

SYNLETT Spotlight 76

Sulfur Trioxide-Amine Adducts

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This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

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Introduction

Many developments have taken place throughout the history of sulfonating reagents from the synthesis of stabilized liquid SO_3 ¹ to the production of chlorosulfonic acid (ClSO_3H) and the development of SO_3 -amine adducts. Reactions involving SO_3 and ClSO_3H prove to be quite violent and are accompanied with heat liberation. With such violent reactivity characteristics a milder reagent was sought. It has been long known that chlorosulfonic acid added dropwise and at low temperatures reacts with aliphatic and aromatic tertiary amines to produce the corresponding sulfur trioxide amine complexes ($\text{O}_3\text{S}^- \text{N}^+\text{R}_3$)

for example, $\text{O}_3\text{S}^- \text{N}^+(\text{CH}_3)_3$,¹ $\text{O}_3\text{S}^- \text{N}^+(\text{CH}_2\text{CH}_3)_3$ and $\text{O}_3\text{S}^- \text{N}^+(\text{CH}_2\text{CH}_2\text{CH}_3)_3$.¹ Sulfur trioxide amine adducts are valuable and versatile sulfonating agents. They may be utilised in the sulfation of alcohols (formation of S–O bonds), sulfonation of acid sensitive heterocycles, aliphatic and aromatic hydrocarbons (formation of S–C bonds) and the sulfamation of amines (formation of S–N bonds).² The resulting products have quite diverse properties, for example, they may act as dyes, detergents, sweeteners, pharmaceutical intermediates, herbicides etc.

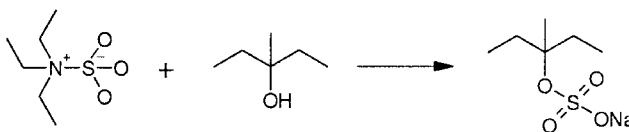
Precautions

All reactions must be carried out in a fumehood. Care must be taken when utilizing concentrated acids, which are highly corrosive and fume as they react with the moisture in the air e.g. chlorosulfonic acid, sulfuric acid, liquid sulfur trioxide. Anhydrous conditions are essential and solvents must be refluxed over appropriate agents and

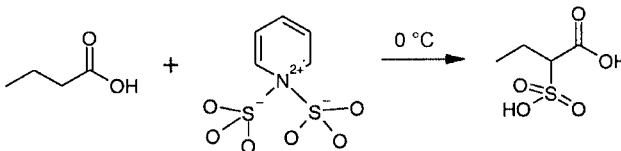
distilled and stored over molecular sieves. Solid reagents are recrystallized from appropriate solvents while liquids are distilled. It is necessary that sulfur trioxide complexes are stored in airtight containers to minimise hydrolysis of the reagent by water vapour.

Abstracts

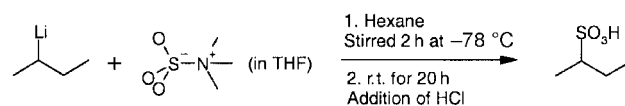
(A) A series of sulfur trioxide complexes have been employed in the sulfation of alcohols.³ There are many examples extensively documented in the literature; *tert*-butyl alcohol and 3-methyl-3-pentanol were successfully converted to their sulfate ester salts by reaction with SO_3 -pyridine or SO_3 - Et_3N .⁴



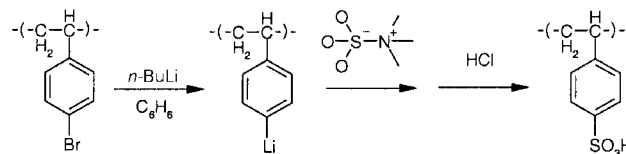
(B) Sulfonation proceeds via oxidation of hydrocarbons resulting in carbocation formation. Saturated aliphatic hydrocarbons possessing a carbonyl component are sulfonated upon the carbon adjacent to this entity. Unsaturated hydrocarbons are sulfonated quite easily forming a β -sultone or a solvated carbenium ion. However, (2SO_3) -pyridine sulfonates butyric acid quantitatively.⁵



