PERKIN 1

Chiral dienes from enantiomerically pure enones. Highly stereoselective intramolecular Diels–Alder reaction involving ethenesulfonates

Guido Galley and Michael Pätzel *

Humboldt-Universität Berlin, Institut für Chemie, Hessische Str. 1-2, D-10115 Berlin, Germany

Chiral dienes 2, easily prepared from α,β-unsaturated γ-alkoxy ketones, are subjected to inter- and intramolecular Diels–Alder reactions. Intermolecular cycloadditions of dienes 2 with 4-phenyl-1,2,4-triazole-3,5(2*H*)-dione 3 are found to be diastereoselective. Thermal or high pressure-induced intramolecular cycloadditions of trienes 8, featuring a sulfonate moiety connecting a diene and a dienophile, are found to proceed with high diastereoselectivity to give sultones 11 and 12. An interesting domino process is observed when enone 5 is reacted with sodium hydride. In this reaction sequence, the decahydropyrano[2,3,4-*de*]chromene derivative 15 was formed. NMR spectroscopic studies allowed the assignments of the configurations of the bi- and tri-cyclic products.

Introduction

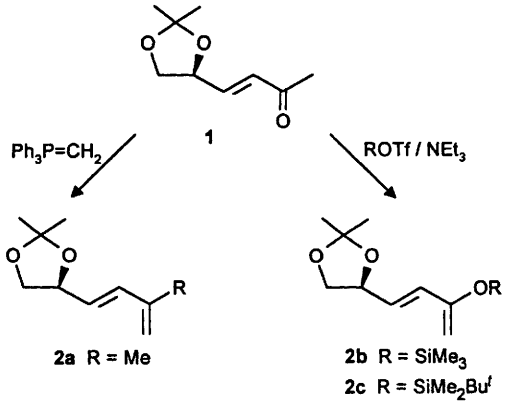
The Diels–Alder reaction is one of the most important reactions in synthetic organic chemistry. It enables the preparation of cyclic compounds with up to four new stereocentres in a single-step reaction. Whereas chirally modified dienophiles are often used to control the absolute configuration of the cycloadducts, only a limited number of homochiral 4π-systems is available at present.[1] The less frequent use of enantiomerically pure dienes may be due to the difficulty of preparing such compounds.[2] Recent reports, particularly on chiral 2-aminobutadienes, show a high degree of stereoselectivity in cycloaddition reactions.[3]

In the course of our studies of diastereoselective cycloadditions of enantiomerically pure enones,[4] we became interested in investigating the suitability of these compounds as starting materials for preparing chiral dienes. In this paper we report the preparation and inter- and intra-molecular Diels–Alder reactions of chiral dienes derived from α,β-unsaturated γ-alkoxy ketones.

Results and discussion

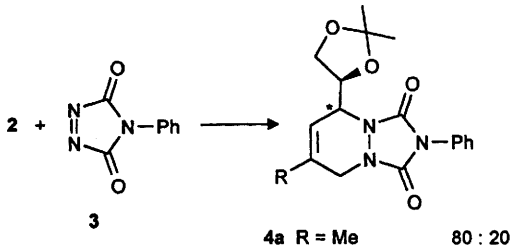
The preparation of chiral dienes starting from enone **1** could be achieved in two different ways. The first employed the Wittig olefination reaction, a method known to convert chiral enals into butadienes without racemisation.[5] This method was used to prepare diene **2a**. The second procedure involved the treatment of enones with powerful silylation agents to synthesise 2-silyloxydienes.[6] To date, only very few examples of enantiomerically pure silyloxydienes are known.[7] Reactions of **1** with alkylsilyl trifluoromethanesulfonates (triflates) afforded chiral dienes **2b** and **2c** in high yield. These silyloxydienes have some advantages over simple dienes like **2a**. Due to their electron rich character, they exhibit higher reactivity in HOMO-diene controlled cycloadditions. In addition, the silyloxy group can easily be converted to a carbonyl group once cycloaddition has been carried out. In asymmetric synthesis, the possibility of controlling the stereochemical outcome of the reaction by introducing steric hindrance, through choice of alkyl substituents R, is also of importance.

Our first attempts to use the dienes **2a–c** in asymmetric cycloadditions failed. No reactions occurred with different olefinic dienophiles, such as maleic anhydride, methyl vinyl ketone, methyl acrylate and β-nitrostyrene at room temperature or even with Lewis acid catalysis [$EtAlCl_2$, $Ti(OPr^i)_3Cl$ or $ZnCl_2$]. Cycloadditions could only be triggered at elevated temperatures or under high pressure conditions; however, these reactions resulted in mixtures of all possible four diastereomers.



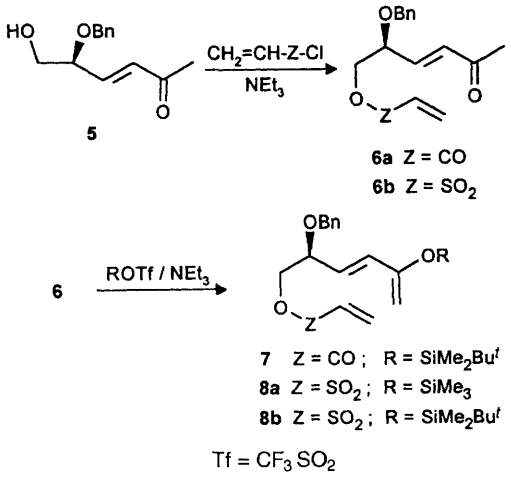
It is known that aza dienophiles show a higher degree of stereodiscrimination than their olefinic counterparts.[8] Hence, dienes **2a–c** were subjected to hetero-Diels–Alder reactions with the very reactive dienophile 4-phenyl-1,2,4-triazol-3,5(4*H*)-dione **3**.[9] At room temperature the cycloadducts **4** were formed immediately and with good diastereoselectivity. However, attempts to separate the diastereomeric products failed and hence the configuration of **4** was not assigned. The cycloadditions of **2a–c**, with hetero dienophiles of wider synthetic interest like imines and sulfinylimines, are currently under investigation.

