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Diels–Alder reactions of enantiopure [(1*S*)-isoborneol-10-sulfinyl]- and [(1*S*-*exo*)-2-bornylsulfinyl]vinylcyclohexenes with maleimides

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

[a] *Dipartimento di Chimica organica e biologica, Chimica analitica e Chimica fisica, 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*

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Abstract

Uncatalyzed cycloadditions of enantiopure [(1*S*)-isoborneol-10-sulfinyl]- and [(1*S*-*exo*)-2-bornylsulfinyl]-vinylcyclohexenes with *N*-phenylmaleimide occur with good facial diastereoselectivity, controlled by the sulfur configuration, even if the extent of this stereoselection appears influenced by the structural features of the terpene residue directly linked to the sulfoxide moiety. Complete *endo* diastereoselectivity is observed in $LiClO_4$ catalyzed cycloadditions of (R_S)-1-{1-[(1*S*)-isoborneol-10-sulfinyl]- and (S_S)-1-{1-[(1*S*-*exo*)-2-bornylsulfinyl]vinyl}cyclohexenes **4** and **5**, respectively. The Diels–Alder reactivity of **5** and (S_S,*E*)-1-{2-[(1*S*-*exo*)-2-bornylsulfinyl]vinyl}cyclohexene **7**, with the chiral auxiliary being in a different position with respect to the diene moiety, is also compared, and the results obtained comfirm that 1-sulfinyldienes are less reactive than 2-sulfinyldienes. $SnCl_4$ catalyzed cycloaddition of **7** with *N*-methylmaleimide is also performed.

1. Introduction

Enantiopure 3-(alkylsulfinyl)-1-methoxybuta-1,3-dienes **1** and **2** have provided stimulating results in their Diels–Alder (DA) reactions with common carbo- and hetero-dienophiles; the stereochemical outcome of thermal cycloadditions with cyclic dienophiles, such as *N*-phenylmaleimide (NPM),[1] and $LiClO_4$ catalyzed cycloadditions with acyclic dienophiles, such as methyl acrylate[2] and ethyl glyoxalate,[3] evidence the great control exerted by the sulfinyl group on both π-facial and *endo/exo* selectivities. The

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

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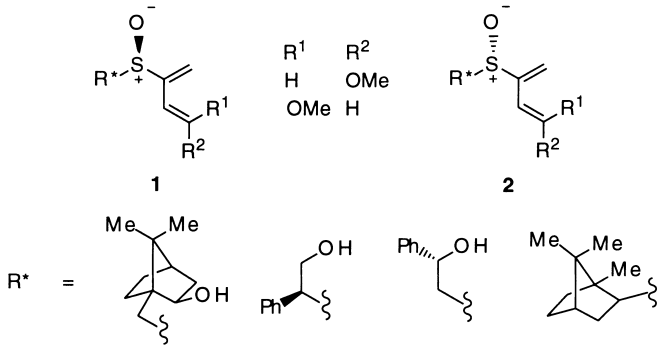
strongly electron donating methoxy substituent and the sulfinyl group, the latter suitably positioned on the diene system to support the OMe electronic characteristics, guarantee complete regioselectivity in DA reactions of **1** and **2**, and have a notable effect on their reactivity, allowing the occurrence of these DA reactions under mild conditions and the production of enantiopure cycloadducts in high yields.

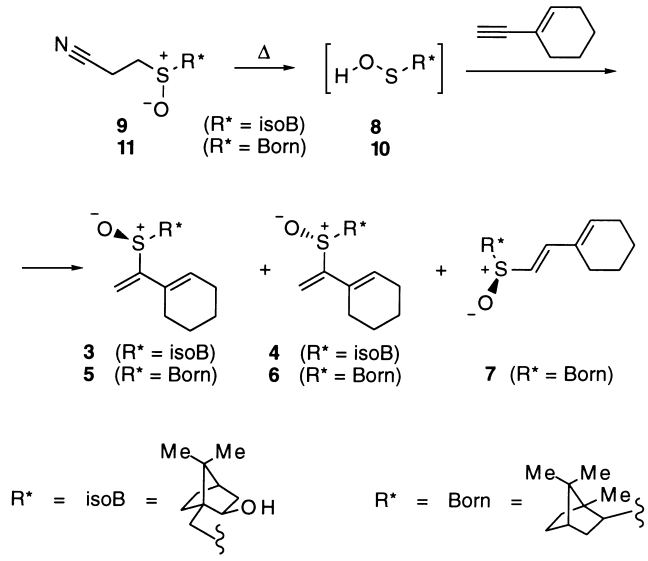


The synthetic strategy for the preparation of these enantiopure 2-(alkylsulfinyl)dienes is based on the regio- and stereoselective addition of (*E*)- or (*Z*)-1-methoxybut-1-en-3-yne to enantiopure alkanesulfenic acids, which can be easily obtained starting from commercially available terpene derivatives.[4–6] The structural features of the terpene residue, directly linked to the sulfur function, play a relevant role in this synthetic strategy, in the chromatographic separation of the DA adducts and in the removal of the chiral auxiliary, which appears less straightforward with respect to 1-(*p*-tolyl)sulfinylbutadienes.[6,7]

Synthesis and reactivity studies of (alkylsulfinyl)vinylcyclohexenes, such as **3**–**7** (Scheme 1), constitute a challenging progression of our investigation into the behaviour of enantiopure sulfinyldienes in asymmetric DA reactions. When one diene double bond participates in a six-membered ring, as in vinylcyclohexenes **3**–**7**, cycloadducts obtained by reacting **3**–**7** with suitable dienophiles can be converted into polycyclic systems, useful precursors of molecules showing a steroid skeleton. The chiral auxiliaries in **3**–**7** are structurally analogous, the isoborneolsulfinyl group (R*SO=isoB-SO) essentially differing from the bornylsulfinyl one (R*SO=Born-SO) in the presence or absence of the hydroxy function: this is in line with our interest in evaluating the influence that intramolecular hydrogen bonding[6] and, in general, the alkyl residue can have on the synthesis and reactivity of alkylsulfinyldienes. Finally, a comparison of the reactivity of 1-sulfinyldiene **7** and 2-sulfinyldienes **3**–**6** in cycloadditions with maleimides enables us to evaluate their potentialities in asymmetric DA reactions.

