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Recent Advances in the Synthesis of Sulfonic Acids

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RECENT ADVANCES IN THE SYNTHESIS OF SULFONIC ACIDS

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This review covers some of the methods for preparation of sulfonic acids reported recently. Phenols can be sulfonated directly using concentrated aqueous sulfuric acid. The products obtained can be analysed by several methods, *e.g.*, HPLC and ^{1}H NMR spectroscopy. Dihydroxy and dimesyloxynaphthalenes have been sulfonated by the use of SO_3. The sulfonation process was found to be dependent on the reaction conditions and the stoichiometry. Sulfur trioxide alone can be used as a sulfonating reagent to produce sulfonic acids, but sulfur trioxide-base complexes have been found to be more convenient sulfonating reagents, with the advantage that they are easier to handle. For example, (*S*)-3-amino-2-oxoazetidine-1-sulfonic acid can be obtained in good yield by the use of a sulfur trioxide-base complex. Sulfur trioxide can be inserted into the metal–carbon bond of various organolithiums and Grignard reagents to produce organic sulfonic acids in high yields.

Keywords: Sulfonic acids; Sulfonation; Sulfur trioxide; Concentrated aqueous sulfuric acid; Organolithiums; (*S*)-3-amino-2-oxoazetidine-1-sulfonic acid

CONTENTS

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1. INTRODUCTION

Sulfonic acids have the general formula RSO_3H, but relatively few have been isolated [1]. The economic usefulness of sulfonic acids depends on the chemical stability and water solubility of the sulfonic group [2, 3]. Several review articles concerning the synthesis of sulfonic acids have been reported [4–9]. Derivatives of sulfonic acids exhibit a wide variety of pharmacological activities [10]. By contrast, sulfonic acid derivatives have rarely been used as reagents or reactants in synthesis, largely due to the fact that their preparation has traditionally entailed cumbersome separation procedures. There are three general methods for the preparation of sulfonic acids [9]. (i) A source of S(VI) is used as a sulfonating reagent. An enormous amount of work using S(VI) reagents for the preparation of sulfonic acids has been reported [9]. The most common reagents are sulfuric acid, sulfur trioxide and chlorosulfonic acid [9]. (ii) A source of sulfur in a lower oxidation state [S(II) or S(IV)] is used to give an intermediate that can be oxidise to the S(VI) state [9]. Various organo-sulfur compounds have been oxidised in this way to the corresponding higher oxidation state species [11]. (iii) One sulfonic acid may be transformed into another by reactions not involving the carbon–sulfur bond [8, 9].

The aromatic sulfonation reaction is very wide in application and many aromatic hydrocarbons, aryl halides, ethers, carboxylic acids, ketones, amines and nitro compounds have been sulfonated [8]. The mechanism is similar to that involved in other electrophilic aromatic

substitution reactions and has been discussed [8]. This review will concentrate on recent work published in this area, particularly on the sulfonation of phenols, where difficulties have been experienced in the past. Although direct sulfonation of aromatic compounds is the most general method for preparation of aromatic sulfonic acids [12], alternative methods are sometimes required, especially in the case of substrates of low or high activity or more complex compounds. The most common method for the preparation of aliphatic sulfonate salts is reaction of aliphatic bromides with sodium sulfite [13], but this reaction is not suitable for vinyl and aryl bromides. Much work has been reported on the insertion reactions of sulfur dioxide with organometallic compounds to form sulfinic acids [14]. However, there are only a few reports of similar reactions of sulfur trioxide being inserted into the bonds between carbon and other elements, mainly relating to elements of main group 4 [15] and mercury [16]. Recently, more reactive organometallic reagents have been reacted with sulfur trioxide–trimethylamine to give sulfonic acids [17]. It is these recent advances that are covered in this review.

2. SULFONATION OF PHENOLS

The sulfonation of phenolic compounds has been studied in the past by various methods [18]. However, a problem in such studies was the separation and analysis of reaction mixtures, so sulfonation of phenols has recently been studied in detail. ^{33}S NMR spectroscopy [19], fast atom bombardment (FAB) mass spectrometry [20] and other methods have been used to elucidate the structures of the sulfonic acids produced. For example, the product composition in the sulfonation of 2- and 3-methylphenols using sulfuric acid and chlorosulfonic acid was studied by means of HPLC [21]. Sulfonation of anisole and phenols takes place very easily in concentrated aqueous sulfuric acid and involves protonation on the oxygen [22]. The actual species undergoing sulfonation in concentrated aqueous sulfuric acid are, however, the unprotonated substrates with $H_3SO_4^+$ and $H_2S_2O_7$ as the sulfonating entities, which are the predominant reacting species in sulfuric acid below 83% and above 88% H_2SO_4, respectively [23]. The sulfonations of phenols were found to follow first-order kinetics with respect to the aromatic substrate [23]. The first-order sulfonation rate

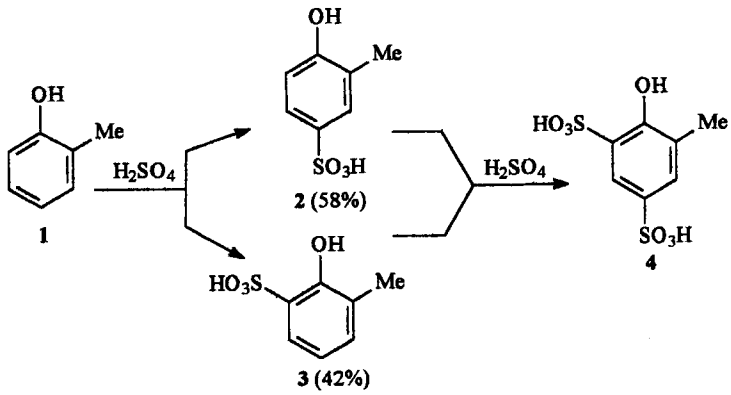
coefficients increased strongly with increasing sulfuric acid concentration [23]. The rates of sulfonation of phenols and their monosulfonic acids were reported to be high in comparison to the rates of the protiodesulfonation of their respective mono- and disulfonic acids [24].

2.1. Sulfonation of Methylphenols

Sulfonation of various methylphenols and dimethylphenols was reported using concentrated aqueous sulfuric acid at 35°C [24]. The sulfonic acid products obtained were analysed using ^{1}H NMR spectroscopy. The assignments were based on the integral area ratios, the multiplicity of the various signals, and the coupling constants. Sulfonation of 2-methylphenol (**1**) with sulfuric acid varying in concentration from 82 to 90% H_2SO_4, gave the 4- and 6-sulfonic acids **2** and **3** in yields of 58 and 42%, respectively, as initial products (Scheme 1) [24]. Compounds **2** and **3** are subsequently sulfonated relatively slowly to afford the corresponding 4,6-disulfonic acid **4** in quantitative yield [24].

Similarly, sulfonation of 4-methylphenol (**5**) with sulfuric acid with the same range of concentration afforded initially the corresponding 2-sulfonic acid **6**, which was eventually sulfonated slowly to give quantitatively the corresponding 2,6-disulfonic acid **7** (Scheme 2) [24].

Sulfonation of 3-methylphenol (**8**) in 85% H_2SO_4 after 18 min gave a mixture of the 2-,4-, and 6-sulfonic acids **9**–**11** and the 4,6-disulfonic



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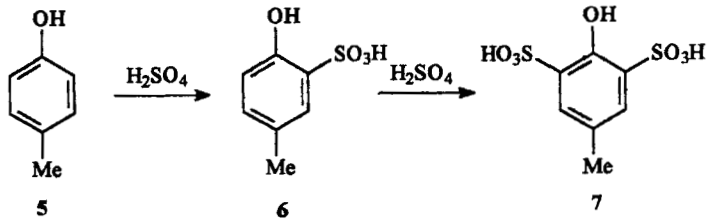
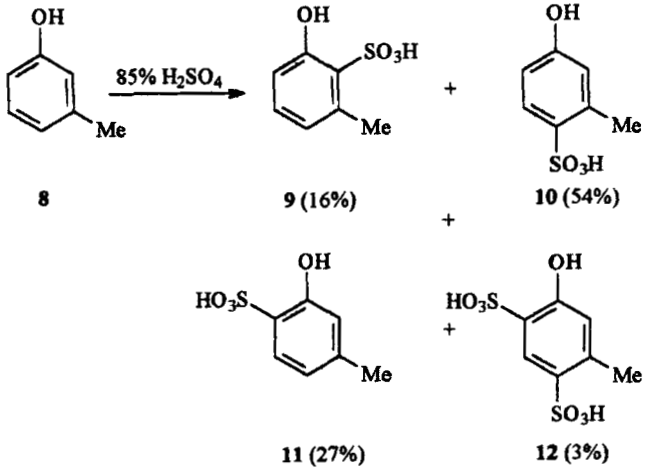


SCHEME 2



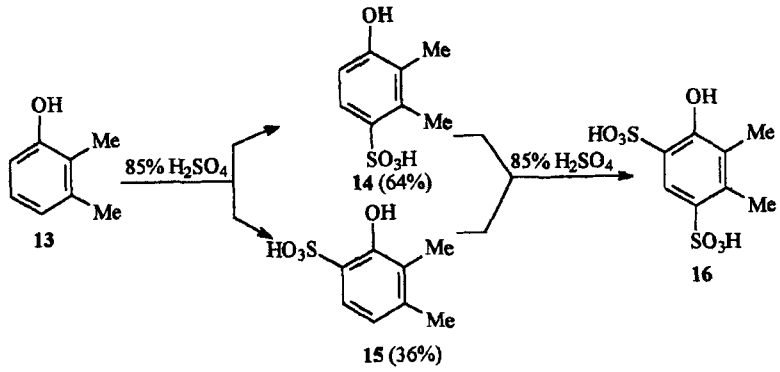
SCHEME 3

acid **12** in yields of 16, 54, 27, and 3%, respectively (Scheme 3). When the reaction time was increased, the corresponding 2,4-disulfonic acid was also formed [24].

2.2. Sulfonation of Dimethylphenols

Sulfonation of 2,3-dimethylphenol (**13**) using 85% H_2SO_4 afforded the corresponding 4- and 6-sulfonic acids **14** and **15** in yields of 64 and 36%, respectively (Scheme 4). Both compounds **14** and **15** were eventually sulfonated to give the corresponding 4,6-disulfonic acid **16** [24].

