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# Synthesis of cyclic sulfamoyl carbamates and ureas via ring-closing metathesis

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**Abstract**—Synthetic routes to a diverse set of cyclic sulfamoyl carbamates and ureas are reported. These routes utilize 3-component coupling, Mitsunobu alkylation, and ring-closing metathesis using the second-generation Grubbs catalyst to achieve the synthesis of the target *S*-heterocyclic compounds. Cyclic *S*-heterocycles ranging from 9- to 11-membered rings have been obtained.


## 1. Introduction

The recent growth of high-throughput screening for biologically active agents has increased the demand for diverse libraries of synthetic compounds.[1] A growing area in combinatorial chemistry[2] is the generation of novel structural scaffolds that are inherently advantageous from both a chemical and a biological standpoint.[3] The ability of the sulfonamide moiety, and related analogs, to serve as non-hydrolyzable amide surrogates has opened the door for their use as key functional groups in the development of new scaffolds. A number of compounds based on this premise have been developed including, biologically active sulfonamides,[4] sulfamides,[5] sulfamoyl carbamates,[6] sulfahydantoins,[7] and sulfamoyl ureas.[8] Recently, novel libraries based on sulfonamide,[9] sulfamoyl urea,[10] sulfahydantoin,[11] and sulfamide[12] scaffolds have been reported. Our interest in the development of new routes to both phosphorus and sulfur-containing heterocycles (*P*- and *S*-heterocycles)[13] leads us to herein report a ring-closing metathesis (RCM) route[13,14] to a diverse set of cyclic sulfamoyl carbamates (**4**) and sulfamoyl ureas (**5**). These compounds represent novel scaffolds possessing multiple points of diversity from which to produce combinatorial libraries.

Sulfamoyl carbamates of structure **2** (Fig. 1) have been primarily used as important synthetic intermediates in the generation of unsymmetric sulfamides[13a,15] and sulfahydantoins.[16] Their popularity originates from their ease

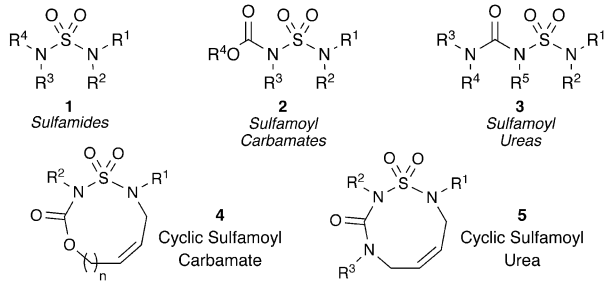


**Figure 1.**

of synthesis utilizing the 3-component coupling with chlorosulfonyl isocyanate (CSI), and facile derivatization by standard alkylation and Mitsunobu alkylation.[17] The result has been the production of linear sulfamoyl carbamates,[18,19] sulfahydantoins,[16] and linear[16,20] and cyclic sulfamides.[13a,15] Sulfamoyl carbamates have been studied as acyl-CoA:cholesterol *O*-acyl-transferase (ACAT) inhibitors[21] in conjunction with sulfamoyl ureas, vide infra. While examples of acyclic sulfamoyl carbamates are prevalent in the literature, reports of cyclic sulfamoyl carbamates are limited, with only two cases reported to date (compounds **6** and **7**, Fig. 2).[22] Furthermore, no examples of

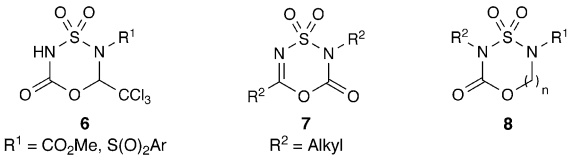


**Figure 2.**

*Keywords*: Cyclic sulfamoyl carbamate; Cyclic sulfamoyl urea; Sulfur heterocycles; RCM; Metathesis.
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cyclic sulfamoyl carbamates of general structure **8** have been reported.

Sulfamoyl ureas have been shown to be active as hypoglycemic agents,[23] ACAT inhibitors,[21] and herbicides.[24] Large libraries of linear sulfamoyl ureas have been synthesized from the 3-component coupling of two amine nucleophiles and CSI. The chemical features of the sulfamoyl urea group are different from that of a sulfamoyl carbamate. The higher p$K_a$ of the urea N–H, compared to the carbamate N–H, has hindered efforts to alkylate the urea N–H using the Mitsunobu reaction. Thus, derivatization of these compounds has previously fallen solely to base alkylation. Cyclic sulfamoyl ureas have been largely unexplored. To date, a single report has appeared detailing the synthesis of cyclic sulfamoyl ureas **9** and **10** (Fig. 3).[25]

The emergence of ring-closing olefin metathesis (RCM)[26,27] over the last decade has fundamentally changed the method of generating both carbocyclic and heterocyclic targets.[27] Specifically, RCM has become a routine transformation for the facile construction of small-, medium-, and large ring-containing systems.[27,28] When coupled with the versatile nature of both titled compounds, several factors provided impetus for this investigation, including: (i) the ease of synthesis and analog generation in both sulfamoyl carbamate and urea classes, (ii) the convenience of using RCM to generate cyclic structures, (iii) the ability of both sulfamoyl carbamate and urea moieties to serve as surrogates for sulfamide or urea groups present in known biologically active systems, and (iv) the correlation to the known biological activities of linear sulfamoyl carbamates and ureas.

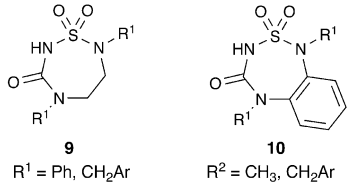



**Figure 3.**

## 2. Results and discussion

Previously, we have utilized sulfamoyl carbamate building blocks as synthetically valuable starting materials to generate a variety of unsymmetic cyclic sulfamides related to the potent HIV protease inhibitors DMP-323 and DMP-450.[15] Our new route utilizes this functional group as the central 'linchpin' in an RCM methodology. The strength of this approach lies in the wide variety of 9–11-membered cyclic sulfamoyl carbamates (**4**) (Fig. 4) and sulfamoyl ureas (**5**) (Fig. 5) that can be accessed from the corresponding dienes of general structure **11** and **12**, respectively. The focal points of this method include the ability to: (i) use 3-component coupling of CSI, allylic alcohols and allylic amines to synthesize sulfamoyl carbamates and sulfamoyl ureas with asymmetry in peripheral areas of the molecules; (ii) functionalize the sulfamoyl carbamate nitrogen via a Mitsunobu reaction; (iii) utilize base-promoted alkylation or the Mitsunobu reaction to functionalize the sulfamoyl urea

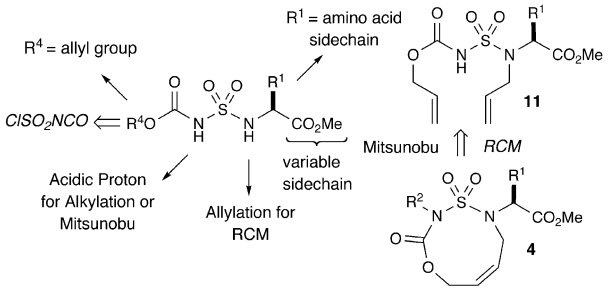



**Figure 4.**

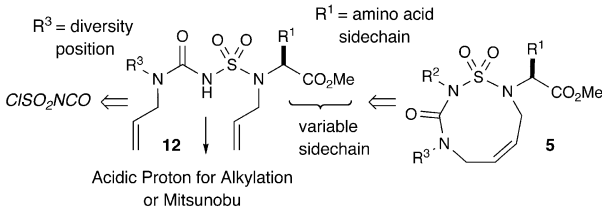
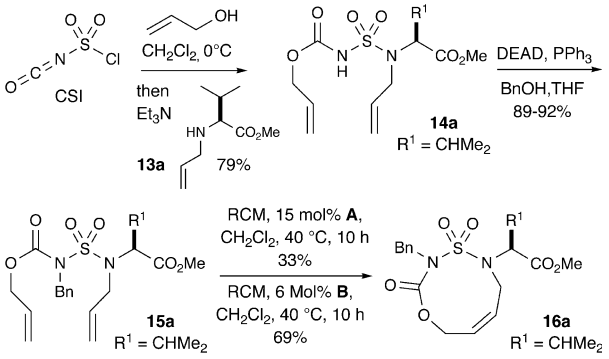



**Figure 5.**

nitrogen; and (iv) generate novel cyclic sulfamoyl carbamates and sulfamoyl ureas utilizing RCM.

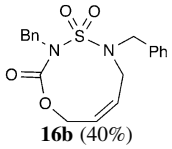
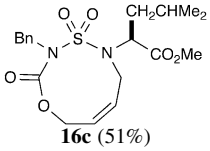
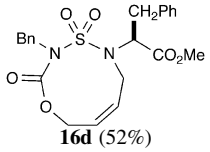
Our initial efforts began with the 3-component coupling of allyl alcohol, CSI, and *N*-allyl (L)-valine methyl ester (**13a**) to produce the corresponding sulfamoyl carbamate **14a** (Scheme 1). Optimization of the reaction conditions led to the use of 1.2 equiv of $Et_3N$ to efficiently facilitate the formation of sulfamoyl carbamate **14a** in 79% yield. Sulfahydantoin formation via intramolecular cyclization between the carbamate nitrogen and the ester group was thwarted under these conditions. Next, it was synthetically desirable to functionalize the carbamate nitrogen in **14a**. Though alkylation of sulfamoyl carbamates with $K_2CO_3$ was a viable option, the Mitsunobu reaction was employed because of its versatility and to reduce possible hydantoin formation. Subjection of **14a** to Mitsunobu conditions gave sulfamoyl carbamate **15a** in excellent yield (89–92%).




**Scheme 1.**

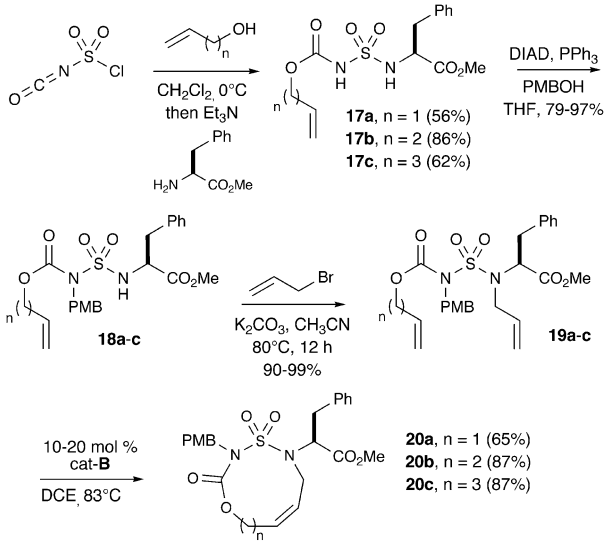
The initial attempts to cyclize diene **15a** using $(PCy_3)_2(Cl)_2Ru{=}CHPh$ (cat-**A**)[29] resulted in formation of 9-membered cyclic sulfamoyl carbamate **16a** in only 33% yield, with a major byproduct tentatively assigned as the dimer arising from cross-metathesis (X-MET).[30] RCM using the more active $(IMesH_2)(PCy_3)(Cl)_2Ru{=}CHPh$ catalyst (cat-**B**)[31] resulted in the formation of desired 9-membered

**Table 1**

| Entry | 3-Component coupling yield | Mitsunobu yield | Product RCM yield |
|---|---|---|---|
| 1 | **14b** (90%) | **15b** (92%) |  **16b** (40%) |
| 2 | **14c** (85%) | **15c** (87%) |  **16c** (51%) |
| 3 | **14d** (86%) | **15d** (81%) |  **16d** (52%) |

cyclic sulfamoyl carbamate **16a** in 69% overall yield, with no observable dimer formation via X-MET. This newly formed sulfamoyl carbamate represents the first example of RCM on this class of compounds and highlights the potential for library production utilizing more elaborate alcohols at the stage of both initial coupling and Mitsunobu alkylation steps.

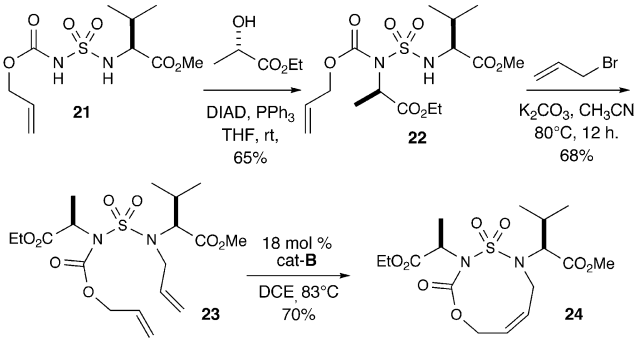
With a general route to cyclic sulfamoyl carbamates in hand, analogous cyclic sulfamoyl carbamates were synthesized using benzylamine and other (L)-amino esters as represented in Table 1. Coupling with CSI and allyl alcohol afforded sulfamoyl carbamates **14b–d** in good yields (85–90%). Benzylation via the Mitsunobu reaction afforded metathesis precursors **15b–d** in 81–92% yields. RCM with 6 mol% of cat-**B** gave cyclic sulfamoyl carbamates **16b–d** in modest yields of 40–52%. The Georg RCM purification procedure,[32] employing DMSO, was utilized to purify compounds throughout this study. Surprisingly, although these yields were marginal, no X-MET dimer was observed, prompting us to further optimize the RCM reaction.




