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SHORT COMMUNICATIONS

N-Chloroacyl Derivatives of Valine Esters

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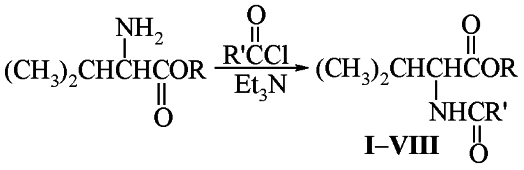
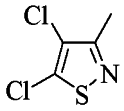
Amino acids derivatives, in particular N-acylamino acids, thanks to their physiological activity are extensively used as pharmaceutical, pesticides, and in production of cosmetics [1]. Therefore the synthesis of new representatives of this class compounds and testing of their biological activity is an important task. Here we report on the synthesis of N-acyl derivatives of valine methyl and ethyl esters containing in the acyl moieties several chlorine atoms.

The acyl derivatives were prepared by reaction of valine methyl and ethyl esters with 3,4,4-trichloro-3-butenoyl, 3,4,4,4-tetrachloro-2-butenoyl, 3,3,4,4,4-



I–VIII

R = CH_3 (**I**–**IV**), CH_2CH_3 (**V**–**VIII**); R' = $CCl_3CCl{=}CH$ (**I, V**), $CCl_2{=}CClCH_2$ (**II, VI**), $CCl_3CCl_2CH_2$ (**III, VII**).



(IV, VIII)

Table 1. ^{1}H NMR spectra of N-acyl derivatives $(CH_3)_2CHCH(COOR)NHCOR'$, δ, ppm

Compd. no.	$(CH_3)_2CH$	R	R'	CH	NH
I	1.00 d (3H, *J* 6.8 Hz), 0.96 d (3H, *J* 6.8 Hz), 2.02–2.48 m (1H)	3.77 s (3H)	7.11 s (1H)	4.70 d (*J* 8.6 Hz), 4.64 d (*J* 8.6 Hz)	6.60–6.80
II	0.90 d (3H, *J* 6.9 Hz), 0.94 d (3H, *J* 6.9 Hz), 1.96–2.40 m (1H)	3.75 s (3H)	3.59 s (2H)	4.61 d (*J* 8.7 Hz), 4.55 d (*J* 8.7 Hz)	6.07–6.40
III	0.90 d (3H, *J* 6.8 Hz), 0.95 d (3H, *J* 6.9 Hz), 1.98–2.41 m (1H)	3.71 s (3H)	3.52 s (2H)	4.65 d (*J* 8.6 Hz), 4.60 d (*J* 8.6 Hz)	6.37–6.63
IV[a]	1.06 d (3H, *J* 6.8 Hz), 1.12 d (3H, *J* 6.7 Hz), 2.12–2.60 m (1H)	3.52 s (3H)	–	5.08 d (*J* 8.8 Hz), 5.02 d (*J* 8.8 Hz)	7.66–7.97
V	0.92 d (3H, *J* 6.7 Hz), 0.96 d (3H, *J* 6.9 Hz), 2.02–2.49 m (1H)	1.29 t (3H, *J* 7.1 Hz), 4.23 q (2H, *J* 7.2 Hz)	7.10 s (1H)	4.69 d (*J* 8.7 Hz), 4.63 d (*J* 8.7 Hz)	6.47–6.82
VI	0.90 d (3H, *J* 6.8 Hz), 0.95 d (3H, *J* 6.8 Hz), 1.98–2.44 m (1H)	1.28 t (3H, *J* 7.1 Hz), 4.21 q (2H, *J* 7.1 Hz)	3.59 s (2H)	4.59 d (*J* 8.7 Hz), 4.53 d (*J* 8.7 Hz)	6.03–6.36
VII	0.95 d (3H, *J* 6.8 Hz), 1.0 d (3H, *J* 6.9 Hz), 1.99–2.47 m (1H)	1.29 t (3H, *J* 7.1 Hz), 4.22 q (2H, *J* 7.1 Hz)	3.57 s (2H)	4.68 d (*J* 8.6 Hz), 4.62 d (*J* 8.6 Hz)	6.47–6.84
VIII[a]	1.04 d (3H, *J* 6.7 Hz), 1.10 d (3H, *J* 6.7 Hz), 2.16–2.65 m (1H)	1.12 t (3H, *J* 7.0 Hz), 4.13 q (2H, *J* 7.0 Hz)	–	5.11 d (*J* 8.8 Hz), 5.05 d (*J* 8.8 Hz)	7.70–8.01

