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$CsF–Si(OEt)_4$ catalyzed addition of (hetero)aromatic amides to ethyl acrylate

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The conjugate addition of some (hetero)aromatic amides to an α,β-unsaturated ester (ethyl acrylate) proceeds efficiently in the presence of an equimolar amount of the $CsF–Si(OEt)_4$ system to afford the corresponding ethyl esters of N-substituted β-amino acids.

Keywords: N-conjugate addition; (hetero)aromatic acetamides; $CsF–Si(OEt)_4$ system; esters of N-substituted β-amino acids

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INTRODUCTION

The conjugate addition of stabilized carbanions to α,β-unsaturated carbonyl compounds (the Michael addition) is a fundamental method of carbon—carbon bond formation.[1] Contrary to C-conjugate addition, in the addition of N-heteronucleophiles there are several unfavorable factors, such as the difficulty of the NH group deprotonation and undesirable side reactions caused by the strong bases usually used as condensation catalysts.[2] There are few examples of N-conjugate addition under the action of non-basic catalysts. The addition of amines to α,β-unsaturated ketones and esters catalyzed by $FeCl_3$,[3] $InCl_3$,[4] lanthanide iodides,[5] and copper[6] has been reported. The N-conjugate additions of a thiolactam and of a urea to methyl acrylate have been studied[7,8] using NaOH in THF and K_2CO_3–$BnEt_3N^+Cl^-$–DMF catalytic systems, respectively. The $CsF–Si(OEt)_4$ system was proposed by Corriu and coworkers[9–12] as promoting Michael type reactions. It reacted selectively and efficiently giving 1,4-addition of ketones, β-cyano or β-keto esters and some other substrates to α,β-unsaturated ketones, esters and nitriles. The addition of some lactams to α,β-unsaturated esters has also been realized under the action of this mild catalytic system.[13] We have surmised that the $CsF–Si(OEt)_4$ system may be suitable for the N-conjugate addition of (hetero)-aromatic amides to ethyl acrylate. In the course of our recent study of the catalytic synthesis of some novel heterocyclic compounds[14] we now report the results of an investigation leading to esters of N-substituted β-amino acids.

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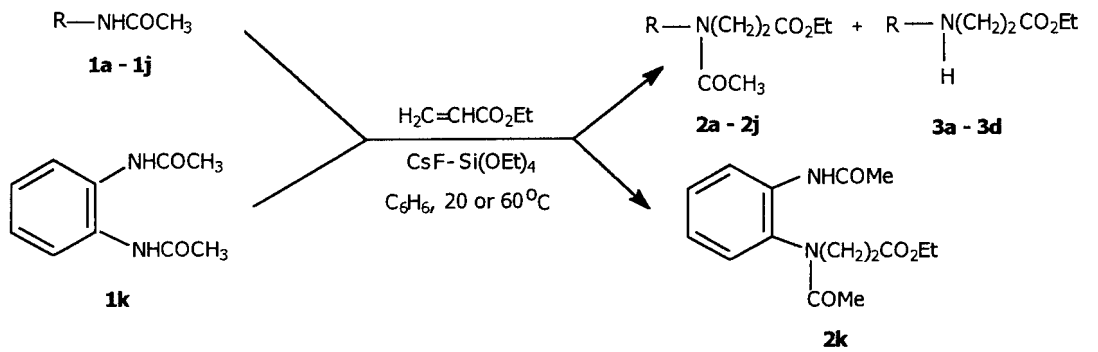
EXPERIMENTAL

General procedure

The reactions of amides with ethyl acrylate (Scheme 1) were carried out in 5 cm^3 Pierce vials under an argon atmosphere in benzene at ambient temperature or 60 °C until the conversion of the starting amides was 85–100% as defined by gas chromatography (GC) and gas chromatography – mass spectrometry (GC–MS) analysis. The Molar ratios of the reagents were as follows amide: $H_2C{=}CHCO_2Et$:$Si(OEt)_4$:CsF = 1:1.1:1.1:1. All the products (Table 1) were isolated by column chromatography (silica gel 60, eluent: chloroform–methanol = 9:1 or 9.5:0.5) as yellow oils. The compound **2k** was obtained as a white solid by recrystallization from benzene, m.p. 107–108 °C (found: C, 61.15; H, 6.86; N, 9.50. $C_{15}H_{20}N_2O_4$ requires C, 61.63; H, 6.90; N, 9.58). The spectral data of the products are listed in Tables 4 and 5.

