Oxonium and quinonoid intermediates in the sulfonation of dimethoxynaphthalenes (DMONs)

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Monoprotonated oxonium cations (such as **2**) and quinonoid dications (such as **5**) of 2,3-, 2,6- and 2,7-dimethoxynaphthalenes are described. Their role as direct substrates in sulfonation reactions is discussed together with details of the sulfonation mechanism for 2,3-dimethoxynaphthalene (2,3-DMON), which is presented as a characteristic example. Steady sulfonation rate constants of 2,6- and 2,7-DMON in 80–88% H_2SO_4 are a result of the DMON protonation equilibria. Binding energies and heats of formation were calculated for several mono- and disulfonic acids of DMONs. Substituent effects are discussed.

Introduction

The study of reactive intermediates is important in the development of concepts of modern reactivity.[1] In recent years extensive studies on the mechanistic aspects of sulfonation have been published.[2] The revival of interest into sulfonation mechanisms of aromatic compounds is largely due to Cerfontain and co-workers who discovered that in aqueous sulfuric acid two reaction mechanisms operate: at lower concentrations of the acid $H_3SO_4^+$ is the principal sulfonating agent, while $H_2S_2O_7$ takes over above *ca.* 83% H_2SO_4.[3] Uncharged substituted benzenes and their ammonium derivatives are sulfonated by $H_2S_2O_7$ with similar slopes of rate profiles[3,4] in aqueous H_2SO_4 but a positive charge on nitrogen near the ring retards sulfonation.[4] In these cases there is only one form of the substrate that reacts with sulfuric acid: neutral (PhR) or ammonium-substituted (PhR^+), except $PhNO_2$, which has two forms in equilibrium:[5] $PhNO_2^0$ and $PhNO_2H^+$ with half-protonation in 99.5% H_2SO_4.

Phenylalkanols[6] are protonated on oxygen (O-protonation) in aqueous H_2SO_4.

Protonated anisole[7] is the principal species present above 77% H_2SO_4 but it has been concluded that sulfonation will proceed predominantly *via* the more reactive, non-protonated form.[7,8] It has been suggested[9,10] that species protonated in the ring appear as the concentration of H_2SO_4 increases. Protonation on C is known to occur at the most electronegative aromatic carbon atom,[11] where sulfonation also takes place and diagnostic absorption bands appear *ca.* 340–350 nm for benzenonium ions.[11,12] Isomers of $C_6H_4(OR)_2$ are in part protonated on oxygen or ring-protonated at C(4) and C(6) in concentrated aqueous sulfuric acid.[13] Subsequently ring sulfonation occurs at the 4- and 6-positions.[13]

We became interested in the basic properties of 6-methoxy-2-naphthylpropionic acid (naproxene) and 2-methoxynaphthalene (neroline) and found a stepwise protonation: first on oxygen,[14a] then a dication is formed[14b] prior to sulfonation.[14c]

Prior to our research only sulfonations of DMONs with SO_3 in CH_3NO_2 have been studied.[2] The aim of the present work was to describe the properties and reactivity of dimethoxynaphthalenes in aqueous H_2SO_4.

Three dimethoxynaphthalenes were chosen in which the classically most reactive 1-position of the naphthalene ring was left unsubstituted to see how reactive it is in sulfonation reactions.

Results and discussion

Protonations

The presence and concentration of protonated forms were quantitatively determined by UV–VIS spectroscopy. The spectra of neutral, uncharged methoxynaphthalenes and dimethoxynaphthalenes in dilute aqueous acidic solutions are alike, with a strong absorption band at 230–240 nm (ε *ca.* 6×10^3 m^2 mol^{-1}, K-band) and several weak overlapping B-bands at 250–350 nm (ε *ca.* 3×10^2 m^2 mol^{-1}). The solubilities of DMONs in aqueous 0 to 50% H_2SO_4 change little and are of the order of 10^{-5} M. However, in 50–75% H_2SO_4 the solubilities increase rapidly, although the absorption coefficients (ε) and the positions of the maxima (λ_{max}) of the absorption bands remain very much the same. Upon dilution with water unchanged DMONs were obtained quantitatively. This indicated reversible protonation at the methoxy oxygen outside the chromophore system of the aromatic ring and an absence of sulfonation in this range of H_2SO_4 concentrations. We applied the solubility method[15] for determination of protonation constants p*K*s, as it permits the detection of true acid–base equilibria before the onset of sulfonation. Quantitative determinations of the O-protonated forms were based on measurements of solubility[15] related to the acidity function H_0 by means of the Krebs and Speakman equation (*cf.* Experimental). Saturation concentrations of the substrates were measured. This made possible the evaluation of protonation constants pK_1 for which the concentrations of the protonated forms $DMONH^+$ and non-protonated forms of $DMON^0$ are equal (half-protonation). Acidity functions are empirical scales[16,17] and therefore the p*K* values we obtained are not true thermodynamic quantities.[18] The symbols "pK_1" and "pK_2" are used to denote the value of H_0 at the first and second half-protonations. The percentage composition of more and less protonated forms of a given substrate could be calculated from[19] $pK_1 = H_0 + \log I_1$, where I_1 is the ionization ratio $[BH^+]/[B]$. Consecutive protonations are also included: for pK_2, $BH^+ + H^+_{solv} \rightleftharpoons BH_2^{2+}$. We used the best general-purpose H_0 scale[19] for 2–99% H_2SO_4 based on twelve nitroaniline indicators.[20] Thus, ionization ratios for all the protonated forms of each substrate at any acidity H_0 of 2–99% H_2SO_4 could be calculated from the p*K* and H_0 values. Our results for pK_1 determinations are collected in Tables 1–3, and give plots that are are linear with correlation factors ≥ 0.95 and slopes near unity (Fig. 1). Fairly constant pK_1 values are obtained from

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Table 1 Determination of the first protonation constant pK_1 of 2,3-DMON ($S_i = 2.5 \times 10^{-5}$ M)

% H_2SO_4	H_0[a]	log I_1[b]	pK_1[c]
49.78	−3.28	0.53	−2.75
50.36	−3.33	0.48	−2.85
58.60	−4.20	1.16	−3.04
61.00	−4.50	1.51	−2.99

[a] H_0, acidity scale according to ref. 20; S_i, minimum solubility in 20–30% H_2SO_4; I_1 and pK_1, see text and Experimental. [b] Standard deviation, $s = 0.13$.[c] Mean: −2.91 (45.4%).

