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Boron-Catalyzed Arylthiooxygenation of *N*-Allylamides: Synthesis of (Arylsulfanyl)oxazolines

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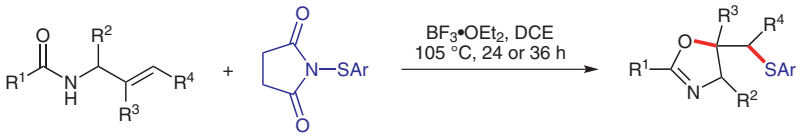

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Abstract Oxazoles and aryl sulfides are chemical entities that are found in many natural products and biologically and pharmaceutically active molecules. It is therefore highly desirable to develop an efficient and practical approach to the synthesis of arylsulfanyl-substituted oxazolines. We developed a simple and efficient method for boron-catalyzed sequential arylsulfanylation and oxygenation of *N*-allylamides. The protocol uses readily available 1-(arylsulfanyl)pyrrolidine-2,5-diones as the arylsulfanylation reagents and inexpensive boron trifluoride etherate as the catalyst; no ligands or additives are required, and it is not necessary to purge the reaction vessel of air. The method therefore provides an efficient and practical strategy for the synthesis of arylsulfanyl-substituted heterocycles.

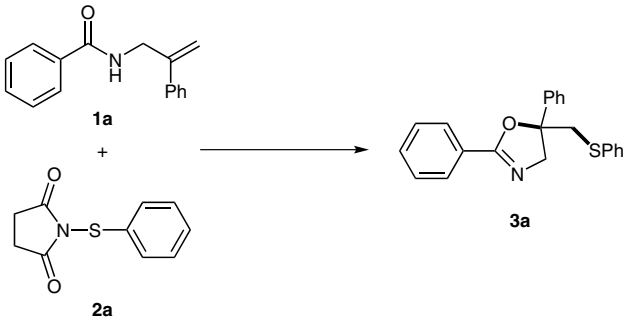
Key words oxazoles, sulfurizations, sulfides, oxygenations

Oxazole moieties are found in many natural products and in many biologically and pharmaceutically active molecules;[1] oxazoles are also useful as building blocks and intermediates in organic synthesis.[1a,2] Similarly, aryl sulfides are indispensable in materials science and in biology, especially the pharmaceutical area,[3] and the formation of C–S bonds is a key step in the synthesis of a broad range of functional molecules.[4] Conventional approaches to aryl sulfides involve transition metal-catalyzed coupling reactions of thiols or disulfides with aryl halides or pseudohalides.[5] Structures that contain both oxazole and aryl sulfide moieties might, therefore, be very useful. Mellor and co-workers reported synthesis of compounds of this type through the reaction of *N*-allylamides with organic disulfides in the presence of manganese(III) acetate.[6] Difunctionalization of alkenes is a promising strategy for the synthesis of various molecules under either transition-metal-mediated or metal-free conditions;[7] this strategy has been used in dioxygenation,[8] aminooxygenation,[9] diamination,[10] fluoroamination,[11] aminohalogenation,[12] azidooxygenation,[13] amino- and oxotrifluoromethylation,[14] carbo- and heterofunctionalization,[15] and dicarbofunctionalization reactions.[16] Inspired by the excellent results that have been achieved, we examined the boron-catalyzed sequential arylsulfanylation and oxygenation of *N*-allylamides to give arylsulfanyl-substituted oxazolines.

We began our search for optimal conditions for such transformations by examining the reaction of *N*-(2-phenylprop-2-en-1-yl)benzamide (**1a**) with 1-(phenylsulfanyl)-pyrrolidine-2,5-dione (**2a**) to give 2,5-diphenyl-5-[(phenylsulfanyl)methyl]-4,5-dihydro-1,3-oxazole (**3a**) in the presence of various catalysts in 1,2-dichloroethane at room temperature under air (Table 1, entries 1–5). Boron trifluoride etherate as catalyst (entry 2) gave oxazole **3a** in 12% yield after 24 hours. Increasing the amount of catalyst gave higher yields (entries 6 and 7). Good to excellent yields were obtained by using 0.2 equivalents of boron trifluoride etherate catalyst at higher temperatures (60 or 105 °C) (entries 8 and 9). The yield decreased when the reaction time was reduced (entry 10), whereas increasing the reaction time to 30 hours had little effect on the yield (entry 11). Next, we examined the effects of various solvents (entries 9 and 12–14), and we confirmed that 1,2-dichloroethane is a suitable solvent (entry 9). In the absence of the catalyst, the product **3a** was obtained in 52% yield (entry 15). Performing the reaction under an atmosphere of nitrogen (entry 16) gave a yield similar to that obtained under air (entry 9).

