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# One-Pot Multistep Bohlmann−Rahtz Heteroannulation Reactions: Synthesis of Dimethyl Sulfomycinamate

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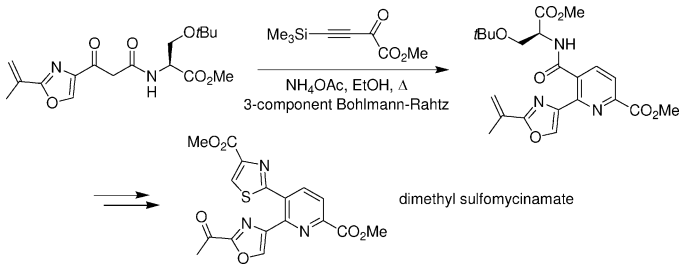


The synthesis of dimethyl sulfomycinamate, the acidic methanolysis product of the sulfomycin family of thiopeptide antibiotics, from methyl 2-oxo-4-(trimethylsilyl)but-3-ynoate is achieved in a 2,3,6-trisubstituted pyridine synthesis that proceeds with total regiocontrol in 13 steps by the Bohlmann−Rahtz heteroannulation of a 1-(oxazol-4-yl)enamine or in 12 steps and 9% yield by three-component cyclocondensation with *N*-[3-oxo-3-(oxazol-4-yl)propanoyl]serine and ammonia in ethanol.

## Introduction

The sulfomycins (**1a**−**c**) are a family of three cyclic peptides isolated from actinomycetes that are members of the thiopeptide or thiazolyl peptide group of antibiotics.[1] This ever-expanding collection of compounds classifies 29 different families of natural products isolated from the mycelial cake of Gram-positive sporulating bacteria and encompasses 76 structurally distinct sulfur-containing secondary metabolites, including a number of well-known antibiotics such as thiostrepton (**2**), nosiheptide (**3**), and the micrococcins (Bycroft−Gowland structure, **4a**,**b**).

Sulfomycin I (**1a**) was isolated from *Streptomyces viridochromogenes* subsp. *sulfomycini* ATCC 29776 and exhibits strong inhibitory activity against Gram-positive bacteria,[2] whereas all of the sulfomycins, I−III, have been isolated from *Streptomyces viridochromogenes* MCRL-0368.[3] An investigation of sulfomycin hydrolysates, combined with FAB mass spectrometric data and $^{1}H$ and $^{13}C$ NMR spectroscopic analyses, elucidated the structure of these natural products. In these studies, the acidic methanolysis of sulfomycin I (**1a**) provided vital evidence and generated a number of different fragments including dimethyl sulfomycinamate (**5**),[4] produced on heating at reflux in methanol for 20 h in the presence of Amberlyst 15 ion-exchange resin, the structure of which was confirmed by X-ray crystallographic data (Scheme 1). Sulfomycin I (**1a**) is structurally distinct from sulfomycin II (**1b**) and III (**1c**) only in the identity of one side chain located on a 2-(2-aminoalkenyl)oxazole residue in the peptide backbone.[5] All of the sulfomycins contain an oxazole−thiazole−pyridine central heterocyclic domain that is common with a number of other thiopeptide antibiotics,[1] including the A10255 factors,[6] berninamycins,[4,7] geninthiocin,[8] methylsulfomycin,[9] promoinducin,[10]

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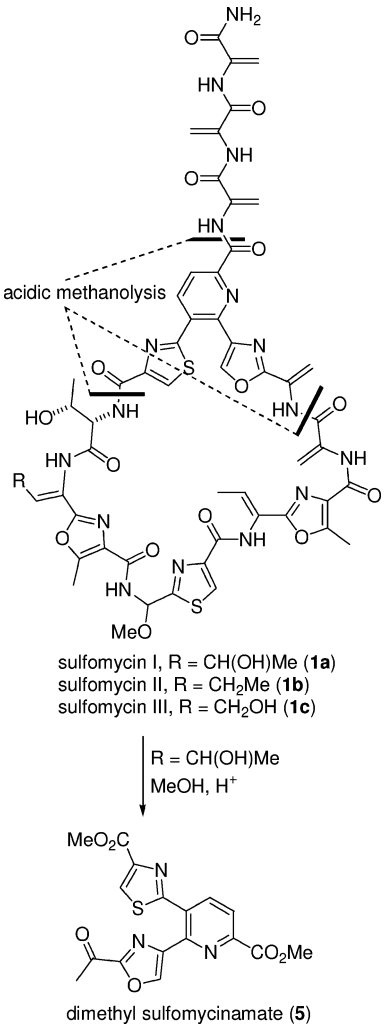
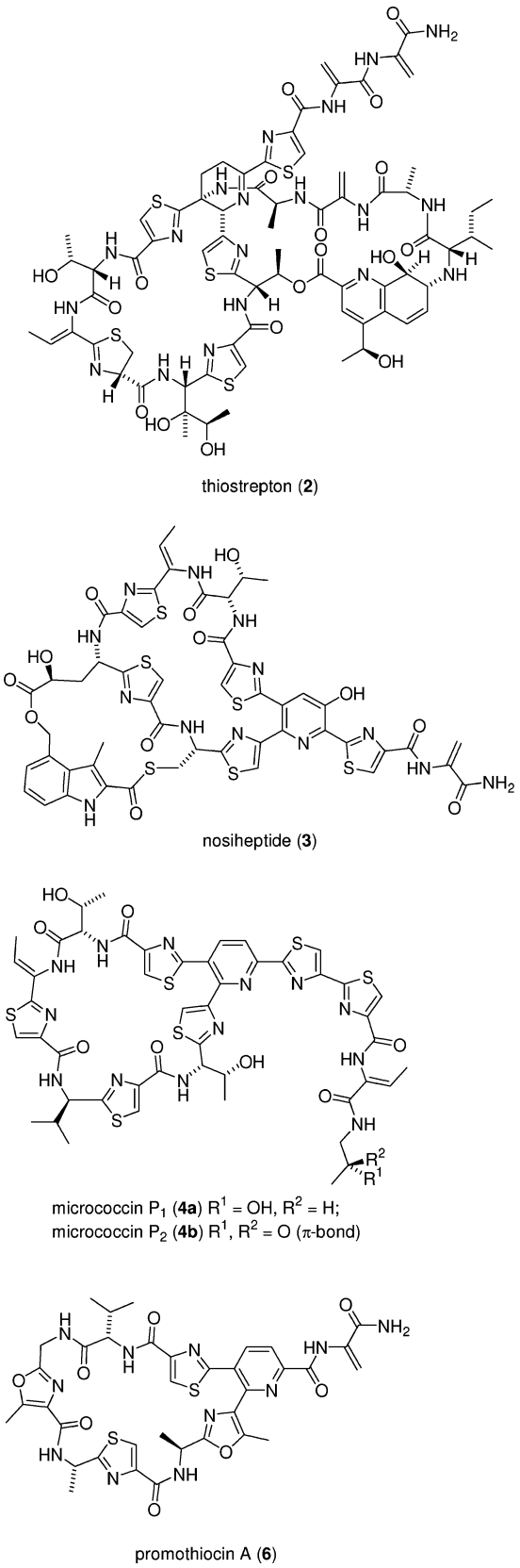
**SCHEME 1. Acidic Methanolysis of Sulfomycin I**




promothiocins (A, **6**),[11] radamycin,[12] thioactin,[13] thioxamycin,[14] and thiotipin.[15] The biological properties of the thiopeptide antibiotics have attracted considerable attention as inhibitors of bacterial protein synthesis with a novel mode of action. The parent of the family, thiostrepton, inhibits the binding of the aminoacyl-tRNA-containing ternary complex to the ribosomal A site[16] at the L11 binding domain on 23S rRNA,[17] and prevents peptide elongation by impeding a conformational change within protein L11 critical for stimulating the GTPase action of the elongation factors.[18] Autoimmunity in thiostrepton producers is achieved by the action of an RNA-pentose methylase enzyme[19] produced constitutively from its own promoter that introduces a single methyl group into the A1067 residue of the 23S rRNA in *Escherichia*

**CHART 1**

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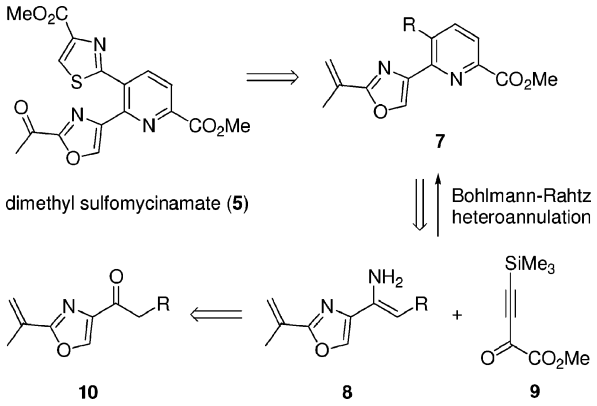
*coli* to give a modified 2′-*O*-methyladenosine-containing ribosome that is completely resistant to the antibiotic,[20] a phenomenon also observed in 23S rRNA mutants of *Halobacterium halobium*.[21] Many of these natural products have also been shown to activate transcription through binding to thiostrepton-induced proteins in bacteria in an autogenously controlled antibiotic resistance system.[22] Furthermore, the biosynthesis of these antibiotics has also emerged as an interesting area of study. The origin of many of the structural motifs in sulfomycin has been investigated by following the incorporation of isotopically labeled amino acids[23] and, based upon related studies on micrococcin $P_1$ (**4a**),[24] would appear to proceed by a template-directed nonribosomal enzymatic process[25] on nonribosomal peptide synthetase (NRPS) multimodular templates.

