ChemCatChem

The European Society Journal for Catalysis

Chemistry Europe

European Chemical Societies Publishing

Supported by GECATS GERMAN CATALYSIS SOCIETY

Accepted Article

Title: Phosphine-Catalyzed (4+1) Annulation: Rearrangement of Allenylic Carbamates to 3-Pyrrolines Through Phosphonium Diene Intermediates

Authors: Ohyun Kwon, Brian Blank, and Ian Andrews

To be cited as: *ChemCatChem* 10.1002/cctc.202000626

Link to VoR: https://doi.org/10.1002/cctc.202000626

WILEY-VCH

10.1002/cctc.202000626

WILEY-VCH

Phosphine-Catalyzed (4+1) Annulation: Rearrangement of Allenylic Carbamates to 3-Pyrrolines through Phosphonium Diene Intermediates

Brian R. Blank,[a] Ian P. Andrews,[a] and Ohyun Kwon*[a]

[a] Dr. B. R. Blank, Dr. I. P. Andrews, Prof. O. Kwon
Department of Chemistry and Biochemistry
University of California, Los Angeles
607 Charles E. Young Drive East, Los Angeles, California, 90095-1569
Group Homepage: https://www.thekwonlab.net/
E-mail: ohyun@chem.ucla.edu

Supporting information for this article is given via a link at the end of the document.

Abstract: We have developed a phosphine-catalyzed (4+1) annulative rearrangement for the preparation of 3-pyrrolines from allenylic carbamates via phosphonium diene intermediates. We employed this methodology to synthesize an array of 1,3-disubstituted- and 1,2,3-trisubstituted-3-pyrrolines, including the often-difficult-to-prepare 2-alkyl variants. A mechanistic investigation employing allenylic acetates and mononucleophiles unexpectedly unveiled that a phosphine-catalyzed (4+1) reaction for the construction of cyclopentene products, previously reported by Tong, might not occur through a phosphonium diene, as had been proposed, but rather through multiple mechanisms working in concert. Consequently, our phosphine-catalyzed rearrangement is most likely the first transformation to involve the unequivocal formation of a phosphonium diene intermediate along the reaction pathway. To demonstrate the synthetic utility of this newly developed reaction, we have completed concise formal syntheses of the pyrrolizidine alkaloids (±)-trachelanthamidine and (±)-supinidine.

Introduction

Pyrrolizidine alkaloids are compounds that have attracted the interest of medicinal chemists for several decades because of their interesting biological activities, including antitumor activity, hepatotoxicity, carcinogenicity, and mutagenicity (Figure 1).[1,2b] Synthetic chemists have also been interested in these compounds because their compact and often highly oxygenated structures are challenging testing grounds for new synthetic methodologies.[2]

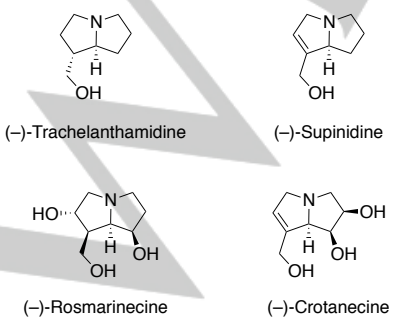


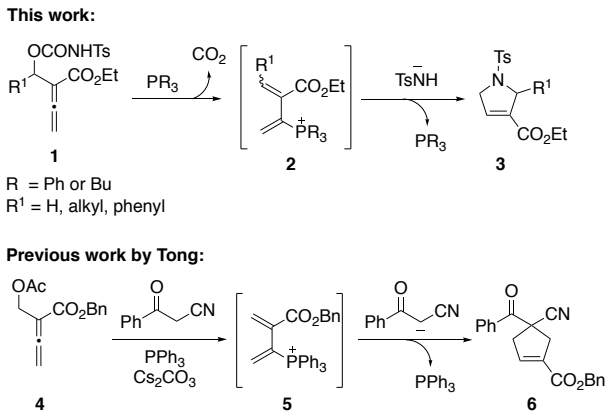
Figure 1. Representative pyrrolizidine alkaloids.

Tertiary phosphines have emerged as excellent nucleophilic catalysts over the last two decades, enabling the rapid and facile construction of multifarious carbocyclic and heterocyclic systems.[3] For example, Lu's phosphine-catalyzed (3+2) reaction between allenoates and *N*-sulfonyl imines produces 1,2,3-trisubstituted-3-pyrrolines in high yield when simply using catalytic PPh_3 (as the only reagent) at room temperature.[4,5] This reaction has since been modified to facilitate the synthesis of 1,2,3,5-tetrasubstituted-3-pyrrolines[6] and the production of enantiomerically enriched 3-pyrrolines.[7] As pyrrolines can be transformed quickly to pyrrolidines[8] through reduction or to pyrroles[4b] and pyrrolidinones[9] through oxidation, a diverse array of five-membered nitrogen heterocycles is readily accessible from this class of compounds. As such, one might expect the allene–imine (3+2) annulation to be widely used in the total synthesis of natural products. It has, however, been limited thus far to imines bereft of an α-proton,[10] with only two exceptions,[6h,7g] even though access to 2-alkyl-substituted 3-pyrrolines would greatly expand the range of natural products that could be assembled through phosphine catalysis.[11]

Over the last few years, several approaches have been designed to circumvent this limitation of Lu's reaction and allow the construction of 2-alkyl-substituted 3-pyrrolines.[12] With these variations, phosphine-catalyzed annulations of imines appear ideally suited for the synthesis of pyrrolizidine alkaloids. Nevertheless, there has been only one attempt to construct a member of this class of natural products.[13] This paucity of examples suggests the need for additional methodological advances toward 2-alkyl-substituted 3-pyrrolines that can be successfully applied to natural product synthesis.

As an alternative to the (3+2) annulations, we envisioned a phosphine-catalyzed annulative rearrangement of allenylic carbamates **1**, proceeding through intermediate phosphonium dienes **2**, to provide 3-pyrrolines **3** (Scheme 1). The first example of a similar reactive species was disclosed when Tong proposed the formation of phosphonium diene **5** as an intermediate in the phosphine-catalyzed (4+1) annulation between allenylic acetate **4** and a carbon-centered bisnucleophile, to yield cyclopentene **6**.[14–17] Additionally, Tong reported a single example whereby a nitrogen (bis)nucleophile was used instead to deliver a 1,3-disubstituted 3-pyrroline in a modest yield of 22%.[14] This aspect of Tong's work was elaborated upon by Fu to allow for the preparation of enantioenriched 1,3,5-trisubstituted-3-pyrrolines.[16] In contrast to

Tong's and Fu's approaches, we anticipated that our annulative rearrangement of allenylic carbamates **1** would expand the substrate scope of 3-pyrrolines that could be obtained through phosphine-catalyzed (4+1) reactions by allowing for the preparation of 1,2,3-trisubstituted-3-pyrrolines. Furthermore, to illustrate its synthetic value, we have applied our new methodology to syntheses of the pyrrolizidine alkaloids (±)-trachelanthamidine and (±)-supinidine (*vide infra*).

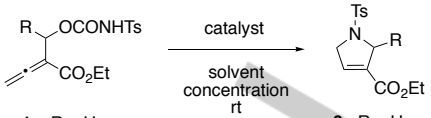


Scheme 1. Phosphine-catalyzed (4+1) reactions.

Results and Discussion

We tested our idea by reacting allenylic carbamate **1a** with PPh_3, obtaining 3-pyrroline **3a** in 19% yield (Table 1, entry 1).[18] Addition of **1a** over 24 h increased the yield to 47% (entry 2), presumably by minimizing undesired decomposition of the substrate.[19] After exploring the effects of the catalyst, the solvent, and the addition time of **1a**, and whether the addition of a combination of external *p*-toluenesulfonamide and base would be beneficial, we determined that the optimal conditions for this transformation involved adding **1a** over 24 h to a solution of PPh_3 in CH_3CN (entry 3).[20] With the optimized conditions for the transformation of allenylic carbamate **1a** determined, we employed allenylic carbamate **1b** in the reaction, but obtained 3-pyrroline **3b** in only 17% yield (entry 4). Slightly increasing the nucleophilicity of the catalyst, by using $PMePh_2$, increased the yield to 33% (entry 5). The application of the more nucleophilic PMe_3 resulted, however, in only a trace of product and mainly decomposition of allenylic carbamate **1b** (entry 6). Employing PEt_3 and PBu_3 as catalysts resulted in a dramatic increase in yield to 55% in both cases (entries 7–8). In contrast, the use of PCy_3 yielded 3-pyrroline **3b** in only 14%, presumably a result of the greater steric bulk of this catalyst (entry 9). Next, we further optimized this transformation by exploring the effects of solvent and concentration.[20] Decreasing the concentration from 0.035 to 0.018 M increased the yield to 66% (entry 10). Lowering the concentration even further to 0.007 M proved detrimental, as the yield decreased to 51% (entry 11). We found that deaerating the solvent was beneficial, resulting in an increase in the yield of desired 3-pyrroline **3b** to 74% (entry 12). To summarize, the final reaction protocol was determined to involve addition of **1b** over 24 h to a solution of PBu_3 in deaerated CH_3CN at a concentration of 0.018 M.

Table 1. Optimization of the phosphine-catalyzed (4+1) reaction.[a]



1a R = H
1b R = Me

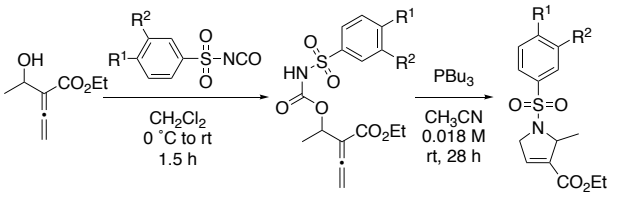
3a R = H
3b R = Me

entry	R	catalyst	solvent	concentration [M]	yield[b] [%]
1[c]	H	PPh_3	CH_2Cl_2	0.035	19
2	H	PPh_3	CH_2Cl_2	0.035	47
3	H	PPh_3	CH_3CN	0.035	69
4	Me	PPh_3	CH_3CN	0.035	17
5	Me	$PMePh_2$	CH_3CN	0.035	33
6	Me	PMe_3	CH_3CN	0.035	trace
7	Me	PEt_3	CH_3CN	0.035	55
8	Me	PBu_3	CH_3CN	0.035	55
9	Me	PCy_3	CH_3CN	0.035	14
10	Me	PBu_3	CH_3CN	0.018	66
11	Me	PBu_3	CH_3CN	0.007	51
12[d]	Me	PBu_3	CH_3CN	0.018	74

[a] Reactions were performed by adding a solution of **1** (0.14 mmol, 1.0 equiv) in solvent (4 mL) over 24 h to a solution of phosphine (0.14 mmol, 1.0 equiv) in solvent (4 mL), followed by stirring for an additional 4 h. [b] All yields reported are isolated yields. [c] Allenylic carbamate **1a** was added to the phosphine in one portion. [d] The solvent was deaerated by bubbling with Ar for 1.5 h.

To further improve the yield of the reaction, we then explored a variety of sulfonamides in an attempt to influence the outcome of the reaction by altering the electronics of the nucleophile. Thus, we prepared four additional allenylic carbamates, **1ba**–**bd**, by reacting allenylic alcohol **7b** with various sulfonyl isocyanates (Table 2).[21] When employed in the (4+1) reaction, *p*-nitrobenzenesulfonyl–substituted carbamate **1ba** resulted in **3ba** being formed in the lowest yield, 37%, presumably because of the weak nucleophilicity of its sulfonamide anion (entry 1). Use of the less electron-poor *m*-trifluoromethylbenzenesulfonyl variant **1bb** resulted in an improved yield of **3bb** (45%, entry 2). Using a simple benzenesulfonyl group increased the yield of **3bc** to 58% (entry 3). The previously obtained 74% yield for the product, **3b**, from the electron-rich *p*-tosyl variant **1b** was likely due to its anion's relatively high nucleophilicity (entry 4). Nevertheless, when using an even more electron-rich *p*-methoxybenzenesulfonyl group, the yield of **3bd** decreased slightly to 72%, presumably because of the lower acidity of its sulfonamide (entry 5). As a result, we continued with our initial choice, *p*-tosyl–substituted carbamates, for further study.

Table 2. Phosphine-catalyzed (4+1) reactions employing various sulfonamide nucleophiles.[a–c]



7b **1b, 1ba–bd** **3b, 3ba–bd**

entry	R^1	R^2	carbamate	yield **1** [%]	3-pyrroline	yield **3** [%]
1	NO_2	H	**1ba**	99	**3ba**	37
2	H	CF_3	**1bb**	79[d]	**3bb**	45
3	H	H	**1bc**	99	**3bc**	58
4	Me	H	**1b**	94	**3b**	74
5	OMe	H	**1bd**	96	**3bd**	72

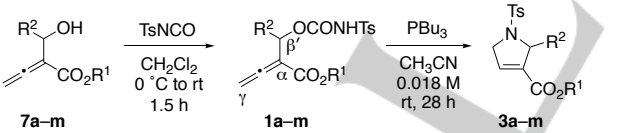
[a] Pertaining to the first step: The isocyanate (1.05 equiv) was added to **7** in dry CH_2Cl_2 (0.4 M) at 0 °C, and stirred for 1 h, and then the solution was

stirred at room temp for 0.5 h. [b] In regards to the phosphine-catalyzed step: Reactions were performed by adding a solution of **1** (0.14 mmol, 1.0 equiv) in CH_3CN (4 mL) over 24 h to a solution of PBu_3 (0.14 mmol, 1.0 equiv) in CH_3CN (4 mL), followed by stirring for an additional 4 h. The solvents employed in these reactions were deaerated by bubbling with Ar for 1.5 h. [c] All yields reported are isolated yields. [d] Yield based on recovered starting material; isolated yield: 22%.

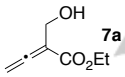
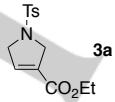
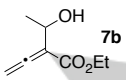
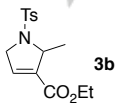
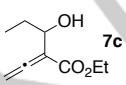
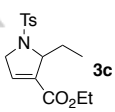
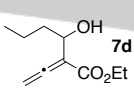
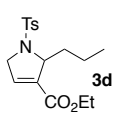
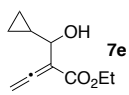
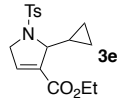
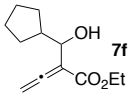
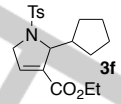
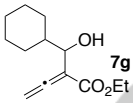
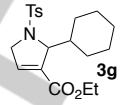
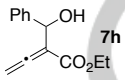
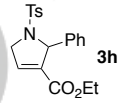
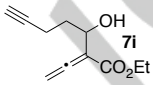
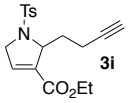
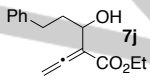
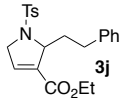
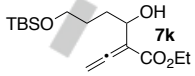
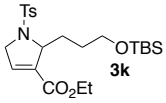
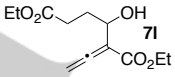
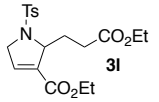
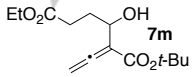
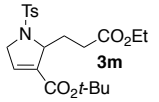
To explore the substrate scope of the (4+1) reaction, we prepared an array of allenylic carbamates **1** from their respective allenylic alcohols **7** (Table 3). We used a Morita–Baylis–Hillman (MBH) reaction between ethyl 2,3-butadienoate and paraformaldehyde or acetaldehyde in the presence of 3-hydroxyquinuclidine to prepare allenylic alcohols **7a** and **7b** in 66 and 79% yield, respectively.[20,22] This approach failed, however, to provide useful yields of more-elaborate allenylic alcohols. Thus, we exploited either a tin(II)- or indium-mediated allenylation of aldehydes to synthesize allenylic alcohols **7c**–**m**.[20,23] Subsequently, we converted allenylic alcohols **7a**–**m** to allenylic carbamates **1a**–**m**, in good to excellent yields, through reactions with tosyl isocyanate (Table 3).

The newly prepared substrates were then subjected to the optimized reaction conditions to deliver 3-pyrrolines **3c**–**m** (Table 3). Allenylic carbamates containing nonfunctionalized linear alkyl chains of various lengths produced their respective 3-pyrrolines **3b**–**d** in moderate to good yields (entries 2–4). Substrates with cycloalkyl groups of various sizes produced pyrrolines **3e**–**g**, albeit with lower reaction efficiencies (entries 5–7). Thus, there appears to be a correlation between the steric bulk at the β′-carbon and the reaction efficiency. The presence of a phenyl ring or unsaturation within the substituent was well tolerated in the reaction, with pyrrolines **3h**–**j** being produced in moderate to good yields (entries 8–10). The reaction was also accepting of siloxy and ester functionalities, with the respective pyrrolines **3k**–**m** being produced in moderate to good yields (entries 11–13). Notably, the latter two compounds served as direct precursors for syntheses of pyrrolizidine alkaloids (*vide infra*).

Table 3. Synthesis of allenylic carbamates **1** and 3-pyrrolines **3**.[a–c]

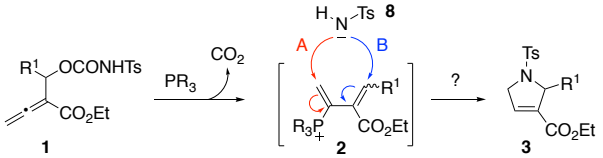


7a–m **1a–m** **3a–m**

entry	allenylic alcohol	yield of **1** [%]	3-pyrroline	yield of **3** [%]
1[d,e]	 **7a**	92	 **3a**	69
2	 **7b**	94	 **3b**	74
3	 **7c**	84	 **3c**	62
4	 **7d**	69	 **3d**	55
5	 **7e**	88	 **3e**	28
6	 **7f**	86	 **3f**	37
7	 **7g**	88	 **3g**	30
8	 **7h**	88	 **3h**	66
9	 **7i**	89	 **3i**	52
10	 **7j**	72	 **3j**	52
11[e]	 **7k**	72	 **3k**	48
12	 **7l**	92	 **3l**	56
13	 **7m**	95	 **3m**	55

[a] Pertaining to the first step: The isocyanate (1.05 equiv) was added to **7** in dry CH_2Cl_2 (0.4 M) at 0 °C, and stirred for 1 h, and then the solution was stirred at room temp for 0.5 h. [b] In regards to the phosphine-catalyzed step: Reactions were performed by adding a solution of **1** (0.14 mmol, 1.0 equiv) in CH_3CN (4 mL) over 24 h to a solution of PBu_3 (0.14 mmol, 1.0 equiv) in CH_3CN (4 mL), followed by stirring for an additional 4 h. The solvents employed in these reactions were deaerated by bubbling with Ar for 1.5 h. [c] All yields reported are isolated yields. [d] PPh_3 was used as the catalyst. [e] Solvent was not deaerated for this reaction.

We surmised that the mechanism of this transformation involved initial displacement of the carbamate by the phosphine, thereby decomposing **1** into phosphonium diene **2**, CO_2, and toluenesulfonamide anion **8**, which then served as the nucleophile in the reaction to construct 3-pyrrolines **3** (Scheme 2). There arises a point of contention, however, when considering how the reaction progresses from phosphonium diene **2** to 3-pyrroline **3**, because it seems feasible that **8** could potentially add to either the β′- or the γ-carbon of phosphonium diene **2**.[24–26]



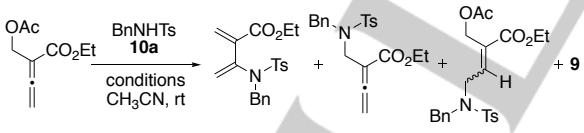
Scheme 2. Conversion of allenylic carbamate **1** to phosphonium diene **2** and 3-pyrroline **3**.

Regarding Tong's (4+1) reaction, it was proposed that the nucleophile initially added to the γ-carbon of the suggested intermediate **5** (Scheme 1), with the argument that the electron-withdrawing effect of a triphenylphosphonium moiety is stronger than that of a carboxylate group.[14] While this scenario is not unreasonable, we felt that experimental evidence to support this hypothesis was lacking. In addition, contrary to this mechanism, Tong later published a reaction between allenylic acetate **4** and butyl toluenesulfonamide in the presence of 20 mol% PPh_3 that produced an allenoate analogous to **12a** (see Table 4) in 76% yield.[27] Consequently, we wished to perform an in-depth investigation of the reactions of an allenylic acetate with nitrogen- and carbon-centered nucleophiles capable of undergoing only monoaddition to the proposed phosphonium diene **2**. As such, if the mononucleophile were to add to the γ-carbon first, a phosphorus ylide would be generated. After protonation of the ylide a second nucleophile could potentially add to the β′-carbon and deliver a trisubstituted olefin. Conversely, initial addition to the β′-carbon would lead to the formation of an allenoate, such as **12a**, upon elimination of the phosphine.

Mechanistic Investigation

Our mechanistic investigation into the (4+1) reaction began by employing allenylic acetate **9** in a series of reactions (Table 4) with benzyl toluenesulfonamide (**10a**). To determine whether a carbon mononucleophile would exhibit similar reactivity to **10a**, we then performed a series of reactions employing 3-methyl-2,4-pentanedione (**10b**) as the pronucleophile (Table 5). We also employed a second carbon monopronucleophile, benzoyl propionitrile (**10c**), in the reactions to determine whether this pair of carbon nucleophiles would demonstrate similar reactivities (Table 6).

Table 4. Investigation of reactions between allenylic acetate **9** and **10a**.[a,b]

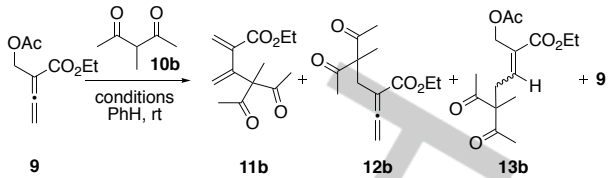


9 **11a** **12a** **13a**

entry	PPh_3 [mol%]	Cs_2CO_3 [mol%]	NaOAc [mol%]	yield **11a** [%]	yield **12a** [%]	yield **13a**[c] [%]	yield **9** [%]
1	20	130	–	77	0	0	0
2	–	130	–	81	0	0	0
3	20	–	–	0	20	15	6
4	110	–	–	0	0	14	0
5	20	–	130	0	19	14	6
6	–	–	130	0	0	0	100

[a] Reactions were performed by adding a solution of **9** (0.190 mmol, 1.0 equiv) in dry CH_3CN (2.8 mL) over 6 h to a solution of **10a** (1.2 equiv) in dry CH_3CN (2.8 mL) containing the following reagents, if required for the reactions listed in the specific entries above: PPh_3 (either 0.2 or 1.1 equiv), Cs_2CO_3 (1.3 equiv), or NaOAc (1.3 equiv). Once the addition was complete, the mixture was stirred for another 1–1.5 h. [b] All yields reported are isolated yields. [c] Allylic acetate **13a** was isolated as a mixture of isomers, with the Z-to-E ratio ranging between 1.11:1 and 1.19:1.

Table 5. Investigation of reactions between allenylic acetate **9** and **10b**.[a,b]

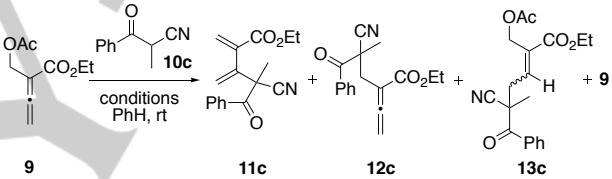


9 **11b** **12b** **13b**

entry	PPh_3 [mol%]	Cs_2CO_3 [mol%]	NaOAc [mol%]	yield **11b** [%]	yield **12b** [%]	yield **13b**[c] [%]	yield **9** [%]
1	20	130	–	0	42	19	0
2	–	130	–	8	74	0	0
3	20	–	–	0	34	19	9
4	110	–	–	0	0	23	0
5	20	–	130	0	34	18	7
6	110	–	130	0	0	24	0
7	–	–	130	0	0	0	100

[a] Reactions were performed by adding a solution of **9** (0.190 mmol, 1.0 equiv) in dry benzene (2.8 mL) over 1 h to a solution of **10b** (1.2 equiv) in dry benzene (2.8 mL) containing the following reagents, if required, for the reactions listed in the specific entries above: PPh_3 (either 0.2 or 1.1 equiv), Cs_2CO_3 (1.3 equiv), or NaOAc (1.3 equiv). Once the addition was complete, the mixture was stirred for another 5–5.5 h. [b] All yields reported are isolated yields. [c] Allylic acetate **13b** was isolated as a mixture of isomers, with the E-to-Z ratio ranging between 1.05:1 and 1.18:1.