Amides (**1a**–**1p**) were synthesized by the reactions of the corresponding amines with acetic anhydride catalyzed by $ZnCl_2$. The reactions were carried out in toluene at 0–5 °C for 0.5 h and then at 20 °C for 1.5 h. The molar ratios of amine to acetic anhydride and $ZnCl_2$ were as follows: 0.5:1.0:0.015; chloroform was used as a solvent



Scheme 1 Reactions of acetamides **1a** – **1k** with ethyl acrylate. R = 3-$F_3CC_6H_4$ (**1a** – **3a**), 4-$F_3CC_6H_4$(**1b** – **3b**), 2-pyridyl (**1c** – **3c**), 4-methyl-2-pyridyl (**1d** – **3d**), 3-methyl-2-pyridyl (**1e, 2e**), Ph (**1f, 2f**), 1-naphthyl (**1g, 2g**), 5-quinolyl (**1h, 2h**), benzyl (**1i, 2i**), 2-picolyl (**1j, 2j**).

for the extraction. After recrystallization from benzene the characteristics of the amides corresponded to known data.[15] The ^{1}H NMR and mass spectra obtained (previously not published) confirm their structures (Tables 2 and 3).

Materials and methods

Benzene and toluene were distilled over $LiAlH_4$. Amines and tetraethoxysilane were distilled or recrystallized; CsF was dried prior to use. Acetic anhydride, $ZnCl_2$ and ethyl acrylate were purchased

Table 1 Interaction of amides **1a – 1k** with ethyl acrylate in the presence of the CsF–$Si(OEt)_4$ system in benzene

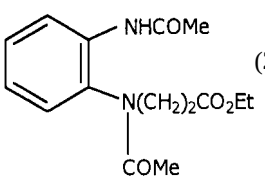
Amide	R	Reaction T(°C)	Reaction time(h)	Product	Isolated yield (GC),(%)
1a	3-$F_3CC_6H_4$	60	62	R—N(COMe)$(CH_2)_2CO_2$Et (**2a**)	42
				R—NH$(CH_2)_2CO_2$Et (**3a**)	(18)
1b	4-$F_3CC_6H_4$	60	62	R—N(COMe)$(CH_2)_2CO_2$Et (**2b**)	27
				R—NH$(CH_2)_2CO_2$Et (**3b**)	22
1c	2-pyridyl	20	24	R—N(COMe)$(CH_2)_2CO_2$Et (**2c**)	39
				R—NH$(CH_2)_2CO_2$Et (**3c**)	24
1d	4-methyl-2-pyridyl	60	50	R—N(COMe)$(CH_2)_2CO_2$Et (**2d**)	(22)
				R—N(COMe)$(CH_2)_2CO_2$Et (**3d**)	42
1e	3-methyl-2-pyridyl	20	24	R—N(COMe)$(CH_2)_2CO_2$Et (**2e**)	47
1f	Ph	20	18	R—N(COMe)$(CH_2)_2CO_2$Et (**2f**)	75
1g	1-naphthyl	60	20	R—N(COMe)$(CH_2)_2CO_2$Et (**2g**)	53
1h	5-quinolyl	60	20	R—N(COMe)$(CH_2)_2CO_2$Et (**2h**)	46
1i	benzyl	60	10	R—N(COMe)$(CH_2)_2CO_2$Et (**2i**)	85
1j	2-picolyl	60	50	R—N(COMe)$(CH_2)_2CO_2$Et (**2j**)	70
1k	1,2-C_6H_4	20	72	 (**2k**)	55

