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Efficient Generation of Highly Functionalized Fused Oxazepine Frameworks Based on a CAN-Catalyzed Four-Component Tetrahydropyridine Synthesis/Ring-Closing Metathesis Sequence

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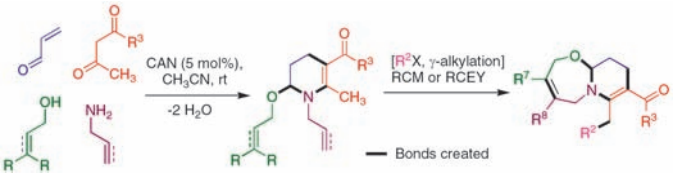

1-Allyl(propargyl)-6-allyl(propargyl)oxy-1,4,5,6-tetrahydropyridines, obtained through a CAN-catalyzed four-component reaction, were transformed into highly functionalized pyrido[2,1-*b*]-[1,3]oxazepines by ring-closing metathesis (RCM) and ring-closing enyne metathesis (RCEYM) processes, which constitute the first examples of the preparation of 1,3-oxazepine systems using metathesis reactions.

Introduction

Peptidomimetics are compounds that mimic the interaction of bioactive peptides with their targets while having improved pharmacokinetic properties such as increased bioavailability and biostability. The use of peptidomimetics has emerged as a powerful tool for overcoming the limitations inherent in the physical characteristics of peptides, thus improving their therapeutic potential, and for this reason peptidomimetics are becoming increasingly important in drug design.[1] Azabicyclo[*x*.*y*.0]alkane frameworks are important building blocks for the construction of conformationally fixed mimics of β-turn (type II) secondary structures of peptides. These unique heterocyclic frameworks can be used to restrain the backbone geometry and side-chain conformations of the native peptide to investigate structure−activity relationships and provide versatile templates for generating combinatorial libraries and for the development of compounds active at enzyme and receptor active sites. Among these β-turn mimics, bicyclic oxazepines derived from the pyrido[2,1-*b*][1,3]oxazepine ring system have received much attention as frameworks for the construction of peptidominetic compounds, specially conformationally restricted dipeptide surrogates that are key structural fragments of inhibitors of angiotensin-converting enzyme (ACE) and neutral endopeptidase (NEP),[2] among other relevant targets.

The synthesis of pyrido[2,1-*b*][1,3]oxazepines has normally been achieved by double cyclization of acyclic precursors containing an ω-hydroxyalkyl chain and ω-formylalkyl[2b] or ω-vinylalkyl[3] substituents attached to a nitrogen atom. We describe here an alternative procedure for the preparation of densely functionalized derivatives of the pyrido[2,1-*b*]-[1,3]oxazepine system, based on the use of our recently described[4] synthesis of 6-alkoxy-1,4,5,6-tetrahydropyridines through a four-component reaction which is followed by generation of the oxazepine moiety by ring-closing metathesis strategies (Scheme 1).

(1) For selected reviews of the role of peptidomimetics in drug design, see: (a) Giannis, A.; Rubsam, F. *Adv. Drug. Res.* **1997**, *29*, 1. (b) Leung, D.; Abbenante, G.; Fairlie, D. P. *J. Med. Chem.* **2000**, *43*, 305. (c) Goodman, M.; Zapf, C.; Rew, Y. *Pept. Sci* **2001**, *60*, 229. (d) Pérez, J. J.; Corcho, F.; Llorens, O. *Curr. Med. Chem.* **2002**, *9*, 2209. (e) Estiarte, M. A.; Rich, D. H. In *Burger's Medicinal Chemistry and Drug Discovery*, 6th ed.; Abraham, D. J., Ed.;Wiley-Interscience: New York, 2003; Vol. 1, p 633. (f) Avendaño, C.; Menéndez, J. C. *Clin. Transl. Oncol.* **2007**, *9*, 563. (g) Clynen, E.; Baggerman, G.; Husson, S. J.; Landuyt, B.; Schoofs, L. *Expert Opin. Drug Discov.* **2008**, *3*, 425.

(2) (a) Robl, J. A. US Patent 5,508,272A (Apr 16, **1996**). (b) Robl, J. A.; Sun, C.-Q.; Stevenson, J.; Ryono, D. E.; Simpkins, L. M.; Cimarusti, M. P.; Dejneka, T.; Slusarchyk, W. A.; Chao, S.; Stratton, L.; Misra, R. N.; Bednarz, M. S.; Asaad, M. M.; Cheung, H. S.; Abboa-Offei, B. E.; Smith, P. L.; Mathers, P. D.; Fox, M.; Schaeffer, T. R.; Seymour, A. A.; Trippodo, N. C. *J. Med. Chem.* **1997**, *40*, 1570.

(3) Chiou, W.-H.; Mizutani, N.; Ojima, I. *J. Org. Chem.* **2007**, *72*, 1871.

(4) Sridharan, V.; Maiti, S.; Menéndez, J. C. *Chem.—Eur. J.* **2009**, *15*, 4565.

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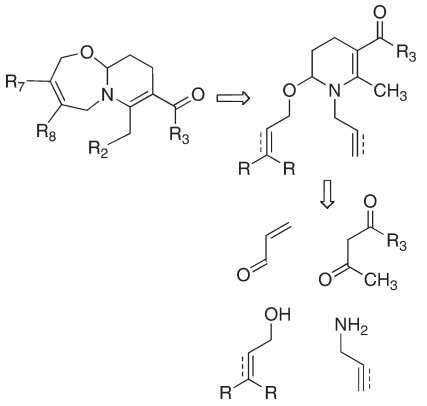
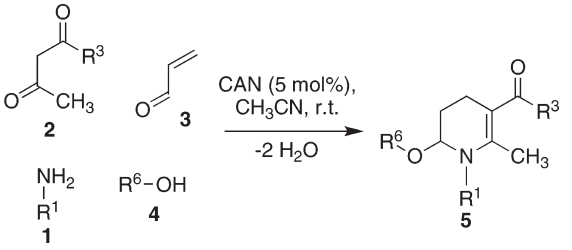
SCHEME 1. Plan for the Synthesis of Pyrido[2,1-*b*]-[1,3]oxazepines



SCHEME 2. Synthesis of Starting 6-Alkoxy-1,4,5,6-tetrahydropyridines



Results and Discussion

The preparation of the tetrahydropyridines **5** needed as starting materials for our study is summarized in Scheme 2 and involved the four-component reaction between primary amines **1**, β-dicarbonyl compounds **2**, α,β-unsaturated aldehydes **3**, and alcohols **4** in acetonitrile, catalyzed by cerium(IV) ammonium nitrate (CAN).[5,6] As shown in Table 1, this reaction tolerated the use of both allyl/propargyl alcohols and allyl/propargyl amines and afforded the corresponding tetrahydropyridines **5a**−**l** in excellent yields.