Table 6. Investigation of reactions between allenylic acetate **9** and **10c**.[a,b]



9 **11c** **12c** **13c**

entry	PPh_3 [mol%]	Cs_2CO_3 [mol%]	yield **11c** [%]	yield **12c** [%]	yield **13c** [%]	yield **9** [%]
1	20	130	18	26	0	5
2	–	130	28	44	0	2
3	20	–	0	7	0	2
4	110	–	0	0	20[c]	0

[a] Reactions were performed by adding a solution of **9** (0.190 mmol, 1.0 equiv) in dry benzene (2.8 mL) over 1 h to a solution of **10c** (1.2 equiv) in dry benzene (2.8 mL) containing the following reagents, if required, for the reaction listed in the specific entries above: PPh_3 (either 0.2 or 1.1 equiv) or Cs_2CO_3 (1.3 equiv). Once the addition was complete, the mixture was stirred for another 8.5, 29, 72, and 9 h for entries 1–4, respectively. [b] All yields reported are isolated yields. [c] Allylic acetate **13c** was isolated as a mixture of isomers, with an E-to-Z ratio of 1.08:1.

Subjecting monopronucleophiles **10a** and **10b** to the standard reaction conditions employed by Tong (20 mol% PPh_3 and 130 mol% Cs_2CO_3 in CH_3CN) resulted in the generation of three different products: diene **11**, allenoate **12**, and allylic acetate **13**. The product distributions for the reactions employing either pronucleophile **10a** or **10b** in the presence of both PPh_3 and Cs_2CO_3 were vastly different from each other (Tables 4 and 5, entry 1). We suspected that diene **11a** was produced through an S_N2' addition of the sulfonamide anion of **10a** to allenylic acetate **9**. In contrast, allenoate **12b** was likely formed through either direct S_N2 displacement of the acetate of **9** by the enolate of **10b** or β′-addition of the enolate to phosphonium diene **2** (*vide infra*). Allylic acetate **13b** was, however, likely formed through either γ-umpolung addition of the enolate of **10b** to allenylic acetate **9** or sequential γ-addition of the enolate of **10b** and β′-addition of acetate onto phosphonium diene **2**. Importantly, we did not observe formation of a trisubstituted olefin in which the

nucleophile had added to both the β′- and γ-carbons. Based on Tong's proposal that the nucleophile should add first to the γ-carbon of the phosphonium diene, we would have expected to observe this product if the phosphonium diene did indeed form during the reaction. Thus, it is unlikely for **13b** to have formed by way of a phosphonium diene, because an excess of the more nucleophilic enolate of **10b** was present during the reaction, relative to the amount of possible acetate ion (when considering the slow addition of **9**), so we should have observed the aforementioned trisubstituted olefin, rather than allylic acetate **13b** that we actually obtained. It seems unlikely that the acetate ion would outcompete the carbon-centered nucleophile for addition to the β′-carbon. For these reasons, we believe that **13b** was delivered through a well-established phosphine-catalyzed γ-umpolung addition.[25,26]

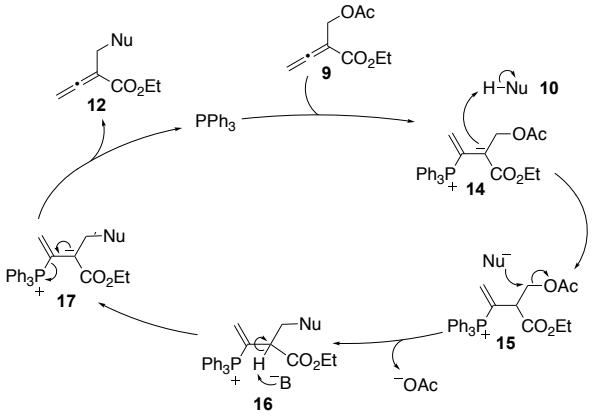
Performing the reaction in the absence of PPh_3 verified our hypothesis that the sulfonamide anion of **10a** underwent S_N2' addition to allenylic acetate **9** to generate diene **11a** (Table 4, entry 2). Employing pronucleophile **10b** in an analogous reaction revealed that production of allenoate **12b** most likely occurred by way of simple S_N2 displacement of the acetate of allenylic acetate **9** by the enolate of **10b** (Table 5, entry 2). More importantly, this result implies that it is not necessary to pass through phosphonium diene **2** *en route* to allenoate **12b**. With the assumption that phosphonium diene **2** is not likely to be generated in the reactions represented in entry 1 of Tables 4 and 5, the difference in reactivity between the nitrogen- and carbon-centered nucleophiles in the presence of both PPh_3 and Cs_2CO_3 can still be explained by considering the involvement of PPh_3. When **10a** was employed, its anion presumably reacted with allenylic acetate **9** in an S_N2' manner to form **11a** faster than PPh_3 could add through conjugate addition, thereby inhibiting the production of allylic acetate **13a**. Conversely, compared with the rate of reaction of the anion of **10a**, the enolate of **10b** likely underwent S_N2 displacement of the acetate at a slower rate, allowing conjugate addition of PPh_3 to allenylic acetate **9**, leading to formation of allylic acetate **13b**.

Next, we tested a second carbon pronucleophile, **10c**, in the reactions to determine whether it would demonstrate reactivity similar to that of **10b** (Table 6, entries 1 and 2). Unexpectedly, we found that the reactivity of **10c** was similar in certain aspects to that of both pronucleophiles **10a** and **10b**, with both diene **11c** and allenoate **12c** being produced from the reactions. In analogy to our discussion above, this outcome implies that the enolate of **10c** reacted faster than PPh_3 with allenylic acetate **9** (Table 6, entry 1). Unlike the enolate of **10b**, however, the enolate of **10c** readily took part in both S_N2 and S_N2' reactions with allenylic acetate **9**, with the S_N2 pathway being the slightly favored mode of reactivity.

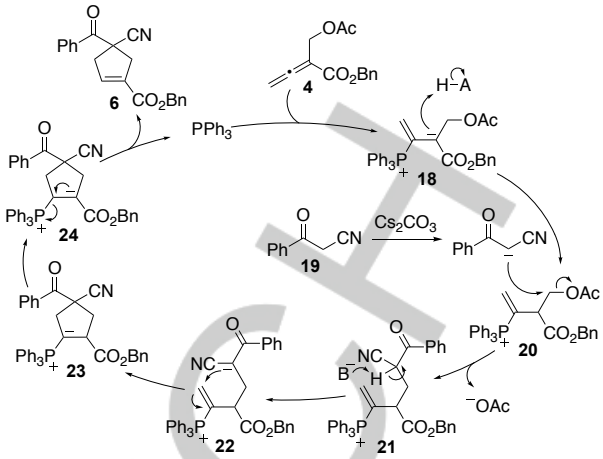
We then turned our attention to performing the reactions in the absence of Cs_2CO_3. In these scenarios, we suspected that if the phosphonium diene were indeed generated, there would be no means to deliver any product. These reactions rely on the fact that Cs_2CO_3 must first deprotonate the pronucleophiles to deliver the active nucleophiles for the reactions. In the absence of an external base, the phosphonium diene would not undergo a reaction with the pronucleophile and, thus, no products would form. In this case, we would expect the phosphonium diene simply to undergo polymerization. Nevertheless, when we employed PPh_3 as the sole catalyst in reactions using pronucleophiles **10a** and **10b**, we isolated allenoates **12a**,**b** and allylic acetates **13a**,**b** (Tables 4 and 5, entry 3). When we used **10c**, the only isolated product was allenoate **12c** (Table 6, entry 3). Thus, because we observed these products from these reactions, we questioned whether it was indeed possible to afford such outcomes by way of a phosphonium diene in the absence of Cs_2CO_3 (*vide infra*). When we subjected **9** and each of the three pronucleophiles **10a**–**c** to excess PPh_3, the only product generated was the respective allylic acetate **13a**–**c** (Tables 4–6, entry 4). It is possible that allenoates **12a**–**c** were produced during these reactions, but were subsequently consumed by the excess of PPh_3 present.[28] Overall, it appears that allenylic acetate **9** and both nitrogen- and carbon-based nucleophiles reacted in a similar manner when exposed solely to PPh_3 in the absence of Cs_2CO_3.

To rationalize the construction of products **12** and **13** in the absence of Cs_2CO_3, we returned to the question of the plausibility of a phosphonium diene intermediate leading to the formation of **12** and **13**. Generation of this intermediate would result in the liberation of acetate into the reaction mixture. As such, we were interested in probing whether acetate was acting as the base in the reaction *en route* to constructing allenoates **12** and allylic acetates **13**. Thus, we performed a series of reactions of **9** with **10a** or **10b** in the presence of PPh_3 and excess NaOAc (Table 4, entry 5; Table 5, entries 5 and 6). If NaOAc was indeed capable of serving as the base in this reaction, the product distribution should have more closely resembled that observed in the presence of Cs_2CO_3. Our results were, however, nearly identical to those observed in the absence of NaOAc (Table 4, entry 3; Table 5, entries 3 and 4). Subsequently, we conducted two experiments of **9** with **10a** or **10b** in the presence of NaOAc alone; no reaction occurred in either case (Table 4, entry 6; Table 5, entry 7). From these findings, we conclude that the acetate ion did not act as a base during any of these reactions. Most importantly, taken together, our results indicate that it is extremely unlikely that the phosphonium diene was generated during these reactions. As discussed earlier, in the absence of an external base, the phosphonium diene would not undergo a reaction with the pronucleophile and, thus, no products would form. Because we have demonstrated that nothing else could serve as the base in the absence of Cs_2CO_3, it would be reasonable to expect that these reactions would not afford any products at all. We did, however, observe product formation, making it clear that the phosphonium diene did not form during these reactions. Ultimately, our findings suggest that, in the absence of an appropriate external base, phosphonium dienolate **14**, generated upon Michael addition of PPh_3 to allenylic acetate **9**, must fulfill the role of a Brønsted base (*vide infra*) and facilitate the formation of **12** and **13**.[29]

With this realization, we propose that a potential pathway toward allenoates **12a**–**c**, in the absence of an external base, proceeds through phosphonium dienolate **14**, as displayed in Scheme 3.[30] The monopronucleophiles **10a**–**c** are subsequently deprotonated by **14**, yielding phosphonium **15**. At this point, the newly formed anion of the nucleophile **10** undergoes an S_N2 reaction at the acetate of **15** to produce phosphonium **16**. Deprotonation of the α-carbon of **16** generates new phosphonium dienolate **17**, which then eliminates PPh_3 to produce allenoate **12**.



Scheme 3. Mechanistic rationale for the formation of allenoate **12** from allenylic acetate **9** in the absence of Cs_2CO_3.



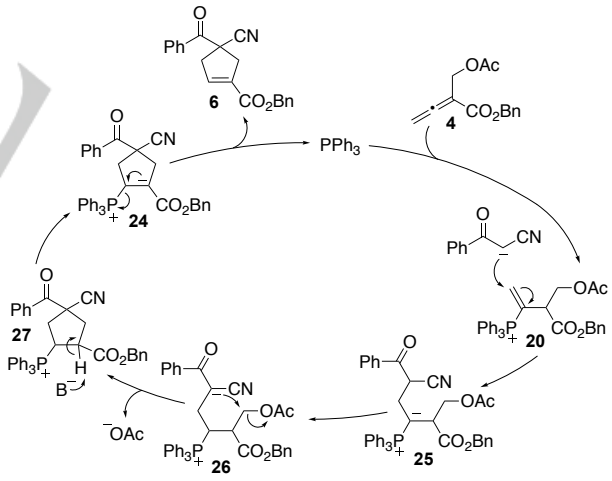
Scheme 4. Plausible mechanism for Tong's (4+1) reaction.

While our proposed mechanisms are more consistent with the observed product distributions, we cannot unequivocally exclude the possibility of phosphonium diene **2** as a reactive intermediate in the formation of allenoates **12a**–**c** and allylic acetates **13a**–**c**. A route proceeding through phosphonium diene **2** is, however, possible only if it employs phosphonium **15** as well; otherwise, there would be no means of introducing the nucleophile to the reaction in the absence of an external base. Therefore, instead of suggesting that **12** and **13** are produced through a complex system of mechanisms employing multiple reactive intermediates working in tandem, we feel it is best to propose a much simpler mechanism for this process, involving phosphonium **15** as a common intermediate, and not requiring formation of phosphonium diene **2**.[31]

Proposed Mechanism for Tong's (4+1) Reaction

Based on the data obtained from our investigations employing the various monopronucleophiles, it is likely that the mechanism proposed by Tong for the phosphine-catalyzed (4+1) reaction of allenylic acetate **4** does not adequately describe the actual events. The most important observation is that this reaction does not have to pass through phosphonium diene **5** *en route* to the formation of cyclopentene **6**. Rather, the data we have obtained suggest a series of alternative mechanisms working in concert to produce **6**. Scheme 4 presents the first plausible mechanism, based on our findings. The addition of PPh_3 to allenylic acetate **4** generates phosphonium dienolate **18**, which then undergoes protonation to yield phosphonium **20**. At this point, the enolate of **19** could displace the acetate, yielding intermediate **21**. Following deprotonation of **21**, zwitterionic intermediate **22** undergoes intramolecular γ-umpolung cyclization to produce phosphorus ylide **23**, which subsequently undergoes proton transfer to **24** and then elimination of PPh_3 to yield cyclopentene **6**.[32]

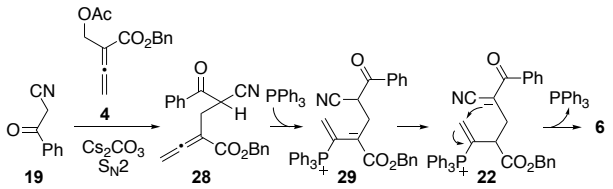
An alternative pathway can be proposed, beginning in the same manner as just discussed. The pathways diverge, however, upon construction of phosphonium **20**. Instead of adding to the β′-carbon, the reaction could proceed initially via γ-umpolung addition of the nucleophile to phosphonium **20**, generating phosphorus ylide **25** (Scheme 5). Following proton transfer, the anion of intermediate **26** undergoes an intramolecular S_N2 reaction, displacing the acetate to form phosphonium **27**. Cyclopentene **6** would then be produced following deprotonation of the α-carbon of **27** and subsequent elimination of PPh_3 from **24**.



Scheme 5. Plausible alternative mechanism for Tong's (4+1) reaction.

A third potential mechanism can also be proposed. Considering that benzoyl acetonitrile (**19**) would likely be converted almost completely to its enolate in the presence of excess Cs_2CO_3, as was the case in Tong's reaction, addition of allenylic acetate **4** to the mixture would mostly result in conversion to allenoate **28** through an S_N2 displacement of the acetate of **4** (Scheme 6). Allenoate **28** then undergoes a phosphine-catalyzed intramolecular γ-umpolung cyclization that begins with addition of PPh_3 to **28**, generating phosphonium dienolate **29**.[32] Following subsequent proton transfer, intermediate **22** is obtained, ultimately producing cyclopentene **6**

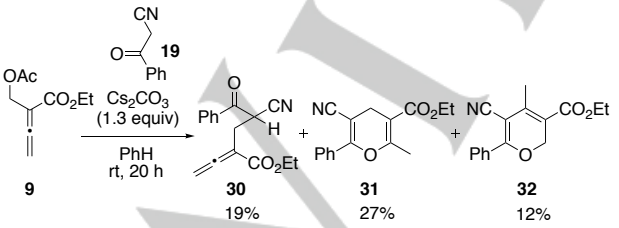
as shown in Scheme 4.



Scheme 6. Alternative pathway for the production of intermediate **22**.

Because the major products obtained when Cs_2CO_3 was employed in the reactions with the carbon-centered monopronucleophiles **10b**,**c** were allenoates **12b**,**c**, it is likely that the predominant pathway in operation during Tong's reaction involves the intramolecular γ-umpolung cyclization presented in either Scheme 4 or 6. This argument is further supported by the fact that when catalytic PPh_3 was employed in the reactions, the formation of the β′-addition products was favored over those produced by γ-umpolung addition. The route presented in Scheme 5 cannot be discounted completely, but it is likely that it constitutes only a minor pathway, if it all.

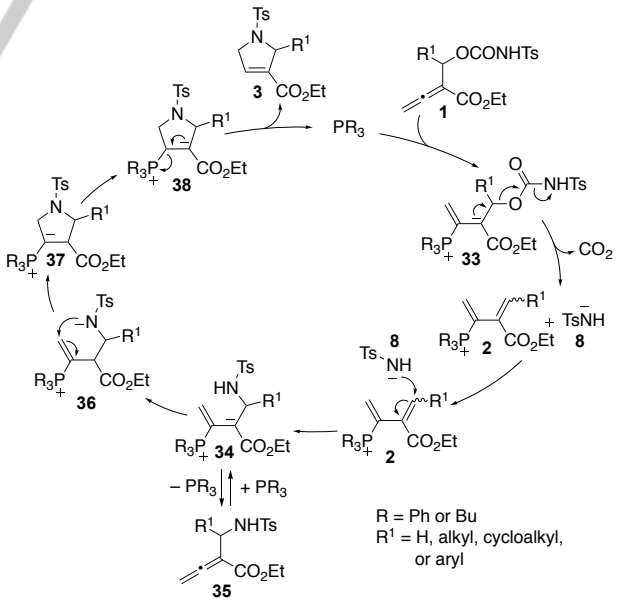
To obtain further evidence to support our proposed mechanism, we ran a reaction between allenylic acetate **9** and benzoyl acetonitrile (**19**) in the presence of Cs_2CO_3 (Scheme 7); we isolated allenoate **30**, 4*H*-pyran **31**, and 2*H*-pyran **32** in yields of 19, 27, and 12%, respectively.[33] Allenoate **30** was likely formed via an S_N2 reaction of the enolate of **19** with allenylic acetate **9**. The presence of this product is important; it provides evidence for the mechanism proposed in Scheme 6 as being the primary reaction pathway for the (4+1) annulation. It is also notable that 4*H*-pyran **31** was likely produced from allenoate **30** through an intramolecular oxa-Michael addition.[34] In contrast, 2*H*-pyran **32** probably arose from an S_N2' addition of the enolate of **19** to allenylic acetate **9** and subsequent intramolecular oxa-Michael addition to the β′-carbon.[34] As such, the total yield of products constructed via the S_N2 pathway was 46%, whereas the yield obtained from the S_N2' pathway was only 12%. This observation ultimately suggests that the mechanism presented in Scheme 6 is the major pathway for the formation of cyclopentene **6** from allenylic acetate **4**, and more accurately depicts what is transpiring during Tong's phosphine-catalyzed (4+1) reaction.



Scheme 7. Reaction between allenylic acetate **9** and **19** in the presence of Cs_2CO_3.

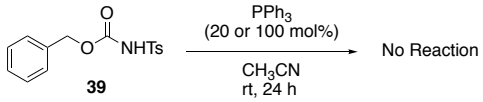
Proposed Mechanism for our Phosphine-Catalyzed Annulative Rearrangement

Based on the knowledge gathered from the studies conducted with monopronucleophiles **10a–c**, it is now apparent that our (4+1) reaction likely begins with addition of phosphine to allenylic carbamate **1** to form phosphonium dienolate **33** (Scheme 8). This intermediate subsequently undergoes β-elimination of the carbamate, generating phosphonium diene **2**, toluenesulfonamide anion **8**, and CO_2. At this point, we return to our initially posed question: To which carbon of phosphonium diene **2** does the anion **8** add to first? As unveiled from our investigation into the reactions between allenylic acetate **9** and monopronucleophiles **10a–c**, a phosphonium diene is not likely to be generated from **9**. Accordingly, we were unable to elucidate the initial site of attack of the sulfonamide anion **8** on phosphonium diene **2**. While we cannot conclusively state that addition to the γ-carbon did not occur first, we believe that **8** was most likely to add to the β′-carbon of phosphonium diene **2**. This mode of addition would be consistent with the lower reaction efficiency observed upon increasing the steric bulk of the alkyl substituent. Following addition to the β′-carbon, phosphonium dienolate **34** would be obtained. Notably, this intermediate could potentially eliminate the phosphine to generate allenoate **35**, instead of undergoing proton transfer to generate the next intermediate in the catalytic cycle. Importantly, we have previously disclosed an intramolecular γ-umpolung cyclization of compounds similar to **35** that produce 3-pyrrolines **3** following exposure to catalytic PPh_3.[18] Such facile conversion of **35** to **3** serves to provide support that **8** adds to the β′-carbon of phosphonium diene **2**. From **34**, the conversion to 3-pyrroline **3** occurs through proton transfer to construct zwitterion **36**, intramolecular γ-umpolung cyclization to yield phosphorus ylide **37**, proton transfer to form **38**, and subsequent elimination of the phosphine.



Scheme 8. Proposed mechanism for our phosphine-catalyzed (4+1) reaction.

We also considered an alternative mechanism that produces **8** through direct S_N2 displacement of the carbamate or addition to the carbonyl by the phosphine. In an attempt to evaluate this alternative pathway, we subjected benzyl tosyl carbamate (**39**) to both catalytic and stoichiometric PPh_3 (Scheme 9). If PPh_3 were able to facilitate the displacement of the carbamate or addition to the carbonyl, it would generate a benzyl phosphonium or benzyloxycarbonyl phosphonium species and sulfonamide anion **8**. From this point, **8** might undergo a subsequent S_N2 reaction to generate benzyl toluenesulfonamide (**10a**). Much to our delight, we observed no reaction between PPh_3 and **39**, suggesting that the sulfonamide anion **8** was not generated through an S_N2 displacement of the carbamate from **1** by PPh_3. Consequently, our transformation in Scheme 8 must proceed by way of an S_N2' reaction, generating phosphonium diene **2** and toluenesulfonamide anion **8**. As such, this reaction is the first example of a phosphine-catalyzed transformation that proceeds unequivocally through a phosphonium diene as a reactive intermediate. We conclude that the reaction developed by Tong is unlikely to proceed through phosphonium diene **5**, whereas our reaction clearly must proceed through phosphonium diene **2** to arrive at 3-pyrrolines **3**.

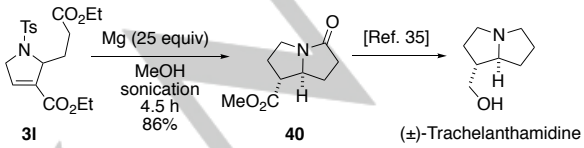


Scheme 9. Reaction of benzyl tosyl carbamate (**39**) with PPh_3.

