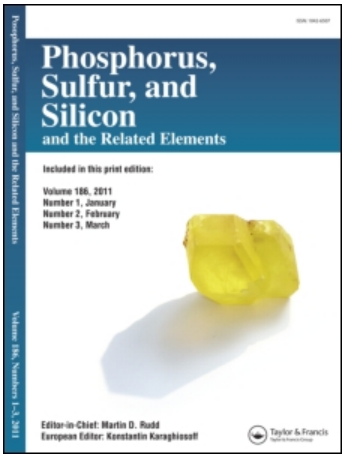


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

THE HALOID DISPLACEMENT BY AMMONIA AND AMINES IN 2(3)-CHLORO-3(2)-ALKYLTHIO-2-METHYLPROPANOIC ACID DERIVATIVES

D. Greiĉiute[a]; J. Kulys[a]; L. Rasteikiene[a]
[a] Institute of Biochemistry of the Academy of Sciences of the Lithuanian SSR, Vilnius, USSR

To cite this Article Greiĉiute, D. , Kulys, J. and Rasteikiene, L.(1977) 'THE HALOID DISPLACEMENT BY AMMONIA AND AMINES IN 2(3)-CHLORO-3(2)-ALKYLTHIO-2-METHYLPROPANOIC ACID DERIVATIVES', Phosphorus, Sulfur, and Silicon and the Related Elements, 3: 3, 261 — 267
To link to this Article: DOI: 10.1080/03086647708079932
URL: http://dx.doi.org/10.1080/03086647708079932

Phosphorus and Sulfur
1977, Vol. 3, pp. 261–267

THE HALOID DISPLACEMENT BY AMMONIA AND AMINES IN 2(3)-CHLORO-3(2)-ALKYLTHIO-2-METHYLPROPANOIC ACID DERIVATIVES

D. GREIČIUTE, J. KULYS* and L. RASTEIKIENE

Institute of Biochemistry of the Academy of Sciences of the Lithuanian SSR, Vilnius, USSR

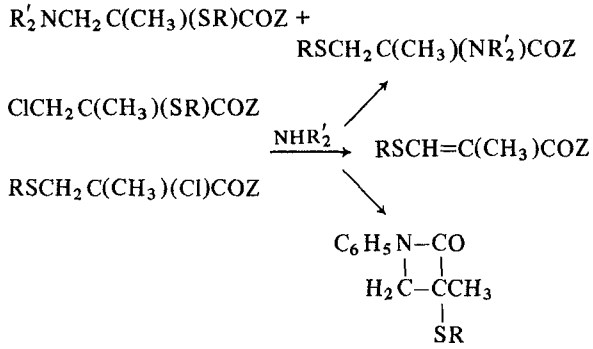
(*Received January 25, 1977*)

The reaction of derivatives of 2(3)-chloro-3(2)-alkylthio-2-methylpropanoic acids with ammonia in nitromethane has been found to yield a mixture of 2- and 3-aminosubstituted compounds. With dimethylamine and diethylamine in nitromethane (sulfolane) a mixture of alkylamino-substituted products as well as HCl elimination products has been obtained. Pure diethylamine has been shown to form mainly the products of HCl elimination. A mechanism for the displacement and elimination reactions via formation of various episulphonium ions as intermediates has been suggested.

RESULTS AND DISCUSSION

Derivatives of 2(3)-chloro-3(2)-alkylthioalkanoic acids easily undergo chlorine substitution when exposed to water, methanol and other nucleophilic reagents.[1-6] This paper deals with the synthesis of aminoalkylthioalkanoic acid derivatives via the transformations of 2(3)-chloro-3(2)-alkylthio-2-methylpropanoic acids by reaction with ammonia and amines in polar aprotic solvents, as well as in pure diethylamine.[7]

The products obtained by the reaction of ammonia and amines with the derivatives of 2(3)-chloro-3(2)-alkylthio-2-methylpropanoic acids according to the following scheme are listed in Table I.