Table 2 Determination of the first protonation constants pK_1 of 2,7-DMON ($S_i = 1.2 \times 10^{-5}$ M)

% H_2SO_4	H_0[a]	log I_1[b]	pK_1[c]
58.0	−4.13	0.23	−3.90
59.9	−4.36	0.53	−3.83
61.0	−4.50	0.77	−3.73
62.0	−4.62	0.72	−3.90
66.0	−5.20	1.08	−4.12

[a] H_0, acidity scale according to ref. 20; S_i, minimum solubility in 20–30% H_2SO_4; I_1 and pK_1, see text and Experimental. [b] Standard deviation $s = 0.12$.[c] Mean: −3.90 (56.0%).

Table 3 Determination of the first protonation constant pK_1 of 2,6-DMON ($S_i = 0.9 \times 10^{-5}$ M)

% H_2SO_4	H_0[a]	log I_1[b]	pK_1[c]
68.35	−5.57	0.37	−5.20
70.0	−5.82	0.48	−5.34
71.13	−5.99	0.64	−5.35
74.7	−6.60	1.11	−5.49
76.03	−6.81	1.59	−5.22

[a] H_0, acidity scale according to ref. 20; S_i, minimum solubility in 20–30% H_2SO_4; I_1 and pK_1, see text and Experimental. [b] Standard deviation $s = 0.12$.[c] Mean: −5.32 (66.7%).

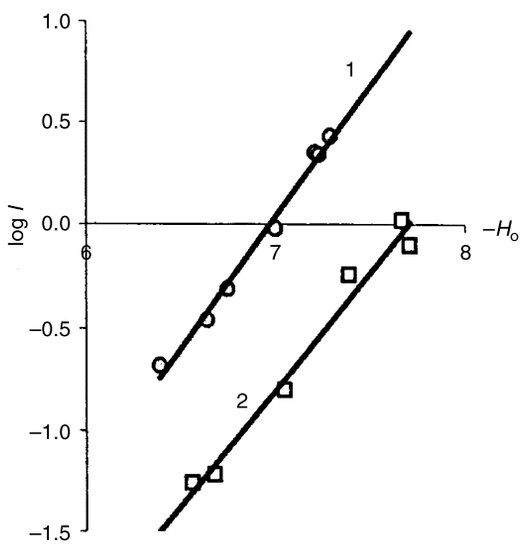


Fig. 1 Log I_2 *vs.* $-H_0$ for: 1: 2,6-DMON, data from Table 4; 2: 2,7-DMON, data from Table 5.

measurements at different acidities, the scatter being due to experimental errors. Taken together, we consider these results as evidence that all three DMONs are reversibly protonated on the methoxy oxygen in aqueous H_2SO_4 (O-protonation) with formation of monoprotonated species, *i.e.*, DMON + $H^+_{solv} \rightleftharpoons DMONH^+$, with pK_1 equal to −2.9 for 2,3-DMON

Table 4 Determination of the second protonation constant pK_2 for 2,7-DMON ($\varepsilon_{max} = 23000$ mol^{-1} dm^3 cm^{-1})

% H_2SO_4	H_0[a]	log I_1[b]	pK_1[c]
73.51	−6.39	−0.68	−7.01
74.95	−6.64	−0.46	−7.10
75.63	−6.75	−0.31	−7.06
77.18	−7.00	−0.02	−7.02
78.52	−7.21	+0.35	−6.86
78.63	−7.23	+0.34	−6.89
78.95	−7.29	+0.43	−6.86

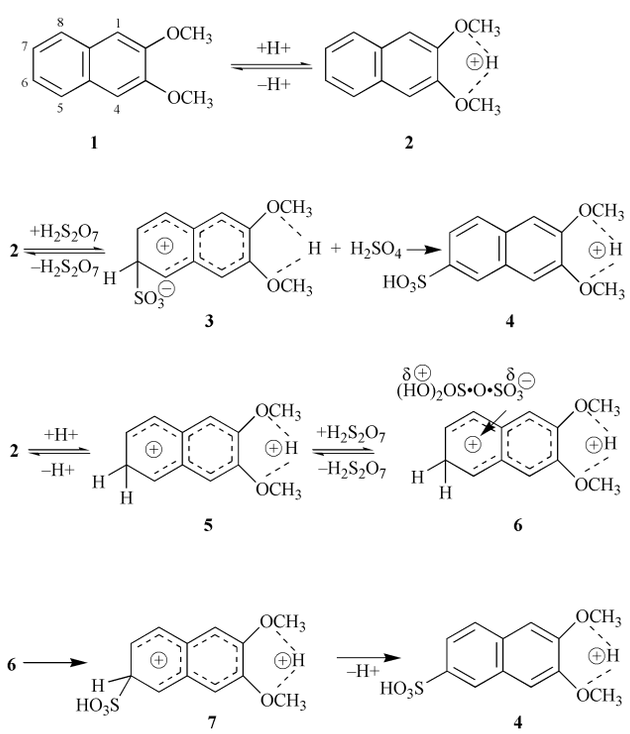
[a] H_0, acidity scale according to ref. 20; S_i, see text and Experimental; ε_{max} = maximum absorption coefficient for 2,7-DMON obtained at higher acidities, extrapolated to time t_0 (preparation of solution). [b] Standard deviation $s = 0.10$.[c] Mean: −7.0 (77.1%).