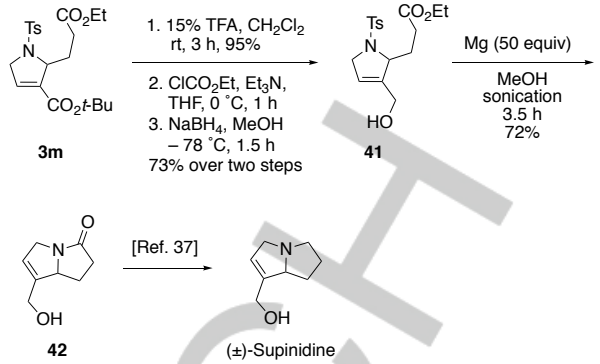
Application in Total Synthesis

We demonstrate the synthetic utility of this phosphine-catalyzed (4+1) reaction through syntheses of the pyrrolizidine alkaloids (±)-trachelanthamidine (Scheme 10) and (±)-supinidine (Scheme 11). A formal synthesis of (±)-trachelanthamidine was achieved by treating pyrroline **3l** with Mg in MeOH—effecting detosylation, lactamization, diastereoselective 1,4-reduction of the α,β-unsaturated ester, and transesterification—to yield the lactam **40** in 86% yield.[35,36]

Our formal synthesis of (±)-supinidine commenced with the trifluoroacetic acid–mediated removal of the *tert*-butyl group from pyrroline **3m** in 95% yield. We then converted the resulting free carboxylic acid to the mixed anhydride, which was reduced with $NaBH_4$ to deliver the allylic alcohol **41** in 73% yield over the two steps. Detosylation using Mg in MeOH and concomitant *in situ* lactamization gave the lactam **42** in 72% yield, thereby completing a formal synthesis of (±)-supinidine in four steps from pyrroline **3m** in 50% overall yield.[37]



Scheme 10. Formal synthesis of (±)-trachelanthamidine.



Scheme 11. Formal synthesis of (±)-supinidine.

Conclusion

We have developed a novel phosphine-catalyzed (4+1) annulative rearrangement of allenylic carbamates **1** to form 3-pyrrolines **3**. This reaction was employed to prepare an array of 1,3-disubstituted and 1,2,3-trisubstituted 3-pyrrolines in moderate to good yields, focusing on the 2-alkyl-substituted variants that have traditionally been difficult to synthesize through phosphine catalysis. This reaction appears to begin with stepwise displacement of the carbamate by the phosphine, generating phosphonium diene **2**, CO_2, and toluenesulfonamide anion **8**, which then adds to the β′-carbon of the phosphonium diene, followed by intramolecular γ-umpolung cyclization to form 3-pyrroline **3**. To discern experimentally which carbon of phosphonium diene **2** underwent addition of the sulfonamide anion, we investigated the reactions of allenylic acetate **4** with several mononucleophiles. The results from this study revealed, unexpectedly, that Tong's phosphine-catalyzed (4+1) reaction to construct cyclopentenes is unlikely to proceed—as had been proposed—through a phosphonium diene, but rather appears to employ multiple mechanisms working in parallel. Of these mechanisms, we propose that the major pathway along which Tong's reaction is likely to travel is a phosphine-catalyzed intramolecular γ-umpolung cyclization. Consequently, our newly developed (4+1) reaction is the first example of a phosphine-catalyzed reaction that must pass unequivocally through a phosphonium diene intermediate. Additionally, our newly developed methodology was applied to concise formal syntheses of the pyrrolizidine natural products (±)-trachelanthamidine and (±)-supinidine.

Experimental Section

General Information. All reactions were performed under an Ar atmosphere with dry solvents in oven-dried round-bottom flasks containing Teflon coated stirrer bars, unless otherwise noted. CH_2Cl_2, CH_3CN, and Et_3N were freshly distilled from CaH_2; tetrahydrofuran (THF), Et_2O, toluene, and benzene were distilled from Na/benzophenone. All other reagents were obtained commercially and used without further purification, unless otherwise stated. Reactions were monitored using thin layer chromatography (TLC), performed on 0.25-mm SiliCycle Glass-Backed Extra-Hard-Layer, 60-Å silica gel plates (TLG-R10011B-323) and

visualized under UV light or through permanganate and iodine staining. Flash column chromatography was performed using SiliCycle SiliaFlash® P60 (230–400 mesh, R12030B) and compressed air. IR spectra were recorded using either a Thermo Nicolet Avatar 370 FT-IR spectrometer or a JASCO FT/IR-4100 spectrometer with an ATR-PRO 450-S accessory. NMR spectra were recorded using Bruker ARX-500, DRX-500, AV-500, or AV-300 instruments calibrated to $CH(D)Cl_3$ as an internal reference (7.26 and 77.00 ppm for ^1H and ^{13}C NMR spectra, respectively). Data for ^1H NMR spectra are reported in terms of chemical shift (δ, ppm), multiplicity, coupling constant (Hz), and integration. Data for ^{13}C NMR spectra are reported in terms of chemical shift (δ, ppm), with multiplicity and coupling constants in the case of C–F coupling. The following abbreviations are used to denote multiplicities: s = singlet; d = doublet; dd = doublet of doublets; dt = doublet of triplets; dq = doublet of quartets; ddd = doublet of doublet of doublets; t = triplet; td = triplet of doublets; tt = triplet of triplets; q = quartet; qd = quartet of doublets; quin = quintet; sex = sextet; m = multiplet. Mass spectra were recorded using an Applied Biosystems Voyager-DE STR MALDI-TOF spectrometer operated in a reflector mode, under positive polarity. The matrix was 2,5-dihydroxybenzoic acid, which was also employed as an internal calibrant. Data were analyzed using the instrument software. One compound's mass was determined using an Agilent 6890-5975 GC-MS instrument; the sample was dissolved in $CHCl_3$. Some samples were also characterized in an Agilent ESI mass spectrometer, with the data analyzed using the instrument's software.

Starting Materials. Ethyl 4-bromo-2-butynoate (**S4**) was prepared following literature procedures;[38] the synthetic route to **S4** is presented in Scheme S1.[20] *tert*-Butyl 4-bromo-2-butynoate (**S7**) was prepared in a manner similar to **S4** (Scheme S2).[20,39] 4-(*tert*-Butyldimethylsilyloxy)butanal[40] and 4-pentynal[41] were prepared following literature procedures.

tert-Butyl 4-hydroxy-2-butynoate (**S6**). 3,4-Dihydro-2*H*-pyran (14.9 mL, 160 mmol) and propargyl alcohol (**S1**; 8.65 mL, 145 mmol) were placed in an oven-dried round-bottom flask containing a magnetic stirrer bar and then cooled to 0 °C using an ice-water bath. *p*-Toluenesulfonic acid (0.276 g, 1.45 mmol) was added to the mixture, which was then stirred at 0 °C for 10 min. The solution was then removed from the bath and warmed to room temperature. After stirring for 2 h at room temperature, dry THF (230 mL) was added and then the solution was cooled to –78 °C. *n*-BuLi (1.6 M solution in hexanes, 99.7 mL, 160 mmol) was slowly added and then the mixture was stirred for 1.5 h at –78 °C. A solution of di-*tert*-butyl dicarbonate (39.5 g, 181 mmol) in dry THF (35 mL) was slowly added (in 20 mL portions) to the mixture over a period of 20 min. The mixture was stirred at –78 °C for 1 h before being removed from the cooling bath and placed in an ice-water bath (0 °C), in which it was stirred for 30 min. The reaction was quenched through the addition of saturated aqueous NH_4Cl (450 mL). The separated aqueous layer was extracted with EtOAc (3 × 150 mL) and then the combined organic layers were washed with brine (100 mL), dried (Na_2SO_4), filtered, and concentrated to yield crude **S5** (43.3 g). This material was subjected to the subsequent reaction without further purification. The crude product was dissolved in absolute EtOH (570 mL) and then pyridinium *p*-toluenesulfonate (3.72 g, 14.5 mmol) was added. The mixture was heated to 55 °C and stirred at that temperature for 2 h. After this time, the reaction was quenched through the addition of saturated aqueous $NaHCO_3$ (500 mL) and then the mixture was concentrated under reduced pressure to remove the EtOH. The aqueous slurry was extracted with Et_2O (5 × 100 mL). The combined organic phases were washed with brine, dried (Na_2SO_4), and concentrated under reduced pressure. The residue was purified through flash column chromatography (100% hexanes to 5% EtOAc/hexanes to 10% EtOAc/hexanes, and finally 15% EtOAc/hexanes) to yield **S6** (18.7 g, 82% over the three steps) as an oil. The spectral data were in agreement with those previously published in the literature.[39]

tert-Butyl 4-bromo-2-butynoate (**S7**). Methanesulfonyl chloride (6.20 mL, 79.8 mmol) was added dropwise to a solution of **S6** (11.3 g, 72.6 mmol) and dry Et_3N (11.0 mL, 76.2 mmol) in dry CH_2Cl_2 (400 mL) that was cooled to 0 °C in an ice-water bath. The solution was then stirred at 0 °C for 1 h, at which point distilled water (200 mL) was added. The separated organic phase was washed sequentially with 2 M HCl (3 × 250 mL), saturated aqueous $NaHCO_3$ (2 × 250 mL), and brine (250 mL), dried (Na_2SO_4), filtered, and concentrated under reduced pressure to yield the crude propargylic mesylate (16.3 g). This material was subjected to the subsequent reaction without further purification. A solution of the crude propargylic mesylate in freshly distilled acetone (20 mL) was added to a solution of anhydrous lithium bromide (reagent stored in a glove box, 23.0 g, 26.5 mmol) in freshly distilled acetone (460 mL). The mixture was heated under reflux for 1.75 h and then cooled to room temperature. The suspension was filtered through Celite using a glass fritted funnel. The filter cake was washed thoroughly with acetone and then the resulting solution was concentrated under reduced pressure. The residue was partitioned between distilled water (300 mL) and hexanes (200 mL). The aqueous phase was extracted with hexanes (2 × 200 mL); the combined organic phases were dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The crude material was purified through flash column chromatography (100% hexanes to 10% EtOAc/hexanes) to yield **S7** (12.6 g, 80% over two steps) as a light-yellow oil. IR (ν, cm^{-1}) 3006, 2982, 2971, 2941, 1738, 1708, 1369, 1278, 1256, 1216, 1152, 1082, 840, 751, 712; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 3.94 (s, 2H), 1.50 (s, 9H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 151.7, 84.0, 78.9, 78.4, 27.8, 11.9; MS (GCMS) calcd for $C_4H_3BrO_2$ $[M - t\text{-Bu}]^+$ *m*/*z* 161.9, found 161.9.

Ethyl 4-oxobutanoate (**S8**). This compound was prepared using a known methodology that had not yet been applied to the synthesis of **S8**.[42] Tri-*n*-butyltin hydride (2.30 mL, 8.40 mmol) was added dropwise over 5 min to a solution of ethyl succinyl chloride (1.14 mL, 8.00 mmol) in freshly distilled *N*-methylpyrrolidinone (8 mL) cooled to 0 °C in an ice-water bath. The mixture was stirred for 30 min at 0 °C and then it was removed from the bath and warmed to room temperature. Once removed from the ice bath, the mixture was stirred for 45 min, at which point the reaction was determined, using TLC (staining with 2,4-dinitrophenylhydrazine produced a yellow spot to reveal the presence of the aldehyde), to be complete. Distilled water (20 mL) and EtOAc (40 mL) were added and the aqueous phase was extracted with EtOAc (3 × 40 mL). The combined organic phases were washed with saturated aqueous NH_4Cl (3 × 40 mL) to ensure removal of NMP. The organic phase was subsequently washed with brine (20 mL), dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was distilled under reduced pressure (head temperature: 100–110 °C; bath temperature: 150 °C) to yield **S8** (0.602 g, 69%) as a colorless oil. The spectral data were in agreement with those previously published.[43]

p-Methoxybenzenesulfonyl isocyanate (**S9**). Prepared by following a literature procedure for a similar compound.[21a] A solution of triphosgene (5.88 g, 19.8 mmol) in dry 1,2-dichlorobenzene (30 mL) was added over 4.5 h, via syringe pump, to a solution of *p*-methoxybenzenesulfonamide (11.0 g, 58.8 mmol) and isopropyl isocyanate (0.550 mL, 5.60 mmol) in dry 1,2-dichlorobenzene (30 mL) at 150 °C. The mixture was then heated at 180 °C for 2 h before being removed from the oil bath and cooled to room temperature, with stirring for 12 h. The solvent and isopropyl isocyanate were distilled off under 3 mmHg of pressure (bath temperature: 155 °C; head temperature: 120 °C). The remaining thick black liquid was then further distilled under 3 mmHg of pressure (bath temperature: 200 °C; head temperature: 160–165 °C) to yield **S9** (7.09 g, 57%) as a clear liquid. Upon cooling, the product solidified in the form of a low-melting white solid, which was stored under Ar at –20 °C. The spectral data were in agreement with those previously reported.[44]

p-Nitrobenzenesulfonyl isocyanate (**S10**). Prepared in an analogous manner to that presented above for **S9**, with *n*-butyl isocyanate employed instead of isopropyl isocyanate. A mixture of *p*-nitrobenzenesulfonamide (5.50 g, 27.2 mmol) and *n*-butyl isocyanate (1.21 mL, 10.9 mmol) in dry

1,2-dichlorobenzene (25 mL) was heated under reflux until the solution became clear-yellow. A solution of triphosgene (3.30 g, 11.1 mmol) in dry 1,2-dichlorobenzene (20 mL) was added to this solution over 3.5 h, via syringe pump, and then the mixture was heated under reflux for another 2 h. At this point, the mixture was removed from the oil bath and cooled to room temperature, with stirring for 12 h. The solvent and *n*-butyl isocyanate were then distilled off under reduced pressure. The remaining thick black liquid was subjected to Kugelrohr distillation to yield **S10** as a light-yellow solid (0.316 g, 5%), which was stored under Ar at –20 °C. The spectral data were in agreement with those previously reported.[45]

Synthesis of Allenylic Alcohols 7. Allenylic alcohols **7a** and **7b** were synthesized through an organocatalytic MBH reaction between ethyl 2,3-butadienoate (**S11**) and either paraformaldehyde or acetaldehyde in the presence of 3-hydroxyquinuclidine (reaction optimization studies for **7a** are presented in the SI).[20] Allenylic alcohols **7c**–**7g** and **7i**–**7m** were prepared from a tin(II)-mediated allenylation of propargyl bromides to aldehydes.[23a] Allenylic alcohol **7h** was prepared according to the procedure described in the literature.[23b]

Ethyl 2-(hydroxymethyl)-2,3-butadienoate (**7a**).[46] Paraformaldehyde (2.82 g, 89.2 mmol) was placed under vacuum in a flask and then immersed in an oil bath at 55 °C for 1 h to remove water. After cooling to room temperature, THF (50 mL) was added and then the flask was placed in an ice/NaCl bath at –15 °C. A solution of 3-hydroxyquinuclidine (472 mg, 3.57 mmol) in THF (25 mL) was added dropwise over 5 min to the suspension of paraformaldehyde. A solution of ethyl 2,3-butadienoate[47] (**S11**, 2.01 g, 17.90 mmol) in THF (25 mL) was added dropwise to the suspension of paraformaldehyde and 3-hydroxyquinuclidine over 5 min. The mixture was stirred at –15 °C for 1 h, at which point the flask was removed from the bath and warmed to room temperature while stirring for 3.75 h. Saturated aqueous NH_4Cl (50 mL) was added and then the aqueous phase was extracted with EtOAc (3 × 50 mL). The combined organic extracts were washed with brine (50 mL), dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was purified through flash column chromatography (15% EtOAc/hexanes) to yield **7a** (1.67 g, 66% yield) as a thick, slightly yellow, oil. All spectral data were in agreement with those previously published.[23b]

Ethyl 2-(1-hydroxyethyl)-2,3-butadienoate (**7b**).[18,48] Ethyl 2,3-butadienoate[47] (**S11**, 2.03 g, 18.1 mmol) was added dropwise over 5 min to a solution of 3-hyoxyquinuclidine (460 mg, 3.55 mmol) in dry Et_2O (10 mL) that was cooled at –15 °C in an ice/NaCl bath. Acetaldehyde (2.00 mL, 35.8 mmol) was then added dropwise over 1 min to this chilled solution [note: the bottle of acetaldehyde had been cooled at –78 °C and kept under Ar prior to use, to ensure that the compound remained as a liquid]. The mixture was stirred at –15 °C for 50 min, at which point the reaction was deemed to be complete (TLC). Saturated aqueous NH_4Cl (10 mL) was added and then the aqueous phase was extracted with EtOAc (3 × 10 mL). The combined organic phases were washed with H_2O (10 mL) and brine (10 mL), dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was purified through flash column chromatography (10% EtOAc/hexanes) to yield **7b** (2.20 g, 79% yield) as a thick, slightly yellow, oil. IR (ν, cm^{-1}) 3433, 2982, 2935, 2907, 1966, 1708, 1266, 1059; ^1H NMR (300 MHz, $CDCl_3$) δ 5.19 (d, *J* = 2.2 Hz, 2H), 4.62–4.51 (m, 1H), 4.17 (d, *J* = 7.1 Hz, 1H), 4.12 (d, *J* = 7.1 Hz, 1H), 3.30 (d, *J* = 4.0 Hz, 1H), 1.25 (d, *J* = 6.4 Hz, 3H), 1.21 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 212.0, 167.1, 104.3, 80.8, 64.7, 61.1, 21.0, 14.1; MS (MALDI) calcd for $C_8H_{12}O_3Na$ $[M + Na]^+$ *m*/*z* 179.07, found 179.04.

General Procedure for the Preparation of Allenylic Alcohols 7c–7g and 7i–7m. Allenylic alcohols **7d**–**7g** and **7i**–**7m** were prepared according to the procedure described below for allenylic alcohol **7c**.

Ethyl 2-(1-hydroxypropyl)-2,3-butadienoate (**7c**).[18] Prepared using a slight modification of the procedure reported by Ma.[23a] $SnCl_2$ (1.19 g, 6.28 mmol) and NaI (0.942 g, 6.28 mmol) were added sequentially, each in one portion, to a solution of ethyl 4-bromo-2-butynoate (**S4**, 1.00 g, 5.24 mmol) in *N,N´*-dimethylpropyleneurea (DMPU; 8 mL). The flask was wrapped in aluminum foil and the hood light turned off to protect the reaction from light. After stirring at room temperature for 7–8 h, the mixture was cooled to 0 °C in an ice-water bath. A solution of propionaldehyde (0.300 mL, 4.19 mmol) in DMPU (4 mL) was added over 15 min. The mixture was stirred at 0 °C for another 2 h and then removed from the ice bath, warmed to room temperature, and stirred for 18–24 h at room temperature while still wrapped in aluminum foil. At this point, the mixture was cooled to 0 °C in an ice-water bath and diluted with Et_2O (15 mL); the reaction was quenched through the addition of saturated aqueous NH_4Cl (15 mL). The separated aqueous phase was extracted with Et_2O (4 x 15 mL). The combined organic phases were washed with brine (15 mL), dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was purified through flash column chromatography (5–10% EtOAc/hexanes) to yield **7c** (373 mg, 52%) as a light-yellow oil. IR (ν, cm^{-1}) 3435, 2978, 2937, 1964, 1708, 1262, 1067; ^1H NMR (400 MHz, $CDCl_3$) δ 5.22 (d, *J* = 1.8 Hz, 2H), 4.31 (br s, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.04 (br s, 1H), 1.65 (quin, *J* = 7.2 Hz, 2H), 1.26 (t, *J* = 7.1 Hz, 3H), 0.93 (t, *J* = 7.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.4, 167.1, 102.9, 80.5, 70.7, 61.2, 28.3, 14.2, 10.2; MS (MALDI) calcd for $C_9H_{14}O_3Na$ $[M + Na]^+$ *m*/*z* 193.08, found 193.09.

Ethyl 2-(1-hydroxybutyl)-2,3-butadienoate (**7d**). This compound was prepared as described above for **7c**, except that butyraldehyde was employed as a reactant. A light-yellow oil was isolated in 55% yield. All spectral data were in agreement with those previously published.[23b]

Ethyl 2-[cyclopropyl(hydroxy)methyl]-2,3-butadienoate (**7e**).[18] This compound was prepared as described above for **7c**, except that cyclopropanecarboxaldehyde was employed as a reactant. A light-yellow oil was isolated in 65% yield. IR (ν, cm^{-1}) 3465, 2986, 1963, 1710, 1256, 1208; ^1H NMR (500 MHz, $CDCl_3$) δ 5.25 (d, *J* = 1.9, 2H), 4.23 (q, *J* = 7.2, 2H), 3.73 (d, *J* = 7.9 Hz, 1H), 3.12 (d, *J* = 3.4 Hz, 1H), 1.28 (t, *J* = 7.2 Hz, 3H), 1.18–1.10 (m, 1H), 0.63–0.56 (m, 1H), 0.52–0.40 (m, 2H), 0.27–0.21 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 212.7, 167.0, 102.9, 80.2, 73.7, 15.8, 14.0, 3.5, 2.6; MS (MALDI) calcd for $C_{10}H_{14}O_3Na$ $[M + Na]^+$ *m*/*z* 205.08, found 205.08.

Ethyl 2-[cyclopentyl(hydroxy)methyl]-2,3-butadienoate (**7f**).[18] This compound was prepared as described above for **7c**, except that cyclopentanecarboxaldehyde was employed as a reactant. Isolated in 62% yield, as a light-yellow oil. IR (ν, cm^{-1}) 3479, 2955, 2869, 1964, 1704, 1255, 1071, 1030; ^1H NMR (500 MHz, $CDCl_3$) δ 5.19 (s, 2H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.19 (br s, 1H), 2.17 (sex, *J* = 8.1 Hz, 1H), 1.88–1.76 (m, 1H), 1.67–1.41 (m, 7H), 1.25 (t, *J* = 4.8 Hz, 3H), 1.18–1.10 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 212.9, 167.1, 102.6, 80.0, 74.1, 61.1, 44.2, 29.44, 29.11, 25.6, 25.5, 14.0; MS (MALDI) calcd for $C_{12}H_{18}O_3Na$ $[M + Na]^+$ *m*/*z* 233.12, found 233.12.

Ethyl 2-[cyclohexyl(hydroxy)methyl]-2,3-butadienoate (**7g**).[18] This compound was prepared as described above for **7c**, except that cyclohexanecarboxaldehyde was employed as a reactant. A light-yellow oil was isolated in 80% yield. IR (ν, cm^{-1}) 3478, 2982, 2927, 2852, 1964, 1710, 1255, 1067; ^1H NMR (500 MHz, $CDCl_3$) δ 5.19 (d, *J* = 1.0 Hz, 2H), 4.19 (q, *J* = 7.1 Hz, 2H), 2.96 (br s, 1H), 1.97 (d, *J* = 12.8 Hz, 1H), 1.76–1.54 (m, 6H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.22–1.09 (m, 3H), 1.02–0.93 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 212.8, 166.9, 101.5, 79.8, 74.7, 61.0, 42.5, 29.7, 28.4, 26.3, 25.9, 25.7, 14.0; MS (MALDI) calcd for $C_{13}H_{20}O_3Na$ $[M + Na]^+$ *m*/*z* 247.13, found 247.12.

Ethyl 2-(1-hydroxy-4-pentynyl)-2,3-butadienoate (**7i**). This compound was prepared as described above for **7c**, except that 4-pentynal[41] was employed as a reactant. A thick light-yellow oil was isolated in 29% yield. IR (ν, cm^{-1}) 3604–3334, 3289, 3063, 2981, 2961, 2929, 2117, 1963, 1939, 1699, 1367, 1268, 1102, 1070, 1050, 852; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 5.27 (d, *J* = 2.0 Hz, 2H), 4.61–4.51 (m, 1H), 4.23 (q, *J* =

7.1 Hz, 2H), 3.11 (d, *J* = 5.2 Hz, 1H), 2.35 (td, *J* = 7.2, 2.6 Hz, 2H), 1.95 (t, *J* = 2.7 Hz, 1H), 1.86 (q, *J* = 7.0 Hz, 2H), 1.29 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 212.1, 166.9, 102.6, 83.6, 80.9, 686, 67.7, 61.3, 33.7, 14.9, 14.1; MS (MALDI) calcd for $C_{11}H_{14}O_3Na$ [M + Na]$^+$ *m*/*z* 217.08, found 217.07.

