Amino-Sulfonation of Alkenes in a Three-Component Reaction[‡]

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Keywords: Amino-sulfonation / Electrophilic additions / Multicomponent reactions / Sulfur trioxide complexes / Taurine

2-Aminoalkanesulfonic acids have been synthesized by a three-component alkene/SO_3·DMF/acetonitrile reaction, followed by hydrolysis. Trifluoromethanesulfonic acid was added to the amino-sulfonation mixture to accelerate the reaction and prevent the competitive formation of by-products. The reported two-step procedure provided a concise and versatile approach to new analogues of the natural amino acid taurine.

Introduction

Taurine (2-aminoethanesulfonic acid) is a conditionally essential amino acid found in very high concentrations in excitable tissues, where it plays key roles in the regulation of several biological processes.[1] The mechanism and site of taurine polyvalent functions are basically unknown. Taurine is a conformationally flexible molecule with only small steric demand, and its analogues are very useful for study of its biological activity and receptor-bound conformations.

The need for new 2-aminosulfonic acids as taurine surrogates prompted us to search for a rapid and general synthetic approach to these compounds.

The amino-sulfonation (AS) of alkenes was an appealing strategy because of the introduction of both the amino and the sulfonic acid moieties in the same step, and also because of the potential to obtain a large assortment of products starting from easily available substrates.

The three-component alkene/SO_3/nitrile reaction has to date been reported in very few papers,[2] its scope being limited because of the poor yields and chemoselectivity.

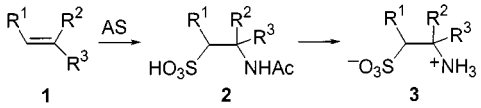
One practical problem in running the AS reaction, especially in a research laboratory, concerned the use of liquid SO_3 or oleum, because of their high reactivity and difficulty in handling. To the best of our knowledge, none of the more stable SO_3 complexes had yet been used in the AS of alkenes, despite their well-known effectiveness and convenience as sulfating and sulfonating reagents.[3]

We now report some examples of a practical two-step conversion of mono-, di-, and trisubstituted alkenes into 2-aminoalkanesulfonic acids, based on the use of the commercially available, solid, and easily handled SO_3·DMF complex.

Results and Discussion

Cyclohexene (**1a**; Scheme 1) has been reported[2d] to afford 41% of *trans*-2-aminocyclohexanesulfonic acid (**3a**) on treatment with 0.5 equiv. of liquid SO_3 and 1 equiv. of CH_3CN in 1,2-dichloroethane, followed by hydrolysis. When we applied the same procedure with the SO_3·DMF complex in place of liquid SO_3, only 7% of **3a** was obtained, probably due to the low solubility of SO_3·DMF. When the reaction was carried out in CH_3CN as a solvent, **3a** was afforded in 36% overall yield.

Other commercially available SO_3 complexes with stronger bases, such as SO_3·Py and SO_3·TMA, did not react at all under the same reaction conditions.



a: R^1,R^2 = -$CH_2(CH_2)_2CH_2$-; R^3 = H
b: R^1,R^2 = -CH_2-CH_2-CH_2-; R^3 = H
c: R^1 = H; R^2 = -$(CH_2)_3CH_3$; R^3 = H
d: R^1 = H; R^2 = Ph; R^3 = H
e: R^1,R^2 = -$CH_2(CH_2)_2CH_2$-; R^3 = CH_3
f: R^1,R^2 = -$CH_2(CH_2)_2CH_2$-; R^3 = NO_2
g: R^1 = H; R^2 = -$(CH_2)_3OBz$; R^3 = H
h: R^1 = Ph; R^2 = H; R^3 = Ph
i: R^1 = H; R^2 = H; R^3 = H

Scheme 1

[‡] Synthesis of Taurine Analogues, 2. − Part 1: Ref.[11]

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The progress of the AS reaction of an equimolecular (0.35 mmol) mixture of cyclohexene (**1a**) and SO_3·DMF in CD_3CN (0.7 mL) (method **A**) at room temp. was monitored by ^1H NMR. Analysis of the spectra showed that the degree of conversion of **1a** after 5 d was only partial. When 1 mol-equiv. of CF_3SO_3H (0.35 mmol) was added to the original mixture (method **B**), however, it was complete after only 2 h.