2. Results and discussion

The procedure based on the pericyclic addition of sulfenic acid **8** (coming from **9**) to 1-ethynylcyclohexene (Scheme 1), and already performed for the synthesis of 2-isoborneolsulfinyldienes **3** and **4**,[4] was adopted to obtain the 2-bornylsulfinyldienes **5** and **6**, starting from the corresponding sulfenic acid **10**. The reaction, which is highly regioselective when **8** is reacted with 1-ethynylcyclohexene, was performed on the sulfenic acid precursor **11** in neat enyne at 110°C and led to the formation of **5** and **6**, together with the 1-sulfinyldiene **7**, in 62.5:30:7.5 relative amounts and 80% total yield. Higher temperatures (150°C) increased the reaction yield up to 90% in favour of the 2-sulfinyldiene **5** (67.8%) and 1-sulfinyldiene **7** (16.7%), both having the sulfoxide in the (S_S) configuration, to the detriment of 2-sulfinyldiene **6** (15.5%). These data can be explained on the basis of an evaluation of the role that the alkylsulfinyl moiety plays in the asymmetric induction characterizing the pericyclic addition sulfenic acid/enyne. A temperature increase induces an increment of the thermodynamically favoured



Scheme 1.

(S_S) products **5** and **7**; the decrease of (R_S)-diene **6** and complete absence of the 1-sulfinyldiene with the same sulfur configuration indicate that the higher steric requirements of the enantiopure bornylsulfinyl auxiliary when the sulfoxide is in the (R_S) configuration penalize the formation of the corresponding sulfinyldienes.

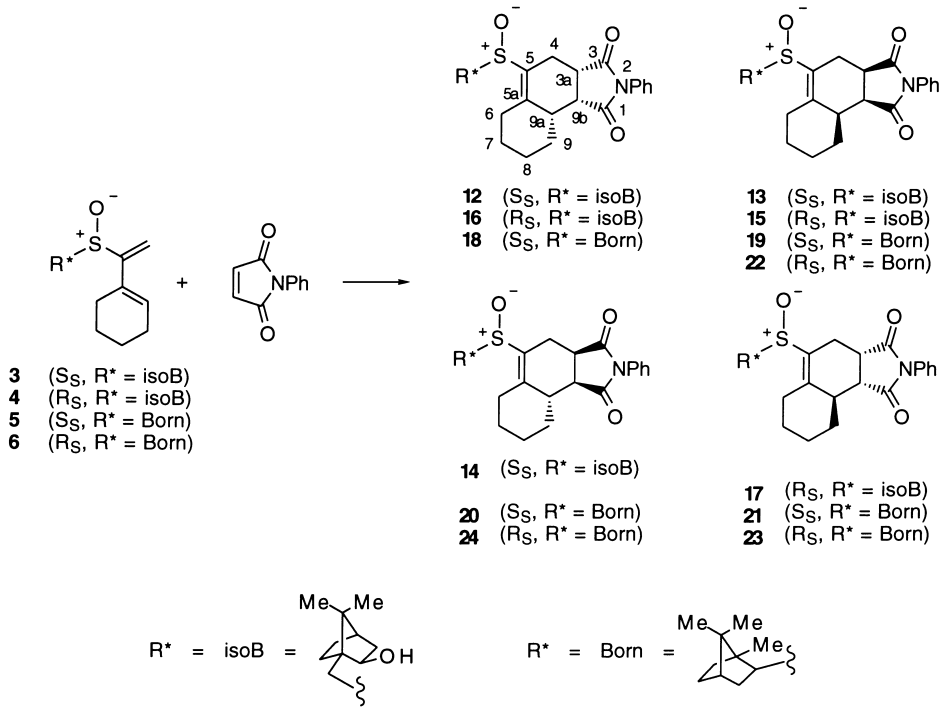
Sulfur absolute configuration in bornylsulfinyldienes **5**–**7** has been attributed on the basis of previously observed stereochemical outcome of the sulfenic acid/enyne addition and dependence of C-2′, 3′ chemical shifts on sulfur configuration.[6] In (R_S)-[(1*S*-*exo*)-2-bornylsulfinyl]vinylcyclohexenes these two carbon resonances appear in the ranges 68–69 and 25–26 ppm, while in the (S_R)-([1*S*-*exo*)-2-bornylsulfinyl]vinylcyclohexenes C-2′ and C-3′ resonate in the ranges 71–78 and 32–33 ppm, respectively.

Results concerning cycloadditions of 2-sulfinyldienes **3**–**6** with *N*-phenylmaleimide (NPM) in thermal and catalyzed conditions (Scheme 2) are reported in Table 1. NPM was chosen to avoid regioselectivity problems and because it is a highly reactive and *endo*-directing dienophile. Absolute configurations of the new stereocentres in cycloadducts **12**–**24** have been assigned on the basis of NMR data and having demonstrated that facial preference of DA attack is unambiguously controlled by sulfur configuration.[1,2,6]

Catalysis by lithium perchlorate, which was chosen for its good ability in enhancing facial diastereoselectivity,[1–3] shortened reaction times and induced complete diastereoselectivity *endo/exo* in favour of the *endo* isomer (entries 3 and 5). The lack of influence on facial diastereoselectivity is probably due to the great steric requirements of both diene and dienophile, which lead to very congested transition states in catalyzed cycloadditions.[1]

It is noteworthy that the bornylsulfinyl auxiliary appears less efficient in the stereocontrol of cycloadditions with NPM than the isoborneolsulfinyl one (compare entries 1 with 4 or 2 with 6), an observation which is in line with our previously reported results[6] and those obtained in the synthesis of sulfinyldienes **3**–**7** (see above). These steric occurrences can again be ascribed to the relevant steric features of the bornyl residue directly linked to the sulfinyl group.

The production of a fair amount of 1-sulfinyldiene **7** allowed for the first time a comparison of the behaviour, in DA cycloadditions, of sulfinyldienes **5** and **7**, differing only in the position of the chiral auxiliary on the diene moiety. Compound **7** was added to NPM in dichloromethane, but no cycloaddition



Scheme 2.

