A Novel Multicomponent Tandem Phosphine-Catalyzed Umpolung Reaction: Facile Access to Highly Functionalized α-Aminonitriles

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Abstract: The first phosphine-catalyzed multicomponent tandem Strecker– γ -umpolung-addition reaction has been developed, which provides a facile access to functionalized allylic α -aminonitriles. The reaction is highly efficient, rapid, versatile and economical, and it is hoped that it will find great practical application in organic synthesis.

Key words: Strecker reaction, umpolung addition, α -aminonitrile, allene, phosphine catalysis

Nucleophilic phosphine catalysis has received considerable attention because it has displayed the diversity of synthetic transformations involving activated allenes as starting materials.¹ Within this field, umpolung addition of nucleophiles to activated allenes plays an important role, which provides an efficient C-C formation reaction. Since the first report by Trost,² there has been increasing interest in phosphine-catalyzed γ -umpolung additions of pronucleophiles to electron-deficient alkynes and allenes.³ However, the construction of synthetically useful intermediates via a multicomponent tandem phosphinecatalyzed umpolung additions has received less attention⁴ in contrast to direct umpolung addition pathways, since it will provide a highly efficient and economic approach to access valuable molecular constructs. a-Aminonitriles are exceptionally versatile intermediates in synthetic chemistry and also proposed as being prebiotic precursors to porphyrins, corrins, and nicotinic acids.⁵ α-Aminonitriles bearing an α -hydrogen have been widely used in the generation of multiple polyfunctional structures.⁶ To the best of our knowledge, the construction of α-aminonitriles including densely functional quaternary carbon centers via a multicomponent tandem umpolung additions to activated allenes by phosphine catalyst is still unexploited.⁷

Recently, we reported the novel tandem cyanation–allylic-alkylation (CAA) reaction and Strecker–allylic-alkylation (SAA) reaction by using amine catalysts, which provided facile accesses to densely functionalized products containing O-substituted or N-substituted quaternary centers.⁸ The accomplishment of these transformations is relied heavily on the combination of the in situ generation of nucleophilic regents, electrophilic regents, and further coupling. Inspired by these, we further envisaged that an attractive multicomponent tandem γ -umpolung reaction

SYNTHESIS 2012, 44, 1849–1853 Advanced online publication: 20.04.2012 DOI: 10.1055/s-0031-1290946; Art ID: SS-2012-C0201-ST © Georg Thieme Verlag Stuttgart · New York could be established by utilizing three-component Strecker reaction and phosphine catalyzed γ -umpolung addition of nucleophiles to activated allenes, which may not only deliver highly functional α -aminonitriles with quaternary carbon centers, but also afford a synthetic complement to SAA reaction. Herein, we demonstrate a novel tandem Strecker– γ -umpolung-addition reaction for the construction of highly functionalized α -aminonitriles (Scheme 1).



Scheme 1 Strategy of multicomponent tandem γ -umpolung reaction

Initially, the reaction of preformed α -aminonitrile **1a** with ethyl buta-2,3-dienoate (2a) in the presence of catalytic triphenylphosphine was investigated. Gratifyingly, this inverse conjugate addition proceeded well in acetonitrile, and affording γ -umpolung adduct **3a** (E/Z = 3.6:1) in 94% yield along with a small amount of β -addition product 4a (Table 1, entry 1). The solvent effects were first examined by using triphenylphosphine as the catalyst. Although γ umpolung addition reactions took place in all screened solvents, sluggish reactions were observed in solvents such as toluen, tetrahydrofuran, and 1,4-dioxane (Table 1, entries 2, 5, 6). When the reactions were carried out in dichloromethane and 1,2-dichloroethane, no β -addition product was detected (Table 1, entries 3, 4). Several commonly used phosphine catalysts were assessed in the nucleophilic addition reaction between 1a and 2a. More nucleophilic phosphanes catalyzed this reaction to give the product 3a in shorter time with slightly higher selectivities. Of these catalysts, tributylphosphine gave 3a in a slightly low yield with the highest E/Z selectivity and an increased amount of β -addition product 4a (Table 1, entry 12). In the absence of catalyst, no conversion of the starting material was observed (Table 1, entry 14). Decreasing the reaction temperature facilitated Michael-type addition (4a) instead of improving E/Z selectivity of the product of γ -umpolung addition reaction (Table 1, entry 13). Further study showed that Z-isomer 3 was easily isomerized into *E*-isomer **3** in the presence of more nucleophilic phosphane catalyst, which may provide a potential to obtain Eisomer with high selectivities (Equation 1).