Table 5 Determination of the second protonation constants pK_2 for 2,6-DMON ($\varepsilon_{max} = 10500$ mol^{-1} dm^3 cm^{-1})

%H_2SO_4	H_0[a]	log I_2[b]	pK_2[c]
74.45	−6.56	−1.26	−7.82
75.23	−6.68	−1.22	−7.90
77.52	−7.05	−0.80	−7.85
79.59	−7.39	−0.24	−7.63
81.21	−7.67	+0.02	−7.65
81.47	−7.71	−0.10	−7.81

[a] H_0, acidity scale according to ref. 20; I_2 and pK_2, see text and Experimental; ε_{max}, maximum absorption coefficient for 2,6-DMON obtained at higher acidities, extrapolated to time t_0 (preparation of solution). [b] Standard deviation $s = 0.11$.[c] Mean: −7.8 (81.4%).

(in 45.4% H_2SO_4), −3.9 for 2,7-DMON (in 56% H_2SO_4) and −5.3 for 2,6-DMON (in 66.7% H_2SO_4). Thus, 2,3-DMON is the strongest base, which may be attributed to theformation of a rather stable five-membered ring with the hydrogen proton forming a hydrogen bridge (**2**, Scheme 1).



Scheme 1

In aqueous sulfuric acid more concentrated than about 75% the UV–VIS spectra change significantly. In fresh solutions a yellow absorption band appears at longer wavelength at 380–430 nm, where in dilute acids the absorbances of DMONs are

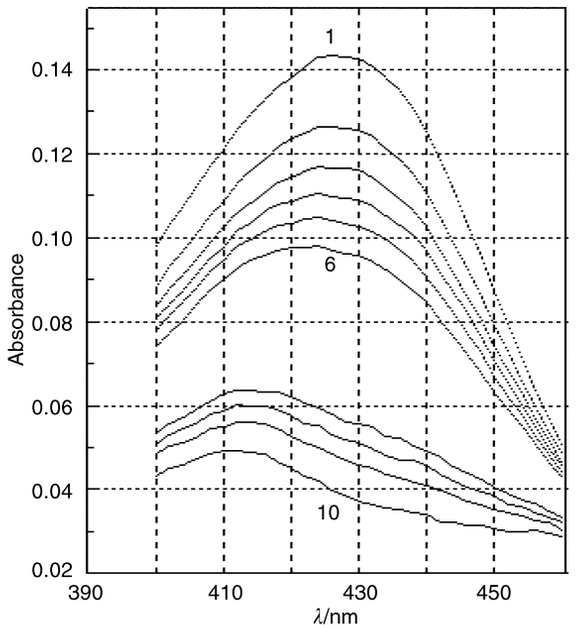


Fig. 2 Decay of the yellow band of 2,3-DMON in 86% H_2SO_4. 1: t_0 + 0.3 min; 6: t_0 + 2.3 min; 10: t_0 + 10 min; t_0 = time of preparation of solution.

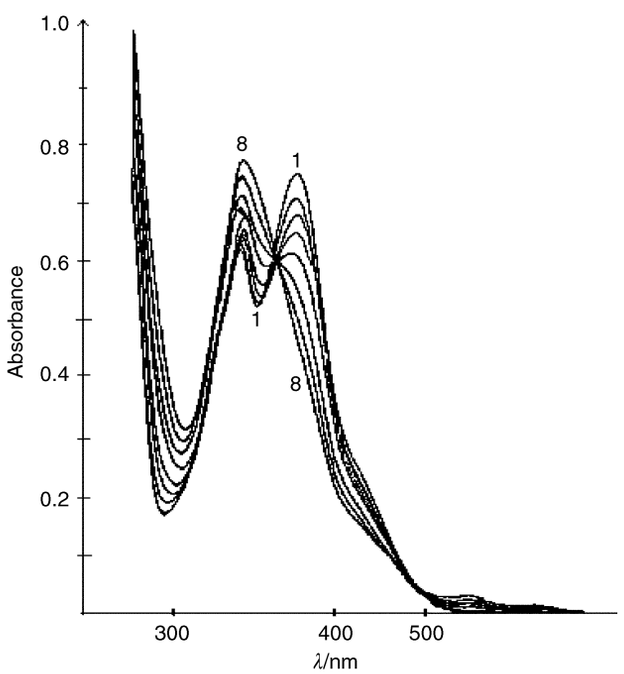


Fig. 3 Evolution of the UV/VIS spectra of 2,6-DMON in 82% H_2SO_4. 1: t_0 + 1.3 min; 8: t_0 + 180 min; t_0 = time of preparation of solution.

nearly zero. Such bands are diagnostic of the presence of carbonium ions.[21] These bands are shown in Figs. 2 and 3. Protonation of 2-methoxynaphthalene and naphthalene in superacids and the formation of a red-coloured carbocation (C-protonation) were observed by Olah *et al.*[22] In aqueous H_2SO_4 we observed discoloration of solutions followed by reprecipitation of the original substances upon dilution (with ice) immediately after dissolution and the appearance of these bands in concentrated perchloric acid. Rapid reversibility with changing acidity indicates a protonation equilibrium. Plots of log ([$DMONH_2^{2+}$]/[$DMONH^+$]) *versus* H_0 are linear as seen in Fig. 1. Fairly constant values of pK_2 are obtained (Tables 4 and 5) although the slopes *vs.* the H_0 scale that we used are somewhat steeper than 1: C-protonations may be less precisely described by this H_0 function. The absorption coefficients ε_0 of the yellow band extrapolated to the time t_0, when plotted against H_0 give a sigmoidal curve characteristic of acid–base titrations,[23] the turning point of which is at the pK_2 value −7.0 (in 77.1% H_2SO_4) for 2,7-DMON and −7.8 (in 81.4% H_2SO_4) for 2,6-DMON. The pK_2 values were calculated from $[\varepsilon_i/(\varepsilon_{max} - \varepsilon_i)] = I_2$; p$K_2 = H_0 + \log I_2$, which is another form of the Henderson equation, where ε_i values are ε_0 values on the sigmoidal curve and ε_{max} is the ε_0 value on the plateau and indicates 100% protonation of the substrate. The rise of the yellow (*i.e.*, carbonium) band from its appearance to full height takes place in an interval of *ca.* 2 H_0 units in accord with the Henderson equation.