Table 1
Asymmetric [4+2] cycloadditions of dienes **3**–**6** to NPM in CH_2Cl_2

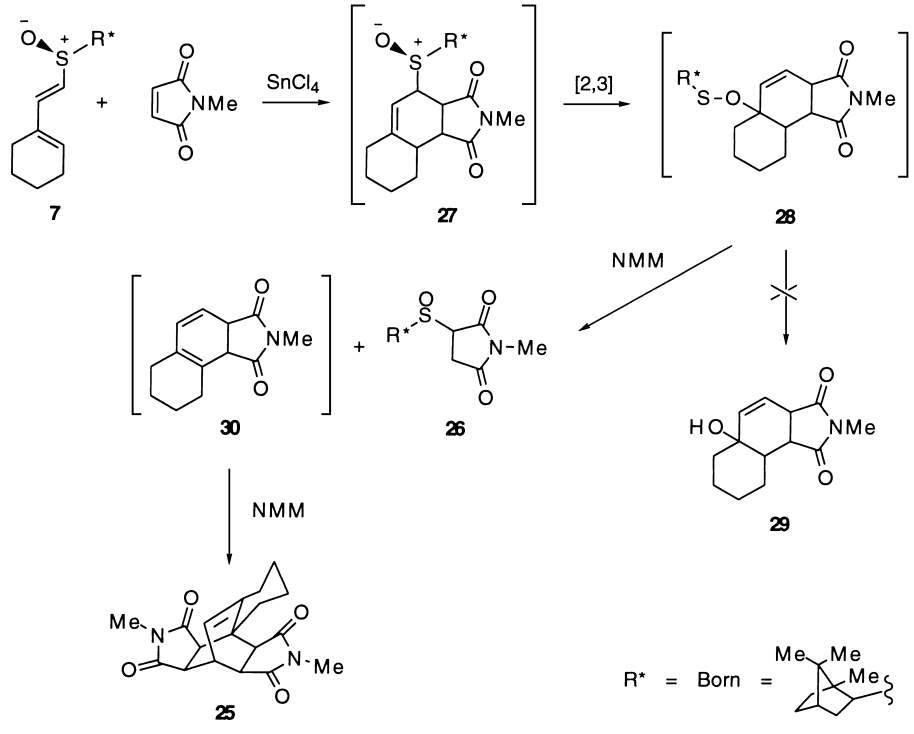
Entry	Diene	Time, h	Temp., °C	Catalyst	yield %	Adducts *endo*	*exo*	(ratio)
1	**3** (S_S)	168	40	none	68	**12** : **13**	**14**	(75 : 15 : 10)
2	**4** (R_S)	192	40	none	70	**15** : **16**	**17**	(90 : 9 : 1)
3	**4** (R_S)	72	25	$LiClO_4$	68	**15** : **16**		(89 : 11)
4	**5** (S_S)	68	40	none	90	**18** : **19**	**20** : **21**	(63 : 9 : 16 : 12)
5	**5** (S_S)	3	40	$LiClO_4$	87	**18** : **19**		(67 : 33)
6	**6** (R_S)	72	40	none	76	**22**	**23** : **24**	(77 : 12 : 11)[a]

[a] The minor *endo* adduct was not isolated from the reaction mixture.

products were observed in the reaction mixture after 15 days at reflux, thus confirming the lower reactivity of 1-sulfinyldienes with respect to 2-sulfinyldienes.[8]

Cycloaddition of **7** with *N*-methylmaleimide (NMM) was also performed in the presence of $SnCl_4$, according to the procedure already described in the literature for (R_S,*E*)-[2-(1-cyclohexenyl)vinyl]-*p*-tolylsulfoxide, the latter showing the *p*-tolyl instead of the bornyl group as part of the sulfur chiral auxiliary.[9] The reaction outcome is depicted in Scheme 3: the expected *meso*-compound **25**[9] was obtained together with a mixture of the four diastereomeric sulfoxides **26**. The major component of this last mixture was isolated by column chromatography, subsequent crystallization (from EtOAc/ligroin), and characterized by X-ray crystallography, which allowed its identification as (3*S*,S_S)-3-[(1*S*-*exo*)-2-

bornylsulfinyl]-1-methylsuccinimide.† The observation of compounds **26** was crucial in understanding our reaction pathway, because they clearly come from trapping of the 'stable'[6] sulfenic acid **10** by NMM, used in large excess (see Experimental). As described previously,[8] DA adducts **27** evolve towards sulfenate intermediates **28** through the well-known [2,3]-sigmatropic rearrangement.[10,11] However, we did not observe the corresponding allylic alcohol **29** since our reaction proceeded via sulfenic acid trapping by NMM from sulfenates **28**, to afford **26** and desulfurated endocyclic diene **30**, the latter again cycloadding NMM with the formation of compound **25**.



Scheme 3.

In this paper we have shown that (alkylsulfinyl)vinylcyclohexenes are notable enantiopure dienes which react easily in DA cycloadditions giving good stereochemical results. When reactions are performed starting from 2-sulfinyldienes **3**–**6** the corresponding cycloadducts can be obtained in enantiomerically pure form and subsequently transformed into molecules of synthetic interest, while the use of 1-sulfinyldiene **7** is less productive from a synthetic point of view. Structural features of the terpene residue linked to the sulfinyl auxiliary not only affect the synthesis of these dienes[6] but also the stereochemical outcome of their DA cycloadditions. However, the large number of terpene systems, available as enantiopure starting products, gives the opportunity for designing numerous sulfinyldienes, useful as efficient partners in stereocontrolled DA reactions.

† The space group of the monoclinic $C_{15}H_{23}NO_3S$ crystal (M=297.42) was $P2_1$ with a=6.9717(8), b=10.2167(13), c=21.773(4) Å, β=91.234(13)°. Other crystal parameters were as follows: V=1550.5(4) Å^3, Z=4, d_{calc}=1.274 g/cm^3. The structure refinement, with all anisotropic non-H atoms, reached $R(F)$=0.0504 with a parameter for extinction correction included in the last cycles. The absolute configuration of both independent molecules appearing into the crystallographic asymmetric unit was identical and well-determined as evidenced by the final enantiomorph Flack parameter that converged to 0.06(13). Tables of bond distances, bond angles, and positional and thermal parameters are available on request from the corresponding author.