In order to increase structural variation in the starting materials for our study, we planned to use the acidity of the C_2-methyl substituent, which is due to its conjugation with the electron-withdrawing group at C-3.[4] Indeed, treatment of some of the tetrahydropyridines previously prepared with LDA followed by alkyl bromides or iodides afforded compounds **5m**−**s**. The yields were excellent in all cases, and no interference from the alkoxy group at C-6 was observed (Scheme 3 and Table 2).

TABLE 1. Scope and Yields of the Synthesis of 6-Alkoxy-1,4,5,6-tetrahydropyridines

entry	compd	R^1	R^3	R^6	yield, %
1	**5a**	allyl	OEt	allyl	88
2	**5b**	allyl	OEt	2-butenyl	85
3	**5c**	allyl	OEt	prenyl	86
4	**5d**	allyl	S-tBu	allyl	87
5	**5e**	allyl	OEt	propargyl	94
6	**5f**	allyl	OMe	propargyl	90
7	**5g**	allyl	OEt	2-hexynyl	86
8	**5h**	allyl	OMe	2-hexynyl	85
9	**5i**	allyl	S-tBu	propargyl	80
10	**5j**	allyl	S-tBu	2-hexynyl	79
11	**5k**	propargyl	OEt	allyl	90
12	**5l**	propargyl	OEt	2-butenyl	87

SCHEME 3. Introduction of Substituents at the C_2-CH_3 Group in 6-Alkoxy-1,4,5,6-tetrahydropyridines

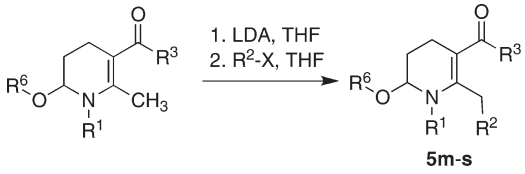


TABLE 2. Scope and Yields of the Synthesis of 6-Alkoxy-1,4,5,6-tetrahydropyridines Bearing Substituents at the C_2-CH_3 Group

entry	compd	R^1	R^2	R^3	R^6	yield, %
1	**5m**	allyl	Me	OEt	allyl	95
2	**5n**	allyl	Me	OMe	allyl	94
3	**5o**	allyl	Et	OMe	allyl	95
4	**5p**	allyl	nBu	OMe	allyl	92
5	**5q**	allyl	$(CH_2)_2Ph$	OEt	allyl	93
6	**5r**	allyl	$(CH_2)_2Ph$	OMe	allyl	95
7	**5s**	propargyl	prenyl	OEt	allyl	90

The next stage of our plan involved the generation of an oxazepine ring by ring-closing metathesis.[7] This may be considered as the most critical step in our synthetic scheme because the preparation of medium-sized rings by RCM may be difficult in some instances (specially from acyclic precursors) owing to entropic factors and transannular repulsions that develop as the ring is formed. Indeed, to our knowledge, the proposed transformations are the first examples of the synthesis of 1,3-oxazepines by ring-closing metathesis.[8] Gratifyingly, and in spite of these potential problems, in our case the reaction proceeded very well, probably favored by the conformational constraints imposed by our semirigid substrate, and compounds **6a**−**h** were isolated in yields higher than 90%. As shown in Table 3, the optimal reaction conditions for the most favorable reactions, involving two allyl substituents, involved the use of 5−10% of the Grubbs-1 catalyst at room temperature (entries 1 and 5−8). The presence of a 2-butenyl substituent did not significantly alter this reactivity (entry 2), while for the case of compound **5c**, bearing a prenyloxy substituent at C-6, reflux conditions were

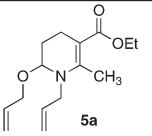
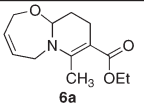
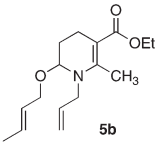
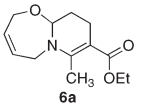
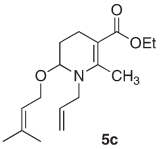
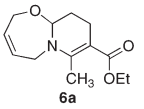
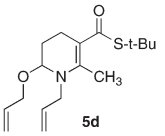
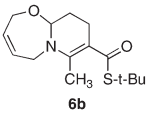
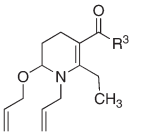
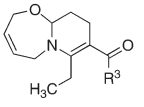
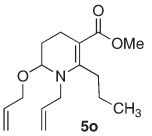
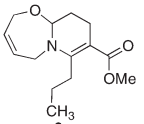
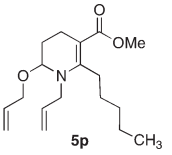
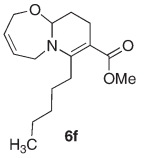
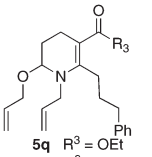
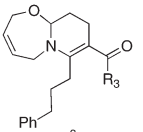
(5) For some reviews of cerium ammonium nitrate-promoted synthetic transformations, see: (a) Nair, V.; Matthew, J.; Prabhakaran, J. *Chem. Soc. Rev.* **1997**, 127. (b) Hwu, J. R.; King, K.-Y. *Curr. Sci.* **2001**, *81*, 1043. (c) Nair, V.; Panicker, S. B.; Nair, L. G.; George, T. G.; Augustine, Z. *Synlett* **2003**, 156. (d) Nair, V.; Balagopal, L.; Rajan, R.; Mathew, J. *Acc. Chem. Res.* **2004**, *37*, 21. (e) Nair, V.; Deepthi, A. *Chem. Rev.* **2007**, *107*, 1862.

(6) For representative recent examples of CAN-catalyzed reactions, taken from the work of our group, see: (a) Sridharan, V.; Ribelles, P.; Ramos, M. T.; Menéndez, J. C. *J. Org. Chem.* **2009**, *74*, 5715. (b) Sridharan, V.; Avendaño, C.; Menéndez, J. C. *Tetrahedron* **2009**, *65*, 2087. (c) Sridharan, V.; Menéndez, J. C. *Org. Lett.* **2008**, *10*, 4303. (d) Sridharan, V.; Avendaño, C.; Menéndez, J. C. *Synthesis* **2008**, 1039. (e) Sridharan, V.; Avendaño, C.; Menéndez, J. C. *Synlett* **2007**, 1079. (f) Sridharan, V.; Avendaño, C.; Menéndez, J. C. *Synlett* **2007**, 881. (g) Sridharan, V.; Avendaño, C.; Menéndez, J. C. *Tetrahedron* **2007**, *63*, 4407. (h) Sridharan, V.; Avendaño, C.; Menéndez, J. C. *Tetrahedron* **2007**, *63*, 673. (i) See also ref 4.

(7) For a review of the synthesis of oxygen and nitrogen heterocycles using ring-closing metathesis reactions, see: Deiters, A.; Martin, S. F. *Chem. Rev.* **2004**, *104*, 2199.

