

# Synthesis of enantiomerically pure, partly saturated (*R*<sub>S</sub>)-[(1*S*)-isoborneol-10-sulfinyl]-substituted [1,2,4]triazolo[1,2-*a*]pyridazine, cinnolines and benzo[*f*]cinnolines

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## Abstract

The facile Diels-Alder cycloaddition reactions of four enantiopure (*R*<sub>S</sub>)-[(1*S*)-isoborneol-10-sulfinyl]-substituted dienes **1a–d** with 4-phenyl-1,2,4-triazoline-3,5-dione (**2**) are reported. The cycloadducts **3a,b** were obtained in enantiopure form and good yields. The (*R*<sub>S</sub>)-7-[(1*S*)-isoborneol-10-sulfinyl]-substituted (5*S*)-5,8-dihydro-5-methoxy-2-phenyl[1,2,4]triazolo[1,2-*a*]pyridazine-1,3(2*H*)-dione (**3a**) features the pyridazine scaffold of azafagomines and their analogues, which are potent inhibitors of various glycosidases; (*R*<sub>S</sub>)-6-[(1*S*)-isoborneol-10-sulfinyl]-2-phenyl[1,2,4]triazolo[1,2-*a*]cinnoline-1,3(2*H*)-diones **3b–d** and **4c,d**, are closely related to fully aromatic cinnolines and their saturated and partially saturated derivatives whose biological activity has been widely recognized.

**Keywords:** Benzo[*f*][1,2,4]triazolo[1,2-*a*]cinnolines, Diels-Alder cycloaddition, stereoselectivity, sulfoxides, [1,2,4]triazolo[1,2-*a*]cinnolines, [1,2,4]triazolo[1,2-*a*]pyridazines

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## Introduction

The Diels-Alder (DA) reaction is a valid tool of contemporary organic synthesis for creating in a single step six-membered cyclic molecules with up to four stereogenic centres.<sup>1</sup> Within this field, we have been working for several years on DA cycloadditions of enantiopure homo and hetero sulfinyl dienes with the aim of investigating scope and limits of the sulfoxide auxiliary, linked to a diene moiety, in the asymmetric DA synthesis of structures, some of which regarded as useful intermediates in the preparation of target molecules.<sup>2</sup>

In this paper we report cycloadditions of (*R*<sub>S</sub>)-[(1*S*)-isoborneol-10-sulfinyl]dienes\* **1a–d** with the commonly employed 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD, **2**), also known as Cookson dienophile (Scheme 1).<sup>3</sup> PTAD is considered a very reactive partner in DA reactions,<sup>4</sup> and it has also been used for trapping labile dienes.<sup>5</sup> In recent works,<sup>6</sup> its intrinsic capability of introducing a N–N moiety into an opportune structure has been exploited for synthesizing some naturally occurring compounds and their analogues. In general, pyridazine derivatives constitute a class of compounds with a wide spectrum of biological activities.<sup>7</sup> In azafagomines,<sup>6</sup> potent inhibitors of various glycosidases, and in cinnolines,<sup>7,8</sup> exhibiting various pharmacological properties, the presence of two neighbouring nitrogen atoms exerts determining effects on structural and electronic properties, and on the bioactivity of such compounds. Scaffold relationship of azafagomines and cinnolines with cycloadducts **3** and **4** renders the DA reaction of sulfinyl-substituted dienes **1** with PTDA a smooth and diastereo-selective route for the preparation of analogues of those bioactive compounds.