Ethyl 2-(1-hydroxy-3-phenylpropyl)-2,3-butadienoate (**7j**). This compound was prepared as described above for **7c**, except that hydrocinnamaldehyde was employed as a reactant. A thick light-yellow oil was isolated in 67% yield. IR (ν, cm^{-1}) 3609–3293, 3059, 3023, 2982, 2928, 1962, 1933, 1703, 1495, 1456, 1391, 1366, 1259, 1097, 1067; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.31–7.26 (m, 2H), 7.22–7.16 (m, 3H), 5.27 (d, *J* = 2.0 Hz, 2H), 4.50–4.39 (m, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 2.89–2.80 (m, 1H), 2.76–2.66 (m, 1H), 2.02–1.93 (m, 2H), 1.29 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 212.2, 167.1, 141.7, 128.4, 128.3, 125.8, 102.9, 80.8, 68.4, 61.2, 36.7, 31.9, 14.1; MS (MALDI) calcd for $C_{15}H_{18}O_3Na$ [M + Na]$^+$ *m*/*z* 269.12, found 269.12.

Ethyl 2-[1-hydroxy-4-(tert-butyldimethylsilyloxy)butyl]-2,3-butadienoate (**7k**). This compound was prepared as described above for **7c**, except that 4-(*tert*-butyldimethylsilyloxy)butanal[40] was employed as a reactant. A thick light-yellow oil was isolated in 44% yield. IR (ν, cm^{-1}) 3580–3253, 2953, 2923, 2889, 2858, 1965, 1939, 1711, 1255, 1097, 1061, 832; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 5.25 (d, *J* = 1.9 Hz, 2H), 4.5–4.39 (br s, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.67–3.63 (m, 2H), 3.65 (td, *J* = 5.8, 1.3 Hz, 1H), 1.78–1.58 (m, 4H), 1.28 (t, *J* = 7.1 Hz, 3H), 0.88 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 212.4, 166.9, 103.3, 80.6, 68.9, 63.0, 61.1, 32.2, 29.0, 25.8, 18.2, 14.1, –5.4; MS (MALDI) calcd for $C_{16}H_{30}O_4SiNa$ [M + Na]$^+$ *m*/*z* 337.18, found 337.17.

Diethyl 3-hydroxy-2-vinylidenehexanedioate (**7l**). This compound was prepared as described above for **7c**, except that ethyl 4-oxobutanoate (**S8**) was employed as a reactant. A thick light-yellow oil was isolated in 61% yield. IR (ν, cm^{-1}) 3644–3248, 2984, 2935, 2905, 1965, 1940, 1737, 1709, 1367, 1253, 1176, 1070; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 5.26 (d, *J* = 2.0 Hz, 2H), 4.49–4.38 (br s, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 4.10 (q, *J* = 7.1 Hz, 2H), 3.24–3.14 (br s, 1H), 2.54–2.36 (m, 2H), 2.01–1.88 (m, 2H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.22 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 212.1, 173.5, 166.8, 102.7, 81.0, 68.2, 61.2, 60.3, 30.5, 30.1, 14.1, 14.1; MS (MALDI) calcd for $C_{12}H_{18}O_5Na$ [M + Na]$^+$ *m*/*z* 265.11, found 265.11.

1-tert-Butyl 6-ethyl 3-hydroxy-2-vinylidenehexanedioate (**7m**). This compound was prepared as described above for **7c**, except that *tert*-butyl 4-bromo-2-butynoate (**S7**) and ethyl 4-oxobutanoate (**S8**) were employed as the reactants. A thick light-yellow oil was isolated in 72% yield. IR (ν, cm^{-1}) 3585–3318, 2981, 2935, 1963, 1941, 1734, 1702, 1367, 1296, 1249, 1168, 846; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 5.19 (d, *J* = 2.0 Hz, 2H), 4.44–4.38 (m, 1H), 4.13 ppm (q, *J* = 7.1 Hz, 2H), 3.19 (d, *J* = 5.7 Hz, 1H), 2.56–2.38 (m, 2H), 2.0–1.92 (m, 2H), 1.48 (s, 9H), 1.25 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 211.9, 173.5, 166.1, 103.8, 81.8, 80.4, 68.3, 60.3, 30.5, 30.2, 27.9, 14.1; MS (MALDI) calcd for $C_{14}H_{22}O_5Na$ [M + Na]$^+$ *m*/*z* 293.14, found 293.14.

Allenylic carbamates 1. Allenylic carbamates **1a** and **1bb** were prepared according to the procedures described below, while allenylic carbamates **1b**–**m**, **1ba**, **1bc**, and **1bd** were prepared according to the procedure described for **1b**.

Ethyl 2-[(tosylcarbamoyloxy)methyl]-2,3-butadienoate (**1a**).[18] *p*-Toluenesulfonyl isocyanate (0.590 mL, 3.71 mmol) was added dropwise quickly to a solution of allenylic alcohol **7a** (0.500 g, 3.52 mmol) in dry CH_2Cl_2 (8.8 mL) at room temperature. The mixture was stirred for 1.5 h at room temperature and then concentrated under reduced pressure. The residue was purified through flash column chromatography (10–30% EtOAc/hexanes) to yield **1a** (1.10 g, 92% yield) as a thick oil that solidified into a white crystalline solid upon standing in the freezer (–20 °C). This compound could also be recrystallized from EtOAc/hexanes as a white crystalline solid. M.p. 111–114 °C; IR (ν, cm^{-1}) 3224, 2985, 1966, 1752, 1711, 1448, 1160; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.26 (s, 1H), 7.90 (d, *J* = 8.3 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 5.18 (t, *J* = 2.1 Hz, 2H), 4.76 (t, *J* = 2.1 Hz, 2H), 4.16 (q, *J* = 7.1 Hz, 2H), 2.42 (s, 1H), 1.22 (t, *J* = 7.1 Hz, 3H): ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.6, 165.1, 150.2, 145.0, 135.5, 129.6, 128.5, 96.3, 81.0, 62.9, 61.5, 21.7, 14.1; MS (MALDI) calcd for $C_{15}H_{17}NO_6SNa$ [M + Na]$^+$ *m*/*z* 362.07, found: 362.06.

Ethyl 2-[1-(tosylcarbamoyloxy)ethyl]-2,3-butadienoate (**1b**).[18] *p*-Toluenesulfonyl isocyanate (0.430 mL, 2.70 mmol) was added dropwise to a solution of allenylic alcohol **7b** (0.400 g, 2.56 mmol) in dry CH_2Cl_2 (6.4 mL), cooled at 0 °C in an ice-water bath. The mixture was stirred for 1 h at 0 °C, at which point it was removed from the bath and warmed to room temperature. After 30 min, the mixture was concentrated under reduced pressure and the residue purified through flash column chromatography (5–20% EtOAc/hexanes) to yield **1b** (0.846 g, 94% yield) as a thick colorless oil. IR (ν, cm^{-1}) 3232, 2988, 1967, 1750, 1717, 1450, 1357, 1286, 1224, 1162; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.4 Hz, 2H), 7.24 (d, *J* = 8.2 Hz, 2H), 5.53–5.48 (m, 1H), 5.20 (dd, *J* = 14.7, 2.1 Hz, 1H), 5.15 (dd, *J* = 14.6, 2.1 Hz, 1H), 4.04 (q, *J* = 7.1 Hz, 2H), 2.35 (s, 3H), 1.28 (d, *J* = 6.5 Hz, 3H), 1.11 (t, *J* = 7.1 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 212.8, 164.7, 149.8, 144.7, 135.6, 129.3, 128.2, 101.8, 82.2, 69.4, 61.2, 60.4, 21.4, 18.9, 14.0, 13.8; MS (MALDI) calcd for $C_{16}H_{19}NO_6SNa$ [M + Na]$^+$ *m*/*z* 376.08, found 376.04.

Ethyl 2-[1-(tosylcarbamoyloxy)propyl]-2,3-butadienoate (**1c**).[18] Isolated in 84% yield as a thick colorless oil. IR (ν, cm^{-1}) 3231, 2981, 2938, 1970, 1750, 1717, 1447, 1162; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.4 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 5.38–5.35 (m, 1H), 5.20, (dd, *J* = 14.6, 1.9 Hz, 1H), 5.15 (dd, *J* = 14.6, 2.0 Hz, 1H), 4.11 (q, *J* = 7.1, 2H), 2.42 (s, 3H), 1.79–1.63 (m, 2H), 1.19 (t, *J* = 7.2 Hz, 3H), 0.82 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) *δ* 213.0, 164.7, 149.7, 144.8, 135.6, 129.4, 128.3, 100.6, 81.7, 74.2, 61.2, 26.3, 21.5, 13.9, 9.3. MS (MALDI) calcd for $C_{17}H_{21}NO_6SNa$ [M + Na]$^+$ *m*/*z* 390.41, found 390.21.

Ethyl 2-[1-(tosylcarbamoyloxy)butyl]-2,3-butadienoate (**1d**). Isolated in 69% yield as a thick light-yellow oil. IR (ν, cm^{-1}) 3432–3088, 2962, 2934, 2873, 1965, 1933, 1751, 1709, 1598, 1496, 1446, 1349, 1284, 1255, 1218, 1160, 1091, 885, 862; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.89 (d, *J* = 8.3 Hz, 2H), 7.31 (d, *J* = 8.1 Hz, 2H), 5.47–5.39 (m, 1H), 5.23 (dd, *J* = 14.5, 1.8 Hz, 1H), 5.16 (dd, *J* = 14.5, 1.9 Hz, 1H), 4.12 (q, *J* = 7.1 Hz, 2H), 2.43 (s, 3H), 1.71–1.61 (m, 2H), 1.29–1.18 (m, 5H), 0.85 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 213.0, 164.7, 149.7, 144.8, 135.6, 129.4, 128.3, 101.0, 81.8, 73.0, 61.2, 35.3, 21.5, 18.3, 14.0, 13.5; MS (MALDI) calcd for $C_{18}H_{23}NO_6SNa$ [M + Na]$^+$ *m*/*z* 404.11, found 404.11.

Ethyl 2-[cyclopropyl(tosylcarbamoyloxy)methyl]-2,3-butadienoate (**1e**).[18] Isolated in 88% yield as a thick oil. IR (ν, cm^{-1}) 3230, 2985, 1964, 1715, 1448, 1353, 1161; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.2 Hz, 2H), 7.28 (d, *J* = 8.2 Hz, 2H), 5.27 (dd, *J* = 14.6, 1.4 Hz, 1H), 5.23 (dd, *J* = 14.6, 1.3 Hz, 1H), 4.88 (d, *J* = 9.0 Hz, 1H), 4.07 (q, *J* = 7.1 Hz, 2H), 2.40 (s, 3H), 1.28–1.21 (m, 1H), 1.15 (t, *J* = 7.1 Hz, 3H), 0.52–0.40 (m, 3H), 0.32–0.28 (m, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 213.7, 164.7, 150.0, 144.6, 135.7, 129.3, 128.2, 100.9, 81.6, 77.2, 61.2, 60.4, 21.5, 14.0, 13.9, 3.9, 2.9; MS (MALDI) calcd for $C_{18}H_{21}NO_6SNa$ [M + Na]$^+$ *m*/*z* 402.10, found: 402.11.

Ethyl 2-[cyclopentyl(tosylcarbamoyloxy)methyl]-2,3-butadienoate (**1f**).[18] Isolated in 86% yield as a thick oil. IR (ν, cm^{-1}) 3229, 2958, 2868, 1964, 1750, 1701, 1447, 1162; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.1 Hz, 2H), 7.28 (d, *J* = 8.2 Hz, 2H), 5.32 (dt, *J* = 8.1, 1.4 Hz, 1H), 5.19 (dd, *J* =14.6, 1.5 Hz, 1H), 5.13 (dd, *J* = 14.5, 1.5 Hz, 1H), 4.09 (q, *J* = 7.1 Hz, 2H), 2.40 (s, 3H), 2.25 (sex, *J* = 8.0 Hz, 1H), 1.61–1.34 (m, 6H), 1.26–1.14 (m, 2H), 1.17 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 213.7, 164.9, 150.0, 144.6, 135.7, 129.3, 128.2, 100.8, 81.5, 76.4, 61.1, 42.8, 28.6, 28.3, 25.2, 25.2, 21.5, 13.9; MS (MALDI) calcd for $C_{20}H_{25}NO_6SNa$ [M + Na]$^+$ *m*/*z* 430.13, found: 429.95.

Ethyl 2-[cyclohexyl(tosylcarbamoyloxy)methyl]-2,3-butadienoate (**1g**).[18] Isolated in 88% yield as a thick oil. IR (ν, cm^{-1}) 3231, 2929, 2854, 1718, 1448, 1161, 1091; ^1H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 8.2 Hz, 2H), 5.23 (dt, *J* = 7.0, 1.6 Hz, 1H), 5.19 (dd, *J* = 14.5, 1.3 Hz, 1H), 5.13 (dd, *J* = 14.5, 1.6 Hz, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 2.43 (s, 3H), 1.73–1.58 (m, 4H), 1.53 (d, *J* = 11.9 Hz, 2H), 1.22 (t, *J* = 7.1 Hz, 3H), 1.19–1.03 (m, 3H), 1.00–0.82 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 213.5, 164.9, 149.9, 144.9, 135.7, 129.5, 128.4, 99.9, 81.5, 77.3, 61.3, 40.8, 29.0, 27.7, 26.1, 25.8, 25.7, 21.7, 14.1; MS (MALDI) calcd for $C_{21}H_{27}NO_6SNa$ [M + Na]$^+$ *m*/*z* 444.15, found: 444.16.

Ethyl 2-[phenyl(tosylcarbamoyloxy)methyl]-2,3-butadienoate (**1h**). Isolated in 88% yield as a white form. IR (ν, cm^{-1}) 3226, 2985, 2922, 1967, 1750, 1706, 1598, 1496, 1443, 1345, 1259, 1222, 1185, 1155, 1089, 869; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.88 (dt, *J* = 8.6, 1.8 Hz, 2H), 7.31–7.26 (m, 7H), 6.44 (t, *J* = 2.4 Hz, 1H), 5.24 (dd, *J* = 14.7, 2.3 Hz, 1H), 5.19 (dd, *J* = 14.7, 2.4 Hz, 1H), 4.17–4.02 (m, 2H), 2.43 (s, 3H), 1.17 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 213.1, 164.4, 149.2, 145.0, 136.7, 135.4, 129.5, 128.7, 128.4, 128.3, 127.2, 102.0, 82.6, 74.3, 61.4, 21.6, 14.0; MS (MALDI) calcd for $C_{21}H_{21}NO_6SNa$ [M + Na]$^+$ *m*/*z* 438.10, found 438.09.

Ethyl 2-[1-(tosylcarbamoyloxy)-4-pentynyl]-2,3-butadienoate (**1i**). Isolated in 89% yield as a thick light-yellow oil. IR (ν, cm^{-1}) 3447–3066, 2987, 2928, 1962, 1936, 1752, 1707, 1595, 1447, 1351, 1276, 1226, 1162, 1085, 862; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.89 (d, *J* = 8.3 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 5.54–5.46 (m, 1H), 5.23 (dd, *J* = 14.7, 1.8 Hz, 1H), 5.16 (dd, *J* = 14.7, 2.0 Hz, 1H), 4.13 (q, *J* = 7.1 Hz, 2H), 2.43 (s, 3H), 2.17–2.08 (m, 2H), 2.04–1.87 (m, 3H), 1.21 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 212.8, 164.5, 149.6, 144.9, 135.5, 129.5, 128.3, 100.4, 82.4, 82.2, 72.1, 69.1, 61.3, 32.1, 21.6, 14.6, 14.0; MS (MALDI) calcd for $C_{19}H_{21}NO_6SNa$ [M + Na]$^+$ *m*/*z* 414.10, found 414.10.

Ethyl 2-[1-(tosylcarbamoyloxy-3-phenylpropyl]-2,3-butadienoate (**1j**). Isolated in 72% yield as a thick light-yellow oil. IR (ν, cm^{-1}) 3366–3107, 3064, 3024, 2988, 2924, 1964, 1932, 1752, 1707, 1599, 1444, 1355, 1287, 1217, 1167, 1088, 1017, 860; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.92 (d, *J* = 8.3 Hz, 2H), 7.32 (d, *J* = 8.2 Hz, 2H), 7.27–7.21 (m, 2H), 7.20–7.13 (m, 1H), 7.11–7.05 (m, 2H), 5.52–5.45 (m, 1H), 5.23 (dd, *J* = 14.6, 1.8 Hz, 1H), 5.17 (dd, *J* = 14.6, 1.9 Hz, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 2.56 (t, *J* = 7.9 Hz, 2H), 2.42 (s, 3H), 2.13–1.93 (m, 2H), 1.21 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 213.0, 164.6, 149.6, 144.9, 140.7, 135.6, 129.5, 128.3, 128.3, 128.2, 126.0, 100.8, 82.0, 72.8, 61.3, 34.9, 31.4, 21.6, 14.0; MS (MALDI) calcd for $C_{23}H_{25}NO_6SNa$ [M + Na]$^+$ *m*/*z* 466.13, found 466.13.

Ethyl 2-[1-(tosylcarbamoyloxy)-4-(tert-butyldimethylsilyloxy)butyl]-2,3-butadienoate (**1k**). Isolated in 72% yield as a thick light-yellow oil. IR (ν, cm^{-1}) 3223, 2953, 2925, 2858, 1963, 1934, 1752, 1718, 1443, 1360, 1258, 1219, 1162, 1091, 839; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.89 (d, *J* = 8.3 Hz, 2H), 7.31 (d, *J* = 8.2 Hz, 2H), 5.48–5.40 (m, 1H), 5.22 (dd, *J* = 14.6, 1.7 Hz, 1H), 5.16 (dd, *J* = 14.6, 1.9 Hz, 1H), 4.12 (q, *J* = 7.1 Hz, 2H), 3.60–3.49 (m, 2H), 2.42 (s, 3H), 1.88–1.64 (m, 2H), 1.51–1.38 (m, 2H), 1.20 (t, *J* = 7.1 Hz, 3H), 0.85 (s, 9H), 0.00 (s, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 213.0, 164.7, 149.7, 144.8, 135.6, 129.4, 128.3, 100.9, 81.9, 73.0, 62.3, 61.2, 29.7, 28.2, 25.8, 21.5, 18.2, 14.0, –5.4; MS (MALDI) calcd for $C_{24}H_{37}NO_7SSiNa$ [M + Na]$^+$ *m*/*z* 534.20, found 534.20.

Diethyl 3-(tosylcarbamoyloxy)-2-vinylidenehexanedioate (**1l**). Isolated in 92% yield as a thick light-yellow oil. IR (ν, cm^{-1}) 2988, 2970, 2940, 1967, 1737, 1722, 1444, 1365, 1257, 1217, 1156, 858; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.89 (d, *J* = 8.3 Hz, 2H), 7.32 (d, *J* = 8.2 Hz, 2H), 5.48–5.43 (m, 1H), 5.24 (dd, *J* = 14.6, 1.8 Hz, 1H), 5.17 (dd, *J* = 14.6, 2.0 Hz, 1H), 4.13 (q, *J* = 7.1 Hz, 2H), 4.10 (q, *J* = 7.1 Hz, 2H), 2.44 (s, 3H), 2.28 (t, *J* = 7.7 Hz, 2H), 2.13–1.98 (m, 2H), 1.23 (t, *J* = 7.1 Hz, 3H), 1.21 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 212.7, 172.6, 164.5, 149.9, 144.7, 135.7, 129.4, 128.2, 100.5, 82.2, 72.0, 61.3, 60.6, 29.8, 28.4, 21.5, 14.1, 14.0; MS (ESI) calcd for $C_{20}H_{25}NO_8SNa$ [M + Na]$^+$ *m*/*z* 462.12, found 462.0.

1-tert-Butyl 6-ethyl 3-(tosylcarbamoyloxy)-2-vinylidenehexanedioate (**1m**). Isolated in 95% yield as a thick light-yellow oil. IR (ν, cm^{-1}) 2981, 2933, 1967, 1732, 1704, 1443, 1367, 1288, 1220, 1153, 1089, 847; ^1H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.88 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 8.1 Hz, 2H), 5.43–5.40 (m, 1H), 5.17 (dd, *J* = 14.4, 2.0 Hz, 1H), 5.11 (dd, *J* = 14.4, 2.2 Hz, 1H), 4.08 (q, *J* = 7.1 Hz, 2H), 2.41 (s, 3H), 2.25 (t, *J* = 7.7 Hz, 2H), 2.07–1.95 (m, 2H), 1.38 (s, 9H), 1.21 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ (ppm) 212.5, 172.6, 163.6, 149.6, 144.8, 135.6, 129.5, 128.3, 101.8, 81.9, 81.9, 72.1, 60.6, 29.9, 28.4, 27.8, 21.5, 14.1; MS (ESI) calcd for $C_{22}H_{29}NO_8SNa$ [M + Na]$^+$ *m*/*z* 490.15, found 490.0.

Ethyl 2-[1-(4-nitrophenylsulfonylcarbamoyloxy)ethyl]-2,3-butadienoate (**1ba**). This compound was prepared as described above for **1b**, except that *p*-nitrobenzenesulfonyl isocyanate (**S10**) was employed as a reactant. A thick light-yellow oil was isolated in 99% yield. IR (ν, cm^{-1}) 3210, 3002, 2970, 2943, 1967, 1739, 1722, 1531, 1437, 1365, 1352, 1159, 1059, 912, 854; ^1H NMR (500 MHz, $CDCl_3$) δ (ppm) 8.37 (d, *J* = 8.9 Hz, 2H), 8.23 (d, *J* = 8.9 Hz, 2H), 5.62–5.56 (m, 1H), 5.34 (dd, *J* = 14.7, 1.9 Hz, 1H), 5.30 (dd, *J* = 14.7, 1.9 Hz, 1H), 4.18–4.06 (m, 2H), 1.37 (d, *J* = 6.5 Hz, 3H), 1.21 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ (ppm) 213.2, 164.8, 150.7, 149.4, 144.0, 129.8, 124.1, 101.4, 82.3, 70.5, 61.4, 18.8, 14.0; MS (ESI) calcd for $C_{15}H_{17}N_2O_8S$ [M + H]$^+$ *m*/*z* 385.1, found 385.0.

Ethyl 2-[1-(phenylsulfonylcarbamoyloxy)ethyl]-2,3-butadienoate (**1bc**). This compound was prepared as described above for **1b**, except that benzenesulfonyl isocyanate was employed as a reactant. A thick light-yellow oil was isolated in 99% yield. IR (ν, cm^{-1}) 3219, 2989, 2970, 2940, 1967, 1741, 1717, 1449, 1364, 1276, 1259, 1217, 1156, 1090, 1060, 911, 845; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.05–7.99 (m, 2H), 7.66–7.59 (m, 1H), 7.56–7.48 (m, 2H), 5.62–5.51 (m, 1H), 5.27 (dd, *J* = 14.6, 2.1 Hz, 1H), 5.20 (dd, *J* = 14.6, 2.1 Hz, 1H), 4.10 (q, *J* = 7.1 Hz, 2H), 1.34 (d, *J* = 6.5 Hz, 3H), 1.18 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 212.8, 164.7, 149.6, 138.5, 133.7, 128.8, 128.2, 101.8, 82.2, 69.7, 61.2, 18.9, 13.9; MS (ESI) calcd for $C_{15}H_{18}NO_6S$ [M + H]$^+$ *m*/*z* 340.1, found 340.0.

