Studies of Reactions of Amines with Sulfur Trioxide. VI.[1] Thermal Reactions of Anilinium, Dimethylanilinium, and Trimethylanilinium Salts of Butylamidosulfuric Acid

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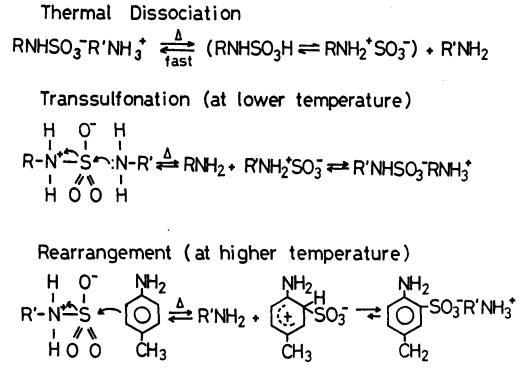
When the title compounds were heated in an evacuated reaction vessel, both transsulfonation and rearrangement occurred. At lower temperatures (80—120 °C) the corresponding phenylamidosulfates and sulfophenylamidosulfates (*transsulfonation products*) were the main products. Increasing temperature led to the formation of ring mono- and disulfonates (*rearrangement products*) at the expense of the transsulfonation products. The sulfonate group always migrated to the *ortho* and/or *para* position(s) to the amino group. In no case was any *meta*-product detected. There was no significant difference in the ease of transsulfonation among the anilinium salts studied except 2,6-dimethyl- and 2,4,6-trimethylanilinium salts. On the other hand, the ease of rearrangement and the orientation of ring sulfonation depended strongly on the structure of the substrate anilines. The thermal reactions of 2,4,6-trimethylanilinium butylamidosulfate produced (2,4,6-trimethylphenylimido)bis(sulfate) in addition to (2,4,6-trimethylphenylamido)sulfate. This is the first isolation of an arylimidobis(sulfate) from such reactions. Mechanisms of the transsulfonation and the rearrangement have been discussed.

Considerable attention has been paid to the chemistry of amidosulfuric acid and its *N*-substituted derivatives in recent years.[2] In particular, rearrangement of arylamidosulfuric acids ($ArNHSO_3H$) to the corresponding ring-sulfonated anilines is of great interest from both mechanistic and preparative viewpoints, because arylamidosulfuric acids have been postulated as intermediates in the sulfonation of aromatic amines with sulfuric acid[3] as well as in the "baking" process.[4-6]

Accordingly we studied the thermal reactions of amine salts of *N*-substituted amidosulfuric acids ($RNHSO_3^-R'NH_3^+$; R=*n*-Bu or *p*-$CH_3C_6H_4$, R'=*n*-Bu or *p*-$CH_3C_6H_4$) and showed[1] that: (1) at lower temperatures (80—120 °C) (4-methylphenylamido)sulfate and 4-methylaniline-*N*,2-disulfonate (transsulfonation products) are the main products; (2) at higher temperatures (120—180 °C) 4-methylaniline-2-sulfonate and 4-methylaniline-2,6-disulfonate (rearrangement products) predominate; and (3) the ease of both transsulfonation and rearrangement[7] depends on the basicity of both the parent amine (RNH_2) and the salt-forming amine ($R'NH_2$). On the basis of these results we proposed a tentative mechanism involving a preequilibrium thermal dissociation into the free acid ($RNHSO_3H$) and the salt-forming amine ($R'NH_2$) followed by a rate-determining nucleophilic attack by $R'NH_2$ on the tetracoordinate sulfur atom of the zwitterionic amidosulfuric acid ($RNH_2^+SO_3^-$) (Scheme 1).



Scheme 1.

In order to obtain a better picture of the mechanism of thermal reaction, we studied the substituent effects both on the ease of transsulfonation and rearrangement and on the orientation of ring sulfonation in a series of methyl-substituted anilinium salts of butylamidosulfuric acid (*n*-$BuNHSO_3^-ArNH_3^+$).

Results and Discussion

Anilinium Butylamidosulfate (1). The thermal reaction of **1** at 100 °C for 8 h produced phenylamidosulfate (**2**) in an 85% yield. Aniline-*N*,4-disulfonate (**3**)[8] was also formed at the temperatures ranging 100—140 °C (Fig. 1). The structure of this new compound, **3**,[9] was unequivocally established by acid hydrolysis; namely, a sulfo-amidosulfate fraction from the reaction of **1** at 115 °C for 8 h gave aniline-4-sulfonic acid on acid hydrolysis. No isomeric aniline-*N*,2-disulfonate (which should give aniline-2-sulfonic

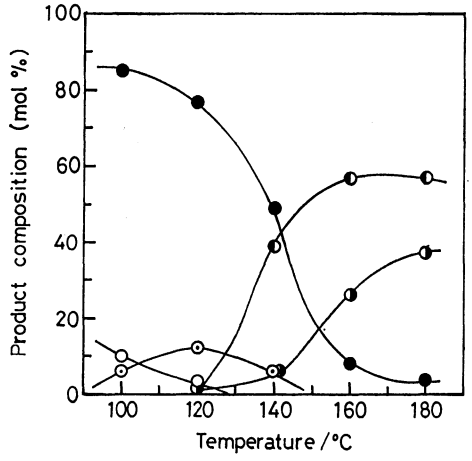


Fig. 1. Thermal reaction of anilinium butylamidosulfate. Reaction time 8 h.
○: *n*-$C_4H_9NHSO_3^-$, ●: $C_6H_5NHSO_3^-$, ◐: $NH_2C_6H_4SO_3^-$, ⊙: $C_6H_4(NHSO_3^-)(SO_3^-)$, ◑: $NH_2C_6H_3(SO_3^-)_2$.

acid on the hydrolysis) was detected on TLC.

The thermal reaction of **1** at 160 °C for 8 h gave a mixture of aniline-2- (**4**) and 4-sulfonate (**5**) (57%)[10] and aniline-2,4-disulfonate (+2,6-disulfonate) (26%);[11] neither **2** nor **3** was detected in the product.

In no run was any evidence obtained for the formation of aniline-3-sulfonic acid (*meta*-compound).

2,3-Dimethylanilinium Butylamidosulfate (6). Thermal reaction of **6** (120 °C, 8 h) gave (2,3-dimethylphenylamido)sulfate (**7**) in an 85% yield (Table 1). The amount of *N*,ring-disulfonate(s) (**8**) was negligibly small. The reaction at 140 °C for 8 h gave a mixture of **7** (13%), **8** (11%), 2,3-dimethylaniline-4-sulfonate (**9**) (27%), 2,3-dimethylaniline-6-sulfonate (**10**) (12%), and 2,3-dimethylaniline-4,6-disulfonate (**11**) (33%).[12]

Reaction of **6** at 160 °C for 8 h produced a mixture of **9** (5%), **10** (32%), and **11** (56%). The structure of **9** was established by direct comparison of its IR spectrum, R_f value (TLC), and melting point with those of an authentic sample prepared umambiguously (see Experimental section).

It is interesting to note here that increasing reaction temperature tends to increase the ratio of **10** : **9** (0.52 : 1 at 140 °C and 1.82 : 1 at 160 °C, respectively[13]).

2,4-Dimethylanilinium Butylamidosulfate (12). The reaction of **12** at 120 °C for 8 h gave (2,4-dimethylphenylamido)sulfate (**13**) in a 93% yield. 2,4-Dimethylaniline-6-sulfonate (**14**)[14] and 2,4-dimethylaniline-*N*,6-disulfonate (**15**) were also formed in small amounts. On the other hand, the thermal reaction of **12** at 160 °C for 8 h gave **14** in a 74% yield, together with **13** and **15**.