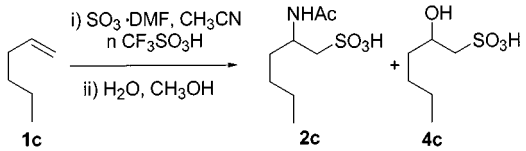
The AS reactions of different alkenes (**1a**−**1f**) with SO_3·DMF (**A**) and with SO_3·DMF/CF_3SO_3H (**B**) in CD_3CN were similarly compared, and a considerable increase in the reaction rate upon addition of CF_3SO_3H was in general observed. In fact, analysis of the reaction mixtures **B** by ^1H NMR at regular intervals showed that the reaction times reported in Table 1 were largely sufficient for the complete disappearance of the olefinic signals, except in the case of **1f**, which did not react at all (Entry 6, Table 1). Without addition of the acid (**A**) the olefinic signals never completely disappeared, even after reaction times twice (**1b**, **1c**) or 100 times (**1a**, **1d**, **1e**) those reported.

Table 1. Synthesis of 2-aminosulfonic acids **3** by AS of alkenes **1**, followed by hydrolysis

Entry	Alkene	AS reaction time[a]	Product	Yield[b] [%]
1	**1a**	1 h 40 min	**3a**	65
2	**1b**	23 h	**3b**	56
3	**1c**	6 d	**3c**	62
4	**1d**	1 h	**3d**	48
5	**1e**	1.5 h	**3e**	50
6	**1f**	30 d	−	−
7	**1g**	3 h	**5**	57
8	**1h**	16 h	**3h**[c]	43[d]
9	**1i**	12 d[e]	**3i**	40[f]

[a] Reaction conditions: i) AS: 10 mmol of **1**, SO_3·DMF and CF_3SO_3H in 20 mL of CH_3CN, room temp. (Entry 5: 0 °C); ii) H_2O or H_2O/MeOH, room temp., overnight; iii) 10% HCl, reflux, 12−24 h. [b] Yield of analytically pure product. [c] Only the *erythro*-**3h** isomer was formed. [d] In this case 52% of starting material **1h** was also recovered. [e] The AS was performed in autoclave with an excess of ethylene at a pressure of 50 atm. [f] Yield of analytically pure taurine (**3i**) relative to SO_3·DMF.

The presence of CF_3SO_3H also affected the chemoselectivity of the reaction, since it prevented the competitive formation of by-products. In particular, 1-hexene (**1c**) slowly reacted with SO_3·DMF in CD_3CN to give, after aqueous workup, an almost equimolecular mixture of **2c** and 2-hydroxysulfonic acid **4c**.[4] In the presence of CF_3SO_3H, however, **1c** exclusively afforded the 2-acetamido acid **2c** (Scheme 2).



n = 0: **2c** and **4c** were formed in *ca.* 1:1 molar ratio
n = 1 mole equiv.: **2c** was the sole product

Scheme 2

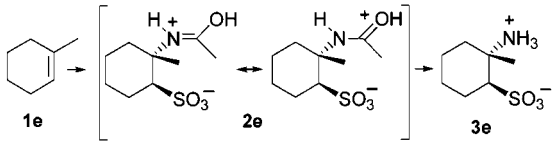
Styrene (**1d**) and 1-methylcyclohexene (**1e**) were transformed into the corresponding 2-amidosulfonic acids **2d** and **2e**, respectively, only in the presence of CF_3SO_3H. The reaction mixtures obtained in the absence of the acid were not resolved, but the amides **2** were absent, as clearly shown by the ^1H NMR spectrum analyses.