3. Experimental

3.1. General methods and materials

Starting product (*S*-epimeric mixture) **11** was prepared following our own methodology.[6] Solvents were purified according to standard procedures. All reactions were monitored by TLC on commercially available precoated plates (Aldrich silica gel 60 F 254) and the products were visualized with iodine or vanillin [vanillin (1 g) dissolved in MeOH (60 ml) and conc. H_2SO_4 (0.6 ml)]. Silica gel used for column chromatography was Aldrich 60. Mps were measured on a microscopic apparatus and are uncorrected. Optical rotations were measured in $CHCl_3$ solutions at 25°C and are given in 10^{-1} deg cm^2 g^{-1}; concentrations *c* are expressed in g/100 ml. Mass spectra were measured by fast atom bombardment (FAB, *m*-nitrobenzyl alcohol as matrix) with a Finnigan MAT 90 instrument. X-Ray diffraction analysis was performed on a Siemens automated four-circle single-crystal diffractometer R3μ/V. ^1H and ^{13}C NMR spectra were recorded on a Varian Mercury 300 spectrometer at 300 and 75 MHz, respectively, in $CDCl_3$ solutions with $SiMe_4$ as internal standard; *J* values are given in hertz; the attributions are supported by attached proton test (APT), heteronuclear shift-correlated and homodecoupling experiments. Proton and carbon indexes, marked with (′), pertain to isoborneol or bornyl moieties. The symbol (″) identifies vinyl nuclei in dienes **5**–**7** and aromatic nuclei in compounds **12**–**24**. 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.

3.2. Thermolysis of sulfoxides *11* in the presence of 1-ethynylcyclohexene

Sulfoxides **4** (1.12 g, 4.7 mmol) were added to 1-ethynylcyclohexene (4.19 g, 39.5 mmol), and the mixture maintained at 110°C. When the reaction appeared complete by TLC (1 h, eluant EtOAc:hexane, 60:40) the enyne excess was removed under reduced pressure and the obtained reaction mixture was separated by column chromatography, beginning the elution with hexane:Et_2O (90:10) and gradually increasing the Et_2O percentage up to 30%. First was eluted (R_S)-1-{1-[(1*S*-*exo*)-2-bornylsulfinyl]vinyl}cyclohexene (**6**): oil; 24% yield; $[\alpha]_D^{25}$ +16.0 (*c* 0.286); δ_H: 5.96 (dt, $J_{2,3}$=4.1, $J_{2,6}$=1.7, H-2), 5.71 and 5.59 (two s, H_2-2″), 2.58 (dd, $J_{2',3'}$=9.2 and 7.4, H-2′), 2.3–1.9 (m, H_2-3, 6), 1.7–1.0 (m, H_2-3′, 4, 5, 5′, 6′, H-4′), 1.14 (s, H_3-10′), 0.99 (s, H_3-8′), 0.86 (s, H_3-9′); δ_C: 152.87 (C-1″), 132.08 (C-1), 128.26 (C-2), 112.21 (C-2″), 68.47 (C-2′), 50.31 (C-1′), 46.71 (C-7′), 45.18 (C-4′), 39.65 and 27.35 (C-5′, 6′), 25.47 (C-3′), 27.35 and 25.12 (C-3, 6), 22.45 and 21.88 (C-4, 5), 20.46 and 19.61 (C-8′, 9′), 13.43 (C-10′). Then (S_S)-1-{1-[(1*S*-*exo*)-2-bornylsulfinyl]vinyl}cyclohexene (**5**) was eluted: low-melting solid; 50% yield; $[\alpha]_D^{25}$ +78.0 (*c* 1.150); δ_H: 6.29 (m, H-2), 5.84 and 5.64 (two s, H_2-2″), 2.56 (m, H-2′), 2.4–2.1 (m, H_2-3, 6), 1.8–1.6 (m, H_A-3′, 5′, 6′, H-4′, H_2-4, 5), 1.4–1.1 (m, H_B-3′, 5′, 6′), 1.25 (s, H_3-10′), 0.94 (s, H_3-8′), 0.88 (s, H_3-9′); δ_C: 155.25 (C-1″), 134.19 (C-1), 129.52 (C-2), 113.82 (C-2″), 77.70 (C-2′), 49.68 (C-1′), 47.86 (C-7′), 45.00 (C-4′), 38.98 and 27.07 (C-5′, 6′), 31.95 (C-3′), 27.02 and 25.59 (C-3, 6), 22.56 and 21.88 (C-4, 5), 20.11 and 19.46 (C-8′, 9′), 13.70 (C-10′); *m/z* (%): 293 (M+1, 11), 137 (100), 95 (14), 81 (43). Finally, the less mobile (S_S,*E*)-1-{2-[(1*S*-*exo*)-2-bornylsulfinyl]vinyl}cyclohexene (**7**) was eluted: oil; 6% yield; $[\alpha]_D^{25}$ +57.9 (*c* 0.350); δ_H: 6.81 (d, $J_{1'',2''}$=15.4, H-2″), 6.13 (d, H-1″), 6.07 (t, $J_{2,3}$=4.0, H-2), 2.66 (t, $J_{2',3'}$=8.0, H-2′), 2.2–2.1 (m, H_2-3, 6), 1.8–1.1 (m, H_2-3′, 4, 5, 5′, 6′, H-4′), 1.24 (s, H_3-10′), 0.97 (s, H_3-8′), 0.89 (s, H_3-9′); δ_C: 142.06 (C-2″), 136.72 (C-1″), 133.85 (C-1), 126.14 (C-2), 73.15 (C-2′), 49.48 (C-1′), 47.58 (C-7′), 44.95 (C-4′), 38.88 and 27.06 (C-5′, 6′), 32.19 (C-3′), 26.17 and 24.39 (C-3, 6), 22.03 and 22.01 (C-4, 5), 20.07 and 19.70 (C-8′, 9′), 13.67 (C-10′); *m/z* (%): 293 (M+1, 6), 137 (91), 81 (100), 55

(85). When the thermolysis was carried out at 150°C, it was complete after 15 min with the following yields of isolated dienes: 14% of compound **6**, 61% of **5** and 15% of **7**.

*3.3. General procedure for Diels–Alder reactions of dienes **3**–**6** with NPM in thermal conditions*

NPM (674.7 mg, 3.9 mmol) was added to a solution of the diene (0.65 mmol) in anhydrous CH_2Cl_2 (7 ml). The reaction mixture was refluxed until the diene totally disappeared, as verified by TLC monitoring (EtOAc:hexane, 70:30). The solvent was removed under vacuum and the crude mixture was column chromatographed beginning the elution with hexane:EtOAc (80:20) and gradually increasing the EtOAc percentage up to 100%. Reaction times and yields are shown in Table 1.

