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Metal-Free Stereoselective Synthesis of (*E*)- and (*Z*)-N-Monosubstituted *β*-Aminoacrylates via Condensation Reactions of Carbamates

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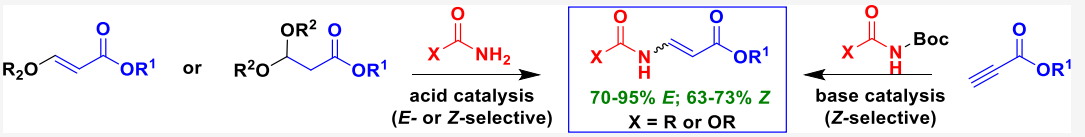

ABSTRACT: N-monosubstituted *β*-aminoacrylates are building blocks, which have been used in the preparation of amino acids and pharmaceuticals. Two efficient, stereoselective methods of preparation, via acid- or base-promoted condensation reactions of carbamates, are described. The base-promoted reaction is *E*-selective, while acid catalysis can, through the choice of solvent, selectively form *E* or *Z*. The acid-catalyzed *E*-selective process proceeds through a crystallization obviating the need for chromatographic purification.

INTRODUCTION

β-Aminoacrylates (**1**, Figure 1), also known as vinylogous carbamates, are versatile building blocks that have found use in

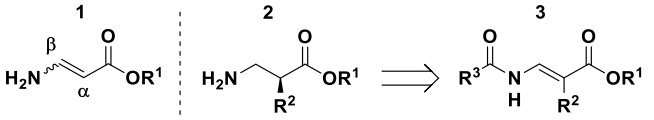

Figure 1. *β*-Aminoacrylates as precursors to β^2-amino acids.

the synthesis of a variety of compounds including heterocycles,[1] amino acids,[2a] and pharmaceuticals.[3] As part of ongoing efforts to incorporate non-natural amino acids into peptides to make them more drug-like,[4] we have become interested in new methods to prepare β^2-amino acids (**2**).[5] Based on the work of Elaridi,[2b] it appeared that (*E*)-*α*-substituted N-monofunctionalized *β*-aminoacrylates (**3**) could be an excellent starting point.

Unfortunately, there are limited reports on the synthesis of the requisite *α*-substituted (*E*)-acrylates (**3**, $R^2 \neq H$)[6] and no approaches that are general and stereocontrolled. However, it seemed reasonable that we could use the (*E*)-*α*-unsubstituted (**3**, $R^2 = H$) analogs as a starting point. It has been reported that similar compounds can be halogenated at the *α*-postion[7] and then subjected to metal-mediated cross coupling.[8] Consequently, those compounds, with nitrogen-protected as a carbamate (**3**, $R^3 = OR$) to facilitate later elaboration, became the focus of our efforts.

A review of the literature shows numerous methods for the preparation of N-acylated *β*-aminoacrylates (**3**, $R^2 = H$). However, in the various reports on this class of substrate, the Z isomer tends to predominate as the exclusive or major product.

Methods utilized (e.g., see Scheme 1) include metal-mediated processes such as amidation/hydroamidation,[9] decarboxylative/decarbonylative eliminations,[10] dehydrogenation,[11] and C−X cross coupling[12] as well as oxidation,[13] acetal condensation,[14] retro-Diels Alder,[15] and heterocycle fragmentation[16] reactions. The vast majority of compounds reported are amides. Of the carbamate-containing examples, nearly all reported reactions favor the formation of the (*Z*)-acrylate. That configurational selectivity has been attributed, by several of the authors, to hydrogen bonding from the N−H to the ester carbonyl during olefin formation.[9a,b] Some of the decarboxylative elimination reactions slightly favor the (*E*)-acrylates but not consistently so. There are also examples of photoisomerization from the (*Z*)- to (*E*)-acrylate.[15] Then, there is the work of Porco[12] who described the cross coupling of amides (no carbamates reported) and (*E*)-*β*-iodoacrylates. However, that process is not entirely stereocontrolled as *Z*-acrylates are sometimes the favored products.

Of the two reports (Newhouse[11] and Ragulin[14]) that describe *E*-selective reactions, neither actually is. Newhouse used a Pd-mediated dehydrogenation to convert *β*-alanines to *β*-aminoacrylates. However, the compounds with a free N−H are actually the *Z* isomers.[17] In the single example by Ragulin,[14] the reaction produces both isomers in nearly equal amounts with the *E* isomer isolated selectively by crystallization (vide infra). Finally, there are examples of *E*-selective reactions that produce products with

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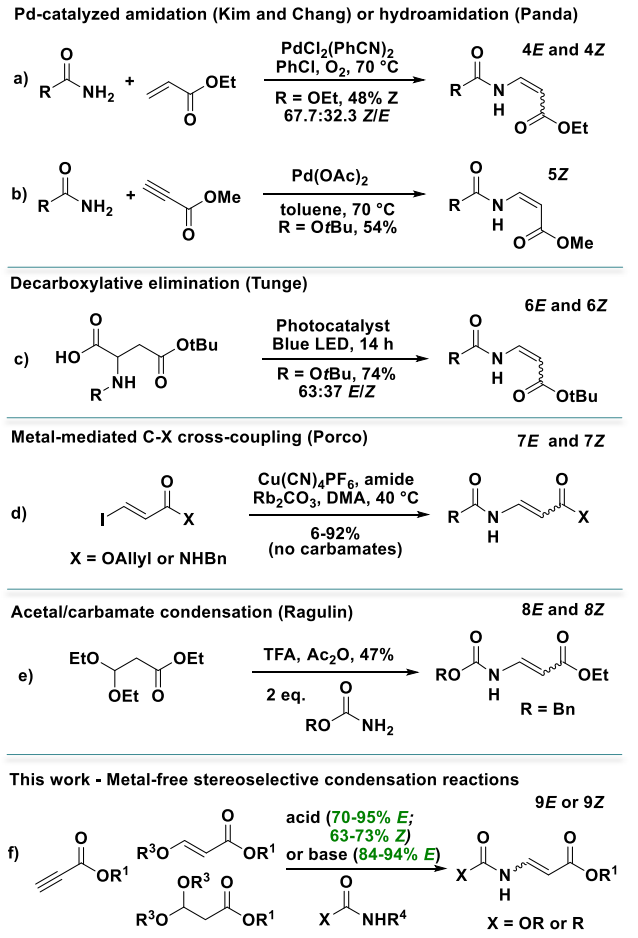
Scheme 1. N-Monoprotected β-Aminoacrylate Syntheses



a fully substituted nitrogen[18] (no N−H), but none with an easily removeable protecting group. Additionally, we hoped to use hydrogen bonding to our advantage.

We now report the development of a pair of efficient metal-free stereoselective processes for the preparation of *N*-carbamate-protected α,β-unsubstituted β-aminoacrylates (**3**, R^2 = H). The first uses an acid-catalyzed condensation to prepare the *E* isomer. Further exploration of the reaction allowed for a *Z*-selective reaction by careful selection of the solvent. The second process relies on base catalysis to prepare the *E* configuration and is amenable to both *N*-carbamates and *N*-amides.

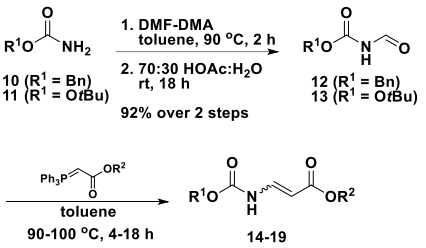
RESULTS AND DISCUSSION

Our initial efforts to stereoselectively access (*E*)-β-aminoacrylates began with an examination of the Wittig reaction of *N*-formyl carbamates. Traditionally, the Wittig reaction of aldehydes with stabilized ylides is expected to generate *trans* olefins with high selectivity. Interestingly, while the reaction of *N*-formyl amides and stabilized ylides has been reported,[6a,9c] the corresponding reaction of *N*-formyl carbamates has not.

The required *N*-Cbz and *N*-Boc-formamides (**12** and **13**) were quickly prepared in a two-step process. Carbamates **10** and **11** were condensed with *N*,*N*-dimethylformamide−dimethyl acetal (DMF−DMA) to give intermediate dimethylaminoimines. Acid hydrolysis of those intermediates gave the desired *N*-formylcarbamates **12** and **13** in high yield and purity without need for chromatography.

The results of the Wittig reaction with *N*-formyl carbamates and various stabilized ester ylides are detailed in Scheme 2.

Scheme 2. Wittig Approach to β-Aminoacrylates



Product	R^1	R^2	*E*:*Z*	% yield
14	Bn	Me	56:44	98%
15	Bn	Et	50.5:49.5	94%
16	Bn	*t*Bu	46.8:53.2	96%
17	*t*Bu	Me	61.2:38.8	92%
18	*t*Bu	Et	53:47	96%
19	*t*Bu	*t*Bu	37.9:62.1	95%

Unfortunately, while products form in high yield, none of the reactions were sufficiently selective for the desired *E* isomer. In fact, the *E*/*Z* ratio dropped as more sterically hindered esters were used. The analogous Horner−Wadsworth−Emmons reaction, using stabilized phosphonate ylides, was also examined, but, no product formation was observed. The main products of those reactions were carbamates **10** and **11**, which presumably occur via N-deformylation due to increased nucleophilicity of the phosphonate relative to the phosphonium ylides.

Several interesting observations resulted from these initial efforts, which had a significant impact on the direction of our subsequent work. First, the *E* isomers are generally solid at ambient temperatures, while the *Z* isomers are oils. Additionally, the *Z* isomers are substantially less polar than their corresponding *E* isomer as evidenced by retention times on silica or C18 stationary phases used in reversed-phase high-performance liquid chromatography (HPLC). That particular property is, likely, due to hydrogen bonding.

On a related note, an example of the importance of hydrogen bonding in the *Z*-selective formation of a similar series of compounds (**20*Z***, Figure 2) was reported by Suh and Kishi. In

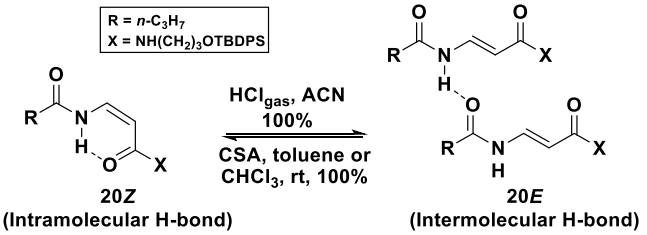


Figure 2. Kishi's study of H-bonding in β-aminoacrylates.

their efforts toward the total synthesis of palytoxin,[19] they prepared a number of amide analogs (vinylogous ureas), which lead to a series of important observations. They observed, in an acid-catalyzed process, that: (1) polar solvents could disrupt the propensity for intramolecular hydrogen bonding, (2) the *E* isomers were, often, observed to be highly crystalline (possibly because of the presence of intermolecular hydrogen bonding) (**20*E***), and (3) potential for *E*/*Z* interconversion exists. Thus, through carefully selected conditions, it might be possible to selectively prepare one isomer or the other.

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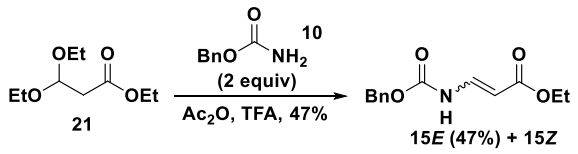
The extension of Kishi's work to the selective synthesis of N-monosubstituted-β-aminoacrylates (vinylogous carbamates) is based on the previously mentioned single reported example by Ragulin.[13] Benzyl carbamate (**10**) and acetal **21** were condensed under acid catalysis to, reportedly, give the (*E*)-β-aminoacrylate exclusively in moderate yield (see Scheme 3). The *E* isomer

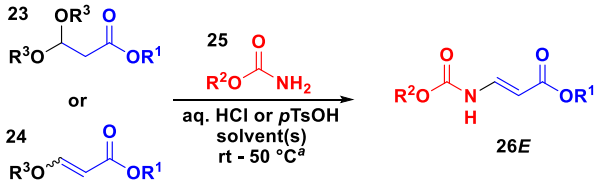
Scheme 3. Known Acid-Catalyzed β-Aminoacylate Synthesis



(**15*E***) was crystallized from the reaction mixture after workup. In our hands, careful examination of the crude reaction showed both the *E* and *Z* isomers were formed in nearly equivalent amounts.[20a]

Armed with these precedents, we examined the possibility of developing an efficient condensation reaction that operates under equilibration/crystallization conditions. When reacting acetal **22** with benzyl carbamate in the presence of aqueous HCl in acetonitrile (ACN)/water, we obtained the desired β-aminoacrylate **14*E*** in great yield and selectivity (93%, see Table 1) as a crystalline solid. Following the reaction profile over

Table 1. *E*-Isomer Synthesis/Crystallization in Polar Solvents



carbamate	R^1	R^2	pdt #	isolated yield
27	Me	Me	**30*E***[b]	90
27	Et	Me	**31*E***	84
28	Me	Et	**32*E***	87
10	Me	Bn	**14*E***[b]	93
10	Et	Bn	**15*E***	81
10	allyl	Bn	**33*E***	75
10	propargyl	Bn	**34*E***	72
10	Bn	Bn	**35*E***	92
29	Me	Fmoc	**36*E***	95
29	Et	Fmoc	**37*E***	70
29	Bn	Fmoc	**38*E***	94

[a]Conditions: 1 equiv carbamate, 1.3 equiv of acetal in solvent with acid—100% 5 N HCl, rt, 18 h for R^2 = Me or Et; 1:1 ACN/5 N HCl, rt, 18 h for R^2 = Bn; and ACN, 50 °C, 18 h for R^2 = FMoc. [b]Reaction could be scaled up to make >100 g. R^3 may or may not equal R^1. See Supporting Information for partner (**23**/**24**) used.

time,[20a,b] the *E* isomer forms rapidly while steadily crystallizing out of solution over time (Figure 3A). Under these conditions, the *Z* isomer remains at a consistently low level. We hypothesize that water might play a double role by serving as an antisolvent for the crystallization of **14*E*** and by disfavoring the intramolecular hydrogen bonding stabilizing **14*Z***. As previously reported,[19] a different behavior was expected, and demonstrated, when the condensation reaction was run in a nonpolar solvent [dichloromethane (DCM) in the presence of 3.0 M HCl in cyclopentyl methyl ether (CPME), Figure 3B]. In this instance, while **14*E*** initially formed at higher concentrations compared to **14*Z***, a plateau occurred after 30 min corresponding to an increase in **14*Z***, further supporting the existence of an equilibrium between these isomers.

To gain further clarity into the equilibrium between aminoacrylates **14*E*** and **14*Z***, each isomer was independently subjected to the condensation conditions. While the olefin configuration was mostly conserved with **14*E*** (Figure 4A), pure **14*Z*** slowly converted into **14*E*** (Figure 4B). In fact, subjecting **14*Z*** to optimized condensation reaction conditions (see Scheme 4), for the formation of **14*E*** from acetal and carbamate, results in near complete isomerization to **14*E*** via simultaneous crystallization.

In order to develop the scope of this reaction for a scalable process, we targeted conditions that would operate under kinetic control as that would give us the crystalline *E* isomer in high yield. Gratifyingly, after screening solvent(s), acids, and temperature, we were able to prepare carbamic acid esters of (*E*)-β-aminoacrylates (**26*E***, Table 1) in good to excellent yield without need for chromatography. Reactions were run in either 100% water, 100% ACN, or mixture of the two depending on solubility of the carbamate (**25**). An excess of the condensation partner was used to ensure complete consumption of the carbamate. Either a 3,3-dialkoxypropionate (**23**) or a 3-alkoxyacryate ester (**24**, cis or trans) can be used as the reaction partner without an effect on yield. The acid used both promotes condensation and facilitates isomerization. Reactions were carried out with aq HCl (5 N) except where ACN was the sole solvent in which case *p*-toluenesulfonic acid (*p*TsOH) was used. Due to solubility issues, Fmoc-amide (**29**) required moderate heating (50 °C) to facilitate the reaction.

In an analogous fashion, reactions may be run under thermodynamic control (toluene, CSA, 50 °C) to selectively form the *Z* isomer (see Table 2). As the most *Z* isomers are oils or low-melting solids, the products must be isolated chromatographically. Overall yields are diminished relative to the synthesis of the *E* isomers due to lower selectivity of the reaction but are still on par with most of the metal-catalyzed processes. As the *Z* isomers have been utilized in number ways,[9c,15] this simplified alternative method to access them should be of use.