(8) For examples of the synthesis of 1,2-oxazepines by ring-closing metathesis, see: (a) Koide, K.; Finkelstein, J. M.; Ball, Z.; Verdine, G. L. *J. Am. Chem. Soc.* **2001**, *123*, 398. (b) Van der Jeught, S.; Stevens, C. V.; Dieltiens, N. *Synlett* **2007**, 3183.

TABLE 3. Synthesis of Pyrido[2,1-*b*][1,3]oxazepines by Ring-Closing Metathesis (RCM) Reactions

Entry	Starting compound	Product	Conditions[a]	**6a**, %
1	 **5a**	 **6a**	Grubbs-1 (5%), reflux, 1 h	92
			Grubbs-1 (5%), rt, 5 h	90
2	 **5b**	 **6a**	Grubbs-1 (5%), reflux, 3 h	75[b]
			Grubbs-1 (5%), rt, 4 h	94
3	 **5c**	 **6a**	Grubbs-1 (5%), rt, 24 h	56
			Grubbs-1 (5%), reflux, 4 h	70[c]
			Grubbs-1 (10%), reflux, 4 h	88
4	 **5d**	 **6b**	Grubbs-1 (5%), reflux, 1 h	93
5	 **5m** R^3 = OEt **5n** R^3 = OMe	 **6c** R^3 = OEt **6d** R^3 = OMe	Grubbs-1 (10%), rt, 6 h (**6c**)	90
			Grubbs-1 (10%), rt, 5 h (**6d**)	95
6	 **5o**	 **6e**	Grubbs-1 (10%), rt, 5 h	92
7	 **5p**	 **6f**	Grubbs-1 (10%), rt, 5 h	92
8	 **5q** R^3 = OEt **5r** R^3 = OMe	 **6g** R^3 = OEt **6h** R^3 = OMe	Grubbs-1 (10%), rt, 6 h (**6g**)	93
			Grubbs-1 (10%), rt, 6 h (**6h**)	92

[a]All reactions were carried out in dichloromethane. [b]Together with 20% of the corresponding elimination product **7**. [c]Together with 23% of the corresponding elimination product **7**.

necessary (entry 3). For reactions involving reflux for several hours, the desired compounds were accompanied by dihydropyridines **7** (see below), arising from an elimination reaction from the starting materials (entries 2 and 3).

We next examined the preparation of fused oxazepine systems by use of a ring-closing enyne metathesis (RCEYM) protocol, which again was unprecedented.[9] These reactions proved more challenging than the standard RCM processes previously studied and required extensive optimization work, which was carried out on the reaction starting from compound **5e**. As shown in Scheme 4 and Table 4, the desired product **6i** was accompanied by variable amounts of the known[10] dihydropyridine **7**, from elimination of a molecule of propargyl

(9) For a review of enyne metathesis, see: Diver, S. T.; Giessert, A. J. *Chem. Rev*. **2004**, *104*, 1317–1382.

(10) Maiti, S.; Menéndez, J. C. *Synlett* **2009**, 2249.

SCHEME 4. Optimization Study of the Ring-Closing Enyne Metathesis Reaction Starting from Compound 5e

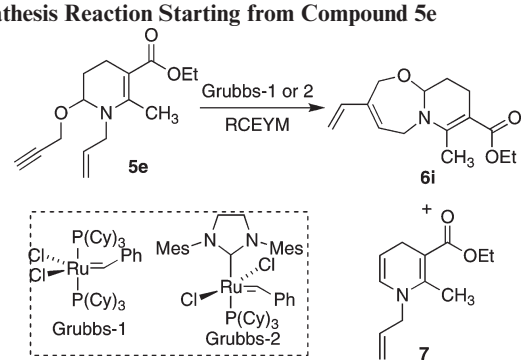


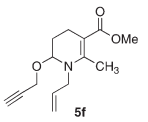
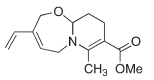
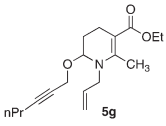
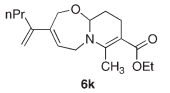
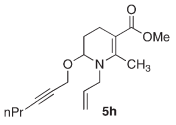
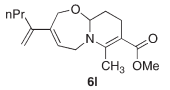
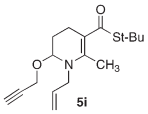
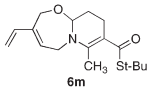
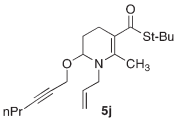
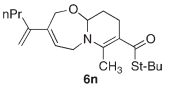
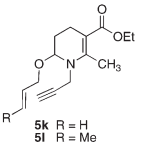
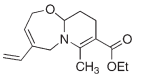
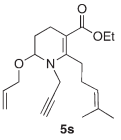
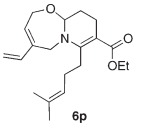
TABLE 4. Yields Obtained in the RCM Optimization Study Starting from Compound 5e

entry	catalyst	ethylene atmosphere	temp, °C	time, h	yield **6i**/**7**, %
1	Grubbs-1 (5%)	no	refluxing CH_2Cl_2	24	32/48
2	Grubbs-1 (10%)	no	refluxing CH_2Cl_2	5	45/46
3	Grubbs-2 (5%)	no	refluxing CH_2Cl_2	24	0/80
4	Grubbs-1 (5%)	yes	rt	24	51/9
5	Grubbs-1 (5%)	yes	refluxing CH_2Cl_2	17	57/33
6	Grubbs-2 (5%)	yes	rt	24	0/37
7	Grubbs-1 (10%)	yes	rt	24	90/0

alcohol from the starting material. Since preliminary experiments showed that the desired RCM reaction in the presence of 5 mol % of the Grubbs-1 catalyst did not take place at room temperature, we carried it out in refluxing dichloromethane, but a long reaction time (24 h) was required. Under these conditions, and not wholly unexpectedly, the major product was dihydropyridine **7** (entry 1). Use of 10 mol % of the Grubbs-1 catalyst allowed a substantial reduction in the reaction time, leading to equimolecular amounts of both products (entry 2). An attempt to use the Grubbs-2 catalyst was disappointing, as the reaction times were similar to those needed for the Grubbs-1 catalyzed reactions, and furthermore, it seemed to favor the undesired elimination (entry 3). At this stage, we decided to study the effect of carrying out the reaction under an ethylene atmosphere.[11] Under these conditions, the use of 5 mol % of Grubbs-1 catalyst allowed us to carry out the reaction at room temperature with very little competing elimination, although the yield of compound **6i** was only 51% (entry 4). Reflux conditions increased conversion, but at the cost of favoring elimination, and the yield of **6i** remained essentially unchanged (entry 5). Grubbs-2 catalyst, as in the previous case, gave only elimination product (entry 6). Finally, we found that the use of 10 mol % of Grubbs-1 catalyst at room temperature for 24 h led to the desired compound **6i** in an excellent 90% yield, without any noticeable competing elimination (entry 7).