1	la catalys solven	catalyst HN ^{Ph} solvent I		HN ^{Ph}		
	+ _CO2Et	Ph CN	CO ²	₂Et + Ph∕ N	CO ₂ Et	
• 2a		(<i>E</i>)- 3 a		4a		
Entry	Catalyst	Solvent	Time (h)	E/Z ^b	Yield (%) ^c	
1	Ph ₃ P	MeCN	2.5	3.6:1	94 (3 a); 2 (4 a)	
2	Ph ₃ P	PhMe	15	d	8 [(<i>E</i>)- 3 a]	
3	Ph ₃ P	CH_2Cl_2	3	3.1:1	64 (3a)	
4	Ph ₃ P	DCE	6	1.9:1	67 (3 a)	
5	Ph ₃ P	THF	15	d	13 [(<i>E</i>)- 3 a]	
6	Ph ₃ P	1,4-dioxane	15	d	<5 (3 a)	
7	Ph ₃ P	t-BuOH	2.5	3.1:1	31 (3 a)	
8	Ph ₃ P	DMF	1	3.8:1	59 (3 a);13 (4 a)	
9	$(4-FC_6H_4)_3P$	MeCN	5	3:1	83 (3 a); 5 (4 a)	
10	Et(Ph) ₂ P	MeCN	0.7	3.5:1	91 (3 a); 5 (4 a)	
11	Et ₂ (Ph)P	MeCN	0.7	5.2:1	88 (3a); 8 (4 a)	
12	Bu ₃ P	MeCN	0.7	7:1	82 (3 a); 16 (4 a)	
13 ^e	Bu ₃ P	MeCN	1	5.1:1	52 (3a); 26 (4a)	
14	none	MeCN	1	_	nr	

Table 1 Optimization of Phosphine-Catalyzed γ -Umpolung Additions of α -Aminonitriles to Electron-Deficient Allenes^a

^a Reactions were performed with **1a** (0.2 mmol), **2a** (0.3 mmol), and catalyst (20 mol%) in solvent (2.0 mL) at 30 °C.

^b Determined by ¹H NMR analysis.

^c Isolated yield. nr = no reaction.

^d No detection.

e Reaction was carried out at 0 °C.



Equation 1

With these preliminary results in hand, next the multicomponent tandem γ -umpolung addition reaction was studied. The results are summarized in Table 2. Straightforwardly mixing benzaldehyde, aniline, TMSCN, triphenylphosphine (20 mol%), and ethyl buta-2,3-dienoate (**2a**) in one flask in acetonitrile resulted in the desired product **3a** in low yield (46%) and side product formation. We hypothesized that the order of reagent mixing may be crucial in order to increase the production of 3. Indeed, charging benzaldehyde, aniline, and TMSCN in one flask, subsequently adding triphenylphosphine (20 mol%) and 2a under optimized solvent, readily furnished the desired product 3a in high yield (Table 2, entry 1). The scope and generality of this novel tandem reaction was evaluated. First, the reactions of different primary amines with benzaldehyde, TMSCN, and 2a were examined. Of note, anilines with electron-withdrawing or -donating substituents at the para-position, can be smoothly employed in this reaction to furnish 3 in good to high yield (Table 2, entries 3, 4). In particular, *N*-PMP substitution of **3** may provide a potential handle for further elaboration, due to their facile deprotection.⁹ However, N-benzyl protected 3c was not observed at all when benzylamine was used (Table 2, entry 5). When secondary amine such as morpholine was used, the tandem reactions did not provide the desired