Cyclopentene (**1b**) and 1-hexene (**1c**) showed lower reactivities than cyclohexene (**1a**), and required 22 h and 6 d, respectively, to be completely consumed even in the presence of the CF_3SO_3H. In contrast, the reactions with styrene (**1d**) and 1-methylcyclohexene (**1e**) were very fast, as they completely reacted in 15 and 10 min, respectively. Finally, the electron-poor 1-nitrocyclohexene (**1f**) was unaffected under the reaction conditions after 1 month, in agreement with the electrophilic character of the addition.

The cyclic and acyclic alkenes **1** were subjected to AS under our optimized reaction conditions (Table 1). Upon completion of the AS reaction and aqueous workup, the 2-acetamidosulfonic acids **2** could be isolated by standard techniques. Alternatively, the crude compounds **2** could be directly hydrolyzed to the corresponding amino derivatives **3** in refluxing aqueous 10% HCl[2d] or NH_2NH_2.[5] The AS reaction of alkenes **1** directly followed by acid hydrolysis gave the 2-aminosulfonic acids **3** in moderate to good overall yields (36−73%) (Table 1). The aminosulfonic acid **3** was the only product detected in the reaction mixture in all the reported examples, except in the case of ethylene (**1i**), which afforded a 4:1 mixture of **3i** and the corresponding 2-hydroxysulfonic acid.

The cyclic 2-aminosulfonic acids **3a** and **3b** were thus prepared in yields significantly higher than those previously obtained with liquid SO_3 and 2 equiv. of alkene[2d] (**3a**: 65 vs. 41%; **3b**: 56 vs. 12%) (Entries 1 and 2, Table 1). The AS of 1-methylcyclohexene (**1e**) was completely regioselective and stereoselective, solely giving the aminosulfonic acid **3e** in 30% yield (30 min, room temp.). An improved yield (50%) of **3e** was obtained when the AS step was run at 0 °C for 1.5 h (Entry 5, Table 1).

The assignment of the structure of **3e** could be achieved indirectly by X-ray analysis[6,7] of a single crystal of the corresponding amide **2e** (Scheme 3). The addition of the sulfonic group had occurred exclusively at the less substituted carbon atom and in a *cis* relationship to the methyl group.

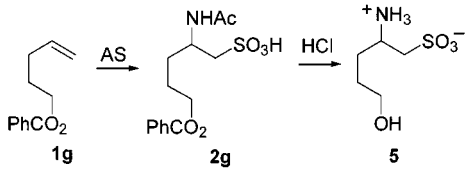


Scheme 3

The study of the structure of the **2e** crystal established that it existed as an inner salt. The amide moiety was protonated at the oxygen atom, in agreement with what has been reported for amides in strongly acidic media and for amide hydrofluoroborates.[8] The observed identical interatomic distances (1.29 Å) between the carbamidic carbon

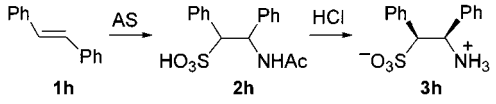
atom and the vicinal nitrogen and oxygen atoms are consistent with a partial double bond character of the two bonds and a sharing of the positive charge between the two heteroatoms (Scheme 3).

Pent-4-enyl benzoate (**1g**) reacted much more rapidly than the analogous terminal alkene 1-hexene (**1c**), conversion being complete after only 3 h (Entry 7, Table 1). After acid hydrolysis the highly water-soluble 5-hydroxyaminosulfonic acid **5** was recovered in 57% yield (Scheme 4).



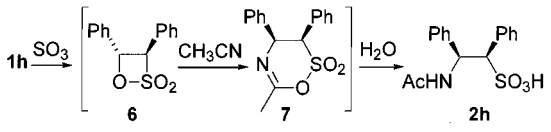
Scheme 4

The two-step process of AS and hydrolysis on *trans*-stilbene (**1h**) exclusively afforded the known *erythro*-2-aminosulfonic acid[9] **3h** (Scheme 5). The lower yield (43%) relative to that obtained with SO_3·DMF may possibly be attributable to the poorer reactivity of the 1,2-disubstituted alkene **1h**, which was recovered unchanged to the extent of 52% after the AS (thus the actual yield with respect to alkene converted was 90%, Entry 8, Table 1).



