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Versatile "Traceless" Sulfone Linker for SPOS: Preparation of Isoxazolinopyrrole 2-Carboxylates

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Abstract: A five-step solid-phase synthesis of isoxazolinopyrrole-2-carboxylates (**6**) that employs a traceless sulfone linker strategy is reported. Resin-bound diene **4**, obtained by acetylation and concomitant β-elimination of acetate from resin-bound allylic alcohol **3**, underwent regioselective 1,3-dipolar cycloadditons with nitrile oxides. Formation of the pyrrole products in a resin-releasing strategy was performed by pyrrole annulation with alkyl isocyanoacetates, which react with the vinyl sulfone moiety to generate the target isoxazolinopyrrole-2-carboxylates (**6**). Use of this chemistry afforded eight isoxazolinopyrrole-2-carboxylates in 6−24% overall yields from polystyrene/divinylbenzene sulfinate **1**.

Combinatorial chemistry and related parallel synthesis techniques are important tools in lead generation, target validation, and lead optimization in drug discovery,[1] and solid-phase organic synthesis (SPOS)[2] has become the most important method in combinatorial synthesis. One continuing objective in SPOS is the development of linker strategies and chemistries applicable to combinatorial techniques wherein the tether is stable through the penultimate step and then readily and efficiently cleaved from the resin. Since the "traceless linker" notion was introduced by Veber[3] and Ellman,[4] these strategies for small organic molecule[5] library production have received much attention.[6] In this regard, we recently reported[7] the preparation of a sulfinate-functionalized resin [from styrene/2% divinylbenzene copolymer beads (PS/DVB)][8] and its "traceless" chemistries.[9] Herein, we report application of a versatile traceless sulfone linker to generate

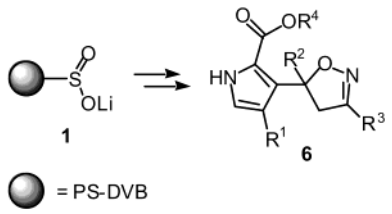

FIGURE 1. Traceless solid-phase synthesis of isoxazolopyrroles.

3-(4,5-dihydroisoxazol-5-yl)pyrrole 2-carboxylates (**6**; Figure 1) from lithium sulfinate resin **1** by S-alkylation with alkyl iodide, sulfone monoanion electrophilic 1,2-addition to α,β-unsaturated aldehydes,[10] acetylation followed by in situ β-elimination, regioselective 1,3-dipolar cycloaddition,[11] and subsequent traceless resin release by pyrrole annulation.[12] Product **6** contains isoxazoline and pyrrole subunits, heterocycles that constitute important structural moieties that occur frequently in natural products and other biologically active compounds.[13] We, therefore, believe these 3-(4,5-dihydroisoxazol-5-yl)-pyrrole 2-carboxylates (**6**) may prove to be useful as a molecular scaffold for library production.

On the basis of our solution-phase studies, we set out to develop a solid-phase route to these isoxazolinopyrroles that exploited the sulfone moiety to (1) mediate a number of synthetic transformation and (2) tracelessly tether the forming small molecule to the resin via a temporary C,S-sulfone bond (see Scheme 1).[14] Our solid-phase synthesis of 3-(4,5-dihydroisoxazol-5-yl)pyrrole-2-carboxylate **6**, which can be monitored by KBr FT-IR, began with benzenesulfinate-functionalized resin **1**. Following our[7,9] published method,[8] lithium benzenesulfinate resin **1** was prepared by treating PS/DVB beads with ^{n}BuLi followed by infusion of excess SO_2.[7] The benzene sulfinate loading (0.8 mmol/g) of these beads was determined by treating lithium benzenesulfinate resin **1** with excess standardized aqueous HCl and then back-titration against standardized aqueous NaOH.

The first real challenge confronted was development of a reliable route to the requisite polymer-bound dienyl sulfone (e.g., **4**). Although several methods for the preparation of 1-sulfonyl-1,3-dienes have been reported, they generally do not lead to variable substitution of the dienes. Among them, the Horner−Emmons reaction of a carbonyl substrate with an α-phosphoryl sulfone and reaction of an α,β-unsaturated aldehyde with a sulfonyl Grignard reagent do accommodate C2−C4 diene substi-