Thus, the pK_2 values for 2,6-and 2,7-DMON represent the second protonation step with addition of a second proton to the ring (C-protonation), $DMONH^+ + H^+ \rightleftharpoons DMONH_2^{2+}$, rather than a change from O-protonation to C-protonation of the monocations. In less than *ca.* 98% H_2SO_4 the activity of H_3O^+ and of free water[3] is sufficient to form and stabilize oxonium cations. Similar results have been obtained for naproxene and neroline.[14b] Dications are also present as O- and C-protonated desoxycorticosterone[24] in 97% H_2SO_4.

Addition of the second H^+ induces a redistribution of the conjugated double bonds and formation of a quinonoid structure such as **5** (Scheme 1) with one hydrogen added to the most nucleophilic center. A new extended chromophore system is formed in the quinonoid dication as indicated by a decrease (at time t_0) of the K-band of DMONs (at 230–240 nm) and a bathochromic shift of the B-bands. Instead, an intense quinonoid band appears at 380–440 nm.

For 2,3-DMON the yellow band appears in 82–97% H_2SO_4. It increases quickly with acidity but no plateau in ε_0 *vs.* $-H_0$ was observed because of very rapid decay of this band. Its λ_{max} at 427 nm indicates that it is due to a quinonoid dication $DMONH_2^{2+}$ such as **5** (Scheme 1), formed in the second protonation step. Species **5** is a diprotic acid that contains labile protons and is also a reaction intermediate in the hydrogen exchange reaction. Protonations on C, although very rapid, are slow in comparison with O-protonations. Nonetheless, the C-protonated forms should not be regarded as complexes that contain a saturated carbon in the naphthalene ring because the aromatic protons are exchanged by tritium and deuterium in 80% sulfuric acid.[25] This exchange is a simple electrophilic aromatic substitution reaction in which D^+ acts as an electrophilic reagent.[25] Such exchange takes place also in the naphthalene ring and protonation of naphthalene in superacidic solutions leads to the formation of stable naphthalenium ions where protons are in rapid equilibrium through a 1,2-hydrogen shift.[22] A broadened $=CH_2$ NMR signal appears in these ions at δ 5–7 ppm indicating labile protons and unsaturated character of this methylene group.[22] Therefore, quinonoid forms ought to be considered as participants in the equilibria with electrophilic reagents present in solution, that is, with proton donors and SO_3 donors at all unsubstituted positions of the ring forming encounter complexes[7] (or π-complexes) such as **6** in Scheme 1. Encounter complexes are much more slowly and quasi-irreversibly transformed into σ-complexes such as **3** and **7**. The latter yield the final sulfonated products, such as **4**, in largely irreversible processes indicated by the single arrows in Scheme 1. Single arrows imply that, given sufficient time and reagent, the sulfonation reactions proceed practically to completion. This does not exclude very slow reverse reactions and under mild conditions the more stable product is formed.

The position in the ring at which protonation occurs preferentially is determined by the structure of the primary monosulfonic derivative. It is well known that protonation occurs at the most electronegative (that is most nucleophilic) aromatic carbon atom.[11] Dihydroxybenzenes upon dissolution in concentrated H_2SO_4 are very rapidly protonated at the same 4- and 6-positions, at which subsequently ring sulfonation occurs.[13] This is in agreement with the principle of microscopic

Table 6 Paralleled determination of decay rates k_{qu} for the quinonoid bands and sulfonation rates k_{grav} determined gravimetrically (in min^{-1})[a]

H_2SO_4	2,6-DMON	2,7-DMON
80% k_{qu}	—	2.3×10^{-3}
k_{grav}	—	2.3×10^{-3}
84% k_{qu}	6.02×10^{-3}	2.7×10^{-3}
k_{grav}	5.98×10^{-3}	2.2×10^{-3}
88% k_{qu}	0.013	2.0×10^{-3}
k_{grav}	0.012	2.5×10^{-3}
92% k_{qu}	0.010	—
k_{grav}	0.014	—

[a] Details are described in the Experimental.

reversibility, as both protonations and sulfonations are reversible electrophilic substitutions that compete for a place, or position, at the same most nucleophilic (that is, electronegative) unsaturated carbon atom. Thus, the reaction sequence depicted in Scheme 1 is proposed. When the SO_3H group is substituted on the ring it imparts strong acidic properties to the sulfonated intermediates and products, which then participate in proton-transfer equilibria that are different to those in which the DMON substrates take part.

Sulfonation substrates

In order to react with cationic substrates such as **2** or **5** the sulfonating entities ought to be polar, but electrically neutral, molecules, such as $H_2S_2O_7$, which can be attracted by the inhomogeneous electric field created by the positive charges of $DMONH^+$, or $DMONH_2^{2+}$. Positively charged sulfonating moieties, such as $H_3SO_4^+$ are repelled (they do react with neutral substrates[7]). Hence, in our sulfonation reactions the overall, or net, charge of the molecule does not change when an intermediate π- or σ-complex is formed.

Sulfonations are slow in comparison with C-protonations, but are also less reversible. Once the sulfonic group is inserted into the aromatic ring it is not easily removed and a sulfonated product is formed with different acidic properties, although the methoxy substituents remain unaffected.[2,14c,23,26] Therefore, the quinonoid forms are not stable—after very rapid formation (<1 s) the yellow bands decrease in concentrated H_2SO_4 in a pseudo-first order reaction in line with the reaction rate constants of the DMON substrate as determined by parallel kinetic spectrophotometric and gravimetric measurements (Table 6 and Experimental).

