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SYNTHESIS OF NEW MONOTERPENE SULFONYLIMIDAZOLES

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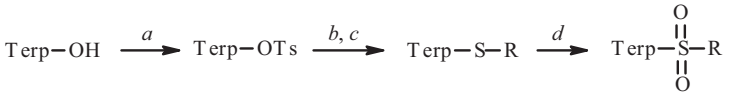
Sulfonylimidazoles of monoterpenes of menthane, pinane, and carane nature were synthesized in 83-98% yields.

Keywords: sulfonylimidazoles, monoterpenoids, neomenthyl, *cis*-myrtanyl, *trans*-myrtanyl, caranyl, cumylhydroperoxide, oxidation.

The design and synthesis of various heterocyclic compounds are of interest because of their pharmacological significance. Compounds containing imidazole and benzimidazole groups are used to treat viral diseases [1–3], arterial hypertonicity [4], and diseases related to hormonal imbalances [5]. It was established recently that the benzimidazole moiety plays an important role in the protein–protein interaction of human growth hormone and its receptor [6]. Compounds containing a sulfonyl group are used as antiviral and anti-inflammatory drugs [7–9]. Monoterpenoids also exhibit a broad spectrum of biological activity [10]. Therefore, the synthesis of monoterpene heterocyclic sulfones is exceedingly timely.

We synthesized for the first time 2-neomenthylsulfonyl-1*H*-imidazole (**1**), 2-(*cis*-myrtanylsulfonyl)-1*H*-imidazole (**2**), 2-(*trans*-myrtanylsulfonyl)-1*H*-imidazole (**3**), 2-(3-caranylsulfonyl)-1*H*-imidazole (**4**), 1-methyl-2-neomenthylsulfonyl-1*H*-imidazole (**5**), 1-methyl-2-(*cis*-myrtanylsulfonyl)-1*H*-imidazole (**6**), 1-methyl-2-(*trans*-myrtanylsulfonyl)-1*H*-imidazole (**7**), 1-methyl-2-(3-caranylsulfonyl)-1*H*-imidazole (**8**), 2-neomenthylsulfonyl-1*H*-benzimidazole (**9**), 2-(*cis*-myrtanylsulfonyl)-1*H*-benzimidazole (**10**), 2-(*trans*-myrtanylsulfonyl)-1*H*-benzimidazole (**11**), and 2-(3-caranylsulfonyl)-1*H*-benzimidazole (**12**) in 83–98% yields (Table 1).

The starting imidazole thioethers were synthesized by reaction of terpene alcohol tosylates with heterocyclic thiols in alcoholic base solution (Scheme 1, *b*). Sulfide derivatives with a benzimidazole moiety were prepared using a Cs_2CO_3–tetrabutylammonium iodide (TBAI) catalytic system (Scheme 1, *c*) [11, 12].



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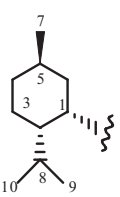

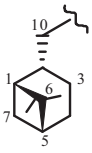

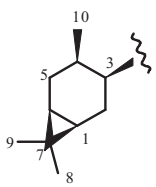

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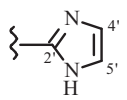

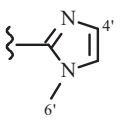

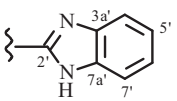

a. TsCl, Py, 23°C; *b*. R-SH, KOH, EtOH, 78°C; *c*. R-SH, TBAI, Cs_2CO_3, EtOH, 78°C; *d*. CHP, CH_2Cl_2, 40°C

Scheme 1

An excess of cumylhydroperoxide (CHP) was used to oxidize the corresponding sulfides (sulfide:CHP ratio 1:2.5) in refluxing CH_2Cl_2.

The structures of the products were confirmed by IR and NMR spectroscopy and elemental analyses. IR spectra of the produced sulfones exhibited absorption bands in the ranges 1100-1150 and 1300–1350 cm^{-1} that were characteristic of a sulfonyl group. PMR and ^{13}C NMR spectra contained resonances for both the heterocyclic radical and the terpene moiety.