In view of the biological properties and considerable interest in the thiopeptide antibiotics, we set out to validate a synthetic route to the sulfomycin family that used an heteroannulation approach to establish the central oxazole−thiazole−pyridine domain and apply this in the synthesis of dimethyl sulfomycinamate (**5**). The synthesis of thiopeptide natural products has attracted much interest, with recent reports on the total synthesis of thiostrepton (**2**),[26] promothiocin A (**6**),[27] and amythiamicin D[28] and significant progress made toward a number of other targets, including the micrococcins (**4a**,**b**),[29] nosiheptide,[30,31] glycothiohexide α,[31] the A10255 factors,[32] cyclothiazomycin,[33] the berninamycins,[34] and the sulfomycins (**1a**−**c**).[35] Prior to our work in this area, the synthesis of the related thiopeptide hydrolysates berninamycinic acid[36] and micrococcinic acid,[37] the latter a derivative of micrococcin $P_1$ (**4a**), had been reported, contributing significantly to structure elucidation studies into their respective thiopeptide families. Furthermore, Kelly and Lang had described an elegant synthesis of dimethyl sulfomycinamate (**5**), using palladium-catalyzed coupling reactions to form the biaryl bonds and so establish the central tris-heterocyclic unit.[38] We now report a new approach to dimethyl sulfomycinamate (**5**) that complements this earlier work, avoids the use of palladium catalysts, and constructs the heterocyclic components from acyclic precursors.[39]

**SCHEME 2. Dimethyl Sulfomycinamate (5) Disconnective Scheme**




Our disconnective scheme for accessing dimethyl sulfomycinamate (**5**) hoped to establish oxazole−pyridine **7** by the Bohlmann−Rahtz heteroannulation[40] of methyl 2-oxo-4-(trimethylsilyl)but-3-ynoate (**9**) and a suitable enamine **8**, bearing a substituent (R) for later elaboration to the thiazole and prepared from oxazolyl ketone **10** by reaction with ammonia (Scheme 2). This two-step pyridine synthesis, for example, proceeds by Michael addition of a 2-aminopropenoate **12**, prepared from the corresponding β-ketoester **11**, and alkynone **13** at 50 °C to give an aminodienone intermediate **14** that is cyclodehydrated at high temperature to give tri- or tetrasubstituted pyridines **15** with total regiocontrol (Scheme 3). In recent years it has found a number of applications in the synthesis of unusual amino acids,[41] pyridine libraries,[42] and nonsteroidal antiinflammatory agents.[43] We have shown that this process is much more facile under acidic

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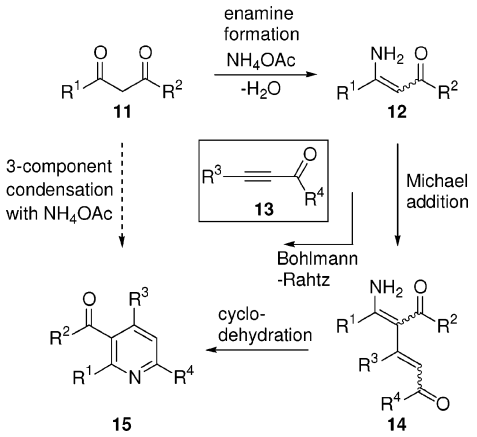
**SCHEME 3. Bohlmann−Rahtz and Related 3-Component Pyridine Synthesis**

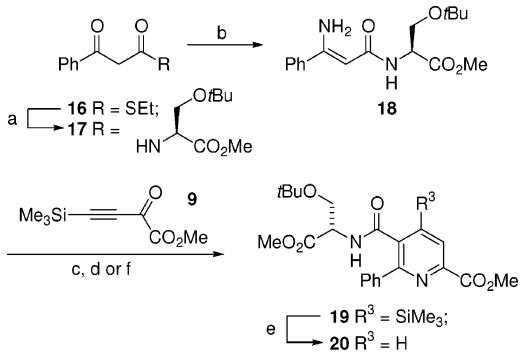



conditions,[44] either with a Brønsted[45] or Lewis acid catalyst,[46] is promoted by microwave irradiation,[47] and can be applied in solution-phase combinatorial chemistry[48] and for the synthesis of pyrido[2,3-*d*]pyrimidines[46,49] and heterocyclic natural products.[50] Yet as both the enamine formation[51] and two-step Bohlmann−Rahtz pyridine synthesis[44] are promoted under acidic conditions, it was proposed that the 3-component condensation of a 1,3-dicarbonylcompound **11**, alkynone **13**, and ammonia should provide a much more direct and efficient approach toward pyridines **15**. This new tandem process would be related to the Hantzsch dihydropyridine synthesis, but would not need subsequent oxidation and could generate the pyridine with total control of regiochemistry. This would constitute a rapid and facile method for the synthesis of pyridines of biological interest that was suitable for the preparation of oxazole−pyridine **7**, containing an acid-sensitive 2-(2-propenyl) group, for elaboration to the 2-acetyloxazole of dimethyl sulfomycinimate (**5**).

## Results and Discussion

We embarked upon our approach to dimethyl sulfomycinamate (**5**) using a model study to establish the substituent (R) required for Bohlmann−Rahtz synthesis of the thiazole−pyridine domain. Starting from *S*-ethyl benzoylthioacetate (**16**) (Scheme 4), copper(I) iodide-promoted thiolate displacement with *O*-*tert*-butyl-L-serine methyl ester according to a modified procedure of Olsen gave *N*-acyl serine **17** (91%),[52] which was heated at reflux with ammonium acetate in toluene−acetic acid to give the Bohlmann−Rahtz precursor **18** (58%). Reaction with methyl 2-oxo-4-(trimethylsilyl)but-3-ynoate (**9**), prepared by the addition of lithium (trimethylsilyl)acetylide to the Weinreb amide derivative of oxalic acid monomethyl ester,[44] under modified Bohlmann−Rahtz conditions with either a Brønsted or Lewis acid catalyst gave the pyridine **19** but in only 25% or 64% yield, respectively. Although the yield of these heteroannulation reactions was disappointing, subsequent protodesilylation with tetrabutylammonium fluoride (TBAF) in THF gave 2,3,6-trisubstituted pyridine **20** with a serine residue in place for elaboration of the 3-thiazolyl substituent. However, when traditional Bohlmann−Rahtz conditions were investigated, the Michael addition appeared facile even at room temperature giving, with spontaneous cyclodehydration, pyridine **20** directly in excellent yield (95%). From pyridine **20**, very efficient introduction of the pyridine 3-substituent was verified for the model system by thionation with Lawesson's reagent (LR) in benzene (96%) followed by cleavage of the *tert*-butyl ether of **21** in trifluoroacetic acid (TFA) at reflux (>98%). Under these conditions, spontaneous cyclization occurred and the generated thiazoline **22** could be readily oxidized, using manganese dioxide in chloroform at 120 °C under microwave irradiation (>98%), to give thiazole−pyridine **23** in excellent overall yield (Scheme 5).

**SCHEME 4. Bohlmann−Rahtz Synthesis of Pyridine 20**[a]




[a] Reagents and conditions: (a) H-L-Ser(*t*Bu)-OMe.HCl, $Et_3N$, CuI, $CH_2Cl_2$, rt, 18 h (91%); (b) $NH_4OAc$, PhMe−AcOH (5:1), reflux, 20 h (58%); (c) **9**, PhMe−AcOH (5:1), 50 °C, 6 h, gave **19** (25%); (d) **9**, $ZnBr_2$ (20 mol %), PhMe, reflux, 6 h, gave **19** (64%); (e) TBAF, THF, rt, 2 h (81%); (f) **9**, MeOH, rt, 60 h, gave **20** (95%).

With the route to the model system established, we sought to validate a faster route to pyridine **7** by the 3-component heteroannulation of potentially acid-sensitive oxazolyl ketone **10**, methyl oxobutynoate **9**, and ammonia, under mild conditions with in situ generation of enamine **8**. Given the surprising facility of the Bohlmann−Rahtz heteroannulation reaction for the synthesis of pyridine **20** in ethanol, without using elevated temperatures or an acid catalyst, we decided to investigate a similar procedure for the 3-component reaction. To this end, a range of 1,3-dicarbonyl compounds **11a**−**d** and alkynones **13a**−**f** were heated at reflux with ammonium

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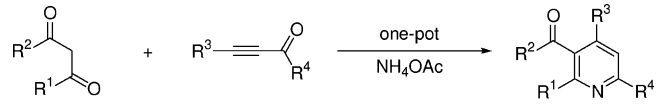
**TABLE 1. One-Pot 3-Component Synthesis of Pyridines 15[a]**

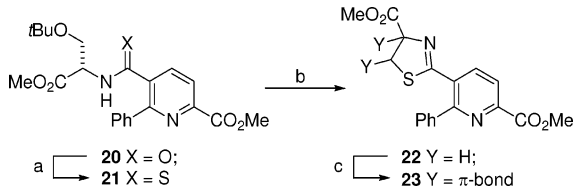



13 14 15

| entry | 11 | $R^1$ | $R^2$ | 13 | $R^3$ | $R^4$ | 15 | yield (%) methods A–C | yield (%) method D |
|---|---|---|---|---|---|---|---|---|---|
| 1 | **a** | Me | EtO | **a** | $Me_3Si$ | Me | **aa** | 55A,[b] 75B[c] | 90[c] |
| 2 | **a** | Me | EtO | **b** | Et | Me | **ab** | 96A, 82B[d] | 38 |
| 3 | **a** | Me | EtO | **c** | Ph | Me | **ac** | 80B | 51[e] |
| 4 | **a** | Me | EtO | **d** | H | Ph | **ad** | 84A,[f] 90B[f] | 95[g] |
| 5 | **a** | Me | OEt | **e** | H | 4′-$C_6H_4Cl$ | **ae** | 97B[f] | 84[g] |
| 6 | **a** | Me | OEt | **f** | H | 4′-$C_6H_4OMe$ | **af** | 98B[f] | 90[g] |
| 7 | **b** | Ph | OEt | **c** | Ph | Me | **bc** | 88A, 70B | <8[h] |
| 8 | **c** | Me | O*t*Bu | **a** | $Me_3Si$ | Me | **ca** | 0A | 98[c,e] |
| 9 | **c** | Me | O*t*Bu | **b** | Et | Me | **cb** | 49A, 55B | 71[e] |
| 10 | **c** | Me | O*t*Bu | **c** | Ph | Me | **cc** | 49A, 60C | 33 |
| 11 | **c** | Me | O*t*Bu | **d** | H | Ph | **cd** | 93C[f] | 89 |
| 12 | **d** | Me | $NH_2$ | **d** | H | Ph | **dd** | 82A[f] | 98[e] |

[a] Reagents and conditions: (A) **13** (2 equiv), $NH_4OAc$ (10 equiv), $ZnBr_2$ (20 mol %), toluene, reflux, 20 h; (B) **13** (2 equiv), $NH_4OAc$ (10 equiv), toluene-acetic acid (5:1), reflux, 20 h; (C) **13** (3 equiv), $NH_4OAc$ (10 equiv), Amberlyst 15, toluene, reflux, 20 h; (D) **13** (1.0 equiv), $NH_4OAc$ (10 equiv), ethanol, reflux, 24 h. Yield refers to isolated yield of pyridine **15** after purification on silica. [b] A mixture of 4-(trimethylsilyl)pyridine and protodesilylated product was obtained (56:44). [c] Only protodesilylated pyridine ($R^4$ = H) was produced. [d] An excess of **13** (3 equiv) was used. [e] Only 1 equiv of $NH_4OAc$ was used. [f] Only 1 equiv of **13** was used. [g] An excess of **14** (1.7 equiv) and $NH_4OAc$ (17 equiv) was used. [h] Not isolated yield, but based upon $^1H$ NMR analysis of the crude product.

