Aromatic Sulfonation. Part 120.[1] Reaction of Dihydroxy- and Dimesyloxynaphthalenes with Sulfur Trioxide in Nitromethane. Directing Effects and the Influence of Initial Sulfation on the Product Distributions†

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The reaction of nine dihydroxynaphthalenes (DHNs) and eight dimesyloxynaphthalenes (DMSNs) with sulfur trioxide in $C^2H_3NO_2$ as solvent has been studied by ^1H NMR spectroscopy. The monosulfonation of the DHNs leads to one or two carbon sulfonated products; only 2,3-DHN yields all the three possible sulfonic acids. The disulfonations of the DHNs yield one or two disulfonic acids which are usually also mono- or di-sulfated. Furthermore, derivatives of two cyclic naphthalenesulfonate sulfate anhydrides and of 8,1-naphthalenesultone are formed. The DMSNs initially yield one or two monosulfonic acids, and, in some cases, subsequently (in part) the corresponding sulfonic anhydrides.

The substitution patterns of the DHNs are generally in agreement with the cation localization energies, obtained by simple Hückel MO calculations. The results of the disulfonations of the DHNs suggest that: (i) sulfonation does not (exclusively) occur *via* the corresponding di(hydrogen sulfates); and (ii) hydrogen sulfate formation is more pronounced for the β- than the α-hydroxy group.

In the (aprotic) sulfur trioxide sulfonation of hydroxyarenes, the initial electrophilic attack occurs on the oxygen, leading to an aryl hydrogen sulfate in an equilibrium reaction $ArOH + SO_3 \rightleftharpoons ArOSO_3H$.[2] When using a deficient amount of SO_3, aromatic ring sulfonation occurs *via* back reaction and subsequent sulfonation of the hydroxyarene, whereas upon using an excess of SO_3, it generally is the hydrogen sulfate derivative that is sulfonated. The hydrogen sulfate group is, contrary to the *ortho/para* directing, activating hydroxy group, a deactivating, *para* directing substituent; therefore, the sulfonation product mixture composition for a given substrate may depend on the amount of SO_3 used.

In recent years we have extended our knowledge on the influence of this initial sulfation step to a large variety of phenols[3–6] and, most recently, naphthols.[1,7] This was done mainly by comparison of the hydroxyarenes with the corresponding methanesulfonate esters (mesyloxyarenes); the mesyloxy group ($-OSO_2Me$) has proved to be an excellent model substituent for the hydrogen sulfate group ($-OSO_2OH$) both in chemical behaviour and for analytical ^1H NMR purposes. ^1H NMR spectroscopy being our major tool in the studies, it proved very convenient that the various substituent chemical shifts of both substituents are very much the same within 0.04 ppm, not only in the benzene series,[8] but also in the more complicated naphthalene series.[1]

From studies of both 1- and 2-naphthol[7] and methoxy substituted naphthols[1] it emerged that the influence of hydrogen sulfate formation is larger for the 2- than the 1-naphthols in that the sulfonic acid product mixture composition changes more dramatically in the former case upon varying the amount of SO_3 from $\leqslant 1.0$ to $\geqslant 4.0$ equiv. The sulfonation of 1-naphthols with an excess of SO_3 still proceeds, at least in part, by reaction of the 1-naphthol itself rather than the 1-naphthyl hydrogen sulfate.

We have now studied the sulfonation of nine dihydroxynaphthalenes (DHNs) with 1.0 and 5.0 equiv. of SO_3 and of eight dimesyloxynaphthalenes (DMSNs) with 1.0 and 3.0 equiv. of SO_3 in $C^2H_3NO_2$ as solvent with ^1H NMR spectroscopy to study the sulfonation behaviour, the degree of sulfation and its effect on the sulfonation, as well as the stability of the various (di)hydrogen (di)sulfates.

Results

The reaction of nine dihydroxynaphthalenes with sulfur trioxide in $C^2H_3NO_2$ as solvent has been studied with ^1H NMR. The results of the ring substitutions are collected in Table 1. A more extensive overview is compiled in the accompanying Supplementary Publication.‡ Furthermore, the reaction of eight dimesyloxynaphthalenes (DMSNs), *i.e.* di(methanesulfonate) esters of the DHNs, with SO_3 has been studied for comparison, the results of which are in Table 2.

The values of the cation localization energies L^+ of the dihydroxynaphthalenes were obtained by simple Hückel MO calculations. In order to include conjugation for the p-lone pair of oxygen, α_O and $\beta_{O,C}$ values of 1.6 and 0.8, respectively, were used for the substrates.[9] In order to include the additional mesomeric conjugation of the oxygen in the positively charged σ-complex, a $\beta_{O,C}$ value of 1.0 was used for these cations. The results are compiled in Table 3.