We propose the following mechanism (see Scheme 5) based on reaction profiling of the condensation and isomerization reactions. The first intermediate is, likely, compound **49**, which would form when carbamate **25** reacts, under acid catalysis, with either acetal **23** or alkoxy acrylate **24**. Under aqueous conditions, **23** or **24** could first hydrolyze to the respective aldehyde before undergoing condensation with the carbamate. It is also conceivable that a second equivalent of carbamate could add in (**49**, R = $NHCO_2R$) as that has been reported to occur when carbamates react with aldehydes. Regardless, all of the possible intermediates could then undergo an elimination reaction to generate either **26*E*** or **26*Z***. At that point, depending on solvent selection, an equilibrium between the compounds, via **50*E***[13b] and **50*Z***, is established that favors one compound over the other. In the case of **26*E***, selectivity is further enhanced through crystallization of the product from solution. Again, a driving force in the reaction is thought to be hydrogen bonding, particularly under conditions that favor the *Z* isomer. It is also possible that the chloride anion plays a role in some of the isomerization process,[21] but it is not essential as the reaction can be catalyzed by organic acids such as camphorsulfonic acid (CAS) or *p*TsOH. It is important to note that in the absence of conditions (e.g., acid or UV light) that promote isomerization,

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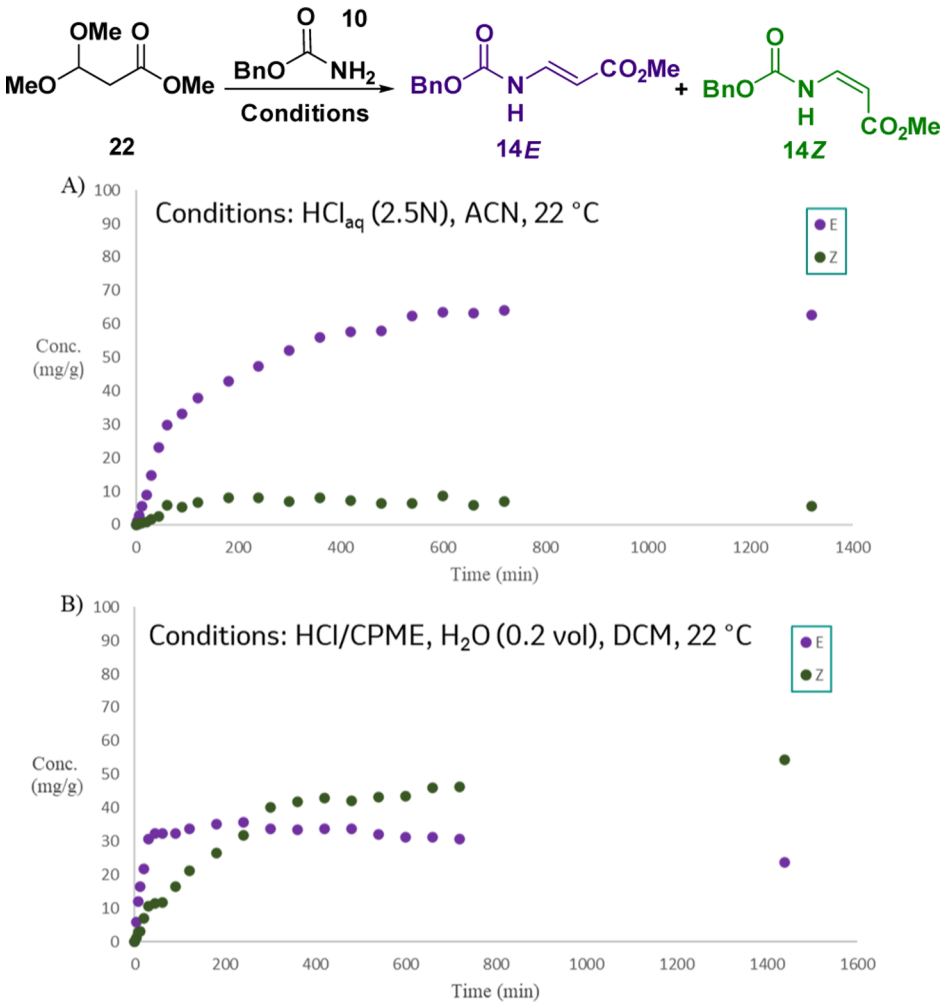

Figure 3. Formation of acrylate **14**: ACN vs DCM/CPME.

the individual isomers are configurationally stable at ambient temperatures in their pure forms.

While the previously discussed chemistry represents a significant improvement in the preparation of these important building blocks, there are a few limitations. The reaction conditions are not compatible with acid-labile functional groups, for example, *t*-butyl carbamate (Boc). Also, the *E*-selective kinetic controlled reaction with crystallization depends on the exclusive (or at least significantly superior) crystallinity of one of the isomers. In order to address these issues, we developed a complementary approach.

Imides have been reported to undergo a base-promoted nucleophilic addition reaction to propiolate esters to produce (*E*)-*β*-aminoacrylates that are fully substituted on nitrogen.[22] We theorized that this process could be modified using an acyclic diacylated nitrogen, where one of the groups on nitrogen is a protecting group, such as Boc, that could be removed after the initial condensation to generate the desired (*E*)-N-monosubstituted *β*-aminoacrylate.

Thus, a series of *N*-Boc carbamates (or amides) were prepared (see Table 3). When subjected to a DABCO-catalyzed reaction, they quickly form (*E*)-N-disubstituted *β*-aminoacrylates (**53*E***). For example, bis-Boc amine **55** undergoes the condensation reaction smoothly in very high yield to produce nearly exclusively the *E* isomer (**62*E***, >90:1). Small amounts (1−5%) of *Z* isomer are sometimes observed but are easily separated after the deprotection step. The fully protected acrylate (**62*E***) is then converted to mono-Boc **17*E*** using Lewis acid catalysis ($MgClO_4$).[23]

The amount of Lewis acid used is key to avoid a sluggish reaction and/or unwanted byproducts. Use of conventional strong acid deprotection methods (e.g., trifluoroacetic acid) leads to lower yields and isomerization of the olefin. This approach also allows for *N*-acyl (alkyl and aryl) analogs to be prepared and is an excellent alternative to the various metal-mediated processes,[9] which primarily afford the *Z* isomer. However, *N*-Boc deprotection of the amide requires stoichiometric amounts of the Lewis acid.

In conclusion, we have developed two fast and efficient routes for the preparation of N-monosubstituted-*β*-aminoacrylates. The first method is a solvent-controlled process to selectively prepare the *E* or *Z* isomer. The second method is a new use of the nucleophilic addition reaction of imides to propiolates to prepare *E* isomers with acid-labile groups or amides on nitrogen. Future publications will detail the functionalization of these substrates and their conversion to β^2-amino acids and heterocycles.

EXPERIMENTAL SECTION

General Information. Commercial grade reagents and solvents were used without further purification. All starting materials not previously reported in the literature have been fully characterized. All compounds previously reported in the literature are spectroscopically

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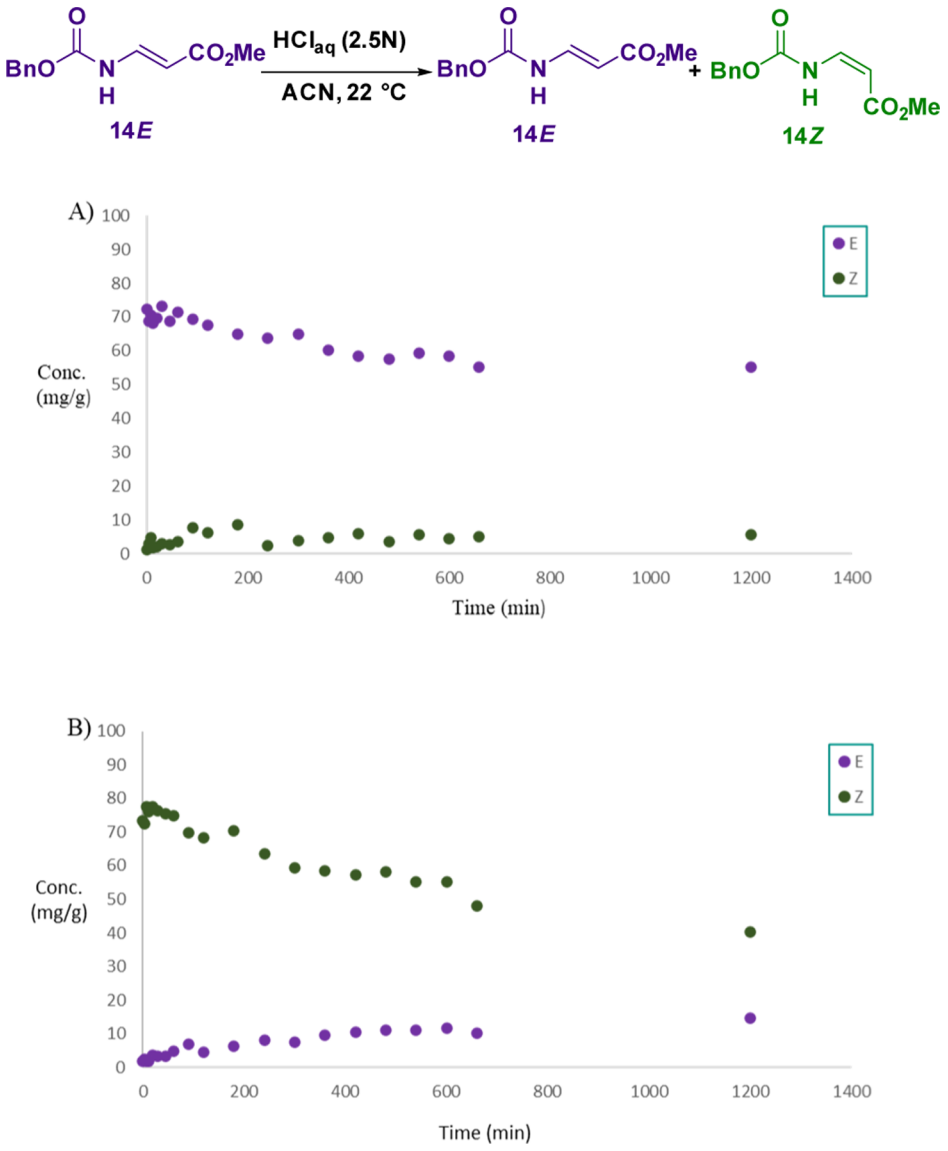
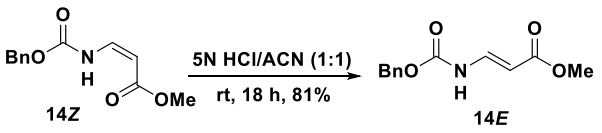


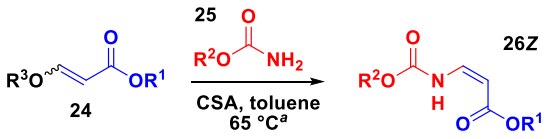
Figure 4. *E*/*Z* isomerization of acrylate **14** in ACN/aqueous HCl.

Scheme 4. *Z* to *E* Isomerization and Crystallization



consistent with the reported values. Reactions are run under a nitrogen atmosphere unless noted. Reactions were monitored by either thin-layer chromatography (EMD Millipore Silica Gel 60 F254 plates with visualization by UV or $KMnO_4$ stain) or ultraperformance liquid chromatography−mass spectrometry (UPLC/MS) (Agilent 1290 Infinity II UPLC with Agilent 6140 MS using ESI) at 1.0 mL/min, 210 and 254 nm, 15−99% gradient eluted with ACN and water (10 mM pH 3.5 ammonium formate) over 1.5 min and then held at 99% ACN for 0.5 min (Zorbax Ecclipse Plus C18 RRHD, 1.8 μm, 2.1 × 50 mm). Kinetics data were collected using a Mettler-Toledo EasyMax 102 and EasySampler 1210 and analyzed by HPLC (Agilent 1260, 0.4 mL/min, 254 nm, 2% ACN/water + 0.3% formic acid for 2.5 min then gradient eluted to 90% over 6 min, and then held for 1.75 min, Waters Acquity UPLC BEH C18, 1.7 μm, 2.1 × 100 mm). ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR spectra were measured on a Bruker system running TopSpin and were internally referenced to $CHCl_3$ (7.24 ppm for ^{1}H;

Table 2. Synthesis of *Z*-Isomers Using Nonpolar Solvents



carbamate	R^1 (=R^3)	R^2	pdt #	isolated yield
27	Me	Me	**30Z**	67
28	Me	Et	**32Z**	66
39	Me	*n*Pr	**44Z**	67
40	Me	*i*Pr	**45Z**	72
10	Me	Bn	**14Z**	73
10	Et	Bn	**15Z**	68
41	Me	menthyl	**46Z**	71
42	Me	Ph	**47Z**	76
43	Me	CCl_3CH_2	**48Z**	63

[a]Conditions: 1 equiv carbamate, 1.3 equiv of acetal, 5 mol % CSA in toluene (0.4−0.5 M) at 65 °C for 5−20 h. Isolated by chromatography.

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Scheme 5. Proposed Reaction Mechanism

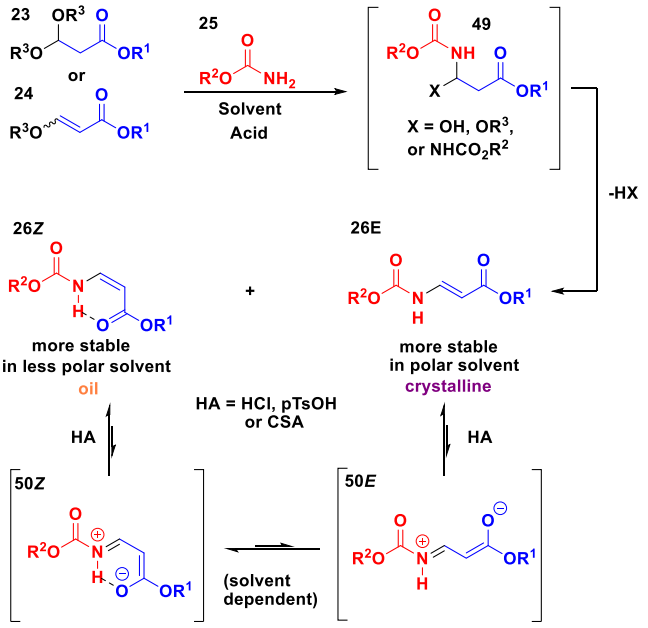
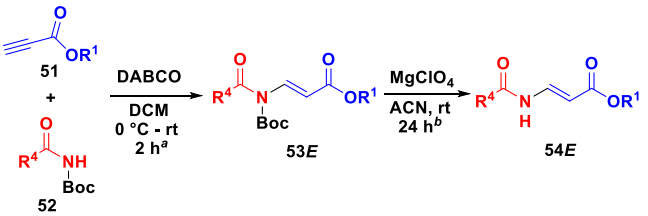


Table 3. Scope of Propiolate Condensation/Deprotection



R_1	imide-R^4 (#)	int. # (yield)	pdt # (yield)
Me	O*t*-Bu (**55**)	**62*E*** (97%)	**17*E*** (91%)
Et	O*t*-Bu (**55**)	**63*E*** (95%)	**18*E*** (95%)
t-Bu	O*t*-Bu (**55**)	**64*E*** (99%)	**19*E*** (93%)
Me	OMe (**56**)	**65*E*** (91%)	**30*E*** (94%)
Et	Me (**57**)	**66*E*** (96%)	**71*E*** (93%)
Me	phenyl (**58**)	**67*E*** (96%)	**72*E*** (85%)
t-Bu	4-CO_2Me-Ph (**59**)	**68*E*** (95%)	**73*E*** (88%)
Me	2-Br-Ph (**60**)	**69*E*** (97%)	**74*E*** (97%)
Me	4-Br-Ph (**61**)	**70*E*** (99%)	**75*E*** (88%)

[a]1 equiv each of propiolate and imide in DCM with 10 mol % DABCO, add propiolate at 0 °C then stir 1−2 h at rt. [b]$MgClO_4$—0.2 equiv to deprotect bis-Boc and 1 equiv to deprotect *N*-Boc, *N*-acyl compounds.