Ethyl 2-[1-(4-methoxyphenylsulfonylcarbamoyloxy)ethyl]-2,3-butadienoate (**1bd**). This compound was prepared as described above for **1b**, except that *p*-methoxybenzenesulfonyl isocyanate (**S9**) was employed as a reactant. A thick light-yellow oil was isolated in 96% yield. IR (ν, cm^{-1}) 3160, 3072, 2979, 1967, 1703, 1597, 1579, 1499, 1466, 1443, 1418, 1362, 1342, 1305, 1265, 1160, 1061, 1023, 846; ^1H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.95 (d, *J* = 8.9 Hz, 2H), 6.97 (d, *J* = 8.9 Hz, 2H), 5.59–5.52 (m, 1H), 5.28 (dd, *J* = 14.6, 1.9 Hz, 1H), 5.24 (dd, *J* = 14.6, 1.9 Hz, 1H), 4.11 (q, *J* = 7.1 Hz, 2H), 3.86 (s, 3H), 1.35 (d, *J* = 6.5 Hz, 3H), 1.9 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ (ppm) 212.9, 164.7, 163.8, 149.7, 130.6, 130.0, 114.0, 102.0, 82.2, 69.6, 61.3, 55.6, 19.0, 14.0; MS (MALDI) calcd for $C_{16}H_{19}NO_7SNa$ [M + Na]$^+$ *m*/*z* 392.08, found 392.07.

Ethyl 2-{1-[3-(trifluoromethyl)phenylsulfonylcarbamoyloxy]ethyl}-2,3-butadienoate (**1bb**). This compound was prepared following a literature procedure to generate sulfonyl isocyanates *in situ*.[21b] A solution of (3-trifluoromethylphenyl)tributyltin[49] (0.587 g, 1.35 mmol) and chlorosulfonyl isocyanate (0.120 mL, 1.35 mmol) in freshly distilled chlorobenzene (2 mL) was heated under reflux for 15.5 h. The flask was removed from the oil bath, cooled to room temperature, and subsequently to 0 °C in an ice-water bath. Allenylic alcohol **7b** (0.200 g, 1.28 mmol) was added dropwise to the cooled mixture. Because of a solubility problem, dry CH_2Cl_2 (2 mL) was added after 10 min. The mixture was then stirred at 0 °C for 30 min, removed from the ice bath, and stirred at room temperature for another 30 min. The reaction was

quenched by adding distilled water (20 mL) and diluted by adding CH_2Cl_2 (20 mL). The separated organic phase was washed with distilled water (3 × 20 mL); the aqueous phase was extracted with CH_2Cl_2 (2 x 20 mL). The combined organic phases were washed with brine (20 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The residue, as a solution in chlorobenzene, was purified through flash column chromatography (100% hexanes to wash away chlorobenzene, then 5–20% EtOAc/hexanes) to yield **1bb** (114 mg, 22% isolated; 145 mg of **7b** was re-isolated, giving a yield of **1bb** of 79% based on this recovered starting material) as a thick, slightly yellow, oil. IR (ν, cm^{-1}) 3224, 2989, 1968, 1934, 1751, 1712, 1440, 1363, 1326, 1281, 1160, 1131, 1103, 1068, 913, 845; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.31–8.22 (m, 2H), 8.18–8.02 (br s, 1H), 7.90 (d, *J* = 7.9 Hz, 1H), 7.70 (d, *J* = 7.8 Hz, 1H), 5.64–5.54 (m, 1H), 5.31 (dd, *J* = 14.8, 2.1 Hz, 1H), 5.26 (dd, *J* = 14.8, 2.2 Hz, 1H), 4.12 (q, *J* = 7.1 Hz, 2H), 1.36 (d, *J* = 6.5 Hz, 3H), 1.19 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 213.1, 164.7, 149.4, 139.7, 131.8, 131.6 (q, J_{C-F} = 33.7 Hz), 130.4 (q, J_{C-F} = 3.4 Hz), 129.8, 125.4 (q, J_{C-F} = 3.9 Hz), 123.1 (q, J_{C-F} = 273.0 Hz), 101.6, 82.2, 70.3, 61.4, 18.8, 14.0; MS (ESI) calcd for $C_{16}H_{17}F_3NO_6S$ [M + H]$^+$ *m*/*z* 408.1, found 408.0.

3-Pyrrolines 3a–m and 3ba–bd. 3-Pyrroline **3a** was prepared according to the procedure described below for **3a**, while 3-pyrrolines **3b–m** and **3ba–bd** were synthesized according to the procedure described for **3b**.

Ethyl 1-tosyl-2,5-dihydropyrrole-3-carboxylate (**3a**). A solution of allenylic carbamate **1a** (50.0 mg, 0.147 mmol) in dry CH_3CN (2 mL) was added to a solution of PPh_3 (38.6 mg, 0.147 mmol) in dry CH_3CN (2 mL) over 24 h via syringe pump. To prevent evaporation of the solvent, the needle was fastened to the syringe by wrapping the joint with Teflon tape and Parafilm. Once the addition was complete, the mixture was stirred for another 4 h. At this point, the solvent was evaporated under reduced pressure. The crude reaction mixture was purified through flash column chromatography (10% EtOAc/hexanes) to yield **3a** (29.9 mg, 69%) as a thick colorless oil. The spectral data were in agreement with those previously reported in the literature.[50]

Ethyl 2-methyl-1-tosyl-2,5-dihydropyrrole-3-carboxylate (**3b**).[18] Argon (g) was bubbled through dry CH_3CN for 1.5 h to prepare a deaerated stock of solvent. In a second flask, a solution of allenylic carbamate **1b** (50.0 mg, 0.142 mmol) in CH_3CN (5–6 mL) was also deaerated by bubbling Ar through it for 1.5 h. A third oven-dried round-bottom flask containing a magnetic stirrer bar was then fitted with a rubber septum, which was covered with Teflon tape and Parafilm. This flask was placed under vacuum for 5 min and then backfilled with Ar; this process was repeated twice. To this flask was added the deaerated CH_3CN (4 mL), followed by tri-*n*-butylphosphine (0.035 mL, 0.1415 mmol). The solution of deaerated carbamate in CH_3CN was then removed from its flask using a syringe; the flask was rinsed with stock CH_3CN (usually ca. 2 mL). The flask was rinsed with more deaerated CH_3CN until the syringe contained 4 mL of solution within it. The syringe was then placed in a syringe pump and the carbamate solution was added to the solution of phosphine over 24 h at room temperature. To prevent evaporation of the solvent, the needle was fastened to the syringe by wrapping the joint with Teflon tape and Parafilm. Upon completion of the addition, the mixture was stirred at room temperature for another 4 h. At this point, the solvent was evaporated under reduced pressure. The residue was purified through flash column chromatography (10% EtOAc/hexanes) to yield **3b** (32.3 mg, 74%) as a thick colorless oil. IR (ν, cm^{-1}) 2985, 2926, 2862, 1717, 1347, 1267, 1164; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.11 (d, *J* = 8.1 Hz, 2H), 7.30 (d, *J* = 7.9 Hz, 2H), 6.53 (s, 1H), 4.78–4.67 (m, 1H), 4.41–4.26 (m, 1H), 4.26–4.12 (m, 3H), 2.41 (s, 3H), 1.53 (t, *J* = 6.3 Hz, 3H), 1.26 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.1, 143.5, 136.5, 135.1, 134.6, 129.7, 127.3, 62.0, 60.7, 54.4, 22.1, 21.4, 14.0; MS (MALDI) calcd for $C_{15}H_{19}NO_4SNa$ [M + Na]$^+$ *m*/*z* 332.09, found: 332.16.

Ethyl 2-ethyl-1-tosyl-2,5-dihydropyrrole-3-carboxylate (**3c**).[18] Isolated in 62% yield as a thick oil. IR (ν, cm^{-1}) 2972, 1718, 1347, 1249, 1164, 1083, 1040; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.2 Hz, 2H), 7.29 (d, *J* = 8.2 Hz, 2H), 6.59–6.57 (m, 1H), 4.81–4.79 (m, 1H), 4.24–4.22 (m, 2H), 4.19–4.13 (m, 2H), 2.41 (s, 3H), 2.08–2.00 (m, 1H), 1.94–1.87 (m, 1H), 1.25 (t, *J* = 7.1 Hz, 3H), 0.83 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.1, 143, 136.2, 134.6, 134.3, 129.7, 127.2, 66.6, 60.7, 55.3, 26.6, 21.4, 14.0, 7.4; MS (MALDI) calcd for $C_{16}H_{21}NO_4SNa$ [M + Na]$^+$ *m*/*z* 346.11, found: 346.13.

Ethyl 2-propyl-1-tosyl-2,5-dihydropyrrole-3-carboxylate (**3d**). Isolated in 55% yield as a thick light-yellow oil. IR (ν, cm^{-1}) 2959, 2932, 2872, 1715, 1645, 1598, 1494, 1458, 1342, 1262, 1243, 1160, 1085, 1044, 1017, 816; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.70 (d, *J* = 8.3 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 6.53 (dd, *J* = 3.8, 2.1 Hz, 1H), 4.82–4.76 (m, 1H), 4.26–4.20 (m, 2H), 4.20–4.11 (m, 2H), 2.41 (s, 3H), 1.97–1.88 (m, 1H), 1.86–1.78 (m, 1H), 1.44–1.35 (m, 1H), 1.30–1.18 (m, 4H), 0.89 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ (ppm) 162.3, 143.6, 136.0, 135.1, 134.7, 129.8, 127.3, 66.1, 60.8, 55.2, 36.1, 21.5, 16.9, 14.1, 14.0; MS (MALDI) calcd for $C_{17}H_{24}NO_4S$ [M + H]$^+$ *m*/*z* 338.14, found 338.14.

Ethyl 2-cyclopropyl-1-tosyl-2,5-dihydropyrrole-3-carboxylate (**3e**).[18] Isolated in 28% yield as a thick oil. IR (ν, cm^{-1}) 3078, 2979, 2916, 2852, 1717, 1346, 1261, 1163; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.3 Hz, 2H), 7.27 (d, *J* = 8.3 Hz, 2H), 6.52–6.50 (m, 1H), 4.54 (t, *J* = 5.2 Hz, 1H), 4.28–4.12 (m, 4H), 2.40 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.12–1.01 (m, 1H), 0.81–0.71 (m, 1H), 0.60–0.37 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.4, 143.5, 136.5, 135.5, 135.0, 129.6, 127.3, 28.3, 60.7, 54.9, 21.4, 16.0, 14.1, 3.4, 2.4; MS (GCMS) calcd for $C_{17}H_{21}NO_4S$ [M]$^+$ *m*/*z* 335.1, found 335.1.

Ethyl 2-cyclopentyl-1-tosyl-2,5-dihydropyrrole-3-carboxylate (**3f**).[18] Isolated in 37% yield as a thick oil. IR (ν, cm^{-1}) 2955, 2870, 1717, 1345, 1257, 1163, 1091; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.3 Hz, 2H), 7.25 (d, *J* = 7.6 Hz, 2H), 6.45–6.40 (m, 1H), 4.92 (t, *J* = 4.1 Hz, 1H), 4.21 (dd, *J* = 18.4, 2.6 Hz, 1H), 4.18–4.09 (m, 3H), 2.39 (s, 3H), 2.31–2.24 (m, 1H), 1.74–1.66 (m, 3H), 1.63–1.45 (m, 4H), 1.33–1.26 (m, 1H), 1.24 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.5, 143.5, 136.4, 135.9, 134.4, 129.6, 127.4, 68.5, 60.6, 55.7, 45.0, 28.5, 27.4, 25.0, 24.4, 21.4, 14.0; MS (MALDI) calcd for $C_{19}H_{25}NO_4SNa$ [M + Na]$^+$ *m*/*z* 386.14, found 386.17.

Ethyl 2-cyclohexyl-1-tosyl-2,5-dihydropyrrole-3-carboxylate (**3g**).[18] Isolated in 30% yield as a thick oil. IR (ν, cm^{-1}) 2985, 2928, 2854, 1717, 1449, 1373, 1345, 1256, 1164; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.2 Hz, 2H), 7.25 (d, *J* = 8.0 Hz, 2H), 6.46–6.45 (m, 1H), 4.70 (t, *J* = 3.4, 1H), 4.20 (dd, *J* = 18.4, 2.7 Hz, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 4.07 (ddd, *J* = 18.4, 4.3, 1.7 Hz, 1H), 2.39 (s, 3H), 1.81–1.68 (m, 4H), 1.66–1.56 (m, 2H), 1.41 (dq, *J* = 12.5, 3.1 Hz, 1H), 1.23 (t, *J* = 7.1 Hz, 3H), 1.26–1.01 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.6, 143.6, 136.5, 135.2, 134.4, 129.6, 127.4, 71.0, 60.7, 55.9, 42.9, 30.1, 27.2, 26.4, 26.3, 26.2, 21.5, 14.0; MS (MALDI) calcd for $C_{20}H_{27}NO_4SNa$ [M + Na]$^+$ *m*/*z* 400.16, found 400.16.

Ethyl 2-phenyl-1-tosyl-2,5-dihydropyrrole-3-carboxylate (**3h**)**.** Isolated in 66% yield as a thick oil. The spectral data were in agreement with those previously reported in the literature.[50]

Ethyl 2-(but-3-ynyl)-1-tosyl-2,5-dihydropyrrole-3-carboxylate (**3i**). Isolated in 52% yield as a thick light-yellow oil. IR (ν, cm^{-1}) 3282, 2979, 2924, 2868, 1715, 1681, 1644, 1597, 1446, 1375, 1341, 1267, 1244, 1161, 1091, 1052, 816; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.70 (d, *J* = 8.3 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 6.56 (dd, *J* = 3.8, 2.0 Hz, 1H), 4.84–4.76 (m, 1H), 4.33–4.21 (m, 2H), 4.17 (q, *J* = 7.1 Hz, 2H), 2.41 (s, 3H), 2.38–2.07 (m, 4H), 1.91 (t, *J* = 2.4 Hz, 1H), 1.26 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 162.0, 143.9, 136.6, 134.5, 134.2, 129.9, 127.4, 84.0, 68.6, 65.3, 60.9, 55.3, 32.9, 21.5, 14.1, 13.4; MS (MALDI) calcd for $C_{18}H_{22}NO_4S$ [M + H]$^+$ *m*/*z* 348.13, found 348.12.

Ethyl 2-phenethyl-1-tosyl-2,5-dihydropyrrole-3-carboxylate (**3j**). Isolated in 52% yield as a thick light-yellow oil. IR (ν, cm^{-1}) 3028, 2979, 2936, 2929, 2861, 1716, 1692, 1647, 1598, 1495, 1455, 1345, 1265,

1243, 1162, 1092, 1051, 815; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.72 (d, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.27–7.23 (m, 2H), 7.18–7.13 (m, 3H), 6.57 (dd, *J* = 3.6, 1.9 Hz, 1H), 4.89–4.82 (m, 1H), 4.32–4.24 (m, 2H), 4.20–4.10 (m, 2H), 2.77–2.67 (m, 1H), 2.59–2.51 (m, 1H), 2.42 (s, 3H), 2.37–2.28 (m, 1H), 2.24–2.15 (m, 1H), 1.25 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ (ppm) 162.1, 143.8, 141.7, 136.4, 134.7, 134.6, 129.9, 128.5, 128.2, 127.4, 125.7, 65.8, 60.9, 55.4, 35.4, 30.0, 21.5, 14.1; MS (MALDI) calcd for $C_{22}H_{26}NO_4S$ [M + H]$^+$ *m*/*z* 400.16, found 400.16.

Ethyl 2-[3-(tert-butyldimethylsilyloxy)propyl]-1-tosyl-2,5-dihydropyrrole-3-carboxylate (**3k**). The same procedure was followed as described above for **3b**, except that the solvent and carbamate were not deaerated prior to the reaction. A thick light-yellow oil was isolated in 48% yield. IR (ν, cm^{-1}) 2953, 2928, 2856, 1718, 1647, 1598, 1553, 1494, 1463, 1349, 1257, 1163, 1090, 834; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.70 (d, *J* = 8.3 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 6.55 (dd, *J* = 3.6, 2.0 Hz, 1H), 4.87–4.79 (m, 1H), 4.27–4.18 (m, 2H), 4.15 (qd, *J* = 7.1, 1.0 Hz, 2H), 3.65–3.59 (m, 1H), 3.58–3.52 (m, 1H), 2.41 (s, 3H), 2.02–1.88 (m, 2H), 1.64–1.56 (m, 1H), 1.47–1.38 (m, 1H), 1.25 (t, *J* = 7.1 Hz, 3H), 0.88 (s, 9H), 0.03 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ (ppm) 162.1, 143.7, 136.2, 134.9, 134.7, 129.8, 127.4, 65.9, 63.0, 60.8, 55.2, 30.2, 26.9, 25.9, 21.5, 18.3, 14.1, –5.3, –5.3; MS (MALDI) calcd for $C_{23}H_{37}NO_5SSiNa$ [M + Na]$^+$ *m*/*z* 490.21, found 490.21.

Ethyl 2-(3-ethoxy-3-oxopropyl)-1-tosyl-2,5-dihydropyrrole-3-carboxylate (**3l**). Isolated in 56% yield as a thick light-yellow oil. IR (ν, cm^{-1}) 2981, 2927, 2868, 1715, 1652, 1644, 1598, 1448, 1344, 1262, 1244, 1161, 1091, 816; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.69 (d, *J* = 8.3 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 6.54 (dd, *J* = 3.5, 1.9 Hz, 1H), 4.86–4.78 (m, 1H), 4.24–4.18 (m, 2H), 4.18–4.05 (m, 4H), 2.44–2.29 (m, 6H), 2.25–2.10 (m, 1H), 1.25 (t, *J* = 7.1 Hz, 3H), 1.24 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 173.2, 161.9, 143.8, 136.6, 134.4, 134.1, 129.8, 127.3, 65.2, 60.9, 60.3, 55.1, 29.1, 29.0, 21.4 14.1, 14.0; MS (ESI) calcd for $C_{19}H_{26}NO_6S$ [M + H]$^+$ *m*/*z* 396.1, found 396.2.

tert-Butyl 2-(3-ethoxy-3-oxopropyl)-1-tosyl-2,5-dihydropyrrole-3-carboxylate (**3m**). Isolated in 55% yield as a thick light-yellow oil. IR (ν, cm^{-1}) 2982, 2924, 2862, 1732, 1713, 1655, 1596, 1456, 1373, 1342, 1285, 1245, 1159, 1094; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.68 (d, *J* = 8.0 Hz, 2H), 7.28 (d, *J* = 8.0 Hz, 2H), 6.44 (dd, *J* = 3.6, 2.0 Hz, 1H), 4.81–4.74 (m, 1H), 4.24–4.15 (m, 2H), 4.10 (q, *J* = 7.1 Hz, 2H), 2.40 (s, 3H), 2.39–2.27 (m, 3H), 2.22–2.07 (m, 1H), 1.44 (s, 9H), 1.24 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 173.2, 161.2, 143.7, 135.9, 135.7, 134.2, 129.8, 127.4, 81.7, 65.2, 60.3, 54.9, 29.1, 29.0, 27.9, 21.4, 14.1; MS (MALDI) calcd for $C_{21}H_{29}NO_6SNa$ [M + Na]$^+$ *m*/*z* 446.16, found 446.19.

Ethyl 2-methyl-1-(4-nitrophenylsulfonyl)-2,5-dihydropyrrole-3-carboxylate (**3ba**). Isolated in 37% yield as a thick light-yellow oil. IR (ν, cm^{-1}) 3107, 2983, 2934, 2872, 1715, 1647, 1606, 1529, 1457, 1400, 1348, 1308, 1266, 1243, 1164, 1092, 1072, 856; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 8.37 (dt, *J* = 9.1, 2.1 Hz, 2H), 8.03 (dt, *J* = 9.1, 2.1 Hz, 2H), 6.57 (dd, *J* = 3.8, 1.9 Hz, 1H), 4.77–4.69 (m, 1H), 4.36 (ddd, *J* = 17.3, 5.4, 2.0 Hz, 1H), 4.24 (dt, *J* = 17.3, 2.3 Hz, 1H), 4.22–4.13 (m, 2H), 1.55 (d, *J* = 6.3 Hz, 3H), 1.27 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ (ppm) 161.8, 150.2, 143.7, 136.7, 134.6, 128.4, 124.5, 62.5, 61.1, 54.6, 22.0, 14.1; MS (ESI) calcd for $C_{14}H_{17}N_2O_6S$ [M + H]$^+$ *m*/*z* 341.1, found 341.0.

Ethyl 2-Methyl-1-[3-(trifluoromethyl)phenylsulfonyl]-2,5-dihydropyrrole-3-carboxylate (**3bb**). Isolated in 45% yield as a thick light-yellow oil. IR (ν, cm^{-1}) 3082, 2930, 1714, 1642, 1606, 1542, 1489, 1461, 1428, 1349, 1322, 1308, 1271, 1245, 1165, 1117, 1066, 814; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 8.10 (s, 1H), 8.03 (d, *J* = 7.9 Hz, 1H), 7.85 (d, *J* = 7.8 Hz, 1H), 7.68 (d, *J* = 7.9 Hz, 1H), 6.57 (dd, *J* = 3.8, 2.0 Hz, 1H), 4.78–4.71 (m, 1H), 4.34 (ddd, *J* = 17.3, 5.4, 2.0 Hz, 1H), 4.23 (dt, *J* = 17.4, 2.4 Hz, 1H), 4.21–4.13 (m, 2H), 1.55 (d, *J* = 6.4 Hz, 3H), 1.27 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ (ppm) 162.0, 139.2, 136.7, 134.9, 131.9 (q, J_{C-F} = 33.5 Hz), 130.4, 130.1, 129.5 (q, J_{C-F} = 3.6 Hz), 124.3 (q, J_{C-F} = 3.7 Hz), 123.2 (q, J_{C-F} = 272.9 Hz), 62.4, 61.0, 54.5, 22.0, 14.1; MS (ESI) calcd for $C_{15}H_{17}F_3NO_4S$ [M + H]$^+$ *m*/*z* 364.1, found 364.0.

Ethyl 2-Methyl-1-(phenylsulfonyl)-2,5-dihydropyrrole-3-carboxylate (**3bc**). Isolated in 58% yield as a thick light-yellow oil. IR (ν, cm^{-1}) 2982, 2934, 2872, 1714, 1644, 1586, 1560, 1446, 1375, 1343, 1265, 1242, 1163, 1092, 1067, 843, 755; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.85–7.81 (m, 2H), 7.59 (tt, *J* = 7.5, 1.5 Hz, 1H), 7.52 (t, *J* = 7.6 Hz, 2H), 6.54 (dd, *J* = 3.7, 1.9 Hz, 1H), 4.76–4.69 (m, 1H), 4.31 (ddd, *J* = 17.4, 5.4, 2.0 Hz, 1H), 4.22 (dt, *J* = 17.5, 2.5 Hz, 1H), 4.19–4.12 (m, 2H), 1.54 (d, *J* = 6.4 Hz, 3H), 1.26 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ (ppm) 162.2, 137.7, 136.6, 135.1, 132.8, 129.2, 127.3, 62.2, 60.8, 54.5, 22.1, 14.1; MS (ESI) calcd for $C_{14}H_{18}NO_4S$ [M + H]$^+$ *m*/*z* 296.1, found 296.0.

Ethyl 1-(4-methoxyphenylsulfonyl)-2-methyl-2,5-dihydropyrrole-3-carboxylate (**3bd**). Isolated in 72% yield as a thick light-yellow oil. IR (ν, cm^{-1}) 2981, 2935, 2873, 1715, 1647, 1595, 1577, 1497, 1460, 1376, 1342, 1305, 1259, 1093, 1064, 1021, 835, 804; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.76 (dt, *J* = 9.5, 2.5 Hz, 2H), 6.97 (dt, *J* = 9.5, 2.5 Hz, 2H), 6.53 (dd, *J* = 3.8, 2.0 Hz, 1H), 4.71–4.64 (m, 1H), 4.28 (ddd, *J* = 17.5, 5.4, 2.0 Hz, 1H), 4.18 (dt, *J* = 17.4, 2.4 Hz, 1H), 4.19–4.11 (m, 2H), 3.85 (s, 3H), 1.53 (d, *J* = 6.3 Hz, 3H), 1.26 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ (ppm) 163.0, 162.2, 136.6, 135.3, 129.4, 129.3, 114.4, 62.1, 60.8, 55.6, 54.5, 22.2, 14.1; MS (ESI) calcd for $C_{15}H_{20}NO_5S$ [M + H]$^+$ *m*/*z* 326.1, found 326.1.

