Pergamon

Tetrahedron: *Asymmetry* 9 (1998) 1577–1587

TETRAHEDRON:
ASYMMETRY

Diels–Alder reactions of (R_S)-3-[(1S)-isoborneol-10-sulfinyl]-1-methoxybuta-1,3-dienes with electron-deficient carbodienophiles. The effects of Lewis acid catalysis

Maria C. Aversa,[a,*] Anna Barattucci,[a] Paola Bonaccorsi,[a] Placido Giannetto,[a]
Manuela Panzalorto[b] and Simona Rizzo[a]

[a] *Dipartimento di Chimica organica e biologica, Università degli Studi di Messina, Salita Sperone 31 (vill. S. Agata), 98166 Messina, Italy*

[b] *Dipartimento di Chimica inorganica, chimica analitica e chimica fisica, Università degli Studi di Messina, Salita Sperone 31 (vill. S. Agata), 98166 Messina, Italy*

Received 3 March 1998; accepted 2 April 1998

Abstract

Uncatalyzed cycloadditions of (R_S,E)-**1** and (R_S,Z)-3-[(1S)-isoborneol-10-sulfinyl]-1-methoxybuta-1,3-diene **2** with maleimide and N-phenylmaleimide occurred with complete *endo* and very high facial diastereoselectivities. The effects of Lewis acid catalysis on these Diels–Alder reactions have been evaluated. $LiClO_4$ catalyzed cycloaddition of **1** with dimethyl maleate gave cyclohexene **13** as the unique product with complete control of *endo* and π-facial diastereoselectivities exerted by the sulfinyl group. A significant improvement in diastereoselectivity was also observed in the $LiClO_4$ catalyzed cycloaddition of **1** with dimethyl fumarate. © 1998 Elsevier Science Ltd. All rights reserved.

---

1. Introduction

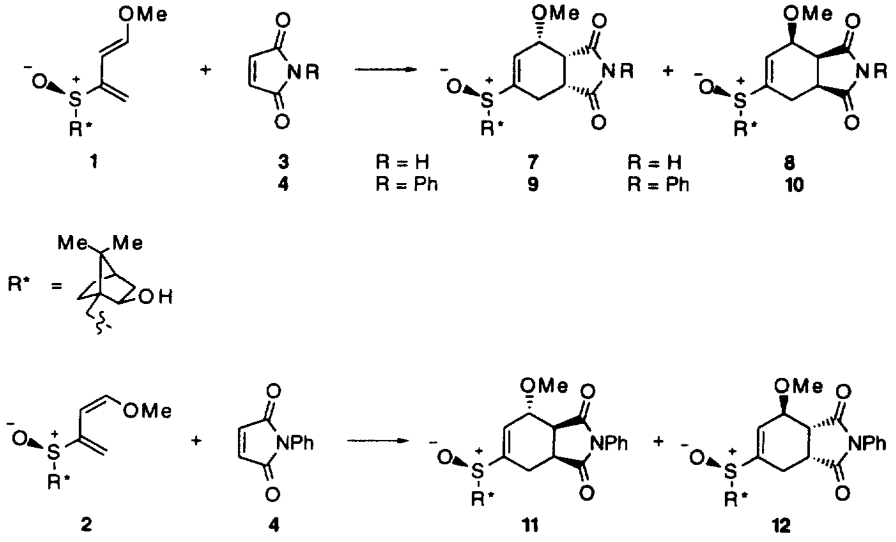
Since the first publication reporting the involvement of enantiomerically pure sulfinyldienes in Diels–Alder reactions,[1] stimulating results have been achieved in this field.[2] The experimental data obtained have emphasized the sulfinyl group efficiency in controlling π-facial diastereoselectivity and the synthetic potential of conjugate sulfinyldienes in the field of natural product chemistry. Electron-deficient cyclic dienophiles, such as maleimides and maleic anhydride, have been widely used in cycloadditions with enantiomerically pure 1- and 2-sulfinyldienes, and complete *endo* and very high facial diastereoselectivities were observed.[2a,c–f] The results concerning π-facial selectivity have been explained on the basis of strong electrostatic repulsions between the sulfinyl oxygen atom of the diene

---

[*] Corresponding author. E-mail: aversa@imeuniv.unime.it

PII: S0957-4166(98)00138-4

and the carbonyl oxygen atoms of the dienophile in the transition state. Nevertheless, 1-sulfinyldienes have shown low reactivity by comparison with 2-sulfinyldienes, since cycloadditions of the former compounds with cyclic electron-deficient dienophiles need high pressures and/or longer reaction times to be completed.[3] Recently, Diels–Alder reactions of 1-sulfinyldienes with either acyclic electron-deficient or cyclic electron-rich dienophiles have been described, and the low reactivity of 1-sulfinyldienes with both types of partners has been attributed to simultaneous electron-donating (+M) and electron-withdrawing (−I) effects of the sulfinyl group which mutually compensate and have minimal influence on both LUMO's and HOMO's energies of these dienes.[4] Following analogous arguments, 2-sulfinyl dienes such as **1** and **2** (Scheme 1 and Scheme 2), which possess a strongly electron-donating methoxy substituent and the sulfinyl group suitably positioned to support the electronic characteristics of the OMe substituent, should be significantly more electron rich than 1-sulfinyldienes and therefore more reactive with electron-deficient dienophiles. However, less attention has been directed towards the Diels–Alder behaviour of these 2-sulfinyldienes, even if they should act as more effective partners in such cycloadditions.[3]



