[Contribution from the Chemical Laboratories of New York University, St. John's University, and Lafayette College]

UNSYMMETRICAL MORPHOLINIUM AND THIAMORPHOLINIUM ALKYL SULFATES[1]

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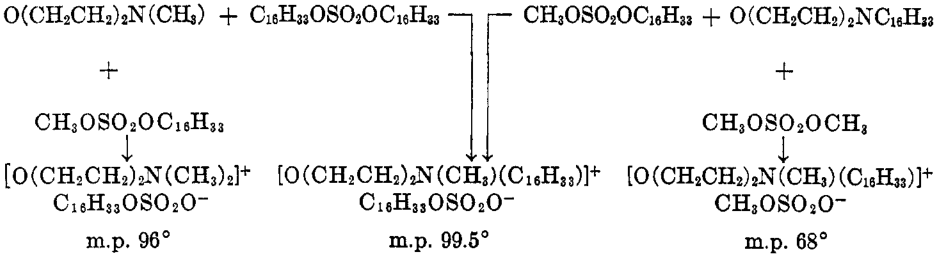
INTRODUCTION

Systematic studies in "Symmetrical Morpholinium Alkyl Sulfates" by Niederl and co-workers (1) have now been extended to the reaction of tertiary aminse with unsymmetrical dialkyl sulfates.

The tertiary amines used in this investigation were N-substituted morpholines such as N-*n*-dodecyl-, N-*n*-tetradecyl-, N-*n*-hexadecyl-, and N-*n*-octadecylmorpholine and the corresponding N-alkylated thiamorpholines, thiamorpholine oxides, and thiamorpholine dioxides previously described by Hart and Niederl (2). The unsymmetrical dialkyl sulfates used were methyl ethyl sulfate, methyl *n*-dodecyl sulfate, methyl *n*-tetradecyl sulfate, and methyl *n*-hexadecyl sulfate, which were prepared by the method of Bushong (3).

While the products obtained by the interaction of symmetrical dialkyl sulfates with tertiary amines needed no further elucidation as to the structure of the resulting quaternary ammonium alkyl sulfates, this was not the case when unsymmetrical dialkyl sulfates were used. It became necessary to investigate the structure of the final quaternary morpholinium alkyl sulfates in order to establish which of the two alkyl radicals of the sulfate migrated to the tertiary amino nitrogen.

By the solution of this problem as illustrated below, it was determined that the smaller alkyl radical of the unsymmetrical dialkyl sulfate migrates to the nitrogen of the tertiary amine.



$O(CH_2CH_2)_2N(CH_3) + C_{16}H_{33}OSO_2OC_{16}H_{33}$ — $CH_3OSO_2OC_{16}H_{33} + O(CH_2CH_2)_2NC_{16}H_{33}$

$O(CH_2CH_2)_2N(CH_3) + CH_3OSO_2OC_{16}H_{33} \rightarrow [O(CH_2CH_2)_2N(CH_3)_2]^+ \; C_{16}H_{33}OSO_2O^-$ m.p. 96°

$\rightarrow [O(CH_2CH_2)_2N(CH_3)(C_{16}H_{33})]^+ \; C_{16}H_{33}OSO_2O^-$ m.p. 99.5°

$O(CH_2CH_2)_2NC_{16}H_{33} + CH_3OSO_2OCH_3 \rightarrow [O(CH_2CH_2)_2N(CH_3)(C_{16}H_{33})]^+ \; CH_3OSO_2O^-$ m.p. 68°

N-Methylmorpholine when reacted with di-*n*-hexadecyl sulfate yielded the same product as when N-*n*-hexadecylmorpholine was treated with methyl *n*-hexadecyl sulfate, while reaction of N-*n*-hexadecylmorpholine with dimethyl sulfate and N-methylmorpholine with methyl *n*-hexadecyl sulfate produced altogether different products.

It may also be pointed out that the use of unsymmetrical dialkyl sulfates not

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only makes it possible to produce quaternary ammonium compounds in which the cation is larger than the anion, as is usual, but also makes readily accessible those in which the cation and anion are equal ("equionics"), or those in which the cation is smaller than the anion.