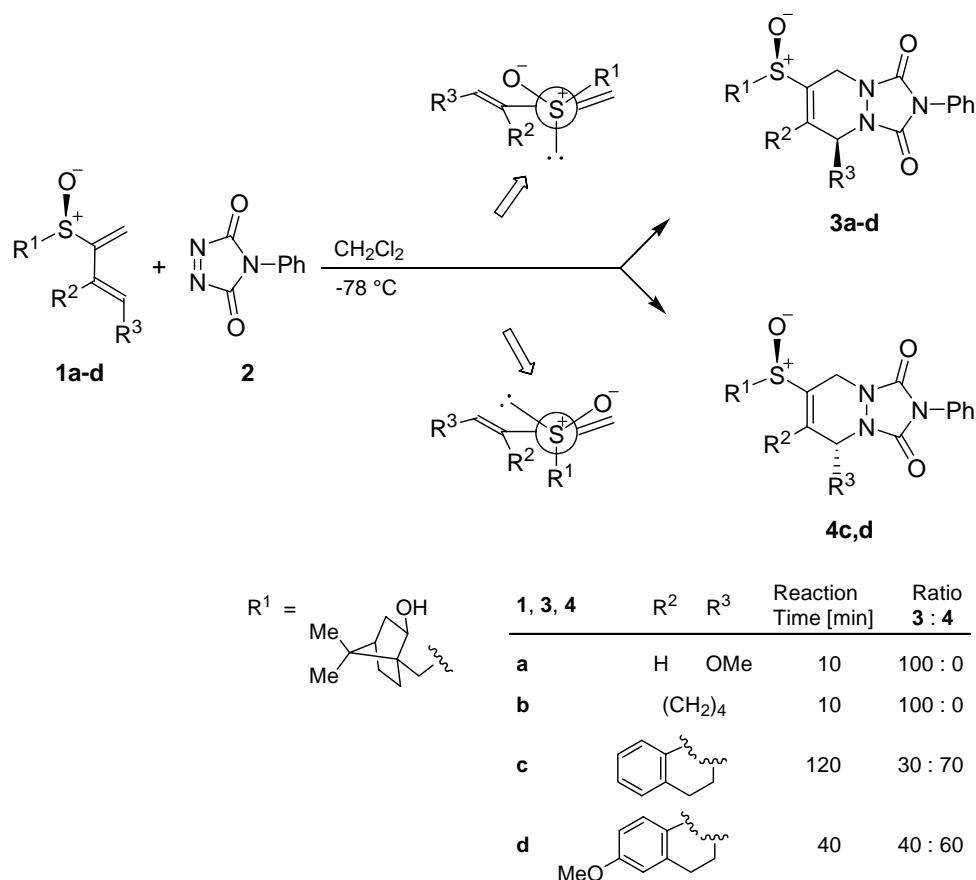
## Results and Discussion

Following our method for the preparation of enantiopure sulfinyl-substituted dienes, the addition of enantiopure sulfenic acids to opportune enynes affords (*R*<sub>S</sub>)-[(1*S*)-isoborneol-10-sulfinyl]-substituted dienes **1**.<sup>2a,d,9</sup> The cycloaddition reactions of dienes **1** with PTAD were performed in CH<sub>2</sub>Cl<sub>2</sub> at –78°C, with yields >95%; reaction times and diastereomer ratios are reported in Scheme 1.

The DA reaction of (*R*<sub>S</sub>,*E*)-3-[(1*S*)-isoborneol-10-sulfinyl]-1-methoxybuta-1,3-diene **1a** with PTDA was completed within 10 min leading to cycloadduct **3a** and occurred with complete stereocontrol. Dienophile **2** approached the diene **1a** from the sterically more readily accessible 1*Re*,2*Re*,3*Si*-face as shown in Scheme 1. Similarly, cycloaddition of (*R*<sub>S</sub>)-1-{1-[(1*S*)-isoborneol-10-sulfinyl]vinyl}cyclohexene **1b** with PTDA furnished the enantiopure cycloadduct **3b** in very good yield (Scheme 1). Configurations of newly-formed stereocenters, C-5 in **3a** and C-10a in **3b**, are assigned by analogy to the stereochemistry of cycloadducts previously obtained from the reaction of dienes **1a,b** with various dienophiles.<sup>2a,10</sup>

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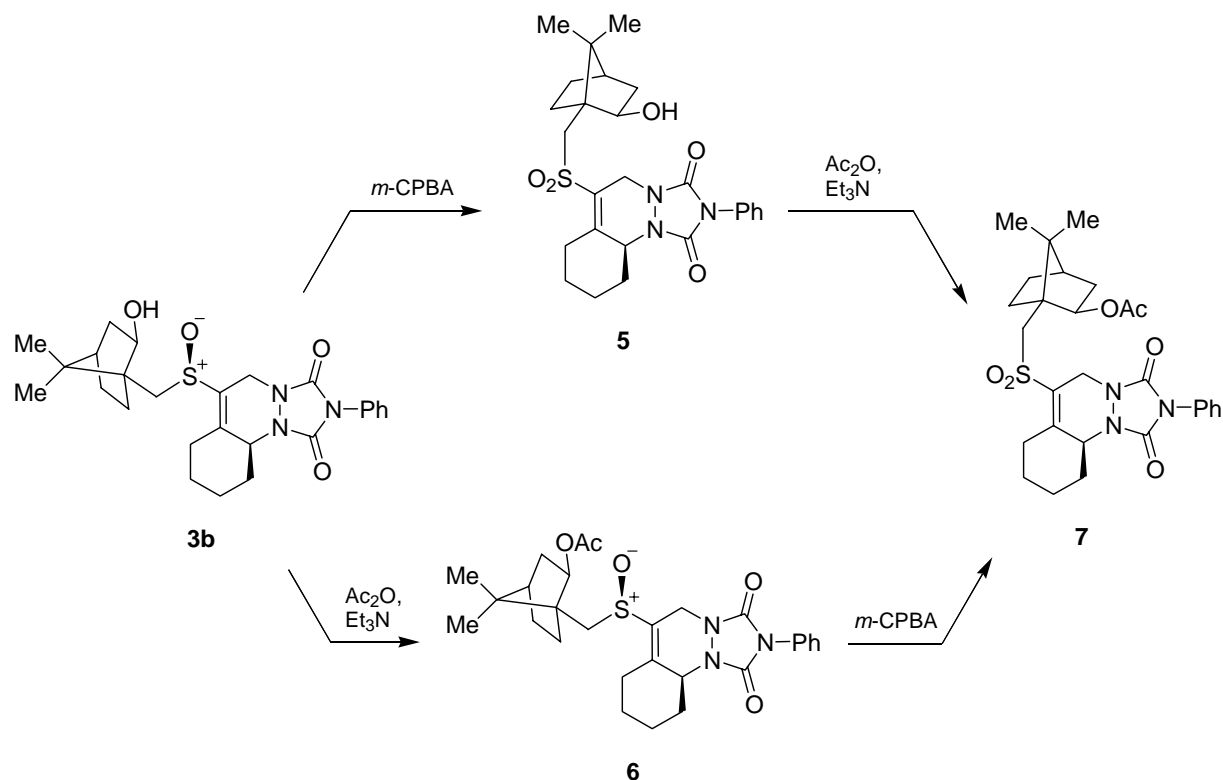
\* The short name “[*(1S)*-isoborneol-10-sulfinyl]” is used for compounds **1**, **3**, and **4** instead of “[*(1S,2R,4R)*-2-hydroxy-7,7-dimethylbicyclo[2.2.1]hept-1-ylmethylsulfinyl]”.