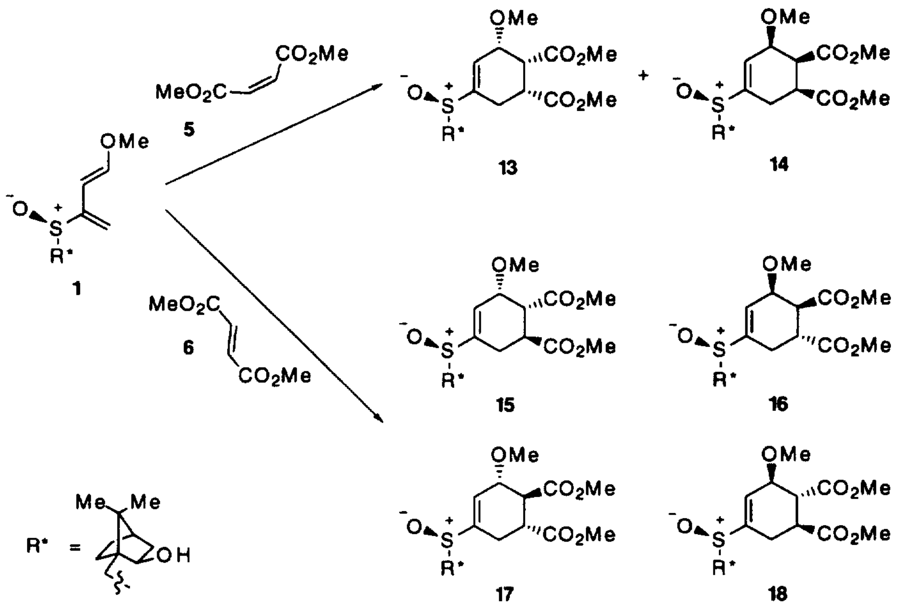
Scheme 1.

In this paper we report the results obtained in Diels–Alder reactions of enantiopure dienes **1** and **2** with maleimide **3** and N-phenylmaleimide (NPM, **4**) (Scheme 1) which corroborate the expected remarkable reactivity of these diene sulfoxides. Acyclic electron-deficient dienophiles, such as dimethyl maleate **5** and fumarate **6**, have also been reacted with diene **1** (Scheme 2) in order to open the way towards the synthesis of enantiopure cyclohexenes, with at least three stereogenic centres, useful intermediates in the total synthesis of natural products. The role of different Lewis acids in affecting the stereoselectivity of these Diels–Alder reactions has been investigated and a rationalization of the obtained results is proposed.

2. Results and discussion

Enantiomerically pure (R_S,E)-diene **1** reacted under mild conditions with maleimide **3**, NPM **4** (Scheme 1), dimethyl maleate **5** and dimethyl fumarate **6** (Scheme 2), giving in each case cycloadducts in high yields.

The results obtained are summarized in Table 1 and deserve some comments. The reactivity of the systems under study, as deduced from the reaction times, corresponded to expectation, *i.e.* the cyclic



Scheme 2.

electron-deficient dienophiles reacted faster than the acyclic ones. Moreover, a comparison with literature data on cycloadditions of different 1- and 2-sulfinyl dienes with maleimides[2a,d] clearly showed the higher reactivity of **1** and encouraged us to test the cycloaddition of (R_S,Z)-diene **2** to NPM **4**. Diene **2** strongly prefers the antiperiplanar conformation and, as a consequence, a reduced reactivity of such a diene in concerted cycloadditions is well stated.[2i,5] However this reaction would open up access to cyclohexenes showing configurations at the new-formed asymmetric centres not easily accessible in other ways. In fact the cycloaddition between **2** and **4** (Scheme 1) occurred in a reasonable length of time and mild conditions (entry 10), in line with the high reactivity of the diene systems under study.

An inspection of Table 1 underlines the complete *endo* selectivity in the cycloadditions under investigation, apart from the special case of dimethyl fumarate. The maleimide planarity can be responsible for its strong *endo* orientating character,[6] and results shown in entries 1, 3, 4 and 10 confirm the expectations. Moreover, literature data on cycloadditions of dimethyl maleate **5** with (E)-1-methoxybuta-1,3-diene report the formation of *endo*:*exo* products in an approximately 70:30 ratio.[5] Our observation (entry 11) of complete *endo* diastereoselectivity in the reaction between **1** and **5** illustrates the remarkable control exerted by the sulfinyl group on the *endo* selectivity when the dienophile is suitably substituted.[2i,4]

High π-facial diastereoselectivity was observed when maleimides **3** and **4** were used as dienophiles in uncatalyzed cycloadditions (entries 1, 3, 4 and 10). The nearly exclusive formation of **7**, **9**, and **11** evidenced the great control exerted by the sulfinyl group on the π-facial selectivity: the cyclic dienophiles approach dienes **1** and **2** on their *Re* faces, which are the more electron rich sides, opposite to the sulfinyl oxygen, the dienes adopting the less sterically hindered conformation along the C–S bond.[2i] $LiClO_4$ catalyzed cycloadditions of diene **1** with **3** and **4** showed a decrease in facial diastereoselectivity, more evident when NPM was the dienophile (entries 2 and 8). On this basis we undertook an investigation of cycloadditions of diene **1** with dienophile **4** in the presence of different Lewis acids (Table 1): all of them led to a diminished facial selectivity which turned over in favour of diastereoisomer **10** when $Eu(fod)_3$ was the catalyst (entry 9). The stereochemical outcome of these catalyzed reactions can be interpreted by considering the *endo* approach of the dienophile once again on the *Re* face of the diene, which adopts the conformation (**a**) where the catalyst is able to co-ordinate both a carbonyl oxygen of the dienophile

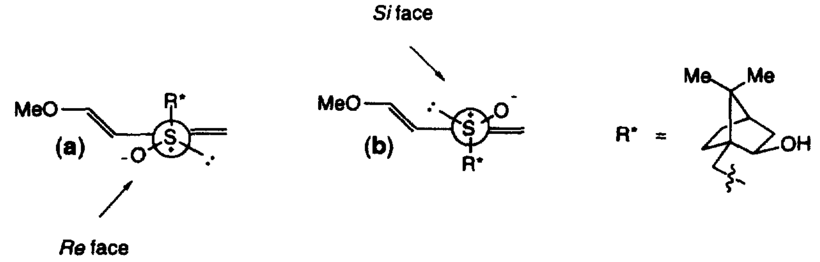
Table 1
Asymmetric [4+2] cycloadditions of dienes **1** and **2** to carbodienophiles, in CH_2Cl_2 as a solvent

