EFFICIENT SYNTHESIS OF β-AMINOACRYLATES AND β-ENAMINONES CATALYZED BY $Zn(OAc)_2 \cdot 2H_2O$

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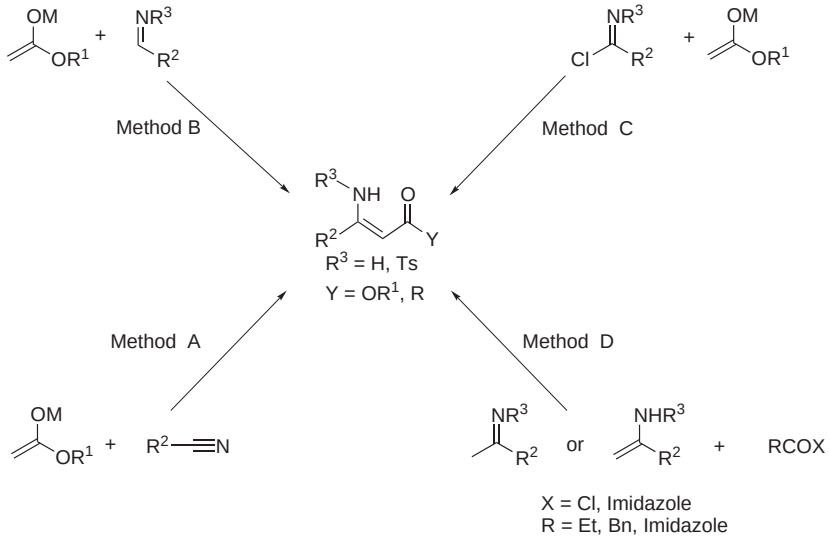
The direct condensation of amines with β-ketoesters and β-diketones to produce functional enamine derivatives has been investigated with zinc Lewis acid catalysts. $Zn(OAc)_2 \cdot 2H_2O$ shows good catalytic activity and leads to a chemo- and stereoselective formation of (Z)-enamine derivatives from aliphatic primary amines and ring-substituted anilines under mild conditions.

Keywords: Zinc catalysts; β-Aminoacrylates; β-Enaminones; Acrylates; Enamines; Lewis acids; Amines; β-Ketoesters.

β-Functionalized enamine derivatives are useful precursors in synthesis, as they combine nucleophilicity of the enamine and electrophilicity of the enone motives. Such derivatives are valuable intermediates for the synthesis of biologically active compounds, such as α-[1] and β-amino acids[2], alkaloids[3], peptides[4], and heterocycles[5]. They exhibit a wide range of biological activities, and have found applications as anti-inflammatory[6], antitumor[6a,7], anticonvulsant agents[6a,8]. β-Enaminones and β-aminoacrylates can be obtained either via the addition of ester or amide enolates to nitriles (method A)[9], tosylimines (method B)[10] and imidoyl halides (method C)[11], or the addition of enamines[12] or ketimines[13] to activated carboxylic acid derivatives (method D) (Scheme 1). More functional derivatives substituted at the C2 position of acrylates have been prepared from active methylene compounds and amide acetals.[14]

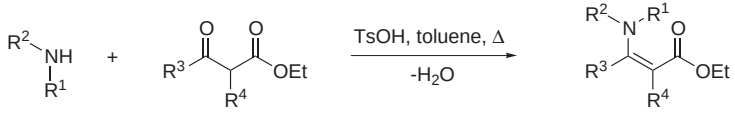
The most commonly used route involves a direct condensation of amines with β-dicarbonyl compounds in an aromatic solvent with azeotropic removal of water at high temperature (Scheme 2)[15,16].

Alternatively, primary amines also react with β-dicarbonyl compounds in water to give enaminones[17]. Some improved procedures have been reported using Al_2O_3 [18], SiO_2 [19], K10-montmorillonite[20], $NaAuCl_4$ [21], or micro-



SCHEME 1

waves[22]. However, these methods suffer from low selectivity (due to transformation of the β-ketoester into β-ketoamide), unsatisfactory yields, and harsh conditions. Therefore, due to the importance of these derivatives in organic chemistry, the development of a more efficient procedure was desired.

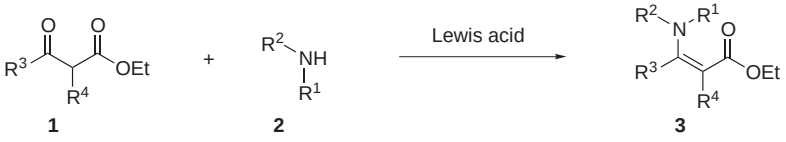


SCHEME 2

Lewis acid-catalyzed reaction are now of great interest because of their unique reactivity and selectivity under mild conditions[23]. Recently, $ZnClO_4 \cdot 6H_2O$ [24], $Bi(TFA)_3$ in water[25a] or molten salt[25b], and $CeCl_3 \cdot 7H_2O$ [26], were found to be very active for the synthesis of β-enaminones or β-aminoacrylates.