Discussion

For the discussion of the sulfonation of the dihydroxynaphthalenes and the dimesyloxynaphthalenes with SO_3 the following basic elements are essential. First, the reactivity of electrophilic substitution is greater for the α- than the β-positions of naphthalene. For the sulfonation of naphthalene with SO_3 in nitromethane at 0 °C, $k_\alpha/k_\beta = 7.3$.[10] Second, the

† For reasons of convenience, all sulfo-products have been numbered as for the substrates.

‡ Supplementary Publication No. 56932 (10 pp.). For details of the Supplementary Publication Scheme, see 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 2*, 1993, issue 1.

Table 1 Sulfonation of the DHNs with SO_3 in nitromethane at 0 °C

Naphth. substs.	SO_3/equiv. (±0.1)	Reaction time/min	Reaction mixture composition (%, ±2)[a,b,c] 1	2	3	4
1,2-$(OH)_2$	1.0	5	4-S (≥99)			
	5.0	5	*O*(2),4-S_2 (33)	*O*(1,2),4-S_3 (67)		
		5 760	*O*(2),4,6-S_3 (70)	*O*(2),4,7-S_3 (30)		
1,3-$(OH)_2$	1.0	5	4-S (≥99)			
	5.0	4	4,7-S_2 (87)	2,4,7-S_3 (7)	**7** (6)	
		3 000		2,4,7-S_3 (24)	**7** (68)	*O*(3),2,4,7-S_4 (8)
1,4-$(OH)_2$	1.0	5	2-S (≤5)[d]			
	4.0	100	*O*(1),2-S_2 (55)	*O*(1,4),2-S_3 (45)		
1,5-$(OH)_2$	1.0	10	2-S (≥99)			
	5.0	30[e]	2,6-S_2 (80)			
		19 000	2,6-S_2 (35)	**5** (21)	**6** (44)	
1,6-$(OH)_2$	1.0	5	2-S (22)	4-S (78)		
	5.0	4	2,4-S_2 (24)	*O*(6),2,4-S_3 (67)	*O*(1,6),2,4-S_4 (9)	
1,7-$(OH)_2$	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-$(OH)_2$	1.0	6	1-S (72)	5-S (9)	6-S (19)	
		2 760	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)	
		37 400	1,5-S_2 (33)	1,6-S_2 (12)	1,7-S_2 (27)	5,7-S_2 (29)
2,6-$(OH)_2$	1.0	10	1-S (≥99)			
	5.0	13	**1** (≥99)			
		7 080	**1** (16)	**2** (36)	1,5-S_2 (34)[f]	
		15 840	**1** (23)	**2** (31)	1,5-S_2 (27)[g]	
		e	1-S (10)		1,5-S_2 (90)	
2,7-$(OH)_2$	1.0	10	1-S (≥99)			
		4 300	1-S (47)	3-S (53)		
	5.0	12	**3** (≥99)			
		1 700	**3** (67)	**3**-3-S (33)		
		13 000		**3**-3-S (44)	1,3,6-S_3 (56)	
		20 220[e]	1,6-S_2 (40)	3,6-S_2 (33)	1,3,6-S_3 (27)	

[a] Stands for SO_3H. The data between brackets are the yields. [b] *O*(*n*) refers to sulfation on the specific position *n*. [c] If the total amount does not add up to 100%, the remaining products could not be identified. [d] Polymer formation was the main reaction. [e] Reaction mixture obtained after alkaline aq. work-up of the mixture. In this case, S stands for SO_3^-. [f,g] 14 and 19% of an additional, unidentified product are present, respectively.

sulfonation with SO_3 of naphthalene at the α-position proceeds with a small kinetic isotope effect of hydrogen (k_H/k_D = 1.9 ± 0.1), illustrating that there is some *peri*-strain in the resulting sulfonic acid between 1-SO_3H and 8-H which is bent away somewhat towards 7-H.[11] Third, 1-OH has a preference to be in the plane of the naphthalene skeleton in a single-*cis* conformation with the C(α)–C(β) bond due to the repulsive *peri* interaction with 8-H; the 2-OH is in *cis*- and *trans*-orientation in approximately equal amounts.[12] Fourth, hydrogen sulfate formation is more effective for 2- than 1-OH[1,7] due to: (i) the steric repulsion between 1-OSO_3H and 8-H; and (ii) the somewhat higher electron density on the oxygen of the 2- as compared with the 1-OH.[13] Fifth, with 1- and 2-mesyloxynaphthalene, sulfonation *ortho* to the mesyloxy group does not occur mainly for steric reasons,[7] the OSO_2Me group being rather bulky; thus, it is anticipated that sulfonation *ortho* to the hydrogen sulfate group will not occur. Sixth, the relative degree of sulfation of a hydroxy substituent will decrease upon increasing the number of sulfonic acid groups introduced for electronic reasons;[2,14] this effect is much more pronounced when the SO_3H group is in an *ortho* or *para* orientation than in a *meta* orientation to the hydroxy group.[2] Seventh and finally, for the substrates 1,2-, 1,4-, 1,5-, 1,7-, 2,3- and 2,6-DHN, the various available positions for electrophilic substitution are each stabilized by conjugation with only one of the two hydroxy groups present, whereas for 1,3-, 1,6- and 2,7-DHN some positions are stabilized by conjugation with both the hydroxy groups, and the others are not stabilized at all. This implies that, in principle, the electronic directing effect of the sulfonic acid group already present will play an important role in the sulfonation of the sulfonic acids of the former six substrates in that it assists the directing effect of one of the hydroxy groups and opposes that of the other.