Sulfonation of 2,4-dimethylphenol (**17**) under similar conditions gave 19% of the 5-sulfonic acid **18**, 79% of the 6-sulfonic acid **19**



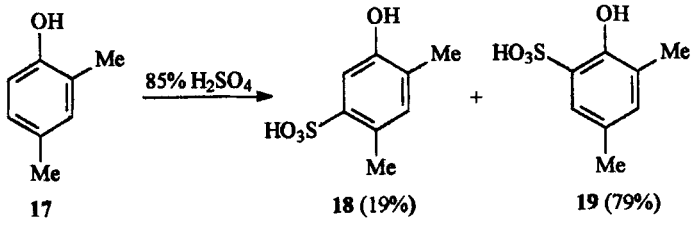
SCHEME 4

(Scheme 5) and 2% of another product which may have been the corresponding 3,5-disulfonic acid [24]. The formation of compound **18** in 19% yield is of interest, since the sulfonic acid substituent is in the position *meta* to the —OH group. This means that the introduction of a methyl group at the 2-position of 4-methylphenol (**5**) apparently activates the 5-position to such an extent that sulfonation *meta* to —OH becomes comparable in rate to that *ortho* to —OH.

Sulfonation of 2,5-dimethylphenol (**20**) with 85% H_2SO_4 after 17 min afforded the corresponding 4-,6- and 4,6-di-sulfonic acids **21**–**23** in yields of 75, 17 and 9%, respectively (Scheme 6) [24]. It was found that compounds **22** and **23** were unstable under the reaction conditions and both were eventually converted into sulfonic acid **21** [24].

Sulfonation of 2,6-dimethylphenol (**24**) with 85% H_2SO_4 afforded the corresponding 3-sulfonic acid **25** and 4-sulfonic acid **26** in yields of 28 and 72%, respectively (Scheme 7) [24]. It was found that the isomer ratio remained constant for about 3 h; thereafter **26** started to precipitate from the reaction mixture.

The authors suggested that three explanations may be considered to account for the high degree of 3-substitution in sulfuric acid sulfonation of **24** [24]. First, the sulfonation of **24** proceeds *via* a sulfate intermediate; secondly, **25** results from sulfonation of the oxygen protonated form of **24**; and thirdly, substantial substitution at the 3-position is due to steric inhibition of resonance [24]. The first explanation is rendered unlikely, as (i) 2,6-dimethylanisole (the *O*-sulfation of which is impossible) in 85% H_2SO_4 was also mainly



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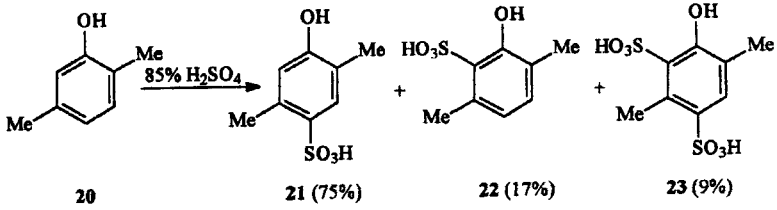

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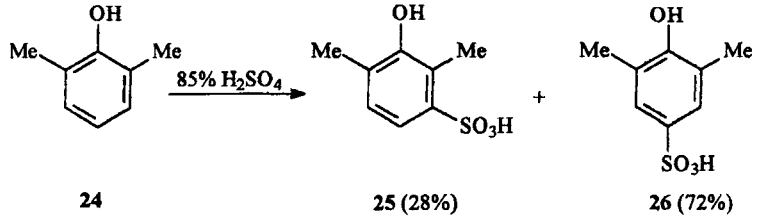


SCHEME 7

sulfonated at the 3-position [25], and (ii) phenyl methanesulfonate (which is an analogue of phenyl hydrogen sulfate) in 86–99% H_2SO_4 gave exclusively the 4-sulfonic acid [23]. The second explanation can also be refuted, as it has been shown previously that a large number of *ortho*- and *para*-substituted phenols and anisoles are sulfonated *via* the unprotonated species, which is very much more reactive than the protonated species (which is the predominant substrate species present) [23]. This leaves the third explanation of steric inhibition of resonance [26].

Sulfonation of 3,4-dimethylphenol (**27**) in 85% H_2SO_4 after 19 min afforded 2-,6-and 2,6-di-sulfonic acids **28–30** in yields of 17, 78 and 5%, respectively (Scheme 8) [24]. When the reaction time was increased the yield of **30** increased to a maximum of 6.5%. It was

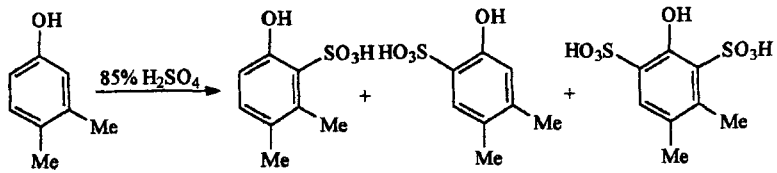
found that compounds **28** and **30** are unstable under the reaction conditions, and after leaving the reaction mixture for one month, compound **29** appeared to be the only product present.

Sulfonation of 3,5-dimethylphenol (**31**) with 85% H_2SO_4 gave exclusively the corresponding 2-sulfonic acid **32** (Scheme 9), which was found to be stable for one week [24].

2.3. Sulfonation of *Tert*-butylphenols

The sulfonation of aromatic substrates containing a *tert*-butyl group [27] has been the subject of several studies. The results showed that, in addition to sulfonation, substantial isomerisation and dealkylation take place [26]. The initial sulfonation products are in general those expected on the basis of the electronic and steric effects of the hydroxy, *t*-butyl, and sulfonic acid substituents [28]. Generally the *t*-butyl group inhibits sulfonation *ortho* to that group as a result of steric hindrance.

Sulfonation of *m*- and *p*-di-*t*-butylbenzenes with ~100% H_2SO_4, gave a small amount (5–9%) of *t*-butylbenzene-2,4-disulfonic acid by sulfo-de-*t*-butylation [27a]. However, sulfonation of 3-*t*-butylphenol (**33**) in 98.5% H_2SO_4 gave the monosulfonic acid **34** after 10 days, while after 85 days with ~100% H_2SO_4 it gave 3-*t*-butylphenol-4,6-



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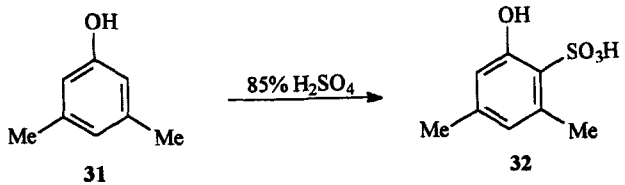
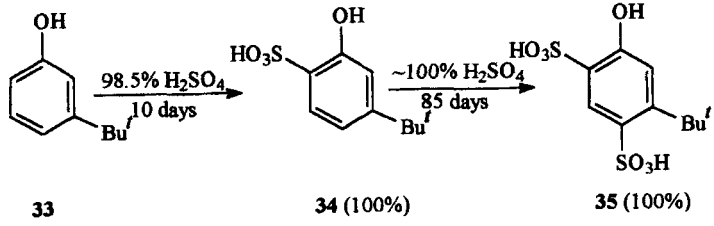


SCHEME 9

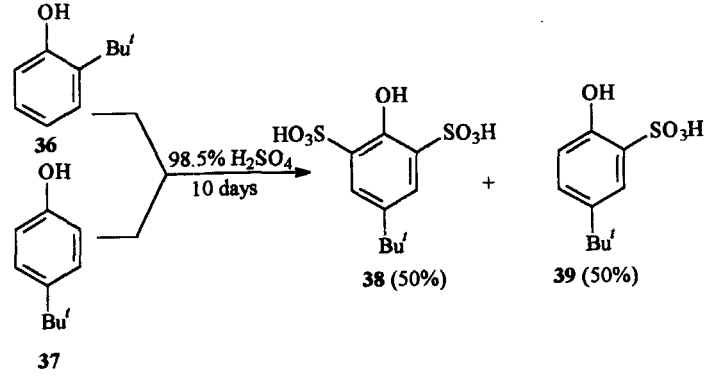
disulfonic acid (**35**) quantitatively (Scheme 10) [28]. Apparently, the presence of the hydroxy group activates the 4-position (which is *ortho* to the 3-*t*-butyl substituent) to such an extent that in these conditions, the sulfo-deprotonation and formation of the 4,6-disulfonic acid is far more favoured than sulfo- and protio-de-*t*-butylation.

2-*t*-Butylphenol (**36**) and 4-*t*-butylphenol (**37**) were sulfonated using 98.5% H_2SO_4 for 10 days to give the same two sulfonic acid products; 4-*t*-butylphenol-2,6-disulfonic acid (**38**) and 4-*t*-butylphenol-2-sulfonic acid (**39**), always in equal proportion (Scheme 11) [28]. Compounds **38** and **39** were obtained from **37** by simple sulfo-deprotonation. The formation of **38** and **39** from **36** is more difficult to understand, but can be explained in terms of either of two alternative reaction sequences; the first involves protonation at C-2, followed by a 1,3-*t*-butyl shift (or two sequential 1,2-*t*-butyl shifts), and subsequent sulfonation at the 2- and 6-positions; the second involves *ipso* attack of the sulfonating



33 **34** (100%) **35** (100%)

SCHEME 10



SCHEME 11

entity at C-2 followed by a 1,3-*t*-butyl shift, and subsequent deprotonation at the 6-position [28].

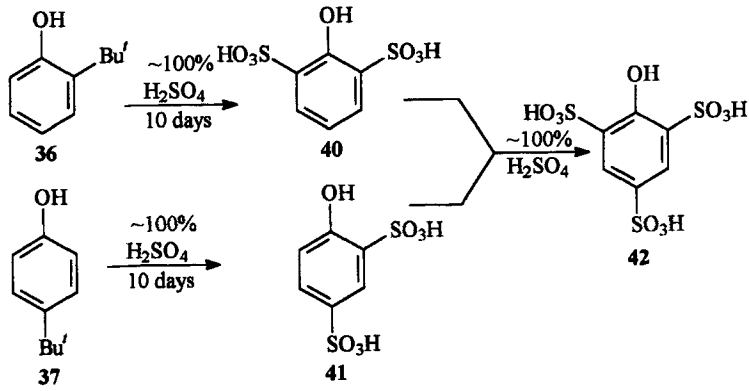
With ~100% H_2SO_4 compounds **36** and **37** afforded phenol-2,6-disulfonic acid (**40**) and phenol-2,4-disulfonic acid (**41**), respectively. If the reaction time was increased, it was found that compounds **40** and **41** were both converted into the 2,4,6-trisulfonic acid **42** (Scheme 12) [28].

