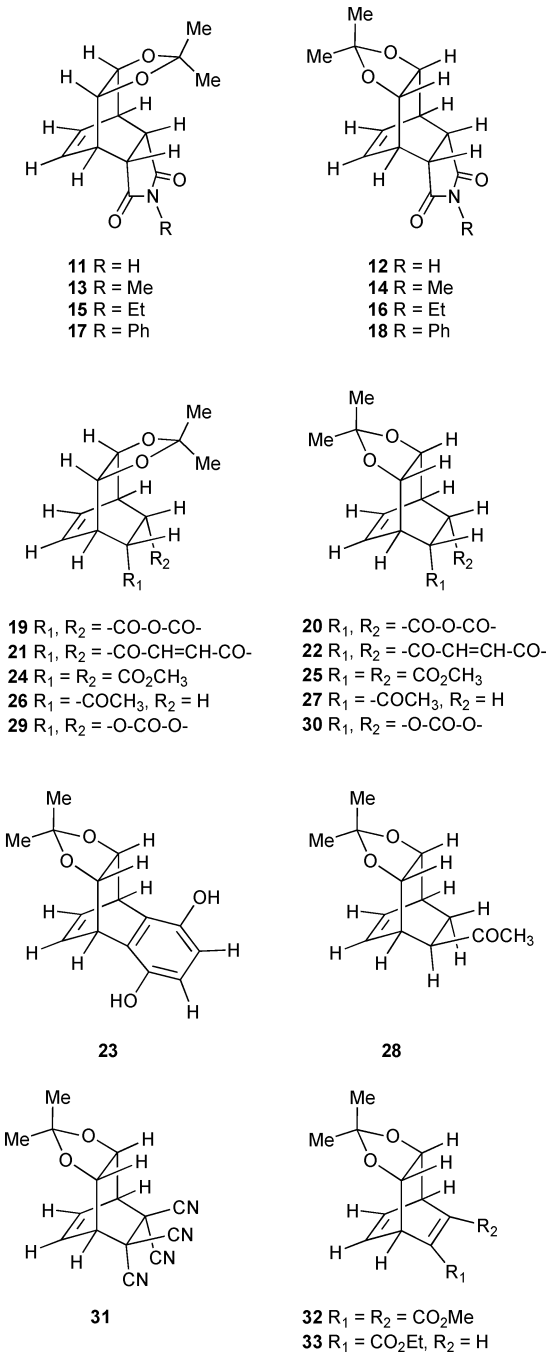


Fig. 2 Adducts derived from diene **6a** and various ethylenic and acetylenic dienophiles.

The results in Table 1 show a much greater range of facial selectivities than the previous studies, from essentially no facial selectivity up to a 1 : 9 ratio. Whereas the three previous studies all used oxygen-substituted dienes (**1a**,[11] **6a**[19] and 5-[(hydroxyimino)methyl]-1,2,3,4,5-pentamethylcyclopentadiene[32]), in this work the dienophile bore an acidic hydrogen (in contrast with *N*-ethyl- and *N*-phenylmaleimide[11,19,32]). The *anti*-addition product was generally more favored by a high solvent dielectric. (In Table 1, the solvents from benzene to water are given

Table 1 Ratios of the *syn* adduct (**11**) to the *anti* adduct (**12**) from the Diels–Alder reactions of maleimide with the acetonide diene **6a** in different solvents

Solvent	Total yield (**11** and **12**) (%)	Ratio of the *syn* adduct (**11**) to the *anti* adduct (**12**)
No solvent	99	27 : 73
Benzene	83	42 : 58
Chloroform	99	46 : 54
Diethyl ether	90	45 : 55
Dichloromethane	99	39 : 61
Pyridine	97	29 : 71
Methanol	94	27 : 73
Acetonitrile	99	21 : 79
Dimethyl sulfoxide	97	14 : 86
Water	89	10 : 90
1 M LiCl in water	81	14 : 86
1 M $LiClO_4$ in water	85	19 : 81
5 M $LiClO_4$ in diethyl ether	92	32 : 68

in the order of increasing dielectric constant.) Addition of salts (LiCl and $LiClO_4$) to the water resulted in slightly reduced facial selectivities. The facial selectivity in a solution of $LiClO_4$ in diethyl ether was better than in just diethyl ether. Thus, synthetically it would be advisable to use a solvent of high dielectric to maximize the yield of an *anti* adduct.

The facial selectivities of the reactions of *N*-methyl-, *N*-ethyl, and *N*-phenylmaleimide with **6a** (leading to products **13–18**) were similar to that of maleimide, *i.e.*, low, when all the reactions were conducted in benzene (Table 2). The facial selectivity in the reaction of the unsymmetrical diol **1b** (X = CF_3) with *N*-ethylmaleimide was consistent with the reactions of **1a**: the ratio was 48 : 53 slightly favoring the *anti* adduct.[18]

Reactions of **6a** with a number of additional carbon-based, ethylenic dienophiles were conducted in benzene (Table 2). Like maleimide, maleic anhydride, *p*-benzoquinone, and dimethyl maleate reacted with low facial selectivities, at best approximately 1 : 2, in favor of the *anti* adducts. The two adducts from the reaction of the quinone behaved very differently during purification on silica. The *syn* adduct **21** was isolated in a straightforward way, but the *anti* adduct **22**, while evident by ^{1}H NMR in the crude product mixture, was obtained as the aromatized compound **23**. The unsymmetrical dienophile 3-buten-2-one was modestly more facially selective than maleimide, producing (*endo*) adducts in a ratio of 1 : 4 in favor of the *anti* adduct. In addition to the two *endo* adducts, the reaction with 3-buten-2-one yielded a small proportion of the *anti-exo* adduct **28**. It was surprising that vinylene carbonate, which reacted sluggishly with **6a**, produced adducts in a ratio of 4 : 1 in favor of the *syn* adduct. The reason for this difference in facial preference is not obvious.

Overall, none of these ethylenic dienophiles gave only one adduct with **6a**. The many results for **6b** suggest that it reacts with much higher facial selectivity than does **6a**. A possible explanation is that an interaction between the annular substituent and the closer oxygen of **6b** makes the difference in transition state energies of the *syn* and *anti* transition states larger with **6b** than with **6a**. The torsional angle from the annular substituent to the closer oxygen of **6b** is very close to 60°. In the *syn* transition state, this angle would be compressed, whereas in the *anti* transition state this angle would become larger. While angular changes at the transition states would be similar with **6a**, the size of a hydrogen on **6a**, *versus* the substituent on **6b**, would make the consequence of the angular change less pronounced.

Tetracyanoethylene presents sterically hindering carbon substituents in both the *endo* and *exo* regions of the Diels–Alder transition state. Thus, it would be reasonable to expect a significant barrier to *syn* addition with this dienophile,[14,21] and, indeed, only its *anti* adduct **31** was observed. On the other hand, there is no steric reason to anticipate a significant barrier to *syn* addition with an acetylenic dienophile. With 5-alkyl-1,3-cyclopentadienes dimethyl acetylenedicarboxylate showed more *syn* adduct than did ethylenic dienophiles,[21] and Paquette's dodecahedrane synthesis relied on an initial *syn* addition of acetylenedicarboxylate to 9,10-dihydrofulvalene.[33] Nevertheless, both dimethyl acetylenedicarboxylate and ethyl propiolate reacted with **6a** to provide only the *anti* adducts **32** and **33**. Unsymmetrical dienes **1b** (X = CF_3, 7-norbornadieneyl, F) had shown the same selectivity.[17,18,20] It can be conjectured that the reluctance of the alkyne to add *syn* to the oxygen functions stems from a repulsive interaction in the *syn* transition state between the π-bond of the alkyne that is orthogonal to the plane of the developing σ-bonds and the lone pair(s) of the oxygen(s) on the diene. There is some computational evidence that a second factor can attenuate *syn* addition. A comparison of computed (HF/6-31G(d)) transition

Table 2 Proportions of *syn* adduct and *anti* adduct from the Diels–Alder reactions of carbon-based dienophiles with the acetonide diene **6a** in benzene

Dienophile	*syn* Adduct	*anti* Adduct	Proportions (%) of the *syn* and the *anti* adducts
Maleimide	**11**	**12**	42 : 58
N-Methylmaleimide	**13**	**14**	47 : 53
N-Ethylmaleimide[a]	**15**	**16**	39 : 61
N-Phenylmaleimide[a]	**17**	**18**	52 : 48[b]
Maleic anhydride	**19**	**20**	40 : 60[c]
p-Benzoquinone	**21**	**22**	32 : 68
Dimethyl maleate	**24**	**25**	32 : 68
3-Buten-2-one[d]	**26**	**27**	21 : 79[e]
Vinylene carbonate	**29**	**30**	81 : 19
Tetracyanoethylene	—	**31**	0 : 100
Dimethyl acetylenedicarboxylate	—	**32**	0 : 100
Ethyl propiolate	—	**33**	0 : 100

[a] Data from ref. 19. [b] Ratio 60 : 40 for the reaction in chloroform, ref. 11. [c] The adducts were not isolated. [d] Reaction in toluene. [e] Only the *endo* adducts are given in the Table. The ratio of **25** : **26** : **27** was 21 : 79 : 14.

states for *syn* and *anti* additions of acetylene and of maleimide to 5-methyl-1,3-cyclopentadiene indicates that more *syn* addition should occur with acetylene (29% *syn* with acetylene *versus* 13% *syn* with maleimide).[15] This is in accord with a simple steric rationalization. However, the corresponding comparisons with 5-chloro- and 5-bromo-1,3-cyclopentadiene reveal that much less *syn* addition should take place with acetylene compared to maleimide (for the chloro-diene, 14% *syn* with acetylene *versus* 88% *syn* with maleimide; and for the bromo-diene, 0.7% *syn* with acetylene *versus* 33% *syn* with maleimide).[15] These results are not consistent with a simple steric argument, but do indicate another, very significant mechanism of inhibition of the *syn* addition. In the case of **6a/b**, the geometry of this interaction is different from that in a 5-substituted 1,3-cyclopentadiene, and **6a/b** has two, not just one, lone-pair-bearing plane-nonsymmetric atoms.

Dimerization

Dimerization of **1a** or its derivatives would be a special case of the addition of a carbon-based dienophile, one in which the dienophile is also plane-nonsymmetric. Dienes **1a** and **1b** do not appear to dimerize spontaneously, but dimerization of **6b** (X = CF_3,[17] Br,[34,35] Cl,[35] vinyl,[36] CN,[37] $SiHMe_2$[38]) is well known, and *trans*-benzylidene **8** (and the *p*-NO_2-phenyl variant) also dimerizes readily giving **34** (Fig. 3).[11] In every instance, the only dimer isolated was the result of *anti* addition of both the diene and the dienophile partners. That only one dimer was produced from **8** was in accord with the high facial selectivity witnessed in the reaction of **8** with *N*-phenylmaleimide.[11] Prolonged storage of the *cis*-benzylidene **7**, which was initially thought not to dimerize,[11] also produced one dimer **35**. This was once again the result of *anti* addition of both the diene and the dienophile partners.

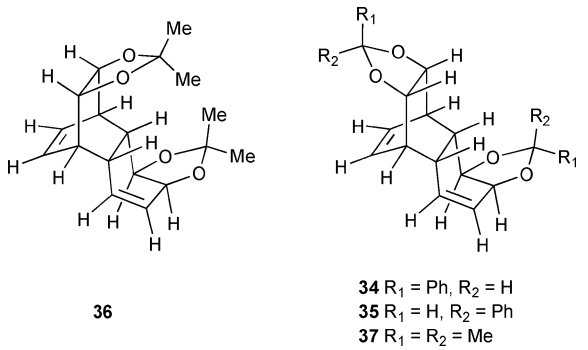


Fig. 3 Dimeric products from acetonides.