This reaction was identified as sulfonation and the products are described in the next paragraph. An agreement between the two sets of measurements collected in Table 6 can be expected when the products of the reaction do not have absorption bands at the wavelength of the photometric measurements, and are more soluble than the substrate in the gravimetric measurements. The latter is generally true for the sulfonated products. At lower acidities the agreement is fair: the decay rate of the quinonoid band is also the overall reaction rate of DMON. At high acidities the products may show absorption bands that are absent at lower acidities. In particular, this is true for 2,7-DMON for which discrepancies arise between photometric and gravimetric measurements and the latter better describe the kinetics of reaction. Of course one could subtract the interfering absorbances by additional measurements at another wavelength.

Parallel kinetic measurements for 2,3-DMON could not be made because of very rapid decay of its quinonoid band: it is 0.4 min^{-1} in 86% H_2SO_4 and *ca.* 7 min^{-1} 97% H_2SO_4. These high rate constants may be due to sulfonation at positions 5 and 6 far from the positively charged oxonium methoxy groups. Their negative effect on the sulfonation rate is therefore reduced.

As discussed in the Protonations section, three forms of each methoxynaphthalene are present when sulfonations take place and may be considered as three sulfonation substrates that are in mutual, rapid protonation equilibria:

$$DMON^0 + 2H_3O^+ \rightleftharpoons DMONH^+ + H_3O^+ \rightleftharpoons DMONH_2^{2+}$$

The sulfonation rate constant k of the substrate added to the solution is a sum of the three separate reaction rates, k_0 (the fastest sulfonation rate of neutral $DMON^0$), the slower sulfonation rate k_1 of monocations $DMONH^+$ and the slowest k_2 of dications $DMONH_2^{2+}$. Their % concentrations (or shares) are constant at each sulfuric acid concentration and can be obtained from measurements at increasing acidities as described above (*cf.* Table 1–5) and calculated using the H_0 scale and pK_1 and pK_2 values.

Examples of % concentrations of the three forms $DMON^0$, $DMONH^+$ and $DMONH_2^{2+}$ at different acidities are given in Table 7. For 2,7-DMON sulfonation proceeds in 80% H_2SO_4 when $DMONH_2^{2+}$ is the prevailing form (76%), while there is only 0.006% of $DMON^0$ (*cf.* Tables 6 and 7). One can see that in solutions more acidic than pK_2, $DMONH_2^{2+}$ prevails (*cf.* Table 7 and **5** in Scheme 1) and $[DMON^0]$ decreases much faster than in less acidic solutions, because $[DMONH^+]$ also decreases. Similar calculations show that in 84–97% H_2SO_4 the concentration of $DMONH_2^{2+}$ is almost constant at nearly 100%, while that of $DMON^0$ decreases to insignificant values.

Similar results are obtained for 2,6-DMON. Also, sulfonation proceeds at a noticeable rate only in solutions in which the quinonoid band appears. The quinonoid spectra of $DMONH_2^{2+}$ are different from the spectra of the sulfonated products so the presence of the latter could be taken into account quantitatively (*cf.* Fig. 3).

Thus, the rate increase cannot be due to neutral $DMON^0$ but the share of $DMONH^+$ is important, in particular, in less concentrated H_2SO_4 where the concentration of monocations such as **2** in Scheme 1 is large and fairly constant, that is, at H_0 values between pK_1 and pK_2 (*cf.* Table 7), if sulfonations proceed in this range. An electrophilic attack by a sulfonating species on a monocation then takes place. The sulfonating entities are in equilibria such as $H_2S_2O_7 + H^+ \rightleftharpoons SO_3 + H_3SO_4^+$.

Assuming usual slopes of rate profiles[3] for cations[4] their sulfonation rates will rise in step with acidity,[7] but in solutions near pK_2 the concentrations of $DMONH^+$ decrease in a similar way. This will stabilize the (large) extent of reaction due to $DMONH^+$ and the overall reaction rate will slow down or may be almost constant if $DMONH_2^{2+}$ reacts much more slowly, *i.e.*, if its rate profile is shifted to higher acidities. This has been observed for the quinonoid band of 2,6-DMON: in 78–88% H_2SO_4 its decay rate is nearly constant at about 0.01 min^{-1}. For 2,7-DMON a stabilization of the reaction rate occurs in 80–88% H_2SO_4 (*cf.* Table 6). In this range of acidities the concentrations of neutral forms and monocations of 2,6- and 2,7-DMON rapidly decrease, while the concentrations of the dications sharply increase. The latter react at a noticeable rate in more acidic solution as indicated by the rapid rise of reaction rate in very concentrated H_2SO_4. For 2,7-DMON this rate is 0.13 min^{-1} in 96% H_2SO_4 and for 2,6-DMON *ca.* 0.4 min^{-1} in 97% H_2SO_4. Above 90% H_2SO_4 the reaction rate rises again and the increase in sulfonation turnover will be due to $DMONH_2^{2+}$, although its percentage concentration is steady at almost 100% in >90% H_2SO_4 because the reaction rate increases with H_0. Protonation near to the aromatic ring retards sulfonation also in the case of 2-naphthol[26] in 91–95% H_2SO_4; 2-naphthol has a strong quinonoid band at λ 385 nm.[14c]

2,3-DMON ($pK_1 = -2.9$; $pK_2 = ca.\ -9.0$) is different as its monocation is the principal substrate for sulfonation in 62–92% H_2SO_4. Again, the concentration of neutral 2,3-DMON rapidly becomes insignificant while the share of 2,3-$DMONH_2^{2+}$ is important or prevalent in very concentrated H_2SO_4. Thus, our results indicate that both mono- and dications of DMONs are

Table 7 Fractions of $DMON^0$, $DMONH^+$ and $DMONH_2^{2+}$ as a function of the H_0, pK_1 and pK_2 values[a]

