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Synthesis of Extended Oxazoles III: Reactions of 2-(Phenylsulfonyl)methyl-4,5-diaryloxazoles

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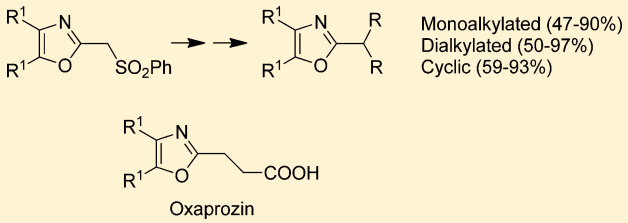
Supporting Information

ABSTRACT: 2-((Phenylsulfonyl)methyl)-4,5-diphenyloxazole is a useful scaffold for synthetic elaboration at the 2-methylene position thereby affording extended oxazoles. The corresponding α-sulfonyl anion reacts smoothly with diverse alkyl halides giving monoalkylated (47−90%), dialkylated (50−97%), and cyclic (59−93%) products. The reductive desulfonylation of the monoalkylated and selected dialkylated products was optimized with a magnesium/mercuric chloride reagent system and afforded desulfonylated products in the range of 66−97%. The anti-inflammatory Oxaprozin was prepared using the α-sulfonyl carbanion strategy along with optimized desulfonylation.



The utilization of α-sulfonyl carbanions in a carbon−carbon bond forming strategy takes advantage of mild reaction conditions and is applicable to the synthetic elaboration of many types of preformed oxygen and nitrogen heterocycles.[1] For example, the Ciufolini group prepared and utilized a dual-functionalized 2-(phenylsulfonylmethyl)-4,5-disubstituted oxazole as a conjunctive intermediate in their synthesis of the siphonazoles.[2] 3-(Phenylsulfonylmethyl)oxindoles, 3- and 4-(arylsulfonyl-methyl)pyridines, 2-(arylsulfonylmethyl)-quinolines, and 2-(phenylsulfonylmethyl)pyrimidines have been designed so that the sulfonyl-activated methylene group facilitates the construction of extended or otherwise more elaborate fused heterocycles.[3] In medicinal chemistry, the need for increased structural diversity and large numbers of therapeutic candidates as potential anti-inflammatories has driven the strategy for extension and elaboration at the 2-position of 2-substituted-4,5-diaryloxazoles.[4] As functioning units in total synthesis, 2-substituted 4,5-diaryloxazoles carry with them a fully masked carboxyl group, thereby allowing a great range of reactions to be performed on the synthon prior to the release of the carboxylate.[5] Hence the strategy whereby the carboxyl group, embedded in 4,5-diaryloxazole framework and oxidatively deprotected in later stages, was put to practice by the Evans group in their synthesis of oasomycin.[6] Therefore, the development of carbon−carbon bond-forming methods at the 2-methylene position of the trisubstituted oxazole would be a complementary strategy to the use of the heterocycle as a protecting group. Our ongoing work with the use of 2,4,5-trisubstituted oxazole scaffolds as "click"[7] components of biofilm inhibitors involved the preparation of several 2-(azidoalkyl)- and 2-(azidoaryl)-substituted 4,5-diaryloxazoles.[8] In a previous communication we described the functionalization of 2-(halomethyl)-4,5-diaryloxazoles using an array of nitrogen, oxygen, and sulfur nucleophiles.[8b] Our examples included the preparation of 2-(phenylthiomethyl)-4,5-diphenyl oxazole **2** from the corresponding 2-(chloromethyl)-4,5-diphenyloxazole **1** and thiophenol (Figure 1). Oxidation of **2** with 3-chloroperbenzoic acid (MCPBA, 2.5 eq/CH_2Cl_2/rt)

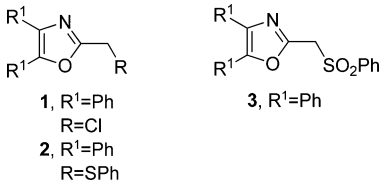


Figure 1. 2-Substituted-4,5-diphenyloxazole scaffolds.

gave the corresponding sulfone **3** (84%) as a crystalline solid. We note that during the MCPBA oxidation the intermediate sulfoxide could be detected and isolated. In our initial experiments, deprotonation of **3** with commercially available potassium *tert*-butoxide (1.1 equiv) in THF followed by slow addition of iodomethane (1.05 eq, 5 °C to rt) gave the 2-(α-sulfonylethyl)-4,5-diphenyloxazole **5** (90%, Table 1). Similarly, the monoalkylated sulfones **6**, **7**, **8**, and **9** could be prepared in isolated yields ranging from 47% to 76% (Table 1). In almost all cases, a small amount of dialkylated product was detected by thin-layer chromatography (TLC) and was easily separable from the monoalkylated product by column chromatography. Dialkylated products were then targeted which required the employment of 2.5 equiv of base followed by 2.5 equiv of an alkylating agent (Table 1, compounds **11**−**14**). For the examples in which the alicyclic sulfones **15**−**17** were prepared (Table 1), conditions similar to the dialkylation experiments were employed. Hence, 2.2 equiv of base followed by 1 equiv of a dihaloalkane was used (see **15**, **16**, and **17**). Interestingly,

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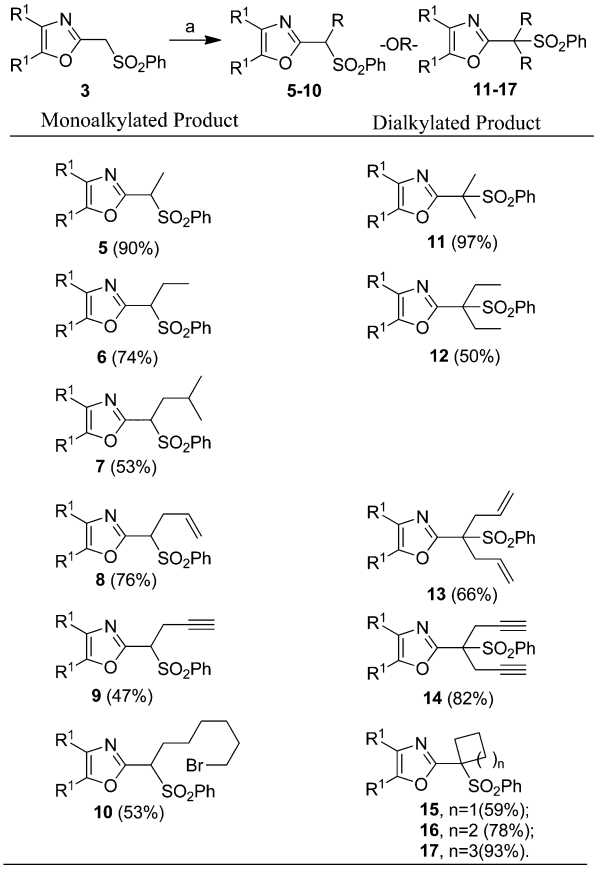
Table 1. Alkylation of 2-(Sulfonylmethyl)-4,5-Diphenyloxazoles[a]

