

Note

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

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J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.6b01280 • Publication Date (Web): 21 Jul 2016

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8 **4,5-Diaryloxazoles**
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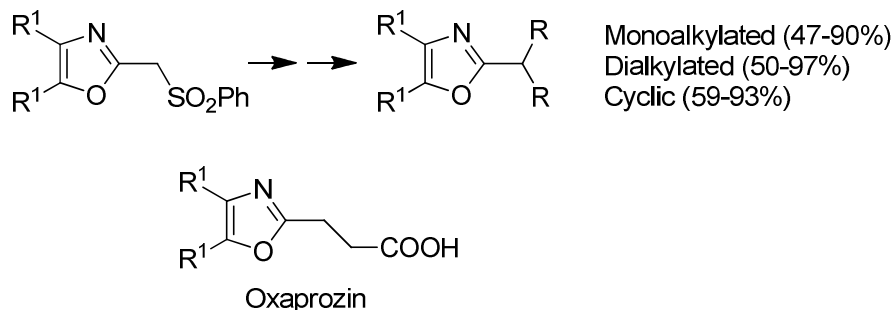
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Abstract

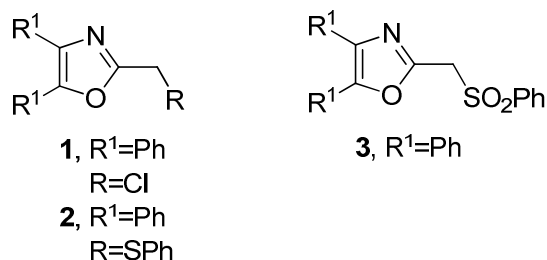


2-((Phenylsulfonyl)methyl)-4,5-diphenyloxazole is a useful scaffold for synthetic elaboration at the 2-methylene position thereby affording extended oxazoles. The corresponding α -sulfonyl anion reacts smoothly with diverse alkyl halides giving monoalkylated (47-90%), dialkylated (50-97%) and cyclic (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.

