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KINETICS OF THE ACETIC ACID-CATALYSED RING-OPENING REACTION OF 2-PHENYL-4,4-DIMETHYL-2-OXAZOLIN-5-ONE WITH SOME AMINOACID ETHYL ESTERS IN CARBON TETRACHLORIDE

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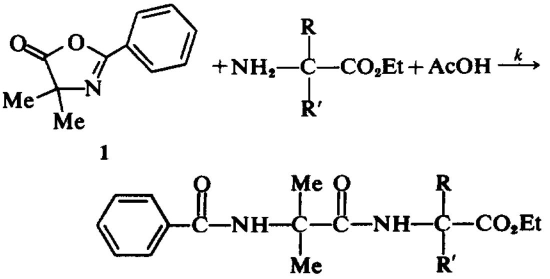
Abstract—The kinetic behaviour of the acetic acid-catalysed reaction of 2-phenyl-4,4-dimethyl-2-oxazolin-5-one (1) with the ethyl esters of glycine (2), DL-α-aminobutyric acid (4), α-aminoisobutyric acid (5), DL-norvaline (6), DL-valine (7), DL-leucine (8) and DL-phenylalanine (9) has been investigated. Within the concentration ranges employed the reactions follow second order kinetics, with no dependence of the experimental rate constant on the initial concentration of 1, just as found previously for the ethyl ester of DL-alanine. To explain the function of the catalyst a cyclic intermediate has been compared with other intermediates proposed for similar reactions. A good correlation has been obtained between the rate constant for the catalysed reaction and Taft's σ^* values, showing that the effects of the substituents on the esters are mainly polar and supporting the structure of the proposed intermediate.

In a previous paper[1] we have discussed the acetic acid-catalysed ring-opening reaction of 2-phenyl-4,4-dimethyl-2-oxazolin-5-one (1) with the ethyl ester of DL-alanine (3) in CCl_4 (Eq 2). This system was described quantitatively using the value of the dimerization constant, K_1, of acetic acid in CCl_4 (Eq 3), and that of the association constant, K_2, for the interaction between the acetic acid monomer and the aminoacid ester in CCl_4 (Eq 4) obtained by IR spectrometry.[2] It was shown that the catalytic species in the system is monomeric acetic acid, and the experimental rate constant, k, was found to be

$$k = k_0 + k'\,[\text{monomer}]^* \qquad \text{(Eq 1)}$$

where k_0 is the specific rate constant for the uncatalysed reaction, and k' is that for the catalysed reaction.



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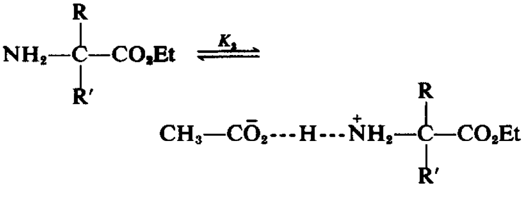
10 (Eq 2)

$$2CH_3{-}CO_2H \xrightleftharpoons{K_1} (CH_3{-}CO_2H)_2 \qquad \text{(Eq 3)}$$



$$NH_2{-}\overset{R}{\underset{R'}{C}}{-}CO_2Et \xrightleftharpoons{K_2} CH_3{-}C\bar{O}_2{\cdots}H{\cdots}\overset{+}{N}H_2{-}\overset{R}{\underset{R'}{C}}{-}CO_2Et$$

ion pair (Eq 4)

In this paper the same treatment is applied to a series of aminoacid ethyl esters with different substituents on the α-C atom, allowing the validity of our previous conclusions[1,2] to be checked, and the nature of the effects of the substituents on the nucleophile to be determined. The aminoacid esters studied, together with the corresponding values of K_2, their association constants with monomeric acetic acid,[2] are shown in Table 1, where R and R'

Table 1. Association constants for the interaction between monomeric acetic acid and some aminoacid ethyl esters

Aminoacid (as Et ester)	R	R'	K_2 M^{-1}
2 Glycine	H	H	282
3 DL-Alanine	H	Me	236
4 DL-α-Aminobutyric acid	H	Et	139
5 α-Aminoisobutyric acid	Me	Me	179
6 DL-Norvaline	H	Pr	104
7 DL-Valine	H	i-Pr	150
8 DL-Leucine	H	i-Bu	108
9 DL-Phenylalanine	H	Ph-CH_2	140