**Scheme 2.**

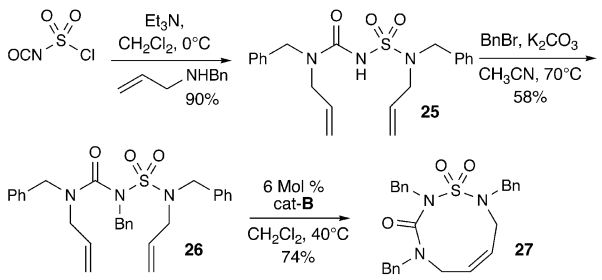
In the second route shown in Scheme 2, 3-component coupling was carried out with various olefinic alcohols, CSI, and (L)-phenylalanine methyl ester to produce corresponding sulfamoyl carbamates **17a–c** in good yields (56–86%). The Mitsunobu reaction was employed to regioselectively install the PMB moiety at the carbamate position (N–$R^2$ position) in sulfamoyl carbamates **18a–c** (79–97%). Allylation under standard conditions produced RCM precursors **19a–c** (90–99%). Subjection to RCM conditions using cat-**B** in refluxing DCE gave corresponding 9-, 10-, and 11-membered cyclic sulfamoyl carbamates **20a–c** in good yields (65–87%).

The initial examples outlined in Schemes 1 and 2 utilized simple Mitsunobu benzylation to install diversity at the sulfamoyl carbamate N–$R^2$ position. Installation of side chains bearing stereogenic centers, as previously shown in the synthesis of unsymmetric sulfamides,[15] were next pursued as outlined in Scheme 3. Thus, alkylation of **21** with naturally occurring (*S*)-ethyl lactate under Mitsunobu conditions, generated **22** in 65% yield. Simple allylation, followed by RCM in DCE afforded cyclic sulfamoyl carbamate **24** in good yield (70%) containing both valine and alanine side chains at the periphery.




**Scheme 3.**

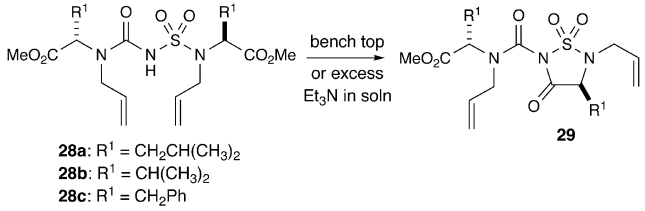
Subsequent efforts were focused toward the exploration of a similar three-step protocol to generate 9-membered cyclic sulfamoyl ureas (Scheme 4). Benzylamine was chosen as the initial test substrate, due to potential problems with sulfahydantoin formation from the use of amino esters, vide infra. Coupling of 2 equiv of benzylamine with CSI gave **25** in 90% yield (Scheme 4). As with the sulfamoyl carbamates, functionalization of the urea nitrogen with a benzyl group was desirable. Unfortunately, sulfamoyl ureas were unable to undergo Mitsunobu benzylations under standard DEAD




**Scheme 4.**

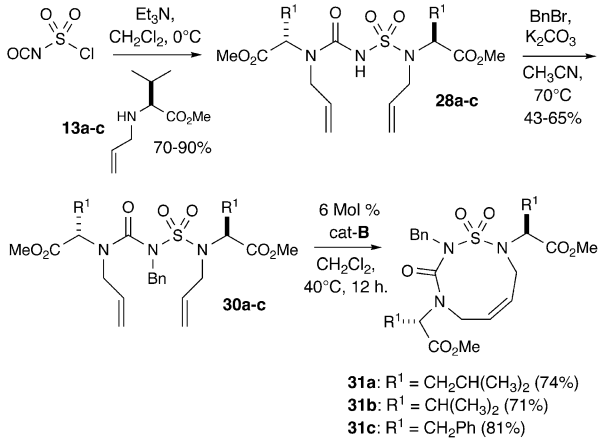
or DIAD conditions. Initial attempts at benzylation using DBU and NaH were found to be surprisingly ineffective despite literature precedent,[21] yielding no noticeable benzylated product. Utilizing our previous method to alkylate sulfamides ($K_2CO_3$, BnBr) resulted in the formation of benzylated sulfamoyl carbamate **26**, albeit in a modest 58% yield. RCM of **26** proved to be efficient as 6 mol% cat-**B** afforded 9-membered cyclic sulfamoyl urea **27** in 74% yield. Importantly, no product from X-MET was observed. This result represents the first known example of RCM on a sulfamoyl urea template, and opens opportunities to diversification strategies.

With a method for the generation of cyclic sulfamoyl ureas in hand, the synthesis of sulfamoyl ureas utilizing allylated aminoesters was explored. Sulfahydantoin formation, arising from attack of the sulfamoyl urea nitrogen into the sulfamide amino ester forming hydantoin **29**, was of major concern (Scheme 5). Thus, our initial use of excess base in the 3-component coupling reaction generated sulfahydantoins as a significant byproduct. In addition, the sulfamoyl ureas were found to form the sulfahydantoin at rt, over time, and in small amounts during column chromatography.




**Scheme 5.**

Despite these concerns, our initial 3-component coupling reaction with allylated amino ester **13a–c** and CSI produced sulfamoyl ureas **28a–c** in good overall yields (Scheme 6). Furthermore, optimal results were obtained with 1.2 equiv of $Et_3N$ and 2.2 equiv of the amino ester. Use of lesser equivalents of the amino ester gave a complex mixture of product, sulfahydantoin and sulfamoyl chloride. For stability reasons, benzylation was therefore utilized as a means of both protection and functionalization. The standard $K_2CO_3$ promoted benzylation of **28a–c** resulted in moderate yields of benzyl-protected RCM precursors **30a–c**

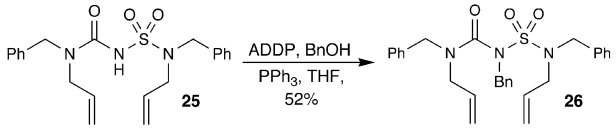



**Scheme 6.**

(43–65%). Surprisingly, these conditions produced only minor amounts of the sulfahydantoin despite elevated temperatures, with no single entry yielding more than 5% of hydantoin byproduct.

Metathesis of the amino ester-derived sulfamoyl ureas met with consistent results as treatment of **30a–c** with 6 mol% of cat-**B** afforded the desired cyclic sulfamoyl ureas **31a–c** in good yields (71–81%). Importantly, no byproducts via X-MET were observed during the RCM.

An alternate route of benzylation was sought in order to circumvent problems associated with generating benzylated sulfamoyl ureas. We felt that if a Mitsunobu reaction could be initiated at the sulfamoyl urea nitrogen, the potential for derivatization would greatly improve. The difficulty is encountered in the inability of the DEAD/$PPh_3$ complex to deprotonate the sulfamoyl ureas containing a less acidic N–H moiety. Mitsunobu reactions with higher p$K_a$ nucleophiles have been realized with the advent of 1,1′-(azodicarbonyl)dipiperidine-tributylphosphine (ADDP)[33] as a more powerful DEAD equivalent. To test the efficacy of this method, benzylamine-derived sulfamoyl urea **25** was subjected to modified conditions with ADDP, to afford benzylated sulfamoyl urea **26** in 52% yield (Scheme 7). To our knowledge, this is the first example of a Mitsunobu reaction using a sulfamoyl urea as the nucleophile. Though the yield was less than that obtained via standard alkylation conditions, these results are encouraging. In addition to nitrogen protection, utilization of more elaborate non-racemic secondary alcohols will provide an excellent pathway for diversification of these sulfamoyl ureas.




**Scheme 7.**

## 3. Conclusion

In conclusion, we have described the first synthesis of both cyclic sulfamoyl carbamates and ureas utilizing RCM. This method represents an extension of our recent sulfamide research and a new direction in the synthesis of novel *S*-heterocycles. Further research on sulfamoyl carbamates will focus on functionalization of the sulfamoyl carbamate nitrogen utilizing secondary allylic alcohols and amines in the 3-component coupling reaction to generate a variety of novel sulfamoyl carbamates and sulfamoyl ureas. In addition, the Mitsunbou reaction will be optimized and exploited as an important means to functionalize the sulfamoyl ureas. Biological screening and further refinement of these compounds is underway and will be reported in due course.

## 4. Experimental

### 4.1. General

All reactions were carried out in flame-dried glassware

under argon. Toluene, THF, $Et_2O$, and $CH_2Cl_2$ were purified by passage through a purification system (Solv-Tek) employing activated $Al_2O_3$.[34] $Et_3N$ was distilled from $CaH_2$. Flash column chromatography was performed with Merck silica gel (EM-9385-9, 230–400 mesh). Thin layer chromatography was performed on silica gel $60F_{254}$ plates (EM-5715-7, Merck). All amino acid precursors were purchased from Advanced Chem Tech. $^1H$ and $^{13}C$ spectra were recorded in $CDCl_3$ on either a Bruker DRX-400 or a Bruker AM-500 spectrometer operating at 400/100 MHz and 500/125 MHz, respectively. High-resolution mass spectrometry (HRMS) and FAB spectra were obtained on a VG Instrument ZAB double-focusing mass spectrometer. Infrared data was obtained on a Nicolet 320 Fourier Transform Infrared Spectrophotometers. Melting points were obtained on a Thomas Hoover capillary melting point apparatus. Optical rotations were carried out on a Rudolph Automatic Polarimeter (AUTOPOL IV).

**4.1.1. *N*-[[[(2-Propenyloxy)carbonyl]amino]sulfonyl]-*N*-(2-propenyl)-(*S*)-valine methyl ester (14a).** To a stirring solution of chlorosulfonyl isocyanate (CSI) (0.61 mL, 7.01 mmol) and $CH_2Cl_2$ (25 mL) at 0 °C was added allyl alcohol (0.40 mL, 7.01 mmol) in $CH_2Cl_2$ (3 mL) and stirred 10 min. The mixture was then transferred, via cannula, to a stirring solution of allylvaline methyl ester (1.23 g, 7.71 mmol) and $Et_3N$ (1.17 mL, 8.41 mmol) in $CH_2Cl_2$ (35 mL) at 0 °C. The resulting mixture was stirred for 12 h. The solvent was removed and EtOAc (80 mL) was added. The solution was washed with 10% $NaHSO_4$ (60 mL), $NaHCO_3$ (2×50 mL), brine (60 mL), dried with $MgSO_4$, filtered, and the solvent removed. Flash chromatography ($SiO_2$, hexanes/EtOAc) afforded 1.86 g (79%) of **14a** as a yellow solid. TLC $R_f$=0.28 (3:1 hexanes/EtOAc). Mp 72 °C; $[\alpha]_D^{25}$ −67.7 (*c* 1.5, $CHCl_3$); $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 7.50 (s, 1H), 5.97 (dddd, *J*=17.5, 10.1, 7.7, 5.4 Hz, 1H), 5.89 (dddd, *J*=16.2, 11.6, 5.8, 5.8 Hz, 1H), 5.33 (dd, *J*=17.1, 1.4 Hz, 1H), 5.25 (dd, *J*=10.5, 1.2 Hz, 1H), 5.22 (dd, *J*=17.2, 1.4 Hz, 1H), 5.13 (dd, *J*=10.1, 1.1 Hz, 1H), 4.62–4.59 (m, 2H), 4.24 (ddd, *J*=16.4, 5.4, 1.4 Hz, 1H), 4.12–4.06 (m, 1H), 4.12–4.06 (m, 1H), 3.69 (s, 3H), 2.21–2.15 (m, 1H), 1.02 (d, *J*=6.6 Hz, 3H), 0.94 (d, *J*=6.6 Hz, 3H); $^{13}C$ ($CDCl_3$, 100 MHz) $\delta$ 170.9, 150.6, 134.8, 131.3, 119.2, 117.8, 67.1, 66.8, 51.7, 49.6, 28.7, 19.6, 19.4; FTIR (neat) 3260, 2967, 1747, 1456, 1370, 1142 $cm^{-1}$; HRMS $(M+H)^+$ calcd for $C_{13}H_{23}N_2O_6S$ 335.1277, found 335.1283.

**4.1.2. *N*-[[[(2-Propenyloxy)carbonyl]amino]sulfonyl]-*N*-(2-propenyl)-benzylamine (14b).** In a procedure similar to the preparation of sulfamoyl carbamate **14a**, allyl alcohol (0.48 mL, 7.08 mmol) and allylbenzylamine (1.25 g, 8.48 mmol) were subjected to 3-component coupling conditions. Flash chromatography ($SiO_2$, hexanes/EtOAc) yielded 1.98 g (90%) of **14b** as a clear liquid. TLC $R_f$=0.27 (3:1 hexanes/EtOAc); $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 7.65 (bs, 1H), 7.35–7.8 (m, 5H), 5.90 (dddd, *J*=16.4, 1.5, 5.8, 5.8 Hz, 1H), 5.78 (dddd, *J*=16.8, 12.9, 6.5, 6.5 Hz, 1H), 5.36 (dd, *J*=17.2, 1.2 Hz, 1H), 5.28 (dd, *J*=10.4, 1.0 Hz, 1H), 5.19 (d, *J*=8.9 Hz, 1H), 5.16 (dd, *J*=16.7, 1.1 Hz, 1H), 4.64 (d, *J*=5.8 Hz, 2H), 4.55 (s, 2H), 3.91 (d, *J*=6.4 Hz, 2H); $^{13}C$ ($CDCl_3$, 100 MHz) $\delta$ 150.9, 135.7, 132.1, 131.2, 128.6, 128.4, 127.9, 119.4, 119.3, 67.1, 51.9, 50.6; FTIR (neat) 3620, 3600, 3260, 3087, 3031, 2928, 1747, 1647, 1606, 1455, 1352, 1150, 778, 700 $cm^{-1}$; HRMS $(M+H)^+$ calcd for $C_{14}H_{19}N_2O_4S$ 311.1066, found 311.1050.