2,5-Dimethylanilinium Butylamidosulfate (16). The reaction of **16** at 100 °C for 8 h gave (2,5-dimethylphenylamido)sulfate (**17**) in a 91% yield. In contrast, the reaction at 120 °C for 8 h produced 2,5-dimethylaniline-4-sulfonate (**18**) (43.5%), and 2,5-dimethylaniline-*N*,4-disulfonate (**19**) (16%), together with **17** (32%). The reaction of **16** at 160 °C for 8 h yielded **18** predominantly; isomeric 2,5-dimethylaniline-6-sulfonate was formed in a small quantity (TLC). It should be noted that most of **19** remained unchanged and no trace of 2,5-dimethylaniline-4,6-disulfonate (**20**) was detected even at 160 °C. This fact indicates that the introduction of a sulfonate group into the 6 position of **18** is highly sterically hindered. This position is flanked by an amino and a methyl groups. Moreover, a buttressing effect of both 2-methyl and 4-sulfonate groups is operative (see also under the headings "3,5-dimethylanilinium butylamidosulfate" and "2,4,5-trimethylanilinium butylamidosulfate").

2,6-Dimethylanilinium Butylamidosulfate (21). In marked contrast with any other anilinium salt studied, **21** was thermally very unstable and showed a great tendency to dissociate into 2,6-dimethylaniline and butylamidosulfuric acid (even at room temperature).[15] Evidently this tendency is ascribable to B strain arising from the salt formation.[16]

It is to be expected that transsulfonation of **21** occurs much more readily than that of the other anilinium salts studied, because the transsulfonation of $RNHSO_3^-R'NH_3^+$ is believed to involve a preequilibrium thermal dissociation into the reacting species ($RNH_2^+SO_3^-$) and the substrate amine ($R'NH_2$) followed by a rate-determining transfer of a sulfonate group from $RNH_2^+SO_3^-$ to $R'NH_2$.[1] In fact, heating at 110 °C for as short as 30 min brought about *ca.* 90% transsulfonation.[17] The reaction for 2 h at the same temperature gave a mixture of (2,6-dimethylphenylamido)sulfate (**22**) (66%), 2,6-dimethylaniline-*N*,4-disulfonate (**23**) (21%), 2,6-dimethylaniline-4-sulfonate (**24**) (7%), and as little as 6% of the starting salt **21**. Heating at 110 °C for 8 h gave **24** in a 44% yield, in addition to **22** (38%) and **23** (15%).

When **21** was heated at 160 °C for 8 h, **24** was produced in a 90% yield. **22** disappeared almost completely (only a trace on TLC). No *meta*-isomer, 2,6-dimethylaniline-3-sulfonate, was detected.

Nitration of 2,6-dimethylaniline (**25**) and its *N*-acetyl derivative (**26**) with nitric acid or with mixed acid is known to occur exclusively at the *meta* position.[18] This anomalous behavior has been attributed to the steric inhibition of resonance.[19] The situation, however, is more complex, because bromination of **25** both in hydrobromic acid and in glacial acetic acid and chlorination of **25** in glacial acetic acid have been reported to give the 4-substituted compounds.[20] Bromination of **26** in hydrobromic acid leads to the formation of the 3-bromo derivative, whereas the bromination in glacial acetic acid gives a mixture of the 3- and the 4-isomers.[20]

These facts led us to examine the orientation of sulfonation of **25**. Our experiments showed that the "baking" of 2,6-dimethylanilinium hydrogensulfate in *o*-dichlorobenzene[21] yields **24** as the sole product, while the sulfonation with 25% oleum gave the *meta*-isomer (**27**) as the main product and, in addition, minor amounts of **24** and (a) disulfonic acid(s). **27** was also produced by reaction of **26** with $ClSO_3H$[22] and subsequent hydrolysis of the acetyl group.

The structure of **24** was established both by direct comparison with an authentic material prepared from 2-nitro-4,6-dimethylaniline and by chemical conversion of **24** to 3,5-dimethylbenzenesulfonic acid (see Experimental section).

Unlike the other *N*,ring-disulfonates, **23** failed to give the bis(tetraphenylphosphonium) salt; therefore, **23** was isolated and characterized as the dipotassium salt (Table 5). Its structure was proved by acid hydrolysis to **24**.

3,4-Dimethylanilinium Butylamidosulfate (28). Thermal reaction of **28** at 120 °C for 8 h gave (3,4-dimethylphenylamido)sulfate (**29**) in an 85% yield. Additionally, 3,4-dimethylaniline-*N*,6-disulfonate (**30**) (18%) was formed. No 3,4-dimethylaniline-6-sulfonate (**31**) was detected (TLC).

On the other hand, the reaction at 160 °C for 8 h produced **31** in a high yield. **29** and **30** were also formed in small amounts. No isomeric 3,4-dimethylaniline-2-sulfonate was found in the product.

3,5-Dimethylanilinium Butylamidosulfate (32). When heated at 110 °C for 8 h, anilinium salt **32** readily underwent transsulfonation to give (3,5-dimethylphenylamido)sulfate (**33**) in a 77% yield, but the subsequent rearrangement of **33** to 3,5-dimethylaniline-2-sulfonate (**34**) proceeded with difficulty and incom-

TABLE 1. THERMAL REACTIONS OF ANILINIUM SALTS OF BUTYLAMIDOSULFURIC ACID, n-$BuNHSO_3^-$-$ArNH_3^+$ [a)]

Ar	Temperature °C	Product composition (mol %)				
		n-$BuNHSO_3^-$	$ArNHSO_3^-$	$Ar(NHSO_3^-)$-(SO_3^-)	$Ar(NH_2)$-(SO_3^-)	$Ar(NH_2)$-$(SO_3^-)_2$
2,3-Dimethylphenyl	120	7.9	84.7	2.2	3.7	1.5
	160	0	1.1	trace	96.8[g)]	
2,4-Dimethylphenyl	120	2.9	92.7	2.2	2.2	0
	160	2.6	14.8	4.0	74.1	0
2,5-Dimethylphenyl	100	4.7	90.8	4.5	trace	0
	120	4.6	31.9	16.0	43.5	0
	160	1.2	trace	15.0	83.8	0
2,6-Dimethylphenyl	110[c)]	5.7	66.2	21.4	6.8	0
	110	3.1	37.8	14.8	44.3	0
	120	6.2	5.4	26.5	61.8	0
	160	1.9	trace	7.9	90.2	0
3,4-Dimethylphenyl	120	5.3	84.7	10.0	0	0
	160	1.7	3.0	7.9	87.3	0
2,4,5-Trimethylphenyl	130[b)]	0	98.3	1.7	0	0
	160	10.5	80.2	1.6	7.8	0
2,4,6-Trimethylphenyl	120[c)]	9.3	90.2	0.4[f)]	0	0
	120	2.6	74.3	23.1[f)]	0	0
	120[d)]	0	93.7	0	0	0
	160	5.2	70.3	19.4[f)]	0	0
	e)	9.5	69.7	6.1[f)]	0	0

a) Reaction time: 8 h. b) Reaction time: 4 h. c) Reaction time: 2 h. d) 2,4,6-Trimethylaniline was used as a reaction medium. e) The reaction was carried out in boiling 1,3,5-trimethylbenzene. f) (2,4,6-Trimethylphenylimido)bis(sulfate). g) A combined analytical yield of 2,3-dimethylaniline-4- and 6-sulfonate and 4,6-disulfonate.

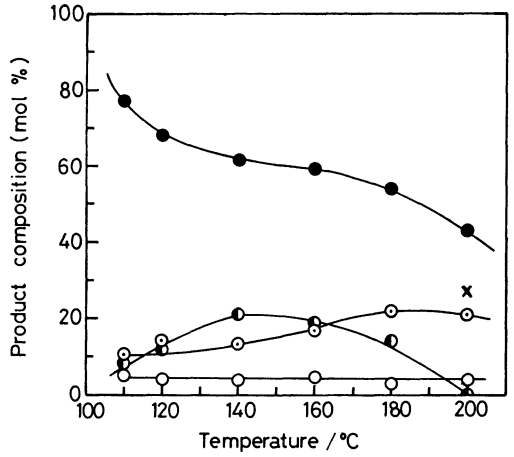


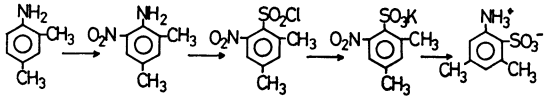
Fig. 2. Thermal reaction of 3,5-dimethylanilinium butylamidosulfate. Reaction time 8 h.
○: n-$C_4H_9NHSO_3^-$, ●: $Me_2C_6H_3NHSO_3^-$, ◐: $Me_2C_6H_2NH_2(SO_3^-)$, ⊙: $Me_2C_6H_2(NHSO_3^-)(SO_3^-)$ × : SO_4^{2-}.

pletely (see Fig. 2). Even after heating of **32** at 180 °C for 8 h, **33** was the main product (54%); 3,5-dimethylaniline-2-sulfonate (**34**) (14%), 3,5-dimethylaniline-*N*, 2-disulfonate (**35**) (22%), and 3,5-dimethylaniline-2,6-(?)-disulfonate (a trace amount) were the minor products. The reaction at 200 °C gave rise to considerable decomposition.

