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N-Allylideneamines Derived from Acrolein: Synthesis and Use as Acceptors of Two Nucleophiles

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Two practical methods have been developed for the preparation of *N*-allylideneamines **1b**,**c**. One involves the isomerization of propargylamines and the other the dehydration of acrolein. *N*-Allylideneamines **1b**,**c** thus prepared were used as efficient substrates for 1,4- and 1,2-double nucleophilic addition reactions.

Introduction

N-Allylideneamines **1** derived from acrolein are important building blocks because they consist of three carbon atoms bearing useful amino and olefin moieties for further functional group manipulations. Although we have already reported that various amino esters can be synthesized by 1,4- and 1,2-double nucleophilic addition to α,β-unsaturated imines and *N*-allylideneamines, the simplest α,β-unsaturated imines are not readily accessible. Because imines **1** have high reactivity and are prone to polymerize even during their preparation, their synthesis is difficult and thus only a few reports are available for the synthesis of this type of imine.[1] Although the use of imine **1** bearing a TBS group at the nitrogen atom was reported by Colvin et al. for β-lactam synthesis, it has not been used for other reactions.[1d,2] The TMS-protected derivative has also been prepared in situ from acrolein and used in the total synthesis of (+/–)-sedridine. However, the formation of this particular derivative was only confirmed by GC analysis.[1c] Another analogous imine protected with an electron-withdrawing group at the nitrogen atom has been reported by Davis and Deng.[1a] Unfortunately, this imine did not work as an effective acceptor in 1,4- and 1,2-nucleophilic addition reactions in our experiments.[3] We therefore embarked on the search for a practical synthesis of stable *N*-allylideneamines **1**. Herein we report the synthesis of *N*-allylideneamines **1** and their subsequent double nucleophilic addition reactions.[4]

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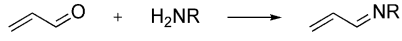
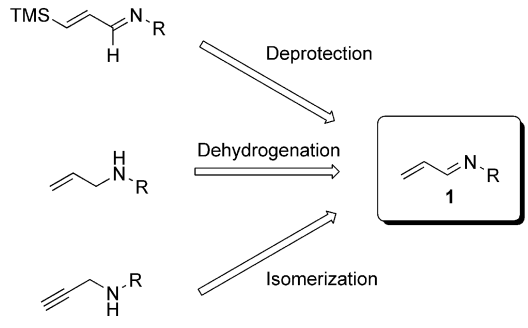
Results and Discussion

The most direct way to synthesize this particular imine involves the dehydration reactions of acrolein and primary amines (Scheme 1). However, several attempts using a variety of dehydration conditions led to the formation of only traces of the imine.



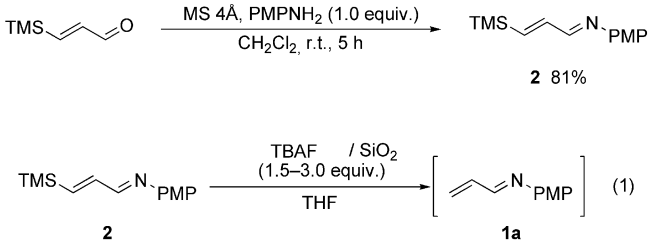
Scheme 1. The dehydration reaction between acrolein and primary amines.

Because there appear to be several routes to prepare *N*-allylideneamine **1** besides dehydration, three approaches, (1) the formation of trimethylsilyl-protected imine followed by desilylation, (2) the dehydrogenation of allylamines, and (3) the isomerization of propargylamines, were next examined (Scheme 2).



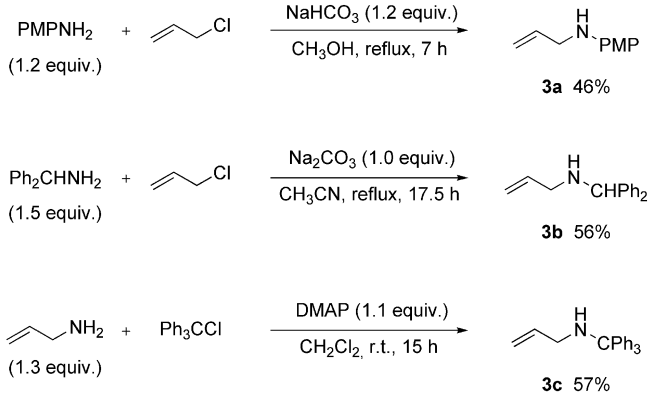
Scheme 2. Strategy for preparing *N*-allylideneamine.

The 3-trimethylsilylated acrolein was readily iminated to give imine **2** in 81% yield. However, desilylation with TBAF only led to the polymerization of the product (Scheme 3).



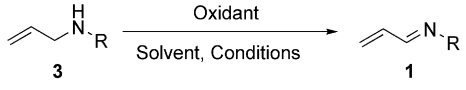
Scheme 3. Imination of the 3-trimethylsilylated acrolein.

Next, the dehydrogenation of allylamines **3** was examined by using a variety of reagents; allylamines **3a**–**c** were prepared by simple allylation of the primary amines (Scheme 4). The results of the dehydrogenation reactions are shown in Table 1.



Scheme 4. Preparation of allylamines **3a**–**c**.

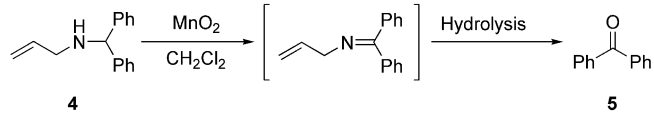
Table 1. Dehydrogenation of allylamines.



Entry	R	Solvent	Oxidant	Conditions	Yield [%]
1	PMP	CH_2Cl_2	MnO_2	r.t., 12 h	–
2	PMP	CH_3CN	MnO_2	reflux, 9 h	–
3	PMP	CH_3CN	DDQ	r.t., 12 h	–
4	$CHPh_2$	CH_2Cl_2	MnO_2	reflux, 8 h	–[a]
5	$CHPh_2$	CH_2Cl_2	SeO_2	r.t., 1 d	–
6	CPh_3	CH_2Cl_2	MnO_2	r.t., 14 h	–

[a] Benzophenone was obtained in 66% yield.

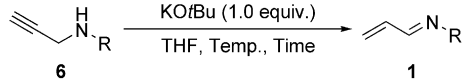
Although various oxidants such as MnO_2, DDQ, and SeO_2 were used, oxidized imine **1** was not obtained (Table 1, Entries 1–5). When the allylamine protected with the diphenylmethyl group was oxidized with MnO_2 at reflux in CH_2Cl_2, only benzophenone (**5**) was obtained (Table 1, Entry 4; Scheme 5). The formation of benzophenone may involve the oxidation of the diphenylmethyl moiety. These results suggest that a relatively stable derivative of the desired *N*-allylideneamine might have a bulky substituent at the nitrogen atom without a hydrogen α to the nitrogen. However, the oxidation product was not formed when an allylamine with a bulky trityl group was used, but recovery of the starting material was observed (Table 1, Entry 6).



Scheme 5. Benzophenone formation.

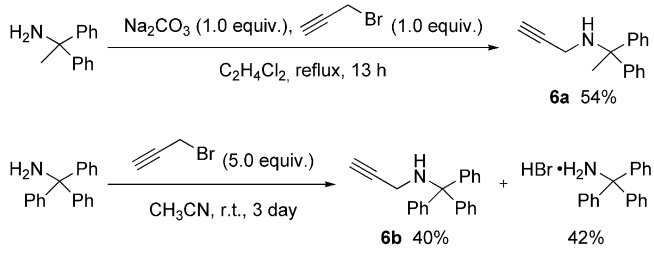
Isomerization of propargylamines **6** was next carried out (Table 2). Starting propargylamines **6** were readily prepared in good yields (Scheme 6). When the diphenylmethyl derivative was used, the reaction afforded the isomerized benzophenone imine (Table 2, Entry 2). With trityl and diphenylethyl groups, desired *N*-allylideneamines **1** were isolated in high yields (Table 2, Entries 4–6).

Table 2. Isomerization of propargylamines **6**.



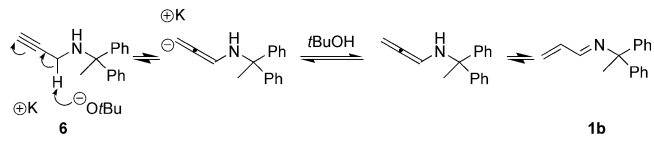
Entry	R	Temp.	Time	*N*-Allylideneamine	Yield [%]
1	PMP	r.t.	3 h	–	–
2	$CHPh_2$	r.t.	5 h	–	–[a]
3	*t*Bu	40 °C	1 h	–	–
4	CCH_3Ph_2	45 °C	1 h	**1b**	86
5	CCH_3Ph_2	r.t.	10 min	**1b**	86
6	CPh_3	r.t.	4 h	**1c**	78

[a] Isomerized benzophenone imine was obtained.



Scheme 6. Preparation of propargylamines **6**.

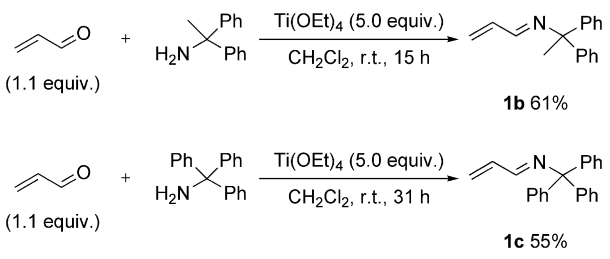
A facile isomerization mechanism is described below. Propargylamines **6** are deprotonated with potassium *tert*-butoxide to afford the alleneamine. Subsequent protonation with *tert*-butyl alcohol gave *N*-allylideneamine **1b** by imine–enamine tautomerism (Scheme 7).



Scheme 7. Mechanism of the isomerisation reaction.

To find more direct alternatives, the dehydration of acrolein with bulky amines was again examined in the presence of $Ti(OEt)_4$, a relatively weak Lewis acid. Indeed, the reac-

tion proceeded smoothly to afford *N*-allylideneamines **1b**,**c** bearing a diphenylethyl or trityl group, respectively (Scheme 8).



Scheme 8. Preparation of *N*-allylideneamines bearing a diphenylethyl or trityl group.

To study the characteristics of these *N*-allylideneamines, the LUMO coefficients of the carbonyl (or imino) and β carbon atoms were calculated, which should provide an indication of the regioselectivities of the nucleophilic addition reactions.[5] Based on molecular orbital calculations, the electronic and steric effects of the substituent at the imino nitrogen atom should be rationalized (Figure 1).[6]

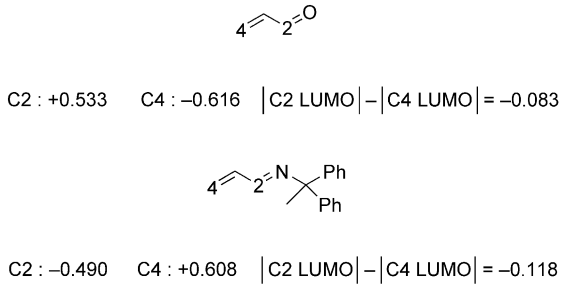
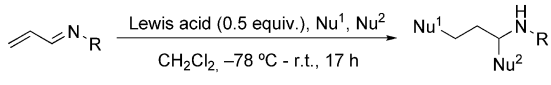


Figure 1. LUMO coefficients of acrolein and *N*-allylideneamine.