*3.4. General procedure for Diels–Alder reactions of dienes **4** and **5** with NPM in the presence of $LiClO_4$*

$LiClO_4$ (29.8 mg, 0.28 mmol) was added to a solution of the diene (0.35 mmol) and NPM (363.7 mg, 2.1 mmol) in anhydrous CH_2Cl_2 (4 ml). The reaction mixture was stirred until the diene had totally disappeared, as verified by TLC monitoring. Isolation and purification of cycloadducts were performed as described previously. Reaction temperatures, times and yields are shown in Table 1.

*3.5. Cycloadducts from (S_S)-isoborneolsulfinyldiene **3** and NPM, reported in order of increasing retention times*

*3.5.1. (3a*S,*9a*S,*9b*R,S_S)-1,3,3a,4,6,7,8,9,9a,9b-Decahydro-5-[(1*S*)-isoborneol-10-sulfinyl]-2-phenylbenz[e]isoindole-1,3-dione **12***

Mp 101–103°C (found: C, 69.54; H, 7.50. $C_{28}H_{35}NO_4S$ requires: C, 69.82; H, 7.32%); δ_H: 7.5–7.2 (m, Ph), 4.04 (t, $J_{2',3'}$=5.5, H-2′), 3.40 (m, H-3a, H_A-4), 3.30 (dd, $J_{3a,9b}$=8.3, $J_{9a,9b}$=6.1, H-9b), 2.95 and 2.74 (AB system, $J_{10'A,10'B}$=13.1, H_2-10′), 2.7–1.3 (m, H_2-3′, 5′, 6, 6′, 7–9, H_B-4, H-4′, 9a), 1.11 (s, H_3-8′), 0.86 (s, H_3-9′); δ_C: 177.17 and 176.64 (C-1, 3), 147.07 (C-5), 132.71 (C-5a), 131.63 (C-1′′), 129.00 (C-2′′, 6′′), 128.44 (C-4′′), 126.47 (C-3′′, 5′′), 76.71 (C-2′), 53.39 (C-10′), 51.10 (C-1′), 48.43 (C-7′), 44.79 (C-4′), 42.84 (C-9b), 41.05 (C-3′), 39.42 and 38.95 (C-3a, 9a), 31.65, 27.59, 27.29, 25.94, 23.03, 22.90 and 19.12 (C-4, 5′, 6, 6′, 7–9), 20.48 and 20.43 (C-8′, 9′); *m/z* (%): 482 (M+1, 57), 329 (12), 55 (100).

*3.5.2. (3a*R,*9a*S,*9b*S,S_S)-1,3,3a,4,6,7,8,9,9a,9b-Decahydro-5-[(1*S*)-isoborneol-10-sulfinyl]-2-phenylbenz[e]isoindole-1,3-dione **14***

Mp 168–170°C (found: C, 69.77; H, 7.45. $C_{28}H_{35}NO_4S$ requires: C, 69.82; H, 7.32%); δ_H: 7.5–7.3 (m, Ph), 3.98 (t, $J_{2',3'}$=5.4, H-2′), 3.4–3.1 (m, H-3a, 9b, H_A-4), 2.91 and 2.77 (AB system, $J_{10'A,10'B}$=13.4, H_2-10′), 2.9–1.2 (m, H_2-3′, 5′, 6, 6′, 7–9, H_B-4, H-4′, 9a), 1.10 (s, H_3-8′), 0.87 (s, H_3-9′); δ_C: 177.75 and 177.40 (C-1, 3), 144.72 (C-5), 131.73 (C-1′′, 5a), 129.18 (C-4′′), 129.17 (C-2′′, 6′′), 126.16 (C-3′′, 5′′), 77.30 (C-2′), 51.10 (C-1′, 10′), 48.68 (C-7′), 44.96 (C-4′), 44.84 (C-9b), 38.02 and 37.97 (C-3a, 9a), 35.75 (C-3′), 31.87, 30.50, 30.44, 27.41, 27.34, 26.16 and 25.39 (C-4, 5′, 6, 6′, 7–9), 20.53 and 10.50 (C-8′, 9′).

*3.5.3. (3a*R,*9a*R,*9b*S,S_S)-1,3,3a,4,6,7,8,9,9a,9b-Decahydro-5-[(1*S*)-isoborneol-10-sulfinyl]-2-phenylbenz[e]isoindole-1,3-dione **13***

Mp 215–217°C (found: C, 69.50; H, 7.65. $C_{28}H_{35}NO_4S$ requires: C, 69.82; H, 7.32%); δ_H: 7.5–7.2 (m, Ph), 4.07 (t, $J_{2',3'}$=5.5, H-2′), 3.50 (dt, $J_{3a,4A}$=1.2, $J_{3a,4B}$=$J_{3a,9b}$=8.3, H-3a), 3.38 (dd, $J_{4A,4B}$=16.5,

H_A-4), 3.33 (dd, $J_{9a,9b}$=6.8, H-9b), 2.79 and 2.50 (AB system, $J_{10'A,10'B}$=13.3, H_2-10′), 2.7–1.1 (m, H_2-3′, 4, 5′, 6, 6′, 7–9, H-4′, 9a), 0.90 (s, H_3-8′), 0.75 (s, H_3-9′); δ_C: 177.84 and 176.48 (C-1, 3), 147.12 (C-5), 133.50 and 131.58 (C-1″, 5a), 129.11 (C-2″, 6″), 128.63 (C-4″), 126.29 (C-3″, 5″), 77.21 (C-2′), 53.70 (C-10′), 51.14 (C-1′), 48.39 (C-7′), 44.87 (C-4′), 43.10 (C-9b), 41.19 (C-3′), 39.84 and 39.41 (C-3a, 9a), 31.78, 27.30, 26.30, 25.01, 22.20, 21.99 and 20.00 (C-4, 5′, 6, 6′, 7-9), 20.32 (C-8′, 9′).