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TABLE 1. Oxidation of Imidazole Thioethers **1**–**12**

Parameters	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Sulfide conversion,* %	99	95	98	100	93	94	91	96	98	97	100	100
Preparative yield of sulfonylimidazoles, %	94	89	91	97	87	83	83	84	96	92	97	98

*Conversion determined from residual sulphide after column chromatography.

Thus, PMR spectra of unsubstituted sulfonylimidazoles exhibited resonances for methine protons in the range 7.06–7.40 ppm and a broad singlet for the NH proton in the range 13.16–13.93 ppm. The ^{13}C NMR spectra showed resonances for methine C atoms in the ranges 119.93–121.45 ppm (C-5′) and 130.40–131.07 (C-4′) and a quaternary C atom in the range 143.11–144.11 ppm (C-2′). PMR spectra of *N*-substituted sulfonylimidazoles were analogous to those of sulfones with an unsubstituted imidazole except that resonances for the methyl appeared near 4.01 ppm and resonances for NH protons were missing. PMR spectra of sulfonylbenzimidazoles exhibited resonances of methine protons in the ranges 7.36–7.62 ppm (H-5′, H-6′) and 7.69–8.14 (H-5′, H-6′) in addition to a broad singlet for the NH proton in the range 13.13–13.86 ppm.

PMR spectra of neomenthane sulfonylimidazoles displayed three characteristic doublets for methyls in the range 0.70–0.96 ppm with SSCC 6.5 Hz and a resonance for a methine proton on the first C atom that appeared as a narrow multiplet in the range 3.80–4.22 ppm. ^{13}C NMR spectra of neomenthane sulfonylimidazoles exhibited a resonance for the first C atom in the range 62.06–62.18 ppm that was characteristic of C atoms bonded to a sulfonyl group.

PMR spectra of *cis*-myrtanylsulfonylimidazoles were characterized by two singlets for methyls in the ranges 1.00–1.20 ppm (Me-8) and 1.15–1.20 (Me-9) and resonances for methylene protons on the tenth C atom in the range 3.61–3.76 ppm. ^{13}C NMR spectra of *cis*-myrtanylsulfonylimidazoles contained a resonance for the tenth C atom in the range 62.37–62.79 ppm that was characteristic of C atoms located near a sulfonyl group.

PMR spectra of *trans*-myrtanylsulfonylimidazoles were similar to those of *cis*-myrtanylsulfonylimidazoles. However, resonances for methyls (Me-8) and methylene protons for the tenth C atom were shifted to stronger field.

PMR spectra of caranylsulfonylimidazoles appeared as two characteristic singlets for methyls in the ranges 0.99–1.02 ppm (Me-8) and 1.00–1.03 (Me-9), one doublet in the range 1.29–1.30 ppm (Me-10) with SSCC 7.0 Hz, and a resonance for a methine proton on the fourth C atom in the range 3.61–3.88 ppm. ^{13}C NMR spectra of caranylsulfonylimidazoles exhibited a resonance for a quaternary C atom in the range 62.70–63.23 ppm that was characteristic of C atoms bonded to a sulfonyl group.

Thus, monoterpene sulfonylimidazoles can be prepared in high yields using oxidation of the corresponding sulfide derivatives and cumylhydroperoxide as the oxidant.

EXPERIMENTAL

IR spectra were recorded in KBr pellets on a Prestige 21 IR-Fourier spectrometer (Shimadzu). Melting points were determined on a Gallencamp–Sanyo instrument. PMR and ^{13}C NMR spectra were recorded in $CDCl_3$ and DMSO-d_6 with $CDCl_3$ internal standard on an Avance-300 spectrometer (Bruker) (300.17 MHz for ^{1}H and 75.48 MHz for ^{13}C). Resonances of ^{1}H and ^{13}C were fully assigned using two-dimensional homo- (^{1}H–^{1}H COSY, ^{1}H–^{1}H NOESY) and heteronuclear experiments (^{1}H–^{13}C HSQC, ^{1}H–^{13}C HMBC). Optical rotation angles were measured on a P3002RS automated digital polarimeter (Kruss). TLC was performed on Sorbfil plates using a heptane:Et_2O solvent system with detection by phosphotungstic acid in EtOH and by $KMnO_4$. Elemental analyses were carried out using an EA 1110 CHNS–O automated analyzer. All reactions were carried out using freshly distilled solvents. Commercially available reagents were used without further purification. Column chromatography was performed over silica gel (Alfa Aesar, 0.06–0.2 mm) using a $CHCl_3$:Et_2O solvent system. Sulfides were prepared according to the literature method [10].