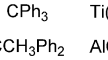
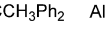
Structures were fully optimized at the HF/6-31G* level of theory by geometry optimization. The calculations were shown to be comparable to the ab initio (HF/STO-3G) method.[7] The values of the LUMO coefficients at each reaction site (the 2- and 4-positions) and the absolute differences between these coefficients for the optimized geometries are given for comparison (Figure 1). Comparison of the LUMO coefficients of acrolein and *N*-allylideneamine **1b** provides an indication of the regioselectivity of the 1,4- and 1,2-addition reactions. Both acrolein and *N*-allylideneamine **1b** have larger coefficients at the 4-position, and the major reaction course based on the HOMO–LUMO interaction would be 1,4-addition. Steric factors suggest that it would be easier for the *N*-allylideneamines to be attacked at the 4-position than acrolein.

1,4- and 1,2-Double nucleophilic additions to *N*-allylideneamine were next examined by using ketene silyl acetals (KSAs) and trimethylsilyl cyanide (TMSCN). When the reaction was carried out with *N*-allylideneamine bearing a trityl group, it decomposed in the presence of Lewis acids such as $AlCl_3$, $TiCl_4$, and Ti(O*i*Pr)$_4$. Similarly, the use of *N*-allylideneamine with a diphenylethyl group also led to the decomposition of the imine in the presence of $AlCl_3$ and $TiCl_4$ (Table 3).

Table 3. Double nucleophilic addition reactions using Lewis acids.

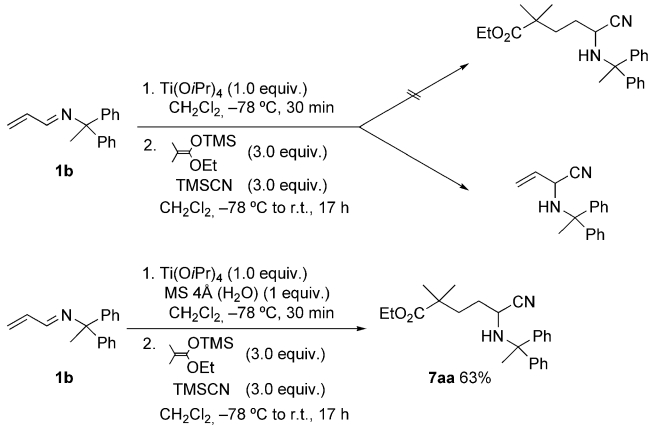


1 **7**

Entry	R	Lewis acid	Nu^1 (equiv.)	Nu^2 (equiv.)	Yield [%]
1	CPh_3	$AlCl_3$	*t*BuC_6H_4SH (1.0)	TMSCN (1.5)	–[a]
2	CPh_3	$TiCl_4$	*t*BuC_6H_4SH (1.0)	TMSCN (1.5)	–[b]
3	CPh_3	Ti(O*i*Pr)$_4$	*t*BuC_6H_4SH (1.0)	TMSCN (1.5)	–
4	CPh_3	Ti(O*i*Pr)$_4$	 (1.5)	TMSCN (1.5)	–
5	CCH_3Ph_2	$AlCl_3$	 (1.5)	TMSCN (1.5)	–
6	CCH_3Ph_2	$TiCl_4$	 (1.5)	TMSCN (1.5)	–

[a] *t*$BuC_6H_4SCPh_3$ was obtained in 43% yield. [b] *t*$BuC_6H_4SCPh_3$ was obtained in 50% yield.

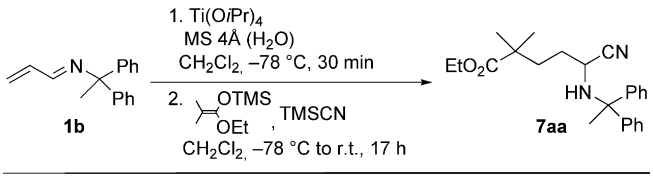
However, when Ti(O*i*Pr)$_4$ was used as a Lewis acid, the formation of the 1,2 adduct of TMSCN as a byproduct was confirmed by ^{1}H NMR spectroscopy (Scheme 9). These results indicate that proton sources might be essential.[4j] The reaction was then carried out in the presence of 4 Å molecular sieves containing one equivalent of H_2O to give the desired 1,4- and 1,2-addition product **7aa** in 63% yield. Because the presence of a limited amount of H_2O affected the double addition, the reaction conditions were examined in detail and the results are summarized in Table 4.



Scheme 9. Double nucleophilic addition reactions of *N*-allylideneamine.

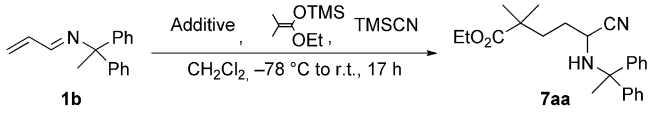
The best result was obtained when the addition was carried out with three equivalents of each nucleophile in the presence of 4 Å MS containing three equivalents of H_2O without the use of Ti(O*i*Pr)$_4$ as a Lewis acid (Table 4, Entry 10). Because the presence of Ti(O*i*Pr)$_4$ was not essential the effect of additives as reaction promoters was next examined and the results are shown in Table 5. *N*-Allylideneamine **1b** was treated with a mixture of ketene silyl acetal and TMSCN in the presence of various additives to give doubly alkylated product **7aa**.

Table 4. Examination of reaction conditions in the synthesis of **7aa**.



Entry	$Ti(iPrO)_4$ [equiv.]	4 Å MS (H_2O) [equiv.]	KSA [equiv.]	TMSCN [equiv.]	Yield [%]
1	1.0	1	3.0	3.0	6
2	1.0	3	3.0	3.0	63
3	1.0	6	3.0	3.0	35
4	1.0	3	1.5	1.5	54
5	0.5	1	3.0	3.0	61
6	0.5	3	3.0	3.0	67
7	0.5	6	3.0	3.0	62
8	0.5	3	1.5	1.5	55
9	–	1	3.0	3.0	23
10	–	3	3.0	3.0	69
11	–	6	3.0	3.0	63
12	–	3	1.5	1.5	65

Table 5. Examination of the effect of additives on the synthesis of **7aa**.

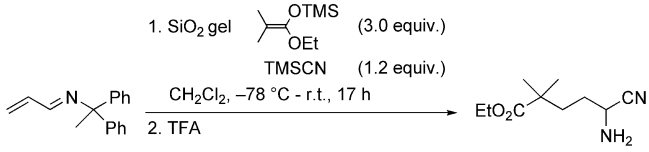


Entry	Additive (equiv.)	KSA [equiv.]	TMSCN [equiv.]	Yield [%]
1	MeOH (3.0)	3.0	3.0	20
2	PhOH (3.0)	3.0	3.0	33
3	AcOH (3.0)	3.0	3.0	27
4	$Na_2SO_4 \cdot 10H_2O$ (0.3)	1.5	1.5	30
5	Amberlyst 15DRY (3.0)	3.0	3.0	13
6	SiO_2 gel (dry, 0.3 g/mmol)	3.0	3.0	21
7	SiO_2 gel (dry, 1.5 g/mmol)	3.0	3.0	80
8	SiO_2 gel (dry, 2.5 g/mmol)	3.0	3.0	83

Dried silica gel was the most effective additive in this reaction.[8] In the presence of 0.3 g/mmol of silica gel, the 1,4- and 1,2-addition product was isolated in 21% yield, whereas the use of 2.5 g/mmol of silica gel gave the 1,4- and 1,2-addition product in 83% yield (Table 5, Entries 6 and 8). The use of other promoters such as MeOH, PhOH, AcOH, $Na_2SO_4 \cdot 10H_2O$, and Amberlyst 15DRY gave 1,4- and 1,2-addition product **7aa** in low yields (Table 5, Entries 1–5).

It was also discovered that the shape and form of the silica gel influenced the product yields (Table 6). Dried spherical silica gel was found to be effective for the reaction. Similarly, the dried irregular analogue gave the product in good yield, although the reproducibility of the reaction was somewhat lost (Table 6, Entry 2). The addition of H_2O led to a decrease in the yield (Table 6, Entries 3 and 4).

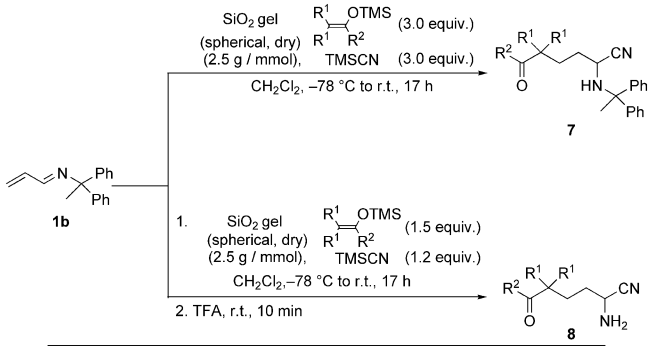
Table 6. Examination of the effect of different forms of silica gel on the reaction.



Entry	SiO_2 gel	Yield [%]
1	Spherical, dry, 2.5 g/mmol	76
2	Irregular, dry, 2.5 g/mmol	65–82
3	Spherical, H_2O (3 equiv.)	42
4	Spherical, H_2O (6 equiv.)	47

The double nucleophilic addition reactions were next carried out with various ketene silyl acetals under the optimized conditions and the results are summarized in Table 7.

Table 7. Examination of 1,4-nucleophiles for the double nucleophilic addition and deprotection reactions with *N*-allylideneamine bearing the diphenylethyl group.



Entry	R^1 R^1 OTMS / R^2	7	Yield of 7 [%]	8	Yield of 8 [%]
1	OTMS, OEt	**7aa**	83	**8a**	78
2	OTMS, OMe	**7ab**	87	**8b**	67
3	OTMS, O*n*Pr	**7ac**	–	**8c**	47
4	OTMS, O*i*Pr	**7ad**	–	**8d**	27
5	OTMS, OMe	**7ae**	87	**8e**	76
6	EtO, EtO, OTMS, OEt	**7af**	–	**8f**	40
7	OTMS, S*t*Bu	**7ag**	56		

The use of ketene silyl acetals derived from ethyl and methyl isobutyrate gave desired 1,4 and 1,2 adducts **7aa** and **7ab** in high yields (Table 7, Entries 1 and 2). The use of ketene silyl thioacetal (KSTA)[4h] also gave the desired 1,4- and 1,2-addition adduct **7ag** in 56% yield (Table 7, Entry 7). Because of the instability of some of the 1,4- and 1,2-addition products,[9] the transformation into the amino nitriles was next carried out. The use of 1.5 equivalents of

ketene silyl acetals and 1.2 equivalents of TMSCN gave the best results. Amino nitrile **8a** was obtained in 78% yield on quenching the reaction with TFA after the double nucleophilic addition reaction (Table 7, Entry 1). Under the best reaction conditions, the double nucleophilic addition of various ketene silyl acetals and TMSCN to *N*-allylideneamine **1b** proceeded smoothly to give the 1,4–1,2 products **8b**–**f** in moderate-to-high yields (Table 7, Entries 2–6).