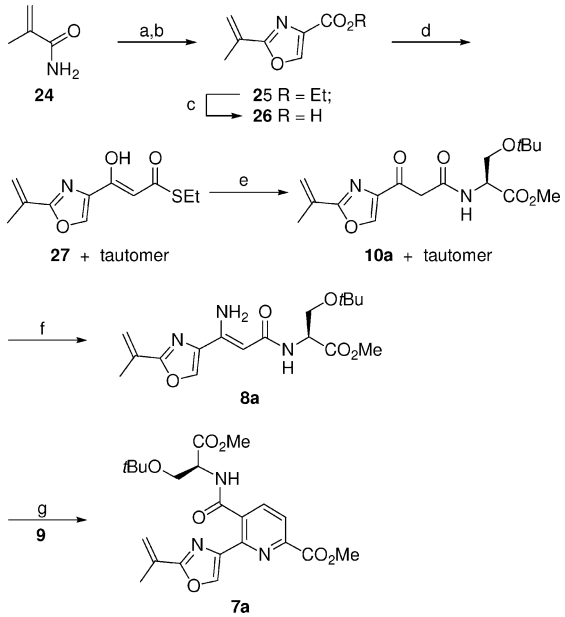
**SCHEME 5. Synthesis of Model Thiazole-Pyridine 23[a]**




[a] Reagents and conditions: (a) LR, benzene, reflux, 66 h (96%); (b) TFA, reflux, 48 h (>98%); (c) $MnO_2$, $CHCl_3$, microwave, 100 °C, 10 min (>98%).

acetate in ethanol and the results compared to a selection of acid-catalyzed 3-component processes, either in toluene in the presence of a Lewis acid catalyst (20 mol % $ZnBr_2$), with acetic acid as a Brønsted acid catalyst, or over Amberlyst 15 acidic ion-exchange resin (Table 1). For the most part, pyridine **15** was generated in higher yield when there was no acid catalyst, except for reactions with less reactive terminally substituted alkynones such as hex-3-yn-2-one **13b** and phenylbutynone **13c**, but was always isolated as a single regioisomeric product. Reactions with 4-(trimethylsilyl)but-3-yn-2-one **13a** in ethanol gave only the protodesilylated pyridines **15aa** and **15ca**. Unfortunately, reactions carried out with a mixture of ethyl benzoyl acetate **11b**, ammonium acetate, and 1-arylprop-2-ynones **13d–f** did not give the desired pyridines and instead produced the corresponding enamine, ethyl 3-amino-3-phenylpropenoate, and a number of side products with degradation of the alkynone. Similarly, the reaction of β-ketoester **11b** with phenylbutynone **13c** gave only a trace of the desired pyridine product **15ca** in the absence of added catalyst (entry 7). However, despite these limitations, the reaction was successful in a number of cases for a wide variety of substrates and thus constitutes a mild method for the regiospecific synthesis of polysubstituted pyridines **15** that would appear to proceed, based upon the isolation

**SCHEME 6. B-R Synthesis of Pyridine 7a[a]**

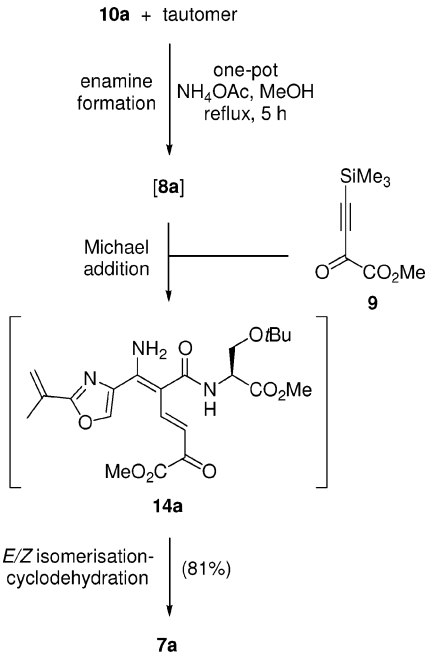



[a] Reagents and conditions: (a) ethyl bromopyruvate, $NaHCO_3$, THF (80%); (b) TFAA, 2,6-lutidine, THF (94%); (c) LiOH, MeOH, $H_2O$ (94%); (d) $EtO_2CCl$, $Et_3N$, THF; LDA, *S*-ethyl thioacetate, THF, −78 °C (75%); (e) HCl.H-L-Ser(*t*Bu)-OMe, $Et_3N$, CuI, $CH_2Cl_2$ (83%); (f) $NH_4OAc$, MeOH (80%); (g) MeOH, rt, 24 h (93%).

of intermediates **12** and **14** (Scheme 3) from reactions halted prior to completion, via enamine formation and subsequent Bohlmann–Rahtz heteroannulation all in one pot.

With all of the model studies established, synthesis of dimethyl sulfomycinamate according to our disconnective scheme (Scheme 2) started from 2-methacrylamide (**24**) (Scheme 6). Oxazole **25** was produced in excellent yield via a two-step modified Hantzsch reaction with ethyl bromopyruvate, in which the condensation was per-

**SCHEME 7. One-Pot Synthesis of Pyridine 7a**

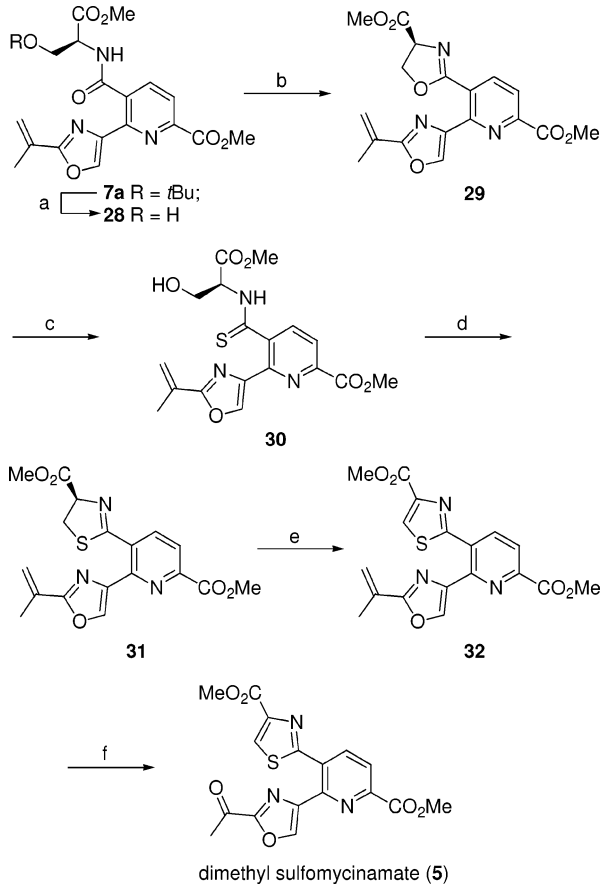



formed under basic conditions with subsequent hydroxythiazoline dehydration, using a mixture of trifluoroacetic anhydride (TFAA) and 2,6-lutidine. Saponification with lithium hydroxide in methanol−water gave carboxylic acid **26**, which was treated with ethyl chloroformate under basic conditions and homologated by reaction with the lithium enolate of *S*-ethyl thioacetate to give *S*-ethyl 3-hydroxypropenoate **27** in equilibrium with its keto tautomer. Reaction with *O-tert*-butyl-L-serine methyl ester hydrochloride in dichloromethane in the presence of copper(I) iodide and triethylamine generated amide **10a** as a mixture of tautomers that was heated at reflux overnight in methanol in the presence of ammonium acetate to give the Bohlmann−Rahtz precursor, enamine **8a**, in a single tautomeric form (80% yield).

The key heteroannulation reaction was first tried for comparison, using enamine **8a** in a standard Bohlmann−Rahtz reaction on the basis of the model study. Stirring a solution of enamine **8a** and methyl oxobutynoate **9** in methanol at room temperature facilitated Michael addition and spontaneous cyclodehydration even under ambient conditions to give pyridine **7a** in excellent yield (93%), as a single regioisomer. However, despite the failure of reactions of ethyl benzoyl acetate **11b** in the absence of an additional acid catalyst (Table 1, entry 7), the pyridine synthesis was improved overall by a one-pot 3-component process. Heating β-ketoamide **10a**, used as a tautomeric mixture, 2-oxobutynoate **9**, and ammonium acetate (10 equiv) at reflux in methanol for 5 h gave pyridine **7a** directly in 81% yield, presumably via enamine **8a** in a one-pot Bohlmann−Rahtz heteroannulation reaction (Scheme 7).

Elaboration of oxazole−pyridine **7a** to dimethyl sulfomycinamate (**5**) by introduction of the 3-thiazolyl substituent was first investigated in accordance with the model route. Thionation by treatment with Lawesson's reagent failed even under forcing conditions and so an alternative strategy (Scheme 8) was adopted according

**SCHEME 8. Synthesis of Dimethyl Sulfomycinamate (5)[a]**




[a] Reagents and conditions: (a) TFA−$CH_2Cl_2$ (1:1), 20 min (96%); (b) Burgess reagent, THF, 70 °C, 1 h (63%); (c) $H_2S$, MeOH, $Et_3N$ (71%); (d) Burgess reagent, THF, 70 °C, 30 min (87%); (e) $MnO_2$, microwave, 100 °C, $CH_2Cl_2$, 150 min (79%); (f) $OsO_4$, $NaIO_4$, MeCN, dioxane, $H_2O$, rt, 12 h (80%).

to good literature precedent.[53] Deprotection of the *tert*-butyl ether **7a** under acidic conditions gave alcohol **28** in excellent yield (96%). Subsequent cyclization to oxazoline **29**, using Burgess reagent, was followed by thionation with hydrogen sulfide in methanol under basic conditions, to give thioamide **30**. Thiazoline **31** formation by cyclization, once again using Burgess reagent, at 70 °C and oxidation by the microwave-assisted procedure, using activated manganese dioxide at 100 °C, in accordance with the model study, gave thiazole **32**. Finally, oxidation with osmium tetroxide/sodium periodate cleaved the isopropenyl unit to give dimethyl sulfomycinamate (**5**), mp 159−161 °C (lit.[4] mp 160.5−161.0 °C) whose spectroscopic and physical properties were in agreement with literature data.[4,38]

In conclusion, methods for the totally regioselective synthesis of 2,3,6-trisubstituted and 2,3,4,6-tetrasubstituted pyridines from β-ketoesters and amides have been developed with use of a one-pot 3-component Bohlmann−Rahtz heteroannulation reaction. This facile transformation proceeds in the presence of zinc(II) bromide, acetic acid, or an immobilized sulfonic acid resin and, in some

(53) Wipf, P.; Miller, C. P.; Venkatraman, S.; Fritch, P. C. *Tetrahedron Lett.* **1995**, *36*, 6395.

cases, is effective in alcoholic solvents at reflux in the absence of any added acid catalyst. Application of this mild procedure to the heteroannulation of an acid-sensitive precursor has established the synthesis of dimethyl sulfomycinamate (**5**), the acidic methanolysis degradation product of the sulfomycin thiopeptide antibiotics, in 12 steps and 9% overall yield to complement the cross-coupling methodology of Kelly and demonstrate an alternative method to access the tris-heterocyclic core of the parent actinomycete metabolites.