**4.1.3. *N*-[[[(2-Propenyloxy)carbonyl]amino]sulfonyl]-*N*-(2-propenyl)-(*S*)-leucine methyl ester (14c).** In a procedure similar to the preparation of sulfamoyl carbamate **14a**, coupling and flash chromatography ($SiO_2$, hexanes/EtOAc) yielded 727 mg (85%) of the sulfamoyl carbamate **14c** as a clear yellow oil. TLC $R_f$=0.28 (3:1 hexanes/EtOAc); $[\alpha]_D^{25}$ −88 (*c* 1.5, $CHCl_3$); $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 7.70 (bs, 1H), 6.00–5.87 (m, 1H), 6.00–5.87 (m, 1H), 5.35 (dd, *J*=17.2, 1.4 Hz, 1H), 5.26 (dd, *J*=10.5, 1.2 Hz, 1H), 5.20 (dd, *J*=17.2, 1.2 Hz, 1H), 5.13 (dd, *J*=10.1, 1.1 Hz, 1H), 4.63–4.60 (m, 2H), 4.63–4.60 (m, 1H), 4.20 (dd, *J*=16.7, 5.4 Hz, 1H), 3.92 (dd, *J*=16.5, 7.3 Hz, 1H), 3.71 (s, 3H), 1.78–1.63 (m, 2H), 1.78–1.63 (m, 1H), 0.96 (d, *J*=6.2 Hz, 3H), 0.91 (d, *J*=6.2 Hz, 3H); $^{13}C$ ($CDCl_3$, 100 MHz) $\delta$ 172.1, 150.9, 134.9, 131.4, 119.1, 117.6, 67.5, 59.5, 52.2, 49.6, 38.9, 24.3, 22.5, 21.3; FTIR (neat) 3620, 3600, 3033, 2954, 1747, 1647, 1606, 1455, 1379, 1147 $cm^{-1}$; HRMS $(M+H)^+$ calcd for $C_{14}H_{25}N_2O_6S$ 349.1433, found 349.1421.

**4.1.4. *N*-[[[(2-Propenyloxy)carbonyl]amino]sulfonyl]-*N*-(2-propenyl)-(*S*)-phenylalanine methyl ester (14d).** In a procedure similar to the preparation of sulfamoyl carbamate **14a**, coupling and flash chromatography ($SiO_2$, hexanes/EtOAc) yielded 1.36 g (86%) of **14d** as a yellow oil. TLC $R_f$=0.21 (3:1 hexanes/EtOAc); $[\alpha]_D^{25}$ −29.3 (*c* 1.5, $CHCl_3$); $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 7.53 (bs, 1H), 7.31–7.21 (m, 5H), 5.95–5.80 (m, 1H), 5.95–5.80 (m, 1H), 5.35 (dd, *J*=17.2 Hz, 1.4 Hz, 1H), 5.26 (dd, *J*=10.4, 1.1 Hz, 1H), 5.24 (dd, *J*=18.1, 1.2 Hz, 1H), 5.16 (dd, *J*=10.2, 1.1 Hz, 1H), 4.79 (dd, *J*=7.5, 7.5 Hz, 1H), 4.62 (dd, *J*=5.7, 1.1 Hz, 1H), 4.15 (ddd, *J*=16.4, 6.0, 1.0 Hz, 1H), 4.01 (ddd, *J*=16.3, 6.4 Hz, 1H), 3.67 (s, 3H), 3.32 (dd, *J*=14.0, 7.8 Hz, 1H), 3.32 (dd, *J*=14.0, 7.8 Hz, 1H), 3.11 (dd, *J*=14.1, 7.5 Hz, 1H); $^{13}C$ ($CDCl_3$,100 MHz) 170.9, 150.6, 136.5, 134.2, 131.3, 129.2, 128.5, 127.0, 119.2, 118.4, 67.1, 62.2, 52.3, 50.2, 36.8; FTIR (neat) 3620, 3600, 3262, 3029, 2953, 1747, 1648, 1605, 1496, 1455, 1367, 1159, 750, 700 $cm^{-1}$; (HRMS $(M+H)^+$ calcd for $C_{17}H_{23}N_2O_6S$ 383.1277, found 383.1275.

**4.1.5. *N*-[[[(2-Propenyloxy)carbonyl]-*N'*-(benzyl)amino]-sulfonyl]-*N*-(2-propenyl)-(*S*)-valine methyl ester (15a).** To a stirring solution of sulfamoyl carbamate **14a** (1.00 g, 3.4 mmol) and DEAD (0.562 mL, 3.57 mmol) in THF (1 mL) under argon, was added a mixture of BnOH (0.370 mL, 3.57 mmol) and $PPh_3$ (936 mg, 3.57 mmol) in THF (1 mL) via dropwise addition from a syringe. The solution was stirred for 6 h, the solvent removed, and purified by flash chromatography to yield 1.20 g (92%) of **15a** as a clear oil. TLC $R_f$=0.45 (3:1 hexanes/EtOAc); $[\alpha]_D^{25}$ −65.9 (*c* 2.0, $CHCl_3$); $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 7.41 (d, *J*=7.9 Hz, 2H), 732–7.23 (m, 3H), 5.97 (dddd, *J*=18.0, 13.0, 7.8, 5.2 Hz, 1H), 5.88 (dddd, *J*=16.3, 10.5, 5.8, 5.8 Hz, 1H), 5.30, (dd, *J*=17.2, 1.4 Hz, 1H), 5.24 (dd, *J*=10.5, 1.1 Hz, 1H), 5.20 (dd, *J*=18.3, 1.1 Hz, 1H), 5.11 (dd, *J*=10.1, 1.0 Hz, 1H), 4.90 (s, 2H), 4.63 (dd, *J*=5.8, 1.2 Hz, 2H), 4.25 (ddd, *J*=16.4, 5.1, 1.4 Hz, 1H), 4.10 (dd, *J*=16.4,

7.9 Hz, 1H), 3.89 (d, $J=10.4$ Hz, 1H), 3.66 (s, 3H), 2.19–2.09 (m, 1H), 1.02 (d, $J=6.6$ Hz, 3H), 0.88 (d, $J=6.6$ Hz, 3H); $^{13}$C ($CDCl_3$, 100 MHz) $\delta$ 170.7, 152.5, 137.1, 135.3, 131.3, 128.3, 128.1, 127.6, 119.2, 117.2, 67.6, 66.3, 52.3, 51.4, 49.7, 28.7, 19.6, 19.2; FTIR (neat) 3033, 2967, 1739, 1649, 1607, 1497, 1435, 1370, 1142, 701, 768 $cm^{-1}$; HRMS $(M+H)^+$ calcd for $C_{20}H_{29}N_2O_6S$ 425.1746, found 425.1729.

**4.1.6. *N*-[[[(2-Propenyloxy)carbonyl]-*N'*-(benzyl)amino]-sulfonyl]-*N*-(2-propenyl)-benzylamine (15b).** In a procedure similar to the preparation of sulfamoyl carbamate **15a**, Mitsunobu reaction and flash chromatography ($SiO_2$, hexanes/EtOAc) afforded 1.19 g (92%) of **15b** as a clear liquid. TLC $R_f=0.51$ (3:1 hexanes/EtOAc); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.45 (d, $J=8.5$ Hz, 2H), 7.35–7.24 (m, 8H), 5.92 (dddd, $J=16.4$, 11.7, 5.9, 5.9 Hz, 1H), 5.65 (dddd, $J=16.8$, 10.5, 6.5, 6.5 Hz, 1H), 5.35 (dd, $J=17.4$, 1.2 Hz, 1H), 5.28 (d, $J=10.4$ Hz, 1H), 5.14 (d, $J=10.2$ Hz, 1H), 5.06 (dd, $J=17.2$, 1.2 Hz, 1H), 4.94 (s, 2H), 4.70 (d, $J=5.8$ Hz, 2H), 4.46 (s, 2H), 3.77 (d, $J=6.4$ Hz, 2H); $^{13}$C ($CDCl_3$, 100 MHz) $\delta$ 152.8, 137.2, 136.0, 132.0, 131.4, 128.5, 128.4, 128.3, 128.2, 127.7, 127.7, 119.4, 119.0, 67.6, 52.0, 51.8, 50.3; FTIR (neat) 3086, 3033, 2983, 1732, 1650, 1606, 1496, 1455, 1372, 1158, 750, 700 $cm^{-1}$; HRMS $(M+H)^+$ calcd for $C_{21}H_{25}N_2O_4S$ 401.1535, found 401.1517.

**4.1.7. *N*-[[[(2-Propenyloxy)carbonyl]-*N'*-(benzyl)amino]-sulfonyl]-*N*-(2-propenyl)-(*S*)-leucine methyl ester (15c).** In a procedure similar to the preparation of sulfamoyl carbamate **15a**, Mitsunobu reaction and flash chromatography ($SiO_2$, hexanes/EtOAc) afforded 721 mg (87%) of **15c** as a clear yellow liquid. TLC $R_f=0.49$ (3:1 hexanes/EtOAc); $[\alpha]_D^{25}$ −81.5 (*c* 5.0, $CHCl_3$); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.41 (d, $J=7.1$ Hz, 2H), 7.33–7.23 (m, 3H), 5.99–5.86 (m, 1H), 5.99–5.86 (m, 1H), 5.33 (dd, $J=17.2$, 1.3 Hz, 1H), 5.26 (dd, $J=10.4$, 1.0 Hz, 1H), 5.16 (dd, $J=17.2$, 1.2 Hz, 1H), 5.10 (dd, $J=10.2$, 1.0 Hz, 1H), 4.93 (d, $J=15.7$ Hz, 1H), 4.75 (d, $J=15.6$ Hz, 1H), 4.67 (d, $J=5.7$ Hz, 2H), 4.40 (dd, $J=8.6$, 6.0 Hz, 1H), 4.17 (d, $J=16.7$, 5.3 Hz, 1H), 3.91 (dd, $J=16.7$, 7.4 Hz, 1H), 3.65 (s, 3H), 1.71–1.56 (m, 2H), 1.71–1.56 (m, 1H), 0.93 (d, $J=6.2$ Hz, 3H), 0.88 (d, $J=6.4$ Hz, 3H); $^{13}$C ($CDCl_3$,100 MHz) $\delta$ 171.9, 153.1, 137.6, 136.0, 131.8, 128.7, 128.6, 128.0, 119.5, 117.4, 68.6, 59.3, 52.6, 52.2, 50.1, 39.8, 24.7, 22.7, 21.8; FTIR (neat) 3033, 2955, 1747, 1649, 1607, 1497, 1455, 1380, 1147, 770, 700 $cm^{-1}$; HRMS $(M+H)^+$ calcd for $C_{21}H_{31}N_2O_6S$ 439.1903, found 439.1904.

**4.1.8. *N*-[[[(2-Propenyloxy)carbonyl]-*N'*-(benzyl)amino]-sulfonyl]-*N*-(2-propenyl)-(*S*)-phenylalanine methyl ester (15d).** In a procedure similar to the preparation of sulfamoyl carbamate **15a**, Mitsunobu and flash chromatography ($SiO_2$, hexanes/EtOAc) afforded 1.24 (81%) of **15d** as a clear oil. TLC $R_f=0.40$ (3:1 hexanes/EtOAc); $[\alpha]_D^{25}$ −27.3 (*c* 1.5, $CHCl_3$); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.42 (d, $J=7.1$ Hz, 2H), 7.33–7.23 (m, 6H), 7.17 (d, $J=6.9$ Hz, 2H), 5.98–5.86 (m, 1H), 5.98–5.86 (m, 1H), 5.33 (dd, $J=17.2$, 1.2 Hz, 1H), 5.27 (dd, $J=10.4$, 1.3 Hz, 1H), 5.26 (dd, $J=16.7$, 1.3 Hz, 1H), 5.17 (dd, $J=10.2$, 1.1 Hz, 1H), 4.94 (d, $J=15.6$ Hz, 1H), 4.86 (d, $J=15.7$ Hz, 1H), 4.69–4.65 (m, 2H), 4.69–4.65 (m, 1H), 4.21 (dd, $J=16.7$, 5.8 Hz, 1H), 4.06 (dd, $J=16.6$, 6.7 Hz, 1H), 3.61 (s, 3H), 3.26 (dd, $J=13.8$, 9.0 Hz, 1H), 3.04 (dd, $J=13.8$, 9.0 Hz, 1H); $^{13}$C ($CDCl_3$,100 MHz) 170.4, 152.6, 137.1, 136.5, 135.1, 131.4, 129.2, 128.5, 128.4, 128.2, 127.7, 126.9, 119.2, 117.6, 67.7, 61.6, 52.2, 51.9, 50.1, 37.1; FTIR 3031, 2952, 1732, 1649, 1605, 1496, 1454, 1384, 1170, 750, 700 $cm^{-1}$; HRMS (neat) $(M+H)^+$ calcd for $C_{24}H_{29}N_2O_6S$ 473.1746, found 473.1744.