Table 2Substrate Scope of Multicomponent Tandem Phosphine-
Catalyzed γ -Umpolung Reaction^a

0 +	$R^2R^3NH_2 + TMS($	CN → catal solve	yst ent Coset	R^3	√ CO₂Et
5	6	_•_	2a	(<i>E</i>)- 3 (major)
Entry	R ¹	NR ² R ³	Time (h)	$E/Z^{\rm b}$	Yield (%) ^c
1	Ph	NHPh	3.5	4.3:1	81(3a)
2^d	Ph	NHPh	1	5:1	76 (3a)
3	Ph	$NH(4-ClC_6H_4)$	2.5	6.4:1	74 (3b)
4 ^e	Ph	NHPMP	3	4.7:1	85 (3d)
5	Ph	NHBn	_	_	nr
6	Ph	N-morpholinyl	_	-	nr
7	$4-ClC_6H_4$	NHPh	2.5	4.6:1	80 (3ab)
8	$4-MeC_6H_4$	NHPh	2.5	4.6:1	75 (3ac)
9	3-MeOC ₆ H ₄	NHPh	2.5	5.9:1	88 (3ad)
10	$2\text{-BrC}_6\text{H}_4$	NHPh	2.5	3.7:1	59 (3ae)
11	2-naphthyl	NHPh	4	4.7:1	59 (3af)
12	2-furyl	NHPh	2.5	3.5:1	81 (3ag)
$13^{d,f}$	(E)-PhCH=CH	NHPh	2	7.4:1	61 (3ah)
14	<i>i</i> -Pr	NHPh	_	_	nr

^a Aldehyde (0.2 mmol), amine (1.05 equiv), and TMSCN (1.05 equiv) were stirred at 30 °C for 50 min. Catalyst (20 mol%), **2a** (0.3 mmol), and solvent were added. The mixture was stirred for mentioned reaction time at 60 °C.

^b Determined by ¹H NMR analysis.

^c Isolated yield. nr = no reaction.

^d Reaction was carried out at 30 °C in the presence of Bu_3P (20 mol%).

^e Compound 2a (0.4 mmol) was added.

^f Compound **2a** was added via syringe pump over 50 min.

product (Table 2, entry 6). A variety of aromatic and heteroaromatic aldehydes were evaluated next with aniline as the amine component. To our delight, the reactions took place efficiently in good yields for all studied aldehydes (Table 2, entries 7–12). The electronic properties of the aromatic system of the aldehyde component do not seem to influence the yield. Aromatic aldehydes with electronwithdrawing or electron-donating substituent at the paraposition furnished the desired products in good yields (Table 2, entries 7, 8). Aromatic aldehyde with *ortho*-substituent at aryl group, which potentially causes steric hindrance effect, also gave moderate yield (Table 2, entry 10). The tandem reaction with aliphatic aldehyde did not give rise to the desired product, which reveals a dramatic dependence on the pK_a value of pronucleophile (Table 2, entry 14). In addition, α,β -unsaturated aldehydes were also applied in this reaction, which would provide more synthetically useful allylic and vinyl substituted α-aminonitrile derivatives, and afforded desired products 3ah in high yield (Table 2, entry 13).

Finally, tandem γ -umpolung addition reactions of substituted allenoates were investigated (Scheme 2). For example, when allenoate with a substituent at the α -position, such as α -methyl-substituted allenoate **2c** was employed, the inverse conjugate addition gave the expected product in moderate yield, albeit as a 1.5:1 mixture of *E*- and *Z*-olefins. However, γ -methyl-substituted allenoate **2b** failed to give rise to the desired product, presumably due to the increasing repulsive force between in situ generated nucleophilic reagent and γ -substituent of allenoate **2b**.



