SYNTHESIS AND REPELLENT PROPERTIES OF N-ALKYLANILIDES AND ESTERS OF BUTANESULFONIC ACID

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There are compounds possessing expressed repellent activity in relation to insects [1-3] among disubstituted amides and esters of organic sulfonic acids. In this connection, it was of interest to us to synthesize and examine a series of N-alkylanilides and esters of butanesulfonic acid as insect repellents, all the more because, according to literature data [4], certain acyl derivatives of alkylanilides, for example butylacetanilide, are active mite repellents.

N-Alkylanilides (I-V) were obtained by reaction of butanesulfonyl chloride with N-alkylanilines in the presence of pyridine.

$$C_4H_9SO_2Cl + C_6H_5NHR \rightarrow \underset{I-V}{C_4H_9SO_2N(C_6H_5)R}.$$

These are thick pale-yellow liquids or colorless crystalline materials without odor (Table 1).

Esters of butanesulfonic acids (VI-XVI) were synthesized by reaction of butanesulfonyl chloride with basic solutions of phenols at room temperature [5-7].

$$C_4H_9SO_2Cl + HOC_6H_4R \rightarrow \underset{VI-XVI}{C_4H_9SO_2OC_6H_4R}.$$

The obtained aromatic esters are thick light-yellow liquids; a portion of the compounds are colorless crystalline materials (Table 2).

Aliphatic esters of butanesulfonic acid (XVII-XXV) were synthesized by reaction of butanesulfonyl chloride with alcohols in pyridine.

$$C_4H_9SO_2Cl + ROH \rightarrow \underset{XVII-XXV}{C_4H_9SO_2OR}.$$

These compounds are colorless or lightly yellow liquids having a unique odor; methoxy- and ethoxyethyl esters (XXIV and XXV) darken strongly upon standing in air. Constants of the synthesized compounds are presented in Table 3.

The repellent activity of the obtained compounds was studied by the method developed at the Miltary-Medicinal Academy [8]. The preparations were applied to a cotton diagonal in a dose of 40 g/m^2, using the flea Ceratophyllus tesquorum as the biological model. The effectiveness of the investigated materials was evaluated from the size of coefficients of repellent effect (CRE) on the day of treatment of the fabric, and in the case of sufficiently expressed repellent properties, additionally after each two weeks until CRE fell below 70%.

All experiments were set in five repetitions using 100 fleas in each of them. Examination was carried out at a temperature of 20-22°C and a relative humidity of the air of 55-75%. Experimental samples were

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TABLE 1. N-Alkylanilides of Butanesulfonic Acid

Compound	R	Yield, %	bp (deg)	mp (deg)	n_D^{20}	Found, % C	H	N	S	Empirical formula	Calculated, % C	H	N	S
I	CH_3	92,1	143—145 (0,3 mm)	52—54	—	58,15	7,87	6,03	13,96	$C_{11}H_{17}NO_2S$	58,12	7,54	6,16	14,10
						58,20	8,00	5,80	13,82					
II	C_2H_5	41,5	142—145 (0,3 mm)	—	1,5159	59,60	8,00	5,95	12,57	$C_{12}H_{19}NO_2S$	59,72	7,93	5,80	13,28
						59,68	8,13	6,00	12,88					
III	C_3H_7	44,5	178—180 (0,75 mm)	—	1,5099	61,10	8,18	5,95	12,35	$C_{13}H_{21}NO_2S$	61,14	8,29	5,49	12,55
						61,43	8,41	5,88	12,40					
IV	C_4H_9	87,4	145—148 (0,2 mm)	30—31	—	62,34	8,47	5,66	11,83	$C_{14}H_{23}NO_2S$	62,42	8,61	5,19	11,90
						62,32	8,32	5,54	11,86					
V	C_5H_{11}	46,6	140—142 (0,25 mm)	27—28	—	63,74	8,58	5,10	11,12	$C_{15}H_{25}NO_2S$	63,34	8,86	4,93	11,27
						63,70	8,58	5,00	11,17					