Sulfonation of the DHNs with 1.0 *Equiv. of Sulfur Trioxide.*—Upon reaction with 1.0 equiv. of SO_3, the DHNs in general yield one or two monosulfonic acids. The observed monosulfonations of 1,7-, 2,6- and 2,7-DHN compare favourably with their nitration on using various nitrocyclohexadienones as reagent.[15] Furthermore, chlorination[16] and nitrosation[17] of 2,7-DHN were observed to occur on C-1.

1,4-Dihydroxynaphthalene (1,4-DHN) forms a tar-like precipitate that does not dissolve in any common solvent, which indicates that a polymer is formed (see Table 1). It appears from weak signals in the initial ^1H NMR spectrum that some 2-sulfonic acid (2-S) is formed. These signals, however, disappear. The polymerization may be initiated by the positively charged sulfonation σ-complex.*

Monosulfonation of 2,3-DHN initially yields a 72:9:19 mixture of the 1-, 5- and 6-S. The 1-S rearranges to 6-S with some

Table 2 Reaction of some dimesyloxynaphthalenes with SO_3 in [$^2H_3$]nitromethane at 20 °C

Naphth. substs.	SO_3/equiv. (±0.1)	Reaction time/min	Reaction mixture composition (%, ±2)[a,b] Substrate	Sulfonic acid products		
1,3-$(OSO_2CH_3)_2$	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-$(OSO_2CH_3)_2$	1.0	7200	(78)	6-S (22)		
	3.0	7000	—	6-S (87)	$(6\text{-S})_2$ (13)	
1,5-$(OSO_2CH_3)_2$	1.0	7500	(≥99)			
	3.0	7500	—	3-S (35)	4-S (21)	**8**-4-S (44)
1,6-$(OSO_2CH_3)_2$	1.0	10	(40)	4-S (60)		
	3.0	10	—	4-S (67)	$(4\text{-S})_2$ (33)	
1,7-$(OSO_2CH_3)_2$	1.0	10	—	4-S (≥99)		
	3.0	10	—	4-S (72)	$(4\text{-S})_2$ (28)	
2,3-$(OSO_2CH_3)_2$	1.0	4000	(68)	5-S (27)	6-S (2)	
	3.0	4000	—	5-S (50)	$(5\text{-S})_2$ (37)	5,7-S_2(10)
2,6-$(OSO_2CH_3)_2$	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-$(OSO_2CH_3)_2$	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. The data between brackets give the yield. [b] All reaction mixture compositions are molar.

Table 3 Localization energies of the dihydroxynaphthalenes

Naph. substs.	Ring position 1	2	3	4	5	6	7	8
1,2-$(OH)_2$			2.0934	1.8050	1.9810	2.1308	2.1310	1.9834
1,3-$(OH)_2$		1.7634		1.5992	1.9142	2.2232	2.0532	2.0600
1,4-$(OH)_2$		1.8656			1.9850	2.1244		
1,5-$(OH)_2$		1.8682	2.1340	1.8170				
1,6-$(OH)_2$		1.8248	2.2400	1.7652	1.7164		1.9930	2.0676
1,7-$(OH)_2$		1.8692	2.1402	1.8080	1.9852	2.0742		1.7654
2,3-$(OH)_2$	1.7728				1.9868	2.1374		
2,6-$(OH)_2$	1.7568		2.0696	1.9844				
2,7-$(OH)_2$	1.7160		1.9960	2.0588				

5-S. This shows that the 1-position is in fact the most reactive, but that there is also some steric strain due to the two adjacent hydroxy groups at this position. This was also shown with 3-methoxy-2-naphthol, which initially yields its 1-S, but rearranges to the 6-isomer.[1] 2,3-Dimethoxynaphthalene (2,3-DMON) is not sulfonated at C-1 at all,[19] which shows that the steric restrictions are more severe for the OMe than the OH substituent.