Scheme 5

The stereochemical outcome of the AS, namely the *anti* addition of the amino and sulfonic group both on cyclic and on acyclic olefins, was consistent with the mechanism previously proposed.[2] In particular, the β-sultone **6** was considered to be the primary intermediate, followed by nucleophilic attack of CH_3CN to afford the oxathiazine **7**, which was converted into the 2-amidosulfonic acid on hydrolysis (Scheme 6). At present there is no evidence concerning the role played by CF_3SO_3H in the three-component reaction, but the experimental results suggested its involvement in promoting the addition of SO_3 to the double bond and enhancing the reactivity of **6** toward acetonitrile.



Scheme 6

The last alkene studied was ethylene (**1i**). The AS reaction was carried out in an autoclave under an ethylene pressure of 50 atm, and the resulting amino acid **3i** was recovered in 40% yield after hydrolysis and crystallization. Although this methodology is less convenient than the current production processes of taurine (**3i**), it represents a new synthetic approach to valuable isotopically labeled taurine. For example, [^{13}C]- and [^{2}H]taurine, useful tools in the investigation of biological processes such as taurine metabolism,[10] can directly be obtained by AS of commercially available [$^{13}C_2$]- and [$^{2}H_4$]ethylene.

Conclusion

This study has demonstrated a broader synthetic utility of the multiple-component AS reaction. The method starts from inexpensive and readily available alkenes and gives access to a highly diverse range of natural and nonnatural 2-aminosulfonic acids in only two steps.

The new modified conditions allow the reaction to be run with greater simplicity and efficiency than previously reported, through the use of a commercially available complex of SO_3 and inclusion of a stoichiometric amount of CF_3SO_3H. This process appears to be quite general for electron-rich carbon−carbon double bonds, and the wide choice of starting olefin provides a useful opportunity for diversification of substituents on the basic 2-aminosulfonic system. A structure-activity relationship study on the nonnatural analogues of taurine by both in vitro and in vivo experiments is currently underway and will be published elsewhere.

Experimental Section

General Remarks: All reactions that required dry conditions were run under nitrogen with anhydrous solvents. Melting points (M.p.) are uncorrected. ^{1}H and ^{13}C NMR spectra (in D_2O, unless otherwise stated) were recorded with a Varian Gemini (^{1}H 200 MHz) or a Bruker DRX 500 (^{1}H 500 MHz). Chemical shifts are given in ppm from TMS. The notation s, d, t, q, m and br indicates singlet, doublet, triplet, quadruplet, multiplet, and broad, respectively. IR spectra (in KBr, unless otherwise stated) were recorded with Perkin−Elmer 881 or BX II spectrophotometers. Mass spectra (MS) were recorded with QMD 1000 Carlo Erba (EI, 70 eV) or PE SCIEX API 365 (ESI) instruments. Microanalyses were measured with a Perkin−Elmer 2400 C instrument.

General Procedure: The appropriate alkene (10 mmol) was added dropwise at room temp. (unless otherwise specified in Table 1) to a solution of SO_3·DMF complex (1.532 g, 10 mmol) and CF_3SO_3H (875 mL, 10 mmol) in CH_3CN (20 mL). The reaction mixture was stirred at room temp. for the time reported in Table 1; H_2O or H_2O/CH_3OH (10 mL) was then added, and stirring was continued overnight. Concentration in vacuo afforded the crude acetylaminosulfonic acid **2**, which could be directly used for subsequent hydrolysis. Small amounts of the intermediate **2** were filtered through ion-exchange resins and characterized spectroscopically. The crude product **2** was dissolved in 10% aqueous HCl solution (10 mL) and then heated at a vigorous reflux overnight. The solution was then partially concentrated in vacuo and diluted with CH_3CN to precipitate the aminosulfonic acid, which was filtered, washed, and recrystallized when necessary (overall yields as reported in Table 1).