**4.1.9. (2*S*)-2-(3-Benzyl-2,4,4-trioxo-3,4,6,9-tetrahydro-2*H*-4$\lambda^6$-[1,4,3,5]oxathiadiazonin-5-yl)-3-methyl-butyric acid methyl ester (16a).** Sulfamoyl carbamate **15a** (200 mg, 0.471 mmol), and $CH_2Cl_2$ (50 mL) were placed in a 100 mL round-bottomed flask and degassed with argon gas for 15 min. Catalyst **B** (12 mg, 0.014 mmol) was added, the flask was quickly fitted with a condenser under argon balloon, and the solution heated to reflux for 12 h. Another equivalent of catalyst was added (12 mg, 0.014 mmol) and the solution stirred for 6 h. The solution was cooled to rt, DMSO (0.2 mL) added, and the solution stirred for 12 h. The solvent was removed under reduced pressure and the material was subjected to flash chromatography ($SiO_2$, hexanes/EtOAc) to yield 128 mg (69%) of **16a** as a white solid. TLC $R_f=0.23$ (3:1 hexanes/EtOAc). Mp 97–98 °C $[\alpha]_D^{25}$ −27.3 (*c* 2.0, $CHCl_3$); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.44 (d, $J=7.2$ Hz, 2H), 7.34–7.25 (m, 3H), 5.73 (dddd, $J=11.4$, 3.6, 1.6, 1.6 Hz, 1H), 5.60–5.53 (m, 1H), 5.30 (d, $J=16.0$ Hz, 1H), 5.00 (d, $J=15.5$ Hz, 1H), 4.90 (d, $J=15.5$ Hz, 1H), 4.82–4.77 (m, 1H), 4.67 (d, $J=16.5$ Hz, 1H), 3.92 (d, $J=11.0$ Hz, 1H), 3.60–3.50 (m, 1H), 3.54 (s, 3H), 2.35–2.26 (m, 1H), 1.02 (d, $J=6.3$ Hz, 3H), 0.99 (d, $J=6.7$ Hz, 3H); $^{13}$C ($CDCl_3$, 100 MHz) $\delta$ 170.7, 153.1, 136.8, 131.3, 128.4, 128.2, 127.7, 125.4, 64.5, 63.7, 52.2, 51.5, 43.3, 25.8, 20.9, 18.6; FTIR (neat) 3023, 2967, 1741, 1600, 1507, 1386, 1136, 767, 701 $cm^{-1}$; HRMS $(M+H)^+$ calcd for $C_{18}H_{25}N_2O_6S$ 397.1433, found 397.1429.

**4.1.10. 2,9-Dibenzyl-1,1-dioxo-1,2,4,5,8,9-hexahydro-1$\lambda^6$-[1,4,2,9]thiaoxdiazonin-3-one (16b).** In a procedure similar to that used for the preparation of **16a**, sulfamoyl carbamate **15b** (200 mg, 0.50 mmol) and cat-**B** (13 mg, 0.015 mmol) in $CH_2Cl_2$ (50 mL) were subjected to RCM. Flash chromatography ($SiO_2$, 3:1 hexane/EtOAc) afforded 74 mg (40%) of **16b** as a brown oil. TLC $R_f=0.40$ (3:1 hexanes/EtOAc); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.48 (d, $J=7.2$ Hz, 2H), 7.37–7.26 (m, 8H), 5.93 (dt, $J=11.5$, 3.2 Hz, 1H), 5.58–5.50 (m, 1H), 5.50 (bs, 2H), 4.92 (s, 2H), 4.14–3.86 (m, 2H), 3.96 (bs, 2H); $^{13}$C ($CDCl_3$, 100 MHz) $\delta$ 153.5, 137.7, 134.6, 132.9, 128.8, 128.6, 128.5, 128.3, 128.2, 127.9, 125.8, 64.6, 51.4, 48.7, 44.3; FTIR (neat) 3220, 3030, 2980, 1729, 1508, 1370, 1167, 753, 699 $cm^{-1}$; HRMS $(M+H)^+$ calcd for $C_{19}H_{21}N_2O_4S$ 373.1222, found 373.1220.

**4.1.11. (2*S*)-2-(3-Benzyl-2,4,4-trioxo-3,4,6,9-tetrahydro-2*H*-4$\lambda^6$-[1,4,3,5]oxathiadiazonin-5-yl)-4-methyl-pentanoic acid methyl ester (16c).** In a procedure similar to that used for the preparation of **16a**, sulfamoyl carbamate **15c** (121 mg, 0.28 mmol) and cat-**B** (17 mg, 0.020 mmol) in $CH_2Cl_2$ (56 mL) were subjected to RCM. Flash chromatography ($SiO_2$, 10:1 heptane/EtOAc) afforded 58 mg (51%) of **16c** as a white solid. TLC $R_f=0.26$ (3:1 hexanes/EtOAc). Mp 78–80 °C; $[\alpha]_D^{25}$ −54.3 (*c* 1.1, $CHCl_3$); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.45 (d, $J=7.0$ Hz, 2H), 7.33–7.23

(m, 3H), 5.73 (dddd, $J$=11.7, 3.7, 1.8, 1.8 Hz, 1H), 5.56–5.51 (m, 1H), 5.28 (dd, $J$=16.7, 3.7 Hz, 1H), 4.96 (d, $J$=15.4, Hz, 1H), 4.89 (d, $J$=15.4 Hz, 1H), 4.79 (dd, $J$=15.2, 7.1 Hz, 1H), 4.71 (d, $J$=16.7 Hz, 1H), 4.45 (dd, $J$=9.2, 5.6 Hz. 1H), 3.69–3.63 (m, 1H), 3.56 (s, 3H), 1.83 (ddd, $J$=14.5, 8.8, 5.7 Hz, 1H), 1.69 (ddd, $J$=14.2, 9.4, 4.7 Hz, 1H), 1.69–1.59 (m, 1H), 0.97 (d, $J$=6.5 Hz, 3H), 0.97 ($J$=6.5 Hz, 3H); $^{13}$C ($CDCl_3$,100 MHz) $\delta$ 171.6, 153.4, 137.0, 131.9, 128.4, 128.4, 127.7, 124.9, 64.9, 56.9, 52.3, 51.4, 43.3, 37.0, 24.3, 22.9, 21.6; FTIR (neat) 3033, 2954, 1739, 1505, 1450, 1385, 1272, 1157, 772, 701 cm$^{-1}$; HRMS $(M+H)^+$ calcd for $C_{19}H_{27}N_2O_6S$ 411.1590, found 411.1583.

**4.1.12. (2*S*)-2-(3-Benzyl-2,4,4-trioxo-3,4,6,9-tetrahydro-2*H*-4λ$^6$-[1,4,3,5]oxathiadiazonin-5-yl)-3-phenyl-propionic acid methyl ester (16d).** In a procedure similar to that used for the preparation of **16a**, RCM and flash chromatography ($SiO_2$, hexanes/EtOAc) yielded 122 mg (52%) of **16d** as a brown solid. TLC $R_f$=0.26 (3:1 hexanes/EtOAc). Mp 83 °C; $[\alpha]_D^{25}$ −45 ($c$ 0.5, $CHCl_3$); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.45 (d, $J$=7.1 Hz, 2H), 7.33–7.23 (m, 8H), 5.75 (ddd, $J$=11.5, 1.9, 1.9 Hz, 1H), 5.66–5.59 (m, 1H), 5.22 (d, $J$=16.2 Hz, 1H), 4.94 (d, $J$=15.5 Hz, 1H), 4.89 (d, $J$=15.5 Hz, 1H), 4.73 (d, $J$=16.8 Hz, 1H), 4.67 (d, $J$=7.5 Hz, 1H), 4.65 (d, $J$=7.5 Hz, 1H), 3.89–3.81 (m, 1H), 3.58 (s, 3H), 3.43 (dd, $J$=14.4, 7.5 Hz, 1H), 3.02 (dd, $J$=14.4, 7.5 Hz, 1H); $^{13}$C ($CDCl_3$,100 MHz) 170.6, 153.2, 136.9, 136.9, 131.9, 129.1, 128.6, 128.4, 128.4, 127.7, 127.0, 125.0, 65.0, 59.9, 52.4, 51.4, 44.1, 35.2; FTIR (neat) 3030, 2950, 1740, 1498, 1386, 1168, 753, 699 cm$^{-1}$; HRMS $(M+H)^+$ calcd for $C_{22}H_{25}N_2O_6S$ 445.1433, found 445.1433.

**4.1.13. *N*-[[[(2-Propenyloxy)carbonyl]amino]sulfonyl]-(*S*)-phenylalanine methyl ester (17a).** To a stirring solution of CSI (1.97 g, 13.9 mmol) in $CH_2Cl_2$, (10 mL) at 0 °C was added allyl alcohol (0.95 mL, 13.9 mmol) via syringe and the reaction was stirred for 1 h. This solution was transferred via cannula to a stirring solution of phenylalanine ester hydrochloride (3.0 g, 13.9 mmol) and $Et_3N$ (3.87 mL, 27.8 mmol) in $CH_2Cl_2$ (25 mL) at 0 °C. The resulting mixture was stirred under Ar for 12 h. The product of the reaction was dissolved in 100 mL of $H_2O$ and extracted with $CH_2Cl_2$ (4×50 mL), dried with $Na_2SO_4$, filtered and concentrated under reduced pressure. The product was purified by flash chromatography ($SiO_2$, 3:1 heptane/EtOAc) to afford 2.65 g (56%) of carbamate **17a** as white solid. TLC $R_f$=0.38 (1:1 heptane/EtOAc). Mp 101–102.5 °C $[\alpha]_D^{25}$ +32.9 ($c$ 0.99, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.33–7.27 (m, 3H and N–H), 7.16 (d, $J$=7.0 Hz, 2H), 5.88 (dddd, J=16.6, 11.3, 5.8, 5.6 Hz, 1H), 5.58 (d, $J$=8.5 Hz, 1H), 5.34 (d, $J$=17.1 Hz, 1H), 5.27 (d, $J$=10.4 Hz, 1H), 4.61, (d, $J$=5.8 Hz, 2H), 4.55–4.51 (m, 1H), 3.72, (s, 3H), 3.13 (d, $J$=5.9 Hz, 2H), $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 171.0, 150.6, 134.7, 130.9, 129.4, 128.7, 127.5, 119.5, 67.4, 57.7, 52.7, 39.0; FTIR (neat) 3271, 1740, 1732, 1647 cm$^{-1;}$ HRMS $(M+H)^+$ calcd for $C_{14}H_{19}N_2O_6S$ 343.0964, found 343.0957.

**4.1.14. *N*-[[[(2-Butenyloxy)carbonyl]amino]sulfonyl]-(*S*)-phenylalanine methyl ester (17b).** In a procedure similar to the preparation of sulfamoyl carbamate **17a**, CSI (1.21 mL, 13.9 mmol), 3-buten-1-ol (1.2 mL, 13.9 mmol), and (L)-phenylalanine methyl ester hydrochloride (3.0 g, 13.9 mmol) and $Et_3N$ (3.87 mL, 27.8 mmol) were subjected to 3-component coupling conditions. Flash chromatography ($SiO_2$, 2:1 heptane/EtOAc) afforded 3.60 g (73%) of the desired carbamate **17b** as a white solid. TLC $R_f$=0.38 (1:1 heptane/EtOAc). Mp 95–97 °C $[\alpha]_D^{25}$ +38.3 ($c$ 1.05, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.32–7.25 (m, 3H and N–H), 7.15 (d, $J$=6.8 Hz, 2H), 5.75 (dddd, $J$=17.0, 10.2, 6.7, 6.7 Hz, 1H), 5.11 (d, $J$=17.1 Hz, 1H), 5.07 (d, $J$=10.3 Hz, 1H), 4.51 (t, $J$=5.8 Hz, 1H), 4.18 (t, $J$=6.6 Hz, 2H), 3.72 (s, 3H), 3.13 (d, $J$=5.8 Hz, 2H), 2.39 (dd, $J$=13.1, 6.5 Hz, 2H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 171.0, 150.8, 134.7, 133.3, 129.4, 128.8, 127.5, 117.8, 65.9, 57.6, 52.7, 38.8, 32.8; FTIR (neat) 3273, 2955, 1744, 1642 cm$^{-1}$ HRMS $(M+H)^+$ calcd for $C_{15}H_{21}N_2O_6S$ 357.1120, found 357.1099.

**4.1.15. *N*-[[[(2-Pentenyloxy)carbonyl]amino]sulfonyl]-(*S*)-phenylalanine methyl ester (17c).** In a procedure similar to the preparation of sulfamoyl carbamate **17a**, CSI (1.21 mL, 13.9 mmol), 4-penten-1-ol (1.44 mL, 13.9 mmol), (L)-phenyl alanine methyl ester hydrochloride (3.0 g, 13.9 mmol) and $Et_3N$ (3.87 mL, 27.8 mmol) were subjected to 3-component coupling conditions. Flash chromatography ($SiO_2$, 3:1 heptane/EtOAc) afforded 3.17 g (62%) of the desired carbamate **17c** as white solid. TLC $R_f$=0.21 (2:1 heptane/EtOAc). Mp 101–103 °C $[\alpha]_D^{25}$ +35.0 ($c$ 1.03, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.35–7.25 (m, 3H), 7.16 (d, $J$=7.1 Hz, 2H), 5.77 (dddd, $J$=16.9, 10.2, 6.6, 6.6 Hz, 1H), 5.58 (dd, $J$=12.6, 8.5 Hz, 1H), 5.04 (dd, $J$=17.2, 1.0 Hz, 1H), 5.00 (dd, $J$=10.2, 1.1 Hz, 1H), 4.52 (dd, $J$=14.3, 5.9 Hz, 1H), 4.14 (t, $J$=6.6 Hz, 2H), 3.72 (s, 3H), 3.13 (d, $J$=5.9 Hz, 2H), 2.08 (q, $J$=7.1 Hz, 2H), 1.73 (quintet, $J$=7.1 Hz, 2H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 171.0, 150.9, 137.0 134.7, 129.4 128.7, 127.4, 115.7, 66.5, 57.7, 52.7, 39.0, 29.7, 27.6; FTIR (neat) 3271, 1744, 1641 cm$^{-1;}$ HRMS $(M+H)^+$ calcd for $C_{16}H_{23}N_2O_6S$ 371.1277, found 371.1280.