Entry	Diene	Dienophile	Temp., °C	Time, h	Catalyst	Total yield, %	Adducts		
							endo	*exo*	(ratio)
1	**1**	**3**	25	0.8	none	90	**7 : 8**		(97 : 3)
2	**1**	**3**	25	0.8	$LiClO_4$	80	**7 : 8**		(88 : 12)
3	**1**	**4**	25	0.5	none	80	**9 :10**		(85 : 15)
4	**1**	**4**	- 20	1.5	none	80	**9 :10**		(87 : 13)
5	**1**	**4**	0	2	$MgBr_2$	83	**9 :10**		(80 : 20)
6	**1**	**4**	25	12	$BF_3.Et_2O$	63	**9 :10**		(75 : 25)
7	**1**	**4**	0	5	$ZnCl_2$	90	**9 :10**		(73 : 27)
8	**1**	**4**	- 20	1.5	$LiClO_4$	86	**9 :10**		(60 : 40)
9	**1**	**4**	- 20	2.5	$Eu(fod)_3$	90	**9 :10**		(36 : 64)
10	**2**	**4**	25	120	none	58	**11:12**		(88 : 12)
11	**1**	**5**	25	43	none	76	**13 : 14**		(74 : 26)
12	**1**	**5**	25	21	$LiClO_4$	80	**13**		(100)
13	**1**	**6**	25	43	none	80	**15 : 16** :	**17 : 18**[a]	(51 : 13 : 20 : 16)
14	**1**	**6**	25	24	$LiClO_4$	87	**15 : 16** :	**17 : 18**	(78 : 6 : 10 : 6)

[a] *Endo/exo* selectivity refers to substituents at C-3 and C-4.

and the sulfinyl oxygen of the diene.[2i] However the dienophile approach to the *Si* face of the diene in conformation (**b**) also becomes effective owing to the catalyst participation and steric requirements of a conformationally biased dienophile such as NPM: conformation (**b**) appears electronically less favoured than (**a**), but this adverse characteristic is counterbalanced in part by reduced steric congestion in the transition state. If it is true, the size of the Lewis acid[2f] should influence the relative stabilities of the transition states originated from the NPM *endo* approach to conformations (**a**) or (**b**): in fact the approach to the *Si* face of the diene **1** in its conformation (**b**) becomes the favourite one when the bulky $Eu(fod)_3$ catalyzes the cycloaddition (entry 9).

(R_S,E)-Diene **1** was reacted with dimethyl maleate at room temperature to avoid possible E/Z isomerization.[5] When the cycloaddition was catalyzed by a suspension of $LiClO_4$, π-facial diastereoselectivity was complete (entry 12), giving **13** as the unique cycloadduct. The interpretation of these stereochemical results is similar to the one previously suggested for the asymmetric cycloaddition of diene **1** and ethyl glyoxalate.[2h] For synthetic purposes it is useful to emphasize that cycloadduct **14** can be obtained as the unique compound of the $LiClO_4$ catalyzed cycloaddition of dimethyl maleate with (S_S,E)-3-[(1*S*)-isoborneol-10-sulfinyl]-1-methoxybuta-1,3-diene,[2i] which is the epimer of diene **1** at the sulfur atom.



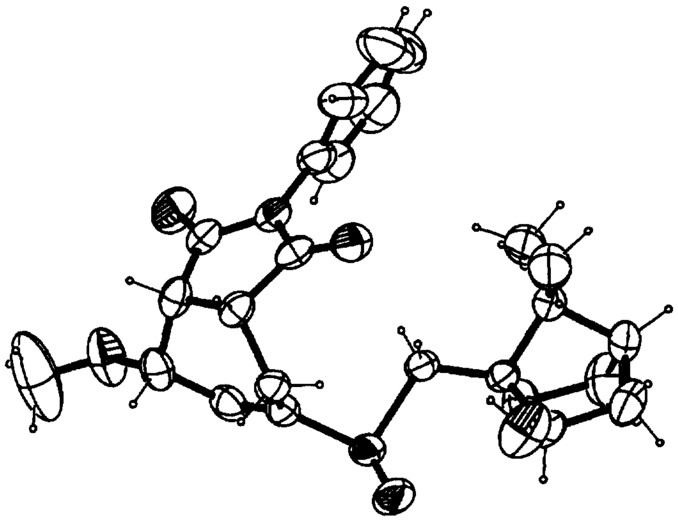


Fig. 1. X-Ray structure of **9**

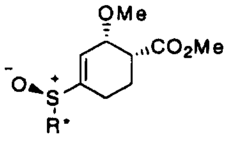
Cycloaddition of **1** with dimethyl fumarate yielded a mixture of four cycloadducts with *trans* arrangement of the methoxycarbonyl groups at C-4 and C-5. The mixture of the four cycloadducts was column chromatographed on silica gel, and cycloadduct **15**, the major product of the reaction which is also the chromatographically more mobile, and cycloadduct **18**, which is the less mobile, were obtained in enantiomerically pure form and fully characterized. $LiClO_4$ catalysis shortened the reaction time and improved facial diastereoselectivity for adduct **15** (entry 14).