Because the 1,4- and 1,2-addition products obtained from *N*-allylideneamine bearing the diphenylethyl group were not stable, the reactions of the *N*-allylideneamine bearing the trityl group were next investigated (Table 8). These reactions also proceeded smoothly to give the 1,4–1,2 adducts **7ba**–**7bi**, which were all reasonably stable, in moderate-to-high yields (Table 8, Entries 1–9). With a disubstituted ketene silyl thioacetal, the *N*-allylideneamine was converted into product **7bg** but in a low yield (Table 8, Entry 7). However, when a trisubstituted ketene silyl acetal was used, 1,4-addition did not proceed (Table 8, Entry 10). Silyl enol ether was also not an effective nucleophile in this reaction (Table 8, Entry 11).

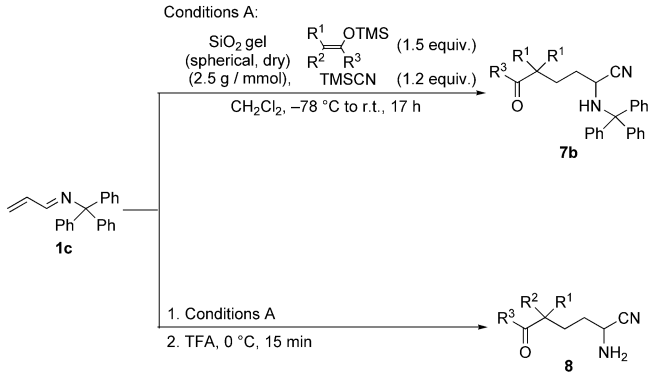
Similarly, transformation to the unprotected amino nitrile after the double nucleophilic addition was next examined (Table 8). It was found that various ketene silyl acetals were good nucleophiles for *N*-trityl-*N*-allylideneamine (**1c**). In fact, by using the ketene silyl acetal derived from isopropyl isobutyrate, amino nitrile **8d** was obtained in good yield, which is in contrast to the result obtained with **1b** (Table 7, Entry 4).

When the trisubstituted ketene silyl thioacetal derived from *S*-cyclohexyl propanethioate was used in the double nucleophilic addition, followed by conversion into an amino nitrile by quenching with TFA, valerolactam **10a** was obtained in high yield by cyclization of the amino nitrile due to the high leaving ability of the alkylthio group (Table 9, Entry 1). Valerolactams are often observed in natural products, and many of them are currently of great interest because of their unique biological activities.[10] Thus, valerolactams were synthesized by using various ketene silyl thioacetals. The 1,4- and 1,2-double nucleophilic addition reactions proceeded smoothly and 1,4–1,2 adducts **9a**–**f** were obtained in moderate-to-good yields (Table 9, Entries 1–6) when trisubstituted ketene silyl thioacetals were used. A tetrasubstituted analogue also gave product **9g** in moderate yield (Table 9, Entry 7). Valerolactams **10** were obtained in moderate-to-high yields under conditions B (Table 9, Entries 1–7).

From these results we have proposed a plausible mechanism for the reaction, as shown in Scheme 10. First, the *N*-allylideneamine was activated with silica gel followed by the 1,4-addition of ketene silyl (thio)acetal to give an intermediary enamine species **11**. Isomerization to the iminium ion was then promoted by silica gel followed by 1,2-addition of TMSCN to give the 1,4- and 1,2-addition product.

The hydrolysis of the nitrile moiety of amino nitrile **8a** was also readily achieved with aqueous HCl in AcOH at reflux to give amino acid **12** in high yield (Scheme 11).

Table 8. Examination of 1,4-nucleophiles for the double nucleophilic addition and deprotection reactions with *N*-allylideneamine bearing the trityl group.



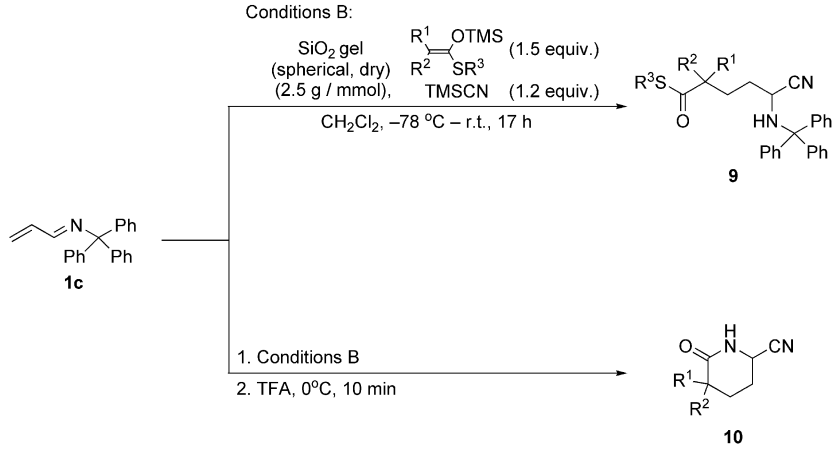
Entry	R^1 OTMS / R^2 R^3	Product	Yield of **7b** [%]	Product	Yield of **8** [%]
1	OTMS, OEt	**7ba**	80	**8a**	56
2	OTMS, OMe	**7bb**	64	**8b**	67
3	OTMS, O*n*Pr	**7bc**	58	**8c**	54
4	OTMS, O*i*Pr	**7bd**	68	**8d**	59
5	OTMS, OMe	**7be**	59	**8e**	61
6	EtO, EtO, OTMS, OEt	**7bf**	51	**8f**	12
7	OTMS, S*t*Bu	**7bg**	22	**8g**	–[a]
8	OTMS, O*t*Bu	**7bh**	59	**8h**	61
9	MeS, OTMS, OEt	**7bi**	24[b]		
10	OTMS, OEt	**7bj**	-		
11	OTMS, Ph	**7bk**	-		

[a] Although the formation of valerolactam was confirmed by ^{1}H NMR spectroscopy, isolation was not successful. [b] *dr* = 53:47.

Conclusions

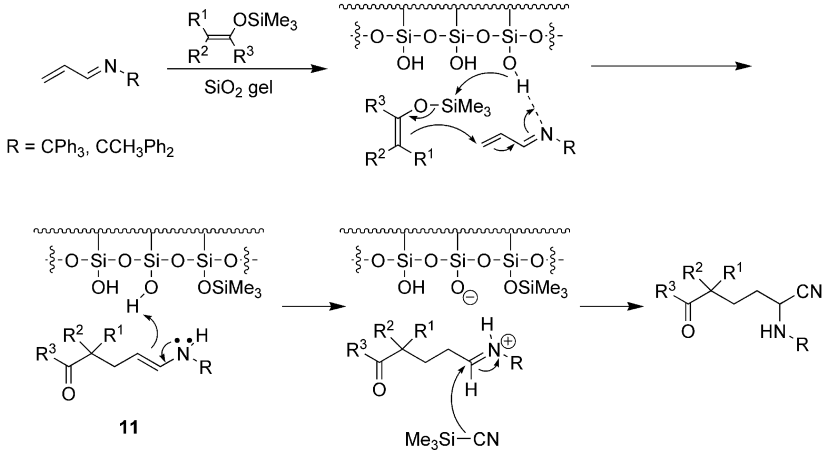
N-Allylideneamines have successfully been prepared in high yields. Although previous double nucleophilic addition reactions used strong Lewis acids such as $TiCl_4$ or $AlCl_3$, it has been discovered that even the use of silica gel, a weak acid, promoted the double nucleophilic addition.[11,12] Tetrasubstituted ketene silyl acetals and trisubstituted ketene silyl thioacetals were found to be useful reagents for this reaction. Amino nitriles and valerolactams were synthesized in good yields using ketene silyl acetals and silyl thioacetals under the influence of TFA, which removed the diphenylethyl and trityl protecting groups. Moreover, hydrolysis of the amino nitrile moiety was readily achieved to yield the amino acid in high yield.

Table 9. Examination of 1,4-nucleophiles for double nucleophilic addition and transformation to valerolactam using *N*-allylideneamine bearing a trityl group.

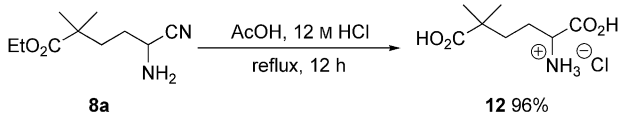


Entry	R^1 OTMS / R^2 SR^3	**9**	**9** (%)	dr	**10**	**10** (%)	dr
1	OTMS, ScHex (*Z*/*E*=92/8)	**9a**	75	50 : 50	**10a**	85	53 : 47
2	OTMS, SEt (*Z*/*E*=89/11)	**9b**	69	71 : 29	**10a**	76[a]	50 : 50
3	OTMS, S*t*Bu (*Z*/*E*=94/6)	**9c**	65	55 : 45	**10a**	71	47 : 53
4	OTMS, S*i*Pr (*Z*/*E*=94/6)	**9d**	68	58 : 42	**10a**	35[b, c]	66 : 34
5	OTMS, SPh (*Z*/*E*=73/23)	**9e**	55[d]	55 : 45	**10a**	64[d]	42 : 58
6	OTMS, S*n*Pr (*Z*/*E*=88/12)	**9f**	45	51 : 49	**10a**	40[c]	46 : 54
7	OTMS, SEt	**9g**	39	–	**10b**	53	–

[a] Ketene silyl thioacetal (*Z*/*E* = 91:9) was used. [b] Ketene silyl thioacetal (*Z*/*E* = 92:8) was used. [c] Treatment with TFA at room temperature for 10 min. [d] The reaction time was 24 h.



Scheme 10. Proposed mechanism for the formation of the amino nitriles.



8a **12** 96%

Scheme 11. Hydrolysis of amino nitrile **8a**.

Experimental Section

General: Infrared spectra were recorded with a JASCO FT/ IR-460 plus spectrometer. ^{1}H and ^{13}C NMR spectra were recorded with a JEOL EX-270, ECX-400P, or A-500 spectrometer using tetramethylsilane as an internal standard. Mass spectra were recorded with a JEOL MS-700D spectrometer. Dichloromethane was distilled from calcium hydride and stored over 4 Å molecular sieves. THF was distilled from benzophenone ketyl immediately before use. MeOH was distilled from magnesium and stored over 3 Å molecular sieves. Products were purified by column chromatography on silica gel (Kanto Chemical Co., Silica 60N) and/or preparative TLC on silica gel (Merck Kiesel Gel PF254).

