Aromatic isomerizations and related reactions. Part 6¹ Reactions of the tetra- and pentamethylbenzenesulfonic acids and hexamethylbenzene in concentrated sulfuric acid; the mechanism of the *Jacobsen* reaction

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Abstract. The chemical behaviour of the sulfonic acids of pentamethylbenzene (PMB) and the three tetramethylbenzenes (TeMB's) in concentrated aqueous sulfuric acid has been studied quantitatively using ¹H and ¹³C NMR and UV spectroscopy. PMB-sulfonic acid yields (protonated) hexamethylbenzene (HMB) and the 2,3,4,5- and 2,3,4,6-TeMB-1-sulfonic acids in an initial ratio of 9/1/8 up to a substrate conversion of 36%; the ratio of HMB to the TeMB-1-sulfonic acids remains 1/1 and the only subsequent reaction is the relatively slow conversion of the 2,3,4,6- into the 2,3,4,5-TeMB-1-sulfonic acid sulfuric acid. 2,3,5,6-TeMB-1-sulfonic acid yields, as initial products, 2,3,5- and 2,4,5-trimethylbenzene(TrMB)-

-1-sulfonic acid together with PMB-1-sulfonic acid in a ratio of ca. 1/3/4. The subsequent products are the 2,3,4,6- and 2,3,4,5-TeMB-1-sulfonic acids, of which the former slowly isomerizes to the latter, together with some HMB.

2,3,4,6-TeMB-1-sulfonic acid yields the stable 2,3,4,5-isomer. It is proposed that the conversion proceeds via *inter*-molecular *trans*-methylations involving 1,3,5-TrMB and PMB as intermediates, the concentrations of which, however, are below the limits of NMR detection.

Based on (i) the desulfonation-sulfonation equilibrium data of the TrMB-, TeMB- and PMB-sulfonic acids, (ii) the strong rate decrease for the conversion of both 2,3,4,6- and 2,3,5,6-TeMB-1-sulfonic acid in 98.4% H₂SO₄ in the presence of added cyclohexane and (iii) the very strong electron-withdrawing and *meta*-directing effect of the SO₃⁻/SO₃H substituent, it is proposed that all the conversions proceed *inter*-molecularly, that the *trans*-methylating reagent is the polymethylbenzene (and not the corresponding sulfonate) and that the substrate undergoing methylation is most likely to be once again the polymethylbenzene rather than its sulfonate ion.

Introduction

As a continuation of our studies on the sulfuric acid sulfonation of poly-tert-butyl-2, polyisopropyl-3 and polyethyl-benzenes⁴ we have carried out an extensive study of the behaviour of polymethylbenzenes and their sulfonic acids in concentrated sulfuric acid which draw our attention to the Jacobsen reaction⁵. The first observations of this reaction, which deals with the migration of alkyl groups in polyalkylbenzenes and of halogens in halogenated alkylbenzenes or polyhalogenobenzenes during the process of sulfonation with concentrated sulfuric acid or weak oleum, were made by Herzog⁶ and Jacobsen⁷. Jacobsen reported that reaction of 1,2,4,5-tetramethylbenzene (1,2,4,5-TeMB) with concentrated sulfuric acid at room temperature yields, in addition to some tar and SO₂, 2,3,4,5-tetramethylbenzene-1-sulfonic acid, 2,3,5- and 2,3,6-trimethylbenzene-1-sulfonic acid and hexamethylbenzene (HMB)^{7a}. In the polymethylbenzene series, only 1,2,3,5- and 1,2,4,5-tetramethylbenzene and pentamethylbenzene (PMB) undergo the Jacobsen reaction⁸. Most investigators have proposed ionic mechanisms⁹, but it remained an intriguing question as to whether it is the arenesulfonic acid or the corresponding hydrocarbon which, by intra- and/or inter-molecular alkyl migration, leads to the

observed isomerization and/or disproportionation products¹¹. The arguments which led most investigators^{5,7,13,14}, with the exception of $Kilpatrick^{15}$, to express a preference for the rearrangement of the arenesulfonic acids are (i) the formation from 1,2,4,5-TeMB of a mixture of 2,3,5- and 2,3,6- instead of 2,4,5-trimethylbenzenesulfonic acid (the original argument of Jacobsen^{7a}), (ii) 2,3,5,6-tetramethylbenzenesulfonic acid in contact with phosphorus pentoxide⁸ or polyphosphoric acid¹³ rearranges into the 2,3,4,5-isomer, whereas 1,2,4,5-TeMB does not, and (iii) the Jacobsen-type rearrangements are not observed on treatment of the polymethylbenzenes with chlorosulfuric acid¹⁴. Since the last two arguments are somewhat weak (see Discussion, last section), we were prompted to test the first, *i.e.* to carry out an accurate structure determination of the trimethylbenzensulfonic acid(s) formed from the TeMB's in concentrated sulfuric acid. Given that objective, the UV spectroscopic method applied by Kilpatrick¹⁵ was considered to be inadequate and we therefore also used the more powerful ¹H and ¹³C NMR techniques.

PMB^{7b,16} and pentaethylbenzene¹⁷ in concentrated sulfuric acid disproportionate and, upon subsequent flash desulfonation, yield a mixture of the corresponding 1,2,3,4-tetraand hexa-alkylbenzene. HMB in concentrated sulfuric acid, upon 365-nm irradiation¹⁸ or in weak oleum¹⁹, yields a radical cation as established by ESR. HMB in 98–100% sulfuric acid is protonated instantaneously; the resulting hexamethylbenzenonium ion is unstable^{15,20} and slowly yields the hexamethylbenzyl (= 4-methylene-1,1,2,3,5,6-hexamethylcyclohexa-2,5-diene) radical cation^{20d}. This conclusion differed from earlier suggestions that the eventual product of HMB in 100% sulfuric acid would be the pentamethylbenzyl carbenium ion^{20b} or 1,3,5-trimethylbenzenesulfonic acid^{20c}.

Koptyug²¹ reported that HMB, upon dissolution in fluorosulfuric acid containing 35% SO₃ at -70 to -40°C, yields the 1,2,3,4,5,6-hexamethylbenzenonium-1-(pyro)sulfonic acid ion. At -25°C, this ion rearranges into the sulfate of 1-hydroxy-1,2,3,4,5,6-hexamethylbenzenonium ion which species, upon addition of 35% sulfuric acid to neutralize the "free" SO₃ in the solution, rearranges into a mixture of 1-hydroxy-2,2,3,4,5,6- and 1-hydroxy-2,3,4,4,5,6hexamethylbenzenomium ion. The interconversion of the former into the latter ion proceeds via the corresponding 1-hydroxy-2,3,3,4,5,6-isomer²².

We have recently shown that the three tetramethylbenzenedisulfonic acids in concentrated aqueous sulfuric acid are unstable²³. As a result of overcrowding²⁴, the three isomers all undergo enhanced protiodesulfonation, the rate order of which decreases in the order 1,2->1,3->1,4-disulfonic acid; the 1,2-isomer, in addition, undergoes intramolecular disulfonic anhydride formation²³.

Results

Hexamethylbenzene (HMB)

The solubilities of the polymethylbenzenes in concentrated aqueous sulfuric acid are very small and decrease strongly when the number of methyl groups are increased²⁵. The homogeneous solution of the relatively strongly basic²⁶ HMB (0.20-0.33 M) in 98.4% H₂SO₄ at 25°C thus contains predominantly the hexamethylbenzenonium ion (1)^{20d} which, due to rapid proton exchange, exhibits, in the ¹H NMR, a singlet absorption at 2.78 ppm (in accordance with the value of $2.35^{20d} + 0.42^{27}$ ppm) and, in the ¹³C NMR, two broadened absorptions at 20.9 (Me's) and 153.3 ppm (ring carbons). The ¹H NMR sharp singlet starts to broaden after 3 h and collapses after 7 h to be eventually replaced by a very broad, undefined absorption at between 1.8 and 4.4 ppm.

The solution of HMB in 98.4% H₂SO₄ is initially yellow and exhibits UV absorption bands at 393 and 279 nm, attributed to the hexamethylbenzenonium ion (1). After 1.9 h, the solution turned red and a new UV band became apparent at 336 nm.

Pentamethylbenzenesulfonic acid

Upon dissolution in 98.4% H_2SO_4 , PMB-sulfonic acid (0.20 M) undergoes, in part, methyl transfer with formation of protonated HMB and 2,3,4,5- and 2,3,4,6-TeMB-1-sulfonic acid, followed by a relatively slow isomerization of the latter, into the former sulfonic acid (Table I)²⁸. Fig. 1A illustrates that part of the 2,3,4,5-TeMB-1-sulfonic acid is formed as a primary product, in addition to the 2,3,4,6isomer, in a ratio of *ca*. 1/8. The disproportionation of PMB-sulfonic acid is impeded by the presence of an equimolar amount of HMB, but not by the presence of 2,3,5,6-TeMB-1-sulfonic acid (Fig. 1B). Again, both the 2,3,4,5- and the 2,3,4,6-TeMB-1-sulfonic acids appear to be primary products formed in a ratio of *ca*. 1/5. Upon dissolving PMB-sulfonic acid (0.20 M) and 1,2,4-TrMB (0.20 M) in 98.4% H_2SO_4 at 25°C, apart from the partial disproportionation of the PMB-sulfonic acid, only sulfonation of 1,2,4-TrMB occurs with formation of 2,3,5- and 2,4,5-TrMB-1-sulfonic acid in a $(25 \pm 3)/(75 \pm 3)$ ratio; methylation of the 1,2,4-TrMB or the TrMB-1-sulfonic acid does not occur.