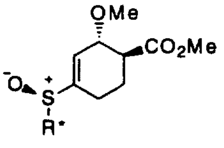
The absolute configuration of cycloadduct **9** was firmly established by X-ray crystallographic analysis (Fig. 1) while the absolute configurations were assigned to the remaining cycloadducts by analogy with **9**, on the basis of NMR data and unambiguous demonstration that the sulfur configuration controls the configurations of the newly-formed asymmetric centres.[2i] Significant spin–spin coupling constants from ^1H NMR spectra of cycloadducts under study are collected in Table 2, together with the corresponding data measured for the epimeric adducts **19** and **20**.[2i] The reported values support the relative configurations assigned to the stereogenic centres in the cyclohexene ring of the adducts **13**, **15** and **17** (and their facial diastereomers) owing to the conformational preferences observed in $CDCl_3$ solution. For instance, the 3-methoxycarbonyl substituent prefers the equatorial position in **15** and **17** (adducts from fumarate) and **19** and **20** (from acrylate) while it appears axially situated in the adduct **13**, obtained from dimethyl maleate. Moreover, the C-3 chemical shift appears strictly related to 3-OMe conformational preference: C-3 resonates at 76–77 ppm in compounds **13**, **14**, **17** and **20** (equatorial 3-OMe) and 72 ppm in **15** and **19**, where 3-OMe is axial.

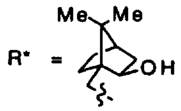
The high degree of stereocontrol found in cycloadditions of electron-deficient cyclic and acyclic dienophiles with sulfinyldienes points out that these enantiopure diene sulfoxides may fulfil a useful role in enantioselective synthesis. In particular, the presence and mutual placement of methoxy and sulfinyl substituents in our enantiopure 3-hydroxyalkylsulfinyl-1-methoxybuta-1,3-dienes,[2i] such as **1** and **2**, seem to have notable effects on their reactivity as *syn*-periplanar conjugate systems, allowing the use of mild conditions in Diels–Alder reactions and obtainment of sterically resolved cycloadducts in high yields. We are now working to transfer all the potential of these enantiopure products in the synthesis of naturally occurring compounds.

Table 2
Selected coupling constants in the ^{1}H NMR spectra of compounds **13**, **15**, **17**, **19** and **20**

Compound	$J_{2,3}$	$J_{3,4}$ (*cis*)	$J_{3ax,4ax}$ (*trans*)	$J_{4,5}$ (*cis*)	$J_{4ax,5ax}$ (*trans*)
13	2.2 (2,3ax)	6.5 (3ax,4eq)		2.6 (4eq,5ax)	
15	4.4 (2,3eq)	4.4 (3eq,4ax)			11.3
17	2.4 (2,3ax)		8.3		10.8
19	4.4 (2,3eq)	4.4 (3eq,4ax)		3.3 (4ax,5eq)	11.9
20	1.9 (2,3ax)		8.1	3.3 (4ax,5eq)	11.4


19


20



3. Experimental

(R_S,E)- and (R_S,Z)-3-[(1*S*)-Isoborneol-10-sulfinyl]-1-methoxybuta-1,3-dienes **1** and **2** were prepared following our previous methodology.[2i] Solvents were purified according to standard procedures, commercial dimethyl maleate was column chromatographed eluting with light petroleum:ethyl acetate 95:5 just before its use, the remaining commercial dienophiles and the Lewis acids were used without further purification. All reactions were monitored by TLC on commercially available precoated plates (Aldrich silica gel 60 F 254) and the products were visualized with vanillin [vanillin (1 g) dissolved in MeOH (60 ml) and H_2SO_4 conc. (0.6 ml)]. Silica gel used for column chromatography was Aldrich 60. Reaction temperatures, times, and yields are shown in Table 1. Mps were measured on a microscopic apparatus and are uncorrected. Optical rotations $[\alpha]_D^{20}$ were measured in $CHCl_3$ solutions and are given in 10^{-1} deg cm^2 g^{-1}; concentrations c are expressed in g/ml. Elemental analyses were performed by REDOX, Milano (Italy). IR spectra were taken with a Perkin–Elmer 1600 FT spectrophotometer in $CHCl_3$ solutions. Mass spectra were measured by Fast Atom Bombardment (FAB, *m*-nitrobenzyl alcohol as the matrix) with a Finnigan MAT 90 instrument. X-Ray diffraction analysis was performed on a Siemens automated four-circle single-crystal diffractometer R3μ/V. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Gemini 300 spectrometer at 300 and 75 MHz respectively in $CDCl_3$ solutions with $SiMe_4$ as the internal standard; J values are given in Hz; the attributions are supported by Attached Proton Test (APT) and decoupling experiments. Diastereomeric adduct ratios were established by integration of well-separated proton signals of the diastereomers in the crude adduct mixtures and are listed in Table 1.

3.1. General procedure for Diels–Alder reactions in thermal conditions

A solution of the diene **1** (or **2**) (100 mg, 0.35 mmol) in 2 ml of anhydrous dichloromethane was added to 2.1 mmol of neat dienophile. The reaction mixture was stirred under argon until the diene totally disappeared, as verified by TLC monitoring (light petroleum:ethyl acetate=1:1). The solvent was removed under vacuum and the crude mixture was column chromatographed eluting with light petroleum:ethyl acetate (8:2).

3.2. General procedure for Diels–Alder reactions in the presence of Lewis acids

Lewis acid (0.42 mmol) was added to a solution of diene **1** (150 mg, 0.53 mmol) and dienophile (3.18 mmol) in anhydrous dichloromethane (3 ml) under argon. The reaction mixture was stirred until the diene had totally disappeared, as verified by TLC monitoring. Isolation and purification of cycloadducts were performed as previously described.

*3.3. Cycloadducts from diene **1** and maleimide **3**, reported in order of increasing retention times*

*3.3.1. (1S,2S,6S,R_S)-4-[(1S)-Isoborneol-10-sulfinyl]-2-methoxy-8-azabicyclo[4.3.0]non-3-ene-7,9-dione **8***

Low melting solid; δ_H 6.90 (dd, $J_{2,3}$ 5.5, $J_{3,5A}$ 2.6, H-3), 4.52 (dd, $J_{1,2}$ 4.5, H-2), 4.12 (dd, $J_{2',3'}$ 7.9 and 3.3, H-2′), 3.32 (s, OMe), 3.26 (m, H-6), 3.10 (dd, $J_{1,6}$ 10.0, H-1), 3.01 and 2.55 (AB system, $J_{10'A,10'B}$ 13.0, H_2-10′), 2.70 (AB ddd, $J_{5A,5B}$ 15.9, $J_{5A,6}$ 7.2, H_A-5), 2.53 (AB ddd, $J_{5B,6}$ 9.0, H_B-5), 1.9–1.1 (m, H_2-3′,5′,6′, H-4′), 1.08 (s, H_3-8′), 0.86 (s, H_3-9′).