***N*-Allylidene-1,1-diphenylethylamine (1b):** 1,1-Diphenylethylamine (493 mg, 2.50 mmol), DCM (5.0 mL), acrolein (0.18 mL, 2.75 mmol), and Ti(OEt)$_4$ (2.6 mL, 12.5 mmol) were placed in a 30-mL two-necked round-bottomed flask equipped with a magnetic stirring bar, a rubber septum, and an argon balloon. The solution was stirred for 15 h at room temperature, quenched with ice/H_2O (5.0 mL), and filtered. The white precipitate was washed with DCM (3 × 10 mL), and the aqueous phase was separated and extracted with DCM (3 × 5.0 mL). The combined organic phases were washed with brine (15 mL), dried (Na_2SO_4), and concentrated. The residue was distilled under reduced pressure (137 °C/0.30 Torr) to give title compound **1b** (359 mg, 61%). White crystals; m.p. 36–37 °C; b.p. 137 °C/0.30 Torr. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.89 (s, 3 H, Ph_2CCH_3), 5.54 [dd, J = 0.9, 17.4 Hz, 1 H, NCHCHCH*H*(*trans*)], 5.74 [dd, J = 0.9, 10.2 Hz, 1 H, NCHCHC*H*H(*cis*)], 6.66 (ddd, J = 8.9, 10.2, 17.4 Hz, 1 H, NCHC*H*CH$_2$), 7.20–7.32 (m, 10 H, Ar*H*), 7.50 (d, J = 8.9 Hz, 1 H, NC*H*CHCH$_2$) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 29.5, 69.4, 126.5, 126.9, 127.8, 128.0, 137.9, 147.2, 161.4 ppm. IR (neat): $\tilde{\nu}$ = 3057, 3024, 2979, 2871, 1641, 1604, 1490, 1444, 1026, 997, 700 cm^{-1}. HRMS (EI): calcd. for $C_{17}H_{17}N$ [M]$^+$ 235.1361; found 235.1350.

***N*-Allylidenetriphenylmethylamine (1c):** Triphenylmethylamine (5.44 g, 21.0 mmol), DCM (42 mL), acrolein (1.5 mL, 23.1 mmol), and Ti(OEt)$_4$ (22 mL, 105 mmol) were placed in a 100-mL two-necked round-bottomed flask equipped with a magnetic stirring bar, a rubber septum, and an argon balloon. The solution was stirred for 31 h at room temperature, quenched with ice/H_2O (15 mL), and filtered. The white precipitate was washed with DCM (3 × 10 mL), and the aqueous phase was separated and extracted with DCM (3 × 5.0 mL). The combined organic phases were washed with brine (15 mL), dried (Na_2SO_4), and concentrated. The residue was recrystallized from toluene to give title compound **1c** (3.43 g, 55%). White crystals; m.p. 173–174 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.56 [dd, J = 0.9, 17.4 Hz, 1 H, NCHCHCH*H*(*trans*)], 5.79 [dd, J = 0.9, 10.1 Hz, 1 H, NCHCHC*H*H(*cis*)], 6.77 (ddd, J = 8.9, 10.1, 17.4 Hz, 1 H, NCHC*H*CH$_2$), 7.17–7.30 (m, 15 H, Ar*H*), 7.51 (d, J = 8.9 Hz, 1 H, NC*H*CHCH$_2$) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 78.5, 126.8, 127.4, 127.7, 129.8, 137.9, 145.5, 162.2 ppm. IR (neat): $\tilde{\nu}$ = 3055, 1637, 1600, 1488, 1445, 1034, 1002, 699 cm^{-1}. HRMS (EI): calcd. for $C_{22}H_{19}N$ [M]$^+$ 297.1518; found 297.1516.

***N*-(1,1-Diphenylethyl)prop-2-ynamine (6a):** Under argon, a suspension of Na_2CO_3 (2.54 g, 23.9 mmol) in $C_2H_4Cl_2$ (50 mL) was stirred at room temperature for 10 min. A solution of 1,1-diphenylethanamine in $C_2H_4Cl_2$ (15 mL) was added to the mixture. After stirring for 10 min, 3-bromoprop-1-yne was added to the mixture. The mixture was heated at reflux for 13 h. H_2O (10 mL) was then added to quench the reaction, and the mixture was extracted with CH_2Cl_2 (3 × 5.0 mL). The combined extracts were dried with Na_2SO_4 and concentrated in vacuo to give the crude product. It was purified by column chromatography on silica gel (*n*-hexane/ethyl acetate, 4:1) to give title compound **6a** (3.06 g, 54%). Yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.81 (s, 3 H, Ph_2CCH_3), 1.87 (br. s, 1 H, N*H*), 2.17 (t, J = 2.4 Hz, 1 H, NCH$_2$CC*H*), 3.15 (d, J = 2.4 Hz, 2 H, NCH_2CCH), 7.20–7.36 (m, 10 H, Ar*H*) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 27.6, 32.8, 62.8, 70.8, 82.9, 126.6, 127.0, 128.1, 147.0 ppm. IR (neat): $\tilde{\nu}$ = 3291, 3058, 3024, 2978, 2834, 1491, 1444, 1373, 1027, 762, 700 cm^{-1}. HRMS (EI): calcd. for $C_{17}H_{17}N$ [M]$^+$ 235.1361; found 235.1363.

General Procedure for the 1,4- and 1,2-Double Nucleophilic Addition Reactions of Ketene Silyl (Thio)acetals and Trimethylsilyl Cyanide (Table 7, Entry 1; product 7aa): Under argon, a suspension of *N*-allylideneamine **1b** (47.1 mg, 0.20 mmol) in CH_2Cl_2 (1.0 mL) was stirred at room temperature for 10 min. Dried silica gel (500 mg) and CH_2Cl_2 (0.30 mL) were added to the mixture, which was cooled to –78 °C. A solution of (1-ethoxy-2-methylprop-1-enyloxy) trimethylsilane (113.0 mg, 0.60 mmol) in CH_2Cl_2 (0.90 mL) was added to the mixture. After stirring for 10 min, a solution of trimethylsilyl cyanide (59.5 mg, 0.60 mmol) in CH_2Cl_2 (0.80 mL) was added to the resulting mixture. The mixture was gradually warmed to room temperature over 17 h. Saturated aqueous $NaHCO_3$ (10 mL) was added to quench the reaction. The mixture was filtered with suction through a Celite pad and washed with ethyl acetate. The mixture was extracted with ethyl acetate (3 × 5.0 mL). The combined extracts were dried with Na_2SO_4 and concentrated in vacuo to give the crude product. Purification on buffered silica gel TLC (*n*-hexane/ethyl acetate, 5:1) gave the compound **7aa** (63.0 mg, 83%). Yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.15 (s, 3 H, COCCH_3CH$_3$), 1.16 (s, 3 H, COCCH$_3$CH_3), 1.23 (t, J = 7.0 Hz, 3 H, COOCH$_2$CH_3), 1.58–1.71 (m, 4 H, NHCHCNCH_2CH_2), 1.95 (s, 3 H, Ph_2CCH_3), 1.97 (br. s, 1 H, N*H*), 3.27 (br. s, 1 H, NHC*H*CN), 4.10 (q, J = 7.0 Hz, 2 H, COOCH_2CH$_3$), 7.21–7.37 (m, 10 H, Ar*H*) ppm. ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = 14.2, 24.9, 25.2, 27.8, 31.3, 35.9, 41.7, 44.8, 60.5, 63.1, 121.8, 126.5, 126.9, 127.1, 127.3, 128.2, 128.3, 145.7, 147.6, 177.2 ppm. IR (neat): $\tilde{\nu}$ = 3334, 3059, 3025, 2978, 2935, 2873, 2289, 1724, 1599, 1474, 1389, 1186, 1142, 762, 702 cm^{-1}. HRMS (EI): calcd. for $C_{24}H_{30}N_2O_2$ [M]$^+$ 378.2307; found 378.2296.

7ab: Yield: 63.5 mg, 87%. Yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.16 (s, 3 H, COCCH_3CH$_3$), 1.17 (s, 3 H, COCCH$_3$CH_3), 1.59–1.68 (m, 4 H, NHCHCNCH_2CH_2), 1.94 (s, 3 H, Ph_2CCH_3), 1.98 (br. s, 1 H, N*H*), 3.27 (br. s, 1 H, NHC*H*CN), 3.64 (s, 3 H, COOCH_3), 7.21–7.37 (m, 10 H, Ar*H*) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 24.9, 25.2, 27.7, 31.2, 35.9, 41.8, 44.8, 51.8, 63.1, 121.7, 126.4, 126.8, 127.1, 127.3, 128.2, 128.3, 145.7, 147.6, 177.6 ppm. IR (neat): $\tilde{\nu}$ = 3546, 3338, 3020, 2979, 2230, 1724, 1642, 1447, 1216, 1144, 757, 703 cm^{-1}. HRMS (EI): calcd. for $C_{23}H_{28}N_2O_2$ [M]$^+$ 364.2151; found 364.2146.

7ae: Yield: 70.5 mg, 87%. Yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.16–1.37 [m, 6 H, COC(CH_2)$_5$], 1.54–1.64 [m, 8 H, COC(CH_2)$_5$ and NHCHCNCH_2CH_2], 1.94 (s, 3 H, Ph_2CCH_3), 2.02–2.04 (m,

1 H, NH), 3.23 (br. s, 1 H, NHCHCN), 3.66 (s, 3 H, $COOCH_3$), 7.21–7.36 (m, 10 H, ArH) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 23.0, 23.0, 25.7, 27.7, 30.4, 33.8, 34.0, 44.8, 46.5, 51.6, 63.1, 121.8, 126.4, 126.9, 127.1, 127.3, 128.2, 128.3, 145.7, 147.6, 176.6 ppm. IR (neat): $\tilde{\nu}$ = 3332, 3085, 3059, 3022, 2936, 2857, 2229, 1725, 1599, 1449, 1210, 1135, 758, 702 cm^{-1}. HRMS (EI): calcd. for $C_{26}H_{32}N_2O_2$ $[M]^+$ 404.2464; found 404.2445.

7ag: Yield: 44.5 mg, 56%. Yellow oil. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.45 (s, 9 H, $SCCH_3CH_3CH_3$), 1.70–1.80 (m, 4 H, $NHCHCNCH_2CH_2$), 1.96 (s including a br. s, 4 H, Ph_2CCH_3 and NH), 2.40 (dt, J = 2.4, 7.0 Hz, 2 H, $COCH_2$), 3.28–3.31 (m, 1 H, NHCHCN), 7.21–7.38 (m, 10 H, ArH) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 21.4, 27.7, 29.8, 34.6, 43.3, 44.1, 48.1, 63.1, 121.8, 126.4, 126.9, 127.2, 127.3, 128.2, 128.4, 145.6, 147.6, 199.4 ppm. IR (neat): $\tilde{\nu}$ = 3332, 3059, 3024, 2962, 2925, 2228, 1681, 1600, 1449, 759, 702 cm^{-1}. HRMS (EI): calcd. for $C_{24}H_{30}N_2OS$ $[M]^+$ 394.2079; found 394.2072.