Preparation of Sulfonyl Derivatives. General Method. A three-necked flask equipped with a stirrer, dropping funnel, and reflux condenser was charged with a solution of starting sulfide (1 mmol) in CH_2Cl_2 (5 mL). Cumylhydroperoxide (2.5 mmol) was added dropwise. The mixture was refluxed for 9 h. The solvent was vacuum distilled. The products were isolated by column chromatography over silica gel (eluent $CHCl_3$:Et_2O, 25:1).

2-{[(1*S*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl]sulfonyl}-1*H*-imidazole (1). Colorless crystals, mp 126–127°C, $[\alpha]_D^{20}$ +36.14° (*c* 0.83, EtOH). IR spectrum (ν, cm^{-1}): 1321 [$\nu_{as}(SO_2)$], 1132 [$\nu_s(SO_2)$].

PMR spectrum (300 MHz, $CDCl_3$ + DMSO-d_6, δ, ppm, J/Hz): 0.70 (3H, d, J = 6.5, Me-7), 0.74 (3H, d, J = 6.5 Me-10), 0.74–0.77 (1H, m, H-4*ax*), 0.80 (3H, d, J = 6.5, Me-9), 1.04 (1H, ddd, J = 14.4, 12.9, 4.7, H-6*ax*), 1.16–1.29 (1H, m, H-2), 1.60–1.87 (4H, m, H-3*ax*, H-3*eq*, H-4*eq*, H-6*eq*), 1.89–2.04 (2H, m, H-8, H-5), 3.80–3.85 (1H, m, H-1), 7.06 (1H, s, H-5′), 7.12 (1H, s, H-4′), 13.16 (1H, br.s, NH).

^{13}C NMR spectrum (75 MHz, $CDCl_3$ + DMSO-d_6, δ, ppm): 21.50 (C-9), 21.69 (C-10), 22.22 (C-7), 24.76 (C-3), 26.48 (C-5), 29.16 (C-8), 35.02 (C-4), 35.97 (C-6), 49.03 (C-2), 62.18 (C-1), 119.93 (C-5′), 130.84 (C-4′), 144.11 (C-2′). $C_{13}H_{22}N_2O_2S$.

2-{[(1*R*,2*S*,5*R*)-6,6-Dimethylbicyclo[3.1.1]heptyl-2]methylsulfonyl}-1*H*-imidazole (2). White powder, mp 173–174°C, $[\alpha]_D^{20}$ –43.91° (*c* 0.22, EtOH). IR spectrum (ν, cm^{-1}): 1318 [$\nu_{as}(SO_2)$], 1142 [$\nu_s(SO_2)$].

PMR spectrum (300 MHz, $CDCl_3$ + DMSO-d_6, δ, ppm, J/Hz): 0.97–1.05 (1H, m, H-7β), 1.00 (3H, s, Me-8), 1.18 (3H, s, Me-9), 1.57 (1H, ddt, J = 15.2, 10.4, 5.4, H-3α), 1.76–2.13 (5H, m, H-1, H-5, H-4α, H-4β, H-3β), 2.35 (1H, dtd, J = 9.9, 6.2, 1.9, H-7α), 2.71–2.81 (1H, m, H-2), 3.47–3.61 (2H, m, H-10α, H-10β), 7.20 (1H, br.s, H-4′), 7.40 (1H, br.s, H-5′), 13.93 (1H, br.s, NH).

^{13}C NMR spectrum (75 MHz, $CDCl_3$ + DMSO-d_6, δ, ppm): 21.55 (C-3), 23.06 (C-8), 25.82 (C-4), 27.53 (C-9), 32.42 (C-7), 34.81 (C-2), 38.38 (C-6), 40.61 (C-5), 46.47 (C-1), 62.79 (C-10), 120.91 (C-5′), 130.30 (C-4′), 142.95 (C-2′). $C_{13}H_{20}N_2O_2S$.