77.0 ppm for ^{13}C), dimethyl sulfoxide (DMSO) (2.50 ppm for ^{1}H; 39.51 ppm for ^{13}C), MeOH (3.3 ppm for ^{1}H; 49.15 ppm for ^{13}C), or D_2O (4.8 ppm for ^{1}H). Chemical shifts are expressed in parts per million (δ) downfield from tetramethylsilane. Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, dt = doublet of triplets, and br = broad), coupling constant (Hz), and integration. HRMS was carried out using a Waters Acquity UPLC coupled to a Waters Xevo XS ToF (pos/neg modes). Silica gel chromatography was performed on a Teledyne ISCO CombiFlash Rf + purification system using prepacked silica gel columns from either ISCO or Biotage (CV = column volume). Note: all ^{1}H NMR of β-aminoacrylates, with free N−H, were run in both $CDCl_3$ and DMSO-d_6 as the N−H proton is diagnostic for *E* vs *Z* in $CDCl_3$ due to H-bonding. The N−H proton in the *E* isomer is typically observed at 6.5−7.5 ppm in $CDCl_3$, whereas it is observed at 9−10 ppm for the H-bonded *Z* isomer. This effect was not observed in DMSO-d_6. Additionally, ^{13}C NMR were run in DMSO-d_6 as small amounts of residual acid in older bottles of $CDCl_3$ can cause isomerization of the olefin during the longer acquisition times.

Wittig Chemistry for β-Aminoacrylate Preparation. *Benzyl Formylcarbamate (**12**).*[24] To a 1000 mL 1-neck flask, with a stir bar, are added benzyl carbamate (**10**) (100 g, 662 mmol), toluene (400 mL, anhydrous), and DMF−DMA (257 mL, 1819 mmol). The reaction is heated at reflux, under N_2, for 3 h. The reaction is cooled to ambient temperature and concentrated in vacuo to a white solid. The solids are slurried in hexanes (500 mL), collected by filtration, and washed with hexanes (3 × 500 mL). The solids are dried on a funnel using a combination of house vacuum/nitrogen sweep via an inverted funnel connected to the nitrogen source to afford (*E*)-benzyl-((dimethylamino)methylene)carbamate as a white solid. Quantitative yield is assumed and used directly in the next reaction. The white solid from the previous step is placed in a 1000 mL 1-neck flask with a stir bar. 272 mL 70% aq HOAc (190 mL HOAc, 82 mL water) is added and the reaction is stirred overnight at ambient temperature (18 h). The reaction is concentrated in vacuo to remove HOAc, and then diluted with water (400 mL) and extracted with EtOAc (2 × 300 mL). The organic layer is washed with saturated NaCl solution (2 × 100 mL), dried over Na_2SO_4, filtered, and concentrated to give an oil, which crystallizes on standing at ambient temperature. The solids are slurried in hexanes (400 mL), filtered, washed with hexanes (3 × 200 mL), and then dried on a funnel using a combination of house vacuum/nitrogen sweep via an inverted funnel connected to the nitrogen source to afford to give (*E*)-benzyl((dimethylamino)methylene)carbamate **12** (109.27 g, 92%) as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.94 (d, *J* = 10.1 Hz, 1H), 8.70 (d, *J* = 8.9 Hz, 1H), 7.59−7.18 (m, 5H), 5.22 (s, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 163.6, 152.5, 134.4, 128.7, 128.6, 128.4, 68.2. HRMS (ESI) (*m*/*z*): ([M − H]$^-$) calcd for $C_9H_9NO_3$, 178.0504; found, 178.0504.

*tert-Butyl Formylcarbamate (**13**).*[25] To a 1000 mL 1-neck flask, with a stir bar under N_2, are added *tert*-butyl carbamate (**11**) (50 g, 427 mmol), toluene (400 mL, anhydrous), and DMF−DMA (181 mL, 1280 mmol). The reaction is heated at 90 °C for 3 h. The reaction is cooled to ambient temperature and concentrated in vacuo. The oily residue is reconcentrated from hexanes (400 mL) and let stand under house vacuum to give (*E*)-*tert*-butyl ((dimethylamino)methylene)carbamate as a waxy solid. Quantitative yield is assumed and used directly in the next reaction. The material from the previous step is placed in a 250 mL 1-neck flask and 70% HOAc/water (2×; 103 mL HOAc/44 mL water) is added. The reaction is stirred overnight at ambient temperature. The reaction is diluted with MTBE (500 mL), washed with water (3 × 250 mL), saturated NaCl solution (150 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue is reconcentrated from chloroform (2 × 300 mL) to give *tert*-butyl formylcarbamate **13** (56.89 g 92%) as a white solid after drying under vacuum: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.86 (d, *J* = 10.4 Hz, 1H), 8.30 (d, *J* = 10.4 Hz, 1H), 1.47 (s, 9H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 163.7, 151.3, 83.5, 27.9. HRMS (ESI) (*m*/*z*): ([M − H]$^-$) calcd for $C_6H_{11}NO_3$, 144.0661; found, 144.0656.

*Methyl (E)-3-(((Benzyloxy)carbonyl)amino)acrylate (**14E**) and Methyl (Z)-3-(((Benzyloxy)carbonyl)amino)acrylate (**14Z**).* To a 250 mL 1-neck flask, with a stir bar and an air condenser under nitrogen, are added methyl 2-(triphenylphosphoranylidene)acetate (18.66 g, 55.8 mmol), benzyl formylcarbamate **12** (5 g, 27.9 mmol), and toluene (100 mL, anhydrous). The reaction is heated at 90 °C (internal temperature) for 4 h. The reaction is cooled to ambient temperature and concentrated in vacuo. The residue is dry loaded onto silica gel (dissolved in DCM, added silica gel, and concentrated to dryness). The silica is packed into a dry load cartridge, placed on top of a silica gel column (ISCO 120 g gold), and chromatographed (conditioned column with hexanes, eluted with 1 CV of hexanes then gradient eluted with 40% EtOAc/hexanes over 6 CV, and then held for 6 CV) to give the 1st eluting compound (*Z*)-methyl 3-(((benzyloxy)carbonyl)amino)acrylate **14*Z*** (2.81 g, 42.8%) as an oil: ^{1}H NMR ($CDCl_3$, 500 MHz): δ ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.79 (s, 1H), 7.41−7.17 (m, 6H), 5.19 (s, 2H), 5.06 (d, *J* = 8.6 Hz, 1H), 3.69 (s, 3H); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 9.79 (d, *J* = 10.4 Hz, 1H), 7.53−7.28 (m, 6H), 5.22 (s, 2H), 5.12 (d, *J* = 8.9 Hz, 1H), 3.64 (s, 3H); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 168.55,

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152.52, 140.20, 135.59, 128.44, 128.25, 128.09, 94.60, 67.37, 51.01. HRMS (ESI) (m/z): ($[M - H]^-$) calcd for $C_{12}H_{13}NO_4$, 234.0767; found, 234.0767; and 2nd eluting compound (*E*)-methyl 3-(((benzyloxy)carbonyl)amino)acrylate **14*E*** (3.6 g, 54.8%) as a white crystalline solid: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.81 (t, J = 13.1 Hz, 1H), 7.47−7.29 (m, 5H), 6.94 (d, J = 12.0 Hz, 1H), 5.35 (d, J = 14.1 Hz, 1H), 5.19 (s, 2H), 3.69 (s, 3H); ^{1}H (DMSO-d_6, 500 MHz): δ 10.61−10.38 (m, 1H), 7.65 (dd, J = 14.0, 11.1 Hz, 1H), 7.48−7.14 (m, 5H), 5.40 (d, J = 14.0 Hz, 1H), 5.18 (s, 2H), 3.61 (s, 3H); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 167.2, 153.4, 140.6, 135.8, 128.5, 128.3, 128.2, 98.2, 67.0, 50.9. HRMS (ESI) (m/z): ($[M - H]^-$) calcd for $C_{12}H_{13}NO_4$, 234.0767, found, 234.0768.

*Ethyl (E)-3-(((Benzyloxy)carbonyl)amino)acrylate (**15E**)*[13] *and Ethyl (Z)-3-(((Benzyloxy)carbonyl)amino)acrylate (**15Z**).* To a 40 mL vial, with a stir bar, are added benzyl formylcarbamate **12** (2.5 g, 13.95 mmol), ethyl(triphenylphosphoranylidene)acetate (7.29 g, 20.93 mmol), and then toluene (15 mL, anhydrous). The reaction is heated at 95 °C for 18 h. The reaction is then cooled to ambient temperature and loaded directly onto a 40 g ISCO gold column that is then placed on top of an 80 g ISCO gold (conditioned with hexanes, eluted with 2 CV hexanes then gradient eluted with 100% MTBE over 8 CV, and then held for 6 CV) to give the 1st eluting compound ethyl (*Z*)-3-(((benzyloxy)carbonyl)amino)acrylate **15*Z*** (1.62 g, 46.6%) as a clear, colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 9.84 (s, 1H), 7.52−7.01 (m, 6H), 5.19 (s, 2H), 5.04 (d, J = 8.9 Hz, 1H), 4.14 (q, J = 7.1 Hz, 2H), 1.26 (t, J = 7.1 Hz, 3H); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 9.82 (d, J = 11.6 Hz, 1H), 7.46−7.22 (m, 6H), 5.21 (s, 2H), 5.10 (d, J = 8.9 Hz, 1H), 4.10 (q, J = 7.1 Hz, 1H), 1.19 (t, J = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 168.2, 152.5, 140.2, 135.6, 128.4, 128.2, 128.1, 94.9, 67.3, 59.7, 14.0. HRMS (ESI) (m/z): ($[M - H]^-$) calcd for $C_{13}H_{15}NO_4$, 248.0923; found, 248.0923; and the 2nd eluting compound ethyl (*E*)-3-(((benzyloxy)carbonyl)amino) acrylate **15*E*** (1.65 g, 47.4%) as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.80 (t, J = 13.1 Hz, 1H), 7.36−7.33 (d, J = 4.4 Hz, 5H), 6.97 (d, J = 12.1 Hz, 1H), 5.34 (d, J = 14.0 Hz, 1H), 4.15 (q, J = 7.1 Hz, 2H), 1.25 (t, J = 7.1 Hz, 3H); ^{1}H (DMSO-d_6, 500 MHz): δ 10.50 (s, 1H), 7.63 (dd, J = 14.0, 11.1 Hz, 1H), 7.51−6.98 (m, 5H), 5.38 (d, J = 14.0 Hz, 1H), 5.18 (s, 2H), 4.07 (q, J = 7.1 Hz, 2H), 1.18 (t, J = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 166.7, 153.4, 140.4, 135.8, 128.5, 128.3, 128.2, 98.6, 67.0, 59.3, 14.2. HRMS (ESI) (m/z): ($[M - H]^-$) calcd for $C_{13}H_{15}NO_4$, 248.0923; found, 248.0924.

*tert-Butyl (E)-3-(((Benzyloxy)carbonyl)amino)acrylate (**16E**)*[10f] *and tert-Butyl (Z)-3-(((Benzyloxy)carbonyl)amino)acrylate (**16Z**).*[10f] To a 40 mL vial, with a stir bar, are added benzyl formylcarbamate **12** (2.5 g, 13.95 mmol), (*tert*-butoxycarbonylmethylene)-triphenylphosphorane (7.88 g, 20.93 mmol), and then toluene (15 mL, anhydrous). The reaction is heated at 95 °C for 18 h. The reaction is then cooled to ambient temperature and loaded directly onto a 40 g ISCO gold column that is then placed on top of an 80 g ISCO gold (conditioned with hexanes, eluted with 2 CV hexanes then gradient eluted with 100% MTBE over 8 CV, and then held for 6 CV) to give the 1st eluting compound *tert*-butyl (*Z*)-3-(((benzyloxy)carbonyl)amino)-acrylate **16*Z*** (1.98 g, 51.2%) as a clear, colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 9.96−9.80 (m, 1H), 7.37−7.31 (m, 5H), 7.19 (t, J = 10.1 Hz, 1H), 5.18 (s, 2H), 4.96 (d, J = 8.6 Hz, 1H), 1.59−1.33 (m, 9H); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 9.82 (d, J = 11.5 Hz, 1H), 7.47−7.33 (m, 5H), 7.25 (dd, J = 11.6, 8.9 Hz, 1H), 5.20 (s, 2H), 5.01 (d, J = 8.9 Hz, 1H), 1.43 (s, 9H); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 168.0, 152.5, 139.6, 135.6, 128.4, 128.2, 128.1, 96.5, 80.3, 67.3, 27.8. HRMS (ESI) (m/z): ($[M - H]^-$) calcd for $C_{15}H_{19}NO_4$, 276.1236; found, 276.1236; and the 2nd eluting compound (*E*)-3-(((benzyloxy)-carbonyl)amino)acrylate **16*E*** (1.74 g, 45.0%) as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.69 (dd, J = 14.0, 12.0 Hz, 1H), 7.39−7.30 (m, 5H), 6.76 (s, 1H), 5.27 (d, J = 14.1 Hz, 1H), 5.18 (s, 2H), 1.45 (s, 9H); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 10.41 (s, 1H), 7.53 (dd, J = 14.0, 11.1 Hz, 1H), 7.45−7.22 (m, 5H), 5.28 (d, J = 14.0 Hz, 1H), 5.17 (s, 2H), 1.41 (s, 9H); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 166.1, 153.4, 139.7, 135.8, 128.5, 128.3, 128.2, 100.4, 79.0, 66.9, 27.9. HRMS (ESI) (m/z): ($[M - H]^-$) calcd for $C_{15}H_{19}NO_4$, 276.1236; found, 276.1236.

*Methyl (E)-3-((tert-Butoxycarbonyl)amino)acrylate (**17E**) and Methyl (Z)-3-((tert-Butoxycarbonyl)amino)acrylate (**17Z**).*[14] To a 250 mL 1-neck flask, with a stir bar and an air condenser under N_2, are added methyl 2-(triphenylphosphoranylidene)acetate (34.6 g, 103 mmol), *tert*-butyl formylcarbamate **13** (7.5 g, 51.7 mmol), and toluene (100 mL, anhydrous). The reaction is heated at 90 °C (internal temperature) for 18 h. The reaction is cooled to ambient temperature and concentrated in vacuo. The residue is dry loaded onto silica gel (dissolved in DCM, added silica gel, and concentrated to dryness). The silica is packed into a dry load cartridge, placed on top of a silica gel column (ISCO 120 g gold), and chromatographed (conditioned with hexanes, eluted with 1 CV hexanes then gradient eluted with 40% EtOAc/hexanes over 6 CV, and then held for 6 CV) to give the 1st eluting compound *(Z)-methyl 3-((tert-butoxycarbonyl)amino)acrylate* **17Z** (3.729 g, 35.9%) as an oil: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 9.56 (s, 1H), 7.23 (t, J = 12.0 Hz, 1H), 4.98 (d, J = 8.9 Hz, 1H), 3.68 (s, 3H), 1.46 (s, 9H); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 9.53 (d, J = 11.8 Hz, 1H), 7.27 (dd, J = 11.8, 8.8 Hz, 1H), 5.05 (d, J = 8.9 Hz, 1H), 3.64 (s, 3H), 1.46 (s, 9H); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 168.7, 151.2, 140.4, 93.4, 81.6, 50.8, 27.5. HRMS (ESI) (m/z): ($[M - H]^-$) calcd for $C_9H_{15}NO_4$, 200.0923; found, 200.0921; and the 2nd eluting compound *(E)-methyl 3-((tert-butoxycarbonyl)amino)acrylate* **17*E*** (5.857 g, 56.3%) as a white solid, which is spectroscopically identical to the material previously reported herein or in the literature:[10] ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.78 (t, J = 13.0 Hz, 1H), 6.73 (d, J = 12.3 Hz, 1H), 5.29 (d, J = 14.0 Hz, 1H), 3.69 (s, 3H), 1.47 (s, 9H); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 10.12 (s, 1H), 7.60 (dd, J = 14.0, 11.2 Hz, 1H), 5.34 (d, J = 14.0 Hz, 1H), 3.59 (s, 3H), 1.44 (s, 9H); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 167.3, 152.2, 140.9, 97.2, 80.9, 50.7, 27.7. HRMS (ESI) (m/z): ($[M - H]^-$) calcd for $C_9H_{15}NO_4$, 200.0923; found, 200.0923.