## Experimental Section

**Lithium Enolate of *S*-Ethyl Thioacetate.** To a stirred solution of DIPA (1.40 mL, 10.0 mmol) in dry THF (10 mL) was added *n*BuLi in hexanes (2.5 M; 4.00 mL, 10.0 mmol) at 0 °C. The mixture was stirred for 10 min and cooled to −65 to −70 °C. Freshly distilled *S*-ethyl thioacetate (0.53 mL, 5.0 mmol) was added and the solution was stirred for 30 min.

***S*-Ethyl Benzoylthioacetate (16) and *S*-Ethyl 3-Hydroxy-3-phenylthiopropenoate.** To a stirred solution of $PhCO_2H$ (0.61 g, 5.0 mmol) in dry THF (10 mL) was added $Et_3N$ (1.39 mL, 10.0 mmol) followed by $EtO_2CCl$ (0.96 mL, 10.0 mmol) at 0 °C. After the mixture was stirred for 30 min at 0 °C, the mixture was filtered and the filtrate added dropwise to a solution of the lithium enolate of *S*-ethyl thioacetate at −68 °C. The mixture was stirred for 20 min and saturated aqueous $NH_4Cl$ solution (50 mL) was added. The resulting mixture was warmed to room temperature and extracted with EtOAc (50 mL). The organic extract was washed with brine, dried ($Na_2SO_4$), and evaporated in vacuo. Purification by flash chromatography on $SiO_2$, eluting with light petroleum−$CHCl_3$ (2:1), gave a mixture of the title compounds[54] (0.73 g, 70%) as a pale yellow oil (found: $M^+$, 208.0557; $C_{11}H_{12}O_2S$ requires $M^+$, 200.0917); IR (film) $\nu_{max}$ 3062, 2970, 2931, 2874, 1698, 1672, 1611, 1574, 1451, 1381, 1266, 1096, 1054, 911, 757, 688; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 13.16 (0.47H, s, OH), 7.88 (1.06H, m), 7.70 (0.94H, m), 7.51 (0.53H, m), 7.39 (1.41H), 7.33 (1.06H, m), 6.00 (0.47H, s), 4.13 (1.06H, s), 2.91 (0.94H, q, $J$ = 7.4 Hz), 2.85 (1.06H, q, $J$ = 7.4 Hz), 1.25 (1.41H, t, $J$ = 7.4 Hz), 1.18 (1.59H, t, $J$ = 7.4 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 195.5 (C), 193.1 (C), 192.5 (C), 169.1 (C), 136.4 (C), 134.2 (CH), 133.3 (C), 132.1 (CH), 129.3 (CH), 129.2 (CH), 129.0 (CH), 126.8 (CH), 97.7 (CH), 54.4 ($CH_2$), 24.5 ($CH_2$), 23.4 ($CH_2$), 15.4 (Me), 14.9 (Me); MS (APcI) *m/z* (rel intensity) 209 ($MH^+$, 2%), 147 (9), 105 (100).

**General Procedure for CuI-Mediated Condensation of *β*-Keto Thioesters with H-Ser(*t*Bu)-OMe.** A solution of the *β*-keto thioester (2.0 mmol) in dry $CH_2Cl_2$ (5 mL) was added to a stirred solution of $Et_3N$ (0.56 mL, 4.0 mmol) and HCl.H-Ser(*t*Bu)-OMe (0.42 g, 2.0 mmol) in dry $CH_2Cl_2$ (15 mL). CuI (0.76 g, 4.0 mmol) was added and the mixture was stirred at room temperature overnight. $CH_2Cl_2$ (5 mL) and dilute hydrochloric acid (1 N; 5 mL) were added and the mixture was filtered. The organic filtrate was washed sequentially with dilute hydrochloric acid (1 N; 10 mL), saturated aqueous sodium hydrogen carbonate solution, and brine, dried ($Na_2SO_4$), and evaporated in vacuo to give the crude product.

**(*S*)-*β*-Ketoamide 17.** *S*-Ethyl benzoylthioacetate (**16**) (0.42 g, 2.0 mmol) was reacted according to the general procedure for CuI-mediated condensation with H-Ser(*t*Bu)-OMe. Purification by flash chromatography on $SiO_2$, eluting with $CH_2Cl_2$−ether (3:1), gave the title compound (0.58 g, 91%) as a colorless solid, mp 48−50 °C (methanol) (found: $MH^+$, 322.1652; $C_{17}H_{23}NO_5$ requires $MH^+$, 322.1649); $[\alpha]^{22}_D$ +28.3 (*c* 2.00, $CHCl_3$); IR (KBr) $\nu_{max}$ 2968, 1752, 1691, 1669, 1639, 1534, 1450, 1364, 1209, 1100, 1051, 1021, 774, 760, 691; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 13.89 (0.18H, s, OH), 7.94 (1.64H, m), 7.69 (0.36H, m), 7.59 (0.82H, d, $J$ = 7.8 Hz, NH), 7.54 (0.82H, m), 7.42 (1.64H, m), 7.35 (0.54H), 6.19 (0.18H, d, $J$ = 8.3 Hz, NH), 5.56 (0.18H, s), 4.75 (0.18H, m), 4.67 (0.82H, m), 3.97 (0.82H, d, $J$ = 16.4 Hz), 3.91 (0.82H, d, $J$ = 16.4 Hz), 3.80 (0.18H, dd, $J$ = 9.1, 2.8 Hz), 3.76 (0.82H, dd, $J$ = 9.1, 3.1 Hz), 3.70 (0.54H, s), 3.66 (2.46H, s), 3.56 (0.18H, dd, $J$ = 9.1, 3.1 Hz), 3.51 (0.82H, dd, $J$ = 9.1, 3.3 Hz), 1.08 (1.62H, s), 1.07 (7.38H, s); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 195.0 (C), 171.6 (C), 171.0 (C), 170.7 (C), 170.0 (C), 165.8 (C), 136.2 (C), 134.1 (C), 133.9 (CH), 130.8 (CH), 128.8 (CH), 128.6 (CH), 128.4 (CH), 125.8 (CH), 88.5 (CH), 73.6 (C), 73.5 (C), 62.1 ($CH_2$), 61.8 ($CH_2$), 53.1 (CH), 52.5 (Me), 52.4 (CH), 52.4 (Me), 45.6 ($CH_2$), 27.3 (Me), 27.3 (Me); MS (APcI) *m/z* (rel intensity) 322 ($MH^+$, 23%), 266 (100).

**(*S*)-Enamine 18.** $NH_4OAc$ (2.52 g, 32.7 mmol) was added to a solution of (*S*)-*β*-ketoamide **17** (1.05 g, 3.27 mmol) in PhMe-AcOH (5:1) (30 mL) under nitrogen and the reaction was heated at reflux overnight, using a Dean−Stark trap. After cooling to room temperature, the mixture was partitioned between EtOAc (50 mL) and saturated aqueous $NaHCO_3$ solution (50 mL) and the aqueous layer was further extracted twice with EtOAc. The combined organic extracts were washed sequentially with saturated aqueous $NaHCO_3$ solution and brine, dried ($Na_2SO_4$), and evaporated in vacuo. Purification by flash chromatography on $SiO_2$, eluting with light petroleum−EtOAc (2:1), gave the title compound (0.61 g, 58%) as a pale yellow oil (Found: $MH^+$, 321.1809; $C_{17}H_{24}N_2O_4$ requires $MH^+$, 321.1809); $[\alpha]^{23}_D$ +27.2 (*c* 1.39, $CHCl_3$); IR (KBr) $\nu_{max}$ 3433, 3307, 2972, 1747, 1627, 1554, 1499, 1364, 1343, 1196, 1090, 771, 700; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.47 (2H, m), 7.34 (3H), 6.52 (2H, br s), 5.90 (1H, d, $J$ = 8.1 Hz), 4.83 (1H, s), 4.74 (1H, m), 3.78 (1H, dd, $J$ = 8.9, 2.9 Hz), 3.68 (3H, s), 3.52 (1H, dd, $J$ = 8.9, 3.4 Hz), 1.07 (9H, s); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 171.8 (C), 169.8 (C), 158.3 (C), 138.3 (C), 129.9 (CH), 128.8 (CH), 126.1 (CH), 87.1 (CH), 73.4 (C), 62.4 ($CH_2$), 52.4 (CH), 52.3 ($CH_3$), 27.3(Me); MS (APcI) *m/z* (rel intensity) 321 ($MH^+$, 100%), 265 (14).

**Monomethyloxalic Acid *N*-Methoxy-*N*-methylamide.** $Et_3N$ (11.4 mL, 81.6 mmol) was added dropwise over a 10-min period to a stirred solution of MeONHMe·HCl (3.98 g, 40.8 mmol) and $MeO_2CCOCl$ (3.75 mL, 40.8 mmol) in dry $CH_2Cl_2$ (270 mL) at 0 °C. The mixture was stirred for 3.5 h, diluted with MeOH (5 mL), and evaporated in vacuo. THF (100 mL) was added and the solution was filtered under suction, washing with THF (2 × 100 mL), and evaporated in vacuo. Purification by distillation gave the title compound (6.47 g, 94%) as a colorless oil, bp 114−120 °C (2−3 Torr) (Found: $MNH_4^+$, 165.0870; $C_5H_9NO_4$ requires $MNH_4^+$, 165.0870); IR (film) $\nu_{max}$ 2945, 1748, 1680, 1394, 1257, 1175, 1092, 999, 962, 784; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 3.83 (3H, s), 3.70 (3H, s), 3.18 (3H, s); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 162.8 (C), 161.8 (C), 62.3 (Me), 52.6 (Me), 31.4 (Me); MS (APcI) *m/z* (rel intensity) 148 ($MH^+$, 57%), 147 (100), 120 (23), 88 (69).