Having determined the optimal conditions for the transformation, we investigated the scope of the boron-catalyzed arylthiooxygenation of various substituted *N*-allylamides **1** with 1-(arylsulfanyl)pyrrolidine-2,5-diones **2** (Table 2).[17] All the substrates examined gave reasonable yields of the corresponding (arylsulfanyl)oxazolines **3**. *N*-Allylarylamides **1** (R^1 = aryl) gave higher yields than *N*-allylalkyl-

Table 1 Optimization of Conditions for the Reaction of *N*-(2-Phenylprop-2-en-1-yl)benzamide (**1a**) with 1-(Phenylsulfanyl)pyrrolidine-2,5-dione (**2a**) to give 2,5-Diphenyl-5-[(phenylsulfanyl)methyl]-4,5-dihydro-1,3-oxazole (**3a**)[a]

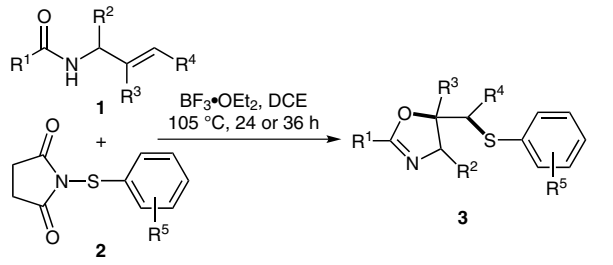


Entry	Catalyst (equiv)	Solvent	Temp (°C)	Time (h)	Yield[b] (%)
1	$FeCl_3$ (0.2)	DCE	r.t.	24	0
2	$BF_3{\cdot}OEt_2$ (0.2)	DCE	r.t.	24	12
3	CuI (0.2)	DCE	r.t.	24	0
4	$CuCl_2$ (0.2)	DCE	r.t.	24	0
5	$Pd(OAc)_2$ (0.2)	DCE	r.t.	24	0
6	$BF_3{\cdot}OEt_2$ (1.0)	DCE	r.t.	24	57
7	$BF_3{\cdot}OEt_2$ (1.5)	DCE	r.t.	24	79
8	$BF_3{\cdot}OEt_2$ (0.2)	DCE	60	24	55
9	**$BF_3{\cdot}OEt_2$ (0.2)**	**DCE**	**105**	**24**	**82**
10	$BF_3{\cdot}OEt_2$ (0.2)	DCE	105	12	59
11	$BF_3{\cdot}OEt_2$ (0.2)	DCE	105	30	82
12	$BF_3{\cdot}OEt_2$ (0.2)	toluene	105	24	23
13	$BF_3{\cdot}OEt_2$ (0.2)	THF	105	24	47
14	$BF_3{\cdot}OEt_2$ (0.2)	MeCN	105	24	69
15	–	DCE	105	24	52
16[c]	$BF_3{\cdot}OEt_2$ (0.2)	DCE	105	24	80

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.3 mmol), catalyst, anhyd solvent (2 mL), sealed Schlenk tube, under air.
[b] Isolated yield.
[c] Under N_2.

amides **1** (R^1 = alkyl) (entry 16). The 1-methyl-2-phenylprop-2-enyl amide **1** (R^2 = Me) also gave a good yield of the corresponding product **3ae** (entry 30). The reaction gave a slightly lower yield when R^3 was hydrogen (entries 17–22) or methyl (entry 23), possibly because intermediate **IV** (see below) is more stable for substrates **1** (R^3 = aryl). Substrates **1** (R^4 = H) were more reactive than **1** (R^4 = Me) (entry 31). The reactivities of the 1-(arylsulfanyl)pyrrolidine-2,5-diones (**2**) were not obviously affected by electronic effects of substituents on the aromatic rings. The arylthiooxygenation of *N*-allylamides **1** with 1-(arylsulfanyl)pyrrolidine-2,5-diones **2** tolerates various functional groups, including

Table 2 Arylthiooxygenation of Substituted *N*-Allylamides **1**[a]