2.4. Sulfonation of Di-*tert*-butylphenols

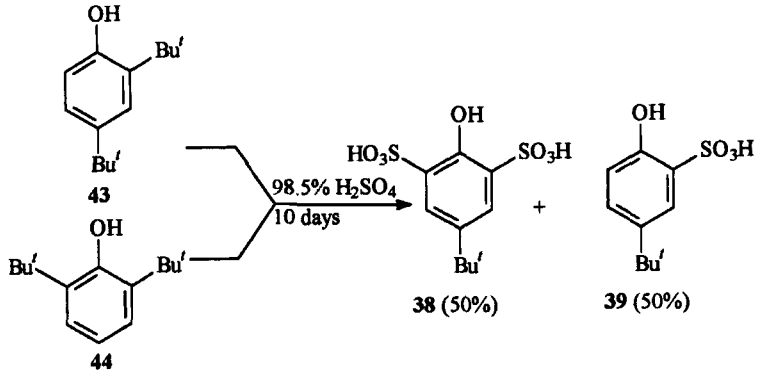
Sulfonation of 2,6-di-*t*-butyl-4-methylphenol with chlorosulfonic acid in chloroform at 0–25°C afforded 6-chlorosulfonyl-2-*t*-butyl-4-methylphenol in quantitative yield [29]. Other studies suggested that the di-*t*-butylation occurred *via* direct sulfo-di-*t*-butylation and not by initial protio-di-*t*-butylation and subsequent sulfo-deprotonation [28].

Sulfonation of both 2,4-di-*t*-butylphenol (**43**) and 2,6-di-*t*-butylphenol (**44**) with 98.5% H_2SO_4 afforded after 10 days of reaction the corresponding sulfonic acids, **38** and **39**, respectively, always in an equal ratio (Scheme 13), as also observed from the mono-*t*-butylphenols [28]. Compounds **38** and **39** were also formed when 2,4,6-tri-*t*-butylphenol was sulfonated with 98.5% H_2SO_4 for 10 days.

Sulfonation of both 2,5-di-*t*-butylphenol (**45**) and 3,5-di-*t*-butylphenol (**46**) with 98.5% H_2SO_4 afforded quantitatively 5-*t*-butylphenol-2-sulfonic acid (**47**) after 10 days of reaction (Scheme 14) [28].



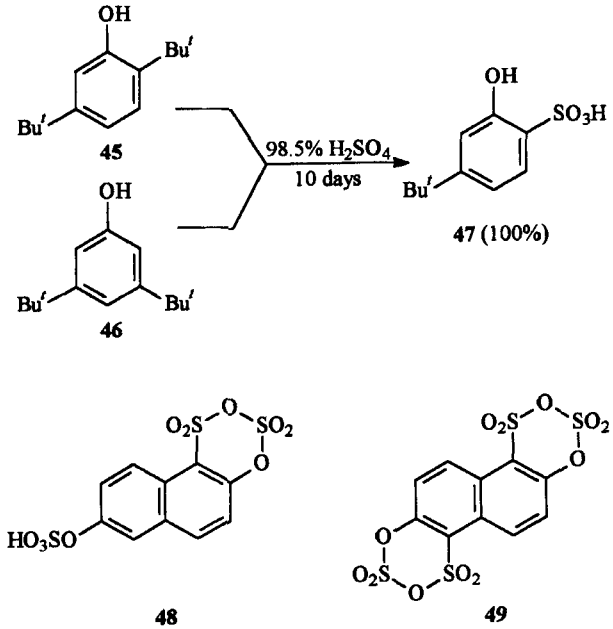
SCHEME 12



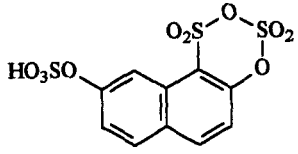
SCHEME 13

Compound **47** was also obtained quantitatively when **45** was sulfonated with two equivalents of SO_3 in CCl_3F as a solvent.

The formation of sulfonic acid **47** from 3,5-di-*t*-butylphenol (**46**) in sulfonation with 98.5% H_2SO_4 could be explained in one of three



SCHEME 14



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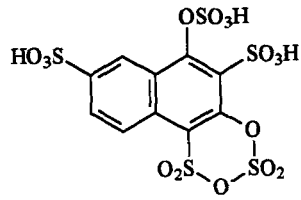

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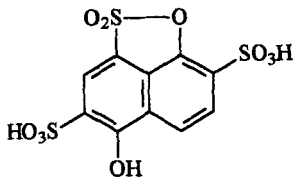

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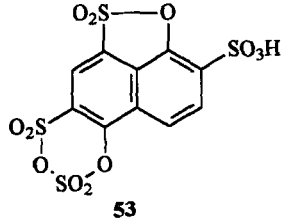

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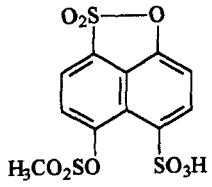

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SCHEME 14 (Continued).

ways: (i) by initial sulfo-de-*t*-butylation of **46** at the 3-position followed by a 1,2-sulfonic acid shift; (ii) by sulfo-deprotonation at the 2-position, followed by protio-de-*t*-butylation; and (iii) by protio-de-*t*-butylation followed by sulfo-deprotonation. A sulfonic acid derivative in which the sulfonic acid substituent is *meta* to the hydroxy group is generally not observed. Further, protio-de-*t*-butylation is more rapid than sulfo-de-*t*-butylation [27b]. Of the three possibilities, the third explanation is therefore more likely for the formation of **47** from **46** [28].

2.5. Sulfonation of Dihydroxynaphthalenes (DHNs)

Sulfonation reactions of dihydroxynaphthalenes (DHNs) with sulfur trioxide in nitromethane as a solvent have been studied with the use of

^{1}H NMR spectroscopy [30]. Upon reaction with 1.0 equivalent of SO_3, the dihydroxynapthalenes (DHNs) in general produce one or two monosulfonic acids. The observed monosulfonations of 1,7-,2,6- and 2,7-DHN compare favourably to give similar product distributions as their nitration using various nitrocyclohexadienones as reagents [31].

Sulfonation of 1,4-dihydroxynaphthalene (1,4-DHN) using SO_3 forms a tar-like precipitate that does not dissolve in any common solvent, which indicates that a polymerization process has taken place. From weak signals in the initial ^{1}H NMR spectrum it appears that some 2-sulfonic acid (2-S) is formed (Tab. I) [30].

It was found that monosulfonation of 2,3-DHN initially gave a 72:9:19 mixture of the 1-,5- and 6-sulfonic acid derivatives, respectively. The 1-sulfonic acid (1-S) was then rearranged to 6-sulfonic acid (6-S), with some 5-S being formed. This shows that the 1-position is the most reactive, but evidently there is also some steric strain in the 1-substituted product due to the two adjacent hydroxy groups (Tab. I) [30].

The fact that 1,6-DHN and 1,7-DHN are not sulfonated at the predicted most reactive positions, *viz.* C-5 and C-8 respectively, is also ascribed to steric factors [30]. For 1,6-DHN, sulfonation on C-5, *i.e.*, *ortho* to the hydroxy group and *peri-* to a hydrogen, will be sterically severely hindered. The same reason applies to 1,7-DHN, for which the steric factor for sulfonation at C-8 will be even larger due to the *peri*-interaction with the hydroxyl group at position 1 [30].

Sulfonation of 1,2-DHN with a large excess of SO_3 gave the *O*(2), 4-S_2 and *O*(1), *O*(2), 4-S_3 derivatives as the initially observed products (Tab. I) [30]. Prolonged sulfonation afforded a 70:30 mixture of *O*(2), 4,6-S_3 and *O*(2),4,7-S_3.

In the sulfonation of 1,4-DHN with a large excess of SO_3, it was found that 1,4-naphthalene bis(hydrogen sulfate) was obtained, together with 2-S, present as its 1-sulfated and disulfated derivatives (*O*(1),2-S_2 and *O*(1),*O*(4),2-S_3, respectively) [30].

Sulfonation of both 1,6- and 1,7-DHNs using an excess of SO_3 gave their corresponding 2,4-S_2 derivatives. These products were expected in view of the directing effect of the hydroxyl group at position 1 [30].

TABLE I Sulfonation of DHNs with SO_3 in nitromethane at 0°C

DHN	*SO_3 equiv.* (± 0.1)	*Time* (*min*)	*Reaction components* (%)[a, b, c]		
1,2-	1.0	5	4-S (≥ 99)		
	5.0	5	*O*(2),4-S_2(33)	*O*(1,2),4-S_3 (67)	
		5760	*O*(2),4,6-S_3 (70)	*O*(2),4,7-S_3 (30)	
1,3-	1.0	5	4-S (≥ 99)		
	5.0	4	4,7-S_2 (87)	2,4,7-S_3 (7)	**51** (6)
1,4-	1.0	5	2-S (≤ 5)		
	4.0	100	*O*(1),2-S_2 (55)	*O*(1,4),2-S_3 (45)	
1,5	1.0	10	2-S (≥ 99)		
	5.0	19000	2,6-S_2 (35)	**52** (21)	**53** (44)
1,6	1.0	5	2-S (22)	4-S (78)	
	5.0	4	2,4-S_2 (24)	*O*(6),2,4-S_3 (9)	*O*(1,6),2,4-S_4 (9)
1,7-	1.0	5	2-S (19)	4-S (81)	
	5.0	14	2,4-S_2 (26)	*O*(7),2,4-S_3 (58)	*O*(1,7),2,4-S_4 (16)
2,3-	1.0	6	1-S (72)	5-S (9)	6-S (19)
		2760	1-S (14)	5-S (18)	6-S (68)
	5.0	8	1,5-S_2 (39)	1,6-S_2 (6)	1,7-S_2 (55)
2,6-	1.0	10	1-S (≥ 99)		
	5.0	13	**48** (≥ 99)		
		7080	**48** (16)	**49** (36)	1,5-S_2 (34)
2,7-	1.0	10	1-S (≥ 99)		
		4300	1-S (47)	3-S (53)	
	5.0	12	**50** (≥ 99)		
		1700	**50** (67)	**50**-3-S (33)	

[a] The yield was determined by the use of ^{1}H NMR.
[b] S Stands for SO_3H.
[c] *O*(*n*) refers to sulfation on the specific position *n*.

Sulfonation of 2,6-DHN with 5 equivalents of SO_3 initially afforded the cyclic sulfonate sulfate anhydride **48**. This was found to react further with SO_3 to produce the bis(cyclic sulfonate sulfate anhydride) **49** and, in later stages, 2,6-DHN-1,5-disulfonic acid (Tab. I) [30].