**Scheme 1.** Cycloaddition reactions of dienes **1a–d** with PTAD.

The reactions of (*R<sub>S</sub>*)-3,4-dihydro-1-{1-[(1*S*)-isoborneol-10-sulfinyl]vinyl}naphthalenes **1c,d** with PTDA required longer reaction times and went along with low facial diastereoselectivity giving rise to mixtures of diastereomeric adducts **3c, 4c** and **3d, 4d**, respectively (Scheme 1). Previously,<sup>2d</sup> we had realized that the highly demanding structural features of dienes **1c,d** strongly influence the stereochemical course in DA cycloadditions. Due to the steric requirements of the substituents of **1c,d** including the isoborneolsulfinyl auxiliary, the dienophile PTAD makes poor topological discrimination between diene faces. We suggest that formation of the major cycloadducts **4c** and **4d** results from PTAD approaching the *Re*-face of dienes **1c** and **1d** in their preferred conformation as shown in Scheme 1. Cycloadducts **3c** and **4c, 3d** and **4d** were easily separated by column chromatography and were isolated as pure diastereomers in good yields. The configuration at the newly formed stereocenter C-12a has been assigned as previously reported.<sup>2d</sup>

Oxidation with *m*-CPBA transformed the sulfinyl function of cycloadduct **3b** into the sulfone group of **5**. Acetylation of the hydroxy group of the isoborneol moiety of **3b** and **5** afforded the *O*-acetylated sulfoxide **6** and sulfone **7**, respectively. Finally, oxidation of **6** with *m*-CPBA also provided enantiopure sulfone **7** (Scheme 2).



Scheme 2

## Experimental Section

**General Procedures.** Reactions were monitored by TLC on commercially available precoated plates (silica gel 60 F 254), products were visualized with acidic vanillin solution. Silica gel 60, 230–400 mesh, was used for column chromatography. Petrol refers to light petroleum, bp 30–40 °C. Melting points were determined with a hot-stage microscope. Optical rotations were measured on a Jasco P-1030 polarimeter for  $\text{CHCl}_3$  solutions whose concentrations are expressed in g / 100 mL.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded on a Varian Mercury 300 spectrometer at 300 and 75 MHz, respectively, in  $\text{CDCl}_3$  solutions with  $\text{SiMe}_4$  as internal standard; assignments are supported by Attached Proton Test (APT) and homodecoupling experiments. Protons and carbon nuclei, marked with ('), pertain to isoborneol moiety; carbon nuclei, marked with ("), pertain to phenyl group. Cycloadduct ratios were established by integration of well-separated proton signals of the diastereomers in the crude adduct mixtures (Scheme 1). Mass spectra were measured by Fast Atom Bombardment (FAB, *m*-nitrobenzyl alcohol as matrix) with a Finnigan MAT 90 instrument.

### General procedure for Diels-Alder reactions of dienes 1 with PTAD

A solution of diene 1 (4.8 mmol) in anhydrous  $\text{CH}_2\text{Cl}_2$  (10 mL) was added to PTAD (841 mg, 4.8 mmol) dissolved in the  $\text{CH}_2\text{Cl}_2$  (30 mL), at  $-78$  °C under a nitrogen atmosphere. The

temperature of the reaction mixture was maintained until the diene was completely consumed, as verified by TLC monitoring (EtOAc/CHCl<sub>3</sub> 7:3). The solvent was then removed in vacuo, and the crude mixture was purified or separated by column chromatography. Generally, the total yield of isolated cycloadducts was >95%.