Entry	R^1	R^2	R^3	R^4	R^5	Time (h)	Product	Yield[b] (%)
1	Ph	H	Ph	H	H	24	**3a**	82
2	4-Tol	H	Ph	H	H	24	**3b**	77
3	3-Tol	H	Ph	H	H	24	**3c**	67
4	2-Tol	H	Ph	H	H	24	**3d**	92
5	$3,5\text{-}Me_2C_6H_3$	H	Ph	H	H	24	**3e**	70
6	$4\text{-}t\text{-}BuC_6H_4$	H	Ph	H	H	36	**3f**	63
7	$4\text{-}MeOC_6H_4$	H	Ph	H	H	36	**3g**	67
8	$4\text{-}FC_6H_4$	H	Ph	H	H	24	**3h**	71
9	$4\text{-}ClC_6H_4$	H	Ph	H	H	24	**3i**	63
10	$4\text{-}BrC_6H_4$	H	Ph	H	H	24	**3j**	74
11	$4\text{-}O_2NC_6H_4$	H	Ph	H	H	24	**3k**	36
12	$3\text{-}O_2NC_6H_4$	H	Ph	H	H	24	**3l**	55
13	2-thienyl	H	Ph	H	H	24	**3m**	56
14	Ph	H	4-Tol	H	H	24	**3n**	62
15	Ph	H	$4\text{-}ClC_6H_4$	H	H	24	**3o**	85
16	*t*-Bu	H	Ph	H	H	24	**3p**	38
17	Ph	H	H	H	H	24	**3q**	65
18	4-Tol	H	H	H	H	24	**3r**	53
19	$3,5\text{-}Me_2C_6H_3$	H	H	H	H	24	**3s**	51
20	2-naphthyl	H	H	H	H	36	**3t**	53
21	$3\text{-}O_2NC_6H_4$	H	H	H	H	24	**3u**	64
22	2-thienyl	H	H	H	H	24	**3v**	67
23	4-Tol	H	Me	H	H	24	**3w**	65
24	Ph	H	Ph	H	4-Me	24	**3x**	75
25	Ph	H	Ph	H	3-Me	24	**3y**	67
26	Ph	H	Ph	H	4-Cl	24	**3z**	90
27	$4\text{-}ClC_6H_4$	H	Ph	H	4-Cl	24	**3aa**	77
28	Ph	H	Ph	H	2-Cl	24	**3ab**	72
29	Ph	H	Ph	H	$4\text{-}NO_2$	24	**3ac**	72
30	4-Tol	Me	Ph	H	H	24	**3ad**	78
31	4-Tol	H	Ph	Me	H	24	**3ae**	54

[a] Reaction conditions: **1** (0.2 mmol), **2** (0.3 mmol), $BF_3{\cdot}OEt_2$ (0.04 mmol), anhyd DCE (2 mL), 105 °C, sealed Schlenk tube, under air.
[b] Isolated yield.

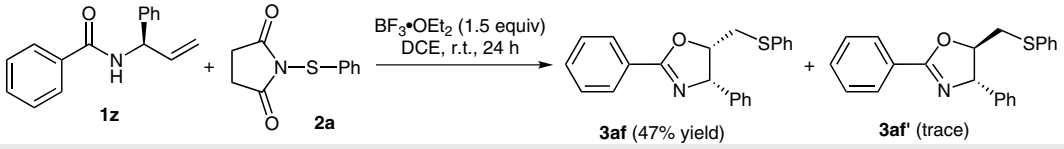
ether (entry 7), fluoro (entry 8), chloro (entries 9, 15, and 26–28), bromo (entry 10), nitro (entries 11, 12, 21, and 29), or 2-thienyl groups (entries 13 and 22).

When the arylthiooxygenation of chiral *N*-[(1*R*)-1-phenylprop-2-en-1-yl]benzamide (**1z**) was investigated in the presence of 1.5 equivalents of boron trifluoride etherate at room temperature for 24 hours, the reaction showed high diastereoselectivity giving (4*S*,5*S*)-2,4-diphenyl-5-[(phenylsulfanyl)methyl]-4,5-dihydro-1,3-oxazole (**3af**) in 47% yield, with only traces of the corresponding (4*S*,5*R*)-isomer **3af'** (Scheme 1).

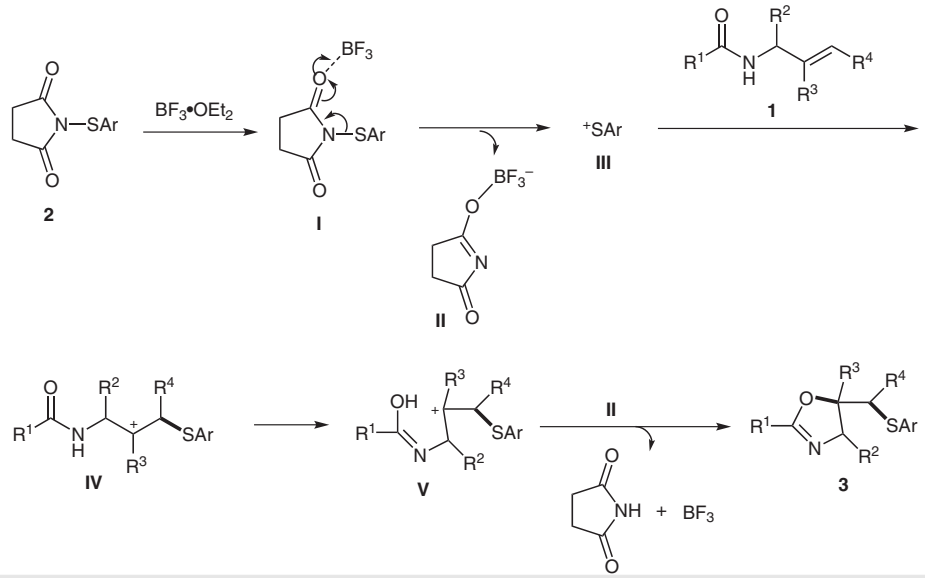
A possible mechanism on the arylthiooxygenation of substituted *N*-allylamides (Scheme 2) is proposed on the basis of the results described above and references from the literature.[18] Treatment of sulfide **2** with boron trifluoride etherate gives complex **I**, which undergoes heterolysis of the N–S bond to form the anionic complex **II** and cation **III**. Electrophilic reaction of **III** with allylic amide **1** gives intermediate **IV**, which isomerizes to give imidic acid **V**. Intramolecular cyclization of **V** in the presence of complex **II** gives the product **3**, with release of succinimide and the catalyst.