2,3,4,5-Tetramethylbenzene-1-sulfonic acid

A solution of this sulfonic acid (0.20 M) in 98.4% H_2SO_4 appeared to be completely stable over a period of at least 21 days. No reaction was observed upon addition of an equimolar amount of HMB (Table II).

2,3,4,6-Tetramethylbenzene-1-sulfonic acid

2,3,4,6-TeMB-1-sulfonic acid in concentrated aqueous sulfuric acid isomerizes to the 2,3,4,5-TeMB-1-sulfonic acid. The conversions have an induction period (Table III). It is remarkable that the rate of conversion – in contrast to the induction period – is independent of the sulfuric acid concentration over the range of 93-98% H₂SO₄ studied (cf. Fig. 2).

The ¹H NMR spectra for 98.4% H₂SO₄ show that, with increasing reaction time, there is both a broadening of the methyl signals and a substantial decrease in the ratio of the aromatic to methyl hydrogens. The latter observation could indicate a partial sulfonation of the substrate and/or of the 2,4,6-TrMB-1-sulfonic acid intermediate (see Discussion) into the 1,3-disulfonic acids. However, the observations in 98.4% H₂SO₄, that 2,4,5,6-TeMB-1,3-disulfonic acid undergoes desulfonation and subsequent isomerization of the resulting 2,3,4,6- into 2,3,4,5-TeMB-1-sulfonic acid (Table II, entries 12 and 13) and that the yield of 2,4,6-TrMeB-1,3--disulfonic acid is only very small, render the first explanation untenable and the second insufficient. Rather, the abnormal ¹H NMR phenomena are thought to be related to the occurrence of radical cations resulting from, for example, $C_6Me_6H^{+20d}$, which could initiate fast electron exchange between species in the reaction mixture. In fact, the ¹³C NMR spectra of the reaction mixtures of 2,3,4,6--TeMB-1-sulfonic acid in 98.4% H₂SO₄ showed no other significant absorption signals than those of 2,3,4,6- and 2,3,4,5-TeMB-1-sulfonic acid³⁰.

Reaction of equimolar amounts of 2,3,4,6-TeMB-1-sulfonic acid and HMB leads, within 0.6 h, to 61% PMB-sulfonic acid and 21% $C_6Me_6H^+$ (Table II, entry 8).

acid and 21% $C_6Me_6H^+$ (Table II, entry 8). An extensive UV study was carried out in which the 2,3,4,6-TeMB-1-sulfonic acid was generated at 25°C in the sulfuric acid solution by desulfonation of 2,4,5,6-TeMB--1,3-disulfonic acid (0.20-0.80 mM)²³ which was used as starting substrate. With a substrate molarity of 8.0×10^{-4} in 98.5% H_2SO_4 , the first order desulfonation reaction is to greater than 95% complete after 80 h²³, while no isomerization of the 2,3,4,6- into the 2,3,4,5-TeMB-1-sulfonic acid was observed over a period of 55 days. At the higher ¹H NMR substrate concentrations (0.2–0.3 M), the isomerization is complete within ca. 60 h (Fig. 2). A similar concentration effect is observed in the UV studies in 95.9% H_2SO_4 , for which the desulfonation half-life is 8.3 h²³; on using 2,4,5,6-TeMB-1,3-disulfonic acid molarities of (7.0 and 5.0) \times 10⁻⁴, the isomerization appears to be complete after 170 h, whereas, for a molarity of 2.0×10^{-4} , it required ca. 240 h. For 2.0×10^{-4} molar solutions of 2,4,5,6-TeMB--1,3-disulfonic acid in 92.9, 90.4 and 86.9% H₂SO₄ (for which sulfuric acid concentrations the desulfonation halflives are 5.8, 4.7 and 3.9 h, respectively²³), the complete conversion into the 2,3,4,5-TeMB-1-sulfonic acid takes ca. 170, 65 and 43 h, respectively.

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Substrate ^a	Addendium	H ₂ SO ₄	Reaction				Composition ($\%, \pm 2$)a		
		(%)	time (h)	PMB-1-S	2,3,5,6-TeMB-1-S	2,3,4,6-TeMB-1-S	2,3,4,5-TeMB-1-S	C ₆ Me ₆ H ⁺	2,3,5-TrMB-1-S	2,4,5-TrMB-1-S
PMB-1-S	I	98.4	0.60	64		15	3	18		
(0.20 M)			0.85	63		14	4	18		
			2.1	65		11	7	17		
_			4.9	49		×	10	18		
_			6.4	4		4	14	18		
			18.8			<2	18			
							01			
(0.12 M)	I	93.1	<0.1	00 \$			2	λ		
(111 71.0)				40		- N	8	97		
PMB-1-S	2,3,5,6-TeMB-1-S	98.4	0.18	44	50	3		ę		
(0.20 M)	(0.20 M)		0.60	39	51	4	7	4		
			1.6	32	44	13	4	Ś	≤0.5	1.5
			4.0	е С б	18	27	13 76	v, v		
PMB-1-S	HMB (0.25 M)	98.4	1.7	95		5	2	, Q	•	5
(0.25 M)			4.5	2		V	2	2		
			19			V -	2			
PMB-I-S	1,2,4-TrMB	98.4	1.0	35		6 \	,		13	35
(W) 07:0)	(111 07.0)		1.0	¢Ç		0 7 V	00	ת	12	39
							,			

^a S stands for SO₃H. ^b The initially homogeneous solution turned slightly turbid after 1 h.

Table I Reaction of PMB-1-sulfonic acid in concentrated sulfuric acid at 25°C.

	C ₆ Me ₆ H ⁺		50 50 50 50							50 21 20
2) ^a	2,4,5,6- -TeMB-1,3-S ₂									
position (%, ±	PMB-S							-		61
Com	2,3,4,5- -TeMB-1-S	> 98 > 98	50 50 50	[∧] 4 0 8 8 9	90 2 2 2 2 9	- c s s s 4	07 88 99 99	> 98	\$\$\$\$%\$?~~	6 9.5 12
	2,3,4,6- -TeMB-1-S			99 7 2 4 7 6 9 7 2 2 4 7 6 9	99 9 A	99 98 75 52	30 16 0.5		99 95 95 95 95 95 95 95 95 95 95 95 95 9	50 18 11.5 6
	keaction time (h)	1.0 500	0.5 3.8 7.0	0.8 7.3 29.0 76.5	1.0 6.3 125	0.6 0.8 1.0 1.6	1.8 2.0 3.4 3.4	0.65	0.9 3.1 7.5 28.0 47	0 6.6 6.6 6.6
Ē	l emp. (°C)	25	25	25	25	60		100	25	25
	н ₂ 004 (%)	98.4	98.4	98.4	98.4	98.4		98.4	93.1	98.4
	Addendum]	HMB (0.20 M)	I	I	I		I	1	НМВ (0.25 м)
	Substrate ^a	2,3,4,5-TeMB-1-S (0.20 M)	2,3,4,5-TeMB-1-S (0.20 M)	1,2,3,5-TeMB (0.31 M)	2,3,4,6-TeMB-1-S (0.20 M)	2,3,4,6-TeMB-1-S (0.20 M)		2,3,4,6-TeMB-1-S (0.20 M)	2,3,4,6-TeMB-1-S (0.20 M)	2,3,4,6-TeMB-1-S (0.25 M)
	Entry	-	7	ñ	4	Ś		9	٢	œ

Table II Behaviour of the suffonic acids of 1,2,3,4- and 1,2,3,5-TeMB in suffuric acid.

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	2,3,4,6- -TeMB-1-S	> 98	91	67	53	12	85
Reaction	time (h)	2.8	7.9	22.4	28.1	44.4	18.6
Temn	(°C)	25					25
US H	(%)	93.1					96.1
	Addendum	cyclohexane			→	(0.008 M)	cvclohexane
	Substrate ^a	2,3,4,6-TeMB-1-S					2.3.4.6-TeMB-1-S
	Entry	6					10

Table II (cont.)