2-{[(1*R*,2*R*,5*R*)-6,6-Dimethylbicyclo[3.1.1]heptyl-2]methylsulfonyl}-1*H*-imidazole (3). White powder, mp 153–154°C, $[\alpha]_D^{20}$ +3.45° (*c* 0.53, EtOH). IR spectrum (ν, cm^{-1}): 1322 [$\nu_{as}(SO_2)$], 1142 [$\nu_s(SO_2)$].

PMR spectrum (300 MHz, $CDCl_3$ + DMSO-d_6, δ, ppm, J/Hz): 0.84 (3H, s, Me-8), 1.20 (3H, s, Me-9), 1.33(1H, d, J = 10.6, H-7β), 1.37–1.49 (1H, m, H-3α), 1.71–1.94 (5H, m, H-1, H-5, H-3β, H-4α, H-4β), 2.10 (1H, ddd, J = 10.6, 5.7, 5.4, H-7α), 2.68 (1H, quin, J = 7.4, H-2), 3.28–3.41 (2H, m, H-10α, H-10β), 7.37 (2H, m, H-4′, 5′), 13.76 (1H, br.s, NH).

^{13}C NMR spectrum (75 MHz, $CDCl_3$ + DMSO-d_6, δ, ppm): 20.00 (C-8), 21.68 (C-3), 23.22 (C-7), 24.16 (C-4), 26.56 (C-9), 30.51 (C-2), 39.55 (C-6), 40.19 (C-5), 45.54 (C-1), 60.41 (C-10), 120.81 (C-5′), 130.42 (C-4′), 143.16 (C-2′). $C_{13}H_{20}N_2O_2S$.

2-{[(1*R*,3*S*,4*R*,6*S*)-4,7,7-Trimethylbicyclo[4.1.0]heptyl]sulfonyl}-1*H*-imidazole (4). White powder, mp 151–152°C, $[\alpha]_D^{20}$ –5.13° (*c* 0.48, EtOH). IR spectrum (ν, cm^{-1}): 1336 [$\nu_{as}(SO_2)$], 1140 [$\nu_s(SO_2)$].

PMR spectrum (300 MHz, $CDCl_3$ + DMSO-d_6, δ, ppm, J/Hz): 0.60 (1H, td, J = 8.7, 7.4, H-1), 0.73 (1H, q, J = 8.5, H-6), 0.91–1.02 (1H, m, H-5α), 1.02 (3H, s, Me-8), 1.03 (3H, s, Me-9), 1.24 (3H, d, J = 7.0, Me-10), 1.24–1.35 (1H, m, H-2α), 2.01 (1H, ddd, J = 13.9, 8.4, 3.8, H-2β), 2.14 (1H, ddd, J = 15.2, 8.4, 8.1, H-5β), 2.49 (1H, sept, J = 7.4, H-4), 3.61 (1H, ddd, J = 11.9, 7.5, 3.8, H-3), 7.29 (2H, br.s, H-4′, 5′), 13.65 (1H, br.s, NH).

^{13}C NMR spectrum (75 MHz, $CDCl_3$ + DMSO-d_6, δ, ppm): 15.12 (C-9), 17.45 (C-2), 17.70 (C-10), 18.36 (C-7), 19.54 (C-6), 21.64 (C-1), 26.36 (C-4), 26.82 (C-5), 28.08 (C-8), 63.23 (C-3), 121.45 (C-5′), 131.07 (C-4′), 143.11 (C-2′). $C_{13}H_{20}N_2O_2S$.

1-Methyl-2-{[(1*S*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl]sulfonyl}-1*H*-imidazole (5). White powder, mp 112–113°C, $[\alpha]_D^{20}$ +48.72° (*c* 0.68, EtOH). IR spectrum (ν, cm^{-1}): 1332 [$\nu_{as}(SO_2)$], 1116 [$\nu_s(SO_2)$].

