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Competitive Formation of β-Amino Acids, Propenoic, and Ylidenemalonic Acids by the Rodionov Reaction from Malonic Acid, Aldehydes, and Ammonium Acetate in Alcoholic Medium

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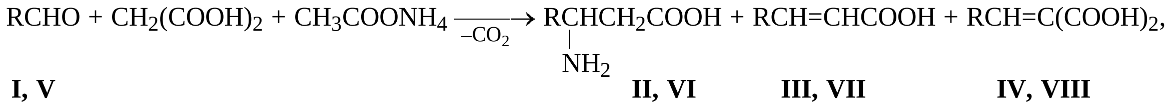
Abstract—The Rodionov reaction of 49 available aliphatic and aromatic aldehydes with malonic acid and ammonium acetate in alcoholic medium, resulting in formation of β-amino acids, propenoic, and ylidenemalonic acids, was studied. Certain regioselectivity regularities of the reaction were revealed. Among the variety of ketones studied, cyclohexanone is the only whose reaction yields a β-amino acid. Unusual dehydrofluorination of 6-chloro-2-fluorocinnamic acid under the Rodionov reaction was discovered.

Amino acids as compounds containing two reaction centers in their molecules present an undeniable interest as intermediates in fine organic synthesis. Among a great variety of amino acids, β-amino acids are hardly available and, therefore, the least studied. One of the known synthetic approaches to β-amino acids involves the Rodionov reaction of aldehydes with malonic acid and ammonia [1–10].

In the present work we made an attempt, in preparative purposes, the analyze Rodionov reaction products for a wide range of carbonyl compounds. Therewith, the most synthetically convenient modification of the Rodionov reaction was used, in which ammonia is generated from ammonium acetate.

It was found that aldehydes **I** and **V** react with malonic acid and ammonium acetate in a 1 : 1.1 : 2.3 molar ratio in 1-butanol or ethanol under reflux to form β-amino acids **II** and **VI**, propenoic acids **III** and **VII**, and ylidenemalonic acids **IV** and **VIII** in various ratios, according to the following scheme.



$$\underset{\textbf{I, V}}{RCHO} + CH_2(COOH)_2 + CH_3COONH_4 \xrightarrow[-CO_2]{} \underset{\textbf{II, VI}}{RCH(NH_2)CH_2COOH} + \underset{\textbf{III, VII}}{RCH{=}CHCOOH} + \underset{\textbf{IV, VIII}}{RCH{=}C(COOH)_2},$$

I–**IV**, R = 4-$CH_3OC_6H_4$ (**a**), 4-$C_2H_5OC_6H_4$ (**b**), 4-$(CH_3)_2CHOC_6H_4$ (**c**), 4-$CH_3(CH_2)_3OC_6H_4$ (**d**), 4-$(CH_3)_2CHCH_2OC_6H_4$ (**e**), 4-$(CH_3)_2CH(CH_2)_2OC_6H_4$ (**f**), 4-$H_2NC(O)CH_2OC_6H_4$ (**g**), 4-$C_6H_5CH_2OC_6H_4$ (**h**), 4-C_2H_5O-3-$CH_3OC_6H_3$ (**i**), 4-$(CH_3)_2CHO$-3-$CH_3OC_6H_3$ (**j**), 4-$(CH_3)_2CHCH_2O$-3-$CH_3OC_6H_3$ (**k**), 4-$H_2NC(O)CH_2O$-3-$CH_3OC_6H_3$ (**l**), 4-$H_2NC(O)\cdot CH_2O$-3-$C_2H_5OC_6H_3$ (**m**), 4-$(CH_3)_2CHO$-3-$C_2H_5OC_6H_3$ (**n**), 3-HOC_6H_4 (**o**), 3-$C_6H_5OC_6H_4$ (**p**), 3-$C_6H_5CH_2OC_6H_4$ (**q**), 3-$C_2H_5OC_6H_4$ (**r**), 2-$C_2H_5OC_6H_4$ (**s**), 2-$(CH_3)_2CHOC_6H_4$ (**t**), 2-$C_6H_5CH_2OC_6H_4$ (**u**), 2,3-$(CH_3O)_2C_6H_3$ (**v**), 3,4-$(CH_3O)_2C_6H_3$ (**w**), 2,5-$(CH_3O)_2C_6H_3$ (**x**), 3,4,5-$(CH_3O)_3C_6H_2$ (**y**), 3,5-$[(CH_3)_3C]_2$-4-HOC_6H_2 (**z**), 3,4-$(CH_3O)_2$-6-BrC_6H_2 (**a'**). **V**–**VIII**, R = 4-FC_6H_4 (**a**), 4-$(CH_3)_2NC_6H_4$ (**b**), 4-$CH_3C_6H_4$ (**c**), 3-BrC_6H_4 (**d**), 4-pyridyl (**e**), 3-pyridyl (**f**), 2-ClC_6H_4 (**g**), 2-$O_2NC_6H_4$ (**h**), 1-(4'-nitrophenyl)pyrrol-2-yl (**i**), 1-(3'-nitrophenyl)pyrrol-2-yl (**j**), 4-Cl-3-$O_2NC_6H_3$ (**k**), 2-furyl (**l**), 5-methyl-2-furyl (**m**), 2-thienyl (**n**), 3-methyl-2-thienyl (**o**), $(CH_3)_2CH$ (**p**), $CH_3CH_2CH_2$ (**q**), $(CH_3)_2CHCH_2$ (**r**), $CH_3(CH_2)_3$ (**s**), $(CH_3)_3CCH_2CH(CH_3)CH_2$ (**t**).

In general, 1-butanol proved to be a preferred solvent from the preparative viewpoint than ethanol, since, having a higher boiling point, it allows more effective separation of reaction products. Therefore, ethanol was applied only with thermally labile furan and thiophene derivatives. The yields of products **II**–**VIII** are listed in Table 1, and the physicochemical characteristics of the products, supportive of their structure, are given in Table 2.

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Table 1. Yields and molecular ions (*m/z*) of amino acids **IIa**–**IIa**' and **VIa**–**VIt**, 3-R-acrylic acids **IIIa**–**IIIa**' and **VIIa**–**VIIt**, and R-methylenemalonic acids **IVa**–**IVa**' and **VIIIa**–**VIIIt**, formed by reactions of aromatic and aliphatic aldehydes with malonic acid and ammonium acetate in alcoholic media[a]