																					_
C ₆ Me ₆ H⁺																					
2,4,5,6- -TeMB-1,3-S ₂													95	81	76 35	16			49	64 / C (/	7 4
PMB-S																					
2,3,4,5- -TeMB-1-S	<2	6	33	88	15	22	34 66		ę	9	Ξ	 86 < 86 <				<2	38	< <	51	200	
2,3,4,6- -TeMB-1-S	> 98	91	67	12	85	78	34 66 34	100	97	94	89	4 V 4 V	\$	19	24	48	59				
time (h)	2.8	6.7	22.4 28 1	44.4	18.6	26.5	31.6 48.8	24.0	50.6	55.2	72.9	071	0.5	4.0	6.0 22.3	45.5	70	120	0,	C.I 8,91	• • •
(°C)	25				25			25					25						25		
(%)	93.1				96.1			98.4					98.4	_					98.4	_	
	cyclohexane (0 011 M) ^b			(0.008 M)	cyclohexane		(0.01 M)	cyclohexane	(0.04 M)°		(0.01 M)	°(M 100.0>)	1						2,3,4,5-TeMB-S	(0.07 M)	
20031410	2,3,4,6-TeMB-1-S (0.16 M)				2,3,4,6-TeMB-1-S	(INI 7C.U)		2,3,4,6-TeMB-1-S	(0.32 M)				2,4,5,6-TeMB-1,3-S ₂	(0.14 M)					2,4,5,6-TeMB-1,3-S ₂	(W 6/0.0)	
	6				10			=					12						13		_

^a S stands for SO₃H. ^b The concentration of cyclohexane *dissolved* in the sulfuric acid solution was determined by ¹H NMR analysis; the limit of detection is 0.0005 M. In addition to the dissolved cyclohexane, there is *ca*. 0.8 ml/3 ml sulfuric acid as supernatant, floating on top of the sulfuric acid solution.

Composition $(\%, \pm 2)^{a}$



Fig. 1. Reaction of PMB-sulfonic acid (0.20 M) in 98.4% H_2SO_4 at 25°C in the absence (A) and the presence (B) of 2,3,5,6-TeMB-1-sulfonic acid (0.02 M). + 2,3,5,6-TeMB-1-S; \bigcirc PMB-S; \bigcirc 2,3,4,6-TeMB-1-S; $\times C_6Me_6H^+$; $\diamondsuit 2,3,4,5$ -TeMB-1-S; $\square 2,3,4-+2,4,5$ -TrMB-1-S.

Substrate	Addendum	H ₂ SO ₄ (%)	Temp. (°C)	Induction period (h)
2,3,4,6-TeMB-1-S (0.31 M)		98.4	25	4 <u>+</u> 1
(0.20 M)		98.4	25	6 ± 2
$(0.8 \times 10^{-3} \text{ M})^{a}$		98.4	25	> 1300
(0.20 M)		98.4	60	0.5
(0.16 M)		93.1	25	1.0
2,3,5,6-TeMB-1-S (0.20 M)		98.4	25	6 + 1
$(0.20 \times 10^{-3} \text{ M})$		98.4	25	35 + 6
$(0.10 \times 10^{-3} \text{ M})$		98.4	25	95 + 15
(0.20 M)		98.4	60	0.1
(0.20 M)		95.0	25	1.0
(0.20 M)		93.1	25	0.6
(0.20 M)	2,3,4,5-TeMB-1-S (0.02 M)	98.4	25	6 + 1
(0.20 M)	PMB-S (0.20 M)	98.4	25	0.9
(0.25 M)	HMB (0.25 M)	98.4	25	< 0.05
(0.20 M)	A ^b	98.4	25	< 0.05
(0.20 M)	Вь	98.4	25	< 0.05
(0.20 M)	C ^b	98.4	25	< 0.05
(0.20 M)	<i>t</i> -BuOH (0.20 M) ²⁹	98.4	25	53
(0.20 M)	$Ac_2O(0.20 M)$	98.4	25	6
(0.20 M)	1,2,4-TrMB (0.05 M)	98.4	25	6
(0.20 M)	O_2 , sat.	98.4	25	6
(0.20 M)	SO_2 , sat.	98.4	25	6
(0.20 M)	$K_2 \tilde{S}_2 O_8 (0.02 \text{ M})^{10}$	98.4	25	6

Table III Induction periods of the reaction of 2,3,4,6- and 2,3,5,6-TeMB-1-sulfonic acids in sulfuric acid.

^a The 2,3,4,6-TeMB-1-sulfonic acid was produced *in situ* by desulfonation of 2,4,5,6-TeMB-1,3-disulfonic acid. ^b The substrate solution was added to an equal volume of (A) a 46 h matured (thus fully converted) solution of 2,3,5,6-TeMB-1-sulfonic acid (0.15 M) in 98.4% H_2SO_4 , (B) a 5.5 day matured (thus fully converted) solution of 2,3,4,6-TeMB-1-sulfonic acid (0.10 M) in 98.4% H_2SO_4 and (C) a solution of 2,3,4,5-TeMB-1-sulfonic acid (0.10 M) in 98.4% H_2SO_4 made up 24 h prior to the addition of 2,3,5,6-TeMB-1-sulfonic acid.

2,3,5,6-Tetramethylbenzene-1-sulfonic acid

2,3,5,6-TeMB-1-sulfonic acid in concentrated sulfuric acid undergoes a reaction which is characterized by an induction period (Fig. 3 and Table III). The initial products are the 2,4,5-³¹ and 2,3,5-TrMB-1-sulfonic acids together with PMB-sulfonic acid (Table IV), indicating disproportionation. The isomer distributions of the TrMB-sulfonic acids are similar to those observed in the direct sulfonation of 1,2,4-TrMB (vide infra). The subsequent products are 2,3,4,5- and 2,3,4,6-TeMB-1-sulfonic acid of which the latter eventually fully isomerizes to the former. The dependence of the product composition upon the reaction time indicates that part of the 2,3,4,5-TeMB-1-sulfonic acid is formed directly from the PMB-sulfonic acid.

It is notable that both the time required to effect the various conversions after the induction period³³ and the final product composition are independent of the concentration of the sulfuric acid employed (93.1-98.4% H₂SO₄). The addition of PMB-sulfonic acid speeds up the conversion of 2,3,5,6-TeMB-1-sulfonic acid due to the disproportionation of PMB-sulfonic acid into 2,3,4,5-+2,3,4,6-TeMB-1-sulfonic acid and $C_6Me_6H^+$ (cf. Figs. 1B and 3). The induction period is now reduced from ca. 6 to 1.0 h (Table III) and the quantity of the TrMB-sulfonic acids formed is strongly reduced, illustrating that the more effective methyl transferring agents are initially PMB-sulfonic acid and later $C_6Me_6H^+$ (or even $C_6Me_7^+$, see Discussion). The strong decrease in the induction period and the increase in the rate of conversion of the 2,3,5,6-TeMB-1-sulfonic acid, upon addition of increasing amounts of HMB, is very apparent (Fig. 4).

The ¹³C NMR spectra of solutions of 2,3,5,6-TeMB-1-sulfonic acid (0.33 M) in 98.4% H_2SO_4 in the absence and in the presence of HMB (0.33 M) qualitatively show the presence of the entities assigned and analyzed by ¹H NMR with the exception of HMB in the reaction of 2,3,5,6-TeMB- -1-sulfonic acid proper, illustrating that the ratio of $C_6Me_6H^+/PMB$ -sulfonic acid is $\ll 1$.

From an additional UV study on 2,3,5,6-TeMB-1-sulfonic acid in 98.4% H_2SO_4 , it appeared that, for a substrate concentration of 2.0×10^{-4} M, the induction period is *ca*. 30 h and the subsequent substrate conversion requires *ca*. 100 h, whereas for a substrate concentration of 1.0×10^{-4} M, the induction period is *ca*. 100 h and the substrate conversion in the subsequent 70 h is only 30%. For comparison, using a substrate concentration of 0.20 M (*cf.* Fig. 3 and Table IV), the induction period is *ca*. 6 h and the subsequent time required to effect the complete substrate conversion *ca*. 23 h.

1,2,4-Trimethylbenzene (1,2,4-TrMB)

Reaction of 1,2,4-TrMB (0.20 M) in 93.1, 95.0 and 98.4% H_2SO_4 at 25°C leads to sulfonation with formation of 2,3,5and 2,4,5-TrMB-1-sulfonic acid in а ratio of $(19 \pm 2)/(81 \pm 2)$, $(25 \pm 2)/(75 \pm 2)$ and $(23 \pm 2)/(77 \pm 2)$, respectively (cf.³⁴). Reaction of 1,2,4-TrMB (0.08 M) in 98.4% H₂SO₄, in the presence of 2,3,4,5-TeMB-1-sulfonic acid (0.16 M) at 25°C, leads only to sulfonation of 1,2,4-TrMB, the resulting sulfonic acid isomer ratio being $(27 \pm 4)/(73 \pm 4)$. Dissolution of a mixture of 1,2,4-TrMB (0.16 M) and HMB (0.20 M) in 98.4% H₂SO₄ at 25°C leads predominantly to sulfonation with formation of 2,3,5- and 2,4,5-TrMB-1-sulfonic acid in a 26/74 ratio. The presence of a small amount ($\leq 10\%$) of PMB-1-sulfonic acid, however, after a reaction time of 0.2 h, is evidence of some trans--methylation.