Table 2 ^{1}H NMR spectra of the amides synthesized

	Chemical shifts (ppm); J (Hz)				
Amide	CH_3CO (s)	CH_3-ring (s) (CH_3CH)	$CH_2(CH)$	Protons of the ring	NH (br s)
1a	2.24	—	—	7.3–7.5 (2 H, m, H-4,6), 7.5–7.8 (1 H, m, H-5),7.75 (1 H, br s, H-2)	7.9
1b	2.20	—	—	7.59 (4 H, br s)	7.4
1c	2.19	—	—	7.00 (1 H, m, H-6), 7.69 (1 H, m, H-4), 8.22 (2 H, m, H-3,5)	8.8
1d	2.38	2.20	—	6.84 (1 H, br s, J = 5.4, H-5), 8.01 (1 H, s, H-3), 8.09 (2 H, d, J = 5.4, H-6)	9.3
1e	2.29	2.25	—	7.04 (1 H, dd, J = 5.0, 2.0, H-5), 7.51 (1 H, m, H-4), 8.18 (1 H, m, H-6)	8.6
1f	2.16	—	—	6.9–7.6 (6 H, m, Ph + NH)	
1g	2.27	—	—	7.2 – 8.1 (7 H, m)	9.1
1h	2.31	—	—	7.41 (1 H, dd, J = 8.8, 3.8, H-3), 7.6–7.8 (2 H, m, H-4.7), 7.98 (1 H, d, J = 8.2, H-6), 8.19 (1 H, d, J = 8.6, H-8), 8.92 (1 H, dd, J = 2.2, <1, H-2)	7.6
1i	1.95	—	4.35 (2 H, d, J = 6.0)	7.22 (5 H, s, Ph)	6.0
1j	2.02	—	4.51 (2 H, d, J = 5.4)	6.9–7.3 (3 H, m, H-3,5 + NH), 7.60 (1 H, td, J = 7.6 and 2.0, H-4), 8.44 (1 H, br d, J = 4.6, H-6)	
1k	2.01 (6 H)	—	—	7.0–7.4 (4 H, m)	8.4 (2 H)
1l	1.93	1.44 (d, J = 7.0)	5.09 (1H, m, J_1 = 7.0)	7.3 (5 H, m, Ph)	5.9
1m	1.93	—	—	0.8–2.1 (10 H, m), 3.7 (1 H, br s)	5.3
1n	2.21	2.35	—	6.52 (1 H, br s, H-5)	10.5
1o	2.42	2.15	—	6.87 (1 H, d, J = 8.0, H-5), 7.55 (1 H, t, J = 8.0, H-4), 7.95 (1 H, d, J = 8.0, H-3)	8.0
1p	2.18 (6 H)	—	—	7.69 (1 H, t, J = 8.2, H-4), 7.87 (2 H, d, J = 8.2, H-3,5)	8.6 (2 H)

from commercial sources (Fluka, Aldrich) and used without purification. Silica gel (Kieselgel 60, 0.063–0.200 mm, Merck) was used for column chromatography.

^{1}H NMR spectra were recorded on Bruker WH-90/DS (90 MHz) and Varian Mercury (200 MHz) spectrometers using $CDCl_3$ as a solvent and Me_4Si as an internal standard. The mass spectra (MS) were obtained on an HP 6890 GC/MS instrument equipped with a capillary column HP-5 MS (30.0 m × 250 μm × 0.25 μm). The GC analyses of the reaction mixtures were performed on a Chrom-4 chromatograph equipped with a flame-ionization detector and glass column (2.4 m ×3 mm) packed with 5% OV-17 on Chromosorb W-AW (60–80 mesh); the carrier gas was nitrogen (60 ml min^{-1}). Elemental analysis was performed using a Carlo Erba EA-1108 instrument.

RESULTS AND DISCUSSION

In this work, the reactions of ethyl acrylate with 14 mono- and two bis-acetamides obtained by the acylation of amines with acetic anhydride were investigated. It was found that the title reaction did not proceed in the presence of CsF or $Si(OEt)_4$ alone. When an equimolar amount of the CsF–$Si(OEt)_4$ system in benzene was used addition took place giving the corresponding ethyl esters of N-substituted β-amino acids (Scheme 1).

The results (Table 1) suggest that the structure of the acetamides has a great influence on the reactivity. The aromatic amides have been found to be much more active than their trifluoromethyl derivatives and heterocyclic amides. Acetamides R—$NHCOCH_3$, where R = Ph(Me)CH (**1l**), C_6H_{11} (**1m**), 5-methyl-2-thiazolyl (**1n**), 6-methyl-2-pyri-