Starting RCHO	$RCH(NH_2)CH_2COOH$			$RCH{=}CHCOOH$		$RCH{=}C(COOH)_2$	
	comp. no.	yield, %	*m/z*, $[M]^{+\cdot}$	comp. no.	yield, %	comp. no.	yield, %
Ia	**IIa**	60	195	**IIIa**	14	**IVa**	0
Ib	**IIb**	60	209	**IIIb**	14	**IVb**	0
Ic	**IIc**	60	223	**IIIc**	15	**IVc**	0
Id	**IId**	45	237	**IIId**	23	**IVd**	0
Ie	**IIe**	54	237	**IIIe**	33	**IVe**	0
If	**IIf**	50	251	**IIIf**	34	**IVf**	0
Ig	**IIg**	0	–	**IIIg**	0	**IVg**[b]	93
Ih	**IIh**	64	271	**IIIh**	12	**IVh**	0
Ii	**IIi**	64	239	**IIIi**	19	**IVi**	0
Ij	**IIj**	57	253	**IIIj**	3	**IVj**	0
Ik	**IIk**	55	267	**IIIk**	17	**IVk**	0
Il	**IIl**	62	268	**IIIl**	25	**IVl**	0
Im	**IIm**	62	282	**IIIm**	20	**IVm**	0
In	**IIn**	57	267	**IIIn**	0	**IVn**	0
Io	**IIo**	52	181	**IIIo**	11	**IVo**	0
Ip	**IIp**	43	257	**IIIp**	31	**IVp**	0
Iq	**IIq**	41	271	**IIIq**	35	**IVq**	0
Ir	**IIr**	22	209	**IIIr**	47	**IVr**	0
Is	**IIs**	21	209	**IIIs**	42	**IVs**	0
It	**IIt**	11	223	**IIIt**	41	**IVt**	0
Iu	**IIu**	26	271	**IIIu**	39	**IVu**	0
Iv	**IIv**	40	225	**IIIv**	23	**IVv**	0
Iw	**IIw**	34	225	**IIIw**	18	**IVw**	0
Ix	**IIx**	0	–	**IIIx**	36	**IVx**	0
Iy	**IIy**	34	255	**IIIy**	22	**IVy**	0
Iz	**IIz**	0	–	**IIIz**	40	**IVz**	0
Ia'	**IIa**'	0	–	**IIIa**'	30	**IVa**'[c]	45
Va	**VIa**	55	183	**VIIa**	17	**VIIIa**	0
Vb	**VIb**	0	–	**VIIb**	33	**VIIIb**	0
Vc	**VIc**	52	179	**VIIc**	21	**VIIIc**	0
Vd	**VId**	62	244	**VIId**	9	**VIIId**	0
Ve	**VIe**	0	–	**VIIe**	62	**VIIIe**	0
Vf	**VIf**	15	166	**VIIf**	38	**VIIIe**	0
Vg	**VIg**	64	199	**VIIg**	9	**VIIIg**	0
Vh	**VIh**	22	210	**VIIh**	0	**VIIIh**[d]	45
Vi	**VIi**	0	–	**VIIi**	2	**VIIIi**[e]	80
Vj	**VIj**	0	–	**VIIj**	4	**VIIIj**[f]	75
Vk	**VIk**	8	244	**VIIk**	27	**VIIIk**[g]	35
Vl	**VIl**	31	155	**VIIl**	34	**VIIIl**	0
Vm	**VIm**	19	169	**VIIm**	45	**VIIIm**	0
Vn	**VIn**	35	171	**VIIn**	37	**VIIIn**	0
Vo	**VIo**	0	–	**VIIo**	31	**VIIIo**[h]	15
Vp	**VIp**	41	131	**VIIp**	41	**VIIIp**	0
Vq	**VIq**	19	131	**VIIq**	59	**VIIIq**	0
Vr	**VIr**	31	145	**VIIr**	46	**VIIIr**	0
Vs	**VIs**	15	145	**VIIs**	51	**VIIIs**	0
Vt	**VIt**	17	201	**VIIt**	–	**VIIIt**	–

[a] The yields are calculated per taken aldehyde. *m/z*, $[M]^{+\cdot}$: [b] 265, [c] 331, [d] 237, [e] 302, [f] 302, [g] 271, [h] 212.

Table 2. Melting or boiling points, ^{1}H NMR and mass spectra, and elemental analyses of compounds **I–XII**

Comp. no.	mp, °C, or bp, °C (*p*, mm Hg)	^{1}H NMR spectrum, δ, ppm^a or mass spectrum (*m/z*)	Found, %		Formula	Calculated, %	
			C	H		C	H
Ic	110–112 (5)	164 $[M]^{+\cdot}$	–	–	$CC_{10}H_{12}O_2$	–	–
Id	123 (5)	178 $[M]^{+\cdot}$	–	–	$CC_{11}H_{14}O_2$	–	–
Ie	105–110 (1.5)	178 $[M]^{+\cdot}$	–	–	$CC_{11}H_{14}O_2$	–	–
If	115–118 (1.5)	0.96 d (6H, 2CH_3), 1.65 m (2H, CH_2), 1.80 m (1H, CH), 4.10 t (2H, OCH_2), 6.96 d ($2H_{arom}$), 7.34 d ($2H_{arom}$), 9.70 s (1H, CHO)	–	–	$CC_{12}H_{16}O_2$	–	–
Ig	135–137	179 $[M]^{+\cdot}$, 162 $[M - NH_3]^+$	60.30	5.10	$CC_9H_9NO_3$	60.33	5.06
Ii	61–63	180 $[M]^{+\cdot}$	–	–	$CC_{10}H_{12}O_3$	–	–
Ij	112–114 (1)	1.28 d (6H, 2CH_3), 3.81 s (3H, OCH_3), 4.70 m (1H, OCH), 7.12 d ($1H_{arom}$), 7.37 s ($1H_{arom}$), 7.50 d ($1H_{arom}$), 9.82 s ($1H_{arom}$)	–	–	$CC_{11}H_{14}O_3$	–	–
Ik	129–131 (1.5)	208 $[M]^{+\cdot}$	–	–	$CC_{12}H_{16}O_3$	–	–
Il	158–159	209 $[M]^{+\cdot}$, 192 $[M - NH_3]^+$	57.35	5.31	$CC_{10}H_{11}NO_4$	57.41	5.30
Im	153–155	223 $[M]^{+\cdot}$, 206 $[M - NH_3]^+$	59.15	5.90	$CC_{11}H_{13}NO_4$	59.19	5.87
In	104–109 (1)	208 $[M]^{+\cdot}$	–	–	$CC_{12}H_{16}O_3$	–	–
Is	125–127 (13)	150 $[M]^{+\cdot}$	–	–	$CC_9H_{10}O_2$	–	–
It	90–93 (1)	164 $[M]^{+\cdot}$	–	–	$CC_{10}H_{12}O_2$	–	–
Iu	158–162 (2) 38–40	212 $[M]^{+\cdot}$	79.20	5.72	$CC_{14}H_{12}O_2$	79.23	5.70
IIa	252–254 (decomp.)	2.47 d (2H, CH_2), 3.76 s (3H, OCH_3), 4.20 t (1H, CHN), 6.96 d ($2H_{arom}$), 7.39 d ($2H_{arom}$)	61.50	6.73	$CC_{10}H_{13}NO_3$	61.53	6.71
IIb	245–246 (decomp.)	1.31 t (3H, CH_3), 2.45 m (2H, CH_2), 4.00 q (2H, OCH_2), 4.19 q (1H, CHN), 6.95 d ($2H_{arom}$), 7.40 d ($2H_{arom}$)	63.13	7.25	$CC_{11}H_{15}NO_3$	63.14	7.23
IIc	244–245 (decomp.)	1.30 d (6H, 2CH_3), 2.48 m (2H, CH_2), 4.20 q (1H, CHN), 4.66 m (1H, OCH), 6.96 d ($2H_{arom}$), 7.38 d ($2H_{arom}$)	64.51	7.69	$CC_{12}H_{17}NO_3$	64.55	7.67
IId	237–239 (decomp.)	0.92 t (3H, CH_3), 1.42 m (2H, CH_2), 1.61 m (2H, CH_2), 2.40 m (2H, CH_2), 3.95 t (2H, OCH_2), 4.25 t (1H, CHN), 6.93 d ($2H_{arom}$), 7.34 d ($2H_{arom}$)	65.80	8.08	$CC_{13}H_{19}NO_3$	65.80	8.07
IIe	253–255 (decomp.)	0.99 d (6H, 2CH_3), 2.00 m (1H, CH), 2.48 m (2H, CH_2), 3.80 d (2H, OCH_2), 4.20 t (1H, CHN), 6.97 d ($2H_{arom}$), 7.36 d ($2H_{arom}$)	65.77	8.09	$CC_{13}H_{19}NO_3$	65.80	8.07
IIf	244–246 (decomp.)	0.94 d (6H, 2CH_3), 1.60 q (2H, CH_2), 1.79 m (1H, CH), 2.35 m (2H, CH_2), 3.97 t (2H, OCH_2), 4.20 q (1H, CHN), 6.90 d ($2H_{arom}$), 7.32 d ($2H_{arom}$)	66.91	8.45	$CC_{14}H_{21}NO_3$	66.91	8.42
IIh	258–262 (decomp.)	2.49 d (2H, CH_2), 4.20 q (1H, CHN), 5.10 s (2H, OCH_2), 6.97 d ($2H_{arom}$), 7.25–7.47 m ($7H_{arom}$)	70.86	6.29	$CC_{16}H_{17}NO_3$	70.83	6.32
IIi	254 (decomp.)	1.32 t (3H, CH_3), 2.27–2.45 m (2H, CH_2), 3.76 s (3H, OCH_3), 4.0 q (2H, OCH_2), 4.18 q (1H, CHN), 6.90 t ($2H_{arom}$), 7.05 s ($1H_{arom}$)	60.24	7.17	$CC_{12}H_{17}NO_4$	60.24	7.16

Table 2. (Contd.)

