Polish J. Chem., **77**, 203–210 (2003)

Amidation-Sulfonation of Selected Unsaturated Monoterpenes

by M. Wełniak

Faculty of Chemistry, Nicolaus Copernicus University, 87-100 Toruń, Poland

(Received September 16th, 2002; revised manuscript December 12th, 2002)

Amidation-sulfonation of (+)-camphene (**1**), (–)-β- and (–)-α-pinene (**3,4**), (+)-limonene (**5**), (+)-2-carene (**16**), and (+)-carvone (**21**) with a mixture of 25% oleum and aceto- or propionitrile is described. Camphene (**1**) gave racemic *exo*-2-amidobornanesulfonic acids (**8,9**), whereas **3** and **4** produced optically active *p*-mentheneamidosulfonic acids (**10–15**). Under the same reaction conditions 1,4-addition to (+)-2-carene (**16**) leading to (1*R*,4*R*)-(–)-4-(1-acetylamino-1-methylethyl)-1-methyl-cyclohex-2-enesulfonic acid (**17**) was observed. Mixtures of diastereomeric structural terpene analogues of N-acetyltaurine were obtained from **5** and **21**. Mechanisms of the investigated reactions are proposed.

Key words: terpenes, Ritter reaction, amidation-sulfonation, rearrangements

As described in [1–3], alkenes react with sulfur trioxide or its complex with 1,4-dioxane to give stereospecifically β-sultones or cyclic sulfonate-sulfate anhydrides (carbyl sulfates). For example, reaction of (+)-camphene (**1**) with sulfur trioxide-1,4-dioxane complex leads to 10-isobornyl sultone (**2**) [3] (Fig. 1). These compounds are readily hydrolyzed in the presence of water or alcohols to form 2-hydroxy-, vinyl- or allyl sulfonic acid [4,5]. When carbyl sulfates are treated with wet acetonitrile it is possible to obtain β-acetamidosulfonic acids [6]. Another method of the last mentioned acids preparation is the Ritter reaction [7] of simple terminal alkenes with a mixture of nitriles and fuming sulfuric acid so far described in few patents [8,9]. The resulted β-amidosulfonic acids were used as foam stabilizers and, after hydrolysis to the respective β-aminosulfonic acids, in plant protection and as viral antimetabolites. This method, to our best knowledge, was not employed in terpene chemistry. In continuation of our studies [10–14] on the Ritter reaction of terpenes, we explored the synthesis of new sulfonated amides by the action of oleum in nitriles on selected chiral monoterpene alkenes. Marschoff and coworkers [15,16] reported that (–)-β-pinene (**3**), (–)-α-pinene (**4**), and (+)-limonene (**5**), upon a reaction in the presence of perchloric acid gave enantiospecifically 3-aza-bicyclo[3.3.1]non-2-ene systems (**6** and **7**) (Fig. 1). The proposed mechanism involved initial protonation of a double bond prior to substitution of an acetonitrile molecule, cyclization and the reaction with another molecule of acetonitrile. As sulfur trioxide can also add to a double bond, we expected that syntheses planned by us will proceed similarly. However, when a stoichiometric amount (with respect to sulfur trioxide) of 25% oleum was used as sulfonating agent, no cyclization was observed for any terpene alkene studied.

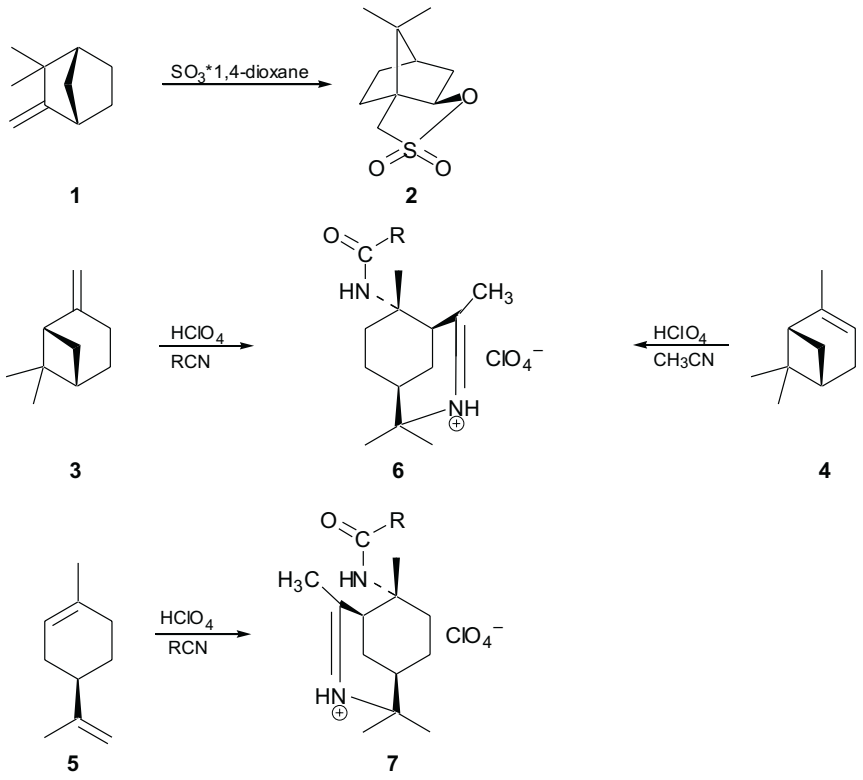


Figure 1.