**(5*S*,*R*<sub>S</sub>)-5,8-Dihydro-7-[(1*S*)-isoborneol-10-sulfinyl]-5-methoxy-2-phenyl[1,2,4]triazolo[1,2-*a*]pyridazine-1,3(2*H*)-dione (3a).** The product obtained from the reaction of PTAD with (*R*<sub>S</sub>,*E*)-3-[(1*S*)-isoborneol-10-sulfinyl]-1-methoxybuta-1,3-diene (**1a**)<sup>2a,9</sup> was purified by column chromatography (petrol/EtOAc 7:3); mp 197–198 °C; [ $\alpha$ ]<sub>D</sub><sup>23</sup> + 4.5 (*c* 0.45). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  7.6–7.4 (5 H, m, Ph), 6.69 (1 H, broad d,  $J_{5,6}$  = 3.7 Hz, H-6), 5.79 (1 H, broad d,  $J_{5,6}$  = 3.7 Hz, H-5), 4.60 (1 H, broad d,  $J_{8A,8B}$  = 16.2 Hz, H<sub>A</sub>-8), 4.10 (2 H, m, H<sub>B</sub>-8, H-2'), 3.67 (3 H, s, OMe), 3.35 and 2.43 (2 H, AB system,  $J_{10'A,10'B}$  = 12.9 Hz, H<sub>2</sub>-10'), 1.8–0.9 (7 H, m, H<sub>2</sub>-3',5',6', H-4'), 1.08 (3 H, s, H<sub>3</sub>-8'), 0.84 (3 H, s, H<sub>3</sub>-9'); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  153.21 and 151.26 (C-1,3), 142.17 (C-7), 130.54 (C-1"), 129.80 (C-6), 129.29 (C-2",6"), 128.59 (C-4"), 125.38 (C-3",5"), 79.41 (C-5), 76.92 (C-2'), 59.09 (OMe), 54.60 (C-10'), 51.49 (C-1'), 48.53 (C-7'), 44.92 (C-4'), 42.24 (C-8), 38.46 (C-3'), 30.63 and 27.07 (C-5',6'), 20.47 and 19.81 (C-8',9'). Anal. Calcd for C<sub>23</sub>H<sub>29</sub>N<sub>3</sub>O<sub>5</sub>S: C, 60.11; H, 6.36. Found: C, 60.01; H, 6.40.

**(10a*S*,*R*<sub>S</sub>)-5,7,8,9,10,10a-Hexahydro-6-[(1*S*)-isoborneol-10-sulfinyl]-2-phenyl[1,2,4]triazolo[1,2-*a*]cinnoline-1,3(2*H*)-dione (3b).** The product obtained from the reaction of PTAD with (*R*<sub>S</sub>)-1-{1-[(1*S*)-isoborneol-10-sulfinyl]vinyl}cyclohexene (**1b**)<sup>9,10</sup> was purified by column chromatography (petrol/EtOAc 7:3): mp 107 °C; [ $\alpha$ ]<sub>D</sub><sup>23</sup> + 11.4 (*c* 1.71). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  7.5–7.3 (5 H, m, Ph), 4.95 (1 H, d,  $J_{5A,5B}$  15.7, H<sub>A</sub>-5), 4.41 (1 H, m, H-10a), 4.20 (1 H, broad d,  $J_{5A,5B}$  15.7, H<sub>B</sub>-5), 4.07 (1 H, m, H-2'), 3.56 and 2.24 (2 H, AB system,  $J_{10'A,10'B}$  12.9, H<sub>2</sub>-10'), 3.12 and 2.62 (2 H, two m, H<sub>2</sub>-7), 2.1–0.9 (13 H, m, H<sub>2</sub>-3',5',6',8–10, H-4'), 1.10 (3 H, s, H<sub>3</sub>-8'), 0.83 (3 H, s, H<sub>3</sub>-9'); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  153.15 and 151.22 (C-1,3), 142.44 (C-6), 130.94 (C-1"), 129.20 (C-2",6"), 128.30 (C-4"), 128.18 (C-6a), 125.37 (C-3",5"), 76.83 (C-2'), 57.10 (C-10a), 53.78 (C-10'), 51.50 (C-1'), 48.40 (C-7'), 45.00 (C-4'), 39.27 (C-5), 38.49 (C-3'), 30.99, 30.53, 27.32, and 24.01 (C-7,8,9,10), 30.72 and 27.08 (C-5',6'), 20.55 and 19.88 (C-8',9'); MS: *m/z* (%) 484 (26) [M+1], 466 (8), 330 (28), 135 (50), 95 (49), 81 (58), 69 (74), 55 (100). Anal. Calcd. for C<sub>26</sub>H<sub>33</sub>N<sub>3</sub>O<sub>4</sub>S: C, 64.57; H, 6.88. Found: C, 64.63; H, 7.01.