trans-2-Acetylaminocyclohexanesulfonic Acid (2a): M.p. > 330 °C. ^{1}H NMR: δ = 3.88 (td, *J* = 11.0, 4.4 Hz, 1 H, 2-H), 2.82 (td, *J* = 11.0, 4.0 Hz, 1 H, 1-H), 2.31−2.15 (m, 1 H), 1.96 (s, 3 H, C*H*$_3$CO), 1.99−1.68 (m, 3 H), 1.55−1.20 (m, 4 H). ^{13}C NMR: δ = 173.2 (s), 62.0 (d), 50.4 (d), 33.2 (t), 28.2 (t), 24.8 (t), 24.7 (t), 22.8 (q). IR ($CHCl_3$): ṽ = 3674, 3001, 1707, 1413, 1356 cm^{-1}. MS: *m*/*z* (%) = 221 (7) [M]$^+$, 178 (7), 140 (22), 98 (21), 81 (40), 60 (100).

trans-2-Aminocyclohexanesulfonic Acid (3a): M.p. 408 °C (CH_3CN/H_2O) (ref.[11] 410 °C, dec.). ^{1}H NMR: δ = 3.41 (dt, *J* = 4.0, 11.4 Hz, 1 H, 2-H), 2.96 (dt, *J* = 4.0, 11.4 Hz, 1 H, 1-H), 2.36−2.10 (m, 2 H), 1.94−1.74 (m, 2 H), 1.64−1.24 (m, 4 H). ^{13}C NMR: δ = 62.3 (d), 52.9 (d), 32.7 (t), 28.9 (t), 26.0 (t), 25.9 (t). IR: ṽ = 3400−2800, 1501, 1240−1105, 1029 cm^{-1}. MS (ESI): 202 [M + Na]$^+$, 180 [M + H]$^+$. $C_6H_{13}NO_3S$ (179.20): calcd. C 40.21, H 7.31, N 7.81; found C 40.52, H 7.59, N 7.65.

trans-2-Acetylaminocyclopentanesulfonic Acid (2b): ^{1}H NMR: δ = 4.37 (q, *J* = 6.9 Hz, 1 H, 2-H), 3.23 (dt, *J* = 9.1, 6.9 Hz, 1 H, 1-H), 2.22−1.42 (m, 6 H), 1.96 (s, 3 H, C*H*$_3$CO). ^{13}C NMR: δ = 175.7 (s), 66.6 (d), 55.7 (d), 35.9 (t), 30.1 (t) 25.6 (t), 24.6 (q).

trans-2-Aminocyclopentanesulfonic Acid (3b): M.p. 324 °C (H_2O/ethanol) (ref.[11] 330 °C, dec.). ^{1}H NMR: δ = 3.84 (m, 1 H, 2-H), 3.40 (ddd, *J* = 9.2, 7.3, 7.0 Hz, 1 H, 1-H), 2.31−2.14 (m, 2 H), 2.07−1.72 (m, 4 H). ^{13}C NMR: δ = 63.4 (d), 54.6 (d), 31.4 (t), 27.8 (t), 23.1 (t). IR: ṽ = 3180−3050, 1220−1160, 1040 cm^{-1}. MS (ESI): 204 [M + K]$^+$, 188 [M + Na]$^+$, 166 [M + H]$^+$. $C_5H_{11}NO_3S$ (165.20): calcd. C 36.35, H 6.71, N 8.48; found C 36.49, H 7.09, N 8.71.

2-Acetylaminohexanesulfonic Acid (2c): ^{1}H NMR (CD_3OD): δ = 4.39 (m, 1 H, 2-H), 3.00 (d, *J* = 6.3 Hz, 2 H, 1-H$_2$), 2.20 (s, 3 H, C*H*$_3$CO), 1.79−1.58 (m, 2 H, 3-H$_2$), 1.38−1.25 (m, 4 H, 4-H$_2$, 5-H$_2$), 0.96−0.89 (m, 3 H, C*H*$_3$). ^{13}C NMR (CD_3OD): δ = 175.2 (s, C=O), 54.8 (t, C-1), 50.6 (d, C-2), 34.6 (t, C-3), 28.9 (t, C-4) 23.3 (t, C-5), 20.6 (q, *C*H$_3$CO), 14.2 (q, *C*H$_3$). MS: *m*/*z* (%) = 224 (3) [M]$^+$, 208 (3), 194 (2), 166 (13), 142 (32), 124 (100), 86 (69), 60 (45). $C_8H_{17}NO_4S$ (223.29): calcd. C 43.03, H 7.67, N 6.27; found C 43.24, H 8.07, N 6.11.