General Procedure for the Transformation into Amino Nitriles for the Deprotection of the 1,4- and 1,2-Double Nucleophilic Adducts (Table 7, Entry 1; product 8a): Under argon, a suspension of *N*-allylideneamine **1b** (47.1 mg, 0.20 mmol) in CH_2Cl_2 (1.0 mL) was stirred at room temperature for 10 min. Dried silica gel (500 mg) and CH_2Cl_2 (0.30 mL) were added to the reaction mixture, which was cooled to –78 °C. A solution of (1-ethoxy-2-methylprop-1-enyloxy)trimethylsilane (56.5 mg, 0.30 mmol) in CH_2Cl_2 (0.90 mL) was added to the mixture. After stirring for 10 min, a solution of trimethylsilyl cyanide (23.8 mg, 0.24 mmol) in CH_2Cl_2 (0.80 mL) was added to the resulting mixture. The mixture was gradually warmed to room temperature over 17 h. The reaction mixture was then cooled to 0 °C, distilled TFA (1.0 mL) was added, and the mixture stirred for 15 min. A 10% aqueous Na_2CO_3 solution (10 mL) was added to quench the reaction. The mixture was filtered with suction through a Celite pad and washed with ethyl acetate and the mixture was extracted with ethyl acetate (3 × 5.0 mL). The combined extracts were dried with Na_2SO_4 and concentrated in vacuo to give the crude product, which was purified by column chromatography on silica gel (*n*-hexane/ethyl acetate, 1:1) to give title compound **8a** (31.0 mg, 78%). Colorless oil. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.20 (s, 6 H, $COCCH_3CH_3$), 1.26 (t, J = 7.0 Hz, 3 H, $COOCH_2CH_3$), 1.65 (br. s, 2 H, NH_2), 1.67–1.75 (m, 4 H, $NH_2CHCNCH_2CH_2$), 3.64–3.67 (m, 1 H, NH_2CHCN), 4.13 (q, J = 7.0 Hz, 2 H, $COOCH_2CH_3$) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 14.2, 25.0, 25.2, 31.0, 36.0, 41.7, 43.6, 60.5, 121.8, 177.1 ppm. IR (neat): $\tilde{\nu}$ = 3592, 3384, 3319, 2978, 2936, 2873, 2228, 1722, 1608, 1475, 1454, 1181, 1152, 1027, 863 cm^{-1}. HRMS (EI): calcd. for $C_{10}H_{18}N_2O_2$ $[M]^+$ 198.1368; found 198.1366.

8b: Yield: 24.7 mg, 67%. Colorless oil. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.21 (s, 6 H, $COCCH_3CH_3$), 1.66–1.76, (m, 4 H, NH_2 and $NH_2CHCNCH_2CH_2$), 3.64–3.66 (m, 1 H, NH_2CHCN), 3.68 (s, 3 H, $COOCH_3$) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 25.0, 25.2, 31.1, 36.1, 41.8, 43.6, 51.9, 121.8, 177.7 ppm. IR (neat): $\tilde{\nu}$ = 3630, 3379, 3314, 2954, 2932, 2875, 2227, 1725, 1623, 1475, 1454, 1196, 1147, 1034, 864 cm^{-1}. HRMS (EI): calcd. for $C_9H_{16}N_2O_2$ $[M]^+$ 184.1212; found 184.1207.

8c: Yield: 20.3 mg, 47%. Colorless oil. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.95 (t, J = 7.6 Hz, 3 H, $COOCH_2CH_2CH_3$), 1.21 (s, 6 H, $COCCH_3CH_3$), 1.62–1.72 (m, 8 H, $NH_2CHCNCH_2CH_2$, $COOCH_2CH_2CH_3$, and NH_2), 3.64–3.66 (m, 1 H, NH_2CHCN), 4.04 (t, J = 6.7 Hz, 2 H, $COOCH_2CH_2CH_3$) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 10.4, 21.9, 25.0, 25.2, 31.1, 36.0, 41.8, 43.6, 66.2, 121.8, 177.2 ppm. IR (neat): $\tilde{\nu}$ = 3680, 3390, 3328, 3021, 2972, 2936, 2879, 2231, 1718, 1473, 1393, 1216, 1181, 760 cm^{-1}. HRMS (EI): calcd. for $C_{11}H_{20}N_2O_2$ $[M]^+$ 212.1525; found 212.1524.

8d: Yield: 11.5 mg, 27%. Colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.16 (s, 6 H, $COCCH_3CH_3$), 1.21 (d, J = 6.4 Hz, 6 H, $COOCHCH_3CH_3$), 1.62 (br. s, 2 H, NH_2), 1.66–1.71 (m, 4 H, $NH_2CHCNCH_2CH_2$), 3.60–3.66 (m, 1 H, NH_2CHCN), 4.97 (sept, J = 6.4 Hz, 1 H, $COOCHCH_3CH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.8, 25.1, 25.3, 31.2, 36.0, 41.7, 43.8, 67.8, 122.0, 176.7 ppm. IR (neat): $\tilde{\nu}$ = 3585, 3382, 3314, 2979, 2936, 2874, 2229, 1718, 1614, 1473, 1375, 1183, 1108 931, 885 cm^{-1}. HRMS (EI): calcd. for $C_{11}H_{20}N_2O_2$ $[M]^+$ 212.1525; found 212.1529.

8e: Yield: 34.4 mg, 76%. Colorless oil. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.21–1.39 [m, 4 H, $COC(CH_2)_5$], 1.55–1.71 [m, 10 H, $COC(CH_2)_5$ and $NH_2CHCNCH_2CH_2$], 2.07 (d, J = 11.3 Hz, 2 H, NH_2), 3.60–3.63 (m, 1 H, NH_2CHCN), 3.70 (s, 3 H, $COOCH_3$) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 23.0, 23.0, 25.7, 30.2, 33.8, 34.0, 35.6, 43.6, 46.4, 51.6, 121.8, 176.6 ppm. IR (neat): $\tilde{\nu}$ = 3288, 3207, 3020, 2938, 2862, 2240, 1721, 1658, 1452, 1209, 756 cm^{-1}. HRMS (EI): calcd. for $C_{12}H_{20}N_2O_2$ $[M]^+$ 224.1525; found 224.1530.

8f: Yield: 20.7 mg, 40%. Colorless oil. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.24 [t, J = 7.0 Hz, 3 H, $COC(CH_2CH_3)_2$], 1.24 [t, J = 7.0 Hz, 3 H, $COC(CH_2CH_3)_2$], 1.33 (t, J = 7.0 Hz, 3 H, $COOCH_2CH_3$), 1.62 (br. s, 2 H, NH_2), 1.69–1.74 (m, 2 H, $NH_2CHCNCH_2CH_2$), 2.04–2.14 (m, 2 H, $NH_2CHCNCH_2CH_2$), 3.45–3.52 [m, 2 H, $COC(CH_2CH_3)_2$], 3.53–3.60 [m, 2 H, $COC(CH_2CH_3)_2$], 3.72 (t, J = 7.3 Hz, 1 H, NH_2CHCN), 4.27 (q, J = 7.0 Hz, 2 H, $COOCH_2CH_3$) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 14.2, 15.1, 29.6, 30.4, 43.0, 57.9, 58.0, 61.6, 101.2, 121.7, 168.9 ppm. IR (neat): $\tilde{\nu}$ = 3676, 3389, 3321, 3018, 2981, 2936, 2898, 2231, 1744, 1618, 1449, 1392, 1216, 1170, 757 cm^{-1}. HRMS (EI): calcd. for $C_{12}H_{22}N_2O_4$ $[M]^+$ 258.1580; found 258.1572.

General Procedure for the 1,4- and 1,2-Double Nucleophilic Addition Reactions of Ketene Silyl (Thio)Acetals and Trimethylsilyl Cyanide (Table 8, Entry 1; conditions A): Under argon, a suspension of *N*-allylideneamine **1c** (59.5 mg, 0.20 mmol) in CH_2Cl_2 (1.0 mL) was stirred at room temperature for 10 min. Dried silica gel (500 mg) and CH_2Cl_2 (0.30 mL) were added and the reaction mixture was cooled to –78 °C. A solution of (1-ethoxy-2-methylprop-1-enyloxy) trimethylsilane (56.5 mg, 0.30 mmol) in CH_2Cl_2 (0.90 mL) was added to the mixture. After stirring for 10 min, a solution of trimethylsilyl cyanide (23.8 mg, 0.24 mmol) in CH_2Cl_2 (0.80 mL) was added to the resulting mixture, which was gradually warmed to room temperature over 17 h. Saturated aqueous $NaHCO_3$ (5.0 mL) was added to quench the reaction and the mixture was filtered with suction through a Celite pad and washed with ethyl acetate. The mixture was extracted with ethyl acetate (3 × 5.0 mL) and the combined extracts were dried with Na_2SO_4 and concentrated in vacuo to give the crude product. Purification on buffered silica gel TLC (*n*-hexane/ethyl acetate, 4:1) gave title compound **7ba** (70.8 mg, 80%). Yellow oil. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.11 (s, 3 H, $COCCH_3CH_3$), 1.14 (s, 3 H, $COCCH_3CH_3$), 1.24 (t, J = 7.0 Hz, 3 H, $COOCH_2CH_3$), 1.45–1.62 (m, 3 H, $NHCHCNCH_2CH_2$), 1.69–1.75 (m, 1 H, $NHCHCNCH_2CH_2$), 2.12 (d, J = 9.8 Hz, 1 H, NH), 3.36–3.41 (m, 1 H, NHCHCN), 4.11 (q, J = 7.0 Hz, 2 H, $COOCH_2CH_3$), 7.21–7.24 (m, 3 H, ArH), 7.29–7.32 (m, 6 H, ArH), 7.50–7.51 (m, 6 H, ArH) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 14.2, 25.0, 25.0, 31.1, 35.8, 41.6, 46.0, 60.5, 71.5, 120.1, 127.0, 128.3, 128.4, 144.9, 177.1 ppm. IR (neat): $\tilde{\nu}$ = 3535, 3328, 3084, 3059, 3020, 2977, 2933, 2871, 2232, 1723, 1597, 1489, 1474, 1450,

1390, 1183, 1140, 1029, 752, 708 cm^{-1}. HRMS (EI): calcd. for $C_{29}H_{32}N_2O_2$ [M]$^+$ 440.2464; found 440.2448.