R = CH_3, $CH_2C_6H_5$, C_6H_5
R' = H, CH_3, C_2H_5
Z = OCH_3, NHC_6H_5

SCHEME 1

As one can see from these data, HCl elimination occurs along with chlorine nucleophilic displacement. Thus the reactions of anilides and methyl esters of 2(3)-chloro-3(2)-alkylthio-2-methylpropanoic acids with ammonia in nitromethane gave only chlorine displacement products: a mixture of the corresponding 2- and 3-aminosubstituted compounds, 14–25, (Tables I, II), the ratio of the amines obtained being equal for both parent isomers (2- or 3-chloroderivatives). In the reaction of 3-chloro-2-methylthio-2-methylpropanoic acid anilide, 2, with ammonia in dioxane β-lactam-1-phenyl-3-methylthio-3-methyl-2-azetidinone was isolated together with aminosubstituted isomers.[4,6]

The reactions of dimethylamine in nitromethane with chloroderivatives, 1–4, 9–13, yielded mixtures of 2- and 3-N-dimethylaminosubstituted products, 26–35, with the same ratio as in the case of ammonia. The reaction of diethylamine with 1–4 and 9–12 in nitromethane resulted in formation of mixtures of 2- and 3-*N*-diethylaminosubstituted compounds, 36–43; the relative quantity of 2-*N*-diethylaminosubstitution being less than in the reactions with ammonia or dimethylamine. The ratio of isomeric diethylaminosubstitution of 36–41, in pure diethylamine, was closer to that of amino- or dimethylamino-substituted products.

In all cases, either with ammonia and amines in nitromethane or with pure diethylamine, considerable increase of the relative amount of 2-aminosubstituted isomers was observed when passing from the methylthiogroup, 1–4, to the benzylthiogroup, 5–8, and particularly to the phenylthiogroup, 9–12.

* To whom correspondence should be addressed.

TABLE I

Reaction of 2(3)-Chloro-3(2)-alkylthio-2-methylpropanoic Acids Derivatives with Ammonia and Amines

		Reaction in nitromethane														Reaction in pure diethylamine				
		Ammonia				Dimethylamine					Diethylamine									
			Product distribution (%)				Product distribution (%)					Product distribution (%)					Product distribution (%)			
No.	Initial compound (isomer ratio, %)	Time (hr)	2-NH_2	3-NH_2	β-lactam	Time (hr)	2-$N(CH_3)_2$	3-$N(CH_3)_2$	Product of HCl elimination	β-lactam	Time (hr)	2-$N(C_2H_5)_2$	3-$N(C_2H_5)_2$	Product of HCl elimination	β-lactam	Time (hr)	2-$N(C_2H_5)_2$	3-$N(C_2H_5)_2$	Product of HCl elimination	β-lactam
1	$CH_3SCH_2C(CH_3)ClCONHC_6H_5$	130	30	70	–	92	32	50	18	–	130	15	69	16	–	148	10	15	75	–
2	$ClCH_2C(CH_3)(SCH_3)CONHC_6H_5$	107	30	70	–	92	31	69	–	–	92	13	87	–	–	122	35	51	14	–
		107	9	9	21[a,c]						86	10	90[b]	–	–					
3	$CH_3SCH_2C(CH_3)ClCOOCH_3$ (40)	182	30	70	–	150	40	60	–	–	160	17	83	–	–	248	12	12	30[c]	–
4	$ClCH_2C(CH_3)(SCH_3)COOCH_3$ (60)																			
5	$C_6H_5CH_2SCH_2C(CH_3)ClCONHC_6H_5$	130	42	58	–															
6	$ClCH_2C(CH_3)(SCH_2C_6H_5)CONHC_6H_5$	130	45	55	–															
7	$C_6H_5CH_2SCH_2C(CH_3)ClCOOCH_3$ (60)	200	40	60	–															
8	$ClCH_2C(CH_3)(SCH_2C_6H_5)COOCH_3$ (40)																			
9	$C_6H_5SCH_2C(CH_3)ClCONHC_6H_5$	242	70	30	–	150	7	3	90	–	150	4	4	90	2	262	–	–	100	–
10	$ClCH_2C(CH_3)(SC_6H_5)CONHC_6H_5$	146	70	30	–	150	52	20	10	18	150	23	23	31	23	300	50	11	26	13
11	$C_6H_5SCH_2C(CH_3)ClCOOCH_3$ (30)	226	75	25	–	225	23	7	70	–	203	15	10	75	–	530	–	–	60[c]	–
12	$ClCH_2C(CH_3)(SC_6H_5)COOCH_3$ (70)																			
13	$ClCH_2C(CH_3)(SC_6H_5)CON(C_6H_5)_2$					150	50	50	–	–										

[a] Reaction in dioxane.