We also examined some reactions of the synthesized products. For example, oxidation of oxazole **3z** with 3-chloroperoxybenzoic acid in dichloromethane at room temperature for 12 hours gave the corresponding sulfone **4** in 73% yield (Scheme 3). Sulfone groups are present in many biologically active molecules[19] and are also valuable as synthetic intermediates in organic synthesis;[20] for example, analogues of **4** can be halogenated or alkylated.[21]

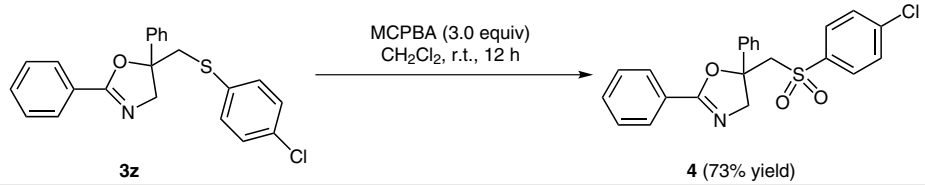
In conclusion, we have developed a simple, efficient, and practical method for the arylthiooxygenation of substituted *N*-allylamides to give arylsulfanyl-substituted oxazoles in good yields. The protocol uses readily available 1-



Scheme 1 Synthesis of the chiral (phenylsulfanyl)oxazoline **3af**



Scheme 2 A possible mechanism for the boron-catalyzed arylthiooxygenation of substituted *N*-allylamides



Scheme 3 Oxidation of (arylsulfanyl)oxazole **3z** to the corresponding sulfone **4**

(arylsulfanyl)pyrrolidine-2,5-diones as the arylsulfanylating reagents and inexpensive boron trifluoride etherate as the catalyst; it requires no ligand or additive, and it is not necessary to expel air from the reaction vessel. The reaction also shows a wide tolerance towards various functional groups. The strategy should therefore have a wide range of applications in synthesis of arylsulfanyl-substituted heterocycles.

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Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0034-1378948.

References

(1) For selected reviews, see: (a) Wipf, P. *Chem. Rev.* **1995**, *95*, 2115. (b) Yeh, V. S. C. *Tetrahedron* **2004**, *60*, 11995. (c) Riego, E.; Hernández, D.; Albericio, F.; Álvarez, M. *Synthesis* **2005**, 1907. (d) Jin, Z. *Nat. Prod. Rep.* **2006**, *23*, 464. For selected papers, see: (e) Adamczeski, M.; Quinoa, E.; Crews, P. *J. Am. Chem. Soc.* **1988**, *110*, 1598. (f) Lindquist, N.; Fenical, W.; Van Duyne, G. D.; Clardy, J. *J. Am. Chem. Soc.* **1991**, *113*, 2303. (g) Li, J.; Jeong, S.; Esser, L.; Harran, P. G. *Angew. Chem. Int. Ed.* **2001**, *40*, 4765. (h) Skepper, C. K.; Quach, T.; Molinski, T. F. *J. Am. Chem. Soc.* **2010**, *132*, 10286.