**(12a*R*,*R*<sub>S</sub>)-6-[(1*S*)-Isoborneol-10-sulfinyl]-2-phenyl-5,11,12,12a-tetrahydrobenzo[*f*]-[1,2,4]triazolo[1,2-*a*]cinnoline-1,3(2*H*)-dione (4c) and (12a*S*,*R*<sub>S</sub>)-6-[(1*S*)-isoborneol-10-sulfinyl]-2-phenyl-5,11,12,12a-tetrahydrobenzo[*f*][1,2,4]triazolo[1,2-*a*]cinnoline-1,3(2*H*)-dione (3c).** The mixture obtained from the reaction of (*R*<sub>S</sub>)-1,2-dihydro-4-{1-[(1*S*)-isoborneol-10-sulfinyl]vinyl}naphthalene (**1c**)<sup>2d</sup> with PTAD was separated by column chromatography (petrol/CHCl<sub>3</sub> 7.5:2.5). With increasing retention times two diastereomers **4c** (major epimer) and **3c** (minor epimer) were isolated.

**4c:** Oil; [ $\alpha$ ]<sub>D</sub><sup>23</sup> + 0.9 (*c* 1.00). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  7.6–6.7 (9 H, m, H-7,8,9,10, Ph), 5.22 (1 H, dd,  $J_{5A,5B}$  = 15.7 Hz,  $J_{5A,12a}$  = 0.6 Hz, H<sub>A</sub>-5), 4.77 (1 H, broad dd,  $J_{12A,12a}$  = 3.8 Hz,  $J_{12A,12B}$  = 11.6 Hz, H-12a), 4.49 (1 H, dd,  $J_{5A,5B}$  = 15.7 Hz,  $J_{5B,12a}$  = 2.1 Hz, H<sub>B</sub>-5), 4.09 (1 H, dd,  $J_{2',3'ax}$  = 8.0 Hz,  $J_{2',3'eq}$  = 3.6 Hz, H-2'), 3.72 and 2.78 (2 H, AB system,  $J_{10'A,10'B}$  = 13.2 Hz, H<sub>2</sub>-

10'), 3.19 (2 H, dd,  $J_{11,12A} = 4.2$  Hz,  $J_{11,12B} = 9.1$  Hz, H<sub>2</sub>-11), 2.85 (1 H, dq,  $J_{11,12A} = 4.2$  Hz,  $J_{12A,12a} = 3.8$  Hz,  $J_{12A,12B} = 12.4$  Hz, H<sub>A</sub>-12), 2.19 (1 H, m, H<sub>B</sub>-12), 1.9-0.9 (7 H, m, H<sub>2</sub>-3',5',6', H-4'), 1.18 (3 H, s, H<sub>3</sub>-8'), 0.93 (3 H, s, H<sub>3</sub>-9'); <sup>13</sup>C NMR(75 MHz, CDCl<sub>3</sub>): δ 152.89 and 151.72 (C-1,3), 140.93 (C-6), 137.22 (C-6a), 130.87 (C-1"), 130.66 (C-10a), 130.60 and 130.12 (C-7,9,10), 129.26 (C-2",6"), 128.71 (C-6b), 128.38 (C-4"), 125.39 (C-3",5"), 125.03 (C-8), 77.19 (C-2'), 54.87 (C-12a), 52.98 (C-10'), 51.81 (C-1'), 48.46 (C-7'), 45.03 (C-4'), 38.53 (C-5), 38.47 (C-3'), 30.77 and 27.33 (C-5',6'), 27.24 and 26.97 (C-11,12), 20.62 and 19.98 (C-8',9'). Anal. Calcd for C<sub>30</sub>H<sub>33</sub>N<sub>3</sub>O<sub>4</sub>S: C, 67.77; H, 6.26. Found: C, 67.39; H 6.38.

**3c:** Oil;  $[\alpha]_D^{23} + 5.7$  (*c* 1.32). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.7–7.2 (9 H, m, H-7,8,9,10, Ph), 4.9–4.5 (3 H, m, H<sub>2</sub>-5, H-12a), 4.00 (1 H, dd,  $J_{2',3'ax} = 7.7$  Hz,  $J_{2',3'eq} = 4.2$  Hz, H-2'), 3.37 and 2.15 (2 H, AB system,  $J_{10'A,10'B} = 12.9$  Hz, H<sub>2</sub>-10'), 3.1-1.0 (11 H, m, H<sub>2</sub>-3',5',6',11,12, H-4'), 1.03 (3 H, s, H<sub>3</sub>-8'), 0.57 (3 H, s, H<sub>3</sub>-9'); MS: *m/z* (%) 532 (4) [M+1], 137 (100), 107 (60). Anal. Calcd for C<sub>30</sub>H<sub>33</sub>N<sub>3</sub>O<sub>4</sub>S: C, 67.77; H, 6.26. Found: C, 67.84; H 6.13.