The optimal conditions thus established for the enyne metathesis were then applied to a range of additional substrates, again in excellent yields. As shown in Table 5, the "yne" component of the reaction can be placed either on nitrogen or on oxygen, allowing us to achieve two types of substitution on

TABLE 5. Synthesis of Pyrido[2,1-*b*][1,3]oxazepines through Ring-Closing Enyne Metathesis (RCEYM) Reactions[a]

Entry	Starting cmpd.	Product	Yield, %
1	**5e**	**6i**	90
2	 **5f**	 **6j**	93
3	 **5g**	 **6k**	91
4	 **5h**	 **6l**	95
5	 **5i**	 **6m**	89
6	 **5j**	 **6n**	88
7	 **5k** R = H **5l** R = Me	 **6o**	87 (from **5k**) 90 (from **5l**)
8	 **5s**	 **6p**	85

[a]Conditions: Grubbs-1, ethylene, rt, 24 h.

the final products, namely vinyl substituents at the C-3 or C-4 positions. On the basis of the previously mentioned difference in reactivity for vinyl and prenyl side chains, it was possible to control the outcome of the metathesis reaction in substrates possessing three potentially reactive substituents with a central alkynyl chain. Thus, compound **5s**, bearing propargyl, allyl, and 4-methyl-3-pentenyl substituents on nitrogen, oxygen, and carbon, respectively, afforded an excellent yield of the pyrido[2,1-*b*]-[1,3]oxazepine **6p** as the only observed product, without any competing or additional metathesis reactions being observed. The fact that compound **5l** gave vinyl derivative **6o**, instead of the expected 2-propenyl derivative, must be due to a cross-metathesis reaction between the initial product (bearing a 2-propenyl chain) and ethylene. There are some examples of related domino enyne−cross-metathesis processes,[12] although

(11) For the acceleration of RCEYM reactions in the presence of ethylene, see: (a) Mori, M.; Sakakibara, N.; Kinoshita, A. *J. Org. Chem.* **1998**, *63*, 6082. For representative examples of the synthetic application of this protocol, see ref 4 and: (b) Saito, N.; Sato, Y.; Mori, M. *Org. Lett.* **2002**, *3*, 803. (c) Núñez, A.; Cuadro, A. M.; Álvarez-Builla, J.; Vaquero, J. J. *Chem. Commun.* **2006**, 2690.

(12) (a) Royer, F.; Vilain, C.; Elkaïm, L.; Grimaud, L. *Org. Lett.* **2003**, *5*, 2007. (b) Lee, H.-Y.; Kim, H. Y.; Tae, H.; Kim, B. G.; Lee, J. *Org. Lett.* **2003**, *5*, 3439.

SCHEME 5. Postcyclization Transformations: Use of Compounds 6k and 6m as Diels−Alder Dienes

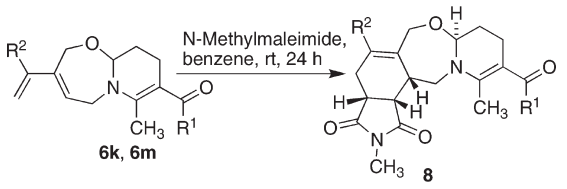


TABLE 6. Results Obtained in the Synthesis of Compounds 8

entry	R^1	R^2	starting material	product	yield, %
1	OEt	*n*-Pr	**6k**	**8a**	96
2	S*t*-Bu	H	**6m**	**8b**	92

we have not found literature precedent for the behavior observed by us in RCEYM reactions carried out under an ethylene atmosphere. Our result is relevant in that it shows that some caution may be needed in the future in the use of ethylene atmospheres in ring-closing enyne metathesis reactions. When the 1-butyl analogue of compound **5l** was submitted to our metathesis conditions in an ethylene atmosphere, we observed about 30% of the corresponding cross-metathesis product in the crude reaction product, which shows that the cross-metathesis reaction between ethylene and the 2-propenyl analogue of **6o** must have been aided by the presence of the conjugated double bond on the adjacent oxazepine ring.

In order to demonstrate the synthetic value of the products arising from the enyne metathesis, we decided to briefly study a protocol combining the ring-closing metathesis reaction with cycloaddition chemistry. Thus, in order to examine the role of some compounds **6** as Diels−Alder dienes,[13] we carried out the reaction between compounds **6k** and **6m** and *N*-methylmaleimide. As shown in Scheme 5 and Table 6, this reaction afforded the tetracyclic compounds **8** at room temperature, in excellent yields and in a completely diastereoselective fashion. The stereochemistry proposed for compounds **8** was based on a literature report for a related case, which was confirmed by X-ray diffraction,[14] and is in agreement with the expected anomeric and *endo* effects. The very brief construction of this hitherto unknown polyheterocyclic framework proves the power of our strategy to efficiently generate structural diversity and complexity in few steps from very simple starting materials.

Finally, we also explored the possibility of carrying out a variation of our tetrahydropyridine synthesis that included an intramolecular last step and which would lead to bicyclic systems related to compounds **6** in one operation. Although some examples of this type of reaction are known in the literature for the generation of pyrido[2,1-*b*]oxazole derivatives (Scheme 6, $n = 1$), it is normally performed as a two-component protocol,[15] and the only three-component version

(13) Ma, S.; Ni, B.; Liang, Z. *J. Org. Chem.* **2004**, *69*, 6305.

(14) For a review of the synthetic applications of the RCEYM/Diels−Alder sequence, see: Kotha, S.; Meshram, M.; Tiwari, A. *Chem. Soc. Rev.* **2009**, *38*, 2065.

(15) (a) De Kok, P. M. T.; Bastiaansen, L. A. M.; Van Lier, P. M.; Vekemans, J. A. J. M.; Buck, H. M. *J. Org. Chem.* **1989**, *54*, 1313. (b) Caballero, E.; Puebla, P.; Medarde, M.; San Feliciano, A. *Tetrahedron* **1993**, *49*, 10079–10088. (c) Noël, R.; Vanucci-Bacqué, C.; Fargeau-Bellassoued, M.-C.; Lhommet, G. *J. Org. Chem.* **2005**, *70*, 9044.

(16) Noël, R.; Fargeau-Bellassoued, M.-C.; Vanucci-Bacqué, C.; Lhommet, G. *Synthesis* **2008**, 1948.