It is particularly noteworthy that the sulfonation occurred almost exclusively at the *ortho* position, the *para*-isomer, 3,5-dimethylaniline-4-sulfonate (**36**) being formed in trace amounts.[23)]

These results show that the transfer of the sulfonate group to the aromatic ring is very subject to steric hindrance. Such preferential or exclusive sulfonation at a less hindered *ortho*- or *para*-position (as observed with **16**, **28**, **32**, and **37**) may be explained in terms of the steric requirements of the attacking species.[24)]

To determine the position of the sulfonate group in **34** we carried out the deamination of **34**; thus, diazotization followed by reduction with $NaBH_4$ in methanol gave *m*-xylene-4-sulfonic acid. The structure of **34** was proved additionally by direct comparison with a sample prepared *via* an unambiguous route outlined below:



The structure of **35** was confirmed by acid hydrolysis to **34**.

A fourth component was isolated chromatographically in only a trace. This substance, which had the smallest R_f value on TLC, seemed to be 3,5-dimethylaniline-*N*,4-disulfonate, because this compound underwent hydrolysis on heating with dil HCl to give a spot corresponding to **36**.

2,4,5-Trimethylanilinium Butylamidosulfate (37). This salt, when heated at 130 °C for 4 h, yielded (2,4,5-trimethylphenylamido)sulfate (**38**) in an almost quantitative yield. 2,4,5-Trimethylaniline has one available position *ortho* to the amino group. This position, however, is highly sterically hindered by 1-amino and 5-methyl substituents. In addition there seems to be a "buttressing" effect of 2- and 4-methyl substituents.

In accord with this view, **38** rearranged to 2,4,5-trimethylaniline-6-sulfonate (**39**) with muth difficulty; thus, the thermal reaction of **37** at 160 °C for 8 h gave a mixture of the starting salt **37** (10.5%), **38** (80%), and **39** (9.4%).[25)] There was no evidence of the formation of either (2,4,5-trimethylphenylimido)bis(sulfate) or 2,4,5-trimethylaniline-*N*,6-disulfonate.

2,4,6-Trimethylanilinium Butylamidosulfate (40). This salt had some tendency to dissociate to 2,4,6-trimethylaniline (**41**) and butylamidosulfuric acid (**42**) at room temperature; consequently, **40** readily underwent transsulfonation to give (2,4,6-trimethylphenylamido)sulfate (**43**). Since **41** has no reactive site in the ring, any ring-sulfonated product cannot be formed. Deficiency of substrate amine **41** in the reaction mixture (caused by condensation of **41** on the cool wall of the reaction vessel) led to the formation of a new compound, (2,4,6-trimethylphenylimido)bis(sulfate) (**44**) in yields of 19—23% (Table 1). This is the first example of isolation of an arylimidobis(sulfate) from such reactions. **44** could also be obtained in an almost quantitative yield by fusion of an equimolar mixture of butylammonium (2,4,6-trimethylphenylamido)sulfate **43** and **42** (Scheme 2).[26]

$$n\text{-BuNHSO}_3^-\ 2,4,6\text{-Me}_3C_6H_2NH_3^+ \rightleftharpoons \underset{\mathbf{40}}{}$$

$$(n\text{-BuNHSO}_3H \rightleftharpoons \underset{\mathbf{42}}{n\text{-BuNH}_2^+SO_3^-})$$

$$+\ 2,4,6\text{-Me}_3C_6H_2NH_2 \quad (\mathbf{41})$$

$$\mathbf{41} + \mathbf{42} \rightleftharpoons 2,4,6\text{-Me}_3C_6H_2NHSO_3^-n\text{-BuNH}_3^+ \quad (\mathbf{43})$$

$$\mathbf{42} + \mathbf{43} \rightleftharpoons 2,4,6\text{-Me}_3C_6H_2N(SO_3^-n\text{-BuNH}_3^+)_2 \quad (\mathbf{44})$$

Scheme 2.

When the thermal reaction of **40** was carried out in **41** or 1,3,5-trimethylbenzene as reaction medium, the formation of **44** was suppressed.

Mechanistic Considerations. The thermal reactions of amine salts of amidosulfuric acids ($RNHSO_3^-R'NH_3^+$) are characterized by the initial thermal dissociation into the free acid ($RNHSO_3H$) and the salt-forming base ($R'NH_2$).[27] The degree of dissociation, of course, depends greatly on the basicity of $R'NH_2$; a decrease in the basicity of $R'NH_2$ favors the dissociation (Scheme 1).

Transsulfonation. There was no significant difference in the rate of transsulfonation among the anilinium salts examined except 2,6-dimethylanilinium and 2,4,6-trimethylanilinium butylamidosulfates. Evidently, in these two cases relief of B strain favors the dissociation.

It has been proved that free amidosulfuric acids exist as zwitterions ($RNH_2^+SO_3^-$) at least in the solid state;[2,28] the zwitterionic form is believed to be the reactive species.[1,2]

There are two possible mechanisms for the transfer of a sulfonate group from the zwitterionic amidosulfuric acid to the substrate amine. One involves rate-determining thermal cleavage of the N–S bond to give the parent amine and SO_3 (Eq. 1), followed by an electrophilic attack of SO_3 on the substrate (Eq. 2). The other involves a bimolecular nucleophilic substitution at the tetracoordinate sulfur atom (Eq. 3).

It should be noted that the transsulfonation occurs in the molten state (*viz.*, non-solvolytic conditions) at such low temperatures that the zwitterion, $n\text{-BuNH}_2^+SO_3^-$, is quite stable. As an example may be cited the fact that the transsulfonation of 2,6-dimethylanilinium butylamidosulfate (**21**) proceeds very rapidly at 110 °C (90% conversion of **21** occurred in 30 min at this temperature). The *gas-phase* reaction between sulfur trioxide and an amine such as trimethylamine is very exothermic.[29] These two facts suggest that, under "*non-solvolytic*" conditions, the dissociative process may be unlikely, whereas the latter process involving synchronous bond-forming and bond-breaking in the transition state is much more likely from the energetical point of view. It has been reported that *N*-substituted amidosulfate salts undergo acid-catalyzed hydrolysis mostly by an A-2 type mechanism (involving a bimolecular nucleophilic attack of water in the transition state) (Eq. 4).[2] It has also been suggested that the catalytic sulfation of 1-hexadecanol with amidosulfuric acid in the presence of DMF may involve the formation of a DMF–SO_3 complex by an S_N2 mechanism (Eq. 5).[30] Further, the rates of sulfation of eleven alcohols with $n\text{-Bu}_3N^+$–SO_3^- have been measured and an S_N2-type mechanism has been proposed (Eq. 6).[31]

Unimolecular Transsulfonation. (S_N1-type dissociative mechanism)

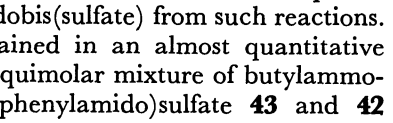
$$n\text{-BuNH}_2^+SO_3^- \underset{\text{slow}}{\overset{\Delta}{\rightleftarrows}} n\text{-BuNH}_2 + SO_3 \quad (1)$$

$$ArNH_2 + SO_3 \underset{\text{fast}}{\rightleftharpoons} (ArNH_2^+SO_3^- \rightleftharpoons ArNHSO_3H)$$

$$\xrightarrow[\text{fast}]{n\text{-BuNH}_2} ArNHSO_3^-n\text{-BuNH}_3^+ \quad (2)$$