Scheme 2 Multicomponent tandem γ -umpolung reaction of substituted allenoates

In conclusion, we have developed a multicomponent tandem γ -umpolung reaction with aldehydes, amines and electron-deficient allenes, which provided an efficient synthetic route for the preparation of densely functionalized α -aminonitriles bearing an N-substituted quaternary carbon centers. A number of aldehydes could be successfully applied to give multifunctional desired products with moderate selectivities. Further studies on synthetic applications and asymmetric catalysis are ongoing in our laboratories and will be reported in due course.

All reactions were carried out under inert atmospheric condition unless otherwise noted, and solvents were dried according to established procedures. Reactions were monitored by TLC visualizing with ultraviolet light (UV), KMnO₄; column chromatography purifications were carried out using silica gel. ¹H NMR spectra were recorded on 300 MHz spectrometer in CDCl₃, and ¹³C NMR spectra were recorded on 100 MHz spectrometer in CDCl₃, with chemical shift values (δ) reported in ppm relative to the internal standard TMS. IR spectra were obtained with a Nicolet Avatar 360 FT-IR. HRMS was measured with Bruker MicrOTOF Q II.

Multicomponent Tandem Phosphine-Catalyzed Umpolung Reaction; Compounds 3; General Procedure

To a dried reaction tube were added the required aldehyde (0.2 mmol) and amine (0.21 mmol). After stirring the mixture at 30 °C for 20 min, TMSCN (0.21 mmol) was added, and the mixture was vigorously stirred. After 50 min, MeCN (2 mL), catalyst (20 mol%), and compound **2** (0.3 mmol) were added under N₂ atmosphere, and the mixture was heated to 60 °C. The reaction was monitored by TLC (eluent: EtOAc-petroleum ether). Upon completion, the stirring bar was removed and the mixture was evaporated under reduced pressure to give the crude products. The crude mixture was purified by column chromatography [silica gel, EtOAc-petroleum ether (bp 60–90 °C)] to provide **3**.

Ethyl (E)-5-Cyano-5-phenyl-5-(phenylamino)pent-2-enoate [(E)-3a]

Yield: 42 mg (66%); colorless oil.

IR (KBr): 3372, 3043, 2924, 2854, 2233, 1716, 1654, 1605, 1499, 1186, 753, 694 $\rm cm^{-1}.$

¹H NMR (300 MHz, CDCl₃): δ = 7.65–7.56 (m, 1 H), 7.47–7.32 (m, 2 H), 7.09 (t, *J* = 7.9 Hz, 1 H), 6.89 (ddd, *J* = 15.2, 8.5, 6.5 Hz, 1 H), 6.79 (t, *J* = 7.4 Hz, 1 H), 6.53 (d, *J* = 7.9 Hz, 1 H), 6.01 (d, *J* = 15.6 Hz, 1 H), 4.37 (br s, 1 H), 4.20 (q, *J* = 7.1 Hz, 1 H), 3.01–2.85 (m, 2 H), 1.29 (t, *J* = 7.1 Hz, 2 H).

¹³C NMR (100 MHz, CDCl₃): δ = 165.16, 143.16, 139.05, 137.54, 129.06, 128.75, 127.24, 125.33, 119.83, 119.33, 115.82, 60.50, 60.22, 46.82, 13.98.

HRMS (ESI): m/z calcd for $C_{20}H_{21}N_2O_2$ ([M + H]⁺): 321.1598; found: 321.1593.

Ethyl (Z)-5-Cyano-5-phenyl-5-(phenylamino)pent-2-enoate [(Z)-3a]

Yield: 9.6 mg (15%); colorless oil.