Studies on the $ArSO_3H \rightleftharpoons ArH$ equilibria

In order to obtain information on the reactive species in the *Jacobsen* reactions, the amount of desulfonated product was



Fig. 2. Conversion of 2,3,4,6-TeMB-1-sulfonic acid in sulfuric acid at $25^{\circ}C$. \odot and \diamond : 93.1% H₂SO₄, 0.20 M; \odot and \diamond : 98.4% H₂SO₄, 0.31 M.

determined for the various polymethylbenzenemonosulfonic acids by extraction of the hydrocarbon with cyclohexane. The results, shown in Table V, illustrate that the equilibrium amount of hydrocarbon increases with decreasing sulfuric acid concentration and increases with increasing steric hindrance between the sulfo group and the adjacent methyls in the polymethylbenzenesulfonic acid, as well as with the total number of methyl groups in the ring.

Using the sulfuric acid solutions remaining after the removal of 50% of the cyclohexane extract containing the polymethylbenzene and which thus contained some cyclohexane extract which was in part dissolved, but mainly present as supernatant, the progress of the *Jacobsen* reactions was followed by ¹H NMR (*cf.* Table II, entries 9–11 and Table IV, entries 11–13). For 98.4% H₂SO₄, both the induction period and the subsequent time required to effect the conversion of the substrate are substantially greater in the presence than in the absence of cyclohexane; for the two lower sulfuric acid concentrations, the differences in the induction periods and the time required to effect the substrate conversion for the experiments with and without

cyclohexane are both relatively small. Considering that the solubility of cyclohexane is greater in 98.4 than in 95.1 and 93.1% H₂SO₄ (cf. Tables II and IV), and that the content of a given polymethylbenzenesulfonic acid being present as polymethylbenzene decreases substantially upon increasing the sulfuric acid concentration from 93.1 to 98.4% H₂SO₄ (cf. Table V), it is thought that the transport of the aromatic hydrocarbon(s) from the sulfuric acid phase to the supernatant cyclohexane is more rapid in 98.4% H₂SO₄ than in the two lower sulfuric acid concentrations and this in turn is thought to lead to a decrease in the rates of the reactions during both the induction period and the subsequent substrate conversion period, as is in fact observed.

Sulfur dioxide formation

In all the reaction mixtures of the substrates which underwent a *Jacobsen* type of rearrangement, the smell of sulfur dioxide was clearly noticeable.

There was no ¹H NMR evidence to indicate the presence of methyl hydrogen sulfate (δ_{Me} 4.2 ppm) in any of the reaction mixtures, thus excluding *trans*-methylation to the HSO₄⁻ ion.

Γ

sulfi	ıric acid.				
	Со	mposition (%)		
B-	2,4,5- -TrMB- -1-S	2,3,4,5- -TeMB- -1-S	2,3,4,6- -TeMB- -1-S	PMB – S	нм

Table IV Behaviour of 2,3,5,6-TeMB-1-sulfonic acid (0.20 M)^a in concentrated

l

Entry	Addendum	H ₂ SO ₄ (%)	Temp. (°C)	Reaction time (h)	2,3,5,6- -TeMB- -1-S	2,3,5- -TrMB- -1-S	2,4,5- -TrMB- -1-S	2,3,4,5- -TeMB- -1-S	2,3,4,6- -TeMB- -1-S	PMB-S	НМВҌ
1	-	93.1ª	25	0.6 2.4 4.6 6.8 10.7 14.8 16.4 22.5 26.8 34.7 46.3	100 91 81 63 30 5 3	1 1 3 4 4 5 5 5 5 5 5	3 6 10 16 19 18 20 19 19 19 18	1 3 6 15 28 27 41 46 52 54	2 5 15 21 20 9 6 -		4 7 13 20 23 24 25 24 25 24 23
2	_	95.0ª	25	0.9 2.5 4.7 6.9 10.8 14.9 20.6 24.6 30.7 39.2 46.8	100 95 87 74 51 13 3 -	0.5 1 2 4 5 5 5 6 5	2 5 9 12 17 18 20 19 18 18	1 2 9 20 34 37 47 52 54	2 8 24 17 11 5 -		2 6 11 6 22 23 25 24 24 23
3	_	98.4ª	25	6.0 11.8 16.0 18.1 22.8 29.5 35.2 42.0 54.5 188	100 82 60 44 14 -	2 3 4 4 4 4 4 4	7 13 15 20 20 19 20 20 20 19	5 10 20 43 50 51 53 55	4 9 18 9 4		9 5 9 24 23 25 23 22
4	_	98.4	60	0.07 0.15 0.30 0.47 0.63 0.80 1.00 1.17	100 92 77 40 10 2 -	0.8 2 5 7 7 6 6	3.2 9 17 22 23 22 22	1 12 21 32 41 41	5 11 6 2 -	1 2 2 3 2 2	4 11 29 30 29 28
5	-	98.4	100	0.16	_	5	25	40	-	3	1 0
6	PMB-S (0.20 M)	98.4	25	see Table I			1				
7	HMB (0.022 M)	98.4	25	0.7 2.6 4.1 5.9 7.2	87 70 52 36 30		 3 7 8 9	3 8 12 14	7 15 20 22	9 14 14 20 21	4 3 4 4 4
8	HMB (0.050 M)	98.4	25	0.4 1.4 4.2 6.0 6.9	62 50 12 5 4		 5 6 5	4 13 19 20	3 9 25 26 26	30 33 38 37 38	5 4 7 7 7
9	HMB (0.12 M)	98.4	25	0.2 1.1 2.3	40 16 4			5 14	14 20	43 52 48	17 13 14
10	HMB (0.20 M)	98.4	25	0.2 0.6 1.5 4,1 7.1	29 20 6 1 -			1 5 21 17	5 24 22 10	47 54 44 33 47	24 20 21 23 26

Table IV	(cont.)
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							Co	mposition ((%)		
Entry	Addendum	H ₂ SO ₄ (%)	Temp. (°C)	Reaction time (h)	2,3,5,6- -TeMB- -1-S	2,3,5- -TrMB- -1-S	2,4,5- -TrMB- -1-S	2,3,4,5- -TeMB- -1-S	2,3,4,6- -TeMB- -1-S	PMB-S	нмвь
11°	cH ^c (0.02 M) ^d ↓ (0.01 M)	93.1	25	2.7 5.7 7.3 21.7 46.9	78 46 32 -	2 4 4 5 5	9 16 16 19 20	10 19 48 50	4 10 5 -	11 20 19 23 25	
12 ^r	cH ^c (0.02 M) ^d (0.01 M)	96.1	25	3.1 8.0 17.5 23.9 28.1 46.2	88 66 30 4 3 -	2 4 5 5	6 10 17 20 20 20 20	6 17 31 41 50	3 12 17 10 -	6 13 20 24 24 25	
13 ^r	cH ^c (0.04 M) ^d ↓ (0.01 M) ↓ (<0.01 M)	98.4	25	23.0 28.6 47.0 52.5 64.3 69.1 87.6	100 83 65 49 31 13 -	2 3 4 5 5	7 12 15 18 19 19	5 9 15 26 52	4 9 13 -	8 15 19 23 24 24	

^a Essentially the same results are obtained on starting with 1,2,4,5-TeMB (0.37 M) which very rapidly dissolves by sulfonation. ^b For the first 15 h after the induction period, the amount of $C_6Me_6H^+$, as estimated from its specific ¹H NMR methyl absorption at 2.78 ppm, is 15% of the amount of PMB-sulfonic acid. ^c cH stands for cyclohexane. ^d The concentration of the *dissolved* cyclohexane was estimated by ¹H NMR. ^{e,f} |2,3,5,6-TeMB-1-S| = 0.16 and 0.32 M, respectively.





Fig. 4. Reaction of 2,3,5,6-TeMB-1-sulfonic acid (0.20 M) in 98.4% H_2SO_4 at 25°C in the absence (A) and in the presence of HMB (B: 0.022 M; C: 0.050 M; D: 0.20 M). + 2,3,5,6-TeMB-1-S; \bigcirc PMB-S; \bigcirc 2,3,4,6-TeMB-1-S; $\times C_6Me_6H^+$; \diamondsuit 2,3,4,5-TeMB-1-S; \square 2,3,4-+2,4,5-TrMB-1-S.

Table V Desulfonation equilibria of polymethylbenzenesulfonic acids in concentrated sulfuric acid at $25^{\circ}C$.

Banzanasulfonio	100 · [ArH	H]/([ArH] + [A	rSO ₃ H])
acid subst.	93.1% H ₂ SO ₄	96.1% H₂SO₄	98.4% H ₂ SO ₄
2,4,5-Me ₃ 2,4,6-Me ₃		≪0.01 0.01ª	≪0.01
2,3,4,5-Me ₄	1	≪0.01	≪0.01
2,3,4,6-Me ₄		1.3	0.2
2,3,5,6-Me ₄	10.0	4.4	0.6 ^ь
Me ₅		26.8	5.6

^a Calculated from extrapolated sulfonation and desulfonation rate coefficients at $12^{\circ}C^{35}$. ^b Upon addition of the cyclohexane 1.8 and 4.0 h after the initial 5 min of shaking of the sulfonate and the sulfuric acid, essentially the same result was obtained.