Intermolecular carbocycle formation through cycloadditions of compounds **2a–c** with olefins gave unsatisfactory results.



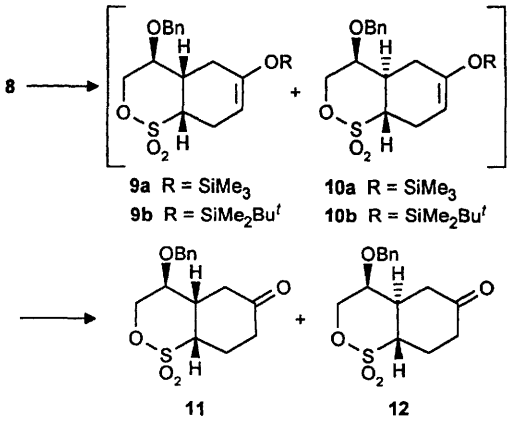
4a R = Me	80 : 20
4b R = $OSiMe_3$	77 : 23
4c R = $OSiMe_2Bu^t$	78 : 22

Attention was then focused on exploring the possibility of intramolecular Diels–Alder reactions. Incorporating the dienophile moiety into enone **5**[4c] at the unprotected hydroxy function, followed by converting the enone function to a diene, would lead to a system that is potentially capable of undergoing an intramolecular Diels–Alder reaction. Because the resulting *diene contains* electron-donating substituents, olefins with electron-withdrawing groups such as acrylates and ethenesulfonates seemed to be the most suitable dienophiles. In this connection, it should be noted that ethenesulfonates take part in intramolecular cyclisations more readily than acrylates, owing to their different conformational preference.[10]



Conversion of **5** to the acrylate **6a** or ethenesulfonate **6b**, followed by treatment with the corresponding silyl trifluoromethanesulfonate, yielded the silyloxydienes **7** or **8**, respectively. Compound **7** was subjected to several different reaction conditions (elevated temperature, high pressure and Lewis acid catalysis), but no cyclisation products were detected. This is a further example of the unsuitability of an ester linkage in intramolecular Diels–Alder reactions.[11]

On the other hand, intramolecular cycloaddition reactions of triene **8**, containing the sulfonate moiety, occurred under thermal and high pressure conditions yielding the sultones **11** and **12**. Because of hydrolytic instability compounds **8** were not isolated but freshly prepared solutions in dichloromethane were used for cycloaddition experiments. The initially formed cycloadducts **9** and **10** could only be detected by TLC and were readily hydrolysed to compounds **11** and **12** during workup.



The choice of reaction conditions had only little influence on yield and ratio of diastereomers (Table 1). Whereas **8a** with the smaller substituent produces three diastereomers, in the case of ***8b*** *the* stereogenic centre within the tether induced the formation of only two isomers (**11** and **12**) out of four possible

Table 1 Results of intramolecular Diels–Alder reactions of trienes **8**

Compound	Conditions	Yield (%)[a] **11** + **12**	**11**:**12**
8a	rt, 10 kbar, 18 h	64	74:17[b]
8b	rt, 10 kbar, 18 h	72	78:22
8b	130 °C, 12 bar, 4 h	67	82:18

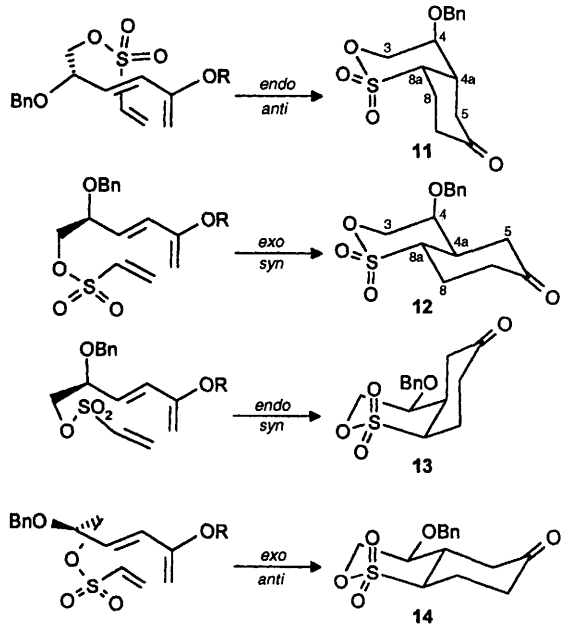
[a] After purification by chromatography for two steps from **6b**. [b] A third isomer (9%) was detected by NMR.

Table 2 Observed and calculated H–H coupling constants for **11** and **12**

	J_{H-H} Hz of **11**		J_{H-H} Hz of **12**	
Coupling protons	Obs.	Calc.	Obs.	Calc.
H-3 and H-4	5.0/5.0	3.2/4.3	1.7/1.7	2.1/2.1
H-4 and H-4a	2.6	2.1	0	1.8
H-4a and H-8a	5.0	4.5	12.1	12.5

cycloadducts. These isomers could be separated by column chromatography and were subjected to extensive NMR studies. As already observed for other ethenesulfonates the reaction could not be accelerated in the presence of $LiClO_4$ or Lewis acids ($EtAlCl_2$, $BF_3{\cdot}OEt_2$ or $ZnCl_2$) as catalysts.[10]

Assignments of the configurations of **11** and **12** followed from NMR spectroscopic and computational studies. C–H COSY and H–H COSY experiments allowed the unequivocal assignment of the chemical shifts and coupling constants of H-4, H-4a and H-8a at the stereogenic centres. In order to compare the measured values with the theoretical coupling constants, the four diastereomers **11**–**14**, arising from the four possible transition states (Scheme 1), were taken into account.



Scheme 1

The structures of the products were optimised using method PM3 of the UniChem® software package.[12] Theoretical coupling constants were calculated[13] from the measured dihedral angles by means of the SpecTool® software.