Table 3 Mass spectra of the amides synthesized

Amide	GC–MS, *m/z* (I_{rel}, %)
1a	203 (16, M^+), 184(8, $[M - F]^+$), 174(2,$[M - HCO]^+$), 168 (8), 161(100,$[M - COCH_2]^+$), 145 (3,$[M - NHCOMe]^+$), 142 (7, $[M - COCH_2 - F]^+$), 133 (3), 114 (11), 113 (5), 111 (8), 69 (2 $[CF_3]^+$), 63(7) 43 (36, $[COMe]^+$)
1b	203 (20, M^+), 184 (4, $[M - F]^+$), 174 (3, $[M - HCO]^+$), 162 (8), 161 (100, $[M - COCH_2]^+$), 142 (25, $[M - COCH_2 - F]^+$), 133 (5), 114 (8), 113 (7), 111 (20), 83 (5), 69 (3, $[CF_3]^+$), 63 (8), 43 (42, $[COMe]^+$)
1c	136 (29, M^+), 121 (2, $[M - Me]^+$), 95 (7), 94 (100, $[M - COCH_2]^+$), 93 (6), 78 (13, Py^+), 68 (5), 67 (98), 66 (10), 51 (9), 43 (40, $[COMe]^+$), 39 (23)
1d	150 (27, M^+), 135 (5, $[M - Me]^+$), 121 (1, $[M - 2Me + H]^+$), 109 (7), 108 (100, $[M - COCH_2]^+$), 92 (7, $[M - NHCOMe]^+$), 81 (50), 80 (45), 65 (9), 53 (15), 43 (27, $[COMe]^+$), 39 (10)
1e	150 (28, M^+), 135 (14, $[M - Me]^+$), 108 (100, $[M - COCH_2]^+$), 107 (25), 92 (9, $[M - NHCOMe]^+$), 91 (10), 81 (32), 80 (40), 65 (6), 53 (18), 43 (29, $[COMe]^+$), 39 (15)
1f	135 (26, M^+), 94 (8), 93 (100, $[M - COCH_2]^+$), 92 (6), 77 (20, Ph^+), 66 (18), 65 (15), 63 (5), 51 (5), 43 (21, $[COMe]^+$), 39 (13)
1g	185 (27, M^+), 144 (14), 143 (100, $[M - COCH_2]^+$), 140 (5), 127 (3, $[M - NHCOMe]^+$), 116 (13), 115 (36), 89 (7), 75 (3), 63 (6), 51 (3) 43 (15, $[COMe]^+$)
1h	186 (25, M^+), 145 (14), 144 (100, $[M - COCH_2]^+$), 117 (20), 116 (15), 90 (7), 89 (14), 76 (3), 63 (7), 51 (5), 43 (23, $[COMe]^+$)
1i	149 (69, M^+), 107 (19), 106 (100, $[M - COMe]^+$), 104 (8), 91(34, $[PhCH_2]^+$), 89 (5), 79 (19), 78 (8), 77 (20, Ph^+), 65 (12), 51 (18), 43 (40, $[COMe]^+$), 39 (10)
1j	150 (10, M^+), 135 (11, $[M - Me]^+$), 108 (12), 107 (100, [M − COMe]), 92 (38, $[M - NHCOMe]^+$), 80 (20), 79 (18), 78 (13), 65 (9), 52 (12), 43 (22, $[COMe]^+$), 39 (9), 30 (8)
1k	192 (21, M^+), 174 (3), 150 (15, $[M - COCH_2]^+$), 135 (14, $[M - NCOMe]^+$), 134 (8), 133 (38, $[M - NHCOMe - H]^+$), 132 (33), 109 (8), 108 (100, $[M - 2COCH_2]^+$), 107 (32), 80 (33), 52 (13), 43 (55, $[COMe]^+$)
1l	163 (36, M^+), 148 (17, $[M - Me]^+$), 120 (32, $[MCOMe]^+$),106 (100, $[M - NCOMe]^+$), 105 (19), 104 (30), 103 (9), 91 (3), 79 (17), 78 (12), 77 (29, Ph^+), 63 (4), 51 (16), 43 (31, $[COMe]^+$), 39 (8)
1m	141 (28, M^+), 98 (19, $[M - COMe]^+$), 82 (6, $[M - NHCOMe - H]^+$), 70 (13), 67 (11), 60 (71), 56 (100), 43 (21, $[COMe]^+$), 41 (26), 39 (20)
1n	156 (22, M^+), 115 (7), 114 (100, $[M - COCH_2]^+$), 73 (8), 72 (23), 71 (14), 70 (13), 44 (19), 43 (38, $[COMe]^+$), 42 (16), 40 (6)
1o	150 (26, M^+), 135 (5, $[M - Me]^+$), 108 (100, $[M - COCH_2]^+$), 92 (9, $[M - NHCOMe]^+$), 81 (58), 80 (31), 66 (7), 65 (9), 53 (9), 43 (23, $[COMe]^+$), 39 (17)
1p	193 (16, M^+), 178 (2, $[M - Me]^+$), 151 (42, $[M - COCH_2]^+$), 136 (5, $[M - COCH - Me]^+$), 110 (7), 109 (100, $[M - 2COCH_2]^+$), 93 (5), 82 (29), 81 (13), 66 (6), 54 (5), 43 (49, $[COMe]^+$), 39 (7)

dyl (**1o**) and 2,6-diacetamidopyridine (**1p**) did not undergo the addition at all. An unusual direction of the reactions was observed in the case of trifluoromethyl derivatives **1a, 1b** and pyridine amides **1c, 1d**: the addition occurred with the elimination of the acetyl group giving the compounds **3a**–**3d**. All the products (Table 1) except **3a** and **2d** were isolated by column chromatography in yields from 22 to 85% and were characterized by ^{1}H NMR and mass spectra. The compounds **3a** and **2d** obtained in low yields were characterized by mass spectra only. The spectra (Tables 4 and 5) confirmed the proposed structures.