% H_2SO_4	H_0	% 2,7-$DMON^0$	% 2,7-$DMONH^+$	% 2,7-$DMONH_2^{2+}$
0.0	7.0	100	0	0
56.0	−3.9	50	50	0.04
68.0	−5.5	2	95	3
77.1	−7.0	0.04	50	50
80.0	−7.5	0.006	24	76
84.0	−8.1	5×10^{-4}	6.9	93.1
90.0	−9.0	8×10^{-6}	1.0	99.0
97.0	−10.2	3×10^{-8}	0.06	99.94
% H_2SO_4	H_0	% 2,6-$DMON^0$	% 2,6-DMONH	% 2,6-$DMONH_2^{2+}$
0.0	7.0	100	0	0
66.7	−5.3	49.9	49.9	0.2
75.0	−6.6	4.5	90	5.5
82.0	−7.8	0.2	49.9	49.9
90.0	−9.0	1×10^{-3}	6	94
97.0	−10.2	5×10^{-6}	0.4	99.6
% H_2SO_4	H_0	% 2,3-$DMON^0$	% 2,3-$DMONH^+$	% 2,3-$DMONH_2^{2+}$
0	7.0	100	0	0
45.4	−2.9	50	50	4×10^{-5}
90.0	−9.0	4×10^{-5}	50	50
97.0	−10.2	3×10^{-7}	6.3	93.7

[a] Examples: 2,7-DMON, $pK_1 = -3.9$, $pK_2 = -7.0$; 2,6-DMON, $pK_1 = -5.3$; $pK_2 = -7.8$; 2,3-DMON, $pK_1 = -2.9$; $pK_2 = ca.\ -9.0$. Data from Tables 1–5 are used in the transformed Henderson equation: $I = [BH^+]/[B]$; $\%BH^+ = 100I/(I+1)$; $\%B = 100\% - \%BH^+$; $\log I_1 = \log([DMONH^+]/[DMON^0]) = pK_1 - H_0$; $\log I_2 = \log([DMONH_2^{2+}]/[DMONH^+]) = pK_2 - H_0$. In solutions more acidic than pK_2 the concentration at time t_0 of neutral $DMON^0$ as a function of H_0 decreases at twice the rate of that of $DMONH^+$, because $DMONH^+$ also decreases.

the direct substrates in sulfonation and not the neutral DMON molecules as the latter are protonated when sulfonations proceed.

Sulfonation products

Mild sulfonation conditions were applied to obtain the first, or early, stable products. The relative ease of sulfonation of aromatic ethers (and phenols) can be explained by the interaction of the lone pair of n-electrons remaining on methoxy oxygen with the naphthalene ring, which retains much of its nucleophilic and aromatic properties in protonated ethers.

In such solutions an electrophilic attack by a sulfonating entity on the relatively electronegative ring carbon atom of the oxonium monocation leads to the formation of the monosulfonic product. In the process the $DMONH^+$ ions are removed from the solution and the concentrations of the more and less protonated forms of the substrate (*i.e.*, of $DMONH_2^{2+}$ and $DMON^0$) also decrease proportionally as indicated by the I values, which are constants at each H_0 value. If the quinonoid band of $DMONH_2^{2+}$ is present, it will decrease in step with the sulfonation rate.

However, with rising acidity in 92–97% H_2SO_4 the initial concentration of the oxonium cations decreases rapidly (*cf.* Table 7) while the sulfonation rate, concentration of $DMONH_2^{2+}$ and the decay of the quinonoid band increase sharply. This means that the dications are also sulfonated, in particular, at acidities where their concentration approaches 100%. Otherwise a levelling or decline of sulfonation rates would be observed. The dications are C-protonated on the ring carbon atom, which decreases the sulfonation rate, but with increasing percentage of H_2SO_4 the sulfonation potential of the solution increases and the reaction rate also increases. The sulfonation potential of solution can be represented by $\log a_{H_2S_2O_7}$, which has been evaluated[3,4b] as a function of % H_2SO_4 and is related *via* the % H_2SO_4 content to the H_0 scale.[20] This sequence of reactions would apply also to other methoxynaphthalenes.

In the case of 2,6-DMON the products have a UV absorption spectrum rather similar to that of the parent 2,6-DMON, but the yellow band is absent. The first SO_3 group is *meta*-positioned with formation of 2,6-DMON-4-monosulfonic acid (2,6-DMON-4-S). The second SO_3 substituent is inserted at position 7. Only one 2,6-DMON-4,7-disulfonic acid (2,6-DMON-4,7-S_2) is obtained.

Sulfonation of 2,3-DMON in 62–80% H_2SO_4 only occurs for monocation **2** at a relatively slow rate, which enabled us to prepare monosulfo-2,3-DMON free of its disulfo derivative. The latter is formed in 91–97% H_2SO_4. Barium salts of 2,3-DMON-monosulfonic acid contained two isomers in the proportion 1:2 of the 2,3-DMON-5-monosulfonic salt (2,3-DMON-5-S) and 2,3-DMON-6-monosulfonic salt (2,3-DMON-6-S), respectively. Only 2,3-DMON-5,7-disulfonic acid (2,3-DMON-5,7-S_2) is obtained after exhaustive sulfonation of 2,3-DMON. Here positions 5,7 and 6,8 are equivalent, which means that in this case the $-SO_3$ group directs the second substituent to a *meta* position.

Sulfonation of 2,7-DMON proceeds *via* O-protonated and C-protonated intermediates with *ortho*-substitution at position 3 (or 6). 2,7-DMON-3-Monosulfonic acid (2,7-DMON-3-S) is formed. Further sulfonation proceeds in 87–97% H_2SO_4 with formation of 2,7-DMON-3,6-disulfonic acid (2,7-DMON-3,6-S_2). In our substrates the β-positions in the naphthalene ring are more reactive than the α-positions.

Both O-protonated monocations as well as O- and C-protonated dications of monosulfonic products can be substrates in further sulfonations of DMONs. This is indicated by the quinonoid spectra[23] of 2,7-DMON-3-S and the absence of such bands[29] for 2,6-DMON-4-S.