The observed coupling constants for the major isomer correlate well with the data for the corresponding protons in the *cis*-fused *endo-anti* product **11**. Typical is the occurrence of only small vicinal coupling constants corresponding to the absence of 1,2-axial-axial proton interaction (see Table 2).

Further evidence of the stereochemistry of the major

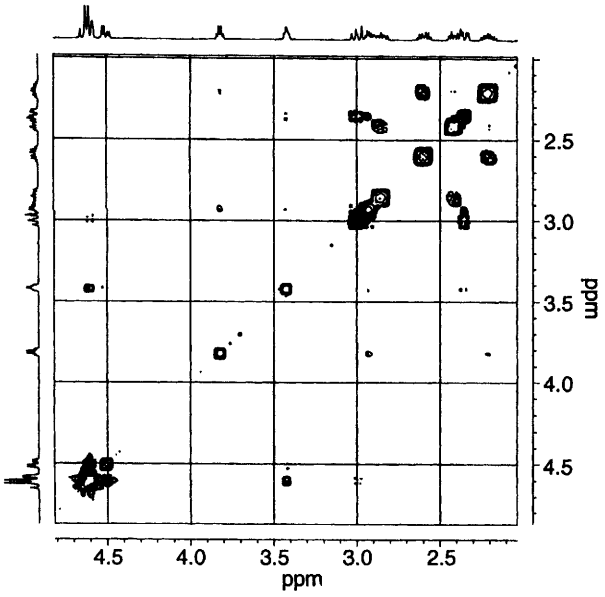


Fig. 1

diastereomer was obtained from a H–H NOESY experiment (Fig. 1). Observed NOE effects between H-3 and H^1-5 and between H-4 and H^2-5 serve as proof of *cis*-annulation and are in agreement only with the *endo-anti* cycloadduct **11**.

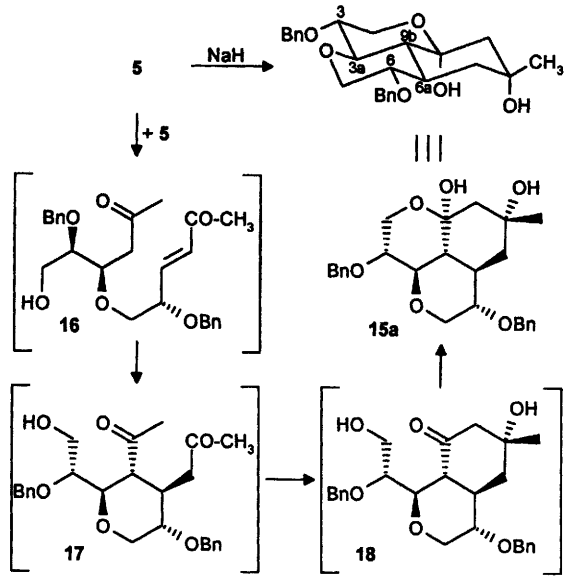
In the minor isomer the large coupling constant of 12.1 Hz between H-4a and H-8a indicates a *trans*-fused bicyclic sultone. The fact that no additional large coupling constant was observed between H-4 and H-4a (as expected for *trans*-fused product **14**) suggests that the minor isomer could be the *trans*-fused *exo-syn* cycloadduct **12**. Table 2 shows that the measured values correlate well with the calculated coupling constants.

Although intramolecular Diels–Alder reactions are often *exo*-selective, the preferred formation of *endo*-adducts in cycloadditions of substrates bearing bulky silyl groups is known.[6a] To explain the stereochemical outcome of the cycloaddition of **8**, steric factors were taken into consideration. In a simple model, assuming a late transition state,[14] the O–O distances between the benzyloxy and the keto (former silyloxy) group were calculated from the PM3 optimised molecules **11**–**14**. The largest value was found in the structure **11** (5.7 Å) followed by **12** (5.3 Å), **13** (5.0 Å) and **14** (4.9 Å). These values serve as measures of the proximity of the large silyloxy and benzyloxy groups and indicate that the cycloadducts **11** and **12** are the less crowded systems. In case of the smaller trimethylsilyl substituent in **8a**, the steric hindrance is lower and the formation of a third diastereomer is plausible.

Metz *et al.*[10] studied the reactions of hexa-3,5-dienylethenesulfonates. Our findings complement those reported by these authors. It can be stated that not only a substituent in the 4-position but also a large substituent in one 5-position is effective for diastereoselection.

In the course of our studies we have also made attempts to connect the dienophile component to enone **5** by an ether linkage. Thus an attempt was made to convert **5** to the corresponding alkoxide ion by treatment with sodium hydride. Surprisingly an interesting cyclisation reaction occurred, which resulted in four products in the ratio of 62:15:13:10. The NMR spectra of these products allowed their identification as dimers of **5**.

The structure of the major isomer was determined by further NMR techniques (H–H and H–C COSY, H–H NOESY). It was assigned as the tricyclic decahydropyrano[2,3,4-*de*]chromene derivative **15a**. From the large coupling constants corresponding to 1,2-diaxial proton interactions *trans*-fusion of all three rings was concluded. The NOESY spectrum further confirmed this assignment (H-9b, H-6 and H-3 were shown to be over the molecule plane, while H-6a and H-3a were under the molecule plane) and also established the equatorial position of the methyl group.



As a possible mechanism for the formation of **15a** from **5**, an interesting domino process is proposed. The first step of the reaction sequence involves a 1,4-addition of the alkoxide ion derived from **5** to a second molecule of **5** to yield dimer **16**. The observed *syn*-selectivity is in agreement with alkoxide additions to other γ-alkoxy α,β-unsaturated carbonyl compounds.[15] This is then followed by an intramolecular Michael addition and an aldol reaction to give **18**. The closure of the third ring is due to an intramolecular hemiacetal formation. In this sequence of reaction five new stereocentres were formed. It is evident that diastereomers of **15** were also produced in this reaction.