In comparison with **7** and **8**, **6a** had shown less facial selectivity with *N*-phenylmaleimide.[11] Diene **6a** was less facially selective in dimerization, also. When **6a** was kept under nitrogen at room temperature for 28 days, the result was conversion to two dimers **36** and **37**, in a ratio of 1 : 6. Measurement of NOE enhancements revealed that the minor isomer was the result of *syn* addition of the diene and *anti* addition of the dienophile (**36**). The major isomer was the result of *anti* addition of both the diene and the dienophile partners (**37**). Compound **37** was the same as the product of debromination of the dimer of **6b** (X = Br).[35] It is not clear why **6a** shows less facial selectivity in its dimerization than does **6b**, but that only two of the four possible *endo*-addition dimers were produced from **6a** indicates that **6a** is more facially selective as a dienophile than as a diene.

Table 3 Proportions of *syn* adduct and *anti* adduct from the Diels–Alder reactions of 4-phenyl-1,2,4-triazoline-3,5-dione with **1a** and derivatives in acetone

Diene	*syn* Adduct	*anti* Adduct	Proportions (%) of *syn* and *anti* adducts
1a	**38**	**39**	76 : 24
2	—	**40**	0 : 100
4a	**41**	**42**	12 : 88
6a	—	**43**	0 : 100
7	—	**44**	0 : 100
8	—	**45**	0 : 100

Azo dienophiles with 1a and derivatives

A survey of additions of **1a** and derivatives **2**, **4a**, **6a**, **7** and **8** with PTAD was carried out. The results are summarized in Table 3. The stereochemistry of the adducts could be determined by measurement of NOE enhancements, in most instances. This was not the case for **42** (Fig. 4), but acetylation of **39**, the minor adduct from **1a**, produced **42**, the major adduct from **4a**.

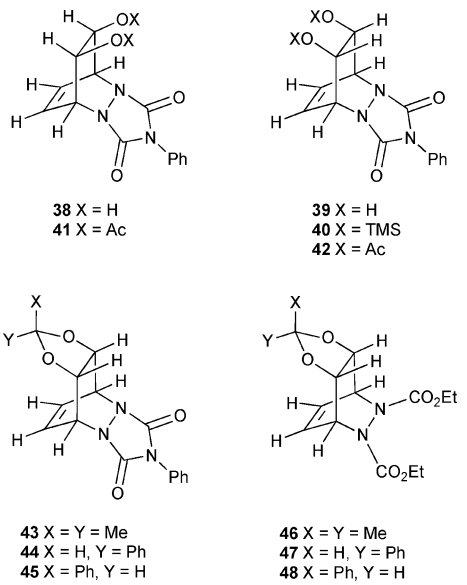


Fig. 4 Adducts derived from PTAD and DEAD.

The computational study with 5-substituted 1,3-cyclopentadienes[15] had revealed inhibition of *syn* addition of 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD) to a diene with a lone-pair-bearing substituent. It was suggested that this interaction was a filled-orbital repulsion. The data in Table 3 suggest that such an interaction might exist with the derivatives of **1a** as well. Whereas PTAD should be less sterically demanding than *N*-phenylmaleimide, the proportions of *anti* adduct with PTAD were much higher. What was again observed was that the simpler dienes **1a** and **4a** seemed to react with less facial selectivity than the substituted dienes **1b** (X = wide variety of substituents), which had reacted with PTAD to give over 97% of the *syn* adduct,[12] and **4b** (X = CH_3), for which only the *anti* adduct had been reported.[16]

It is tempting to ascribe the *syn* selectivity of **1a**/**b** to hydrogen bonding between the addends.

The only products detected from the Diels–Alder reactions of PTAD with dienes **6a**, **7** and **8** were the *anti* adducts **43**, **44** and **45**. The same facial selectivity was observed when diethyl azodicarboxylate (DEAD) was employed as an azo dienophile with **6a**, **7** and **8**. There are many examples of additions of heterodienophiles to **6b**, and, in every instance, only the *anti* adducts were reported.[17,18,20,24,26,27]

Conclusions

The reactions of **6a** with maleimide in various solvents showed a significant range of facial selectivities, from essentially 1 : 1 up to 1 : 9. Different ethylenic dienophiles added to **6a** (in benzene) with modest facial selectivities, in contrast with reportedly high selectivities for the substituted dienes **6b**. Acetylenic dienophiles added to **6a** exclusively *anti.* There was also a marked tendency for azo dienophiles (PTAD and DEAD) to add *anti* to the oxygen functions of the diene, although the reaction of PTAD and **1a** gave mainly the *syn* adduct.

Experimental

General

Melting points are uncorrected. NMR spectra are at 300 MHz for ^{1}H and 74.5 MHz for ^{13}C. Shifts are relative to internal tetramethylsilane. Nuclear Overhauser effect (NOE) measurements were made using difference spectra. Assignments are based on 2-D homo- and heterocorrelation experiments, APT spectra (for ^{13}C) and the NOE measurements. ^{13}C NMR shifts that are not assigned may be followed in parentheses by the number of attached hydrogens. Mass spectra were obtained by electron impact ionization at 70 eV. "Chromatography" refers to flash chromatography on silica gel; elution was with hexanes containing an increasing proportion of ethyl acetate.

Diene **1a** was obtained from the Aldrich Chemical Co. Dienes **2**,[11] **4a**,[11] **6a**,[11,39,40] **7**,[11] and **8**[11] were prepared by literature methods from **10**.[39,40] Diels–Alder reactions were conducted at RT except in those cases in which no product was evident by TLC after a few hours at RT. Solvents were evaporated, and the ratios of the adducts were obtained by careful integration of the ^{1}H NMR spectra. In most instances, the adducts could be separated by chromatography.

Diels–Alder reactions of acetonide 6a with carbon-based dienophiles

Solutions of **6a** and the dienophile in benzene were maintained at RT for a few hours. If TLC revealed some reaction progress, the mixture was stirred at RT until reaction was complete (by TLC). If TLC showed no reaction progress, the solution was heated at reflux until reaction was complete (by TLC). (Under these conditions *cis*-stilbene and styrene failed to undergo any Diels–Alder addition to **6a**.) After removal of the solvent the crude reaction mixture was analysed by ^{1}H NMR in order to obtain the proportions of the adducts by integration. Adducts were then purified by chromatography. Benzene solutions of some pure adducts (**11–14**, **24**, **25**, **29**, **30**, **31** and **33**) were heated under reflux for 12 to 16 h. In no case was there evidence, by TLC or by ^{1}H NMR, of equilibration to a mixture of adducts.

Diels–Alder reaction of 6a with maleimide

A solution of **6a** (124 mg, 0.817 mmol) and maleimide (158 mg, 1.63 mmol) in benzene (4.0 ml) at RT for 16 h gave **11** (182 mg, 45% after recrystallization from benzene) and **12** (152 mg, 38% after recrystallization from benzene) as colourless crystals.

For (3aα,4α,4aβ,7aβ,8α,8aα)-4a,7a,8,8a-tetrahydro-2,2-dimethyl-4,8-etheno-4*H*-1,3-dioxolo[4,5-*f*]isoindole-5,7(3a*H*,6*H*)-dione **11**: mp 172–174 °C; ν_{max}/cm^{-1} 1754; δ_H ($CDCl_3$) 8.40 (1 H, very br, N-H), 6.20 (2 H, m, 9-H and 10-H), 4.15 (2 H, dd, *J* 1.6 and 2.2, 3a-H and 8a-H), 3.39 (2 H, m, 4-H and 8-H), 3.36 (2 H, narrow m, 4a-H and 7a-H), 1.49 (3 H, s, 2-Me$_\beta$) and 1.35 (3 H, s, 2-Me$_\alpha$); saturation at δ 6.20 led to NOEs at δ 4.15 (1%) and 3.39 (9%), saturation at δ 4.15 led to NOEs at δ 6.20 (1.5%), 3.39 (14%) and 1.35 (2%), saturation at δ 3.39 led to NOEs at δ 6.20 (8%) and 4.15 (7%), saturation at δ 3.36 led to NOE at δ 1.49 (1%), saturation at δ 1.49 led to NOE at δ 3.36 (5%) and saturation at δ 1.35 led to NOE at δ 4.15 (8%); δ_C ($CDCl_3$) 179.7 (C-5 and C-7), 131.6 (C-9 and C-10), 112.5 (C-2), 73.7 (C-3a and C-8a), 39.0 (C-4a and C-7a), 36.5 (C-4 and C-8), 26.3 (2-Me$_\beta$) and 24.2 (2-Me$_\alpha$); *m*/*z* 250 (5%, M$^+$ + 1), 234.0775 (64, M$^+$ − CH_3, $C_{12}H_{12}NO_4$ requires 234.0766), 192 (51), 191 (63), 163 (40), 162 (35), 146 (36), 135 (48), 120 (64), 119 (32), 118 (48), 117 (39), 100 (74), 92 (78), 91 (82), 85 (53), 78 (49), 65 (55) and 43 (100).

For (3aα,4β,4aα,7aα,8β,8aα)-4a,7a,8,8a-tetrahydro-2,2-dimethyl-4,8-etheno-4*H*-1,3-dioxolo[4,5-*f*]isoindole-5,7(3a*H*,6*H*)-dione **12**: mp 233–234 °C; ν_{max}/cm^{-1} 1701; δ_H ($CDCl_3$) 8.27 (1 H, very br, N-H), 6.13 (2 H, m, 9-H and 10-H), 4.28 (2 H, narrow m, 3a-H and 8a-H), 3.44 (2 H, br m, 4-H and 8-H), 2.81 (2 H, t, *J* 1.4, 4a-H and 7a-H), 1.34 (3 H, s, 2-Me$_\beta$) and 1.29 (3 H, s, 2-Me$_\alpha$); saturation at δ 6.13 led to NOE at δ 3.44 (7%), saturation at δ 4.28 led to NOEs at δ 3.44 (9%), 2.81 (13%) and 1.29 (2%), saturation at δ 3.44 led to NOEs at δ 6.13 (8%), 4.28 (4%) and 2.81 (5%), saturation at δ 2.81 led to NOEs at δ 4.28 (11%) and 3.44 (8%), saturation at δ 1.34 led to NOE at δ 6.13 (1.5%) and saturation at δ 1.29 led to NOE at δ 4.28 (7%); δ_C ($CDCl_3$) 177.3 (C-5 and C-7), 129.7 (C-9 and C-10), 109.8 (C-2), 77.2 (C-3a and C-8a), 41.7 (C-4a and C-7a), 36.3 (C-4 and C-8), 25.3 (2-Me$_\beta$) and 24.9 (2-Me$_\alpha$); *m*/*z* 250 (0.7%, M$^+$ + 1), 234.0773 (30, M$^+$ − CH_3, $C_{12}H_{12}NO_4$ requires 234.0766), 192 (17), 191 (23), 163 (14), 162 (12), 146 (12), 135 (15), 120 (23), 100 (32), 92 (55), 91 (72) and 43 (100).