As a part of our program directed toward the preparation of optically active amine compounds via enantioselective hydrogenation[2,27], we investigated the use of an efficient Lewis acid catalyst for the synthesis of *N*-substi-

tuted β-aminoacrylates **3** via direct condensation of primary or secondary amines **2** with β-ketoester **1** (Scheme 3).



SCHEME 3

RESULTS AND DISCUSSION

The Lewis acid-catalyzed condensation of amines with β-ketoesters or β-diketones has recently been described[24–26]. With the objective of carrying out enamine formation and hydrogenation in one pot, we were interested in a cheap and efficient catalyst that could be safely used under reductive conditions in the presence of hydrogen. Thus, we tested the activity of various zinc salts (5 mole %) for the direct formation of aminoacrylate **4** from benzylamine **2a** (1.5 equivalents) and ethyl 2-oxocyclopentane-1-carboxylate **1a** (1 equivalent) in dichloromethane at room temperature in the presence of magnesium sulfate (Table I).

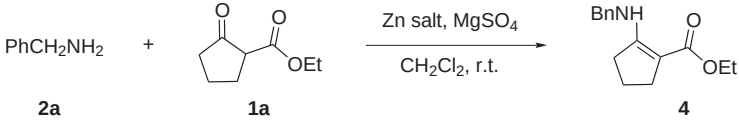


TABLE I
Reaction of benzylamine (**2a**) with ethyl 2-oxocyclopentane-1-carboxylate (**1a**) in the presence of zinc catalyst[a]

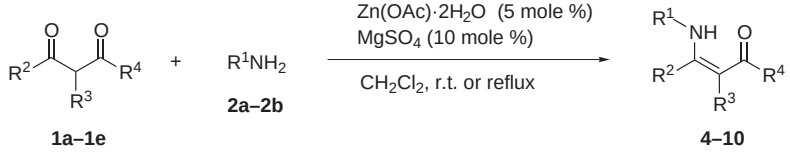
Lewis Acid	Yield, %
$Zn(ClO_4)_2 \cdot 6H_2O$	74
$Zn(OAc)_2 \cdot 2H_2O$	90
$Zn(citrate) \cdot 2H_2O$	80[b]
$ZnBr_2$	50
$Zn(D\text{-gluconate})_2 \cdot 3H_2O$	13
$ZnSO_4 \cdot 7H_2O$	0

[a] Conditions: 0.75 mmol of benzylamine **2a**, 0.5 mmol of carboxylate **1a**, dried $MgSO_4$ and zinc salt (5 mole %) in 5 ml of CH_2Cl_2, 2 days; [b] 3 days.

It is notable that the reaction does not occur without a catalytic amount of previously dried magnesium sulfate, and is very slow in the presence of sole magnesium sulfate. The necessity of the presence of such a dehydrating agent might be related to in situ formation of an active zinc species. Indeed, the required amount of magnesium sulfate depends only on the amount of water present in the starting zinc salt (30 mole % of $MgSO_4$ for $Zn(ClO_4)_2 \cdot 6H_2O$; 10 mole % for $Zn(OAc)_2 \cdot 2H_2O$).

Among the different salts, $Zn(ClO_4)_2 \cdot 6H_2O$, $Zn(OAc)_2 \cdot 2H_2O$, $ZnBr_2$, and Zn(citrate)$\cdot 2H_2O$ appear to be the most efficient catalysts. $Zn(OAc)_2 \cdot 2H_2O$, which provided the expected aminoacrylate in 90% yield, is also the cheapest zinc salt. In addition, this Lewis acid not only promotes the condensation reaction smoothly but also chemoselectively[28], as we never observed the formation of a β-ketoamide or β-enaminoacrylamide.

We extended this condensation reaction of an alkylamine to a variety of β-ketoesters (**1a**–**1c**) and β-diketones (**1d**, **1e**) with $Zn(OAc)_2 \cdot 2H_2O$ as the Lewis acid catalyst (Table II). In dichloromethane at reflux, in the presence of 5 mole % $Zn(OAc)_2 \cdot 2H_2O$ and 10 mole % $MgSO_4$, aminoacrylate **8** was isolated in a good yield (73%). With compounds **1a**, **1b** and **1d**, a lower temperature could be used. Aminoacrylates **4**–**7** and **9** were obtained in high yields (73–98%) by performing the condensation at room tempera-



1a–1e **4–10**

TABLE II
Zinc-catalyzed condensation of alkylamines with β-ketoesters and β-diketones[a]