To the best of our knowledge there are only three examples of compounds carrying the decahydropyrano[2,3,4-*de*]chromene framework. These are the heptanortriterpernoids entilin A, B and C isolated from tropical hardwood trees.[16]

Experimental

All solvents and reagents were purchased from commercial sources and used as received, unless otherwise stated. High pressure-induced cycloadditions were performed in a piston-cylinder high pressure apparatus for pressures up to 14 kbar, manufactured by Andreas Hofer Hochdrucktechnik GmbH, Mülheim/Ruhr, Germany. The reactions and the purity of compounds were monitored by TLC performed on pre-coated silica gel plates with a fluorescence indicator (Merck 60 F_{254}). Column chromatography was carried out on Merck Kieselgel 60 (0.040–0.063). The ^1H (300 MHz) and ^{13}C (75 MHz) NMR spectra were recorded on a Bruker AC-300 spectrometer in $CDCl_3$ solutions. Chemical shifts are given in δ values relative to residual proton or carbon resonances of $CDCl_3$ (7.26 or 77.0 respectively). *J* Values are given in Hz. The following abbreviations are used: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad singlet. Elemental analyses were performed in a Leco CHNS-932 apparatus. Optical rotations were measured on a Perkin Elmer 241 polarimeter using a 2 ml cell. [α] Values are given in 10^{-1} deg cm^2 g^{-1}.

(1′*E*,4*S*)-2,2-Dimethyl-4-(3′-methylbuta-1′,3′-dienyl)-1,3-dioxolane 2a

To a cooled solution (−78 °C) of diisopropylamine (505 mg, 5 mmol) in dry THF (10 ml) was added butyllithium (1.6 M, 3.8 ml, 6 mmol). After removal of the cooling bath the mixture was stirred for 15 min, then methyltriphenylphosphonium bromide

(1.79 g, 5 mmol) was added under argon. The mixture was stirred until the solid was almost completely dissolved, then cooled to −60 °C and a solution of enone **1**[17] (850 mg, 5 mmol) in THF (10 ml) was added dropwise. After removal of the cooling bath the mixture was stirred for 1 h and poured into water–hexane (100 ml, 1:1). The mixture was filtered by suction over Celite and the water layer was extracted three times with hexane. After drying ($MgSO_4$) the combined organic layers were concentrated under reduced pressure. Passing the residue through a silica gel plug (eluent: hexane–ethyl acetate 7:3, v/v) afforded diene **2a** (638 mg, 76%) as a colourless liquid (Found: C, 71.7; H, 10.0. $C_{10}H_{16}O_2$ requires C, 71.4; H, 9.6%); $[\alpha]_{546}^{25}$ +23.0 (*c* 1.0 in CH_2Cl_2); δ_H(300 MHz; $CDCl_3$) 6.32 (1 H, d, *J* 15.6, 2′-H), 5.52 (1 H, dd, *J* 7.7 and 15.6, 1′-H), 4.93 (2 H, s, 4′-H), 4.48 (1 H, q, *J* 7.6, 4-H), 4.02 (1 H, dd, *J* 6.1 and 8.1, 5-H), 3.52 (1 H, t, *J* 8.1, 5-H), 1.78 (3 H, s, 3′-*Me*), 1.37 and 1.32 (both 3 H, s, Me); δ_C(75 MHz; $CDCl_3$) 140.8 (C-3′), 136.2 (C-1′), 126.3 (C-2′), 117.5 (C-4′), 109.1 (OCO), 77.0 (C-4), 69.4 (C-5), 26.5 and 25.7 (both Me), 18.3 (3′-*Me*).

(1′*E*,4*S*)-2,2-Dimethyl-4-(3′-trimethylsilyloxylbuta-1′,3′-dienyl)-1,3-dioxolane 2b

To a cooled solution (10 °C) of enone **1**[17] (680 mg, 4 mmol) in dry dioxane (25 ml) were added dropwise triethylamine (560 mg, 5.5 mmol) and trimethylsilyl trifluoromethanesulfonate (1.0 g, 4.5 mmol). The mixture was stirred for 5 min, the cooling bath was then removed and the stirring continued at room temperature for 1 h at which time TLC showed the completion of the reaction. The mixture was concentrated under reduced pressure at 40 °C and passed through a silica gel plug (eluent: hexane–ethyl acetate 7:3, v/v) to give **2b** (891 mg, 92%) as a colourless liquid (Found: C, 59.5; H, 9.2. $C_{12}H_{22}O_3Si$ requires C, 59.5; H, 9.15%); $[\alpha]_{546}^{25}$ +24.1 (*c* 1.1 in CH_2Cl_2); δ_H(300 MHz; $CDCl_3$) 6.09 (1 H, dd, *J* 15.1 and 0.7, 2′-H), 5.85 (1 H, dd, *J* 7.1 and 15.1, 1′-H), 4.53 (1 H, q, *J* 7.1, 4-H), 4.30 (2 H, s, 4′-H), 4.05 (1 H, dd, *J* 6.1 and 8.1, 5-H), 3.55 (1 H, t, *J* 7.9, 5-H), 1.39 and 1.35 (both 3 H, s, Me), 0.18 (9 H, s, Si*Me*$_3$); δ_C(75 MHz; $CDCl_3$) 153.9 (C-3′), 130.6 (C-1′), 127.4 (C-2′), 109.3 (OCO), 96.6 (C-4′), 76.2 (C-4), 69.5 (C-5), 26.6 and 25.8 (both Me), −0.1 (Si*Me*$_3$).