TABLE 2. Aromatic Esters of Butanesulfonic Acid

Compound	R	Yield, %	mp (deg)	d_4^{20}	n_D^{20}	Found, % C	H	S	Empirical formula	Calculated, % C	H	S
VI[1]	H	73,4	123—126 (1—2 mm)	—	1,5026	—	—	—	—	—	—	—
VII[1]	o-CH_3	55,3	118—121 (0,5 mm)	—	1,5040	—	—	—	—	—	—	—
VIII	m-CH_3	71,1	124—127 (0,6 mm)	1,1433	1,5042	57,47	7,22	13,60	$C_{11}H_{16}O_3S$	57,86	7,06	14,04
						57,80	7,23	13,91				
IX	p-CH_3	61,9	122—125 (0,5 mm)	1,1408	1,5038	57,71	6,85	13,90	$C_{11}H_{16}O_3S$	57,86	7,06	14,04
						57,64	6,75	13,85				
X[2]	o-CH_3O	66,4	138—142 (0,6 mm)	—	—	53,73	7,05	13,17	$C_{11}H_{16}O_4S$	54,08	6,60	13,12
						53,85	7,08	12,92				
XI	m-CH_3O	71,3	134—138 (0,2mm)	1,1964	1,5101	53,85	7,03	12,94	$C_{11}H_{16}O_4S$	54,08	6,60	13,12
						53,88	6,85	12,81				
XII	p-CH_3O	70,1	150—152 (0,6 mm)	1,1947	1,5108	54,00	7,10	13,43	$C_{11}H_{16}O_4S$	54,08	6,60	13,12
						53,77	6,95	13,16				
XIII	2-iso-C_3H_7-5-CH_3	43,0	138—140 (0,8 mm)	1,0802	1,5102	62,02	8,70	12,00	$C_{14}H_{22}O_3S$	62,18	8,21	11,86
						62,52	8,54	11,80				
XIV[1]	o-Cl	68,2	125—129 (0,7 mm)	—	1,5170	—	—	—	—	—	—	—
XV[1]	p-Cl	79,0	144—146 (1 mm)	—	1,5162	—	—	—	—	—	—	—
XVI[3]	o,p-Cl	78,5	128—132 (0,3 mm)	1,3496	1,5295	42,59	4,65	10,92	$C_{10}H_{12}Cl_2O_3S$	42,41	4,27	11,31
						42,38	4,30	10,99				

*Literature data: VI, bp. 166° (10 mm), n_D^{20} 1.5011 [5]; VII, bp 150-152° (5 mm), n_D^{20} 1.5035 [6]; XIV, bp 180-181° (13 mm), n_D^{20} 1.5120 [7]; XV, bp 186-189° (7 mm), n_D^{20} 1.5165 [5].

† bp 42.5-43.5°.

‡ Found, %: Cl 24.65; 24.81. Calculated, %: Cl 25.07.