Dicarbonyl compound	R^2	R^3	R^4	Amine	R^1	Product	Temperature	Yield %
1a	$(CH_2)_3$		OEt	**2a**	Bn	**4**	r.t.	50[b]
1a	$(CH_2)_3$		OEt	**2a**	Bn	**4**	r.t.	90
1a	$(CH_2)_3$		OEt	**2b**	(*S*)-PhCHCH$_3$	**5**	r.t.	95[b]
1a	$(CH_2)_3$		OEt	**2b**	(*S*)-PhCHCH$_3$	**5**	r.t.	95
1b	CH_3	H	OEt	**2a**	Bn	**6**	r.t.	78
1b	CH_3	H	OEt	**2b**	(*S*)-PhCHCH$_3$	**7**	r.t.	79
1c	Ph	H	OEt	**2a**	Bn	**8**	reflux	73
1d	CH_3	H	CH_3	**2a**	Bn	**9**	r.t.	98
1e	Ph	H	Ph	**2a**	Bn	**10**	reflux	no reaction

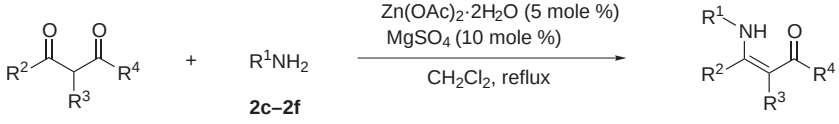
[a] Conditions: 0.75 mmol of amine, 0.5 mmol of carboxylate **1**, dried $MgSO_4$ (10 mole %) and zinc acetate (5 mole %) in 5 ml of CH_2Cl_2, 16 h. [b] Zinc bromide (5 mole %) was used.

ture. As a limitation of this process, the reaction between diketone **1e** and various alkylamines did not occur. This absence of reactivity might be due to the conjugation of the carbonyl and phenyl groups, which lead to a dramatic decrease in the electrophilic character of the carbonyl moiety.

The nucleophilicity of the enamines can be assessed by ^{1}H or ^{13}C NMR. Indeed, the vinylic protons of compounds **6**–**9** are located in the high-field area (around 4.3–5.0 ppm, compared with the usual vinylic proton: δ > 5.5 ppm) and the corresponding carbons in the ^{13}C spectra are present at 83–96 ppm (110–120 ppm for a usual C(sp^2)).

It is notable that, based on literature data[29], the enamino esters and enamino ketones were isolated exclusively as the hydrogen-bonded (*Z*)-isomers. Thus, in the ^{1}H NMR spectrum of compound **6**, only a CH_3 signal at 1.90 ppm, characteristic of the (*Z*)-isomers was observed, whereas no signal was detected at a lower field (δ > 2.2 ppm for the (*E*)-isomers).

In order to extend the scope of the reaction, we investigated the addition of aromatic amines **2c**–**2f** to the carbonyl reagents **1a**–**1e** (Table III). All experiments were conducted in dichloromethane at reflux using 1 equivalent



1a–1e **2c–2f** **11–22**

TABLE III
Zinc-catalyzed condensation of aromatic amines with β-ketoesters and β-diketones[a]

Dicarbonyl compound	R^2	R^3	R^4	Amine	R^1	Product	Reaction time, days	Yield %
1a	$(CH_2)_3$		OEt	**2c**	Ph	**11**	2	99
1a	$(CH_2)_3$		OEt	**2d**	3,4,5-$(MeO)_3C_6H_2$	**12**	4	75
1a	$(CH_2)_3$		OEt	**2e**	2,4,6-$Me_3C_6H_2$	**13**	3	45
1a	$(CH_2)_3$		OEt	**2f**	4-IC_6H_4	**14**	5	36
1b	CH_3	H	OEt	**2c**	Ph	**15**	2	57
1b	CH_3	H	OEt	**2d**	3,4,5-$(MeO)_3C_6H_2$	**16**	2	55
1b	CH_3	H	OEt	**2e**	2,4,6-$Me_3C_6H_2$	**17**	2	69
1b	CH_3	H	OEt	**2f**	4-IC_6H_4	**18**	2	21
1c	Ph	H	OEt	**2c**	Ph	**19**	4	53
1c	Ph	H	OEt	**2f**	4-IC_6H_4	**20**	4	42
1d	CH_3	H	CH_3	**2c**	Ph	**21**	2	86
1e	Ph	H	Ph	**2c**	Ph	**22**	5	no reaction

[a] Conditions: 0.75 mmol of amine, 0.5 mmol of carboxylate **1**, dried $MgSO_4$ (10 mole %) and zinc acetate (5 mole %) in 5 ml of CH_2Cl_2.

of β-ketoesters **1a**–**1c** or β-diketones **1d**, **1e**, 1.5 equivalents of an amine in the presence of 5 mole % of $Zn(OAc)_2 \cdot 2H_2O$, and previously dried $MgSO_4$ (10 mole %). As shown in Table III, the yields were usually lower than those obtained with alkyl amines. They ranged from 21% for **18** to 86% for **21** and 99% for **11**. The steric hindrance on the aromatic ring has no real influence on the yield (cf., e.g., the yields in the synthesis of **15**, **18** or **19**). The influence of electronic properties seems to be more important. Thus, with aniline, the anilinoacrylates were produced in up to 99% yields (**11**, **15**, **19**, **21**), whereas, with 4-iodoaniline, the corresponding products (**14**, **18**, **20**) were isolated in moderate yields ranging from 21 to 42%. As also previously observed with alkylamines, no reaction occurred between an aromatic amine and the diketone **1e**.