*Ethyl (E)-3-((tert-Butoxycarbonyl)amino)acrylate (**18E**) and Ethyl (Z)-3-((tert-Butoxycarbonyl)amino)acrylate (**18Z**).*[14] To a 40 mL vial, with a stir bar, are added *tert*-butyl formylcarbamate **13** (2.03 g, 13.95 mmol), ethyl (triphenylphosphoranylidene)acetate (7.29 g, 20.93 mmol), and then toluene (15 mL, anhydrous). The reaction is heated at 95 °C for 18 h. The reaction is then cooled to ambient temperature and loaded directly onto a 40 g ISCO gold column that is then placed on top of an 80 g ISCO gold (conditioned with hexanes, eluted with 2 CV hexanes then gradient eluted with 100% MTBE over 8 CV, and then held for 6 CV) to give the 1st eluting compound ethyl (*Z*)-3-((*tert*-butoxycarbonyl)amino)acrylate **18*Z*** (1.35 g, 45.0%) as a clear, colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 9.60 (s, 1H), 7.21 (t, J = 10.5 Hz, 1H), 4.97 (d, J = 8.9 Hz, 1H), 4.14 (d, J = 7.2 Hz, 2H), 1.46 (s, 9H), 1.26 (t, J = 7.1 Hz, 3H); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 9.57 (d, J = 11.7 Hz, 1H), 7.26 (dd, J = 11.7, 8.8 Hz, 1H), 5.04 (d, J = 8.9 Hz, 1H), 4.11 (q, J = 7.1 Hz, 2H), 1.46 (s, 9H), 1.21 (t, J = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 168.4, 151.2, 140.4, 93.7, 81.5, 59.5, 27.5, 14.0. HRMS (ESI) (m/z): ($[M + H]^+$) calcd for $C_{10}H_{17}NO_4$, 216.1236; found, 216.1238; and the 2nd eluting compound ethyl (*E*)-3-((*tert*-butoxycarbonyl)amino)acrylate **18*E*** (1.52 g, 50.9%) as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.77 (t, J = 13.1 Hz, 1H), 6.83 (d, J = 12.3 Hz, 1H), 5.27 (d, J = 14.1 Hz, 1H), 4.14 (q, J = 7.1 Hz, 2H), 1.47 (s, 9H), 1.24 (t, J = 7.1 Hz, 3H); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 7.59 (dd, J = 14.0, 11.3 Hz, 1H), 5.32 (d, J = 14.0 Hz, 1H), 4.05 (q, J = 7.1 Hz, 2H), 1.44 (s, 9H), 1.18 (t, J = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 166.9, 152.3, 140.7, 97.5, 80.9, 59.1, 27.8, 14.2. HRMS (ESI) (m/z): ($[M + H]^+$) calcd for $C_{10}H_{17}NO_4$, 216.1236; found, 216.1234.

*tert-Butyl (E)-3-((tert-Butoxycarbonyl)amino)acrylate (**19E**) and tert-Butyl (Z)-3-((tert-Butoxycarbonyl)amino)acrylate (**19Z**).*[10d] To a 40 mL vial, with a stir bar, are added *tert*-buty formylcarbamate **13** (2.03 g, 13.95 mmol), (*tert*-butoxycarbonylmethylene)triphenylphosphorane (7.88 g, 20.93 mmol), and then toluene (15 mL, anhydrous). The reaction is heated at 95 °C for 18 h. The reaction is then cooled to ambient temperature and loaded directly onto a 40 g ISCO gold column that is then placed on top of an 80 g ISCO gold (conditioned with hexanes, eluted with 2 CV hexanes then gradient eluted with 100% MTBE over 8 CV, and then held for 6 CV) to give the 1st eluting compound *tert*-Butyl (*Z*)-3-((*tert*-butoxycarbonyl)amino)acrylate **19*Z***

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(2.0 g, 58.9%) as a clear, colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 9.61 (s, 1H), 7.18−7.11 (m, 1H), 4.89 (d, J = 8.9 Hz, 1H), 1.46 (s, 18H); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 9.60 (d, J = 11.7 Hz, 1H), 7.19 (dd, J = 11.7, 8.9 Hz, 1H), 4.95 (d, J = 8.9 Hz, 1H), 1.46 (s, 9H), 1.44 (s, 9H); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 168.2, 151.2, 139.7, 95.4, 81.4, 80.0, 27.8, 27.6; HRMS (ESI) (m/z): ([M − H]$^-$) calcd for $C_{12}H_{21}NO_4$, 242.1393; found, 242.1391 and the 2nd eluting compound *tert*-butyl (*E*)-3-((*tert*-butoxycarbonyl)amino)acrylate **19*E*** (1.22 g, 35.9%) as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.66 (t, J = 13.1 Hz, 1H), 6.58 (s, 1H), 5.20 (d, J = 14.0 Hz, 1H), 1.47 (s, 9H), 1.45 (s, 9H); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 10.05 (s, 1H), 7.51 (dd, J = 14.0, 11.2 Hz, 1H), 5.24 (d, J = 14.0 Hz, 1H), 1.45 (s, 9H), 1.41 (s, 9H); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 166.3, 152.3, 139.9, 99.3, 80.8, 78.8, 27.9, 27.8. HRMS (ESI) (m/z): ([M − H]$^-$) calcd for $C_{12}H_{21}NO_4$, 242.1393; found, 242.1393.

Acid-Catalyzed Conversion of 10*Z* to 10*E* Acrylate Using Crystallization to Drive the Reaction. *Methyl (E)-3-(((Benzyloxy)-carbonyl)amino)acrylate (**14E**).* To a 20 mL vial with a stir bar are added *methyl (Z)-3-(((benzyloxy)carbonyl)amino)acrylate* **14Z** (2.5 g, 10.63 mmol), ACN (5 mL), and 5 N aqueous HCl (5 mL). The reaction is stirred at ambient temperature for 18 h. The reaction was seeded with **14*E*** after 1 h. After 18 h, a thick precipitate forms that is collected by filtration, washed first with 1:1 ACN/water (30 mL) then hexanes (20 mL), and dried under house vacuum/nitrogen sweep (inverted funnel) to give methyl (*E*)-3-(((benzyloxy)carbonyl)amino)acrylate **14*E*** (2.027 g, 81%) as a white solid. The material is spectroscopically identical to that described herein.

E*-Selective Acid-Promoted Synthesis of *β*-Aminoacrylates.** *Methyl (E)-3-((Methoxycarbonyl)amino)acrylate (**30E**).*[26] Method A: To a 1000 mL 4-neck round bottom flask with a large egg-shaped stir bar are added methyl carbamate **27** (56.8 g, 757 mmol), methyl (*E*)-3-methoxyacrylate (102 mL, 946 mmol), and 5 N aqueous HCl (500 mL). The reaction is stirred at ambient temperature for 18 h. The solution turns yellow and a thick precipitate is generated. The solids are collected by filtration, washed with water (2 × 200 mL), hexanes (2 × 200 mL), and dried under a combination of house vacuum/nitrogen sweep (inverted funnel) to give *methyl (E)-3-((methoxycarbonyl)amino)-acrylate* **30*E (108.7 g, 90%) as a light yellow solid: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.86−7.76 (m, 1H), 6.95 (d, J = 12.1 Hz, 1H), 5.37 (d, J = 14.1 Hz, 1H), 3.79 (s, 3H), 3.70 (s, 3H); ^{1}H (DMSO-d_6, 500 MHz): δ 10.36 (d, J = 10.6 Hz, 1H), 7.61 (dd, J = 14.0, 11.2 Hz, 1H), 5.37 (d, J = 14.0 Hz, 1H), 3.69 (s, 3H), 3.60 (s, 3H); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 167.3, 154.0, 140.8, 98.0, 52.8, 50.9. HRMS (ESI) (m/z): ([M − H]$^-$) calcd for $C_6H_9NO_4$, 158.0454; found, 158.0453.

Method B: To a 1-neck (29/42)1000 mL flask with a stir bar are added methyl carbamate **27** (25 g, 333 mmol), methyl 3,3-dimethoxypropionate (61.4 mL, 433 mmol), and 5 N aqueous HCl (300 mL). The reaction is stirred at ambient temperature for 18 h. The solution turns yellow with a thick precipitate. The solids were collected by filtration, washed with water (2 × 200 mL) and hexanes (2 × 200 mL), and dried under a combination of house vacuum/nitrogen sweep (inverted funnel) to give *methyl (E)-3-((methoxycarbonyl)amino)-acrylate* **30*E*** (46.69 g, 88%) as a light yellow solid. ^{1}H NMR matches reported values (vide supra).

*Ethyl (E)-3-((Methoxycarbonyl)amino)acrylate (**31E**).* Method A: To a 200 mL 1-neck flask, with a stir bar, are added methyl carbamate **27** (5.0 g, 66.6 mmol) and 5 N aqueous HCl (50 mL). Then, ethyl 3-ethoxyacrylate (12.51 mL, 87 mmol) is added. All solids dissolve before a white solid begins to precipitate within approximately 30 min. The reaction is stopped after 3.5 h. The initial crystalline material from this reaction can redissolve under extended reaction times resulting in an unfilterable gel. The solids are collected by filtration, washed with water (100 mL) followed by hexanes (100 mL), and finally dried under a combination of house vacuum/nitrogen sweep (inverted funnel) to give *ethyl (E)-3-((methoxycarbonyl)amino)acrylate* **31*E*** (9.75 g, 84.6%) as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.78 (t, J = 13.0 Hz, 1H), 7.39 (d, J = 11.9 Hz, 1H), 5.36 (d, J = 14.0 Hz, 1H), 4.15 (q, J = 7.1 Hz, 2H), 3.77 (s, 3H), 1.24 (t, J = 7.1 Hz, 3H); ^{1}H (DMSO-d_6, 500 MHz): δ 10.36 (d, J = 9.8 Hz, 1H), 7.60 (dd, J = 14.0, 11.1 Hz, 1H), 5.36 (d, J = 14.0 Hz, 1H), 4.07 (q, J = 7.1 Hz, 2H), 3.70 (s, 3H), 1.18 (t, J = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 166.8, 154.0, 140.6, 98.3, 59.3, 52.8, 14.2. HRMS (ESI) (m/z): ([M − H]$^-$) calcd for $C_7H_{11}NO_4$, 172.0610; found, 172.0610.

Method B: To a 200 mL 1-neck flask, with a stir bar, are added methyl carbamate **27** (5.0 g, 66.6 mmol) and 5 N aqueous HCl (50 mL). Then, ethyl 3,3-diethoxypropanoate (16.84 mL, 87 mmol) is added. All solids dissolve before a white solid begins to precipitate within approximately 30 min. The reaction is stopped after 2.5 h. The solids are collected by filtration, washed with water (100 mL) followed by hexanes (100 mL), and finally dried under a combination of house vacuum/nitrogen sweep (inverted funnel) to give *ethyl (E)-3-((methoxycarbonyl)amino)acrylate* **31*E*** (9.7 g, 84.1%) as a white solid. The material is spectroscopically identical to that described in Method A.

*Methyl (E)-3-((Ethoxycarbonyl)amino)acrylate (**32E**).*[27] To a 500 mL 1-neck flask, with a stir bar, are added ethyl carbamate **28** (25 g, 281 mmol), methyl (*E*)-3-methoxyacrylate (37.7 mL, 351 mmol), and 5 N aqueous HCl (250 mL). The reaction is stirred at ambient temperature for 18 h. The reaction turns yellow and a thick precipitate forms. The slurry is filtered, washed with water (150 mL) followed by hexanes (100 mL), and then dried under a combination of house vacuum/nitrogen sweep (inverted funnel) to give *methyl (E)-3-((ethoxycarbonyl)amino)-acrylate* **32*E*** (42.3 g, 87%) as a light-yellow solid: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.78 (t, J = 12.9 Hz, 1H), 7.63 (s, 1H), 5.37 (d, J = 13.9 Hz, 1H), 4.19 (q, J = 7.1 Hz, 2H), 3.67 (s, 3H), 1.24 (t, J = 7.1 Hz, 3H); ^{1}H (DMSO-d_6, 500 MHz): δ 10.35 (d, J = 10.8 Hz, 1H), 7.62 (dd, J = 14.0, 11.2 Hz, 1H), 5.37 (d, J = 14.0 Hz, 1H), 4.14 (q, J = 7.1 Hz, 2H), 3.60 (s, 3H), 1.22 (t, J = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 167.3, 153.4, 140.8, 97.8, 61.6, 50.8, 14.2. HRMS (ESI) (m/z): ([M − H]$^-$) calcd for $C_7H_{11}NO_4$, 172.0610; found, 172.0611.

*Methyl (E)-3-(((Benzyloxy)carbonyl)amino)acrylate (**14E**).* Method A: To a 1 L 3-neck flask fitted with an overhead stirrer are added benzyl carbamate **10** (50 g, 331 mmol), ACN (165 mL), (*E*)-methyl 3-methoxyacrylate (45 mL, 419 mmol), and finally 5 N aqueous HCl (165 mL). After approximately 30−40 min, all solids dissolve. The reaction is stirred for 18 h at ambient temperature. A thick white precipitate is formed during this time. The solids are collected by filtration, washed first with 70:30 water/ACN (400 mL) then hexanes (400 mL), and finally dried under a combination of house vacuum/nitrogen sweep (inverted funnel) for 2 h to give *(E)-methyl 3-(((benzyloxy)carbonyl)-amino)acrylate* **14*E*** (72.44 g, 93%) as a white solid. The material is spectroscopically identical to that previously prepared herein.

Method B: To a 500 mL 1-neck flask, with a stir bar, are added benzyl carbamate **10** (20 g, 132 mmol), ACN (66 mL), methyl 3,3-dimethoxypropanoate (23.82 mL, 168 mmol), and then 5 N aqueous HCl (66 mL). All solids dissolved after approximately 30−40 min. The reaction is stirred at ambient temperature for 18 h. A thick white precipitate formed during this time. The solids are collected by filtration, washed first with 70:30 water/CAN (250 mL) then hexanes (200 mL), and finally dried under a combination of house vacuum/nitrogen sweep (inverted funnel) for 2 h to give *methyl (E)-3-(((benzyloxy)carbonyl)amino)acrylate* **14*E*** (25.32 g, 81%) as a white solid. Note: A large stir bar or an overhead stirrer is essential on a larger scale as inefficient stirring, due to the thick precipitate, can lead to diminished yields. The material is spectroscopically identical to that described in Method A.

*Ethyl (E)-3-(((Benzyloxy)carbonyl)amino)acrylate (**15E**).*[13] To a 250 mL 1-neck flask, with stir bar, are added benzyl carbamate **10** (20.6 g, 136 mmol), ACN (68 mL), (*E*)-ethyl 3-ethoxyacrylate (24.95 g, 173 mmol), and then 5 N aqueous HCl (68 mL). All solids dissolved though reaction remain cloudy and never become fully clear. The reaction is stirred at ambient temperature for 18 h. A thick white precipitate forms during this time. The solids are collected by filtration, washed first with 30% ACN/water (200 mL) then hexanes (200 mL), then dried under a combination of house vacuum/nitrogen sweep (inverted funnel) to give *(E)-ethyl 3-(((benzyloxy)carbonyl)amino)acrylate* **15*E*** (27.49 g, 81%) as a white solid. The material is spectroscopically identical to that previously prepared herein.

*Allyl (E)-3-ethoxyacrylate (**33a**).* To a 200 mL 1-neck flask, with a stir bar, are added 3-ethoxyacrylic acid (20 g, 172 mmol), K_2CO_3 (35.7 g, 258 mmol), DMF (100 mL anhydrous), and allyl bromide (25 g, 207

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mmol). The reaction is stirred at ambient temperature for 18 h. The reaction is partitioned between water (400 mL) and EtOAc (400 mL). The organic layer is washed with 10% aqueous lithium chloride solution (2 × 100 mL), saturated sodium chloride solution (100 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo to give *allyl (E)-3-ethoxyacrylate* **33a** (26.29 g, 98%) as a clear, colorless oil. ^{1}H NMR is consistent with the known desired product.[28] No further purification is required.