**(12aR<sub>S</sub>)-6-[(1S)-isoborneol-10-sulfinyl]-9-methoxy-2-phenyl-5,11,12,12a-tetrahydrobenzo[f][1,2,4]triazolo[1,2-*a*]cinnoline-1,3(2*H*)-dione (4d)** and **(12aS<sub>R</sub>)-6-[(1S)-isoborneol-10-sulfinyl]-9-methoxy-2-phenyl-5,11,12,12a-tetrahydrobenzo[f][1,2,4]triazolo[1,2-*a*]cinnoline-1,3(2*H*)-dione (3d)**. The mixture obtained from the reaction of (*R*<sub>S</sub>)-1,2-dihydro-4-{1-[(1*S*)-isoborneol-10-sulfinyl]vinyl}-7-methoxynaphthalene (**1d**)<sup>2d</sup> with PTAD was separated by column chromatography (petrol/CHCl<sub>3</sub> 7.5:2.5). With increasing retention times two diastereomers **4d** (major epimer) and **3d** (minor epimer) were isolated.

**4d:** Oil,  $[\alpha]_D^{23} + 2.6$  (*c* 3.83). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.6–6.6 (8 H, m, H-7,8,10, Ph), 5.16 (1 H, d,  $J_{5A,5B} = 15.7$  Hz, H<sub>A</sub>-5), 4.71 (1 H, m, H-12a), 4.49 (1 H, broad d, H<sub>B</sub>-5), 4.10 (1 H, m, H-2'), 3.85 (3 H, s, OMe), 3.72 and 2.75 (2 H, AB system,  $J_{10'A,10'B} = 13.1$  Hz, H<sub>2</sub>-10'), 3.16 (2 H, dd,  $J_{11,12A} = 4.2$  Hz,  $J_{11,12B} = 9.4$  Hz, H<sub>2</sub>-11), 2.87 (1 H, m, H<sub>A</sub>-12), 2.17 (1 H, m, H<sub>B</sub>-12), 1.9–0.9 (7 H, m, H<sub>2</sub>-3',5',6', H-4'), 1.18 (3 H, s, H<sub>3</sub>-8'), 0.92 (3 H, s, H<sub>3</sub>-9'); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 161.27 (C-9), 152.83 and 151.78 (C-1,3), 140.55 (C-6), 138.97 (C-6a), 130.91 (C-1"), 130.86 (C-7), 129.23 (C-2",6"), 128.34 (C-4"), 126.69 (C-10a), 125.38 (C-3",5"), 123.29 (C-6b), 113.97 (C-10), 111.04 (C-8), 76.56 (C-2'), 55.42 (OMe), 55.19 (C-12a), 52.91 (C-10'), 51.74 (C-1'), 48.42 (C-7'), 45.03 (C-4'), 38.53 (C-5), 38.46 (C-3'), 30.30 and 27.31 (C-5',6'), 27.37 and 23.70 (C-11,12), 20.62 and 19.98 (C-8',9'); MS: *m/z* 562 (3) [M+1], 137 (100), 107 (45). Anal. Calcd for C<sub>31</sub>H<sub>35</sub>N<sub>3</sub>O<sub>5</sub>S: C, 66.29; H, 6.28. Found: C, 66.00; H 6.15.

**3d:** Oil;  $[\alpha]_D^{23} - 3.2$  (*c* 0.74). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.7–6.7 (8 H, m, H-7,8,10, Ph), 4.89 (1 H, d,  $J_{5A,5B} = 16.7$  Hz, H<sub>A</sub>-5), 4.50 (2 H, m, H<sub>B</sub>-5, H-12a), 4.02 (1 H, dd,  $J_{2',3'ax} = 7.8$  Hz,  $J_{2',3'eq} = 4.0$  Hz, H-2'), 3.84 (3 H, s, OMe), 3.41 and 2.20 (2 H, AB system,  $J_{10'A,10'B} = 12.7$  Hz, H<sub>2</sub>-10'), 3.1–1.0 (11 H, m, H<sub>2</sub>-3',5',6',11,12, H-4'), 1.05 (3 H, s, H<sub>3</sub>-8'), 0.63 (3 H, s, H<sub>3</sub>-9'); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 160.92 (C-9), 152.87 and 152.18 (C-1,3), 139.12 (C-6), 138.73 (C-6a), 132.41 (C-1"), 130.88 (C-7), 129.25 (C-2",6"), 128.78 (C-4"), 128.46 (C-10a), 125.49 (C-3",5"), 122.58 (C-6b), 113.65 (C-10), 112.50 (C-8), 76.77 (C-2'), 56.60 (C-12a), 55.39 (OMe), 53.61 (C-10'), 51.41 (C-1'), 48.25 (C-7'), 44.98 (C-4'), 38.43 (C-3',5), 30.32 and 28.90 (C-5',6'), 23.70 and 22.96 (C-11,12), 20.31 and 19.87 (C-8',9'); MS: *m/z* 562 (1) [M+1], 408 (4) [M+1-isoborneol],