SCHEME 6. CAN-Catalyzed Three-Component Synthesis of Pyrido[2,1-*b*]oxazoles and Pyrido[2,1-*b*][1,3]oxazines 10

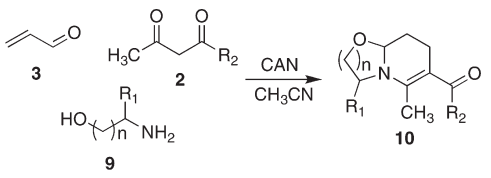


TABLE 7. Results Obtained in the Synthesis of Compounds 10

entry	compd	R^1	R^2	*n*	yield, %
1	**10a**	H	OEt	1	79
2	**10b**	*n*-Bu (R)	OEt	1	86[a]
3	**10c**	H	OEt	2	90
4	**10d**	H	OMe	2	82
5	**10e**	H	O*t*Bu	2	89
6	**10f**	H	S*t*Bu	2	88

[a]As a 7:3 diastereomer mixture.

that we are aware of proceeds in rather low yield (47% average).[16] As shown in Scheme 6 and Table 7, CAN was an excellent catalyst for the generation of this type of framework (compounds **10a**,**b**, entries 1 and 2) from β-dicarbonyl compounds **2**, acrolein **3**, and amino alcohols **9** ($n = 1$). The same conditions could also be applied to the synthesis of pyrido[2,1-*b*][1,3]oxazines **10c−f** by using amino alcohols **9** where $n = 2$ (entries 3−6). However, the reactions involving the use of 4-aminobutanol and 5-aminopentanol, which would have afforded pyrido[2,1-*b*][1,3]oxazepine and pyrido-[2,1-*b*][1,3]oxazocine derivatives, respectively, gave a complex mixture. This result proved that the three-component reaction is not suitable for the generation of medium-sized rings and is therefore complementary to the RCM-based protocol described in this paper.

In conclusion, we have extended and generalized the CAN-catalyzed four-component synthesis of 1,4,5,6-tetrahydropyridines to include the preparation of 1-allyl(propargyl)-6-allyl-(propargyl)oxy-1,4,5,6-tetrahydropyridines, some of which were further functionalized through a regioselective γ-deprotonation−allylation process. These starting materials were transformed into highly functionalized pyrido[2,1-*b*][1,3]oxazepine frameworks related to bioactive peptidomimetic compounds using ring-closing metathesis (RCM) and ring-closing enyne metathesis (RCEYM) processes, which constitute the first examples of the preparation of 1,3-oxazepine systems using metathesis chemistry. A modified version of the CAN-catalyzed tetrahydropyridine synthesis involving an intramolecular final step was also developed, which was complementary to the metathesis-based method in that it allowed very efficient access to pyrido[2,1-*b*]oxazoles and pyrido[2,1-*b*][1,3]oxazines.

Experimental Section

General Procedure for the Four-Component 6-Alkoxy-1,4,5,6-tetrahydropyridine Synthesis: Preparation of Compounds 5a−l. To a stirred solution of amine **1** (3.9 mmol, 1.3 equiv) and β-keto ester **2** (3 mmol, 1 equiv) in acetonitrile (5 mL) was added CAN (5 mol %). Stirring was continued for 30 min at room temperature. Acrolein **3** (3.3 mmol, 1.1 equiv) and alcohol **4** (6 mmol, 2 equiv) were then added, and stirring was continued for another 1 h. After completion of the reaction, the mixture was diluted with CH_2Cl_2 (60 mL), washed with water followed by brine, and dried (anhydrous Na_2SO_4). The solvent was evaporated under

reduced pressure, and the residue was purified by rapid column chromatography on activated neutral alumina (grade II−III), eluting with a petroleum ether−ethyl acetate mixture (95:5, v/v) to give pure compounds **5**. Data for representative compounds (**5a**, **5d**, and **5k**) follow. Characterization data for all compounds **5a**−**l** can be found in the Supporting Information.

(±)-Ethyl 1-allyl-6-allyloxy-2-methyl-1,4,5,6-tetrahydropyridine-3-carboxylate (5a): colorless viscous liquid; IR (neat) 2979.5, 2931.3, 1681.7, 1579.9, 1381.2, 1273.9, 1119.8, 1055.1 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 1.27 (t, J = 7.1 Hz, 3H), 1.45−1.58 (m, 1H), 2.01−2.11 (m, 1H), 2.26−2.35 (m, 1H), 2.42 (s, 3H), 2.52−2.60 (m, 1H), 3.79−3.89 (m, 1H), 3.99−4.19 (m, 5H), 4.47 (bs, 1H), 5.09−5.34 (m, 4H), 5.75−6.02 (m, 2H); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 15.0, 16.6, 18.4, 25.4, 52.2, 59.3, 68.3, 86.0, 97.4, 116.2, 117.5, 135.0, 135.2, 152.3, 169.4. Anal. Calcd for $C_{15}H_{23}NO_3$: C, 67.90; H, 8.74; N, 5.28. Found: C, 67.62; H, 8.51; N, 5.20.

(±)-*S*-*tert*-Butyl 1-allyl-6-allyloxy-2-methyl-1,4,5,6-tetrahydropyridine-3-carbothioate (5d): colorless viscous liquid; IR (neat) 2958.4, 2922.9, 1628.4, 1544.2, 1253.5, 1058.1 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 1.50 (s, 9H), 1.52−1.64 (m, 1H), 2.04−2.14 (s, 1H), 2.38 (s, 3H), 2.42−2.55 (m, 1H), 2.57−2.67 (m, 1H), 3.81−4.19 (m, 4H), 4.44 (bs, 1H), 5.08−5.35 (m, 4H), 5.75−6.10 (m, 2H); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 17.2, 18.9, 25.5, 30.7, 46.9, 52.1, 68.4, 85.5, 106.2, 116.4, 117.7, 134.6, 134.9, 150.6, 191.5. Anal. Calcd for $C_{17}H_{27}NO_2S$: C, 65.98; H, 8.79; N, 4.53. Found: C, 65.63; H, 8.53; N, 4.50.

(±)-Ethyl 6-allyloxy-2-methyl-1-(prop-2-ynyl)-1,4,5,6-tetrahydropyridine-3-carboxylate (5k): colorless viscous liquid; IR (neat) 3253.1, 2978.6, 2936.4, 2115.5, 1681.9, 1584.6, 1433.2, 1274.4, 1120.0, 1058.8 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 1.28 (t, J = 7.1 Hz, 3H), 1.49−1.63 (m, 1H), 2.00−2.10 (m, 1H), 2.29 (t, J = 2.4 Hz, 1H), 2.32−2.40 (m, 1H), 2.48−2.56 (m, 1H), 2.51 (s, 3H), 4.00−4.19 (m, 6H), 4.62 (t, J = 2.2 Hz, 1H), 5.15−5.37 (m, 2H), 5.88−6.15 (m, 1H); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 14.9, 16.8, 18.6, 25.7, 39.6, 59.6, 68.3, 72.6, 80.2, 86.5, 100.3, 117.6, 135.1, 150.8, 169.3. Anal. Calcd for $C_{15}H_{21}NO_3$: C, 68.42; H, 8.04; N, 5.32. Found: C, 68.10; H, 7.90; N, 5.20.