**4.1.16. *N*-[[[(2-Propenyloxy)carbonyl]-*N*′-(4-methoxybenzyl)-amino]sulfonyl]-(*S*)-phenylalanine methyl ester (18a).** To a stirring solution of $Ph_3P$ (1.85 g, 7.04 mmol) in THF (4 mL) at rt was added PMBOH (973 mg, 7.04 mmol) via syringe and the solution stirred for 30 min. This mixture was transferred via cannula to a stirring solution of sulfamoyl carbamate **17a** (2.41 g, 7.04 mmol) and DIAD (1.42 g, 7.04 mmol) in THF (5 mL) and the reaction was stirred for 3 h and concentrated under reduced pressure. Flash chromatography ($SiO_2$, 4:1 heptane/EtOAc) afforded 3.17 g (97%) of the desired alkylated sulfamoyl carbamate **18a** as a yellow oil. TLC $R_f$=0.49 (1:1 heptane/EtOAc). $[\alpha]_D^{25}$ +2.9 ($c$ 1.02, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.35 (d, $J$=8.6 Hz, 2H), 7.31–7.28 (m, 3H), 7.07 (d, $J$=6.3 Hz, 2H), 6.87 (d, $J$=8.5 Hz, 2H), 5.90 (dddd, $J$=16.6, 11.2, 5.8, 5.4 Hz, 1H), 5.74 (d, $J$=8.2 Hz, 1H), 5.36 (d, $J$=17.2 Hz, 1H), 5.28 (d, $J$=10.4 Hz, 1H), 4.85 (d, $J$=15.3 Hz, 1H), 4.73 (d, $J$=15.3 Hz, 1H), 4.71–4.74 (m, 2H), 4.06 (dd, $J$=14.0, 5.9 Hz, 1H), 3.82 (s, 3H), 3.61 (s, 3H), 3.03 (d, $J$=9.4 Hz, 2H), $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 170.6, 159.4, 152.6, 136.2, 134.8, 131.0, 130.1, 129.3, 128.6, 127.3, 119.4, 113.9, 67.4, 57.0, 55.2, 52.4, 50.3, 38.9; FTIR (neat) 3304, 2979, 1736, 1728, 1612, 1514 cm$^{-1}$

HRMS $(M+H)^+$ calcd for $C_{22}H_{27}N_2O_7S$ 463.1539, found 463.1566.

**4.1.17. *N*-[[[(2-Butenyloxy)carbonyl]-*N′*-(4-methoxybenzyl)-amino]sulfonyl]-(*S*)-phenylalanine methyl ester (18b).** In a procedure similar to the preparation of sulfamoyl carbamate **18a**, compound **17b** (3.56 g, 9.99 mmol), DIAD (1.97 mL, 9.99 mmol), $Ph_3P$ (2.62 g, 9.99 mmol) and PMBOH (1.25 mL g, 9.99 mmol) were utilized in the Mitsunobu reaction. Flash chromatography ($SiO_2$, 5:1 heptane/EtOAc) afforded 3.94 g (83%) of the desired alkylated product **18b** as a yellow oil. TLC $R_f=0.55$ (1:1 heptane/EtOAc). $[\alpha]_D^{25}$ +3.0 (*c* 1.00, $CHCl_3$); $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta$ 7.33 (d, $J=8.5$ Hz, 2H), 7.27–7.24 (m, 3H), 7.05 (d, $J=7.0$ Hz, 2H), 6.84 (d, $J=8.5$ Hz, 2H), 5.75–5.69 (m, 1H and N–H), 5.10 (d, $J=17.2$ Hz, 1H), 5.00 (d, $J=10.2$ Hz, 1H), 4.82 (d, $J=15.2$ Hz, 1H), 4.68 (d, $J=15.2$ Hz, 1H), 4.24 (t, $J=6.5$ Hz, 2H), 4.02 (dd, $J=14.2$, 5.9 Hz, 1H), 3.80 (s, 3H), 3.59 (s, 3H), 2.98 (d, J=5.9 Hz, 2H), 2.40 (dd, $J=12.8$, 6.4 Hz, 2H), $^{13}C$ NMR ($CDCl_3$, 125 MHz) $\delta$ 170.6, 159.3, 152.8, 134.8, 134.0, 130.2, 129.4, 129.2, 128.6, 127.3, 117.8, 113.8, 66.4, 56.9, 55.3, 52.4, 50.2, 39.0, 32.9; FTIR (neat) 3319, 3055, 2926, 1744, 1728, 1612, 1514 $cm^{-1}$ HRMS $(M+NH_4)^+$ calcd for $C_{23}H_{32}N_3O_7S$ 494.1961, found 494.1953.

**4.1.18. *N*-[[[(2-Pentenyloxy)carbonyl]-*N′*-(4-methoxybenzyl)-amino]sulfonyl]-(*S*)-phenylalanine methyl ester (18c).** In a procedure similar to the preparation of sulfamoyl carbamate **18a**, compound **17c** (3.0 g, 8.1 mmol), DIAD (1.59 mL, 8.1 mmol), $Ph_3P$ (2.12 g, 8.1 mmol) and PMBOH (1.0 mL, 8.1 mmol) were utilized in the Mitsunobu reaction. Flash chromatography ($SiO_2$, 4:1 heptane/EtOAc) afforded 3.08 g (78%) of the desired alkylated product **18c** as a yellow oil. TLC $R_f=0.54$ (1:1 heptane/EtOAc). $[\alpha]_D^{25}$ +3.3 (*c* 1.01, $CHCl_3$);$^1H$ ($CDCl_3$, 500 MHz) $\delta$ 7.34 (d, $J=8.6$ Hz, 2H), 7.31–7.27 (m, 3H), 7.08 (d, $J=6.5$ Hz, 2H), 6.87 (d, $J=8.6$ Hz, 2H), 5.78 (dddd, $J=16.9$, 10.2, 6.6, 6.6 Hz, 1H), 5.73 (d, $J=5.5$ Hz, 1H), 5.03 (dd, $J=16.9$, 1.5 Hz, 1H), 5.00 (d, $J=9.0$ Hz, 1H), 4.85 (d, $J=15.3$ Hz, 1H), 4.72 (d, $J=15.3$, 1H), 4.24–4.17 (m, 2H), 4.06 (dd, $J=13.9$, 5.9 Hz, 1H), 3.82 (s, 3H), 3.62 (s, 3H), 3.01 (d, $J=5.8$ Hz, 2H), 2.08 (dt, $J=7.4$, 7.1 Hz, 2H), 1.75 (quintet, $J=7.1$ Hz, 2H); $^{13}C$ ($CDCl_3$, 125 MHz) $\delta$ 170.6, 159.3, 152.8, 137.0, 134.8, 129.9, 129.3, 129.1, 128.6, 127.3, 115.6, 113.8, 67.0, 57.0, 55.2, 52.4, 50.2, 38.9, 29.7, 27.6; FTIR (neat) 3296, 1728, 1612, 1514 $cm^{-1}$; HRMS $(M+NH_4)^+$ calcd for $C_{24}H_{34}N_3O_7S$ 508.2117, found 508.2094.

**4.1.19. *N*-(2-Propenyl)-*N*-[[[(2-propenyloxy)carbonyl]-*N′*-(4-methoxybenzyl)-amino]sulfonyl]-(*S*)-phenylalanine methyl ester (19a).** To a stirring solution of **18a** (3.06 g, 6.62 mmol) in $CH_3CN$ (25 mL) was added $K_2CO_3$ (9.15 g, 66.2 mmol), and allyl bromide (2.86 mL, 33.1 mmol). The reaction was stirred under reflux for 24 h. The product was filtered and purified by flash chromatography ($SiO_2$, 5:1 heptane/EtOAc) to afford 2.01 g (60%) of the pure product **19a** as a yellow oil. TLC $R_f=0.51$ (1:1 heptane/EtOAc). $[\alpha]_D^{25}$ −15.1 (*c* 1.09, $CHCl_3$); $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 7.37 (d, $J=8.6$ Hz, 2H), 7.30–7.21 (m, 3H), 7.12 (d, $J=6.9$ Hz, 2H), 6.82 (d, $J=8.6$ Hz, 2H), 5.97–5.85 (m, 2H), 5.35 (d, $J=17.1$ Hz, 1H), 5.28 (d, $J=10.4$ Hz, 1H), 5.25 (d, $J=17.6$ Hz, 1H), 5.17 (d, $J=10.2$ Hz, 1H), 4.87 (d, $J=15.4$ Hz, 1H), 4.77 (d, $J=15.4$ Hz, 1H), 4.65 (d, $J=5.9$ Hz, 2H), 4.55 (dd, $J=8.9$, 6.2 Hz, 1H), 4.17 (dd, $J=16.7$, 5.7 Hz, 1H), 4.00 (dd, $J=16.7$, 6.8 Hz, 1H), 3.77 (s, 3H), 3.59 (s, 3H), 3.22 (dd, $J=13.7$, 9.0 Hz, 1H), 2.97 (dd, $J=13.7$, 6.2 Hz, 1H), $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 170.3, 159.1, 152.5, 136.2, 134.9, 131.2, 129.9, 129.1, 129.0, 128.4, 126.8, 119.4, 117.6, 113.6, 67.7, 61.1, 55.1, 52.0, 51.4, 50.0, 36.8; FTIR (neat) 3350, 2982, 1732, 1649, 1612, 1585, 1514 $cm^{-1}$; HRMS $(M+H)^+$ calcd for $C_{25}H_{31}N_2O_7S$ 503.1852, found 503.1863.

**4.1.20. *N*-(2-Propenyl)-*N*-[[[(2-butenyloxy)carbonyl]-*N′*-(4-methoxybenzyl)amino]sulfonyl]-(*S*)-phenylalanine methyl ester (19b).** In a procedure similar to the preparation of sulfamoyl carbamate **19a**, **18b** (1.58 g, 3.3 mmol), $K_2CO_3$ (912 mg, 6.6 mmol), and allyl bromide (0.29 mL, 3.30 mmol) was subjected to the allylation procedure. Flash chromatography ($SiO_2$, 100% EtOAc) afforded 1.68 g (98%) of **19b** as a yellow oil. TLC $R_f=0.60$ (1:1 heptane/EtOAc). $[\alpha]_D^{25}$ −19.8 (*c* 0.98, $CHCl_3$); $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta$ 7.35 (d, $J=8.6$ Hz, 2H), 7.29–7.22 (m, 3H), 7.13 d, $J=7.0$ Hz, 2H), 6.81 (d, $J=11.5$ Hz, 2H), 5.91 (dddd, $J=16.9$, 10.2, 6.3, 6.1 Hz, 1H), 5.75 (dddd, $J=17.0$, 10.3, 6.7, 6.7 Hz, 1H), 5.25 (dd, $J=17.2$, 1.1 Hz, 1H), 5.16 (dd, $J=10.3$, 1.0 Hz, 1H), 5.12 (dd, $J=17.2$, 1.5 Hz, 1H), 5.10 (dd, $J=9.3$, 1.3 Hz, 1H), 4.83 (d, $J=15.5$ Hz, 1H), 4.74 (d, $J=15.5$ Hz, 1H), 4.58 (dd, $J=8.9$, 6.2 Hz, 1H), 4.20 (t, $J=6.3$ Hz, 2H), 4.17 (d, $J=5.7$ Hz, 1H)), 4.02 (dd, $J=16.6$, 6.7 Hz, 1H), 3.77 (s, 3H), 3.59 (s, 3H), 3.22 (dd, $J=13.7$, 9.0 Hz, 1H), 2.97 (dd, $J=13.7$, 6.1 Hz, 1H), 2.42 (dd, $J=13.5$, 6.7 Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 125 MHz) $\delta$ 170.4, 159.3, 152.7, 136.3, 135.0, 133.3, 129.9, 129.2, 129.1, 128.4, 126.8, 117.8, 117.7, 113.7, 66.3, 61.2, 55.2, 52.0, 51.4, 49.9, 36.9, 33.0; FTIR (neat) 2955, 1728, 1612, 1514 $cm^{-1}$; HRMS $(M+Na)^+$ calcd for $C_{26}H_{32}N_2O_7SNa$ 539.1828, found 539.1834.

**4.1.21. *N*-(2-Propenyl)-*N*-[[[(2-pentenyloxy)carbonyl]-*N′*-(4-methoxybenzyl)amino]sulfonyl]-(*S*)-phenylalanine methyl ester (19c).** In a procedure similar to the preparation of sulfamoyl carbamate **19a**, **18c** (513 mg, 3.3 mmol), $K_2CO_3$ (1.45 g, 10.5 mmol), allyl bromide (0.45 mL, 5.23 mmol) in $CH_3CN$ (20 mL) was subjected to the allylation procedure. Flash chromatography ($SiO_2$, 4:1 heptane/EtOAc) afforded 506 mg (91%) of **19c** as a yellow oil. TLC $R_f=0.67$ (1:1 heptane/EtOAc). $[\alpha]_D^{25}$ −20.2 (*c* 0.92, $CHCl_3$); $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 7.38 (d, $J=8.7$ Hz, 2H), 7.33–7.25 (m, 3H), 7.17 (d, $J=6.8$ Hz, 2H), 6.86 (d, $J=8.7$ Hz, 2H), 5.95 (dddd, $J=16.9$, 10.2, 6.5, 5.9 Hz. 1H), 5.80 (dddd, $J=16.9$, 10.2, 6.6, 6.6 Hz, 1H), 5.29 (dd, $J=17.2$, 1.2 Hz, 1H), 5.20 (dd, $J=10.2$, 1.1 Hz, 1H), 5.05 (dd, $J=17.1$, 1.6 Hz, 1H), 5.04 (d, $J=10.0$, 1.5 Hz, 1H), 4.89 (d, $J=15.5$ Hz, 1H), 4.79 (d, $J=15.5$ Hz, 1H), 4.61 (dd, $J=8.9$, 6.2 Hz, 1H), 4.22 (dd, $J=16.3$, 5.7 Hz, 1H), 4.19 (t, $J=7.0$ Hz, 2H), 4.07 (dd, $J=16.6$, 6.7 Hz, 1H), 3.80 (s, 3H), 3.63 (s, 3H), 3.26 (dd, $J=13.7$, 8.9 Hz, 1H), 3.01 (dd, $J=13.7$, 6.2 Hz, 1H), 2.11 (q, $J=7.1$ Hz, 2H), 1.79 (quintet, $J=7.0$ Hz, 2H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 170.3, 159.1, 152.7, 136.9, 136.2, 134.9, 129.6, 129.1, 129.0, 128.3, 126.8, 117.6, 115.5, 113.6, 66.5, 61.1, 55.1, 52.0, 51.4, 49.9, 36.8, 29.6, 27.6;

FTIR (neat) 1728, 1612, 1514 $cm^{-1}$; HRMS $(M+NH_4)^+$ calcd for $C_{27}H_{38}N_3O_7S$ 548.2430, found 540.2431.