2-Aminohexanesulfonic Acid (3c): M.p. > 300 °C (CH_3CN/H_2O). ^{1}H NMR: δ = 3.69 (m, 1 H, 2-H), 3.30 (A part of an ABX system, J_{AB} = 15.0 Hz, J_{AX} = 3.3 Hz, 1 H, 1-H), 3.13 (B part of an ABX system, J_{AB} = 15.0 Hz, J_{BX} = 9.5 Hz, 1 H, 1-H), 1.84−1.72 (m, 2 H, 3-H$_2$), 1.47−1.27 (m, 4 H, 4-H$_2$, 5-H$_2$), 0.90 (m, 3 H, C*H*$_3$). ^{13}C NMR: δ = 52.2 (t, C-1), 49.3 (d, C-2), 32.3 (t, C-3), 26.9 (t, C-4), 22.2 (t, C-5), 13.6 (q, C*H*$_3$). IR: ṽ = 1250−1190, 1041 cm^{-1}. MS (ESI): 220 [M + K]$^+$, 204 [M + Na]$^+$, 182 [M + H]$^+$. $C_6H_{15}NO_3S$ (181.25): calcd. C 39.75, H 8.34, N 7.73; found C 40.05, H 8.11, N 7.63.

2-Hydroxyhexanesulfonic Acid (4c): M.p. 218−220 °C (ethyl acetate/CH_3OH). ^{1}H NMR: δ = 4.09 (m, 1 H, 2-H), 3.09 (A part of an ABX system, J_{AB} = 14.9 Hz, J_{AX} = 4.7 Hz, 1 H, 1-H), 3.00 (B part of an ABX system, J_{AB} = 14.9 Hz, J_{BX} = 7.4 Hz, 1 H, 1-H), 1.69−1.50 (m, 2 H, 3-H$_2$), 1.49−1.34 (m, 4 H, 4-H$_2$, 5-H$_2$), 0.91−0.81 (m, 3 H, C*H*$_3$). ^{13}C NMR: δ = 68.2 (d, C-2), 57.6 (t, C-1), 36.1 (t, C-3), 27.2 (t, C-4) 22.4 (t, C-5), 13.8 (q, C*H*$_3$). IR: ṽ = 3387, 2955, 2924, 2517, 1227, 1170, 1051 cm^{-1}. MS (ESI): 431 [2 M + 3 Na]$^+$, 227 [M + 2 Na]$^+$, 182 [M]$^+$, 163 [M − H_2O]$^+$, 95 (CH_2SO_3H), 80 (SO_3H). $C_6H_{14}O_4S$ (182.20): calcd. C 39.55, H 7.74; found C 39.94, H 7.63.

2-Acetylamino-2-phenylethanesulfonic Acid (2d): ^{1}H NMR ([D$_6$]DMSO): δ = 8.60−8.45 (m, 1 H, N*H*CO), 7.38−7.15 (m, 5 H, Ph), 5.19−5.02 (m, 1 H, 2-H), 3.13−2.96 (AB system, 2 H, 1-H$_2$), 1.80 (s, 3 H, C*H*$_3$).