*Allyl (E)-3-(((Benzyloxy)carbonyl)amino)acrylate (**33E**).* To a 500 mL 1-neck flask, with a stir bar, are added benzyl carbamate **10** (15 g, 99 mmol), ACN (130 mL), 5 N aqueous HCl (150 mL), and then allyl (*E*)-3-ethoxyacrylate **33a** (20.15 g, 129 mmol) in ACN (20 mL). The reaction is further diluted with water (100 mL) and stirred at RT for 48 h. The reaction slowly produces a crystalline precipitate. The solids are collected by filtration, washing first with 1:2 ACN/water (100 mL) then hexanes (100 mL), and then dried using a combination of house vacuum/nitrogen sweep (inverted funnel) to give *allyl (E)-3-(((benzyloxy)carbonyl)amino)acrylate* **33*E*** (17.94 g, 70%) as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.83 (t, J = 13.0 Hz, 1H), 7.42−7.29 (m, 5H), 6.95 (d, J = 12.1 Hz, 1H), 5.91 (ddt, J = 17.2, 10.4, 5.7 Hz, 1H), 5.37 (d, J = 14.1 Hz, 1H), 5.30 (dd, J = 17.2, 1.6 Hz, 1H), 5.23−5.15 (m, 3H), 4.72−4.47 (m, 2H); ^{1}H (DMSO-d_6, 500 MHz): δ 10.55 (d, J = 10.2 Hz, 1H), 7.66 (dd, J = 14.0, 11.1 Hz, 1H), 7.49−7.00 (m, 5H), 5.93 (ddt, J = 17.3, 10.6, 5.4 Hz, 1H), 5.41 (d, J = 14.0 Hz, 1H), 5.28 (dd, J = 17.2, 1.7 Hz, 1H), 5.21−5.18 (d, J = 14.3 Hz, 3H), 4.57 (dt, J = 5.5, 1.5 Hz, 2H); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 166.3, 153.4, 140.8, 135.8, 133.1, 128.5, 128.3, 128.2, 117.5, 98.1, 67.0, 63.9. HRMS (ESI) (m/z): ([M − H]$^-$) calcd for $C_{14}H_{15}NO_4$, 260.0923; found, 260.0923.

*Prop-2-yn-1-yl 3,3-Dimethoxypropanoate (**34a**).* To a 200 mL 1-neck flask, with a stir bar, are added methyl 3,3-dimethoxypropanoate (15 mL, 106 mmol) and 2 N aqueous sodium hydroxide solution (61.0 mL, 122 mmol). The mixture is heated at 50 °C (internal temp) for 1 h and then cooled to ambient temperature. The reaction is diluted with DCM (150 mL) and transferred to a separatory funnel with the aid of water (25 mL). 5 N aqueous HCl (25.6 mL) is added and mixed well. The aqueous layer is washed with DCM (2 × 100 mL). The combined organic layers are dried over Na_2SO_4, filtered, and concentrated in vacuo to give the intermediate, 3,3-dimethoxypropanoic acid,[29] as a clear, colorless oil, which is used directly in the next step. To the acid from the previous step, in a 1 L 1-neck flask, with a stir bar, are added DCM (200 mL), followed by EDCI (23.37 g, 122 mmol), 4-dimethylaminopyridine (DMAP) (0.648 g, 5.30 mmol), and prop-2-yn-1-ol (7.10 mL, 122 mmol). The reaction is stirred at ambient temperature for 18 h. The reaction is washed with 1 N aqueous HCl (100 mL), saturated $NaHCO_3$ solution (100 mL), saturated NaCl solution (100 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo to give *prop-2-yn-1-yl 3,3-dimethoxypropanoate* **34a** (12.17 g, 66.7%) as a clear, colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 4.82 (t, J = 5.9 Hz, 1H), 4.68 (d, J = 2.4 Hz, 2H), 3.34 (s, 6H), 2.68 (d, J = 6.0 Hz, 2H), 2.46 (t, J = 2.5 Hz, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 168.8, 100.9, 77.3, 74.9, 53.4, 52.0, 38.5. LRMS (ESI) (m/z): ([M − H]$^+$) calcd for $C_8H_{12}O_4$, 173.0; found, 173.0.

*Prop-2-yn-1-yl (E)-3-(((Benzyloxy)carbonyl)amino)acrylate (**34E**).* To a 250 mL 1-neck flask, with a stir bar, are added benzyl carbamate **10** (8.3 g, 54.9 mmol) and prop-2-yn-1-yl 3,3-dimethoxypropanoate **34a** (12.29 g, 71.4 mmol) in ACN (50 mL), followed by 5 N aqueous HCl (50 mL). The reaction is stirred at ambient temperature for 2 days. The solids are collected by filtration, first washing with water (2 × 25 mL) then hexanes (50 mL), and then drying under a combination of house vacuum/nitrogen sweep (inverted funnel) to give *prop-2-yn-1-yl (E)-3-(((benzyloxy)carbonyl)amino)acrylate* **34*E*** (10.2 g, 71.7%) as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.85 (t, J = 13.0 Hz, 1H), 7.37−7.30 (m, 5H), 7.23 (s, 1H), 5.38 (d, J = 14.1 Hz, 1H), 5.18 (s, 2H), 4.70 (d, J = 2.4 Hz, 2H), 2.44 (t, J = 2.5 Hz, 1H); ^{1}H (DMSO-d_6, 500 MHz): δ 10.61 (s, 1H), 7.69 (dd, J = 14.0, 11.2 Hz, 1H), 7.45−7.23 (m, 5H), 5.42 (d, J = 14.0 Hz, 1H), 5.19 (s, 2H), 4.72 (d, J = 2.5 Hz, 2H), 3.51 (t, J = 2.4 Hz, 1H); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 166.0, 153.3, 141.5, 135.7, 128.5, 128.3, 128.2, 97.4, 78.8, 77.3, 67.1, 51.1. HRMS (ESI) (m/z): ([M − H]$^-$) calcd for $C_{14}H_{13}NO_4$, 258.0767; found, 258.0767.

*Benzyl (E)-3-Ethoxyacrylate (**35a**).* To a 200 mL 1-neck flask, with a stir bar, are added 3-ethoxyacrylic acid (20 g, 172 mmol), K_2CO_3 (35.7 g, 258 mmol), DMF (100 mL, anhydrous), and benzyl bromide (21.51 mL, 181 mmol). The reaction is stirred at ambient temperature for 18 h. The reaction is partitioned between water (300 mL) and MTBE (500 mL). The organic layer is washed with 10% aqueous LiCl solution (3 × 150 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo to give *benzyl (E)-3-ethoxyacrylate* **35a** (34.77 g, 98%) as a clear, colorless oil. ^{1}H NMR is consistent with the known desired product.[28] No further purification is required.

*Benzyl (E)-3-(((Benzyloxy)carbonyl)amino)acrylate (**35E**).*[30] To a 1 L 4-neck flask, with an extra-large stir bar, are added benzyl carbamate **6** (25.5 g, 169 mmol), a solution of benzyl (*E*)-3-ethoxyacrylate **35a** (34.77 g, 169 mmol) in ACN (200 mL), and then 5 N aqueous HCl (200 mL). The reaction is stirred at ambient temperature for 18 h. A thick suspension forms during this period. The solids are collected by filtration, first washing with 1:1 ACN/water (500 mL) then hexanes (300 mL), and then drying using a combination of house vacuum/nitrogen sweep (inverted funnel) to give *benzyl (E)-3-(((benzyloxy)-carbonyl)amino)acrylate* **35*E*** (48.07 g, 92%) as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.84 (dd, J = 14.0, 12.0 Hz, 1H), 7.40−7.29 (m, 10H), 6.99 (d, J = 12.1 Hz, 1H), 5.39 (d, J = 14.1 Hz, 1H), 5.18 (s, 2H), 5.15 (s, 2H); ^{1}H (DMSO-d_6, 500 MHz): δ 10.56 (s, 1H), 7.68 (d, J = 14.0 Hz, 1H), 7.54−7.00 (m, 10H), 5.43 (d, J = 14.0 Hz, 1H), 5.18 (s, 2H), 5.12 (s, 2H); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 166.6, 153.3, 141.0, 136.5, 135.8, 128.5, 128.4, 128.3, 128.2, 127.9, 127.9, 98.2, 67.0, 64.9. HRMS (ESI) (m/z): ([M − H]$^-$) calcd for $C_{18}H_{17}NO_4$, 310.1080; found, 310.1079.

*Methyl (E)-3-((((9H-Fluoren-9-yl)methoxy)carbonyl)amino)-acrylate (**36E**).* To a 20 mL vial, with a stir bar, are added 9-fluorenylmethyl carbamate **29** (1.0 g, 4.18 mmol), *p*TsOH monohydrate (0.040 g, 0.209 mmol), ACN (8 mL), and methyl (*E*)-3-methoxyacrylate (0.584 mL, 5.43 mmol). The suspension is stirred at 50 °C (heating block temperature) for 18 h. The reaction is monitored by UPLC/MS. The solids never completely dissolve. The reaction is cooled to ambient temperature and the solids are collected by filtration, washed with ACN (30 mL) and hexanes (50 mL), and then dried under a combination of house vacuum/nitrogen sweep (inverted funnel) to give methyl (*E*)-3-((((9*H*-fluoren-9-yl)methoxy)carbonyl)amino)-acrylate **36*E*** (1.29 g, 95%) as a white solid: ^{1}H (DMSO-d_6, 500 MHz): δ 10.41 (d, J = 10.6 Hz, 1H), 7.90 (dt, J = 7.5, 0.9 Hz, 2H), 7.69 (d, J = 7.5 Hz, 2H), 7.59 (dd, J = 14.1, 11.0 Hz, 1H), 7.48−7.38 (m, 2H), 7.35 (td, J = 7.4, 1.2 Hz, 2H), 5.39 (d, J = 14.0 Hz, 1H), 4.57 (d, J = 6.3 Hz, 2H), 4.31 (t, J = 6.3 Hz, 1H), 3.60 (s, 3H); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 167.2, 153.4, 143.4, 140.8, 140.5, 127.7, 127.1, 125.0, 120.2, 98.3, 66.5, 50.9, 46.4. HRMS (ESI) (m/z): ([M + H]$^+$) calcd for $C_{19}H_{17}NO_4$, 324.1236, found, 324.1232.

*Ethyl (E)-3-((((9H-Fluoren-9-yl)methoxy)carbonyl)amino)acrylate (**37E**).* To a 40 mL vial, with stir bar, are added 9-fluorenylmethyl carbamate **29** (2.0 g, 8.36 mmol), *p*TsOH monohydrate (0.079 g, 0.418 mmol), ACN (8 mL), and ethyl (*E*)-3-ethoxyacrylate (1.567 g, 10.87 mmol). The suspension is stirred at 50 °C (heating block temperature) for 18 h. The reaction is monitored by UPLC/MS. The solids never completely dissolve. The reaction is cooled to ambient temperature and the solids are collected by filtration, washed with ACN (50 mL) and hexanes (50 mL), and then dried under a combination of house vacuum/nitrogen sweep (inverted funnel) to give *ethyl (E)-3-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)acrylate* **37*E*** (1.974 g, 70%) as a white solid: ^{1}H (DMSO-d_6, 500 MHz): δ 10.39 (d, J = 11.1 Hz, 1H), 7.90 (d, J = 7.5 Hz, 2H), 7.69 (d, J = 7.4 Hz, 2H), 7.57 (dd, J = 14.0, 11.1 Hz, 1H), 7.42 (t, J = 7.4 Hz, 2H), 7.35 (dd, J = 8.1, 6.8 Hz, 2H), 5.36 (d, J = 14.0 Hz, 1H), 4.58 (d, J = 6.2 Hz, 2H), 4.31 (t, J = 6.3 Hz, 1H), 4.06 (q, J = 7.0 Hz, 2H), 1.23−1.08 (m, 2H); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 166.7, 153.4, 143.4, 140.8, 140.4, 127.7, 127.1, 124.9, 120.2, 98.7, 66.5, 59.3, 46.4, 14.3. HRMS (ESI) (m/z): ([M + H]$^+$) calcd for $C_{20}H_{19}NO_4$, 338.1392; found, 338.1388.

*Benzyl (E)-3-((((9H-Fluoren-9-yl)methoxy)carbonyl)amino)-acrylate (**38E**).* To a 40 mL vial, with a stir bar, are added 9-

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fluorenylmethyl carbamate **29** (2.0 g, 8.36 mmol), *p*TsOH monohydrate (0.079 g, 0.418 mmol), ACN (16 mL), and benzyl (*E*)-3-ethoxyacrylate **35a** (2.241 g, 10.87 mmol). The suspension is stirred at 50 °C (heating block temperature) for 18 h. The reaction is monitored by UPLC/MS. The solids never completely dissolve. The reaction is cooled to ambient temperature and the solids are collected by filtration, washed with ACN (50 mL) and hexanes (50 mL), and then dried under a combination of house vacuum/nitrogen sweep (inverted funnel) to give *benzyl (E)-3-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)acrylate* **38*E*** (3.1475 g, 94%) as a white solid.: ^{1}H (DMSO-d_6, 500 MHz): δ ^{1}H NMR 10.48−10.39 (m, 1H), 7.90 (d, J = 7.5 Hz, 2H), 7.69 (d, J = 7.5 Hz, 2H), 7.63 (dd, J = 14.0, 11.1 Hz, 1H), 7.47−7.22 (m, 9H), 5.43 (d, J = 14.0 Hz, 1H), 5.11 (s, 2H), 4.58 (d, J = 6.3 Hz, 2H), 4.31 (t, J = 6.2 Hz, 1H); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 166.6, 153.4, 143.4, 140.9, 140.8, 136.5, 128.4, 127.93, 127.91, 127.7, 127.1, 124.9, 120.2, 98.3, 66.5, 64.9, 46.4. HRMS (ESI) (m/z): ([M + H]$^+$) calcd for $C_{25}H_{21}NO_4$, 400.1549; found, 400.1544.

Z-Selective Acid-Promoted Synthesis of β-Aminoacrylates. *Methyl (Z)-3-((Methoxycarbonyl)amino)acrylate (**30Z**).*[31] To a 200 mL 1-neck flask, with a stir bar and an air condenser, are added methyl carbamate **27** (2 g, 26.6 mmol), (1*S*)-(+)-10-CAS (0.309 g, 1.332 mmol), toluene (52 mL, anhydrous), and then methyl (*E*)-3-methoxyacrylate (3.72 mL, 34.6 mmol). The reaction is heated at 65 °C for 18 h. The reaction is cooled to ambient temperature and loaded directly onto a 40 g ISCO gold silica gel column, which is then placed on top of an 80 g ISCO gold column (conditioned with hexanes, eluted with 2 CV of hexanes then gradient eluted with 60% MTBE/hexanes over 8 CV, and then held for 6 CV) to give *methyl (Z)-3-((methoxycarbonyl)amino)acrylate* **30Z** (2.82 g, 67%) as a clear, colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 9.73 (s, 1H), 7.31−7.10 (m, 1H), 5.03 (d, J = 8.9 Hz, 1H), 3.77 (s, 3H), 3.69 (s, 3H); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 9.71 (d, J = 11.5 Hz, 1H), 7.33 (dd, J = 11.7, 8.9 Hz, 1H), 5.12 (d, J = 8.9 Hz, 1H), 3.77 (s, 3H), 3.68 (s, 3H); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 168.6, 153.1, 140.3, 94.3, 53.1, 51.0. HRMS (ESI) (m/z): ([M − H]$^-$) calcd for $C_6H_9NO_4$, 158.0454; found, 158.0449.

*Methyl (Z)-3-((Ethoxycarbonyl)amino)acrylate (**32Z**).*[27] To a 200 mL 1-neck flask, with a stir bar and an air condenser, are added ethyl carbamate [urethane] **28** (2 g, 22.45 mmol), (1*S*)-(+)-10-CAS (0.261 g, 1.122 mmol), toluene (44 mL, anhydrous), and then methyl (*E*)-3-methoxyacrylate (3.14 mL, 29.2 mmol). The reaction is heated at 65 °C for 18 h. The reaction is cooled to ambient temperature and loaded directly onto a 40 g ISCO gold silica gel column, which is then placed on top of an 80 g ISCO gold column (conditioned with hexanes, eluted with 2 CV of hexanes then gradient eluted with 60% MTBE/hexanes over 8 CV, and then held for 6 CV) to give methyl *(Z)-3-((ethoxycarbonyl)amino)acrylate* **32Z** (2.56 g, 66%) as a clear, colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 9.70 (s, 1H), 7.24 (t, J = 5.8 Hz, 1H), 5.03 (d, J = 8.9 Hz, 1H), 4.21 (q, J = 7.1 Hz, 2H), 3.69 (d, J = 0.8 Hz, 3H), 1.27 (t, J = 7.1 Hz, 3H); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 9.65 (d, J = 11.7 Hz, 1H), 7.30 (dd, J = 11.7, 8.9 Hz, 1H), 5.09 (d, J = 8.9 Hz, 1H), 4.18 (q, J = 7.1 Hz, 2H), 3.65 (s, 3H), 1.24 (t, J = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 168.6, 152.5, 140.3, 94.2, 62.1, 51.0, 14.0. HRMS (ESI) (m/z): ([M + H]$^+$) calcd for $C_7H_{11}NO_4$, 174.0766; found, 174.0762.