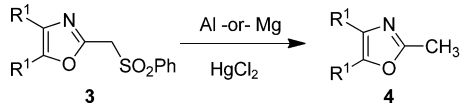


[a]Reagents/Conditions: (a) KO*t*-Bu/THF/5 °C to rt; **5**,**11**/MeI; **6**,**12**/EtI; **7**/iso-BuI; **8**,**13**/allyl-Br; **9**,**14**/propargyl-Br; **10**/1,6-dibromohexane; **15**/1,3-diiodopropane; **16**/1,4-dibromobutane; **17**/1,5-dibromopentane.

alkylation of **3** with 1,6-dibromohexane under conditions of dialkylation provided only the bromohexyl homologue **10** (Table 1) and no seven-member sulfonyloxazole despite heating over extended reaction periods.

Examination of the reagents and conditions for reductive desulfonylation of many of the synthetic intermediates and products listed in Table 1 were warranted as well as determination of the optimal conditions for β-elimination of the phenylsulfonyl group.[9] Such complementary transformations involving deletion of the sulfonyl group would broaden the scope and utility of the heterocyclic sulfone alkylation scheme. While reductive desulfonylation with Raney nickel precluded its employment with substrates **8**, **9**, **13**, and **14** due to unwanted reduction of unsaturated sites, we found it ineffective with simple substrates such as sulfonylmethyloxazole **3**. Attempted reductive desulfonylation of **3** with amalgamated active metals such as zinc and magnesium, including the classical "15-second" amalgamated aluminum foil method of Corey,[10] were of no consequence and led to the recovery of only unreacted substrate. Interestingly, some definitive changes to the Corey aluminum-mediated desulfonylation method, however, did lead to positive results (eq 1).

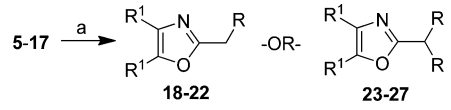
The addition of solid mercuric chloride to a mixture of food-grade aluminum foil and sulfone **3** in methanol was optimal for the conversion of the 2-(phenylsulfonylmethyl)oxazole **3** to the 2-methyloxazole **4** (eq 1). The heterogeneous mixture required



(1)

heating at reflux until the aluminum metal disappeared and afforded the 2-methyl-4,5-diphenyloxazole **4** cleanly in 96% yield after workup and chromatography. In separate experiments, the 2-(phenylsulfonylmethyl)oxazole **3** was desulfonylated to provide **4** in 98% isolated yield using magnesium turnings with solid mercuric chloride in methanol.[11] However, the aluminum/$HgCl_2$ desulfonylation was not optimal for unsaturated substrate **8** or **9** (Table 2), so the same conditions

Table 2. Magnesium/$HgCl_2$/Methanol-Mediated Desulfonylation of 4−17[a]



Sulfone	Product (%)	Sulfone	Product (%)
5	**18** (97%)[b]	**11**	**23** (90%)
6	**19** (76%)	**12**	**24** (82%)
7	**20** (66%)	**15,16,17**	**25**, n=1(69%); **26**, n=2 (92%), **27**, n=3(97%),
8	**21** (97%)[b]		
9	**22** (96%)[b]		

[a]Reagents/Conditions: magnesium(turnings)/$HgCl_2$/MeOH/rt/2 h. [b]Using aluminum: **18** (95%); **21**, **22** (<33%).

for the magnesium-mediated reductive desulfonylation of **3** were applied to the entire range of mono- and dialkylated sulfone substrates **5**−**9**, **11**−**12**, and **15**−**17**. The desulfonylated products **18**−**24** and **25**−**27** (Table 2) were obtained as pure compounds after column chromatography on silica gel. The synthetic utility of oxazole sulfone **3** is demonstrated by our synthesis of the nonsteroidal anti-inflammatory Oxaprozin **32** (Scheme 1).[12] In contrast to our earlier communication where we described the preparation of Oxaprozin using the electrophilic (chloroalkyl)oxazole synthon **1**,[8a] we now employ the readily prepared and versatile nucleophilic scaffold **3**. Deprotonation of **3** (5 °C/KO*t*-Bu/THF) followed by addition of ethyl bromoacetate (5 °C to rt) afforded the β-sulfonyl ester **28** (72%). Base-mediated (5 °C/KO*t*-Bu/THF) elimination of the phenylsulfonyl group from **28** provided the α,β-unsaturated ester **29** (65%). Catalytic reduction of the unsaturated ester **29**

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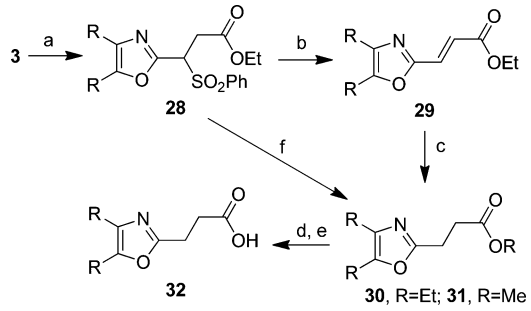
Scheme 1. Synthesis of Oxaprozin 32 from Sulfone 3[a]



[a]Reagents/Conditions: (a) KO-*t*-Bu/ethyl bromoacetate/THF/5 °C to rt/16 h (72%); (b) KO-*t*-Bu/THF/5−10 °C/2 h (65%); (c) H_2/10% Pd−C/MeOH/rt/16 h (80%); (d) 20% aqueous NaOH/rt/16 h; (e) Conc. HCl/75 °C/3 h (68%, from d); (f) Mg/$HgCl_2$/MeOH/rt/16 h (97%).

(H_2/10% Pd−C/MeOH) gave Oxaprozin ethyl ester **30** (80%). Alternatively, **28** could be reductively desulfonylated (Mg/$HgCl_2$/MeOH) which gives rise to the methyl ester **31** of oxaprozin through transesterification. Mild hydrolysis of the ethyl ester group of **30** with dilute aqueous acid then afforded Oxaprozin **32** (68%).