**Methyl 2-Oxo-4-(trimethylsilyl)but-3-ynoate (9).** A solution of *n*BuLi in hexanes (2.5 M; 3.1 mL, 7.82 mmol) was added dropwise over 10 min to a stirred solution of TMSCCH (0.7 mL, 6.8 mmol) in dry THF (30 mL) at −78 °C. The solution was stirred for 30 min and added dropwise to a solution of monomethyloxalic acid *N*-methoxy-*N*-methylamide (1.0 g, 6.8 mmol) in dry THF (60 mL) at −78 °C. The mixture was stirred for 30 min, warmed to room temperature, and poured over ice (20 g). Aqueous orthophosphoric acid solution (20%; 30 mL) was added. The mixture was concentrated in vacuo and partitioned between $H_2O$ (20 mL) and ether (50 mL), further extracting the aqueous layer twice with ether. The combined organic extracts were washed sequentially with aqueous orthophosphoric acid solution (10%; 20 mL), saturated aqueous sodium hydrogen carbonate solution, and brine, dried ($Na_2SO_4$), and evaporated in vacuo. Purification by flash chromatography on $SiO_2$, eluting with light petroleum−ether (5:1), gave the title compound (0.61 g, 49%) as a yellow oil (Found: $M^+$, 184.0545; $C_8H_{12}O_3Si$ requires $M$, 184.0550); IR (film) $\nu_{max}$ 2960, 2150, 1746, 1685, 1438, 1254, 1103, 850, 763; $^1$H NMR

(54) Hayashi, Y.; Miyamoto, Y.; Shoji, M. *Tetrahedron Lett.* **2002**, *43*, 4079.

(400 MHz, $CDCl_3$) $\delta$ 3.71 (3H, s), 0.08 (9H, s); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 168.8 (C), 159.3 (C), 107.0 (C), 100.0 (C), 53.7 (Me), −1.0 (Me); MS (EI) *m/z* (rel intensity) 184 ($M^+$, 3%), 169 (20), 158 (100).

**(*S*)-Pyridine-3-carboxamide 20.** A solution of (*S*)-enamine **18** (26 mg, 0.08 mmol) and methyl 2-oxo-4-(trimethylsilyl)but-3-ynoate (**9**) (19 mg, 0.10 mmol) in MeOH (15 mL) was stirred at room temperature for 60 h and evaporated in vacuo. Purification by flash chromatography on $SiO_2$, eluting with light petroleum−EtOAc (1:1), gave the title compound (32 mg, 95%) as a pale yellow oil (Found: $MH^+$, 415.1863; $C_{22}H_{26}N_2O_6$ requires $MH^+$, 415.1864); $[\alpha]^{23}_D$ +48.3 (*c* 2.83, $CHCl_3$); IR (KBr) $\nu_{max}$ 3428, 3341, 2976, 1750, 1654, 1522, 1433, 1392, 1364, 1321, 1228, 1192, 1168, 1096, 972, 859, 740, 699; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.09 (2H, app s), 7.66 (2H, m), 7.37 (3H), 6.28 (1H, d, $J$ = 8.3 Hz), 4.66 (1H, m), 3.95 (3H, s), 3.64 (1H, dd, $J$ = 9.0, 2.9 Hz), 3.63 (3H, s), 3.18 (1H, dd, $J$ = 9.0, 3.2 Hz), 0.91 (9H, s); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 170.3 (C), 167.4 (C), 165.2 (C), 156.7 (C), 148.7 (C), 138.4 (CH), 138.2 (C), 133.6 (C), 129.5 (CH), 129.2 (CH), 128.7 (CH), 123.2 (CH), 73.4 (C), 61.3 ($CH_2$), 53.2 (CH), 53.1 (Me), 52.5 (Me), 27.1 (Me); MS (APcI) *m/z* (rel intensity) 415 ($MH^+$, 100%).

**General Procedure for One-Step Bohlmann−Rahtz Reactions Catalyzed by AcOH.** A solution of the enamine (∼1 mmol) and alkynone (1.2−2.4 equiv) in PhMe−AcOH (5:1) (5 mL) was stirred at 50 °C for 6 h. The mixture was partitioned between PhMe (30 mL) and saturated aqueous $NaHCO_3$ solution (30 mL). The aqueous layer was twice further extracted with PhMe and the combined organic extracts were washed sequentially with saturated aqueous $NaHCO_3$ solution and brine, dried ($Na_2SO_4$), and evaporated in vacuo to give the crude pyridine product.

**General Procedure for One-Step Bohlmann−Rahtz Reactions Catalyzed by $ZnBr_2$.** A solution of the enamine (∼1 mmol, 1 equiv), alkynone (1.2−2.4 equiv), and $ZnBr_2$ (15−20 mol %) in PhMe (6 mL) was heated at reflux for 6 h and then allowed to cool. After the addition of $H_2O$ (6 mL), the mixture was stirred for 20 min and extracted with EtOAc (2 × 10 mL). The combined organic extracts were washed with brine, dried ($Na_2SO_4$), and evaporated in vacuo to give the crude pyridine product.

**(*S*)-4-(Trimethylsilyl)pyridine 19.** (*S*)-Enamine **18** (65 mg, 0.20 mmol) and methyl 2-oxo-4-(trimethylsilyl)but-3-ynoate (**9**) (74 mg, 0.40 mmol) were reacted according to the general procedure for one-step Bohlmann−Rahtz reactions catalyzed by AcOH or $ZnBr_2$. Purification by flash chromatography on $SiO_2$, eluting with light petroleum−EtOAc (2:1), gave the title compound [24 mg, 25% for AcOH (reaction time 80 min); 62 mg, 64% for $ZnBr_2$ (reaction time 70 min)] as a pale yellow oil (Found: $MH^+$, 487.2257; $C_{25}H_{34}N_2O_6Si$ requires $MH^+$, 487.2259); $[\alpha]^{22}_D$ +51.0 (*c* 2.91, $CHCl_3$); IR ($CHCl_3$) $\nu_{max}$ 3431, 2960, 1742, 1664, 1508, 1439, 1365, 1261, 1213, 1096, 1020, 846, 807; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.20 (1H, s), 7.62 (2H, m), 7.32 (3H, m), 6.12 (1H, d, $J$ = 8.5 Hz), 4.62 (1H, m), 3.94 (3H, s), 3.55 (3H, s), 3.50 (1H, dd, $J$ = 8.9, 2.8 Hz), 2.90 (1H, dd, $J$ = 8.9, 3.2 Hz), 0.87 (9H, s), 0.33 (9H, s); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 170.2 (C), 168.7 (C), 165.9 (C), 155.6 (C), 151.9 (C), 146.8 (C), 139.2 (C), 139.1 (C), 129.1 (CH), 129.0 (CH), 128.6 (CH), 128.5 (CH), 73.2 (C), 61.6 ($CH_2$), 53.1 (CH), 53.0 (Me), 52.3 (Me), 27.1 (Me), −0.6 (Me); MS (APcI) *m/z* (rel intensity) 487 ($MH^+$, 100%), 431 (11).

**(*S*)-Pyridine 20 from Silyl Ether 19.** A solution of TBAF in THF (1 M; 0.06 mL, 0.06 mmol) was added to a solution of silyl ether **19** (26 mg, 0.05 mmol) in THF (10 mL) at 0 °C. The mixture was stirred at this temperature for 2 h, concentrated in vacuo, and partitioned between $H_2O$ (10 mL) and $CHCl_3$ (10 mL). The aqueous layer was twice further extracted with chloroform and the combined organic extracts were dried ($Na_2SO_4$) and evaporated in vacuo. Purification by flash chromatography on silica, eluting with light petroleum−EtOAc (1:1), gave the title compound (17 mg, 81%) as a pale yellow oil with identical physical and spectroscopic properties.

**(*S*)-Thioamide 21.** A solution of (*S*)-amide **20** (67 mg, 0.16 mmol) and Lawesson's reagent (52 mg, 0.13 mmol) in PhH (25 mL) was heated under reflux for 66 h. The mixture was allowed to cool, evaporated in vacuo, and purified by flash chromatography on $SiO_2$, eluting with light petroleum−EtOAc (4:3), to give the title compound (66 mg, 96%) as a pale yellow oil (Found: $MH^+$, 431.1637; $C_{22}H_{26}N_2O_5S$ requires $MH^+$, 431.1635); $[\alpha]^{28}_D$ +99.7 (*c* 1.52, $CHCl_3$); IR (KBr) $\nu_{max}$ 3294, 2973, 1744, 1512, 1432, 1392, 1364, 1321, 1223, 1153, 1095, 915, 848, 802, 743, 700; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.13 (1H, d, $J$ = 8.0 Hz), 8.04 (1H, d, $J$ = 8.0 Hz), 7.72 (1H, d, $J$ = 7.9 Hz), 7.71 (2H, m), 7.35 (3H), 5.12 (1H, m), 3.95 (3H, s), 3.64 (1H, dd, $J$ = 9.2, 2.5 Hz), 3.62 (3H, s), 3.14 (1H, dd, $J$ = 9.2, 3.1 Hz), 0.89 (9H, s); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 198.3 (C), 169.1 (C), 165.2 (C), 154.0 (C), 148.3 (C), 140.1 (C), 139.5 (CH), 138.1 (C), 129.3 (CH), 129.0 (CH), 128.6 (CH), 123.1 (CH), 73.7 (C), 60.5 ($CH_2$), 58.8 (CH), 53.1 (Me), 52.7 (Me), 27.1 (Me); MS (EI) *m/z* (rel intensity) 430 ($M^+$, 100%).

**Thiazoline 22.** A solution of (*S*)-thioamide **21** (61 mg, 0.14 mmol) in TFA (10 mL) was heated under reflux for 48 h. The solution was allowed to cool and evaporated in vacuo. Purification by flash chromatography on $SiO_2$, eluting with light petroleum−EtOAc (2:3), gave the title compound (50 mg, 99%) as a colorless solid, mp 121−122.5 °C (MeOH); (Found: $MH^+$, 357.0904; $C_{18}H_{16}N_2O_4S$ requires $MH^+$, 357.0904); $[\alpha]^{28}_D$ +3.8 (*c* 1.05, $CHCl_3$); IR (KBr) $\nu_{max}$ 2955, 1740, 1723, 1584, 1440, 1426, 1320, 1227, 1177, 1130, 1104, 1027, 804, 749, 701; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.07 (2H, app s), 7.57 (2 H, m), 7.35 (3H), 5.15 (1H, app t, $J$ = 9.1 Hz), 3.94 (3H, s), 3.73 (3H, s), 3.62 (1H, dd, $J$ = 11.2, 8.5 Hz), 3.52 (1H, dd, $J$ = 11.2, 9.6 Hz); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 171.2 (C), 170.4 (C), 165.2 (C), 158.1 (C), 148.8 (C), 138.8 (CH), 138.1 (C), 131.4 (C), 129.6 (CH), 129.4 (CH), 128.3 (CH), 123.0 (CH), 77.8 (CH), 53.2 (Me), 53.0 (Me), 36.9 ($CH_2$); MS (APcI) *m/z* (rel intensity) 357 ($MH^+$, 100%).