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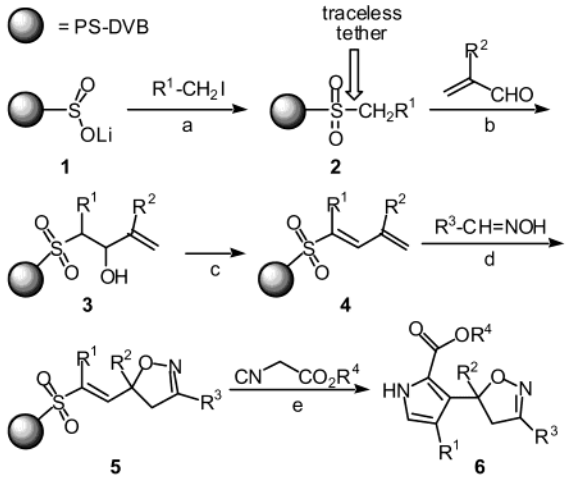
SCHEME 1. Solid-Phase Synthesis of 3-(4,5-Dihydroisoxazol-5-yl)pyrrole 2-Carboxylates (6)[a]



[a] Reagents and conditions: (a) THF or DME, reflux, 24 h. (b) (i) ^{n}BuLi (1.2 equiv), THF, −78 °C, 1 h; (ii) −78 °C → rt, 12 h. (c) DBU (6 equiv), Ac_2O (4 equiv), THF, rt, 1 day. (d) Aqueous NaOCl (5 equiv), CH_2Cl_2, 0 °C → rt, 12 h. (e) NaH (2.2 equiv), HMDS (2.2 equiv), DMSO (15 equiv), THF, rt, 1 day.

tution paterns, and each results in variable (*E*)-C−C double-bond formation.[15] However, neither method provides for C1 substitution of 1-sulfonyl 1,3-dienes.

The solid-phase route reported in the Scheme 1 for conversion of **1** to **4** does accommodate C1−C4 substitution [although C2 substitution is ruled out in the present application by the fact that C2 ends up as an sp^2 quaternary carbon in the final isoxazolopyrrole product-(**6**)] and provides the targeted (*E*)-C−C double bond in excellent yields. To initiate this process, S-alkylation of benzenesulfinate resin **1** was achieved by treatment with excess alkyl iodide. As anticipated by the HSAB principle,[16] reaction of this ambident sulfinate anion with a soft alkylating agent, e.g., methyl iodide, gives the sulfone product (**2**) exclusively.[17] However, S-alkylation with ethyl iodide requires refluxing in DME and, in a solution-phase model reaction, led to formation of ca. 3% of ethyl benzenesulfinate product (i.e., O-alkylation).

Reaction of the resulting THF-swollen phenylalkyl sulfone resin (**2**) with ^{n}BuLi generated the Cα anion, which underwent a condensation reaction with α,β-unsaturated aldehydes to afford allylic alcohol resin **3**. It should be noted that a stoichiometric amount of ^{n}BuLi was used in this step, as the use of excess ^{n}BuLi in solution-phase model studies produced a complex mixture of products. Also, while the use of either dimsyl anion or LDA to generate •-sulfonyl monocarbanions for reaction with epoxide or alkyl halide electrophiles has been demonstrated,[18] no product (**3**; ● = Ph) was isolated when **2** (● = Ph) was treated with dimsyl anion. The use of excess LDA (3 equiv) in reaction **2** → **3** (● = Ph) is

TABLE 1. Synthesis of 6 (see Scheme 1) Using PS/2%-DVB

entry	product	R^1	R^2	R^3	R^4	% yield[a]
1	**6a**	H	H	C_6H_5	Et	16
2	**6a**	H	H	C_6H_5	Et	16[b]
3	**6a**	H	H	C_6H_5	Et	16[c]
4	**6b**	H	H	4-$MeOC_6H_4$	Et	17
5	**6c**	H	H	4-CNC_6H_4	Et	24
6	**6d**	H	H	2-Py	Et	19
7	**6e**	H	H	$(CH_2)_5CH_3$	Et	13
8	**6f**	Me	Me	C_6H_5	Et	12
9	**6g**	H	Me	C_6H_5	Et	24
10	**6h**	H	H	C_6H_5	CH_2Ph	6

[a] Purified yield based on the sulfinate loading of resin **1**. [b] PS/1%-DVB was used in place of PS/2%-DVB. [c] Identical to entry 1 except that LDA was used in place of ^{n}BuLi in step **2** → **3**.

effective (80% yield of **3**; $R^1 = R^2 = H$) but offers no advantage over the use of ^{n}BuLi (95% yield of **3**; $R^1 = R^2 = H$) (Table 1, entry 3). Finally, resin-bound diene **4** was obtained from this β-hydroxy sulfone by hydroxyl acetylation and concomitant DBU-mediated β-elimination of acetate (reaction **3** → **4**).