In summary, we have demonstrated the synthetic utility of a basic trisubstituted heterocyclic scaffold that has potential applications in synthetic and medicinal chemistry. Single and multiple carbon−carbon bond-forming reactions may be executed as well as effective removal of the activating phenylsulfonyl group within the diaryloxazole scaffold. A new synthesis of the extended oxazole nonsteroidal anti-inflammatory compound Oxaprozin was demonstrated and utilized the sulfonylmethyl synthon **3** which further demonstrated that it is well-suited for its application in the preparation of diverse analogues.

EXPERIMENTAL SECTION

Solvents and reagents are ACS grade and were used as commercially supplied. Analytical thin-layer chromatography (TLC) utilized 0.25 mm precut glass-backed plates (Silica Gel 60 F_{254}). Thin-layer chromatograms were visualized during chromatographic and extraction runs by rapidly dipping the plates in anisaldehyde/ethanol/sulfuric acid stain or phosphomolybdic acid/ethanol stain and heating (hot plate). Column chromatography was carried out in gravity mode using silica gel 60 (70−230 mesh) and used combinations of hexanes and ethyl acetate. Melting points were determined on a capillary melting point apparatus and are uncorrected. Reaction mixtures, extracts, and chromatographic fractions were concentrated with a standard rotary evaporator under water aspirator vacuum. Nuclear magnetic resonance (^{1}H and ^{13}C NMR) spectra were recorded with 400 MHz (100 MHz, ^{13}C) or 700 MHz (175 MHz, ^{13}C) instruments using $CDCl_3$ as a solvent and TMS as the internal standard. Infrared spectra (Fourier Transform Infrared Spectroscopy, FTIR) were analyzed as films and are reported in wavenumbers (cm^{-1}).

4,5-Diphenyl-2-((phenylsulfonyl)methyl)oxazole (3). To a prechilled solution of 4,5-diphenyl-2-((phenylthio)methyl)oxazole **2** (1.0 g, 2.91 mmol) in dichloromethane (40 mL) was added MCPBA (1.26 g, 7.27 mmol) while stirring. The reaction mixture was stirred at room temperature (3 h). After completion of the reaction as indicated by TLC, the reaction mixture was washed with saturated aqueous $NaHCO_3$ (2 × 30 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated. The crude residue was submitted to gravity-column chromatography on silica gel (hexane/ethyl acetate, 9:1) to afford **3** as white crystals (0.92 g, 84%); mp 94−96 °C; R_f = 0.26 (hexane/ethyl acetate, 5:1); FT-IR (neat film): 3067, 2972, 1558, 1318, 1148 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, J = 8.4 Hz, 2H), 7.70−7.67 (m, 1H), 7.57−7.47 (m, 6H), 7.35−7.34 (m, 6H), 4.66 (s, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.5, 147.6, 138.2, 136.2, 134.3, 131.6, 129.3, 129.1, 128.7, 128.65, 128.60, 128.4, 128.1, 127.9, 126.6, 55.9 ppm; HRMS (ESI-TOF) m/z calcd for $C_{22}H_{17}NO_3S$ $[M + H]^+$ 376.1007, found 376.1019.

General Procedure for the Preparation of Alkylated Sulfones (5−17). To a stirred solution of 2-(phenylsulfonyl)-methyl-4,5-diphenyloxazole **3** (0.27 mmol, 1.0 equiv) in dry THF (10 mL) was added potassium *tert*-butoxide (0.29 mmol, 1.1 equiv) at 5 °C. Stirring of the resultant yellow reaction mixture was continued under a nitrogen atmosphere (30 min). The alkyl halide (0.028 mmol, 1.05 equiv) was then slowly added to the reaction mixture by syringe, and the reaction mixture was allowed to warm to room temperature and stirring was continued (16 h). At the end of the reaction period, cold water (10 mL) was added to the reaction mixture followed by extraction with dichloromethane (2 × 20 mL). The organic layers were combined, washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated. The crude residue was submitted to gravity-column chromatography (hexane/ethyl acetate, 9:1) to afford the corresponding products **5−10**. For the preparation of the dialkylated compounds **11−14** the same procedure was used with the exception that potassium *tert*-butoxide (0.66 mmol, 2.5 equiv) and corresponding alkylating reagent (0.66 mmol, 2.5 equiv) were employed. For the cyclic compounds **15−17**, potassium *tert*-butoxide (0.58 mmol, 2.2 equiv) and dihaloalkane (0.29 mmol, 1.1 equiv) were employed. The methods for purification of **11−17** were the same as those for the monoalkyl sulfones **5−10**.

4,5-Diphenyl-2-(1-(phenylsulfonyl)ethyl)oxazole (5). Off-white solid (93 mg, 90%); mp 95−97 °C; R_f = 0.25 (hexane/ethyl acetate, 4:1); FT-IR (neat film): 3069, 2974, 1562, 1446, 1319, 1147 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73−7.70 (m, 2H), 7.56 (t, J = 7.4 Hz, 1H), 7.45−7.38 (m, 6H), 7.27−7.25 (m, 6H), 4.57 (q, J = 7.6 Hz, 1H), 1.82 (d, J = 6.8 Hz, 3H) ppm; ^{13}C NMR (175 MHz, $CDCl_3$) δ 155.5, 147.0, 136.7, 136.0, 134.2, 131.7, 129.3, 128.99, 128.97, 128.7, 128.6, 128.4, 128.1, 128.0, 126.6, 60.5, 12.2 ppm; HRMS (ESI-TOF) m/z calcd for $C_{23}H_{19}NO_3S$ $[M + H]^+$ 390.1164, found 390.1180.

4,5-Diphenyl-2-(1-phenylsulfonyl)propyl)oxazole (6). Colorless oil (80 mg, 74%); R_f = 0.25 (hexane/ethyl acetate, 4:1); FT-IR (neat film): 3060, 2974, 1558, 1446, 1319, 1148 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78−7.76 (m, 2H), 7.65−7.61 (m, 1H), 7.51−7.46 (m, 6H), 7.37−7.32 (m, 6H), 4.43 (dd, J = 11.6 Hz, 4.0 Hz, 1H), 2.49−2.39 (m, 1H), 2.38−2.31 (m, 1H), 1.06 (t, J = 7.6 Hz, 3H) ppm; ^{13}C NMR (175 MHz, $CDCl_3$) δ 154.8, 147.1, 137.2, 136.0, 134.1, 131.7, 129.2, 129.0, 128.9, 128.7, 128.6, 128.4, 128.2, 127.9, 126.5, 67.3, 20.5, 11.7 ppm; HRMS (ESI-TOF) m/z calcd for $C_{24}H_{21}NO_3S$ $[M + H]^+$ 404.1320, found 404.1332.