Discussion

General considerations

The reactions of 1,2,4-TrMB, the three TeMB's, PMB and their monosulfonic acids have been studied in 93.1–98.4% H_2SO_4 . In this sulfuric acid region, the aromatic hydrocarbons are sulfonated extremely rapidly to their monosulfonic acids³⁶; the subsequent, further sulfonation to the disulfonic acids (of 1,2,4-TrMB and the three TeMB's) is extremely slow³⁷. In fact, in the acid region 93.1–98.4% H_2SO_4 , the disulfonic acids of the three TeMB's undergo irreversible desulfonation with formation of the monosulfonic acids²³. This then leaves the polymethylbenzenes and their monosulfonic acids – of which the former species are present only in very small amounts – to be considered as the entities engaged in the *Jacobsen* reactions.

With a sulfuric acid concentration ranging from 90-98% H_2SO_4 , the higher polymethylbenzenes will be protonated in part^{15,20d,38}. The corresponding sulfonic acids will be present predominantly in the unprotonated ArSO₃H form and, for the remaining part, as the ArSO₃⁻ anion³⁹.

In the sulfuric acid concentrations used in the present study, PMB-, 2,4,5-TrMB-, 2,4,6-TrMB- and the three TeMB--sulfonic acids are in equilibrium with very small amounts of the corresponding hydrocarbon, the relative amounts of which increase with decreasing sulfuric acid concentration and, as far as the structure of the arenesulfonic acid is concerned, in the order 2,4,5-TrMB- \approx 2,3,4,5-TeMB- \ll 2,4,6-TrMB- < 2,3,4,6-TeMB- < 2,3,5,6-TeMB- < PMB--1-sulfonic acid (cf. Table V).

The trans-methylation (i.e. protiodemethylation) reactivity of the reagent will be very much greater for a given hydrocarbon than for the corresponding sulfonic acid, due to the strong electron withdrawing effect of the sulfo substituent (which is both inductive and mesomeric in nature) 40 , rendering the degree of protonation of an aromatic carbon site very much higher (at least by a factor of 10⁵) for the arene than its sulfonic acid and even its sulfonate ion, which will be more reactive than the sulfonic acid in view of its negative charge⁴¹. The trans-methylation by the polymethylbenzene will proceed via initial protonation of the arene and subsequent methyl transfer to the nucleophilic substrate, followed by deprotonation of the resulting methylation σ -complex (steps [1]-[3]), where Ar stands for $C_6Me_nH_{4-n}$, R for H and Me, and HB for H_2SO_4 . The strong inhibition of the Jacobsen reactions of 2,3,4,6- and 2,3,5,6-TeMB-1-sulfonic acid in 98% H_2SO_4 , due to the presence of a small amount of added cyclohexane (see

Results, section Studies on the $ArSO_3H \rightleftharpoons ArH$ equilibria), substantiates the reasoning that it is the aromatic hydrocarbon and not the corresponding sulfonic acid or sulfonate ion which is the methyl donor.

ArRMe + HB
$$\rightleftharpoons$$
 RA \dot{r} (I) + B⁻ [1]

I + ArHMe
$$\longrightarrow$$
 RArH + MeAr^{+/} (II) [2]

$$II + B^{-} \longrightarrow ArMe_2 + HB$$
 [3]

On the assumption that the rate of trans-methylation is determined mainly by the initial protonation (equilibrium[1]) and presuming additivity of the methyl substituent effects, the reactivity order of the polymethylbenzene reagents to methylate a given aromatic substrate will follow the order 1,3,5-TrMB (0.0001) \ll 1,2,3-TrMB (0.05) < 1,2,4-TrMB $(0.10) \ll 1,2,3,4$ -TeMB (1.8) < 1,2,4,5-TeMB (2.4) <1,2,3,5-TeMB (22) \ll PMB (270) in which the datum in parentheses is a measure of the relative degree of protonation of the methyl-carrying aromatic carbons⁴³. Taking further into account the relative concentrations of the various polymethylbenzenes present in concentrated sulfuric acid (cf. Table V), it follows that the rate order for the initial substrate conversion in the Jacobsen reactions of the polymethylbenzenesulfonic acids will follow the order 2,3,4-, 2,3,5- and 2,4,6-TrMB-1-sulfonic acid < 2,3,4,5- $\ll 2,3,5,6$ - < 2,3,4,6--TeMB-1-sulfonic acid < PMB-1-sulfonic acid. In fact, the former four compounds do not undergo a Jacobsen conversion and PMB-1-sulfonic acid is the most reactive compound.

The substrate being methyl-deprotonated may be a given polymethylbenzene, its sulfonate anion or its sulfonic acid. The substrate reactivity of the sulfonate anion is thought to be at least a factor of 10⁵ smaller than that of the polymethylbenzene and the reactivity of the unionized sulfonic acid will be substantially smaller than that of the corresponding sulfonate anion because of the difference in charge⁴¹. Presuming additivity of the methyl substituent effects⁴⁵, the reactivity order of the polymethylbenzene substrate will increase in the order 1,2-DMB (0.10) < 1,2,4-TrMB (0.25) < 1,2,3-TrMB (0.32) < 1,2,4,5-TeMB (0.71) < 1,2,3,4-TeMB (1.3) <1,3,5-TrMB (5.6) < 1,2,3,5-TeMB (15) < PMB (30), the datum in parentheses being a realtive measure of the overall rate of methyl deprotonation of the listed polymethylbenzene substrates by a given polymethylbenzene reagent. For the polymethylbenzenesulfonate anion substrate, presuming additivity of the methyl and sulfonate substituents⁴⁵, the relative reactivity order of the polymethylbenzenesulfonate anion substrates will increase in the order 2,3,5-TrMB-1-S [6] (0.02) \simeq [4] (0.02) < 2,3,4,5-TeMB-1-S (0.06) < 2,3,5,6-TeMB-1-S (0.07) < 2,4-DMB-1-S [3] (0.09) < [5] (0.16) < 2,4,5-TrMB-1-S [3] (0.35) < 2,3,4-TrMB-1-S [5] (0.63) < 2,4,6-TrMB-1-S [3 + 5] (15) < 2,3,4,6-TeMB-1-S (30), in which the data in square brackets refer to the position(s) of substitution while those in parentheses give a relative measure of the rate of that substitution.

The sulfonation of arene – in casu the polymethylbenzenes – in 89-99% H₂SO₄ as solvent has previously been shown to proceed by means of H₂S₂O₇ as reacting electro-phile^{34,40b}.

Hexamethylbenzene

HMB, upon dissolution in concentrated sulfuric acid $\ge 98\%$ H₂SO₄, is, for the greater part, protonated. After an induction period of *ca*. 1 h, the sulfuric acid solution contains the 2,3,4,4,5,6-hexamethylbenzyl radical cation $(3)^{20d}$. This species is thought to result from *inter*-molecular methylation of the HMB hydrocarbon by the hexamethylbenzenonium ion and subsequent hydrogen atom transfer from the resulting heptamethylbenzenonium ion $(2)^{46,48}$, as shown in Scheme 1. In the ¹³C NMR spectrum of HMB in 98.4% H₂SO₄, taken after 12 h, only the strong absorptions of HMB are apparent; the signals of PMB-1-sulfonic acid and **2** are lost in the noise of the spectrum indicating that equilibrium [5] lies far to the left.



<u>3</u>

$$\frac{1}{2} = R^{1} = H; R^{3} = R^{5} = R^{6} = Me$$

- $2 R^1 = R^3 = R^5 = R^6 = Me$
- $4 \qquad R^1 = R^6 = H ; R^3 = R^5 = Me$
- 5 $R^1 = R^5 = H$; $R^3 = R^6 = Me$
- . 6 R¹=R³=R⁶=H ; R⁵= Me
- 7 $R^1 = R^3 = R^5 = H$; $R^6 = Me$

Pentamethylbenzene-1-sulfonic acid

PMB-1-sulfonic acid, in both 98.4 and 93.1% H₂SO₄, rapidly forms, *i.e.* within 0.6 h of starting to dissolve the PMB-1-sulfonate in the sulfuric acid, the 2,3,4,5- and 2,3,4,6-TeMB-1-sulfonic acids in a ratio of 1/7 (cf. Fig. 1). Subsequently, a relatively slow isomerization of the latter into the former sulfonic acid is observed. The initial formation of the 2,3,4,5- and 2,3,4,6-TeMB-1-sulfonic acid together with HMB may be explained on the basis of the reaction

discussed later. The Jacobsen reaction of PMB-1-sulfonic acid is impeded by the presence of an equimolar amount of HMB (*cf.* Table I). Apparently, the overall non-productive steps [4] and [17] are now faster than the steps [11]-[14] which would lead to the 2,3,4,5- and 2,3,4,6-TeMB-1-sulfonic acids.

of the 2,3,4,6- into the 2,3,4,5-TeMB-1-sulfonic acid will be

2,3,4,5-Tetramethylbenzene-1-sulfonic acid

As already noted by $Kilpatrick^{15}$, this sulfonic acid is – in contrast to its 2,3,4,6- and 2,3,5,6-isomers – completely stable in 55–97% H₂SO₄. This is the result of (i) the significantly lower desulfonation rate coefficient of 2,3,4,5-TeMB--1-sulfonic acid as compared with those of the two other isomers¹⁵ which both suffer from overcrowding due to the presence of two methyls *ortho* to the sulfo group and (ii) the relatively high sulfonation rate coefficient for 1,2,3,4-TeMB, for which the degree of steric hindrance will be substantially less than for the sulfonation of 1,2,3,5- and 1,2,4,5-TeMB.