(1′*E*,4*S*)-4-(3′-*tert*-Butyldimethylsilyloxybuta-1′,3′-dienyl)-2,2-dimethyl-1,3-dioxolane 2c

The procedure employed for the preparation of **2b** was followed using *tert*-butyldimethylsilyl trifluoromethanesulfonate instead of trimethylsilyl trifluoromethanesulfonate **2c** (1.02 g, 90%) was obtained as a colourless liquid (Found: C, 63.1; H, 10.2. $C_{15}H_{28}O_3Si$ requires C, 63.3; H, 9.9%); $[\alpha]_{546}^{25}$ + 17.0 (*c* 1.2 in CH_2Cl_2); δ_H(300 MHz; $CDCl_3$) 6.12 (1 H, d, *J* 15.2, 2′-H), 5.92 (1 H, dd, *J* 7.1 and 15.2, 1′-H), 4.56 (1 H, q, *J* 7.1, 4-H), 4.31 (2 H, s, 4′-H), 4.09 (1 H, dd, *J* 6.3 and 7.9, 5-H), 3.58 (1 H, t, *J* 7.9, 5-H), 1.42 and 1.38 (3 H, s, Me), 0.95 (9 H, s, C*Me*$_3$), 0.16 (6 H, s, Si*Me*$_2$); δ_C(75 MHz; $CDCl_3$) 154.1 (C-3′), 130.7 (C-1′), 127.5 (C-2′), 109.3 (OCO), 96.5 (C-4′), 76.2 (C-4), 69.5 (C-5), 26.6 and 25.9 (Me), 25.8 (C*Me*$_3$), 18.2 (Si*C*Me$_3$), −4.7 (Si*Me*$_2$).

Cycloadditions with 4-phenyl-1,2,4-triazole-3,5(2*H*)-dione 3

4-Phenyl-1,2,4-triazole-3,5(2*H*)-dione **3** (88 mg, 0.5 mmol) in CH_2Cl_2 (3 ml) was treated with a solution of diene **2** (0.5 mmol) in CH_2Cl_2 (2 ml) at room temperature. The red colour of **3** was discharged and a solid was deposited. The solvent was removed and the residue analysed using ^{13}C and ^1H NMR techniques.

5-[(4*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-7-methyl-2-phenyl-2,3,5,8-tetrahydro-1*H*-[1,2,4]triazolo[1,2-*a*]pyridazine-1,3-dione 4a. Major isomer: δ_H(300 MHz; $CDCl_3$) 7.27–7.46 (5 H, m, ArH), 5.63 (1 H, dd, *J* 11.6 and 1.7, 6-H), 4.42–4.45 (2 H, m, 5-H and CH–O), 3.86–4.09 (4 H, m, 8-H and CH_2O), 1.81 (3 H, s, 7-*Me*), 1.33 and 1.25 (each 3 H, s, Me); δ_C(75 MHz; $CDCl_3$) 152.1 and 150.6 (C-1, C-3), 131.1 (ArC), 130.1 (C-7), 129.0, 128.0, 125.4 (ArCH), 116.0 (C-6), 109.8 (OCO), 76.2 (CH–O), 66.7 (CH_2O), 54.9 (C-5), 46.6 (C-8), 26.1 and 25.0 (both Me), 20.2 (7-*Me*).

5-[(4*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-2-phenyl-7-trimethylsilyloxy-2,3,5,8-tetrahydro-1*H*-[1,2,4]triazolo[1,2-*a*]-pyridazine-1,3-dione 4b. Major isomer: δ_H(300 MHz; $CDCl_3$) 7.31–7.51 (5 H, m, ArH), 5.10 (1 H, d, *J* 4.8, 6-H), 4.63–4.67 (1 H, m, 5-H), 4.47 (1 H, q, *J* 5.8, CH–O), 3.86–4.21 (4 H, m, 8-H and CH_2O), 1.40 and 1.31 (each 3 H, s, Me), 0.26 (9 H, s, Si*Me*$_3$); δ_C(75 MHz; $CDCl_3$) 151.9 and 150.5 (C-1, C-3), 143.4 (C-7), 131.0 (ArC), 129.0, 128.1, 125.4 (ArCH), 110.2 (OCO), 97.5 (C-6), 76.3 (CH–O), 66.6 (CH_2O), 53.4 (C-5), 45.8 (C-8), 26.4 and 25.6 (both Me), 1.2 and 0.0 (Si*Me*$_3$).

7-(*tert*-Butyldimethylsilyloxy)-5-[(4*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]-2-phenyl-2,3,5,8-tetrahydro-1*H*-[1,2,4]triazolo-[1,2-*a*]pyridazine-1,3-dione 4c. Major isomer: δ_H(300 MHz; $CDCl_3$) 7.31–7.51 (5 H, m, ArH), 5.09 (1 H, d, *J* 4.8, 6-H), 4.62 (1 H, t, *J* 5.0, 5-H), 4.43 (1 H, q, *J* 5.7, CH–O), 3.88–4.13 (4 H, m, 8-H and CH_2O), 1.40 and 1.30 (each 3 H, s, Me), 0.93 (9 H, s, C*Me*$_3$), 0.22 and 0.20 (each 3 H, s, Si*Me*$_2$); δ_C(75 MHz; $CDCl_3$) 152.1 and 150.4 (C-1, C-3), 146.0 (C-7), 131.0 (ArC), 129.0, 128.0, 125.3 (ArCH), 109.6 (OCO), 97.8 (C-6), 76.5 (CH–O), 66.7 (CH_2O), 53.8 (C-5), 45.9 (C-8), 26.1 and 25.0 (both Me), 25.3 (C*Me*$_3$), 17.8 (Si*C*Me$_3$), −4.6 and −4.8 (Si*Me*$_2$).