7bb: Yield: 55.3 mg, 64%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.12 (s, 3 H, COCCH_3CH$_3$), 1.15 (s, 3 H, COCCH$_3$CH_3), 1.43–1.61 (m, 3 H, NHCHCNCH_2CH_2), 1.68–1.75 (m, 1 H, NHCHCNCH_2CH$_2$), 2.12 (d, J = 9.2 Hz, 1 H, NH), 3.36–3.39 (m, 1 H, NHCHCN), 3.66 (s, 3 H, COOCH_3), 7.22–7.26 (m, 3 H, ArH), 7.28–7.33 (m, 6 H, ArH), 7.50–7.54 (m, 6 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.1, 25.2, 31.2, 36.0, 41.9, 46.2, 52.0, 71.6, 120.3, 127.2, 128.4, 128.5, 145.0, 177.7 ppm. IR (neat): $\tilde{\nu}$ = 3327, 3085, 3058, 3020, 2974, 2950, 2870, 2235, 1728, 1596, 1489, 1448, 1390, 1199, 1138, 1032, 753, 708 cm^{-1}. HRMS (EI): calcd. for $C_{28}H_{30}N_2O_2$ [M]$^+$ 426.2307; found 426.2290.

7bc: Yield: 53.1 mg, 58%. Yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.94 (t, J = 7.3 Hz, 3 H, COOCH$_2$CH$_2$CH_3), 1.12 (s, 3 H, COCCH_3CH$_3$), 1.15 (s, 3 H, COCCH$_3$CH_3), 1.46–1.53 (m, 2 H, NHCHCNCH$_2$CH_2), 1.55–1.61 (m, 1 H, NHCHCNCH_2CH$_2$), 1.62–1.68 (m, 2 H, COOCH$_2$CH_2CH$_3$), 1.70–1.76 (m, 1 H, NHCHCNCH_2CH$_2$), 2.11 (d, J = 10.1 Hz, 1 H, NH), 3.36–3.41 (m, 1 H, NHCHCN), 4.02 (t, J = 6.7 Hz, 2 H, COOCH_2CH$_2$CH$_3$), 7.21–7.27 (m, 3 H, ArH), 7.29–7.36 (m, 6 H, ArH), 7.46–7.55 (m, 6 H, ArH) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 10.4, 22.0, 25.0, 25.1, 31.1, 35.9, 41.8, 46.0, 66.1, 71.4, 120.1, 127.0, 128.3, 128.4, 144.9, 177.1 ppm. IR (neat): $\tilde{\nu}$ = 3327, 3059, 3020, 2970, 2933, 2877, 2232, 1724, 1597, 1490, 1452, 1391, 1183, 1139, 1034, 753, 708 cm^{-1}. HRMS (EI): calcd. for $C_{30}H_{34}N_2O_2$ [M]$^+$ 454.2620; found 454.2611.

7bd: Yield: 62.6 mg, 68%. Yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.10 (s, 3 H, COCCH_3CH$_3$), 1.13 (s, 3 H, COCCH$_3$CH_3), 1.22 (d, J = 6.1 Hz, 3 H, COOCHCH_3CH$_3$), 1.23 (d, J = 6.1 Hz, 3 H, COOCHCH$_3$CH_3), 1.49–1.64 (m, 3 H, NHCHCNCH_2CH_2), 1.70–1.75 (m, 1 H, NHCHCNCH_2CH$_2$), 2.12 (d, J = 10.1 Hz, 1 H, NH), 3.37–3.41 (m, 1 H, NHCHCN), 4.98 (sept, J = 6.1 Hz, 1 H, COOCHCH$_3$CH$_3$), 7.22–7.25 (m, 3 H, ArH), 7.29–7.32 (m, 6 H, ArH), 7.50–7.51 (m, 6 H, ArH) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 21.7, 25.0, 25.0, 31.2, 35.8, 41.6, 46.0, 67.6, 71.4, 120.0, 127.0, 128.3, 128.4, 144.9, 176.6 ppm. IR (neat): $\tilde{\nu}$ = 3326, 3059, 3020, 2979, 2933, 2872, 2234, 1717, 1596, 1489, 1450, 1372, 1184, 930, 755, 708 cm^{-1}. HRMS (EI): calcd. for $C_{30}H_{34}N_2O_2$ [M]$^+$ 454.2620; found 454.2623.

7be: Yield: 27.6 mg, 59%. Yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.11–1.36 [m, 6 H, COC(CH_2)$_5$], 1.39–1.48 [m, 2 H, COC-(CH_2)$_5$], 1.50–1.56 (m, 3 H, NHCHCNCH_2CH_2), 1.64–1.70 (m, 1 H, NHCHCNCH_2CH$_2$), 1.95–2.03 [m, 2 H, COC(CH_2)$_5$], 2.08 (d, J = 9.8 Hz, 1 H, NH), 3.32–3.37 (m, 1 H, NHCHCN), 3.67 (s, 3 H, COOCH_3), 7.22–7.25 (m, 3 H, ArH), 7.29–7.31 (m, 6 H, ArH), 7.48–7.50 (m, 6 H, ArH) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 23.0, 25.7, 30.4, 33.9, 33.9, 46.1, 46.5, 51.6, 71.5, 120.2, 127.1, 128.3, 128.4, 144.9, 176.5 ppm. IR (neat): $\tilde{\nu}$ = 3329, 3059, 3020, 2936, 2857, 2232, 1724, 1597, 1490, 1452, 1208, 755, 708 cm^{-1}. HRMS (EI): calcd. for $C_{31}H_{34}N_2O_2$ [M]$^+$ 466.2620; found 466.2627.

7bf: Yield: 51.8 mg, 51%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.19 [t, J = 7.3 Hz, 3 H, COC(OCH$_2$CH_3)$_2$], 1.22 [t, J = 7.3 Hz, 3 H, COC(OCH$_2$CH_3)$_2$], 1.32 (t, J = 7.3 Hz, 3 H, COOCH$_2$CH_3), 1.60–1.72 (m, 2 H, NHCHCNCH$_2$CH_2), 1.90–1.98 (m, 1 H, NHCHCNCH_2CH$_2$), 2.08–2.15 (m, 2 H, NHCHCNCH_2CH$_2$ and NH), 3.45 [q, J = 7.3 Hz, 2 H, COC(OCH_2CH$_3$)$_2$], 3.47 [q, J = 7.3 Hz, 2 H, COC(OCH_2CH$_3$)$_2$], 3.52–3.59 (m, 1 H, NHCHCN), 4.27 (q, J = 7.3 Hz, 2 H, COOCH_2CH$_3$), 7.21–7.27 (m, 3 H, ArH), 7.28–7.32 (m, 6 H, ArH), 7.47–7.49 (m, 6 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.4, 15.2, 29.9, 30.4, 45.5, 58.0, 61.7, 71.5, 101.3, 119.9, 127.2, 127.3, 128.0, 128.4, 128.5, 144.9, 168.9 ppm. IR (neat): $\tilde{\nu}$ = 3330, 3059, 3016, 2979, 2932, 2231, 1745, 1597, 1490, 1449, 1370, 1185, 1120, 753, 707 cm^{-1}. HRMS (EI): calcd. for $C_{31}H_{36}N_2O_4$ [M]$^+$ 500.2675; found 500.2652.

7bg: Yield: 20.1 mg, 22%. Yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.46 (s, 9 H, COSCCH_3CH_3CH_3), 1.58–1.64 (m, 1 H, NHCHCNCH_2CH$_2$), 1.65–1.75 (m, 2 H, NHCHCNCH$_2$CH_2), 1.82–1.90 (m, 1 H, NHCHCNCH_2CH$_2$), 2.13 (d, J = 10.1 Hz, 1 H, NH), 2.36–2.46 (m, 2 H, COCH_2), 3.38–3.43 (m, 1 H, NHCHCN), 7.12–7.27 (m, 3 H, ArH), 7.29–7.33 (m, 6 H, ArH), 7.50–7.55 (m, 6 H, ArH) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 21.3, 29.8, 34.7, 43.5, 45.5, 48.1, 71.4, 120.0, 127.1, 127.7, 127.9, 128.3, 128.4, 144.9, 199.3 ppm. IR (neat): $\tilde{\nu}$ = 3685, 3619, 3020, 2974, 2927, 2232, 1710, 1676, 1599, 1448, 1422, 1365, 1216, 929, 770, 669, 626 cm^{-1}. HRMS (EI): calcd. for $C_{29}H_{32}N_2OS$ [M]$^+$ 456.2235; found 456.2242.

7bh: Yield: 55.7 mg, 59%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.08 (s, 3 H, COCCH_3CH$_3$), 1.11 (s, 3 H, COCCH$_3$CH_3), 1.45 (s, 9 H, COOCCH_3CH_3CH_3), 1.47–1.74 (m, 4 H, NHCHCNCH_2CH_2), 2.13 (d, J = 10.1 Hz, 1 H, NH), 3.37–3.42 (m, 1 H, NHCHCN), 7.22–7.25 (m, 3 H, ArH), 7.28–7.33 (m, 6 H, ArH), 7.50–7.52 (m, 6 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.2, 28.1, 31.4, 36.1, 42.3, 46.1, 71.6, 80.3, 120.2, 127.2, 128.0, 128.4, 128.5, 145.0, 176.5 ppm. IR (neat): $\tilde{\nu}$ = 3326, 3060, 3018, 2976, 2931, 2871, 2232, 1718, 1597, 1489, 1452, 1391, 1368, 1214, 1140, 755, 708 cm^{-1}. HRMS (EI): calcd. for $C_{31}H_{36}N_2O_2$ [M]$^+$ 468.2777; found 468.2763.

7bi: Yield: 22.8 mg, 24%. Yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$, *dr* = 53:47 mixture): δ = 1.25–1.30 (m, 3 H, COOCH$_2$CH_3), 1.37 (s, 1.59 H, COCCH_3), 1.38 (s, 1.41 H, COCCH_3), 1.60–1.63 (m, 1.06 H, NHCHCNCH_2CH$_2$), 1.71–1.77 (m, 2 H, NHCHCNCH$_2$-CH_2), 1.86–1.95 (m, 0.94 H, NHCHCNCH_2CH$_2$), 2.04 (s, 1.59 H, COCSCH_3), 2.07 (s, 1.41 H, COCSCH_3), 2.13–2.17 (m, 1 H, NH), 3.44 (br. s, 1 H, NHCHCN), 4.11–4.21 (m, 2 H, COOCH_2CH$_3$), 7.23–7.30 (m, 3 H, ArH), 7.32–7.33 (m, 6 H, ArH), 7.50–7.52 (m, 6 H, ArH) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 12.4, 12.5, 14.2, 21.1, 21.7, 30.9, 31.0, 32.3, 32.3, 45.8, 45.9, 49.5, 49.5, 60.4, 61.3, 61.4, 71.5, 71.6, 120.0, 120.0, 127.1, 128.4, 128.4, 144.8, 172.7, 172.7 ppm. IR (neat): $\tilde{\nu}$ = 3326, 3084, 3059, 2980, 2929, 2249, 1716, 1598, 1490, 1447, 1244, 733, 708 cm^{-1}. HRMS (EI): calcd. for $C_{29}H_{32}N_2O_2S$ [M]$^+$ 472.2185; found 472.2181.