[b] Reaction in sulfolane.

[c] Reaction is not completed.

TABLE II
PMR Parameters of Derivatives of 2(3)-Chloro-3(2)-benzylthio-2-methylpropanoic Acids, 2(3)-Amino-3(2)-alkylthio-2-methylpropanoic Acids and Products of HCl Elimination

No.	Compound	Chemical shift, ppm							Coupling constant, J_{ab}, Hz
		δ_{CH_3}	$\delta C\begin{matrix}H_a\\H_b\end{matrix}$	δ_{SCH_3}	δ_{OCH_3}	δ_{NCH_3}	$\delta_{NCH_2CH_3}$	δ_{NHCO}	
5	$C_6H_5CH_2SCH_2C(CH_3)ClCONHC_6H_5$	1.78	2.83 3.08	3.65[a]				8.50	14
6	$ClCH_2C(CH_3)(SCH_2C_6H_5)CONHC_6H_5$	1.58	3.70 4.03	3.73[a]				8.45	11.3
7	$C_6H_5CH_2SCH_2C(CH_3)ClCOOCH_3$	1.69	2.80 3.10	3.65[a]	3.71				14
8	$ClCH_2C(CH_3)(SCH_2C_6H_5)COOCH_3$	1.50	3.38 3.98	3.76[a]	3.69				11
14	$CH_3SCH_2C(CH_3)(NH_2)CONHC_6H_5$	1.32	2.45 3.25	2.03				9.75	14
15	$NH_2CH_2C(CH_3)(SCH_3)CONHC_6H_5$	1.39	2.92 3.02	2.03				10.93	13
16	$CH_3SCH_2C(CH_3)(NH_2)COOCH_3$	1.30	2.59 2.86	2.11	3.69				14
17	$NH_2CH_2C(CH_3)(SCH_3)COOCH_3$	1.41	2.72 3.01	2.03	3.72				14
18	$C_6H_5CH_2SCH_2C(CH_3)(NH_2)CONHC_6H_5$	1.28	2.25 2.35	3.56 3.72[a]				9.60	14
19	$NH_2CH_2C(CH_3)(SCH_2C_6H_5)CONHC_6H_5$	1.45	3.00	3.80[a]				10.45	
20	$C_6H_5CH_2SCH_2C(CH_3)(NH_2)COOCH_3$	1.25	2.49 2.78	3.68[a]	3.60				13
21	$NH_2CH_2C(CH_3)(SCH_2C_6H_5)COOCH_3$	1.41	2.75 3.03	3.73[a]	3.65				13
22	$C_6H_5SCH_2C(CH_3)(NH_2)CONHC_6H_5$	1.28	3.03 3.49					9.52	14
23	$NH_2CH_2C(CH_3)(SC_6H_5)CONHC_6H_5$	1.22	2.92 2.98					10.47	14
24	$C_6H_5SCH_2C(CH_3)(NH_2)COOCH_3$	1.32	3.02 3.38		3.42				14
25	$NH_2CH_2C(CH_3)(SC_6H_5)COOCH_3$	1.42	3.28[b]		3.58				
26	$CH_3SCH_2C(CH_3)[N(CH_3)_2]CONHC_6H_5$	1.22	2.68 2.88	1.98		2.30		9.08	14
27	$(CH_3)_2NCH_2C(CH_3)(SCH_3)CONHC_6H_5$	1.37	2.59 2.78	2.06		2.47		10.65	13.5
28	$CH_3SCH_2C(CH_3)[N(CH_3)_2]COOCH_3$	1.37	2.46 2.83	2.08	3.68	2.26			13.5
29	$(CH_3)_2NCH_2C(CH_3)(SCH_3)COOCH_3$	1.44	2.74 2.82	2.03	3.71	2.26			13
30	$C_6H_5SCH_2C(CH_3)[N(CH_3)_2]CONHC_6H_5$	1.27	3.26			2.37		9.01	
31	$(CH_3)_2NCH_2C(CH_3)(SC_6H_5)CONHC_6H_5$	1.23	2.78			2.48		10.25	
32	$C_6H_5SCH_2C(CH_3)[N(CH_3)_2]COOCH_3$	1.41	3.28 3.46		3.60	2.28			13
33	$(CH_3)_2NCH_2C(CH_3)(SC_6H_5)COOCH_3$	1.15	2.70 2.94		3.56	2.24			13
34	$C_6H_5SCH_2C(CH_3)[N(CH_3)_2]CON(C_6H_5)_2$	1.03	3.11			2.17			
35	$(CH_3)_2NCH_2C(CH_3)(SC_6H_5)CON(C_6H_5)_2$	1.28	2.09			2.29			
36	$CH_3SCH_2C(CH_3)[N(C_2H_5)_2]CONHC_6H_5$	1.36	2.88[b]	2.01			1.15	9.36	
37	$(C_2H_5)_2NCH_2C(CH_3)(SCH_3)CONHC_6H_5$	1.38	2.74[b]	2.04			1.05	10.65	
38	$CH_3SCH_2C(CH_3)[N(C_2H_5)_2]COOCH_3$	1.41	3.10	2.06	3.62		1.04		
39	$(C_2H_5)_2NCH_2C(CH_3)(SCH_3)COOCH_3$	1.42	2.56[b]	2.03	3.66		0.95		
40	$C_6H_5SCH_2C(CH_3)[N(C_2H_5)_2]CONHC_6H_5$	1.26	3.25 3.45				1.16	9.32	14
41	$(C_2H_5)_2NCH_2C(CH_3)(SC_6H_5)CONHC_6H_5$	1.42	2.83[b]				1.05	10.43	
42	$C_6H_5SCH_2C(CH_3)[N(CH_2H_5)_2]COOCH_3$	1.25	3.39[b]		3.57		1.13		
43	$(C_2H_5)_2NCH_2C(CH_3)(SC_6H_5)COOCH_3$	1.47	2.67[b]		3.61		1.05		
44	$CH_3SCH{=}C(CH_3)CONHC_6H_5$	1.93	6.37[c]	2.45				8.63	
45	$C_6H_5SCH{=}C(CH_3)CONHC_6H_5$	2.07	6 63[c]					8.60	
46	$CH_3SCH{=}C(CH_3)COOCH_3$	1.81		2.42	3.65				
47	$C_6H_5SCH{=}C(CH_3)COOCH_3$	1.93	7.49[c]		3.69				