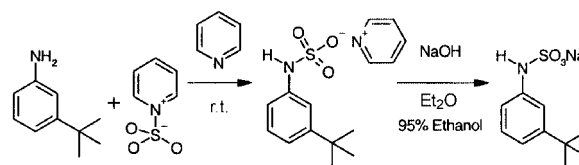
(C) Sulfonation is also achieved via insertion of SO_3 into a carbon-metal bond. Organometallic compounds treated with $\text{SO}_3\text{-Me}_3\text{N}$, a mild reagent, react to produce the corresponding sulfonic acids – a process suitable for both aliphatic and aromatic hydrocarbons.⁶



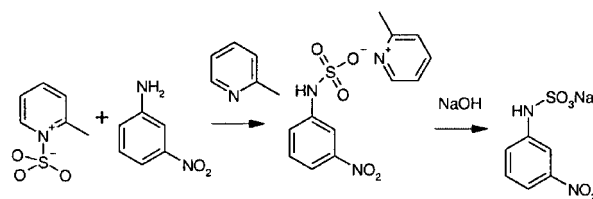
(D) 2% Cross-linked *p*-bromopolystyrene, may also be converted to its corresponding aromatic polystyrenesulfonic acid via sulfonation of its lithium derivative.⁷



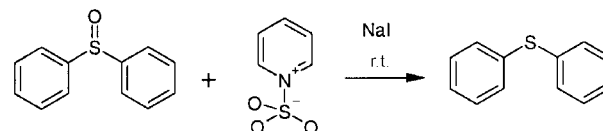
(E) Initially amines were sulfamated by treatment with chlorosulfonic acid.^{8,9} Both mono- and disubstituted sulfamates may be prepared with ease. $\text{SO}_3\text{-Pyridine}$ is used extensively in the sulfamation of primary amines.¹⁰ The amine salt formed is treated with hydroxide and the alkali sulfamate extracted and recrystallised finally from 95% ethanol.



(F) Electron donating groups, for example methyl, ethoxy etc., promote sulfamation however electron-withdrawing groups such as nitro substituents hinder the reaction. Utilizing α -picoline (2-methylpyridine) however overcomes this problem and the resulting sulfamate may be extracted in good yield.¹¹



(F) $\text{SO}_3\text{-amine}$ adducts, such as $\text{SO}_3\text{-pyridine}$, may be affectively utilized in the reduction of aromatic (diphenyl sulfoxide) and aliphatic sulfoxides at room temperatures resulting in quantitative yields of the corresponding sulfide.¹²



References

- (1) Gilbert, E. E. *Sulfonation and Related Reactions*, Chap. I; Interscience: New York, **1965**, 1–30.
- (2) (a) Cremly, R. J. *Chlorosulfonic Acid A versatile Reagent*, Chap. I; Royal Society of Chemistry: London, **2002**, 1–6.
(b) Cremly, R. J. *Chlorosulfonic Acid A versatile Reagent*, Chap. IX; Royal Society of Chemistry: London, **2002**, 97–110.
- (3) Gilbert, E. E. *Sulfonation and Related Reactions*, Chap. VI; Interscience: New York, **1965**, 339–401.
- (4) Sogo Yakuko Co., Ltd., Jpn. Kokai Tokkyo JP 82 59,853; 1982. Chem. Abstr. **1982**, 97, 91730.
- (5) Gilbert, E. E. *Sulfonation and Related Reactions*; Interscience: New York, **1965**, Chap. II, 31–124.
- (6) Smith, K.; Hou, D. *J. Org. Chem.* **1996**, 61, 1530.
- (7) Smith, K.; Hou, D. *Sulfur Lett.* **2000**, 24, 193.
- (8) Gilbert, E. E. *Sulfonation and Related Reactions*, Chap. VII; Interscience: New York, **1965**, 403–424.
- (9) Audrieth, L. F.; Sveda, M. *J. Org. Chem.* **1944**, 39, 89.
- (10) Boyland, E.; Manson, D.; Orr, S. F. D. *Biochem. J.* **1957**, 65, 417.
- (11) Sureau, R. F. M.; Obellianne, P. M. J. U.S. Patent 2, 789, 132, 1957. Chem. Abstr. **1957**, 51, 15571.
- (12) Olah, G. A.; Vankar, Y. D.; Arvanaghi, M. *Synthesis* **1979**, 984.