*3.3.2. (1R,2R,6R,R_S)-4-[(1S)-Isoborneol-10-sulfinyl]-2-methoxy-8-azabicyclo[4.3.0]non-3-ene-7,9-dione **7***

Mp 72–73°C; $[\alpha]_D^{20}$ +125.0 (c 0.0137); δ_H 6.82 (dd, $J_{2,3}$ 5.0, $J_{3,5B}$ 2.1, H-3), 4.44 (dd, $J_{1,2}$ 4.9, H-2), 4.09 (dd, $J_{2',3'}$ 8.1 and 4.0, H-2′), 3.32 (s, OMe), 3.29 and 2.28 (AB system, $J_{10'A,10'B}$ 12.9, H_2-10′), 3.26 (m, H-6), 3.17 (dd, $J_{1,6}$ 9.8, H-1), 2.87 (AB dd, $J_{5A,5B}$ 16.3, $J_{5A,6}$ 8.3, H_A-5), 2.78 (AB ddd, $J_{5B,6}$ 7.0, H_B-5), 1.9–1.1 (m, H_2-3′,5′,6′, H-4′), 1.09 (s, H_3-8′), 0.83 (s, H_3-9′); δ_C 178.45 and 175.28 (C-7,9), 147.49 (C-4), 130.98 (C-3), 76.90 (C-2′), 71.84 (C-2), 57.56 (OMe), 53.52 (C-10′), 51.40 (C-1′), 48.37 (C-7′), 46.08 and 45.03 (C-1,4′), 38.45 (C-3′), 38.28 (C-6), 30.84 and 27.12 (C-5′,6′), 20.51 (C-8′), 19.85 (C-9′), 18.96 (C-5); m/z (%) 382 (M+1, 47), 149 (100), 135 (75).

*3.4. Cycloadducts from diene **1** and NPM **4**, reported in order of increasing retention times*

*3.4.1. (1S,2S,6S,R_S)-4-[(1S)-Isoborneol-10-sulfinyl]-2-methoxy-8-phenyl-8-azabicyclo[4.3.0]non-3-ene-7,9-dione **10***

Mp 204–205°C; $[\alpha]_D^{20}$ −110 (c 0.0001); δ_H 7.5–7.3 (m, Ph), 6.95 (dd, $J_{2,3}$ 5.2, $J_{3,5A}$ 2.6, H-3), 4.62 (dd, $J_{1,2}$ 4.6, H-2), 4.12 (dd, $J_{2',3'}$ 7.6 and 3.6, H-2′), 3.35 (s, OMe), 3.34 (m, H-6), 3.20 (dd, $J_{1,6}$ 9.9, H-1), 3.01 and 2.58 (AB system, $J_{10'A,10'B}$ 13.0, H_2-10′), 2.79 (AB ddd, $J_{5A,5B}$ 16.1, $J_{5A,6}$ 7.0, H_A-5), 2.64 (AB dd, $J_{5B,6}$ 9.3, H_B-5), 1.9–1.1 (m, H_2-3′,5′,6′, H-4′), 1.06 (s, H_3-8′), 0.84 (s, H_3-9′); δ_C 177.92 and 174.75 (C-7,9), 148.13 (C-4), 131.78 (C-1″), 129.22 (C-3), 128.81 (C-2″,4″,6″), 126.55 (C-3″5″), 76.70 (C-2′), 71.89 (C-2), 57.45 (OMe), 54.68 (C-10′), 51.51 (C-1′), 48.36 (C-7′), 45.50 and 45.14 (C-1,4′), 38.46 (C-3′), 37.22 (C-6), 30.99 and 27.13 (C-5′,6′), 21.67 (C-5), 20.48 (C-8′), 19.79 (C-9′); m/z (%) 458 (M+1, 47), 149 (60), 135 (100).

3.4.2. (1R,2R,6R,R$_S$)-4-[(1S)-Isoborneol-10-sulfinyl]-2-methoxy-8-phenyl-8-azabicyclo[4.3.0]non-3-ene-7,9-dione ***9***

Mp 213–214°C; $[\alpha]_D^{20}$ +210 (c 0.0001) (found: C, 65.49; H, 6.79; $C_{25}H_{31}NO_5S$ requires C, 65.62; H, 6.83%); δ_H 7.5–7.3 (m, Ph), 6.87 (dd, $J_{2,3}$ 5.1, $J_{3,5B}$ 2.5, H-3), 4.54 (dd, $J_{1,2}$ 4.7, H-2), 4.10 (m, H-2′), 3.38 (m, H-6), 3.34 (s, OMe), 3.33 and 2.30 (AB system, $J_{10'A,10'B}$ 12.8, H_2-10′), 3.24 (dd, $J_{1,6}$ 9.8, H-1), 3.01 (AB dd, $J_{5A,5B}$ 16.5, $J_{5A,6}$ 9.0, H_A-5), 2.88 (AB ddd, $J_{5B,6}$ 6.9, H_B-5), 1.9–1.1 (m, H_2-3′,5′,6′, H-4′), 1.09 (s, H_3-8′), 0.81 (s, H_3-9′); δ_C 177.72 and 174.65 (C-7,9), 148.17 (C-4), 131.77 (C-1″), 130.56 (C-3), 129.17 (C-2″,6″), 128.75 (C-4″), 126.49 (C-3″5″), 76.92 (C-2′), 71.98 (C-2), 57.61 (OMe), 53.59 (C-10′), 51.43 (C-1′), 48.35 (C-7′), 45.13 and 45.04 (C-1,4′), 38.43 (C-3′), 36.99 (C-6), 30.85 and 27.11 (C-5′,6′), 20.46 (C-8′), 19.85 (C-9′), 18.90 (C-5); ν_{max} 3500 (OH), 3007, 2954, 1716 (CO), 1388, 1096, 1078 cm^{-1}; m/z (%) 458 (M+1, 65), 137 (99), 135 (100).