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.87 (3H, d, J = 6.5, Me-7), 0.88–1.04 (1H, m, H-4*ax*), 0.95 (3H, d, J = 6.3, Me-10), 0.96 (3H, d, J = 6.5, Me-9), 1.23 (1H, ddd, J = 14.6, 12.8, 4.8, H-6*ax*), 1.35–1.45 (1H, m, H-2), 1.81–2.04 (4H, m, H-3*ax*, H-3*eq*, H-4*eq*, H-6*eq*), 2.09–2.28 (2H, m, H-8, H-5), 4.01 (3H, s, Me-6′), 4.09–4.14 (1H, m, H-1), 6.99 (1H, s, H-5′), 7.18 (1H, d, J = 0.9, H-4′).

^{13}C NMR spectrum (75 MHz, $CDCl_3$, δ, ppm): 21.78 (C-9), 21.82 (C-10), 22.31 (C-7), 25.01 (C-3), 26.62 (C-5), 29.23 (C-8), 35.20 (C-4), 35.37 (C-6′), 36.17 (C-6), 49.55 (C-2), 62.06 (C-1), 125.26 (C-5′), 129.24 (C-4′), 143.11 (C-2′). $C_{14}H_{24}N_2O_2S$.

1-Methyl-2-{[(1*R*,2*S*,5*R*)-6,6-dimethylbicyclo[3.1.1]heptyl-2]methylsulfonyl}-1*H*-imidazole (6). Light-yellow powder, mp 80–81°C, $[\alpha]_D^{20}$ –27.58° (*c* 0.30, EtOH). IR spectrum (ν, cm^{-1}): 1316 [$\nu_{as}(SO_2)$], 1124 [$\nu_s(SO_2)$].

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.98–1.07 (1H, m, H-7β), 1.04 (3H, s, Me-8), 1.20 (3H, s, Me-9), 1.61 (1H, ddt, J = 15.6, 10.3, 5.4, H-3α), 1.79–2.04 (4H, m, H-1, H-5, H-4α, H-4β), 2.06–2.19 (1H, m, H-3β), 2.35 (1H, dtd, J = 9.9, 6.1, 1.8, H-7α), 2.76–2.87 (1H, m, H-2), 3.59–3.64 (2H, m, H-10α, H-10β), 4.01 (3H, s, Me-6′), 7.02 (1H, s, H-5′), 7.16 (1H, s, H-4′).

^{13}C NMR spectrum (75 MHz, $CDCl_3$, δ, ppm): 21.72 (C-3), 23.08 (C-8), 25.91 (C-4), 27.58 (C-9), 32.51 (C-7), 34.65 (C-2), 35.15 (C-6′), 38.42 (C-6), 40.69 (C-5), 46.47 (C-1), 62.37 (C-10), 125.38 (C-5′), 129.00 (C-4′), 142.51 (C-2′). $C_{14}H_{22}N_2O_2S$.

1-Methyl-2-{[(1*R*,2*R*,5*R*)-6,6-dimethylbicyclo[3.1.1]heptyl-2]methylsulfonyl}-1*H*-imidazole (7). Light-yellow powder, mp 68–69°C, $[\alpha]_D^{20}$ +3.82° (*c* 0.61, EtOH). IR spectrum (ν, cm^{-1}): 1324 [$\nu_{as}(SO_2)$], 1122 [$\nu_s(SO_2)$].

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.88 (3H, s, Me-8), 1.23 (3H, s, Me-9), 1.37 (1H, d, J = 10.3, H-7β), 1.43–1.57 (1H, m, H-3α), 1.75–1.98 (5H, m, H-1, H-5, H-3β, H-4α, H-4β), 2.12 (1H, ddd, J = 10.6, 5.7, 5.5, H-7α), 2.76 (1H, quin, J = 7.4, H-2), 3.38–3.50 (2H, m, H-10α, H-10β), 4.01 (3H, s, Me-6′), 7.00 (1H, s, H-5′), 7.15 (1H, s, H-4′).