[a] Signal of $SCH_2C_6H_5$ methylene protons.
[b] Signals of methylene protons are overlapped.
[c] Methine signals.

In addition to the substitution products in the reaction of parent, 1, and 9–12 with amines in nitromethane HCl elimination products, 44, 45, 47, were obtained. In pure diethylamine the reaction mainly proceeds with HCl elimination to give unsaturated products, 44–47, from chloroderivatives 1–4 and 9–12, both isomeric anilides, either, 1, 2, or 9, 10, forming the same elimination products, 44, 45. The yield of unsaturated phenylthioderivatives was higher than that of methylthio-derivatives. Anilide, 10, in pure diethylamine as well as with amines in nitromethane was found to form, along with aminoderivatives, β-lactam-1-phenyl-3-phenylthio-3-methyl-2-azetidinone.[4,6]

The kinetic measurements of the transformation of 2-chloroanilides, 1 and 9, in the solution of diethylamine in nitromethane showed the rate of formation of diethylamine hydrochloride to be independent of diethylamine concentration. The estimated values of first-order reaction constants are given in Table III. In the case of isomeric 3-chloroanilides, 2 and 10, the relative rate of hydrochloride formation falls with time, this being caused by isomerization of 3-chloroderivatives 2 and 10 to less reactive 2-chloroderivatives, 1 and 9.[3] The initial rate of the reaction, however, does not depend on the amine concentration, indicating that 3-chloroanilides 2 and 10 also react by a monomolecular mechanism.