**Thiazole 23.** A mixture of thiazoline **22** (36 mg, 0.10 mmol) and activated $MnO_2$ (174 mg, 2.0 mmol) in $CH_2Cl_2$ (3 mL) was irradiated at 100 °C (initial power 300 W) for 10 min in a sealed pressure-rated reaction tube (10 mL), using a CEM Discover Microwave Synthesizer. The mixture was cooled rapidly to room temperature in a flow of compressed air for 5 min, filtered through Celite, washed with $CH_2Cl_2$ (2 × 10 mL), and evaporated in vacuo to give the title compound (35 mg, 100%) as a pale yellow solid, mp 173−175 °C (MeOH) (Found: $MH^+$, 355.0747; $C_{18}H_{14}N_2O_4S$ requires $MH^+$, 355.0747); IR (KBr) $\nu_{max}$ 2962, 1719, 1262, 1096, 1023, 801; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.53 (1H, d, $J$ = 8.1 Hz), 8.15 (1H, d, $J$ = 8.1 Hz), 8.06 (1H, s), 7.41−7.32 (5H), 3.95 (3H, s), 3.91 (3H, s); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 165.3 (C), 165.1 (C), 161.7 (C), 158.2 (C), 148.2 (C), 146.8 (C), 139.3 (CH), 138.1 (C), 130.9 (C), 130.2 (CH), 130.0 (CH), 129.6 (CH), 128.9 (CH), 123.7 (CH), 53.2 (Me), 52.6 (Me); MS (APcI) *m/z* (rel intensity) 355 ($MH^+$, 100%).

**General Procedure for Traditional Two-Step Bohlmann−Rahtz Reactions.** A solution of the enamine (∼1 mmol, 1 equiv) and alkynone (1.2−2.4 equiv) in EtOH (5 mL) was stirred at 50 °C for 5 h, cooled, and then evaporated in vacuo to give the dienone intermediate. The residue was heated at 140−160 °C in a flask fitted with a drying tube for 1−2 h and allowed to cool to give the crude pyridine product.

**General Procedure for One-Pot 3-Component Bohlmann−Rahtz Pyridine Synthesis with Acetic Acid.** $NH_4OAc$ (10 equiv) was added to a solution of the $\beta$-ketoester **11** (∼2.2 mmol, 1 equiv) and alkynone **13** (∼2 equiv) in PhMe−AcOH (5:1) (12 mL). The mixture was heated at reflux for 20 h and partitioned between saturated aqueous $NaHCO_3$ solution (20 mL) and EtOAc (20 mL). The aqueous layer was twice further extracted with EtOAc and the combined organic extracts were washed sequentially with saturated aqueous $NaHCO_3$ solution and brine, dried ($MgSO_4$), and evaporated in vacuo to give the crude pyridine **15**.

**General Procedure for One-Pot 3-Component Bohlmann−Rahtz Pyridine Synthesis with Zinc(II) Bromide.** $NH_4OAc$ (10 equiv) was added to a stirred solution of the $\beta$-ketoester **11** (∼2.2 mmol, 1 equiv) and alkynone **13** (∼2 equiv) in PhMe (12 mL) with zinc(II) bromide (20 mol %). The mixture was heated at reflux for 20 h then cooled and $H_2O$ (6 mL) was added. After heating at reflux for a further 20 min, the solution was allowed to cool and partitioned between $H_2O$ (20 mL) and EtOAc (20 mL). The aqueous layer was twice further extracted with EtOAc and the combined organic extracts were washed with brine, dried ($MgSO_4$), and evaporated in vacuo to give the crude pyridine **15**.

**General Procedure for One-Pot 3-Component Bohlmann−Rahtz Pyridine Synthesis with Amberlyst 15 Ion-Exchange Resin.** $NH_4OAc$ (10 equiv) was added to a stirred solution of the $\beta$-ketoester **11** (∼2.2 mmol, 1 equiv) and alkynone **13** (∼2 equiv) in PhMe (12 mL) in the presence of Amberlyst 15 ion-exchange resin (0.20 g). The mixture was heated at reflux for 20 h and partitioned between $H_2O$ (20 mL) and EtOAc (20 mL). The aqueous layer was twice further extracted with EtOAc and the combined organic extracts were washed with brine, dried ($MgSO_4$), and evaporated in vacuo to give the crude pyridine **15**.

**General Procedure for One-Pot 3-Component Bohlmann−Rahtz Pyridine Synthesis in Alcoholic Solvent.** A solution of the $\beta$-ketoester **11** (1 mmol), alkynone **13** (0.6−3.0 mmol), and $NH_4OAc$ (1−10 mmol) in EtOH (10 mL) was stirred at reflux for 24 h, allowed to coo, and evaporated in vacuo. The residue was partitioned between saturated aqueous $NaHCO_3$ solution (30 mL) and EtOAc (30 mL) and the aqueous layer was further extracted with EtOAc. The combined organic extracts were washed sequentially with saturated aqueous $NaHCO_3$ solution and brine, dried ($Na_2SO_4$), and evaporated in vacuo. Purification by column chromatography on $SiO_2$, eluting either with $CH_2Cl_2$−light petroleum (1:1) or EtOAc−light petroleum (1:3), gave pyridine **15**.

**Ethyl 4-Hydroxy-2-(2-propenyl)-2-oxazoline-4-carboxylate.** Ethyl bromopyruvate (0.9 mL, 7.17 mmol) was added to a stirred solution of methacrylamide (**24**) (0.5 g, 6.02 mmol) and dry $NaHCO_3$ (ground and dried in an oven at 115 °C for 2 d prior to use) (2.5 g, 29.76 mmol) in dry THF (60 mL). The mixture was heated at reflux for 18 h, filtered through Celite, and evaporated in vacuo. Purification by recrystallization (light petroleum−ether) gave the title compound as a colorless solid (0.96 g, 80%), mp 80−81 °C (EtOAc) (Found: C, 54.0; H, 6.4; N, 6.7. Calcd for $C_9H_{13}NO_4$: C, 54.3; H, 6.6; N, 7.0) (Found: $MH^+$, 200.0916; $C_9H_{13}NO_4$ requires *MH*, 200.0917); IR (Nujol) $\nu_{max}$ 1749, 1654, 1602, 1459, 1376, 1224, 1154, 1083, 1016, 954; $^1$H NMR (400 MHz; *d*$_4$-methanol) $\delta$ 5.89 (1H, m), 5.52 (1H, m), 4.59 (1H, d, $J$ = 10.0 Hz), 4.15 (2H, q, $J$ = 7.1 Hz), 4.12 (1H, d, $J$ = 10.0 Hz), 1.86 (3H, m), 1.21 (3H, t, $J$ = 7.1 Hz); $^{13}$C NMR (100 MHz; *d*$_4$-methanol) $\delta$ 170.6 (C), 168.6 (C), 132.2 (C), 123,8 ($CH_2$), 97.1 (C), 76.1 ($CH_2$), 62.0 ($CH_2$), 17.9 (Me), 13.0 (Me); MS (APcI) *m/z* 200 ($MH^+$, 100%), 182 (32).

**Oxazole 25.** A solution of 2,6-lutidine (8.12 mL, 77.12 mmol) and TFAA (4.73 mL, 33.49 mmol) in dry THF (10 mL) was added to a solution of ethyl 4-hydroxy-2-(2-propenyl)-2-oxazoline-4-carboxylate (5.55 g, 27.86 mmol) at 0 °C. After the solution was stirred for 30 min, $H_2O$ (50 mL) was added and the mixture was evaporated in vacuo. Purification by flash chromatography on $SiO_2$, gradient eluting with light petroleum to light petroleum−EtOAc (3:1), gave the title compound as a colorless oil (5.06 g, 94%) (Found: $MH^+$, 182.0810; $C_9H_{11}NO_3$ requires *MH*, 182.0817); IR (film) $\nu_{max}$ 3155, 2984, 1744, 1575, 1543, 1448, 1391, 1315, 1254, 1176, 115, 982, 916, 763; $^1$H NMR (400 MHz; $CDCl_3$) $\delta$ 8.12 (1H, s), 6.15 (1H, d, $J$ = 1.4 Hz), 5.39 (1H, dd, $J$ = 1.4, 0.9 Hz), 4.32 (2H, q, $J$ = 7.1 Hz), 2.12 (3H, s), 1.30 (3H, t, $J$ = 7.1 Hz); $^{13}$C NMR (100 MHz; $CDCl_3$) $\delta$ 163.1 (C), 161.3 (C), 143.5 (CH), 134.2 (C), 131.1 (C), 119.9 ($CH_2$), 61.2 ($CH_2$), 19.0 (Me), 14.3 (Me); MS (EI) *m/z* 181 ($M^+$, 100%).

**Carboxylic Acid 26.** LiOH monohydrate (6.49 g, 0.155 M) was added to a solution of ethyl ester **25** (4.76 g, 26.44 mmol) in MeOH−$H_2O$ (1:1) (100 mL). The mixture was stirred at room temperature for 2 h, concentrated in vacuo, and partitioned between $H_2O$ (100 mL) and $CHCl_3$ (50 mL). The aqueous layer was twice further extracted with $CHCl_3$, acidified to pH 2−3 with dilute hydrochloric acid (3 N), and thrice extracted with $CHCl_3$. The combined organic extracts were washed with brine, dried ($MgSO_4$), and evaporated in vacuo to give the title compound as a colorless solid (3.14 g, 78%), mp 121.5−122 °C (EtOAc) (Found: C, 54.6; H, 4.6; N, 8.9. Calcd for $C_9H_{13}NO_4$: C, 54.9; H, 4.6; N, 9.2) (Found: $MH^+$, 154.0498; $C_7H_7NO_3$ requires *MH*, 154.0499); IR (Nujol) $\nu_{max}$ 3136, 1691, 1562, 1462, 1377, 1260, 1186, 1124, 984, 910, 853, 766, 665; $^1$H NMR (400 MHz; $CDCl_3$) $\delta$ 10.26 (1H, br s), 8.23 (1H, s), 6.00 (1H, s), 5.44 (1H, s), 2.14 (3H, s); $^{13}$C NMR (100 MHz; $CDCl_3$) $\delta$ 166.1 (C), 163.5 (C), 145.0 (CH), 133.4 (C), 130.9 (C), 120.6 ($CH_2$), 19.0 (Me); MS (APcI) *m/z* 154 ($MH^+$, 100%), 136 (80).