Two total sets of peaks of all protons are observed in ^{1}H NMR spectra for **2i** and **2j** compounds. Such a doubling of signals could be caused by the stability of the pyramidal structure of the amide atom of nitrogen in the Ph(2-Py)—CH_2—$N(COCH_3)CH_2$ fragment. Analogous to other compounds of trivalent nitrogen,[16] the barrier to inversion is possibly explained by repulsion between the nitrogen lone pair and the Ph 2-R, electrons in **2i** and **2j** respectively. On absence of CH_2 group between the amide nitrogen and the aromatic cycle, conjugation in the Ar(Het)—N chain increases, the barrier to inversion decreases and doubling of the signals did not occur as observed in the ^{1}H NMR spectra for all other compounds studied (Table 4).

The reaction of 1,2-diacetamidobenzene (**1k**) with ethyl acrylate leads to mono-addition product (**2k**), which was confirmed by mass spectra (Table 5)

Table 4 ^{1}H NMR spectra of the esters of N-substituted β-amino acids obtained

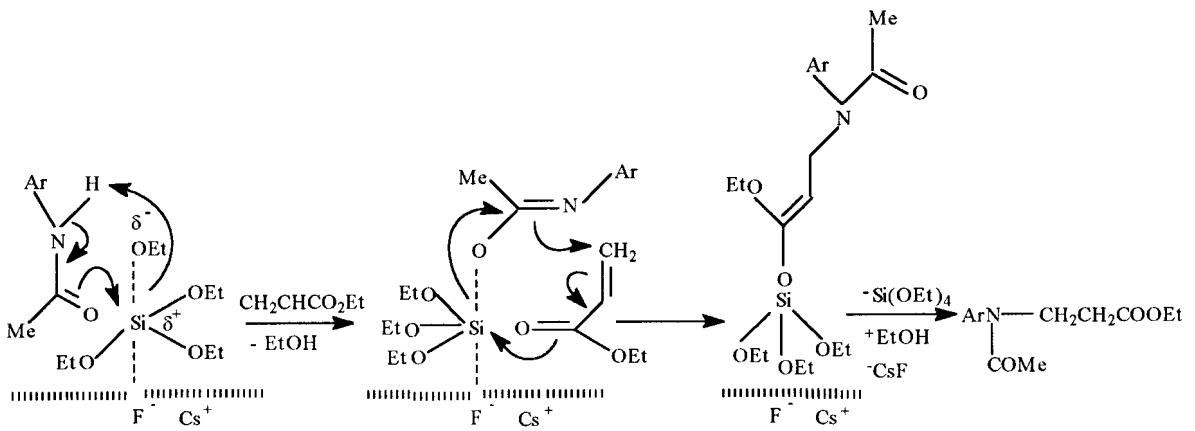
Compound	Chemical shifts (ppm), *J* (Hz)								
	Et		CH_3CO(s)	C*H*$_3$-ring(s)	CH_2CO	CH_2N	Ring-C*H*$_2$(s)	Protons of the ring (s)	NH(br,s)
	CH_3 (t)	CH_2 (q)							
2a	1.20 *J* = 7.0	4.01	1.84	—	2.55, t *J* = 7.0	4.00, t	—	7.2–7.6 (4H, m, Ar)	—
2b	1.19 *J* = 7.0	4.04	1.40	—	2.62, t *J* = 7.0	4.15, t	—	7.3–7.7 (4H, m, J_1 = 8.5, Ar)	—
3b	1.24 *J* = 7.0	4.15	—	—	2.60, t *J* = 6.6	3.48, t	—	6.6–7.4 (4H, m, J_1 = 8.8, Ar)	4.4
2c	1.18 *J* = 7.2	4.04	1.99	—	2.66, t *J* = 7.0	4.12, t	—	7.2–7.3 (2H, m, H-3,5), 7.77 (1H, td, *J* = 7.6, 1.6, H-4), 8.51 (1H, dd, *J* = 4.8, 1.6, H-6)	—
3c	1.26 *J* = 7.2	4.15	—	—	2.63, t *J* = 6.4	3.64, t	—	6.39 (1H, d, *J* = 8.4, H-3), 6.56 (1H, m, *J* = 7.2, 5.0, H-5), 7.38 (1H, m, *J* = 8.4, 7.2, 3.8, H-4), 8.07 (1H, d, *J* = 5.0, H-6)	5.0
3d	1.30 *J* = 7.6	4.13	—	2.27	2.62, t *J* = 6.8	3.62, m,	—	6.22 (1H, s, H-3), 6.40 (1H, d, *J* = 5.5, H-5), 7.89 (1H, d, *J* = 5.5, H-6)	4.4
2e	1.17 *J* = 7.2	4.01	1.75	2.31	2.70 (4H, t, *J* = 7.04)		—	7.22 (1H, dd, *J* = 7.4, 4.8, H-5), 7.65 (1H, dd, *J* = 7.4, 2.0, H-4), 8.34 (1H, dd, *J* = 4.8,2.0, H-6)	—
2f	1.07 *J* = 7.0	3.69	1.66	— —	2.41, t,	3.84, t, *J* = 7.2	—	6.9–7.4 (5H, m, Ph)	—
2g	1.16 *J* = 7.2	4.02	1.77	—	2.67 (m, *J* = 7.8, 5.8, 2.0)	3.4–3.8 (1H, m, *J* = 12.5, 7.8, 2.0) 4.3–4.7 (1H, m, *J* = 12.5, 7.8, 2.0)	—	7.37 (1H, dd, *J* = 7.2, 1.2, H-2), 7.5–7.6 (3H, m, H-3, 6, 7), 7.8–8.0 (3H, m, H-4, 5, 8)	—
2h	1.15 *J* = 7.4	4.00	1.73	—	2.63 (m, *J* = 7.6, 5.3, 1.6)	3.68 (1H, m, *J* = 8.0, 7.6, 1.6) 4.48 (1H, m *J* = 8.0, 7.6, 1.6)	—	7.44 (1H, dd, *J* = 7.4, 1.6, H-8), 7.51 (1H, dd, *J* = 8.5, 4.2, H-3),7.75 (1H, dd, *J* = 7.4, H-7) 8.16 (2H, dt, *J* = 8.5, 1.6, H-4, 6) 9.0 (1H, dd, *J* = 4.2, 1.6, H-2)	