109 (29), 95 (49), 81 (56), 69 (78), 55 (100). Anal. Calcd for  $C_{31}H_{35}N_3O_5S$ : C, 66.29; H, 6.28. Found: C, 66.45; H, 6.30.

**(10a*S*)-5,7,8,9,10,10a-Hexahydro-6-[(1*S*)-isoborneol-10-sulfonyl]-2-phenyl[1,2,4]triazolo[1,2-*a*]cinnoline-1,3(2*H*)-dione (5)**. A solution of carefully dried (over  $P_2O_5$ ) *m*-CPBA (98%, 176 mg 1 mmol) in anhydrous  $CH_2Cl_2$  (10 mL) was slowly added to a solution of sulfoxide **3b** (242 mg, 0.5 mmol) in anhydrous  $CH_2Cl_2$  (10 mL) at 0 °C. The reaction mixture was allowed to reach room temperature and stirred until sulfoxide **3b** completely disappeared, as checked by TLC monitoring (EtOAc/petrol 1:1). Anhydrous KF (200 mg) was then added, and the mixture was stirred overnight. After filtration the solvent was evaporated under reduced pressure to give sulfone **5** as practically pure, amorphous solid in almost quantitative yield.  $^1H$  NMR (300 MHz,  $CDCl_3$ ):  $\delta$  7.5–7.4 (5 H, m, Ph), 4.66 (1 H, d,  $J_{5A,5B} = 16.6$  Hz,  $H_A$ -5), 4.42 (1 H, m, H-10a), 4.28 (1 H, dt,  $J_{5A,5B} = 16.6$  Hz,  $J_{long-range} = 2.5$  Hz,  $H_B$ -5), 4.18 (1 H, dd,  $J_{2',3'ax} = 8.0$  Hz,  $J_{2',3'eq} = 4.1$  Hz, H-2'), 3.75 and 2.72 (2 H, two m,  $H_2$ -7), 3.47 and 2.91 (2 H, AB system,  $J_{10'A,10'B} = 13.4$  Hz,  $H_2$ -10'), 2.1–1.1 (13 H, m,  $H_2$ -3',5',6',8-10, H-4'), 1.08 (3 H, s,  $H_3$ -8'), 0.85 (3 H, s,  $H_3$ -9');  $^{13}C$  NMR (75 MHz,  $CDCl_3$ ):  $\delta$  152.68 and 151.30 (C-1,3), 150.67 (C-6), 130.72 (C-1"), 129.18 (C-2",6"), 128.34 (C-4"), 127.19 (C-6a), 125.29 (C-3",5"), 76.14 (C-2'), 57.86 (C-10a), 55.21 (C-10'), 51.01 (C-1'), 49.30 (C-7'), 44.05 (C-4'), 43.87 (C-5), 39.14 (C-3'), 31.95, 30.50, 28.02, and 23.88 (C-7,8,9,10), 30.87 and 27.42 (C-5',6'), 20.51 and 19.83 (C-8',9'); MS: *m/z* (%) 482 (5) [M+1- $H_2O$ ], 330 (3), 281 (10), 135 (23), 109 (33), 95 (52), 81 (61), 69 (76), 55 (100). Anal. Calcd for  $C_{26}H_{33}N_3O_5S$ : C, 62.50; H, 6.66. Found: C, 62.37; H 6.70.