RESULTS AND DISCUSSION

The reaction of camphene (**1**) with 25% oleum in acetonitrile at –30°C to 20°C for 18 h gave racemic *exo*-2-acetamido-10-bornanesulfonic acid (**8**) in 46% yield. Its structure was confirmed by ^{1}H-, ^{13}C-NMR and IR spectroscopy. The ^{1}H-NMR spectrum showed, apart from other signals, an AB-type pattern for the $-CH_2SO_3H$ group. The *exo*-position of the acetamide substituent was corroborated by the doublet of doublets at δ 3.82 (J = 9 Hz, J = 4.5 Hz) characteristic of the 2-substituted bornane derivatives [17]. The ^{13}C-NMR spectrum revealed the presence of an acetamide group at δ 173.94. The IR spectrum displayed strong absorption bands at 655, 1170 and 1209 cm^{-1} characteristic for sulfonic acids. The formation of **8** can be explained by an initial addition of sulfur trioxide to the double bond of camphene (**1**) followed by the Wagner-Meerwein rearrangement, 6,2-hydride shift leading to racemization, and an attack of acetonitrile from the *exo*-side (Fig. 2). In propionitrile, *exo*-2-propioamido-10-bornane sulfonic acid (**9**) was obtained in 46% yield. Optically active acids **10** and **11** were obtained in 63% and 45% yield, by amidation-sulfonation of (–)-β-pinene (**3**) in aceto- or propionitrile. Initial addition of sulfur trioxide to a double bond le-

ads to a tertiary carbonium ion **12**, which is transformed into a cation **13** with a cyclobutane ring opening and simultaneous formation of an internal double bond (Fig. 2). The cation **13** is attacked by acetonitrile to form **10** with a retention of configuration at the C-4 atom. The structure of **10** was supported by the presence of signals at δ 129.27 and δ 130.29 for trisubstituted double bond in the ^{13}C-NMR spectrum. The initial attack of sulfur trioxide on a double bond followed by the rearrangement to the *p*-menthene system was also observed for (–)-α-pinene (**4**). The *trans* position of the sulfonyl group relative to the isopropyl group in acetamidosulfonic acid (**14**) is probably due to steric effects. This assumption is supported by the coupling constant value of a doublet centered at δ 3.35 (J = 4 Hz, 1H) characteristic of axial-equatorial interactions. The reaction of (+)-2-carene (**16**) in acetonitrile gave amidoacid **17**. Its structure was established by ^{1}H- and ^{13}C-NMR spectroscopy (see Experimental). The structure of **17** points to its formation by the 1,4-addition process to a conjugated system of the double bond and the cyclopropane ring. An analogous situation was described in [18] for a free-radical addition of ethanethiol to **16**. We have no direct evidence of the stereochemistry of the C-1 atom but we assume *R*-configuration, due a steric hindrance in the initial stage of amidation-sulfonation. The addition of sulfur trioxide to (+)-limonene (**5**) proceeded selectively to the isopropenyl group producing the cation **18**, which reacted with acetonitrile to give a mixture of diastereomers **19a**/**b** as indicated by duplicated signals in the ^{13}C-NMR spectrum (see Experimental). For comparison, (+)-carvone (**21**) was subjected to the same amidation-sulfonation reaction an analogous regioselectivity was observed, and a mixture of diastereomeric products **22a**/**b** was obtained (Fig. 2). The ^{1}H-NMR spectrum of a mixture **22a/22b** in D_2O displayed three methyl groups at δ 1.26, 1.55 and 1.80, two one-proton separated doublets centered at δ 2.97 (J = 5 Hz) and δ 3.05 (J = 5 Hz) for each diastereomer. An additional doublet (δ 3.56, J = 14 Hz) is attributed to the second proton of the $-CH_2SO_3H$ group of both components of the mixture. The structure of the compounds investigated **22a**/**22b** was confirmed by NOE experiments. Thus, irradiation of a doublet δ 3.56 characteristic for the $-CH_2SO_3H$ group resulted in enhancement of signals at δ 2.97 and 3.05 (25%) and a multiplet of the H-1 cyclohexenyl proton (δ 1.80, 7%) in agreement with the postulated structure. The ^{1}H-NMR spectrum of a mixture of **22a/22b** in DMSO-d_6 showed a doublet (δ 8.01, J = 2 Hz) for NH proton. Upon irradiation it displayed NOE correlation with a methyl singlet (δ 1.75) attributed to a $-CH_3$ group connected to the C-2 (14%) and a multiplet of the H-1 cyclohexenyl proton (δ 2.94, 5%) with the methyl group (CH_3CONH-) at δ 1.42 (25%). It is noteworthy that ^{1}H-NMR spectrum in DMSO-d_6 showed, contrary to that in D_2O, two methyl singlets for an acetamide group and two separate AB systems for a $-CH_2SO_3H$ group (see Experimental) for each diastereomer. Additionally, molecular structures of acids **22a**/**22b** and **23a**/**23b** were assigned by high resolution mass spectrometry as $C_{12}H_{19}NO_5S$ and $C_{13}H_{21}NO_5S$, respectively.