[a] Solvent deuterobenzene.

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Table 2. Yields, physico-chemical characteristics, and elemental analyses of N-acyl derivatives of valine esters

Compd. no.	Yield, %	mp, °C	IR spectrum, ν, cm^{-1}			Found, %				Formula	Calculated, %			
			NH	CO (amide)	COOR	C	H	Cl	N		C	H	Cl	N
I	80	86–88	1545	1647	1738	35.53	3.80	42.14	3.92	$C_{10}H_{13}Cl_4NO_3$	35.64	3.89	42.08	4.16
II	82	75–77	1546	1651	1745	39.85	4.78	35.01	4.58	$C_{10}H_{14}Cl_3NO_3$	39.69	4.66	35.15	4.63
III	81	110–113	1553	1657	1746	32.30	3.91	47.52	3.56	$C_{10}H_{14}Cl_5NO_3$	32.16	3.78	47.46	3.75
IV	78	48–50	1540	1659	1745	38.84	4.06	22.62	8.79	$C_{10}H_{12}Cl_2N_2O_3S$	38.60	3.89	22.79	9.00
V	79	77–78	1545	1640	1733	37.79	4.54	40.62	3.76	$C_{11}H_{15}Cl_4NO_3$	37.64	4.31	40.40	3.99
VI	80	72–75	1545	1653	1726	41.97	5.01	33.72	4.18	$C_{11}H_{16}Cl_3NO_3$	41.73	5.09	33.59	4.42
VII	80	103–106	1557	1656	1741	34.28	4.27	45.93	3.52	$C_{11}H_{16}Cl_5NO_3$	34.09	4.16	45.74	3.61
VIII	75	40–42	1543	1660	1737	40.74	4.40	21.67	8.48	$C_{11}H_{14}Cl_2N_2O_3S$	40.63	4.34	21.80	8.61

pentachlorobutanoyl chlorides, and 4,5-dichlorothiazole-3-carbonyl chloride in the presence of triethylamine in ethyl ether solution.

Compounds **I–VIII** synthesized are solids soluble in the majority of organic solvents. Their composition and structure were confirmed by ^{1}H NMR spectra (Table 1), IR spectra, and elemental analyses (Table 2).

Acyl derivatives of valine esters. General preparation procedure. To a solution of 2 mmol of an appropriate valine ester in 75 ml of anhydrous ethyl ether was added 0.21 g (2.08 mmol) of triethylamine and then dropwise 2 mmol of acyl chloride in 25 ml of ether. The reaction mixture was stirred for 5 h and then filtered. The filtrate was concentrated by distilling off the solvent in a vacuum and then treated with 40 ml of cold hexane. The precipitate was separated from the solvent, washed with cold hexane, and dried in a vacuum. The compounds were purified by reprecipitation with hexane from ether solution. Yields of compounds and their melting points are listed in Table 2.

IR spectra were measured on Fourier IR spectrometer Protege-460 from samples pelleted with KBr. ^{1}H NMR spectra were registered on spectrometer Tesla BS-567A from solutions in deuterochloroform or deuterobenzene, chemical shifts were measured relative to TMS. The initial valine methyl [2] and ethyl [3] esters and acyl chlorides [4] were prepared by known procedures.

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