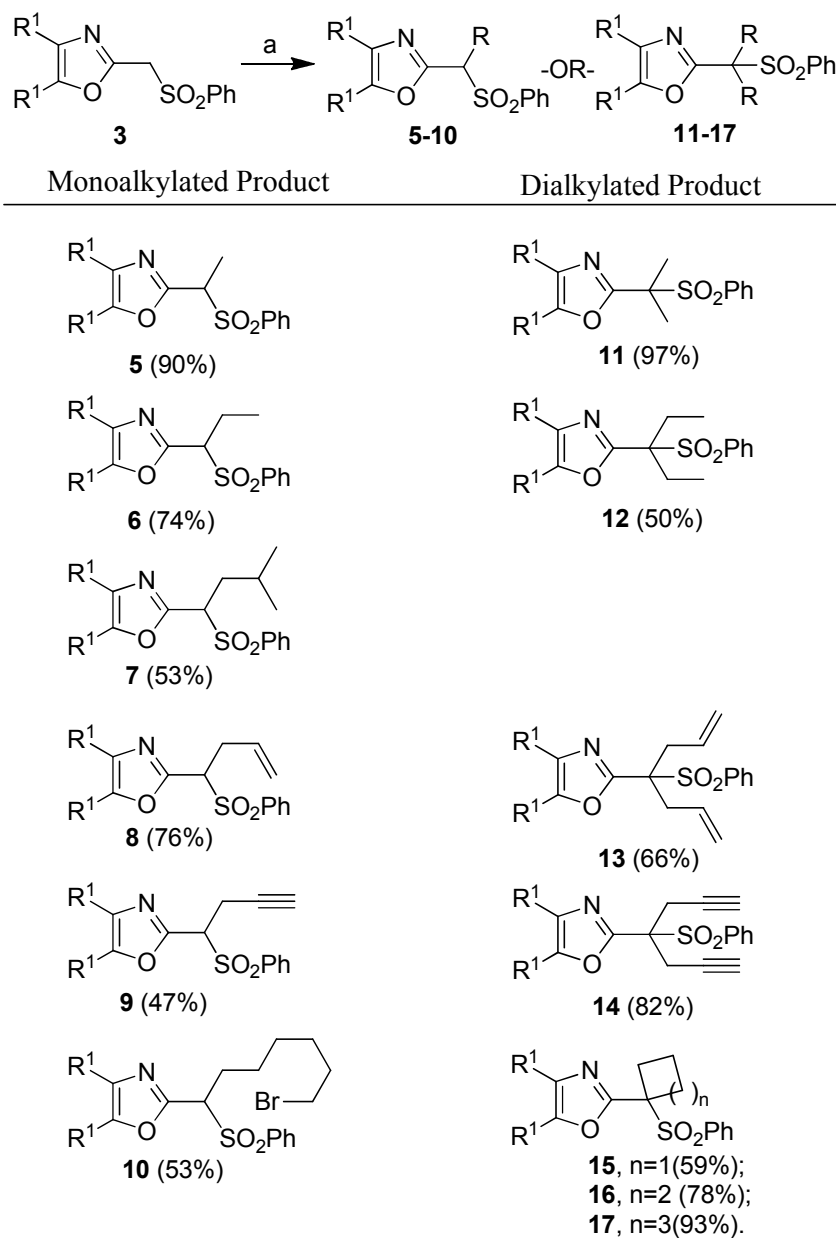
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6 The utilization of α -sulfonyl carbanions in carbon-carbon bond forming strategy takes
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8 advantage of mild reaction conditions and is applicable to the synthetic elaboration of many
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10 types of pre-formed oxygen and nitrogen heterocycles.¹ For example, the Ciufolini group
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12 prepared and utilized a dual-functionalized 2-(phenylsulfonylmethyl)-4,5-disubstituted oxazole
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14 as a conjunctive intermediate in their synthesis of the siphonazoles.² 3-(Phenylsulfonylmethyl)
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16 oxindoles, 3- and 4-(arylsulfonyl-methyl) pyridines, 2-(arylsulfonylmethyl) quinolines and 2-
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18 (phenylsulfonylmethyl)pyrimidines have been designed so that the sulfonyl-activated methylene
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20 group facilitates the construction of extended or otherwise more elaborate fused heterocycles.³ In
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22 medicinal chemistry, the need for increased structural diversity and large numbers of therapeutic
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24 candidates as potential anti-inflammatories has driven the strategy for extension and elaboration
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26 at the 2-position of 2-substituted-4,5-diaryloxazoles.⁴ As functioning units in total synthesis, 2-
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28 substituted 4,5-diaryloxazoles carry with them a fully-masked carboxyl group, thereby allowing
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30 a great range of reactions to be performed on the synthon prior to the release of the carboxylate.⁵
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32 Hence the strategy whereby the carboxyl group, embedded in 4,5-diaryloxazole framework and
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34 oxidatively deprotected in later stages, was put to practice by the Evans group in their synthesis
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36 of oasomycin.⁶ Therefore, the development of carbon-carbon bond-forming methods at the 2-
37
38 methylene position of the trisubstituted oxazole would be a complementary strategy to the use of
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40 the heterocycle as a protecting group. Our ongoing work with the use of 2,4,5-trisubstituted
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42 oxazole scaffolds as “click”⁷ components of biofilm inhibitors involved the preparation of
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44 several 2-(azidoalkyl)- and 2-(azidoaryl)-substituted 4,5-diaryloxazoles.⁸ In a previous
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46 communication we described the functionalization of 2-(halomethyl)-4,5-diaryloxazoles using an
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48 array of nitrogen, oxygen and sulfur nucleophiles.^{8b} Our examples included the preparation of 2-
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(phenylthiomethyl)-4,5-diphenyl oxazole **2** from the corresponding 2-(chloromethyl)-4,5-diphenyloxazole **1** and thiophenol (**Fig. 1**). Oxidation of **2** with 3-chloroperbenzoic acid

Fig. 1. 2-Substituted-4,5-Diphenyloxazole Scaffolds



(MCPBA, 2.5 eq/CH₂Cl₂/rt) 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 eq) 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 equivalents of base followed by 2.5 equivalents of 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 equivalents of base followed by one equivalent of dihaloalkane was used (See **15**, **16** and **17**). Interestingly, 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

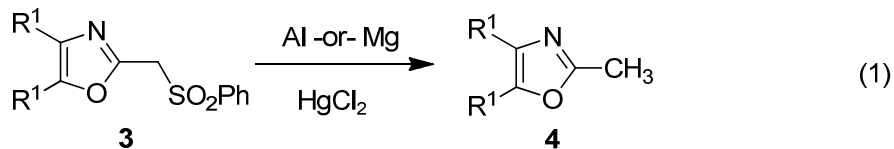
Table 1. Alkylation of 2-(Sulfonylmethyl)-4,5-Diphenyloxazoles¹

¹Reagents/Conditions: (a) KOt-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.