Sulfonic acids such as **4** in Scheme 1 are strong acids and dissociate in solutions of lower acidity.

Conclusions

a) In our research we found that 2,3-, 2,6- and 2,7-DMONs are reversibly protonated in concentrated H_2SO_4. The pK_1 and pK_2 values have been determined and the results are presented in Table 7.

Table 8 Binding energies (BE) and heats of formation (HF) (in kcal mol^{-1}) of mono- and disulfonic acids of 2,3-, 2,6- and 2,7-DMON[a]

2,3-DMON	HF	BE	2,6-DMON	HF	BE	2,7-DMON	HF	BE
1-S	−145.84	−3185.94	1-S	−148.90	−3188.99	1-S	−148.80	−3188.90
5-S	−150.43	−3190.53	3-S	−147.81	−3187.91	*3-S*	*−148.96*	*−3189.06*
6-S	*−151.83*	*−3191.92*	*4-S*	*−149.31*	*−3189.41*	4-S	−149.42	3189.52
5,1-S_2	−262.69	−3547.86	4,1-S_2	−258.71	−3543.88	3,1-S_2	−262.06	−3547.24
5,7-S_2	*−268.18*	*−3553.36*	*4,7-S_2*	*−266.63*	*−3551.81*	*3,6-S_2*	*−265.51*	*−3550.69*
5,8-S_2	−260.65	−3545.83	4,8-S_2	−261.81	−3546.99	3,8-S_2	−261.82	−3547.00
5,4-S_2	−184.79	−3469.96	4,3-S_2	−253.02	−3538.20	3,5-S_2	−254.42	−3539.60
5,6-S_2	−257.54	−3542.72	4,5-S_2	−191.28	−3476.46		−260.72	−3545.90
6,1-S_2	−264.54	−3549.72						
6,4-S_2	−255.57	−3540.75						
6,7-S_2	−262.35	−3547.52						

[a] Isomers obtained in this work are in italic type. The sulfonic group is abbreviated as S preceded by a number indicating its position on the naphthalene ring.

b) The sulfonation rate constants are, within experimental error, the same as the decay rate constants of the quinonoid dications. These results are collected in Table 6.
c) As a result of protonation the neutral DMON^0 molecules disappear from solutions in which sulfonation proceeds and therefore are not the direct substrates of sulfonation.
d) The immediate substrates of sulfonation in acids of medium strength are the respective monocations of DMON and at acidities higher than pK_2 these are the dications of DMON.
e) Barium or sodium salts of mono- and disulfonic acids of 2,3- and 2,6-DMON have been isolated and their structure was established by NMR spectroscopy. All the products we have prepared and identified are printed in italic type in Table 8.
f) Further sulfonation of dimethoxynaphthalenes proceeds on the naphthalene ring with the fewer substituents. At room temperatures in aqueous H_2SO_4 up to 97% only a second SO_3 group is substituted.

In order to clarify the observed substituent effects theoretical calculations of binding energies (BE) and heats of formation (HF in kcal mol^{-1}) were made.

In Table 8 are the results calculated after geometry optimisation by AM1 semiempirical methods (a HyperChem® program) for all possible monosulfonic acids and those disulfonic acids that are derived from obtained monosulfonic acids. It was found that the mono- and disulfonic acids we obtained have the lowest values of binding energies and heats of formation for a given DMON substrate; only 2,7-DMON-3-S differs slightly. This may explain the site of substitution of the first and the second SO_3 group and the formation of the products observed by us. The calculated reactivities of various naphthalene ring positions in the neutral primary substrates appear to be less significant, if the presence of protonated forms of DMONs is considered.

Experimental

Experimental procedures and methods including evaluation of results were similar for all three title compounds. The products we have isolated have been identified before in non-aqueous solutions by means of NMR by others.[2] The structures of our products are also based principally on NMR spectra, but the UV spectra were considered as the β-bands confirm the presence of a naphthalene ring. Also elemental analyses of all products for C and H were obtained together with some mineralizations in 72% $HClO_4$ if the carbon content was lower than calculated and the presence of inorganic salts was suspected.

Determination of the first protonation constants

Pulverized DMON (*ca*. 0.2 g) was placed in a 50 or 100 ml conical flask with a glass stopper, 15–25 ml of H_2SO_4 of a concentration determined by alkalimetry were added and the suspension was stirred. Every 1 or 2 hours the spectra of the solutions were recorded in quartz cuvettes. A shallow minimum of solubility, S_i, was found in 20–30% H_2SO_4. The increase of solubility, S_H, was attributed to the formation of a protonated form if a plateau of solubility was reached (sometimes the next day) and if, after ice was added, the concentration returned to S_i. We used an extended form of the Krebs and Speakman equation[27,28]

$$pK_1 = H_0 + \log[(S_H/S_i) - 1] \quad (1)$$

equivalent to the standard (Henderson) equation, which describes the acid–base titration curve, but adapted to the range of the H_0 acidity scale, $-H_0 = pK_1 - \log I$; S_i is the concentration of the uncharged form B of the DMON. BH^+ is the protonated form $DMONH^+$; S_H is the solubility measured at higher acid concentrations and is the sum of B and BH^+.

$$[(S_H/S_i) - 1] = [(BH^+ + B)/B] - 1 = (BH^+/B) = I \quad (2)$$

$$\%B = 100\% - \%BH^+ \; [\%BH^+ = 100\, I(I + 1)] \quad (3)$$

Parallel determinations of decay rates k_{qu} for the quinonoid band and sulfonation rates k_{grav} were achieved gravimetrically: A 26–80 mg sample of a DMON was weighed in a 100 ml conical flask with a glass stopper on an analytical balance and 40–70 ml of H_2SO_4 of known concentration was added and the solution was stirred. Small samples of DMONs and larger volumes of the weaker acids were used to obtain rapid and complete dissolution (time t_0). Final concentrations of DMONs were 0.002–0.01 M. Just after dissolution 0.1–0.2 ml of the (coloured) solution were transferred to a 10 ml flask and filled to the mark with another portion of the same acid. After mixing, the spectra of this diluted solution were taken in a cyclic mode. The reactions are of (pseudo)-first order and the decay rates k_{qu} of the quinonoid bands were obtained from $k_{qu} = [\ln(A_0 - A_\infty)]/(A_t - A_\infty)]/t$. A_0 is the absorbance extrapolated to time t_0, A_∞ is the (small) final absorbances; t is time measured from t_0.