Bimolecular Transsulfonation (S_N 2-type mechanism)

$$n\text{-BuNH}_2^+SO_3^- + ArNH_2 \rightleftharpoons$$



pentacoordinate transition state

$$\rightleftharpoons n\text{-BuNH}_2 + ArNH_2^+SO_3^- \rightleftarrows ArNHSO_3^-n\text{-BuNH}_3^+ \quad (3)$$

$$R^1R^2NSO_3^- \underset{\rightleftharpoons}{H^+} R^1R^2NH^+SO_3^- \xrightarrow[\text{slow}]{H_2O} R^1R^2NH_2^+HSO_4^- \quad (4)$$

$$NH_3^+SO_3^- + DMF \underset{\rightleftharpoons}{\text{slow}} NH_3 + DMF\cdot SO_3 \xrightarrow{ROH} ROSO_3^-NH_4^+ \quad (5)$$

$$n\text{-Bu}_3N^+SO_3^- + RO^- \xrightarrow{\text{slow}} \left[n\text{-Bu}_3N\cdots\overset{\displaystyle O}{\overset{\|}{S}}\cdots{}^-OR\right] \longrightarrow ROSO_3^- + n\text{-Bu}_3N \quad (6)$$

Rearrangement. There are at least three possible mechanisms to be considered for the rearrangement.[32]

(a) Intramolecular Pathway: Any mechanism which does not involve the N–S bond cleavage before a ring-sulfonation, encounters geometrical difficulties; that is, direct transfer of the sulfonate group from the amino nitrogen to the *para*-position of the ring is improbable because of the large distance which would have to be

spanned in the transition state.[33]

In order to account for the intramolecularity of the nitramine rearrangement, Dewar has proposed a π-complex mechanism involving initial cleavage of the N-NO_2 bond, followed by a series of 1,2-shifts *via* π-complex intermediates.[34] The very ready rearrangement of butylammonium (2,6-dimethylphenylamido)-sulfate (**22**) to 2,6-dimethylaniline-4-sulfonate (**24**) could not be accounted for by this scheme, because the migration of the sulfonate group passing through the ring to the *para*-position should be highly sterically hindered (Fig. 3).

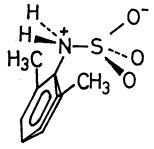
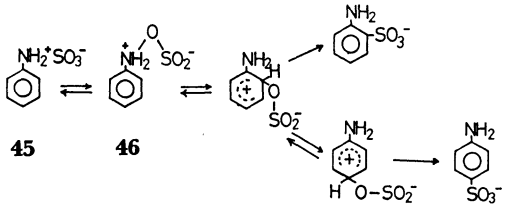


Fig. 3. (2,6-Dimethylphenylamido)sulfuric acid zwitterion.

Hughes and coworkers proposed the "cartwheel" mechanism in order to explain the intramolecular migration of the nitro group from the amino nitrogen to the *para*-position in the ring.[35] If a similar mechanism were to operate, the amidosulfuric acid rearrangement could be written as follows:



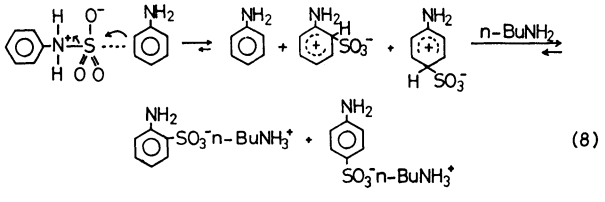
45 **46**

This mechanism seems unlikely from the following reasons. First, there is neither evidence nor analogy for such initial isomerization of **45** to *N*-phenylhydroxylamine-*O*-sulfite (sulfitoamine), **46**.[36] Secondly, **46**, a postulated intermediate in the reaction of *N*-phenylhydroxylamine with SO_2, has neither been isolated nor characterized.

It should be noted that the formation of disulfonated products does not eliminate the possibility of an intramolecular process, because a sulfonate group exchange between an arylamidosulfate and an aniline occurs very rapidly in the presence of the anilinium chloride (Eq. 7).[37]

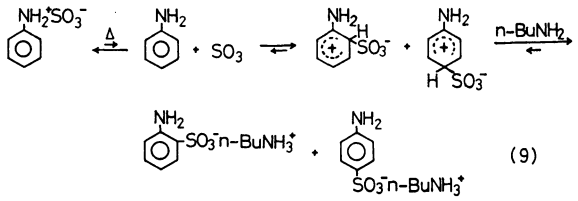
$$ArNHSO_3^- + Ar'NH_2 \overset{H^+}{\rightleftharpoons} ArNH_2 + Ar'NHSO_3^- \quad (7)$$

(b) S_N2-type Intermolecular Pathway: A second possible mechanism is an S_N2-type intermolecular pathway involving a nucleophilic attack by a substrate amine at the tetracoordinate sulfur atom of the zwitterion (ligand-exchange) to form (a) σ-complex(es) leading to *ortho* and/or *para* sulfonates (Eq. 8).



(8)

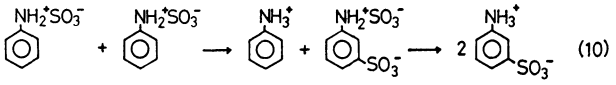
(c) S_N1-type Intermolecular Pathways: A third possible mechanism is an S_N1-type intermolecular process, which involves a unimolecular thermal cleavage of the zwitterion, $ArNH_2^+$–SO_3^-, to the substrate aromatic amine ($ArNH_2$) and SO_3 molecule. The latter species attacks at the *ortho*- and/or *para*-position(s) in the substrate (Eq. 9).



(9)

It is well known that, in marked contrast with amidosulfuric acid itself and its *N*-alkyl derivatives, arylamidosulfuric acids are very unstable and have a great tendency to undergo a hydrolytic and thermolytic N–S bond cleavage.[38] Further, it should be emphasized that (a) the composition of the product formed in the rearrangement of anilinium butylamidosulfate (160 °C, 8 h) closely resembled that of the product obtained by heating free phenylamidosulfuric acid, $C_6H_5NH_2^+SO_3^-$, in dioxane at 100 °C for 30 min (in the solid state)[28] and (b) in no case was any *meta*-sulfonated product detected.

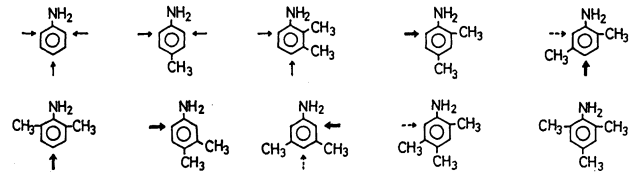
These facts support the S_N1-type intermolecular mechanism (Eq.9). A mechanism whereby the sulfonate group is transferred directly from the amino nitrogen to the *ortho*- and/or *para*-position(s) of another molecule (Eq. 10) is excluded. If this mechanism were operative, one would expect *meta* substitution (positively charged nitrogen).[3]



(10)

We suggested previously[1] that the transsulfonation and the rearrangement may occur concurrently. However, in the present study we have found that the former process proceeds much more rapidly than the latter; therefore, it seems more likely that both processes proceed consecutively.

Orientation of Ring Sulfonation. In marked contrast to the transsulfonation, the rearrangement was very subject to steric hindrance; *viz.*, both the ease and the orientation of the rearrangement were governed by steric factors. Relief of the steric strain around the amido-nitrogen markedly accelerated the rearrangement as observed with 2,6-dimethylanilinium butylamidosulfate. Two methyl substituents *ortho* to the reactive site hindered the introduction of a sulfonate group as observed typically with 3,5-dimethylanilinium butylamidosulfate. Moreover, a buttressing effect of 2- and 4-methyl substituents may operate. Thus, 2,4,5-trimethylanilinium butylamidosulfate underwent transsulfonation as rapidly as the other anilinium salts, but the subsequent rearrangement was very much retarded. The absence of 3,4-dimethylaniline-2-sulfonate in the



→ indicates the position where sulfonation occurs.
⇒ indicates the position where sulfonation occurs (almost) exclusively.
⇢ indicates the position where sulfonation occurs to only a small extent.