CONCLUSION

We have shown that $Zn(OAc)_2 \cdot 2H_2O$, an inexpensive zinc salt, was able to catalyze the condensation of primary alkylamines and ring-substituted anilines with β-ketoesters and β-diketones under safe and mild conditions, providing a straightforward and selective route to aminoacrylate and enaminone derivatives in moderate to very good yields.

EXPERIMENTAL

^1H and ^{13}C NMR spectra were recorded on 200 MHz Bruker AC 200 spectrometers. Chemical shifts are reported in ppm (δ-scale) referenced to the residual proton resonances of the solvents. Coupling constants (*J*) are given in Hz. Mass spectra (MS) were obtained on a GC-MS Hewlett–Packard HP 5971 apparatus. Thin-layer chromatography (TLC) was performed on Merck silica gel 60 F 254 plates. Silica gel Merck Geduran SI (40–63 μm) was used for column chromatography. For compounds **5**, **19**, **20**, the proton of the amine was not observed in the proton NMR spectrum.

General Procedure for the Preparation of Aminoacrylates

Magnesium sulfate was first heated at 200 °C under vacuum over 15 min. To this previously dried magnesium sulfate (10 mole %), zinc acetate (5 mole %), dichloromethane (5 ml/mmol), the dicarbonyl derivative (1 equiv.), and finally a primary amine (1.5 equiv.) were successively added under argon. The reaction mixture was stirred at room temperature or at reflux until completion, as detected by TLC analysis. The solution was then filtered through Celite, and concentrated under vacuum. The crude oily mixture was purified on silica gel by flash chromatography (eluent: heptane/ethyl acetate, 7:3).

Ethyl 2-(benzylamino)cyclopent-1-ene-1-carboxylate (**4**). ^1H NMR (200.13 MHz, $CDCl_3$): 1.26 t, 3 H, *J* = 7.1; 1.78 quint, 2 H, *J* = 7.7; 2.53 m, 4 H; 4.15 q, 2 H, *J* = 7.1; 4.35 d, 2 H, *J* = 6.3; 7.15–7.40 m, 5 H; 7.84 br s, 1 H (NH). ^{13}C NMR (50.3 MHz, $CDCl_3$): 14.4, 20.5, 28.8,

31.6, 47.9, 53.2, 93.0, 126.3 (2 C); 126.8, 128.3 (2 C); 138.9, 164.1, 168.0. HRMS: calculated for $C_{15}H_{19}NO_2$: 245.14158, found: 245.1409.

Ethyl 2-[((S)-1′-phenylethylamino)]cyclopent-1-ene-1-carboxylate (**5**). ^{1}H NMR (200.13 MHz, $CDCl_3$): 1.26 t, 3 H, *J* = 7.2; 1.46 d, 3 H, *J* = 6.8; 1.72 m, 2 H; 2.25 m, 1 H; 2.48 t, 2 H, *J* = 7.4; 2.55 m, 1 H; 4.18 q, 2 H, *J* = 6.8; 4.52 q, 1 H, *J* = 7.2; 7.24 m, 5 H; 7.82 br s, 1 H (NH). ^{13}C NMR (50.3 MHz, $CDCl_3$): 14.8, 20.9, 24.9, 28.9, 32.3, 54.3, 58.5, 93.5, 125.5 (2 C); 127.0, 128.7 (2 C); 145.3, 164.2, 168.6. HRMS: calculated for $C_{16}H_{21}NO_2$: 259.15723, found: 259.1577.

Ethyl 3-(benzylamino)but-2-enoate[17,20] (**6**). ^{1}H NMR (200.13 MHz, $CDCl_3$): 1.25 t, 3 H, *J* = 7.1; 1.90 s, 3 H; 4.10 q, 2 H, *J* = 7.1; 4.40 d, 2 H, *J* = 6.4; 4.55 s, 1 H; 7.31 m, 5 H; 8.98 s, 1 H (NH). ^{13}C NMR (50.3 MHz, $CDCl_3$): 14.4, 19.1, 46.6, 58.1, 83.0, 126.7 (2 C); 127.1, 128.5 (2 C); 138.6, 161.6, 170.3. IR (ν, cm^{-1}): 1658, 1600. HRMS: calculated for $C_{13}H_{17}NO_2$: 219.12593, found: 219.1244.