(2) (a) Turchi, I. J.; Dewar, M. J. S. *Chem. Rev.* **1975**, *75*, 389. (b) Wasserman, H. H.; McCarthy, K. E.; Prowse, K. S. *Chem. Rev.* **1986**, *86*, 845. (c) Jin, Z. *Nat. Prod. Rep.* **2003**, *20*, 584. (d) Wipf, P.; Aoyama, Y.; Benedum, T. E. *Org. Lett.* **2004**, *6*, 3593. (e) Jin, Z. *Nat. Prod. Rep.* **2009**, *26*, 382. (f) Wan, C.; Gao, L.; Wang, Q.; Zhang, J.; Wang, Z. *Org. Lett.* **2010**, *12*, 3902. (g) He, W.; Li, C.; Zhang, L. *J. Am. Chem. Soc.* **2011**, *133*, 8482. (h) Cano, I.; Álvarez, E.; Nicasio, M. C.; Pérez, P. J. *J. Am. Chem. Soc.* **2011**, *133*, 191. (i) Badillo, J. J.; Arevalo, G. E.; Fettinger, J. C.; Franz, A. K. *Org. Lett.* **2011**, *13*, 418.

(3) (a) Liu, L.; Stelmach, J. E.; Natarajan, S. R.; Chen, M.-H.; Singh, S. B.; Schwartz, C. D.; Fitzgerald, C. E.; O'Keefe, S. J.; Zaller, D. M.; Schmatz, D. M.; Doherty, J. B. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 3979. (b) Kaldor, S. W.; Kalish, V. J.; Davies, J. F.; Shetty, B. V.; Fritz, J. E.; Appelt, K.; Burgess, J. A.; Campanale, K. M.; Chirgadze, N. Y.; Clawson, D. K.; Dressman, B. A.; Hatch, S. D.; Khalil, D. A.; Kosa, M. B.; Lubbehusen, P. P.; Muesing, M. A.; Patick, A. K.; Reich, S. H.; Su, K. S.; Tatlock, J. H. *J. Med. Chem.* **1997**, *40*, 3979.

(4) (a) Hartwig, J. F. *Angew. Chem. Int. Ed.* **1998**, *37*, 2046. (b) Wolfe, J. P.; Wagaw, S.; Marcoux, J.-F.; Buchwald, S. L. *Acc. Chem. Res.* **1998**, *31*, 805. (c) Hassan, J.; Sévignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 1359. (d) Beletskaya, I. P.; Cheprakov, A. V. *Coord. Chem. Rev.* **2004**, *248*, 2337. (e) Corbet, J.-P.; Mignani, G. *Chem. Rev.* **2006**, *106*, 2651. (f) Tran, L. D.; Popov, I.; Daugulis, O. *J. Am. Chem. Soc.* **2012**, *134*, 18237. (g) Yang, Y.; Hou, W.; Qin, L.; Du, J.; Feng, H.; Zhou, B.; Li, Y. *Chem. Eur. J.* **2014**, *20*, 416.

(5) For reviews on transition-metal-catalyzed C–S coupling reaction, see: (a) Kondo, T.; Mitsudo, T.-a. *Chem. Rev.* **2000**, *100*, 3205. (b) Ley, S. V.; Thomas, A. W. *Angew. Chem. Int. Ed.* **2003**, *42*, 5400. (c) Eichman, C. C.; Stambuli, J. P. *Molecules* **2011**, *16*, 590. (d) Liu, H.; Jiang, X. *Chem. Asian J.* **2013**, *8*, 2546.

(6) (a) Abd El Samii, Z. K. M.; Al Ashmawy, M. I.; Mellor, J. M. *J. Chem. Soc., Perkin Trans. 1* **1988**, 2517. (b) Abd El Samii, Z. K. M.; Al Ashmawy, M. I.; Mellor, J. M. *Tetrahedron Lett.* **1987**, *28*, 1949.

(7) (a) McDonald, R. I.; Liu, G.; Stahl, S. S. *Chem. Rev.* **2011**, *111*, 2981. (b) Muñiz, K. *Angew. Chem. Int. Ed.* **2009**, *48*, 9412. (c) Jacques, B.; Muñiz, K. In *Catalyzed Carbon–Heteroatom Bond Formation*; Yudin, A. K., Ed.; Wiley-VCH: Weinheim, **2011**, Chap. 4, 119.

(8) (a) Li, Y.; Song, D.; Dong, V. M. *J. Am. Chem. Soc.* **2008**, *130*, 2962. (b) Wang, A.; Jiang, H.; Chen, H. *J. Am. Chem. Soc.* **2009**, *131*, 3846. (c) Giglio, B. C.; Schmidt, V. A.; Alexanian, E. J. *J. Am. Chem. Soc.* **2011**, *133*, 13320.