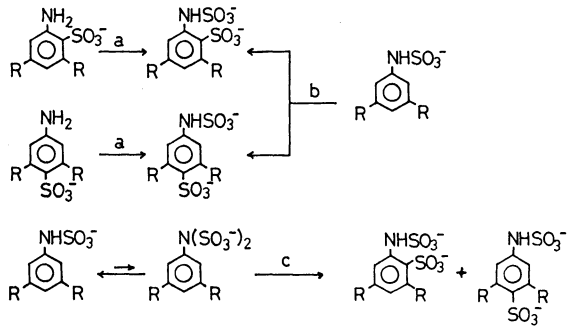
Fig. 4. The orientation of ring sulfonation.

product of the rearrangement of 3,4-dimethylanilinium butylamidosulfate is also ascribable to this effect.

Formation of N, *Ring-disulfonates.* Deficiency of the substrate aniline caused by the partial condensation of the dissociated amine on the cool part of the reaction vessel gave rise to the formation of disulfonates compounds. Thus, the thermal reaction of **1** gave aniline-*N*,4- (**3**) and 2,4-disulfonates in addition to aniline-2- and 4-sulfonates and phenylamidosulfate (Fig. 1). No trace of the *N*,2-disulfonate was found in the product mixture. In contrast, the same reaction of **32** yielded 3,5-dimethylaniline-*N*,2-disulfonate (**35**), together with (3,5-dimethylphenylamido)sulfate and 3,5-dimethylaniline-2-sulfonate. 4-Sulfonate (**36**) and *N*,4-disulfonate (**47**) were formed in only traces.

There are three possible pathways to an *N*,ring-disulfonate: (1) *N*-sulfonation of a ring monosulfonate (route a); (2) ring sulfonation of an arylamidosulfate (route b); (3) rearrangement of an arylimidobis(sulfate) (route c) which could be formed by the *N*-sulfonation of the corresponding arylamidosulfate (Scheme 3).

The results described above can best be interpreted in terms of route a. The exclusive formation of **3** is accounted for by the preferential *N*-sulfonation of aniline-4-sulfonate. The *N*-sulfonation of aniline-2-sulfonate must be sterically unfavored. If route b were to be followed, **47** should be formed instead of **35**. Formation of **36** and **47** in only traces supports pathway b. Route c is unlikely, because this route is sterically unfavorable as compared with route a.



R = H, CH_3

Scheme 3.

Experimental

General experimental details have been described previously.[1)]

Material. *Anilinium Salts of Butylamidosulfuric Acid (**42**)*: These compounds were prepared simply by neutralization of the free acid (**42**) with an appropriate aniline in methanol.[1)]

2,6-Dimethylanilinium and 2,4,6-trimethylanilinium salts were prepared as follows and immediately used for the reactions: a large excess of the aniline was added to a methanol solution of **42**; the mixture was evaporated *in vacuo* to give a slurry of the salt. This was filtered, washed with benzene, and dried in a desiccator (Table 2).

Isolation and Identification of the Reaction Products. For details see Ref. 1. *Amidosulfates* were isolated by liquid chromatography (cellulose Whatman CF-11, dioxane–H_2O 4 : 1) or by extraction with EtOH of the product mixtures obtained (as the sodium salts) from the reactions at lower temperatures. The crude amidosulfates thus obtained were readily purified and characterized as the tetraphenylphosphonium salts (Table 3).

Table 2. Analytical and spectral data for anilinium salts of butylamidosulfuric acid *n*-$BuNHSO_3^-$ $ArNH_3^+$

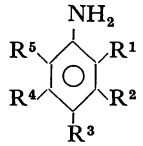
$ArNH_3^+$	Formula	N(%) (Calcd)	S(%) (Calcd)	IR spectra ($\tilde{\nu}$/cm^{-1})			
				νNH	$\nu_s SO_3^-$	$\nu_{as} SO_3^-$	Other prominent bands
Anilinium	$C_6H_{18}N_2O_3S$	11.46 (11.37)	13.15 (13.02)	3280	1048	1187 1229	748, 683
2,3-Dimethylanilinium	$C_8H_{22}N_2O_3S$	10.25 (10.21)	11.60 (11.68)	3210	1026	1147 1231	912, 880, 769, 705
2,4-Dimethylanilinium	$C_8H_{22}N_2O_3S$	10.20 (10.21)	11.65 (11.68)	3260	1026	1156 1235	916, 876, 807, 720
2,5-Dimethylanilinium	$C_8H_{22}N_2O_3S$	10.15 (10.21)	11.73 (11.68)	3268	1024	1156 1235	871, 828, 708
2,6-Dimethylanilinium	$C_8H_{22}N_2O_3S$	9.72 (10.21)	11.97 (11.68)	3260	1033	1161 1236	890, 777, 706
3,4-Dimethylanilinium	$C_8H_{22}N_2O_3S$	10.18 (10.21)	11.70 (11.68)	3240	1044	1170	807
3,5-Dimethylanilinium	$C_8H_{22}N_2O_3S$	9.98 (10.21)	11.68 (11.68)	3224	1038	1232	917, 855, 756—746, 684
2,4,5-Trimethylanilinium	$C_9H_{24}N_2O_3S$	9.68 (9.71)	11.14 (11.12)	3240	1027 1069	1160 1233	918, 876, 735
2,4,6-Trimethylanilinium	$C_9H_{24}N_2O_3S$	9.58 (9.71)	11.52 (11.12)	3260	1051	1186 1229	858

TABLE 3. ANALYTICAL AND SPECTRAL DATA FOR TETRAPHENYLPHOSPHONIUM AMIDOSULFATES,[a] $ArNHSO_3^-(C_6H_5)_4P^+$, ISOLATED FROM THE THERMAL REACTIONS OF n-$BuNHSO_3^-ArNH_3^+$

Ar	Formula	N(%) (Calcd)	S(%) (Calcd)	P(%) (Calcd)	IR spectra[b] ($\tilde{\nu}$/cm^{-1}) νNH	$\nu_s SO_3^-$	$\nu_{as} SO_3^-$	Other prominent bands
Phenyl	$C_{30}H_{26}NO_3PS$	2.72 (2.74)	6.50 (6.27)	5.97 (6.05)	3260	1039	1210 1227	885
2,3-Dimethylphenyl	$C_{32}H_{30}NO_3PS$	2.63 (2.60)	6.04 (5.94)	5.87 (5.74)	3308	1033	1210 1225	921, 834, 807, 778
2,4-Dimethylphenyl	$C_{32}H_{30}NO_3PS$	2.65 (2.60)	6.08 (5.94)	5.70 (5.74)	3280	1037	1206 1225	937, 864, 837
2,5-Dimethylphenyl	$C_{32}H_{30}NO_3PS$	2.62 (2.60)	6.03 (5.94)	5.82 (5.74)	3260	1035	1188 1231	950, 857, 813
2,6-Dimethylphenyl	$C_{32}H_{30}NO_3PS$	2.58 (2.60)	5.85 (5.94)	5.73 (5.74)	—	1036	1208 1228	875, 779, 745
3,4-Dimethylphenyl	$C_{32}H_{30}NO_3PS$	2.65 (2.60)	6.16 (5.94)	5.85 (5.74)	3236	1036	1205 1226	958, 868, 846, 816
3,5-Dimethylphenyl	$C_{32}H_{30}NO_3PS$	2.56 (2.60)	6.07 (5.94)	5.89 (5.74)	3216	1037	1203 1227	955, 844
2,4,5-Trimethylphenyl	$C_{33}H_{32}NO_3PS$	2.40 (2.53)	5.85 (5.79)	5.73 (5.59)	—	1029	1217	874
2,4,6-Trimethylphenyl	$C_{33}H_{32}NO_3PS$	2.38 (2.53)	6.04 (5.79)	5.61 (5.59)	3240	1033	1200 1218	864, 847, 819

a) Melting points of these phosphonium salts depended greatly on the rate of heating, probably because of the lability of the N-sulfonate group and hence the definite values could not be obtained. b) Absorbtions due to the tetraphenylphosphonium cation are omitted.