Table 4 continued.

Compound	Chemical shifts (ppm), *J* (Hz)								
	Et		CH_3CO(s)	CH_3-ring(s)	CH_2CO	CH_2N	Ring-CH_2(s)	Protons of the ring (s)	NH(br,s)
	CH_3 (t)	CH_2 (q)							
2i	1.22 & 1.26 *J* = 7.0	4.08 & 4.10	2.09 & 2.21	—	2.50, m & 2.60, m	3.55, m & 3.61, m	4.59	7.22 (5H, m)	—
2j	1.22 & 1.23 *J* = 7.2	4.08 & 4.09	2.10 & 2.23	—	2.59,m & 2.63, m	3.68, m & 3.70, m	4.68 & 4.69	7.19 & 7.1–7.3 (2H, m, H-3,5) 7.59 & 7.63 (1H, m, H-4) 8.51 & 8.58 (1H, m, H-6)	—
2k	1.31 *J* = 7.2	4.15	1.80 & 2.27 (Me-CONH)	—	2.1–2.7 (m, *J* = 14.0, 12.0, 5.4)	3.44 (1H, dt, *J* = 14.0, 5.4) 4.58 (1H, m, 12.0, 5.4)	—	7.09 (2H, m, H-4,5) 7.38 (1H, m, H-3) 8.40 (1H, m, H-6)	9.1

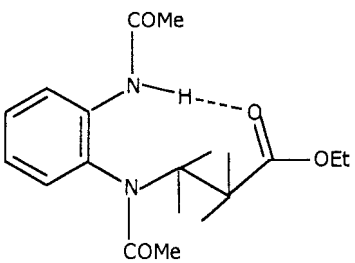
Table 5 Mass spectra of the esters of N-substituted β-amino acids obtained