2,3,5,6-Tetramethylbenzene-1-sulfonic acid

The essential phenomena of the Jacobsen reaction of 2,3,5,6-TeMB-1-sulfonic acid are the following. Firstly, the substrate conversion is characterized by an induction period, the length of which increases by a factor of ca. 10, upon increasing the sulfuric acid concentration from 93.1 to 98.4% H_2SO_4 and by a factor of *ca*. 16, upon decreasing the substrate concentration from 0.20 to 0.00010 M (cf. Table III). Secondly, for 98.4% H₂SO₄, both the induction period and the subsequent time required to effect the complete substrate conversion increase with decreasing substrate concentration and, for a substrate concentration of 0.20 M, upon adding some - only in part dissolved - cyclohexane. Thirdly, the time to effect the substrate conversion (after the induction period) is, for a substrate concentration of 0.20 M, independent of the sulfuric acid concentration³³, as is the final product composition. The observation that the induction period increases strongly with decreasing substrate concentration indicates that the rate limiting reactions during that period are (at least) bimolecular. The observation that the time required to effect the complete substrate conversion increases strongly with decreasing



Scheme 1



Scheme 2

substrate concentration illustrates the *inter*-molecular nature of the methyl migration. The observation for 98.4% H_2SO_4 , that both the induction period and the subsequent time period required to effect the substrate conversion are strongly enhanced by the addition of some – only in part dissolved – cyclohexane, is thought to illustrate the fact that the effective reagent in the *trans*-methylation is 1,2,4,5-TeMB and not its sulfonate or sulfonic acid. The very much higher reactivity of the former entity, as compared with the latter two species, in methylating aromatic nucleophiles (see General considerations) substantiates this presumption.

The observed product formation may be discussed in terms of the reaction steps depicted in Scheme 3. The initial step is *trans*-methylation by 1,2,4,5-TeMB (steps [19] and [20]). The resulting 1,2,4-TrMB is subsequently sulfonated to yield 2,3,5- and 2,4,5-TrMB-1-sulfonic acid in the same ratio as observed on sulfonation of 1,2,4-TrMB proper (step [21])^{45,52}. The PMB then engages in the type of disproportionation reactions previously depicted in Scheme 2 to form HMB, 2,3,4,6- and 2,3,4,5-TeMB-1-sulfonic acid (steps [11]–[16]) and possibly, via step [22], to yield additional 1,2,4-TrMB and HMB. Finally the 2,3,4,6-TeMB--1-sulfonic acid slowly isomerizes to the 2,3,4,5-isomer via the *inter*-molecular mechanism discussed below.

In agreement with the proposed mechanism, the rate of conversion of 2,3,5,6-TeMB-1-sulfonic acid is very much greater in the presence (cf. Fig. 1B) than in the absence (cf. Fig. 3) of added PMB-1-sulfonic acid.

2,3,4,6-Tetramethylbenzene-1-sulfonic acid

The general phenomena of the Jacobsen reaction of 2,3,4,6--TeMB-1-sulfonic acid are similar to those of the 2.3.5.6--isomer (vide supra). Both the induction period and the subsequent time required for the conversion of 2,3,4,6-TeMB--1-sulfonic acid into the 2,3,4,5-isomer strongly increase with decreasing substrate concentration, illustrating that the rate-limiting steps in both time periods are (at least) bi-molecular. The observed isomerization may then be discussed in terms of the reactions depicted in Scheme 4 which are in essence quite similar to those discussed for the Jacobsen reaction of 2,3,5,6-TeMB-1-sulfonic acid (vide supra). The initial reaction is the trans-methylation of 1,2,3,5-TeMB yielding 1,3,5-TrMB⁵³ and PMB (steps [24] and [25]). This disproportionation proceeds via the arenonium ion 7, formed on protonation of 1,2,3,5-TeMB at C(2), which ion is more stable due to a higher degree of conjugative methyl stabilization than the ions resulting from protonation at C(1) or $C(5)^{50}$. The ions 4 and 5, formed by protonation of PMB (steps [11] and [12]), subsequently act as methyl donors to 1,3,5-TrMB and/or its sulfonate^{53,54} (steps [27]) and to 1,2,3,5-TeMB and/or its sulfonate (steps [28]) or may engage in reactions leading to the formation of HMB (cf. Scheme 2). Independent experiments with 98.4% H₂SO₄ at 25°C showed that both PMB-1-sulfonic acid and HMB methylate 2,4,6-TrMB-1-sulfonic acid⁵⁵. In 98.4% H_2SO_4 , the 2,4,6-TrMB-1-sulfonic acid formed from the

+	нв	<u>~</u>	1,2,4,5 - TeMB	+	BS03H			[18]
			Me					
+	н+	<u> </u>		51 ~				[19]
+	1,2,4,5-TeMB		1,2,4 - TrMB	+	РМВ	+	н+	[20a]
+	2,3,5,6-TeMB-1-SO3		1,2,4 - TrMB	+	PMB-1-	ѕо₃н		{20b}
+	H ₂ S ₂ O ₇	~~`	2,3,5-+ 2,4,5-Tr	MB-1-5	50 ₃ H +	H₂S	04	[21]
+	H ₂ S ₂ O ₇		PMB-1-SO3H	+	H ₂ SO4			[-10]
+	РМВ		1,2,4 -TrMB	+	НМВ	+	н+	[22]
+	н ⁺	\rightleftharpoons	4	+	5~			[11+12]
+	РМВ		1, 2, 3, 4 - TeMB	+	НМВ	+	н⁺	[13]
+	РМВ		1,2,3,5 - TeMB	+	НМВ	+	н +	[14]
+	H25207	<u> </u>	2.3.4.5- TeMB-1-	50,н	+	Ж	50 <u>,</u>	[15]
·		~		<u>-</u> <u>-</u> <u>-</u>		- 2-	-4	•
+	H ₂ S ₂ O ₇		2.3.4.6-TeMB-1-	SO3H	+	Hys	50 4	[16]
	* * * * * * *	 + HB + H⁺ 1,2,4,5-TeMB + 1,2,4,5-TeMB + 2,3,5,6-TeMB-1-SO₃ + H₂S₂O₇ + H₂S₂O₇ + PMB + H⁺ PMB + H₂S₂O₇ + H₂S₂O₇ + H₂S₂O₇ + H₂S₂O₇ 	HB Image: state of the	+ HB 1,2,4,5 - TeMB + H ⁺ Image: state st	+ HB + 1.2.4.5 - TeMB + + H ⁺ + - Me + + H ⁺ + - (6) + 1.2.4.5 - TeMB 1.2.4 - TrMB + + 1.2.4.5 - TeMB 1.2.4 - TrMB + + 2.3.5.6 - TeMB-1 - SO_3 - 1.2.4 - TrMB + + H ₂ S ₂ O ₇ - 2.3.5 - + 2.4.5 - TrMB-1 - 5 + + H ₂ S ₂ O ₇ - 2.3.5 - + 2.4.5 - TrMB-1 - 5 + + H ₂ S ₂ O ₇ - - 2.3.5 - TrMB-1 - 5 + H ₂ S ₂ O ₇ - - - - + H ⁺ - - + - + H ⁺ - - - - - + H ⁺ - - - - - - - + H ⁺ - - - - - - - - - - - - - - - - -	+ HB + 1.2.4.5-TEMB + BSO ₃ H + H ⁺ + + + (6) + 1.2.4.5-TEMB 1.2.4-TrMB + PMB + 1.2.4-TrMB + PMB + 2.3.5.6-TEMB-1-SO ₃ - 1.2.4-TrMB + PMB-1- + H ₂ S ₂ O ₇ + - 2.3.5-+2.4.5-TrMB-1-SO ₃ H + + H ₂ S ₂ O ₇ + - 2.3.5-+2.4.5-TrMB-1-SO ₃ H + + H ₂ S ₂ O ₇ + - 2.3.5-+2.4.5-TrMB-1-SO ₃ H + + H ₂ S ₂ O ₇ + - - - PMB-1-SO ₃ H + + H ₂ S ₂ O ₇ + + - <t< th=""><th>+ HB + 1.2.4.5 - TEMB + BSO₃H + H⁺ + + + (6) + 1.2.4.5 - TEMB 1.2.4 - TrMB + PMB + + 1.2.4.5 - TEMB 1.2.4 - TrMB + PMB + + 1.2.4.5 - TEMB 1.2.4 - TrMB + PMB + + 2.3.5.6 - TEMB-1 - SO₃ - 1.2.4 - TrMB + PMB-1 - SO₃H + H₂SO₄ + H₂S₂O₇ - - 2.3.5 - TEMB-1 - SO₃H + H₂SO₄ + H₂S₂O₇ - - PMB-1 - SO₃H + H₂SO₄ + H₃S₂O₇ -<th>+ HB 1.2.4.5 - TEMB BSO_3H + H⁺ H⁺ H⁺ H⁺ H⁺ + H⁺ H⁺ H⁺ H⁺ H⁺ + 1.2.4 - TrMB PMB H⁺ + 1.2.4 - TrMB PMB H⁺ + 2.3.5.6 - TEMB - 1 - SO_3 1.2.4 - TrMB PMB - 1 - SO_3H + H_2S_2O_7 Image: Colored and the colored and</th></th></t<>	+ HB + 1.2.4.5 - TEMB + BSO ₃ H + H ⁺ + + + (6) + 1.2.4.5 - TEMB 1.2.4 - TrMB + PMB + + 1.2.4.5 - TEMB 1.2.4 - TrMB + PMB + + 1.2.4.5 - TEMB 1.2.4 - TrMB + PMB + + 2.3.5.6 - TEMB-1 - SO ₃ - 1.2.4 - TrMB + PMB-1 - SO ₃ H + H ₂ SO ₄ + H ₂ S ₂ O ₇ - - 2.3.5 - TEMB-1 - SO ₃ H + H ₂ SO ₄ + H ₂ S ₂ O ₇ - - PMB-1 - SO ₃ H + H ₂ SO ₄ + H ₃ S ₂ O ₇ - - <th>+ HB 1.2.4.5 - TEMB BSO_3H + H⁺ H⁺ H⁺ H⁺ H⁺ + H⁺ H⁺ H⁺ H⁺ H⁺ + 1.2.4 - TrMB PMB H⁺ + 1.2.4 - TrMB PMB H⁺ + 2.3.5.6 - TEMB - 1 - SO_3 1.2.4 - TrMB PMB - 1 - SO_3H + H_2S_2O_7 Image: Colored and the colored and</th>	+ HB 1.2.4.5 - TEMB BSO_3H + H ⁺ H ⁺ H ⁺ H ⁺ H ⁺ + H ⁺ H ⁺ H ⁺ H ⁺ H ⁺ + 1.2.4 - TrMB PMB H ⁺ + 1.2.4 - TrMB PMB H ⁺ + 2.3.5.6 - TEMB - 1 - SO_3 1.2.4 - TrMB PMB - 1 - SO_3H + H_2S_2O_7 Image: Colored and the colored and