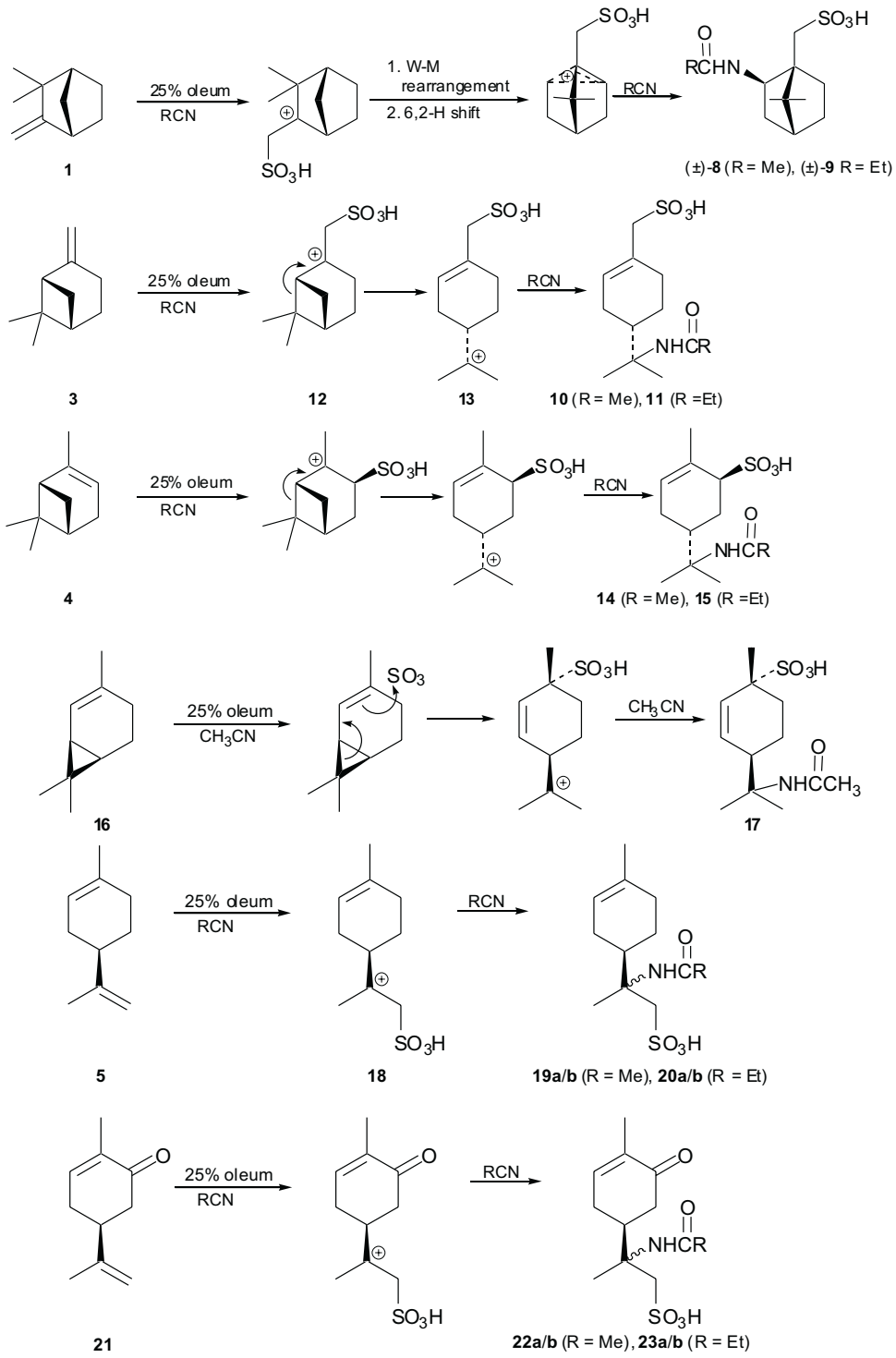
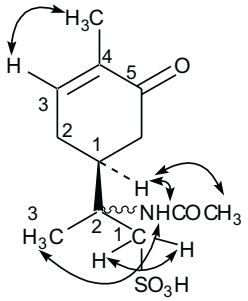

25% oleum
RCN
1. W-M rearrangement
2. 6,2-H shift
RCN
1
(±)-8 (R = Me), (±)-9 R = Et)
3
12
13
10 (R = Me), 11 (R =Et)
4
14 (R = Me), 15 (R =Et)
CH3CN
16
17
5
18
19a/b (R = Me), 20a/b (R = Et)
21
22a/b (R = Me), 23a/b (R = Et)

Figure 2.