(9) (a) Zhu, R.; Buchwald, S. L. *Angew. Chem. Int. Ed.* **2012**, *51*, 1926. (b) Wang, H.; Wang, Y.; Liang, D.; Liu, L.; Zhang, J.; Zhu, Q. *Angew. Chem. Int. Ed.* **2011**, *50*, 5678. (c) Desai, L. V.; Sanford, M. S. *Angew. Chem. Int. Ed.* **2007**, *46*, 5737. (d) Liu, G.; Stahl, S. S. *J. Am. Chem. Soc.* **2006**, *128*, 7179. (e) Alexanian, E. J.; Lee, C.; Sorensen, E. J. *J. Am. Chem. Soc.* **2005**, *127*, 7690. (f) Fuller, P. H.; Kim, J.-W.; Chemler, S. R. *J. Am. Chem. Soc.* **2008**, *130*, 17638. (g) Lovick, H. M.; Michael, F. E. *J. Am. Chem. Soc.* **2010**, *132*, 1249. (h) de Haro, T.; Nevado, C. *Angew. Chem. Int. Ed.* **2011**, *50*, 906.

(10) (a) Ingalls, E. L.; Sibbald, P. A.; Kaminsky, W.; Michael, F. E. *J. Am. Chem. Soc.* **2013**, *135*, 8854. (b) Zhao, B.; Peng, X.; Zhu, Y.; Ramirez, T. A.; Cornwall, R. G.; Shi, Y. *J. Am. Chem. Soc.* **2011**, *133*, 20890. (c) Röben, C.; Souto, J. A.; González, Y.; Lishchynskyi, A.; Muñiz, K. *Angew. Chem. Int. Ed.* **2011**, *50*, 9478. (d) Iglesias, Á.; Pérez, E. G.; Muñiz, K. *Angew. Chem. Int. Ed.* **2010**, *49*, 8109. (e) Sibbald, P. A.; Rosewall, C. F.; Swartz, R. D.; Michael, F. E. *J. Am. Chem. Soc.* **2009**, *131*, 15945. (f) Muñiz, K.; Hövelmann, C. H.; Streuff, J. *J. Am. Chem. Soc.* **2008**, *130*, 763. (g) Bar, G. L. J.; Lloyd-Jones, G. C.; Booker-Milburn, K. I. *J. Am. Chem. Soc.* **2005**, *127*, 7308.

(11) (a) Wu, T.; Yin, G.; Liu, G. *J. Am. Chem. Soc.* **2009**, *131*, 16354. (b) Li, Z.; Song, L.; Li, C. *J. Am. Chem. Soc.* **2013**, *135*, 4640. (c) Kong, W.; Feige, P.; de Haro, T.; Nevado, C. *Angew. Chem. Int. Ed.* **2013**, *52*, 2469.

(12) (a) Michael, F. E.; Sibbald, P. A.; Cochran, B. M. *Org. Lett.* **2008**, *10*, 793. (b) Muñiz, K.; Höelmann, C. H.; Campos-Gómez, E.; Barluenga, J.; González, J. M.; Streuff, J.; Nieger, M. *Chem. Asian J.* **2008**, *3*, 776. (c) Bovino, M. T.; Chemler, S. R. *Angew. Chem. Int. Ed.* **2012**, *51*, 3923.

(13) (a) Zhang, B.; Studer, A. *Org. Lett.* **2013**, *15*, 4548. (b) Trahanovsky, W. S.; Robbins, M. D. *J. Am. Chem. Soc.* **1971**, *93*, 5256.

(14) For selected examples, see: (a) Deb, A.; Manna, S.; Modak, A.; Patra, T.; Maity, S.; Maiti, D. *Angew. Chem. Int. Ed.* **2013**, *52*, 9747. (b) Jiang, X.-Y.; Qing, F.-L. *Angew. Chem. Int. Ed.* **2013**, *52*, 14177. (c) Zhu, R.; Buchwald, S. L. *Angew. Chem. Int. Ed.* **2013**, *52*, 12655. (d) Egami, H.; Kawamura, S.; Miyazaki, A.; Sodeoka, M. *Angew. Chem. Int. Ed.* **2013**, *52*, 7841. (e) Zhu, R.; Buchwald, S. L. *J. Am. Chem. Soc.* **2012**, *134*, 12462. (f) Feng, C.; Loh, T.-P. *Chem. Sci.* **2012**, *3*, 3458. (g) Li, Y.; Studer, A. *Angew. Chem. Int. Ed.* **2012**, *51*, 8221. (h) Yasu, Y.; Koike, T.; Akita, M. *Angew. Chem. Int. Ed.* **2012**, *51*, 9567.