Diels–Alder reaction of 6a with *N*-methylmaleimide

A solution of **6a** (108 mg, 0.712 mmol) and *N*-methylmaleimide (79 mg, 0.71 mmol) in benzene (1.0 ml), stirred at RT for 17 h, yielded **13** (74 mg, 40%) and **14** (71 mg, 38%) as colourless crystals.

For (3aα,4α,4aβ,7aβ,8α,8aα)-4a,7a,8,8a-tetrahydro-2,2,6-trimethyl-4,8-etheno-4*H*-1,3-dioxolo[4,5-*f*]isoindole-5,7(3a*H*,6*H*)-dione **13**: mp 218–220 °C; ν_{max}/cm^{-1} 1689; δ_H ($CDCl_3$) 6.12 (2 H, dd, *J* 3.0 and 4.5, 9-H and 10-H), 4.15 (2 H, dd, *J* 1.7 and 2.2, 3a-H and 8a-H), 3.41 (2 H, m, 4-H and 8-H), 3.32 (2 H, narrow m, 4a-H and 7a-H), 2.91 (3 H, s, N–Me), 1.48 (3 H, s, 2-Me$_\beta$) and 1.35 (3 H, s, 2-Me$_\alpha$); saturation at δ 4.15 led to NOEs at δ 6.12 (2%),

3.41 (10%) and 1.35 (2%) and saturation at δ 1.48 led to NOE at δ 3.32 (5%); δ_C ($CDCl_3$) 179.4 (C-5 and C-7), 131.5 (C-9 and C-10), 112.4 (C-2), 73.9 (C-3a and C-8a), 37.7 (C-4a and C-7a), 36.6 (C-4 and C-8), 26.3 (2-Me_β), 24.7 (N–Me) and 24.2 (2-Me_α); *m/z* 264 (2%, $M^+ + 1$), 248.0913 (35, $M^+ - CH_3$, $C_{13}H_{14}NO_4$ requires 248.0922), 206 (51), 205 (47), 204 (16), 177 (32), 176 (25), 160 (21), 146 (37), 120 (43), 119 (21), 118 (22), 100 (73), 92 (100), 91 (100), 85 (39), 78 (28), 77 (22), 65 (33) and 43 (100).

For (3aα,4β,4aα,7aα,8β,8aα)-4a,7a,8,8a-tetrahydro-2,2,6-trimethyl-4,8-etheno-4*H*-1,3-dioxolo[4,5-*f*]isoindole-5,7(3a*H*,6*H*)-dione **14**: mp 190–192 °C; ν_{max}/cm^{-1} 1691; δ_H ($CDCl_3$) 6.05 (2 H, dd, *J* 3.1 and 4.4, 9-H and 10-H), 4.30 (2 H, narrow m, 3a-H and 8a-H), 3.46 (2 H, m, 4-H and 8-H), 2.92 (3 H, s, N–Me), 2.76 (2 H, narrow m, 4a-H and 7a-H), 1.33 (3 H, s, 2-Me_β) and 1.29 (3 H, s, 2-Me_α); saturation at δ 4.30 led to NOEs at δ 3.46 (9%), 2.76 (14%) and 1.29 (2%) and saturation at δ 1.33 led to NOE at δ 6.05 (2%); δ_C ($CDCl_3$) 177.4 (C-5 and C-7), 129.6 (C-9 and C-10), 109.7 (C-2), 77.3 (C-3a and C-8a), 40.4, 36.4, 25.3 and 24.9 (3C); *m/z* 264 (1%, $M^+ + 1$), 248.0922 (41, $M^+ - CH_3$, $C_{13}H_{14}NO_4$ requires 248.0922), 206 (45), 205 (41), 204 (16), 177 (32), 176 (22), 160 (20), 146 (33), 120 (41), 118 (22), 100 (54), 92 (100), 91 (96), 85 (37), 78 (29), 65 (25) and 43 (93).

Diels–Alder reaction of 6a with maleic anhydride

A solution of **6a** (124 mg, 0.817 mmol) and maleic anhydride (159 mg, 162 mmol) in benzene (4.0 ml) was stirred at RT for 16 h. After a ^1H NMR spectrum was taken, the product was passed through a very short silica gel column in order to remove less polar impurities. A mixture of adducts (334 mg, 83%) was obtained. Attempts to separate the adducts by chromatography led to hydrolysis. Assignment of the structures was based on similarity of the NMR spectra to other adduct mixtures. In the ^1H NMR spectra, the olefinic signal was always slightly downfield in the *syn* adduct, the carbinolic signal was always slightly downfield in the *anti* adduct, and the signal for the hydrogens α to the carbonyls was always at least 0.5 ppm downfield for the *syn* adduct.

For (3aα,4α,4aβ,7aβ,8α,8aα)-3a,4,4a,7a,8,8a-hexahydro-2,2-dimethyl-4,8-ethenofuro[3,4-*f*]-1,3-benzodioxole-5,7-dione **19**: δ_H ($CDCl_3$) (data from the adduct mixture) 6.20 (2 H, dd, *J* 2.9 and 4.3), 4.15 (2 H, narrow m), 3.40 (2 H, m), 3.38 (2 H, narrow m), 1.49 (3 H, s) and 1.35 (3 H, s).

For (3aα,4β,4aα,7aα,8β,8aα)-3a,4,4a,7a,8,8a-hexahydro-2,2-dimethyl-4,8-ethenofuro[3,4-*f*]-1,3-benzodioxole-5,7-dione **20**: δ_H ($CDCl_3$) (data from the adduct mixture) 6.13 (2 H, dd, *J* 3.0 and 4.5), 4.28 (2 H, narrow m), 3.44 (2 H, m), 2.82 (2 H, apparent t, *J* 1.4), 1.34 (3 H, s) and 1.29 (3 H, s).

Diels–Alder reaction of 6a with *p*-benzoquinone

A solution of **6a** (358 mg, 2.34 mmol) and *p*-benzoquinone (385 mg, 3.53 mmol) in benzene (2.0 ml) was stirred at RT for 72 h. Chromatography (20% EtOAc in hexanes) could not separate the adducts cleanly. Compound **21** (84 mg, 9%) was obtained as colourless crystals following recrystallization four times from EtOAc–hexanes and hexanes. The other adduct was isolated as the aromatized compound **23** (511 mg, 56%) after recrystallization three times from EtOAc–hexanes and hexanes.

For (3aα,4α,4aβ,8aβ,9α,9aα)-3a,4,9,9a-tetrahydro-2,2-dimethyl-4,9-etheno-1,3-dioxolo[4,5-*b*]naphthalene-5,8(4a*H*,8a*H*)-dione **21**: mp 122–123 °C; ν_{max}/cm^{-1} 1703; δ_H ($CDCl_3$) 6.69 (2 H, s, 6-H and 7-H), 6.17 (2H, dd, *J* 2.9 and 4.4, 10-H and 11-H), 4.10 (2 H, apparent t, *J* 1.9, 3a-H and 9a-H), 3.51 (4 H, apparent br s, 4-H, 4a-H, 8a-H and 9-H), 1.51 (3 H, s, 2-Me_β) and 1.36 (3 H, s, 2-Me_α); saturation at δ 6.17 led to NOEs at δ 4.10 (1%) and 3.51 (2%), saturation at δ 4.10 led to NOEs at δ 6.17 (2%) and 3.51 (4%), saturation at δ 1.51 led to NOE at δ 3.51 (3%) and saturation at δ 1.36 led to NOE at δ 4.10 (8%); δ_C ($CDCl_3$) 199.4 (C-5 and C-8), 141.8 (C-6 and C-7), 132.8 (C-10 and C-11), 122.2 (C-2), 73.9 (C-3a and C-9a), 42.0, 39.2, 26.5 (2-Me_β) and 24.3 (2-Me_α); *m/z* 260 (7%, M^+), 245.0815 (50, $M^+ - CH_3$, $C_{14}H_{13}O_4$ requires 245.0812), 231 (8), 203 (11), 202 (13), 185 (18), 173 (23), 157 (13), 145 (16), 129 (17), 120 (29), 100 (46), 91 (44), 82 (54), 54 (33) and 43 (100).

For (3aα,4β,4aα,8aα,9β,9aα)-3a,4,9,9a-tetrahydro-2,2-dimethyl-4,9-etheno-1,3-dioxolo[4,5-*b*]naphthalene-5,8(4a*H*,8a*H*)-dione **22**: δ_H ($CDCl_3$) (data from the adduct mixture before chromatography) 6.70 (2 H, s, 6-H and 7-H), 6.10 (2 H, dd, *J* 3.0 and 4.5, 10-H and 11-H), 4.33 (2 H, narrow m, 3a-H and 9aH), 3.53 (2 H, m, 4-H and 9-H), 2.82 (2 H, narrow m, 4a-H and 8a-H), 1.32 (3 H, s, 2-Me) and 1.29 (3 H, s, 2-Me).

For (3aα,4β,4aα,8aα,9β,9aα)-3a,4,9,9a-tetrahydro-2,2-dimethyl-4,9-etheno-1,3-dioxolo[4,5-*b*]naphthalene-5,8-diol **23**: mp 151–152 °C; δ_H ($CDCl_3$) 6.68 (2 H, s, 6-H and 7-H), 6.41 (2 H, dd, *J* 3.0 and 4.3, 10-H and 11-H), 4.57 (2 H, m, 4-H and 9-H), 4.27 (2 H, t, *J* 1.7, 3a-H and 9a-H), 1.37 (3 H, s, 2-Me_β) and 1.25 (3 H, s, 2-Me_α); saturation at δ 6.41 led to NOE at δ 4.57 (7%), saturation at δ 4.57 led to NOEs at δ 6.41 (7%) and 4.27 (4%), saturation at δ 4.27 led to NOEs at δ 4.57 (10%) and 1.25 (1.5%), saturation at δ 1.37 led to NOE at δ 6.41 (3%) and saturation at δ 1.25 led to NOE at δ 4.27 (9%); δ_C ($CDCl_3$) 146.9, 135.9, 131.5, 113.7, 78.4, 39.4, 25.7 and 25.5 (two aromatic signals are likely overlapped); *m/z* 260.1031 (10%, M^+, $C_{15}H_{16}O_4$ requires 260.1047), 245 (27), 231 (19), 203 (13), 202 (29), 185 (24), 173 (36), 145 (18), 129 (15), 120 (47), 100 (90), 91 (57), 85 (22), 82 (88), 77 (16), 65 (22), 54 (51) and 43 (100).

Diels–Alder reaction of 6a with dimethyl maleate

A solution of **6a** (120 mg, 0.794 mmol) and dimethyl maleate (229 mg, 1.58 mmol) in benzene (1.0 ml) was stirred at RT for 5 days. TLC still showed much unreacted **6a**, but the mixture was concentrated, and flash chromatography provided **24** (25 mg, 11%) and **25** (83 mg, 35%) as colourless solids.