Selected NOE's for **22a/22b**

Figure 3.

In conclusion, we have described a simple synthetic method of an unknown amidosulfonic monoterpene acids **8–15**, **17**, **19a/b**, **20a/b**, **22a/b**, and **23a/b**. Considering the relative ease of hydrolysis of acetamides to amines, it may be also a route to the respective aminosulfonic acids. According to literature, sulfonated amides or amines, especially structural analogues of taurine, the known component of bile acid, exhibit various biological activities [19–27]. For example, potassium salt of *N*-acetyltaurine reveals neuromuscular action [19] and *N*-acetyl-2-(4-chlorophenyl)propanesulfonic acid is a powerful specific antagonist of GABA [20].

EXPERIMENTAL

Melting points were measured on a Boetius apparatus and were uncorrected. ^{1}H- and ^{13}C- NMR spectra were recorded in D_2O or DMSO-d_6 solutions with a Varian Gemini 200 spectrometer. IR absorption spectra were taken with Perkin Elmer Spectrum RX spectrophotometer in hexachlorobutadiene. Optical rotations were measured with a POL S-2 polarimeter. (+)-Camphene (**1**), (1*S*)-(–)-β-pinene (**3**), (1*S*)-(–)-α-pinene (**4**), (*R*)-(+)-limonene (**5**), (+)-2-carene (**16**), and (*S*)-(+)-carvone (**21**) were purchased from Aldrich.

Amidation-sulfonation of (+)-camphene (1), (+)-limonene (5), and (+)-carvone (21). General Procedure. 2cc of 25% oleum (40 mmol of SO_3) was added dropwise at –30 °C to 40 mmol (5.4 g of **1** and **5** or 6.0 g of **21**) in acetonitrile or propionitrile (30 cc). The reaction mixture was allowed to attain room temperature and stirred for 24 h to observe gradual precipitation of a crystalline product. The resulted solids were filtered off and rinsed with Et_2O to give: a) for alkene **1**: (+/–)-*exo*-2-acetamido-10-bornanesulfonic acid (**8**): 5.1 g (46%). M.p. 256–258°C (dec.) (EtOH/EtOAc (2:1)). ^{1}H-NMR (D_2O), δ: 0.72 (s, 3H, CH_3), 0.80 (s, 3H, CH_3), 1.08 (m, 1H), 1.32–1.92 (m, 6H), 1.84 (s, 3H, CH_3), 2.70 (d, 1H, J = 14 Hz) and 3.19 (d, 1H, J = 14 Hz) for $-CH_2SO_3H$, 3.82 (dd, J = 9 Hz, J = 4.5 Hz $H_{2\text{-}endo}$); ^{13}C-NMR (D_2O), δ: 20.40 (CH_3), 20.52 (CH_3), 22.60 (CH_3), 27.54 (CH_2), 33.71 (CH_2), 40.30 (CH_2), 45.17 (CH), 49.22 (C), 49.80 (C), 50.56 (C), 56.60 (CH), 173.94 (C). IR (cm^{-1}): 655, 1170, 1209, 1563, 1651, 3224. Anal. Calcd. for $C_{12}H_{21}NO_4S$: C, 52.33; H, 7.68. Found C, 52.25; H 7.82 or (+/–)-*exo*-2-propioamido-10-bornanesulfonic acid (**9**): 5.3 g (46%). M.p. 245–247°C (dec.) (EtOH). ^{1}H-NMR (D_2O), δ: 0.72 (s, 3H, CH_3), 0.80 (s, 3H, CH_3), 0.92 (t, 3H, J = 8 Hz, CH_3), 1.05–1.85 (m, 7H), 2.09 (q, 2H, J = 16 Hz, J = 8 Hz, CH_2), 2.70 (d, 1H, J = 14 Hz) and 3.17 (d, 1H, J = 14 Hz) for $-CH_2SO_3H$; 3.79 (dd, 1H, J = 10 Hz, J = 4Hz, $H_{2\text{-}endo}$); ^{13}C-NMR (D_2O), δ: 10.67 (CH_3), 20.39 (CH_3), 20.50 (CH_3), 27.51 (CH_2), 29.78 (CH_2), 33.64 (CH_2), 40.41 (CH_2), 45.15 (CH), 49.20 (C), 49.75 (CH_2), 50.53 (C), 56.35 (CH_2), 177.77 (C). IR (cm^{-1}): 655, 982, 1035, 1145, 1234, 1561, 1678, 3182. Anal. Calcd. for $C_{13}H_{23}NO_4S$: C, 53.95; H 8.02. Found C, 54.10; H 8.08; b) for (+)-limonene (**5**): (2*R*/*S*)-2-[(*S*)-4-methyl-cyclohex-3-enyl]-2-propionyl-amino-propane-1-