(3*E*,2*S*)-2-Benzyloxy-5-oxohex-3-enyl acrylate 6a

To a solution of **5**[4c] (220 mg, 1.0 mmol) in CH_2Cl_2 (4 ml) was added acryloyl chloride (127 mg, 1.4 mmol) and the mixture was stirred and cooled to 0–5 °C. A solution of triethylamine (143 mg, 1.4 mmol) in CH_2Cl_2 (1 ml) was then added dropwise using a syringe. After stirring the mixture overnight, it was poured into saturated aqueous NH_4Cl (5 ml) and the aqueous layer was extracted several times with CH_2Cl_2. The combined organic layers were dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2, hexane–ethyl acetate 1:1, v/v) to yield **6a** (167 mg, 61%) as a colourless oil; δ_H(300 MHz; $CDCl_3$) 7.22–7.31 (5 H, m, ArH), 6.63 (1 H, dd, *J* 4.4 and 16.1, 3-H), 6.35 (1 H, dd, *J* 1.3 and 17.3, CH_2=), 6.32 (1 H, d, *J* 17.1, 4-H), 6.08 (1 H, dd, *J* 10.4 and 17.3, CH_2=), 5.79 (1 H, dd, *J* 10.3 and 1.3, CH–COO), 4.59 (1 H, d, *J* 12.0, CH_2-Ph), 4.45 (1 H, d, *J* 12.0, CH_2-Ph), 4.18–4.26 (3 H, m, 2-H and 1-H), 2.22 (3 H, s, 6-H); δ_C(75 MHz; $CDCl_3$) 197.8 (C-5), 165.7 (COO), 142.4 (C-3), 137.4 (ArC), 132.5 (C-4), 131.5 (CH_2=), 128.5 (*C*H–COO), 128.5, 127.9, 127.7 (ArCH), 75.9 (C-2), 71.5 (CH_2-Ph), 65.2 (C-1), 27.3 (C-6).

(3*E*,2*S*)-2-Benzyloxy-5-oxohex-3-enyl ethenesulfonate 6b

The same procedure as employed for the preparation of **6a** was followed. Ethenesulfonyl chloride[18] was used instead of acryloyl chloride. From 3 mmol of **5** was obtained 670 mg of **6b** (72%) as a colourless oil (Found: C, 57.9; H, 5.85; S, 10.8. $C_{15}H_{18}SO_5$ requires C, 58.05; H, 5.85; S, 10.3%); $[\alpha]_{546}^{25}$ −29.7 (*c* 1.1 in CH_2Cl_2); δ_H(300 MHz; $CDCl_3$) 7.23–7.33 (5 H, m, ArH), 6.57 (1 H, dd, *J* 5.8 and 16.1, 3-H), 6.46 (1 H, dd, *J* 9.6 and 16.6, CH_2=), 6.33 (1 H, dd, *J* 4.1 and 16.6, CH_2=), 6.30 (1 H, d, *J* 16.1, 4-H), 6.03 (1 H, d, *J* 9.6, CH–SO_3), 4.58 (1 H, d, *J* 11.8, CH_2-Ph), 4.46 (1 H, d, *J* 11.8, CH_2-Ph), 4.26 (1 H, q, *J* 4.9, 2-H), 4.06–4.17 (2 H, m, 1-H), 2.22 (3 H, s, 6-H); δ_C(75 MHz; $CDCl_3$) 197.7 (C-5), 140.8 (C-3), 137.1 (ArC), 133.2 (C-4), 132.2 (CH–SO_3), 130.6 (CH_2=), 128.5, 128.1, 127.8 (ArCH), 75.8 (C-2), 71.8 (CH_2-Ph), 70.7 (C-1), 27.5 (C-6).

(3*E*,2*S*)-2-Benzyloxy-5-(*tert*-butyldimethylsilyloxy)hexa-3,5-dienyl acrylate 7

To an ice cooled solution (0 °C) of **6a** (137 mg, 0.5 mmol) in dry THF (4 ml) were added dropwise triethylamine (82 mg, 0.8 mmol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (211 mg, 0.8 mmol). The mixture was then stirred for 15 min at room temperature, concentrated under reduced pressure and

passed through a silica gel plug (eluent: hexane–ethyl acetate 8:2, v/v) to give **7** (136 mg, 70%) as a colourless oil; δ_H(300 MHz; $CDCl_3$) 7.30–7.32 (5 H, m, ArH), 6.38 (1 H, dd, *J* 1.5 and 17.3, CH_2=), 6.15 (1 H, d, *J* 14.9, 4-H), 6.11 (1 H, dd, *J* 10.4 and 17.3, CH–COO), 5.91 (1 H, dd, *J* 6.9 and 15.3, 3-H), 5.81 (1 H, dd, *J* 10.4 and 1.5, CH_2=), 4.64 (1 H, d, *J* 12.1, CH_2-Ph), 4.41 (1 H, d, *J* 12.1, CH_2-Ph), 4.35 (2 H, d, *J* 5.3, 6-H), 4.13–4.22 (3 H, m, 2-H and 1-H), 0.96 (9 H, s, C*Me*$_3$), 0.17 (6 H, s, Si*Me*$_2$); δ_C(75 MHz; $CDCl_3$) 165.9 (COO), 154.1 (C-5), 138.1 (ArC), 132.0 (C-3), 130.9 (CH_2=), 128.4, 128.3, 127.7 (ArCH), 127.6 (*C*H–COO), 126.5 (C-4), 97.0 (C-6), 76.6 (C-2), 70.6 (CH_2-Ph), 66.4 (C-1), 25.7 (C*Me*$_3$), 18.2 (Si*C*Me$_3$), −4.7 (Si*Me*$_2$).