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

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2
3 the optimal conditions for β -elimination of the phenylsulfonyl group.⁹ Such complementary
4 transformations involving deletion of the sulfonyl group would broaden the scope and utility of
5 the heterocyclic sulfone alkylation scheme. While reductive desulfonylation with Raney nickel
6 precluded its employment with substrates **8**, **9**, **13**, and **14** due to unwanted reduction of
7 unsaturated sites, we found it ineffective with simple substrates such as sulfonylmethyloxazole **3**.
8 Attempted reductive desulfonylation of **3** with amalgamated active metals such as zinc and
9 magnesium, including the classical '15 second' amalgamated aluminum foil method of Corey,¹⁰
10 were of no consequence, and led to the recovery of only unreacted substrate. Interestingly, some
11 definitive changes to the Corey aluminum-mediated desulfonylation method, however, did lead
12 to positive results (Eq. 1).
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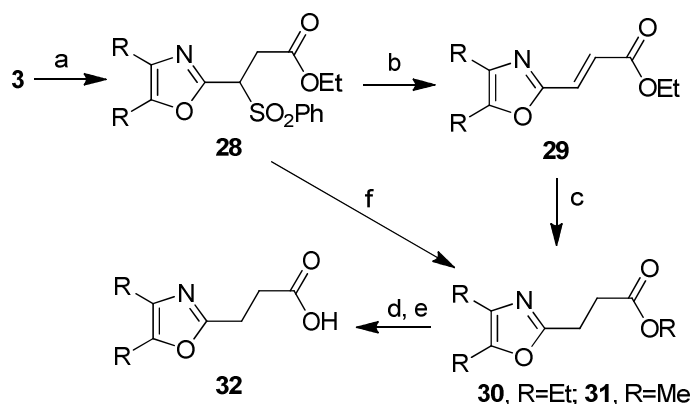
The addition of solid mercuric chloride to a mixture of food-grade aluminum foil and sulfone **3** in methanol was optimal for the conversion of the 2-(phenylsulfonylmethyl)oxazole **3** to the 2-methyloxazole **4** (Eq. 1). The heterogeneous mixture required heating at reflux until the aluminum metal 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/HgCl₂ desulfonylation was not optimal for unsaturated substrates **8** or **9** (Table 2), so the same conditions for the magnesium-mediated reductive desulfonylation of **3** were applied to the entire range of monalkylated and dialkylated sulfone substrates **5-9**, **11-12** and **15-17**. The

Table 2. Magnesium/HgCl₂/methanol-mediated desulfonation of **4-17**.¹

Sulfone	Product (%)	Sulfone	Product (%)
5	 18 (97%) ²	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%) ²		
9	 22 (96%) ²		

¹Reagents/Conditions:(a)magnesium(turnings)/HgCl₂/MeOH/
rt/2 h. ²Using aluminum: **18** (95%); **21**, **22** (<33%).

desulfonated 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 non-steroidal 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

Scheme 1. Synthesis of Oxaprozin **32** from Sulfone **3**.

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) H₂/10% Pd-C/MeOH/rt/16h (80%); (d) 20% aqueous NaOH/rt/16h; (e) Conc. HCl/75°C/3h (68%, from d); (f) Mg/HgCl₂/MeOH/rt/16h (97%);

nucleophilic scaffold **3**. Deprotonation of **3** (5°C/KOt-Bu/THF) followed by addition of ethyl bromoacetate (5°C to rt) afforded the β -sulfonyl ester **28** (72%). Base-mediated (5°C/KOt-Bu/THF) elimination of the phenylsulfonyl group from **28** provided the α,β -unsaturated ester **29** (65%). Catalytic reduction of the unsaturated ester **29** (H₂/10% Pd-C/MeOH) gave Oxaprozin ethyl ester **30** (80%). Alternatively, **28** could be reductively desulfonated (Mg/HgCl₂/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 non-steroidal 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

Solvents and reagents are ACS grade and were used as commercially supplied. Analytical thin-layer chromatography (TLC) utilized 0.25 mm pre-cut glass-backed plates (Silica Gel 60 F₂₅₄). 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 ethylacetate. 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 (¹H and ¹³C NMR) spectra were recorded with 400 MHz (100 MHz, ¹³C) or 700 MHz (175 MHz, ¹³C) instruments using CDCl₃ as a solvent and TMS as 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 pre-chilled 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 NaHCO₃ (2 X 30 mL). The combined organic layers were dried over anhydrous Na₂SO₄, 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; ¹H NMR (400 MHz, CDCl₃) 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; ¹³C NMR (100

