SHORT PAPER

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Synthesis of taurine analogues. Part 1: 2-aminosulfonic acids from alkene–sulfur monochloride adducts†

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(±)*Trans*-2-aminocyclohexanesulfonic acid and (±)*trans*-2-aminocyclopentanesulfonic acid were prepared respectively from cyclohexene and cyclopentene by sulfur monochloride addition, followed by oxidation to 2-chlorosulfonic acid and substitution of chlorine.

Taurine (2-aminoethanesulfonic acid) can be synthesised from 1,2-dichloro- or 1,2-dibromoethane by sequential substitution of one halogen atom by the SO_3H group and the other one by the NH_2 group.[1] This procedure cannot compete in cost with the isolation from natural sources. However, the preparation of taurine analogues or of isotopically labelled taurine requires the availability of reliable preparation methods.[2] Taurine analogues are required for studies on receptor interactions related to a variety of biological activities of taurine, while labelled taurine might prove very helpful in investigations on its metabolism.[3] Among methods applied so far, in addition to the double substitution mentioned above, the simultaneous introduction of the two functionalities by reaction of alkenes with acetonitrile and sulfur trioxide has been reported: the resulting acetamide was then hydrolysed to the 2-aminosulfonic acid.[4] Individual procedures have been reported for analogues derived from cyclopentene and cyclohexene[5] leading to the *trans* racemic compounds.

We report here the attempts to use the addition of sulfur monochloride to alkenes as the first step of a sequence leading to 2-aminosulfonic acids (taurine analogues). Cyclopentene (**1**) or cyclohexene (**2**) was treated with sulfur monochloride, as reported.[6] The crude mixture of sulfides (**3** or **4**) was then added to *m*-chloroperbenzoic acid (MCPBA) in methylene chloride and the corresponding 2-chlorosulfonate (**5** or **6**) obtained (Scheme 1).

The addition of sulfur monochloride to the alkene only in part follows the expected 1:2 stoichiometry, as already pointed out.[6] In fact, the carbocyclic rings are joined by one or more S atoms, in the molar ratios reported in the experimental section, as clearly indicated by the GC–MS data of the crude mixtures **3** or **4**.

The oxidation step was attempted with various reagents and the best results were obtained with nitric acid or with MCPBA. The last was preferred because of the easier work-up.

Conversion of the 2-chlorosulfonates **5** and **6** into the amino derivatives **9** and **10** could not be achieved directly, as a basic reagent (NH_3 , K phthalimide) caused mainly elimination. Substitution by azido group to the intermediates **7** and **8**, followed by catalytic hydrogenation, afforded the products **9** (37% from cyclopentene) and **10** (50% from cyclohexene): even this procedure gave some elimination product (20% in either case). (See Scheme 1).

The *trans* configuration of the products **9** and **10** was established by comparison of their NMR data with those reported.[5] The addition of sulfur monochloride occurred with a *trans* diastereoselectivity, in agreement with previous findings (ref.6, p.3996). The chlorosulfonate **6** was also found to be *trans*, as indicated by the coupling constant of the CH–CH system. Retention of configuration during the azide substitution is reasonably ascribed to diastereoselective attack on the intermediate carbocation. We assume the same configurations for the intermediate cyclopentane derivatives **5** and **7**.

For the adducts **4**, inversion of the step sequence was attempted, *i.e.* azide substitution was followed by S oxidation. The overall result was not improved, as the severe reaction conditions required for the substitution (refluxing DMF) caused extensive decomposition: the azido sulfides were identified in the reaction mixture, but their isolation was not attempted.

Experimental

Melting points are uncorrected. ^1H and ^{13}C spectra were recorded at 200 and 50.33 MHz respectively with a Varian Gemini instrument by using D_2O as solvent. MS (EI) were recorded at 70 eV by GC inlet or by direct inlet.

2-Chlorosulfonic acids **5** *and* **6**, *sodium salts:* Sulfur monochloride (50 mmol) was added dropwise to an excess (150 mmol) of cyclopentene (**1**) or cyclohexene (**2**) over 2 h. After stirring at room temperature for 3 days, then concentrating *in vacuo*, the chlorosulfides **3** and **4** were obtained as clear syrups (ratios 35:25:40 for **3a**:**3b**:**3c** and 3:5:2 for **4a**:**4b**:**4c**, as determined by GC–MS).

The sulfides mixture (**3** or **4**) was added dropwise to an ice-cold solution containing 5 times its weight of MCPBA (70%) in dichloromethane. Cooling was removed, the solution refluxed for 5 h, then extracted 4 times with water. The white solid was removed and the clear aqueous phase concentrated and neutralised with 0.5 M NaOH solution. The chlorosulfonic acids **5** or **6** were obtained as sodium salts on concentration to dryness.