(15) For selected examples, see: (a) Egami, H.; Shimizu, R.; Kawamura, S.; Sodeoka, M. *Angew. Chem. Int. Ed.* **2013**, *52*, 4000. (b) Wei, W.-T.; Zhou, M.-B.; Fan, J.-H.; Liu, W.; Song, R.-J.; Liu, Y.; Hu, M.; Xie, P.; Li, J.-H. *Angew. Chem. Int. Ed.* **2013**, *52*, 3638. (c) Zhou, M.-B.; Song, R.-J.; Ouyang, X.-H.; Liu, Y.; Wei, W.-T.; Deng, G.-B.; Li, J.-H. *Chem. Sci.* **2013**, *4*, 2690. (d) Wu, T.; Mu, X.; Liu, G. *Angew. Chem. Int. Ed.* **2011**, *50*, 12578. (e) Piou, T.; Neuville, L.; Zhu, J. *Angew. Chem. Int. Ed.* **2012**, *51*, 11561. (f) Li, Y.-M.; Sun, M.; Wang, H.-L.; Tian, Q.-P.; Yang, S.-D. *Angew. Chem. Int. Ed.* **2013**, *52*, 3972. (g) Chen, Y.-R.; Duan, W.-L. *J. Am. Chem. Soc.* **2013**, *135*, 16754. (h) Zhang, C.; Li, Z.; Zhu, L.; Yu, L.; Wang, Z.; Li, C. *J. Am. Chem. Soc.* **2013**, *135*, 14082. (i) Matcha, K.; Narayan, R.; Antonchick, A. P. *Angew. Chem. Int. Ed.* **2013**, *52*, 7985.

(16) For selected examples, see: (a) Mu, X.; Wu, T.; Wang, H.-y.; Guo, Y.-l.; Liu, G. *J. Am. Chem. Soc.* **2012**, *134*, 878. (b) Xu, P.; Xie, J.; Xue, Q.; Pan, C.; Cheng, Y.; Zhu, C. *Chem. Eur. J.* **2013**, *19*, 14039. (c) Dong, X.; Song, R.; Wang, Q.; Tang, X.-Y.; Shi, M. *Chem. Eur. J.* **2013**, *19*, 16910. (d) Egami, H.; Shimizu, R.; Sodeoka, M. *J. Fluorine Chem.* **2013**, *152*, 51. (e) Yang, F.; Klumpha, P.; Liang, Y.-M.; Lipshutz, B. H. *Chem. Commun.* **2014**, *50*, 936. (f) Lu, Q.; Liu, C.; Peng, P.; Liu, Z.; Fu, L.; Huang, J.; Lei, A. *Asian J. Org. Chem.* **2014**, *3*, 273. (g) Fu, W.; Xu, F.; Fu, Y.; Zhu, M.; Yu, J.; Xu, C.; Zou, D. *J. Org. Chem.* **2013**, *78*, 12202. (h) Zhou, B.; Hou, W.; Yang, Y.; Feng, H.; Li, Y. *Org. Lett.* **2014**, *16*, 1322. (i) Shi, L.; Yang, X.; Wang, Y.; Yang, H.; Fu, H. *Adv. Synth. Catal.* **2014**, *356*, 1021. (j) Shi, L.; Wang, Y.; Yang, H.; Fu, H. *Org. Biomol. Chem.* **2014**, *12*, 4070. (k) Kong, W.; Casimiro, M.; Merino, E.; Nevado, C. *J. Am. Chem. Soc.* **2013**, *135*, 14480.

(17) **5-(Arylsulfanyl)-4,5-dihydro-1,3-oxazoles 3a–af; General Procedure**

A 25-mL Schlenk tube containing a magnetic stirrer was charged with allylamide **1** (0.2 mmol), 1-(arylthio)pyrrolidine-2,5-dione **2** (0.3 mmol), and anhyd DCE (2.0 mL). $BF_3{\cdot}OEt_2$ (0.04 mmol) was added, the tube was sealed, and the mixture was stirred at 105 °C until the reaction was complete (TLC). The solution was concentrated in a rotary evaporator and the residue was purified by column chromatography (silica gel, PE–EtOAc). Data for three representative products are given below.

5-Phenyl-5-[(phenylsulfanyl)methyl]-2-(4-tolyl)-4,5-dihydro-1,3-oxazole (3b)

Eluent: PE–EtOAc (5:1); colorless film; yield: 55 mg (77%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.79 (d, *J* = 7.4 Hz, 2 H), 7.42–7.29 (m, 7 H), 7.21–7.13 (m, 5 H), 4.47 (d, *J* = 14.7 Hz, 1 H), 4.22 (d, *J* = 14.7 Hz, 1 H), 3.62 (d, *J* = 13.9 Hz, 1 H), 3.51 (d, *J* = 13.9 Hz, 1 H), 2.40 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.2, 143.7, 141.9, 136.5, 130.4, 129.1, 128.9, 128.7, 128.3, 127.9, 126.5, 124.9, 124.8, 88.6, 66.5, 46.1, 21.7.

ESI-MS: *m/z* = 360.4 $[M + H]^+$.