2-Amino-2-phenylethanesulfonic Acid (3d): M.p. 314−315 °C (ethanol/H_2O) (ref.[12] 306−308 °C). ^{1}H NMR ([D$_6$]DMSO): δ = 7.63−7.29 (m, 5 H, Ph), 4.66−4.41 (m, 1 H, H-2), 3.26−3.05 (m, 1 H, 1-H), 2.92−2.78 (m, 1 H, 1-H). ^{13}C NMR ([D$_6$]DMSO): δ = 137.2 (s, *ipso* C), 128.9 (d, 2 C$_{Ar}$), 128.8 (d, C$_{Ar}$), 127.4 (d, 2 C$_{Ar}$), 54.0 (t, C-1), 52.2 (d, C-2). IR:[13] ṽ = 3206−2864, 1246−1128, 1049 cm^{-1}. MS (ESI): 240 [M + K]$^+$, 224 [M + Na]$^+$, 202 [M + H]$^+$. $C_8H_{11}NO_3S$ (201.24): calcd. C 47.75, H 5.51, N 6.96; found C 47.66, H 5.30, N 6.76.

(1R*,2R*)-2-Acetylamino-2-methylcyclohexanesulfonic Acid (2e): M.p. 194−197 °C. ^{1}H NMR ([D$_6$]DMSO): δ = 10.60−9.90 (br. s, SO_3 *H*), 8.60−8.40 (br. s, N*H*), 2.76 (dd, *J* = 12.2, 3.0 Hz, 1 H, 1-H), 2.44 (d, *J* = 15.4 Hz, 1 H), 1.99 (dd, *J* = 13.3, 2.7 Hz, 1 H), 1.70 (s, 3 H, C*H*$_3$CO), 1.63 (d, *J* = 12.8 Hz, 1 H), 1.48−1.43 (m, 3 H), 1.34 (s, 3 H, C*H*$_3$), 1.32−1.05 (m, 3 H). ^{13}C NMR: δ = 173.7 (s, C=O), 62.3 (d, C-1), 56.6 (s, C-2), 37.8 (t), 25.6 (t) 25.2 (t), 24.0 (q), 22.5 (t), 19.6 (q). IR: ṽ = 3265, 3185, 3098, 2941, 2852, 2377, 1661, 1544, 1428, 1247, 1110, 993 cm^{-1}. MS: *m*/*z* (%) = 192 (3) [M − COMe]$^+$, 178 (3), 154 (39), 112 (31), 95 (65), 81 (18), 70 (64), 60 (100). $C_9H_{17}NO_4S$ (235.30): calcd. C 45.94, H 7.28, N 5.95; found C 46.29, H 7.16, N 5.99.

(1R*,2R*)-2-Amino-2-methylcyclohexanesulfonic Acid (3e): M.p. > 340 °C (CH_3CN/CH_3OH/H_2O). ^{1}H NMR: δ = 3.09 (dd, *J* = 12.1, 3.7 Hz, 1 H, 1-H), 2.19−2.14 (m, 1 H), 1.94−1.80 (m, 2 H), 1.80−1.59 (m, 3 H), 1.53 (s, 3 H, C*H*$_3$), 1.47−1.31 (m, 2 H). ^{13}C NMR: δ = 63.7 (d, C-1), 56.2 (s, C-2), 38.7 (t), 25.1 (t), 24.9 (t), 21.9 (t), 18.0 (q, *C*H$_3$). IR: ṽ = 3466, 2951, 2360, 1240−1147, 1032 cm^{-1}. MS (ESI): 232 [M + K]$^+$,216 [M + Na]$^+$, 194 [M + H]$^+$. $C_7H_{15}NO_3S$ (193.26): calcd. C 43.501, H 7.82, N 7.25; found C 43.28, H 7.87, N 7.03.

2-Amino-5-hydroxypentanesulfonic Acid (5): ^{1}H NMR: δ = 3.84−3.62 (m, 3 H, 2-H and 5-H$_2$), 3.32 (A part of an ABX system, J_{AB} = 14.7 Hz, J_{AX} = 3.5 Hz, 1 H, 1-H), 3.17 (B part of an ABX system, J_{AB} = 14.7 Hz, J_{BX} = 8.8 Hz, 1 H, 1-H), 1.97−1.61 (m, 4 H, 3-H$_2$ and 4-H$_2$). ^{13}C NMR: δ = 51.0 (t), 47.7 (d, C-2), 43.9 (t), 29.0 (t), 26.9 (t). MS (ESI): 222 [M + K]$^+$, 206 [M + Na]$^+$, 184 [M + H]$^+$.