Ethyl 3-[((S)-1′-phenylethylamino)]but-2-enoate (**7**). ^{1}H NMR (200.13 MHz, $CDCl_3$): 1.28 t, 3 H, *J* = 7.1; 1.52 d, 3 H, *J* = 6.8; 1.78 s, 3 H; 4.18 q, 2 H, *J* = 7.1; 4.50 s, 1 H; 4.62 q, 1 H, *J* = 7.1; 7.31 m, 5 H; 8.99 s, 1 H (NH). ^{13}C NMR (50.3 MHz, $CDCl_3$): 15.1, 20.1, 25.4, 53.3, 58.8, 83.6, 125.8 (2 C); 127.5, 129.2 (2 C); 145.4, 161.9, 171.1.

Ethyl 3-(benzylamino)-3-phenylacrylate (**8**). ^{1}H NMR (200.13 MHz, $CDCl_3$): 1.28 t, 3 H, *J* = 7.1; 4.21 q, 2 H, *J* = 7.1; 4.30 d, 2 H, *J* = 6.5; 4.70 s, 1 H; 7.29 m, 10 H; 8.91 br s, 1 H (NH). ^{13}C NMR (50.3 MHz, $CDCl_3$): 14.5, 48.3, 58.8, 86.2, 126.8 (2 C); 127.1, 127.8 (2 C); 128.3 (2 C); 129.0 (2 C); 129.2, 136.0, 139.2, 164.7, 170.3. HRMS: calculated for $C_{18}H_{19}NO_2$: 281.14158, found: 281.1408.

4-(Benzylamino)pent-3-en-2-one[20] (**9**). ^{1}H NMR (200.13 MHz, $CDCl_3$): 1.91 s, 3 H; 2.03 s, 3 H; 4.43 d, 2 H, *J* = 6.4; 5.03 s, 1 H; 7.31 m, 5 H; 8.91 br s, 1 H (NH). ^{13}C NMR (50.3 MHz, $CDCl_3$): 19.3, 29.3, 47.1, 96.3, 127.1 (3 C); 128.0, 129.2 (2 C); 138.4, 164.0.

Ethyl 2-anilinocyclopent-1-ene-1-carboxylate (**11**). ^{1}H NMR (200.13 MHz, $CDCl_3$): 1.32 t, 3 H, *J* = 7.2; 1.87 quint, 2 H, *J* = 7.6; 2.60 t, 2 H, *J* = 7; 2.82 t, 2 H, *J* = 7.5; 4.22 q, 2 H, *J* = 7.1; 7.08 m, 3 H, *J* = 6.8; 7.29 m, 2 H, *J* = 7.9; 9.68 br s, 1 H (NH). ^{13}C NMR (50.3 MHz, $CDCl_3$): 15.1, 22.2, 29.2, 34.1, 59.4, 98.1, 121.1 (2 C); 123.5, 129.6 (2 C); 141.1, 160.8, 168.9.

Ethyl 2-(3,4,5-trimethoxyanilino)cyclopent-1-ene-1-carboxylate (**12**). ^{1}H NMR (200.13 MHz, $CDCl_3$): 1.24 t, 3 H, *J* = 6.0; 1.97 m, 2 H; 2.35 m, 2 H; 2.55 m, 1 H; 2.80 m, 1 H; 3.81 s, 3 H; 3.82 s, 6 H; 4.18 q, 2 H, *J* = 6.0; 6.30 s, 2 H; 10.21 s, 1 H (NH). ^{13}C NMR (50.3 MHz, $CDCl_3$): 14.6, 22.2, 29.1, 34.0, 56.0 (2 C); 59.4, 61.4, 97.8, 99.3 (2 C); 135.1 (2 C); 153.3 (2 C); 161.0, 168.9. HRMS: calculated for $C_{17}H_{23}NO_5$: 321.15762, found: 321.1579.

Ethyl 2-(2,4,6-trimethylanilino)cyclopent-1-ene-1-carboxylate (**13**). ^{1}H NMR (200.13 MHz, $CDCl_3$): 1.28 t, 3 H, *J* = 7.1; 1.80 quint, 2 H, *J* = 7.3; 2.25 m, 2 H; 2.28 s, 6 H; 2.30 s, 3 H; 2.60 t, 2 H, *J* = 7.2; 4.24 q, 2 H, *J* = 7.1; 6.85 s, 2 H; 8.47 br s, 1 H (NH). ^{13}C NMR (50.3 MHz, $CDCl_3$): 15.1, 18.4 (2 C); 21.0, 21.1, 29.4, 32.8, 59.6, 98.9, 127.1 (2 C); 129.1 (2 C); 136.6, 140.1, 164.3, 168.6. HRMS: calculated for $C_{17}H_{23}NO_2$: 273.17288, found: 273.1724.