^{13}C NMR spectrum (75 MHz, $CDCl_3$, δ, ppm): 20.07 (C-8), 21.83 (C-3), 23.25 (C-7), 24.23 (C-4), 26.62 (C-9), 30.25 (C-2), 35.13 (C-6′), 39.57 (C-6), 40.26 (C-5), 45.62 (C-1), 61.15 (C-10), 125.29 (C-5′), 129.00 (C-4′), 142.80 (C-2′). $C_{14}H_{22}N_2O_2S$.

1-Methyl-2-{[(1*R*,3*S*,4*R*,6*S*)-4,7,7-trimethylbicyclo[4.1.0]heptyl]sulfonyl}-1*H*-imidazole (8). Light-beige powder, mp 97–98°C, $[\alpha]_D^{20}$ –5.59° (*c* 0.59, EtOH). IR spectrum (ν, cm^{-1}): 1308 [$\nu_{as}(SO_2)$], 1126 [$\nu_s(SO_2)$].

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.59 (1H, td, J = 8.7, 7.4, H-1), 0.74 (1H, q, J = 8.5, H-6), 0.98–1.08 (1H, m, H-5α), 1.01 (3H, s, Me-8), 1.03 (3H, s, Me-9), 1.20 (3H, d, J = 7.0, Me-10), 1.23–1.34 (1H, m, H-2α), 1.99 (1H, ddd, J = 13.9, 8.5, 3.7, H-2β), 2.13 (1H, dt, J = 15.3, 8.2, H-5β), 2.48 (1H, sept, J = 7.4, H-4), 3.74 (1H, ddd, J = 12.0, 7.4, 3.7, H-3), 4.01 (3H, s, Me-6′), 7.00 (1H, s, H-4′), 7.17 (1H, s, H-5′).

^{13}C NMR spectrum (75 MHz, $CDCl_3$, δ, ppm): 15.18 (C-9), 17.31 (C-2), 17.65 (C-10), 18.38 (C-7), 19.56 (C-6), 21.67 (C-1), 26.36 (C-4), 26.88 (C-5), 28.14 (C-8), 35.32 (C-6′), 62.70 (C-3), 125.22 (C-5′), 129.11 (C-4′), 142.35 (C-2′). $C_{14}H_{22}N_2O_2S$.

2-{[(1*S*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl]sulfonyl}-1*H*-benzimidazole (9). Pale-yellow powder, mp 223–224°C, $[\alpha]_D^{20}$ 0° (*c* 0.14, EtOH), $[\alpha]_D^{20}$ –33.57° (*c* 0.14, $CHCl_3$). IR spectrum (ν, cm^{-1}): 1332 [$\nu_{as}(SO_2)$], 1134 [$\nu_s(SO_2)$].

PMR spectrum (300 MHz, $CDCl_3$ + DMSO-d_6, δ, ppm, J/Hz): 0.71 (3H, d, J = 6.5, Me-7), 0.74–0.93 (1H, m, H-4*ax*), 0.78 (3H, d, J = 6.5, Me-10), 0.83 (3H, d, J = 6.7, Me-9), 1.10 (1H, ddd, J = 14.4, 12.9, 4.7, H-6*ax*), 1.26–1.36 (1H, m, H-2), 1.78–2.01 (4H, m, H-3*ax*, H-3*eq*, H-4*eq*, H-6*eq*), 2.05–2.19 (2H, m, H-8, H-5), 4.16–4.22 (1H, m, H-1), 7.36–7.42 (2H, m, H-5′, 6′), 7.69–7.74 (2H, m, H-4′, 7′), 13.86 (1H, br.s, NH).

^{13}C NMR spectrum (75 MHz, $CDCl_3$ + DMSO-d_6, δ, ppm): 21.66 (C-9), 21.66 (C-10), 22.16 (C-7), 25.03 (C-3), 26.48 (C-5), 29.42 (C-8), 35.03 (C-4), 35.96 (C-6), 49.27 (C-2), 62.09 (C-1), 112.43 (C-4′), 120.80 (C-7′), 123.02 (C-5′), 125.05 (C-6′), 148.51 (C-2′). $C_{17}H_{24}N_2O_2S$.