(1R*,2S*)-2-Amino-1,2-diphenylethanesulfonic Acid (3h): M.p. > 255 °C dec. (EtOH/H_2O) (ref.[9] 306−308 °C). ^{1}H NMR ([D$_6$]DMSO): δ = 8.60−8.20 (br. s), 7.38−7.01 (m, 10 H, 2 Ph), 5.00 (m, 1 H, 2-H), 4.11 (d, *J* = 2.9 Hz, 1 H, 1-H). ^{13}C NMR ([D$_6$]DMSO): δ = 135.2 (s, *ipso* C), 132.7 (s, *ipso* C), 130.3 (d, 2 C$_{Ar}$), 128.3 (d), 128.1 (d, 2 C$_{Ar}$), 127.8 (d, 2 C$_{Ar}$), 127.6 (d), 127.5 (d, 2 C$_{Ar}$), 67.1 (d, C-1), 56.1 (d, C-2).

Taurine (3i): The AS was performed in a autoclave with an excess of ethylene at a pressure of 50 atm. The spectroscopic data were identical with those of a commercial sample of taurine.

[1] For example see: [1a] S. W. Schaffer, J. B. Lombardini, J. Azuma, *Amino Acids* **2000**, *18*, 305−318. [1b] J. D. Militante, J. B. Lombardini, S. W. Schaffer, *Cardiovasc. Res.* **2000**, *46*, 393−402. [1c] H. Satoh, N. Sperelakis, *Gen. Pharmac.* **1998**, *30*, 451−463. [1d] R. J. Huxtable, *Physiol. Rev.* **1992**, *72*, 101−163.

[2] [2a] G. L. Broussalian, U. S. Patent 3,303,137, **1967**; *Chem. Abstr.* **1966**, *66*, 67063d. [2b] I. D. Khalistova, V. A. Podgornova, *Russ. J. Appl. Chem.* **1994**, *67*, 1185−1188. [2c] V. A. Podgornova, I. D. Khalistova, B. F. Ustavshchikov, *Russ. J. Appl. Chem.* **1996**, *69*, 110−113. [2d] S. M. Liebowitz, J. B.

Lombardini, P. S. Salva, *Biochem. Pharmacol.* **1987**, *36*, 2109−2114.
[3] For a review see: E. E. Gilbert, *Chem. Rev.* **1962**, *62*, 549−589.
[4] Similarly, long-chain terminal alkenes gave mixtures of 2-acylamino and 2-hydroxy sulfonate on treatment with liquid SO_3 and an alkanenitrile (ref.[2a]).
[5] D. D. Keith, J. A. Tortora, R. Yang, *J. Org. Chem.* **1978**, *43*, 3711−3713.
[6] Dr. Cristina Faggi is acknowledged for carrying out the X-ray analysis.
[7] The authors have deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre; depository number CCDC-167422. The data can be obtained free of charge on application to Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].
[8] [8a] G. Fraenkel, C. Franconi, *J. Am. Chem. Soc.* **1960**, *82*, 4478−4483. [8b] S. S. Hecht, E. S. Rothman, *J. Org. Chem.* **1973**, *38*, 395−396.
[9] E. Grunder, G. Leclerc, *Synthesis* **1999**, 135−137.
[10] B. D. Andresen, F. T. Davis, P. P. Taskes, C. E. King, *J. Labelled Compd. Radiopharm.* **1978**, *15*, 731−738.
[11] F. Machetti, M. Cacciarini, F. Catrambone, F. M. Cordero, S. Romoli, F. De Sarlo, *J. Chem. Res. (S)* **2000**, 120−121.
[12] A. Lambert, J. D. Rose, *J. Chem. Soc.* **1949**, 46−49.
[13] E. Meyle, E. Keller, H.-H. Otto, *Liebigs Ann. Chem.* **1985**, 802−812.

Received August 13, 2001
[O01396]