*3.5. Cycloadducts from diene **2** and NPM **4**, reported in order of increasing retention times*

3.5.1. (1R,2S,6R,R$_S$)-4-[(1S)-Isoborneol-10-sulfinyl]-2-methoxy-8-phenyl-8-azabicyclo[4.3.0]non-3-ene-7,9-dione ***12***

Mp 205–207°C; δ_H 7.5–7.2 (m, Ph), 6.94 (dd, $J_{2,3}$ 5.7, $J_{3,5A}$ 3.0, H-3), 4.60 (dd, $J_{1,2}$ 2.3, H-2), 4.08 (dd, $J_{2',3'}$ 7.7 and 3.5, H-2′), 3.67 (dd, $J_{1,6}$ 8.8, H-1), 3.45 (m, H-6), 3.42 (s, OMe), 2.95 (AB ddd, $J_{5A,5B}$ 15.8, $J_{5A,6}$ 7.4, H_A-5), 2.74 and 2.65 (AB system, $J_{10'A,10'B}$ 13.1, H_2-10′), 2.68 (AB dd, $J_{5B,6}$ 2.3, H_B-5), 1.9–1.1 (m, H_2-3′,5′,6′, H-4′), 0.88 (s, H_3-8′), 0.71 (s, H_3-9′); δ_C 177.88 and 175.26 (C-7,9), 149.15 (C-4), 131.33 (C-1″), 129.31 (C-2″,6″), 129.00 (C-3), 128.19 (C-4″), 126.20 (C-3″,5″), 76.86 (C-2′), 72.22 (C-2), 57.17 (OMe), 54.12 (C-10′), 51.43 (C-1′), 48.36 (C-7′), 45.93 and 45.12 (C-1,4′), 38.50 (C-3′), 37.77 (C-6), 30.90 and 27.10 (C-5′,6′), 22.70 (C-5), 20.18 (C-8′), 19.54 (C-9′); m/z (%) 458 (M+1, 18), 138 (58), 137 (100).

3.5.2. (1S,2R,6S,R$_S$)-4-[(1S)-Isoborneol-10-sulfinyl]-2-methoxy-8-phenyl-8-azabicyclo[4.3.0]non-3-ene-7,9-dione ***11***

Mp 152–153°C; $[\alpha]_D^{20}$ +50 (c 0.0001); δ_H 7.5–7.2 (m, Ph), 6.84 (dd, $J_{2,3}$ 5.7, $J_{3,5A}$ 2.4, H-3), 4.58 (dd, $J_{1,2}$ 2.4, H-2), 4.08 (dd, $J_{2',3'}$ 8.2 and 4.0, H-2′), 3.65 (dd, $J_{1,6}$ 8.8, H-1), 3.47 (m, H-6), 3.45 (s, OMe), 3.15 and 2.36 (AB system, $J_{10'A,10'B}$ 13.0, H_2-10′), 2.87 (AB ddd, $J_{5A,5B}$ 15.6, $J_{5A,6}$ 7.3, H_A-5), 2.78 (AB dd, $J_{5B,6}$ 2.6, H_B-5), 1.9–1.1 (m, H_2-3′,5′,6′, H-4′), 1.07 (s, H_3-8′), 0.79 (s, H_3-9′); δ_C 177.43 and 175.17 (C-7,9), 148.13 (C-4), 131.34 (C-1″), 129.23 (C-2″,6″), 129.06 (C-3), 128.93 (C-4″), 126.18 (C-3″,5″), 76.96 (C-2′), 72.25 (C-2), 57.17 (OMe), 54.11 (C-10′), 51.46 (C-1′), 48.36 (C-7′), 45.53 and 45.08 (C-1,4′), 38.45 (C-3′), 37.89 (C-6), 30.96 and 27.13 (C-5′,6′), 22.38 (C-5), 20.40 (C-8′), 19.80 (C-9′); ν_{max} 3500 (OH), 3009, 2954, 1713 (CO), 1387, 1088, 1078 cm^{-1}; m/z (%) 458 (M+1, 48), 137 (41), 135 (100).

*3.6. Cycloadducts from diene **1** and dimethyl maleate **5**, reported in order of increasing retention times*

3.6.1. (3S,4S,5S,R$_S$)-4,5-Dimethoxycarbonyl-1-[(1S)-isoborneol-10-sulfinyl]-3-methoxycyclohexene ***14***

Mp 170–172°C; $[\alpha]_D^{20}$ +8.2 (c 0.0062); δ_H 6.50 (ddd, $J_{2,3}$ 2.1, $J_{2,6A}$ 2.8, $J_{2,6B}$ 1.4, H-2), 4.24 (ddd, $J_{3,4}$ 6.2, $J_{3,6A}$ 2.8, $J_{3,6B}$ 1.4, H-3), 4.11 (dd, $J_{2',3'}$ 8.2 and 4.2, H-2′), 3.74 and 3.72 (two s, 2×CO_2Me), 3.63 (dd, $J_{4,5}$ 3.6, H-4), 3.53 (s, 3-OMe), 3.20 and 2.58 (AB system, $J_{10'A,10'B}$ 13.4, H_2-10′), 3.03 (ddd, $J_{5,6A}$ 10.3, $J_{5,6B}$ 6.0, H-5), 2.85 (AB ddt, $J_{6A,6B}$ 16.7, H_A-6), 2.42 (AB ddt, H_B-6), 1.9–1.0 (m, H_2-3′,5′,6′, H-4′), 1.09 (s, H_3-8′), 0.86 (s, H_3-9′); δ_C 172.02 and 170.40 (2×CO), 143.21 (C-1), 126.28 (C-2), 77.07 (C-2′), 76.11 (C-3), 57.67 (3-OMe), 54.31 (C-10′), 52.47 and 51.83 (2×CO_2*Me*), 51.52 (C-1′), 48.35

(C-7′), 45.15 (C-4′), 43.31 (C-4), 40.39 (C-5), 38.43 (C-3′), 30.95 and 27.19 (C-5′,6′), 23.58 (C-6), 20.57 (C-8′), 19.88 (C-9′); m/z (%) 429 (M+1, 38), 135 (100), 107 (36).