2-{[(1*R*,2*S*,5*R*)-6,6-Dimethylbicyclo[3.1.1]heptyl-2]methylsulfonyl}-1*H*-benzimidazole (10). Light-beige powder, mp 158–159°C, $[\alpha]_D^{20}$ –22.79° (*c* 0.38, EtOH). IR spectrum (ν, cm^{-1}): 1322 [$\nu_{as}(SO_2)$], 1144 [$\nu_s(SO_2)$].

PMR spectrum (300 MHz, $CDCl_3$ + DMSO-d_6, δ, ppm, J/Hz): 0.98 (1H, d, J = 10.0, H-7β), 1.01 (3H, s, Me-8), 1.15 (3H, s, Me-9), 1.65 (1H, ddt, J = 15.6, 10.3, 5.4, H-3α), 1.76–2.01 (4H, m, H-1, H-5, H-4α, H-4β), 2.06–2.19 (1H, m, H-3β), 2.33 (1H, dtd, J = 9.9, 6.0, 1.8, H-7α), 2.80–2.91 (1H, m, H-2), 3.68–3.76 (2H, m, H-10α, H-10β), 7.42–7.48 (2H, m, H-5′, 6′), 7.71–7.84 (2H, m, H-4′, 7′), 13.57 (1H, br.s, NH).

^{13}C NMR spectrum (75 MHz, $CDCl_3$ + DMSO-d_6, δ, ppm): 21.63 (C-3), 23.05 (C-8), 25.81 (C-4), 27.47 (C-9), 32.42 (C-7), 34.65 (C-2), 38.40 (C-6), 40.58 (C-5), 46.46 (C-1), 62.41 (C-10), 112.65 (C-4′), 121.53 (C-7′), 124.20 (C-5′), 126.25 (C-6′), 133.40 (C-3a′), 142.95 (C-7a′), 148.01 (C-2′). $C_{17}H_{22}N_2O_2S$.

2-{[(1*R*,2*R*,5*R*)-6,6-Dimethylbicyclo[3.1.1]heptyl-2]methylsulfonyl}-1*H*-benzimidazole (11). White powder, mp 166–167°C, $[\alpha]_D^{20}$ +2.13° (*c* 0.39, EtOH). IR spectrum (ν, cm^{-1}): 1328 [$\nu_{as}(SO_2)$], 1138 [$\nu_s(SO_2)$].

PMR spectrum (300 MHz, $CDCl_3$ + DMSO-d_6, δ, ppm, J/Hz): 0.85 (3H, s, Me-8), 1.19 (3H, s, Me-9), 1.36 (1H, d, J = 10.3, H-7β), 1.51 (1H, dq, J = 13.8, 9.0, H-3α), 1.76–1.98 (5H, m, H-1, H-5, H-3β, H-4α, H-4β), 2.12 (1H, ddd, J = 10.6, 5.7, 5.5, H-7α), 2.83 (1H, quin, J = 7.5, H-2), 3.45–3.59 (2H, m, H-10α, H-10β), 7.42–7.48 (2H, m, H-5′, 6′), 7.73–7.82 (2H, m, H-4′, 7′), 13.13 (1H, br.s, NH).

^{13}C NMR spectrum (75 MHz, $CDCl_3$ + DMSO-d_6, δ, ppm): 20.03 (C-8), 21.77 (C-3), 23.23 (C-7), 24.16 (C-4), 26.54 (C-9), 30.40 (C-2), 39.61 (C-6), 40.21 (C-5), 45.63 (C-1), 61.17 (C-10), 113.0 (C-4′), 120.70 (C-7′), 123.40 (C-5′), 125.03 (C-6′), 148.22 (C-2′). $C_{17}H_{22}N_2O_2S$.

2-{[(1*R*,3*S*,4*R*,6*S*)-4,7,7-Trimethylbicyclo[4.1.0]heptyl]sulfonyl}-1*H*-benzimidazole (12). White powder, mp 130–131°C, $[\alpha]_D^{20}$ +9.25° (*c* 1.07, EtOH). IR spectrum (ν, cm^{-1}): 1306 [$\nu_{as}(SO_2)$], 1140 [$\nu_s(SO_2)$].