Simultaneously at the same temperature the reaction in the conical flask proceeded under stirring. After 90–350 min the reaction was stopped by pouring the solution on to a weighed amount of ice, the flask was rinsed with ice-cold water. In the combined solutions the percentage of H_2SO_4 was in the S_i region of DMON, between 20 and 35%. The solution immediately turned white, and a white precipitate formed. This was left overnight at room temperature. Then the precipitated DMON was slowly filtered on a sintered-glass crucible No.4, washed with cold water, dried at 55 °C and weighed.

The reaction rate $k_{grav} = \ln[(\text{initial weight of DMON})/(\text{final weight of DMON})]/t$.

2,3-DMON was prepared from 2,3-dihydroxynaphthalene by standard methylation with dimethyl sulfate. The product was purified by double crystallisation from ethyl alcohol. Melting point 116 °C (uncorrected). Calculated: C, 76.52; H, 6.38; found: C, 76.51; H, 6.42%. ^{1}H NMR: δ 3.87 (s, 2 × OCH_3), 7.22 (s, H1, H4), 7.27 (m, H6, H7), 7.66 (m, H5, H8).

2,6- and 2,7-DMON of 99% purity were obtained from Sigma Chemical Co., and were used as supplied: 2,6-DMON mp 153 °C; ^{1}H NMR: δ 3.83 (s, 2 × OCH_3), 7.12 (dd, ^3J = 8.9 Hz, ^4J = 2.3 Hz, H3, H7), 7.25 (d, ^4J = 2.3 Hz, H1, H5), 7.71 (d, ^3J = 8.9 Hz, H4, H8). 2,7-DMON mp 138 °C; ^{1}H NMR: δ 3.84 (s, 2 × OCH_3), 6.97 (dd, ^3J = 8.9 Hz, ^4J = 2.0 Hz, H3, H6), 7.22 (d, ^4J = 2.0 Hz, H1, H8), 7.71 (d, ^3J = 8.9 Hz, H4, H5).

Preparation of monosulfonic salts

1 g of DMON was dissolved at room temperature in 20 g of 80% H_2SO_4. The solution was stirred for 18 hours, then 50 g of ice were added with stirring. Unreacted DMON precipitated out, was filtered off and identified. The filtrate was neutralized stepwise with $Ba(OH)_2 \cdot 8H_2O$. $BaSO_4$ was filtered off and washed with distilled water. Then $BaSO_4$ was discarded, the filtrates were combined and extracted with diethyl ether to remove traces of DMON and were evaporated to dryness. The product was extracted with ethyl alcohol from the residue. After evaporation $[C_{10}H_5(OCH_3)_2SO_3]_2Ba$ (*ca*. 0.4 g) was obtained, purity 95% according to elemental analysis. (2,3-DMON-5-S)$_2$Ba was enriched by repeated extraction with methanol of the dry ethanol extract. ^{1}H NMR: δ 3.83 and 3.91 (s, 2 × OCH_3), 7.17 (s, H1), 7.32 (m, H7), 7.76 (d, H6), 7.88 (dd, H8), 7.90 (s, H4). (2,3-DMON-6-S)$_2$Ba ^{1}H NMR: δ 3.77 and 3.78 (s, 2 × OCH_3), 6.99 (s, H1), 7.09 (s, H4), 7.57 (dd, H7), 7.64 (d, H8), 8.01 (s, H5).

Preparation of disulfonic salts

1 g of DMON was dissolved with stirring at room temperature in 20 g of 94% H_2SO_4. After 20 h the homogeneous solution was diluted with 50 g of ice and worked up as described above for the monosulfonic salt. About 0.5 g of 2,3-DMON-5,7 S_2Ba was obtained, 95–97% purity. ^{1}H NMR: δ 3.79 and 3.98 (s, 2 × OCH_3), 7.31 (s, H1), 7.98 (s, H4), 8.31 and 8.35 (d, ^4J = 1.2 Hz, H6, H8). Mono- and disulfonic acids and salts of 2,6-DMON were prepared by similar procedures[29] to those for 2,3-DMON. 2,6-DMON-4-S: δ 3.78 and 3.85 (s, 2 × OCH_3), 7.08 (m, H7), 7.25 (s, H5), 7.55 (s, H1), 7.65 (d, ^4J = 1.8Hz, H8), 8.15 (s, H3). 2,6-DMON-4,7-S_2: δ 3.76 (s, OCH_3-C2), 4.01 (s, OCH_3-C6), 7.56 (s, H1), 8.15–8.25 (m, H3, H5, H8).

The spectra of the sulfonic salts of 2,7-DMON have been published[23] and the ^{1}H NMR assignments are confirmed by the ^{1}H NMR spectrum of the sodium salt of 2,7-dihydroxynaphthalene-3,6-disulfonic acid: δ 4.72 (s, 2 × OH), 7.11 (s, H1, H8), 8.25 (s, H4, H5).

The preparation of mono- and disulfonates of 2,7-DMON is described in our earlier paper.[23]

All measurements and reactions were performed at room temperature (that is, 22–24 °C). UV spectra were recorded with an ATI Unicam UV4 spectrophotometer and the ^{1}H NMR with a Bruker AC 200 and a DRX 500 spectrometer; pH measurements were made with a Radiometer PHM-80 instrument.

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