***S*-Ethyl Thioester 27.** $EtO_2CCl$ (0.54 mL, 5.7 mmol) was added dropwise to a stirred solution of carboxylic acid **26** (800 mg, 5.22 mmol) and $Et_3N$ (0.80 mL, 5.7 mmol) in dry THF (11 mL) at 0 °C. After being stirred for 30 min, the mixture was filtered and cooled to −78 °C and a solution of the lithium enolate of *S*-ethyl thioacetate (0.83 mL, 7.8 mmol) in THF (16 mL) was added dropwise. The mixture was stirred at −78 °C for 30 min and partitioned between saturated aqueous $NH_4Cl$ solution (60 mL) and EtOAc (60 mL). The organic extract was washed with brine, dried ($Na_2SO_4$), and evaporated in vacuo. Purification by flash chromatography on $SiO_2$, eluting with $CH_2Cl_2$, gave a mixture of the title compound*s* (0.94 g, 75%) as a pale yellow oil (Found: $MH^+$, 240.0688; $C_{11}H_{13}NO_3S$ requires $MH^+$, 240.0689); IR (KBr) $\nu_{max}$ 2966, 2925, 1704, 1648, 1589, 1538, 1452, 1408, 1330, 1246, 1120, 1080, 775, 722; $^1$H NMR (400 MHz; $CDCl_3$) $\delta$ 12.54 (0.65H, s, OH), 8.15 (0.35H, s), 7.93 (0.65H, s), 6.20 (0.65H, s), 5.94 (0.35H, s), 5.91 (0.65H, s), 5.40 (0.35H, s), 5.37 (0.65H, s), 4.10 (0.70H, s), 2.90 (1.30H, q, $J$ = 7.4 Hz), 2.86 (0.70H, q, $J$ = 7.4 Hz), 2.09 (3H, s), 1.24 (1.95H, t, $J$ = 7.4 Hz), 1.19 (1.05H, t, $J$ = 7.4 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 195.5 (C), 192.0 (C), 186.9 (C), 163.0 (C), 162.8 (C), 161.0 (C), 142.8 (CH), 140.7 (C), 139.7 (CH), 136.6 (C), 131.2 (C), 131.0 (C), 120.1 ($CH_2$), 119.6 ($CH_2$), 98.3 (CH), 54.5 ($CH_2$), 24.0 ($CH_2$), 22.9 ($CH_2$), 18.91 (Me), 18.88 (Me), 14.8 (Me), 14.5 (Me); MS (APcI) *m/z* 240 ($MH^+$, 100%), 210 (44).

**(*S*)-Serine Methyl Ester 10a.** A solution of *S*-ethyl thioester **27** (274 mg, 1.14 mmol) in dry $CH_2Cl_2$ (5 mL) was added to a stirred solution of $Et_3N$ (0.32 mL, 2.29 mmol) and HCl·H-L-Ser(*t*Bu)-OMe (242 mg, 1.14 mmol) in dry $CH_2Cl_2$ (15 mL). CuI (485 mg, 2.29 mmol) was added and the mixture was stirred at room temperature overnight. After being partitioned between $CH_2Cl_2$ (5 mL) and dilute hydrochloric acid (1 N; 5 mL), the mixture was filtered. The organic extract was washed sequentially with dilute hydrochloric acid (1 N), saturated aqueous $NaHCO_3$ solution, and brine, dried ($Na_2SO_4$), and evaporated in vacuo. Purification by flash column chromatography on $SiO_2$, eluting with light petroleum−EtOAc (4:1), gave a mixture of the title compound*s* (0.33 g, 83%) as a pale yellow oil (Found: $MH^+$, 353.1701; $C_{17}H_{24}N_2O_6$ requires $MH^+$, 353.1707); $[\alpha]^{24}_D$ +41.7 (*c* 1.1, $CHCl_3$); IR (KBr) $\nu_{max}$ 3366, 2971, 1750, 1694, 1661, 1609, 1549, 1438, 1364, 1248, 1204, 1093, 1054, 1020, 915, 812, 780, 737; $^1$H NMR (400 MHz; $CDCl_3$) $\delta$ 13.36 (0.36H, s, OH), 8.24 (0.64H, s), 7.87 (0.36H, s), 7.72 (0.64H, d, $J$ = 8.2 Hz), 6.42 (0.36H, d, $J$ = 8.5 Hz), 5.95 (0.64H, s), 5.90 (0.36H, s), 5.79 (0.36H, s), 5.42 (0.64H, s), 5.35 (0.36H, s), 4.71 (0.36H, m), 4.66 (0.64H, m), 3.93 (0.64H, d, $J$ = 15.6 Hz), 3.89 (0.64H, d, $J$ = 15.6 Hz), 3.78 (0.36H, dd, $J$ = 8.9, 2.9 Hz), 3.74 (0.64H, dd, $J$ = 9.1, 3.0 Hz), 3.68 (1.08H, s), 3.65 (1.92H, s), 3.54 (0.36H, dd, $J$ = 8.9, 3.2 Hz), 3.49 (0.64H, dd, $J$ = 9.1, 3.2 Hz), 2.11 (1.92H, s), 2.08 (1.08H, s), 1.06 (1.08H, s), 1.04 (1.92H, s); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 188.8 (C), 171.3 (C), 170.8 (C), 170.6 (C), 165.2 (C), 162.8 (C), 162.7 (C), 162.2 (C), 143.2 (CH), 140.7 (C), 138.1 (CH), 137.4 (C), 131.2 (C), 130.9 (C), 120.2 ($CH_2$), 119.2 ($CH_2$), 89.9 (CH), 73.4 (C),

73.3 (C), 61.9 ($CH_2$), 61.8 ($CH_2$), 53.1 (CH), 52.4 (Me), 52.3 (Me), 52.3 (CH), 47.0 ($CH_2$), 27.2 (Me), 27.2 (Me), 18.9 (Me), 18.8 (Me); MS (APcI) *m/z* 353 ($MH^+$, 44%), 297 (100), 279 (12), 120 (37).

**(*S*)-Enamine 8a.** $NH_4OAc$ (293 mg, 3.8 mmol) was added to a stirred solution of **10a** (269 mg, 0.76 mmol) in dry MeOH (15 mL) under $N_2$. After being heated at reflux overnight, the reaction mixture was cooled to room temperature and evaporated in vacuo. The residue was partitioned between EtOAc (30 mL) and $H_2O$ (30 mL) and the aqueous layer further extracted with EtOAc. The combined organic extracts were washed sequentially with saturated aqueous $NaHCO_3$ solution and brine, dried ($Na_2SO_4$), and evaporated in vacuo. Purification by flash chromatography on $SiO_2$, eluting with light petroleum−EtOAc (1:1), gave the title compound (214 mg, 80%) as a pale yellow oil (Found: $MH^+$, 352.1871; $C_{17}H_{25}N_3O_5$ requires *MH*$^+$, 352.1867); $[\alpha]^{24}_D$ +51.2 (*c* 1.0, $CHCl_3$); IR (KBr) $\nu_{max}$ 3452, 3324, 2974, 1748, 1644, 1598, 1540, 1363, 1198, 1098, 1050, 1021, 976, 913, 778; $^1H$ NMR (400 MHz; $CDCl_3$) $\delta$ 7.79 (1H, s), 6.82 (2H, br s), 5.90 (1H, s), 5.89 (1H, d, $J$ = 8.5 Hz), 5.36 (1H, s), 5.00 (1H, s), 4.72 (1H, m), 3.78 (1H, dd, $J$ = 8.9, 2.9 Hz), 3.68 (3H, s), 3.51 (1H, dd, $J$ = 8.9, 3.2 Hz), 2.10 (3H, s), 1.08 (9H, s); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 171.8 (C), 169.8 (C), 162.6 (C), 147.8 (C), 138.6 (C), 135.5 (CH), 131.3 (C), 119.1 ($CH_2$), 84.2 (CH), 73.4 (C), 62.4 ($CH_2$), 52.34 (CH), 52.30 (Me), 27.3 (Me), 19.0 (Me); MS (APcI) *m/z* 353 (100%), 352 ($MH^+$, 67).

**(*S*)-Pyridine 7a from Enamine 8a.** A solution of (*S*)-enamine **8a** (88 mg, 0.25 mmol) and methyl 2-oxo-4-(trimethylsilyl)but-3-ynoate (**9**) (61 mg, 0.33 mmol) in MeOH (10 mL) was stirred at room temperature for 24 h and evaporated in vacuo. Purification by flash chromatography on $SiO_2$, eluting with light petroleum−EtOAc (1:2), gave the title compound (104 mg, 93%) as a pale yellow oil (Found: $MH^+$, 446.1925; $C_{22}H_{27}N_3O_7$ requires *MH*$^+$, 446.1927); $[\alpha]^{29}_D$ +12.0 (*c* 1.8, $CHCl_3$); IR (KBr) $\nu_{max}$ 2966, 1751, 1670, 1540, 1436, 1364, 1323, 1262, 1099, 801, 760; $^1H$ NMR (400 MHz; $CDCl_3$) $\delta$ 8.18 (1H, s), 8.05 (1H, d, $J$ = 8.0 Hz), 8.01 (1H, d, $J$ = 8.0 Hz), 7.00 (1H, d, $J$ = 8.0 Hz), 5.93 (1H, s), 5.35 (1H, s), 4.85 (1H, m), 3.95 (3H, s), 3.80 (1H, dd, $J$ = 9.1, 3.0 Hz), 3.69 (3H, s), 3.57 (1H, dd, $J$ = 9.1, 3.2 Hz), 2.10 (3H, s), 1.01 (9H, s); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 170.5 (C), 167.0 (C), 165.0 (C), 162.6 (C), 148.5 (C), 147.5 (C), 139.5 (C), 139.0 (CH), 138.1 (CH), 133.3 (C), 131.4 (C), 123.6 (CH), 119.0 ($CH_2$), 73.6 (C), 61.8 ($CH_2$), 53.5 (CH), 53.1 (Me), 52.5 (Me), 27.2 (Me), 19.0 (Me); MS (APcI) *m/z* 446 ($MH^+$, 100%).

**(*S*)-Pyridine 7a from *β*-Ketoester 10a.** A solution of (*S*)-*β*-ketoester **10a** (35 mg, 0.1 mmol), methyl 2-oxo-4-(trimethylsilyl)but-3-ynoate (**9**) (49 mg, 0.25 mmol), and $NH_4OAc$ (77 mg, 1.0 mmol) in MeOH (10 mL) was stirred at reflux for 5 h. After cooling, the mixture was evaporated in vacuo. The residue was partitioned between saturated aqueous $NaHCO_3$ solution (5 mL) and EtOAc (8 mL) and the aqueous layer was further extracted with EtOAc. The combined organic extracts were washed sequentially with saturated aqueous $NaHCO_3$ solution and brine, dried ($Na_2SO_4$), and evaporated in vacuo. Purification by column chromatography on $SiO_2$, eluting with EtOAc−light petroleum (2:1), gave the title compound (36 mg, 81%) as a pale yellow oil with identical physical and spectroscopic properties.