The equal ratio of aminosubstituted products in the displacement reactions of isomeric 2- and 3-chloroanilides 1 and 2 and 9 and 10 with ammonia shows that these products form from the same intermediate.[3,6] It is expected that the intermediate, similarly to other nucleophilic chlorine displacement reactions in 2-chloro-thioethers, is the episulphonium ion.[8,9] The formation of this ion in the reactions of the compounds under investigation apparently represents the rate-limiting step of the process. It is for this reason that the reactions are described by first-order kinetics. In this way the ratio of 2- and 3-aminosubstituted products is determined by the electronic and steric factors of the episulphonium ions. In these ions, formed from phenylthioderivatives, the 2-carbon atom is attacked more easily. The introduction in the nucleophile of a bulky ethyl radical, as in the case of diethylamine, apparently leads to steric hindrance of the attack on the 2-carbon atom with the result that the yield of 2-amino isomers falls. The formation of HCl elimination products by the first-order reaction mechanism (Tables I, III, compounds 9 and 10) favors the suggestion that this elimination proceeds via intermediates whose formation is the rate-limiting step of the transformation. Supposedly these intermediates involve an asymmetric, undissociated episulphonium ion similar to that suggested in literature,[10,11] in which the alkylthiogroup is linked with the 3-carbon atom. The decrease of electron density in such ions, when the methylthiogroup is changed to the phenylthio group, increases the rate of HCl elimination. The substitution of polar solvent nitro-methane by less polar diethylamine also results in formation of undissociated episulphonium ion and again in an increase of the HCl elimination rate.

TABLE III
Kinetic Data of 2(3)-Chloro-3(2)-alkylthio-2-methylpropanoic Acids Anilides Reaction with Diethylamine in Nitromethane at 50° (Concentration of Anilides 0.04 M)

No.	Amine concentration (M)	$k \times 10^3$, min^{-1}
1	1.0	2.1
	0.5	2.3
2	1.0	57
	0.5	40
9	1.0	0.46
	0.5	0.44
10	1.0	2.0
	0.5	2.0

Similarly to the reactions of anilides of these haloid alkanoic acids with alkali[4,5] or sodium methylate,[6] the production of β-lactams in reactions with amines is associated with the formation of imine forms of the anilides. This process is competitative with the monomolecular transformation of haloid derivatives. In nonpolar medium, e.g. dioxane (Table I), since the imine forms of anilides are stable, the formation of episulphonium ions is thermodynamically unfavorable, consequently the yield of lactams in this medium increases considerably.

EXPERIMENTAL

Derivatives of 2(3)-chloro-3(2)-methyl(phenyl)thio-2-methylpropanoic acids, 1–4 and 9–13, were prepared according to previously reported techniques.[1,3,4,12]

Derivatives of 2(3)-chloro-3(2)-benzylthio-2-methylpropanoic acids, 6–8, were obtained by addition of benzylsulphenyl chloride to derivatives of methacrylic acid according to the well known procedure.[12] 3-Benzylthio-2-chloro-2-methylpropanoic acid anilide, 5, was obtained by heating of isomeric anilide, 6, in acetonitrile.[3] The yield and microanalysis data are summarized in Table IV.

General method of synthesis of derivatives of 2(3)-amino-3(2)-alkylthio-2-methylpropanoic acids, 14–43.[7]

0.01 Mole of derivative of 2(3)-chloro-3(2)-alkylthio-2-methylpropanoic acid, 1–13, was dissolved in 100 ml of 1 N amine solution in nitromethane (sulfolane, dioxane) or in pure diethylamine. Reaction mixture was heated at 50° in a sealed tube for a definite time. The solvent was removed under

TABLE IV
Analytical Data of Derivatives of 2(3)-Chloro-3(2)-benzylthio-2-methylpropanoic Acids, 2(3)-Amino-3(2)-alkylthio-2-methylpropanoic Acids and Products of HCl Elimination