General Procedure for the Transformation Into Amino Nitriles for Deprotection of the 1,4- and 1,2-Double Nucleophilic Adducts (Table 8, Entry 8; product 8h): The 1,4- and 1,2-double nucleophilic addition reaction was performed according to the procedure described above under Conditions A. After 17 h the reaction mixture was cooled to 0 °C, distilled TFA (1.0 mL) was added, and the mixture was stirred for 15 min. A 10% aqueous Na_2CO_3 (10 mL) solution was added to quench the reaction and the mixture was filtered with suction through a Celite pad and washed with ethyl acetate. The mixture was extracted with ethyl acetate (3 × 5.0 mL) and the combined extracts were dried with Na_2SO_4 and concentrated in vacuo to give the crude product, which was purified by column chromatography on silica gel (*n*-hexane/ethyl acetate, 1:1) to give title compound **8h** (28.0 mg, 61%). Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.15 (s, 6 H, COCCH_3CH_3), 1.44 (s, 9 H, COOCCH_3CH_3CH_3), 1.60 (br. s, 1 H, NH$_2$CHCNCH$_2$CH_2), 1.68–1.70 (m, 3 H, NHCHCNCH_2CH_2), 3.63–3.66 (m, 1 H, NH$_2$CHCN) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.2, 25.3, 28.1, 31.3, 36.1, 42.3, 43.8, 80.4, 122.0, 176.5 ppm. IR (neat): $\tilde{\nu}$ = 3385, 3314, 2977, 2933, 2872, 2230, 1717, 1611, 1456, 1392, 1370, 1148, 756 cm^{-1}. HRMS (EI): calcd. for $C_{12}H_{22}N_2O_2$ [M]$^+$ 226.1681; found 226.1682.

General Procedure for the 1,4- and 1,2-Double Nucleophilic Addition Reactions of Ketene Silyl Thioacetals and Trimethylsilyl Cyanide (Table 9, Entry 1; Conditions B): Under argon, a suspension of *N*-allylideneamine **1c** (59.5 mg, 0.20 mmol) in CH_2Cl_2 (1.0 mL) was stirred at room temperature for 10 min. Dried silica gel (500 mg) and CH_2Cl_2 (0.30 mL) were added and the reaction mixture was cooled to –78 °C. A solution of (*Z*)-[1-(cyclohexylthio)prop-1-enyloxy]trimethylsilane (*Z*/*E* = 92:8, 73.3 mg, 0.30 mmol) in CH_2Cl_2 (0.90 mL) was added to the mixture. After stirring for 10 min, a solution of trimethylsilyl cyanide (23.8 mg, 0.24 mmol) in CH_2Cl_2 (0.80 mL) was added and the mixture was gradually warmed to room temperature over 17 h. Saturated aqueous $NaHCO_3$ (5.0 mL) was added to quench the reaction and the mixture was filtered with suction through a Celite pad and washed with ethyl acetate. The mixture was extracted with ethyl acetate (3 × 5.0 mL) and the combined extracts were dried with Na_2SO_4 and concentrated in vacuo to give the crude product. Purification on buffered silica gel TLC (toluene/ethyl acetate, 20:1) gave title compound **9a** (74.5 mg, 75%, *dr* = 50:50, as determined by ^{1}H NMR analysis). Clear oil. ^{1}H NMR (400 MHz, $CDCl_3$, *dr* = 50:50 mixture): δ = 1.14 (d, *J* = 6.4 Hz, 1.5 H, COCHC*H*$_3$), 1.15 (d, *J* = 6.4 Hz, 1.5 H, COCHC*H*$_3$), 1.23–1.37 (m, 1 H, NHCHCNCH$_2$C*H*$_2$), 1.43–1.54 [m, 4.5 H, COSCH(C*H*$_2$)$_5$], 1.56–1.74 [m, 6 H, NHCHCNCH$_2$C*H*$_2$ and COSCH(C*H*$_2$)$_5$], 1.93–1.94 [m, 2.5 H, NHCHCNC*H*$_2$CH$_2$ and COSCH(C*H*$_2$)$_5$], 2.14 (d, *J* = 10.1 Hz, 1 H, NHC*H*CN), 2.54 (tq, *J* = 6.4, 6.8 Hz, 1 H, COC*H*CH$_3$), 3.37–3.53 [m, 2 H, NHC*H*CN and COSC*H*(CH$_2$)$_5$], 7.23–7.26 (m, 3 H, Ar*H*), 7.30–7.34 (m, 6 H, Ar*H*), 7.51–7.53 (m, 6 H, Ar*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.8, 18.0, 25.7, 26.1, 29.7, 29.8, 30.0, 33.1, 33.2, 42.4, 45.7, 45.9, 48.0, 48.1, 71.5, 120.0, 120.2, 127.2, 128.4, 128.6, 145.0, 202.8 ppm. IR (neat): $\tilde{\nu}$ = 3678, 3345, 3060, 3019, 2934, 2856, 2231, 1710, 1677, 1597, 1449, 1216, 760, 708 cm^{-1}. HRMS (EI): calcd. for $C_{32}H_{36}N_2OS$ [M]$^+$ 496.2548; found 496.2540.

9b: Yield: 61.1 mg, 69%. Clear oil. ^{1}H NMR (400 MHz, $CDCl_3$, *dr* = 71:29 mixture): δ = 1.14 (d, *J* = 6.9 Hz, 0.87 H, COCHC*H*$_3$), 1.15 (d, *J* = 6.9 Hz, 2.13 H, COCHC*H*$_3$), 1.25 (t, *J* = 7.3 Hz, 0.87 H, COSCH$_2$C*H*$_3$), 1.26 (t, *J* = 7.3 Hz, 2.13 H, COSCH$_2$C*H*$_3$), 1.44–1.80 (m, 3.71 H, NHCHCNC*H*$_2$C*H*$_2$), 1.88–1.93 (m, 0.29 H, NHCHCNC*H*$_2$CH$_2$), 2.11 (d, *J* = 9.6 Hz, 1 H, N*H*), 2.55 (tq, *J* = 6.9, 6.9 Hz, 1 H, COC*H*CH$_3$), 2.81–2.94 (m, 2 H, COSC*H*$_2$CH$_3$), 3.39–3.45 (m, 1 H, NHC*H*CN), 7.18–7.27 (m, 3 H, Ar*H*), 7.29–7.36 (m, 6 H, Ar*H*), 7.49–7.51 (m, 6 H, Ar*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.9, 17.7, 18.0, 23.3, 29.6, 29.8, 33.0, 33.2, 45.8, 45.9, 47.9, 48.0, 71.6, 120.0, 120.2, 126.5, 127.2, 128.0, 128.2, 128.4, 128.6, 128.7, 145.0, 203.0 ppm. IR (neat): $\tilde{\nu}$ = 3682, 3617, 3345, 3019, 2975, 2933, 2874, 2232, 1679, 1598, 1452, 1216, 767, 669 cm^{-1}. HRMS (EI): calcd. for $C_{28}H_{30}N_2OS$ [M]$^+$ 442.2079; found 442.2061.

9c: Yield: 61.2 mg, 65%. Clear oil. ^{1}H NMR (400 MHz, $CDCl_3$, *dr* = 55:45 mixture): δ = 1.11 (t, *J* = 6.4 Hz, 3 H, COCHC*H*$_3$), 1.47 (s, 4.05 H, COSCC*H*$_3$C*H*$_3$C*H*$_3$), 1.48 (s, 4.95 H, COSCC*H*$_3$C*H*$_3$C*H*$_3$), 1.56–1.74 (m, 3.55 H, NHCHCNC*H*$_2$C*H*$_2$), 1.86–1.99 (m, 0.45 H, NHCHCNC*H*$_2$CH$_2$), 2.12 (d, *J* = 10.3 Hz, 0.45 H, N*H*), 2.13 (d, *J* = 10.3 Hz, 0.55 H, N*H*), 2.43–2.49 (m, 1 H, COC*H*CH$_3$), 3.35–3.48 (m, 1 H, NHC*H*CN), 7.19–7.27 (m, 3 H, Ar*H*), 7.29–7.33 (m, 6 H, Ar*H*), 7.49–7.51 (m, 6 H, Ar*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.6, 17.8, 29.5, 29.7, 29.8, 29.8, 32.9, 33.1, 45.6, 45.7, 47.9, 48.2, 71.4, 119.9, 120.0, 127.1, 128.1, 128.3, 128.4, 144.9, 203.7 ppm. IR (neat): $\tilde{\nu}$ = 3682, 3618, 3346, 3019, 2968, 2929, 2869, 2232, 1674, 1453, 1367, 1216, 961, 771, 669, 621 cm^{-1}. HRMS (EI): calcd. for $C_{30}H_{34}N_2OS$ [M]$^+$ 470.2392; found 470.2382.

9d: Yield: 62.1 mg, 68%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$, *dr* = 58:42 mixture): δ = 1.13 (d, *J* = 6.9 Hz, 1.26 H, COCHC*H*$_3$), 1.15 (d, *J* = 6.9 Hz, 1.74 H, COCHC*H*$_3$), 1.30–1.33 (m, 6 H, COSCHC*H*$_3$C*H*$_3$), 1.44–1.84 (m, 3.55 H, NHCHCNC*H*$_2$C*H*$_2$), 1.88–1.97 (m, 0.45 H, NHCHCNC*H*$_2$C*H*$_2$), 2.14 (d, *J* = 10.1 Hz, 1 H, N*H*), 2.53 (tq, *J* = 6.9, 6.9 Hz, 1 H, COC*H*CH$_3$), 3.40–3.46 (m, 1 H, NHC*H*CN), 3.58–3.70 (m, 1 H, COSC*H*CH$_3$CH$_3$), 7.22–7.26 (m, 3 H, Ar*H*), 7.29–7.34 (m, 6 H, Ar*H*), 7.50–7.52 (m, 6 H, Ar*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.7, 18.0, 23.1, 23.1, 29.6, 29.8, 33.0, 33.2, 34.6, 34.6, 45.7, 45.9, 48.0, 48.0, 71.5, 71.6, 120.0, 120.2, 127.1, 127.2, 128.4, 128.4, 128.6, 145.0, 145.0, 203.1 ppm. IR (neat): $\tilde{\nu}$ = 3678, 3343, 3060, 3020, 2971, 2931, 2869, 2232, 1677, 1597, 1490, 1451, 1372, 1216, 752, 709, 669 cm^{-1}. HRMS (EI): calcd. for $C_{29}H_{32}N_2OS$ [M]$^+$ 456.2235; found 456.2234.