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3 MHz, CDCl₃) δ 151.5, 147.6, 138.2, 136.2, 134.3, 131.6, 129.3, 129.1, 128.7, 128.65, 128.60,
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5 128.4, 128.1, 127.9, 126.6, 55.9 ppm; HRMS (ESI-TOF) m/z calcd for C₂₂H₁₇NO₃S [M+H]⁺
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7 376.1007, found 376.1019.
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11 **General procedure for the Preparation of Alkylated Sulfones (5-17).** To a stirred solution of
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13 2-(phenylsulfonyl)methyl-4,5-diphenyloxazole **3** (0.27 mmol, 1.0 equiv) in dry THF (10 mL)
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15 was added potassium *tert*-butoxide (0.29 mmol, 1.1 equiv) at 5°C. Stirring of the resultant
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17 yellow reaction mixture was continued under a nitrogen atmosphere (30 min). The alkyl halide
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19 (0.028 mmol, 1.05 equiv) was then slowly added to the reaction mixture by syringe, and the
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21 reaction mixture was allowed to warm to room temperature and stirring was continued (16 h). At
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23 the end of the reaction period, cold water (10 mL) was added to the reaction mixture followed by
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25 extraction with dichloromethane (2 x 20 mL). The organic layers were combined, washed with
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27 brine, dried over anhydrous Na₂SO₄, filtered and concentrated. The crude residue was submitted
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29 to gravity-column chromatography (hexane/ethyl acetate, 9:1) to afford the corresponding
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31 products **5-10**. For the preparation of the dialkylated compounds **11-14** the same procedure was
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33 used with the exception that, potassium *tert*-butoxide (0.66 mmol, 2.5 equiv) and corresponding
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35 alkylating reagent (0.66 mmol, 2.5 equiv) were employed. For the cyclic compounds **15-17**,
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37 potassium *tert*-butoxide (0.58 mmol, 2.2 equiv) and dihaloalkane (0.29 mmol, 1.1 equiv) were
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39 employed. The methods for purification of **11-17** were the same as for the monoalkyl sulfones **5-**
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47 **10**.
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50 **4,5-Diphenyl-2-(1-(phenylsulfonyl)ethyl)oxazole (5).** Off-white solid (93 mg, 90%); mp 95-97
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52 °C; R_f = 0.25 (hexane/ethyl acetate, 4:1); FT-IR (neat film): 3069, 2974, 1562, 1446, 1319, 1147
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54 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.73-7.70 (m, 2H), 7.56 (t, J = 7.4 Hz, 1H), 7.45-7.38 (m,
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56 6H), 7.27-7.25 (m, 6H), 4.57 (q, J = 7.6 Hz, 1H), 1.82 (d, J = 6.8 Hz, 3H) ppm; ¹³C NMR (175
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MHz, CDCl₃) 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 C₂₃H₁₉NO₃S [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; ¹H NMR (400 MHz, CDCl₃) 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; ¹³C NMR (175 MHz, CDCl₃) 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 C₂₄H₂₁NO₃S [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; ¹H NMR (400 MHz, CDCl₃) 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; ¹³C NMR (175 MHz, CDCl₃) 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 C₂₆H₂₅NO₃S [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; ¹H NMR (700 MHz, CDCl₃) 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 $\text{C}_{25}\text{H}_{21}\text{NO}_3\text{S}$ $[\text{M}+\text{H}]^+$ 416.1320, found 416.1338.

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 $\text{C}_{25}\text{H}_{19}\text{NO}_3\text{S}$ $[\text{M}+\text{H}]^+$ 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 $\text{C}_{28}\text{H}_{28}\text{BrNO}_3\text{S}$ $[\text{M}+\text{H}]^+$ 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 $^\circ\text{C}$; $R_f = 0.34$ (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 $\text{C}_{24}\text{H}_{21}\text{NO}_3\text{S}$ $[\text{M}+\text{H}]^+$ 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 $\text{C}_{26}\text{H}_{25}\text{NO}_3\text{S}$ $[\text{M}+\text{H}]^+$ 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 $\text{C}_{28}\text{H}_{25}\text{NO}_3\text{S}$ $[\text{M}+\text{H}]^+$ 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),