For dimethyl (3a*R*,4*S*,7*R*,7a*S*,8*S*,9*R*)-3a,4,7,7a-tetrahydro-2,2-dimethyl-4,7-ethano-1,3-benzodioxole-8,9-dicarboxylate **24**: mp 134–135 °C; ν_{max}/cm^{-1} 1738 and 1732; δ_H ($CDCl_3$) 6.29 (2 H, dd, *J* 3.0 and 4.8, 5-H and 6-H), 4.05 (2 H, br t, $J \approx 2.1$, 3a-H and 7a-H), 3.61 (6 H, s, 2 × OCH_3), 3.54 (2 H, br s, 8-H and 9-H), 3.14 (2 H, br m, 4-H and 7-H), 1.53 (3 H, s, 2-Me_{endo}) and 1.34 (3 H, s, 2-Me_{exo}); saturation at δ 6.29 led to NOEs at δ 4.05 (1%) and 3.14 (4%), saturation at δ 4.05 led to NOEs at δ 6.29 (1%), 3.14 (5%) and 1.34 (1.5%), saturation at δ 3.54 led to NOEs at δ 3.14 (3%) and 1.53 (0.8%), saturation at δ 1.53 led to NOE at δ 3.54 (3%) and saturation at δ 1.34 led to NOE at δ 4.05 (5%); δ_C ($CDCl_3$) 173.6, 131.6, 112.0, 74.0, 51.7, 40.0, 37.4, 26.3 and 24.3; *m/z* 296.1258 (4%, M^+, $C_{15}H_{20}O_6$ requires 296.1258), 281 (16), 265

(23), 238 (51), 207 (16), 206 (22), 179 (28), 178 (20), 147 (100), 119 (37), 100 (58), 91 (56), 59 (37) and 43 (57).

For dimethyl (3a*R*,4*R*,7*S*,7a*S*,8*R*,9*S*)-3a,4,7,7a-tetrahydro-2,2-dimethyl-4,7-ethano-1,3-benzodioxole-8,9-dicarboxylate **25**: mp 196–197 °C: ν_{max}/cm^{-1} 1742 and 1725; δ_H ($CDCl_3$) 6.20 (2 H, dd, *J* 3.3 and 4.5, 5-H and 6-H), 4.22 (2 H, narrow m, 3a-H and 7a-H), 3.63 (6 H, s, 2 × OCH_3), 3.21 (2 H, br m, 4-H and 7-H), 2.86 (2 H, br s, 8-H and 9-H), 1.34 (3 H, s, 2-Me_{endo}) and 1.28 (3 H, s, 2-Me_{exo}); saturation at δ 6.20 led to NOE at δ 3.21 (8%), saturation at δ 4.22 led to NOEs at δ 3.21 (10%), 2.86 (15%) and 1.28 (2%), saturation at δ 3.21 led to NOEs at δ 6.20 (10%), 4.22 (5%) and 2.86 (4%), saturation at δ 2.86 led to NOEs at δ 4.22 (15%) and 3.21 (9%), saturation at δ 1.34 led to NOE at δ 6.20 (2%) and saturation at δ 1.28 led to NOE at δ 4.22 (7%); δ_C ($CDCl_3$) 172.3 (2 × CO_2), 129.4 (C-5 and C-6), 109.2 (C-2), 77.5 (C-3a and C-7a), 52.0 (2 × OCH_3), 42.9 (C-8 and C-9), 39.5 (C-4 and C-7), 25.3 (2-Me_{endo}) and 25.0 (2-Me_{exo}); *m*/*z* 296.1249 (4%, M^+, $C_{15}H_{20}O_6$ requires 296.1258), 281 (27), 265 (20), 238 (16), 207 (20), 206 (29), 179 (27), 178 (17), 147 (100), 119 (33), 100 (32), 91 (56), 85 (28), 59 (42) and 43 (62).

Diels–Alder reaction of 6a with 3-buten-2-one

A solution of **6a** (126 mg, 0.833 mmol), a large excess (1.0 ml) of 3-buten-2-one, and hydroquinone (10 mg) in toluene (5.0 ml), heated at reflux for 72 h, provided **27** (119 mg, 64%) after recrystallization from hexane, and a fraction (17 mg, 9%) containing a mixture of **26** and **28**.

For (3a*R**,4*R**,7*R**,7a*S**,8*R**)-8-acetyl-3a,4,7,7a-tetrahydro-2,2-dimethyl-4,7-ethano-1,3-benzodioxole **26**: δ_H ($CDCl_3$) (data from a mixture with **28**) 6.22 (1 H, overlapped), 6.06 (1 H, br t, *J* 7.2), 4.00–4.11 (2 H, m), 3.8 (2 H, m, overlapped), 2.84 (1 H, m), 2.13 (3 H, s), 2.13 (1 H, m, overlapped), 1.54 (3 H, s, 2-Me), 1.53 (1 H, m, overlapped) and 1.35 (3 H, s, 2-Me).

For (3a*R**,4*S**,7*S**,7a*S**,8*S**)-8-acetyl-3a,4,7,7a-tetrahydro-2,2-dimethyl-4,7-ethano-1,3-benzodioxole **27**: mp 61–62 °C; ν_{max}/cm^{-1} 1710; δ_H ($CDCl_3$) 6.17 (1 H, t, *J* 7.5, 5-H), 5.97 (1 H, t, *J* 7.5, 6-H), 4.28 (1 H, dd, *J* 3.1 and 7.2, 7a-H), 4.22 (1 H, dd, *J* 3.2 and 7.2, 3a-H), 3.23 (1 H, m, 7-H), 2.92 (1 H, m, 4-H), 2.48 (1 H, ddd, *J* 2.0, 5.1 and 9.8, 8-H), 2.16 (3 H, s, COMe), 1.81 (1 H, ddd, *J* 3.3, 5.1 and 13.4, 9-H_{endo}), 1.46 (1 H, ddd, *J* 2.3, 9.8 and 13.4, 9-H_{exo}), 1.34 (3 H, s, 2-Me_{endo}) and 1.29 (3 H, s, 2-Me_{exo}); saturation at δ 6.17 led to NOEs at δ 5.97 (3%) and 2.92 (2%), saturation at δ 5.97 led to NOEs at δ 6.17 (4%) and 3.23 (3%), saturation at δ 4.28 led to NOEs at δ 3.23 (4%), 2.48 (8%) and 1.29 (0.6%), saturation at δ 4.22 led to NOEs at δ 2.92 (3%), 1.46 (4%) and 1.29 (approx. 0.5%), saturation at δ 3.23 led to NOEs at δ 5.97 (5%); 4.28 (3%), 2.48 (2%) and 2.16 (1%), saturation at δ 2.92 led to NOEs at δ 6.17 (5%), 4.22 (3%), 1.81 (3%) and 1.46 (1.5%), saturation at δ 2.48 led to NOEs at δ 4.28 (7%), 4.22 (1%), 3.23 (3%) and 1.46 (4%), saturation at δ 1.81 led to NOEs at δ 2.92 (5%) and 1.46 (9%), saturation at δ 1.46 led to NOEs at δ 4.22 (5%), 2.92 (2%), 2.48 (5%) and 1.81 (14%), saturation at δ 1.34 led to NOEs at δ 6.17 (1%) and 5.97 (1.5%) and saturation at δ 1.29 led to NOEs at δ 4.28 (7%) and 4.22 (6%); δ_C ($CDCl_3$) 207.5 (CO), 132.4 (C-5), 127.8 (C-6), 108.6 (C-2), 78.3 (C-3a and C-7a), 46.9 (C-8), 37.1 (C-7), 34.5 (C-4), 28.4 (COMe), 25.4 (2-Me_{endo}), 24.9 (2-Me_{exo}) and 22.9 (C-9); *m*/*z* 222.1247 (1%, M^+, $C_{13}H_{18}O_3$ requires 222.1256), 207 (13), 164 (20), 147 (7), 121 (62), 104 (19), 103 (37), 100 (26), 91 (22), 85 (20), 77 (23) and 43 (100).

For (3a*R**,4*S**,7*S**,7a*S**,8*R**)-8-acetyl-3a,4,7,7a-tetrahydro-2,2-dimethyl-4,7-ethano-1,3-benzodioxole **28**: δ_H ($CDCl_3$) (data from a mixture with **26**) 6.13–6.26 (2 H, m), 4.17 (1 H, br dd, *J* 3.0 and 7.2), 4.1 (1 H, overlapped), 3.8 (1 H, overlapped, 7-H), 2.94 (1 H, m, 4-H), 2.53 (1 H, ddd, *J* 2.7, 5.5 and 10.8, 8-H), 2.23 (3 H, s, $COCH_3$), 1.86 (1 H, ddd, *J* 2.1, 5.5 and 13.5, 9-H), 1.37 (1 H, overlapped, 9-H), 1.32 (3 H, s, 2-Me) and 1.23 (3 H, s, 2-Me).

Diels–Alder reaction of 6a with vinylene carbonate

A solution of **6a** (152 mg, 1.00 mmol) and vinylene carbonate (0.12 ml, 2.0 mmol) in benzene (8 ml), heated under reflux for 8 days, gave **29** (182 mg, 38%) and **30** (43 mg, 9%) as colourless solids after recrystallization from hexane.

For (3aα,4β,4aβ,7aβ,8β,8aα)-3a,4,4a,7a,8,8a-hexahydro-6,6-dimethyl-4,8-ethenobenzo[1,2-*d*:4,5-*d*′]bis[1,3]dioxol-2-one **29**: mp 167–169 °C; ν_{max}/cm^{-1} 1796; δ_H ($CDCl_3$) 6.23 (2 H, dd, *J* 3.0 and 4.5, 9-H and 10-H), 5.17 (2 H, br s, 3a-H and 8a-H), 4.21 (2 H, t, *J* 2.1, 4a-H and 7a-H), 3.47 (2 H, m, 4-H and 8-H), 1.46 (3 H, s, 6-Me_α) and 1.30 (3 H, s, 6-Me_β); saturation at δ 6.23 led to NOEs at δ 4.21 (1%) and 3.47 (5%), saturation at δ 5.17 led to NOEs at δ 3.47 (5%) and 1.46 (0.7%), saturation at δ 4.21 led to NOEs at δ 6.23 (2%), 3.47 (8%) and 1.30 (1.5%), saturation at δ 3.47 led to NOEs at δ 6.23 (7%), 5.17 (5%) and 4.21 (5%), saturation at δ 1.46 led to NOE at δ 5.17 (6%) and saturation at δ 1.30 led to NOE at δ 4.21 (9%); δ_C ($CDCl_3$) 155.0 (C-2), 130.5 (C-9 and C-10), 112.1 (C-6), 74.3 (C-3a and C-8a), 73.7 (C-4a and C-7a), 38.4 (C-4 and C-8), 25.8 (6-Me_α) and 23.2 (6-Me_β); *m*/*z* 239 (1%, $M^+ + 1$), 223.0604 (45, $M^+ - CH_3$, $C_{11}H_{11}O_5$ requires 223.0605), 180 (43), 119 (14), 107 (42), 95 (27), 94 (68), 91 (27), 79 (46), 77 (29), 66 (21) and 43 (100).

For (3aα,4β,4aα,7aα,8β,8aα)-3a,4,4a,7a,8,8a-hexahydro-6,6-dimethyl-4,8-ethenobenzo[1,2-*d*:4,5-*d*′]bis[1,3]dioxol-2-one **30**: mp 205–207 °C; ν_{max}/cm^{-1} 1772; δ_H ($CDCl_3$) 6.16 (2 H, dd, *J* 3.3 and 4.2, 9-H and 10-H), 4.67 (2 H, br s, 3a-H and 8a-H), 4.20 (2 H, br s, 4a-H and 7a-H), 3.47 (2 H, m, 4-H and 8-H), 1.35 (3 H, s, 6-Me_β) and 1.27 (3 H, s, 6-Me_α); saturation at δ 6.16 led to NOE at δ 3.47 (5%), saturation at δ 4.67 led to NOEs at δ 4.20 (10%) and 3.47 (7%), saturation at δ 4.20 led to NOEs at δ 4.67 (13%), 3.47 (7%) and 1.27 (2%), saturation at δ 3.47 led to NOEs at δ 6.16 (6%), 4.67 (3%) and 4.20 (3%), saturation at δ 1.35 led to NOE at δ 6.16 (2%) and saturation at δ 1.27 led to NOE at δ 4.20 (7%); δ_C ($CDCl_3$) 154.5, 128.4, 110.1, 74.5, 74.0, 38.8, 25.0 and 24.6; *m*/*z* 239 (0.5, $M^+ + 1$), 223.0606 (53, $M^+ - CH_3$, $C_{11}H_{11}O_5$ requires 223.0605), 180 (9), 119 (14), 118 (29), 107 (48), 95 (25), 94 (43), 91 (26), 79 (35), 77 (23), 59 (40) and 43 (100).