Comp. no.	mp, °C, or bp, °C (*p*, mm Hg)	^{1}H NMR spectrum, δ, ppm^a or mass spectrum (*m/z*)	Found, %		Formula	Calculated, %	
			C	H		C	H
IIj	242–244 (decomp.)	1.28 d (6H, $2CH_3$), 2.28–2.42 m (2H, CH_2), 3.80 s (3H, OCH_3), 4.19 m (1H, CHN), 4.69 m (1H, OCH), 6.84–6.94 m ($2H_{arom}$), 7.06 s ($1H_{arom}$)	61.52	7.58	$CC_{13}H_{19}NO_4$	61.64	7.56
IIk	241–242 (decomp.)	0.98 t (6H, $2CH_3$), 1.99 m (1H, CH), 2.28–2.40 m (2H, CH_2), 3.70 d (2H, OCH_2), 3.76 s (3H, OCH_3), 4.19 m (1H, CHN), 6.85–6.94 m ($2H_{arom}$), 7.07 s ($1H_{arom}$)	62.88	7.95	$CC_{14}H_{21}NO_4$	62.90	7.92
IIl	220 (decomp.)	2.45–2.55 m (2H, CH_2), 3.83 s (3H, OCH_3), 4.20 t (1H, CHN), 4.39 s (2H, OCH_2), 6.91 s ($2H_{arom}$), 7.12 s ($1H_{arom}$), 7.30 d (2H, NH_2)	53.70	6.01	$CC_{12}H_{16}N_2O_5$	53.73	6.01
IIm	217–219 (decomp.)	1.30 t (3H, CH_3), 2.45–2.55 m (2H, CH_2), 4.00 q (2H, OCH_2), 4.18 q (1H, CHN), 4.40 s (2H, OCH_2), 6.90 d ($2H_{arom}$), 7.11 s ($1H_{arom}$), 7.30 d (2H, NH_2)	55.31	6.44	$CC_{13}H_{18}N_2O_5$	55.31	6.43
IIn	239–241 (decomp.)	1.23 d (6H, $2CH_3$), 1.33 t (3H, CH_3), 2.30–2.40 m (2H, CH_2), 4.00 q (2H, OCH_2), 4.18 q (1H, CHN), 4.47 m (1H, OCH), 6.85–6.96 m ($2H_{arom}$), 7.04 s ($1H_{arom}$)	62.91	7.88	$CC_{14}H_{21}NO_4$	62.90	7.92
IIo	240–242 (decomp.)	2.35 m (2H, CH_2), 4.18 q (1H, CHN), 6.70 d (1H, CH), 6.82 d ($2H_{arom}$), 7.13 t ($1H_{arom}$)	59.65	6.13	$CC_9H_{11}NO_3$	59.66	6.12
IIp	210–211 (decomp.)	2.40 d (2H, CH_2), 4.25 t (1H, CHN), 6.86–6.91 d.d ($1H_{arom}$), 7.00 d ($2H_{arom}$), 7.11–7.21 m ($3H_{arom}$), 7.33–7.42 m ($5H_{arom}$)	70.00	5.90	$CC_{15}H_{15}NO_3$	70.02	5.88
IIq	224–225 (decomp.)	2.38 d (2H, CH_2), 4.23 t (1H, CHN), 5.10 s (2H, OCH_2), 6.92 d ($1H_{arom}$), 6.95 d ($1H_{arom}$), 7.12 s ($1H_{arom}$), 7.27 t ($1H_{arom}$), 7.33–7.46 m ($5H_{arom}$)	70.75	6.31	$CC_{16}H_{17}NO_3$	70.83	6.32
IIr	210 (decomp.)	1.32 t (3H, CH_3), 2.35 m (2H, CH_2), 4.02 q (2H, OCH_2), 4.22 t (1H, CHN), 6.83 d (1H, CH), 6.93 d (1H, CH), 6.99 s ($1H_{arom}$), 7.25 t ($1H_{arom}$)	63.15	7.28	$CC_{11}H_{15}NO_3$	63.14	7.23
IIs	210 (decomp.)	1.38 t (3H, CH_3), 2.18 q (1H, CH_2), 2.36 q (1H, CH_2), 4.08 q (2H, OCH_2), 4.75 q (1H, CHN), 6.95 t ($1H_{arom}$), 7.03 d ($1H_{arom}$), 7.24 d ($1H_{arom}$), 7.34 t ($1H_{arom}$)	63.11	7.23	$CC_{11}H_{15}NO_3$	63.14	7.23
IIt	210 (decomp.)	1.33 d (6H, $2CH_3$), 2.28 d (2H, CH_2), 4.45 t (1H, CH), 4.67 m (1H, OCH), 6.90 t ($1H_{arom}$), 7.02 d ($1H_{arom}$), 7.25 d ($1H_{arom}$), 7.37 t ($1H_{arom}$)	64.50	7.66	$CC_{12}H_{17}NO_3$	64.55	7.67
IIu	214–216 (decomp.)	2.35 m (2H, CH_2), 4.56 q (1H, CHN), 5.17 s (2H, OCH_2), 6.97 t ($1H_{arom}$), 7.08 d ($1H_{arom}$), 7.27 t ($1H_{arom}$), 7.34 t ($1H_{arom}$), 7.40 m ($3H_{arom}$), 7.48 d ($2H_{arom}$)	70.80	6.35	$CC_{16}H_{17}NO_3$	70.83	6.32
IIv	220 (decomp.)	2.30–2.43 m (2H, CH_2), 3.75 s (3H, OCH_3), 3.83 s (3H, OCH_3), 4.50 q (1H, CHN), 6.89 d ($1H_{arom}$), 6.96–7.05 m ($2H_{arom}$)	58.65	6.72	$CC_{11}H_{15}NO_4$	58.66	6.71

Table 2. (Contd.)