Synthesis Performed for the Mechanistic Investigation

Allenylic Acetate 9

Ethyl 2-(ethanoyloxymethyl)-2,3-butadienoate (**9**). 2,6-Lutidine (265 µL, 2.28 mmol) was added dropwise to a solution of allenylic alcohol **7a** (0.200 g, 1.41 mmol) in dry CH_2Cl_2 (10 mL) at 0 °C (ice-water bath) and then the solution was stirred at 0 °C for 5 min. At this point, acetyl chloride (225 µL, 3.10 mmol) was added dropwise to the stirred solution. After stirring at 0 °C for 1 h, the mixture was removed from the ice bath and warmed to room temperature, where it was stirred for an additional 17 h. The reaction was quenched by adding 2 M HCl (10 mL) to remove excess 2,6-lutidine from the mixture. The layers were then separated and the aqueous phase was extracted with CH_2Cl_2 (2 × 5 mL) and then with Et_2O (3 × 5 mL). Each set of organic layers was washed with brine (10 mL). The combined organic phases were dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was purified through flash column chromatography (0–10% EtOAc/hexanes) to yield **9** (219 mg, 85%) as a colorless oil. IR (ν, cm^{-1}) 2888, 1969, 1942, 1742, 1709, 1447, 1368, 1264, 1219, 1126, 1044, 1024, 857; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.25 (t, *J* = 2.2 Hz, 2H), 4.73 (t, *J* = 2.2 Hz, 2H), 4.18 (q, *J* = 7.1, 2H), 2.02 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 214.4, 170.3, 165.1, 96.8, 80.3, 61.2, 60.8, 20.7, 14.1; MS (MALDI) calcd for $C_9H_{12}O_4Na$ [M + Na]$^+$ *m*/*z* 207.06, found 207.05.

Reactions Between Allenylic Acetate 9 and Monopronucleophiles 10a–c

General Procedure for the Reactions of Allenylic Acetate 9 with Benzyl Toluenesulfonamide 10a. An oven-dried round-bottom flask containing a magnetic stirrer bar was charged with *N*-benzyl-4-methylbenzenesulfonamide[51] (**10a**, 1.2 equiv) and then the following reagents were added, if required, for the reactions listed in the specific entries of Table 4: PPh_3 (either 0.2 or 1.1 equiv), Cs_2CO_3 (1.3 equiv), or NaOAc (1.3 equiv); followed by dry CH_3CN (2.8 mL). A solution of allenylic acetate **9** (0.190 mmol, 1.0 equiv) in dry CH_3CN (2.8 mL) was added over 6 h via syringe pump. Once the addition was complete, the mixture was stirred for another 1–1.5 h. At this point the solvent was evaporated under reduced pressure. The residue was purified through

flash column chromatography (0–30% EtOAc/hexanes) to yield the products displayed in Table 4. Diene **11a** eluted from the column when the eluent was between 7.5 and 10% EtOAc/hexanes. Allenoate **12a** eluted between 10 and 15% EtOAc/hexanes. Lastly, allylic acetate **13a** eluted during elution with 30% EtOAc/hexanes. The characterization data of the products **11a**, **12a**, and **13a** are provided below.

General information regarding characterization of allylic acetates **13a**–**c**: Allylic acetates **13a**–**c** were isolated from the reactions as mixtures of (*E*) and (*Z*) isomers, where the isomeric ratios ranging between 1.11:1 and 1.19:1 (*Z*:*E*) for **13a** (see Table 4, entries 3–5), between 1.05:1 and 1.18:1 (*E*:*Z*) for **13b** (see Table 5, entries 1 and 3–6), and 1.08:1 (*E*:*Z*) for **13c** (see Table 6, entry 4) (see below for the syntheses of allylic acetates **13b**,**c**). For characterization purposes, the compounds were separated using preparatory TLC (silica gel). Each isomer was fully characterized and the data are presented below. The structures of the (*E*) and (*Z*) isomers of **13b** were assigned based on NOE experiments (these data are located within the section of the SI containing the ^{1}H and ^{13}C spectra).[19] The (*E*) isomer is referred to herein as allylic acetate **13ba**, while the (*Z*) isomer is known as allylic acetate **13bb**. The isomers of allylic acetates **13a**,**c** were then assigned based on analogy to the isomers of allylic acetate **13b**, with the (*E*) isomers referred to as allylic acetates **13aa** and **13ca**, respectively, and the (*Z*) isomers are known as allylic acetates **13ab** and **13cb**, respectively.

Ethyl 3-(N-benzyl-4-methylphenylsulfonamido)-2-methylene-3-butenoate (**11a**). Isolated as a colorless thin film. IR (ν, cm^{-1}) 3033, 2995, 2970, 2925, 1739, 1704, 1626, 1586, 1473, 1455, 1360, 1345, 1232, 1165, 1141, 1092, 1022, 920; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71 (dt, *J* = 8.4, 1.8 Hz, 2H), 7.33–7.23 (m, 7H), 6.09 (s, 1H), 5.81 (d, *J* = 0.8 Hz, 1H), 5.62 (s, 1H), 4.86 (s, 1H), 4.52 (s, 2H), 4.15 (q, *J* = 7.1 Hz, 2H), 2.43 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 165.7, 143.6, 140.7, 138.0, 135.8, 135.5, 129.5, 129.2, 128.4, 128.0, 127.9, 127.9, 118.0, 61.0, 54.1, 21.6, 14.1; MS (MALDI) calcd for $C_{21}H_{23}NO_4SNa$ [M + Na]$^+$ *m*/*z* 408.12, found 408.10.

Ethyl 2-[(N-benzyl-4-methylphenylsulfonamido)methyl]-2,3-butadienoate (**12a**). Isolated as a colorless thin film. IR (ν, cm^{-1}) 2925, 2854, 1967, 1706, 1453, 1338, 1258, 1157, 1092, 1055, 912; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72 (dt, *J* = 8.2, 1.9 Hz, 2H), 7.33–7.21 (m, 7H), 5.01 (t, *J* = 2.9 Hz, 2H), 4.43 (s, 2H), 4.08 (q, *J* = 7.1, 2H), 4.04 (t, *J* = 2.8 Hz, 2H), 2.43 (s, 3H), 1.20 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 214.2, 165.8, 143.2, 137.8, 136.1, 129.6, 128.5, 127.8, 127.3, 97.1, 81.0, 61.2, 51.9, 45.4, 21.5, 14.1; MS (MALDI) calcd for $C_{21}H_{23}NO_4SNa$ [M + Na]$^+$ *m*/*z* 408.12, found 408.13.

(E)-Ethyl 4-(N-benzyl-4-methylphenylsulfonamido)-2-(ethanoyloxymethyl)but-2-enoate (**13aa**). Isolated as a thin film. IR (ν, cm^{-1}) 2979, 2958, 2924, 2852, 1738, 1715, 1457, 1341, 1243, 1160, 1093, 1028, 935, 737; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76–7.72 (m, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.31–7.27 (m, 3H), 7.25–7.23 (m, 2H), 6.61 (t, *J* = 6.7 Hz, 1H), 4.56 (s, 2H), 4.32 (s, 2H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.99 (d, *J* = 6.7 Hz, 2H), 2.45 (s, 3H), 1.96 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.6, 165.3, 143.8, 142.7, 136.4, 135.3, 130.0, 128.7, 128.7, 128.6, 128.2, 127.3, 61.1, 57.5, 52.2, 45.2, 21.6, 20.8, 14.1; MS (MALDI) calcd for $C_{23}H_{27}NO_6SNa$ [M + Na]$^+$ *m*/*z* 468.15, found 468.10.

(Z)-Ethyl 4-(N-benzyl-4-methylphenylsulfonamido)-2-(ethanoyloxymethyl)but-2-enoate (**13ab**). Isolated as a thin film. IR (ν, cm^{-1}) 2979, 2959, 2925, 2852, 1747, 1714, 1457, 1339, 1243, 1224, 1161, 1095, 1043, 1028, 740; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75–7.70 (m, 2H), 7.36–7.32 (m, 2H), 7.31–7.26 (m, 4H), 7.25–7.23 (m, 1H), 5.99 (t, *J* = 5.7 Hz, 1H), 4.50 (d, *J* = 1.0 Hz, 2H), 4.29 (s, 2H), 4.25 (d, *J* = 5.8 Hz, 2H), 4.11 (q, *J* = 7.2 Hz, 2H), 2.45 (s, 3H), 2.00 (s, 3H), 1.20 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.3, 164.9, 143.7, 143.6, 136.3, 135.7, 129.9, 128.7, 128.6, 128.0, 127.4, 127.3, 63.8, 60.8, 52.9, 47.2, 21.6, 20.9, 14.1; MS (MALDI) calcd for $C_{23}H_{27}NO_6SNa$ [M + Na]$^+$ *m*/*z* 468.15, found 468.12.

General Procedure for Reactions of Allenylic Acetate 9 with 10b or 10c. An oven-dried round-bottom flask containing a magnetic stirrer bar was charged with the following reagents, if required, for the reaction listed as a specific entry in either Table 5 or 6: PPh_3 (either 0.2 or 1.1 equiv), Cs_2CO_3 (1.3 equiv), or NaOAc (1.3 equiv); followed by dry benzene (2.8 mL) and the respective monopronucleophile [1.2 equiv of freshly distilled material of either 3-methyl-2,4-pentanedione (**10b**) or benzoyl propionitrile (**10c**)[52]]. A solution of allenylic acetate **9** (0.190 mmol, 1.0 equiv) in dry benzene (2.8 mL) was then added over 1 h via a syringe pump. Once the addition was complete, the mixture was stirred for another 5–5.5 h (true only for **10b**; when **10c** was used, the reaction times were 8.5, 29, 72, and 9 h for entries 1–4, respectively). At this point the solvent was evaporated under reduced pressure. The residue was purified through flash column chromatography (0–25% EtOAc/hexanes) to yield the products displayed in Tables 5 and 6. Diene **11b** or **11c** eluted from the column when the eluent was between 5 and 7.5% EtOAc/hexanes. Allenoate **12b** or **12c** eluted between 10 and 15% EtOAc/hexanes. Lastly, allylic acetate **13b** or **13c** eluted during the 25% EtOAc/hexanes portion. Characterization data for products **11b/c**, **12b/c**, and **13b/c** are provided below.

Ethyl 4-ethanoyl-4-methyl-2,3-dimethylene-5-oxohexanoate (**11b**). Isolated as a thin film. IR (ν, cm^{-1}) 2983, 2957, 2925, 2852, 1718, 1704, 1553, 1542, 1458, 1355, 1320, 1232, 1208, 1144, 1091; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.29 (d, *J* = 1.5 Hz, 1H), 5.72 (d, *J* = 1.5 Hz, 1H), 5.50 (s, 1H), 5.18 (s, 1H), 4.17 (q, *J* = 7.2 Hz, 2H), 2.24 (s, 6H), 1.38 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.5, 165.8, 145.0, 141.3, 128.7, 122.0, 70.0, 61.4, 26.8, 19.0, 14.0; MS (MALDI) calcd for $C_{13}H_{18}O_4Na$ [M + Na]$^+$ *m*/*z* 261.11, found 261.13.

Ethyl 4-ethanoyl-4-methyl-5-oxo-2-vinylidenehexanoate (**12b**). Isolated as a colorless oil. IR (ν, cm^{-1}) 2985, 2935, 1966, 1943, 1698, 1447, 1424, 1359, 1259, 1214, 1116, 1068, 857; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.10 (t, *J* = 2.4 Hz, 2H), 4.16 (q, *J* = 7.1, 2H), 2.87 (t, *J* = 2.4 Hz, 2H), 2.12 (s, 6H), 1.31 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 214.6, 206.3, 166.9, 95.7, 79.9, 66.5, 61.4, 31.6, 26.7, 17.7, 14.2; MS (MALDI) calcd for $C_{13}H_{18}O_4Na$ [M + Na]$^+$ *m*/*z* 261.11, found 261.09.

(E)-Ethyl 5-ethanoyl-2-(ethanoyloxymethyl)-5-methyl-6-oxohept-2-enoate (**13ba**). Isolated as a thin film. IR (ν, cm^{-1}) 2979, 2960, 2921, 2851, 1710, 1698, 1552, 1462, 1362, 1247, 1223, 1175, 1095, 1070, 1026, 964; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.77 (t, *J* = 7.6 Hz, 1H), 4.85 (s, 2H), 4.21 (q, *J* = 7.1 Hz, 2H), 2.85 (d, *J* = 7.7 Hz, 2H), 2.13 (s, 6H), 2.04 (s, 3H), 1.37 (s, 3H), 1.28 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.9, 170.7, 165.8, 142.2, 130.3, 66.0, 61.1, 57.8, 33.1, 26.5, 20.9, 18.4, 14.2; MS (MALDI) calcd for $C_{15}H_{22}O_6Na$ [M + Na]$^+$ *m*/*z* 321.13, found 321.14.

(Z)-Ethyl 5-ethanoyl-2-(ethanoyloxymethyl)-5-methyl-6-oxohept-2-enoate (**13bb**). Isolated as a thin film. IR (ν, cm^{-1}) 2957, 2924, 2852, 1716, 1701, 1555, 1463, 1389, 1246, 1183, 1095, 1028; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.05 (tt, *J* = 7.4, 1.0 Hz, 1H), 4.71 (d, *J* = 1.0 Hz, 2H), 4.24 (q, *J* = 7.1 Hz, 2H), 3.15 (d, *J* = 7.4 Hz, 2H), 2.14 (s, 6H), 2.05 (s, 3H), 1.37 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.7, 170.5, 165.5, 141.3, 129.7, 66.0, 65.1, 60.8, 33.4, 26.6, 20.9, 18.5, 14.2; MS (MALDI) calcd for $C_{15}H_{22}O_6Na$ [M + Na]$^+$ *m*/*z* 321.13, found 321.17.

Ethyl 4-cyano-4-methyl-2,3-dimethylene-5-oxo-5-phenylpentanoate (**11c**). Isolated as a thin film. IR (ν, cm^{-1}) 2956, 2923, 2851, 2240, 1716, 1694, 1597, 1555, 1449, 1385, 1373, 1316, 1287, 1229, 1134, 1105, 1024, 959; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13–8.09 (m, 2H), 7.62–7.56 (m, 1H), 7.49–7.43 (m, 2H), 6.42 (d, *J* = 1.2 Hz, 1H), 5.69 (d, *J* = 1.2 Hz, 1H), 5.52 (s, 1H), 5.42 (s, 1H), 4.27–4.12 (m, 2H), 1.90 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 191.0, 165.4, 142.7, 139.4, 133.9, 133.8, 130.8, 129.9, 128.4, 121.3, 120.3, 61.6, 51.5, 25.3, 14.0;

MS (MALDI) calcd for $C_{17}H_{17}NO_3Na$ [M + Na]$^+$ *m*/*z* 306.11, found 306.10.

Ethyl 4-cyano-4-methyl-5-oxo-5-phenyl-2-vinylidenepentanoate (**12c**). Isolated as a colorless oil. IR (ν, cm^{-1}) 3065, 2986, 2925, 2851, 1965, 1938, 1709, 1689, 1597, 1448, 1367, 1304, 1258, 1221, 1080, 972, 860; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17–8.13 (m, 2H), 7.64–7.58 (m, 1H), 7.53–7.48 (m, 2H), 5.24 (dt, *J* = 14.3, 2.7 Hz, 1H), 5.17 (dt, *J* = 14.3, 2.7 Hz, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.26 (dt, *J* = 15.1, 3.0 Hz, 1H), 2.80 (dt, *J* = 15.1, 2.4 Hz, 1H), 1.76 (s, 3H), 1.28 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 214.8, 193.6, 166.4, 134.2, 133.8, 129.4, 128.7, 121.4, 95.5, 81.9, 61.6, 45.6, 36.0, 24.4, 14.2; MS (MALDI) calcd for $C_{17}H_{17}NO_3Na$ [M + Na]$^+$ *m*/*z* 306.11, found 306.08.

(E)-Ethyl 5-cyano-2-(ethanoyloxymethyl)-5-methyl-6-oxo-6-phenylhex-2-enoate (**13ca**). Isolated as a thin film. IR (ν, cm^{-1}) 2958, 2924, 2852, 2238, 1736, 1716, 1690, 1552, 1487, 1448, 1384, 1371, 1241, 1173, 1160, 1092, 1081, 1027; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17–8.13 (m, 2H), 7.66–7.61 (m, 1H), 7.55–7.50 (m, 2H), 7.02 (dd, *J* = 8.0, 7.4 Hz, 1H), 4.92 (d, *J* = 12.1 Hz, 1H), 4.87 (d, *J* = 12.1 Hz, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 3.19 (dd, *J* = 15.2, 7.2 Hz, 1H), 2.91 (dd, *J* = 15.1, 8.1 Hz, 1H), 2.05 (s, 3H), 1.76 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.8, 170.7, 165.6, 139.9, 134.2, 133.5, 131.7, 129.4, 128.9, 120.9, 61.3, 57.8, 45.1, 36.6, 24.3, 20.9, 14.2; MS (MALDI) calcd for $C_{19}H_{21}NO_5Na$ [M + Na]$^+$ *m*/*z* 366.13, found 366.12.

(Z)-Ethyl 5-cyano-2-(ethanoyloxymethyl)-5-methyl-6-oxo-6-phenylhex-2-enoate (**13cb**). Isolated as a thin film. IR (ν, cm^{-1}) 2958, 2921, 2851, 2260, 1745, 1716, 1690, 1648, 1553, 1490, 1457, 1450, 1377, 1234, 1179, 1096, 1027; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17–8.14 (m, 2H), 7.66–7.61 (m, 1H), 7.54–7.49 (m, 2H), 6.30–6.26 (m, 1H), 4.79 (dd, *J* = 13.1, 0.8 Hz, 1H), 4.75 (dd, *J* = 13.1, 0.8 Hz, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 3.41 (dd, *J* = 15.7, 6.7 Hz, 1H), 3.30 (dd, *J* = 15.7, 8.0 Hz, 1H), 2.07 (s, 3H), 1.73 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 193.2, 170.4, 165.1, 138.3, 134.0, 133.8, 131.2, 129.4, 128.8, 121.2, 64.5, 61.0, 45.4, 36.8, 23.8, 20.9, 14.2; MS (MALDI) calcd for $C_{19}H_{21}NO_5Na$ [M + Na]$^+$ *m*/*z* 366.13, found 366.14.

Reaction Between Allenylic Acetate 9 and Benzoyl Acetonitrile 19.[53] A solution of allenylic acetate **9** (35.0 mg, 0.190 mmol) in dry benzene (2.8 mL) was added over 1 h via a syringe pump to a suspension of Cs_2CO_3 (80.5 mg, 0.247 mmol) and benzoyl acetonitrile (**19**; 33.1 mg, 0.228 mmol) in dry benzene (2.8 mL). Once the addition was complete, the mixture was stirred for an additional 19 h. The reaction was then quenched by adding saturated aqueous NH_4Cl (5 mL). The separated aqueous phase was extracted with Et_2O (3 × 5 mL). The combined organic phases were washed with brine (10 mL), dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was purified through flash column chromatography (0–15% EtOAc/hexanes) to yield allenoate **30** (9.8 mg, 19%) and a co-eluted mixture of 4*H*-pyran **31** and 2*H*-pyran **32**. To fully separate **31** from **32**, the mixture was subjected to preparatory TLC to yield 4*H*-pyran **31** (13.8 mg, 27%) and 2*H*-pyran **32** (5.9 mg, 12%).

Ethyl 4-cyano-5-oxo-5-phenyl-2-vinylidenepentanoate (**30**). Isolated as a colorless oil. IR (ν, cm^{-1}) 2982, 2958, 2922, 2851, 2209, 1967, 1733, 1671, 1625, 1446, 1354, 1270, 1251, 1168, 1027, 863, 769; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80–7.75 (m, 2H), 7.49–7.42 (m, 3H), 4.98 (d, *J* = 2.1 Hz, 1H), 4.55 (d, *J* = 2.1 Hz, 1H), 4.23 (qd, *J* = 7.1, 1.8 Hz, 2H), 3.59 (dd, *J* = 5.8, 5.0 Hz, 1H), 2.93 (dd, *J* = 16.4, 4.8 Hz, 1H), 2.76 (dd, *J* = 16.4, 6.0 Hz, 1H), 1.28 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.6, 162.4, 151.0, 131.7, 131.0, 128.5, 127.8, 119.2, 97.0, 82.2, 61.9, 40.9, 26.6, 14.1; MS (MALDI) calcd for $C_{16}H_{15}NO_3SNa$ [M + Na]$^+$ *m*/*z* 292.10, found 292.08.

Ethyl 5-cyano-2-methyl-6-phenyl-4H-pyran-3-carboxylate (**31**). Isolated as thin film. IR (ν, cm^{-1}) 2954, 2919, 2850, 2210, 1715, 1672, 1631, 1447, 1382, 1368, 1245, 1211, 1173, 1154, 1078, 770; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79–7.75 (m, 2H), 7.51–7.43 (m, 3H), 4.23 (q, *J* = 7.1 Hz, 2H), 3.28 (d, *J* = 1.3 Hz, 2H), 2.38 (apparent t, *J* = 1.3 Hz, 3H), 1.32 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.2, 159.6, 159.3, 131.3, 130.8, 128.6, 127.5, 101.5, 85.1, 60.8, 24.6, 18.5, 14.3; MS (MALDI) calcd for $C_{16}H_{15}NO_3Na$ [M + Na]$^+$ *m*/*z* 292.10, found 292.06.

Ethyl 5-cyano-4-methyl-6-phenyl-2H-pyran-3-carboxylate (**32**). Isolated as a thin film. IR (ν, cm^{-1}) 2957, 2924, 2852, 2212, 1710, 1692, 1632, 1545, 1491, 1447, 1394, 1337, 1289, 1251, 1176, 1058; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94–7.90 (m, 2H), 7.58–7.53 (m, 1H), 7.51–7.46 (m, 2H), 5.04 (d, *J* = 1.2 Hz, 2H), 4.26 (q, *J* = 7.1 Hz, 2H), 2.51 (apparent t, *J* = 1.2 Hz, 3H), 1.34 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.8, 164.3, 142.7, 132.7, 130.6, 129.5, 128.7, 110.7, 92.2, 67.3, 60.8, 17.3, 14.3; MS (MALDI) calcd for $C_{16}H_{15}NO_3Na$ [M + Na]$^+$ *m*/*z* 292.10, found 292.06.

Reactions Between Benzyl Tosyl Carbamate 39 and PPh_3. PPh_3 (0.2 or 1.0 equiv) was added to a solution of benzyl tosyl carbamate[54] (**39**; 0.350 mmol, 1.0 equiv) in dry CH_3CN (10 mL) and then the mixture was stirred at room temperature while monitoring using both TLC and ^{1}H NMR spectroscopy. After 24 h, it was determined that no reaction had occurred. A ^{1}H NMR spectrum of the crude product isolated at this time revealed a very clean mixture of only **39** and PPh_3. Furthermore, the ^{31}P NMR spectrum of this crude sample featured only one signal, that of PPh_3, indicating that there was no other form of phosphine present. As such, it was determined that that no reaction had occurred.