Ethyl 2-(4-iodoanilino)cyclopent-1-ene-1-carboxylate (**14**). ^{1}H NMR (200.13 MHz, $CDCl_3$): 1.28 t, 3 H, *J* = 7.1; 1.90 quint, 2 H, *J* = 7.4; 2.58 t, 2 H, *J* = 7.4; 2.80 t, 2 H, *J* = 7.4; 4.20 q, 2 H, *J* = 7.1; 6.80 d, 2 H, *J* = 8.7; 7.58 d, 2 H, *J* = 8.7; 9.61 s, 1 H (NH). ^{13}C NMR (50.3 MHz, $CDCl_3$): 15.0, 22.2, 29.1, 34.0, 59.5, 99.8, 122.6 (2 C); 129.9, 138.4 (2 C); 140.9, 154.3, 159.9.

Ethyl 3-anilinobut-2-enoate[17,20,22] (**15**). ^{1}H NMR (200.13 MHz, $CDCl_3$): 1.21 t, 3 H, *J* = 6.4; 1.99 s, 3 H; 4.10 q, 2 H, *J* = 6.4; 4.78 s, 1 H; 7.10 m, 5 H; 10.35 s, 1 H (NH). ^{13}C NMR

(50.3 MHz, $CDCl_3$): 14.6, 20.4, 58.7, 86.1, 124.4 (2 C); 124.9, 129.3 (2 C); 139.4, 159.0, 170.4. HRMS: calculated for $C_{12}H_{15}NO_2$: 205.11028, found: 205.1118.

Ethyl 3-(3,4,5-trimethoxyanilino)but-2-enoate (**16**). ^{1}H NMR (200.13 MHz, $CDCl_3$): 1.24 t, 3 H, *J* = 6.0; 1.97 s, 3 H; 3.81 s, 3 H; 3.82 s, 6 H; 4.18 q, 2 H, *J* = 6.4; 4.62 s, 1 H; 6.30 s, 2 H; 10.21 s, 1 H (NH). ^{13}C NMR (50.3 MHz, $CDCl_3$): 14.6, 20.3, 56.2 (2 C); 58.8, 61.1, 85.7, 92.7 (2 C); 135.1 (2 C); 153.3 (2 C); 159.2, 171.0. HRMS: calculated for $[M - CH_3]^+$ (main peak) $C_{14}H_{18}NO_5$: 280.11850, found: 280.1193.

Ethyl 3-(2,4,6-trimethylanilino)but-2-enoate (**17**). ^{1}H NMR (200.13 MHz, $CDCl_3$): 1.28 t, 3 H, *J* = 7.2; 1.62 s, 1 H; 2.20 t, 6 H, *J* = 5.5; 2.31 s, 2 H; 4.18 q, 2 H, *J* = 7.1; 4.72 s, 1 H; 6.80 s, 2 H; 6.95 s, 3 H; 9.71 s, 1 H (NH).

Ethyl 3-(4-iodoanilino)but-2-enoate (**18**). ^{1}H NMR (200.13 MHz, $CDCl_3$): 1.29 t, 3 H, *J* = 7.1; 2.02 s, 3 H; 4.15 q, 2 H, *J* = 7.1; 4.78 s, 1 H; 6.86 d, 2 H, *J* = 8.4; 7.65 d, 2 H, *J* = 8.4. ^{13}C NMR (50.3 MHz, $CDCl_3$): 14.4, 19.1, 59.4, 87.6, 89.5, 117.7 (2 C); 126.3, 138.5 (2 C); 139.7, 161.6, 170.3.

Ethyl 3-anilino-3-phenylacrylate (**19**). ^{1}H NMR (200.13 MHz, $CDCl_3$): 1.28 t, 3 H, *J* = 7.0; 4.21 q, 2 H, *J* = 7.0; 4.99 s, 1 H; 6.65 d, 2 H, *J* = 6.8; 6.98 t, 1 H, *J* = 7.3; 7.11 t, 2 H, *J* = 7.5; 7.30 m, 3 H; 7.49 t, 1 H; 7.98 d, 1 H, *J* = 7.1. ^{13}C NMR (50.3 MHz, $CDCl_3$): 14.9, 59.7, 91.6, 122.6 (2 C); 126.4, 128.6 (2 C); 128.8 (2 C); 128.9 (2 C); 129.9, 136.4, 140.8, 159.5, 170.5.

Ethyl 3-(4-iodoanilino)-3-phenylacrylate (**20**). ^{1}H NMR (200.13 MHz, $CDCl_3$): 1.31 t, 3 H, *J* = 7.1; 4.21 q, 2 H, *J* = 7.2; 5.02 s, 1 H; 6.42 d, 2 H, *J* = 8.7; 7.23–7.50 m, 5 H; 7.98 d, 2 H, *J* = 7.1. ^{13}C NMR (50.3 MHz, $CDCl_3$): 14.9, 59.9, 92.7, 124.2 (2 C); 126.4, 128.9 (2 C); 129.0 (2 C); 130.1, 134.2, 137.9 (2 C); 140.7, 158.7, 170.4.