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3 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,
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5 131.6, 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;
6
7 HRMS (ESI-TOF) m/z calcd for $\text{C}_{28}\text{H}_{21}\text{NO}_3\text{S}$ $[\text{M}+\text{H}]^+$ 452.1320, found 452.1336.
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11 **4,5-Diphenyl-2-(1-(phenylsulfonyl)cyclobutyl)oxazole (15)**. Colorless oil (65 mg, 59%); $R_f =$
12 0.33 (hexane/ethyl acetate = 1:4); FT-IR (neat film): 3064, 2953, 1553, 1446, 1306, 1147 cm^{-1} ;
13
14 ^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),
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16 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)
17
18 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,
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20 128.8, 128.6, 128.5, 128.3, 128.2, 128.0, 126.5, 65.4, 28.1, 15.7 ppm; HRMS (ESI-TOF) m/z
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22 calcd for $\text{C}_{25}\text{H}_{21}\text{NO}_3\text{S}$ $[\text{M}+\text{H}]^+$ 416.1320, found 416.1329.
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29 **4,5-Diphenyl-2-(1-(phenylsulfonyl)cyclopentyl)oxazole (16)**. Colorless oil (89 mg, 78%); $R_f =$
30 = 0.43 (hexane/ethyl acetate, 4:1); FT-IR (neat film): 3062, 2960, 1686, 1446, 1305, 1140 cm^{-1} ;
31
32 ^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,
33
34 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
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36 (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,
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38 128.3, 128.0, 126.5, 74.4, 33.0, 25.4 ppm; HRMS (ESI-TOF) m/z calcd for $\text{C}_{26}\text{H}_{23}\text{NO}_3\text{S}$ $[\text{M}+\text{H}]^+$
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40 430.1477, found 430.1494.
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47 **4,5-Diphenyl-2-(1-(phenylsulfonyl)cyclohexyl)oxazole (17)**. Colorless oil (110 mg, 93%); $R_f =$
48 0.47 (hexane/ethyl acetate, 4:1); FT-IR (neat film): 3069, 2952, 1690, 1505, 1446, 1296, 1146
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50 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),
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52 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)
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54 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,
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3 128.6, 128.54, 128.52, 128.4, 128.3, 128.0, 126.6, 69.2, 28.0, 24.7, 22.6 ppm; HRMS (ESI-TOF)
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5 m/z calcd for $C_{27}H_{25}NO_3S$ $[M+H]^+$ 444.1633, found 444.1650.
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9 **Typical Procedure for Aluminum/HgCl₂-Mediated Desulfonylation for Synthesis of 4 (Eq.**
10 **1) and 18 (Table 2).** To a solution of the alkylated 2-(sulfonylethyl)-4,5-diphenyloxazole **5** (0.12
11 mmol, 1.0 equiv) and crystals of mercuric chloride (0.034 mmol, 0.3 equiv), in methanol (15
12 mL), was added an excess of food-grade aluminum foil (2.32 mmol, 20 equiv) with vigorous
13 stirring under a nitrogen atmosphere. The resulting heterogeneous mixture was heated at reflux
14 until the metal disappeared. The reaction mixture was then allowed to cool to room temperature
15 and filtered through a Celite bed followed by washing with methanol (2 x 15mL). The filtrate
16 was concentrated to a crude residue which was submitted to gravity-column chromatography on
17 silica gel to provide 2-methyl-4,5-diphenyloxazole **4** (96%) or 2-ethyl-4,5-diphenyloxazole **18**
18 (97%).
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33 **General procedure for Magnesium/HgCl₂-Mediated Desulfonylation of Alkylated Sulfones**