TABLE 4. ANALYTICAL AND SPECTRAL DATA FOR HEXYLAMMONIUM SALTS OF AMINOBENZENESULFONIC ACIDS (I) ISOLATED FROM THE THERMAL REACTIONS OF n-$BuNHSO_3^-ArNH_3^+$

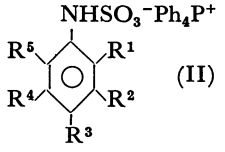


(I)

R^1	R^2	R^3	R^4	R^5	Mp/°C	Formula	N(%) (Calcd)	S(%) (Calcd)	IR spectra ($\tilde{\nu}$/cm^{-1}) νNH	$\nu_s SO_3^-$	$\nu_{as} SO_3^-$	Other prominent bands
SO_3H	H	H	H	H	190—190.5	$C_{12}H_{22}N_2O_3S$	10.13 (10.21)	11.66 (11.68)	3340 3408	1015 1110	1160 1200	748, 710
H	H	SO_3H	H	H	141—142	$C_{12}H_{22}N_2O_3S$	10.15 (10.21)	11.55 (11.68)		1037 1125	1162	822, 701
CH_3	CH_3	SO_3H	H	H	138.5—139.5	$C_{14}H_{26}N_2O_3S$	9.30 (9.26)	10.51 (10.60)	3352	1031	1175	650 971, 816, 711
CH_3	CH_3	H	H	SO_3H	172—173	$C_{14}H_{26}N_2O_3S$	9.15 (9.26)	10.53 (10.60)	3336 3428	1038 1079	1178 1221	800, 750, 700
CH_3	H	CH_3	H	SO_3H	153—154	$C_{14}H_{26}N_2O_3S$	9.22 (9.26)	10.48 (10.60)		1031	1172 1210	870, 797, 745
CH_3	H	SO_3H	CH_3	H	178.5—179.5	$C_{14}H_{26}N_2O_3S$	9.28 (9.26)	10.52 (10.60)	3340 3410	1065	1180	797, 728, 676 978, 912, 866
CH_3	H	SO_3H	H	CH_3	125—126.5	$C_{14}H_{26}N_2O_3S$	9.06 (9.26)	10.59 (10.60)	3360 3425	1034	1130 1220	888, 750, 737
H	CH_3	CH_3	H	SO_3H	214—216	$C_{14}H_{26}N_2O_3S$	9.31 (9.26)	10.51 (10.60)	3340 3420	1058	1165 1221	725, 663 985, 895, 868
SO_3H	CH_3	H	CH_3	H	138—139[a]	$C_{12}H_{22}N_2O_3S$[a]	10.25 (10.21)	11.64 (11.68)	3350 3430	1012 1075	1178	910, 830, 681
SO_3H	H	SO_3H	H	H	137—138	$C_{18}H_{37}N_3O_6S_2$	9.31 (9.22)	14.00 (14.07)	3365	1029 1090	1186 1215	817, 752, 691
CH_3	CH_3	SO_3H	H	SO_3H	178—179	$C_{20}H_{41}N_3OS_2$	8.60 (8.69)	13.40 (13.26)		1047	1182	750, 699 960, 878, 800
CH_3	H	CH_3	H	CH_3	—	$C_9H_{11}K_2NO_6S_2 \cdot H_2O$[b]	3.55 (3.61)	16.52 (16.50)	—	1028 1079	1223,1194 1284,1246	929, 730, 689

a) Butylammonium salt. b) Dipotassium (2,4,6-trimethylphenylimido)bis(sulfate) monohydrate.

TABLE 5. ANALYTICAL AND SPECTRAL DATA FOR BIS(TETRAPHENYLPHOSPHONIUM) AMIDOSULFATES (II)[a] ISOLATED FROM THE THERMAL REACTIONS OF *n*-BuNHSO$_3$-ArNH$_3$$^+$



(II)

R^1	R^2	R^3	R^4	R^5	Formula	N(%) (Calcd)	S(%) (Calcd)	P(%) (Calcd)	IR spectra[c] ($\tilde{\nu}$/cm^{-1}) νNH	$\nu_s SO_3^-$	$\nu_{as} SO_3^-$	Other prominent bands
H	H	SO_3^- Ph_4P^+	H	H	$C_{54}H_{45}NO_6P_2S_2$	1.30 (1.51)	7.04 (6.90)	6.51 (6.66)	3250	1026	1206	890, 841
CH_3	H	SO_3^- Ph_4P^+	CH_3	H	$C_{56}H_{49}NO_6P_2S_2$	1.57 (1.46)	6.50 (6.69)	6.45 (6.47)	3245	1048 1076	1179 1220	870, 812, 797
CH_3	H	SO_3K	H	CH_3	$C_8H_9K_2NO_6S_2$[b]	3.90 (3.92)	17.85 (17.94)	—	3225	1041	1175 1218	920, 904, 806
H	CH_3	CH_3	H	SO_3^- Ph_4P^+	$C_{56}H_{49}NO_6P_2S_2$	1.75 (1.46)	6.75 (6.69)	6.39 (6.47)	3240	1035	1202	865, 814
SO_3^- Ph_4P^+	CH_3	H	CH^3	H	$C_{56}H_{49}NO_6P_2S_2$	1.42 (1.46)	6.85 (6.69)	6.55 (6.47)	3230	1032	1211	841

a) See footnote a) to Table 3. b) Dipotassium salt. c) Absorptions due to the tetraphenylphosphonium cation are omitted.

Amino-monosulfonic acids were easily isolated by treatment with hydrochloric acid of the sodium salt mixtures obtained from the reactions at higher temperature. These acids were characterized as the hexylammonium or butylammonium salts (Table 4).

Sulfo-amidosulfates (*N*, ring-disulfonates) were isolated by liquid chromatography or by fractional precipitation with $(C_6H_5)_4PCl$ from the disulfonate fractions (obtained as the insoluble residues of the foregoing ethanol extraction). The tetraphenylphosphonium amidosulfates were more soluble in acetone than the bis(tetraphenylphosphonium) *N*, ring-disulfonates; hence, the former salts can readily be removed by washing the precipitate with a small volume of acetone. Disodium 2,6-dimethylaniline-*N*,4-disulfonate could not be converted to the corresponding bis(phosphonium)salt by the double-decomposition method (Table 5).

(2,4,6-Trimethylphenylimido)bis(sulfate) was isolated by liquid chromatography. Isolation was also achieved as follows: the product from the reaction of **40** (2 mmol, 120 °C, 8 h) was dissolved in water and the solution was passed through a column of Dowex 50W (K^+ form). The eluate was evaporated to dryness and the residue was extracted three times with 99.5% ethanol. The residual solid [composed of potassium (2,4,6-trimethylphenylamido)sulfate and dipotassium (2,4,6-trimethylphenylimido)bis(sulfate)] was then dissolved in water (3 ml) containing a few drops of aqueous KOH; to this solution was added 60 ml of hot ethanol with vigorous stirring. The mixture was filtered immediately and the filtrate was left at room temperature overnight. The precipitate was collected by filtration; for further purification this was dissolved in hot water containing a few drops of aqueous KOH, and reprecipitated with hot ethanol, giving the pure *imidobis(sulfate)* as colorless needles (Table 4).

Confirmation of the Structures of the Products Isolated from the Thermal Reactions. Deamination of 2,6-Dimethylaniline-4-sulfonic Acid: The aminosulfonic acid [obtained from the thermal reaction (160 °C, 5 h) of **22**] was deaminated by diazotization followed by reduction with $NaBH_4$ in MeOH (5—10 °C, 5 h),[39] yielding *m*-xylene-5-sulfonic acid; this was converted to the sulfonamide, mp 133—134 °C (lit,[40] 133—134 °C), mixed mp 132—133.5 °C.[41]

Deamination of 3,5-Dimethylaniline-2-sulfonic Acid: The aminosulfonic acid isolated from the thermal reaction (180 °C, 8 h) of **33** was deaminated in the same way as described above. The product was identical with authentic *m*-xylene-4-sulfonic acid;[42] its anilinium salt melted at 203—204 °C (lit,[40] 197—199 °C); mixed mp 202.5—203.5 °C; IR: 1551, 1194 (SO_3^-), 1168, 1089 (SO_3^-), 1018, 833 (2H), 746 (5H), and 680 (5H) cm^{-1}.