Sulfonation of 2,7-DHN using a large excess of SO_3 initially afforded the cyclic anhydride **50**, which reacted further with SO_3 to produce the corresponding 3-sulfonic acid derivative, **50**-3-S (Tab. I) [30]. Also, sulfonation of 1,3-DHN with 5 equivalents of SO_3 initially produced 1,3-DHN-4,7-disulfonic acid, which sulfonated further to produce a mixture of products that all contain sulfonic acid groups on the 2-,4- and 7-positions, of which the most abundant product was **51** (Tab. I) [30].

It was found that sulfonation of 1,5-DHN using 5 equivalents of SO_3 afforded after a long time a mixture of three products, one of which is 1,5-DHN-2,6-disulfonic acid. The other two products both contain sulfonic acid groups at the 2-,4- and 6-positions and on at least one of the oxygens and were assigned by ^1H NMR spectroscopy as naphthalenesultones **52** and **53**, respectively (Tab. I) [30].

The substitution patterns for sulfonations of dihydroxynaphthalenes (DHNs) were found to be in agreement with the cation localization energies of 1,2-,1,3-,1,4-,2,3-,2,6- and 2,7-DHNs, obtained by simple Hückel MO calculations [30]. This observation indicated that the products formed in these cases are the kinetically controlled products [30]. The lack of correlation with 1,5-,1,6- and 1,7-DHNs may be due to steric factors [30]. The results of the disulfonation of DHNs suggested that sulfonation did not occur *via* the corresponding bis(hydrogen sulfates) and that hydrogen sulfate formation was more pronounced for β- than α-hydroxy groups [30].

2.6. Sulfonation of Dimesyloxynaphthalenes (DMSNs)

Sulfonation of dimesyloxynaphthalenes (DMSNs) with sulfur trioxide in [$^2H_3$]nitromethane as a solvent generally resulted in the formation of one or two sulfonic acid derivatives (Tab. II) [30]. Sulfonation using an excess of SO_3 led to the formation of the corresponding intermolecular sulfonic anhydrides, a reaction that is common with

TABLE II Reactions of some DMSNs with SO_3 in [$^2H_3$]nitromethane at 20°C

DMSN	SO_3 equiv (±0.1)	Time (min)	Reaction components (%)[a] Substrate	Sulfonic acid products (%)[b]		
1,3-	1.0	10	(47)	4-S (3)	5-S (44)	7-S (6)
	3.0	10	–	5-S (75)	$(5\text{-S})_2$ (25)	
1,4-	1.0	7200	(78)	6-S (22)		
	3.0	7000	–	6-S (87)	$(6\text{-S})_2$ (13)	
1,5-	1.0	7500	(≥ 99)			
	4.0	7500	–	3-S (35)	4-S (21)	**54** (44)
1,6	1.0	10	(40)	4-S (60)		
	5.0	10	–	4-S (67)	$(4\text{-S})_2$ (33)	
1,7	1.0	10	–	4-S (≥ 99)		
	3.0	10	–	4-S (72)	$(4\text{-S})_2$ (28)	
2,3-	1.0	4000	(68)	5-S (27)	6-S (2)	
	3.0	4000	–	5-S (50)	$(5\text{-S})_2$ (37)	$5,7\text{-S}_2$ (10)
2,6-	1.0	5000	(37)	1-S (26)	4-S (37)	
	3.0	5000	–	1-S (21)	4-S (34)	$(4\text{-S})_2$ (13)
2,7-	1.0	10	(87)	1-S (10)		3-S (3)
	3.0	10	–	1-S (49)	$(1\text{-S})_2$ (21)	3-S (30)

[a] S and $(S)_2$ stand for SO_3H and $(SO_2)_2O$, respectively.
[b] The data in brackets are the yields.

deactivated naphthalenes. Sulfonation *ortho* to the mesyloxy substituent is observed only with 2,6- and 2,7-DMSN. 2,7-DMSN, the two substituents of which both direct to C-1 and C-3, gives a mixture of 1-S and 3-S [30]. For 2,6-DMSN, the formation of 1-sulfonic acid (1-S) in 26% yield indicates that *ortho*-substitution is not prohibited sterically, but apparently only retarded [30]. Substitution *peri* to the OSO_2Me group takes place only in the case of a strong electron directing effect by another substituent, as with 1,5-DMSN, which is sulfonated at C-4 [30].

When 1,5-dimesyloxynaphthalene (1,5-DMSN), was treated with 1.0 equivalent of SO_3, no reaction took place. This is not unexpected, as the most reactive available positions, *viz.* C-2 and C-4, are both sterically hindered. Upon prolonged sulfonation using 3 equivalents of sulfur trioxide, 1,5-DMSN-3- and 1,5-DMSN-4-sulfonic acid derivatives were formed, along with sulfonic acid derivative **54**, in 35, 21 and 44% yields, respectively [30].

The inhibition of sulfonation at a *peri* position was found to be the same for a hydroxyl and a mesyloxy group, whereas the inhibition of sulfonation at an *ortho* position was found to be less for a hydroxyl group than for a mesyloxy group [30].

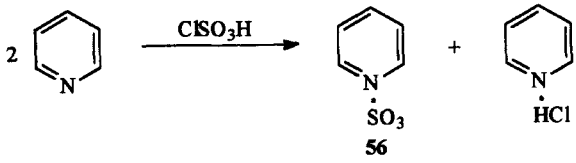
3. CONVERSION OF ORGANOLITHIUMS TO SULFONIC ACIDS USING SULFUR TRIOXIDE-BASE COMPLEXES

Sulfur trioxide, being an electron acceptor (or Lewis acid) combines with an electron donor (a Lewis base) to form a coordination compound, also known as an "adduct" or a "complex". The bases employed may be tertiary amines, including those which are fairly strong bases (trimethyl- or triethylamine), or considerably weaker (pyridine or dimethylaniline). The reactivity of the complex varies inversely with the strength of the base used [32]. When the adduct is employed for sulfonating an organic compound, SO_3 is released and the base forms a salt with the new sulfonic acid **55** (Scheme 15). Even the weakest sulfur trioxide-base complex is a much milder reagent than free SO_3. It is possible to moderate the reactivity of SO_3 to any desired degree by the correct choice of a complexing basic material.

The sulfur trioxide–pyridine complex has often been prepared by direct reaction of SO_3 with the base [32]. Reaction of pyridine with $ClSO_3H$ also yields SO_3-pyridine (**56**), along with a mole of pyridinium hydrochloride (Scheme 16) [33, 34].

The complex **56** has also been prepared along with two moles of pyridinium hydrochloride by adding ice to a mixture of pyridine and sulfuryl chloride [35]. The stability of the pyridine complex **56** is quite high. It is insoluble in cold water and cold aqueous alkali, but rapidly decomposes completely upon warming in either medium [33a]. It is insoluble in pyridine, nitrobenzene, cyclohexane, methylcyclohexane,

SCHEME 15



SCHEME 16

n-hexane, chloroform, carbon tetrachloride, dioxane, diethylether, *n*-butyl benzenesulfonate and acetone at 25°C [36] but is soluble in dimethylformamide [37]. Complex **56** has been used extensively as a laboratory reagent for sulfonating alcohols, sterols, carbohydrates, acid-sensitive heterocycles and alkadienes. These reactions are run at a moderate temperature, usually below 120°C in the presence of excess pyridine.

Sulfur trioxide–trimethylamine complex has been prepared by direct vapour phase interaction of SO_3 and trimethylamine without a solvent [37]. However, solvents such as chloroform [38] or liquid SO_2 [39] have also been used. Alternative methods for the preparation of sulfur trioxide–trimethylamine complex have involved reaction of trimethylamine with $ClSO_3H$ [40] using chlorobenzene as solvent at 10°C or with cold aqueous SO_3-pyridine [41]. The sulfur trioxide–trimethylamine complex is the most stable of those studied to date. It is considerably more stable than that derived from pyridine and has been used in the laboratory for sulfonating alcohols, starch and phenol.

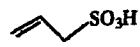
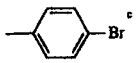
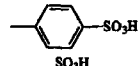
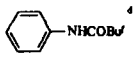
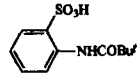
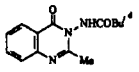
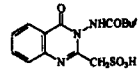
There is a lack of reports concerning reactions of reactive organometallic reagents with sulfur trioxide. Recently, however, the reaction of organolithium reagents with sulfur trioxide–trimethylamine complex to produce sulfonic acids **57** (Scheme 17) was reported by Smith and Hou [17].

A series of experiments was conducted to find conditions under which the reaction of organolithium reagents with a sulfur trioxide-base complex would produce sulfonic acids **57** in high yields. It was found that the reaction of the sulfur trioxide–pyridine complex with *n*-butyllithium, in diethyl ether or tetrahydrofuran (THF), and at −78°C rising to room temperature, resulted in the production of a complex mixture of products, including the product of addition of butyllithium to pyridine [17]. Treatment of the commercial sulfur trioxide–trimethylamine complex (STTAC) with *n*-butyllithium in diethyl ether also gave a complex mixture [17]. However, when the

$$R{-}Li + SO_3 \cdot NMe_3 \longrightarrow NMe_3 + R{-}SO_3Li \longrightarrow \underset{\mathbf{57}}{R{-}SO_3H}$$

SCHEME 17

TABLE III Yields for sulfonic acids **57** prepared according to Scheme 17

Starting material	*Product*	*57*[a]	*Yield* (%)[b]
n-BuLi	*n*-$BuSO_3H$	**a**	76
sec-BuLi	sec-$BuSO_3H$	**b**	74
t-BuLi	*t*-$BuSO_3H$	**c**	69
MeLi	CH_3SO_3H	**d**	60
PhLi	$PhSO_3H$	**e**	78
		**f**	78
		**g**	62
		**h**	79
		**i**	65

[a] Purity (%) is in the range of 95–99.
[b] Yields of isolated purified product.
[c] *Via* the corresponding organolithium reagent.
[d] *Via* the corresponding lithium dianions.

reaction of commercial STTAC with *n*-butyllithium was carried out in THF as solvent a mixture containing the desired butanesulfonate and one other major component, possibly lithium butanesulfinate, was obtained [42]. 1-Butanesulfonic acid (**57a**) was obtained in 76% yield (Tab. III) when *n*-butylithium was added dropwise to a stirred suspension of purified STTAC in dry THF at −78°C for 2 h followed by removal of the solvent and treatment of the residue with 6 M hydrochloric acid [17]. A similar procedure was applied to the synthesis of a range of sulfonic acids **57a–57i** from the corresponding organolithium and Grignard reagents [43] (Tab. III).