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*The following abbreviated expressions shall be used subsequently to denote, respectively, the concentrations of the oxazolinone 1, the ester, total acetic acid, and acetic acid monomer: [oxa], [ester], [AcOH] and [monomer].

refer to the groups on the aminoacid esters as shown in Eq 2. A value of 2252 M^{-1} was used for K_1.[1,2]

RESULTS AND DISCUSSION

As already observed for **3**,[1] the ring-opening reaction was found to be second order within the ranges of concentrations employed for **1** and the aminoacid esters:

$$v = k\,[\text{oxa}]\,[\text{ester}] \qquad (\text{Eq } 5)$$

where the specific rate constant, k, is as described in Eq 1. The value of k was obtained from the relation

$$k = \frac{2{\cdot}303}{t(a-b)} \log \frac{b(a-x)}{a(b-x)} \qquad (\text{Eq } 6)$$

and when t was plotted against

$$\log \frac{b(a-x)}{a(b-x)},$$

straight lines with correlations better than 0·99 were obtained in all cases.

The concentration of acetic acid monomer may be obtained from the following relation:[1]

$$[\text{monomer}]^3 + \frac{2K_1 + K_2}{2K_1K_2}[\text{monomer}]^2 + \frac{K_2[\text{ester}] - K_2[\text{AcOH}] + 1}{2K_1K_2}[\text{monomer}] - \frac{[\text{AcOH}]}{2K_1K_2} = 0 \qquad (\text{Eq } 7)$$

The effects of the variation of [ester] are shown in Tables 2.1, 3.1, 4.1, 5.1, 6.1, 7.1 and 8.1 (no results are given for **4** because at the higher concentrations the solutions are unstable and a precipitate is formed); in the second column of each table are listed the monomer concentrations calculated from Eq 7, and in the fourth column the values of k' calculated from Eq 1 assuming that, as a first approximation, k_0 is negligible.

Table 2.1. Influence of the variation of [**2**] when [oxa] = 82·50 × 10^{-4} M and [AcOH] = 16·85 × 10^{-4} M

[**2**] M × 10^4	[monomer] M × 10^4	$k \times 10^3$ M^{-1} sec^{-1}	k'_{calc} M^{-2} sec^{-1}
28·44	4·505	76·21	169·2
56·87	3·701	66·31	179·2
85·31	3·526	65·57	186·0
113·24	3·143	59·49	189·3
199·05	2·305	43·77	189·9
264·52	1·888	34·82	184·8
278·77	1·813	36·66	202·2
304·56	1·692	31·02	183·3
330·65	1·584	30·70	193·8
396·78	1·360	27·19	199·9

$\bar{k}'_{calc} = 187{\cdot}8\ M^{-2}\,\text{sec}^{-1}$

Table 2.2. Influence of the variation of [AcOH] when [oxa] = 82·50 × 10^{-4} M and [**2**] = 278·77 × 10^{-4} M

[AcOH] M × 10^4	[monomer] M × 10^4	$k \times 10^3$ M^{-1} sec^{-1}	$k_{calc} \times 10^3$ M^{-1} sec^{-1}
6·74	0·746	15·62	14·01
10·11	1·108	22·88	20·81
13·48	1·463	29·67	27·48
16·85	1·813	36·66	34·05
20·22	2·155	42·24	40·47
23·59	2·437	49·54	45·77
26·96	2·822	54·97	53·00

$k' = 191{\cdot}9\ M^{-2}\,\text{sec}^{-1}$
$k_0 = 1{\cdot}55 \times 10^{-3}\ M^{-1}\,\text{sec}^{-1}$
$r = 0{\cdot}999$

Table 3.1. Influence of the variation of [**3**] when [oxa] = 100·50 × 10^{-4} M and [AcOH] = 16·85 × 10^{-4} M

[**3**] M × 10^4	[monomer] M × 10^4	$k \times 10^3$ M^{-1} sec^{-1}	k'_{calc} M^{-2} sec^{-1}
33·58	4·509	24·87	54·01
61·45	4·090	20·94	49·95
146·34	3·021	14·81	47·35
167·95	2·861	13·61	45·80
181·10	2·748	13·23	46·25
222·06	2·442	11·65	45·66
294·05	2·029	10·04	46·95
307·86	1·971	9·33	44·77