*Methyl (Z)-3-((Propoxycarbonyl)amino)acrylate (**44Z**).* To a 200 mL 1-neck flask, with a stir bar and an air condenser, are added propyl carbamate **39** (2 g, 19.39 mmol), (1*S*)-(+)-10-CAS (0.225 g, 0.970 mmol), toluene (40 mL, anhydrous), and then methyl (*E*)-3-methoxyacrylate (2.71 mL, 25.2 mmol). The reaction is heated at 65 °C for 18 h. The reaction is cooled to ambient temperature and loaded directly onto a 40 g ISCO gold silica gel column, which is then placed on top of an 80 g ISCO gold column (conditioned with hexanes, eluted with 2 CV of hexanes then gradient eluted with 50% MTBE/hexanes over 8 CV, and then held for 6 CV) to give methyl *(Z)-3-((propoxycarbonyl)amino)acrylate* **44Z** (2.43 g, 67%) as a clear, colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 9.76 (s, 1H), 7.35−7.22 (m, 4.9 Hz, 1H), 5.08 (d, J = 8.9 Hz, 1H), 4.16 (t, J = 6.7 Hz, 2H), 3.74 (s, 3H), 1.71 (q, J = 7.1 Hz, 2H), 0.98 (t, J = 7.4 Hz, 3H); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 9.67 (d, J = 11.7 Hz, 1H), 7.30 (dd, J = 11.8, 8.8 Hz, 1H), 5.09 (d, J = 8.9 Hz, 1H), 4.09 (t, J = 6.6 Hz, 2H), 3.65 (s, 3H), 1.84−1.43 (m, 2H), 0.90 (t, J = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 168.6, 152.6, 140.4, 94.2, 67.4, 51.0, 21.6, 9.9. HRMS (ESI) (m/z): ([M − H]$^-$) calcd for $C_8H_{13}NO_4$, 186.0767; found, 186.0766.

*Methyl (Z)-3-((Isopropoxycarbonyl)amino)acrylate (**45Z**).* To a 200 mL 1-neck flask, with a stir bar and an air condenser, are added propyl carbamate **40** (2 g, 19.39 mmol), (1*S*)-(+)-10-CAS (0.225 g, 0.970 mmol), toluene (40 mL, anhydrous), and then methyl (*E*)-3-methoxyacrylate (2.71 mL, 25.2 mmol). The reaction is heated at 65 °C for 18 h. The reaction is cooled to ambient temperature and loaded directly onto a 40 g ISCO gold silica gel column, which is then placed on top of an 80 g ISCO gold column (conditioned with hexanes, eluted with 2 CV of hexanes then gradient eluted with 50% MTBE/hexanes over 8 CV, and then held for 6 CV) to give *methyl (Z)-3-((isopropoxycarbonyl)amino)acrylate* **45Z** as a clear, colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz) d ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.62 (s, 1H), 7.27−7.16 (m, 1H), 5.16−4.78 (m, 2H), 3.66 (s, 3H), 1.23 (d, J = 6.3 Hz, 6H); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 9.60 (d, J = 11.7 Hz, 1H), 7.30 (dd, J = 11.7, 8.9 Hz, 1H), 5.08 (d, J = 8.9 Hz, 1H), 4.91 (p, J = 6.2 Hz, 1H), 3.65 (s, 3H), 1.24 (d, J = 6.3 Hz, 6H); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 168.7, 152.0, 140.4, 94.0, 69.9, 51.0, 21.4. HRMS (ESI) (m/z): ([M − H]$^-$) calcd for $C_8H_{13}NO_4$, 186.0767; found, 186.0764.

*Methyl (Z)-3-(((Benzyloxy)carbonyl)amino)acrylate (**14Z**).* To a 200 mL 1-neck flask, with a stir bar and an air condenser, are added benzyl carbamate **10** (8.0 g, 52.9 mmol), (1*S*)-(+)-10-CAS (0.615 g, 2.65 mmol), toluene (120 mL, anhydrous), and then methyl (*E*)-3-methoxyacrylate (7.40 mL, 68.8 mmol). The reaction is heated at 65 °C for 18 h. The reaction is cooled to ambient temperature and loaded directly onto a 125 g ISCO column, which is then placed on top of a 220 g ISCO gold column (conditioned with hexanes, eluted with 2 CV hexanes then gradient eluted with 30% MTBE/hexanes over 6 CV, and then held for 6 CV) to give methyl *(Z)-3-(((benzyloxy)carbonyl)amino)acrylate* **14Z** (9.07 g, 73%) as a clear colorless oil. The material is spectroscopically identical to that previously prepared herein.

*Ethyl (Z)-3-(((Benzyloxy)carbonyl)amino)acrylate (**15Z**).* To a 200 mL 1-neck flask, with a stir bar and an air condenser, are added benzyl carbamate **10** (8.0 g, 52.9 mmol), (1*S*)-(+)-10-CAS (0.615 g, 2.65 mmol), toluene (120 mL, anhydrous), and then ethyl (*E*)-3-ethoxyacrylate (10.01 mL, 68.8 mmol). The reaction is stirred at 65 °C (heating block temp) for 18 h. The reaction is cooled to ambient temperature and loaded directly onto a 125 g ISCO column, which is then placed on top of a ISCO 220 g gold column (conditioned with hexanes, eluted with 2 CV hexanes then gradient eluted with 30% MTBE/hexanes over 6 CV, and then held for 4 CV) to give *ethyl (Z)-3-(((benzyloxy)carbonyl)amino)acrylate* **15Z** (9.0 g, 68%) as a clear, colorless oil. The material is spectroscopically identical to that previously prepared herein.

*(1R,2S,5R)-2-Isopropyl-5-methylcyclohexyl Carbamate (**41**).* To a 500 mL 1-neck flask, with a stir bar, is added tetrahydrofuran (THF) (100 mL, anhydrous). The flask is cooled in an ice/water bath and then (−)-menthyl chloroformate (15 mL, 70.6 mmol) is added, followed by the careful addition of ammonium hydroxide solution (150 mL, 956 mmol, 28−30 wt %) over 10 min. The reaction is stirred for 5 min under cooling and then for 18 h at ambient temperature. The reaction is diluted with EtOAc (350 mL) and water (200 mL). The organic layer is washed with saturated aqueous $NaHCO_3$ solution (100 mL), saturated aqueous NaCl solution (50 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo to give (1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl carbamate **41** (14.01 g, 100%) as a white crystalline solid. ^{1}H NMR is consistent with the known desired product.[32] No further purification is required.

*Methyl (Z)-3-(((((1R,2S,5R)-2-Isopropyl-5-methylcyclohexyl)oxy)carbonyl)amino)acrylate (**46Z**).* To a 40 mL vial, with a stir bar, are added (1*S*)-(+)-10-CAS (0.117 g, 0.502 mmol), (1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl carbamate **41** (2 g, 10.04 mmol), toluene (20 mL, anhydrous), and then methyl (*E*)-3-methoxyacrylate (1.403 mL, 13.05 mmol). The capped vial is heated at 65−70 °C for 18 h. The reaction is cooled to ambient temperature and loaded directly onto a 40 g ISCO gold column, which is then placed on top of an 80 g ISCO gold

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column (conditioned with hexanes, eluted with 2 CV hexanes then gradient eluted with 20% MTBE/hexanes over 8 CV, and then held for 6 CV) to give methyl (*Z*)-3-(((((1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl)oxy)carbonyl)amino)acrylate **46*Z*** (2.02 g, 71%) as a clear, colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 9.77−9.56 (m, 1H), 7.32−7.21 (m, 1H), 5.02 (d, *J* = 8.9 Hz, 1H), 4.62 (td, *J* = 10.9, 4.4 Hz, 1H), 3.69 (s, 3H), 2.02 (dt, *J* = 11.6, 3.5 Hz, 1H), 1.88 (pd, *J* = 7.0, 2.7 Hz, 1H), 1.65 (dt, *J* = 12.8, 2.9 Hz, 2H), 1.53−1.41 (m, 1H), 1.35 (t, *J* = 11.7 Hz, 1H), 1.08−0.96 (m, 2H), 0.91−0.82 (m, 7H), 0.74 (d, *J* = 6.9 Hz, 3H); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 9.65 (d, *J* = 11.7 Hz, 1H), 7.31 (dd, *J* = 11.7, 8.9 Hz, 1H), 5.10 (d, *J* = 8.9 Hz, 1H), 4.59 (td, *J* = 10.9, 4.4 Hz, 1H), 3.65 (s, 3H), 1.99−1.91 (m, 1H), 1.84 (pd, *J* = 7.0, 2.6 Hz, 1H), 1.63 (dt, *J* = 13.4, 3.5 Hz, 2H), 1.52−1.42 (m, 1H), 1.39 (ddt, *J* = 14.4, 11.3, 3.2 Hz, 1H), 1.03 (qd, *J* = 11.7, 8.8 Hz, 2H), 0.87 (t, *J* = 7.1 Hz, 7H), 0.74 (d, *J* = 7.0 Hz, 3H); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 168.6, 152.2, 140.4, 94.2, 75.7, 51.0, 46.4, 40.4, 33.6, 30.8, 25.8, 23.0, 21.7, 20.3, 16.2. HRMS (ESI) (*m*/*z*): ([M − H]$^-$) calcd for $C_{15}H_{25}NO_4$, 282.1706; found, 282.1701.

*Methyl (Z)-3-((Phenoxycarbonyl)amino)acrylate (**47Z**).* To a 200 mL 1-neck flask, with a stir bar and an air condenser, are added phenyl carbamate **42** (2 g, 14.58 mmol), (1*S*)-(+)-10-CAS (0.169 g, 0.729 mmol), toluene (30 mL, anhydrous), and then methyl (*E*)-3-methoxyacrylate (2.04 mL, 19.0 mmol). The reaction is heated at 65 °C for 18 h. The reaction is cooled to ambient temperature and loaded directly onto a 40 g ISCO gold silica gel column, which is then placed on top of an 80 g ISCO gold column (conditioned with hexanes, eluted with 2 CV of hexanes then gradient eluted with 30% MTBE/hexanes over 8 CV, and then held for 6 CV) to give *methyl (Z)-3-((phenoxycarbonyl)amino)acrylate* **47Z** (2.46 g, 76%) as a clear, colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz): δ ^{1}H NMR (500 MHz, Chloroform-*d*): δ 10.08 (d, *J* = 11.3 Hz, 1H), 7.37 (t, *J* = 7.9 Hz, 2H), 7.31 (dd, *J* = 11.5, 8.9 Hz, 1H), 7.23 (t, *J* = 7.4 Hz, 1H), 7.18−7.09 (m, 2H), 5.17 (d, *J* = 8.9 Hz, 1H), 3.74 (s, 3H); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 10.06 (d, *J* = 11.6 Hz, 1H), 7.45 (dd, *J* = 8.6, 7.4 Hz, 2H), 7.39 (dd, *J* = 11.6, 8.9 Hz, 1H), 7.30 (td, *J* = 7.4, 1.2 Hz, 1H), 7.27 (dd, *J* = 8.5, 1.4 Hz, 2H), 5.24 (d, *J* = 8.9 Hz, 1H), 3.70 (s, 2H); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 168.4, 151.2, 150.1, 139.9, 129.5, 126.1, 121.6, 95.8, 51.2. . HRMS (ESI) (*m*/*z*): ([M + H]$^+$) calcd for $C_{11}H_{11}NO_4$, 222.0766; found, 222.0759.

*2,2,2-Trichloroethyl Carbamate (**43**).* To a 250 mL 1-neck flask, with a stir bar, and cooled in ice/water is added ammonium hydroxide solution (145 mL, 1090 mmol, 28−30 wt %), followed by 2,2,2-trichloroethyl chloroformate (15 mL, 109 mmol) over 10 min. The reaction is stirred for 45 min at 0 °C. The reaction is diluted with DCM (400 mL). The organic layer is washed with water (50 mL), saturated NaCl solution (50 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo to give *2,2,2-trichloroethyl carbamate* **43** (20.9 g, 100%) as a white solid. ^{1}H NMR is consistent with the known desired product.[33] No further purification is required.

*Methyl (Z)-3-(((2,2,2-trichloroethoxy)carbonyl)amino)acrylate (**48Z**).* To a 40 mL vial, with a stir bar, are added 2,2,2-trichloroethyl carbamate **43** (1.0 g, 5.20 mmol), (1*S*)-(+)-10-CAS (0.060 g, 0.260 mmol), toluene (10 mL, anhydrous), and then methyl (*E*)-3-methoxyacrylate (0.726 mL, 6.76 mmol). The reaction is heated at 65 °C for 5 h and then stirred for 18 h at ambient temperature. The reaction is cooled to ambient temperature and loaded directly onto a 24 g ISCO gold column that is then placed on top of an 80 g ISCO gold column (conditioned with hexanes, eluted with 2 CV hexanes then gradient eluted with 40% MTBE/hexanes over 8 CV, and then held for 8 CV) to give *methyl (Z)-3-(((2,2,2-trichloroethoxy)carbonyl)amino)acrylate* **48Z** (0.9002 g, 63%) as a clear, colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 10.00 (d, *J* = 11.2 Hz, 1H), 7.31−7.11 (m, 1H), 5.17 (d, *J* = 8.9 Hz, 1H), 4.80 (s, 2H), 3.73 (s, 3H); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 9.97 (d, *J* = 11.5 Hz, 1H), 7.34 (dd, *J* = 11.5, 8.9 Hz, 1H), 5.23 (d, *J* = 8.9 Hz, 1H), 4.98 (s, 2H), 3.68 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 168.5, 151.2, 139.6, 96.2, 95.0, 74.3, 51.2. HRMS (ESI) (*m*/*z*): ([M + H]$^+$) calcd for $C_7H_8Cl_3NO_4$, 275.9597; found, 275.9593.

Imide Nucleophiles for Synthesis of (*E*)-β-Aminoacrylates. *Methyl (E)-3-((Bis-tert-butoxycarbonyl)amino)acrylate (**62E**).* To a 1 L 1-neck flask, with a stir bar, are added DiBOC amine **55** (36.6 g, 169 mmol), DABCO (1.891 g, 16.86 mmol), DCM (100 mL), and then methyl propiolate (15 mL, 169 mmol). The reaction is stirred at ambient temperature for 18 h. The reaction is concentrated in vacuo and the residue is dissolved in a minimum volume and DCM and loaded on to a 50 g Biotage Snap column, which is then placed on top of a 220 g ISCO gold column (conditioned with hexanes, eluted with 1 CV hexanes then gradient eluted with 20% MTBE/hexanes over 3 CV, and then held for 6 CV) to give *methyl (E)-3-((bis-tert-butoxycarbonyl)-amino)acrylate* **62E** (49.18 g, 97%) as a clear, colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.83 (d, *J* = 14.5 Hz, 1H), 5.59 (d, *J* = 14.5 Hz, 1H), 3.70 (s, 3H), 1.52 (s, 18H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 167.53, 150.06, 138.61, 101.60, 84.75, 51.31, 27.64. HRMS (ESI) (*m*/*z*): ([M − H]$^-$) calcd for $C_{14}H_{23}NO_6$, 300.1447; found, 300.1443.

*Methyl (E)-3-((tert-Butoxycarbonyl)amino)acrylate (**17E**).*[17] To a 40 mL vial, with a stir bar, is added magnesium perchlorate (0.370 g, 1.66 mmol), followed by a solution of methyl (*E*)-3-((*tert*-butoxycarbonyl)amino)acrylate **62E** (1.66 g, 8.26 mmol) in ACN (20 mL, anhydrous). The reaction is stirred at ambient temperature for 24 h. The reaction is diluted with MTBE (200 mL), washed with saturated aqueous $NaHCO_3$ solution (50 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude is chromatographed on silica, loaded in a minimal amount of DCM onto a 24 g ISCO gold column, and then placed on top of an 80 g ISCO gold column (conditioned with hexanes, eluted with 1 CV hexanes then gradient eluted with 40% MTBE/hexanes over 6 CV, and then held for 6 CV) to give *methyl (E)-3-((tert-butoxycarbonyl)amino)acrylate* **17E** (1.51 g, 91%) as a white solid. The material is spectroscopically identical to that previously prepared herein.