34 **5-17.** To a stirred solution of an alkylated 2-(phenylsulfonyl)methyl-4,5-diphenyloxazole (0.12
35 mmol, 1.0 equiv. from **Table 1**) in methanol (5 mL) was added magnesium turnings (1.73 mmol,
36 15 equiv) and crystals of mercuric chloride (0.012 mmol, 0.1 equiv) at room temperature. The
37 reaction mixture was stirred at room temperature (2 h) while monitoring the reaction progress by
38 TLC. After the reaction was complete, the reaction mixture was filtered through a Celite bed
39 followed by washing with methanol (2 x 10 mL). The filtrate was concentrated and the resultant
40 crude residue was submitted to gravity-column chromatography on silica gel (hexane/ethyl
41 acetate) to afford the pure products **18-27** listed in **Table 2**.
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3 **2-Methyl-4,5-diphenyloxazole (4).**¹³ Colorless oil (30 mg, 96%); R_f = 0.42 (hexane/ethyl
4 acetate, 4:1); FT-IR (neat film): 3061, 2985, 1572, 1438, 1052 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3)
5 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
6 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
7 ppm.
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16 **2-Ethyl-4,5-diphenyloxazole (18).**¹⁴ Colorless oil (31 mg, 97 %); R_f = 0.46 (hexane/ethyl
17 acetate, 4:1); FT-IR (neat film): 3059, 2984, 1570, 1444, 1059 cm^{-1} ; ^1H NMR (700 MHz, CDCl_3)
18 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,
19 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,
20 135.0, 132.6, 129.2, 128.6, 128.5, 128.3, 127.94, 127.92, 126.4, 21.8, 11.3 ppm.
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29 **4,5-Diphenyl-2-propyloxazole (19).**¹⁵ white solid (24.8 mg, 76 %); mp 62-64 °C [Lit. 64 °C]¹⁵;
30 R_f : 0.60 (hexane/ethyl acetate, 4:1); FT-IR (neat film): 3061, 2982, 1571, 1441, 1056 cm^{-1} ; ^1H
31 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),
32 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
33 NMR (175 MHz, CDCl_3) δ 163.6, 145.0, 135.0, 132.6, 129.2, 128.6, 128.5, 128.2, 127.92,
34 127.91, 126.4, 30.1, 20.7, 13.8 ppm.
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44 **2-Isopentyl-4,5-diphenyloxazole (20).** Colorless oil (22.3 mg, 66 %); R_f = 0.65 (hexane/ethyl
45 acetate, 4:1); FT-IR (neat film): 3064, 2956, 1570, 1444, 1059 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3)
46 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),
47 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,
48 135.0, 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-
49 TOF) m/z calcd for $\text{C}_{20}\text{H}_{21}\text{NO}$ [$\text{M}+\text{H}$]⁺ 292.1701, found 292.1697.
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3 **2-(But-3-enyl)-4,5-diphenyloxazole (21).** Colorless oil (32 mg, 97%); $R_f = 0.53$ (hexane/ethyl
4 acetate, 4:1); FT-IR (neat film): 3064, 2924, 1675, 1448, 1211, 1059 cm^{-1} ; ^1H NMR (400 MHz,
5 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, $J =$
6 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, $J = 7.8$
7 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,
8 136.6, 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;
9 HRMS (ESI-TOF) m/z calcd for $\text{C}_{19}\text{H}_{17}\text{NO}$ $[\text{M}+\text{H}]^+$ 276.1388, found 276.1402.

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13 **2-(But-3-ynyl)-4,5-diphenyloxazole (22).** Colorless oil (32 mg, 96%); $R_f = 0.45$ (hexane/ethyl
14 acetate, 4:1); FT-IR (neat film): 3296, 2919, 1580, 1448, 1211, 1059 cm^{-1} ; ^1H NMR (400 MHz,
15 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, $J = 7.6$
16 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,
17 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,
18 27.7, 16.6 ppm; HRMS (ESI-TOF) m/z calcd for $\text{C}_{19}\text{H}_{15}\text{NO}$ $[\text{M}+\text{H}]^+$ 274.1232, found 274.1247.

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22 **2-Isopropyl-4,5-diphenyloxazole (23).**¹⁶ Colorless oil (29 mg, 90%); $R_f = 0.64$ (hexane/ethyl
23 acetate, 4:1); FT-IR (neat film): 3064, 2973, 1671, 1448, 1210 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3)
24 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
25 (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,
26 128.6, 128.5, 128.2, 128.0, 127.9, 126.3, 28.5, 20.5 ppm.