$\bar{k}'_{calc} = 47{\cdot}59\ M^{-2}\,\text{sec}^{-1}$

Table 3.2. Influence of the variation of [AcOH] when [oxa] = 85·54 × 10^{-4} M and [**3**] = 115·44 × 10^{-4} M

[AcOH] M × 10^4	[monomer] M × 10^4	$k \times 10^3$ M^{-1} sec^{-1}	$k_{calc} \times 10^3$ M^{-1} sec^{-1}
3·37	0·850	5·14	4·56
6·74	1·591	8·64	8·08
10·11	2·259	11·43	11·27
13·48	2·778	15·07	13·74
16·85	3·410	16·99	16·74
20·22	3·892	19·69	19·02
30·33	5·258	27·63	25·54

$k' = 50{\cdot}42\ M^{-2}\,\text{sec}^{-1}$
$k_0 = 0{\cdot}51 \times 10^{-3}\ M^{-1}\,\text{sec}^{-1}$
$r = 0{\cdot}997$

Tables 2.2, 3.2, 4.2, 5.2, 6.2, 7.2, 8.2 and 9 show the effect of the variation of [AcOH]; the values of [monomer] calculated from Eq 7 are given in the second column of each table, and the values of k obtained from Eq 1 using the average values of k' in the fourth column.

Table 4.1. Influence of the variation of [5] when [oxa] = 82·21 × 10^{-4} M and [AcOH] = 16·85 × 10^{-4} M

[5] M × 10^4	[monomer] M × 10^4	$k \times 10^3$ M^{-1} sec^{-1}	k'_{calc} M^{-2} sec^{-1}
51·75	4·416	15·88	35·96
103·49	3·833	13·53	35·30
155·24	3·348	11·38	33·99
206·99	2·948	9·52	32·29
242·84	2·712	8·53	31·72
248·55	2·678	8·83	32·97
258·73	2·618	8·17	31·21
310·48	2·344	7·25	30·93

$\bar{k}'_{calc} = 33{\cdot}05$ M^{-2} sec^{-1}

Table 4.2. Influence of the variation of [AcOH] when [oxa] = 82·21 × 10^{-4} M and [5] = 242·84 × 10^{-4} M

[AcOH] M × 10^4	[monomer] M × 10^4	$k \times 10^3$ M^{-1} sec^{-1}	$k_{calc} \times 10^3$ M^{-1} sec^{-1}
6·74	1·197	3·80	3·96
10·11	1·732	5·51	5·72
13·48	2·235	7·07	7·39
16·85	2·713	8·53	8·97
20·22	3·160	9·74	10·44
26·96	4·015	12·60	13·27
33·70	4·799	15·57	15·86

$k' = 32{\cdot}2$ M^{-2} sec^{-1}
$k_0 = -0{\cdot}147 \times 10^{-3}$ M^{-1} sec^{-1}
$r = 0{\cdot}999$

Table 5.1. Influence of the variation of [6] when [oxa] = 82·21 × 10^{-4} M and [AcOH] = 16·85 × 10^{-4} M

[6] M × 10^4	[monomer] M × 10^4	$k \times 10^3$ M^{-1} sec^{-1}	k'_{calc} M^{-2} sec^{-1}
45·92	4·710	17·73	37·64
65·52	4·557	16·83	36·93
98·84	4·293	15·64	36·43
112·96	4·197	15·01	35·76
131·05	4·070	15·18	37·30
158·82	3·884	13·89	35·76
198·57	3·641	13·23	36·34
223·35	3·498	11·80	33·73
279·19	3·208	10·56	32·92
308·54	3·068	9·68	31·55

$\bar{k}'_{calc} = 35{\cdot}44$ M^{-2} sec^{-1}

Table 5.2. Influence of the variation of [AcOH] when [oxa] = 82·21 × 10^{-4} M and [6] = 129·00 × 10^{-4} M