Proof of the Constitutions of Aniline-N,4-disulfonate and 3,5-Dimethylaniline-N,2-disulfonate. Disodium aniline-*N*,ring-disulfonate [obtained from the thermal reaction of **2** (110 °C, 8 h)] was hydrolyzed by refluxing for 30 min with dil HCl. After cooling, the mixture was neutralized with $Ba(OH)_2$, filtered, and the filtrate was passed through a column of Amberlite IR-120B (H^+ form). The effluent was evaporated to dryness and the residual solid washed in a minimum quantity of ethanol. The product thus obtained gave a single spot on TLC. Its R_f value and IR spectrum were entirely in agreement with those of authentic aniline-4-sulfonic acid.

In the same manner, acid hydrolysis of disodium 3,5-dimethylaniline-*N*,ring-disulfonate gave 3,5-dimethylaniline-2-sulfonic acid, deamination of which yielded *m*-xylene-4-sulfonic acid.

Preparation of Authentic Compounds. (1) 2,3-Dimethylaniline-4-sulfonic Acid:[43] *Nitration of 2,3-Dimethylacetanilide*:[44,45] To a stirred solution of 2,3-dimethylacetanilide (mp 130—131 °C) (8.0 g) in concd H_2SO_4 (20 ml) was added HNO_3 (d 1.42; 3.3 ml) at 5—10 °C over a period of half an hour. The mixture was poured into ice water (250 ml) and the precipitate was filtered, washed, and dried.

2,3-Dimethyl-4-nitroaniline:[44] The foregoing nitroacetanilide was hydrolyzed by refluxing for 1 h with 60% sulfuric acid (100 ml). The product (6.91 g) was chromatographed on silica gel by use of CCl_4–acetone (15 : 1 v/v) as an eluent. The 4-nitro compound thus obtained was recrystallized from CCl_4; the pure product (2.48 g) melted at 114—115 °C (lit,[46] 115.5—116.5 °C).

2,3-Dimethyl-4-nitro-1-benzenesulfonic Acid: 2,3-Dimethyl-4-nitroaniline (2.2 g) was diazotized in the usual way and the excess of nitrous acid was destroyed with NH_2SO_3H. The mixture was poured in one portion into a cold, saturated solution of SO_2 (8.7 g) in CH_3COOH to which a solution of $CuCl_2$ (0.37 g) in water (0.80 ml) had been added. The

temperature was raised gradually to 40 °C. The mixture was stirred for 1 h at this temperature, then poured into water (150 ml), and neutralized carefully with a $NaHCO_3$ solution; the oily layer was extracted twice with benzene and the extract was washed with aqueous $NaHCO_3$, dried, and concentrated *in vacuo* to give the crude sulfonyl chloride. A mixture of the sulfonyl chloride, 50% aq MeOH (15 ml), and Na_2CO_3 (0.60 g) was boiled for 1 h. The reaction mixture was evaporated and the residual solid was dissolved in water (10 ml), filtered, and evaporated to dryness. The residue was again dissolved in methanol (35 ml). After filtration, the filtrate was concentrated to give the *sodium nitro-sulfonate*. IR: 1517 (NO_2), 1356 (NO_2), 1178 (SO_3^-) 1067 (SO_3^-), 1039, 828(2H), 802, and 663 (SO_3^-) cm^{-1}; *S*-(1-naphthylmethyl)isothiouronium salt, mp 222—222.5 °C.

2,3-Dimethylaniline-4-sulfonic Acid: The crude nitrosulfonate was reduced with activated iron powder (2.5 g). Work-up in the usual way gave the pure *sulfonic acid* as needles; IR: 1503, 1206 (SO_3), 1082, 1052 (SO_3), 818 (2H), and 695 cm^{-1}. Found: S, 14.58%. Calcd for $C_8H_{11}NO_3S \cdot H_2O$: S, 14.62%. The *hexylammonium salt* (from EtOH–AcOEt 1 : 2) melted at 138.5—139.5 °C. Found: S, 10.51%. Calcd for $C_{14}H_{26}N_2O_3S$: S, 10.60%.

(2) 2,5-Dimethylaniline-4-sulfonic Acid: Treatment of 2,5-dimethylacetanilide (mp 138—139 °C, 1.0 g) with $ClSO_3H$ (4.2 ml) (80 °C, 1 h)[47] and subsequent recrystallization from C_6H_6–AcOEt(1 : 1) gave N-*acetyl-2,5-dimethylaniline-4-sulfonyl chloride* (0.55 g); mp 159—160 °C (lit, [47]160 °C), IR: 1660 (CO), 1560 (NH_3^+), 1360 (SO_2), 1275, 1121 (SO_2), 895 (1H), and 829 cm^{-1}.

A mixture of the sulfonyl chloride (0.30 g), ethanol (1 ml), and concd HCl (5 ml) was refluxed for 1h. After cooling the *sulfonic acid* was collected and recrystallized from H_2O. IR: 1219, 1083, 1055, 900, and 873 cm^{-1}. Its *hexylammonium salt* melted at 178.5—179.5 °C. Found: S, 10.52%. Calcd for $C_{14}H_{26}O_3N_2S$: S, 10.60%. The sulfonic acid was converted to its sodium salt, which was then refluxed for 1 h with Ac_2O in pyridine to give the N-*acetyl derivative*. Its p-*toluidinium salt* melted at 232—233 °C. The same *N*-acetylated sulfonic acid was also prepared according to Junghahn's procedure.[48]

(3) 2,6-Dimethylaniline-3-sulfonic Acid: This acid was prepared by two methods.

(a) Sulfonation of 2,6-Dimethylaniline with Oleum: To 25% oleum (32 ml) was added, drop by drop, 2,6-dimethylaniline (5.1 ml) and the mixture was heated for 4 h at 80—90 °C. The reaction mixture was poured on cracked ice and neutralized with $BaCO_3$. After removal of $BaSO_4$ the filtrate was concentrated and treated with concd HCl (5 ml), giving the 3-sulfonic acid in a 30% yield. IR: 1607, 1185 (SO_3^-), 1044 (SO_3^-), 822 (2H), 741, and 694 cm^{-1}.

(b) Chlorosulfonylation of 2,6-Dimethylacetanilide.[49] To ice-cooled $ClSO_3H$ (18.69 g) was added the acetanilide (3.00 g) with stirring. The mixture was stirred at 5 °C for 15 min, then at 25 °C for 1 h, and finally at 40 °C for 10 min, and poured on cracked ice, yielding the *sulfonyl chloride*. IR: 3290 (NH), 1665 (CO), 1505, 1367 (SO_2), 1202, 1168 (SO_2), and 814 (2H) cm^{-1}. The sulfonyl chloride was treated with concd ammonia, giving N-*acetyl-2,6-dimethylbenzene-3-sulfonamide*. Recrystallization from water gave the pure sulfonamide; mp 263—264 °C. IR: 3345 (NH), 3235 (NH), 1638 (CO), 1327 (SO_2), 1120 (SO_2), and 810 (2H) cm^{-1}. The foregoing sulfonyl chloride was heated under reflux with concd HCl for 1 h to give the *3-sulfonic acid*.

(4) 2,6-Dimethylaniline-4-sulfonic Acid: This acid was prepared by "baking" 2,6-dimethylanilinium hydrogensulfate in *o*-dichlorobenzene (180 °C, 6 h).[21,51] No isomeric 3-sulfonic acid was detected. IR: 1618, 1529, 1438, 1222, 1190, 1154, 1111, 1045 (SO_3^-), 883 (1H), and 723 cm^{-1}.

(5) 3,4-Dimethylaniline-6-sulfonic Acid: This acid was prepared in a 76% yield by baking 3,4-dimethylanilinium hydrogensulfate in *o*-dichlorobenzene (171—175 °C, 3 h).[43,51,52] IR: 1603, 1553, 1502, 1258, 1167 (SO_3^-), 1048 (SO_3^-), 880 (1H), 787, 732, and 660 cm^{-1}.