General Procedure for the γ-Alkylation Reactions: Preparation of Compounds 5m−t. To a solution of the suitable 1,4,5,6-tetrahydropyridine derivative **5** (1 mmol) in dry tetrahydrofuran (10 mL) was added LDA [prepared from diisopropylamine (2 equiv) and *n*-BuLi (1.6 M hexane solution, 2.05 equiv), 30 min, 0 °C]. The reaction mixture was stirred at −5 to 0 °C for 30 min, and then allyl iodide or propargyl bromide (1.1 equiv) was added. The resulting solution was stirred at 0 °C for the 2 h, and, after the completion of the reaction was verified by TLC, a few drops of cold saturated aqueous NH_4Cl solution were added and the organic layer was concentrated to dryness. The residue was dissolved in dichloromethane and washed with water. The organic layer was dried over Na_2SO_4 and concentrated to dryness. The crude residue was chromatographed on neutral Al_2O_3 (activity grade IV), eluting with a 98:2 petroleum ether−ethyl acetate mixture containing 0.25% Et_3N. Data for representative examples (compounds **5m** and **5o**) follow. Characterization data for all compounds **5m**−**t** can be found in the Supporting Information.

(±)-Ethyl 1-allyl-6-allyloxy-2-ethyl-1,4,5,6-tetrahydropyridine-3-carboxylate (5m): colorless viscous liquid; IR (neat) 2979.9, 1682.3, 1574.1, 1267.6, 1175.3, 1120.7, 1050.3 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.17 (t, J = 7.3 Hz, 3H), 1.30 (t, J = 7.0 Hz, 3H), 1.44−1.56 (m, 1H), 2.00−2.09 (m, 1H), 2.33−2.61 (m, 3H), 3.16−3.28 (m, 1H), 3.76−3.88 (m, 1H), 4.01−4.04 (m, 2H), 4.09−4.22 (m, 3H), 4.48 (br s, 1H), 5.09−5.35 (m, 4H), 5.65−5.94 (m, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 13.9, 14.9, 18.6, 22.6, 25.7, 51.9, 59.3, 68.1, 85.8, 96.9, 116.4, 117.4, 135.3 (2C), 157.4, 168.8. Anal. Calcd for $C_{16}H_{25}NO_3$: C, 68.79; H, 9.02; N, 5.01. Found: C, 68.48; H, 8.95; N, 5.16.

(±)-Methyl 1-allyl-6-allyloxy-2-propyl-1,4,5,6-tetrahydropyridine-3-carboxylate (5o): colorless viscous liquid; IR (neat) 2959.3, 1684.3, 1570.4, 1264.0, 1174.4, 1120.4, 1054.2, 919.6 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.01 (t, J = 7.4 Hz, 3H), 1.41−1.66 (m, 3H), 1.99−2.09 (m, 1H), 2.26−2.59 (m, 3H), 3.11−3.23 (m, 1H), 3.67 (s, 3H), 3.75−3.85 (m, 1H), 4.00−4.03 (m, 2H), 4.08−4.17 (m, 1H), 4.47 (br s, 1H), 5.09−5.34 (m, 4H), 5.75−5.97 (m, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 14.7, 18.5, 23.1, 25.8, 31.3, 50.9, 52.1, 68.1, 85.7, 96.9, 116.5, 117.4, 135.2, 135.3, 156.5, 169.2. Anal. Calcd for $C_{16}H_{25}NO_3$: C, 68.79; H, 9.02; N, 5.01. Found: C, 68.69; H, 8.86; N, 5.12.

General Procedure for the RCM and RCEYM Reactions of Compounds 5. Synthesis of Fused Oxazepines 6. To a solution of the suitable 6-alkoxy-1,4,5,6-tetrahydropyridine derivative **5** (1 mmol) in dry dichloromethane (10 mL) was added Grubbs first-generation catalyst (5 or 10 mol %, as specified in Tables 3 and 4), and the reaction mixture was stirred or refluxed in the presence or absence of ethylene gas under the conditions mentioned in Tables 3 and 4. After the completion of the reaction was verified by TLC, the reaction mixture was concentrated to dryness and the crude residue was purified by chromatography on neutral Al_2O_3 (activity IV) column, eluting with a 90:10 petroleum ether−ethyl acetate mixture. Data for representative examples (compounds **6a**, **6d**, **6g**, and **6l**) follow. Characterization data for all compounds **6** can be found in the Supporting Information.

(±)-Ethyl 7-methyl-5,9,10,10a-tetrahydro-2*H*-pyrido[2,1-*b*][1,3]oxazepine-8-carboxylate (6a): colorless viscous liquid; IR (neat) 2973.1, 2932.5, 1679.7, 1579.0, 1431.0, 1272.9, 1096.5 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 1.28 (t, J = 7.1 Hz, 3H), 1.77−1.83 (m, 1H), 1.92−2.01 (m, 1H), 2.44 (s, 3H), 2.44−2.51 (m, 2H), 3.73−3.82 (m, 1H), 4.09−4.39 (m, 5H), 4.87 (dd, J = 4.4, 3.6 Hz, 1H), 5.78−5.97 (m, 2H); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 15.0, 16.8, 19.4, 27.4, 49.3, 59.5, 65.3, 87.9, 97.6, 130.3, 131.2, 152.4, 169.6. Anal. Calcd for $C_{13}H_{19}NO_3$: C, 65.80; H, 8.07; N, 5.90. Found: C, 65.45; H, 7.92; N, 5.85.

(±)-Methyl 7-ethyl-5,9,10,10a-tetrahydro-2*H*-pyrido[2,1-*b*][1,3]oxazepine-8-carboxylate (6d): colorless viscous liquid; IR (neat) 2944.7, 1683.8, 1569.6, 1270.2, 1176.0, 1125.6, 1100.5 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.17 (t, J = 7.3 Hz, 3H), 1.67−1.81 (m, 1H), 1.92−2.03 (m, 1H), 2.45−2.62 (m, 3H), 3.15−3.29 (m, 1H), 3.68 (s, 3H), 3.71−3.83 (m, 1H), 4.20−4.41 (m, 3H), 4.85 (t, J = 3.6 Hz, 1H), 5.79−5.89 (m, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 13.8, 19.2, 22.9, 27.2, 49.2, 50.9, 65.4, 87.6, 96.0, 130.4, 130.6, 157.9, 169.2. Anal. Calcd for $C_{13}H_{19}NO_3$: C, 65.80; H, 8.07; N, 5.90. Found: C, 65.61; H, 7.93; N, 5.80.