[AcOH] M × 10^4	[monomer] M × 10^4	$k \times 10^3$ M^{-1} sec^{-1}	$k_{calc} \times 10^3$ M^{-1} sec^{-1}
6·74	2·074	7·81	7·38
10·11	2·845	10·70	10·12
13·48	3·487	13·63	12·40
16·85	4·084	15·78	14·53
20·22	4·632	17·47	16·48
26·96	5·616	20·77	19·98
33·70	6·501	22·89	23·12

$k' = 34{\cdot}46$ M^{-2} sec^{-1}
$k_0 = 1{\cdot}185 \times 10^{-3}$ M^{-1} sec^{-1}
$r = 0{\cdot}996$

Table 6.1. Influence of the variation of [7] when [oxa] = 82·50 × 10^{-4} M and [AcOH] = 16·85 × 10^{-4} M

[7] M × 10^4	[monomer] M × 10^4	$k \times 10^3$ M^{-1} sec^{-1}	k'_{calc} M^{-2} sec^{-1}
92·58	4·069	12·39	30·45
138·86	3·648	10·91	29·91
185·15	3·285	9·79	29·79
231·44	2·975	8·66	29·11
277·73	2·707	7·91	29·22
324·02	2·477	7·15	28·87

$\bar{k}'_{calc} = 29{\cdot}56$ M^{-2} sec^{-1}

Table 6.2. Influence of the variation of [AcOH] when [oxa] = 82·50 × 10^{-4} M and [7] = 229·03 × 10^{-4} M

[AcOH] M × 10^4	[monomer] M × 10^4	$k \times 10^3$ M^{-1} sec^{-1}	$k_{calc} \times 10^3$ M^{-1} sec^{-1}
6·74	1·390	4·05	4·11
10·11	1·939	5·85	5·73
13·48	2·482	7·44	7·34
16·85	2·991	9·07	8·84
20·22	3·469	10·07	10·25
26·96	4·376	12·37	12·93
33·70	5·171	14·43	15·28

$k' = 27{\cdot}14$ M^{-2} sec^{-1}
$k_0 = 0{\cdot}590 \times 10^{-3}$ M^{-1} sec^{-1}
$r = 0{\cdot}998$

Just as in the case of 3, it is seen that as [ester] is increased, the specific rate constant, k, decreases, and this can be accounted for satisfactorily if it is assumed that the most important catalytic species is the acetic acid monomer; this assumption is supported by the good agreement between the experimental values of k and those calculated from Eq 1 for the variation of [AcOH]. There is also good agreement between the values of k' obtained from a correlation of k with [monomer], and those calculated from Eq 1 for the variation of [ester].

The specific rate constant for the uncatalysed reaction, k_0, can be obtained from the correlation of [monomer] with k for the variation of [AcOH]. However, the resulting values of k_0 are not significant because they are too small; in fact, negative values are obtained for some of them. But k' can be

Table 7.1. Influence of the variation of [8] when [oxa] = $82{\cdot}21 \times 10^{-4}$ M and [AcOH] = $16{\cdot}85 \times 10^{-4}$ M

[8] M × 10^4	[monomer] M × 10^4	$k \times 10^3$ M^{-1} sec^{-1}	k'_{calc} M^{-2} sec^{-1}
34·94	4·801	13·80	33·65
69·89	4·502	12·78	28·39
104·83	4·230	10·82	25·58
153·26	3·882	11·29	29·08
204·35	3·564	9·63	27·02
255·44	3·274	8·67	26·48
294·31	3·082	7·61	24·69

$\bar{k}'_{calc} = 28{\cdot}37\ M^{-2}\ sec^{-1}$

Table 7.2. Influence of the variation of [AcOH] when [oxa] = $82{\cdot}21 \times 10^{-4}$ M and [8] = $195{\cdot}79 \times 10^{-4}$ M

[AcOH] M × 10^4	[monomer] M × 10^4	$k \times 10^3$ M^{-1} sec^{-1}	$k_{calc} \times 10^3$ M^{-1} sec^{-1}
6·74	1·745	4·45	4·95
10·11	2·433	6·39	6·90
13·48	3·047	8·41	8·64
16·85	3·641	10·03	10·33
20·22	4·136	11·54	11·73
26·96	5·090	14·36	14·44
33·70	5·948	16·64	16·87