4-Anilinopent-3-en-2-one[17,20] (**21**). ^{1}H NMR (200.13 MHz, $CDCl_3$): 1.98 s, 3 H; 2.11 s, 3 H; 5.19 s, 1 H; 7.22 m, 5 H. ^{13}C NMR (50.3 MHz, $CDCl_3$): 20.3, 29.6, 98.0, 125.2 (2 C); 125.9, 129.5 (2 C); 139.1, 160.6, 196.6.

REFERENCES

1. Felice E., Fioraventi S., Pellacani L., Tardella P. A.: *Tetrahedron Lett.* **1999**, *40*, 4413; and references therein.
2. a) Jerphagnon T., Renaud J.-L., Demonchaux P., Ferreira P., Bruneau C.: *Adv. Synth. Catal.* **2004**, *346*, 33, and references therein; b) Jerphagnon T., Renaud J.-L., Demonchaux P., Ferreira P., Bruneau C.: *Tetrahedron: Asymmetry* **2003**, *14*, 1973; c) Liu M., Sibi M. P.: *Tetrahedron* **2002**, *58*, 7991; d) Zhou Y. G., Tang W., Wang W. B., Li W., Zhang X.: *J. Am. Chem. Soc.* **2002**, *124*, 4952; e) Tang W., Wi S., Zhang X.: *J. Am. Chem. Soc.* **2003**, *125*, 9570; f) Heller D., Drexler H. J., You J., Baumann W., Drauz K., Krimmer H. P., Börner A.: *Chem. Eur. J.* **2002**, *8*, 5196; g) Holz J., Monsees A., Jiao H., You J., Komarov I. V., Fischer C., Drauz K., Börner A.: *J. Org. Chem.* **2003**, *68*, 1701; h) Lee S. I., Zhang Y. J.: *Org. Lett.* **2002**, *4*, 2429; i) Yasutake M., Gridnev I. D., Higashi N., Imamoto T.: *Org. Lett.* **2001**, *3*, 1701; j) Peña D., Minnaard A. J., De Vries J. G., Feringa B. L.: *J. Am. Chem. Soc.* **2002**, *124*, 14552; k) Peña D., Minnaard A. J., Boogers J. A. F., De Vries A. H. M., De Vries J. G., Feringa B. L.: *Org. Biomol. Chem.* **2003**, *1*, 1087; l) Peña D., Minnaard A. J., De Vries A. H. M., De Vries J. G., Feringa B. L.: *Org. Lett.* **2003**, *5*, 475.
3. a) Blot J., Baidou A., Bellec C., Fargeau-Bellasoued M.-C., Célérier J.-P., Lhommet G., Gardette D., Gramain J.-C.: *Tetrahedron Lett.* **1997**, *38*, 8511; b) Michael J. P., de Koning C. B., Gravestock D., Hosken G. D., Howard A. S., Jungmann C. M., Krause R. W. M.,

Parsons A. S., Pelly S. C., Stanbury T. V.: *Pure Appl. Chem.* **1999**, *71*, 979; c) David C., Blot J., Bellec C., Fargeau-Bellasoued M.-C., Haviari G., Célérier J.-P., Lhommet G., Gramain J.-C., Gardette D.: *J. Org. Chem.* **1999**, *64*, 3122; d) Michael J. P., Parsons A. S.: *Tetrahedron* **1999**, *55*, 10915.