2-(3-Methyl-1-(phenylsulfonyl)butyl)-4,5-diphenyloxazole (7). Colorless oil (61 mg, 53%); R_f = 0.36 (hexane/ethyl acetate, 4:1); FT-IR (neat film): 3064, 1447, 1322, 1149, 1084 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J = 7.6 Hz, 2H), 7.62 (t, J = 7.6 Hz, 1H), 7.51−7.46 (m, 6H), 7.35−7.33 (m, 6H), 4.58 (dd, J = 11.6 Hz, 4.0 Hz, 1H), 2.36 (ddd, J = 16.8 Hz, 12.0 Hz, 4.4 Hz, 1H), 2.17 (ddd, J = 16.8 Hz, 9.2 Hz, 4.4 Hz, 1H), 1.70−1.64 (m, 1H), 0.95 (t, J = 6.8 Hz, 6H) ppm; ^{13}C NMR (175 MHz, $CDCl_3$) δ 155.0, 147.0, 137.3, 135.9, 134.0, 131.7, 129.1, 128.94, 128.93, 128.6, 128.5, 128.3, 128.2, 127.9, 126.5, 64.5, 34.8, 26.0, 23.0, 21.3 ppm; HRMS (ESI-TOF) m/z calcd for $C_{26}H_{25}NO_3S$ $[M + H]^+$ 432.1633, found 432.1648.

4,5-Diphenyl-2-(1-(phenylsulfonyl)but-3-enyl)oxazole (8). Colorless oil (84 mg, 76%); R_f = 0.28 (hexane/ethyl acetate, 4:1); FT-IR (neat film): 3065, 2915, 1553, 1447, 1299, 1134 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.78 (d, J = 8.4 Hz, 2H), 7.64 (t, J = 7.7 Hz, 1H), 7.51−7.45 (m, 6H), 7.34−7.31 (m, 6H), 5.78−5.72 (m, 1H), 5.20 (d, J = 16.8 Hz, 1H), 5.09 (d, J = 9.8 Hz, 1H), 4.57 (dd, J = 11.2, 4.2 Hz, 1H), 3.17−3.08 (m, 2H) ppm; ^{13}C NMR (175 MHz, $CDCl_3$) δ 154.4, 147.1, 137.0, 136.0, 134.2, 132.0, 131.7, 129.2, 129.0, 128.9, 128.7, 128.5, 128.4, 128.1, 127.9, 126.6, 119.3, 65.2, 30.7 ppm; HRMS (ESI-TOF) m/z calcd for $C_{25}H_{21}NO_3S$ $[M + H]^+$ 416.1320, found 416.1338.

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4,5-Diphenyl-2-(1-(phenylsulfonyl)but-3-ynyl)oxazole (9). Colorless oil (52 mg, 47%); R_f = 0.24 (hexane/ethyl acetate, 4:1); FT-IR (neat film): 3286, 3068, 1448, 1310, 1150 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, J = 8.0 Hz, 2H), 7.65 (t, J = 7.6 Hz, 1H), 7.53−7.47 (m, 6H), 7.38−7 33 (m, 6H), 4.72 (dd, J = 8.8 Hz, 7.2 Hz, 1H), 3.30−3.28 (m, 2H), 1.99 (t, J = 2.4 Hz, 1H) ppm; ^{13}C NMR (175 MHz, $CDCl_3$) δ 153.7, 147.4, 136.6, 136.1, 134.5, 131.6, 129.2, 129.1, 129.0, 128.6, 128.5, 128.4, 128.1, 127.9, 126.6, 126.1, 77.9, 71.6, 64.2, 17.5 ppm; HRMS (ESI-TOF) m/z calcd for $C_{25}H_{19}NO_3S$ $[M + H]^+$ 414.1164, found 414.1179.

2-(7-Bromo-1-(phenylsulfonyl)heptyl)-4,5-diphenyloxazole (10). Colorless oil (76 mg, 53%); R_f = 0.54 (hexane/ethyl acetate, 4:1); FT-IR (neat film): 3069, 2959, 1690, 1447, 1321, 1148, 687 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.78−7.76 (m, 2H), 7.61 (t, J = 8.0 Hz, 1H), 7.52−7.47 (m, 6H), 7.38−7.33 (m, 6H), 4.51 (dd, J = 10.0 Hz, 5.2 Hz, 1H), 3.36 (t, J = 7.2 Hz, 2H), 2.40−2.37 (m, 2H), 1.83−1.80 (m, 2H), 1.45−1.37 (m, 6H) ppm; ^{13}C NMR (175 MHz, $CDCl_3$) δ 154.8, 147.0, 137.1, 136.0, 134.0, 131.6, 129.0, 128.92, 128.89, 128.6, 128.5, 128.3, 128.0, 127.8, 126.5, 65.7, 33.6, 32.4, 28.0, 27.6, 26.7, 26.3 ppm; HRMS (ESI-TOF) m/z calcd for $C_{28}H_{28}BrNO_3S$ $[M + H]^+$ 538.1052, found 538.1066.

4,5-Diphenyl-2-(2-(phenylsulfonyl)propan-2-yl)oxazole (11). Off-white solid (104 mg, 97%); mp = 103−106 °C; R_f = 0.34 (hexane/ethyl acetate, 4:1); FT-IR (neat film): 3065, 2939, 1446, 1305, 1154 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.67−7.60 (m, 3H), 7.49−7.44 (m, 6H), 7.35−7.33 (m, 6H), 1.93 (s, 6H) ppm; ^{13}C NMR (175 MHz, $CDCl_3$) δ 158.8, 146.9, 135.9, 135.3, 134.0, 131.9, 130.1, 128.9, 128.7, 128.63, 128.59, 128.3, 128.2, 128.0, 126.5, 64.2, 20.5 ppm; HRMS (ESI-TOF) m/z calcd for $C_{24}H_{21}NO_3S$ $[M + H]^+$ 404.1320, found 404.1341.

4,5-Diphenyl-2-(3-(phenylsulfonyl)pentan-3-yl)oxazole (12). Colorless oil (57 mg, 50%); R_f = 0.41 (hexane/ethyl acetate, 4:1); FTIR (neat film): 3062, 2936, 1442, 1306, 1154 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.59−7.57 (m, 2H), 7.53 (t, J = 7.6 Hz, 1H), 7.47−7.36 (m, 6H), 7.35−7.32 (m, 6H), 2.70−2.63 (m, 2H), 2.42−2.35 (m, 2H), 1.61 (t, J = 7.6 Hz, 6H) ppm; ^{13}C NMR (175 MHz, $CDCl_3$) δ 158.1, 146.5, 136.8, 135.8, 133.6, 132.0, 129.6, 128.8, 128.6, 128.53, 128.50, 128.3, 128.0, 126.4, 72.0, 22.3, 8.4 ppm; HRMS (ESI-TOF) m/z calcd for $C_{26}H_{25}NO_3S$ $[M + H]^+$ 432.1633, found 432.1624.