(6) 3,5-Dimethylaniline-2-sulfonic Acid: This compound was prepared by three different methods.[43] *(a) Synthesis via 2,4-Dimethyl-6-nitroaniline*: The procedure was almost the same as that for the synthesis of 2,3-dimethylaniline-4-sulfonic acid. 2,4-Dimethyl-6-nitroacetanilide, mp 171.5—172.8 °C (from H_2O) (lit,[53] 172 °C); 2,4-dimethyl-6-nitroaniline, mp 67—68 °C (from CCl_4) (lit,[54] 67—68 °C); potassium 4,6-dimethyl-2-nitrobenzene-1-sulfonate, IR; 1529 (NO_2), 1377 (NO_2), 1208 (SO_3^-), 1093, 1032 (SO_3^-), 852 (1H), and 773 cm^{-1}; 3,5-dimethylaniline-2-sulfonic acid (from H_2O), IR: 1200 (SO_3^-), 1162, 1123, 1087, 1015 (SO_3^-), 866 (1H), and 683 (SO_3^-) cm^{-1}; p-*toluidinium* N-*acetyl-3,5-dimethylaniline-2-sulfonate* melted at 180.5—181.5 °C (from H_2O), IR; 1662 (CO), 1580 (amide), 1322, 1184 (SO_3^-), 1082, 1017 (SO_3^-), 858 (1H), and 806 (2H). *(b) Sulfonation of 3,5-Dimethylaniline with 100% Sulfuric Acid*: Sulfonation of 3,5-dimethylaniline (2.5 g) with 100% H_2SO_4 (3.0 g) (170 °C, 1 h) gave almost exclusively the *2-sulfonic acid* (TLC, IR).[55] *(c) Sulfonation of 3,5-Dimethylaniline with Chlorosulfuric Acid*: Sulfonation of 3,5-dimethylaniline (2.0 g) with $ClSO_3H$ (3.25 g) in 1,1,2,2-tetrachloroethane (150 °C, 45 min)[56] also gave the *2-sulfonic acid* as the main product, together with the 4-sulfonic and 2,6-(?)-disulfonic acids.

(7) 3,5-Dimethylaniline-4-sulfonic Acid: This acid was prepared by chlorosulfonation of 3,5-dimethylacetanilide.[57] The sulfonyl chloride obtained was moderately soluble in water unlike the normal sulfonyl chlorides and considerably susceptible to hydrolysis. Accordingly, this chloride was immediately converted to the corresponding *sulfonamide*, which melted at 230—231 °C after repeated crystallization from dil alcohol. IR: 3245 (NH), 1660 (C=O), 1593 (NH), 1543, 1319 (SO_2), 1150 (SO_2), 872, 850, and 740 cm^{-1}.

The sulfonyl chloride was subjected to hydrolysis with aqueous K_2CO_3 (100 °C, 1 h), followed by acidification to give the *4-sulfonic acid*. IR: 1476, 1242 (SO_3^-), 1148, 1118, 1080, 1003 (SO_3^-), 860 (1H), and 680 (SO_3^-) cm^{-1}; the butylammonium salt melted at 168.5—170 °C.

*Formation of (2,4,6-Trimethylphenylimido)bis(sulfate) (**44**) by Reaction of (2,4,6-Trimethylphenylamido)sulfate (**43**) with Butylamidosulfuric Acid (**42**).* An intimate mixture of **43** (0.56 g) and **42** (0.30 g) was heated at 120 °C for 4 h in an evacuated tube; the product was dissolved in aqueous KOH. The solution was evaporated to dryness; the residual solid was dissolved in hot water (8 ml) containing two drops of aqueous KOH. This solution was added, with vigorous stirring, to boiling 99.5% ethanol (100 ml). The precipitated crystals were collected, and dried. Its IR spectrum was completely in accord with that of the material isolated from the thermal reaction of **40**.

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7) In the present paper, the term "*transsulfonation*" refers to the transfer of a sulfonate group from one amino nitrogen to another and the term "*rearrangement*" refers to the migration of a sulfonate group from aromatic amino nitrogen to the ring.
8) This compound may be called (4-sulfophenylamido) sulfate or *N*-(4-sulfophenyl)sulfamate in accordance with IUPA Crules.
9) Aniline-*N*,2- and *N*,4-disulfonic acids have been postuated as intermediates in the sulfonation of aniline with sulfuric acid (Ref. 3).
10) The *ortho*: *para* ratios as calculated from the weights of the isolated products ranged from 0.66 : 1 to 0.82 : 1.
11) Product compositions are expressed in mol%.
12) In this paper, aminosulfonic acids are consistently named as the sulfonic acid derivative of the parent aniline in order to facilitate comparison; thus, the names of 2,3-dimethylaniline-4- and 6-sulfonate are used instead of 4-amino-2,3-dimethylbenzenesulfonic acid and 2-amino-3,4-dimethylbenzenesulfonic acid, respectively.
13) The ratios were calculated from the weights of the isolated products on the assumption that all of **8** was the *N*,4-disulfonate and that **11** comes equally both from **9** and from **10**.
14) See also A. Junghahn, *Ber.*, **35**, 3747 (1902).
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17) Immediately after the reaction had started, boiling of the reactant **21** and refluxing of 2,6-dimethylaniline occurred, but rapidly subsided in a few minutes. This observation is consistent with the ready transsulfonation of **21**.
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21) A. Burger and J. F. Siuda, *Arzneim. Forsch.*, **18**, 1220 (1968).
22) British Patent 1027060; *Chem. Abstr.*, **65**, 10905h (1966).
23) Sulfonation of 3,5-dimethylaniline with 100% H_2SO_4 and with $ClSO_3H$ also gave the 2-sulfonic acid almost exclusively (see Experimental section). A similar *ortho*-sulfonation of 3,5-dimethylphenol has been reported (F. Raschig, D. R. P. 283306; *Chem. Zentral.*, **1915 I**, 926).
24) Nitration of 3,5-dimethylaniline with mixed acid has been reported to give the 2- and 4-nitro compounds in yields of 55 and 24%, respectively [B. M. Wepster and P. E. Verkade, *Recl. Trav. Chim. Pays-Bas*, **68**, 88 (1949)]. Further, nitration of 3,5-dimethylanisole with nitric acid in $HClO_4$ has been reported to give *ca.* 1 : 1 mixtures of the 2- and 4-nitro isomers [R. B. Moodie, K. Schofield, and P. N. Thomas, *J. Chem. Soc., Perkin Trans. 2*, **1978**, 318]). In the present rearrangement the reacting species is probably SO_3, which is much larger than the species, NO_2^+, involved in nitration.
25) Paal and Hubalek have reported that (2,4,5-trimethylphenylamido)sulfuric acid as well as its ammonium salt did not rearrange to **39** at the temperatures up to 250 °C [C. Paal and M. Hubalek, *Ber.*, **50**, 1110 (1917).]. To the contrary a German patent claims that **39** is obtained by treatment of 2,4,5-trimethylaniline with an equimolar amount of $ClSO_3H$ in *o*-dichlorobenzene [I. G. Farbenindustrie A-G., DRP 541258; *Chem. Zentral.*, **1931 II**, 2057; *Chem. Abstr.*, **26**, 1942 (1932).]. It has been reported that *N*-bromo-2,4,5-trichloroacetanilide does not undergo the Orton rearrangement [M. J. S. Dewar and J. M. W. Scott, *J. Chem. Soc.*, **1957**, 1445.].
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33) In order to rationalize the alledged intramolecular rearrangement of phenylamidosulfuric acid in an excess of 97% sulfuric acid, Vrba and Allan postulated the deformation of the benzene ring so that the migrating SO_3H group was close to the *para*-position [Z. Vrba and Z. J. Allan, *Collect. Czech. Chem. Commun.*, **33**, 2502 (1968).]. However, this cannot be applied to our case.
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41) Authentic *m*-xylene-5-sulfonic acid was prepared by sulfonation of *m*-xylene with concd H_2SO_4 (200 °C, 3 h) (see Ref. 40). Its *sulfonamide* melted at 133.5—134 °C; IR: 3340 (NH), 3250 (NH), 1328 (SO_2), 1305, 1155 (SO_2), 894, and 860 (1H) cm^{-1}.
42) Authentic *m*-xylene-4-sulfonic acid was prepared by sulfonation of *m*-xylene with an equal volume of concd H_2SO_4 (80—90 °C, 2 h).
43) After the present work had been completed, we became aware of the publications on the syntheses of 2,3-dimethyl-

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