(±)*Trans-2-chlorocyclopentanesulfonic acid sodium salt* (**5**): ^1H NMR δ 4.50–4.48 (m, 1H), 3.86–3.74 (m, 1H), 2.16–1.64 (m, 6H)

(±)*Trans-2-chlorocyclohexanesulfonic acid sodium salt* (**6**): ^1H NMR δ 4.12 (td, *J*= 4.0 and 10.4 Hz, 1H), 3.0 (td, *J*= 4.0 and 10.4 Hz, 1H), 2.43-2.10 (m, 2H), 1.95-1.2 (m, 4H); ^{13}C NMR δ 67.6 (d), 61.5 (d), 39.2 (t), 30.6 (t), 27.2 (t), 26.2 (t); MS (*m/z*, %) 198 (M^+, 40), 117 (60), 81 (44)

2-Aminosulfonic acids **9** *and* **10**: Sodium azide (2:1 molar ratio) was added to a 5% solution of 2-chlorosulfonate (**5** or **6**) in dimethylformamide (DMF). After reflux (3h) the solvent was evaporated, the solid residue was dissolved in 2M HCl and concentrated again, to give the *2-azidosulfonic acids* **7** or **8**, containing minor amounts of the unsaturated sulfonic acids.

(±)*Trans-2-azidocyclopentanesulfonic acid* (**7**): ^1H NMR δ 3.5 (m, 1H), 2.6 (m, 1H), 2.2–1.2 (m, 6H).

(±)*Trans-2-azidocyclohexanesulfonic acid* (**8**): ^1H NMR δ 3.6 (m, 1H), 2.8 (m, 1H), 2.4–1.0 (m, 8H); ^{13}C NMR δ 64.7 (d), 64.0 (d), 34.6 (t), 30.4 (t), 27.1 (t), 26.9 (t).

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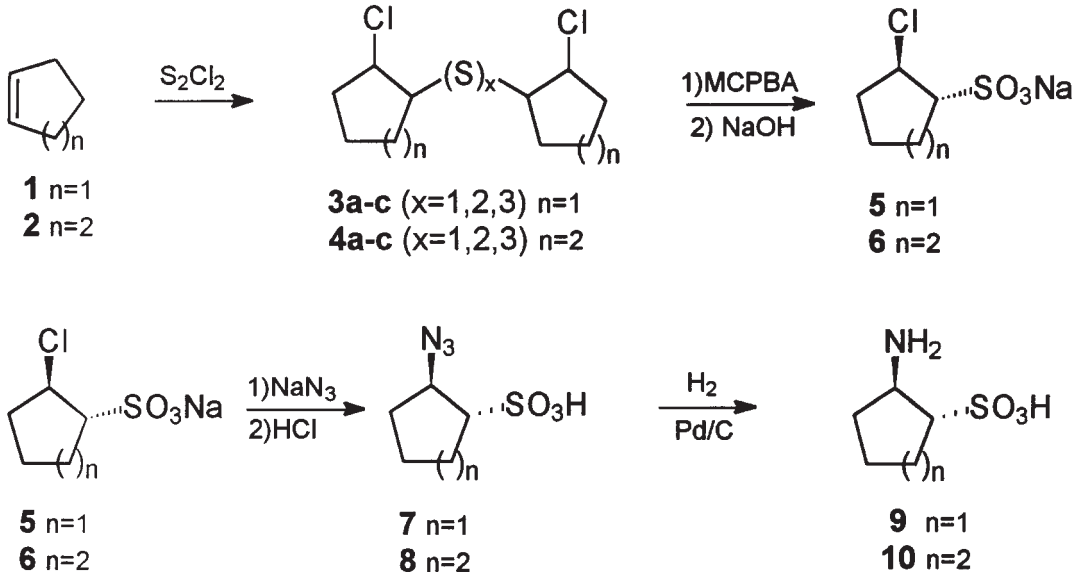
† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*



Scheme 1

The crude product **7** or **8** was hydrogenated in methanol with Pd/C (10%) under hydrogen at atmospheric pressure for 3 days. The crude solid, obtained after removal of the catalyst and of the solvent, was dissolved in water and passed through a column of Dowex 50 WX4 H^+ form. After evaporation of the solvent the solid was recrystallized from water–ethanol.

(±)*Trans-2-aminocyclopentanesulfonic acid* (**9**): 37% overall yield from cyclopentene. mp 324 °C dec. (lit.[5], 330 °C dec); ^{1}H NMR δ 3.80 (m, 1H), 3.36 (m, 1H), 2.16–2.34 (m, 2H), 1.68–2.00 (m, 4H); ^{13}C NMR δ 63.4 (d), 54.6 (d), 31.4 (t), 27.8 (t), 23.1 (t).

(±)*Trans-2-aminocyclohexanesulfonic acid* (**10**): 50% overall yield from cyclohexene. mp 408 °C dec (lit.[4b] 410 °C dec). ^{1}H NMR δ 3.41 (td, *J*= 4.0 and 11.4 Hz, 1H), 2.96 (td, *J*= 4.0 and 11.4 Hz, 1H) 2.36–2.10 (m, 2H), 1.94–1.74 (m, 2H), 1.64–1.24 (m, 4H). ^{13}C NMR δ 62.3 (d), 52.9 (d), 32.7 (t), 28.9 (t), 26.0 (t), 25.9 (t).

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