4,5-Diphenyl-2-(4-(phenylsulfonyl)hepta-1,6-dien-4-yl)-oxazole (13). Colorless oil (80 mg, 66%); R_f = 0.4 (hexane/ethyl acetate, 4:1); FT-IR (neat film): 3060, 2923, 1683, 1446, 1307, 1146 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 7.6 Hz, 2H), 7.55 (t, J = 7.4 Hz, 1H), 7.49−7.46 (m, 2H), 7.44−7.41 (m, 4H), 7.37−7.33 (m, 6H), 5.98 (ddt, J = 17.4, 10 Hz, 7.6 Hz, 2H), 5.27 (dd, J = 17.2, 1.6 Hz, 2H), 5.22 (d, J = 10 Hz, 2H), 3.31 (dd, J = 14.8, 7.2 Hz, 2H), 3.15 (dd, J = 14.8, 7.2 Hz, 2H) ppm; ^{13}C NMR (175 MHz, $CDCl_3$) δ 157.2, 146.8, 136.2, 135.8, 134.0, 131.8, 131.1, 129.8, 129.0, 128.64, 128.62, 128.5, 128.3, 128.2, 127.9, 126.5, 120.4, 70.2, 34.5 ppm; HRMS (ESI-TOF) m/z calcd for $C_{28}H_{25}NO_3S$ $[M + H]^+$ 456.1633, found 456.1645.

4,5-Diphenyl-2-(4-(phenylsulfonyl)hepta-1,6-diyn-4-yl)-oxazole (14). Colorless oil (99 mg, 82%); R_f = 0.30 (hexane/ethyl acetate, 4:1); FT-IR (neat film): 3293, 1448, 1325, 1149, 1083 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, J = 7.2 Hz, 2H), 7.60 (t, J = 7.6 Hz, 1H), 7.52−7.44 (m, 6H), 7.36−7.34 (m, 6H), 3.59 (dd, J = 17.6 Hz, 2.8 Hz, 2H), 3.47 (dd, J = 17.6, 2.8 Hz, 2H), 2.14 (t, J = 2.8 Hz, 2H) ppm; ^{13}C NMR (175 MHz, $CDCl_3$) δ 155.8, 147.4, 136.0, 135.4, 134.4, 131.6, 130.0, 129.1, 128.9, 128.65, 128.57, 128.4, 128.0, 127.9, 126.7, 72.6, 68.3, 21.6 ppm; HRMS (ESI-TOF) m/z calcd for $C_{28}H_{21}NO_3S$ $[M + H]^+$ 452.1320, found 452.1336.

4,5-Diphenyl-2-(1-(phenylsulfonyl)cyclobutyl)oxazole (15). Colorless oil (65 mg, 59%); R_f = 0.33 (hexane/ethyl acetate, 1:4); FT-IR (neat film): 3064, 2953, 1553, 1446, 1306, 1147 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J = 7.6 Hz, 2H), 7.61−7.58 (m, 1H), 7.53−7.45 (m, 6H), 7.37−7.32 (m, 6H), 3.29−3.21 (m, 2H), 2.87−2.80 (m, 2H), 2.28−2.21 (m, 1H), 2.10−2.09 (m, 1H) ppm; ^{13}C NMR (175 MHz, $CDCl_3$) δ 158.2, 147.0, 136.2, 135.9, 133.9, 131.9, 129.3, 128.9, 128.8, 128.6, 128.5, 128.3, 128.2, 128.0, 126.5, 65.4, 28.1, 15.7 ppm; HRMS (ESI-TOF) m/z calcd for $C_{25}H_{21}NO_3S$ $[M + H]^+$ 416.1320, found 416.1329.

4,5-Diphenyl-2-(1-(phenylsulfonyl)cyclopentyl)oxazole (16). Colorless oil (89 mg, 78%); R_f = 0.43 (hexane/ethyl acetate, 4:1); FT-IR (neat film): 3062, 2960, 1686, 1446, 1305, 1140 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, J = 7.2 Hz, 2H), 7.58 (t, J = 7.2 Hz, 1H), 7.50−7.42 (m, 6H), 7.37−7.33 (m, 6H), 2.75−2.71 (m, 4H), 2.00−1.97 (m, 2H), 1.77−1.73 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.8, 147.1, 137.0, 136.0, 133.8, 132.0, 129.6, 128.9, 128.7, 128.6, 128.5, 128.3, 128.0, 126.5, 74.4, 33.0, 25.4 ppm; HRMS (ESI-TOF) m/z calcd for $C_{26}H_{23}NO_3S$ $[M + H]^+$ 430.1477, found 430.1494.

4,5-Diphenyl-2-(1-(phenylsulfonyl)cyclohexyl)oxazole (17). Colorless oil (110 mg, 93%); R_f = 0.47 (hexane/ethyl acetate, 4:1); FT-IR (neat film): 3069, 2952, 1690, 1505, 1446, 1296, 1146 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.61−7.57 (m, 3H), 7.51−7.41 (m, 6H), 7.37−7.33 (m, 6H), 2.78−2.75 (m, 2H), 2.21−2.15 (m, 2H), 1.88−1.86 (m, 2H), 1.67−1.65 (m, 1H), 1.37−1.32 (m, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.0, 147.0, 136.1, 135.6, 133.8, 132.0, 130.0, 128.8, 128.6, 128.54, 128.52, 128.4, 128.3, 128.0, 126.6, 69.2, 28.0, 24.7, 22.6 ppm; HRMS (ESI-TOF) m/z calcd for $C_{27}H_{25}NO_3S$ $[M + H]^+$ 444.1633, found 444.1650.

Typical Procedure for Aluminum/$HgCl_2$-Mediated Desulfonylation for Synthesis of 4 (eq 1) and 18 (Table 2). To a solution of **3** or the alkylated 2-(sulfonylethyl)-4,5-diphenyloxazole **5** (0.12 mmol, 1.0 equiv) and crystals of mercuric chloride (0.034 mmol, 0.3 equiv), in methanol (15 mL), was added an excess of food-grade aluminum foil (2.32 mmol, 20 equiv) with vigorous stirring under a nitrogen atmosphere. The resulting heterogeneous mixture was heated at reflux until the metal disappeared. The reaction mixture was then allowed to cool to room temperature and filtered through a Celite bed followed by washing with methanol (2 × 15 mL). The filtrate was concentrated to a crude residue which was submitted to gravity-column chromatography on silica gel to provide 2-methyl-4,5-diphenyloxazole **4** (96%) or 2-ethyl-4,5-diphenyloxazole **18** (97%).