Scheme 3

2,3,4,6-TeMB-1-sulfonic acid substrate will, to a minor extent, undergo irreversible²³ sulfonation^{37,55} to yield some 2,4,6-TrMB-1,3-disulfonic acid.

The occurrence of an induction period in the Jacobsen reactions of 2,3,4,6- and 2,3,5,6-TeMB-1-sulfonic acid suggests autocatalysis. The PMB formed in the primary disproportionation (cf. Schemes 3 and 4) is apparently too poor a trans-methylation reagent, as compared with HMB which is formed as a secondary product by disproportionation reactions involving PMB as methyl acceptor. The much higher reactivity of HMB is logical if one considers (i) that PMB in concentrated sulfuric acid is predominantly present as its sulfonic acid which is unreactive in trans-methylation (vide supra) and (ii) that PMB is predominantly protonated at $C(6)^{51}$ and apparently only to a very minor extent at C(1) and C(2), *i.e.* at the positions required to form the trans-methylating carbenium ions 4 and 5 (cf. Schemes 2 and 4).

Comparison with homologous polyalkylbenzenesulfonic acids

The monosulfonic acids of 1,2,3,5- and 1,2,4,5-tetraethylbenzene are unstable in 98.4% H_2SO_4 and are converted *without* and induction period into 2,3,4,5-tetraethylbenzene-

-1-sulfonic acid as the only final product. Dealkylation does not occur⁴. The least stable sulfonic acid is the 2,3,5,6--isomer which rearranges in part via the 2,3,4,6-isomer and in part directly to the 2,3,4,5-isomer (in a ratio of 1.3/1) by intra-molecular 1,2-ethyl shifts of the appropriately ring--protonated arenesulfonic acids. The conversion of the 2,3,5,6-tetraethylbenzene-1-sulfonic acid is complete within ca: 1 h and that of the 2,3,4,6-isomer within ca. 8 h which is far more rapid than those of the methyl analogues (vide supra). 1,2,4,5-Tetraisopropylbenzene initially yields the corresponding sulfonic acid which is unstable and undergoes dealkylation, yielding eventually a mixture of 2,4,5-triand 3,5-diisopropylbenzene-1-sulfonic acid and 2-propyl hydrogen sulfate³. The conversions of both 2,3,4,6- and 2,3,5,6-tetraethylbenzene-1-sulfonic acid show simple first--order substrate kinetics⁴, whereas the conversion of the corresponding methyl homologues do not (cf. Figs. 2 and 3). This again illustrates that the conversion of 2,3,4,6- and 2,3,5,6-TeMB-1-sulfonic acid does not proceed intra--molecularly.

In conclusion, this study would appear to firmly establish that (i) the Jacobsen reaction of polymethylbenzenesulfonic acids – contrary to those of the corresponding tetraethyl-

1							
Q	+	нв	<u>~</u>	1,2,3,5 - Te MB	+	BSO₃H	[23]
' 1,2,3,5-ТеМВ	+	н*	<u> </u>	+ (7))		[24]
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	+	1,2,3,5 -TeMB	>	1,3,5-TrMB	+	PMB + H ⁺	[25a]
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	+	2,3,4,6 - Te MB - 1 - SO ₃	>	1,3,5 - T r MB	+	Р <b>ВМ-1-</b> SO ₃ H	(25b)
1,3,5-TrMB	+	H ₂ S ₂ O ₇		2,4,6 - Tr MB-1-SO) ₃ H +	H ₂ SO4	[26]
PMB-1-SO ₃ H	+	нв	<u></u>	РМВ	+	BS0 ₃ H	[10]
РМВ	+	н+	<u> </u>	4			[11]
РМВ	+	н*	<u> </u>	5			[12]
<u>لا</u>	+	1, 3,5 - TrMB		1, 2, 3, 4 - TeMB	+	1,2,3,5-TeMB + H ⁺	[27a]
<u></u>	+	2,4,6 - Tr MB-1-SO ₃	>	1,2,3,4 - TeMB	+	2,3,4,6 - TeMB-1-SO ₃ H	[27b]
4	+	1,2,3,5 - TeMB	>	1.2.3.4 - TeMB	+	рмв + н ⁺	[28a]
4~	+	2,3,4,6 - TeMB		1,2,3,4 - TeMB	+	РМВ-1-S0 ₃ Н	[28b]
1,2,3,4 - TeMB	+	H ₂ S ₂ O ₇	•	2,3,4,5-TeMB-1-5	50 , Н	+ H ₂ SO ₄	[15]
5~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	+	1,3,5 - Tr MB-1-S03		2 1,2,3,5 - TeME	3 +	н⁺	[290]
5~	+	2,4,6-TrMB-1-S03		1,2,3,5 - TeMB	+	2,3,4,6 - TeMB-1- SO ₃ H	[29b]

Scheme 4

benzenesulfonic acids - proceeds inter-molecularly and that the methyl transferring species are the ring-protonated polymethylbenzenes and not the ring-protonated polymethylbenzenesulfonates or sulfonic acids. The previously presented arguments suggesting a preference for the arenesulfonic acids as the substrate species involved in the rearrangements. viz. (i) that 2,3,5,6-TeMB-1-sulfonic acid in contact with phosphorus pentoxide8 or polyphosphoric acid13 rearranges 2,3,4,5-isomer, into the whereas 1,2,4,5--TeMB does not and (ii) that the Jacobsen rearrangements are not observed on using chlorosulfuric acid¹⁴ instead of sulfuric acid as solvent, are very weak. As for the first argument, the reaction mixture containing the 2,3,5,6--TeMB-1-sulfonic acid will be more acidic than those of the 1,2,4,5-TeMB and this acidity difference may very well explain the occurrence of the rearrangement on using the sulfonic acid and its non-occurrence on using the arene. As for the second argument, the non-occurrence of the Jacobsen rearrangement on using chlorosulfuric acid as solvent may, in our view, be explained in terms of the predominant conversion of the arenesulfonic acid into its sulfonyl chloride⁵⁶, rendering the degree of free arene in this system much smaller than in the sulfuric acid system.

Experimental

The ¹H and ¹³C NMR spectra were recorded using Varian HA-100 and XL-100 spectrometers. The ¹H and ¹³C chemical shifts are relative to neat TMS (capillary) which was used as external reference. The UV spectra were recorded on a Cary 14 spectrometer.

Materials

The polymethylbenzenes were high-quality commercial compounds and were used without further purification. The three potassium TeMB-sulfonates were prepared as previously described²³; potassium PMB-sulfonate was similarly prepared.

co ...