4. DIRECT SULFUR TRIOXIDE INSERTION INTO CARBON-ELEMENT BONDS

Sulfur trioxide itself can be inserted into the carbon–metal bond directly in some cases involving less electropositive metals. For example, aryltrimethylsilanes react with SO_3 in carbon tetrachloride to give compounds of the type $ArSO_2OSiMe_3$, **58**, which can be hydrolysed easily to afford the corresponding sulfonic acids **57** (Scheme 18) [44].

$$Ar-SiMe_3 \xrightarrow{SO_3} \underset{\mathbf{58}}{Ar-SO_2-OSiMe_3} \xrightarrow[-Me_3SiOH]{H_2O} \underset{\mathbf{57}}{Ar-SO_3H}$$

SCHEME 18

$$p\text{-}Me_3Si-C_4H_4-SiMe_3 \xrightarrow{SO_3} \xrightarrow{H_2O} \underset{\mathbf{59}}{p\text{-}Me_3Si-C_4H_4-SO_3H}$$

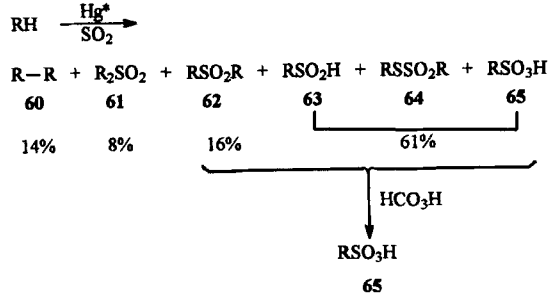
SCHEME 19

The reaction has also been applied to the synthesis of some organosilicon-substituted benzenesulfonic acids such as **59** (Scheme 19) [44].

This reaction has obvious synthetic appeal since it can be employed to introduce a sulfonic acid group into an aromatic compound at a specified position under mild conditions. Quantitative aspects of the above reaction were probed by Bott, Eaborn and Hashimoto and it emerged that $Ar-SiMe_3$ is cleaved in preference to the $C_6H_5-SiAr_3$ or $Ar-Si(C_6H_5)_3$ bond [45]. Benzyl–Si bonds were not cleaved under the conditions used and *o*-, *m*- and *p*-[trimethylsilylmethyl]benzenesulfonic acids were obtained from the corresponding [(trimethylsilyl)methylphenyl]trimethylsilanes. There was no evidence for normal sulfonations *i.e.*, attack at Ar–H bonds. This is consistent with the results of bromination and acid cleavage, where $Ar-SiMe_3$ bonds are also far more reactive than Ar–H bonds. Little information on substituent effects in the SO_3 reaction is available.

5. MISCELLANEOUS SULFONATION

Mercury-photosensitized sulfination of alkanes (RH) with SO_2 resulted in the production of sulfinate esters **62** and sulfinic acids **63** in high conversion and yield [46]. Oxidation of this mixture using performic acid afforded the corresponding sulfonic acids **65** in high yield (Scheme 20) [46]. The initial reaction afforded a surprisingly large number of products [46]. The formation of dehydrodimer **60** means that the trapping of the $R^{\cdot}$ by SO_2 is not completely effective. Sulfone **61** (8%) and sulfinate esters **62** (16%) were also obtained, but as minor products. The major species formed were sulfinic acid **63** and its disproportionation products, thiosulfonate **64** and sulfonic acid **65**



SCHEME 20

itself [46]. It was found that both RSO_2H **63** and RSO_2R **64** were oxidized easily to the corresponding desired sulfonic acid **65** during the performic acid reaction (Scheme 20).

Various conditions were examined in order to maximize the yield of the oxidizable fraction, consisting of **62–64**, relative to the non-oxidizable species **60** and **61**. It was found that it was necessary to increase the SO_2 flow rate to 20 ml/min to ensure that sufficient trapping gas was being supplied. A flow of H_2 doped into the SO_2 proved beneficial, perhaps because H atoms are formed from Hg^* and H_2, and these H atoms may recombine with intermediate $RSO_2^{\cdot}$. A 15 ml/min flow of hydrogen gave the highest eventual yields of sulfonic acid [46].

By applying these new conditions, cyclohexane, for example, at 30°C afforded 80% by weight of RSO_2H and 17% of RSO_2R. No dimer was formed, indicating that all $R^{\cdot}$ radicals were completely trapped by SO_2. Oxidation of the mixture with performic acid produced cyclohexanesulfonic acid in 99% yield [46]. The same procedure was applied successfully to the production of various sulfonic acids, which were then separated by solvent extraction [46].

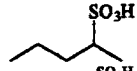
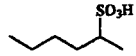
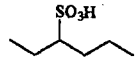
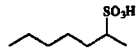
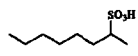
Mercury-photosensitized hydrosulfination of alkenes with H_2 and SO_2 gave, after oxidative workup, sulfonic acids **65** [46]. H atoms formed from the reaction of Hg^* and H_2 react with alkenes to give alkyl radicals, which lead to the formation of hydrodimerization products. One of the advantages of using an alkene is the high regioselectivity of radical formation [47]. For example, with *n*-hexane, all secondary C—H bonds are equally reactive, giving a statistical mixture of radicals, but with 3-hexene, essentially only the 3-hexyl

radical is formed. Thus, from sulfination/oxidation of *n*-hexane both 2- and 3-hexanesulfonic acids were formed in yields of 43 and 51%, respectively [46]. By contrast, hydrosulfination of 1-hexene gave 2-hexanesulfonic acid in 71% yield, free from other isomers (1- and 3-isomers) [46]. Similarly, hydrosulfination of 3-hexene gave 3-hexanesulfonic acid in a yield of 75%, again free of other isomers (Tab. IV) [46].

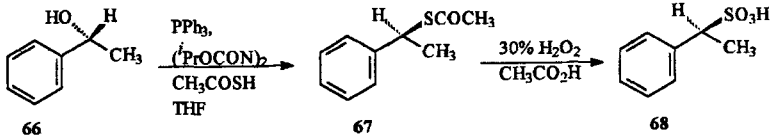
Chiral (*S*)-1-phenylethanesulfonic acid (**68**) was obtained directly from the *S*-alkylthioacetate **67** in a single step [48]. The conversion took place by treatment of a solution of **67** in acetic acid with 30% hydrogen peroxide at 60°C (Scheme 21) [49]. Thioacetate **67** was in turn prepared in 72% yield and 96% ee from the *R*-alcohol **66** using Mitsunobu conditions [50].

Alkanesulfonamides and alkanesulfonates can conveniently be deprotonated at the α-position and reactions of the α-metalated species produced with electrophiles gives a wide range of alkanesulfonic acid derivatives [51]. Reactions of cyanohydrins with mesyl

TABLE IV Sulfonic acids **57** from Hg^{*}-sensitized hydrosulfination of olefins

Substrate	*Product*[a]	*Weight %*[b]
1-pentene		91
1-hexene		71
3-hexene		75
1-heptene		88
1-octene		80

[a] $RSO_3H \cdot 3H_2O$.
[b] Refers to sulfonic acid in the final product mixture of involatile material after photochemical and oxidation steps.



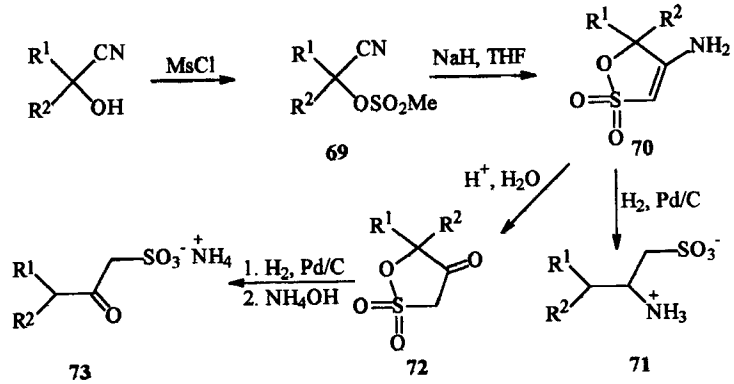
SCHEME 21

chloride afford the corresponding cyanohydrin mesylates **69** [52]. Deprotonation of **69** to give the α-carbanion, followed by intramolecular addition to the nitrile group, gives 4-amino-5 *H*-1,2-oxathiole-2,2-dioxides (**70**). Compounds **70** are useful intermediates for the synthesis of β-amino and β-ketosulfonic acids **71** and **73** (Scheme 22) [52]. Hydrogenation of compounds **70** in the presence of a palladium–charcoal catalyst gives the β-amino sulfonic acids **71** in good yields [52], while hydrolysis of compounds **70** affords 1,2-oxathiolan-4-ones **72** [52]. Catalytic hydrogenation of **72** affords β-keto sulfonic acids **73** (isolated as ammonium salts) in good yields (Scheme 22) [52].

Alkanesulfonic acids (*e.g.*, $MeSO_3H$) have been prepared in high yield and high selectivity by the reaction of alkanethiol derivatives (*e.g.*, Me–SH) with Cl_2 in the presence of aqueous HCl at $-10°C$ to $+115°C/1.05-8.16$ atm [53]. Alkanesulfonic acids (RSO_3H) have also been prepared by the photoxidation of sulfur derivatives (RSR^1; R^1 = H, R, SR) in aqueous or alcoholic MeCN at 200–400 nm [54].

Perfluoroalkanesulfonic acids have been prepared in high yield and selectivity by the reaction of oxone® with perfluoroalkyl compounds (*e.g.*, 1-iodoperfluorooctane) in propanoic acid as solvent [55]. Fluorinated sulfonic acids have been prepared by hydrolysis of the corresponding fluorinated sulfonyl fluorides in the presence of a tertiary amine [56].

Recently, preparations of 2,6-disubstituted benzenesulfonic acids by electrophilic substitution have been reported [57]. Phenols were safely,



SCHEME 22

selectively, and quantitatively sulfonated in dialkyl carbonates as solvents [58]. Resorcinol was treated with $ClSO_3H$ in dimethyl carbonate to give 99% conversion [58].

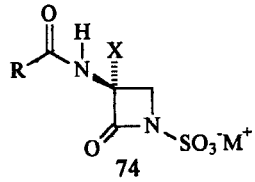
6. PREPARATION OF SULFAZECINS

A novel type of monocyclic β-lactam antibiotic [*e.g.*, 3-(acylamino)-2-oxoazetidine-1-sulfonic acids **74**], which is characterised by the presence of an SO_3^- group bonded to the azetidinone nitrogen, has been isolated from certain bacteria [59].