Initial compound, No. (isomer ratio, %)	Reaction product, No. (product distribution, %)	Yield, %	M.p., B.p., °C (mm Hg)	Found, %					Formula	Calculated, %				
				C	H	N	S	Cl		C	H	N	S	Cl
	5	41	45–47 (from petroleum ether)	63.81	5.90	4.30	9.69	12.00	$C_{17}H_{18}ClNOS$	63.85	5.63	4.38	10.01	11.11
	6	74	80–82 (from ether and petroleum ether)	63.80	5.70	4.58	9.58	10.58	$C_{17}H_{18}ClNOS$	63.85	5.63	4.38	10.01	11.11
	7, 8 (60, 40)	60	130–138(3)	55.87	5.82	–	12.10	13.42	$C_{12}H_{15}ClO_2S$	55.70	5.80	–	12.37	13.73
1	14,15 (30, 70)	93	–	59.30	7.10	12.67	13.63	–	$C_{11}H_{16}N_2OS$	58.93	7.14	12.50	14.28	–
2		69	–	58.99	7.43	12.55	13.40	–	$C_{11}H_{16}N_2OS$	58.93	7.14	12.50	14.28	–
3, 4 (40, 60)	16, 17 (30, 70)	56	66 (3)	44.48	8.00	8.83	21.30	–	$C_6H_{13}NO_2S$	44.17	7.97	8.59	19.63	–
6	18, 19 (45, 55)	90	–	68.09	6.65	9.40	10.21	–	$C_{17}H_{20}N_2OS$	68.00	6.67	9.33	10.67	–
7, 8 (60, 40)	20, 21 (40, 60)	74	130–133 (3)	59.80	7.40	5.48	12.43	–	$C_{12}H_{17}NO_2S$	60.25	7.11	5.85	13.38	–
9	22, 23 (70, 30)	86	–	67.17	6.20	9.91	10.90	–	$C_{16}H_{18}N_2OS$	67.13	6.29	9.79	11.19	–
10		78	–	67.30	6.30	9.80	11.40	–	$C_{16}H_{18}N_2OS$	67.13	6.29	9.79	11.19	–
11, 12 (30, 70)	24, 25 (75, 25)	48	107 (3)	58.83	6.62	6.09	13.05	–	$C_{11}H_{15}NO_2S$	58.67	6.67	6.22	14.22	–
1	26, 27 (38, 62)	81	–	62.20	7.89	11.29	12.90	–	$C_{13}H_{20}N_2OS$	61.90	7.94	11.11	12.70	–
2		88	–	61.77	7.93	11.24	12.83	–	$C_{13}H_{20}N_2OS$	61.90	7.94	11.11	12.70	–

TABLE IV—*continued*

Initial compound, No. (isomer ratio, %)	Reaction product, No. (product distribution, %)	Yield, %	M.p., B.p., °C (mm Hg)	Found, %					Formula	Calculated, %				
				C	H	N	S	Cl		C	H	N	S	Cl
3, 4 (40, 60)	28, 29 (40, 60)	56	69 (3)	50.26	9.07	7.49	16.62	–	$C_8H_{17}NO_2S$	50.25	8.90	7.33	16.75	–
10	30, 31 (75, 25)	70	–	68.68	7.00	9.23	11.30	–	$C_{18}H_{22}N_2OS$	68.79	7.01	9.82	10.19	–
11, 12 (30, 70)	32, 33 (75, 25)	24	112 (3)	61.30	7.25	5.51	13.30	–	$C_{13}H_{19}NO_2S$	61.66	7.55	5.53	12.64	–
13	34, 35 (50, 50)	78	–	73.83	6.79	7.23	8.00	–	$C_{24}H_{26}N_2OS$	73.84	6.92	7.18	8.20	–
1	36, 37 (13, 87)	72	–	64.49	8.80	10.10	10.75	–	$C_{15}H_{24}N_2OS$	64.28	8.57	10.00	11.43	–
2		96	–	64.20	8.70	10.08	11.13	–	$C_{15}H_{24}N_2OS$	64.28	8.57	10.00	11.43	–
2	36, 37 (10, 90)[a]	98	–	64.20	8.80	10.09	11.45	–	$C_{15}H_{24}N_2OS$	64.28	8.57	10.00	11.43	–
2	36, 37 (50, 50)[b]	65	–	64.23	8.70	9.66	11.57	–	$C_{15}H_{24}N_2OS$	64.28	8.57	10.00	11.43	–
3, 4 (40, 60)	38, 39 (17, 83)	69	80 (3)	54.54	9.39	6.84	13.24	–	$C_{10}H_{21}NO_2S$	54.79	9.59	6.47	14.61	–
10	40, 41 (50, 50)	72	–	70.04	7.35	8.27	9.26	–	$C_{20}H_{26}N_2OS$	70.17	7.60	8.19	9.36	–
11, 12 (30, 70)	42, 43 (20, 80)	16	116 (3)	63.78	8.00	5.01	11.56	–	$C_{15}H_{23}NO_2S$	64.06	8.18	4.98	11.39	–
1	44	47	145–147 (from methanol)	63.47	6.17	7.02	15.02	–	$C_{11}H_{13}NOS$	63.77	6.28	6.77	15.46	–
9	45	68	155–157 (from methanol)	71.30	5.80	5.02	11.43	–	$C_{16}H_{15}NOS$	71.37	5.57	5.20	11.89	–