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30 **2-(Pentan-3-yl)-4,5-diphenyloxazole (24).** Colorless oil (28 mg, 82%); $R_f = 0.68$ (hexane/ethyl
31 acetate, 4:1); FT-IR (neat film): 3064, 2962, 1566, 1444, 1058 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3)
32 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),
33 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,
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3 134.9, 132.8, 129.3, 128.6, 128.5, 128.2, 128.0, 127.9, 126.3, 43.0, 26.30, 11.9 ppm; HRMS
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5 (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.
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9 **2-Cyclobutyl-4,5-diphenyloxazole (25).** Colorless oil (23 mg, 69%); R_f = 0.52 (hexane/ethyl
10 acetate, 4:1); FT-IR (neat film): 2944, 2860, 1566, 1444, 1059 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$)
11 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,
12 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,
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14 135.1, 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-
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16 TOF) m/z calcd for $C_{19}H_{17}NO$ $[M+H]^+$ 276.1388, found 276.1397.
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24 **2-Cyclopentyl-4,5-diphenyloxazole (26).** Colorless oil (31 mg, 92 %); R_f = 0.55 (hexane/ethyl
25 acetate, 4:1); FT-IR (neat film): 3064, 2957, 1681, 1448, 1210 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$)
26 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),
27
28 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
29
30 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
32 31.5, 25.6 ppm. HRMS (ESI-TOF) m/z calcd for $C_{20}H_{19}NO$ $[M+H]^+$ 290.1545, found 290.1560
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39 **2-Cyclohexyl-4,5-diphenyloxazole (27).**¹⁶ Colorless oil (33 mg, 97%); R_f = 0.66 (hexane/ethyl
40 acetate, 4:1); FT-IR (neat film): 2913, 2854, 1566, 1443, 1056 cm^{-1} ; 1H NMR (700 MHz, $CDCl_3$)
41 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,
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43 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
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45 (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,
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47 37.6, 30.7, 25.8, 25.7 ppm.
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54 **Ethyl 3-(4,5-diphenyloxazol-2-yl)-3-(phenylsulfonyl)propanoate (28).** To a prechilled solution
55 of 2-(phenylsulfonyl)methyl-4,5-diphenyloxazole **3** (100 mg, 0.27 mmol) in dry THF (15 mL)
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3 was added potassium *tert*-butoxide (33 mg, 0.29 mmol) under a nitrogen atmosphere. The
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5 resulting yellow solution was stirred (5°C) for 30 min. To the reaction mixture was slowly added
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7 ethyl bromoacetate (49 mg, 32.4 μ L, 0.29 mmol) and stirring was continued (16 h) at room
8
9 temperature. Upon completion of reaction as indicated by TLC, the reaction mixture was
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11 quenched with cold water (20 mL) and extracted with dichloromethane (2 x 20 mL). The organic
12
13 layers were combined, dried over anhydrous sodium sulfate and concentrated to obtain a crude
14
15 oily residue. The residue was submitted to gravity-column chromatography on silica gel
16
17 (hexane/ethyl acetate, 4:1) afford pure ethyl 3-(4,5-diphenyloxazol-2-yl)-3-
18
19 (phenylsulfonyl)propanoate **28** as off-white solid (88 mg, 72%); mp = 30-33 °C; R_f = 0.25
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21 (hexane/ethyl acetate, 4:1); FT-IR (neat film): 3062, 1733, 1447, 1324, 1148 cm^{-1} ; ^1H NMR (400
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23 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
24
25 (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
26
27 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)
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29 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,
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31 127.9, 126.6, 61.5, 61.4, 31.9, 14.1 ppm; HRMS (ESI-TOF) m/z calcd for $\text{C}_{26}\text{H}_{23}\text{NO}_5\text{S}$ $[\text{M}+\text{H}]^+$
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33 462.1375; found 462.1379.