sulfonic acids (**19a**/**b**): 6.0 g (55%); $[\alpha]_D^{22}$ = 11.9 (c = 3.2, MeOH); M.p. 218–219°C (dec.), (MeOH/EtOAc (1:1)) (diastereomeric ratio *ca.* 1:1 (NMR)). ^{1}H-NMR (D_2O), δ: 1.20 and 1.22 (2s, 6H, $2CH_3$), 1.48 (b.s, 6H, 2 CH_3), 1.55–2.00 (m, 12H), 1.78 and 1.82 (2s, 6H, $2CH_3$, 2 $NHCOCH_3$), 2.15 (m, 2H), 3.02 (d, 1H, J = 9 Hz) and 3.4 (d, 1H, J = 15 Hz) for $–CH_2SO_3H$ of one diastereomer, 3.08 (d, 1H, J = 9 Hz) and 3.58 (d, 1H, J = 15 Hz) for $–CH_2SO_3H$ of the second diastereomer, 5.30 (m, 2H, for both diastereomers); ^{13}C-NMR (D_2O), δ: 19.85 ($2CH_3$), 23.31 ($2CH_3$), 23.45 (CH_3), 23.64 (CH_3), 23.85 (CH_2), 24.77 (CH_2), 26.11 (CH_2), 26.88 (CH_2), 31.44 (CH_2) and 31.53 (CH_2), 40.89 (CH) and 41.13 (CH), 54.97 (CH_2) and 55.10 (CH_2), 58.67 (C), 58.81 (C), 121.11 (CH), and 121.23 (CH), 136.55 (C) and 136.65 (C), 174.72 (C) and 174.92 (C) for two diastereomers **19a/b**. IR (cm^{-1}): 1031, 1131, 1234, 1574, 1673, 3105, 3263. Anal. Calcd. for $C_{12}H_{21}NO_4S$: C 52.33; H 7.68. Found C, 52.41; H, 7.48 or (2*R*/*S*)-2-[(*S*)-4-methyl-cyclohex-3-enyl]-2-propionylamino-propane-1-sulfonic acids (**20a/b**): 5.1 g (44%). M.p. 198–199°C (MeOH/EtOH (1:1)). $[\alpha]_D^{22}$ = 17.4 (c = 12.3, MeOH). ^{1}H-NMR (D_2O) δ: 0.90 (t, 6H, J = 7 Hz, $2CH_3$ for $–NHCOCH_2CH_3$), 1.20 (s, 3H, CH_3) and 1.22 (s, 3H, CH_3) for two diastereomers, 1.44 (s, 6H, $2CH_3$), 1.50–2.30 (m, 14H), 2.04 (q, 2H, J = 16 Hz, J = 6 Hz) and 2.06 (q, 2H, J = 16 Hz, J = 6 Hz) for $–NHCOCH_2CH_3$ of **20a** and **20b**, 2.98 (d, 1H, J = 9 Hz) and 3.43 (d, 1H, J = 13 Hz) for $–CH_2SO_3H$ of one diastereomer, 3.05 (d, 1H, J = 9 Hz) and 3.56 (d, 1H, J = 13 Hz) for $–CH_2SO_3H$ of the second diastereomer, 5.85 (bs, 2H, 2HC=C). ^{13}C–NMR (D_2O), δ: 10.26 ($2CH_3$), 19.58 ($2CH_3$), 23.28 ($2CH_3$), 23.72 (CH_2), 24.68 (CH_2), 26.02 (CH_2), 26.76 (CH_2), 30.60 (CH_2), 30.69 (CH_2), 31.34 (2 CH_2), 40.86 (CH), 40.99 (CH), 55.08 (2 CH_2), 58.11 (C), 58.20 (C), 121.10 (2 CH), 136.41 (C), 136.48 (C), 178.17 (C) and 178.30 (C); IR (cm^{-1}): 1080, 1142, 1250, 1570, 1668, 3280. Anal. Calcd. for $C_{13}H_{23}NO_4S$: 53.95; H, 8.02. Found C, 53.90; H, 8.12; c) for (+)-carvone (**21**): (2*R*/*S*)-acetylamino-2-[(*S*)-4-methyl-5-oxo-cyclohex-3-enyl]-propane-1-sulfonic acids (**22a/b)**: 5.1 g (44%). M.p. 215–216°C (EtOH); $[\alpha]_D^{22}$ = –40.6 (c = 3.2, EtOH); ^{1}H-NMR (D_2O), δ: 1.26 (s, 6H, $2CH_3$), 1.55 (s, 6H, $2CH_3$), 1.80 (s, 6H, $2CH_3$), 2.05–2.38 (m, 8H), 1.80 (m, 2H, H-4 of both diastereomers), 2.97 (d, 1H, J = 4 Hz) and 3.05 (d, 1H, J = 4 Hz) for $–CH_2SO_3H$ of one isomer and 3.56 (d, 2H, J = 14 Hz) for $–CH_2SO_3H$ of both isomers, 6.85 (bs, 2H, HC=C). ^{1}H-NMR (DMSO-d_6) δ: 1.38 (s, 3H, CH_3) and 1.42 (s, 3H, CH_3) for two isomers, 1.62 (s, 6H, $2CH_3$), 1.75 (s, 6H, $2CH_3$), 2.10–2.35 (m, 8H), 2.55 (d, 1H, J = 4Hz) and 2.82 (d, 1H, J = 6Hz) for $–CH_2SO_3H$ of one diastereomer, 2.65 (d, 1H, J = 4 Hz) and 2.90 (d, 1H, J = 6 Hz) for $–CH_2SO_3H$ of the second isomer, 2.98 (m, 2H, H-4 for both isomers), 6.82 (bs, 2H, HC=C for both isomers) and 8.01 (d, 2H,J = 2Hz, NH); ^{13}C-NMR (D_2O), δ: 14.50 (CH_3), 14.52 (CH_3), 19.12 (CH_3), 19.30 (CH_3), 22.73 ($2CH_3$), 26.13 (CH_2), 26.86 (CH_2), 37.84 (CH_2), 38.64 (CH_2), 40.64 (CH), 40.80 (CH), 53.57 ($2CH_2$), 56.28 (2C), 134.09 (C), 134.20 (C), 149.20 (CH), 149.38 (CH), 173.85 (2C), 204.10 (C), 204.58 (C), NOE (D_2O), δ: 3.56→2.97 and 3.05 (25%), 3.56→1.80 (7%). NOE (DMSO-d_6), 8.01→1.75 (14%), 8.01→2.98 (5%) and 8.01→1.42 (2.5%). IR (cm^{-1}): 992, 1120, 1270, 1558, 1640, 1652, 3268. ES MS (negative mode): 288.0, 228.9, 79.8. Anal. Calcd. for $C_{12}H_{19}NO_5S$: C, 48.43; H, 6.62. Found C, 48.53; H, 6.70 or (2*R*/*S*)-2-[(*S*)-4-methyl-5-oxo-cyclohex-3-enyl)-propane-1-sulfonic acids (**23a**/**b**): 5.6 g (46%). M.p. 210–212°C (MeOH). $[\alpha]_D^{22}$ = –13.3 (c = 3.0, EtOH). ^{1}H-NMR (DMSO-d_6) δ: 0.95 (t, 6H, J = 7Hz, $2CH_2CH_3$), 1.41 (s, 3H, CH_3) and 1.43 (s, 3H, CH_3) for two isomers, 1.63 (s, 6H, $2CH_3$) for both isomers, 2.01 (q, 4H, J = 16 Hz, J = 7 Hz, 2 CH_2CH_3), 2.10–2.35 (m, 8H), 2.61 (d, 1H, J = 6 Hz) and 2.87 (d, 1H, J = 6 Hz) for $–CH_2SO_3H$ of one isomer and 2.68 (d, 1H, J = 6 Hz) and 2.94 (d, 1H, J = 6 Hz) for the second isomer ($–CH_2SO_3H$), 2.99 (m, 2H, H-4 of both isomers), 6.82 (bs, 2H, 2 HC=C), 8.05 (d, 2H, J = 4 Hz, 2 NH); ^{13}C-NMR (DMSO-d_6), δ: 9.82 ($2CH_3$), 15.12 ($2CH_3$), 21.15 ($2CH_3$), 26.86 ($2CH_2$), 29.83 ($2CH_2$), 39.03 ($2CH_2$), 40.79 (CH), 41.01 (CH), 54.56 (C), 55.87 (CH_2), 55.88 (CH_2), 133.75 (C), 133.92 (C), 146.21 (2 CH), 172.60 (2C), 199.51 (C), and 199.46 (C). ES MS (negative mode): 302.0, 228.9, 79.8. IR (cm^{-1}): 981, 1108, 1262, 1563, 1644, 1652, 1666 and 3252. Anal. Calcd. for $C_{13}H_{21}NO_5S$; C, 51.46; H, 6.97. Found C, 51.62; H, 7.10.