Diels–Alder reaction of 6a with tetracyanoethylene

A solution of **6a** (122 mg, 0.802 mmol) and tetracyanoethylene (102 mg, 0.802 mmol) in benzene (2.0 ml), heated under reflux for 24 h, yielded **31** (141 mg, 63%) as a pale brown solid.

For (3aα,4α,7α,7aα)-8,8,9,9-tetracyano-3a,4,7,7a-tetrahydro-2,2-dimethyl-4,7-ethano-1,3-benzodioxole **31**: mp 218–220 °C; ν_{max}/cm^{-1} 2233 (weak); δ_H ($CDCl_3$/CD_2Cl_2/CD_3COCD_3) 6.52/6.53/6.63 (2 H, dd, *J* 3.0 and 4.7, 5-H and 6-H), 4.76/4.79/4.87 (2 H, br s, 4-H and 7-H), 3.85/3.92/4.34 (2 H, m, 4-H and 7-H), 1.34/1.32/1.40 (3 H, s, 2-Me) and 1.34/1.32/1.33 (3 H, s, 2-Me); in $CDCl_3$ solution, saturation at δ 6.52 led to NOE at δ

3.85 (7%), saturation at δ 4.76 led to NOEs at δ 3.85 (11%) and 1.34 (0.7%); saturation at δ 3.85 led to NOEs at δ 6.52 (7%) and 4.76 (4%) and saturation at δ 1.34 led to NOEs at δ 6.52 (1.5%) and 4.76 (9%); δ_C ($CDCl_3$/CD_2Cl_2/CD_3COCD_3) 130.7/131.1/132.0, 111.6/111.8/112.8, 110.7/111.4/111.7, 109.9/110.6/111.6, 72.3/72.8/73.5, 42.8/43.1/43.4, 25.0/25.1/25.4 and 25.0/25.1/25.2; *m/z* 280 (0.7%, M^+), 265.0730 (30, $M^+ - CH_3$, $C_{14}H_9N_4O_2$ requires 265.0725), 100 (17), 95 (57), 85 (12), 59 (48), 58 (17) and 43 (100); analysis: found C, 64.08; H, 4.29; N, 20.04%; $C_{15}H_{12}N_4O_2$ requires C, 64.26; H, 4.32; N, 20.00%.

Diels–Alder reaction of 6a with dimethyl acetylenedicarboxylate

A solution of **6a** (118 mmol, 0.782 mmol) and dimethyl acetylenedicarboxylate (111 mg, 0.782 mmol) in benzene (2.0 ml) was stirred at RT for 17 h. This provided **32** (198 mg, 86%) as colourless crystals after recrystallization from hexane.

For dimethyl (3aα,4β,7β,7aα)-4,7-dihydro-2,2-dimethyl-4,7-etheno-1,3-benzodioxole-5,6-dicarboxylate **32**: mp 93–94 °C; ν_{max}/cm^{-1} 1732 and 1714; δ_H ($CDCl_3$) 6.39 (2 H, dd, *J* 3.1 and 4.4, 8-H and 9-H), 4.39 (2 H, narrow m, 3a-H and 7a-H), 4.23 (2 H, m, 4-H and 7-H), 3.79 (6 H, s, 2 × CO_2Me), 1.34 (3 H, s, 2-Me_β) and 1.26 (3 H, s, 2-Me_α); saturation at δ 6.39 led to NOEs at δ 4.23 (11%) and 1.34 (0.2%), saturation at δ 4.39 led to NOEs at δ 4.23 (7%) and 1.26 (1.5%), saturation at δ 4.23 led to NOEs at δ 6.39 (9%) and 4.39 (5%), saturation at δ 1.34 led to NOE at δ 6.39 (2%) and saturation at δ 1.26 led to NOE at δ 4.39 (9%); δ_C ($CDCl_3$) 165.8 (2 × C=O), 141.3 (C-5 and C-6), 131.2 (C-8 and C-9), 113.6 (C-2), 78.1 (C-3a and C-7a), 52.4 (2 × OMe), 44.2 (C-4 and C-7), 25.7 (2-Me_β) and 25.5 (2-Me_α); *m/z* no M^+, 279 (4%), 207 (4), 205 (3), 163 (20), 100 (85), 85 (100) and 43 (22); analysis: found C, 61.33; H, 6.20%; $C_{15}H_{18}O_6$ requires C, 61.22; H, 6.16%.

Diels–Alder reaction of 6a with ethyl propiolate

A solution of **6a** (62 mg, 0.46 mmol) and ethyl propiolate (43 mg, 0.40 mmol) in benzene (0.5 ml) was stirred at RT for 3 days. Adduct **33** (63 mg, 61%) was obtained as a sweet-smelling oil.

For ethyl (3a*R**,4*R**,7*S**,7a*S**)-4,7-dihydro-2,2-dimethyl-4,7-etheno-1,3-benzodioxole-5-carboxylate **33**: ν_{max}/cm^{-1} 1713, 1634 and 1598; δ_H ($CDCl_3$) 7.21 (1 H, dd, *J* 1.7 and 6.4, 6-H), 6.40 (1 H, br ddd, *J* 1.6, 6.0 and 6.8, 9-H), 6.30 (1 H, ddd, *J* 1.7, 6.0 and 6.7, 8-H), 4.39 (1 H, m, 4-H), 4.26 (2 H, m, 3a-H and 7a-H), 4.19 (2 H, dq, *J* 0.6 and 7.1, OCH_2CH_3), 4.00 (1 H, m, 7-H), 1.35 (3 H, s, 2-Me_{endo}), 1.29 (3 H, t, *J* 7.1, OCH_2CH_3) and 1.26 (3 H, s, 2-Me_{exo}); saturation at δ 7.21 led to NOEs at δ 4.26 (0.6%) and 4.00 (5%), saturation at δ 6.40 led to NOE at δ 4.39 (4%), saturation at δ 6.30 led to NOE at δ 4.00 (3%), saturation at δ 4.39 led to NOE at δ 6.40 (4%), saturation at δ 4.26 led to NOEs at δ 7.21 (3%), 4.39 (5%), 4.00 (1.5%) and 1.26 (2%), saturation at δ 4.00 led to NOEs at δ 7.21 (8%) and 6.30 (5%), saturation at δ 1.35 led to NOEs at δ 6.40 (1.5%) and 6.30 (1.5%) and saturation at δ 1.26 led to NOE at δ 4.26 (8%); δ_C ($CDCl_3$) 164.4 (0), 144.1 (1), 138.7 (0), 132.4 (1), 130.7 (1), 113.2 (0), 78.3 (1), 78.1 (1), 60.7 (2), 43.1 (1), 41.6 (1), 25.8 (3), 25.5 (3) and 14.2 (3); *m/z* no M^+, 235.0957 (3%, $M^+ - CH_3$, $C_{13}H_{15}O_4$ requires 235.0969), 163 (10), 147 (5), 135 (7), 105 (25), 100 (96), 91 (10), 85 (100), 77 (16), 60 (14) and 43 (30).

Dimerization of 7

Diene **7** dimerized to **35** spontaneously during storage, forming colourless crystals.

For (2α,3aβ,5aα,6β,6aα,8β,9aα,10β,10aα,10bβ)-3a,5a,6,6a,9a,10,10a,10b-octahydro-2,8-diphenyl-6,10-ethenonaphtho[1,2-*d*:6,7-*d*′]bis[1,3]dioxole **35**: mp 152–154 °C; ν_{max}/cm^{-1} 3057, 1522, 1445 and 1055; δ_H ($CDCl_3$) 7.48–7.24 (10 H, m), 6.17 (2 H, m, 11-H and 12-H), 5.84 (1 H, s, 2-H), 5.68 (2 H, broadened AB, 4-H and 5-H), 5.61 (1 H, s, 8-H), 4.39–4.31 (3 H, m, 3a-H, 6a-H and 9a-H), 4.30 (1 H, br d, *J* 5.7, 10b-H), 3.14 (1 H, m, 10-H), 3.07 (1 H, m, 6-H) and 2.44 (2 H, broadened AB, 5a-H and 10a-H); saturation at δ 6.17 led to NOEs at δ 3.14 (4%) and 3.07 (4%), saturation at δ 5.84 led to NOEs at δ 7.48–7.42 (2%) and 4.30 (7%), saturation at δ 5.61 led to NOEs at δ 7.48–7.42 (3%) and a multiplet at 4.38 (3%), saturation at δ 4.30 led to NOEs at δ 5.84 (12%) and 3.14 (13%), saturation at δ 3.14 led to NOEs at δ 6.17 (4%), 4.30 (12%) and 2.44 (2%), saturation at δ 3.07 led to NOEs at δ 6.17 (4%), 5.68 (5%) and 2.44 (2%) and saturation at δ 2.44 led to NOEs at δ 5.68 (3%), double-doublets at 4.38 and 4.33 (9%), 3.14 (4%) and 3.07 (5%); δ_C ($CDCl_3$) 137.9, 136.1, 132.9 (C-11 or C-12), 129.7, 129.2 (C-11 or C-12), 129.1 (C-4 or C-5), 128.3 (4C), 127.4, 127.1, 126.4 (C-4 or C-5), 103.5 (C-2), 103.1 (C-8), 79.7 (C-10b), 79.0 (2C), 70.6, 40.8 (C-6 and C-10), 34.5 and 33.5; *m/z* 400 (1.6%, M^+), 399 (4), 171 (14), 170 (28), 159 (37), 145 (27), 144 (25), 141 (20), 129 (22), 120 (31), 105 (100), 94 (40), 91 (72), 78 (31), 77 (55) and 66 (30); analysis: found C, 78.11; H, 5.99%; $C_{26}H_{24}O_4$ requires C, 77.98; H, 6.04%.

Dimerization of 6a

A sample of **6a** (214 mg, 1.41 mmol) was kept at RT for 28 d. Flash chromatography (10% EtOAc in hexanes) gave **36** (41 mg, 19%) and **37** (129 mg, 60%) as colourless solids.