TABLE I

UNSYMMETRICAL DIALKYL SULFATES

COMPOUND	EMP. FORMULA	M.P. (B.P.), °C	YIELD %	%S	
				Calc'd	Found
Methyl ethyl sulfate	$C_3H_8O_4S$	(100–102/45 mm.)	15	22.87	22.84
Methyl *n*-dodecyl sulfate	$C_{13}H_{28}O_4S$	47	35	11.43	11.39
Methyl *n*-tetradecyl sulfate	$C_{15}H_{32}O_4S$	54	15	10.39	10.34
Methyl *n*-hexadecyl sulfate	$C_{17}H_{36}O_4S$	61	20	9.52	9.49

TABLE II

UNSYMMETRICAL N-ALKYL-N-METHYLMORPHOLINIUM ALKYL SULFATES

$[O(CH_2CH_2)_2N(CH_3)(R)]^+ \, OSO_2OR'^-$

R	R'	EMP. FORMULA	M.P. (°C)	% NITROGEN	
				Calc'd	Found
n-Hexadecyl	Ethyl	$C_{23}H_{49}NO_5S$	45	3.10	3.05
Methyl	*n*-Dodecyl	$C_{18}H_{39}NO_5S$	60	3.67	3.64
n-Dodecyl	*n*-Dodecyl	$C_{29}H_{61}NO_5S$	87	2.61	2.68
n-Tetradecyl	*n*-Dodecyl	$C_{31}H_{65}NO_5S$	80	2.48	2.42
n-Hexadecyl	*n*-Dodecyl	$C_{33}H_{69}NO_5S$	88	2.37	2.31
Methyl	*n*-Tetradecyl	$C_{20}H_{43}NO_5S$	98	3.42	3.46
n-Dodecyl	*n*-Tetradecyl	$C_{31}H_{65}NO_5S$	58	2.48	2.44
n-Tetradecyl	*n*-Tetradecyl	$C_{33}H_{69}NO_5S$	78	2.37	2.36
n-Hexadecyl	*n*-Tetradecyl	$C_{33}H_{73}NO_5S$	75	2.26	2.28
Methyl	*n*-Hexadecyl	$C_{22}H_{47}NO_5S$	96	3.20	3.15
n-Dodecyl	*n*-Hexadecyl	$C_{33}H_{69}NO_5S$	92	2.37	2.37
n-Tetradecyl	*n*-Hexadecyl	$C_{35}H_{73}NO_5S$	82	2.26	2.30
n-Hexadecyl	*n*-Hexadecyl	$C_{37}H_{77}NO_5S$	99	2.16	2.11

EXPERIMENTAL

Unsymmetrical dialkyl sulfates. The methyl ethyl, methyl *n*-dodecyl, methyl *n*-tetradecyl, and methyl *n*-hexadecyl sulfates were prepared by slight modifications of the method of Bushong (3). Of these compounds, only the first has been previously described (4, 5, 6). In each case the chlorosulfonate of the higher alcohol was prepared and reacted with sodium methoxide in anhydrous ether at low temperature. The methyl ethyl sulfate was purified by distillation *in vacuo*, the others by crystallization from ether.

Unsymmetrical N-alkyl-N-methylmorpholinium alkyl sulfates. These compounds were prepared by reacting equivalent quantities (from 0.003 to .01 mole) of the N-alkylmorpholine and the appropriate unsymmetrical dialkyl sulfate, without solvent, at 115° for six hours in a tightly stoppered Pyrex test tube heated in an oil-bath. The reaction mixture was then allowed to remain overnight at room temperature. The resultant waxy product was washed with 3 cc. of ether at 33°, cooled, and centrifuged. The ether layer containing the more soluble unreacted starting materials was decanted. The washed product was recrystallized three times from ethyl acetate, and dried on a porous tile. In cases where there was evidence of spontaneous exothermic reaction the heating was limited to 50° for three hours. The yields for this group of compounds varied from 32–45%.