$k' = 33{\cdot}51\ M^{-2}\ sec^{-1}$
$k_0 = -2{\cdot}428 \times 10^{-3}\ M^{-1}\ sec^{-1}$
$r = 0{\cdot}974$

Table 8.1. Influence of the variation of [9] when [oxa] = $82{\cdot}21 \times 10^{-4}$ M and [AcOH] = $16{\cdot}85 \times 10^{-4}$ M

[9] M × 10^4	[monomer] M × 10^4	$k \times 10^3$ M^{-1} sec^{-1}	k'_{calc} M^{-2} sec^{-1}
51·93	4·527	9·91	21·89
64·91	4·393	9·80	22·31
97·72	4·076	9·65	23·68
130·29	3·790	8·72	23·01
168·87	3·490	7·62	21·83
209·97	3·205	7·86	24·52
262·47	2·889	6·13	21·22
305·14	2·660	5·80	21·80

$\bar{k}'_{calc} = 22{\cdot}53\ M^{-2}\ sec^{-1}$

Table 8.2. Influence of the variation of [AcOH] when [oxa] = $82{\cdot}21 \times 10^{-4}$ M and [9] = $129{\cdot}83 \times 10^{-4}$ M

[AcOH] M × 10^4	[monomer] M × 10^4	$k \times 10^3$ M^{-1} sec^{-1}	$k_{calc} \times 10^3$ M^{-1} sec^{-1}
10·11	2·578	6·10	5·81
13·48	3·218	7·74	7·25
16·85	3·800	8·83	8·56
20·22	4·333	10·38	9·76
26·96	5·306	11·51	11·95
33·70	6·177	13·44	13·92

$k' = 19{\cdot}80\ M^{-2}\ sec^{-1}$
$k_0 = 1{\cdot}284 \times 10^{-3}\ M^{-1}\ sec^{-1}$
$r = 0{\cdot}994$

Table 9. Influence of the variation of [AcOH] when [oxa] = $82{\cdot}83 \times 10^{-4}$ M and [4] = $110{\cdot}60 \times 10^{-4}$ M

[AcOH] M × 10^4	[monomer] M × 10^4	$k \times 10^3$ M^{-1} sec^{-1}
10·11	2·726	10·68
13·48	3·380	13·55
16·85	3·967	16·26
20·22	4·515	18·68
26·96	5·496	23·09
33·70	6·375	26·06

$k' = 42{\cdot}80\ M^{-2}\ sec^{-1}$
$k_0 = -0{\cdot}819 \times 10^{-3}\ M^{-1}\ sec^{-1}$
$r = 0{\cdot}999$

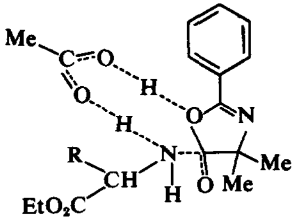
assigned relatively exact values that are of the order of 10^5 times larger than those of k_0.

Correlation with Taft's parameter σ^*.[3] When the values of k' are correlated with σ^*, straight lines with slope $\rho^* = 1{\cdot}256$ ($r = 0{\cdot}993$) are obtained. From the intercept, log k_0 is found to be 1·674, which compares favourably with the experimental value of 1·702 for the log of the catalytic constant of **3**. Since σ^* is considered to be a measure of the polar effect in aliphatic and *ortho*-substituted benzene compounds, it can be assumed that the effects of the substituents on the catalytic constant are mainly polar. The benzyl group of **9** is excluded from this correlation because it behaves anomalously.

The fact that a Taft correlation can be obtained would show some kind of electronic effect of the substituent, and the fact that the value of ρ^* is greater than 0 would disagree with the existence of a rate limiting step for the formation of a tetrahedral intermediate between the aminoacid ester and **1**.

The observed effects of the substituents, and the fact that a nonpolar solvent is used, have led us to believe that a cyclic intermediate can exist in the acetic acid-catalysed aminolysis of **1**. One molecule each of ester, **1** and acetic acid monomer would participate in the formation of this intermediate (**10**), that is in agreement with the rate equation and in which the rate limiting step would be the breaking of the N—H bond; the acetic acid would provide a proton that promotes the breaking of the C—O bond, and it would accept one from the amino group, thus aiding in the formation of the C—N bond.