TABLE 3. Aliphatic Esters of Butanesulfonic Acid

Compound	R	Yield, %	Bp(deg)	d_4^{20}	n_D^{20}	Found, % C	Found, % H	Found, % S	Empirical formula	Calculated, % C	Calculated, % H	Calculated, % S
XVII	C_5H_{11}	68,8	110—114 (0,9 mm)	1,0128	1,4361	51,92 51,99	10,08 9,87	15,18 14,87	$C_9H_{20}O_3S$	51,88	9,67	15,38
XVIII	iso-C_5H_{11}	68,3	104—107 (1 mm)	1,0411	1,4360	51,68 51,95	10,13 10,07	15,12 15,20	$C_9H_{20}O_3S$	51,88	9,67	15,38
XIX	C_6H_{13}	77,9	115—117 (0,7 mm)	1,0066	1,4384	53,80 53,92	9,97 9,99	14,33 14,17	$C_{10}H_{22}O_3S$	54,02	9,97	14,42
XX	C_7H_{15}	74,2	140—143 (1 mm)	0,9916	1,4420	55,84 56,24	10,28 9,80	13,43 13,85	$C_{11}H_{24}O_3S$	55,89	10,24	13,57
XXI	C_8H_{17}	78,8	140—144 (1 mm)	0,9806	1,4423	57,89 58,15	10,70 10,59	12,74 12,30	$C_{12}H_{26}O_3S$	57,56	10,47	12,81
XXII	C_9H_{19}	76,1	153—155 (1 mm)	0,9760	1,4440	59,65 59,62	10,53 10,75	12,53 12,57	$C_{13}H_{28}O_3S$	59,04	10,67	12,12
XXIII	$C_{10}H_{21}$	75,5	150—157 (1 mm)	0,9607	1,4454	60,22 60,16	11,14 10,90	11,40 11,35	$C_{14}H_{30}O_3S$	60,38	10,86	11,52
XXIV	$CH_2CH_2OCH_3$	33,7	95—98 (0,6 mm)	1,1311	1,4400	42,89 42,55	8,56 8,55	16,22 16,02	$C_7H_{16}O_4S$	42,84	8,21	16,34
XXV	$CH_2CH_2OC_2H_5$	69,0	125—127 (0,4 mm)	1,0986	1,4384	45,13 45,33	8,71 8,82	14,89 14,78	$C_8H_{18}O_4S$	45,69	8,62	15,25

TABLE 4. Repellent Activity of Derivatives of Butanesulfonic Acid in Relation to Fleas C. tesquorum (dose 40 g/m^2, exposure 1 min)

Compound	CRE (%) after treatment of the cloth	CRE (%) weeks after treatment					Compound	CRE, % after treatment of the cloth	CRE, % weeks after treatment				
		2	4	6	8	10			2	4	6	8	10
I	87	73	16	—	—	—	XIV	90	77	84	62	—	—
II	93	68	—	—	—	—	XV	81	61	—	—	—	—
III	49	—	—	—	—	—	XVI	64	—	—	—	—	—
IV	18	—	—	—	—	—	XVII	81	65	—	—	—	—
V	0	—	—	—	—	—	XVIII	100	62	—	—	—	—
VI	90	77	84	69	—	—	XIX	90	47	—	—	—	—
VII	95	67	—	—	—	—	XX	91	63	—	—	—	—
VIII	87	83	75	80	88	55	XXI	76	63	—	—	—	—
IX	75	68	—	—	—	—	XXII	91	46	—	—	—	—
X	63	—	—	—	—	—	XXIII	92	63	—	—	—	—
XI	81	56	—	—	—	—	XXIV	98	91	81	17	—	—
XII	90	62	—	—	—	—	XXV	97	96	81	75	73	45
XIII	47	—	—	—	—	—	N,N-Diethyl-m-toluamide	100	100	85	46	—	—

stored under these same conditions. Diethyltoluamide served as a standard. Results of examinations are presented in Table 4. As is seen, of the synthesized groups of compounds the most effect had the aliphatic esters of butanesulfonic acid, the CRE of the majority of which was greater than 90% upon fresh impregnation of the cloth. However, with the exception of the methoxyethyl (XXIV) and ethoxyethyl (XXV) esters, similar in strength and duration of effect to diethyltoluamide, taken as a standard, all compounds of this group were found to be unstable and virtually lost activity already in the course of the first two weeks.

All compounds of the group of aromatic esters of butanesulfonic acid also showed significant repellant activity, but among the most strongly acting of them, the phenyl (VI), o-cresyl (VII), m-cresyl (VIII), p-methoxyphenyl (XII), and o-chlorophenyl (XIV) esters, only (VI), (VIII), and (XIV) did not yield in length of effect to diethyltoluamide.

Of the N-alkylanilides of butanesulfonic acid, the methyl- and ethylanilides (I and II) showed expressed effectiveness, but at low stability. The remaining compounds of the given homologous series were found to be virtually inactive.

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