Comp. no.	mp, °C, or bp, °C (*p*, mm Hg)	^{1}H NMR spectrum, δ, ppm^a or mass spectrum (*m/z*)	Found, %		Formula	Calculated, %	
			C	H		C	H
IIw	248–249 (decomp.)	2.27–2.45 m (2H, CH_2), 3.79 s (3H, OCH_3), 3.82 s (3H, OCH_3), 4.48 q (1H, CHN), 6.85–6.95 m ($2H_{arom}$), 7.07 s ($1H_{arom}$)	58.60	6.69	$CC_{11}H_{15}NO_4$	58.66	6.71
IIy	226–227 (decomp.)	2.40 m (2H, CH_2), 3.64 s (3H, OCH_3), 3.77 s (6H, $2OCH_3$), 4.18 q (1H, CHN), 6.76 s ($2H_{arom}$)	56.46	6.71	$CC_{12}H_{17}NO_5$	56.46	6.71
IIIa	170–173	178 $[M]^{+\cdot}$, 161 $[M – OH]^+$, 134 $[M – CO_2]^+$	–	–	$CC_{10}H_{10}O_3$	–	–
IIIb	198–200	192 $[M]^{+\cdot}$, 175 $[M – OH]^+$, 147 $[M – COOH]^+$	–	–	$CC_{11}H_{12}O_3$	–	–
IIIc	154–157	1.38 d (6H, $2CH_3$), 4.60 m (1H, OCH), 6.30 d (1H, CH=), 6.90 d($2H_{arom}$), 7.48 d ($2H_{arom}$), 7.74 d (1H, CH=)	–	–	$CC_{12}H_{14}O_3$	–	–
IIId	155–160	220 $[M]^{+\cdot}$, 203 $[M – OH]^+$, 176 $[M – CO_2]^+$	–	–	$CC_{13}H_{16}O_3$	–	–
IIIe	161–163	1.00 d (6H, $2CH_3$), 2.00 m (1H, CH), 3.80 d (2H, OCH_2), 6.33 d (1H, CH=), 6.96 d ($2H_{arom}$), 7.53 d (1H, CH=), 7.60 d ($2H_{arom}$)	70.85	7.29	$CC_{13}H_{16}O_3$	70.89	7.32
IIIf	155–156	0.96 d (6H, $2CH_3$), 1.67 m (2H, CH_2), 1.82 m (1H, CH), 4.11 t (2H, OCH_2), 6.34 d (1H, CH=), 6.96 d ($2H_{arom}$), 7.54 d (1H, CH=), 7.61 d ($2H_{arom}$)	71.80	7.75	$CC_{14}H_{18}O_3$	71.77	7.74
IIIg	260–262	4.50 s (2H, OCH_2), 6.42 d (1H, CH=), 6.98 d ($2H_{arom}$), 7.38 s (1H, NH_2), 7.43 d (1H, CH=), 7.53 s (1H, NH_2), 7.60 d ($1H_{arom}$)	59.73	5.00	$CC_{11}H_{11}NO_4$	59.73	5.01
IIIh	198–201	5.16 s (2H, OCH_2), 6.30 d (1H, CH=), 7.06 d ($2H_{arom}$), 7.33–7.54 m ($7H_{arom}$), 7.58 d (1H, CH=)	75.50	5.59	$CC_{16}H_{14}O_3$	75.58	5.55
IIIi	177–179	1.32 t (3H, CH_3), 3.80 s (3H, OCH_3), 4.06 q (2H, OCH_2), 6.38 d (1H, CH=), 6.93 d ($1H_{arom}$), 7.15 d ($1H_{arom}$), 7.26 s ($1H_{arom}$), 7.47 d (1H, CH=)	64.80	6.38	$CC_{12}H_{14}O_4$	64.85	6.35
IIIj	152–155	1.30 d (6H, $2CH_3$), 3.78 s (3H, OCH_3), 4.68 m (1H, OCH), 6.50 d (1H, CH=), 6.93 t ($1H_{arom}$), 7.15 d ($1H_{arom}$), 7.27 t ($1H_{arom}$), 7.80 d (1H, CH=)	66.10	6.85	$CC_{13}H_{16}O_4$	66.09	6.83
IIIk	145–147	0.98 d (6H, $2CH_3$), 2.01 m (1H, CH), 3.75 d (2H, OCH_2), 3.80 s (3H, OCH_3), 6.41 d (1H, CH=), 6.95 d ($1H_{arom}$), 7.16 d ($1H_{arom}$), 7.27 s ($1H_{arom}$), 7.50 d (1H, CH=)	67.18	7.25	$CC_{14}H_{18}O_4$	67.18	7.25
IIIl	265–267	3.83 s (3H, OCH_3), 4.48 s (2H, OCH_2), 6.45 d (1H, CH=), 6.88 d ($1H_{arom}$), 7.18 d ($1H_{arom}$), 7.30 s (1H, NH2), 7.34 s ($1H_{arom}$), 7.38 s (1H, NH_2), 7.52 d (1H, CH=)	60.72	5.49	$CC_{12}H_{13}O_5$	60.76	5.52
IIIm	250–254	1.32 t (3H, CH_3), 4.08 q (2H, OCH_2), 4.50 s (2H, OCH_2), 6.46 d (1H, CH=), 6.90 d ($1H_{arom}$), 7.19 d ($1H_{arom}$), 7.30 s (1H, NH_2), 7.35 s ($1H_{arom}$), 7.41 s (1H, NH_2), 7.54 d (1H, CH=)	62.14	6.06	$CC_{13}H_{15}O_5$	62.14	6.02
IIIo	192–194	164 $[M]^{+\cdot}$, 147 $[M – OH]^+$, 120 $[M – CO_2]^+$	65.80	4.85	$CC_9H_8O_3$	65.85	4.91

Table 2. (Contd.)

Comp. no.	mp, °C, or bp, °C (*p*, mm Hg)	^{1}H NMR spectrum, δ, ppm[a] or mass spectrum (*m/z*)	Found, %		Formula	Calculated, %	
			C	H		C	H
IIIp	200–202	6.50 d (1H, CH=), 6.90 d.d (1H_{arom}), 7.02 d (2H_{arom}), 7.13–7.21 m (3H_{arom}), 7.36–7.46 m (3H_{arom}), 7.53 d (1H, CH=)	75.04	4.97	$CC_{15}H_{12}O_3$	74.99	5.03
IIIq	153–154	5.17 s (2H, OCH_2), 6.53 d (1H, CH=), 6.95–7.43 m (9H_{arom}), 7.50 d (1H, CH=)	75.48	5.53	$CC_{16}H_{14}O_3$	75.58	5.55
IIIr	132–134	192 $[M]^{+\cdot}$, 148 $[M - CO_2]^+$, 133 $[M - CO_2 - CH_3]^+$	68.70	6.27	$CC_{11}H_{12}O_3$	68.74	6.29
IIIs	135–136	1.38 t (3H, CH_3), 4.10 q (2H, OCH_2), 6.50 d (1H, CH=), 6.96 t (1H_{arom}), 7.04 d (1H_{arom}), 7.37 t (1H_{arom}), 7.65 d (1H_{arom}),7.81 d (1H, CH=)	68.64	6.23	$CC_{11}H_{12}O_3$	68.74	6.29
IIIt	108–110	1.30 d (6H, 2CH_3), 4.68 m (1H, OCH), 6.50 d (1H, CH=), 6.95 t (1H_{arom}), 7.08 d (1H_{arom}), 7.35 t (1H_{arom}), 7.67 d (1H_{arom}), 7.82 d (1H, CH=)	69.96	6.88	$CC_{12}H_{14}O_3$	69.89	6.84
IIIu	135–145	254 $[M]^{+\cdot}$, 210 $[M - CO_2]^+$	75.64	5.57	$CC_{16}H_{14}O_3$	75.58	5.55
IIIv	181–183	208 $[M]^{+\cdot}$, 164 $[M - CO_2]^+$	63.56	5.78	$CC_{11}H_{12}O_4$	63.46	5.81
IIIw	180–183	208 $[M]^{+\cdot}$, 164 $[M - CO_2]^+$	63.53	5.78	$CC_{11}H_{12}O_4$	63.46	5.81
IIIx	146–151	208 $[M]^{+\cdot}$, 164 $[M - CO_2]^+$	63.52	5.84	$CC_{11}H_{12}O_4$	63.46	5.81
IIIy	127–128	238 $[M]^{+\cdot}$, 194 $[M - CO_2]^+$	60.44	5.88	$CC_{12}H_{14}O_5$	60.50	5.92
IIIz	[b]	1.39 s (18H, 6CH_3), 6.25 d (1H, CH=), 7.36 s (2H_{arom}), 7.51 d (1H, CH=), 12.00 d (1H, OH)	73.83	8.78	$CC_{17}H_{24}O_3$	73.88	8.75
IIIa'	195–200	3.80 s (3H, OCH_3), 3.83 s (3H, OCH_3), 6.56 d (1H, CH=), 7.21 s (1H_{arom}), 7.39 s (1H_{arom}), 7.73 d (1H, CH=)	46.12	3.90	$CC_{11}H_{11}BrO_4$	46.02	3.86
IVg	290 (decomp.)	4.46 s (2H, OCH_2), 6.90 d (2H_{arom}), 7.32 s (1H, NH_2), 7.50 s (1H, NH_2), 7.79 s (1H, CH=), 7.92 d (2H_{arom})	54.34	4.21	$CC_{12}H_{11}NO_6$	54.34	4.18
IVa'	255–263 (decomp.)	3.70 s (3H, OCH_3), 3.80 s (3H, OCH_3), 7.14 s (1H_{arom}), 7.53 s (1H_{arom}), 7.91 s (1H, CH=)	43.43	3.33	$CC_{12}H_{11}BrO_6$	43.53	3.35
VIa	242–244 (decomp.)	2.33–2.44 m (2H, CH_2), 4.26 q (1H, CHN), 7.18 t (2H_{arom}), 7.45 t (2H_{arom})	59.00	5.48	$CC_9H_{10}FNO_2$	59.01	5.50
VIc	240–242 (decomp.)	2.25–2.35 m (5H, CH_2 and CH_3), 4.25 t (1H, CHN), 7.19 d (2H_{arom}), 7.30 d (2H_{arom})	67.00	7.30	$CC_{10}H_{13}NO_2$	67.02	7.31
VId	243–245 (decomp.)	2.40 d (2H, CH_2), 4.27 t (1H, CHN), 7.31 t (1H_{arom}), 7.41 d (1H_{arom}), 7.48 d (1H_{arom}), 7.64 s (1H_{arom})	44.25	4.10	$CC_9H_{10}BrNO_2$	44.29	4.13
VIf	224–228 (decomp.)	2.50–2.60 m (2H, CH_2), 4.31 t (1H, CHN), 7.36 t (1H_{arom}), 7.83 d (1H_{arom}), 8.47 d (1H_{arom}), 8.60 s (1H_{arom})	57.78	6.01	$CC_8H_{10}N_2O_2$	57.82	6.07
VIg	210 (decomp.)	2.41 m (2H, CH_2), 4.59 q (CHN), 7.27 t (1H_{arom}), 7.35 t (1H_{arom}), 7.40 d (1H_{arom}), 7.62 d (1H_{arom})	54.10	5.02	$CC_9H_{10}ClNO_2$	54.15	5.05
VIh	–	2.44 m (2H, CH_2), 4.54 q (1H, CHN), 7.48 t (1H_{arom}), 7.68 t (1H_{arom}), 7.83 q (2H_{arom})	–	–	$CC_9H_{10}N_2O_4$	–	–