Amidation-sulfonation of (–)-β-pinene (3), (–)-α-pinene (4) and (+)-2-carene (16). General Procedure. 2cc of 25% oleum (40 mmol of SO_3) was added dropwise at –30°C to 5.4 g (40 mmol) of the respective alkene in acetonitrile or propionitrile (30 cc). The reaction mixture was allowed to attain room temperature and stirred for 2 h to observe a formation of a gummy product. Then, the liquid was decanted and the residue was treated with 100 cc of Et_2O to observe slow transformation into solid when stirred. The products obtained were filtered off, washed with Et_2O and crystallized to obtain: a) for (–)-β-pinene (**3**): (–)-[(4*S*)-1-acetylamino-1-methyl-ethyl)-cyclohex-1-enyl]-methanesulfonic acid (**10**): 6.9 g (63%). M.p. 210–212°C (dec.) (EtOH : Et_2O, 1:1). $[\alpha]_D^{23}$ = –69.9° (c = 2.3, MeOH). ^{1}H-NMR (DMSO-d_6), δ: 1.05 (s, 3H, CH_3), 1.08 (s, 3H, CH_3), 1.15–2.12 (m, 7H), 1.77 (s, 3H, CH_3), 3.14 (s, 2H, $–CH_2SO_3H$), 5.46 (m, 1H,