*Ethyl (E)-3-((Bis-tert-butoxycarbonyl)amino)acrylate (**63E**).* To a 500 mL 1-neck flask, with a stir bar and cooled in an ice/water bath, are added DiBOC amine **55** (21.44 g, 99 mmol), DABCO (1.107 g, 9.87 mmol), DCM (200 mL), and then ethyl propiolate (10 mL, 99 mmol) in DCM (40 mL). After addition is complete, the cooling bath is removed, and the reaction is stirred at ambient temperature for 1 h. The reaction is split into batches and each is loaded directly onto a 125 g ISCO column that is then placed on top of a 220 g ISCO gold column (conditioned with hexanes, eluted with 1 CV hexanes then gradient eluted with 20% MTBE/hexanes over 4 CV, and then held for 4 CV) to give *ethyl (E)-3-(bis(tert-butoxycarbonyl)amino)acrylate* **63E** (29.6 g, 95%) as a clear, colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.81 (d, *J* = 14.5 Hz, 1H), 5.56 (d, *J* = 14.5 Hz, 1H), 4.15 (q, *J* = 7.1 Hz, 2H), 1.50 (s, 18H), 1.24 (t, *J* = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 167.1, 150.1, 138.4, 102.1, 84.7, 60.1, 27.7, 14.3. HRMS (ESI) (*m*/*z*): ([M + H]$^+$) calcd for $C_{15}H_{25}NO_6$, 316.1760; found, 316.1768.

*Ethyl (E)-3-((tert-Butoxycarbonyl)amino)acrylate (**18E**).*[14] To a 40 mL vial, with stir bar, are added ethyl (*E*)-3-(bis(*tert*-butoxycarbonyl)-amino)acrylate **63E** (2.5 g, 7.93 mmol), ACN (20 mL, anhydrous), and then magnesium perchlorate (0.354 g, 1.585 mmol). The reaction is stirred at ambient temperature for 18 h. The reaction is diluted with EtOAc (200 mL), saturated aqueous $NaHCO_3$ solution (50 mL), and saturated aqueous NaCl solution (25 mL). The organic layer is dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude is loaded in DCM onto a 24 g ISCO gold column that is then placed on top of an 80 g ISCO gold column (conditioned with hexanes, eluted with 1 CV hexanes then gradient eluted with 40% EtOAc/hexanes over 6 CV, and then held for 6 CV to give *ethyl (E)-3-((tert-butoxycarbonyl)amino)-acrylate* **18E**) (1.613 g, 95%) as a white solid. The material is spectroscopically identical to that previously prepared herein.

*tert-Butyl (E)-3-((Bis-tert-butoxycarbonyl)amino)acrylate (**64E**).* To a 500 mL 1-neck flask, with a stir bar and cooled in an ice/water bath, are added DiBOC amine **55** (25.8 g, 119 mmol), DABCO (1.334 g, 11.89 mmol), DCM (260 mL), and then *tert*-butyl propiolate (16.32 mL, 119 mmol) in DCM (40 mL). After addition is complete, the cooling bath is removed, and the reaction is stirred at ambient temperature for 1 h. The reaction is concentrated in vacuo then redissolved in a minimum amount of DCM and loaded onto a 125 g ISCO column that is then placed on top of a 330 g ISCO gold column (conditioned with hexanes, eluted with 1 CV hexanes then gradient eluted with 20% MTBE/hexanes over 5 CV, and then held for 5 CV) to give *tert-butyl (E)-3-(bis(tert-butoxycarbonyl)amino)acrylate* **64E** (40.34 g, 99%) as a clear, colorless oil that solidifies on standing: ^{1}H NMR

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($CDCl_3$, 500 MHz): δ 7.68 (d, J = 14.5 Hz, 1H), 5.46 (d, J = 14.5 Hz, 1H), 1.48 (s, 18H), 1.41 (s, 9H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 166.4, 150.2, 137.6, 103.9, 84.5, 80.0, 28.1, 27.6. HRMS (ESI) (m/z): ($[M + H]^+$) calcd for $C_{17}H_{29}NO_6$, 344.2073; found, 344.2068.

*tert-Butyl (E)-3-((tert-Butoxycarbonyl)amino)acrylate (**19E**).*[10d] To a 40 mL vial, with a stir bar, are added *tert*-butyl (*E*)-3-(bis(*tert*-butoxycarbonyl)amino)acrylate **64*E*** (2.5 g, 7.28 mmol), ACN (20 mL, anhydrous), and then magnesium perchlorate (0.325 g, 1.456 mmol). The reaction is stirred at ambient temperature for 18 h. The reaction is diluted with EtOAc (200 mL), saturated aqueous $NaHCO_3$ solution (50 mL), and saturated aqueous NaCl solution (25 mL). The organic layer is dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude material is loaded in a minimal amount of DCM onto a 24 g ISCO gold column that is then placed on top of an 80 g ISCO gold column (conditioned with hexanes, eluted with 1 CV hexanes then gradient eluted with 40% EtOAc/hexanes over 6 CV, and then held for 6 CV) to give *tert-butyl (E)-3-((tert-butoxycarbonyl)amino)acrylate* **19*E*** (1.65 g, 93%) as a clear, colorless oil that solidified on standing. The material is spectroscopically identical to that previously prepared herein.

*Methyl (E)-3-(((Methoxycarbonyl),(tert-butoxycarbonyl))amino)-acrylate (**65E**).* To a 200 mL 1-neck flask, with a stir bar, are added *tert*-butyl methyl iminodicarbonate **56** (5.0 g, 28.5 mmol), DABCO (0.320 g, 2.85 mmol), and DCM (100 mL, anhydrous), and then methyl propiolate (2.54 mL, 28.5 mmol) is added dropwise. The reaction is stirred at ambient temperature for 18 h. The reaction is concentrated to reduce the volume of DCM to ~20 mL and loaded onto a 24 g ISCO gold column, which is then placed on top of an ISCO 120 g gold column (conditioned with DCM and eluted with 16 V of 100% DCM) to give *methyl (E)-3-((tert-butoxycarbonyl) (methoxycarbonyl)amino)acrylate* **65*E*** (6.75 g, 91%) as a clear, colorless liquid: ^1H NMR matches the desired product: ^1H NMR ($CDCl_3$, 500 MHz): δ ^1H NMR 7.82 (d, J = 14.5 Hz, 1H), 5.70 (d, J = 14.5 Hz, 1H), 3.88 (s, 3H), 3.71 (s, 3H), 1.52 (s, 10H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 167.2, 152.2, 149.6, 138.2, 103.3, 85.3, 54.4, 51.3, 27.4. HRMS (ESI) (m/z): ($[M + H]^+$) calcd for $C_{11}H_{17}NO_6$, 260.1134; found, 260.1133.

*Methyl (E)-3-((Methoxycarbonyl)amino)acrylate (**30E**).* To a 40 mL vial, with a stir bar, are added methyl (*E*)-3-((*tert*-butoxycarbonyl)(methoxycarbonyl)amino)acrylate **65*E*** (2.5 g, 9.64 mmol), ACN (20 mL, anhydrous), and then magnesium perchlorate (0.430 g, 1.929 mmol). The reaction is stirred at ambient temperature for 18 h. The reaction is diluted with EtOAc (200 mL), saturated aqueous $NaHCO_3$ solution (25 mL), and saturated aqueous NaCl solution (25 mL). The organic layer is dried over Na_2SO_4, filtered, and concentrated in vacuo. The solid is slurried in DCM (50 mL) and hexane (50 mL) is added. The solids are collected by filtration, washed with hexanes (30 mL), and then dried under a combination of house vacuum/nitrogen sweep (inverted funnel) to give *methyl (E)-3-((methoxycarbonyl)amino)-acrylate* **30*E*** (1.444 g, 95%) as a white solid. The material is spectroscopically identical to that described herein.

*Ethyl (E)-3-(N-(tert-Butoxycarbonyl)acetamido)acrylate (**66E**).* To a 200 mL 1-neck flask, with a stir bar, are added *tert*-butyl acetylcarbamate **57** (8.48 g, 53.3 mmol), DABCO (0.598 g, 5.33 mmol), and DCM (100 mL, anhydrous) and then ethyl propiolate (5.4 mL, 53.3 mmol) is added dropwise over 5 min at 0 °C. The reaction is stirred for 5 min under cooling and then at ambient temperature for 18 h. The reaction is concentrated to a minimal volume of DCM, loaded onto a 50 g Biotage Snap column, and then placed on top of an ISCO 120 g gold column (conditioned with hexanes, eluted with 1 CV hexanes then gradient eluted with 20% EtOAc/hexanes over 8 CV, and then held for 8 CV) to give *ethyl (E)-3-(N-(tert-butoxycarbonyl)acetamido)acrylate* **66*E*** (13.22 g, 96%) as a clear, colorless oil: ^1H NMR ($CDCl_3$, 500 MHz): δ 7.89 (d, J = 14.6 Hz, 1H), 5.96 (d, J = 14.6 Hz, 1H), 4.18 (q, J = 7.1 Hz, 2H), 2.40 (s, 3H), 1.56 (s, 9H), 1.26 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 170.4, 167.0, 151.0, 137.0, 107.2, 85.6, 60.1, 27.5, 25.6, 14.0. HRMS (ESI) (m/z): ($[M + H]^+$) calcd for $C_{12}H_{19}NO_5$, 258.1341; found, 258.1343.

*Ethyl (E)-3-Acetamidoacrylate (**71E**).* To a 40 mL vial, with a stir bar, are added magnesium perchlorate (0.868 g, 3.89 mmol), ethyl (*E*)-3-(*N*-(*tert*-butoxycarbonyl)acetamido)acrylate **66*E*** (1.0 g, 3.89 mmol), and ACN (10 mL, anhydrous). The reaction is stirred at ambient temperature for 18 h. The reaction is diluted with EtOAc (80 mL) then washed with saturated aqueous $NaHCO_3$ solution (40 mL), 10% aqueous NH_4Cl solution (40 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude was purified by loading in DCM onto an 80 g ISCO gold column (conditioned with hexanes, eluted with 1 CV hexanes then gradient eluted with 50% EtOAc/hexanes over 6 CV, and then held for 6 CV) to give *ethyl (E)-3-acetamidoacrylate* **71*E*** (0.57 g, 93%) as a white solid: ^1H NMR ($CDCl_3$, 500 MHz): δ 7.99 (dd, J = 14.1, 11.7 Hz, 1H), 7.82 (d, J = 11.9 Hz, 1H), 5.41 (d, J = 14.1 Hz, 1H), 4.16 (q, J = 7.1 Hz, 2H), 2.12 (s, 3H), 1.26 (t, J = 7.1 Hz, 3H); ^1H NMR (DMSO-d_6, 500 MHz): δ 10.68 (d, J = 11.2 Hz, 1H), 7.79 (dd, J = 14.2, 11.1 Hz, 1H), 5.41 (d, J = 14.2 Hz, 1H), 4.08 (q, J = 7.1 Hz, 2H), 2.01 (s, 3H), 1.19 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (DMSO-d_6, 125 MHz): δ 168.7, 167.0, 138.3, 99.3, 59.4, 22.9, 14.24. HRMS (ESI) (m/z): ($[M - H]^-$) calcd for $C_7H_{11}NO_3$, 156.0661; found, 156.0664.

*tert-Butyl Benzoylcarbamate (**58**).* To a 200 mL 1-neck flask, with a stir bar, are added methyl benzoate (2.132 mL, 17.07 mmol), *tert*-butyl carbamate (2 g, 17.07 mmol), and THF (23 mL, anhydrous). The reaction is cooled to an internal temp of −20 to −25 °C and lithium *tert*-butoxide (34.1 mL, 34.1 mmol, 1.0 M in THF) is added dropwise over 10 min maintaining the temperature below −20 °C. After addition is complete, the reaction is stirred for 10 min under cooling then at ambient temperature over 18 h. The reaction is partitioned between EtOAc (200 mL) and saturated aqueous NH_4Cl (100 mL). 2 N aqueous HOAc is added until the pH of the aqueous layer becomes less than 4. The organic layer is washed with saturated aqueous NaCl solution (50 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude is slurried in minimal EtOAc and hexane (~100 mL) is added. The solids are filtered, washed with hexanes, and then dried under a combination of house vacuum/nitrogen stream (inverted funnel) to give *tert*-butyl benzoylcarbamate **58** (3.02 g, 80%) as an off-white solid. ^1H NMR is consistent with the known desired product.[34] No further purification is required.

*Methyl (E)-3-(N-(tert-Butoxycarbonyl)benzamido)acrylate (**67E**).* To a 40 mL vial, with a stir bar, are added *tert*-butyl benzoylcarbamate **58** (1.0 g, 4.52 mmol), DABCO (0.051 g, 0.452 mmol), and DCM (12 mL, anhydrous). The reaction is cooled in an ice/water bath and methyl propiolate (0.402 mL, 4.52 mmol) is added. After addition is complete, the cooling bath is removed, and the reaction is stirred at ambient temperature for 1 h. The reaction is loaded directly on a 24 g ISCO gold column that is then placed on top of an 80 g ISCO gold column (conditioned with hexanes, eluted with 1 CV hexanes then gradient eluted with 30% MTBE/hexanes over 8 CV, and then held for 6 CV) to give *methyl (E)-3-(N-(tert-butoxycarbonyl)benzamido)acrylate* **67*E*** (1.32 g, 96%) as a clear, colorless oil: ^1H NMR ($CDCl_3$, 500 MHz): δ 8.02 (d, J = 14.6 Hz, 1H), 7.70 (dd, J = 8.4, 1.3 Hz, 2H), 7.62−7.55 (m, 1H), 7.47−7.40 (m, 2H), 5.80 (d, J = 14.6 Hz, 1H), 3.70 (s, 3H), 1.18 (s, 9H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 170.6, 167.6, 150.6, 138.7, 134.5, 133.5, 128.8, 128.7, 103.7, 85.0, 51.4, 27.3. HRMS (ESI) (m/z): ($[M - H]^-$) calcd for $C_{16}H_{19}NO_5$, 304.1185; found, 304.1185.

*Methyl (E)-3-Benzamidoacrylate (**72E**).*[35] To a 40 mL vial, with a stir bar, are added magnesium perchlorate (0.951 g, 4.26 mmol) and then a solution of methyl (*E*)-3-(*N*-(*tert*-butoxycarbonyl)benzamido)-acrylate **67*E*** (1.3 g, 4.26 mmol) in ACN (15 mL, anhydrous). The reaction is stirred at ambient temperature for 2 days. The reaction is diluted with EtOAc (200 mL) and saturated aqueous $NaHCO_3$ solution (50 mL). The organic layer is washed with 10% aqueous LiCl solution (2 × 75 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude is purified on silica (80 g ISCO gold column, conditioned with hexanes, loaded directly onto the column in DCM, eluted with 1 CV hexanes, gradient eluted with 50% EtOAc over 4 CV, and then held for 6 CV) to give *methyl (E)-3-benzamidoacrylate* **72*E*** (0.745 g, 85%) as a white solid: ^1H NMR ($CDCl_3$, 500 MHz): δ 8.36 (d, J = 11.7 Hz, 1H), 8.23 (dd, J = 14.3, 11.8 Hz, 1H), 7.89−7.71 (m, 2H), 7.57 (td, J = 7.4, 1.4 Hz, 1H), 7.51−7.33 (m, 2H), 5.62 (d, J = 14.2, Hz, 1H), 3.73 (s, 3H); ^1H NMR (DMSO-d_6, 500 MHz): δ 11.20−11.03 (m, 1H), 8.08 (dd, J = 14.1, 9.7 Hz, 1H), 8.04−7.92 (m, 2H), 7.70−7.62 (m, 1H), 7.60−7.52 (m, 2H), 5.79 (dd, J = 14.2, 2.2 Hz, 1H), 3.67 (s, 3H); $^{13}C\{^1H\}$ NMR (DMSO-d_6, 125 MHz): δ 167.4, 165.0, 139.0, 132.8,

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132.3, 128.7, 128.0, 100.9, 51.0. HRMS (ESI) (m/z): ([M − H]$^-$) calcd for $C_{11}H_{11}NO_3$, 204.0661; found, 204.0665.