(3*E*,2*S*)-2-benzyloxy-5-(trimethylsiloxy)hexa-3,5-dienyl ethenesulfonate 8a

To an ice cooled solution (0 °C) of **6b** (420 mg, 1.35 mmol) in dry THF (8 ml) were added dropwise triethylamine (163 mg, 1.6 mmol) and trimethylsilyl trifluoromethanesulfonate (356 mg, 1.6 mmol). The mixture was stirred for 1 h at room temperature and was then concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2, washed with saturated aqueous NaCl and dried ($MgSO_4$). This solution was used for cycloaddition experiments. Because of hydrolytic instability only an analytical sample was purified by column chromatography (SiO_2, hexane–ethyl acetate 7:3, v/v). Thus 0.3 mmol of **6b** afforded **8a** (69 mg, 60%) as a colourless oil (and **6b**, 33 mg, 35%, *via* hydrolysis); $[\alpha]_{546}^{25}$ −38.8 (*c* 1.0 in CH_2Cl_2); δ_H(300 MHz; $CDCl_3$) 7.22–7.31 (5 H, m, ArH), 6.40 (1 H, dd, *J* 9.3 and 16.7, CH–SO_3), 6.30 (1 H, dd, *J* 16.7 and 0.8, CH_2=), 6.13 (1 H, d, *J* 15.3, 4-H), 5.98 (1 H, d, *J* 9.6, CH_2=), 5.72 (1 H, dd, *J* 7.2 and 15.3, 3-H), 4.57 (1 H, d, *J* 11.7, CH_2-Ph), 4.35 (1 H, d, *J* 11.7, CH_2-Ph), 4.33–4.35 (2 H, m, 6-H), 4.09–4.17 (1 H, m, 2-H), 4.05 (2 H, d, *J* 5.5, 1-H), 0.18 (9 H, s, Si*Me*$_2$); δ_C(75 MHz; $CDCl_3$) 153.5 (C-5), 137.6 (ArC), 132.9 (C-3), 132.5 (CH–SO_3), 130.0 (CH_2=), 128.4, 128.1, 127.8 (ArCH), 124.9 (C-4), 97.8 (C-6), 76.5 (C-2), 71.9 (CH_2-Ph), 70.8 (C-1), 0.0 (Si*Me*$_2$).

(3*E*,2*S*)-2-Benzyloxy-5-(*tert*-butyldimethylsiloxy)hexa-3,5-dienyl ethenesulfonate 8b

The same procedure as employed for the preparation of **8a** was followed. *tert*-Butyldimethylsilyl trifluoromethanesulfonate was used instead of trimethylsilyl trifluoromethanesulfonate. The solution in CH_2Cl_2 was used for cycloaddition experiments. Because of hydrolytic instability only an analytical sample was purified by column chromatography (SiO_2, hexane–ethyl acetate 7:3, v/v). Thus 0.4 mmol of **6b** afforded **8b** (93 mg, 55%) as a colourless oil (and **6b**, 47 mg, 38%, *via* hydrolysis); $[\alpha]_{546}^{25}$ −32.4 (*c* 1.1 in CH_2Cl_2); δ_H(300 MHz; $CDCl_3$) 7.24–7.36 (5 H, m, ArH), 6.48 (1 H, dd, *J* 9.6 and 16.7, CH–SO_3), 6.35 (1 H, d, *J* 16.7, CH_2=), 6.18 (1 H, dd, *J* 15.4 and 0.6, 4-H), 6.01 (1 H, d, *J* 9.6, CH_2=), 5.82 (1 H, dd, *J* 7.1 and 15.3, 3-H), 4.62 (1 H, d, *J* 11.8, CH_2-Ph), 4.44 (1 H, d, *J* 11.8, CH_2-Ph), 4.38 (2 H, d, *J* 7.9, 6-H), 4.16–4.23 (1 H, m, 2-H), 4.11 (2 H, d, *J* 5.7, 1-H), 0.96 (9 H, s, C*Me*$_3$), 0.18 (6 H, s, Si*Me*$_2$); δ_C(75 MHz; $CDCl_3$) 153.8 (C-5), 137.7 (ArC), 133.1 (C-3), 132.6 (CH–SO_3), 129.8 (CH_2=), 128.4, 127.8 (ArCH), 124.9 (C-4), 97.6 (C-6), 76.6 (C-2), 71.8 (CH_2-Ph), 70.9 (C-1), 25.8 (C*Me*$_3$), 18.3 (Si*C*Me$_3$), −4.6 (Si*Me*$_2$).

Intramolecular Diels–Alder reactions of trienes 8

(a) High pressure-induced cycloaddition. A solution of **8** in CH_2Cl_2 (0.3–0.5 M) was introduced into a PTFE tube. After sealing, the tubes were immersed in the transmitter liquid of the high pressure apparatus. The piston was inserted and the pressure was raised to 10 kbar. The mixture was kept under these conditions for 18 h. After decompression the tube was opened and the solvent was removed. Column chromatography (SiO_2, hexane–ethyl acetate 7:3, v/v) of the residue yielded the pure compounds **11** and **12** (see Table 1) and unreacted **6b** (56 mg, 10% from **8a**; 62 mg, 11% from **8b**).

(b) Thermal cycloaddition. A solution of **8b** in CH_2Cl_2 (0.05–0.1 M) was heated at 130 °C in an autoclave for 4 h. The solvent was evaporated under reduced pressure. Column chromatography (SiO_2, hexane–ethyl acetate 7:3, v/v) of the residue yielded the pure compounds **11** and **12** (see Table 1) and unreacted **6b** (74 mg, 13%).

(4*S*,4a*S*,8a*S*)-3-Benzyloxy-3,4,4a,7,8,8a-hexahydrobenzoxathiin-6(5*H*)-one 1,1-dioxide 11