HC=C), 7.40 (s, 1H, NH); ^{13}C-NMR (D_2O), δ: 23.82 (CH_3), 24.09 (CH_3), 24.25 (CH_3), 24.55 (CH_2), 27.41 (CH_2), 30.04 (CH_2), 41.05 (CH), 57.34 (C), 59.79 (CH_2), 129.97 (C), 130.29 (CH), 174.13 (C). IR (cm^{-1}): 1072, 1223, 1562, 1663, 3170. Anal. Calcd. for $C_{12}H_{21}NO_4S$: C, 52.33; H, 7.68. Found C, 52,15; H, 7.75 or (–)-[(4*S*)-(1-methyl-1-propionyl-amino-ethyl)-cyclohex-1-enyl]-methanesulfonic acid (**11**): 5.2 g (45%). M.p. 193–194°C (EtOH). $[\alpha]_D^{22}$= –37.5 (c = 3.2, EtOH). ^{1}H-NMR (D_2O), δ: 0.90 (t, 3H, J = 8 Hz, CH_3), 1.08 (s, 3H, CH_3), 1.10 (s, 3H, CH_3), 1.20–2.20 (m, 7H), 2.02 (q, 2H, J = 14 Hz, J = 8 Hz, –CH_2CH_3), 3.38 (s, 2H, –C**H**$_2SO_3H$), 5.60 (m, 1H, HC=C); ^{13}C-NMR (D_2O), δ: 10.80 (CH_3), 23.85 (CH_3), 24.20 (CH_3), 24.52 (CH_2), 27.36 (CH_2), 29.98 (CH_2), 30.89 (CH_2), 57.11 (C), 59.73 (CH_2), 129.97 (C), 130.22 (CH), 178.31 (C). IR (cm^{-1}): 1040, 1170, 1556, 1650, 3290. Anal. Calcd. for $C_{21}H_{13}NO_4S$: C, 53.95; H, 8.02. Found C, 53.83; H, 7.95. b) for (–)-α-pinene (**4**): (1*S*,5*R*)-(–)-5-(1-acetylamino-1-methyl-ethyl)-2-methylcyclohex-2-enesulfonic acid (**14**): 5.6 g (51%). M.p. 214–216°C (Et_2O/EtOH (2:1)). $[\alpha]_D^{22}$ = –86.8° (c = 5.0, H_2O). ^{1}H-NMR (D_2O), δ: 1.10 (s, 3H, CH_3), 1.15 (s, 3H, CH_3), 1.28 (m, 2H), 1.75 (s, 3H, CH_3), 1.78 (s, 3H, CH_3), 1.85 (m, 1H), 2.15 (d, 1H, J = 12 Hz, CH), 2.40 (m, 1H), 3.35 (d, 1H, J = 4 Hz, CH), 5.62 (bs, 1H, HC=C); ^{13}C-NMR (D_2O), δ: 23.66 (CH_3), 23.92 (CH_3), 24.10 (CH_3), 24.14 (CH_3), 27.05 (CH_2), 27.51 (CH_2), 57.05 (C), 62.68 (CH), 129.18 (C), 129.28 (CH), 174.15 (C). IR (cm^{-1}): 1134, 1164, 1213, 1249, 1564, 1644, 3091, 3344. Anal. Calcd. for $C_{12}H_{21}NO_4S$: C, 52.33; H, 7.68. Found C, 52.48; H, 7.81 or (1*S*,5*R*)-(–)-2-methyl-5-(1-methyl-1-propionylamino-ethyl)-cyclohex-2-enesulfonic acid (**15**): 5.3 g (46%). M.p. 219–221°C (Et_2O/EtOH (2:1)). $[\alpha]_D^{22}$ = –44.0° (c = 5.0, H_2O). ^{1}H-NMR (D_2O), δ: 0.93 (t, 3H, J = 8 Hz, CH_3), 1.08 (s, 3H, CH_3), 1.17 (s, 3H, CH_3), 1.45 (m, 1H), 1.72 (s, 3H, CH_3), 1.85 (m, 1H), 2.03 (q, 2H, J = 12 Hz, J = 6 Hz, –C**H**$_2CH_3$), 2.17 (d, 1H, J = 12 Hz), 2.40 (m, 1H), 3.45 (d, 1H, J = 5 Hz), 5.60 (bs, 1H, HC=C); ^{13}C-NMR (D_2O), δ: 10.28 (CH_3), 23.67 (CH_3), 23.80 (CH_3), 23.99 (CH_3), 26.26 (CH_2), 26.92 (CH_2), 35.74 (CH_2), 54.92 (C), 61.03 (CH), 124.96 (CH), 130.84 (C), 172.97 (C). IR (cm^{-1}): 635, 1019, 1151, 1176, 1555, 1640, 3185, 3334. Anal. Calcd. for $C_{13}H_{23}NO_4S$: C, 53.95; H, 8.02. Found C, 53.82; H, 8.10. c) for (+)-2-carene (**16**):(1*R*,4*R*)-(–)-(1-acetylamino-1-methyl-ethyl)-1-methyl-cyclohex-2-enesulfonic acid (**17**): 4.8 g (44%). M.p. 218–219°C. $[\alpha]_D^{22}$ = 70.6° (c = 3.0, MeOH). ^{1}H-NMR (DMSO-d_6), δ: 1.08 (s, 3H, CH_3), 1.15 (s, 3H, CH_3), 1.19 (s, 3H, CH_3), 1.60 (m, 3H), 1.77 (s, 3H, CH_3), 1.94 (m, 1H), 2.80 (m, 1H), 5.55 (d, 1H, J = 10 Hz), 5.70 (dd, 1H, J = 10 Hz, J = 2 Hz), 7.44 (s, 1H, NH); ^{13}C-NMR (D_2O), δ: 20.87 (CH_2), 23.10 (CH_3), 23.38 (CH_3), 23.78 (CH_3), 24.13 (CH_3), 30.41 (CH_2), 42.84 (CH), 57.68 (C), 60.34 (C), 129.82 (CH), 131.92 (CH), 174.64 (C). IR (cm^{-1}): 1021, 1150, 1226, 1557, 1651, 1672, 3026, 3156. Anal. Calcd. for $C_{12}H_{21}NO_4S$: C, 52.33; H, 7.68. Found C, 52.50; H, 7.58.