Product	GC–MS, *m/z* (I_{rel}, %)
2a	303 (2, M^+), 284 (3, $[M - F]^+$), 261 (25, $[M - COCH_2]^+$), 260 (15), 258 (8, $[M - OEt]^+$), 232 (2, $[M - COCH_2 - Et]^+$), 216 (7, $[M - COCH_2 - OEt]^+$), 203 (3 $[M - CHCH_2CO_2 Et]^+$ 188 (6, $[M - COCH_2 - CO_2Et]^+$), 175 (9) 174 (100, $[M - COCH_2 - H_2CO_2Et]^+$), 145 (14, $[M - N(COMe)CH_2CH_2CO_2Et]^+$), 43 (32, $[COMe]^+$)
3a	261 (26, M^+), 260 (16), 216 (7, $[M - OEt]^+$), 188 (6, $[M - CO_2Et]^+$), 175 (10), 174 (100, $[M - CH_2CO_2Et]^+$), 172 (15), 161 (6, $[M - CHCH_2CO_2Et]+$), 145(14, $[M - NHCH_2CH_2CO_2Et]^+$), 127 (5), 110(5), 95(5), 55(6)
2b	303 (2, M^+), 261 (24, $[M - COCH_2]^+$), 260 (16), 258 (8, $[M - OEt]^+$), 242 (3, $[M - COCH_2 - F]^+$), 232 (2, $[M - COCH_2 - Et]^+$), 216 (7, $[M - COCH_2 - OEt]$ 203 (3, $[M - CHCH_2CO_2eT]^+$), 188 (6,$[M- COCH_2-CO_2Et]^+$), 175 (9), 174(100, $[M-COCH_2-CH_2CO_2Et]^+$), 172 (14), 161 (5, $[M - COCH_2-CHCH_2CO_2Et]^+$), 145(13,$[M-N(COMe)CH_2CH_2CO_2Et]^+$), 55(5), 43(32, $[COMe]^+$)
3b	261 (23, M^+), 244 (7), 242 (2, $[M - F]^+$), 215 (3, $[M - OEt - H]^+$), 202 (5), 188 (6, $[M - CO_2Et]^+$), 175 (10), 174 (100, $[M - CH_2CO_2Et]^+$), 172 (15), 161 (5, $[M - CHCH_2CO_2Et]^+$), 145(15, $[M - NHCH_2CH_2CO_2Et]^+$), 127 (5), 55(10)
2c	236 (7, M^+), 221 (2, $[M - Me]^+$), 207 (5, $[M - Et]^+$), 194 (27, $[M - COCH_2]^+$), 193 (22, $[M - COMe]^+$), 191 (14, $[M - OEt]^+$), 163 (5, $[M - CO_2Et]^+$), 149 (8, $[M - COCH_2- OEt]^+$), 147 (29, $[M - COMe - OEt - H]^+$), 120 (8) 121 (88, $\{PyNHCH_2CH_2]^+$), 119 (20), 108 (7), 107 (100), $[PyNHCH_2]^+$), 105 (7), 94 (13, $[PyNH_2]^+$), 79 (19, PyH^+), 78(45,Py^+), 67(5), 51 (9) 43(36, $[COMe]^+$)
3c	194 (23, M^+), 149 (10, $[M - OEt]^+$), 147 (6), 122 (8), 121 (93, $[PyNHCH_2CH_2]^+$), 119 (12), 108 (7), 107 (100, $[PyNHCH_2]^+$), 105 (5), 94 (13, $[PyNH_2]^+$), 79 (19, PyH^+), 78 (48,Py^+), 73 (6), 67 (13), 5 (12), 39(13)
2d	250 (8, M^+), 249 (9, $[M - H]^+$), 221 (3, $[M - HCO]^+$), 208 (18), 207 (25, $[M - COMe]^+$), 205 (14, $[M - OEt]^+$), 177 (6, $[M - COEt]^+$), 163 (7), 162 (6), 161 (32, $[M - COMe - OEt - H]^+$), 150(3), 136 (8) 135(86, $[M - COCH_2 - CO_2Et]^+$), 133(11), 122 (9), 121 (100, $[M - COCH - CH_2CO_2Et]^+$), 119(6) 108 (13, $[C_5H_3N(Me)NH_2]^+$), 93 (15), 92 (36) $[C_5H_3N(Me)]^+$), 80 (8), 65 (19), 55 (7), 43 (30 [COMe]), 39(8)
3d	208 (18, M^+), 163 (9, $[M - OEt]^+$), 161 (5), 136 (9), 135 (100, $[M - CO_2Et]^+$), 133 (10), 122 (7), 121 (88, $[M - CH_2CO_2Et]^+$), 108 (22, $[C_5H_3N(Me)NH]^+$), 93 (12), 92(33, $[C_5H_3N(Me)]^+$), 81(5), 80(9), 66(8), 65(19), 53(8), 39(9)
2e	250 (3, M^+), 235 (25, $[M - Me]^+$), 208 (14), 207 (45, $[M - COMe]^+$), 205 (15, $[M - OEt]^+$), 177 (6, $[M - CO_2Et]^+$), 163 (9), 162 (7), 161 (44, $[M - COMe - OEt - H]^+$), 150 (7), 136(9), 135(98, $[M - COCH_2 - CO_2Et]^+$),133(24), 122(7), 121 (100, $[M - COCH_2 - CH_2CO_2Et]^+$), 119(16), 108 (18, $[C_5H_3N(Me)NH_2]^+$), 93(21), 92(46), $[C_5H_3N(Me)]^+$), 80(12), 65(25), 53(8), 43(38, $[COMe]^+$)