[a] Reaction in sulfolane.
[b] Reaction in pure diethylamine.

reduced pressure. Absolute ether was added and precipitated amine hydrochloride filtered. Stirred filtrate was acidified dropwise at 0° with 0.1 N solution of HCl in dry ether. The hydrochloride was filtered, dissolved in water, the solution washed with ether and neutralized by adding sodium carbonate solution dropwise. (In case of sulfolane the reaction mixture was poured in water). Reaction products were extracted into ether and dried with $MgSO_4$. The clear solution was evaporated under reduced pressure. The residue in the case of methyl esters was distilled in vacuo; HCl elimination products were crystallized. Reaction mixtures and isolated products were analysed by PMR. Yield and microanalysis data are listed in Table IV.

PMR spectra of the compounds were recorded in CCl_4 on an R-22 spectrometer at 90 MHz. As reference HMDS was used. Chemical shifts against TMS are given in Table II. The determination of structure of anilides of 2(3)-amino-3(2)-alkylthio-2-methylpropanoic acids was based upon investigation of H-bonding between anilide protons and the 3-aminogroup and by acetylation of aminogroups and double resonance analysis.[13] The structure of esters of 2(3)-amino-3(2)-alkylthio-2-methylpropanoic acids was determined on the basis of chemical shifts of the corresponding groups established for anilides. In the case of alkylaminoderivatives the position of alkylaminogroups was determined by variable temperature investigations and on the basis of broadening of a quadrupole signal-line of protons neighboring nitrogen.

Kinetic measurements were made on a self-recording conductometer.[2] The apparatus was calibrated with the solution of diethylamine hydrochloride in nitromethane for each diethylamine concentration. The concentrations of the latter (1.0 M and 0.05 M) in kinetic measurements were chosen so that in the reaction practically only diethylamine hydrochloride would be formed as an ionic product. The reaction constants for the compounds 2 and 10 were determined from the initial rates and for compounds 1 and 9 either by a modified Gugenheim method or by means of a semilogarithmic transformation.[2,3]

Nitromethane was distilled through a column. Ammonia, dimethylamine and diethylamine were purified with alkali and the latter was distilled.

REFERENCES

1. L. Rasteikiene, D. Greičiute, M. G. Lin'kova and I. L. Knunyants, *Izv. Akad. Nauk SSSR, Ser. Khim.* **488** (1972)
2. L. Rasteikiene, L. Gurviciene and J. Kulys, *Zh. Vses. Khim. Obshchest.* **17**, 701 (1972).
3. D. Greičiute, J. Kulys and L. Rasteikiene, *Zh. Org. Khim.* **9**, 1837 (1973).
4. D. Greičiute, J. Kulys and L Rasteikiene, *Zh. Org. Khim.* **10**, 436 (1974).
5 D. Greičiute, J. Kulys and L. Rasteikiene, *Liet. TSR Mokslu Akad. Darb., Ser. B (3)* 71 (1975).
6. D. Greičiute, J. Kulys and L. Rasteikiene, *Zh. Org. Khim.* **11**, 1157 (1957).
7. J. Kulys, D. Greičiute and L. Rasteikiene, U.S.S.R. Patent application, No. 2009662/23-4, claims allowed. Oct. 1975.
8 P. D. Bartlett and C. G. Swain, *J. Am. Chem. Soc.* 71, 1406 (1949).
9. N. Kharasch in *Organic Sulfur Compounds*, Vol. I, N. Kharasch, Ed. (Pergamon Press, Inc., New York, N.Y., 1961) Chapter 32, p. 375.
10. G. H. Schmid and V. M Csizmadia, *Can. J. Chem.* **50**, 2465 (1972).
11. R. Bird and Ch. J. M. Stirling, *J. Chem. Soc.* Perkin Trans. **II**, 1221 (1973).
12. M. G. Lin'kova, D. Greičiute, Z. Stumbrevičiute and I. L. Knunyants, *Izv. Akad. Nauk SSSR, Ser. Khim.* 1872 (1968).
13. D. Greičiute, J. Kulys and L. Rasteikeine, *Liet. TSR Mokslu Akad. Darb., Ser. B (5)* **85** (1976).