Another possible intermediate is **11**, in which the



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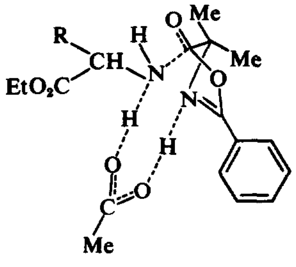

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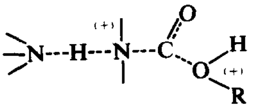
acetic acid shares its proton with the ring N atom, thus giving rise to a partial positive charge that facilitates the attack by the nucleophile, and at the same time promoting the removal of a proton from the amino group, this being probably the rate limiting step.

These conclusions are supported by the observations of several authors on the aminolysis of esters in different solvents,[4–9] some of whom have found the reactions to be catalysed by acids.[7–9]

Jencks and Carriuolo[7] have suggested the existence of intermediate **12** in aqueous solution. Satchell and Secemski,[8] using ether as solvent, propose **13** as an intermediate when a carboxylic acid is used as the catalyst, the acid acting in the dual role of promoting the release of a proton from the amino group and providing one for the formation of the OH group; such an intermediate would be energetically favoured by solvents of low dielectric constant, since no charges are involved that would be difficult to stabilize in such solvents. do Amaral *et al.*[9] propose intermediate **14** for the carboxylic acid-catalysed aminolysis of phenyl acetates in aqueous solution, i.e. an intermediate that requires both general acid and base catalysis; by varying the substituents on the phenyl group they found a value of 0·8 for Hammett's ρ.



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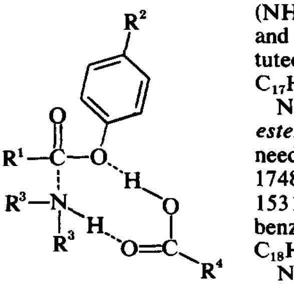

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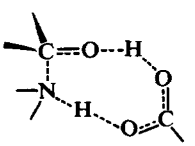

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EXPERIMENTAL

IR spectra and kinetic measurements were obtained on a Leitz model IIIG spectrophotometer. M.ps were determined on a Leitz microscope hot stage and are uncorrected. Elemental analyses were performed by Mr. Juan García in this Faculty.

Materials. AcOH and CCl_4 (E. Merck, Darmstadt, reagent grade) were kept over silica gel and were used without further purification. 2-Phenyl-4,4-dimethyl-2-oxazolin-5-one (**1**) was prepared as described.[1] The aminoacid esters **2**, **3**, **4**, **5**, **6**, **7**, **8**, **9** were prepared as described.[1,2] The products of the ring-opening reactions between **1** and the aminoacid ethyl esters were prepared as described for the reaction product of **1** and **3**.[1]

N-(N'-Benzoyl-α-aminoisobutyryl)glycine ethyl ester (**10**: R = R' = H), yield: 66% colorless, silky needles, m.p. 122°; IR (KBr): 3356 and 3300 (NH), 1730 (ester C=O), 1664 and 1637 (amide I), 1541 and 1522 (amide II), and 719 and 694 cm^{-1} (monosubstituted benzene ring). (Found: C, 61·26; H, 6·90; N, 9·12; $C_{15}H_{20}N_2O_4$ requires: C, 61·63; H, 6·90; N, 9·58%).

N-(N'-*Benzoyl-α-aminosiobutyryl*)-DL-*alanine ethyl ester* (**10**: R = H; R' = Me), yield and properties as described.[1]

N-(N'-*Benzoyl-α-aminoisobutyryl*)-DL-*α-aminobutyric acid ethyl ester* (**10**: R = H; R' = Et), yield: 88% small, colorless crystals, m.p. 112·5°; IR (KBr): 3300 and 3268 (NH), 1742 (ester C=O), 1658 and 1637 (amide I), 1546 and 1539 (amide II), and 728 and 696 cm^{-1} (monosubstituted benzene ring). (Found: C, 64·10; H, 7·52; N, 8·71; $C_{17}H_{24}N_2O_4$ requires: C, 63·73; H, 7·55; N, 8·74%).