General Procedure for Magnesium/$HgCl_2$-Mediated Desulfonylation of Alkylated Sulfones 5−9, 11−12, 5−17. To a stirred solution of an alkylated 2-(phenylsulfonyl)methyl-4,5-diphenyloxazole (0.12 mmol, 1.0 equiv from Table 1) in methanol (5 mL) were added magnesium turnings (1.73 mmol, 15 equiv) and crystals of mercuric chloride (0.012 mmol, 0.1 equiv) at room temperature. The reaction mixture was stirred at room temperature (2 h) while monitoring the reaction progress by TLC. After the reaction was complete, the reaction mixture was filtered through a Celite bed followed by washing with methanol (2 × 10 mL). The filtrate was concentrated, and the resultant crude residue was submitted to gravity-column chromatography on silica gel (hexane/ethyl acetate) to afford the pure products **18**−**27** listed in Table 2.

2-Methyl-4,5-diphenyloxazole (4).[13] Colorless oil (30 mg, 96%); R_f = 0.42 (hexane/ethyl acetate, 4:1); FT-IR (neat film): 3061, 2985, 1572, 1438, 1052 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.65−7.63 (m, 2H), 7.59−7.56 (m, 2H), 7.36−7.30 (m, 6H), 2.56 (s, 3H) ppm; ^{13}C NMR (175 MHz, $CDCl_3$) δ 160.2, 145.3, 135.2, 132.5, 129.1, 128.6, 128.5, 128.3, 128.0, 127.8, 126.4, 14.0 ppm.

2-Ethyl-4,5-diphenyloxazole (18).[14] Colorless oil (31 mg, 97%); R_f = 0.46 (hexane/ethyl acetate, 4:1); FT-IR (neat film): 3059, 2984, 1570, 1444, 1059 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.63 (dd, J = 8.4 Hz, 1.4 Hz, 2H), 7.58 (d, J = 8.4 Hz, 1.4 Hz, 2H), 7.36−7.29 (m, 6H), 2.88 (q, J = 7.7 Hz, 2H), 1.41 (t, J = 7.7 Hz, 3H) ppm; ^{13}C NMR (175 MHz, $CDCl_3$) δ 164.5, 145.0, 135.0, 132.6, 129.2, 128.6, 128.5, 128.3, 127.94, 127.92, 126.4, 21.8, 11.3 ppm.

4,5-Diphenyl-2-propyloxazole (19).[15] White solid (24.8 mg, 76%); mp = 62−64 °C [Lit. 64 °C];[15] R_f = 0.60 (hexane/ethyl acetate, 4:1); FT-IR (neat film): 3061, 2982, 1571, 1441, 1056 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.65 (dd, J = 8.4 Hz, 1.6 Hz, 2H), 7.59 (dd, J = 8.4 Hz, 1.6 Hz, 2H), 7.39−7.31 (m, 6H), 2.83 (t, J = 8.0 Hz, 2H), 1.92−1.86 (m, 2H), 1.07 (t, J = 7.6 Hz, 3H) ppm; ^{13}C NMR (175 MHz, $CDCl_3$) δ 163.6, 145.0, 135.0, 132.6, 129.2, 128.6, 128.5, 128.2, 127.92, 127.91, 126.4, 30.1, 20.7, 13.8 ppm.

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2-Isopentyl-4,5-diphenyloxazole (20). Colorless oil (22.3 mg, 66%); R_f = 0.65 (hexane/ethyl acetate, 4:1); FT-IR (neat film): 3064, 2956, 1570, 1444, 1059 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 8.0 Hz, 2H), 7.58 (d, J = 7.6 Hz, 2H), 7.38−7.29 (m, 6H), 2.86 (t, J = 8.0 Hz, 2H), 1.79−1.66 (m, 3H), 0.98 (d, J = 6.4 Hz, 6H) ppm; ^{13}C NMR (175 MHz, $CDCl_3$) δ 163.9, 145.0, 135.0, 132.7, 129.2, 128.6, 128.5, 128.3, 128.0, 126.4, 36.0, 27.8, 26.3, 22.3 ppm; HRMS (ESI-TOF) m/z calcd for $C_{20}H_{21}NO$ $[M + H]^+$ 292.1701, found 292.1697.

2-(But-3-enyl)-4,5-diphenyloxazole (21). Colorless oil (32 mg, 97%); R_f = 0.53 (hexane/ethyl acetate, 4:1); FT-IR (neat film): 3064, 2924, 1675, 1448, 1211, 1059 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 7.2 Hz, 2H), 7.58 (d, J = 6.8 Hz, 2H), 7.38−7.29 (m, 6H), 5.94 (ddt, J = 17.2, 10.4, 6.4 Hz, 1H), 5.14 (dd, J = 17.2, 1.6 Hz, 1H), 5.06 (d, J = 10.4 Hz, 1H), 2.96 (t, J = 7.8 Hz, 2H), 2.62 (dd, J = 14.8, 7.0 Hz, 2H) ppm; ^{13}C NMR (175 MHz, $CDCl_3$) δ 162.9, 145.1, 136.6, 135.0, 132.6, 129.1, 128.6, 128.5, 128.3, 127.97, 127.90, 126.4, 115.9, 31.0, 27.8 ppm; HRMS (ESI-TOF) m/z calcd for $C_{19}H_{17}NO$ $[M + H]^+$ 276.1388, found 276.1402.

2-(But-3-ynyl)-4,5-diphenyloxazole (22). Colorless oil (32 mg, 96%); R_f = 0.45 (hexane/ethyl acetate, 4:1); FT-IR (neat film): 3296, 2919, 1580, 1448, 1211, 1059 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 6.8 Hz, 2H), 7.58 (d, J = 7.2 Hz, 2H), 7.38−7.30 (m, 6H), 3.10 (t, J = 7.6 Hz, 2H), 2.76 (td, J = 7.6 Hz, 2.0 Hz, 2H), 2.03 (t, J = 2.6 Hz, 1H) ppm; ^{13}C NMR (175 MHz, $CDCl_3$) δ 161.4, 145.5, 135.1, 132.4, 129.0, 128.6, 128.5, 128.4, 128.1, 128.0, 126.5, 82.3, 69.5, 27.7, 16.6 ppm; HRMS (ESI-TOF) m/z calcd for $C_{19}H_{15}NO$ $[M + H]^+$ 274.1232, found 274.1247.