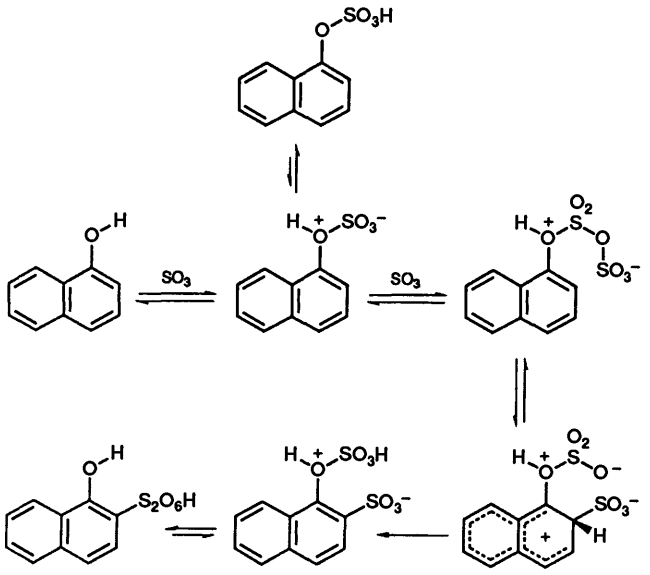
The initially formed 2,7-DHN-1-S slowly rearranges into the 3-S. 2,7-DMON was observed to yield a 1:1 mixture of the 1- and 3-S[19] as a result of enhanced *peri* strain between 1- and 8-H as a result of buttressing by the methoxy groups. A similar effect may be responsible for the present rearrangement.

Relation to the Hückel MO Calculations.—The sulfonation product ratios initially obtained upon reaction with 1.0 equiv. of SO_3, agree with the cation localization energy calculations (see Table 3) for 1,2-, 1,3-, 1,4-, 2,3-, 2,6 and 2,7-DHN. This observation implies that the products formed in these cases are indeed the kinetically controlled products.

The lack of correlation with 1,5-, 1,6- and 1,7-DHN is ascribed to steric factors. As for 1,5-DHN, the localization energy calculations predict sulfonation to occur on C-4; furthermore, nitration with nitrocyclohexadienones yields 45% of the 4-nitro derivative in addition to 55% of the 2-isomer;[15] nitration has smaller steric needs than sulfonation.[20] From these two observations we conclude that the absence of 4-S in the sulfonation of 1,5-DHN is due to steric factors.

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. 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; furthermore, the differences in localization energy between C-2 and C-4 on the one hand, and C-5 on the other are very small (0.1086 and 0.0488, respectively). Thus, the steric factor is dominant over the localization energy. The same reasoning applies for 1,7-DHN, for which the steric factor for sulfonation at C-8 will be even larger due to the *peri* interaction with the 1-OH. For the same reason, the two corresponding DMONs are not sulfonated at the corresponding C-5 and C-8 positions.[19]

* The polymerization may originate from reaction of the positively charged sulfonation σ-complex with the substrate or with 2,3-dihydro-1,4-naphthoquinone, the tautomer of 1,4-DHN that will be present in a small amount. 1,4-Naphthoquinone proper, when reacted with SO_3, also yields a polymer-like precipitate.[18]



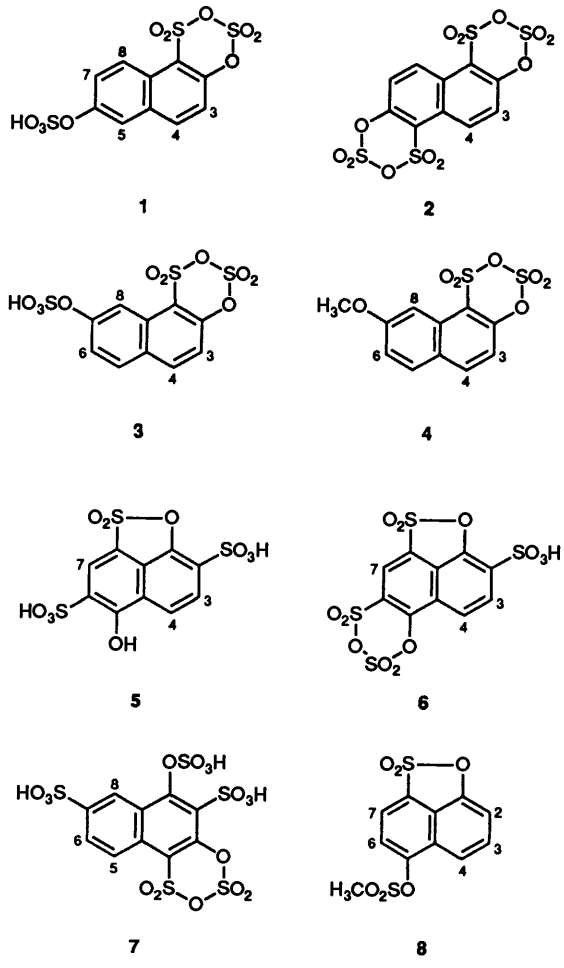
Scheme 1 Mechanism for *intra*molecular sulfonation of 1-naphthols