Acknowledgment

The assistance in ES MS measurements done at EPSRC National Center, Swansea, Wales, is gratefully acknowledged.

REFERENCES

1. Roberts D.W. and Williams D.L., *Tetrahedron*, **43**, 1027 (1987).
2. Nagayama M., Okamura O., Noda S., Mandai H. and Mori A., *Bull. Soc. Chim. Jpn*., **47**, 2158 (1974).
3. Lipp P. and Holl M., *Chem. Ber*., **62**, 499 (1929).
4. Nakanishi S. and Yoshimura F., *Kogyo Kagaku Zasshi*, **74**, 2297 (1971); *C.A*., **76**, 45782 s (1972).
5. Bordwell F.G. and Osborne C.E., *J. Am. Chem. Soc*., **81**, 2000 (1959).
6. Sheehan J.C. and Zoller U., *J. Org. Chem*., **40**, 1179 (1975).
7. Ritter J.J. and Kalish J., *J. Am. Chem. Soc*., **70**, 4048 (1948).
8. Killam H.S., U.S. Pat. 3544597; *C.A*., **74**, 141314v (1971).
9. Arlt D., Neth. Pat. 6611091; *C.A.,* **67**, 11213f (1967).
10. Wełniak M., *Polish J. Chem.,* **70**, 752 (1996).
11. Wełniak M., *Polish J. Chem.,* **72**, 1021 (1998).
12. Wełniak M., *Polish J. Chem.,* **75**, 55 (2001).
13. Wełniak M., *Polish J. Chem.,* **76**, 37 (2002).
14. Wełniak M., *Polish J. Chem.,* **76**, 1405 (2002).

15. Rodriguez J.B., Gros E.G., Caram J.A. and Marschoff C.M., *Tetrahedron Lett.,* 7825 (1995).
16. Samaniego W.N., Baldessari A., Ponce M.A., Rodriguez J.B., Gros E.G. Caram J.A. and Marschoff C.M., *Tetrahedron Lett*., 6967 (1994).
17. Flaut T.I. and Erman W.F., *J. Am. Chem. Soc.*, **85**, 3212 (1963).
18. Pattenden G. and Smithies A.J., *J. Chem. Soc. Perkin Trans. 1*, 57 (1995).
19. Durlach J.P., Ger. Pat. 2810918; *C.A*., **90**, 122047 z (1978).
20. Abbenante G.Y. and Prager R.H., *Austr. J. Chem*., **95**, 1791 (1992).
21. Abbenante G.Y. and Prager R.H., *ibid*. p. 1801.
22. Petegnief V., Lleu, P-L., Gupta R.C., Bourguignon I-J. and Rabel G., *Biochem. Pharmacol*., **49**, 399 (1995).
23. Satake M., Chiba Y., Mahuta M., Fujita T., Kohama Y. and Mimura T., *Yakugaku Zasshi*, **107**, 917 (1987); *C.A*., **108**, 48744w (1988).
24. Shue H.J., Chen X., Blytkin D.J., Carruthers N.I. and Spitler J.H., *Bioorg. Med. Chem. Lett.,* **6**, 1709 (1996).
25. Campagna F., Carotti A., Casini G., Palluotto F. and Pierno S., *Farmaco*, **49**, 653 (1994).
26. Rosowsky A., Forsch R.A., Moran R.G., Kohler W. and Freisheim J.H*., J. Med. Chem.,* **31**, 1326 (1988).
27. Kunihiko H., Hiroe M., Hirohide M., Yoshio T. and Kazuharu I., *J. Chem. Soc. Perkin Trans. 1*, 1479 (1989).