2-Isopropyl-4,5-diphenyloxazole (23).[16] Colorless oil (29 mg, 90%); R_f = 0.64 (hexane/ethyl acetate, 4:1); FT-IR (neat film): 3064, 2973, 1671, 1448, 1210 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, J = 6.8 Hz, 2H), 7.59 (d, J = 6.8 Hz, 2H), 7.38−7.29 (m, 6H), 3.22−3.15 (m, 1H), 1.43 (d, J = 7.2 Hz, 6H) ppm; ^{13}C NMR (175 MHz, $CDCl_3$) δ 167.6, 144.8, 134.9, 132.7, 129.2, 128.6, 128.5, 128.2, 128.0, 127.9, 126.3, 28.5, 20.5 ppm.

2-(Pentan-3-yl)-4,5-diphenyloxazole (24). Colorless oil (28 mg, 82%); R_f = 0.68 (hexane/ethyl acetate, 4:1); FT-IR (neat film): 3064, 2962, 1566, 1444, 1058 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.67−7.65 (m, 2H), 7.60−7.58 (m, 2H), 7.38−7.28 (m, 6H), 2.80 (tt, J = 14.4 Hz, 6.0 Hz, 1H), 1.90−1.75 (m, 4H), 0.96 (t, J = 7.2 Hz, 6H) ppm; ^{13}C NMR (175 MHz, $CDCl_3$) δ 166.3, 144.8, 134.9, 132.8, 129.3, 128.6, 128.5, 128.2, 128.0, 127.9, 126.3, 43.0, 26.30, 11.9 ppm; HRMS (ESI-TOF) m/z calcd for $C_{20}H_{21}NO$ $[M + H]^+$ $C_{20}H_{21}NO$ $[M + H]^+$ 292.1701, found 292.1713.

2-Cyclobutyl-4,5-diphenyloxazole (25). Colorless oil (23 mg, 69%); R_f = 0.52 (hexane/ethyl acetate, 4:1); FT-IR (neat film): 2944, 2860, 1566, 1444, 1059 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.65−7.63 (m, 2H), 7.60−7.58 (m, 2H), 7.38−7.29 (m, 6H), 3.76−3.68 (m, 1H), 2.60−2.50 (m, 2H), 2.46−2.38 (m, 2H), 2.16−1.98 (m, 2H) ppm; ^{13}C NMR (175 MHz, $CDCl_3$) δ 165.8, 144.9, 135.1, 132.7, 129.2, 128.6, 128.5, 128.2, 128.0, 127.9, 126.4, 33.2, 27.4, 18.7 ppm; HRMS (ESI-TOF) m/z calcd for $C_{19}H_{17}NO$ $[M + H]^+$ 276.1388, found 276.1397.

2-Cyclopentyl-4,5-diphenyloxazole (26). Colorless oil (31 mg, 92%); R_f = 0.55 (hexane/ethyl acetate, 4:1); FT-IR (neat film): 3064, 2957, 1681, 1448, 1210 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 6.8 Hz, 2H), 7.58 (d, J = 7.2 Hz, 2H), 7.38−7.28 (m, 6H), 3.31 (q, J = 8.0 Hz, 1H), 2.18−2.10 (m, 2H), 2.06−1.97 (m, 2H), 1.89−1.80 (m, 2H), 1.75−1.69 (m, 2H) ppm; ^{13}C NMR (175 MHz, $CDCl_3$) δ 166.8, 144.8, 134.9, 132.8, 129.3, 128.6, 128.5, 128.2, 128.0, 127.9, 126.3, 38.6, 31.5, 25.6 ppm. HRMS (ESI-TOF) m/z calcd for $C_{20}H_{19}NO$ $[M + H]^+$ 290.1545, found 290.1560

2-Cyclohexyl-4,5-diphenyloxazole (27).[16] Colorless oil (33 mg, 97%); R_f = 0.66 (hexane/ethyl acetate, 4:1); FT-IR (neat film): 2913, 2854, 1566, 1443, 1056 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.66−7.64 (m, 2H), 7.60−7.58 (m, 2H), 7.38−7.29 (m, 6H), 2.91−2.88 (m, 1H), 2.17−2.15 (m, 2H), 1.88−1.86 (m, 2H), 1.75−1.67 (m, 3H), 1.45−1.39 (m, 2H), 1.35−1.32 (m, 1H) ppm; ^{13}C NMR (175 MHz, $CDCl_3$) δ 166.9, 144.6, 134.9, 132.8, 129.3, 128.6, 128.5, 128.2, 128.0, 127.9, 126.3, 37.6, 30.7, 25.8, 25.7 ppm.

Ethyl 3-(4,5-Diphenyloxazol-2-yl)-3-(phenylsulfonyl)-propanoate (28). To a prechilled solution of 2-(phenylsulfonyl)-methyl-4,5-diphenyloxazole **3** (100 mg, 0.27 mmol) in dry THF (15 mL) was added potassium *tert*-butoxide (33 mg, 0.29 mmol) under a nitrogen atmosphere. The resulting yellow solution was stirred (5 °C) for 30 min. To the reaction mixture was slowly added ethyl bromoacetate (49 mg, 32.4 μL, 0.29 mmol), and stirring was continued (16 h) at room temperature. Upon completion of reaction as indicated by TLC, the reaction mixture was quenched with cold water (20 mL) and extracted with dichloromethane (2 × 20 mL). The organic layers were combined, dried over anhydrous sodium sulfate, and concentrated to obtain a crude oily residue. The residue was submitted to gravity-column chromatography on silica gel (hexane/ethyl acetate, 4:1) to afford pure ethyl 3-(4,5-diphenyloxazol-2-yl)-3-(phenylsulfonyl)propanoate **28** as an off-white solid (88 mg, 72%); mp = 30−33 °C; R_f = 0.25 (hexane/ethyl acetate, 4:1); FT-IR (neat film): 3062, 1733, 1447, 1324, 1148 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, J = 7.6 Hz, 2H), 7.66 (t, J = 7.2 Hz, 1H), 7.54−7.49 (m, 4H), 7.45−7.41 (m, 2H), 7.35−7.32 (m, 6H), 5.04 (dd, J = 6.0 Hz, 2.0 Hz, 1H), 4.18−4.08 (m, 2H), 3.42 (d, J = 8.0 Hz, 1H), 3.42 (d, J = 5.6 Hz 1H), 1.21 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (175 MHz, $CDCl_3$) δ 169.2, 154.3, 147.2, 136.7, 136.0, 134.5, 131.8, 129.3, 129.2, 129.0, 128.6, 128.5, 128.4, 128.1, 127.9, 126.6, 61.5, 61.4, 31.9, 14.1 ppm; HRMS (ESI-TOF) m/z calcd for $C_{26}H_{23}NO_5S$ $[M + H]^+$ 462.1375; found 462.1379.