Sulfonation with a Large Excess of Sulfur Trioxide; Influence of Hydrogen Sulfate Formation.—Upon reacting 1,2-DHN with a large excess of SO_3, the initially observed products are the *O*(2),4-S_2 and *O*(1),*O*(2),4-S_3. These species then yield a 70:30 mixture of the *O*(2),4,6- and *O*(2),4,7-S_3. The 4,7-S_2 is expected to be the main product as it is the result of the directing effect of both the 1-OX (X = H, SO_2OH) and the 4-SO_3H substituents, whereas the 4,6-S_2 results from the directing effect of the 2-OX group only; this latter observation implies that the species that is further sulfonated is at least not sulfated at 2-OH.

Upon sulfonating 1,4-DHN with a large excess of SO_3, the 1,4-naphthylene di(hydrogen sulfate) is formed together with the 2-S, present as the 1-sulfated and disulfated derivatives [*O*(1),2-S_2 and *O*(1),*O*(4),2-S_3, respectively]. Remarkably, the corresponding 1,4-dimesyloxynaphthalene (1,4-DMSN), upon reaction with sulfur trixoide, yields the 6-S (see Table 2). This indicates that the substrate species undergoing sulfonation in the case of 1,4-DHN is not the di(hydrogen sulfate), as this would lead to the formation of the 6-S. Thus, sulfonation occurs either *via* desulfation and subsequent sulfonation of the 1,4-DHN proper, or of its mono(hydrogen sulfate). In the latter case, it is to be expected that sulfonation occurs at the C adjacent to the hydroxy rather than adjacent to the hydrogen sulfate group for both steric and electronic reasons. An alternative mechanistic possibility is *intra*molecular transfer of SO_3 from one of the hydrogen sulfate groups to the adjacent carbon (see Scheme 1), as was shown to occur in the sulfonation of phenol using solvents that do not engage in a Lewis complex formation with SO_3[21] and was postulated to occur in the sulfonation of 1-naphthol.[22]

Reaction of both 1,6- and 1,7-DHN with an excess of SO_3 yields their 2,4-S_2. This again is to be expected in view of the directing effect of 1-OH. The absence of any sulfonation in the ring containing β-OH is parallel with our earlier observation[1,7] that hydrogen sulfate formation is more effective for β- than α-OH. The corresponding 1,6- and 1,7-DMSNs are only sulfonated on C-4, which indicates—again—that sulfonation at a position adjacent to the OSO_2Me (and thus, probably, also to the OSO_2OH) group does, in general, not occur. 1,7-DMON is in fact disulfonated to form the 4,8-S_2 in an 80% yield;[19] in contrast, 1,7-DHN is not sulfonated at C-8 at all. These observations clearly illustrate that it is in fact the 7-naphthyl hydrogen sulfate derivative that reacts upon sulfonation with an excess of SO_3.

It is noteworthy that, with three of the α,β-DHNs a mixture



of the β-sulfated and disulfated derivatives is obtained, as is shown in Table 4, again illustrating that sulfation of β-OH is more effective than that of α-OH.

Upon reaction of 2,6-DHN with 5.0 equiv. of SO_3, the cyclic sulfonate sulfate anhydride **1** is initially formed, as is apparent from a comparison of the ^1H NMR data with those of the corresponding 6-mesyloxy-2-naphthol which yields the 6-SO_2Me analogue of **1**.[1] The cyclic anhydride **1** reacts further with SO_3 to yield the bis(cyclic sulfonate sulfate anhydride) **2** and, in a later stage, 2,6-DHN-1,5-S_2.