**4.1.22. (2*S*)-2-[3-(4-Methoxy)benzyl)-2,4,4-trioxo-3,4,6,9-tetrahydro-2*H*-4λ$^6$-[1,4,3,5]oxathiadiazonin-5-yl]-3-phenyl-propionic acid methyl ester (20a).** Compound **19a** (202 mg, 0.40 mmol) was dissolved in DCE (80 mL, 0.005 *M*) and the solution was degassed with Ar for 15 min followed by reflux for 30 min. Cat-**B** (75 mg, 22 mol%) was added to the refluxing solution in three equal portions over a period of 48 h. The reaction was cooled to rt, DCE was removed under reduced pressure, followed the addition of DMSO (0.32 mL, 50 equiv relative to catalyst) in $CH_2Cl_2$ (50 mL). The reaction was stirred at rt for 24 h and the solvent was removed under reduced pressure. Flash chromatography ($SiO_2$, 4:1 heptane/EtOAc) afforded 124 mg (65%) of **19b** as a yellow oil. TLC $R_f$=0.47 (1:1 heptane/EtOAc). $[\alpha]_D^{25}$ −60.6 (*c* 1.11, $CHCl_3$); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.39 (d, *J*=8.9 Hz, 2H), 7.30 (d, *J*=7.4 Hz, 2H), 7.24–7.22 (m, 3H), 6.81 (d, *J*=8.7 Hz, 2H), 5.74 (dd, *J*=11.5 Hz, 1.7 Hz, 1H), 5.59 (dd, *J*=9.2, 1.8 Hz, 1H), 5.24–5.14 (m, 1H), 4.83 (s, 2H), 4.71–4.67 (m, 1H), 4.61 (t, *J*=7.3 Hz, 1H), 3.80–3.75 (m, 1H), 3.75 (s, 3H), 3.53 (s, 3H), 3.41 (dd, *J*=14.4, 7.6 Hz, 1H), 2.98 (dd, *J*=14.4, 7.6 Hz, 1H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 170.8, 159.2, 153.1, 136.1, 132.0, 130.1, 129.0, 128.8, 128.6, 127.0, 124.5, 113.7, 64.9, 59.4, 55.2, 52.5, 50.7, 43.6, 34.8; FTIR (neat) 2950, 1740, 1612, 1514 $cm^{-1}$; HRMS $(M+NH_4)^+$ calcd for $C_{23}H_{29}N_3O_7S$ 492.1804, found 492.1793.

**4.1.23. (2*S*)-2-[3-(4-Methoxybenzyl)-2,4,4-trioxo-3,4,9,10 tetrahydro-2*H*,6*H*-4λ$^6$-[1,4,3,5]oxathiadiazonin-5-yl]-3-phenyl-propionic acid methyl ester (20b).** In a procedure similar to the preparation of cyclic sulfamoyl carbamate **20a**, **19b** (209 mg, 0.40 mmol) and cat-**B** (34 mg, 10 mol%) in DCE (80 mL) was subjected to the RCM procedure. Flash chromatography ($SiO_2$, 4:1 heptane/EtOAc) afforded 173 mg (87%) of **20b** as an ivory-colored solid, Mp=43–50 °C. TLC $R_f$=0.16 (2:1 heptane/EtOAc). $[\alpha]_D^{25}$ −97.5 (*c* 0.96, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.39 (d, *J*=8.6 Hz, 2H), 7.31 (d, *J*=7.2 Hz, 2H), 7.27–7.24 (m, 3H). 6.78 (d, *J*=8.6 Hz, 2H), 5.85 (dd, *J*=16.6, 5.2 Hz, 1H), 5.62 (ddd, *J*=11.0, 11.0, 5.5 Hz, 1H), 4.82 (d, *J*=15.1 Hz, 1H), 4.76 (d, *J*=15.1 Hz, 1H), 4.59 (bs,1H), 4.52 (t, *J*=7.4 Hz, 1H), 4.18–4.14 (m, 1H), 4.08 (dd, *J*=11.3, 1.1 Hz, 1H), 3.74 (s, 4H), 3.52 (s, 3H), 3.45 (dd, *J*=14.4, 7.0 Hz, 1H), 3.00 (dd, *J*=14.4, 7.8 Hz, 1H), 2.74–2.68 (m, 1H), 2.25–2.21 (m, 1H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 171.3, 159.2, 152.5, 136.5, 131.5, 130.3, 129.1, 129.1, 128.5, 126.9, 113.5, 65.6, 59.2, 55.2, 52.5, 50.8, 44.7, 35.0, 25.3; FTIR (neat) 1732, 1612, 1514 $cm^{-1}$; HRMS $(M+NH_4)^+$ calcd for $C_{24}H_{32}N_3O_7S$ 506.1961, found 506.1955.

**4.1.24. (2*S*)-2-[3-(4-Methoxybenzyl)-2,4,4-trioxo-1-oxa-4λ$^6$-thia-3,5-diaza-cycloundec-7-en-5-yl]-3-phenyl-propionic acid methyl ester (20c) (hydrogenated for characterization).** In a procedure similar to the preparation of cyclic sulfamoyl carbamate **20a**, **19c** (206 mg, 0.39 mmol) and cat-**B** (43 mg, 0.05 mmol) in DCE (78 mL) was subjected to the RCM procedure. Flash chromatography ($SiO_2$, 5:1 heptane/EtOAc) afforded 170 mg (87%) of **20c** (1.6:1 E:Z) as a yellow oil. TLC $R_f$=0.50 (1:1 heptane/EtOAc); HRMS $(M+NH_4)^+$ calcd for $C_{25}H_{34}N_3O_7S$ 520.2117, found 520.2091. A portion of this compound was immediately subjected to the following hydrogenation protocol: Cyclic sulfamoyl carbamate **20c** (57 mg, 0.11 mmol) was weighed into a round-bottomed flask followed by the addition of 5% Pd/C (29 mg) and EtOAc (10 mL). The flask was evacuated using suction followed by the insertion of two $H_2$ balloons. The reaction was stirred at rt for 2 h. The crude product was filtered through celite and concentrated under reduced pressure to afford 54 mg (95%) of a white solid. TLC $R_f$=0.49 (1:1 heptanes/EtOAc). Mp 99–102 °C; $[\alpha]_D^{25}$ −9.7 (*c* 0.82, $CHCl_3$); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.44 (d, *J*=8.5 Hz, 2H), 7.24–7.17 (m, 3H), 6.91 (d, *J*=6.0 Hz, 2H), 6.76 (d, *J*=8.5 Hz, 2H), 5.03 (d, *J*=15.0 Hz, 1H), 4.81 (d, *J*=15.0 Hz, 1H), 4.22 (m, 1H), 4.10 (t, *J*=10.1 Hz, 1H), 3.90 (dd, *J*=9.8, 3.7 Hz, 1H), 3.73 (s, 3H), 3.68–3.51 (m, 2H), 3.58 (s, 3H), 3.17 (t, *J*=10.5 Hz, 1H), 2.87 (dd, *J*=13.3, 4.2 Hz, 1H), 2.05–1.92 (m, 2H), 1.78–1.66 (m, 2H), 1.56–1.51 (m, 2H), 1.32–1.28 (m, 2H); $^{13}$C ($CDCl_3$, 100 MHz) $\delta$ 169.9, 159.2, 152.9, 136.0, 130.5, 129.1, 129.0, 128.4, 126.7, 113.6, 69.2, 60.6, 55.1, 52.0, 51.5, 46.9, 34.9, 25.8, 23.4, 23.3, 22.1; FTIR (neat) 2953, 1743, 1726, 1612, 1514 $cm^{-1}$; HRMS $(M+Na)^+$ calcd for $C_{25}H_{32}N_2O_7SNa$ 527.1828, found 527.1820.

**4.1.25. *N*-[[[(2-Propenyloxy)carbonyl]amino]sulfonyl]-(*S*)-valine methyl ester (21).** CSI (29.8 mmol; 4.2 g) was dissolved in $CH_2Cl_2$ (10 mL), the solution was cooled to 0 °C, and allyl alcohol (1.73 g, 29.8 mmol) was added via syringe. In an adjacent round-bottomed flask, valine methyl ester hydrochloride (5.0 g, 29.8 mmol) was dissolved in $CH_2Cl_2$ (25 mL), cooled to 0 °C, and $Et_3N$ (6.03 g, 59.6 mmol) was added via syringe. Each solution was stirred at 0 °C under Ar for approximately 1h. The CSI/alcohol solution was cannulated into the amino acid solution and the reaction was stirred for 12 h under Ar at 0 °C while slowly warming to rt. The crude product was dissolved in $H_2O$ (100 mL) and extracted with $CH_2Cl_2$ (4×50 mL), dried ($Na_2SO_4$), filtered, and concentrated under reduced pressure. Flash chromatography ($SiO_2$, 4:1 heptane/EtOAc) afforded 6.12 g (70%) of the desired carbamate **21** as white solid. TLC $R_f$=0.35 (1:1 heptane/EtOAc). Mp 93–95 °C $[\alpha]_D^{25}$ +43.6 (*c* 1.03, $CHCl_3$); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 5.92 (dddd, *J*=17.0, 10.4, 5.8, 5.8 Hz, 1H), 5.67 (d, *J*=9.4 Hz, 1H), 5.37 (dd, *J*=17.2, 1.3 Hz, 1H), 5.29 (dd, *J*=10.4, 1.1 Hz, 1H), 4.66–4.63 (m, 2H), 4.07 (dd, *J*=9.4, 5.0 Hz, 1H), 3.75 (s, 3H), 2.20–2.11 (m, 1H), 1.02 (d, *J*=6.8 Hz, 3H), 0.91 (d, *J*=6.9 Hz, 3H), $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 171.6, 150.7, 131.0, 119.4, 67.3, 62.2, 52.5, 31.4, 18.8, 17.2; FTIR (neat) 3276, 3205, 2966, 1744, 1720, 1651 $cm^{-1}$; HRMS $(M+H)^+$ calcd for $C_{10}H_{19}N_2O_6S$ 295.0964, found 295.0947.

**4.1.26. *N*-[[[[*N*′-(2-Propenyloxy)carbonyl]-*N*′-(1*R*)-1-ethoxycarbonyl-ethyl]amino]sulfonyl]-(*S*)-valine methyl ester (22).** Compound **21** (2.66 g, 9.0 mmol) was dissolved in THF (3 mL) followed by the addition of DIAD (1.82 g, 9.0 mmol) dropwise via syringe. In an adjacent round-bottomed flask, $Ph_3P$ (2.37 g, 9.0 mmol) was dissolved in THF (4 mL) followed by the addition of (*S*)-ethyl lactate (1.02 mL, 9.0 mmol) via syringe. Each solution was stirred under Ar atmosphere at rt for 1 h after which the $Ph_3P$/ethyl lactate solution was cannulated into the solution of

**21**/DIAD and the resulting reaction mixture stirred under at rt for 24 h. The reaction was concentrated under reduced pressure. Flash chromatography ($SiO_2$, 9:1 heptane/EtOAc) afforded 2.30 g (65%) of the desired alkylated product **22** as a yellow oil. TLC $R_f$=0.53 (1:1 heptane/EtOAc). $[\alpha]_D^{25}$ + 73.0 (*c* 1.18, $CHCl_3$); $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta$ 6.08 (d, $J$=7.4 Hz, 1H), 5.95 (dddd, $J$=16.6, 11.1, 5.7, 5.4 Hz, 1H), 5.39 (d, $J$=17.2 Hz, 1H), 5.30 (d, $J$=10.5 Hz, 1H), 4.96 (q, $J$=7.0 Hz, 1H), 4.71 (t, $J$=5.6 Hz, 2H), 4.23–4.17 (m, 2H), 4.12 (dd, $J$=7.0, 3.5 Hz, 1H), 3.77 (s, 3H), 2.22–2.15 (m, 1H), 1.59 (d, $J$=7.0 Hz, 3H), 1.27 (t, $J$=7.1 Hz, 3H), 1.02 (d, $J$=6.8 Hz, 3H), 0.86 (d, $J$=6.9 Hz, 3H), $^{13}C$ NMR ($CDCl_3$, 125 MHz) $\delta$ 171.4, 170.0, 151.7, 131.0, 119.3, 68.1, 61.9, 61.8, 56.6, 52.5, 31.9, 18.8, 17.0, 16.5, 14.1; FTIR (neat) 3304, 2966, 1740, 1726, 1649 $cm^{-1}$; HRMS $(M+H)^+$ calcd for $C_{15}H_{27}N_2O_8S$ 395.1488, found 395.1472.