3.6. Cycloadducts from (R_S*)-isoborneolsulfinyldiene* ***4*** *and NPM, reported in order of increasing retention times*

*3.6.1. (3a*S*,9a*R*,9b*R,R_S*)-1,3,3a,4,6,7,8,9,9a,9b-Decahydro-5-[(1*S*)-isoborneol-10-sulfinyl]-2-phenylbenz[e]isoindole-1,3-dione (**17**)*

Mp 222–224°C (found: C, 69.79; H, 7.40. $C_{28}H_{35}NO_4S$ requires: C, 69.82; H, 7.32%); δ_H: 7.5–7.2 (m, Ph), 4.10 (dd, $J_{2',3'}$=8.1 and 4.3, H-2′), 3.51 and 2.07 (AB system, $J_{10'A,10'B}$=12.6, H_2-10′), 3.4–1.4 (m, H-3a, 4′, 9b, H_2-3′, 4, 5′, 6, 6′, 7–9), 1.13 (s, H_3-8′), 0.83 (s, H_3-9′).

*3.6.2. (3a*R*,9a*R*,9b*S,R_S*)-1,3,3a,4,6,7,8,9,9a,9b-Decahydro-5-[(1*S*)-isoborneol-10-sulfinyl]-2-phenylbenz[e]isoindole-1,3-dione (**15**)*

Mp 210–212°C; $[\alpha]_D^{25}$ −47.1 (*c* 0.955) (found: C, 69.44; H, 7.70. $C_{28}H_{35}NO_4S$ requires: C, 69.82; H, 7.32%); δ_H: 7.5–7.2 (m, Ph), 4.08 (dd, $J_{2',3'}$=8.3 and 4.1, H-2′), 3.41 (m, H-3a), 3.40 and 2.12 (AB system, $J_{10'A,10'B}$=13.0, H_2-10′), 3.30 (dd, $J_{3a,9b}$=8.3, $J_{9a,9b}$=6.4, H-9b), 2.7–1.1 (m, H_2-3′, 4, 5′, 6, 6′, 7–9, H-4′, 9a), 1.10 (s, H_3-8′), 0.80 (s, H_3-9′); δ_C: 176.97 and 176.46 (C-1, 3), 147.68 (C-5), 131.96 and 131.56 (C-1″, 5a), 128.99 (C-2″, 6″), 128.43 (C-4″), 126.37 (C-3″, 5″), 76.76 (C-2′), 52.65 (C-10′), 51.25 (C-1′), 48.09 (C-7′), 44.92 (C-4′), 42.74 (C-9b), 39.32 and 38.87 (C-3a, 9a), 38.37 (C-3′), 30.88, 27.36, 27.05, 25.94, 23.00, 22.85 and 18.92 (C-4, 5′, 6, 6′, 7–9), 20.37 and 19.81 (C-8′, 9′); *m/z* (%): 482 (M+1, 24), 135 (37), 95 (50), 81 (70), 69 (100).

*3.6.3. (3a*S*,9a*S*,9b*R,R_S*)-1,3,3a,4,6,7,8,9,9a,9b-Decahydro-5-[(1*S*)-isoborneol-10-sulfinyl]-2-phenylbenz[e]isoindole-1,3-dione (**16**)*

Mp 180–182°C; $[\alpha]_D^{25}$ +89.3 (*c* 0.740) (found: C, 69.90; H, 7.55. $C_{28}H_{35}NO_4S$ requires: C, 69.82; H, 7.32%); δ_H: 7.5–7.2 (m, Ph), 4.04 (dd, $J_{2',3'}$=8.1 and 4.2, H-2′), 3.50 (dt, $J_{3a,4A}$=2.1, $J_{3a,4B}$=$J_{3a,9b}$=8.1, H-3a), 3.44 and 1.70 (AB system, $J_{10'A,10'B}$=13.2, H_2-10′), 3.36 (dd, $J_{4A,4B}$=16.5, H_A-4), 3.33 (dd, $J_{9a,9b}$=7.9, H-9b), 2.7–1.1 (m, H_2-3′, 5′, 6, 6′, 7–9, H_B-4, H-4′, 9a), 1.00 (s, H_3-8′), 0.52 (s, H_3-9′); δ_C: 177.50 and 176.32 (C-1, 3), 148.52 (C-5), 131.54 (C-1″, 5a), 129.14 (C-2″, 6″), 128.62 (C-4″), 126.00 (C-3″, 5″), 76.89 (C-2′), 53.00 (C-10′), 51.25 (C-1′), 48.21 (C-7′), 44.97 (C-4′), 43.00 (C-9b), 39.75 and 39.55 (C-3a, 9a), 38.38 (C-3′), 31.06, 27.15, 26.11, 24.81, 21.99, 21.86 and 20.32 (C-4, 5′, 6, 6′, 7–9), 20.00 and 19.57 (C-8′, 9′); *m/z* (%): 482 (M+1, 67), 149 (60), 135 (100), 107 (52), 91 (52), 55 (59).

3.7. Cycloadducts from (S_S*)-bornylsulfinyldiene* ***5*** *and NPM, reported in order of increasing retention times*

*3.7.1. (3a*S*,9a*S*,9b*R,S_S*)-1,3,3a,4,6,7,8,9,9a,9b-Decahydro-5-[(1*S*-exo*)-2-bornylsulfinyl]-2-phenylbenz[e]isoindole-1,3-dione* ***18***

Mp 83–85°C; $[\alpha]_D^{25}$ +109.3 (*c* 1.480) (found: C, 72.00; H, 7.64. $C_{28}H_{35}NO_3S$ requires: C, 72.22; H, 7.58%); δ_H: 7.4–7.2 (m, Ph), 3.37 (dt, $J_{3a,4A}$=2.1, $J_{3a,4B}$=$J_{3a,9b}$=8.6, H-3a), 3.37 (dd, $J_{4A,4B}$=15.4, H_A-4), 3.30 (dd, $J_{9a,9b}$=5.5, H-9b), 2.7–1.1 (m, H-2′, 4′, 9a, H_B-4, H_2-3′, 5′, 6, 6′, 7–9), 1.27 (s, H_3-10′), 0.90 (s,

H_3-8′, 9′); δ_C: 176.98 and 176.50 (C-1, 3), 151.24 (C-5), 131.64 and 130.88 (C-1″, 5a), 128.97 (C-2″, 6″), 128.96 (C-4″), 126.61 (C-3″, 5″), 70.03 (C-2′), 48.90 (C-1′), 47.54 (C-7′), 44.79 (C-4′), 43.13 (C-9b), 39.74 and 38.94 (C-3a, 9a), 38.66, 32.29, 27.34, 22.14, 21.86, 20.28 and 20.26 (C-4, 5′, 6, 6′, 7–9), 27.03 (C-3′), 19.93 and 19.33 (C-8′, 9′), 13.38 (C-10′); *m/z* (%): 466 (M+1, 5), 137 (51), 81 (100).