IR (KBr): 3372, 3027, 2957, 2925, 2237, 1715, 1653, 1603, 1499, 1204, 753, 698 $\rm cm^{-1}.$

¹H NMR (300 MHz, CDCl₃): δ = 7.63–7.60 (m, 2 H), 7.40–7.35 (m, 3 H), 7.12–7.06 (m, 2 H), 6.77–6.72 (m, 1 H), 6.51–6.49 (m, 2 H), 6.23–6.09 (m, 2 H), 5.42 (br s, 1 H), 4.25 (q, *J* = 7.1 Hz, 2 H), 3.48 (ddd, *J* = 9.0, 8.1, 0.5 Hz, 1 H), 3.29 (ddd, *J* = 8.7, 7.1, 0.9 Hz, 1 H), 1.34 (t, *J* = 7.1 Hz, 3 H).

 ^{13}C NMR (100 MHz, CDCl₃): δ = 166.52, 143.53, 139.92, 138.04, 129.06, 128.85, 128.69, 125.60, 125.30, 119.55, 119.34, 115.38, 60.76, 60.53, 43.13, 14.11.

HRMS (ESI): m/z calcd for $C_{20}H_{21}N_2O_2$ ([M + H]⁺): 321.1598; found: 321.1596.

Ethyl 3-[Cyano(phenyl)(phenylamino)methyl]but-3-enoate (4a) (Table 1, entry 13)

Yield: 17 mg (26%); colorless oil.

IR (KBr): 3348, 3057, 2925, 2853, 2239, 1728, 1647, 1603, 1499, 1198, 754, 698 $\rm cm^{-1}.$

¹H NMR (300 MHz, CDCl₃): δ = 7.61–7.59 (m, 2 H), 7.41–7.39 (m, 3 H), 7.18–7.13 (m, 2 H), 6.85–6.80 (m, 1 H), 6.67–6.64 (m, 2 H), 5.85 (s, 1 H), 5.38 (s, 1 H), 5.21 (br s, 1 H), 4.14 (q, *J* = 7.1 Hz, 2 H), 3.13 (s, 2 H), 1.29–1.24 (t, *J* = 7.1 Hz, 3 H).

 13 C NMR (125 MHz, CDCl₃): δ = 171.89, 143.46, 139.49, 136.45, 129.16, 129.08, 128.92, 126.66, 120.09, 119.93, 118.77, 116.13, 66.18, 61.56, 37.14, 14.13.

HRMS (ESI): m/z calcd for $C_{20}H_{21}N_2O_2^+$ ([M + H]⁺): 321.1598; found: 321.1601.

SPECIAL TOPIC

Ethyl (E)-5-(4-Chlorophenylamino)-5-cyano-5-phenylpent-2enoate [(E)-3b]

Yield: 45 mg (64%); yellow oil.

IR (KBr): 3365, 3030, 2983, 2936, 2231, 1718, 1657, 1600, 1494, 1198, 819, 732, 700 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): $\delta = 7.59 - 7.56$ (m, 2 H), 7.46-7.36 (m, 3 H), 7.09–7.04 (m, 2 H), 6.89 (ddd, J = 15.4, 8.8, 6.3 Hz, 1 H), 6.49-6.44 (m, 2 H), 6.04 (dt, J = 15.6, 1.2 Hz, 1 H), 4.29 (br s, 1 H),4.22 (q, J = 7.1 Hz, 2 H), 3.00 (ddd, J = 14.2, 6.3, 1.6 Hz, 1 H), 2.89 (ddd, J = 14.3, 8.8, 1.1 Hz, 1 H), 1.31 (t, J = 7.1 Hz, 3 H).

¹³C NMR (125 MHz, CDCl₃): δ = 165.17, 141.54, 138.74, 137.22, 129.48, 129.26, 129.00, 128.02, 125.38, 119.02, 117.24, 60.91, 60.12, 47.46, 14.21.

HRMS (ESI): m/z calcd for $C_{20}H_{20}ClN_2O_2$ ([M + H]⁺): 355.1208; found: 355.1209.

Ethyl (E)-5-Cyano-5-(4-methoxyphenylamino)-5-phenylpent-2enoate [(*E*)-3d]

Yield: 49 mg (70%); yellow oil.