5-[(Phenylsulfanyl)methyl]-2-(2-thienyl)-4,5-dihydro-1,3-oxazole (3v)

Eluent: PE–EtOAc (5:1); colorless film; yield: 37 mg (67%).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.49 (d, *J* = 3.3 Hz, 1 H), 7.40 (d, *J* = 7.4 Hz, 3 H), 7.27 (t, *J* = 7.7 Hz, 2 H), 7.20 (t, *J* = 7.4 Hz, 1 H), 7.03 (t, *J* = 4.3 Hz, 1 H), 4.84–4.79 (m, 1 H), 4.11 (dd, *J* = 14.8, 9.4 Hz, 1 H), 3.85 (dd, *J* = 14.8, 6.7 Hz, 1 H), 3.31 (dd, *J* = 13.8, 5.4 Hz, 1 H), 3.05 (dd, *J* = 13.8, 7.2 Hz, 1 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 159.7, 134.9, 130.5, 130.4, 130.2, 130.0, 129.2, 127.6, 126.9, 78.9, 59.7, 38.4.

ESI-MS: *m/z* = 298.3 $[M + Na]^+$.

4-Methyl-5-phenyl-5-[(phenylsulfanyl)methyl]-2-(4-tolyl)-4,5-dihydro-1,3-oxazole (3ad)

Eluent: PE–EtOAc (5:1); light-yellow film; yield: 58 mg (78%).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.78 (d, *J* = 8.1 Hz, 2 H), 7.36 (t, *J* = 7.4 Hz, 2 H), 7.33–7.28 (m, 5 H), 7.19 (d, *J* = 8.0 Hz, 2 H), 7.15 (d, *J* = 7.3 Hz, 2 H), 7.11 (t, *J* = 7.2 Hz, 1 H), 4.46 (q, *J* = 6.9 Hz, 1 H), 3.67 (s, 2 H), 2.40 (s, 3 H), 0.84 (d, *J* = 6.9 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.1, 142.1, 139.0, 136.8, 130.4, 129.1, 128.9, 128.5, 128.3, 127.7, 126.4, 125.9, 124.6, 91.4, 70.4, 45.4, 21.7, 19.4.

ESI-MS: *m/z* = 374.1 $[M + H]^+$.

(18) (a) Prakash, G. K. S.; Mathew, T.; Hoole, D.; Esteves, P. M.; Wang, Q.; Rasul, G.; Olah, G. A. *J. Am. Chem. Soc.* **2004**, *126*, 15770. (b) Tian, H.; Zhu, C.; Yang, H.; Fu, H. *Chem. Commun.* **2014**, *50*, 8875.

(19) (a) Ettari, R.; Nizi, E.; Di Francesco, M. E.; Dude, M.-A.; Pradel, G.; Vičík, R.; Schirmeister, T.; Micale, N.; Grasso, S.; Zappalà, M. *J. Med. Chem.* **2008**, *51*, 988. (b) Bachovchin, D.; Zuhl, A.; Speers, A.; Wolfe, M.; Weerapana, E.; Brown, S.; Rosen, H.; Cravatt, B. *J. Med. Chem.* **2011**, *54*, 5229. (c) Neamati, N.; Mazumder, A.; Zhao, H.; Sunder, S.; Burke, T. R. Jr.; Schultz, R. J.; Pommier, Y. *Antimicrob. Agents Chemother.* **1997**, *41*, 385. (d) Colwell, W. T.; Chan, G.; Brown, V. H.; DeGraw, J. I.; Peters, J. H.; Morrison, N. E. *J. Med. Chem.* **1974**, *17*, 142. (e) Sharpe, T. R.; Cherkofsky, S. C.; Hewes, W. E.; Smith, D. H.; Gregory, W. A.; Haber, S. B.; Leadbetter, M. R.; Whitney, J. G. *J. Med. Chem.* **1985**, *28*, 1188. (f) Jones, T. R.; Webber, S. E.; Varney, M. D.; Rami Reddy, M.; Lewis, K. K.; Kathardekar, V.; Mazdiyasni, H.; Deal, J.; Nguyen, D.; Welsh, K. M.; Webber, S.; Johnston, A.; Matthews, D. A.; Smith, W. W.; Janson, C. A.; Bacquet, R. J.; Howland, E. F.; Booth, C. L. J.; Herrmann, S. M.; Ward, R. W.; White, J.; Bartlett, C. A.; Morse, C. A. *J. Med. Chem.* **1997**, *40*, 677.

(20) (a) *Tetrahedron Organic Chemistry Series*; Vol. 10; Simpkins, N. S., Ed.; Elsevier: Amsterdam, **1993**, 1. (b) Procter, D. J. *J. Chem. Soc., Perkin Trans. 1* **2000**, 835.

(21) Shen, T.; Yuan, Y.; Song, S.; Jiao, N. *Chem. Commun.* **2014**, *50*, 4115.