PMR spectrum (300 MHz, $CDCl_3$ + DMSO-d_6, δ, ppm, J/Hz): 0.61 (1H, td, J = 8.7, 7.4, H-1), 0.72 (1H, q, J = 8.4, H-6), 0.93–1.09 (1H, m, H-5α), 0.99 (3H, s, Me-8), 1.00 (3H, s, Me-9), 1.30 (3H, d, J = 7.0, Me-10), 1.26–1.39 (1H, m, H-2α),

2.06 (1H, ddd, J = 14.1, 8.2, 3.5, H-2β), 2.16 (1H, ddd, J = 15.4, 8.4, 8.2, H-5β), 2.57 (1H, sept, J = 7.4, H-4), 3.88 (1H, ddd, J = 11.8, 7.6, 3.8, H-3), 7.43–7.49 (1H, m, H-6′), 7.62 (1H, ddd, J = 8.0, 2.0, 0.9, H-5′), 8.05 (1H, dt, J = 7.9, 1.2, H-7′), 8.14 (1H, t, J = 1.8, H-4′), 13.75 (1H, br.s, NH).

^{13}C NMR spectrum (75 MHz, $CDCl_3$ + DMSO-d_6, δ, ppm): 15.13 (C-9), 17.60 (C-2), 17.84 (C-10), 18.44 (C-7), 19.52 (C-6), 21.55 (C-1), 26.35 (C-4), 26.85 (C-2), 28.04 (C-8), 63.00 (C-3), 128.32 (C-7′), 129.84 (C-6′), 130.27 (C-4′), 131.14 (C-7a′), 133.79 (C-5′), 134.72 (C-3a′), 147.96 (C-2′). $C_{17}H_{22}N_2O_2S$.

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REFERENCES

1. T. Roth, M. L. Morningstar, P. L. Boyer, S. H. Hughes, R. W. Buckheit, and C. J. Michejda, *J. Med. Chem.*, **40**, 4199 (1997).
2. J. S. Kim, B. Gatto, C. Yu, A. Liu, L. F. Liu, and E. J. LaVoie, *J. Med. Chem.*, **39**, 992 (1996).
3. A. R. Porcari, R. V. Devivar, L. S. Kucera, J. C. Drach, and L. B. Townsend, *J. Med. Chem.*, **41**, 1252 (1998).
4. R. L. Lombardy, F. A. Tanious, K. Ramachandran, R. R. Tidwell, and W. D. Wilson, *J. Med. Chem.*, **39**, 1452 (1996).
5. H. Zarrinmayeh, A. M. Nunes, P. L. Z. D. M. Ornstein, M. B. Arnold, D. A. Schober, S. L. B. R. F. Gackenheimer, P. A. Hipskind, T. C. Britton, B. E. Cantrell, and D. R. Gehlert, *J. Med. Chem.*, **41**, 2709 (1998).
6. Z. Gua, D. Zhou, and P. G. Schultz, *Science*, **288**, 2042 (2000).
7. M. Artico, R. Silvestri, E. Pagnozzi, B. Bruno, E. Novellino, G. Greco, S. Massa, A. Ettorre, A. G. Loi, F. Scintu, and P. L. Colla, *J. Med. Chem.*, **43**, 1886 (2000).
8. J. J. Talley, S. R. Bertenshaw, D. L. Brown, J. S. Carter, M. Graneto, M. S. Kellog, C. M. Koboldt, J. Yuan, Y. Y. Zhang, and K. Seibert, *J. Med. Chem.*, **43**, 1661 (2000).
9. A. Scozzafava and C. T. Supuran, *J. Med. Chem.*, **43**, 1858 (2000).
10. V. V. Plemenkov, *Chemistry of Isoprenoids: Student Aid* [in Russian], Izd. Altaiskogo Univ., Barnaul (2007).
11. R. N. Salvatore, R. A. Smith, A. K. Nischwitz, and T. Gavin, *Tetrahedron Lett.*, **46**, 8931 (2005).
12. M. Ya. Demakova, D. V. Sudarikov, S. A. Rubtsova, P. A. Slepukhin, and A. V. Kuchin, *Khim. Prir. Soedin.*, 789 (2011).