IR (KBr): 3410, 2997, 2924, 2854, 2231, 1718, 1654, 1513, 1240, 1200, 825, 762, 700 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.63–7.59 (m, 2 H), 7.45–7.37 (m, 3 H), 6.89 (ddd, J = 15.3, 8.8, 6.3 Hz, 1 H), 6.71–6.65 (m, 2 H), 6.55–6.50 (m, 2 H), 6.01 (dt, J = 15.8, 1.2 Hz, 1 H), 4.21 (q, J = 7.1 Hz, 2 H), 4.00 (br s, 1 H), 3.69 (s, 3 H), 2.98 (ddd, J = 14.2, 6.3, 1.6 Hz, 1 H), 2.88 (ddd, J = 14.2, 8.7, 1.1 Hz, 1 H), 1.30 (t, J = 7.1 Hz, 3 H).

¹³C NMR (125 MHz, CDCl₃): δ = 165.23, 154.29, 139.16, 137.90, 136.63, 129.27, 129.05, 127.70, 125.68, 119.49, 118.58, 114.47, 61.21, 60.77, 55.48, 47.28, 14.20.

HRMS (ESI): m/z calcd for $C_{21}H_{23}N_2O_3$ ([M + H]⁺): 351.1703; found: 351.1703.

Ethyl (E)-5-(4-Chlorophenyl)-5-cyano-5-(phenylamino)pent-2enoate [(E)-3ab]

Yield: 46 mg (66%); yellow oil.

IR (KBr): 3361, 3057, 3032, 2981, 2926, 2231, 1703, 1654, 1603, 1498, 1199, 830, 750, 693 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.57–7.53 (m, 2 H), 7.42–7.38 (m, 2 H), 7.16–7.10 (m, 2 H), 6.94–6.81 (m, 2 H), 6.52 (d, J = 7.7 Hz, 1 H), 6.04 (d, J = 15.6 Hz, 1 H), 4.23 (q, J = 7.2 Hz, 1 H), 4.25 (br s, 1 H), 2.98 (ddd, J = 14.2, 6.3, 1.6 Hz, 1 H), 2.88 (ddd, J = 14.4, 8.7, 0.8 Hz, 1 H), 1.31 (t, *J* = 7.1 Hz, 3 H).

¹³C NMR (125 MHz, CDCl₃): $\delta = 160.35$, 137.91, 133.72, 131.60, 130.32, 124.85, 124.39, 123.38, 122.22, 115.88, 114.16, 111.35, 56.16, 54.92, 42.65, 9.46.

HRMS (ESI): m/z calcd for $C_{20}H_{20}ClN_2O_2$ ([M + H]⁺): 355.1208; found: 355.1204.

Ethyl (E)-5-Cyano-5-(phenylamino)-5-p-tolylpent-2-enoate [(*E*)-3ac]

Yield: 41 mg (62%); yellow oil.

IR (KBr): 3359, 3032, 2983, 2925, 2229, 1716, 1646, 1604, 1498, 1273, 820, 753, 691 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.47 (d, J = 8.3 Hz, 2 H), 7.21 (d, J = 8.0 Hz, 2 H), 7.14–7.08 (m, 2 H), 6.96–6.84 (m, 1 H), 6.81 (t, J = 7.4 Hz, 1 H), 6.56–6.53 (m, 2 H), 6.03 (dt, J = 15.6, 1.2 Hz, 1 H), 4.25–4.18 (m, 3 H), 2.98 (ddd, J = 14.2, 6.3, 1.6 Hz, 1 H), 2.88 (ddd, J = 14.3, 8.8, 1.1 Hz, 1 H), 2.36 (s, 3 H), 1.30 (t, J = 7.1 Hz, 3 H).