3.6.2. (3R,4R,5R,R$_S$)-4,5-Dimethoxycarbonyl-1-[(1S)-isoborneol-10-sulfinyl]-3-methoxycyclohexene ***13***

Mp 135–137°C; $[\alpha]_D^{20}$ +43.4 (c 0.0268) (found: C, 58.68; H, 7.51; $C_{21}H_{32}O_7S$ requires C, 58.86; H, 7.53%); δ_H 6.34 (br d, $J_{2,3}$ 2.2, H-2), 4.22 (br d, $J_{3,4}$ 6.5, $J_{3,6A}$ 2.1, H-3), 4.07 (dd, $J_{2',3'}$ 8.3 and 4.2, H-2′), 3.76 and 3.71 (two s, 2×CO_2Me), 3.66 (dd, $J_{4,5}$ 2.6, H-4), 3.52 (s, 3-OMe), 3.50 and 2.40 (AB system, $J_{10'A,10'B}$ 13.2, H_2-10′), 3.0–2.8 (m, H-5, H_2-6), 1.9–0.9 (m, H_2-3′,5′,6′, H-4′), 1.11 (s, H_3-8′), 0.83 (s, H_3-9′); δ_C 172.12 and 170.39 (2×CO), 143.76 (C-1), 129.92 (C-2), 76.97 (C-2′), 76.36 (C-3), 57.75 (3-OMe), 52.69 (C-10′), 52.46 and 51.80 (2×CO_2*Me*), 51.34 (C-1′), 48.26 (C-7′), 45.07 (C-4′), 42.55 (C-4), 39.82 (C-5), 38.42 (C-3′), 30.75 and 27.11 (C-5′,6′), 20.48 (C-8′), 19.88 (C-9′), 19.85 (C-6); ν_{max} 3400 (OH), 3002, 2854, 1737 (CO), 1438, 1072, 1004 cm^{-1}; m/z (%) 429 (M+1, 100), 149 (44), 135 (61), 57 (43).

3.7. Isolated cycloadducts from diene 1 and dimethyl fumarate 6[7] reported in order of increasing retention times

3.7.1. (3R,4R,5S,R$_S$)-4,5-Dimethoxycarbonyl-1-[(1S)-isoborneol-10-sulfinyl]-3-methoxycyclohexene ***15***

Low melting solid; $[\alpha]_D^{20}$ +120.8 (c 0.0078); δ_H 6.75 (br dd, $J_{2,3}$ 4.4, $J_{2,6A}$ 0.8, $J_{2,6B}$ 2.5, H-2), 4.27 (t, $J_{3,4}$ 4.4, H-3), 4.10 (dd, $J_{2',3'}$ 7.5 and 3.7, H-2′), 3.76 (s, 2×CO_2Me), 3.40 (s, 3-OMe), 3.18 (dt, $J_{4,5}$=$J_{5,6B}$ 11.3, $J_{5,6A}$ 5.0, H-5), 3.11 and 2.41 (AB system, $J_{10'A,10'B}$ 12.9, H_2-10′), 3.07 (dd, H-4), 2.56 (AB ddd, $J_{6A,6B}$ 17.0, H_A-6), 2.20 (AB ddd, H_B-6), 1.9–1.1 (m, H_2-3′,5′,6′, H-4′), 1.08 (s, H_3-8′), 0.84 (s, H_3-9′); δ_C 174.85 and 171.19 (2×CO), 144.54 (C-1), 125.70 (C-2), 77.20 (C-2′), 72.10 (C-3), 57.83 (3-OMe), 53.81 (C-10′), 52.33 and 52.06 (2×CO_2*Me*), 51.49 (C-1′), 48.40 (C-7′), 47.32 (C-4′), 45.10 (C-4), 38.44 (C-3′), 37.00 (C-5), 30.84 and 27.14 (C-5′,6′), 26.89 (C-6), 20.53 (C-8′), 19.86 (C-9′); ν_{max} 3400 (OH), 2367, 1734 (CO), 1540 cm^{-1}; m/z (%) 429 (M+1, 100), 149 (88), 135 (77).

3.7.2. (3R,4S,5R,R$_S$)-4,5-Dimethoxycarbonyl-1-[(1S)-isoborneol-10-sulfinyl]-3-methoxycyclohexene ***17***

Low melting solid; $[\alpha]_D^{20}$ +23.9 (c 0.0116); δ_H 6.52 (br dt, $J_{2,3}$ 2.4, $J_{2,6A}$ 1.0, $J_{2,6B}$ 2.4, H-2), 4.30 (dt, $J_{3,4}$ 8.3, $J_{3,6A}$ 1.7, $J_{3,6B}$ 2.9, H-3), 4.08 (m, H-2′), 3.77 and 3.73 (two s, 2×CO_2Me), 3.42 (s, 3-OMe), 3.10 (m, $J_{4,5}$ 10.8, $J_{5,6A}$ 5.4, $J_{5,6B}$ 9.8, H-5), 3.34 and 2.34 (AB system, $J_{10'A,10'B}$ 13.0, H_2-10′), 2.95 (dd, H-4), 2.78 (AB ddt, $J_{6A,6B}$ 17.5, H_A-6), 2.50 (AB ddt, H_B-6), 1.9–1.1 (m, H_2-3′,5′,6′, H-4′), 1.10 (s, H_3-8′), 0.84 (s, H_3-9′); δ_C 173.13 and 172.25 (2×CO), 143.22 (C-1), 129.19 (C-2), 77.19 (C-2′,3), 57.21 (3-OMe), 53.41 (C-10′), 52.46 and 52.44 (2×CO_2*Me*), 51.45 (C-1′), 48.37 (C-7′), 47.36 (C-4′), 45.09 (C-4), 40.88 (C-5), 38.45 (C-3′), 30.80 and 27.13 (C-5′,6′), 22.86 (C-6), 20.54 (C-8′), 19.90 (C-9′); m/z (%) 429 (M+1, 37), 149 (100), 135 (56), 69 (38), 57 (39), 55 (46).