For (3aα,5aβ,6α,6aα,9aα,10α,10aβ,10bα)-3a,5a,6,6a,9a,10,10a,10b-octahydro-2,2,8,8-tetramethyl-6,10-ethenonaphtho[1,2-*d*:6,7-*d*′]bis[1,3]dioxole **36**: mp 92–93 °C; ν_{max}/cm^{-1} 2985, 2935, 1375, 1238, 1207 and 1061; δ_H ($CDCl_3$) 6.07 (2 H, narrow m, 11-H and 12-H), 5.56 (1 H, ddd, *J* 1.3, 3.4 and 10.3, 5-H), 5.49 (1 H, br d, *J* 10.3, 4-H), 4.19 (1 H, m, 3a-H), 4.06 (3 H, m, 6a-H, 9a-H and 10b-H), 3.01 (1 H, br d, *J* 9.0, 5a-H), 2.96 (1 H, br d, *J* 9.0, 10a-H), 2.80 (2 H, m, 6-H and 10-H), 1.55 (3 H, s, 8-Me_β), 1.38 (3 H, s, 2-Me_β), 1.35 (3 H, s, 8-Me_α) and 1.33 (3 H, s, 2-Me_α); saturation at δ 6.07 led to NOEs at δ 4.19 (3%), 4.06 (0.6%) and 2.80 (5%), saturation at δ 5.56 led to NOEs at δ 2.96 (3%) and 2.80 (1%), saturation at δ 5.49 led to NOEs at δ 4.19 (2%) and 3.01 (4%), saturation at δ 4.19 led to NOEs at δ 6.07 (2%) and 5.49 (4%), saturation at δ 4.06 led to NOEs at δ 6.07 (2%), 2.96 (4%), 2.80 (11%) and 1.35 (1.5%), saturation at δ 2.80 led to NOEs at δ 6.07 (7%), 5.56 (4%), 4.06 (8%), 3.01 (4%) and 2.96 (3%) and saturation at δ 1.55 led to NOEs at δ 3.01 (5%), 2.96 (5%) and 1.35 (1%); δ_C ($CDCl_3$) 134.6 (C-12), 131.1 (C-11), 130.3 (C-5), 126.8 (C-4), 111.9 (C-8), 107.4 (C-2), 77.9 (C-10b), 75.2 (C-6a or C-9a), 74.7 (C-6a or C-9a), 71.2 (C-3a), 40.8 (C-6 or C10), 40.3 (C-6 or C10), 30.5 (C-5a and C-10a), 28.4 (2-Me_β), 26.8 (2-Me_α), 26.3 (8-Me_β) and 24.4 (8-Me_α); *m/z* no M^+, 289 (15%), 275 (2), 231 (3), 188 (40), 171 (85), 159 (30), 153 (19), 145 (20), 143 (26), 129 (26), 100 (50), 91 (34) and 43 (100); analysis: found C, 70.98; H, 7.91%; $C_{18}H_{24}O_4$ requires C, 71.03; H, 7.95%.

For (3aα,5aβ,6α,6aβ,9aβ,10α,10aβ,10bα)-3a,5a,6,6a,9a,10,10a,10b-octahydro-2,2,8,8-tetramethyl-6,10-ethenonaphtho[1,2-*d*:6,7-*d*′]bis[1,3]dioxole **37**: mp 149–151 °C (lit.[35] 150–151 °C); ν_{max}/cm^{-1} 2987, 2930, 2911, 2884, 1456, 1365, 1236, 1046 and 886; δ_H ($CDCl_3$) 5.99 (2 H, narrow m, 11-H and 12-H), 5.60 (1 H, dd, *J* 3.8 and 10.3, 5-H), 5.51 (1 H, d, *J* 10.3, 4-H), 4.30 (2 H, m, 6a-H and 9a-H), 4.20–4.14 (2 H, m, 3a-H and 10b-H), 2.87 (2 H, m, 6-H and 10-H), 2.36 (1 H, br d, *J* 9.1, 5a-H), 2.23 (1 H, d, *J* 9.1, 10a-H), 1.36 (3 H, s, 2-Me$_\beta$), 1.34 (3 H, s, 2-Me$_\alpha$), 1.32 (3 H, s, 8-Me$_\alpha$) and 1.29 (3 H, s, 8-Me$_\beta$); saturation at δ 5.99 led to NOEs at δ 4.17 (4%), 2.87 (5%) and 1.32 (0.3%), saturation at δ 5.60 led to NOEs at δ 2.87 (2%) and 2.36 (2%), saturation at δ 5.51 led to NOE at δ 4.17 (2%), saturation at δ 4.30 led to NOEs at δ 2.87 (3%), 2.36 (5%) 2.23 (10%) and 1.29 (1%), saturation at δ 4.17 led to NOEs at δ 5.99 (2%), 5.51 (4%), 2.87 (6%), 2.23 (3%) and 1.34 (0.7%), saturation at δ 2.87 led to NOEs at δ 5.99 (7%), 5.60 (6%), 4.30 (4%), 4.17 (10%), 2.36 (3%) and 2.23 (3%), saturation at δ 2.36 led to NOEs at δ 5.60 (4%), 4.30 (4%) and 2.87 (2%), saturation at δ 2.23 led to NOEs at δ 4.30 (4%), 4.17 (1.5%) and 2.87 (0.7%), saturation at δ 1.36 led to NOE at δ 5.51 (4%), saturation at δ 1.34 led to NOE at δ 4.17 (9%), saturation at δ 1.32 led to NOE at δ 5.99 (2%) and saturation at δ 1.29 led to NOE at δ 4.30 (6%); δ_C ($CDCl_3$) 132.4 (C-12), 129.3 (C-5), 128.8 (C-11), 126.6 (C-4), 108.6 (C-8), 107.6 (C-2), 78.6 (C-6a or C-9a), 78.3 (C-6a or C-9a), 77.6 (C-10b), 70.9 (C-3a), 41.0 (C-6 or C-10), 40.7 (C-6 or C-10), 34.3 (C-10a), 33.1 (C-5a), 28.3 (2-Me$_\beta$), 26.8 (2-Me$_\alpha$), 25.4 (8-Me$_\alpha$) and 25.0 (8-Me$_\beta$); *m*/*z* no M$^+$, 289 (12%), 246 (8), 230 (7), 188 (49), 171 (20), 158 (26), 145 (19), 143 (18), 131 (20), 129 (22), 119 (22), 100 (30), 95 (72), 91 (36) and 43 (100); analysis: found C, 71.00; H, 7.84%; $C_{18}H_{24}O_4$ requires C, 71.03; H, 7.95%.

Diels–Alder reactions with 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD)

A solution of PTAD in acetone was added dropwise to an equimolar amount of the diene in acetone. The initial carmine colour of the PTAD faded as the solution was stirred at RT for 16–18 h. The solution was concentrated under vacuum, and the residue was analysed by ^{1}H NMR spectroscopy in order to obtain the proportions of the adducts in Table 3. The adducts were isolated by chromatography (20–30% EtOAc in hexanes). Yields are for the isolated adducts.

Diels–Alder reaction of 1a with PTAD

PTAD (171 mg, 0.98 mmol) and **1a** (109 mg, 0.89 mmol) provided **38** (193 mg, 68%), as colourless crystals, and some impure **39** (19 mg, 7% if pure).

For (5*R*,8*S*,10*S*,11*R*)-5,8-dihydro-10,11-dihydroxy-2-phenyl-5,8-ethano-1*H*-[1,2,4]triazolo[1,2-*a*]-pyridazine-1,3(2*H*)-dione **38**: mp 226–228 °C; ν_{max}/cm^{-1} 1779 (m) and 1738; δ_H ($CDCl_3$/CD_3OD) 7.50–7.38/7.50–7.40 (5 H, m), 6.51/6.57 (2 H, dd, *J* 3.2 and 4.1, 6-H and 7-H), 5.00/4.89 (2 H, m, 5-H and 8-H), 3.95/3.94 (2 H, m, 10-H and 11-H), 3.21/3.30 (2 H, OH); in CD_3OD solution, saturation at δ 6.57 led to NOEs at δ 4.89 (4%) and 3.94 (1.5%), saturation at δ 4.89 led to NOEs at δ 6.57 (5%) and 3.94 (5%) and saturation at δ 3.94 led to NOEs at δ 6.57 (3%) and 4.89 (9%); δ_C (CD_3OD) 156.1, 131.6 (likely overlapping the quaternary aromatic signal), 130.1, 129.5, 127.4, 63.6 and 57.4; *m*/*z* 287.0893 (3%, M$^+$, $C_{14}H_{13}N_3O_4$ requires 287.0905), 258 (8), 228 (16), 227 (83), 119 (42), 91 (12) and 80 (100).

For (5*R*,8*S*,10*R*,11*S*)-5,8-dihydro-10,11-dihydroxy-2-phenyl-5,8-ethano-1*H*-[1,2,4]triazolo[1,2-*a*]-pyridazine-1,3(2*H*)-dione **39**: δ_H ($CDCl_3$) 7.50–7.35 (5 H, m), 6.56 (2 H, br t, *J* 3.6), 5.04 (2 H, m), 4.44 (2 H, m) and 2.76 (2 H, OH).

Diels–Alder of 2 with PTAD

PTAD (60 mg, 0.33 mmol) and **2** (85 mg, 0.33 mmol) provided **40** (103 mg, 72%) as colourless crystals.

For (5*R*,8*S*,10*R*,11*S*)-5,8-dihydro-2-phenyl-10,11-bis(trimethylsilyloxy)-5,8-ethano-1*H*-[1,2,4]triazolo[1,2-*a*]pyridazine-1,3(2*H*)-dione **40**: mp 62–63 °C; ν_{max}/cm^{-1} 1718; δ_H ($CDCl_3$) 7.48–7.36 (5 H, m), 6.55 (2 H, dd, *J* 3.2 and 4.0, 6-H and 7-H), 4.81 (2 H, m, 5-H and 8-H), 4.34 (2 H, narrow m, 10-H and 11-H) and 0.21 (18 H, s, 2 × OTMS); saturation at δ 6.55 led to NOE at δ 4.81 (10%), saturation at δ 4.81 led to NOEs at δ 6.55 (10%) and 4.34 (8%), saturation at δ 4.34 led to NOEs at δ 4.81 (16%) and 0.21 (0.7%) and saturation at δ 0.21 led to NOEs at δ 6.55 (1.5%), 4.81 (5%) and 4.34 (5%); δ_C ($CDCl_3$) 155.6, 130.1, 129.6 (C-6 and C-7), 129.2, 128.4, 125.5, 68.4 (C-10 and C-11), 54.5 (C-5 and C-8) and 0.23 (2 × OTMS); *m*/*z* no M$^+$, 416 (3%), 300 (1), 297 (1), 227 (100), 204 (25), 147 (16), 119 (17), 80 (43) and 73 (61); analysis: found C, 55.70; H, 6.66; N, 9.74%; $C_{20}H_{29}N_3O_4Si_2$ requires C, 55.66; H, 6.71; N, 9.74%.

Diels–Alder reaction of 4a with PTAD

PTAD (145 mg, 0.830 mmol) and **4a** (163 mg, 0.830 mmol) provided **41** (39 mg, 13%) and **42** (238 mg, 77%) as colourless crystals.

For (5*R*,8*S*,10*S*,11*R*)-10,11-bis(acetyloxy)-5,8-dihydro-2-phenyl-5,8-ethano-1*H*-[1,2,4]triazolo[1,2-*a*]pyridazine-1,3(2*H*)-dione **41**: mp 224–225 °C; ν_{max}/cm^{-1} 1744 (m) and 1707; δ_H ($CDCl_3$) 7.51–7.36 (5 H, m), 6.60 (2 H, apparent dd, *J* 3.1 and 4.2, 6-H and 7-H), 5.10 (2 H, m, 5-H and 8-H), 5.04 (2 H, narrow m, C-10 and C-11), 2.15 (6 H, s, 2 × OAc); saturation at δ 6.60 led to NOEs at δ 5.10 (10%) and 5.04 (1.5%), saturation at δ 5.10 led to NOEs at δ 6.60 (9%) and 5.04 (7%) and saturation at δ 5.04 led to NOEs at δ 6.60 (2%) and 5.10 (12%); δ_C ($CDCl_3$) 169.8, 155.4, 131.1, 130.1, 129.2, 128.5, 125.6, 63.4, 53.1 and 20.6; *m*/*z* 371 (3%, M$^+$), 329 (3), 269 (9), 228 (22), 227 (100), 119 (25), 80 (56) and 43 (71); analysis: found C, 58.27; H, 4.61; N, 11.34%; $C_{18}H_{17}N_3O_6$ requires C, 58.20; H, 4.62; N, 11.32%.