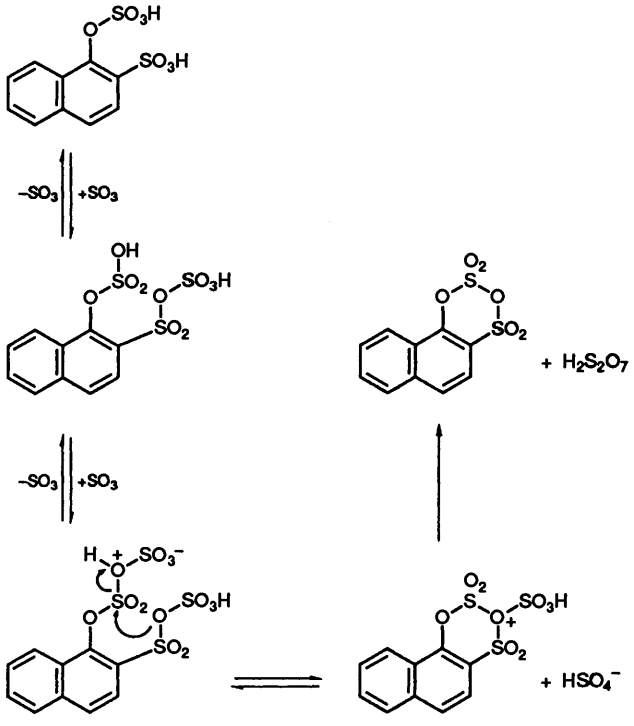
Upon sulfonation of 2,7-DHN with a large excess of SO_3, the initially observed cyclic anhydride **3** reacts to yield **3**-3-S, which compound, after longer reaction times, is converted into 2,7-DHN-1,3,6-S_3. Notably, **3** is sulfonated *ortho* to the cyclic anhydride moiety rather than to the hydrogen sulfate group at C-6, which behaviour is in contrast with that of **1**. Also, the 7-OMe analogue **4** is sulfonated at C-6 rather than C-3.[1] Apparently, in **3**, C-3 is more electron rich than C-6, which implies that the carbon bonded oxygen of the cyclic anhydride moiety is less electron withdrawing than that of the hydrogen sulfate group.* In **1**, there is as an alternative the (more reactive) α-position C-5, that is available for sulfonation as it is comparatively free of steric restrictions. For **3**, sulfonation at the comparable α-position C-8 would encounter too much steric hindrance by the 1-SO_2OH group to occur at all. 2,7-DHN-1,3,6-S_3 is eventually desulfonated to yield the 1,6-S_2. Aqueous

* The same may also be concluded from the ^1H NMR chemical shifts of the various hydrogens, which are also a measure for the electron density on a given carbon position. For **7**, 3-H is slightly more up-field than 6-H, and will thus be more electron rich.

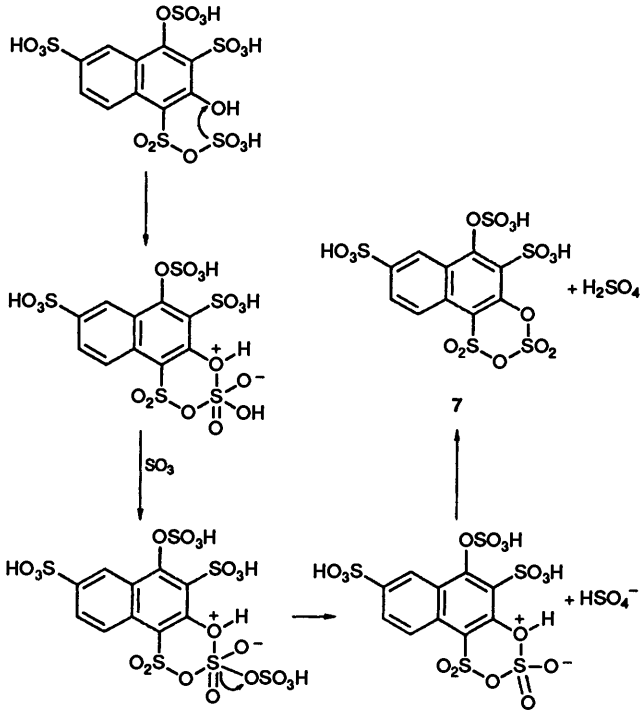
Table 4 Amount of sulfation initially observed in the reaction of the α,β-DHNs with 5.0 equiv. of SO_3[a]

α,β-$(OH)_2$	Reaction time/min	Relative amount of sulfation (%, ±2) α-OS	β-OS	α,β-$(OS)_2$	β:α (β + α,β):(α + α,β)
1,2	5	—	33	67	1.49
1,6	24	—	56	21	3.67
1,7	20	—	58	16	4.63

[a] No initial sulfation was observed in the reaction of 1,3-DHN.