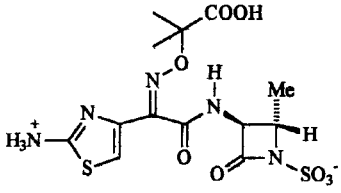
These compounds are called monobactams or sulfazecins and show interesting activity towards β-lactamase. Aztreonam (**75**) and carumonam (**76**) showed specific activity against *gram-negative* bacteria coupled with high β-lactamase activity. These compounds showed significant biological properties, which have allowed them to be brought into clinical use. Since 4-substituted monobactams are not accessible through microbiological methods, their preparation requires the development of total syntheses of the corresponding 3-amino monobatamic acid (3-AMA) derivatives **77**–**79** [60]. One of the most efficient methodologies for the general preparation of 3-AMA derivatives involves the biomimetic cyclization of suitably derivatized 2-amino-3-hydroxyacids [61].

cis-4-Methyl-3-AMA (**78**) can be prepared as shown in Scheme 23 [62]. Sulfonation of 3-[*N*,*N*′-bis-(*t*-butoxycarbonyl)hydrazino]-4-methylazetidin-2-one (**80**) was carried out using pyridine-SO_3 complex in hot pyridine and the resulting azetidinesulfonic acid was isolated through extraction of its tetra-*n*-butylammonium salt **81** [62]. Attempted further purification through silica gel chromatography afforded the azetidinesulfonic acid **82** instead of the expected salt **81** [62]. When **82** was subjected to acidic cleavage of the *t*-butylurethane with CF_3COOH, the hydrazinium salt **83** was obtained. Hydrogenation of **83** over PtO_2 in ethanol afforded **78** (Scheme 23) [62].

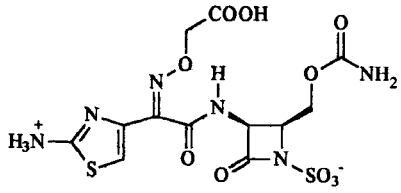
Attempted coupling of L-*Z*-β-chloroalanine (*Z* = benzyloxycarbonyl) **84** and tetra-*n*-butylammonium sulfamate has been reported [63]. However, the sulfamate anion was found to be an extremely poor nucleophile and only a moderate yield of **85** was obtained when



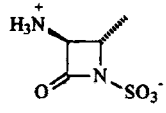
74



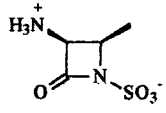
75 aztreonam



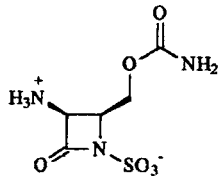
76 carumonam



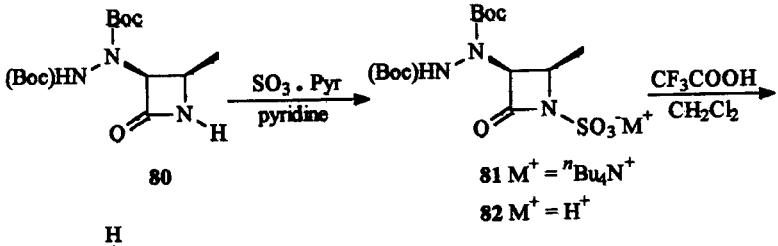
trans-4-methyl-3AMA
77



cis-4-methyl-3AMA
78



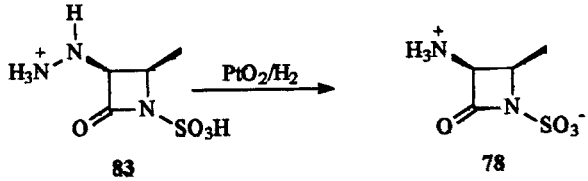
cis-4-carbamoyloxymethyl-3AMA
79



80

81 $M^+ = {}^nBu_4N^+$

82 $M^+ = H^+$



83

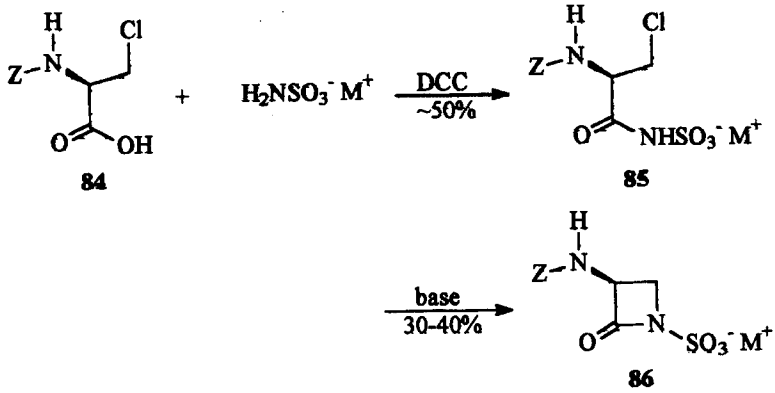
78

SCHEME 23

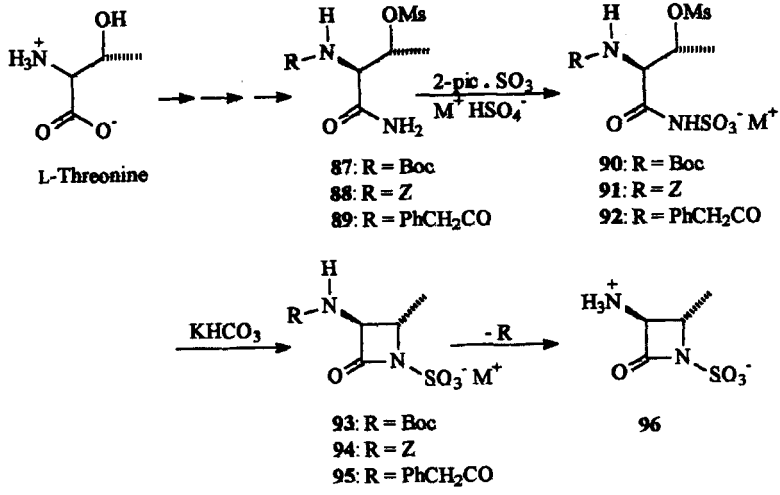
dicyclohexylcarbodiimide (DCC) was used as the coupling reagent (Scheme 24) [63]. The azetidinone **86** was obtained, but in low yields (30–40%), when sulfamate **85** was treated with a base [63]. The low yield of **86** obtained encouraged the authors to investigate other synthetic pathways.

A better route to acylsulfamates involves initial transformation of the amino acid to a protected α-amino amide and subsequent sulfonation of the primary amide. Scheme 25 shows the application of this approach for the transformation of L-threonine to sulfamates **90–92**. Cyclization of **90–92** under basic conditions afforded the corresponding azetidines **93–95**, which were deprotected to afford zwitterion **96** [63].

Attempted sulfonation of **87** with freshly prepared pyridine-sulfur trioxide complex [33c] under different reaction conditions gave **90**, but in low yield [63]. An attempt was therefore made to apply different amine sulfur trioxide complexes. It was found that treatment of **87** with 2.5–3.0 equivalents of 2-picoline-sulfur trioxide complex [33c] (pic · SO_3) in dichloromethane at room temperature for 4–5 h, followed by addition of a large excess of 0.5 M aqueous KH_2PO_4, then addition of tetra-*n*-butylammonium hydrogen sulfate (1.0 equivalent) and finally extraction with dichloromethane, gave the desired acylsulfamate **90** in greater than 90% yield [63]. However, the yield became even better when the reaction mixture was heated under reflux for 18–20 h to produce **90** in 90–95% crude yields. Analysis of the



SCHEME 24



SCHEME 25

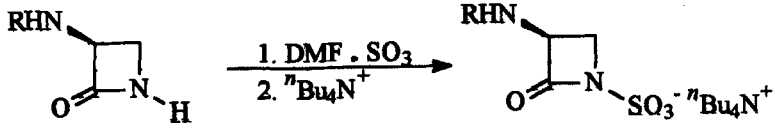
crude tetra-*n*-butylammonium salt by TLC indicated it to be essentially homogeneous, as did ^1H and ^{13}C NMR analyses [63]. By applying the same reaction conditions, the *Z*-amide **88** was converted to sulfamate **91** in 85–90% crude yield. The addition of **90** to a refluxing mixture of 1,2-dichloroethane and water containing 4 equivalents of potassium carbonate resulted in a rapid reaction to give the azetidinone **93** in good yield (Scheme 25) [63]. A cleaner reaction was observed when potassium bicarbonate was used as the base instead of potassium carbonate. Under these conditions (reflux, 15 min), sulfamates **90** and **91** were converted to azetidinones **93** and **94**, respectively, in 90–99% yields. The products were found to be virtually homogenous by TLC and spectral analysis [63].

Deprotection of the amino function of azetidinones **93–95** was carried out under standard conditions on the crude isolated products. Thus the Boc-azetidinone **93** was dissolved 0.3 M formic acid (97%) and the resulting solution was stirred, which led to the precipitation of analytically pure **96** in 65–70% yield [63]. Hydrogenolysis of *Z*-azetidinone **94** over 5% Pd–C in ethanol, followed by the addition of formic acid, resulted in the precipitation of **96** in 50% yield [63]. Treatment of a solution of **95** in methylene chloride with excess phosgene in pyridine at 0°C, followed by addition of methanol again resulted in the precipitation of **96** in 41% yield [63].

The reactions of the Boc-protected azetidinone **97** and *Z*-protected azetidinone **98** with DMF · SO_3 [33c] in DMF at 0°C for 20 minutes gave the corresponding sulfonic acid derivatives, **99** and **100**, respectively, in good yields and analytically pure (Scheme 26) [64]. However, it was observed that the yield of **99** decreased as the length of reaction increased. The authors suggested that the product might be the DMF solvate of the azetidinonesulfonic acid, with the Boc group being partially lost during the reaction. Another problem raised, with respect to large-scale work, was that rigorously anhydrous conditions were also necessary to achieve a high yield [64].