For (5*R*,8*S*,10*R*,11*S*)-10,11-bis(acetyloxy)-5,8-dihydro-2-phenyl-5,8-ethano-1*H*-[1,2,4]triazolo[1,2-*a*]pyridazine-1,3(2*H*)-dione **42**: mp 219–220 °C: ν_{max}/cm^{-1} 1749 and 1717; δ_H ($CDCl_3$) 7.48–7.36 (5 H, m), 6.58 (2 H, dd, *J* 3.1 and 4.0, 6-H and 7-H), 5.46 (2 H, narrow m, 10-H and 11-H), 5.10 (2 H, m, 5-H and 8-H), 2.05 (6 H, s, 2 × OAc); saturation at δ 6.58 led to NOE at δ 5.10 (11%), saturation at δ 5.46 led to NOEs at δ 5.10 (16%) and 2.05 (0.5%), saturation at δ 5.10 led to NOEs at δ 6.58 (8%) and 5.46 (8%) and saturation at δ 2.05 led to NOEs at δ 6.58 (1.5%), 5.46 (1.5%) and 5.10 (1%); δ_C ($CDCl_3$) 169.2, 155.4, 130.9, 129.5 (C-6 and C-7), 129.1, 128.4, 125.3, 67.0 (C-10 and C-11), 51.4 (C-5 and C-8) and 20.2 (2 × OAc); *m*/*z* 371 (1%, M$^+$), 329 (1), 311 (1), 269 (12), 228 (15), 227 (76), 119 (28), 80 (62) and 43 (100);

analysis: found C, 58.35; H, 4.63; N, 11.38%; $C_{18}H_{17}N_3O_6$ requires C, 58.20; H, 4.62; N, 11.32%.

Conversion of 39 to 42

A solution of **39** (12 mg, 0.042 mmol) in pyridine (1.0 ml) and acetic anhydride (0.5 ml) was stirred at RT overnight. Aqueous work-up afforded **42** (14 mg, 90%).

Diels–Alder reaction of 6a with PTAD

PTAD (121 mg, 0.689 mmol) and **6a** (105 mg, 0.689 mmol) provided **43** (256 mg, 97%) as colourless crystals.

For (3aα,4β,10β,10aα)-3a,4,10,10a-tetrahydro-2,2-dimethyl-7-phenyl-4,10-etheno-6*H*-1,3-dioxolo[4,5-*d*][1,2,4]triazolo[1,2-*a*]-pyridazine-6,8(7*H*)-dione **43**: mp 248–250 °C; ν_{max}/cm^{-1} 1713; δ_H ($CDCl_3$) 7.46–7.36 (5 H, m), 6.42 (2 H, dd, *J* 3.4 and 3.8, 11-H and 12-H), 5.15 (2 H, m, 4-H and 10-H), 4.66 (2 H, narrow m, 3a-H and 10a-H), 1.35 (6 H, s, 2 × CH_3); saturation at δ 6.42 led to NOE at δ 5.15 (10%), saturation at δ 5.15 led to NOEs at δ 6.42 (9%) and 4.66 (6%), saturation at δ 4.66 led to NOEs at δ 5.15 (14%) and 1.35 (1%) and saturation at δ 1.35 led to NOEs at δ 6.42 (3%) and 4.66 (11%); δ_C ($CDCl_3$) 155.6, 130.7, 129.1, 128.8 (C-11 and C-12), 128.4, 125.5, 112.1, 73.8 (C-3a and C-10a), 52.3 (C-4 and C-10), 25.4 (CH_3) and 25.3 (CH_3); *m*/*z* 327.1210 (2%, M^+, $C_{17}H_{17}N_3O_4$ requires 327.1217), 312 (11), 269 (23), 240 (41), 227 (100), 121 (29), 119 (59), 95 (73), 91 (18), 80 (67), 78 (42) and 43 (83).

Diels–Alder reaction of 7 with PTAD

PTAD (110 mg, 0.63 mmol) and **7** (126 mg, 0.63 mmol) provided **44** (130 mg, 55%) as colourless crystals.

For (2α,3aβ,4α,10α,10aβ)-3a,4,10,10a-tetrahydro-2,7-diphenyl-4,10-etheno-6*H*-1,3-dioxolo[4,5-*d*]-[1,2,4]triazolo[1,2-*a*]pyrida-zine-6,8(7*H*)-dione **44**: mp 193–195 °C; ν_{max}/cm^{-1} 1719; ^{1}H NMR δ_H ($CDCl_3$) 7.47–7.35 (10 H, m), 6.53 (2 H, dd, *J* 3.2 and 4.0, 11-H and 12-H), 5.80 (1 H, s, 2-H), 5.29 (2 H, m, 4-H and 10-H) and 4.73 (2 H, narrow m, 3a-H and 10a-H); saturation at δ 6.53 led to NOEs at δ 7.40 (1%) and 5.29 (11%), saturation at δ 5.80 led to NOEs at δ 7.40 (3%) and 4.73 (7%), saturation at δ 5.29 led to NOEs at δ 6.53 (7%) and 4.73 (7%) and saturation at δ 4.73 led to NOEs at δ 5.80 (17%) and 5.29 (15%); δ_C ($CDCl_3$) 155.5, 134.6, 131.0, 130.1, 129.1 (C-11, C-12 and aromatic signal), 128.4, 127.2, 125.4, 105.6 (C-2), 74.1 (C-3a and C-10a) and 52.1 (C-5 and C-10); *m*/*z* 375.1225 (8%, M^+, $C_{21}H_{17}N_3O_4$ requires 375.1217), 269 (58), 240 (58), 227 (65), 153 (18), 121 (37), 119 (61), 105 (33), 91 (32), 81 (100), 80 (78), 78 (57) and 77 (36).

Diels–Alder reaction of 8 with PTAD

PTAD (146 mg, 0.83 mmol) and **8** (167 mg, 0.63 mmol) provided **45** (196 mg, 62%) as colourless crystals.

For (2α,3aα,4β,10β,10aα)-3a,4,10,10a-tetrahydro-2,7-diphenyl-4,10-etheno-6*H*-1,3-dioxolo[4,5-*d*]-[1,2,4]triazolo[1,2-*a*]pyridazine-6,8(7*H*)-dione **45**: mp 238–239 °C; ν_{max}/cm^{-1} 1718; δ_H ($CDCl_3$) 7.48–7.36 (10 H, m), 6.61 (2 H, dd, *J* 3.4 and 3.8, 11-H, 12-H), 6.10 (1 H, s, 2-H), 5.27 (2 H, m, 4-H and 10-H) and 4.82 (2 H, narrow m, 3a-H and 10a-H); saturation at δ 6.61 led to NOEs at δ 6.10 (7%) and 5.27 (8%), saturation at δ 6.10 led to NOEs at δ 7.38 (1%) and 6.61 (3%), saturation at δ 5.27 led to NOEs at δ 6.61 (5%) and 4.82 (6%) and saturation at δ 4.82 led to NOEs at δ 7.38 (1%) and 5.27 (11%); δ_C ($CDCl_3$) 155.5 (C=O), 137.8, 131.0, 129.9 (C-11 and C-12), 129.3, 129.1, 128.5, 125.8, 125.4, 106.8 (C-2), 74.7 (C-3a and C-10a) and 52.3 (C-4 and C-10); *m*/*z* 375.1218 (12%, M^+, $C_{21}H_{17}N_3O_4$ requires 375.1218), 269 (88), 240 (83), 227 (94), 121 (51), 119 (89), 105 (24), 91 (34), 80 (100), 78 (81) and 77 (37).

Diels–Alder reactions with diethyl azodicarboxylate (DEAD)

A solution of DEAD and the diene in benzene was stirred at RT for 24 h. The solution was concentrated under vacuum, and the residue was analyzed by ^{1}H NMR spectroscopy. In all three instances, signals for only one adduct with DEAD were evident, although a minor amount (12%) of dimer was noted in the reaction of **8**. Adducts were purified by chromatography (30% EtOAc in hexanes). Yields are for the isolated adducts.

Diels–Alder reaction of 6a with DEAD

DEAD (123 mg, 0.71 mmol) and **6a** (108 mg, 0.71 mmol) provided **46** (223 mg, 96%) as a colourless oil.

For diethyl (3aα,4β,7β,7aα)-3a,4,7,7a-tetrahydro-2,2-dimethyl-4,7-etheno-1,3-dioxolo[4,5-*d*]pyridazine-5,6-dicarboxylate **46**: ν_{max}/cm^{-1} 1737 and 1725; δ_H ($CDCl_3$) 6.51 (1 H, br t, $J \approx 6.3$), 6.36 (1 H, br t, $J \approx 7.0$), 5.15 (1 H, br m), 5.04 (1 H, br m), 4.47 (2 H, br m), 4.40–4.10 (4 H, br m), 1.36–1.23 (6 H, m), 1.32 (3 H, s) and 1.29 (3 H, s); saturation at δ 6.40 led to NOEs at δ 5.15 (10%) and 5.04 (11%), saturation at δ 5.10 led to NOEs at δ 6.51 (11%), 6.36 (11%) and 4.47 (8%), saturation at δ 4.47 led to NOEs at δ 5.15 (14%), 5.04 (14%) and 1.29 (0.5%), saturation at δ 1.32 led to NOEs at δ 6.51 (4%) and 6.36 (3%) and saturation at δ 1.29 led to NOE at δ 4.47 (9%); δ_C ($CDCl_3$) (Many signals were broadened, which did not allow detection of the carbonyls.) 133.5, 128.7, 111.0, 73.7, 73.1, 62.9, 62.6, 53.5, 51.3, 25.5, 25.4, 14.4 and 14.3; *m*/*z* 326 (1.5%, M^+), 311.1253 (7, $M^+ - CH_3$, $C_{14}H_{19}N_2O_6$ requires 311.1243), 268 (2), 226 (6), 196 (6), 195 (5), 167 (14), 153 (20), 123 (16), 95 (29), 81 (100), 80 (13) and 43 (22).

Diels–Alder reaction of 7 with DEAD

DEAD (266 mg, 1.52 mmol) and **7** (153 mg, 0.76 mmol) provided **47** (142 mg, 50%) as a pale yellow oil.