**4.1.27. *N*-(2-Propenyl)-*N*-[[[[*N′*-(2-propenyloxy)carbonyl]-*N′*-(1*R*)-1-ethoxycarbonyl-ethyl]amino]sulfonyl]-(*S*)-valine methyl ester (23).** Compound **22** (1.10 g, 2.79 mmol) was weighed into a round-bottomed flask, followed by the addition of $K_2CO_3$ (771 mg, 5.58 mmol), allyl bromide (0.24 mL, 2.79 mmol) and $CH_3CN$ (25 mL). The reaction was stirred under reflux at 85 °C for 6 h. The product was filtered and concentrated under reduced pressure. Flash chromatography ($SiO_2$, 6:1 heptane/EtOAc) afforded 825 mg (68%) of **23** as a yellow oil. TLC $R_f$=0.38 (2:1 heptane/EtOAc). $[\alpha]_D^{25}$ −22.2 (*c* 1.05, $CHCl_3$); $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta$ 6.02 (dddd, $J$=17.3, 10.2, 5.8, 5.8 Hz, 1H), 5.90 (dddd, $J$=16.4, 10.6, 5.8, 5.8 Hz, 1H), 5.36 (dd, $J$=17.2, 1.2 Hz, 1H), 5.29 (dd, $J$=10.2, 1.0 Hz, 1H), 5.22 (dd, $J$=17.3, 1.2 Hz, 1H), 5.12 (dd, $J$=10.2, 1.1 Hz, 1H), 4.99 (q, $J$=7.0 Hz, 1H), 4.64 (d, $J$=5.8 Hz, 2H), 4.23–4.21 (m, 2H), 4.19 (d, $J$=7.1 Hz, 2H), 4.13 (d, $J$=10.3 Hz, 1H), 3.70 (s, 3H), 2.22–2.14 (m, 1H), 1.61 (d, $J$=7.0 Hz, 3H), 1.26 (t, $J$=7.1 Hz, 3H), 1.03 (d, $J$=6.6 Hz, 3H), 0.94 (d, $J$=6.6 Hz, 3H); $^{13}C$ NMR ($CDCl_3$, 125 MHz) $\delta$ 171.0, 170.0, 151.9, 135.3, 131.0, 119.6, 117.5, 67.9, 66.2, 61.7, 56.8, 51.7, 49.5, 28.9, 19.7, 19.4, 16.1, 14.0; FTIR (neat) 2968, 1742, 1647 $cm^{-1}$; HRMS $(M+H)^+$ calcd for $C_{18}H_{31}N_2O_8S$ 435.1801, found 435.1778.

**4.1.28. (2*S*)-2-((1*R*)-1-Ethoxycarbonyl-ethyl])-2,4,4-trioxo-3,4,6,9-tetrahydro-2*H*-4λ⁶-[1,4,3,5]oxathiadiazonin-5-yl)-3-methyl-butyric acid methyl ester (24).** In a procedure similar to the preparation of cyclic sulfamoyl carbamate **20a**, **23** (24 mg, 0.055 mmol), cat-**B** (4 mg, 8 mol%) in DCE (11 mL) was subjected to the RCM procedure. Flash chromatography ($SiO_2$, 9:1 heptane/EtOAc) afforded 15 mg (68%) of **24** as a yellow oil. TLC $R_f$=0.45 (1:1 heptane/EtOAc). $[\alpha]_D^{25}$ −77.9 (*c* 1.00, $CHCl_3$); $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 5.72–5.69 (m, 1H), 5.54–5.51 (m, 1H), 5.33–5.29 (m, 1H), 4.95 (q, $J$=7.0 Hz, 1H), 4.89–4.85 (m, 1H), 4.73–4.69 (m, 1H), 4.33–4.18 (m, 2H), 3.96 (d, $J$=10.9 Hz, 1H), 3.57 (s, 3H), 3.57 (m, 1H), 2.37–2.27 (m, 1H), 1.62 (d, $J$=7.0 Hz, 3H), 1.31 (t, $J$=7.1 Hz, 3H), 1.04 (d, $J$=6.3 Hz, 3H), 0.98 (d, $J$=6.8 Hz, 3H); $^{13}C$ NMR ($CDCl_3$, 125 MHz) $\delta$ 170.7, 169.7, 152.6, 130.9, 124.6, 65.3, 61.8, 56.0, 51.8, 43.2, 29.7, 25.9, 20.5, 18.6, 15.6, 14.0; FTIR (neat) 2970, 1744, 1647, 1450, 1386 $cm^{-1}$; HRMS $(M+H)^+$ calcd for $C_{16}H_{27}N_2O_8S$ 407.1488, found 407.1497.

**4.1.29. *N*-(Benzyl)-*N*-(2-propenyl)-*N′*-[[*N″*-(2-propenyl)-*N″*-(benzyl)amino]sulfonyl]-urea (25).** To a stirring solution of benzylallylamine (2.18 g, 14.8 mmol) and $Et_3N$ (2.96 mL, 21.2 mmol) in $CH_2Cl_2$ (45 mL) at 0 °C under argon was added CSI (615 μL, 2.40 mmol) in $CH_2Cl_2$ (3 mL) dropwise over 5 min. The solution was stirred for 12 h, and $CH_2Cl_2$ (130 mL) added. The solution was washed with 10% $NaHSO_4$ (50 mL), $NaHCO_3$ (50 mL), brine (50 mL), dried ($MgSO_4$), and the solvent removed. Flash chromatography ($SiO_2$, hexanes/EtOAc) afforded 2.75 g of **25** (97%) as a white solid. TLC $R_f$=0.30 (2:1 hexanes/EtOAc). Mp 54–58 °C; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 7.36–7.26 (m, 10H), 5.87–5.71 (m, 1H), 5.87–5.71 (m, 1H), 5.25–5.20 (m, 1H), 5.25–5.20 (m, 1H), 5.15–5.11 (m, 1H), 5.15–5.11 (m, 1H), 4.57 (s, 2H), 4.50 (s, 2H), 3.91 (d, $J$=5.6 Hz, 2H), 3.85 (d, $J$=5.1 Hz, 2H); $^{13}C$ ($CDCl_3$,125 MHz) 152.8, 136.6, 132.8, 128.9, 128.9, 128.5, 128.5, 128.4, 127.9, 127.7, 127.6, 118.7, 118.0, 52.1, 50.6, 50.4, 49.7; FTIR (neat) 3306, 3031, 2927, 1696, 1651, 1606, 1586, 1455, 1392, 1153, 740, 699 $cm^{-1}$; HRMS $(M+H)^+$ calcd for $C_{21}H_{26}N_3O_3S$ 400.1695, found 400.1711.

**4.1.30. *N*-(Benzyl)-*N*-(2-propenyl)-*N′*-(benzyl)-*N′*-[[*N″*-(2-propenyl)-*N″*(benzyl)amino]sulfonyl]-urea (26).** Sulfamoyl urea **25** (500 mg, 1.25 mmol), $K_2CO_3$ (863 mg, 6.25 mmol), $CH_3CN$ (40 mL) and BnBr (744 μL, 6.25 mmol) were added sequentially to a 100 mL round-bottomed flask, a condenser was attached, and the mixture stirred at 70 °C for 16 h. The solution was filtered, the solvent removed under reduced pressure, and the crude mixture was submitted to flash chromatography ($SiO_2$, hexanes/EtOAc) to yield 355 mg (58%) of **26** as a clear oil. TLC $R_f$=0.44 (3:1 hexanes/EtOAc); $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 7.38–7.17 (m, 15H), 5.91 (dddd, $J$=16.9, 10.4, 6.5, 6.5 Hz, 1H), 5.77 (dddd, $J$=16.3, 10.4, 5.9, 5.9, 1H), 5.48 (s, 2H), 5.19, (dd, $J$=10.2, 1.0 Hz, 1H), 5.11 (dd, $J$=15.4, 1.1 Hz, 1H), 5.10 (dd, $J$=8.6, 1.2 Hz, 1H), 5.09 (dd, $J$=18.3, 1.2 Hz, 1H), 4.56 (s, 2H), 4.30 (s, 2H), 3.96 (d, $J$=5.9 Hz, 2H), 3.75 (d, $J$=6.5 Hz, 2H); $^{13}C$ ($CDCl_3$, 100 MHz) 157.1, 137.2, 136.3, 135.4, 133.8, 132.3, 129.1, 128.8, 128.7, 128.6, 128.5, 128.2, 127.7, 127.5, 127.3, 118.4, 118.0, 74.0, 51.5, 51.4, 51.0, 50.9; FTIR (neat) 3031, 2925, 1743, 1566, 1496, 1454, 1313, 1153, 739, 699 $cm^{-1}$; HRMS $(M+H)^+$ calcd for $C_{28}H_{32}N_3O_3S$ 490.2168, found 490.2158.

**4.1.31. 2,4,9-Tribenzyl-1,1-dioxo-1,2,4,5,8,9-hexahydro-1λ⁶-[1,2,4,9]thiatriazonin-3-one (27).** Sulfamoyl urea **26** (53 mg, 0.72 mmol), and $CH_2Cl_2$ (50 mL) were placed in a 100 mL round-bottomed flask and degassed with argon gas for 10 min. Cat-**B** (3 mg, 0.023 mmol) was added, the flask was quickly fitted with a condenser containing an argon balloon, and the solution was heated to reflux for 10 h during which another equivalent of cat-**B** was added. The solution was cooled to rt, DMSO (0.1 mL) added, and the solution stirred for 12 h. The solvent was removed and flash chromatography ($SiO_2$, hexanes/EtOAc) gave 41 mg (74%) of **27** as a white solid. Mp 92 °C; TLC $R_f$=0.24 (3:1 hexanes/EtOAc); $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 7.39–7.27 (m, 15H), 5.87 (dd, $J$=15.4, 7.6 Hz, 1H), 5.45 (dd, $J$=17.0,

8.4 Hz, 1H), 5.33 (s, 2H), 4.60 (s, 2H), 4.35 (s, 2H), 3.71 (s, 2H), 3.71 (s, 2H); $^{13}$C ($CDCl_3$, 100 MHz) $\delta$ 154.0, 136.6, 135.6, 135.2, 129.3, 128.8, 128.7, 128.6, 128.5, 128.5, 128.4, 128.1, 128.0, 127.9, 127.6, 71.1, 55.6, 50.7, 46.8, 40.6; FTIR (neat) 3030, 2956, 1741, 1680, 1508, 1455, 1365, 1163, 751, 699 $cm^{-1}$; HRMS $(M+H)^+$ calcd for $C_{26}H_{28}N_3O_3S$ 462.1851, found 462.1861.

**4.1.32. *N*-(2-Propenyl)-*N*-[[[*N′*-(2-propenyl)-*N′*-(1*S*)-1-methoxycarbonyl-3-methyl-butyl]carbonyl]amino]-sulfonyl]-(*S*)-leucine methyl ester (28a).** To a stirring solution of *N*-allyl (L)-leucine methyl ester (975 mg, 5.26 mmol) and $Et_3N$ (0.40 mL, 2.90 mmol) in $CH_2Cl_2$ at 0 °C under argon was added CSI (0.21 mL, 2.40 mmol) in $CH_2Cl_2$ (3 mL) slowly over 10 min. The solution was stirred for 12 h while slowly being raised to rt. The solvent was removed under reduced pressure and EtOAc (80 mL) added. The solution was washed with 10% $NaHSO_4$ (50 mL), $NaHCO_3$ (50 mL), brine (50 mL), dried with $MgSO_4$, and the solvent removed. Column chromatography ($SiO_2$, hexanes/EtOAc) afforded 890 mg (78%) of **28a** as a yellow oil. TLC $R_f$=0.20 (3:1 hexanes/EtOAc); $[\alpha]_D^{25}$ −131.6 (*c* 3.1, $CHCl_3$); FTIR (neat) 3347, 2958, 2870, 1732, 1682, 1642, 1549, 1455, 1368, 1168 $cm^{-1}$; HRMS $(M+H)^+$ calcd for $C_{21}H_{38}N_3O_7S$ 476.2430, found 476.2433.

**4.1.33. *N*-(2-Propenyl)-*N*-[[[*N′*-(2-propenyl)-*N′*-(1*S*)-1-methoxycarbonyl-2-methyl-propyl]carbonyl]amino]-sulfonyl]-(*S*)-valine methyl ester (28b).** In a procedure similar to the preparation of **28a**, 3-component coupling and flash chromatography ($SiO_2$, hexanes/EtOAc) yielded 921 mg (56%) of **28b** as a clear oil, which was taken on directly to the next step. TLC $R_f$=0.17 (3:1 hexanes/EtOAc); $[\alpha]_D^{25}$ −87.3 (*c* 1.05, $CHCl_3$); FTIR (neat) 3292, 3081, 2967, 1740, 1684, 1551, 1458, 1355, 1164 $cm^{-1}$; HRMS $(M+H)^+$ calcd for $C_{19}H_{34}N_3O_7S$ 448.2117, found 448.2118.

**4.1.34. *N*-(2-Propenyl)-*N*-[[[*N′*-(2-propenyl)-*N′*-(1*S*)-1-methoxycarbonyl-2-phenyl-ethyl]carbonyl]amino]-sulfonyl]-(*S*)-phenylalanine methyl ester (28c).** In a procedure similar to the preparation of sulfamoyl urea **28a** coupling and flash chromatography ($SiO_2$, hexanes/EtOAc) yielded 1.01 g (90%) of **28c** as a clear oil, which was taken on directly to the next step. TLC $R_f$=0.28 (3:1 hexanes/EtOAc); $[\alpha]_D^{25}$ −30.8 (*c* 1.1, $CHCl_3$); FTIR (neat) 3306, 3032, 2964, 1738, 1556, 1455, 1327, 1155, 745, 699 $cm^{-1}$; HRMS $(M+H)^+$ calcd for $C_{27}H_{34}N_3O_7S$ 544.2117, found 544.2118.