¹³C NMR (125 MHz, CDCl₃): δ = 165.26, 143.13, 139.21, 138.96, 134.74, 130.02, 129.02, 127.69, 125.36, 120.25, 119.42, 116.08, 60.80, 59.94, 47.57, 21.10, 14.22.

HRMS (ESI): m/z calcd for $C_{21}H_{23}N_2O_2$ ([M + H]⁺): 335.1754; found: 335.1755.

Ethyl (E)-5-Cyano-5-(3-methoxyphenyl)-5-(phenylamino)pent-2-enoate [(E)-3ad]

Yield: 52 mg (75%); yellow oil.

IR (KBr): 3364, 3063, 2927, 2854, 2235, 1718, 1658, 1603, 1499, 1194, 1041, 787, 753, 697 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.33 (t, J = 8.0 Hz, 1 H), 7.23–7.17 (m, 1 H), 7.16–7.06 (m, 3 H), 6.97–6.85 (m, 2 H), 6.81 (t, J = 7.4Hz, 1 H), 6.55 (d, J = 7.7 Hz, 2 H), 6.03 (d, J = 15.6 Hz, 1 H), 4.27(br s, 1 H), 4.22 (q, J = 7.2 Hz, 2 H), 2.99 (ddd, J = 14.1, 6.3, 1.5 Hz, 1 H), 2.95–2.83 (m, 1 H), 1.30 (t, J = 7.1 Hz, 3 H).

¹³C NMR (125 MHz, CDCl₃): δ = 165.22, 160.36, 143.04, 139.46, 139.06, 130.45, 129.04, 127.77, 120.35, 119.24, 117.68, 116.04, 114.37, 111.22, 60.82, 60.12, 55.38, 47.41, 14.21.

HRMS (ESI): m/z calcd for $C_{21}H_{23}N_2O_3$ ([M + H]⁺): 351.1703; found: 351.1701.

Ethyl (E)-5-(2-Bromophenyl)-5-cyano-5-(phenylamino)pent-2**enoate** [(*E*)-3ae] Yield: 37 mg (46%); yellow oil.

IR (KBr): 3377, 3058, 2958, 2926, 2237, 1718, 1655, 1603, 1499, 1193, 752, 693 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): $\delta = 7.77$ (dd, J = 8.0, 1.5 Hz, 1 H), 7.62 (dd, J = 7.9, 1.3 Hz, 1 H), 7.38–7.33 (m, 1 H), 7.26–7.20 (m, 1 H), 7.16–7.11 (m, 2 H), 6.92 (ddd, *J* = 15.4, 8.5, 6.4 Hz, 1 H), 6.82 (t, J = 7.4 Hz, 1 H), 6.60–6.57 (m, 2 H), 6.08 (dt, J = 15.6, 1.2 Hz, 1 H), 4.40 (br s, 1 H), 4.21 (q, J = 7.1 Hz, 2 H), 3.44 (ddd, J = 14.6, 6.4, 1.5 Hz, 1 H), 3.21 (ddd, J = 14.8, 8.6, 0.7 Hz, 1 H), 1.30 (t, J = 7.1 Hz, 3 H).

¹³C NMR (125 MHz, CDCl₃): δ = 165.17, 142.53, 138.98, 136.05, 133.86, 130.65, 130.21, 128.98, 128.13, 127.69, 120.25, 119.84, 118.10, 115.81, 60.82, 60.68, 42.40, 14.20.

HRMS (ESI): m/z calcd for $C_{20}H_{20}BrN_2O_2$ ([M + H]⁺): 399.0703; found: 399.0704.

Ethyl (E)-5-Cyano-5-(naphthalen-2-yl)-5-(phenylamino)pent-2-enoate [(*E*)-3af]

Yield: 36 mg (49%); white oil.