Formal Synthesis of (±)-Trachelanthamidine[35]

Methyl 5-oxohexahydropyrrolizine-1-carboxylate (**40**). A suspension of pyrroline **3l** (25.0 mg, 0.0630 mmol) and freshly crushed (using a hammer) Mg turnings (38.4 mg, 1.58 mmol) in dry MeOH (3.2 mL) under a balloon of Ar was subjected sonication for 4.25 h. The reaction was stopped by diluting the mixture with CH_2Cl_2 (50 mL) and adding saturated aqueous NH_4Cl (30 mL). The separated organic phase was further washed with saturated aqueous NH_4Cl (3 × 30 mL). The initial aqueous layer was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic phases were washed with brine (20 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The residue was purified through flash column chromatography (100% hexanes to 50–80% EtOAc/hexanes to 100% EtOAc; to visualize the product, the TLC plates were stained in an I_2 chamber) to yield **40** (10 mg, 86% yield) as a light-yellow oil. The spectroscopic data were in agreement with those previously reported in the literature.[55]

Formal Synthesis of (±)-Supinidine

2-(3-Ethoxy-3-oxopropyl)-1-tosyl-2,5-dihydropyrrole-3-carboxylic acid (**S12**). Trifluoroacetic acid (0.63 mL) was added to a solution of pyrroline **3m** (53 mg, 0.13 mmol) in dry CH_2Cl_2 (3.6 mL) and then the mixture was stirred at room temperature for 3 h. At this point, the solvent was evaporated and the residue purified through flash column chromatography (10–30% EtOAc/hexanes then 30% EtOAc/hexanes containing 1% AcOH) to yield **S12** (43.7 mg, 95% yield) as a colorless thin film. IR (ν, cm^{-1}) 3624–3028, 2980, 2927, 1717, 1704, 1643, 1598, 1452, 1398, 1377, 1343, 1268, 1233, 1160, 1092, 1067, 1039, 817; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 8.66–7.86 (br s, 1H), 7.67 (d, *J* = 8.2 Hz, 2H), 7.29 (d, *J* = 8.1 Hz, 2H), 6.63 (s, 1H), 4.82–4.77 (br s, 1H), 4.28–4.17 (m, 2H), 4.09 (q, *J* = 7.1 Hz, 2H), 2.49–2.29 (m, 6H), 2.19–2.10 (m, 1H), 1.23 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ (ppm) 173.8, 166.5, 144.1, 139.2, 134.1, 134.0, 130.0, 127.4, 65.0, 60.7, 55.4, 29.1, 29.0, 21.6, 14.1; MS (MALDI) calcd for $C_{17}H_{21}NO_6SNa$ [M + Na]$^+$ *m*/*z* 390.10, found 390.09.

Ethyl 3-[3-(hydroxymethyl)-1-tosyl-2,5-dihydropyrrol-2-yl]propanoate (**41**). An oven-dried conical vial containing a magnetic spin vane was charged with carboxylic acid **S12** (21 mg, 0.057 mmol) and dry THF (500 μL) and then the solution was cooled to 0 °C in an ice-water bath. Et_3N (16 μL, 0.11 mmol) and ethyl chloroformate (97%, 8.0 μL, 0.081 mmol)

were added dropwise sequentially to the cooled solution. The ice bath was removed and the solution stirred at room temperature for 1.2 h. The mixture was filtered through a short pad of Celite, which was then washed thoroughly with EtOAc. The filtrate was concentrated under reduced pressure and azeotropic removal of water was performed using benzene. The crude material was then dissolved in dry MeOH (1 mL) and transferred to a new oven-dried conical vial containing a magnetic spin vane. After the solution had been cooled to –78 °C, $NaBH_4$ (6.0 mg, 0.14 mmol) was added and then the mixture was stirred for 30 min at that temperature. A second portion of $NaBH_4$ (6.0 mg, 0.14 mmol) was added and then the reaction was stirred for a further 1 h at –78 °C. The reaction was quenched through the addition of saturated aqueous NH_4Cl (2 mL) and then the mixture was slowly warmed to room temperature. The mixture was diluted with EtOAc (20 mL) and then another portion of saturated aqueous NH_4Cl (10 mL) was added. The separated aqueous phase was extracted with EtOAc (3 × 30 mL). The combined organic phases were washed with brine (30 mL), dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was purified through flash column chromatography (0–60% EtOAc/hexanes) to yield **41** (14.7 mg, 73% yield) as a thin film. IR (ν, cm^{-1}) 3666–3194, 2981, 2927, 2870, 1727, 1598, 1494, 1448, 1396, 1377, 1337, 1305, 1288, 1259, 1157, 1093, 1036, 814; ^1H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.68 (d, *J* = 8.3 Hz, 2H), 7.28 (d, *J* = 8.2 Hz, 2H), 5.53–5.49 (m, 1H), 4.61–4.56 (m, 1H), 4.11 (q, *J* = 7.1 Hz, 2H), 4.15–4.00 (m, 4H), 2.55–2.47 (m, 1H), 2.40 (s, 3H), 2.37–2.27 (m, 2H), 1.97–1.88 (m, 1H), 1.25 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ (ppm) 174.0, 143.7, 141.6, 134.3, 129.8, 127.4, 120.8, 65.7, 60.6, 59.0, 55.1, 28.6, 28.6, 21.5, 14.2; MS (ESI) calcd for $C_{17}H_{24}NO_5S$ $[M + H]^+$ *m/z* 354.1, found 354.1.

7-(Hydroxymethyl)-5,7a-dihydropyrrolizin-3(2H)-one (**42**).[37] A suspension of allylic alcohol **41** (14 mg, 0.040 mmol) and freshly crushed (using a hammer) Mg turnings (25 mg, 1.03 mmol) in dry MeOH (2 mL) under a balloon of Ar was subjected to sonication for 1.5 h. At this point, a second portion of freshly crushed Mg turnings (25 mg, 1.03 mmol) was added to the mixture, which was sonicated for another 2 h (at this point, all the Mg had dissolved). The reaction was then stopped by diluting the mixture with CH_2Cl_2 (50 mL) and adding saturated aqueous NH_4Cl (30 mL). The separated organic phase was washed with saturated aqueous NH_4Cl (3 × 30 mL). The initial aqueous phase was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic phases were then washed with brine (20 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The residue was purified through flash column chromatography in a Pasteur pipette (100% hexanes to 50% EtOAc/hexanes to 100% EtOAc to 10–50% MeOH/EtOAc; to visualize the product, the TLC plates were stained in an I_2 chamber or stained with $KMnO_4$) to yield **42** (4.4 mg, 72% yield) as a light-yellow oil. IR (ν, cm^{-1}) 3556–3095, 2979, 2917, 2865, 1672, 1643, 1529, 1461, 1406, 1328, 1307, 1281, 1222, 1169, 1054, 1010, 834; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 5.74 (dd, *J* = 3.6, 2.1 Hz, 1H), 4.75–4.63 (m, 1H), 4.46–4.35 (doublet of multiplets, *J* = 15.7 Hz, 1H), 4.32–4.26 (m, 2H), 3.78–3.67 (doublet of multiplets, *J* = 15.9 Hz, 1H), 2.80–2.65 (m, 1H), 2.49–2.29 (m, 2H), 1.98–1.81 (m, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 177.9, 143.6, 122.9, 67.3, 59.0, 49.5, 33.9, 29.2; MS (MALDI) calcd for $C_8H_{12}NO_2$ $[M + H]^+$ *m/z* 154.09, found 154.08.

Supporting Information

Supporting information for this article can be found under http://dx.doi.org/10.1002/cctc____. This material is available free of charge via the internet at the website provided. The supporting information includes: synthetic routes to propargyl bromides **S4** and **S7**, reaction optimization for the syntheses of allenylic alcohol **7a** and 3-pyrrolines **3a–b**, deuterium labeling studies, proposed mechanisms for the formation of pyrans **31** and **32**, and copies of ^1H and ^{13}C NMR spectra for all new compounds (PDF).

Acknowledgements

This material is based upon studies supported by the NIH (GM 071779) and the NSF under equipment grant no. CHE-1048804.

Keywords: phosphine-catalysis • phosphonium diene • 3-pyrroline • pyrrolizidine alkaloid • (4+1) annulative rearrangement

[1] a) A. R. Mattocks, *Nature* **1968**, *217*, 723–728; b) C. C. J. Culvenor, D. T. Downing, J. A. Edgar, M. V. Jago, *Ann. NY Acad. Sci*. **1969**, *163*, 837–847; c) A. R. Mattocks, *Chemistry and Toxicology of Pyrrolizidine Alkaloids*, Academic Press, London, **1986**, pp. 1–363.

[2] For reviews, see: a) X. L. M. Despinoy, H. McNab, *Tetrahedron* **2000**, *56*, 6359–6383; b) J. R. Liddell, *Nat. Prod. Rep*. **2002**, *19*, 773–781, and references therein; c) J. A. Vanecko, F. G. West, *Heterocycles* **2007**, *74*, 125–143; d) T. Hudlicky, J. W. Reed, *The Way of Synthesis: Evolution of Design and Methods for Natural Products*, Wiley VCH, Weinheim, **2007**, pp. 617–655.

[3] For examples, see the following reviews: a) X. Lu, C. Zhang, Z. Xu, *Acc. Chem. Res*. **2001**, *34*, 535–544; b) D. H. Valentine Jr., J. H. Hillhouse, *Synthesis* **2003**, *2003*, 317–334; c) J. L. Methot, W. R. Roush, *Adv. Synth. Catal.* **2004**, *346*, 1035–1050; d) X. Lu, Y. Du, C. Lu, *Pure Appl. Chem*. **2005**, *77*, 1985–1990; e) V. Nair, R. S. Menon, A. R. Sreekanth, N. Abhilash, A. T. Biju, *Acc. Chem. Res*. **2006**, *39*, 520–530; f) C. K.-W. Kwong, M. Y. Fu, C. S.-L. Lam, P. H. Toy, *Synthesis* **2008**, *2008*, 2307–2317; g) L.-W. Ye, J. Zhou, Y. Tang, *Chem. Soc. Rev*. **2008**, *37*, 1140–1152; h) S. E. Denmark, G. L. Beutner, *Angew. Chem. Int. Ed.* **2008**, *47*, 1560–1638; i) C. E. Aroyan, A. Dermenci, S. J. Miller, *Tetrahedron* **2009**, *65*, 4069–4084; j) B. J. Cowen, S. J. Miller, *Chem. Soc. Rev*. **2009**, *38*, 3102–3116; k) A. Marinetti, A. Voituriez, *Synlett* **2010**, *2010*, 174–194; l) B. Kolesinska, *Cent. Eur. J. Chem*. **2010**, *8*, 1147–1171; m) T. M. V. D. Pinho e Melo, *Monatsh. Chem.* **2011**, *142*, 681–697; n) C. Lalli, J. Brioche, G. Bernadat, G. Masson, *Curr. Org. Chem*. **2011**, *15*, 4108–4127; o) S.-X. Wang, X. Han, F. Zhong, Y. Wang, Y. Lu, *Synlett* **2011**, *2011*, 2766–2778; p) Z. Zhou, Y. Wang, C. Tang, *Curr. Org. Chem*. **2011**, *15*, 4083–4107; q) Q.-Y. Zhao, Z. Lian, Y. Wei, M. Shi, *Chem. Commun*. **2012**, *48*, 1724–1732; r) Y. C. Fan, O. Kwon, in *Science of Synthesis: Asymmetric Organocatalysis*, Vol. 1, (Ed.: B. List), Georg Thieme, Stuttgart, **2012**; pp. 723–782; s) Z. Chai, G. Zhao, *Catal. Sci. Technol*. **2012**, *2*, 29–41; t) Y. C. Fan, O. Kwon, *Chem. Commun*. **2013**, *49*, 11588–11619; u) S. Xu, Z. He, *RSC Adv*. **2013**, *3*, 16885–16904; v) Y. Wang, J. Pan, Z. Chen, X. Sun, Z. Wang, *Mini-Rev. Med. Chem*. **2013**, *13*, 836–844; w) Z. Wang, O. Kwon, in *Diversity-Oriented Synthesis: Basics and Applications in Organic Synthesis Drug Discovery, and Chemical Biology*, (Ed.: A. Trabocchi), John Wiley & Sons, Hoboken, **2013**, pp. 97–133; x) C. Gomez, J.-F. Betzer, A. Voituriez, A. Marinetti, *ChemCatChem* **2013**, *5*, 1055–1065; y) L.-W. Xu, *ChemCatChem* **2013**, *5*, 2775–2784; z) Y. Xiao, Z. Sun, H. Guo, O. Kwon, *Beilstein J. Org. Chem*. **2014**, *10*, 2089–2121; aa) Y. Wei, M. Shi, *Chem. Asian J*. **2014**, *9*, 2720–2734; bb) Z. Wang, X. Xu, O. Kwon, *Chem. Soc. Rev*. **2014**, *43*, 2927–2940; cc) S. Xu, Y. Tang, *Lett. Org. Chem*. **2014**, *11*, 524–533; dd) P. Xie, Y. Huang, *Org. Biomol. Chem*. **2015**, *13*, 8578–8595; ee) Y. C. Fan, O. Kwon, in *Lewis Base Catalysis*, Vol. 2 (Eds.: E. Vedejs, S. E. Denmark), Wiley-VCH, Weinheim, **2016**, pp. 715–804; ff) Y. Xiao, H. Guo, O. Kwon, *Aldrichimica Acta* **2016**, *49*, 3–13; gg) T. Wang, X. Han, F. Zhong, W. Yao, Y. Lu, *Acc. Chem. Res*. **2016**, *49*, 1369–1378; hh) W. Li, J. Zhang, *Chem. Soc. Rev*. **2016**, *45*, 1657–1677; ii) Z. Lao, P. H. Toy, *Beilstein J. Org. Chem*. **2016**, *12*, 2577–2587; jj) A. Voituriez, N. Saleh, *Tetrahedron Lett*. **2016**, *57*, 4443–4451; kk) R. Zhou, Z. He, *Eur. J. Org. Chem*. **2016**, *2016*, 1937–1954; ll) Y. L. Sun, Y. Wei, M. Shi, *ChemCatChem* **2017**, *9*, 718–727; mm) Y. N. Gao, M. Shi, *Chin. Chem.*

Lett. **2017**, *28*, 493–502; nn) Y. Wei, M. Shi, *Org. Chem. Front*. **2017**, *4*, 1876–1890; oo) H. Li, Y. Lu, *Asian J. Org. Chem*. **2017**, *6*, 1130–1145; pp) P. Karanam, G. M. Reddy, S. R. Koppolu, W. Lin, *Tetrahedron Lett*. **2018**, *59*, 59–76; qq) S. B. Nallapati, S.-C. Chuang, *Asian J. Org. Chem*. **2018**, *7*, 1743–1757; rr) H. Ni, W.-L. Chan, Y. Lu. *Chem. Rev*. **2018**, *118*, 9344–9411; ss) H. Guo, Y. C. Fan, Z. Sun, Y. Wu, O. Kwon, *Chem. Rev*. **2018**, *118*, 10049–10293; tt) E.-Q. Li, Y. Huang, *Chem. Commun*., **2020**, *56*, 680–694.

[4] a) Z. Xu, X. Lu, *Tetrahedron Lett*. **1997**, *38*, 3461–3464; b) X. Lu, Z. Xu, *J. Org. Chem*. **1998**, *63*, 5031–5041; c) Z. Xu, X. Lu, *Tetrahedron Lett*. **1999**, *40*, 549–552.

[5] Modifications of Lu's reaction. For an example of [3 + 2] annulations of allenoates with N-thiophosphorylimines, see: a) B. Zhang, S. Xu, G. Wu, Z. He, *Tetrahedron* **2008**, *64*, 9471–9479. For examples of [3 + 2] cycloadditions between allenoates and cyclic aldimines or ketimines, see: b) X.-Y. Chen, R.-C. Lin, S. Ye, *Chem. Commun*. **2012**, *48*, 1317–1319; c) H. Yu, L. Zhang, Z. Yang, Z. Li, Y. Zhao, Y. Xiao, H. Guo, *J. Org. Chem*. **2013**, *78*, 8427–8436; d) Y.-Q. Wang, Y. Zhang, H. Dong, J. Zhang, J. Zhao, *Eur. J. Org. Chem*. **2013**, *2013*, 3764–3770; e) L.-J. Yang, S. Wang, J. Nie, S. Li, J.-A. Ma, *Org. Lett*. **2013**, *15*, 5214–5217; f) L.-J. Yang, S. Li, S. Wang, J. Nie, J.-A. Ma, *J. Org. Chem*. **2014**, *79*, 3547–3558. For examples of 2,3-pentadienenitriles being employed in the [3 + 2] annulation with imines, see: g) S. S. Kinderman, J. H. van Maarseveen, H. Hiemstra, *Synlett* **2011**, *2011*, 1693–1696. For an example of [3 + 2] annulations of allenoates with N-aryl fluorinated imines, see: h) Z. Zhu, Y. Guo, X. Wang, F. Wu, Y. Wu, *J. Fluorine Chem*. **2017**, *195*, 102–107.

[6] For the synthesis of 1,2,3,5-tetrasubstituted-3-pyrrolines from allenoates, see: a) X.-F. Zhu, C. E. Henry, O. Kwon, *Tetrahedron* **2005**, *61*, 6276–6282; b) G.-L. Zhao, M. Shi, *J. Org. Chem*. **2005**, *70*, 9975–9984; c) X. Tang, B. Zhang, Z. He, R. Gao, Z. He, *Adv. Synth. Catal*. **2007**, *349*, 2007–2017; d) reference [5a]; e) I. P. Andrews, O. Kwon, *Org. Synth*. **2011**, *88*, 138–151; f) A. C. Shaikh, O. Kwon, *Org. Synth.* **2019**, *96*, 214–231. For the synthesis of 1,2,3,5-tetrasubstituted-3-pyrrolines from 2-alkynoates, see: g) reference [4c]. For the synthesis of 1,2,3,5-tetrasubstituted-3-pyrrolines from 3-alkynoates and alkyl sulfonyl imines, see: h) M. Sampath, P. Y. B. Lee, T. P. Loh, *Chem. Sci.* **2011**, *2*, 1988–1991. For the synthesis of 1,2,3,5-tetrasubstituted-3-pyrrolines from alkynyl ketones, see: i) L.-G. Meng, P. Cai, Q. Guo, Xue, S. *J. Org. Chem*. **2008**, *73*, 8491–8496. For the synthesis of 1,2,3,5-tetrasubstituted-3-pyrrolines from 2,3-pentadienenitriles see: j) reference [5g].

[7] For examples of asymmetric phosphine-catalyzed allene–imine (3+2) annulations to construct 3-pyrrollines, see: a) A. Scherer, J. A. Gladysz, *Tetrahedron Lett.* **2006**, *47*, 6335–6337; b) L. Jean, A. Marinetti, *Tetrahedron Lett.* **2006**, *47*, 2141–2145; c) N. Fleury-Brégeot, L. Jean, P. Retailleau, A. Marnetti, *Tetrahedron* **2007**, *63*, 11920–11927; d) Y.-Q. Fang, E. N. Jacobsen, *J. Am. Chem. Soc*. **2008**, *130*, 5660–5661; e) A. Panossian, N. Fleury-Brégeot, A. Marinetti, *Eur. J. Org. Chem.* **2008**, *2008*, 3826–3833; f) N. Pinto, N. Fleury-Brégeot, A. Marinetti, *Eur. J. Org. Chem.* **2009**, *2009*, 146–151; g) X. Han, F. Zhong, Y. Wang, Y. Lu, *Angew. Chem. Int. Ed*. **2012**, *51*, 767–770; h) reference [5c]; i) C. E. Henry, Q. Xu, Y. C. Fan, T. J. Martin, L. Belding, T. Dudding, O. Kwon, *J. Am. Chem. Soc*. **2014**, *136*, 11890–11893; j) T.-H. Nguyen, M. Toffano, C. Bournaud, G. Vo-Thanh, *Tetrahedron Lett.* **2014**, *55*, 6377–6380; k) X. Han, W.-L. Chan, W. Yao, Y. Wang, Y. Lu, *Angew. Chem. Int. Ed.* **2016**, *55*, 6492–6496; l) M. G. Sankar, M. Garcia-Castro, C. Golz, C. Strohmann, K. Kumar, *RSC. Adv*. **2016**, *6*, 56537–56543; m) M. G. Sankar, M. Garcia-Castro, C. Golz, C. Strohmann, K. Kumar, *Angew. Chem. Int. Ed*. **2016**, *55*, 9709–9713; n) A. J. Smaligo, S. Vardhineedi, O. Kwon, *ACS Catal.* **2018**, *8*, 5188–5192.

[8] S. Gowrisankar, H. S. Kim, H. S. Lee, J. N. Kim, *Bull. Korean Chem. Soc*. **2007**, *28*, 1844–1846.

[9] M. P. Green, J. C. Prodger, C. J. Hayes, *Tetrahedron Lett*. **2002**, *43*, 6609–6611.

[10] For an example of phosphine-catalyzed allene–imine (3+2) annulations in total synthesis, see: a) reference [4b]. For an example of phosphine-catalyzed *in situ* isomerization of 3-butynoates to 2,3-butadienoates and subsequent (3+2) annulation with N-sulfonyl alkylimines in total synthesis, see: b) reference [6h]. For examples of asymmetric phosphine-catalyzed allene–imine (3+2) annulations in total synthesis, see: c) reference [7g]; d) I. P. Andrews, O. Kwon, *Chem. Sci.* **2012**, *3*, 2510–2514; e) L. Cai, K. Zhang, O. Kwon, *J. Am. Chem. Soc*. **2016**, *138*, 3298–3301.

[11] Provided below are applications of phosphine catalysis in total synthesis in addition to the examples presented in reference [10]. For examples of phosphine-catalyzed allene–alkene (3+2) annulations in total synthesis, see: a) Y. Du, X. Lu, *J. Org. Chem*. **2003**, *68*, 6463–6456; b) J.-C. Wang, M. J. Krische, *Angew. Chem. Int. Ed*. **2003**, *42*, 5855–5857; c) R. A. Jones, M. J. Krische, *Org. Lett*. **2009**, *11*, 1849–1851. For examples of phosphine-catalyzed (4+2) annulations with imines in total synthesis, see: d) Y. S. Tran, O. Kwon, *Org. Lett*. **2005**, *7*, 4289–4291; e) R. A. Villa, Q. Xu, O. Kwon, *Org. Lett*. **2012**, *14*, 4634–4637; f) G. A. Barcan, A. Patel, K. N. Houk, O. Kwon, *Org. Lett.* **2012**, *14*, 5388–5391. For an example of phosphine–palladium(0) dual catalysis in total synthesis, see: g) P. Webber, M. J. Krische, *J. Org. Chem*. **2008**, *73*, 9379–9387. For examples of phosphine/palladium sequential catalysis in total synthesis, see: h) Y. C.; Fan, O. Kwon, *Org. Lett*. **2012**, *14*, 3264–3267. For examples of phosphine-catalyzed intramolecular Rauhut–Currier reactions in total synthesis, see: i) D. J. Mergott, S. A. Frank, W. R. Roush, *Org. Lett*. **2002**, *4*, 3157–3160; j) K. Agapiou, M. J. Krische, *Org. Lett*. **2003**, *5*, 1737–1740; k) J. L. Methot, W. R. Roush, *Org. Lett*. **2003**, *5*, 4223–4226; l) D. J. Mergott, S. A. Frank, W. R. Roush, *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 11955–11959; m) S. M. Winbush, D. J. Mergott, W. R. Roush, *J. Org. Chem*. **2008**, *73*, 1818–1829. For examples of phosphine-catalyzed α-arylation in total synthesis, see: m) P. Koech, M. J. Krische, *Tetrahedron* **2006**, *62*, 10594–10602. For an example of bifunctional Brønsted iminophosphorane (BIMP) organocatalysis in total synthesis, see: n) H. Shi, I. N. Michaelides, B. Darses, P. Jakubec, Q. N. N. Nguyen, R. S. Paton, D. J. Dixon, *J. Am. Chem. Soc*. **2017**, *139*, 17755–17758.