Unsymmetrical N-alkyl-N-methylthiamorpholinium alkyl sulfates. Equivalent quantities (approximately 0.003 mole) of the N-alkyl thiamorpholine, oxide, or dioxide and di-*n*-hexadecyl sulfate were added to 5 cc. of toluene which had been dried over sodium. The solution was refluxed for four hours, using an oil-bath, with an external temperature of 160–170°. Lower temperatures were found to give incomplete reaction. The toluene was distilled off *in vacuo*, a little alcohol was added, and distilled *in vacuo* to remove the last traces of toluene. The residue was taken up in ethyl acetate and crystallized from this solvent.

TABLE III

UNSYMMETRICAL N-ALKYL-N-METHYLTHIAMORPHOLINIUM ALKYL SULFATES

R	R′	EMP. FORMULA	M.P. (°C)	% NITROGEN	
				Calc'd	Found
THIAMORPHOLINIUM $[S(CH_2CH_2)_2N(CH_3)(R)]^+ OSO_2OR'^-$					
n-Dodecyl	*n*-Hexadecyl	$C_{33}H_{69}NO_4S_2$	76	2.30	2.28
n-Tetradecyl	*n*-Hexadecyl	$C_{35}H_{73}NO_4S_2$	112	2.20	2.23
n-Hexadecyl	*n*-Hexadecyl	$C_{37}H_{77}NO_4S_2$	92	2.10	2.13
n-Octadecyl	*n*-Hexadecyl	$C_{39}H_{81}NO_4S_2$	98	2.02	2.00
THIAMORPHOLINIUM-1-OXIDE $[OS(CH_2CH_2)_2N(CH_3)(R)]^+ OSO_2OR'^-$					
n-Dodecyl	*n*-Hexadecyl	$C_{33}H_{69}NO_5S_2$	127	2.24	2.21
n-Tetradecyl	*n*-Hexadecyl	$C_{35}H_{73}NO_5S_2$	128	2.14	2.12
n-Hexadecyl	*n*-Hexadecyl	$C_{37}H_{77}NO_5S_2$	110	2.05	2.04
n-Octadecyl	*n*-Hexadecyl	$C_{39}H_{81}NO_5S_2$	105	1.97	1.93
THIAMORPHOLINIUM-1-DIOXIDE $[O_2S(CH_2CH_2)_2N(CH_3)(R)]^+ OSO_2OR'^-$					
n-Dodecyl	*n*-Hexadecyl	$C_{33}H_{69}NO_6S_2$	130	2.18	2.16
n-Tetradecyl	*n*-Hexadecyl	$C_{35}H_{73}NO_6S_2$	88	2.09	2.07
n-Hexadecyl	*n*-Hexadecyl	$C_{37}H_{77}NO_6S_2$	105	2.01	2.03
n-Octadecyl	*n*-Hexadecyl	$C_{39}H_{81}NO_6S_2$	98	1.93	1.90

In cases where decolorization was necessary, this was done with Darco in alcohol solution. The compounds were finally recrystallized twice from acetone, and twice from ethyl acetate, or from an ethyl acetate–alcohol mixture. The melting points were taken on a Fisher-Johns electrical melting-point apparatus, and the point of complete liquefication determined.

SUMMARY

Work in the field of quaternary morpholinium and thiamorpholinium types of "invert soaps" has been extended to include the preparation of two series of unsymmetrical N,N-dialkyl-morpholinium and -thiamorpholinium alkyl sulfates possessing a balance between the carbon atom content of the anion and cation (equionics).

It has been established that, in the N-alkylation of tertiary amines by unsymmetrical dialkyl sulfates, the smaller alkyl group migrates to the nitrogen of the tertiary amine.

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REFERENCES

(1) NIEDERL, SALZBERG, AND SHATYNSKI, *J. Am. Chem. Soc.*, **70,** 618 (1948).
(2) HART AND NIEDERL, *J. Am. Chem. Soc.*, **66,** 1610 (1944); **68,** 714 (1946).
(3) BUSHONG, *Am. Chem. J.*, **30,** 212 (1903).
(4) BEHREND, *Ber.*, **9,** 1334 (1876).
(5) BERT, *Compt. rend.*, **178,** 1182 (1924).
(6) THAYER, *J. Am. Chem. Soc.*, **46,** 1044 (1926).