N-(N'-*Benzoyl-α-aminoisobutyryl*)-*α-aminoisobutyric acid ethyl ester* (**10**: R = R' = Me), yield: 69% small, colorless crystals, m.p. 113·5°; IR (KBr): 3390 and 3333 (NH), 1727 (ester C=O), 1658 and 1637 (amide I), 1546 and 1527 (amide II), and 727 and 693 cm^{-1} (monosubstituted benzene ring). (Found. C, 63·77; H, 7·56; N, 8·30; $C_{17}H_{24}N_2O_4$ requires: C, 63·73; H, 7·55; N, 8·74%).

N-(N'-*Benzoyl-α-aminoisobutyryl*)-DL-*norvaline ethyl ester* (**10**: R = H; R' = Pr), yield: 96·2% colorless, silky needles, m.p 134·5–135°; IR (KBr): 3300 and 3268 (NH), 1748 (ester C=O), 1658 and 1637 (amide I), 1546 and 1531 (amide II), and 721 and 691 cm^{-1} (monosubstituted benzene ring). (Found: C, 64·76; H, 7·73; N, 8·31; $C_{18}H_{26}N_2O_4$ requires: C, 64·65; H, 7·84; N, 8·38%).

N-(N'-*Benzoyl-α-aminoisobutyryl*)-DL-*valine ethyl ester* (**10**: R = H, R' = i-Pr), yield: 90·6% colorless, silky needles, m.p. 96°; IR (KBr): 3390 and 3322 (NH), 1724 (ester C=O), 1658 and 1639 (amide I), 1546 and 1531 (amide II), and 730 and 694 cm^{-1} (monosubstituted benzene ring). (Found: C, 64·81; H, 8·08; N, 7·80; $C_{18}H_{26}N_2O_4$ requires: C, 64·65; H, 7·84; N, 8·38%).

N-(N'-*Benzoyl-α-aminoisobutyryl*)-DL-*leucine ethyl ester* (**10**: R = H; R' = i-Bu), yield: 99% white powder, m.p. 138·5°; IR (KBr). 3311 (NH), 1730 (ester C=O), 1658 and 1639 (amide I), 1546 and 1529 (amide II), and 721 and 691 cm^{-1} (monosubstituted benzene ring).

(Found: C, 65·39; H, 8·16; N, 7·95; $C_{19}H_{28}N_2O_4$ requires: C, 65·49; H, 8·10; N, 8·04%).

N-(N'-*Benzoyl-α-aminoisobutyryl*)-DL-*phenylalanine ethyl ester* (**10**: R = H; R' = Ph—CH_2), yield: 90% small, colorless crystals, m.p. 160°; IR (KBr): 3290 (NH), 1724 (ester C=O), 1655 and 1637 (amide I), 1546 and 1534 (amide II), and 721 and 692 cm^{-1} (monosubstituted benzene ring). (Found: C, 69·51; H, 6·88; N, 7·37; $C_{22}H_{26}N_2O_4$ requires C, 69·09; H, 6·85; N, 7·33%).

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REFERENCES

[1] H. Rodríguez, C. Chuaqui, S. Atala and A. Márquez, *Tetrahedron* **27**, 2425 (1971)

[2] N. Offermanns, A. Márquez, C. Chuaqui, H. Rodríguez, S. Atala and R. Pérez, *Ibid.* **28**

[3] R. W. Taft, Jr., *Separation of Polar, Steric and Resonance effects in Reactivity* (Edited by M. S. Newman), *Steric Effects in Organic Chemistry*, Chap. 13. Wiley, New York, (1956).

[4] R. L. Betts and L. P. Hammett, *J. Am. Chem. Soc.* **59**, 1568 (1937).

[5] W. H. Watanabe and L. R. de Fonso, *Ibid.* **78**, 4542 (1956).

[6] J. F. Bunnett and G. T. Davis, *Ibid.* **82**, 655 (1960).

[7] W. P. Jencks and J. Carriuolo, *Ibid.* **82**, 675 (1960).

[8] D. P. N. Satchell and I. I. Secemski, *J. Chem. Soc.* B 130 (1969).

[9] L. do Amaral, K. Koehler, D. Bartenbach, T. Pletcher and E. H. Cordes, *J. Am. Chem. Soc.* **89**, 3537 (1967).

[10] A. N. Sharpe and S. Walker, *J. Chem. Soc.* 2974 (1961).