*3.7.2. (3a*R,*9a*S,*9b*S,S$_S$*)-1,3,3a,4,6,7,8,9,9a,9b-Decahydro-5-[(1*S-exo*)-2-bornylsulfinyl]-2-phenylbenz[e]isoindole-1,3-dione* ***20***

Mp 66–68°C (found: C, 71.90; H, 7.38. $C_{28}H_{35}NO_3S$ requires: C, 72.22; H, 7.58%); δ_H: 7.5–7.3 (m, Ph), 3.4–1.1 (m, H-2′, 3a, 4′, 9a, 9b, H_2-3′, 4, 5′, 6, 6′, 7–9), 1.25 (s, H_3-10′), 0.92 (s, H_3-8′), 0.89 (s, H_3-9′); δ_C: 177.66 and 177.40 (C-1, 3), 147.68 (C-5), 131.71 and 129.64 (C-1″, 5a), 129.11 (C-2″, 6″), 128.50 (C-4″), 126.03 (C-3″, 5″), 69.55 (C-2′), 49.09 (C-1′), 47.61 (C-7′), 44.74 (C-4′), 44.65 (C-9b), 38.24 and 37.99 (C-3a, 9a), 38.80, 35.32, 31.55, 29.63, 26.95, 26.21 and 17.63 (C-4, 5′, 6, 6′, 7–9), 25.16 (C-3′), 19.45 and 19.40 (C-8′, 9′), 13.48 (C-10′); *m/z* (%): 466 (M+1, 4), 137 (20), 95 (50), 81 (65), 69 (73), 55 (100).

*3.7.3. (3a*S,*9a*R,*9b*R,S$_S$*)-1,3,3a,4,6,7,8,9,9a,9b-Decahydro-5-[(1*S-exo*)-2-bornylsulfinyl]-2-phenylbenz[e]isoindole-1,3-dione* ***21***

Mp 188–190°C (found: C, 72.00; H, 7.70. $C_{28}H_{35}NO_3S$ requires: C, 72.22; H, 7.58%); δ_H: 7.5–7.2 (m, Ph), 3.45 (dt, $J_{3a,4A}$=2.6, $J_{3a,4B}$=$J_{3a,9b}$=8.8, H-3a, H_A-4), 3.35 (dd, $J_{9a,9b}$=7.7, H-9b), 3.07 (dd, $J_{4A,4B}$=17.3), 2.9–1.2 (m, H-2′, 4′, 9a, H_B-4, H_2-3′, 5′, 6, 6′, 7–9), 1.22 (s, H_3-10′), 0.92 (s, H_3-8′), 0.86 (s, H_3-9′); δ_C: 177.84 and 176.45 (C-1, 3), 149.83 (C-5), 131.61 and 130.18 (C-1″, 5a), 128.93 (C-2″, 6″), 128.40 (C-4″), 125.90 (C-3″, 5″), 68.27 (C-2′), 49.18 (C-1′), 47.56 (C-7′), 44.68 (C-4′), 42.15 (C-9b), 39.31 and 38.63 (C-3a, 9a), 38.82, 31.12, 29.60, 27.48, 24.24, 23.54 and 17.83 (C-4, 5′, 6, 6′, 7–9), 26.70 (C-3′), 19.46 and 19.42 (C-8′, 9′), 13.54 (C-10′); *m/z* (%): 466 (M+1, 5), 137 (65), 55 (100).

*3.7.4. (3a*R,*9a*R,*9b*S,S$_S$*)-1,3,3a,4,6,7,8,9,9a,9b-Decahydro-5-[(1*S-exo*)-2-bornylsulfinyl]-2-phenylbenz[e]isoindole-1,3-dione* ***19***

Mp 140–142°C (found: C, 72.25; H, 7.63. $C_{28}H_{35}NO_3S$ requires: C, 72.22; H, 7.58%); δ_H: 7.5–7.2 (m, Ph), 3.4–3.3 (m, H-3a, H_A-4), 3.30 (dd, $J_{3a,9b}$=8.9, $J_{9a,9b}$=5.6, H-9b), 2.7–1.2 (m, H-2′, 4′, 9a, H_B-4, H_2-3′, 5′, 6, 6′, 7–9), 1.23 (s, H_3-10′), 0.88 (s, H_3-8′, 9′); *m/z* (%): 466 (M+1, 23), 312 (30), 137 (100), 81 (70).

*3.8. Cycloadducts from (*R$_S$*)-bornylsulfinyldiene* ***6*** *and NPM, reported in order of increasing retention times*

*3.8.1. (3a*R,*9a*R,*9b*S,R$_S$*)-1,3,3a,4,6,7,8,9,9a,9b-Decahydro-5-[(1*S-exo*)-2-bornylsulfinyl]-2-phenylbenz[e]isoindole-1,3-dione* ***22***

Mp 193–195°C; $[\alpha]_D^{25}$ −19.0 (*c* 0.835) (found: C, 72.21; H, 7.70. $C_{28}H_{35}NO_3S$ requires: C, 72.22; H, 7.58%); δ_H: 7.5–7.2 (m, Ph), 3.37 (dt, $J_{3a,4A}$=2.3, $J_{3a,4B}$=$J_{3a,9b}$=8.6, H-3a), 3.29 (dd, $J_{9a,9b}$=5.6, H-9b), 3.27 (split dd, $J_{4A,4B}$=15.8, H_A-4), 2.7–1.0 (m, H-2′, 4′, 9a, H_B-4, H_2-3′, 5′, 6, 6′, 7–9), 0.99 (s, H_3-8′), 0.95 (s, H_3-10′), 0.85 (s, H_3-9′); δ_C: 177.05 and 176.60 (C-1, 3), 147.83 (C-5), 134.25 and 131.68 (C-1″, 5a), 129.04 (C-2″, 6″), 128.47 (C-4″), 126.62 (C-3″, 5″), 68.80 (C-2′), 49.96 (C-1′), 47.28 (C-7′), 45.22 (C-4′), 43.25 (C-9b), 39.78 and 39.05 (C-3a, 9a), 39.18, 29.65, 27.41, 26.89, 22.45, 21.78 and 20.37 (C-4, 5′, 6, 6′, 7–9), 25.06 (C-3′), 19.88 and 19.86 (C-8′, 9′), 13.28 (C-10′); *m/z* (%): 466 (M+1, 4), 312 (7), 279 (4), 205 (9), 55 (100).