**(10a*S,R\_S*)-5,7,8,9,10,10a-Hexahydro-6-[(1*S*,2*R*,4*R*)-2-acetoxy-7,7-dimethylbicyclo[2.2.1]-hept-1-ylmethylsulfinyl]-2-phenyl[1,2,4]triazolo[1,2-*a*]cinnoline-1,3(2*H*)-dione (6)**. To a solution of sulfoxide **3b** (242 mg, 0.5 mmol) in  $Ac_2O$  (3 mL)  $Et_3N$  (1.05 mL, 7.5 mmol) was added. The reaction mixture was kept at reflux until the starting material completely disappeared, as checked by TLC monitoring (EtOAc/petrol 1:1). The mixture was allowed to cool to room temperature,  $H_2O$  (20 mL) was added, and the mixture was extracted with  $Et_2O$  (3 x 20 mL). The combined organic layers were dried over  $Na_2SO_4$ . After evaporation of the solvent in vacuo, the crude product was purified by column chromatography (petrol/EtOAc 6:4); product **6** was isolated as a thick oil (131 mg, 50%).  $^1H$  NMR (300 MHz,  $CDCl_3$ ):  $\delta$  7.5–7.3 (5 H, m, Ph), 4.98 (1 H, d,  $J_{5A,5B} = 15.5$  Hz,  $H_A$ -5), 4.82 (1 H, dd,  $J_{2',3'ax} = 8.0$  Hz,  $J_{2',3'eq} = 2.8$  Hz, H-2'), 4.41 (1 H, m, H-10a), 4.15 (1 H, dt,  $J_{5A,5B} = 15.5$  Hz,  $J_{long-range} = 2.5$  Hz,  $H_B$ -5), 3.32 and 2.56 (2 H, AB system,  $J_{10'A,10'B} = 13.1$  Hz,  $H_2$ -10'), 3.20 and 2.60 (2 H, two m,  $H_2$ -7), 2.10 (3 H, s, Ac), 2.0–0.9 (13 H, m,  $H_2$ -3',5',6',8-10, H-4'), 1.05 (3 H, s,  $H_3$ -8'), 0.90 (3 H, s,  $H_3$ -9');  $^{13}C$  NMR (75 MHz,  $CDCl_3$ ):  $\delta$  170.04 [C(O)Me], 153.21 and 151.19 (C-1,3), 142.64 (C-6), 130.90 (C-1"), 129.17 (C-2",6"), 128.85 (C-6a), 128.24 (C-4"), 125.27 (C-3",5"), 78.25 (C-2'), 57.08 (C-10a), 51.96 (C-10'), 49.69 (C-1'), 49.45 (C-7'), 44.56 (C-4'), 39.48 (C-5), 38.86 (C-3'), 30.93, 30.44, 27.38, and 24.04 (C-7,8,9,10), 30.70 and 26.95 (C-5',6'), 21.30 [C(O)Me], 20.31 and 19.89 (C-8',9'). Anal. Calcd for  $C_{28}H_{35}N_3O_5S$ : C, 63.98; H, 6.71. Found: C, 64.00; H, 6.51.

**(10a*S*,*R*<sub>S</sub>)-5,7,8,9,10,10a-Hexahydro-6-[(1*S*,2*R*,4*R*)-2-acetoxy-7,7-dimethylbicyclo[2.2.1]-hept-1-ylmethylsulfonyl]-2-phenyl[1,2,4]triazolo[1,2-*a*]cinnoline-1,3(2*H*)-dione (7)**. Oxidation of **6** was carried out as described for the preparation of **5**, and sulfone **7**, after purification by column chromatography (EtOAc/petrol 1:1), was isolated as a thick oil in almost quantitative yield. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.5–7.4 (5 H, m, Ph), 5.00 (1 H, dd,  $J_{2',3'ax} = 8.4$  Hz,  $J_{2',3'eq} = 3.2$  Hz, H-2'), 4.60 (1 H, d,  $J_{5A,5B} = 16.5$ , H<sub>A</sub>-5), 4.40 (1 H, m, H-10a), 4.24 (1 H, broad d,  $J_{5A,5B} = 16.5$ , H<sub>B</sub>-5), 3.84 and 2.73 (2 H, two m, H<sub>2</sub>-7), 3.44 and 2.92 (2 H, AB system,  $J_{10'A,10'B} = 13.4$  Hz, H<sub>2</sub>-10'), 2.06 (3 H, s, Ac), 2.0–1.3 (13 H, m, H<sub>2</sub>-3',5',6',8-10, H-4'), 1.02 (3 H, s, H<sub>3</sub>-8'), 0.92 (3 H, s, H<sub>3</sub>-9'); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 169.41 [C(O)Me], 152.68 and 151.40 (C-1,3), 149.97 (C-6), 130.74 (C-1"), 129.23 (C-2",6"), 128.38 (C-4"), 127.69 (C-6a), 125.33 (C-3",5"), 78.12 (C-2'), 57.92 (C-10a), 53.93 (C-10'), 50.02 (C-1'), 49.24 (C-7'), 43.99 (C-4'), 43.95 (C-5), 39.61 (C-3'), 32.01, 30.01, 28.03, and 23.92 (C-7,8,9,10), 30.46 and 27.14 (C-5',6'), 21.24 [C(O)Me], 20.37 and 19.94 (C-8',9'). Anal. Calcd for C<sub>28</sub>H<sub>35</sub>N<sub>3</sub>O<sub>6</sub>S: C, 62.09; H, 6.51. Found: C, 62.17; H, 6.50.

Sulfone **7** was obtained, though in lower yield, by acetylation of sulfone **5**, following the procedure described for the conversion of **3b** into **6**.

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