**4.1.35. *N*-(2-Propenyl)-*N*-[[[*N′*-(2-propenyl)-*N′*-(1*S*)-1-methoxycarbonyl-3-methyl-butyl]carbonyl]-*N″*-(benzyl)-amino]sulfonyl]-(*S*)-leucine methyl ester (30a).** In a procedure similar to the preparation of **26**, benzylation and flash chromatography ($SiO_2$, hexanes/EtOAc) gave 140 mg (43%) of **30a** as a white solid. TLC $R_f$=0.46 (3:1 hexanes/EtOAc). Mp 46–47 °C; $[\alpha]_D^{25}$ −47.3 (*c* 0.85, $CHCl_3$); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.39–7.29 (m, 5H), 6.02 (dddd, *J*=17.0, 10.2, 6.6, 6.6 Hz, 1H), 5.41 (dddd, *J*=16.9, 10.1, 6.7, 6.7 Hz, 1H), 5.22 (dd, *J*=17.2, 1.0 Hz, 1H), 5.14 (d, *J*=10.2 Hz, 1H), 5.04 (dd, *J*=17.9, 1.2 Hz, 1H), 5.01 (d, *J*=10.6, Hz, 1H), 4.52–4.49 (m, 1H), 4.50 (s, 2H), 4.17–4.01 (m, 2H), 4.17–4.01 (m, 2H), 3.85 (dd, *J*=15.4, 7.2 Hz, 1H), 3.65 (s, 3H), 3.60 (s, 3H), 1.82–1.71 (m, 2H), 1.82–1.71 (m, 2H), 1.65–1.55 (m, 1H), 1.55–1.45 (m, 1H), 0.99 (d, *J*=5.5 Hz, 3H), 0.94 (d, *J*=6.0 Hz, 3H), 0.82 (d, *J*=6.5 Hz, 3H), 0.82 (d, *J*=6.5 Hz, 3H); $^{13}$C ($CDCl_3$,100 MHz) 172.1, 171.1, 155.4, 135.3, 135.3, 133.8, 129.8, 128.4, 128.1, 118.5, 117.6, 74.5, 59.1, 57.3, 52.0, 51.6, 51.5, 49.5, 39.5, 376, 24.6, 24.4, 22.8, 22.4, 21.9, 21.8; FTIR (neat) 3347, 3080, 2958, 2870, 1732, 1681, 1642, 1548, 1455, 1368, 1168 $cm^{-1}$; HRMS $(M+H)^+$ calcd for $C_{28}H_{44}N_3O_7S$ 566.2900, found 566.2875.

**4.1.36. *N*-(2-Propenyl)-*N*-[[[*N′*-(2-propenyl)-*N′*-(1*S*)-1-methoxycarbonyl-2-methyl-propyl]carbonyl]-*N″*-(benzyl)amino]-sulfonyl]-(*S*)-valine methyl ester (30b).** In a procedure similar to the preparation of **26**, benzylation and flash chromatography ($SiO_2$, hexanes/EtOAc) gave 117 mg (62%) of **30b** as a clear oil. TLC $R_f$=0.43 (3:1 hexanes/EtOAc); $[\alpha]_D^{25}$ −56.5 (*c* 0.6, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.34–7.25 (m, 5H), 6.06 (dddd, *J*=17.2, 10.1, 6.1, 6.1 Hz, 1H), 5.50–5.38 (m, 1H), 5.21 (dd, *J*=17.2, 1.1 Hz, 1H), 5.12 (dd, *J*=10.1, 1.0 Hz, 1H), 5.04 (d, *J*=17.2 Hz, 1H), 4.97 (d, *J*=10.1 Hz, 1H), 4.44 (s, 2H), 4.17 (d, *J*=10.3 Hz, 1H), 4.16–4.11 (m, 2H), 4.07 (dd, *J*=19.1, 5.8 Hz, 1H), 4.03–3.99 (m, 1H), 3.98–3.93 (m, 1H), 3.72 (s, 3H), 3.53 (s, 3H), 2.25–2.18 (m, 2H), 1.10 (d, *J*=6.6 Hz, 3H), 0.95 (d, *J*=6.6 Hz, 3H), 0.87 (d, *J*=6.5 Hz, 3H), 0.48 (bs, 3H); $^{13}$C ($CDCl_3$, 125 MHz) $\delta$ 171.4, 170.5, 156.0, 135.2, 133.8, 129.9, 128.6, 128.5, 128.2, 118.0, 117.8, 67.1, 65.3, 51.6, 51.3, 48.8, 28.9, 28.2, 20.3, 19.9, 19.6, 18.9, 17.9, 17.8; FTIR (neat) 3080, 2966, 2877, 1742, 1676, 1456, 1436, 1364, 1161, 749, 700 $cm^{-1}$; HRMS $(M+H)^+$ calcd for $C_{26}H_{40}N_3O_7S$ 538.2587, found 538.2571.

**4.1.37. *N*-(2-Propenyl)-*N*-[[[*N′*-(2-propenyl)-*N′*-(1*S*)-1-methoxy-carbonyl-2-phenyl-ethyl]carbonyl]-*N″*-(benzyl)-amino]-sulfonyl]-(*S*)-phenylalanine methyl ester (30c).** In a procedure similar to the preparation of sulfamoyl urea **26**, benzylation and flash chromatography ($SiO_2$, hexanes/EtOAc) afforded 505 mg (65%) of **30c** as a clear oil. TLC $R_f$=0.36 (3:1 hexanes/EtOAc); $[\alpha]_D^{25}$ −104.9 (*c* 3.0, $CHCl_3$); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.34–7.26 (m, 8H), 7.22–7.14 (m, 5H), 7.06–7.04 (m, 2H), 6.02 (dddd, *J*=16.8, 10.2, 6.5, 6.5 Hz, 1H), 5.39–5.33 (m, 1H), 5.28 (dd, *J*=17.2, 1.3 Hz, 1H), 5.22 (dd, *J*=10.2, 1.1 Hz, 1H), 4.97 (dd, *J*=10.1, 1.1 Hz, 1H), 4.94 (d, *J*=17.2 Hz, 1H), 4.78 (dd, *J*=7.9, 6.8 Hz, 1H), 4.29 (s, 2H), 4.14–4.02 (m, 2H), 4.14–4.02 (m, 2H), 3.70 (s, 3H), 3.52–3.44 (m, 1H), 3.50–3.40 (m, 1H), 3.46 (s, 3H), 3.43–3.37 (m, 1H), 3.18 (dd, *J*=13.9, 6.7 Hz, 1H), 2.89 (dd, *J*=14.2, 7.2 Hz, 1H); $^{13}$C ($CDCl_3$,100 MHz) 170.9, 170.1, 155.4, 138.2, 137.1, 135.3, 134.6, 133.4, 129.5, 129.5, 129.4, 128.6, 128.5, 128.4, 128.1, 127.0, 126.5, 119.2, 118.7, 62.2, 61.4, 52.1, 51.9, 51.4, 49.4, 49.4, 36.8, 35.2; FTIR (neat) 3064, 3030, 2951, 1744, 1675, 1605, 1586, 1496, 1455, 1367, 1160, 749, 700 $cm^{-1}$; HRMS $(M+H)^+$ calcd for $C_{34}H_{40}N_3O_7S$ 634.2587, found 634.2582.

**4.1.38. (2*S*)-2-[2-Benzyl-4-[(1*S*)-1-methoxycarbonyl-3-methyl-butyl]-1,1,3-trioxo-1,2,3,4,5,8-hexahydro-1λ$^6$-[1,2,4,9] thiatriazonin-9-yl]-4-methyl-pentanoic acid methyl ester (31a).** In a procedure similar to that used for the preparation of **27**, RCM and flash chromatography ($SiO_2$, hexanes/EtOAc) afforded 35 mg (74%) of **31a** as a

white solid. Mp 86–87 °C; TLC $R_f$=0.31 (3:1 hexanes/EtOAc); $[\alpha]_D^{25}$ −91.8 (*c* 0.65, $CHCl_3$); $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 7.41–7.37 (m, 2H), 7.40–7.26 (m, 3H), 5.78 (dd, *J*=18.7, 8.7 Hz, 1H), 5.51 (dd, *J*=18.8, 8.6, Hz, 1H), 4.90–4.86 (m, 1H), 4.80 (dd, *J*=8.4, 5.6 Hz, 1H), 4.55 (d, *J*=13.2 Hz, 1H), 4.47 (d, *J*=13.2 Hz, 1H), 4.09 (dd, *J*=15.0, 8.8 Hz, 1H), 3.95–3.78 (m, 2H), 3.95–3.78 (m, 1H), 3.77 (s, 3H), 3.62 (s, 3H), 1.86–1.77 (m, 2H), 1.76–1.61 (m, 2H), 1.57–1.48 (m, 2H), 1.02 (d, *J*=6.0 Hz, 3H), 1.02 (d, *J*=6.0 Hz, 3H), 0.84 (d, *J*=6.5 Hz, 3H), 0.84 (d, *J*=6.5 Hz, 3H); $^{13}C$ ($CDCl_3$,100 MHz) 172.3, 171.7, 154.7, 134.5, 130.7, 130.2, 128.2, 128.0, 127.8, 59.7, 58.3, 52.3, 51.9, 51.6, 42.0, 40.2, 39.7, 38.3, 24.9, 24.3, 23.1, 22.9, 21.7, 21.7; FTIR (neat) 3033, 2956, 1742, 1693, 1680, 1380, 1164, 752, 700 $cm^{-1}$; HRMS $(M+H)^+$ calcd for $C_{26}H_{40}N_3O_7S$ 53.2587, found 538.2573.

**4.1.39. (2*S*)-2-[2-Benzyl-4-[(1*S*)-1-methoxycarbonyl-2-methyl-propyl)-1,1,3-trioxo-1,2,3,4,5,8-hexahydro-1λ$^6$-[1,2,4,9] thiatriazonin-9-yl]-3-methyl-butyric acid methyl ester (31b).** In a procedure similar to that used for the preparation of **27**, RCM and flash chromatography ($SiO_2$, hexanes/EtOAc) afforded 75 mg (71%) of **31b** as a clear oil. TLC $R_f$=0.13 (3:1 hexanes/EtOAc); $[\alpha]_D^{25}$ −101.2 (*c* 0.75, $CHCl_3$); $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 7.38–7.29 (m, 5H), 5.95 (dd, *J*=18.6, 8.6 Hz, 1H), 5.62 (dd, *J*=18.0, 8.7 Hz, 1H), 5.45 (d, *J*=12.2 Hz, 1H), 5.37 (d, *J*=12.2 Hz, 1H), 4.48 (dd, *J*=13.8, 9.3 Hz, 1H), 4.29–4.12 (m, 2H), 4.29–4.12 (m, 2H), 4.01 (dd, *J*=15.3, 7.7 Hz, 1H), 3.71 (s, 3H), 3.68 (s, 3H), 2.23–2.13 (m, 1H), 2.15–2.05 (m, 1H), 1.07 (d, *J*=6.7 Hz, 3H),) 0.95 (d, *J*=6.5 Hz, 3H), 0.89 (d, *J*=6.7 Hz, 3H), 0.88 (d, *J*=6.7 Hz, 3H);); $^{13}C$ ($CDCl_3$,100 MHz) 172.5, 170.4, 156.1, 135.1, 131.8, 128.6, 128.6128.5, 126.2, 72.4, 67.1, 65.9, 51.9, 51.4, 42.9, 40.0, 29.3, 28.7, 19.8, 19.5, 19.4, 19.3; FTIR (neat) 3030, 2965, 1740, 1579, 1472, 1291, 1156, 753, 701 $cm^{-1}$; HRMS $(M+H)^+$ calcd for $C_{24}H_{36}N_3O_7S$ 510.2274, found 510.2273.

**4.1.40. (2*S*)-2-[2-Benzyl-4-[(1*S*)-1-methoxycarbonyl-2-phenyl-ethyl]-1,1,3-trioxo-1,2,3,4,5,8-hexahydro-1λ$^6$-[1,2,4,9] thiatriazonin-9-yl]-3-phenyl-propionic acid methyl ester (31c).** In a procedure similar to that used for the preparation of cyclic sulfamoyl urea **27**, RCM and flash chromatography ($SiO_2$, hexanes/EtOAc) afforded 84 mg (81%) of **31c** as a clear oil. TLC $R_f$=0.20 (3:1 hexanes/EtOAc); $[\alpha]_D^{25}$ −110.3 (*c* 0.82, $CHCl_3$); $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 7.34–7.24 (m, 8H), 7.23–7.16 (m, 5H), 7.06–7.02 (m, 2H), 5.69 (dd, *J*=18.3, 7.7 Hz, 1H), 5.24 (dd, *J*=19.0, 8.6 Hz, 1H), 4.96 (dd, *J*=7.8, 7.8 Hz, 1H), 4.57 (dd, *J*=7.6, 6.7 Hz, 1H), 4.47 (d, *J*=13.4 Hz, 1H), 4.23–4.19 (m, 1H), 4.10 (dd, *J*=15.6, 8.0 Hz, 1H), 4.03 (dd, *J*=14.7, 8.9 Hz, 1H), 3.91 (dd, *J*=15.6, 7.5 Hz, 1H), 3.73 (s, 3H), 3.64 (dd, *J*=14.7, 8.1 Hz, 1H), 3.60 (s, 3H), 3.40 (dd, *J*=14.4, 7.1 Hz, 1H), 3.29 (dd, *J*=14.3, 6.4 Hz, 1H), 3.07 (dd, *J*=14.3, 8.2 Hz, 1H), 2.91 (dd, *J*=14.3, 7.9 Hz, 1H); $^{13}C$ ($CDCl_3$,100 MHz) 171.1, 170.4, 159.3, 137.4, 136.1, 134.7, 130.5, 129.2, 129.2, 128.7, 128.4, 128.2, 128.2, 128.1, 127.9, 127.2, 126.6, 63.4, 62.2, 52.2, 52.2, 51.7, 44.3, 41.4, 36.9, 35.4; FTIR (neat) 3032, 2958, 1742, 1649, 1545, 1455, 1365, 1164, 750, 700 $cm^{-1}$; HRMS $(M+H)^+$ calcd for $C_{32}H_{36}N_3O_7S$ 606.2274, found 606.2281.

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