(±)-Ethyl 7-(3-phenylpropyl)-5,9,10,10a-tetrahydro-2*H*-pyrido[2,1-*b*][1,3]oxazepine-8-carboxylate (6g): colorless viscous liquid; IR (neat) 3025.8, 2933.8, 2857.3, 1681.5, 1573.9, 1453.4, 1361.5, 1269.3, 1144.9, 1096.0 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.29 (t, J = 7.1 Hz, 3H), 1.63−1.84 (m, 2H), 1.85−2.04 (m, 2H), 2.44−2.55 (m, 3H), 2.63−2.86 (m, 2H), 3.13−3.25 (m, 1H), 3.54−3.63 (m, 1H), 3.91 (dd, J = 4.9 and 17.8 Hz, 1H), 4.14 (q, J = 7.1 Hz, 2H), 4.20−4.25 (m, 1H), 4.28−4.36 (m, 1H), 4.76 (t, J = 3.5 Hz, 1H), 5.59−5.66 (m, 1H), 5.72−5.81 (m, 1H), 7.17−7.29 (m, 5H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 15.0, 19.4, 27.3, 28.9, 31.0, 36.2, 49.1, 59.4, 65.4, 87.8, 97.0, 126.2, 128.7 (2C), 129.0 (2C), 130.5, 130.6, 142.5, 155.9, 168.9. Anal. Calcd for $C_{21}H_{27}NO_3$: C, 73.87; H, 7.97. N, 4.10; Found: C, 73.65; H, 7.63; N, 3.97.

(±)-Methyl 7-Methyl-3-(1-butylvinyl)-5,9,10,10a-tetrahydro-2*H*-pyrido[2,1-*b*][1,3]oxazepine-8-carboxylate (6l): colorless viscous liquid; IR (neat) 2957.4, 2930.9, 1683.7, 1577.7, 1426.9, 1275.0, 1178.9, 1108.5 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 0.91 (t, J = 7.3 Hz, 3H), 1.38−1.53 (m, 2H), 1.84−1.98 (m, 2H), 2.19 (t, J = 7.4 Hz, 2H), 2.31−2.60 (m, 2H), 2.43 (s, 3H), 3.66 (s, 3H), 3.91 (d, J = 18.0 Hz, 1H), 4.24 (dd, J = 17.4, 5.9 Hz, 1H), 4.39 (d, J = 15.3 Hz, 1H), 4.48 (d, J = 15.3 Hz, 1H), 4.89−4.96 (m,

3H), 5.91 (dd, J = 5.1, 4.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 14.3, 17.0, 19.8, 21.9, 27.0, 36.9, 47.8, 51.0, 65.3, 88.1, 96.9, 111.9, 125.3, 142.3, 147.0, 153.6, 169.8. Anal. Calcd for $C_{17}H_{25}NO_3$: C, 70.07; H, 8.65; N, 4.81. Found: C, 69.88; H, 8.55; N, 4.71.

General Procedure for the Diels−Alder Reaction between Compounds 6k,m and *N*-Methylmaleimide. A solution of compounds **6k** or **6m** (1 mmol) and *N*-methylmaleimide (1 mmol) in benzene (10 mL) was stirred at room temperature for 24 h. The reaction mixture was evaporated to dryness, and the residue was purified by II−III activity alumina chromatography, eluting with a 75:25 petroleum ether−ethyl acetate mixture.

(±)-(3a*R,7a*S**,13a*S**,13b*R**)-Ethyl 2,11-dimethyl-1,3-dioxo-5-propyl-2,3a,4,6,7a,8,9,13,13a,13b-decahydroisoindolo[5,6-*e*]pyrido-[2′,1′-*b*][1,3]oxazepine-10-carboxylate (8a):** white solid; mp 179−180 °C; IR (neat) 2959.5, 2935.3, 1697.9, 1574.7, 1433.7, 1277.8, 1114.3, 1017.8 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz) δ 0.75 (t, J = 7.3 Hz, 3H), 0.98−1.12 (m, 1H), 1.27 (t, J = 7.1 Hz, 3H), 1.29−1.43 (m, 1H), 1.57−1.70 (m, 1H), 1.91−2.01 (m, 2H), 2.13−2.34 (m, 3H), 2.46−2.61 (m, 3H), 2.50 (s, 3H), 2.90 (s, 3H), 3.07 (dd, J = 8.7, 4.6 Hz, 1H), 3.18 (t, J = 7.6 Hz, 1H), 4.05−4.20 (m, 5H), 4.58 (bs, 1H), 4.74 (d, J = 14.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 13.9, 14.9, 15.9, 18.5, 21.5, 25.2, 27.2, 30.6, 35.1, 41.3, 41.6, 44.1, 51.2, 59.5, 67.9, 90.8, 99.2, 132.9, 137.6, 150.5, 169.5, 178.6, 179.8. Anal. Calcd for $C_{23}H_{32}N_2O_5$: C, 66.32; H, 7.74; N, 6.73. Found: C, 66.11; H, 7.65; N, 6.60.

(±)-(3a*R,7a*S**,13a*S**,13b*R**)-*S*-*tert*-Butyl 2,11-dimethyl-1,3-dioxo-2,3a,4,6,7a,8,9,13,13a,13b-decahydroisoindolo[5,6-*e*]pyrido-[2′,1′-*b*][1,3]oxazepine-10-carbothioate (8b):** white solid; mp 205−206 °C; IR (neat) 2956.1, 2920.3, 1697.7, 1537.0, 1433.0, 1313.3, 1019.7 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.17−1.30 (m, 2H), 1.50 (s, 9H), 1.55−1.75 (m, 1H), 1.98−2.06 (m, 1H), 2.14−2.59 (m, 2H), 2.45 (s, 3H), 2.73 (dd, J = 15.5, 7.2 Hz, 1H), 2.93 (s, 3H), 3.11−3.24 (m, 2H), 4.01−4.38 (m, 4H), 4.53 (s, 1H), 5.84−5.87 (m, 1H); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 16.4, 19.3, 25.1, 25.4, 27.2, 30.6, 40.7, 41.0, 43.6, 47.1, 51.0, 74.1, 90.6, 108.0, 125.9, 141.2, 148.3, 178.3, 179.7, 192.2. Anal. Calcd for $C_{22}H_{30}N_2O_4S$: C, 63.13; H, 7.22; N, 6.69. Found: C, 62.98; H, 7.12; N, 6.62.

General Procedure for the Three-Component Synthesis of Compounds 10. To a stirred solution of the suitable amino alcohol **9** (3.9 mmol, 1.3 equiv) and β-keto ester, **2** (3 mmol, 1 equiv) in acetonitrile (5 mL) was added CAN (5 mol %). Stirring was continued for 30 min at room temperature, acrolein (3.3 mmol, 1.1 equiv) was then added, and stirring was continued for another 1 h. After completion of the reaction, as indicated by TLC, the mixture was diluted with CH_2Cl_2 (60 mL), washed with water and brine, and dried (anhydrous Na_2SO_4), and the solvent was evaporated under reduced pressure. Compounds **10** were purified by rapid alumina column chromatography on activated, neutral alumina, eluting with a petroleum ether−ethyl acetate mixture (95:5, v/v).