3.8. X-Ray structure determination of (1R,2R,6R,R$_S$)-4-[(1S)-isoborneol-10-sulfinyl]-2-methoxy-8-phenyl-8-azabicyclo[4.3.0]non-3-ene-7,9-dione ***9***

Suitable crystals of compound **9** have been obtained by slow evaporation of an ethyl acetate solution. A summary of crystallographic data, collected at room temperature, and structure refinement is given in Table 3. Reflection intensities were evaluated by profile fitting of a 96-step peak scan among 2θ

Table 3
Crystal data and measurements conditions for the adduct **9**

Formula	$C_{25}H_{31}NO_5S$
Crystal System	Orthorombic
Space Group	$P2_1 2_1 2_1$
a/Å	9.778(7)
b/Å	10.868(4)
c/Å	21.942(9)
Volume/Å^3	2332(2)
Z	4
M	479.66
D_x/mg/m^3	1.366
μ/mm^{-1}	0.178
F(000)	1040
Radiation	MoKα (l = 0.71073 Å)
Temperature	293 K
θ_{min}, θ_{max} /°	3.5, 55
Index ranges	0/12, -4/14,-7/28
Collected reflections	3053
Independent reflections	2038
Number of refined parameters	289
R(F)[I>2σ(I)]	0.0468
ωR^2 (all data)	0.01188

shells procedure[8] and then corrected for Lorentz polarization effects. Standard deviations σ(I) were estimated from counting statistics. The structure was solved by direct methods subsequently completed by a combination of least squares technique and Fourier syntheses (SHELXTL-PLUS[9]) and refined by the full-matrix least squares technique (SHELXL-97[10]) based on F^2. H atoms were constrained to idealized geometries: assigned isotropic displacement parameters were 1.5 times the U_{iso} value of their C atoms for methyl hydrogens and 1.2 U_{iso} for all the other H atoms. Data reduction, structure solution and drawings were performed with SHELXTL-PLUS package,[9,10] and the geometrical calculations were obtained from PARST programme,[11] respectively. All calculations were performed on a μ-VAX 3400 and an AXP DecStation 3000/400.

Acknowledgements

Financial support by MURST and Regione Siciliana are gratefully acknowledged.

References

1. Adams, H.; Jones, D. N.; Aversa, M. C.; Bonaccorsi, P.; Giannetto, P. *Tetrahedron Lett.* **1993**, *34*, 6481–6484.
2. (a) Gosselin, P.; Bonfand, E.; Hayes, P.; Retoux, R.; Maignan, C. *Tetrahedron: Asymmetry* **1994**, *5*, 781–784; (b) Aversa, M. C.; Bonaccorsi, P.; Giannetto, P.; Jones, D. N. *Tetrahedron: Asymmetry* **1994**, *5*, 805–808; (c) Carreño, M. C.; Cid, M. B.; Colobert, F.; García Ruano, J. L.; Solladié, G. *Tetrahedron: Asymmetry* **1994**, *5*, 1439–1442; (d) Arce, E.; Carreño, M.

C.; Cid, M. B.; García Ruano, J. L. *J. Org. Chem.* **1994**, *59*, 3421–3426; (e) Carreño, M. C.; Cid, M. B.; García Ruano, J. L. *Tetrahedron: Asymmetry* **1996**, *7*, 2151–2158; (f) Yang, T.; Chu, H.; Lee, D.; Jiang, Y.; Chou, T. *Tetrahedron Lett.* **1996**, *37*, 4537–4540; (g) Gosselin, P.; Bonfand, E.; Maignan, C. *J. Org. Chem.* **1996**, *61*, 9049–9052; (h) Aversa, M. C.; Barattucci, A.; Bonaccorsi, P.; Bruno, G.; Giannetto, P.; Panzalorto, M. *Tetrahedron: Asymmetry* **1997**, *8*, 2989–2995; (i) Aversa, M. C.; Barattucci, A.; Bonaccorsi, P.; Giannetto, P.; Jones, D. N. *J. Org. Chem.* **1997**, *62*, 4376–4384.

3. Compare Ref. 1 with Ref. 4, and Ref. 2a with Ref. 2d.
4. Carreño, M. C.; Cid, M. B.; García Ruano, J. L.; Santos, M. *Tetrahedron: Asymmetry* **1997**, *8*, 2093–2097.
5. Sustmann, R.; Tappanchai, S.; Bandmann, H. *J. Am. Chem. Soc.* **1996**, *118*, 12555–12561.
6. García Ruano, J. L.; Carretero, J. C.; Carreño, M. C.; Martín Cabrejas, L. M.; Urbano, A. *Pure & Appl. Chem.* **1996**, *68*, 925–930.
7. Minor products **16** and **18** were recognized in the crude adduct mixture by typical ^{1}H NMR resonances such as vinyl proton multiplets at δ 6.72 and 6.57 respectively.
8. Diamond, R. *Acta Crystallogr., Sect. A* **1969**, *25*, 43–55.
9. SHELXTL-PLUS 1991, V.4.2, Siemens Analytical X-Ray Instruments Inc., Madison, Wisconsin.
10. Sheldrick, G. M. 1997, SHELXL-97, Program for the Refinement of Crystal Structures, University of Göttingen, Germany.
11. Nardelli, M. *Comput. Chem.* **1983**, *7*, 95–98 (locally modified version).