Table 2. (Contd.)

Comp. no.	mp, °C, or bp, °C (*p*, mm Hg)	^{1}H NMR spectrum, δ, ppm^a or mass spectrum (*m/z*)	Found, %		Formula	Calculated, %	
			C	H		C	H
VIk	220 (decomp.)	2.40 d (2H, CH_2), 4.62 t (1H, CHN), 7.50 d (1H$_{arom}$), 7.82 d (1H$_{arom}$), 8.02 s (1H$_{arom}$)	44.24	3.68	$CC_9H_9ClN_2O_4$	44.19	3.71
VIl	224–227 (decomp.)	2.47 m (2H, CH_2), 4.25 q (1H, CHN), 6.30 d (1H$_{arom}$), 6.40 t (1H$_{arom}$), 7.58 d (1H$_{arom}$)	54.28	5.90	$CC_7H_9NO_3$	54.19	5.85
VIm	207–209 (decomp.)	2.31 s (3H, CH_3), 2.46 m (2H, CH_2), 4.28 q (1H, CHN), 6.17 d (1H$_{arom}$), 6.45 d (1H$_{arom}$)	56.88	6.61	$CC_8H_{11}NO_3$	56.80	6.55
VIn	226–228 (decomp.)	2.45–2.60 m (2H, CH_2), 4.50 t (1H, CHN), 6.96 t (1H$_{arom}$), 7.05 d (1H$_{arom}$), 7.41 d (1H, CHS)	49.12	5.28	$CC_7H_9NO_2S$	49.11	5.30
VIp	210–212 (decomp.)	0.88 q (6H, 2CH_3), 1.67 m (1H, CH), 1.92 q (1H, CH_2), 2.16 q (1H, CH_2), 2.82 m (1H, CHN)	54.94	10.02	$CC_6H_{13}NO_2$	54.94	9.99
VIq	205–207 (decomp.)	0.96 t (3H, CH_3), 1.42 m (2H, CH_2), 1.65 m (2H, CH_2), 2.39–2.62 m (2H, CH_2), 3.52 m (1H, CHN)	54.96	9.97	$CC_6H_{13}NO_2$	54.94	9.99
VIr	250 (decomp.)	0.93 m (6H, 2CH_3), 1.51 t (2H, CH_2), 1.71 m (1H, CH), 2.38–2.61 m (2H, CH_2), 3.56 m (1H, CHN)	57.80	10.37	$CC_7H_{15}NO_2$	57.90	10.41
VIs	215–218 (decomp.)	0.88 t (3H, CH_3), 1.22–1.50 m (6H, 3CH_2), 1.94 q (1H, CH_2), 2.16 q (1H, CH_2), 3.02 m (1H, CHN)	57.85	10.37	$CC_7H_{15}NO_2$	57.90	10.41
VIt	228–230 (decomp.)	0.82 d (3H, CH_3), 0.92 s (9H, 3CH_3), 1.03–1.27 m (2H, CH_2), 1.28–1.53 m (2H, CH_2), 1.54–1.75 m (1H, CH), 2.10–2.43 m (2H, CH_2), 3.17 m (1H, CHN)	65.60	11.56	$CC_{11}H_{23}NO_2$	65.63	11.52
VIIa	209–210	6.45 d (1H, CH=), 7.21 q (2H$_{arom}$), 7.48 d (1H, CH=), 7.71 q (2H$_{arom}$)	65.00	4.23	$CC_9H_7FO_2$	65.06	4.25
VIIb	227–230 (decomp.)	3.00 s (6H, 2CH_3), 6.08 d (1H, CH=), 6.63 d (2H$_{arom}$), 7.34 d (2H$_{arom}$), 7.40 d (1H, CH=)	68.90	7.00	$CC_{11}H_{13}NO_2$	69.09	6.85
VIIc	195–198	162 $[M]^{+\cdot}$, 118 $[M - CO_2]^+$, 103 $[M - CO_2 - CH_3]^+$	74.08	6.20	$CC_{10}H_{10}O_2$	74.06	6.21
VIId	177–180	227 $[M]^{+\cdot}$, 183 $[M - CO_2]^+$	47.54	3.09	$CC_9H_7BrO_2$	47.61	3.11
VIIe	275–280	7.52 d (2H$_{arom}$), 8.02 d (1H, CH=), 8.60 d (2H$_{arom}$), 8.68 d (1H, CH=)	64.40	4.70	$CC_8H_7NO_2$	64.42	4.73
VIIf	232–235 (decomp.)	6.68 d (1H, CH=), 7.42 t (1H$_{arom}$), 7.51 d (1H, CH=), 8.08 d (1H$_{arom}$), 8.58 d (1H$_{arom}$), 8.80 s (1H, CHN)	64.38	4.68	$CC_8H_7NO_2$	64.42	4.73
VIIg	206–209	6.57 d (1H, CH=), 7.41 m (2H$_{arom}$), 7.52 d (1H$_{arom}$), 7.84–7.90 q (2H, CH= and H$_{arom}$)	59.18	3.85	$CC_9H_7ClO_2$	59.20	3.86
VIIi	191–196	6.10 d (1H, CH=), 6.42 t (1H$_{arom}$), 7.10 s (1H$_{arom}$), 7.27 d (1H, CH=), 7.40 s (1H, CH), 7.72 d (2H, 2CH), 8.34 d (2H, 2CH)	60.43	3.87	$CC_{13}H_{10}N_2O_4$	60.47	3.90
VIIj	186–192	6.20 d (1H, CH=), 6.42 t (1H$_{arom}$), 7.04 d (1H$_{arom}$), 7.22 d (1H, CH=), 7.35 s (1H$_{arom}$), 7.87 d (2H$_{arom}$), 8.17 s (1H$_{arom}$), 8.33 m (1H$_{arom}$)	60.40	3.88	$CC_{13}H_{10}N_2O_4$	60.47	3.90

Table 2. (Contd.)