4. Beholz L. G., Benovsky P., Ward D. L., Barta N. S., Stille J. R.: *J. Org. Chem.* **1997**, *62*, 1033.
5. a) Elassar A.-Z. A., El-Khair A. A.: *Tetrahedron* **2003**, *59*, 8463; b) Agami C., Dechoux L., Hebbe V.: *Tetrahedron Lett.* **2002**, *43*, 2521; c) Hassneen H. M., Abdallah T. A.: *Molecules* **2003**, *8*, 333.
6. a) Michael J. P., de Koning C. B., Hosken G. D., Stanbury T. V.: *Tetrahedron* **2001**, *57*, 9635; b) Dannhardt G., Bauer A., Nowe U.: *J. Prakt. Chem.* **1998**, *340*, 256.
7. Boger D. L., Ishizaki T., Wysocki J. R. J., Munk S. A., Kitos P. A., Suntornwat O.: *J. Am. Chem. Soc.* **1989**, *111*, 6461.
8. Azzaro M., Geribaldi S., Videau B.: *Synthesis* **1981**, 880.
9. a) Lee A. S.-Y., Cheng R. Y.: *Tetrahedron Lett.* **1997**, *38*, 443; b) Bird T. G. C., Olivier A.: *Bioorg. Med. Chem.* **1996**, *6*, 515; c) Hannick S. M., Kishi Y.: *J. Org. Chem.* **1983**, *48*, 3833.
10. Jiang N., Qu Z., Wang J.: *Org. Lett.* **2001**, *3*, 2989.
11. a) Fustero S., Pina B., Salavert E., Navarro A., Ramirez de Arellano M. C., Simón-Fuentes A.: *J. Org. Chem.* **2002**, *67*, 4667; b) Fustero S., Pina B., Garciá de la Torre M., Navarro A., Ramirez de Arellano M. C., Simón-Fuentes A.: *Org. Lett.* **1999**, *1*, 977.
12. a) Katritzky A. R., Fang Y., Donkor A., Xu J.: *Synthesis* **2000**, 2029; b) Bartoli G., Cimarelli C., Dalpozzo R., Palmieri G.: *Tetrahedron* **1995**, *51*, 8613.
13. Fustero S., Garciá de la Torre M., Jofrè V., Pérez Carlon R., Navarro A., Simón-Fuentes A.: *J. Org. Chem.* **1998**, *63*, 8825.
14. a) Stanovnik B., Svete J.: *Chem. Rev.* **2004**, *104*, 2433; b) Abdulla R. F., Brinkmeyer R. S.: *Tetrahedron* **1979**, *35*, 1675.
15. a) Baraldi P. G., Simoni D., Manfredini S.: *Synthesis* **1983**, 902, and references therein; b) Ferraz H. M. C., Oliveira E. O., Payret-Arrua M. E., Brandt C. A.: *J. Org. Chem.* **1995**, *60*, 7357; c) Amougay A., Letsch O., Pete J. P.: *Tetrahedron* **1996**, *52*, 2405; d) Valduga C. L., Squizani A., Braibante H. S., Braibante M. E. F.: *Synthesis* **1997**, 1019; e) Leflemme N., Dallemagne P., Rault S.: *Synthesis* **2002**, 1740; f) Calvet S., David O., Vanucci-Bacqué C., Fargeau-Bellasoued M.-C., Lhommet G.: *Tetrahedron* **2003**, *59*, 6333.
16. A similar protocol was described for the synthesis of *N*-acetylenamines: Dupau P., Hay A.-E., Alameda Angulo C., Dixneuf P. H., Bruneau C.: *Collect. Czech. Chem. Commun.* **2002**, *67*, 235.
17. Stefani H. A., Costa I. M., de O. Silva D.: *Synthesis* **2000**, 1526.
18. Valduga C. L., Braibante H. S., Braibante M. E. F.: *J. Heterocycl. Chem.* **1998**, *35*, 189.
19. Rechsteiner B., Texier-Boullet F., Hamelin J.: *Tetrahedron Lett.* **1993**, *34*, 5071.
20. Braibante M. E. F., Braibante H. S., Missio L., Andricopulo A.: *Synthesis* **1994**, 898.
21. Arcadi A., Bianchi G., Di Giuseppe S., Marinelli F.: *Green Chem.* **2003**, *5*, 64.
22. Brandt C. A., da Silva A. C. M. P., Pancote C. G., Brito C. L., da Silveira M. A. B.: *Synthesis* **2004**, 1557.
23. Yamamoto H. (Ed.): *Lewis Acid Reagents*. Oxford University Press, Oxford 1999.
24. Bartoli G., Bosco M., Locatelli M., Marcantoni E., Melchiorre P., Sambri L.: *Synlett* **2004**, 239.

25. a) Khosropour A. R., Khodaei M. M., Kookhazadeh M.: *Tetrahedron Lett.* **2004**, *45*, 1725; b) Khodaei M. M., Khosropour A. R., Kookhazadeh M.: *Can. J. Chem.* **2005**, *83*, 209.
26. Khodaei M. M., Khosropour A. R., Kookhazadeh M.: *Synlett* **2004**, 1980.
27. a) Renaud J.-L., Dupau P., Hay A.-E., Guingouain M., Dixneuf P. H., Bruneau C.: *Adv. Synth. Catal.* **2003**, *345*, 230; b) Dupau P., Bruneau C., Dixneuf P. H.: *Synlett* **1999**, 1932; c) Dupau P., Bruneau C., Dixneuf P. H.: *Tetrahedron: Asymmetry* **1999**, *10*, 3467; d) Dupau P., Bruneau C., Dixneuf P. H.: *Adv. Synth. Catal.* **2001**, *343*, 331; e) Dupau P., Hay A.-E., Bruneau C., Dixneuf P. H.: *Tetrahedron: Asymmetry* **2001**, *12*, 863.
28. For some recent publications on the selectivity in Lewis acid catalyzed reactions, see: a) Sekar G., Singh V. K.: *J. Org. Chem.* **1999**, *64*, 2537; b) Braga A. L., Dornelles L., Silveira C. C., Wessjohann L. A.: *Synthesis* **1999**, 562.
29. Fabiano E., Golding B. T.: *J. Chem. Soc., Perkin Trans. 1* **1991**, 3371.