Ethyl 3-(4,5-Diphenyloxazol-2-yl)acrylate (29). To a cooled (5 °C) solution of sulfonyloxazole ester **28** (225 mg, 0.49 mmol) in dry THF was added potassium *tert*-butoxide (60.2 mg, 0.54 mmol) under nitrogen, and the reaction mixture was then stirred at 5−10 °C (2 h) while being monitored by TLC. After completion of the reaction, the reaction mixture was extracted with dichloromethane (2 × 25 mL) followed by washing the extracts with water and brine with subsequent drying over anhydrous Na_2SO_4. Removal of the drying agent and concentration of the filtrate gave a crude residue which was submitted to gravity-column chromatography (hexane/ethyl acetate, 4:1) to provide unsaturated oxazole ester **29** as a colorless oil (100 mg, 65%); R_f = 0.49 (hexane/ethyl acetate, 4:1); FT-IR (neat film): 3064, 1712, 1653, 1256, 1159 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.67−7.62 (m, 4H), 7.51 (d, J = 16.0 Hz, 1H), 7.40−7.36 (m, 6H), 6.83 (d, J = 16.0 Hz, 1H), 4.29 (q, J = 7.2 Hz, 2H), 1.35 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (175 MHz, $CDCl_3$) δ 165.8, 157.6, 147.0, 137.8, 134.9, 133.0, 131.8, 129.9, 129.2, 129.0, 128.8, 128.7, 128.5, 128.5, 128.2, 128.0, 126.7, 124.8, 61.0, 14.2 ppm; HRMS (ESI-TOF) m/z calcd for $C_{20}H_{17}NO_3$ $[M + H]^+$ 320.1287, found 320.1281.

Ethyl 3-(4,5-Diphenyloxazol-2-yl)propanoate (30).[17] The unsaturated oxazole ester **30** (160 mg, 0.50 mmol) was dissolved in methanol (25 mL), and then 10% Pd/C (16 mg, 10% wt/wt) was added at room temperature. The reaction mixture was purged with nitrogen while stirring followed by the addition of hydrogen gas (balloon), and then stirring was continued (16 h) under an atmosphere of hydrogen. Upon completion of reaction, the reaction mixture was filtered through a bed of Celite while washing with methanol (2 × 30 mL). The combined filtrates were concentrated, and the crude residue was submitted to gravity-column chromatography (hexane/ethyl acetate, 4:1) to afford **30** as an off-white solid (129 mg, 80%); mp = 68−70 °C [Lit. 69.5−71 °C];[17] R_f = 0.36 (hexane/ethyl acetate, 4:1); FT-IR (neat film): 3068, 2980, 1734, 1444, 1060 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 7.2 Hz, 2H), 7.58 (d, J = 7.6 Hz, 2H), 7.38−7.30 (m, 6H), 4.19 (q, J = 6.8 Hz, 2H), 3.19 (t, J = 7.2 Hz, 2H), 2.91 (t, J = 7.6 Hz, 2H), 1.27 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (175 MHz, $CDCl_3$) δ 172.0, 161.8, 145.4, 135.1, 132.5, 129.0, 128.6, 128.5, 128.4, 128.0, 127.9, 126.5, 60.8, 31.2, 23.6, 14.2 ppm.

Methyl 3-(4,5-Diphenyloxazol-2-yl)propanoate (31).[13] To a clear solution of sulfonyloxazole ester **28** (80 mg, 0.173 mmol) in methanol (10 mL) was added magnesium turnings (63 mg, 2.60 mmol) followed by solid mercuric chloride (4.7 mg, 0.017 mmol) at room temperature. The resulting reaction mixture was stirred (2 h) while the reaction progress was monitored by TLC. After completion of the reaction, the heterogeneous mixture was then filtered through a

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Celite bed followed by washing with methanol (2 × 15 mL). The methanolic filtrates were combined and concentrated to afford a crude residue. The residue was submitted to gravity-column chromatography (hexane/ethyl acetate, 4:1) to provide ester **31** as an off-white solid (52 mg, 97%); mp = 58−61 °C [Lit. 58−59 °C];[13] R_f = 0.29 (hexane/ethyl acetate, 4:1); FT-IR (neat film): 3061, 2957, 1731, 1438, 1056 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J = 7.2 Hz, 2H), 7.57 (d, J = 7.2 Hz, 2H), 7.38−7.29 (m, 6H), 3.73 (s, 3H), 3.19 (t, J = 7.6 Hz, 1H), 2.92 (t, J = 7.6 Hz, 3H) ppm; ^{13}C NMR (175 MHz, $CDCl_3$) δ 172.5, 161.7, 145.4, 135.1, 132.5, 129.0, 128.6, 128.5, 128.4, 128.0, 127.9, 126.5, 51.9, 30.9, 23.5 ppm.

3-(4,5-Diphenyloxazol-2-yl)propanoic Acid (Oxaprozin) (32).[13] Ethyl ester **30** (128 mg, 0.39 mmol) or methyl ester **31** (65 mg, 0.21 mmol) and 20% aqueous NaOH solution (3 mL) were stirred overnight at room temperature. Upon completion of reaction as indicated by TLC, the reaction mixture was slowly acidified to pH 3−4 using conc. HCl (3 mL) at room temperature and stirring was continued (3 h). After the neutralization was complete the reaction mixture was diluted with cold water (15 mL) and extracted with dichloromethane (2 × 15 mL). The organic extracts were combined, dried over anhydrous Na_2SO_4, and concentrated to give a white solid residue. The residue was submitted to gravity-column chromatography (chloroform/methanol, 9:1) to afford pure Oxaprozin **32** as a white solid (80 mg, 68%, from the ethyl ester **30** or 60 mg, 97%, from the methyl ester **31**); mp = 158−160 °C [Lit. 160.5−161.5 °C];[13] R_f = 0.27 (methanol/chloroform, 1:9); FT-IR (neat) 3156, 2948, 1714, 1568; ^1H NMR (400 MHz, $CDCl_3$) δ 7.62−7.50 (m, 2H), 7.56−7.54 (m, 2H), 7.37−7.30 (m, 6H), 3.17 (t, J = 7.2 Hz, 2H), 2.94 (t, J = 7.2 Hz, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.8, 161.9, 145.5, 134.8, 132.0, 128.7, 128.6, 128.5, 128.1, 127.9, 126.4, 31.0, 23.2 ppm.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01280.

Copies of spectra for compounds **3**−**32** (PDF)

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Notes

The authors declare no competing financial interest.

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