*3.8.2. (3aS,9aR,9bR,R$_S$)-1,3,3a,4,6,7,8,9,9a,9b-Decahydro-5-[(1*S*-exo)-2-bornylsulfinyl]-2-phenylbenz[e]isoindole-1,3-dione* ***23***

Mp 94–96°C (found: C, 72.26; H, 7.38. $C_{28}H_{35}NO_3S$ requires: C, 72.22; H, 7.58%); δ_H: 7.5–7.3 (m, Ph), 3.31 (ddd, $J_{3a,4A}$=7.6, $J_{3a,4B}$=8.7, $J_{3a,9b}$=5.7, H-3a), 3.19 (ddd, $J_{6A,6B}$=11.3, $J_{6A,7}$=3.7 and 1.5, H_A-6), 3.02 (ddd, $J_{4A,4B}$=18.5, H_A-4), 2.86 (dd, $J_{9,9a}$=4.6, $J_{9a,9b}$=9.1, H-9a), 2.72 (dd, H-9b), 2.6–1.1 (m, H-2′, 4′, H_2-3′, 5′, 6′, 7–9, H_B-4, 6), 0.98 (s, H_3-8′), 0.90 (s, H_3-10′), 0.84 (s, H_3-9′); δ_C: 177.90 and 177.38 (C-1, 3), 145.08 (C-5), 133.06 and 131.78 (C-1″, 5a), 129.15 (C-2″, 6″), 128.55 (C-4″), 126.09 (C-3″, 5″), 68.56 (C-2′), 49.99 (C-1′), 47.37 (C-7′), 45.36 (C-4′), 44.68 (C-9b), 39.03 and 38.37 (C-3a, 9a), 25.50 (C-3′), 38.85, 30.99, 30.96, 29.23, 27.40, 26.50 and 18.07 (C-4, 5′, 6, 6′, 7–9), 19.94 and 19.75 (C-8′, 9′), 13.28 (C-10′).

*3.8.3. (3aR,9aS,9bS,R$_S$)-1,3,3a,4,6,7,8,9,9a,9b-Decahydro-5-[(1*S*-exo)-2-bornylsulfinyl]-2-phenylbenz[e]isoindole-1,3-dione* ***24***

Mp 75–77°C (found: C, 72.11; H, 7.68. $C_{28}H_{35}NO_3S$ requires: C, 72.22; H, 7.58%); δ_H: 7.5–7.2 (m, Ph), 3.5–3.1 (m, H-3a, 9b, H_A-4), 2.7–1.0 (m, H-2′, 4′, H_2-3′, 5′, 6, 6′, 7–9, H_B-4), 0.96 (s, H_3-8′), 0.86 (s, H_3-10′), 0.80 (s, H_3-9′).

*3.9. Reaction of (S$_S$,E)-1-{2-[(1*S*-exo)-2-bornylsulfinyl]vinyl}cyclohexene (***7***) with NMM in the presence of $SnCl_4$*

$SnCl_4$ (0.064 ml, 0.55 mmol) was added to a solution of the diene **7** (200 mg, 0.685 mmol) and NMM (456 mg, 4.1 mmol) in anhydrous CH_2Cl_2 (5 ml) under stirring at room temperature. When the reaction appeared complete by TLC (48 h, eluant hexane:EtOAc, 70:30) further CH_2Cl_2 (5 ml) was added, and the organic layer washed with H_2O for $SnCl_4$ removal, and dried over Na_2SO_4. The solvent was then evaporated under vacuum and the crude mixture was column chromatographed beginning the elution with hexane:EtOAc (90:10) and gradually increasing the EtOAc percentage up to 40%. First the diastereomeric mixture of four sulfoxides **26** (55% yield) was eluted. The crystallization from EtOAc:ligroin of suitable combined fractions gave (3*S*,*S*$_S$)-3-[(1*S*-*exo*)-2-bornylsulfinyl]-1-methylsuccinimide (main product among sulfoxides **26**): mp 143–145°C; $[\alpha]_D^{25}$ +159.1 (*c* 0.215) (found: C, 60.50; H, 7.75. $C_{15}H_{23}NO_3S$ requires: C, 60.58; H, 7.79%); δ_H: 3.80 (dd, $J_{3,4A}$=4.7, $J_{3,4B}$=9.1, H-3), 3.46 (AB dd, $J_{3A,3B}$=18.1, H_A-4), 3.02 (1-Me), 2.73 (AB dd, H_B-4), 2.54 (dd, $J_{2',3'}$=9.2 and 6.7, H-2′), 1.9–1.2 (m, H_2-3′, 5′, 6′, H-4′), 1.19 (s, H_3-10′), 1.02 (s, H_3-8′), 0.91 (s, H_3-9′); δ_C: 174.48 and 173.50 (C-2, 5), 69.23 (C-2′), 56.74 (C-3), 49.98 (C-1′), 47.72 (C-7′), 44.82 (C-4′), 39.18 (C-4), 31.54 and 24.01 (C-5′, 6′), 26.91 (C-3′), 25.49 (1-Me), 20.02 and 19.74 (C-8′, 9′), 13.59 (C-10′); MS/FAB in the presence of NaI: *m/z* (%): 320 (M+Na, 73), 137 (44), 81 (45), 41 (45), 23 (100). The final fractions of the column contained *meso*-2,12-dimethyl-1,2,3,3a,4,6,7,8,9a,9b,10,11,12,14-tetradecahydro-4,9a[3′,4′]-*endo*-pyrrolobenz[e]isoindole-1,3,11,13-tetrone **25**[9] (20% yield): δ_H: 5.69 (dt, $J_{4,5}$=6.3, $J_{5,6}$=2.0, H-5), 3.67 (dt, $J_{3a,4}$=$J_{4,10}$=3.0, H-4), 2.93 (dd, $J_{3a,9b}$=$J_{10,14}$=8.1, H-3a, 10), 2.90 (s, Me), 2.75 (t, $J_{8,9}$=6.9, H_2-9), 2.71 (d, H-9b, 14), 2.10 (dt, $J_{6,7}$=6.4, H_2-6), 1.8–1.3 (m, H_2-7, 8).

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