Scheme 2 Mechanism for the conversion of 2-sulfo-1-naphthyl hydrogen sulfate into the corresponding cyclic sulfonate sulfate anhydride



Scheme 3 Mechanism for the conversion of 3-hydroxy-2,7-disulfo-4-pyrosulfo-1-naphthyl hydrogen sulfate into **7**

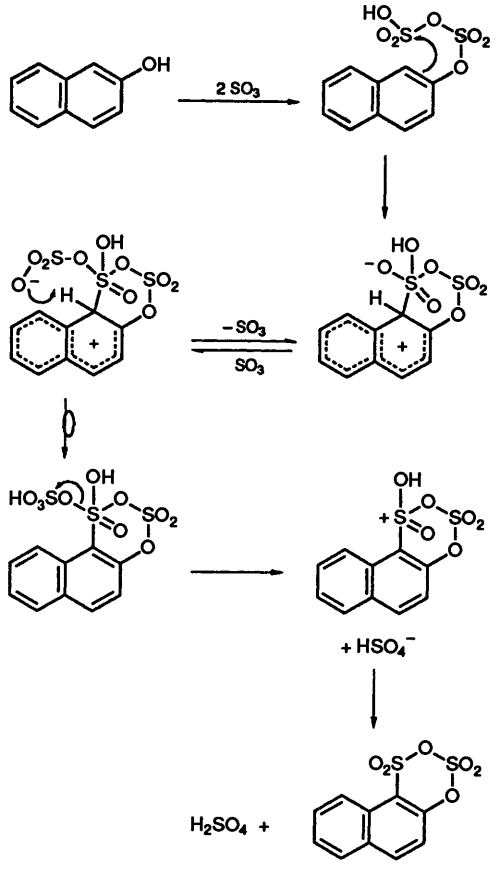
work-up of the reaction mixture affords a mixture of the alkali 2,7-DHN-1,6-disulfonate [1,6-$(S^-)_2$], 3,6-$(S^-)_2$ and 1,3,6-$(S^-)_3$ in a 40:33:27 ratio. Both protodesulfonations occur to relieve the steric strain between the three adjacent substituents.

Ring Closing Reactions.—Reaction of 1,5-DHN with 5.0 equiv. of SO_3 initially yields a complex and uninterpretable ^1H NMR spectrum; aqueous alkaline work-up of this mixture after 30 min yields 80% of the 1,5-DHN-2,6-$(S^-)_2$. After very prolonged reaction times in nitromethane, three products emerge, one of which is 1,5-DHN-2,6-S_2; the other products both contain sulfo groups at the 2-, 4- and 6-position, and on at least one of the oxygens. Comparison with the results of the sulfonation of 8,1-naphthalenesultone[1] and using the ^1H NMR substituent shift effects of the various substituents that may be present,[1] it was concluded that the products are the naphthalenesultones **5** and **6**. This assignment is further substantiated by the observation that aqueous work-up of both **5** and **6** yields 1,5-DHN-2,4,6-$(S^-)_3$. A mechanism for the formation of the 8,1-naphthalenesultone derivative **5** from 1,5-DHN-2,4,6-S_3 has been given previously.[1] A mechanism for the formation of **6** is depicted in Scheme 2.

The initially observed product in the sulfonation of 1,3-DHN, *viz.* 1,3-DHN-4,7-S_2, is converted into a mixture of products that all contain sulfo groups on the 2-, 4- and 7-positions, of which the most remarkable product is **7**. As **7** is observed prior to the final trisulfo-3-naphthyl hydrogen sulfate, it is probably formed from the 4-pyrosulfonic acid as precursor, as depicted in Scheme 3, rather than *via* the corresponding hydrogen sulfate. The driving force for the formation of **7** is relief of steric strain in the overcrowded six-membered carbon ring containing the four substituents. Subsequently, protodesulfonation occurs, leading to the dihydroxy derivative 1,3-DHN-2,4,7-S_3, of which the corresponding tri(potassium sulfonate) is the product isolated after aqueous work-up.

The cyclic anhydrides **1–3** that are initially observed upon reaction of 2,6- and 2,7-DHN are thought to be formed as depicted in Scheme 4, analoguous to the formation of the cyclic sulfonate sulfate anhydride in the sulfonation of 2-naphthol with a large excess of SO_3.[7]

Comparison of the Steric Restrictions of the Hydroxy and Methoxy Group.—From a Catalin–Stuart molecular model study it appeared that the steric restrictions for sulfonation at a *peri* position are essentially the same for a hydroxy and a methoxy group, whereas the steric hindrance for sulfonation at an *ortho* position is less for a hydroxy than for a methoxy group. The consequences of this may be exemplified by the sulfonation of 1,5-DHN and 1,5-DMON with 1.0 equiv. of SO_3, the former substrate yielding the 2-S, whereas the latter yields the 4-S exclusively.[19] Also, 5-methoxy-1-naphthol yields the 2-S rather than the 4-S.[1] Furthermore the smaller steric requirements for the hydroxy as compared with the methoxy group are apparent



Scheme 4 Mechanism for the conversion of 2-naphthol *via* 2-naphthyl hydrogen pyrosulfate into the cyclic sulfonate sulfate anhydride 1,3,2,4-naphtho[2,1]dioxadithiin 2,2,4,4-tetraoxide

from the initial formation of 2,3-DHN-1-S, which is in contrast with the absence of 2,3-DMON-1-S[19] and 3-methoxy-2-naphthol-4-S,[1] all on sulfonation of the corresponding substrates.