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42 **Ethyl 3-(4,5-diphenyloxazol-2-yl)acrylate (29).** To a cooled (5°C) solution of sulfonyloxazole
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44 ester **28** (225 mg, 0.49 mmol) in dry THF was added potassium *tert*-butoxide (60.2 mg, 0.54
45
46 mmol) under nitrogen and the reaction mixture was then stirred at 5-10°C (2 h) while monitoring
47
48 by TLC. After completion of the reaction, the reaction mixture was extracted with
49
50 dichloromethane (2 x 25 mL) followed by washing the extracts with water and brine then drying
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52 over anhydrous Na_2SO_4 . Removal of the drying agent and concentration of the filtrate gave a
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54 crude residue which was submitted to gravity-column chromatography (hexane/ethylacetate, 4:1)
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3 to provide unsaturated oxazole ester **29** as a colorless oil (100 mg, 65%); $R_f = 0.49$ (hexane/ethyl
4 acetate, 4:1); FT-IR (neat film): 3064, 1712, 1653, 1256, 1159 cm^{-1} ; ^1H NMR (CDCl_3 , 400
5 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,
6 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
7 165.8, 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,
8 128.2, 128.0, 126.7, 124.8, 61.0, 14.2 ppm; HRMS (ESI-TOF) m/z calcd for $\text{C}_{20}\text{H}_{17}\text{NO}_3[\text{M}+\text{H}]^+$
9 320.1287, found 320.1281.
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21 **Ethyl 3-(4,5-diphenyloxazol-2-yl)propanoate (30).**¹⁷ The unsaturated oxazole ester **30** (160
22 mg, 0.50 mmol) was dissolved in methanol (25 mL) then 10% Pd/C (16 mg, 10% wt/wt) was
23 added at room temperature. The reaction mixture was purged with nitrogen while stirring
24 followed by the addition of hydrogen gas (balloon) and then stirring was continued (16 h) under
25 an atmosphere of hydrogen. Upon completion of reaction, the reaction mixture was filtered
26 through a bed of Celite while washing with methanol (2 x 30 mL). The combined filtrates were
27 concentrated and the crude residue was submitted to gravity-column chromatography
28 (hexane/ethyl acetate, 4:1) to afford **30** as an off-white solid (129 mg, 80%); mp 68-70 $^\circ\text{C}$ [Lit.
29 69.5-71 $^\circ\text{C}$]¹⁷; $R_f = 0.36$ (hexane/ethyl acetate, 4:1); FT-IR (neat film): 3068, 2980, 1734, 1444,
30 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),
31 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),
32 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,
33 129.0, 128.6, 128.5, 128.4, 128.0, 127.9, 126.5, 60.8, 31.2, 23.6, 14.2 ppm.
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52 **Methyl 3-(4,5-diphenyloxazol-2-yl)propanoate (31).**¹³ To a clear solution of sulfonyloxazole
53 ester **28** (80 mg, 0.173 mmol) in methanol (10 mL) was added magnesium turnings (63 mg, 2.60
54 mmol) followed by solid mercuric chloride (4.7 mg, 0.017 mmol) at room temperature. The
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3 resulting reaction mixture was stirred (2 h) while monitoring the reaction progress by TLC. After
4 completion of the reaction, the heterogeneous mixture was then filtered through a Celite bed
5 followed by washing with methanol (2 x 15 mL). The methanolic filtrates were combined and
6 concentrated to afford a crude residue. The residue was submitted to gravity-column
7 chromatography (hexane/ethylacetate, 4:1) to provide ester **31** as an off-white solid (52 mg,
8 97%); mp 58-61°C [Lit. 58-59 °C]¹³; $R_f = 0.29$ (hexane/ethyl acetate, 4:1); FT-IR (neat film):
9 3061, 2957, 1731, 1438, 1056 cm^{-1} ; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.63 (d, $J = 7.2$ Hz, 2H),
10 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, $J = 7.6$
11 Hz, 3H) ppm; $^{13}\text{C NMR}$ (175 MHz, CDCl_3) δ 172.5, 161.7, 145.4, 135.1, 132.5, 129.0, 128.6,
12 128.5, 128.4, 128.0, 127.9, 126.5, 51.9, 30.9, 23.5 ppm.

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28 **3-(4,5-Diphenyloxazol-2-yl)propanoic acid (Oxaprozin) (32).**¹³ Ethyl ester **30** (128 mg, 0.39
29 mmol) or methyl ester **31** (65 mg, 0.21 mmol) and 20% aqueous NaOH solution (3 mL) was
30 stirred overnight at room temperature. Upon completion of reaction as indicated by TLC, the
31 reaction mixture was slowly acidified to pH 3-4 using conc. HCl (3 mL) at room temperature and
32 stirring was continued (3 h). After the neutralization was complete the reaction mixture was
33 diluted with cold water (15 mL) and extracted with dichloromethane (2 x 15 mL). The organic
34 extracts were combined, dried over anhydrous Na_2SO_4 and concentrated to give a white solid
35 residue. The residue was submitted to gravity-column chromatography (chloroform/methanol,
36 9:1) to afford pure Oxaprozin **32** as white solid (80 mg, 68%, from the ethyl ester **30**) or (60 mg,
37 97%, from the methyl ester **31**). mp = 158-160 °C [Lit. 160.5-161.5 °C]¹³; $R_f = 0.27$
38 (methanol/chloroform, 1:9); FT-IR (neat) 3156, 2948, 1714, 1568; $^1\text{H NMR}$ (400 MHz, CDCl_3)
39 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, $J =$
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3 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,
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5 128.5, 128.1, 127.9, 126.4, 31.0, 23.2 ppm.
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12 **ACKNOWLEDGMENT** The measurement of high-resolution mass spectra by Dr. Bo Wang of
13
14 the Texas A&M University Laboratory for Biological Mass Spectrometry is acknowledged.
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16 Financial support from the NIH/NIDCR through grant 1RO1DE023206 is gratefully
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18 acknowledged.
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24 **Supporting Information Available.** Copies of spectra for compounds **3-32** are included.
25
26 This material is available free of charge via the Internet at <http://pubs.acs.org>
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