*Methyl 4-((tert-butoxycarbonyl)carbamoyl)benzoate (**59**).* To a 100 mL 1-neck flask, with a stir bar, are added methyl 4-(((*tert*-butoxycarbonyl)amino)methyl)benzoate (2.0 g, 7.54 mmol), sodium periodate (5.64 g, 26.4 mmol), ruthenium(IV) oxide hydrate (0.114 g, 0.754 mmol), and then EtOAc (25 mL) and water (50 mL). The reaction is stirred at ambient temperature for 5 h. The reaction is diluted with EtOAc (125 mL), filtered through Celite, and washed with EtOAc (25 mL). The organic layer is separated, 2-propanol (2 mL) is added, and the solution is stirred for 18 h at ambient temperature (consumes residual Ru oxidant). The solution is filtered through Celite, washed with EtOAc, and concentrated in vacuo. The residual yellow solid is taken up 1:1 DCM/MTBE (50 mL) and hexane (200 mL) is added. The precipitated solids are collected by filtration, washed with hexane, and dried under a combination of house vacuum/nitrogen sweep (inverted funnel) to give *methyl 4-((tert-butoxycarbonyl)carbamoyl)-benzoate* **59** (1.96 g, 93%) as an off-white solid. ^{1}H NMR is consistent with the known desired product.[36] No further purification is required.

*Methyl (E)-4-((3-(tert-Butoxy)-3-oxoprop-1-en-1-yl)(tert-butoxycarbonyl)carbamoyl)benzoate (**68E**).* To a 40 mL vial, with a stir bar, are added DABCO (0.072 g, 0.644 mmol) and a solution of methyl 4-((*tert*-butoxycarbonyl)carbamoyl)benzoate **59** (1.8 g, 6.44 mmol) in DCM (7 mL, anhydrous). The mixture is cooled in an ice/water bath and a solution of *tert*-butyl propiolate (0.813 g, 6.44 mmol) in DCM (7 mL, anhydrous) is added. After the addition is complete, the cooling bath is removed, and the reaction is stirred at ambient temperature for 4 h. The reaction mixture is loaded directly onto a 24 g ISCO gold column that is then placed on top of an 80 g ISCO gold column (conditioned with hexanes, eluted with 2 CV hexanes then gradient eluted with 20% MTBE/hexanes over 8 CV, and then held for 6 CV) to give *methyl (E)-4-((3-(tert-butoxy)-3-oxoprop-1-en-1-yl) (tert-butoxycarbonyl)carbamoyl)benzoate* **68*E*** (2.53 g, 97%) as a clear, colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.11 (d, J = 8.4 Hz, 2H), 7.90 (d, J = 14.6 Hz, 1H), 7.75 (d, J = 8.5 Hz, 2H), 5.85 (d, J = 14.6 Hz, 1H), 3.94 (s, 3H), 1.46 (s, 9H), 1.18 (s, 9H); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 8.12 (d, J = 8.4 Hz, 1H), 7.86 (d, J = 8.5 Hz, 2H), 7.78 (d, J = 14.5 Hz, 2H), 5.82 (d, J = 14.6 Hz, 1H), 3.91 (s, 3H), 1.45 (s, 9H), 1.13 (s, 9H); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 170.0, 165.5, 165.3, 150.0, 138.5, 137.5, 133.3, 129.6, 128.6, 106.3, 85.4, 79.9, 52.5, 27.8, 26.8. . HRMS (ESI) (m/z): ([M − H]$^-$) calcd for $C_{21}H_{27}NO_7$, 404.1710; found, 404.1709.

*Methyl (E)-4-((3-(tert-Butoxy)-3-oxoprop-1-en-1-yl)carbamoyl)-benzoate (**73E**).* To a 100 mL 1-neck flask, with a stir bar, are added methyl (*E*)-4-((3-(*tert*-butoxy)-3-oxoprop-1-en-1-yl) (*tert*-butoxycarbonyl)carbamoyl)benzoate **68** (2.28 g, 5.62 mmol), ACN (28 mL, anhydrous), and then magnesium perchlorate (1.255 g, 5.62 mmol). The reaction is stirred at ambient temperature for 2 days. The reaction is diluted with EtOAc (200 mL), saturated aqueous $NaHCO_3$ solution (50 mL), and saturated NaCl solution (50 mL). The organic layer is dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude is loaded in a minimal amount of DCM onto a 24 g ISCO gold column and then placed on top of an 80 g ISCO gold column (conditioned with hexanes, eluted with 1 CV hexanes then gradient eluted with 80% EtOAc/hexanes over 8 CV, and then held for 6 CV) to give *methyl (E)-4-((3-(tert-butoxy)-3-oxoprop-1-en-1-yl)carbamoyl)-benzoate* **73*E*** (1.51 g, 88%) as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.32 (s, 1H), 8.13−8.02 (m, 3H), 7.88 (d, J = 8.5 Hz, 2H), 5.57 (d, J = 14.2 Hz, 1H), 3.93 (s, 3H), 1.48 (s, 9H); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 11.19 (d, J = 10.3 Hz, 1H), 8.14−8.10 (m, 2H), 8.09−8.05 (m, 2H), 7.94 (dd, J = 14.1, 10.3 Hz, 1H), 5.70 (d, J = 14.2 Hz, 1H), 3.90 (s, 3H), 1.46 (s, 9H); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 166.2, 165.5, 164.3, 137.8, 136.4, 132.9, 129.4, 128.3, 103.8, 79.4, 52.5, 27.9. HRMS (ESI) (m/z): ([M − H]$^-$) calcd for $C_{16}H_{19}NO_5$, 304.1185; found, 304.1187.

*tert-Butyl (2-Bromobenzoyl)carbamate (**60**).* To a 200 mL 1-neck flask, with a stir bar, are added ethyl 2-bromobenzoate (5 mL, 31.5 mmol), *tert*-butyl carbamate (3.69 g, 31.5 mmol), and anhydrous THF (40 mL). The reaction was cooled to −20 to −25 °C (monitored with internal thermometer) and a lithium *tert*-butoxide solution (63.0 mL, 63.0 mmol, 1.0 M in THF) is added dropwise over 10 min at a rate to maintain the temperature below −20 °C. After addition is complete, the reaction is stirred for 10 min after which the cooling bath is removed and the reaction is stirred at ambient temperature for 18 h. The reaction is partitioned between EtOAc (300 mL) and 2 N aqueous HOAc (150 mL). The organic solvent layer is washed with saturated NaCl solution (50 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude is purified on silica (loaded in DCM onto a 25 g Biotage SNAP column and placed on top of an ISCO 120 g gold column that was conditioned with hexane, eluted with 1 CV hexanes then gradient eluted with 50% EtOAc/hexanes over 6 CV, and then held for 6 CV) to give *tert-butyl (2-bromobenzoyl)carbamate* **57** (6.63 g, 70.1%) as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.86 (s, 1H), 7.55 (dd, J = 8.0, 1.1 Hz, 1H), 7.39 (dd, J = 7.6, 1.9 Hz, 1H), 7.34 (td, J = 7.5, 1.2 Hz, 1H), 7.27 (td, J = 7.7, 1.8 Hz, 1H), 1.39 (s, 9H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 167.4, 149.3, 137.1, 132.9, 131.4, 128.7, 127.4, 118.7, 83.1, 27.7. HRMS (ESI) (m/z): ([M − H]$^-$) calcd for $C_{12}H_{14}BrNO_3$, 298.0079; found, 298.0078.

*tert-Butyl (E)-3-(2-Bromo-N-(tert-butoxycarbonyl)benzamido)-acrylate (**69E**).* To a 200 mL 1-neck flask, with a stir bar, are added *tert*-butyl (2-bromobenzoyl)carbamate **60** (6.6 g, 21.99 mmol), DABCO (0.247 g, 2.199 mmol), and DCM (100 mL, anhydrous). The mixture is cooled in an ice/water bath and methyl propiolate (1.956 mL, 21.99 mmol) is added dropwise over 2−3 min. After addition is complete, the cooling bath is removed and the reaction is stirred at ambient temperature for 24 h. The reaction is concentrated in vacuo and then loaded in a minimal volume of DCM onto a 24 g ISCO gold column that is then placed on top of a 120 g ISCO gold column (conditioned with hexanes, eluted with 1 CV hexanes then gradient eluted with 30% MTBE/hexanes over 6 CV, and then held for 6 CV) to give *methyl (E)-3-(2-bromo-N-(tert-butoxycarbonyl)benzamido)acrylate* **69*E*** (8.4 g, 99%) as a clear, colorless oil (contains trace amounts of *Z* isomer that is not separable at this stage using silica gel chromatography): ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.00 (d, J = 14.7 Hz, 1H), 7.58 (dd, J = 7.8, 1.2 Hz, 1H), 7.40−7.28 (m, 3H), 6.27 (d, J = 14.6 Hz, 1H), 3.73 (s, 3H), 1.15 (s, 9H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 168.6, 167.6, 150.2, 138.0, 137.3, 133.3, 131.9, 129.0, 127.4, 119.6, 107.5, 85.7, 51.6, 27.1. HRMS (ESI) (m/z): ([M + H]$^+$) calcd for $C_{16}H_{18}BrNO_5$, 384.0446; found, 384.0448.

*tert-Butyl (E)-3-(2-Bromobenzamido)acrylate (**74E**).* To a 500 mL 1-neck flask, with stir bar, are added methyl (*E*)-3-(2-bromo-*N*-(*tert*-butoxycarbonyl)benzamido)acrylate **69*E*** (8.5 g, 22.12 mmol), ACN (100 mL, anhydrous), and then magnesium perchlorate (4.94 g, 22.12 mmol). The reaction is stirred at ambient temperature for 2 days. The reaction is diluted with EtOAc (400 mL), saturated aqueous $NaHCO_3$ solution (100 mL), and water (100 mL). The organic layer is washed with saturated aqueous NaCl solution (50 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude material is dissolved in a minimal amount of DCM and loaded onto a 50 g Biotage Snap column that is then placed on top of a 120 g ISCO gold column (conditioned with hexanes, eluted with 1 CV hexanes then gradient eluted with 50% EtOAc/hexanes over 6 CV, and then held for 6 CV) to give *methyl (E)-3-(2-bromobenzamido)acrylate* **74*E*** (6.1 g, 97%) as a clear, colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.30 (d, J = 11.6 Hz, 1H), 8.12 (dd, J = 14.1, 11.5 Hz, 1H), 7.60 (dd, J = 7.9, 1.2 Hz, 1H), 7.56 (dd, J = 7.6, 1.8 Hz, 1H), 7.38 (td, J = 7.5, 1.3 Hz, 1H), 7.32 (td, J = 7.7, 1.8 Hz, 1H), 5.58 (d, J = 14.1 Hz, 1H), 3.71 (s, 3H); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 11.26 (d, J = 10.8 Hz, 1H), 7.97 (dd, J = 14.2, 10.8 Hz, 1H), 7.75 (dd, J = 7.9, 1.2 Hz, 1H), 7.58 (dd, J = 7.6, 1.9 Hz, 1H), 7.53 (td, J = 7.4, 1.3 Hz, 1H), 7.47 (td, J = 7.7, 1.8 Hz, 1H), 5.67 (d, J = 14.2 Hz, 1H), 3.68 (s, 3H); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 167.1, 165.9, 138.0, 136.9, 133.0, 132.1, 129.1, 127.8, 118.9, 101.6, 51.1. HRMS (ESI) (m/z): ([M − H]$^-$) calcd for $C_{11}H_{10}BrNO_3$, 281.9766; found, 281.9766.

*tert-Butyl (4-Bromobenzoyl)carbamate (**61**).* To a 100 mL 1-neck flask, with a stir bar, are added *tert*-butyl (4-bromobenzyl)carbamate (2.0 g, 6.99 mmol), sodium periodate (5.23 g, 24.46 mmol), ruthenium(IV) oxide hydrate (0.106 g, 0.699 mmol), and then EtOAc (25 mL) and water (50 mL). The reaction is stirred at ambient temperature for 5 h. The reaction is diluted with EtOAc (125 mL) and filtered through Celite (washing with 50 mL EtOAc). The EtOAc layer

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is separated and 2-propanol (2 mL) is added to it. The mixture is stirred at ambient temperature for 18 h to consume the residual Ru oxidant. The solution is filtered through Celite, washed with EtOAc (50 mL), and concentrated in vacuo. The residual yellow solid is taken up 1:1 DCM/MTBE (50 mL) and hexane (200 mL) is added to cause precipitation. The solids are collected by filtration, washed with hexane (50 mL), and dried under a combination of house vacuum/nitrogen sweep (inverted funnel connected to the N_2 source) to give *tert*-butyl (4-bromobenzoyl)carbamate **61** (1.73 g, 82%) as an off-white solid. ^{1}H NMR is consistent with the known desired product.[37] No further purification is required.

*tert-Butyl (E)-3-(4-Bromo-N-(tert-butoxycarbonyl)benzamido)-acrylate (**70E**).* To a 40 mL vial, with a stir bar, are added *tert*-butyl (4-bromobenzoyl)carbamate **61** (1.5 g, 5.00 mmol), DABCO (0.056 g, 0.500 mmol), and DCM (20 mL, anhydrous). The solution is cooled in an ice/water bath and methyl propiolate (0.445 mL, 5.00 mmol) is added dropwise over 2−3 min. After addition is complete, the cooling bath is removed, and the reaction is stirred at ambient temperature for 2 h. The reaction is loaded directly on a 24 g ISCO gold column that is then placed on top of an 80 g ISCO gold column (conditioned with hexanes, eluted with 1 CV hexanes then gradient eluted with 30% MTBE/hexanes over 6 CV, and then held for 6 CV) to give *methyl (E)-3-(4-bromo-N-(tert-butoxycarbonyl)benzamido)acrylate* **70*E*** (1.9 g, 99%) as a clear, colorless oil (LCMS shows a small amount of the Z isomer, which is not separable on silica): ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.99 (d, J = 14.6 Hz, 1H), 7.65−7.53 (m, 4H), 5.78 (d, J = 14.6 Hz, 1H), 3.70 (s, 3H), 1.24 (s, 9H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 169.8, 167.5, 150.4, 138.5, 133.3, 132.1, 130.2, 128.6, 104.1, 85.4, 51.5, 27.5. HRMS (ESI) (m/z): ([M − H]$^-$) calcd for $C_{16}H_{18}BrNO_5$, 382.0290; found, 382.0293.

*tert-Butyl (E)-3-(4-Bromobenzamido)acrylate (**75E**).* To a 200 mL 1-neck flask, with a stir bar, are added magnesium perchlorate (2.300 g, 10.31 mmol) and a solution of methyl (*E*)-3-(4-bromo-*N*-(*tert*-butoxycarbonyl)benzamido)acrylate **70*E*** (3.6 g, 9.37 mmol) in ACN (60 mL, anhydrous). The reaction is stirred at ambient temperature for 2 days. The reaction is diluted with EtOAc (250 mL) and saturated aqueous $NaHCO_3$ solution (100 mL). The organic layer is washed with 10% aqueous LiCl solution (2 × 50 mL), saturated aqueous NaCl solution (50 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude was dry loaded onto silica and placed on top of a 120 g ISCO gold column (conditioned with hexanes, eluted with 1 CV hexanes then gradient eluted with 50% EtOAc/hexanes over 6 CV, and then held for 6 CV) to give *methyl (E)-3-(4-bromobenzamido)acrylate* **75*E*** as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.33 (d, J = 11.7 Hz, 1H), 8.19 (dd, J = 14.1, 11.6 Hz, 1H), 7.71 (d, J = 8.6 Hz, 2H), 7.61 (d, J = 8.6 Hz, 2H), 5.63 (d, J = 14.1 Hz, 1H), 3.73 (s, 3H); ^{1}H NMR (MeOD, 500 MHz): δ 8.16 (d, J = 14.2 Hz, 1H), 7.83 (d, J = 8.6 Hz, 2H), 7.68 (d, J = 8.6 Hz, 2H), 5.76 (d, J = 14.2 Hz, 1H), 3.72 (s, 3H); ^{13}C{^{1}H} NMR (MeOD, 125 MHz): δ 170.1, 166.8, 140.3, 133.2, 133.1, 130.9, 128.7, 103.0, 52.1. HRMS (ESI) (m/z): ([M − H]$^-$) calcd for $C_{11}H_{10}BrNO_3$, 281.9766; found, 281.9768.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c01212.

Results from repeating previously reported acetal condensation reaction; reaction monitoring details and data; and copies of ^{1}H and ^{13}C spectra (PDF)

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Notes

The authors declare no competing financial interest.

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