Comp. no.	mp, °C, or bp, °C (*p*, mm Hg)	^{1}H NMR spectrum, δ, ppm[a] or mass spectrum (*m/z*)	Found, %		Formula	Calculated, %	
			C	H		C	H
VIIk	212–214	6.54 d (1H, CH=), 7.57 d (1H, CH=), 7.64 d ($1H_{arom}$), 7.83 d ($1H_{arom}$), 8.14 s ($1H_{arom}$)	47.54	2.70	$CC_9H_6ClNO_4$	47.49	2.66
VIIl	141–145	138 $[M]^{+\cdot}$, 94 $[M - CO_2]^+$	60.81	4.40	$CC_7H_6O_3$	60.87	4.38
VIIm	138–140	2.32 s (3H, CH_3), 6.03 d (1H, CH=), 6.27 d ($1H_{arom}$), 6.80 d ($1H_{arom}$), 7.31 d (1H, CH=)	63.13	5.30	$CC_8H_8O_3$	63.15	5.30
VIIn	143–145	6.19 d (1H, CH=), 7.12 t ($1H_{arom}$), 7.50 d ($1H_{arom}$), 7.67 d ($1H_{arom}$), 7.72 d (1H, CH=)	54.48	3.94	$CC_7H_6O_2S$	54.53	3.92
VIIo	173–175	2.36 s (3H, CH_3), 6.02 d (1H, CH=), 6.80 d ($1H_{arom}$), 7.30 d (1H, CH=), 7.43 d ($1H_{arom}$)	57.07	4.83	$CC_8H_8O_2S$	57.12	4.79
VIIp[c]	116 (20)	114 $[M]^{+\cdot}$, 70 $[M - CO_2]^+$	–	–	$CC_6H_{10}O_2$	–	–
VIIq[d]	118 (25)	114 $[M]^{+\cdot}$, 70 $[M - CO_2]^+$	–	–	$CC_6H_{10}O_2$	–	–
VIIr[e]	130 (25)	128 $[M]^{+\cdot}$, 84 $[M - CO_2]^+$	–	–	$CC_7H_{12}O_2$	–	–
VIIs[f]	128 (25)	128 $[M]^{+\cdot}$, 84 $[M - CO_2]^+$	–	–	$CC_7H_{12}O_2$	–	–
VIIIh	200–205 (decomp.)	7.37 d ($1H_{arom}$), 7.52 t ($1H_{arom}$), 7.64 t ($1H_{arom}$), 8.06 d ($1H_{arom}$), 8.13 s (1H, CH=)	50.57	3.02	$CC_{10}H_7NO_6$	50.64	2.97
VIIIi	215–220 (decomp.)	6.40 t ($1H_{arom}$), 7.26 t ($1H_{arom}$), 7.58 d ($2H_{arom}$), 7.69 s (1H, CH=), 8.00 q (1H, CHN), 8.40 d ($2H_{arom}$)	55.58	3.29	$CC_{14}H_{10}N_2O_6$	55.64	3.33
VIIIj	208–210 (decomp.)	6.38 t ($1H_{arom}$), 7.26 t ($1H_{arom}$), 7.66 s (1H, CH=), 7.76 d ($1H_{arom}$), 7.84 t ($1H_{arom}$), 8.04 d ($1H_{arom}$), 8.14 s ($1H_{arom}$), 8.30 d ($1H_{arom}$)	55.56	3.30	$CC_{14}H_{10}N_2O_6$	55.64	3.33
VIIIk	190–194 (decomp.)	7.60 d ($1H_{arom}$), 7.77 s (1H, CH=), 7.91 d ($1H_{arom}$), 8.46 s ($1H_{arom}$)	44.25	2.23	$CC_{10}H_6ClNO_6$	44.22	2.23
VIIIo	198–200 (decomp.)	2.38 s (3H, CH_3), 7.00 d ($1H_{arom}$), 7.70 d ($1H_{arom}$), 8.34 s (1H, CH=)	50.98	3.78	$CC_9H_8O_4S$	50.94	3.80
IX	–	6.59 d (1H, CH=), 7.35 d ($1H_{arom}$), 7.45 d ($1H_{arom}$), 7.60 t ($1H_{arom}$), 8.17 d (1H, CH=)	–	–	$CC_9H_6ClFO_2$	–	–
X	247–253 (decomp.)	7.28 d ($1H_{arom}$), 7.40 d ($1H_{arom}$), 7.52 t ($1H_{arom}$), 8.08 s (1H, CH=); 180 $[M]^{+\cdot}$	59.80	2.73	$CC_9H_5ClO_2$	59.86	2.79
XI	220 (decomp.)	2.66 t (2H, CH_2), 4.69 m (1H, CH), 7.16 t ($1H_{arom}$), 7.20–7.35 m ($3H_{arom}$); 202 $[M]^{+\cdot}$, 158 $[M - CO_2]^+$	53.30	4.03	$CC_9H_8ClFO_2$	53.35	3.98
XII	270 (decomp.)	1.25–1.47 m (6H, $3CH_2$), 1.47–1.58 m (4H, $2CH_2$), 2.09 s (2H, CH_2)	61.10	9.58	$CC_8H_{15}NO_2$	61.12	9.62

[a] The ^{1}H NMR spectra of all the synthesized acids lack signals of the COOH, NH_2, and OH protons since these protons are in fast exchange with protons of water contained in the solvent, as evidenced by the presence in the spectra of one broad signal in the region of 3.3 ppm. [b] Oily substance. [c] n_D^{20} 1.4480. [d] n_D^{20} 1.4490. [e] n_D^{20} 1.4468. [f] n_D^{20} 1.4475.

As seen from Table 1, *O*-alkyl derivatives of 4-hydroxybenzaldehyde **Ia**–**If** give β-amino acids **IIa**–**IIf** in high yields that slightly fall down with increasing alkyl chain length. Therewith, chain branching favors higher yields of β-amino acids. The yield of compound **IIe** is higher than that of **IId**. The yields of cinnamic acids increase in parallel with radical chain length, from compound **IIIa** to compound **IIIf**. Surprisingly, acetamide derivative **Ig** in the same conditions gives exclusively ylidenemalonic acid **IVg** that is stable in the solid state up to 290°C.

With *O*-alkyl derivatives **Ii**–**Il** and their homologs **Im** and **In**, the major reaction products, too, are β-amino acids **IIi**–**IIn**. Cinnamic acids **IIIi**–**IIIn** are formed in small amounts (from 3 to 25%), and alkylidenes **IVl** and **IVm**, related to compounds **IVg**, were not found at all.

With 3-hydroxybenzaldehyde, the yield of β-amino acids **IIo**–**IIr** decreases in going from unsubstituted aldehyde **Io** to aromatic **Ip**, aliphatic–aromatic **Iq**, and aliphatic **Ir**. The yields of cinnamic acids **IIIo**–**IIIr** decrease in the same order. In going to 2-hydroxybenzaldehyde derivatives **Is**–**Iu**, the major reaction product are cinnamic acids **IIIs**–**IIIu**. The yields of β-amino acids **IIs**–**IIr** are lower (11–26%).

In general, with all the alkoxy derivatives, the following trends are revealed: The yield of β-amino acids decreases, depending on the position of the substituent, in the order *para* > *meta* > *ortho* and, depending of the radical in the same position, in the order $C_6H_5CH_2 > C_2H_5 > CH(CH_3)_2 > CH_2CH(CH_3)_2 > CH_2CH_2CH(CH_3)_2$.