	6-Me					3.03				2.97	23.1								
	5-Me	2.65	20.9	2.65	19.3*			2.71	20.9					2.78				r.s)	
	4-Me			2.65	19.7*	2.75	3.19	2.66	17.1*	2.70	21.4			3.10	2.70	18.1	2.78	14) 20.9 (bi	
	3-Me	2.65	20.4					2.66	16.4	2.60	16.1	2.66	20.8		2.66	17.1*			
c,d	2-Me	2.95	16.2	2.95	20.2	3.03	3.45	2.94	17.3*	2.97	18.7	2.89	18.2	3.33	2.95	19.5*			
β (ppm)	C(6)H	8.04	127.3	8.10	129.9*			8.03	127.6		136.8								
	C(5)H		137.4		136.7	7.49	7.85		136.1*	7.42	133.8								
	C(4)H	7.77	138.7		146.9				145.4		145.5	7.66	138.8			144.1		53.2	
	C(3)H		141.3	7.60	135.0 [†]	7.49			139.8		137.5*		137.8			136.7*			
	C(2)		134.0*		136.0^{\dagger}				134.1*		138.4*		136.1*			135.2*			
ĺ	C(1)		133.3*		129.1*				130.2		130.5		133.8*			131.7			
NMDa	VIAN	H1	D ^{E1}	18H1	D ^{E1}	H'	H1	Hi	1 ³ C	H_1	D ^{E1}	H	D ^{E1}	H_1	H		H	D ^{E1}	
Benzene	substituents ^b	2,3,5-Me ₁ -1-S ^e		2,4,5-Me,-1-S ^e		2,4,6-Me ₃ -1-S	2,4,6-Me ₃ -1,3-S ₂	2,3,4,5-Me ₄ -1-S		2,3,4,6-Me ₄ -1-S		2,3,5,6-Me ₄ -1-S		2,4,5,6-Me ₄ -1,3-S ₂	Me1-S		Me	1	

Table VI NMR data^a of the polymethylbenzenesulfonic acids and HMB in 98.4% H_2SO_4 .

^a For ¹H and ¹³C NMR, the solute concentrations were 0.20 and 0.33 M, respectively. ^b S stands for SO₃H. ^e The assignments are in accordance with those of a systematic study using ²H₂O as solvent²⁴. ^d The chemical shifts are relative to neat external TMS (¹H NMR) and virtual internal TMS (¹³C NMR). ^e From the spectrum of a 1/3 mixture of 2,3,5- and 2,4,5-TrMB-1-sulfonic acid. ^{*†} The assignments may be reversed.

Table VII UV absorption data	³ of	f the polymet	hylbenzenesulfonic	acids	and	HMB	in 98.4	% H,	SO4	
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Benzene substituents ^b	$\lambda_{max}(\epsilon \cdot 10^{-3})$	$\lambda_{\min}(\epsilon \cdot 10^{-3})$					
$2,3,5-+2,4,5-Me_3-1-S$ (23/77)	233(13.8); 283(3.5)	215(9.1); 253(0.7)					
2,3,4,5-Me ₄ -1-S	237(15.6); 282(3.6)	219(8.2); 257(0.9)					
2,3,4,6-Me ₄ -1-S	237(15.1); 287(5.0)	220(10.1); 259(0.7)					
2,3,5,6-Me₄-1-S	225(10.9)°; 293(5.8)	256(0.2)					
Me _s -1-S	242(11.4); 291(4.7); 385(1.6)	229(9.3); 266(2.2); 355(0.9)					
Me ₆	279(8.7); 335(7.7); 393(11.7)	252(4.5); 302(2.5); 357(4.2)					

^a λ expressed in nm and ϵ in M⁻¹·cm⁻¹. ^b S stands for SO₃H. ^c Shoulder.

Analysis

The quantitative analyses of the reaction mixtures in concentrated sulfuric acid were performed using a ¹H NMR multicomponent analysis³² on the basis of the specific aromatic hydrogen absorptions of the various components (see Table VI). Further – more qualitative – information on the composition of the sulfuric acid solutions was obtained from their ¹³C NMR and UV spectra by comparison with the spectra of the pure components in the same solvent (cf. Tables VI and VII, respectively).

The ¹H NMR methyl singlet of $C_6Me_6H^+$ at *ca.* 2.8 ppm and the three methyl singlets of PMB-sulfonic acid in 98.4% H₂SO₄ slowly start to collapse after 7 h. These absorptions were therefore used as specific absorptions in the multi-component ¹H NMR analysis³² only for reaction mixtures with a reaction time <9 h.

For the relatively slow experiments starting with 2,3,5,6-TeMB--1-sulfonate, the total amount of products not having aromatic hydrogens (*i.e.* PMB-sulfonic acid and hexamethylbenzenonium ion) was determined from the ratio of the total methyl to the total aromatic ¹H NMR absorption; it always appeared to be equal, within experimental error, to the sum of the 2,3,5- and 2,4,5--TrMB-1-sulfonic acids. For experiments starting with PMB-sulfonate and a reaction time >9 h, the amount of C₆Me₆H⁺ originally formed was taken to be the sum of the 2,3,4,6- and 2,3,4,5-TeMB--1-sulfonic acids formed.

The content of ArH present in a solution of a given polymethylbenzenesulfonic acid in sulfuric acid was determined as follows. 250 mg of a given potassium tri- and tetramethylbenzenesulfonate or 200 mg of potassium pentamethylbenzenesulfonate were added to 3.00 ml of sulfuric acid and the mixture shaken vigorously for 5 min using a vibromixer. 2.00 ml of cyclohexane were then added and the mixture shaken for a further 30 s. After 2 min, to allow for separation, 1.00 ml of the supernatant cyclohexane extract was removed and diluted with cyclohexane sufficiently to allow its arene concentration to be determined using UV spectroscopy. In the case of PMB-sulfonate, after the 6 min required for the analytical procedure, the PMB was found to contain some HMB, rendering the accuracy of PMB determination somewhat low.

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starting material and 2,3,4,5-TeMB-1-sulfonic acid, i.e. the minor and major component, respectively.

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 ${}^{SO_3-}f_p = 0.2 \times 10^{-8}$, *i.e.* those reported for the sulfonation by the H₂S₂O₇ mechanism in concentrated sulfuric acid^{40b}, whereas $\frac{SO_3}{f_0}$ was taken to be 0.1×10^{-8} .

- ⁴⁶ The alternative route of hydrogen atom loss from C₆Me₆H⁺ and subsequent inter-molecular methylation of the resulting hexamethylphenyl radical cation ion by another molecule of $C_6Me_6H^+$ is considered less likely, since there is no common opinion as to whether the hexamethylphenyl radical cation is formed under the conditions of the present study^{18,19,20d,47}
- ⁴⁷ M. C. R. Symons and R. Hulme, Nature 206, 293 (1965).
- ⁴⁸ HMB is easily methylated to form the heptamethylbenzenonium ion on reaction with (i) methanol in concentrated sulfuric acid, (ii) dimethyl sulfate and (iii) methyl chloride with aluminium chloride as catalyst49
- ⁴⁹ W. von E. Doering, M. Saunders, H. G. Boynton, H. W. Earhart, E. F. Wadley and G. Labor, Tetrahedron 4, 178 (1958).
- ⁵⁰ Upon protonation of PMB, 1,2,3,5- and 1,2,4,5-TeMB, the only observed carbenium ions are those formed by protonation at C(6), C(4) and C(3), respectively⁵¹
- ⁵¹ D. M. Brouwer, E. L. Mackor and C. Maclean, Recl. Trav. Chim. Pays-Bas 84, 1564 (1965).
- The products formed by methyl loss from the ring protonated 2,3,5,6-TeMB-1-sulfonate ion would be the 2,3,5- and 2,3,6--TrMB-1-sulfonic acids, of which the latter would be the predominant species in view of the significantly larger degree of protonation of 2,3,5,6-TeMB-1-sulfonate at C(3) than at C(2), due to the strong -1 effect of the 1-SO₃⁻ substituent⁴⁰. In fact, the main demethylation products are different, viz. the 2,3,5and 2,4,5-TrMB-1-sulfonic acids, of which the latter predominates.
- 53 The limit of ¹H NMR detection of 2,4,6-TrMB-1-sulfonic acid in concentrated sulfuric acid in the presence opf 2,3,4,6-TeMB--1-sulfonic acid is thought to be high (10 - 15%), due to the small differences in the chemical shifts of the singlet signals of the two sulfonic acids and the fact that these absorptions are substantially broadened in the concentrated sulfuric acid solvent.
- Marvell and Graybill report the presence of traces of 1,3,5--TrMB in the flash desulfonation distillate of the reaction mixture of 2,3,5,6-TeMB-1-sulfonic acid in polyphosphoric acid¹³
- 55 A. Koeberg-Telder and H. Cerfontain, Recl. Trav. Chim. Pays-Bas, to be published.
- 56 L. Harding, J. Chem. Soc. 1261 (1921); A. A. Spryskov and Y. L. Kuz'mina, J. Gen. Chem. USSR 28, 184 (1958).