Ethyl 5-methyl-2,3,8,8a-tetrahydro-7*H*-oxazolo[3,2-*a*]pyridine-6-carboxylate (10a): colorless viscous liquid; IR (neat) 2954.8, 2932.5, 1677.2, 1560.4, 1415.3, 1277.2, 1095.4 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.27 (t, J = 7.1 Hz, 3H), 1.35−1.48 (m, 1H), 2.18−2.32 (m, 2H), 2.44 (s, 3H), 2.66−2.74 (m, 1H), 3.48−3.58 (m, 2H), 3.88−3.98 (m, 1H), 4.13 (q, J = 7.1 Hz, 2H), 4.17−4.25 (m, 1H), 4.64 (dd, J = 9.9, 3.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 15.0, 18.2, 21.7, 26.9, 46.2, 59.2, 66.0, 87.7, 93.9, 151.8, 169.3. Anal. Calcd for $C_{11}H_{17}NO_3$: C, 62.54; H, 8.11; N, 6.63. Found: C, 62.31; H, 7.99; N, 6.48.

Ethyl 3-butyl-5-methyl-2,3,8,8a-tetrahydro-7*H*-oxazolo[3,2-*a*]pyridine-6-carboxylate (10b): colorless viscous liquid, two diastereoisomers **A** and **B** (7:3); IR (neat) 2956.8, 2932.8, 1679.0, 1567.4, 1416.0, 1274.7, 1097.4 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz) δ 0.87−0.99 (m, 3H, **A** + **B**), 1.19−1.73 (m, 10H, **A** + **B**), 2.08−2.28 (m, 2H, **A** + **B**), 2.44 (s, 3H, **A** + **B**), 2.61−2.70 (m, 1H, **A** + **B**), 3.70−3.82 (m, 1H, **A** + **B**), 3.89−3.97 (m, 1H, **A** + **B**), 4.04−4.17 (m, 3H, **A** + **B**), 4.60 (dd, J = 9.8, 2.3 Hz, 0.3H, **B**), 4.77 (dd, J = 9.6, 3.8 Hz, 0.7H, **A**); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 14.4, 15.0, 17.9, 18.6, 21.0, 22.6, 22.9, 23.1, 26.9, 27.9, 28.1, 29.0, 34.2, 34.4, 57.3, 57.5, 59.1, 59.2, 70.2, 70.6, 87.3, 88.3, 94.1, 95.3, 150.8, 151.8, 169.3. Anal. Calcd for $C_{15}H_{25}NO_3$: C, 67.38; H, 9.42; N, 5.24. Found: C, 67.01; H, 9.22; N, 5.13.

Ethyl 6-methyl-3,4,9,9a-tetrahydro-2*H*,8*H*-pyrido[2,1-*b*][1,3]-oxazine-7-carboxylate (10c): colorless viscous liquid; IR (neat) 2956.6, 2854.9, 1682.0, 1582.2, 1434.0, 1272.8, 1111.6, 1046.6 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.28 (t, J = 7.1 Hz, 3H), 1.43−1.50 (m, 1H), 1.69−1.98 (m, 3H), 2.36−2.47 (m, 2H), 2.38 (s, 3H), 3.15 (td, J = 13.6, 2.7 Hz, 1H), 3.86 (td, J = 11.6, 2.6 Hz, 1H), 3.98−4.09 (m, 1H), 4.12−4.17 (m, 3H), 4.54 (t, J = 3.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 14.9, 16.7, 19.2, 26.8, 27.2, 47.0, 59.4, 68.2, 85.3, 99.6, 152.0, 169.4. Anal. Calcd for $C_{12}H_{19}NO_3$: C, 63.98; H, 8.50; N, 6.22. Found: C, 63.80; H, 8.41; N, 6.18.

Methyl 6-methyl-3,4,9,9a-tetrahydro-2*H*,8*H*-pyrido[2,1-*b*]-[1,3]oxazine-7-carboxylate (10d): white solid; mp 69−70 °C; IR (neat) 2949.0, 2853.7, 1684.0, 1581.4, 1430.5, 1274.9, 1115.5, 1047.5 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.44−1.50 (m, 1H), 1.71−1.97 (m, 3H), 2.28−2.50 (m, 2H), 2.38 (s, 3H), 3.16 (td, J = 13.6, 2.7 Hz, 1H), 3.67 (s, 3H), 3.86 (td, J = 11.9, 2.6 Hz, 1H), 3.98−4.17 (m, 2H), 4.54 (t, J = 3.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 16.7, 19.2, 26.8, 27.2, 47.1, 51.1, 68.2, 85.3, 99.3, 152.4, 169.8. Anal. Calcd for $C_{11}H_{17}NO_3$: C, 62.54; H, 8.11; N, 6.63. Found: C, 62.34; H, 8.00; N, 6.61.

***tert*-Butyl 6-methyl-3,4,9,9a-tetrahydro-2*H*,8*H*-pyrido[2,1-*b*]-[1,3]oxazine-7-carboxylate (10e):** colorless viscous liquid; IR (neat) 2962.8, 2927.1, 1681.6, 1584.5, 1364.8, 1278.2, 1116.2, 1043.9 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.41−1.52 (m, 1H), 1.50 (s, 9H), 1.67−1.96 (m, 3H), 2.28−2.42 (m, 2H), 2.32 (s, 3H), 3.12 (td, J = 13.6, 2.7 Hz, 1H), 3.86 (td, J = 12.1, 2.6 Hz, 1H), 3.95−4.02 (m, 1H), 4.11−4.18 (m, 1H), 4.53 (t, J = 3.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 16.8, 19.7, 26.7, 27.2, 28.9, 47.0, 68.2, 78.9, 85.4, 101.6, 150.7, 169.2. Anal. Calcd for $C_{14}H_{23}NO_3$: C, 66.37; H, 9.15; N, 5.53. Found: C, 66.11; H, 9.01; N, 5.41.

***S*-*tert*-Butyl 6-methyl-3,4,9,9a-2*H*,8*H*-pyrido[2,1-*b*][1,3]oxazine-7-carbothioate (10f):** viscous liquid; IR (neat) 2959.0, 2919.7, 1629.2, 1547.5, 1430.3, 1273.7, 1072.6 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.43−1.53 (m, 1H), 1.51 (s, 9H), 1.72−2.00 (m, 3H), 2.33 (s, 3H), 2.44−2.52 (m, 2H), 3.17 (td, J = 13.6, 2.7 Hz, 1H), 3.85 (td, J = 12.0, 2.6 Hz, 1H), 3.99−4.17 (m, 2H), 4.51 (t, J = 3.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 17.2, 19.9, 27.0, 27.4, 30.6, 46.9, 47.0, 68.2, 84.9, 108.2, 149.9, 192.1. Anal. Calcd for $C_{14}H_{23}NO_2S$: C, 62.42; H, 8.61; N, 5.20. Found: C, 62.13; H, 8.41; N, 5.03.

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Supporting Information Available: Copies of ^{1}H NMR and ^{13}C NMR spectra for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.