The Rodionov reaction with 2,3- and 3,4-dimethoxybenzaldehydes **Iv** and **Iw** results in preferential formation of amino acids **IIv** and **IIw** in moderate yields that, however, double those of cinnamic acids **IIIv** and **IIIw**. At the same time, 2,5-dimethoxybenzaldehyde (**Ix**) provides no β-amino acid at all, and the only isolated product in this case was cinnamic acid **IIIx**.

The reaction of 3,4,5-trimethoxybenzaldehyde (**Iy**) with malonic acid and ammonium acetate affords β-amino acid **IIy** and cinnamic acid **IIIy** (1.5 : 1). The other trisubstituted benzaldehydes studied, **Iz** and **Ia**', gave no β-amino acids under the same conditions. The major products here were cinnamic acids **IIIz** and **IIIa**' and arylmethylenemalonic acid **IVa**'.

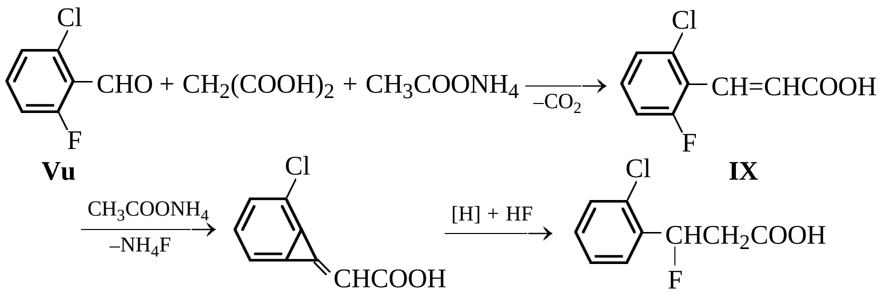
Monosubstituted compounds, 4-fluoro-, 4-methyl-, 3-bromo, and 2-chlorobenzaldehydes (**Va, Vc, Vd**, and **Vg**, respectively) provide β-amino acids **VIa**, **VIc**, **VId**, and **VIg** as major products and cinnamic acids **VIIa**, **VIIc**, **VIId**, and **VIIg** as minor products. The Rodionov reaction with 4-(dimethylamino)benzaldehyde (**Vb**) results in exclusive formation of cinnamic acid **VIIb**.

4- and 3-Pyrininecarboxaldehydes **Ve** and **Vf** covert primarily into pyridylacrylic acids **VIIe** and **VIIf**, but with aldehyde **Vf**, 15% of β-amino acid **VIf** was isolated.

Nitro substitution in the aromatic ring favors formation of ylidenemalonic acids by the scheme **Vh**–**Vk** > **VIIIh**–**VIIIk**. In certain cases, we could isolate (compound **VIk**) or detect (compound **VIh**) β-amino acids and propenoic acids **VIIi**–**VIIk**.

The Rodionov reactions with furan- and thiophenecarboxaldehydes (**Vl** and **Vn**) give readily separable mixtures of β-amino acids **VIl**, **VIn** and acrylic acids **VIIl**, **VIIn**, respectively, in 1 : 1 ratios. Methyl substitution in the aldehyde heteroring (aldehydes **Vm** and **Vo**) decreases the yields of β-amino acids [19 and 0% with compounds **VIm** and **VIo**, respectively) and increases the yields of Knoevenagel condensation products [the yields of acrylic acid derivatives **VIIm** and **VIIo** are 45 and 31%, respectively, and that of malonic acid derivative **VIIIo** is 15%].

6-Chloro-2-fluorobenzaldehyde (**Vu**) reacts with malonic acid and ammonium acetate in a more complicated fashion. Due to the known ability of the fluorine atom in the *ortho* position of the benzene ring to interaction with α-hydrogen atoms of the aliphatic fragment, the reaction gives a mixture of compounds **X** and **XI** as major reaction products.

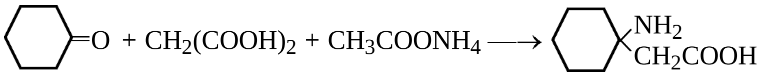


X, 25% **XI**, 23%

Apparently, the reaction involve intermediate formation of an “ordinary” cinnamic acid **IX** that undergoes consecutive dehydrofluorination to compound **X** and reductive hydrofluorination to acid **XI**.

Aliphatic aldehydes **Vp**–**Vt**, like aromatic aldehydes, enter into the Rodionov reaction to form a readily separable mixture of β-amino acids **VIp**–**VIt** and acrylic acids **VIIp**–**VIs**. Therewith, as follows from Table 1, the yields of isomeric β-amino acids **VIp**, **VIq** and **VIr**, **VIs** are much higher in the case of branched aldehydes **Vp** and **Vr**.

Aiming at preparing β-amino acids, we also brought into the Rodionov reaction certain readily available ketones. It was found that such ketones as acetophenone, benzophenone, cyclopentane dione, dimedone, acetone, and methyl ethyl ketone give no β-amino acids. Cyclohexanone was the only whose Rodionov reaction gave β-amino acid **XII** in high yield.



XII, 69%

It should be noted that the coupling constants of the CH=CH protons in the ^{1}H NMR spectra of all the cinnamic acids **III** and **VII** formed by the Rodionov reaction span the range 15.7–15.9 Hz, which suggests [11, 12] *trans* structures.

Isolated ylidenemalonic acids **IVg** and **IVa**' and pyrrole-2-ylmethylenemalonic acids **VIIIi** and **VIIIj** exhibit a high thermal stability. Their decarboxylation to corresponding propenoic acids **IIIg**, **IIIa**' and **VIIi**, **VIIj** could be accomplished only in pyridine under reflux. In wet pyridine, decarboxylation competes with hydrolysis of ylidenemalonic acids to aldehydes; moreover, hydrolysis is more facile that decarboxylation.

$$\underset{\textbf{VIIIi, VIIIj}}{RCH{=}C(COOH)_2} + H_2O \xrightarrow{t^\circ,\ PyH} \underset{\textbf{Vi, Vj}}{RCHO} + \underset{\textbf{VIIi, VIIj}}{RCH{=}CHCOOH} + CH_3COOH + CO_2$$

β-Amino acids **II** and **VI** are stable in air and have high decomposition points (>200°C). Most of them are poorly soluble in organic solvents, and most aromatic acids are also water-insoluble.

In summary in may be said that, inspite of the widely varied yields of β-amino acids in our studied version of the Rodionov reaction, this synthetic approach can be used to success in preparative purposes even on the semimicro scale, since the molecular weights of β-amino acids are much larger than those of the corresponding aldehydes.

EXPERIMENTAL

The ^{1}H NMR spectra were measured on a Bruker AM-360 spectrometer at 360.14 MHz in DMSO-d_6, except for amino acids **VIq**, **VIr** and compound **IIIc**, whose spectra were measured in D_2O and $CDCl_3$. The mass spectra were obtained on a QP-5000 spectrometer at 70 eV. The mass spectra of the synthesized β-amino acids all contain molecular ion peaks $[M]^{+\cdot}$ (10–30% of the base peak) and $[M - NH_2]$ ion peaks; the base peaks are from $[M - CH_2COOH]^+$ ions.

Aldehydes **Vi** and **Vj** were prepared as described in [13] from 2-furaldehyde and the corresponding nitroaniline.

Alkoxybenzaldehydes Ic–**Ig, Ii**–**In, and Is**–**Iu** *(general procedure).* A mixture of 1 mol of 2-, 3-, or 4-hydroxybenzaldehyde, vanillin or 3-ethoxy-4-hydroxybenzaldehyde, 103.5 g of anhydrous potash, and 350 ml of *N*,*N*-dimethylformamide was stirred for 30 min at 100°C. The reaction mixture warmed up to 100–115°C, and 1.3 mol of alkyl bromide or 1.4 mol of αchloroacetamide was added to it at that temperature (the first reagent was added dropwise). The mixture was stirred for 2 h at 110°C, cooled to 70°C, diluted with 800 ml of water, stirred for 30 min, and cooled to 20°C. Aldehydes **Ig**, **Ii**, **Il**, and **Im** and were filtered off, thoroughly washed with water, and dried. In the other cases, the reaction mixture was treated with chloroform 2×350 ml, the extracts were evaporated, and aldehydes **Ic**–**If**, **Ij**, **Ik**, **In**, and **Is**–**Iu** were isolated bu fractionation in a vacuum. Yields 85–90%. Given are comp. no. and n_D^{20}: **Ic**, 1.5437; **Id**, 1.5370; **Ie**, 1.5344; **If**, 1.5270; **Ij**, 1.5587; **Ik**, 1.5520; **In**, 1.5437; **Is**, 1.5423; **It**, 1.5288.