Colourless oil (Found: C, 57.5; H, 5.9; S, 10.7. $C_{15}H_{18}SO_5$ requires C, 58.1; H, 5.85; S, 10.3%); $[\alpha]_{546}^{25}$ +38.2 (*c* 1.1 in CH_2Cl_2); δ_H(300 MHz; $CDCl_3$) 7.29–7.38 (5 H, m, ArH), 4.62 (1 H, d, *J* 11.6, CH_2-Ph), 4.58 (1 H, dd, *J* 12.9 and 2.6, 3′-*H*), 4.56 (1 H, d, *J* 11.6, CH_2-Ph), 4.48 (1 H, dd, *J* 12.5 and 4.7, 3′-H), 3.79 (1 H, q, *J* 5.0, 8a-H), 3.40 (1 H, td, *J* 5.0 and 2.6, 4-H), 4.58 (1 H, t, *J* 10.5, 5-H), 2.86 (1 H, q, *J* 5.0, 4a-H), 2.79 (1 H, dd, *J* 6.0 and 4.0, 7-H), 2.58 (1 H, dt, *J* 14.8 and 6.0, 8-H), 2.41 (1 H, t, *J* 6.0, 7-H), 2.33 (1 H, dd, *J* 13.5 and 4.6, 5-H), 2.18 (1 H, dt, *J* 14.8 and 5.0, 8-H); δ_C(75 MHz; $CDCl_3$) 207.1 (C-6), 136.8 (ArC), 128.7, 128.4, 127.8 (ArCH), 72.0 (CH_2-Ph), 71.9 (C-4), 70.6 (C-3), 53.0 (C-8a), 42.1 (C-4a), 40.4 (C-5), 37.4 (C-7), 23.6 (C-8); *m*/*z* (CI) 311 ($M + H^+$, 100).

(4*S*,4a*R*,8a*S*)-3-Benzyloxy-3,4,4a,7,8,8a-hexahydrobenzoxathiin-6(5*H*)-one 1,1-dioxide

Colourless needles, mp 219 °C (Found: C, 58.3; H, 5.5.; S, 10.7. $C_{15}H_{18}SO_5$ requires C, 58.1; H, 5.85; S, 10.3%); $[\alpha]_{546}^{25}$ +229 (*c* 0.5 in CH_2Cl_2); δ_H(300 MHz; $CDCl_3$) 7.24–7.38 (5 H, m, ArH), 4.76 (1 H, d, *J* 11.6, CH_2-Ph), 4.63 (1 H, dd, *J* 12.8 and 1.7, 3-H), 4.50 (1 H, dd, *J* 12.9 and 1.7, 3-H), 4.45 (1 H, d, *J* 11.8, CH_2-Ph), 3.70 (1 H, td, *J* 12.1 and 3.4, 8a-H), 3.36 (1 H, s, 4-H), 2.79 (1 H, t, *J* 13.8, 5-H), 2.55–2.63 (2 H, m, 4a-H and 8-H), 2.55 (1 H, dt, *J* 14.5 and 2.3, 7-H), 2.37 (1 H, td, *J* 14.5 and 6.3, 7-H), 2.26 (1 H, ddd, *J* 14.5, 4.0 and 2.1, 5-H), 1.99 (1 H, qd, *J* 13.3 and 4.6, 8-H); δ_C(75 MHz; $CDCl_3$) 206.6 (C-6), 136.5 (ArC), 128.7, 128.5, 128.1 (ArCH), 71.8 (C-4), 71.7 (CH_2-Ph), 71.3 (C-3), 55.2 (C-8a), 43.3 (C-4a), 41.8 (C-5), 39.2 (C-7), 23.5 (C-8).

(3*R*,3a*R*,6*S*,6a*R*,8*R*,9a*S*,9b*R*)-3,6-Bis(benzyloxy)-8-methyldecahydro-2*H*-pyrano[2,3,4-*de*]chromene-8,9a-diol 15

To sodium hydride (48 mg, 2 mmol) in dry THF (4 ml) was added a solution of **5**[4c] (440 mg, 2 mmol) in dry THF (2 ml) at room temperature. The mixture was stirred for 1 h, saturated aqueous NaCl was added to it and then the mixture was extracted with diethyl ether three times. The combined organic extracts were dried ($MgSO_4$) and concentrated. Column chromatography (SiO_2, hexane–ethyl acetate 1:1, v/v) of the residue yielded **15** (165 mg, 37%, major compound), 40 mg of a second diastereomer (9%) and a mixture of two further products (61 mg, 8% and 6%). **15**: Colourless needles, mp 105 °C (Found: C, 70.8; H, 7.1. $C_{26}H_{32}O_6$ requires C, 70.9; H, 7.3%); $[\alpha]_{546}^{25}$ +7.0 (*c* 1.0 in CH_2Cl_2); δ_H(300 MHz; $CDCl_3$) 7.24–7.37 (10 H, m, ArH), 4.80 (1 H, d, *J* 12.0, CH_2-Ph), 4.60 (1 H, d, *J* 11.8, CH_2-Ph), 4.58 (1 H, d, *J* 12.0, CH_2-Ph), 4.48 (1 H, d, *J* 11.8, CH_2-Ph), 4.30 (1 H, br, OH), 4.13 (1 H, dd, *J* 8.7 and 2.2, 5-H), 3.73 (1 H, t, *J* 10.7, 2-H), 3.67 (1 H, dd, *J* 10.8 and 5.9, 2-H), 3.64 (1 H, t, *J* 10.8, 3a-H), 3.47 (1 H, td, *J* 10.7 and 5.8, 3-H), 3.23 (1 H, t, *J* 10.3, 5-H), 3.16 (1 H, dd, *J* 10.2 and 3.8, 6-H), 3.10 (1 H, br, OH), 2.17 (1 H, dd, *J* 15.1 and 3.3, 7-H), 1.92 (1 H, qd, *J* 11.8 and 3.3, 6a-H), 1.78 (1 H, dd, *J* 13.9 and 1.9, 9-H), 1.51 (1 H, d, *J* 13.9, 9-H), 1.22 (3 H, s, CH_3), 1.04 (1 H, t, *J* 10.5, 9b-H), 0.97 (1 H, t, *J* 13.4, 7-H); δ_C(75 MHz; $CDCl_3$) 138.5, 138.1 (ArC), 128.4, 128.3, 127.9, 127.7 (ArCH), 96.3 (C-9a), 77.7 (C-3), 77.6 (C-3a), 76.7 (C-6), 73.1 (CH_2-Ph), 72.2 (CH_2-Ph), 70.9 (C-8), 68.8 (C-5), 61.6 (C-2), 48.6 (C-9b), 47.2 (C-9), 41.6 (C-7), 37.1 (C-6a), 30.8 (CH_3).

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