Sulfonation of the Dimesyloxynaphthalenes (DMSNs).—Sulfonation of the DMSNs leads to the formation of one or two sulfonic acids (Table 2). Upon using an excess of SO_3, the formation of the corresponding intermolecular sulfonic anhydrides is observed, a reaction that is common with deactivated naphthalenes.[23] Sulfonation *ortho* to the mesyloxy substituent is only observed with 2,6- and 2,7-DMSN. This is understandable for 2,7-DMSN, of which the two substituents both direct to C-1 and C-3. For 2,6-DMSN, this is not the case, and the formation of up to 26% of 1-S illustrates that *ortho*-substitution is sterically not prohibited, but apparently only retarded. Substitution *peri* to the OSO_2Me group only occurs in the case of a strong electronic directing effect by another substituent, as with 5-methoxy-1-mesyloxynaphthalene[1] and 1,5-DMSN, which are in fact sulfonated at C-8 and C-4, respectively.

1,5-DMSN, when treated with 1.0 equiv. of SO_3, does not react. This is not unexpected, as the most reactive available positions, *viz.* C-2 and C-4, are both sterically severely hindered. Upon reaction with 3.0 equiv. of SO_3, after long reaction times, 1,5-DMSN-3- and 4-S are formed and in addition **8**-4-S. **8**-4-S is probably formed *via* the naphthalenesultone derivative **8** as intermediate, as sulfonation of any formed 1,5-DMSN-4-S is anticipated to be very slow. A mechanism for the formation of 8,1-naphthalenesultones from 8-sulfo-1-mesyloxynaphthalenes was given previously.[1,*]

In conclusion, it appears that the dihydroxynaphthalenes (DHNs) are monosulfonated in accordance with predictions based on Hückel MO localization energy calculations, provided that allowance is made for steric hindrance. The product distribution of the further sulfonation is not predicted by this criterion due to hydrogen sulfate formation. Upon using a large excess of SO_3, the DHNs are not sulfonated *via* their di-(hydrogen sulfate) derivatives, as the substitution patterns of the DHNs strongly deviate from those obtained with the corresponding DMSNs. It is, again, shown that hydrogen sulfate formation is more effective for β- than for α-OH groups. Some interesting ring closing reactions are observed, and in two cases, trisulfonic acids are formed.

Experimental

The dihydroxynaphthalenes were obtained commercially and used as such. The dimesyloxynaphthalenes were synthesized from the corresponding DHNs following a described procedure using methanesulfonyl chloride (2.2 equiv.).[24] The ^1H NMR spectra were recorded on Bruker AC-200 and WM-250 spectrometers.

Sulfonation Procedure and Analysis.—A solution of the desired amount of SO_3 in $C^2H_3NO_2$ (0.5 cm^3) was added to a solution of substrate (0.10 mmol) in $C^2H_3NO_2$ (0.5 cm^3) at 0 °C under argon. A sample of the resulting homogeneous mixture was then transferred into an NMR tube and subsequently ^1H NMR spectra were recorded at ambient temperatures (20–22 °C) for product assignment and quantitative analysis allowing appropriate time intervals. The mixtures thus obtained were worked up with H_2O, subsequently neutralized with 10% aq. potassium hydroxide and the water removed by freeze drying. Subsequently, a ^1H NMR spectrum of the resulting potassium sulfonate salt mixture, dissolved in ^2H_2O, was recorded.

The structural assignments of the sulfo products of the SO_3 sulfonations were made on the basis of the observed ^1H NMR chemical shifts, absorption area ratios and coupling constants in combination with the shielding parameters of the OH, OSO_3H, OSO_2Me, SO_3^-, SO_3H, 8,1-SO_2O–, 1,2-SO_2OSO_2O– and $(SO_2)_2O$ substituents.[1,19] The assignments are compiled in the Supplementary Publication which accompanies this paper. The compositions of the sulfonation reaction mixtures and the sulfonated product mixtures were determined by multicomponent ^1H NMR analysis on the basis of specific absorptions of the various components.[25]

* Interestingly, the 1-OSO_2Me group engages in a reaction which involves scission of the O–S bond, whereas the 2-OSO_2Me group does not; in addition to the 'hydrogen sulfate effect' this is an illustration that the O–S bond is more stable when the oxygen is bonded at a β-carbon than at an α-carbon of naphthalene.

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Paper 2/05573B
Received 19*th October* 1992
Accepted 12*th January* 1993