[12] For the construction of a 2-Me– and a 2-Pr–substituted 3-pyrroline in low yields through phosphine-catalyzed (3+2) annulations of an MBH carboxylate and an imine, see: a) S. Zheng, X. Lu, *Org. Lett*. **2008**, *10*, 4481–4484. For the use of an *i*-Pr–substituted sulfonyl imine in phosphine-catalyzed annulation with 6-oxo-2,4-dienoates to construct *i*-Pr–substituted 3-pyrrolines, see: b) M. Schuler, D. Duvvuru, P. Retailleau, J.-F. Betzer, A. Marinetti, *Org. Lett*. **2009**, *11*, 4406–4409; c) D. Duvvuru, J.-F. Betzer, P. Retailleau, G. Frison, A. Marinetti, *Adv. Synth Catal*. **2011**, *353*, 483–493. For the synthesis of 2-alkyl–substituted 3-pyrrolines through phosphine-catalyzed (3+2) annulations between 3-alkynoates and alkyl sulfonyl imines, see: d) reference [6h]. For the synthesis of 2-alkyl–substituted 3-pyrrolines through phosphine-catalyzed (3+2) annulations between allenoates and alkyl diphenylphosphinoyl imines, see: e) reference [7g].

[13] In reference [7g], the diphenylphosphinoyl group was deprotected and the 3-pyrroline nitrogen was reprotected as a tosylamide to complete the formal synthesis of trachelanthamidine.

[14] Q. Zhang, L. Yang, X. Tong, *J. Am. Chem. Soc*. **2010**, *132*, 2550–2551.

[15] For asymmetric versions of Tong's phosphine-catalyzed (4+1) reaction between allenylic acetates and carbon-centered 1,1-bisnucleophiles see: a) X. Han, W. Yao, T. Wang, Y. R. Tan, Z. Yan, J. Kwiatkowski, Y. Lu, *Angew. Chem. Int. Ed.* **2014**, *53*, 5643–5647; b) D. T. Ziegler, L. Riesgo, T. Ikeda, Y. Fujiwara, G. C. Fu, *Angew. Chem. Int. Ed*. **2014**, *53*, 13183–13187.

[16] For an asymmetric version of Tong's phosphine-catalyzed (4+1) reaction between allenylic acetates and nitrogen-centered 1,1-bisnucleophiles, see: S. Kramer, G. C. Fu. *J. Am. Chem. Soc*. **2015**, *137*, 3803–3806.

[17] Very recently, Huang modified Tong's proposed reactive intermediate and suggested a very elaborated phosphonium diene—a 1,4-(bis)electrophilic α,β-unsaturated ketenyl phosphonium species—as an intermediate in a phosphine-catalyzed (4+1) annulation between allenyl imides and either methyl ketimines or enamines; see: a) Z.-H. Cao, Y.-H. Wang, S. J. Kalita, U. Schneider, Y.-Y. Huang. *Angew. Chem. Int. Ed*. **2020**, *59*, 1884–1890. b) Within the same manuscript, Huang disclosed two examples of a phosphine-catalyzed (4+1) annulation between allenyl imides and a nitrogen (bis)nucleophile that delivered

1,2-dihydropyrrol-5-ones. c) Within this same manuscript, Huang also disclosed one example of a chiral phosphine being used to deliver one 1,2-dihydropyrrol-5-one with modest enantioselectivity.

[18] For the synthesis of allenylic carbamates **1**, see: I. P. Andrews, B. R. Blank, O. Kwon, *Chem. Commun*. **2012**, *48*, 5373–5375.

[19] One possible route for the decomposition of allenylic carbamate **1** is through phosphine-catalyzed polymerization; for examples, see: a) V. L. Horner, W. Jurgeleit, K. Klüpfel, *Liebigs Ann. Chem*. **1955**, *591*, 108–117; b) N. Takashina, C. C. Price, *J. Am. Chem. Soc*. **1962**, *84*, 489–491.

[20] See the Supporting Information for more details.

[21] The *p*-methoxybenzenesulfonyl isocyanate and *p*-nitrobenzenesulfonyl isocyanate were prepared following a procedure developed for related sulfonyl isocyanates: a) W. Su, Y. Li (Univ Zhejiang Polytechnic), CN 1475482, **2004**. *m*-Trifluoromethylbenzenesulfonyl isocyanate was prepared *in situ* according to a procedure described previously; see: b) M. Amswald, W. P. Neumann, *Chem. Ber*. **1991**, *124*, 1997–2000.

[22] a) B. T. H. Hue, J. Dijkink, S. Kuiper, S. van Schaik, J. H. van Maarseveen, H. Hiemstra, *Eur. J. Org. Chem*. **2006**, *2006*, 127–137. For reviews of the MBH reaction, see: b) D. Basavaiah, P. Dharma Rao, R. Suguna Hyma, *Tetrahedron* **1996**, *52*, 8001–8062; c) P. Langer, *Angew. Chem. Int. Ed*. **2000**, *39*, 3049–3052; d) D. Basavaiah, A. J. Rao, T. Satyanarayana, *Chem. Rev*. **2003**, *103*, 811–892; e) G. Masson, C. Housseman, J. Zhu, *Angew. Chem. Int. Ed*. **2007**, *46*, 4614–4628; f) D. Basavaiah, K. V. Rao, R. J. Reddy, *Chem. Soc. Rev*. **2007**, *36*, 1581–1588; g) Y.-L. Shi, M. Shi, *Eur. J. Org. Chem*. **2007**, *2007*, 2905–2916; h) V. Singh, S. Batra, *Tetrahedron* **2008**, *64*, 4511–4574; i) V. Declerck, J. Martinez, F. Lamaty, *Chem. Rev*. **2009**, *109*, 1–48; j) G. N. Ma, J. J. Jiang, M. Shi, Y. Wei, *Chem. Commun*. **2009**, 5496–5514; k) Y. Wei, M. Shi, *Acc. Chem. Res*. **2010**, *43*, 1005–1018; l) Y. Wei, M. Shi, *Acc. Chem. Res*. **2010**, *43*, 1005–1018; m) Y. Wei, M. Shi, *Chin. Sci. Bull*. **2010**, *55*, 1699–1711; n) R. O. M. A. de Souza, L. S. M. Miranda, *Mini-Rev. Org. Chem*. **2010**, *7*, 212–220; o) J. Mansilla, J. M. Saa, *Molecules* **2010**, *15*, 709–734; p) D. Basavaiah, B. S. Reddy, S. S. Badsara, *Chem. Rev*. **2010**, *110*, 5447–5674; q) P. H.-Y. Cheong, C. Y. Legault, J. M. Um, N. Çelebi-Ölçüm, K. N. Houk, *Chem. Rev*. **2011**, *111*, 5042–5137; r) M. Shi, F. Wang, M.-X. Zhao, Y. Wei, *Chemistry of the Morita–Baylis–Hillman Reaction*, Royal Society of Chemistry, Cambridge, **2011**, pp. 1–551; s) D. Basavaiah, G. Veeraraghavaiah, *Chem. Soc. Rev*. **2012**, *41*, 68–78; t) Y. Wei, M. Shi, *Chem. Rev*. **2013**, *113*, 6659–6690; u) F.-L. Hu, M. Shi, *Org. Chem. Front*. **2014**, *1*, 587–595; v) S. Bhowmik, S. Batra, *Curr. Org. Chem*. **2014**, *18*, 3078–3119; w) K. C. Bharadwaj, *RSC Adv*. **2015**, *5*, 75923–75946; x) B. Satpathi, S. S. V. Ramasastry, *Synlett* **2016**, *2016*, *27*, 2178–2182; y) D. Basavaiah, G. C. Reddy, *ARKIVOC* **2016**, *ii*, 172–205; z) H. Pellissier, *Tetrahedron* **2017**, *73*, 2831–2861; aa) D. Basavaiah, R. T. Naganaboina, *New J. Chem.*, **2018**, *42*, 14036–14066.

[23] Allenylic alcohols **7c**–**7g** and **7i**–**7m** were prepared through tin(II)-mediated allenylation of propargyl bromides to aldehydes: a) Y. Deng, X. Jin, S. Ma, *J. Org. Chem*. **2007**, *72*, 5901–5904. Allenylic alcohol **7h** was prepared through indium-mediated allenylation of propargyl bromides to aldehydes: b) C. Park, P, H. Lee, *Org. Lett*. **2008**, *10*, 3359–3362.

[24] For examples of phosphine-catalyzed β′-umpolung additions to allenes, see: a) T. J. Martin, V. G. Vakhshori, Y. S. Tran, O. Kwon, *Org. Lett*. **2011**, *13*, 2586–2589; b) X.-Y. Guan, Y. Wei, M. Shi, *Eur. J. Org. Chem*. **2011**, *2011*, 2673–2677.

[25] Cristau demonstrated the first example of γ-umpolung addition to allenes employing stoichiometric phosphine; see: a) H.-J. Cristau, J. Viala, H. Christol, *Tetrahedron Lett*. **1982**, *23*, 1569–1572; b) H.-J. Cristau, M. Fonte, E. Torreilles, *Synthesis* **1989**, *1989*, 301–303. For examples of non-asymmetric γ-umpolung additions to allenoates and alkynoates employing catalytic phosphine, see: c) B. M. Trost, C.-J. Li, *J. Am. Chem. Soc*. **1994**, *116*, 3167–3168; d) B. M. Trost, C.-J. Li, *J. Am. Chem. Soc*. **1994**, *116*, 10819–10820; e) C. Zhang, X. Lu, *Synlett* **1995**, *1995*, 645–646; f) B. M. Trost, G. R. Drake, *J. Org. Chem*. **1997**, *62*, 5670–5671; g) C. Alvarez-Ibarra, A. G. Csákÿ, C. Gómez de la Oliva, *Tetrahedron Lett*. **1999**, *40*, 8465–8467; h) C. Alvarez-Ibarra, A. G. Csákÿ, C. Gómez de la Oliva, *J. Org. Chem*. **2000**, *65*, 3544–3547; i) C. Lu, X. Lu, *Org. Lett*. **2002**, *4*, 4677–4679; j) B. Liu, R. Davis, B. Joshi, D. W. Reynolds, *J. Org. Chem*. **2002**, *67*, 4595–4598; k) R. Skouta, R. S. Varma, C.-J. Li, *Green Chem*. **2005**, *7*, 571–575; l) D. Virieux, A.-F. Guillouzic, H.-J. Cristau, *Tetrahedron* **2006**, *62*, 3710–3720; m) Z. Lu, S. Zheng, X. Zhang, X. Lu, *Org. Lett*. **2008**, *10*, 3267–3270; n) Y. Lin, D. Bernardi, E. Doris, F. Taran, *Synlett* **2009**, *2009*, 1466–1470; o) A. L. Cardoso, A. M. Beja, M. R. Silva, J. M. de los Santos, F. Palacios, P. E. Abreu, A. A. C. C. Pais, T. M. V. D. Pinho e Melo, *Tetrahedron* **2010**, *66*, 7720–7725; p) J.-M. Chen, Y.-Z. Fang, Z.-L Wei, W.-W. Liao, *Synthesis* **2012**, *44*, 1849–1853; q) C.-K. Pei, Y. Jiang, M. Shi, *Eur. J. Org. Chem*. **2012**, *2012*, 4206–4216; r) J. M. de los Santos, Z. Ochoa, F. Palacios, *ARKIVOC* **2012**, *iv*, 54–62; s) P. Xie, W. Lai, Z. Geng, Y. Huang, R. Chen, *Chem. Asian J*. **2012**, *7*, 1533–1537; t) reference [18]; u) Q.-F. Zhou, K.; Zhang, O. Kwon, Tetrahedron Lett. **2015**, *56*, 3273–3276; v) S. Takizawa, K. Kishi, Y. Yoshida, S. Mader, F. A. Arteaga, S. Lee, M. Hoshino, M. Rueping, M. Fujita, H. Sasai, *Angew. Chem. Int. Ed*. **2015**, *54*, 15511–15515; w) Z. Huang, X. Yang, F. Yang, T. Lu, Q. Zhou, *Org. Lett*. **2017**, *19*, 3524–3527; x) J.-Q. Zhang, S.-M. Li, C.-F. Wu, X.-L. Wang, T.-T. Wu, Y. Du, Y.-Y. Yang, L.-L. Fan, Y.-X. Dong, J.-T. Wang, L. Tang, *Catal. Commun*. **2020**, *138*, 105838–105845.

[26] For examples of asymmetric γ-umpolung additions to allenoates using catalytic phosphine, see: a) Z. Chen, G. Zhu, Q. Jiang, D. Xiao, P. Cao, X. Zhang, *J. Org. Chem*. **1998**, *63*, 5631–5635; b) Z. Pakulski, O. M. Demchuk, J. Frelek, R. Luboradzki, K. M. Pietrusiewicz, *Eur. J. Org. Chem*. **2004**, *2004*, 3913–3918; c) Y. K. Chung, G. C. Fu, *Angew. Chem. Int. Ed*. **2009**, *48*, 2225–2227; d) S. W. Smith, G. C. Fu, *J. Am. Chem. Soc*. **2009**, *131*, 14231–14233; e) J. Sun, G. C. Fu, *J. Am. Chem. Soc*. **2010**, *132*, 4568–4569; f) R. Sinisi, J. Sun, G. C. Fu, *Proc. Natl. Acad. Sci. U.S.A*. **2010**, *107*, 20652–20654; g) Y. Fujiwara, J. Sun, G. C. Fu, *Chem. Sci*. **2011**, *2*, 2196–2198; h) N. Lu, L. Meng, D. Chen, G. Zhang, *J. Mol. Catal. A: Chem*. **2011**, *339*, 99–107; i) R. J. Lundgren, A. Wilsily, N. Marion, C. Ma, Y. K. Chung, G. C. Fu, *Angew. Chem. Int. Ed*. **2013**, *52*, 2525–2528; j) V. Kumar, S. Mukherjee, *Chem. Commun*. **2013**, *49*, 11203–11205; k) T. Wang, W. Yao, F. Zhong, G. H. Pang, Y. Lu, *Angew. Chem. Int. Ed*. **2014**, *53*, 2964–2968; l) Y.-Q.; Fang, P. M. Tadross, E. N. Jacobsen, *J. Am. Chem. Soc*. **2014**, *136*, 17966–17968; m) J. Chen, Y. Cai, G. Zhao, *Adv. Synth. Catal*. **2014**, *356*, 359–363; n) M. Kalek, G. C. Fu, *J. Am. Chem. Soc*. **2015**, *137*, 9438–9442; o) T. Wang, D. L. Hoon, Y. Lu, *Chem. Commun*. **2015**, *51*, 10186–10189; p) T. Wang, Z. Yu, D. L. Hoon, K.-W. Huang, Y. Lan, Y. Lu, *Chem. Sci*. **2015**, *6*, 4912–4922; q) T. Wang, Z. Yu, D. L. Hoon, C. Y. Phee, Y. Lan, Y. Lu, *J. Am. Chem. Soc*. **2016**, *138*, 265–271; r) D. T. Ziegler, G. C. Fu, *J. Am. Chem. Soc*. **2016**, *138*, 12069–12072; s) Y.-N. Gao, M. Shi, *Eur. J. Org. Chem*. **2017**, *2017*, 1552–1562; t) P. Chen, J. Zhang, *Org. Lett*. **2017**, *19*, 6550–6553; u) H. Qiu, X. Chen, J. Zhang, *Chem. Sci*. **2019**, 10, 10510–10515; v) H. Wang, C. Guo, *Angew. Chem. Int. Ed*., **2019**, *58*, 2854–2858; w) Y. Tasdan, G.-J. Mei and Y. Lu, *Sci. Bull*., **2020**, *65*, 557–563.

[27] No experimental details for this reaction, nor characterization data of the product, were provided: J. Hu, B. Tian, X. Wu, X. Tong, *Org. Lett*. **2012**, *14*, 5074–5077.

[28] This statement is based on the fact that **12a** decomposed upon exposure to catalytic PPh_3.

[29] For examples of phosphine-initiated general base catalysis, see: a) D. A. White, M. M. Baizer, *Tetrahedron Lett*. **1973**, *14*, 3597–3600; b) V. Sriramurthy, G. A. Barcan, O. Kwon, *J. Am. Chem. Soc*. **2007**, *129*, 12928–12929; c) V. Sriramurthy, O. Kwon, *Org. Lett*. **2010**, *12*, 1084–1087; d) Y. C. Fan, O. Kwon, *Molecules* **2011**, *16*, 3802–3825; e) J. Szeto, V. Sriramurthy, O. Kwon, *Org. Lett*. **2011**, *13*, 5420–5423; f) S. Khong, O. Kwon, *Molecules* **2012**, *17*, 5626–5650; g) S. Khong, O. Kwon, *J. Org. Chem*. **2012**, *77*, 8257–8267; h) S. Khong, O. Kwon, *Asian J. Org. Chem*. **2014**, *3*, 453–457; i) V. R. Gandi, Y. Lu, *Chem. Commun*. **2015**, *51*, 16188–16190; j) N. K. Vaishanv, M. K. Zaheer, R. Kant, K. Mohanan, *Eur. J. Org. Chem*. **2019**, *2019*, 6138–6142.

[30] This mechanism can also be applied to the phosphine-catalyzed reaction discussed in reference [27]. In that example, Tong proposed that the allenoate analogous to **12a** was produced through generation of phosphonium diene **5**, β′-addition of the sulfonamide anion, and

elimination of the phosphine. As we have demonstrated, however, the acetate ion is not sufficiently basic to generate the active nucleophile, suggesting that Tong's proposal is likely incorrect. The phosphonium dienolate **18** is, presumably, the actual Brønsted base, implying that the mechanism presented in Scheme 3 is likely in operation for the reaction in reference [27] as well.

[31] Deuterium labeling studies employing allenylic acetate **9** and trideuteroacetate **9-D** corroborated our mechanistic rationale. See the Supporting Information for details.

[32] For examples of phosphine-catalyzed intramolecular γ-umpolung cyclizations of alkynoates, see: a) reference [25d]; b) reference [26c]; c) reference [26i]. For an example of phosphine-catalyzed intramolecular γ-umpolung cyclization of allenoates, see: d) reference [18].

[33] Tong performed an analogous reaction employing allenylic acetate **4** and reported the isolation of only the analogous compound to 2*H*-pyran **32** in 21% yield; see the Supporting Information of reference [14].

[34] The mechanism for the formation of this pyran is presented in the Supporting Information.

[35] G. A. Kraus, K. Neuenschwander, *Tetrahedron Lett*. **1980**, *21*, 3841–3844.

[36] For an example of detosylation/lactamization, see: L. C. Pattenden, H. Adams, S. A. Smith, J. P. A. Harrity, *Tetrahedron* **2008**, *64*, 2951–2961.

[37] a) D. A. Burnett, J.-K. Choi, D. J. Hart, Y.-M. Tsai, *J. Am. Chem. Soc*. **1984**, *106*, 8201–8209; b) Y. Nagao, W.-M. Dai, M. Ochiai, M. Shiro, *Tetrahedron* **1990**, *46*, 6361–6380.

[38] a) A. G. Myers, B. Zhang, *Org. Synth.* **1999**, *76*, 178; b) I. MacInnes, J. Walton, *J. Chem. Soc. Perkin Trans. II*. **1987**, 1077–1082.

[39] M. V. Chelliah, S. Chackalamannil, Y. Xia, M. C. Clasby, W. J. Greenlee, Y. Wang, E. P. Veltri, W. Wu, M. P. Graziano, T. Kosoglou, M. Chintala (Schering-Plough), US 20050267155 A1, **2005**; *Chem. Abstr*. **2005**, *144*, 6954.

[40] E. J. Kang, E. J. Cho, M. K. Ji, Y. E. Lee, D. M. Shin, S. Y. Choi, Y. K. Chung, J.-S. Kim, H.-J. Kim, S.-G. Lee, M. S. Lah, E. Lee, *J. Org. Chem*. **2005**, *70*, 6321–6329.

[41] a) T. C. Adams, A. C. Dupont, J. P. Carter, J. F. Kachur, M. E. Guzewska, W. J. Rzeszotarski, S. G. Farmer, L. Noronhablob, C. Kaiser, *J. Med. Chem*. **1991,** *34*, 1585–1593; b) M. Rubinshtein, C. R. James, J. L. Young, Y. J. Ma, Y. Kobayashi, N. C. Gianneschi, J. Yang, *Org. Lett*. **2010**, *12*, 3560–3563.

[42] P. Le Ménez, A. Hamze, O. Provot, J.-D. Brion, M. Alami, *Synlett* **2010**, *2010*, 1101–1103.

[43] a) H. Helmboldt, J. E. Aho, P. M. Pihko, *Org. Lett*. **2008**, *10*, 4183–4185; b) M. Winter, F. Naf, A. Furrer, W. Pickenhagen, W. Giersch, A. Meister, B. Willhalm, W. Thommen, G. Ohloff, *Helv. Chim. Acta*. **1979**, *62*, 135–139.

[44] For construction of this compound using phosgene gas and for its spectral data, see: a) H. Ulrich, B. Tucker, A. A. R. Sayigh, *J. Org. Chem*. **1966**, *31*, 2658–2661; b) A. A. R. Sayigh, H. Ulrich (Upjohn), US 3371114 (A), **1968**.

[45] G. Besenyei, L. I. Simándi, *Tetrahedron Lett*. **1993**, *34*, 2839–2842.

[46] This procedure was modified from one previously published for a similar compound: see reference [22a].

[47] R. Na, C. Jing, Q. Xu, H. Jiang, X. Wu, J. Shi, J. Zhong, M. Wang, D. Benitez, E. Tkatchouk, W. A. Goddard, H. Guo, O. Kwon, *J. Am. Chem. Soc*. **2011**, *133*, 13337–13348.

[48] This procedure was modified from one for the construction of similar compounds while employing DABCO as the organocatalyst: a) S. Tsuboi, S. Takatsuka, M. Utaka, *Chem. Lett*. **1988**, *17*, 2003–2004; b) S. Tsuboi, H. Kuroda, S. Takatsuka, T. Fukawa, T. Sakai, M. Utaka, *J. Org. Chem*. **1993**, *58*, 5952–5957.

[49] M. Barnard, P. J. Smith, R. F. M. White, *J. Organomet. Chem*. **1974**, *77*, 189–197.

[50] J. M. Kim, K. Y. Lee, S. Lee, J. N. Kim, *Tetrahedron Lett*. **2004**, *45*, 2805–2808.

[51] W. Huang, Q. Shen, J. Wang, X. Zhou, *J. Org. Chem*. **2008**, *73*, 1586–1589.

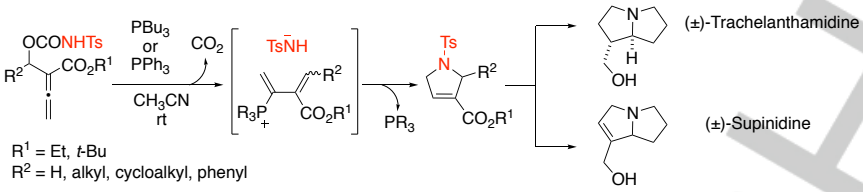
[52] K. Drauz, A. Kleemann, E. Wolf-Heuss (Degussa Aktiengesellschaft), US 4716237 (A), **1987**.

[53] a) The structures of allenoate **30** and 4*H*-pyran **31** obtained from this reaction were assigned based on similarity to analogous structures reported in the following paper: C. Li, Q. Zhang, X. Tong, *Chem. Commun*. **2010**, *46*, 7828–7830. b) The structure of 2*H*-pyran **32** obtained from this reaction was assigned based on similarity to an analogous structure presented in the Supporting Information of the following paper: reference [14].

[54] S. A. Reed, C. White, *J. Am. Chem. Soc*. **2008**, *130*, 3316–3318.

[55] S. Ishikawa, F. Noguchi, A. Kamimura, *J. Org. Chem*. **2010**, *75*, 3578–3586.

Entry for the Table of Contents



From allenes to pyrrolizidines: A phosphine-catalyzed (4+1) annulative rearrangement of allenylic carbamates yields 1,3-disubstituted- and 1,2,3-trisubstituted-3-pyrrolines, including difficult-to-prepare 2-alkyl variants, via phosphonium diene intermediates. This new methodology has been employed as the key step in concise formal syntheses of the pyrrolizidine alkaloids (±)-trachelanthamidine and (±)-supinidine.