2f	235 (3, M^+), 206 (2, $[M - Et]^+$), 193 (22, $[M - COCH_2]^+$), 192 (16, $[M - COMe]^+$), 190 (8, $[M - OEt]^+$), 148 (9, $[M - COCH_2\text{-}OEt]^+$), 120 (6, $[PhNHCH_2CH_2]^+$), 105 (9), 106(100, $[PhNHCH_2]^+$), 104(13), 93(6), 77(17, Ph^+), 65(5), 51(7), 43(32,$[COMe]^+$)
2g	285 (10, M^+), 244 (6), 243 (35, $[M - COCH_2]^+$), 242 (7), 240 (10, $[M - OEt]^+$), 215 (2), 198 (5, $[M - CH_2CO_2Et]^+$), 185 (4, $[M - CHCH_2CO_2Et]^+$) 168(7, $[M - COMe - HCO_2Et]^+$), 157(13), 156 (100, $[M - COCH_2 - CH_2CO_2Et]^+$), 155(20), 154 (39), 143 (15), 142(51, $[M - COCH_2 - CH_2CH_2CO_2Et]^+$), 141(7), 140(6) 129(20), 128(18) 127(30, $[M - N(COMe)CH_2CH_2C0_2Et]^+$), 126 (7), 115(21), 101(43), 77(6), 73(13), 63(4), 55(7), 43(67, $[COMe]^+$)
2h	186 (25, M^+), 145 (14), 144 (100, $[M - COCH_2]^+$), 117 (20), 116 (15), 90 (7), 89 (14), 76 (3), 63 (7), 51 (5), 43 (23, $[COMe]^+$)
2i	249 (1, M^+), 207 (12), 206 (85, $[M - COMe]^+$), 204 (10), 174 (3), 162 (8, $[M - CH_2CO_2Et]^+$), 160 (7), 148 (3, $[M - CH_2CH_2CO_2Et]^+$), 132 (6, $[PhCH_2NCH_2CH]^+$), 120(25, $[PhCH_2NHCH_2]^+$), 118 (35, $[PhCH_2NCH]^+$), 116(9), 106(34, $[PhCH_2NH]^+$), 92(9), 91(100, $[PhCH_2]^+$), 77 (5, Ph^+), 65(19), 51 (4), 43(51, $[COMe]^+$), 42(10), 39(6)
2j	250 (1, M^+), 235 (1, $[M - Me]^+$), 205 (3, $[M - OEt]^+$), 177 (1, $[M - CO_2Et]^+$), 163 (4, $[M - CH_2CO_2Et]^+$), 160 (7), 133 (5, $[PyCH_2NHCH_2CH]^+$), 121(11), $[PyCH_2NHCH_2]^+$), 107 (6, $[PyCH_2NH]^+$), 94(7), 93(100, $[PyCH_2]^+$), 92(16), 79 (3, PyH^+), 78(3,Py^+), 65(8), 43 (16, $[COMe]^+$),
2k	292 (13, M^+), 277 (5, $[M - Me]^+$), 249 (7, $[M - COMe]^+$), 247 (6), 234 (10), 233 (55, $[M - COMe - Me - H]^+$), 232 (23), 219 (2, $[M - CO_2Et]^+$), 205 (10, $[M - CH_2CO_2Et]^+$), 203(10), 189 (15), 163(37), 161(35, $[C_6H_4(NHCO)NCO]^+$), 134(11), 133(27, $[C_6H_4(NCHO)NH]^+$), 132(15), 121 (64), 119 (100, $[C_6H_4NHCO]^+$), 107(11, $[C_6H_4(NH)NH_2]^+$), 92(17), $[C_6H_4NH]^+$), 80(11), 65 (15), 55(10), 43(95, $[COMe]^+$), 39(5)



Scheme 3 Proposed mechanism of N-conjugate addition of aromatic amides to ethyl acrylate.

and elemental analysis. In the ^{1}H NMR spectrum (Table 4) of **2k**, the signals of the —$NCH_2CH_2CO_2$ protons formed complete multiplets of ABMN type, while this group gives two simple triplets of the A_2M_2 type in the spectra of the other compounds (Table 2). This means that free rotation around the H_2C—CH_2 bond is absent in **2k**, clearly due to strong NH…O=C hydrogen bond formation. The large chemical shift of the NH proton ($\delta = 9.1$) confirms this presumption. Thus, the structure of **2k** was elucidated by ^{1}H NMR as follows (Scheme 2):



Scheme 2.

Analogous to C—C bond formation[17–19] the proposed mechanism of N-conjugate addition involves coordination of the fluoride ion to $Si(OEt)_4$, generating the basic species EtO. The latter promotes enolate formation from the amide. Fast silylation of this intermediate leads to the silyl enol ether, which enables 1,4-addition of α,β-unsaturated ester. The complex obtained reacts *in situ* with the alcohol present in the mixture to give the N-substituted adduct (Scheme 3).

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