Reaction of aldehydes I and V and cyclohexanone with malonic acid and ammonium acetate *(general procedure).* A mixture of aldehyde **I** or **V**, or cyclohexanone, 114.4 g of malonic acid, and 177.1 g of ammonium acetate in 600 ml of 1-butanol was refluxed for 1.5–3 h until CO_2 no longer evolved. The precipirate that formed (with aldehydes **Ia**–**Io**, **Iw**, **Ia**', **Va**, **Vc**, **Vd**, or **Vg**–**Vm**) was filtered off while hot, washed in succession with boiling 1-butanol (2 × 250 ml), 250 ml of boiling ethanol, 250 ml of water, and 50 ml of ethanol at 25°C to obtain compounds **IIa**–**IIf**, **IIh**–**IIo**, **IIw**, **IVg**, **IVa**', **VIa**, **VIc**, **VId**, **VIg** and mixtures of compounds **VIh**, **VIIIh** and **VIIIi**–**VIIIl**, that were dried at 100°C. The mother liquor was cooled to 20°C to obtain additional crops of compound **IIj**, cinnamic acids **IIIl** and **IIIm**, and amino acid **VIk**. They were filtered off, washed with cold ethanol, and dried. After cooling, the mother liquors were reduced by half and poured into 750 ml of water. The precipitate that formed was filtered off, washed with water, and dried at 100°C to obtain compounds **IIIa**–**IIIf**, **IIIh**–**IIIk**, **IIIo**, and **IIIw**, a mixture of compounds **IIIa**' and **IVa**' (2 : 1), and compounds **VIIa**, **VIIc**, **VIId**, and **VIIg**–**VIIk**, that were additionally purified, if required, by recrystallization from ethanol (**IIIb**–**IIIf**), precipitation with water from acetone (**IIIj**), or by reprecipitation with HCl form aqueous alkalini washed with ether (**IIIh**, **IIIi**, and **IIIk**). Most of amino acids **II** and **VI** are pure by no less than 98%. Compounds **IIl** and **IIm** were brought to this purity by additional recrystallization from water.

Amino acid **IIq** was filtered off from the reaction mixture cooled to 15°C, washed in with cold ethanol, water, and acetone. The mother liquor was reduced by half, poured into 500 ml of water, compound **IIIq** precipitated and was filtered off and recrystallized from 50% aqueous ethanol.

The reaction mixture was cooled to 15°C to precipitate acid **IIv** that was filtered off and washed with cold ethanol, water, and ethanol (100 each). The mother liquor was poured into 700 ml of water, and the precipitate that formed was filtered off and dried.

The precipitate was washed with acetone to extract cinnamic acid **IIIv** that was then precipitated with water and filtered off. The acetone-insoluble precipitate contained an additional portion of acid **IIv**. Acid **VIIb** was obtain in a similar way.

The postreaction mixtures of aldehydes **Ip**, **Ir**–**Iu**, **Ix**–**Iz**, **Ve**, **Vf**, and **Vp**–**Vt**, as well as cyclohexanone with malonic acid in the presence of ammonium acetate looked like transparent solutions. All volatile compounds boiling to 135°C were distilled off. Therewith, is a colorless film of ammonium malonate deposited in the Liebig condenser, the reaction mixture was diluted with 300 ml of 1-butanol, and distillation was repeated. The residue was distilled in a vacuum of 10–20 mm Hg, until the boiling point of the distillate reached 128–130°C or 130–135°C (with aldehydes **Vp**–**Vt**). In latter case, the distillate was distilled once more to isolate acrylic acids **VIIp**–**Vs**. The viscous still bottom was cooled to 20°C and treated with stirring with 700 ml of acetone, allowed to stand for no less than 10 h, and the precipitates that formed were filtered off, washed with acetone, and dried at 100°C to obtain compounds **IIp** and **IIr**, mixtures of acids **IIv** and **IIIv** and **IIt** and **IIIt**, acids **IIu** and **IIy**, a mixture of acids **VIf**, **VIIf**, and acids **VIp**–**VIt**, and **XII**. To separate mixtures of acids **IIs** and **IIIs**, **IIt** and **IIIt**, and **VIf** and **VIIf**, amino acids **IIs**, **IIt**, and **VIf** were extracted with water, the aqueous extracts were evaporated, and acids **IIs**, **IIt**, **VIf**, and **VIIf** were washed with acetone. Water-insoluble compounds **IIIs** and **IIIt** were then isolated by recrystallization from 60% aqueous ethanol. The mother liquors were reduced by 35% and poured into 650 ml of water. The precipitates that formed were filtered off, washed with water, and dried to obtain acids **IIIp** and **IIIr** (purified by recrystallization from 50% aqueous ethanol) and **IIIu**, **IIIx**, **IIIy**, and **VIIe**. Cinnamic acid **IIIz** is a viscous oily substance. It was isolated by decantation of the aqueous layer which was then diluted with 300 ml of water, extracted with ether, and removal of the solvent.

Furan and thiophene derivatives were synthesized from aldehydes **Vl**, **Vm**, **Vn**, and **Vo** in a similar way using as solvent 1-butanol instead of ethanol. With aldehydes **Vl** and **Vm**, the reaction mixture was poured into 4 l of water, the tarry residue was filtered off, the filtrate was treated with ether (2 × 350 ml), and the ether was removed. Amino acids **VIl** and **VIm** were isolated from the aqueous layer and acrylic acids **VIIl** and **VIIm**, from the ether extract. With aldehydes **Vn** and **Vn**, the synthesis was 8 h long, after which 154 g of ammonium acetate was added to the reaction mixture, and it was refluxed for an additional 4 h. After cooling, compounds **VIn** and **VIIIo**, respectively, precipitated and were filtered off and dried at 100°C. The mother liquors were evaporated, the residue was poured into 500 ml of water, and the precipitate was filtered off and recrystallized from aqueous ethanol to obtain acids **VIIn** and **VIIo**, repsectively.

In the case of the reaction of aldehyde **Vu** with malonic acid and ammonium acetate, the reaction mixture was filtered to separate insoluble acid **X**, and the filtrate was cooled to 15°C to precipitate acid **XI**.

Both products were washed with cold ethanol and dried at 75°C. In the mother liquor, a little compound **IX** was detected by ^{1}H NMR.

Decarboxylation of ylidenemalonic acids. A mixture of 30 g of compound **IVg**, **IVa**', **VIIIi**, or **VIIIj**, 100 ml of dry pyridine, and 5 ml of piperidine was refluxed until gas evolution was no longer observed (~4 h) and then poured onto a mixture of 300 g of ice, 160 ml of conc. H_2SO_4, and 500 ml of water. The precipitate that formed was washed with water and dried to obtain 24 (96%) of acid **IIIg**, 20 (77%) of acid **IIIa**', 22 (86%) of acid **VIIi**, or 21.2 g (83%) of acid **VIIj**, respectively. Under the same conditions, using technical grade wet pyridine, from acids VIIIi and **IIIj** we obtained 20.3 g of a mixture of compounds **Vi** and **VIIi** (51 : 49, ^{1}H NMR data) and 18.4 g of a mixture of compounds **Vj** and **VIIj** (68 : 32, ^{1}H NMR data), respectively.

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