When a solution of (*S*)-3-[(*t*-butoxycarbonyl)amino]-2-azetidinone (**97**) in pyridine was heated to 80°C, then 3 equivalents of pyridine-sulfur trioxide complex added and the mixture stirred for 30 min and then worked up, the sulfonate **99** was obtained in 89–91% yield [64]. This procedure was found to be dependent on the quality of pyr · SO_3 and on the length of the reaction, but independent of the solvent purity. In the case of azetidinones **101** and **102**, which contain a methyl group, it was found that the reaction time should exceed 45 min to obtain maximum yields of **103** and **104**, respectively (Scheme 27) [64]. Deprotection of **99**, **103** and **104** was achieved by dissolving them in 97% formic acid, then stirring for 4.5 h at room temperature, followed by the addition of dichloromethane and work up to afford the corresponding zwitterions **105**–**107** in various yields (Scheme 27) [64]. It was found that the differences in yields were due to solubility differences between the three products and exactly paralleled the observed solubilities of the zwitterions in water; **107** > **105** > **106**. In all cases, the products were isolated by simple filtration and found to be analytically pure.

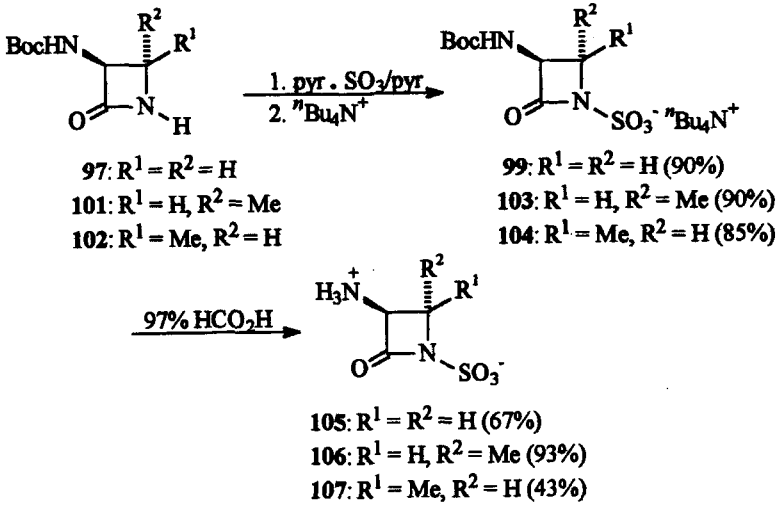
Treatment of **74a** with phosgene in acetonitrile-pyridine at 45°C for 2 h gave chloroester **110** and acetonitrile rather than the expected



97: R = Boc
98: R = Z

99: R = Boc
100: R = Z

SCHEME 26



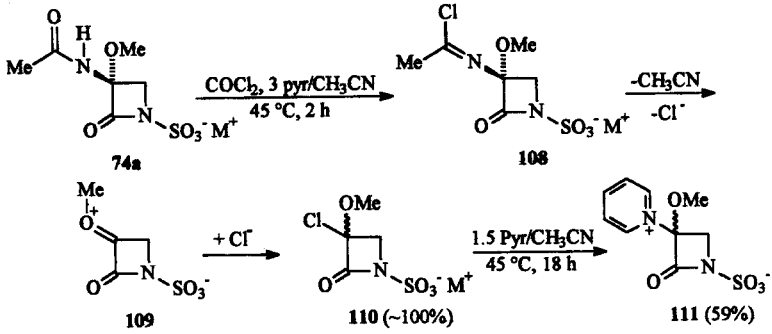
SCHEME 27

imino chloride **108** (Scheme 28) [65]. The structure of **110** was inferred from spectral properties and from mechanistic argument [66], and was confirmed by conversion of **110** into **111**. Treatment of **110** with 1.5 equivalents of pyridine in acetonitrile at 45°C for 18 h afforded **111** in 59% yield [65].

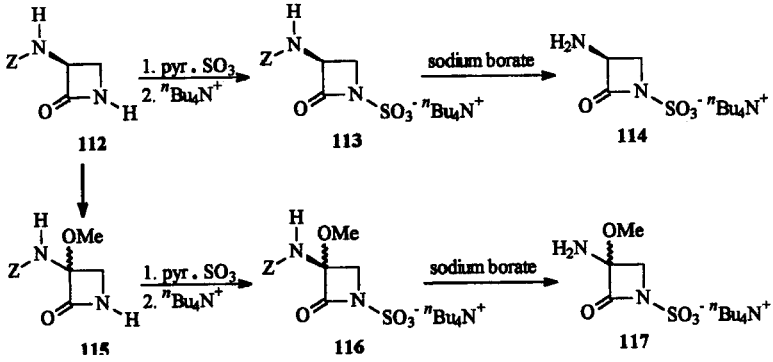
Sulfonation of **115** was found to be much slower than sulfonation of **112** due to steric effects and electron withdrawal by the methoxy group, but proceeded in high yield with excess pyridine-sulfur trioxide to give **116** after ion-pair extraction (Scheme 29) [65]. Hyrogenolysis of **116** using 10 mol% sodium borate in acetonitrile or methanol gave **117** in high yield (Scheme 29) [65].

When sodium borate was omitted, the crude product showed virtually no CH_3O resonance (^1H NMR), suggesting that acid-catalysed decomposition *via* zwitterion **118** had intervened (Scheme 30) [65]. Moreover, it was found that **117** was converted into zwitterion **118** under acid conditions [65].

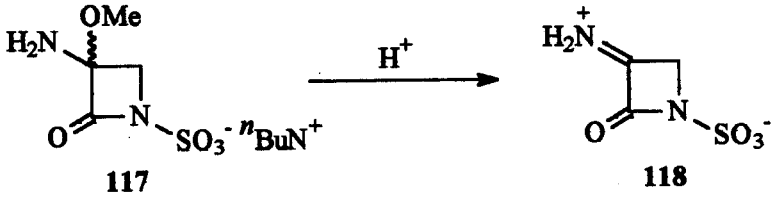
Racemic monobactams **74** (X=OMe) could be obtained from acylation of **117** using acid chlorides. When acylating agents derived from enantiomerically-pure α-amino acids were used, the resulting mixture of diastereomeric monobactams could be separated to provide biologically active 3*R* enantiomers of **74** (X=OMe) [65].



SCHEME 28



SCHEME 29



SCHEME 30

7. CONCLUSIONS

The sulfonations of phenolic compounds using sulfuric acid have been studied by several methods. Dihydroxy and dimesyloxynaphthalenes

were sulfonated successfully under different reaction conditions using SO_3 to afford a complex mixture of products. Some biologically active compounds were prepared in high yield and selectivity by the use of sulfur trioxide-base complexes. Trimethylamine-sulfur trioxide reacts with organolithiums in THF to give lithium sulfonates. Subsequent treatment with acid affords the corresponding sulfonic acids in good yields. This reaction is suitable for both aliphatic and aromatic sulfonic acids. Some sulfonic acids could be prepared by direct insertion of SO_3 into carbon-element bonds.

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References

[1] Barrett, G. C. (1973). *Organic Compounds of Sulfur, Selenium and Tellurium* (The Royal Chemical Society, London), Vol. 2, Chapter 1.
[2] Quaedvlieg, M. (1955). *Methoden der Organischen Chemie* (Thieme Verlag, Stuttgart), Vol. IX, Chapter 14.
[3] Muth, F. (1955). *Methoden der Organischen Chemie* (Thieme Verlag, Stuttgart), Vol. IX, Chapter 16.
[4] Howells, R. D. and McCown, J. D. (1977). *Chem. Rev.*, **77**, 69.
[5] Barrett, G. C. (1970). *Organic Compounds of Sulfur, Selenium and Tellurium* (The Royal Chemical Society, London), Vol. 1, Chapter 2.
[6] Barrett, G. C. (1975). *Organic Compounds of Sulfur, Selenium and Tellurium* (The Royal Chemical Society, London), Vol. 3, Chapter 1.
[7] Gilbert, E. E. (1969). *Synthesis*, Vol. 3.
[8] Gilbert, E. E. (1965). *Sulfonation and Related Reactions* (Interscience, New York), pp. 62–83, 87–124, 215–239.
[9] Andersen, K. K. (1979). *Comprehensive Organic Chemistry* (Pergamon Press), Chapter 11, pp. 331–338.
[10] See for example; (a) Berké, B., Chéze, C., Vercauteren, J. and Deffieux, G. (1998). *Tetrahedron Lett.*, **39**, 5771; (b) Fanchon, C. (1996). *Eur. Pat. Appl. EP 728,474*; *Chem. Abstr.*, **125**, 256772 (1996); (c) Boelle, J.-P., Laugier, J.-P. and Forestier, S. (1995). *Eur. Pat. Appl. EP 671,160*; *Chem. Abstr.*, **123**, 296250 (1995); (d) Fuku, Y. (1997). *Jpn. Kokai Tokyo Koho JP 09,110,613*; *Chem. Abstr.*, **127**, 33590 (1997); (e) Wieczorek, J. J. (1997). *PCT Int. Appl. WO 97 18,190*; *Chem. Abstr.*, **127**, 50395 (1997).
[11] Uemura, S. (1991). *Comprehensive Organic Synthesis* (Pergamon Press), Chapter 6, pp. 757–784.
[12] Sandler, S. R. and Karo, W. (1968). *Organic Functional Group Preparations* (Academic Press, New York), p. 506.