9e: Yield: 54.0 mg, 55%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$, *dr* = 55:45 mixture): δ = 1.24 (d, *J* = 6.9 Hz, 1.35 H, COCHC*H*$_3$), 1.26 (d, *J* = 6.9 Hz, 1.65 H, COCHC*H*$_3$), 1.54–1.85 (m, 3.55 H, NHCHCNC*H*$_2$C*H*$_2$), 1.95–2.06 (m, 0.45 H, NHCHCNC*H*$_2$C*H*$_2$), 2.16 (d, *J* = 9.6 Hz, 1 H, N*H*), 2.72 (tq, *J* = 6.7, 6.9 Hz, 1 H, COC*H*CH$_3$), 3.38–3.50 (m, 1 H, NHC*H*CN), 7.19–7.58 (m, 20 H, Ar*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.7, 18.0, 29.6, 29.8, 33.0, 33.2, 45.8, 45.9, 47.8, 47.8, 71.6, 71.6, 120.0, 120.2, 127.2, 127.6, 128.0, 128.5, 128.6, 129.3, 129.5, 134.6, 145.0, 145.0, 200.7 ppm. IR (neat): $\tilde{\nu}$ = 3682, 3620, 3345, 3062, 3019, 2976, 2934, 2231, 1706, 1597, 1491, 1449, 1216, 749, 709, 621 cm^{-1}. HRMS (EI): calcd. for $C_{32}H_{30}N_2OS$ [M]$^+$ 490.2079; found 490.2100.

9f: Yield: 41.5 mg, 45%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$, *dr* = 51:49 mixture): δ = 0.98 (t, *J* = 7.3 Hz, 1.47 H, COSCH$_2$CH$_2$C*H*$_3$), 0.98 (t, *J* = 7.3 Hz, 1.53 H, COSCH$_2$CH$_2$C*H*$_3$), 1.14 (d, *J* = 6.9 Hz, 1.47 H, COCHC*H*$_3$), 1.15 (d, *J* = 6.9 Hz, 1.53 H, COCHC*H*$_3$), 1.45–1.84 (m, 5.49 H, NHCHCNC*H*$_2$C*H*$_2$ and COSCH$_2$C*H*$_2$CH$_3$), 1.88–1.97 (m, 0.51 H, NHCHCNC*H*$_2$C*H*$_2$ and COSCH$_2$C*H*$_2$CH$_3$), 2.11 (d, *J* = 10.1 Hz, 0.49 H, N*H*), 2.11 (d, *J* = 10.1 Hz, 0.51 H, N*H*), 2.57 (tq, *J* = 6.9, 6.9 Hz, 1 H, COC*H*CH$_3$), 2.80–2.92 (m, 2 H, COSC*H*$_2$CH$_2$CH$_3$), 3.35–3.45 (m, 1 H, NHC*H*CN), 7.18–7.33 (m, 9 H, Ar*H*), 7.49–7.51 (m, 6 H, Ar*H*) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 13.3, 17.6, 17.9, 22.9, 29.5, 29.6, 30.5, 32.9, 33.0, 45.6, 45.7, 47.9, 47.9, 71.4, 71.4, 119.9, 120.0, 127.0, 127.0, 127.9, 128.3, 128.4, 144.8, 202.9 ppm. IR (neat): $\tilde{\nu}$ = 3683, 3618, 3346, 3019, 2972, 2933, 2875, 2233, 1679, 1598, 1521, 1452, 1217, 770, 670 cm^{-1}. HRMS (EI): calcd. for $C_{29}H_{32}N_2OS$ [M]$^+$ 456.2235; found 456.2234.

9g: Yield: 35.8 mg, 39%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.15 (s, 3 H, COC*H*$_3$CH$_3$), 1.19 (s, 3 H, COCH$_3$C*H*$_3$), 1.25 (t, *J* = 7.3 Hz, 3 H, COSCH$_2$C*H*$_3$), 1.46–1.63 (m, 3 H, NHCHCNC*H*$_2$C*H*$_2$), 1.73–1.81 (m, 1 H, NHCHCNC*H*$_2$CH$_2$), 2.12 (d, *J* = 10.1 Hz, 1 H, N*H*), 2.86 (q, *J* = 7.3 Hz, 2 H, COSC*H*$_2$CH$_3$), 3.36–3.41 (m, 1 H, NHC*H*CN), 7.22–7.33 (m, 9 H, Ar*H*), 7.50–7.54 (m, 6 H, Ar*H*) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 14.7, 23.0, 25.2, 25.3, 30.8, 36.4, 46.0, 49.0, 71.5, 120.0, 127.0, 127.9, 128.3, 128.4, 144.9, 205.7 ppm. IR (neat): $\tilde{\nu}$ = 3683, 3618, 3346, 3019, 2974, 2933, 2234, 1669, 1599, 1521, 1424, 1218, 771, 670 cm^{-1}. HRMS (EI): calcd. for $C_{29}H_{32}N_2OS$ [M]$^+$ 456.2235; found 456.2234.

General Procedure for the Transformation Into Valerolactams for the Deprotection of 1,4- and 1,2-Double Nucleophilic Adducts (Table 9, Entry 1; product 10a): The 1,4- and 1,2- double nucleophilic addition reaction was performed according to the procedure described above under conditions B. After 17 h TFA (1.0 mL) was added and the mixture was stirred for 10 min at room temperature. A 10% aqueous Na_2CO_3 solution (10 mL) was added to quench the reaction and the mixture was filtered with suction through a Celite pad and washed with ethyl acetate. The mixture was ex-

tracted with ethyl acetate (3 × 5.0 mL) and the combined extracts were dried with Na_2SO_4 and concentrated in vacuo to give the crude product, which was purified by column chromatography on silica gel (*n*-hexane/ethyl acetate, 1:1) to give the title compound *cis*-**10a** (12.4 mg) and *trans*-**10a** (11.2 mg, 85%, *dr* = 53:47). Data for *cis*-**10a**: Yellow solid; m.p. 107–108 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.26 (d, J = 7.3 Hz, 3 H, COCHCH_3), 1.60–1.66 (m, 1 H, CH_3CHCH_2), 2.05–2.11 (m, 1 H, CH_3CHCH_2), 2.17–2.29 (m, 2 H, CNCHCH_2), 2.54 (tq, J = 6.7, 7.3 Hz, 1 H, CH_3CHCH_2), 4.42–4.44 (m, 1 H, NHCHCN), 6.50 (br. s, 1 H, NH) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 17.3, 24.8, 26.6, 35.4, 43.7, 118.2, 174.5 ppm. IR (neat): $\tilde{\nu}$ = 3288, 2942, 2876, 2241, 1617, 1475, 777 cm^{-1}. HRMS (EI): calcd. for $C_7H_{10}N_2O$ [M]$^+$ 138.0793; found 138.0797. Data for *trans*-**10a**: Yellow solid; m.p. 157–158 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.29 (d, J = 7.0 Hz, 3 H, COCHCH_3), 1.83–1.91 (m, 1 H, CH_3CHCH_2), 2.05–2.13 (m, 2 H, CH_3CHCH_2), 2.17–2.21 (m, 1 H, CNCHCH_2), 2.36–2.44 (m, 1 H, CH_3CHCH_2), 4.45–4.47 (m, 1 H, NHCHCN), 6.68 (br. s, 1 H, NH) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 16.7, 26.1, 26.7, 36.3, 44.0, 118.6, 174.3 ppm. IR (neat): $\tilde{\nu}$ = 3443, 3265, 2970, 2943, 2878, 2243, 1629, 1472, 778 cm^{-1}. HRMS (EI): calcd. for $C_7H_{10}N_2O$ [M]$^+$ 138.0793; found 138.0795.

10b: Yield: 16.4 mg, 53%. Yellow solid; m.p. 122–123 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.24 (s, 3 H, COCCH_3CH$_3$), 1.28 (s, 3 H, COCCH$_3$CH_3), 1.74–1.79 (m, 1 H, CH_3CH_3CCH_2), 1.99–2.05 (m, 1 H, CH_3CH_3CCH_2), 2.07–2.12 (m, 1 H, CNCHCH_2), 2.17–2.24 (m, 1 H, CNCHCH_2), 4.43–4.45 (m, 1 H, NHCHCN), 6.75 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.5, 26.9, 26.9, 33.2, 38.0, 44.1, 118.5, 177.7 ppm. IR (neat): $\tilde{\nu}$ = 3199, 2952, 2875, 2241, 1656, 1481, 1237, 827 cm^{-1}. HRMS (EI): calcd. for $C_8H_{12}N_2O$ [M]$^+$ 152.0950; found 152.0944.

Transformation Into Glutamic Acid Derivative 12 (Scheme 11): Under argon, acetic acid (3.0 mL) and hydrochloric acid (12 M, 1.5 mL) were added to ethyl 5-amino-5-cyano-2,2-dimethylpentanoate (**8a**; 79.3 mg, 0.40 mmol) and heated at reflux for 12 h. The reaction mixture was cooled and the solvent evaporated in vacuo to afford the crude product, which was purified by ion-exchange chromatography on Amberlyst 15DRY® to give title compound **12** (86.7 mg, 96%). Yellow powder; m.p. 191–195 °C. ^{1}H NMR (400 MHz, D_2O with 3-trimethylsilyl-1-propanesulfonic acid, sodium salt as the internal standard): δ = 1.17 (s, 3 H, COCCH_3CH$_3$), 1.18 (s, 3 H, COCCH$_3$CH_3), 1.64–1.80 (m, 4 H, NH_3CHCOOHCH_2CH_2), 4.21 (t, J = 6.2 Hz, 1 H, NH_3CHCOOHCH$_2$CH$_2$) ppm. ^{13}C NMR (100 MHz, D_2O with 3-trimethylsilyl-1-propanesulfonic acid, sodium salt as the internal standard): δ = 24.5, 28.6, 28.7, 35.6, 39.8, 57.6, 178.9, 184.4 ppm. IR (neat): $\tilde{\nu}$ = 2926, 1737, 1697, 1493, 1415, 1212 cm^{-1}. HRMS (EI): calcd. for $C_8H_{16}ClNO_4$ [M]$^+$ 225.0768; found 225.0767.

Supporting Information (see footnote on the first page of this article): ^{13}C NMR spectra of all new compounds.

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[2] Although we examined the 1,4- and 1,2-double nucleophilic addition using the imine protected with the TBS group, the 1,4–1,2 product was not obtained.

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[7] Results for the s-*cis* isomers are nearly the same as those for the s-*trans*; the difference in the method of calculation (HF/STO-3G or PM3) has little influence on a qualitative conclusion.

[8] For examples using silica gel as a reaction promoter, see: M. Shimizu, M. Tanaka, T. Itho, I. Hachiya, *Synlett* **2006**, 1687–1690.

[9] We confirmed by ^{1}H NMR spectroscopy that 1,4- and 1,2-addition products **7ac**, **7ad**, and **7af** were converted into 1,4 adducts by a retro-Strecker reaction (Table 7, Entries 3, 4, and 6). Because the adducts were not stable, the addition reactions with **1b** were not examined in detail.

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[12] A control experiment was carried out by using acrolein as the substrate in place of the imine **1c**. Under the conditions A in Table 8, the reaction gave the 1,4- and 1,2-addition product in 36% yield.

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