IR (KBr): 3370, 3061, 2955, 2852, 2245, 1715, 1659, 1605, 1499, 1188, 754, 693 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): $\delta = 8.14$ (s, 1 H), 7.91–7.85 (m, 3 H), 7.67 (dd, J = 8.7, 1.9 Hz, 1 H), 7.57–7.51 (m, 2 H), 7.08 (t, J = 7.9Hz, 1 H), 7.00–6.90 (m, 1 H), 6.80 (t, J = 7.4 Hz, 1 H), 6.58 (d, J = 8.2 Hz, 2 H), 6.06 (d, J = 15.6 Hz, 1 H), 4.33 (s, 1 H), 4.21 (q, J = 7.1 Hz, 2 H), 3.12–2.94 (m, 2 H), 1.29 (t, J = 7.1 Hz, 3 H).

¹³C NMR (125 MHz, CDCl₃): δ = 165.16, 143.06, 138.93, 135.29, 133.43, 133.23, 129.58, 129.10, 128.39, 127.95, 127.75, 126.97, 126.87, 125.23, 122.36, 120.48, 119.30, 116.17, 60.83, 60.38, 47.50, 14.20.

HRMS (ESI): m/z calcd for $C_{24}H_{23}N_2O_2$ ([M + H]⁺): 371.1754; found: 371.1747.

Ethyl (E)-5-Cyano-5-(furan-2-yl)-5-(phenylamino)pent-2-enoate [(E)-3ag]

Yield: 39 mg (63%); yellow oil.

IR (KBr): 3376, 3029, 2926, 2854, 2242, 1716, 1658, 1603, 1500, 1185, 752, 695 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.45 (dd, J = 1.8, 0.9 Hz, 1 H), 7.22-7.15 (m, 2 H), 6.93-6.82 (m, 2 H), 6.75-6.70 (m, 2 H), 6.51 (dd, J = 3.4, 0.9 Hz, 1 H), 6.38 (dd, J = 3.4, 1.9 Hz, 1 H), 6.04 (dt, J = 3.4, 1.9 Hz, 1 HJ = 15.6, 1.4 Hz, 1 H), 4.21 (q, J = 7.1 Hz, 2 H), 4.05 (br, 1 H), 3.16 (ddd, J = 5.0, 4.5, 1.4 Hz, 1 H), 3.10 (ddd, J = 9.3, 6.1, 1.4 Hz, 1 H),1.30 (t, J = 7.1 Hz, 3 H).

 ^{13}C NMR (125 MHz, CDCl₃): δ = 165.26, 148.59, 143.60, 142.93, 138.54, 129.15, 127.59, 121.46, 117.70, 117.30, 110.88, 109.98, 60.78, 56.10, 43.35, 14.20.

HRMS (ESI): m/z calcd for $C_{18}H_{19}N_2O_3$ ([M + H]⁺): 311.1390; found: 311.1385.

Ethyl (2*E*,6*E*)-5-Cyano-7-phenyl-5-(phenylamino)hepta-2,6-dienoate [(*E*)-3ah]

Yield: 38 mg (54%); red oil.

IR (KBr): 3364, 3029, 2925, 2854, 2231, 1717, 1653, 1603, 1498, 1187, 751, 693 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.42–7.31 (m, 5 H), 7.24–7.18 (m, 2 H), 7.06–6.96 (m, 2 H), 6.92–6.87 (m, 3 H), 6.13 (d, *J* = 15.9 Hz, 1 H), 6.10 (dt, *J* = 15.6, 1.5 Hz, 1 H), 4.23 (q, *J* = 7.1 Hz, 2 H), 3.96 (br s, 1 H), 3.01–2.86 (m, 2 H), 1.31 (t, *J* = 7.1 Hz, 3 H).

 ^{13}C NMR (125 MHz, CDCl₃): δ = 165.29, 143.36, 138.87, 134.90, 133.89, 129.25, 128.85, 127.83, 127.57, 126.99, 120.97, 118.64, 116.83, 60.86, 57.97, 44.48, 14.23.

HRMS (ESI): m/z calcd for $C_{22}H_{23}N_2O_2$ ([M + H]⁺): 347.1754; found: 347.1751.

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Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

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