**(*S*)-Alcohol 28.** A solution of pyridine **7a** (60 mg, 0.14 mmol) in TFA−$CH_2Cl_2$ (1:1) (20 mL) was stirred at room temperature for 20 min and evaporated in vacuo. Purification by flash column chromatography on $SiO_2$, eluting with EtOAc, gave the title compound (50 mg, 96%) as colorless crystals, mp 74−76 °C (aqueous EtOH) (Found: $MH^+$, 390.1301; $C_{18}H_{19}N_3O_7$ requires *MH*$^+$, 390.1296); $[\alpha]^{25}_D$ −8.8 (*c* 0.5, $CHCl_3$); IR (KBr) $\nu_{max}$ 3439, 2954, 1734, 1654, 1542, 1438, 1323, 1293, 1234, 1174, 1140, 760; $^1H$ NMR (400 MHz; $CDCl_3$) $\delta$ 8.22 (1H, s), 7.89 (1H, d, $J$ = 7.9 Hz), 7.84 (1H, d, $J$ = 7.9 Hz), 7.50 (1H, d, $J$ = 7.1 Hz), 5.89 (1H, s), 5.35 (1H, s), 4.70 (1H, m), 4.32 (1H, br s), 4.01 (1H, dd, $J$ = 8.2, 3.1 Hz), 3.94 (1H, dd, $J$ = 8.2, 3.7 Hz), 3.91 (3H, s), 3.68 (3H, s), 2.05 (3H, s); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 170.5 (C), 167.6 (C), 164.9 (C), 162.8 (C), 148.0 (C), 147.2 (C), 142.2 (C), 139.7 (CH), 137.8 (CH), 132.8 (C), 131.0 (C), 123.5 (CH), 119.9 ($CH_2$), 62.2 ($CH_2$), 55.6 (CH), 53.2 (Me), 52.8 (Me), 18.9 (Me); MS (APcI) *m/z* 390 ($MH^+$, 100%).

**(*S*)-Oxazoline 29.** A solution of (*S*)-alcohol **28** (41 mg, 0.10 mmol) and Burgess reagent (28 mg, 0.11 mmol) in dry THF (5 mL) was stirred at 70 °C for 1 h and evaporated in vacuo. Purification by flash chromatography on $SiO_2$, eluting with EtOAc−light petroleum (2:1), gave the title compound (24 mg, 63%) as a pale yellow oil (Found: $MH^+$, 372.1191; $C_{18}H_{17}N_3O_6$ requires *MH*$^+$, 372.1191); $[\alpha]^{29}_D$ +29.1 (*c* 0.87, $CHCl_3$); IR (KBr) $\nu_{max}$ 2956, 1741, 1654, 1437, 1325, 1286, 1228, 1139, 1052, 958, 762; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.25 (1H, s), 8.06 (1H, d, $J$ = 8.0 Hz), 8.01 (1H, d, $J$ = 8.0 Hz), 5.93 (1H, s), 5.36 (1H, s), 4.94 (1 H, dd, $J$ = 10.7, 8.6 Hz), 4.64 (1H, app t, $J$ = 8.6 Hz), 4.57 (1H, dd, $J$ = 10.7, 8.6 Hz), 3.95 (3H, s), 3.77 (3H, s), 2.11 (3H, s); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 171.2 (C), 165.9 (C), 164.9 (C), 162.3 (C), 149.6 (C), 149.0 (C), 140.2 (C), 139.8 (CH), 139.1 (CH), 131.3 (C), 124.9 (C), 123.1 (CH), 118.8 ($CH_2$), 70.3 ($CH_2$), 68.8 (CH), 53.1 (Me), 52.8 (Me), 19.0 (Me); MS (APcI) *m/z* (rel intensity) 372 ($MH^+$, 100%).

**(*S*)-Thioamide 30.** A solution of oxazoline **29** (23 mg, 0.06 mmol) in MeOH−$Et_3N$ (2:1) (3 mL) was saturated with $H_2S$, stirred at room temperature for 3.5 h, and evaporated in vacuo. Purification by flash chromatography on $SiO_2$, eluting with ether−acetone (5:1), gave the title compound (17 mg, 71%) as a pale yellow oil (Found: $MH^+$, 406.1062; $C_{18}H_{19}N_3O_6S$ requires *MH*$^+$, 406.1067); $[\alpha]^{20}_D$ −29.6 (*c* 0.90, $CHCl_3$); IR (KBr) $\nu_{max}$ 3400, 2956, 1736, 1542, 1437, 1388, 1293, 1262, 1232, 1140, 1087, 1027, 802, 761; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 9.18 (1H, d, $J$ = 6.1 Hz), 8.31 (1H, s), 7.91 (1H, d, $J$ = 8.0 Hz), 7.81 (1H, d, $J$ = 8.0 Hz), 5.89 (1H, s), 5.37 (1H, s), 5.18 (1H, m), 4.34 (1H, dd, $J$ = 11.9, 3.2 Hz), 4.05 (1H, dd, $J$ = 11.9, 2.9 Hz), 3.93 (3H, s), 3.83 (1H, br s), 3.77 (3H, s), 2.04 (3H, s); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 197.9 (C), 169.6 (C), 164.9 (C), 162.7 (C), 146.7 (C), 144.8 (C), 140.2 (CH), 139.7 (C), 138.5 (C), 137.7 (CH), 130.8 (C), 123.3 (CH), 120.1 ($CH_2$), 61.2 ($CH_2$), 61.0 (CH), 53.2 (Me), 52.9 (Me), 18.9 (Me); MS (APcI) *m/z* (rel intensity) 406 ($MH^+$, 87%), 181 (68), 130 (100).

**(*R*)-Thiazoline 31.** A solution of thioamide **30** (33 mg, 0.08 mmol) and Burgess reagent (24 mg, 0.10 mmol) in dry THF (5 mL) was stirred at 70 °C for 30 min and evaporated in vacuo. Purification by flash chromatography on $SiO_2$, eluting with EtOAc, gave the title compound (27 mg, 87%) as a pale yellow oil (Found: $MH^+$, 388.0962; $C_{18}H_{17}N_3O_5S$ requires *MH*$^+$, 388.0962); $[\alpha]^{23}_D$ +18.4 (*c* 1.06, $CHCl_3$); IR (KBr) $\nu_{max}$ 2952, 1742, 1618, 1436, 1323, 1281, 1227, 1137, 931, 851, 759; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.16 (1H, s), 8.02 (1H, d, $J$ = 8.0 Hz), 7.91 (1H, d, $J$ = 8.0 Hz), 5.92 (1H, s), 5.35 (1H, s), 5.21 (1H, app t, $J$ = 9.7 Hz), 3.95 (3H, s), 3.77 (3H, s), 3.77 (1H, dd, $J$ = 11.2, 9.7 Hz), 3.67 (1H, dd, $J$ = 11.2, 9.7 Hz), 2.12 (3H, s); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 170.8 (C), 169.6 (C), 165.0 (C), 162.4 (C), 148.6 (C), 148.5 (C), 139.4 (C), 139.3 (CH), 138.6 (CH), 131.4 (C), 130.8 (C), 123.2 (CH), 78.6 (CH), 53.1 (Me), 53.0 (Me), 37.0 ($CH_2$), 19.1 (Me); MS (APcI) *m/z* (rel intensity) 388 ($MH^+$, 100%).

**Thiazole 32.** A mixture of thiazoline **31** (27 mg, 0.07 mmol) and activated $MnO_2$ (121 mg, 1.39 mmol) in $CH_2Cl_2$ (3 mL) was irradiated at 100 °C (initial power 300 W) for 150 min in a sealed pressure-rated reaction tube (10 mL), using a CEM Discover Microwave Synthesizer. The mixture was cooled rapidly to room temperature in a flow of compressed air for 5 min, filtered through Celite, washed with $CH_2Cl_2$ (2 × 10 mL), and evaporated in vacuo. Purification by flash chromatography on $SiO_2$, eluting with EtOAc−light petroleum (2:1), gave the title compound (21 mg, 79%) as a pale yellow oil (Found: $MH^+$, 386.0812; $C_{18}H_{15}N_3O_5S$ requires *MH*$^+$, 386.0805); IR (KBr) $\nu_{max}$ 2956, 2919, 1724, 1560, 1542, 1438, 1322, 1229, 1139, 1087, 761; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.27 (1H, s), 8.20 (1H, d, $J$ = 8.0 Hz), 8.10 (1H, d, $J$ = 8.0 Hz), 7.96 (1H, s), 5.83 (1H, s),

5.30 (1H, s), 3.97 (3H, s), 3.91 (3H, s), 1.95 (3H, s); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 165.0 (C), 164.6 (C), 162.3 (C), 161.7 (C), 149.2 (C), 148.6 (C), 146.9 (C), 140.0 (CH), 139.3 (C), 139.1 (CH), 131.3 (C), 130.7 (C), 129.8 (CH), 123.6 (CH), 118.8 ($CH_2$), 53.2 (Me), 52.7 (Me), 18.9 (Me); MS (APcI) *m/z* (rel intensity) 386 ($MH^+$, 100%).

**Dimethyl Sulfomycinamate (5).** A solution of $OsO_4$ (1.2 mg, 4.7 $\mu$mol) in MeCN (60 $\mu$L) was added to a solution of alkene **32** (16 mg, 0.04 mmol) in dioxane−$H_2O$ (1:1) (8 mL). Sodium periodate (17 mg, 0.08 mmol) was added and the mixture was stirred at room temperature overnight. After extracting twice with $CH_2Cl_2$, the combined organic extracts were washed sequentially with saturated aqueous $NaHCO_3$ solution, $H_2O$, and brine, dried ($Na_2SO_4$), and evaporated in vacuo. Purification by flash chromatography on $SiO_2$, eluting with EtOAc−light petroleum (2:1), gave the title compound (12 mg, 80%) as colorless crystals, mp 159.0−161.0 °C (ether−hexane) (lit.[4] mp 160.5−161.0 °C) (lit.[38] mp 157.3−160.2 °C) (Found: $MH^+$, 388.0604; $C_{17}H_{13}N_3O_6S$ requires $MH^+$, 388.0595); IR (KBr) $\nu_{max}$ 3150, 2954, 1728, 1702, 1573, 1534, 1477, 1435, 1373, 1338, 1316, 1219, 1128, 1096, 1005, 963, 869, 842, 768; $^1$H NMR (400 MHz; $CDCl_3$) $\delta$ 8.33 (1H, s), 8.31 (1H, s), 8.16 (2H, app s), 3.98 (3H, s), 3.91 (3H, s), 2.41 (3H, s); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 185.6 (C), 164.7 (C), 164.2 (C), 161.6 (C), 157.0 (C), 148.8 (C), 148.0 (C), 147.2 (C), 142.7 (CH), 140.4 (CH), 140.3 (C), 130.7 (C), 129.7 (CH), 124.2 (CH), 53.3 (Me), 52.8 (Me), 26.6 (Me); MS (APcI) *m/z* 388 ($MH^+$, 100%).

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**Supporting Information Available:** Experimental procedures, characterization data for pyridines **15**, and $^1$H NMR spectra for the synthesis of dimethyl sulfomycinamate (**5**). This material is available free of charge via the Internet at http://pubs.acs.org.

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