For diethyl (2α,3aβ,4α,7α,7aβ)-3a,4,7,7a-tetrahydro-2-phenyl-4,7-etheno-1,3-dioxolo[4,5-*d*]pyridazine-5,6-dicarboxylate **47**: ν_{max}/cm^{-1} 1737 and 1703; δ_H ($CDCl_3$) 7.37 (5 H, br m), 6.62 (1 H, br t, $J \approx 6.1$), 6.48 (1 H, br t, $J \approx 7.2$), 5.69 (1 H, s), 5.30 (1 H, br m), 5.20 (1 H, br m), 4.56 (1 H, br m), 4.52 (1 H, br m), 4.34–4.10 (4 H, m) and 1.35–1.23 (6 H, m); saturation at δ 6.62 and 6.48 led to NOEs at δ 7.37 (0.6%), 5.30 (4%) and 5.20 (4%), saturation at δ 5.69 led to NOEs at δ 7.37 (2%) and 4.56 and 4.52 (3%), saturation at δ 5.30 and 5.20 led to NOEs at δ 6.62 (6%), 6.48 (6%) and 4.56 and 4.52 (5%), saturation at δ 4.54 led to NOEs at δ 5.69 (6%), 5.30 (4%) and 5.20 (5%) and saturation at δ 4.22 led to NOE at δ 1.35–1.23 (1%); δ_C ($CDCl_3$) (Many signals were broadened, which did not allow detection of the carbonyls.) 135.1, 133.8, 129.8, 129.0, 128.3, 127.2, 104.7, 73.9, 73.4 (br), 63.0, 62.7, 53.3 (br), 51.0 (br), 14.4 and 14.3; *m*/*z* 374.1472 (0.5%, M^+, $C_{19}H_{22}N_2O_6$ requires 374.1478), 302 (3), 268 (3), 239 (5), 196 (10), 195 (8), 167

(19), 153 (22), 123 (18), 105 (12), 95 (11), 91 (8), 81 (100), 80 (12), 78 (10) and 77 (12).

Diels–Alder reaction of 8 with DEAD

DEAD (483 mg, 2.77 mmol) and **8** (222 mg, 1.10 mmol) provided **48** (224 mg, 54%) as a pale pink oil.

For diethyl (2α,3aα,4β,7β,7aα)-3a,4,7,7a-tetrahydro-2-phenyl-4,7-etheno-1,3-dioxolo[4,5-*d*]pyridazine-5,6-dicarboxylate **48**: ν_{max}/cm^{-1} 1720; δ_H ($CDCl_3$) 7.35 (5 H, narrow m), 6.69 (1 H, br t, $J \approx 6.1$), 6.56 (1 H, br t, $J \approx 6.6$), 6.02 (1 H, s, 2-H), 5.27 (1 H, br m), 5.17 (1 H, br m), 4.69 (1 H, br m), 4.56 (1 H, br m), 4.31–4.10 (4 H, m, OCH_2CH_3) and 1.27 (6 H, br t, J 7.0, OCH_2CH_3); saturation at δ 6.69 and 6.56 led to NOEs at δ 6.02 (8%), 5.27 (10%) and 5.17 (10%), saturation at δ 6.02 led to NOEs at δ 7.35 (1%), 6.69 (1%) and 6.56 (1%), saturation at δ 5.27 and 5.17 led to NOEs at δ 6.69 (11%), 6.56 (11%), 4.69 (9%) and 4.56 (9%) and saturation at δ 4.69 and 4.56 led to NOEs at δ 5.27 (12%) and 5.17 (12%); δ_C ($CDCl_3$) (Many signals were broadened, which did not allow detection of the carbonyls.) 138.1, 134.3, 130.1, 129.1, 128.3, 125.8, 106.0, 74.7, 73.7 (br), 62.9, 62.6, 53.3, 51.3 (br), 14.3 and 14.2; *m/z* 374.1466 (0.7, M^+, $C_{19}H_{22}N_2O_6$ requires 374.1476), 302 (3), 268 (2), 239 (4), 196 (9), 195 (7), 167 (16), 153 (21), 123 (16), 105 (18), 95 (11), 91 (9), 81 (100), 80 (11), 78 (11) and 77 (15).

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References

1 D. T. Gibson, M. Hensley, H. Yoshioka and T. J. Mabry, *Biochemistry*, 1970, **9**, 1626.
2 D. T. Gibson and V. Subramanian, in *Microbial Degradation of Organic Compounds*, ed. D. T. Gibson, Marcel Dekker, New York, 1984, ch. 7 and references therein; T. Hudlicky and C. H. Boros, *Synthesis*, 1992, 174.
3 Reviews: H. A. J. Carless, *Tetrahedron: Asymmetry*, 1992, **3**, 795; T. Hudlicky and A. J. Thorpe, *Chem. Commun.*, 1996, 1993.
4 M. G. Banwell, A. J. Edwards, G. J. Harfoot and K. A. Jolliffe, *J. Chem. Soc., Perkin Trans. 1*, 2002, 2439; M. G. Banwell, A. J. Edwards, M. D. McLeod and S. G. Stewart, *Aust. J. Chem.*, 2004, **57**, 641.
5 D. A. Spiegel, J. T. Njardarson and J. L. Wood, *Tetrahedron*, 2002, **58**, 6545.
6 H. Uno, T. Ishikawa, T. Hoshi and N. Ono, *Tetrahedron Lett.*, 2003, **44**, 5163.
7 M. G. Banwell and G. J. Harfoot, *Aust. J. Chem.*, 2004, **57**, 895.
8 M. G. Banwell, A. J. Edwards, G. J. Harfoot and K. A. Jolliffe, *Tetrahedron*, 2004, **60**, 535.
9 M. E. Salvati, A. Balog, W. Shan, D. D. Wei, D. Pickering, R. M. Attar, J. Geng, C. A. Rizzo, M. M. Gottardis, R. Weinmann, S. R. Krystek, J. Sack, Y. An and K. Kish, *Bioorg. Med. Chem. Lett.*, 2005, **15**, 271.
10 Recent syntheses in which the use of **1a**/**b** was not as a Diels–Alder diene: J. M. Ready, S. E. Reisman, M. Hirata, M. M. Weiss, K. Tamaki, T. V. Ovaska and J. L. Wood, *Angew. Chem., Int. Ed.*, 2004, **43**, 1270; G. Özer, N. Saracoglu, A. Menzek and M. Balci, *Tetrahedron*, 2005, **61**, 1545.
11 J. R. Gillard and D. J. Burnell, *Can. J. Chem.*, 1992, **70**, 1296. (Earlier communication:; J. R. Gillard and D. J. Burnell, *J. Chem. Soc., Chem. Commun.*, 1989, 1439).
12 D. R. Boyd, M. R. J. Dorrity, M. V. Hand, J. F. Malone, N. D. Sharma, H. Dalton, D. J. Gray and G. N. Sheldrake, *J. Am. Chem. Soc.*, 1991, **113**, 666; S. M. Resnick, D. S. Torok and D. T. Gibson, *J. Org. Chem.*, 1995, **60**, 3546; D. R. Boyd, N. D. Sharma, B. Byrne, M. V. Hand, J. F. Malone, G. N. Sheldrake, J. Blacker and H. Dalton, *J. Chem. Soc., Perkin Trans. 1*, 1998, 1935.
13 D. W. Jones, *J. Chem. Soc., Chem. Commun.*, 1980, 739; J. B. Macaulay and A. G. Fallis, *J. Am. Chem. Soc.*, 1990, **112**, 1136; M. A. McClinton and V. Sik, *J. Chem. Soc., Perkin Trans. 1*, 1992, 1891; D. F. Harvey and E. M. Grezner, *J. Org. Chem.*, 1996, **61**, 159.
14 M. A. Wellman, L. C. Burry, J. E. Letourneau, J. N. Bridson, D. O. Miller and D. J. Burnell, *J. Org. Chem.*, 1997, **62**, 939, and references therein.
15 J. D. Xidos, R. A. Poirier, C. C. Pye and D. J. Burnell, *J. Org. Chem.*, 1998, **63**, 105.
16 V. M. Kobal, D. T. Gibson, R. E. Davis and A. Garza, *J. Am. Chem. Soc.*, 1973, **95**, 4420.
17 C. A. Pittol, R. J. Pryce, S. M. Roberts, G. Ryback, V. Sik and J. O. Williams, *J. Chem. Soc., Perkin Trans. 1*, 1989, 1160.
18 P. J. Geary, R. J. Pryce, S. M. Roberts, G. Ryback and J. A. Winders, *J. Chem. Soc., Chem. Commun.*, 1990, 204.
19 W. Downing, R. Latouche, C. A. Pittol, R. J. Pryce, S. M. Roberts, G. Ryback and J. O. Williams, *J. Chem. Soc., Perkin Trans. 1*, 1990, 2613.
20 M. F. Mahon, K. Molloy, C. A. Pittol, R. J. Pryce, S. M. Roberts, G. Ryback, V. Sik, J. O. Williams and J. A. Winders, *J. Chem. Soc., Perkin Trans. 1*, 1991, 1255.
21 J. E. Letourneau, M. A. Wellman and D. J. Burnell, *J. Org. Chem.*, 1997, **62**, 7272.
22 M. G. Banwell and J. R. Dupuche, *Chem. Commun.*, 1996, 869.
23 J. Zezula, T. Hudlicky and I. Ghiviriga, I., *Collect. Czech. Chem. Commun.*, 2001, **66**, 1269.
24 T. Hudlicky, H. F. Olivo and B. McKibben, *J. Am. Chem. Soc.*, 1994, **116**, 5108.
25 M. G. Banwell, D. C. R. Hockless, J. W. Holman, R. W. Longmore, K. J. McRae and H. T. T. Pham, *Synlett*, 1999, 1491.
26 I. C. Cotterill, S. M. Roberts and J. O. Williams, *J. Chem. Soc., Chem. Commun.*, 1988, 1628.
27 K. Schürrle, B. Beier and W. Piepersberg, *J. Chem. Soc., Perkin Trans. 1*, 1991, 2407; T. Hudlicky and H. F. Olivo, *J. Am. Chem. Soc.*, 1992, **114**, 9694; S. Elango, Y.-C. Wang, C.-L. Cheng and T.-H. Yan, *Tetrahedron Lett.*, 2002, **43**, 3757.
28 A. C. Spivey, C. G. Mañas and I. Mann, *Chem. Commun.*, 2005, 4426.
29 J. R. Gillard, M. J. Newlands, J. N. Bridson and D. J. Burnell, *Can. J. Chem.*, 1991, **69**, 1337.
30 A. P. Henderson, E. Mutlu, A. Leclercq, C. Bleasdale, W. Clegg, R. A. Henderson and B. T. Golding, *Chem. Commun.*, 2002, 1956.
31 C. C. Pye, J. D. Xidos, R. A. Poirier and D. J. Burnell, *J. Phys. Chem. A*, 1997, **101**, 3371.
32 M. Ishida, H. Kobayashi, S. Tomohiro and S. Inagaki, *J. Chem. Soc., Perkin Trans. 2*, 2000, 1625.
33 L. A. Paquette, J. C. Weber, T. Kobayashi and Y. Miyahara, *J. Am. Chem. Soc.*, 1988, **110**, 8591.
34 S. V. Ley, A. J. Redgrave, S. C. Taylor, S. Abmed and D. W. Ribbons, *Synlett*, 1991, 741.
35 T. Hudlicky, E. E. Boros, H. F. Olivo and J. S. Merola, *J. Org. Chem.*, 1992, **57**, 1026.
36 T. Hudlicky and C. H. Boros, *Tetrahedron Lett.*, 1993, **34**, 2557; M. R. Stabile, T. Hudlicky and M. L. Meisels, *Tetrahedron: Asymmetry*, 1995, **6**, 537.
37 C. H. Tran, D. H. G. Crout, W. Errington and G. M. Whited, *Tetrahedron: Asymmetry*, 1996, **7**, 691.
38 J. C. Mcauliffe, G. M. Whited and W. C. Smith, *PCT Int. Appl.*, 2002, 156.
39 N. C. Yang, M.-J. Chen and P. Chen, *J. Am. Chem. Soc.*, 1984, **106**, 7310.
40 A. Baran, H. Seçen and M. Balci, *Synthesis*, 2003, 1500.