[13] (a) Houlton, H. G. and Tartar, H. V. (1938). *J. Am. Chem. Soc.*, **60**, 544; (b) Wagner, F. C. and Reid, E. E. (1931). *J. Am. Chem. Soc.*, **53**, 3407.
[14] (a) Allen, P. (1942). *J. Org. Chem.*, **7**, 23; (b) Marvel, C. S. and Johnson, R. S. (1948). *J. Org. Chem.*, **13**, 822; (c) Pinnick, H. W. and Reynolds, M. A. (1979). *J. Org. Chem.*, **44**, 160.
[15] (a) Eaborn, C. and Hashimoto, T. (1961). *Chem. Ind.*, p. 1081; (b) Bott, R. W., Eaborn, C. and Hashimoto, T. (1965). *J. Organometal. Chem.*, **3**, 442; (c) Bott, R. W., Eaborn, C. and Hashimoto, T. (1963). *J. Chem. Soc.*, p. 3906; (d) Schmidbaur, H., Sechser, L. and Schmidt, M. (1969). *Chem. Ber.*, **102**, 376; (e) Schmidbaur, H., Sechser, L. and Schmidt, M. (1968). *J. Organometal. Chem.*, **15**, 77; (f) Gelius, R. and Muller, R. (1967). *Z. Anorg. Allg. Chem.*, **351**, 42; (g) Dubac, J. and Mazerolles, P. (1969). *J. Organometal. Chem.*, **20**, 5.
[16] Salib, K. A. R. and Senior, J. B. (1970). *J. Chem. Soc., Chem. Commun.*, p. 1259.
[17] Smith, K. and Hou, D. (1996). *J. Org. Chem.*, **61**, 1530.
[18] Spryskov, A. A. and Gnedin, B. G. (1964). *Izv. Vyssh. Uchebn. Zaved Khim. Khim. Tekhnol.*, **7**, 61; *Chem. Abstr.*, **61**, 6403 (1964).
[19] Crumrine, D. S. and Gillece-Castro, B. (1985). *J. Org. Chem.*, **50**, 4408.
[20] Monaghan, J. J., Barber, M., Bordoli, R. S., Sedgwick, D. and Tyler, A. N. (1982). *Org. Mass Spectroscopy*, **17**, 529.
[21] Strandlund, G. and Lagerström, P.-O. (1979). *Acata Chem. Scand., Ser. B*, **33**, 261.
[22] (a) Arnett, E. M. and Wu, C. Y. (1960). *J. Am. Chem. Soc.*, **82**, 5660; (b) Koeberg-Telder, A., Lambrechts, H. J. A., and Cerfontain, H. (1983). *Recl. Trav. Chim. Pays-Bas*, **102**, 293; (c) Lambrechts, H. J. A. and Cerfontain, H. (1983). *Recl. Trav. Chim. Pays-Bas*, **102**, 293.
[23] (a) Cerfontain, H., Lambrechts, H. J. A., Schaasberg-Nienhuis, Z. R. H., Coombes, R. G., Hadjigeorgiou, P. and Tucker (1985). *J. Chem. Soc., Perkin Trans., 2*, p. 659; (b) Koeberg-Telder, A., Lambrechts, H. J. A. and Cerfontain, H. (1985). *J. Chem. Soc., Perkin Trans., 2*, p. 1241.
[24] Lambrechts, H. J. A., Schaasberg-Nienhuis, Z. R. H. and Cerfontain, H. (1985). *J. Chem. Soc., Perkin Trans., 2*, p. 669.
[25] Cerfontain, H., Koeberg-Telder, A., Lambrechts, H. J. A. and de Wit, P. (1984). *J. Org. Chem.*, **49**, 4917.
[26] Wheland, G. W. (1955). *Resonance in Organic Chemistry* (Wiley, New York), p. 508.
[27] (a) Cerfontain, H. (1968). *Mechanistic Aspects in Aromatic Sulfonation and Desulfonation* (Interscience, New York), pp. 53–57, 181, 182; (b) Ris, C. and Cerfontain, H. (1975). *J. Chem. Soc., Perkin Trans., 2*, p. 1438 and references cited therein.
[28] Lambrechts, H. J. A., Mul, J. and Cerfontain, H. (1985). *J. Chem. Soc., Perkin Trans., 2*, p. 677.
[29] Weinstein, A. H. (1967). *J. Org. Chem.*, **32**, 3669.
[30] Ansink, H. R. W., Zelvelder, E., de Graaf, E. J. and Cerfontain, H. (1993). *J. Chem. Soc., Perkin Trans., 2*, p. 721.
[31] (a) Roussel, J., Lemaire, M., Guy, A. and Guetté, J.-P. (1986). *Tetrahedron Lett.*, **27**, 27; (b) Lemaire, M., Guy, A., Roussel, J. and Guetté, J.-P. (1987). *Tetrahedron*, **43**, 835.
[32] Hall, H. K. Jr. (1956). *J. Phys. Chem.*, **60**, 63.
[33] (a) Baumgarten, P. (1926). *Ber.*, **59B**, 1166; (b) Scully, J. F. and Brown, E. V. (1954). *J. Org. Chem.*, **19**, 894; (c) Hofmann, K. and Simchen, G. (1979). *Synthesis*, 699.
[34] (a) Sisler, H. H. and Audrieth, L. F. (1946). *Inorg. Synth.*, **2**, 173; (b) Wagner, J. (1886). *Ber.*, **19**, 1157.
[35] Baumgarten, P. (1927). *Ber.*, **60**, 1177.
[36] Terent'ev, A. P. and Kadatskii, G. M. (1952). *Zhur. Obshchei Khim.*, **22**, 153; *Chem. Abstr.*, **46**, 11178 (1952).

[37] Burg, A. B. (1943). *J. Am. Chem. Soc.*, **65**, 1629.
[38] National Starch products, Inc. (1957). *British Patent, 755,461*; *Chem. Abstr.*, **51**, 8460 (1957).
[39] Gilbert, E. E. and Nychka, H. R. (1960). *US Patent, 2,928,836*; *Chem. Abstr.*, **54**, 12165 (1960).
[40] Hardy, W. B. and Hardy, E. M. (1954). *US Patent, 2,647,129*; *Chem. Abstr.*, **48**, 4851 (1954).
[41] Baumgarten, P. (1926). *Ber.*, **59B**, 1976.
[42] Burg, A. B. (1943). *J. Am. Chem. Soc.*, **65**, 1629.
[43] (a) Chetcuti, M. J., Chisholm, M. H., Folting, K., Haitko, D. A., Huffman, J. C. and Janos, J. (1983). *J. Am. Chem. Soc.*, **1050**, 1163; (b) Führer, W. and Gschwend, H. W. (1979). *J. Org. Chem.*, **44**, 1133; (c) Smith, K. and Pritchard, G. (1990). *Angew. Chem., Int. Ed Engl.*, **29**, 282; (d) Smith, K., El-Hiti, G. A., Abdo, M. A. and Abdel-Megeed, M. F. (1995). *J. Chem. Soc., Perkin Trans., 1*, p. 1029.
[44] Eaborn, C. and Hashimoto, T. (1961). *Chem. Ind.*, p. 1081.
[45] Bott, R. W., Eaborn, C. and Hashimoto, T. (1965). *J. Organometal. Chem.*, **3**,442.
[46] Ferguson, R. R. and Crabtree, R. H. (1991). *J. Org. Chem.*, **56**, 5503.
[47] (a) Muedas, C. A., Ferguson, R. R. and Crabtree, R. H. (1989). *Tetrahedron Lett.*, **30**, 3389; (b) Muedas, C. A., Ferguson, R. R., Brown, S. H. and Crabtree, R. H. (1991). *J. Am. Chem. Soc.*, **113**, 2233.
[48] Corey, E. J. and Cimprich, K. A. (1992). *Tetrahedron Lett.*, **33**, 4099.
[49] Agami, C., Prince, B. and Puchot, C. (1990). *Synthesis Commun.*, **20**,3289.
[50] Volante, R. P. (1981). *Tetrahedron Lett.*, 3119.
[51] Patai, S. and Rappoport, Z. (Eds.) (1991). *The Chemistry of Sulfonic Acids, Esters and Their Derivatives* (John Wiely & Sons, New York), pp. 408–412.
[52] Poszávácz, L. and Simig, G. (1997). *J. Org. Chem.*, **62**, 7021.
[53] Schon, S. G., Wheaton, G. A. and Overgaard, T. H. (1995). *Eur. Pat. Appl. EP 675, 107*; *Chem. Abstr.*, **123**, 339140 (1995).
[54] Banchereau, E., Lacombe, S. and Ollivier, J. (1996). *Eur. Pat. Appl. EP 714, 888*; *Chem. Abstr.*, **125**, 114180 (1996).
[55] Marzouk, H., Petit, L., Tordeux, M., Berecibar, A. and Wakselman, C. (1997). *PCT Int. Appl. WO 9724,309*; *Chem. Abstr.*, **127**, 108706 (1997).
[56] Hommeltoft, S. I., Ekelund, O. and Zavilla, J. (1997). *US. US 5,648,522*; *Chem. Abstr.*, **127**, 135552 (1997).
[57] Spangler, L. A. and Weaver, D. G. (1997). *U.S. US 5,670,691*; *Chem. Abstr.*, **127**, 307205 (1997).
[58] Ban, Y., Shimizu, T., Tabuchi, K. and Shimozaki, T. (1997). *Jpn. Kokai Tokyo Koho JP 09,227,499*; *Chem. Abstr.*, **127**, 234175 (1997).
[59] (a) Imada, A., Kitano, K., Kintaka, K., Murali, M. and Asai, M. (1981). *Nature (London)*, **289**, 590; (b) Sykes, R. B., Cimarusti, C. M., Bonner, D. P., Bush, K., Floyed, D. M., Georgopapadakou, N. H., Koster, W. H., Liu, W. C., Parker, W. L., Principe, P. A., Rathnum, M. L., Slusarchyk, W. A., Trejo, W. H. and Wells, J. S. (1981). *Nature (London)*, **291**, 489.
[60] See for example; (a) van der Steen, F. H. and van Koten, O. (1991). *Tetrahedron*, **47**, 7503; (b) Andreoli, P., Billi, L., Cainelli, G., Panunzio, M., Bandini, E., Martelli, G. and Spunta, G. (1991). *Tetrahedron*, **47**, 9061; (c) Obi, K., Ito, Y. and Terashima, S. (1990). *Chem. Pharm. Bull.*, **38**, 917; (d) Fernández-Resa, P., Herranz, R., Conde, S. and Arribas, E. (1989). *J. Chem. Soc., Perkin Trans.*, **1**, p. 67; (e) Brown, M. J. and Overman, L. E. (1991). *J. Org. Chem.*, **56**, 1933; (f) Teng, M. and Miller, M. J. (1993). *J. Am. Chem. Soc.*, **115**, 548; (g) van der Steen, F. H., Kleijn, H., Spek, A. L. and van Koten, G. (1990). *J. Chem. Soc., Chem. Commun.*, p. 503.
[61] Miller, M. J. (1986). *Acc. Chem. Res.*, **19**, 49.
[62] Banfi, L., Cascio, G., Guanti, G., Manghisi, E., Narisano, E. and Riva, R. (1994). *Tetrahedron*, **50**, 11967.

[63] Floyd, D. M., Fritz, A. W. and Cimarusti, C. M. (1982). *J. Org. Chem.*, **47**, 176.
[64] Floyd, D. M., Fritz, A. W., Plusces, J., Weaver, E. R. and Cimarusti, C. M. (1982). *J. Org. Chem.*, **47**, 5160.
[65] Cimarusti, C. M., Applegate, H. E., Chang, H. W., Floyd, D. M., Koster, W. H., Slusarchyk, W. A. and Young, M. G. (1982). *J. Org. Chem.*, **47**, 179.
[66] Vaughan, W. R. and Carlson, R. D. (1962). *J. Am. Chem. Soc.*, **84**, 769.