With this diene scaffold in hand, we set out to engineer the regioselective construction of the isoxazolino and pyrrolo heterocycles. Solid-phase 1,3-dipolar cycloaddition of nitrile oxides, generated via the Huisgen method with aqueous NaOCl,[19] to acrylate resin in THF has been reported by Cheng's group.[11b] Our initial trials using THF as a solvent in solution-phase studies produced incomplete reaction, but simply switching to CH_2Cl_2 solved this problem. Thus, treatment of resin-bound diene **4** with nitrile oxides, generated by reaction of aldoximes with an excess of commercially available bleach (5 equiv) in CH_2Cl_2, gave resin bound isoxazolines **5** regioselectively. As reported in the literature[20] and also demonstrated by us,[14] nitrile oxides add with high regioselectivity to the less substituted double bond of 1-substituted butadienes. Moreover, the regioselectivity of 1,3-dipolar cycloadditions to 1,3-butadiene has been rationalized computationally by analyzing the transitional structure associated with isoxazoline formation.[21] Typically, reaction **4** → **5** was not amenable to IR analysis, but employing 4-cyanobenzaldehyde oxime as a nitrile oxide precursor allowed this transformation to be monitored by the appearance of a cyano stretch in the KBr FT-IR (**6c**; 2227 cm-1). Subsequent reaction of resin **5** with alkyl isocyanoacetate anion generated by sodium hydride in the presence of HMDS and DMSO in THF furnished the desired 3-(4,5-dihydroisoxazol-5-yl)pyrrole-2-carboxylates **6** (Table 1).[22]

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As reported by Magnus,[22a] the ester moiety of the alkyl isocyanoacetate plays a pivotal role in the formation of the desired pyrrole heterocycle. Specifically, the desired product **6** is obtained by aromatization of the pyrrole ring by removal of the relatively acidic ester Cα-proton followed by sulfinate elimination of the resin bound sulfonyl moiety. This process not only delivers the targeted pyrrole ring, but it also releases the product from the resin. As a consequence of this release mechanism, isoxazolinopyrroles **6** is obtained in good purity from **1** through the five-step process outlined in the Scheme 1. Step **2** → **3**, which utilizes only 1 equiv of the ^{n}BuLi, is thought to be largely responsible for the relatively low overall yields for reaction **1** → **6** (6−24%). Excess nitrile oxide was employed in reaction **4** → **5**. However, on the basis of the fact that using excess dipole reagent in the solution-phase variant does not lead to bis-addition, we do not believe excess dipole reagent is detrimental to the overall yield (i.e., a bis-adduct would not be released from the resin). It should also be noted that PS/1%-DVB and PS/2%-DVB beads gave the same overall yield of **6** (entry 1 and 2, Table 1).

We have demonstrated a solid-phase traceless sulfone linker method for construction of the isoxazolinopyrrole heterocycles that accommodates four points of diversification (see R^1−R^4 in **6**). This chemistry appears to be well suited for combinatorial library production.

Experimental Section

General Procedures. All reactions, unless otherwise noted, were performed under an inert atmosphere of dry nitrogen. PS/1%-DVB and PS/2%-DVB beads were purchased from Acros. Tetrahydrofuran was distilled from sodium/benzophenone ketyl immediately prior to use. Methylene chloride and 1,2-dimethoxyethane (DME) were distilled from CaH_2. Melting points were uncorrected. All infrared spectra were analyzed by FT-IR. ^{1}H and ^{13}C NMR were measured in $CDCl_3$ at 300 and 75 MHz, respectively. Elemental analyses were determined at MidWest Microlab, Indianapolis, IN.

General Procedure for the Preparation of Isoxazolinopyrrole 6. As a typical example, the preparation of **6a** is described as follows.

Ethyl 3-(3-Phenyl-4,5-dihydroisoxazol-5-yl)-1*H*-pyrrole-2-carboxylate (6a). Polymer **1** (3.61 g) was swollen in THF (50 mL), and iodomethane (2 mL) was added at room temperature and then refluxed under nitrogen (24 h). The resin was collected by filtration using a medium sintered glass fritted Buchner funnel, washed with H_2O (2 × 15 mL), THF/H_2O (1:1, 2 × 20 mL), THF (2 × 20 mL), and ether (2 × 10 mL), and dried overnight affording polymer-bound methyl sulfone **2** as yellow beads: IR (KBr) 1599, 1492, 1451, 1301, 1142 cm^{-1}.

Polymer **2** (3.1 g) was swollen in THF (37 mL) at −78 °C, and *n*-BuLi (2 mL, 3.2 mmol, 1.6 M) was added. After the mixture was stirred for 1 h, acrolein (0.18 g, 3.2 mmol) was added at −78 °C, and the reaction was allowed to warm to room temperature for 12 h. The reaction was quenched with aqueous saturated NH_4Cl solution (10 mL), and polymer **3** was filtered out and washed with H_2O (2 × 20 mL), THF/H_2O (1:1, 2 × 25 mL), THF (2 × 20 mL), and ether (2 × 10 mL) and dried overnight: IR (KBr) 3499, 1597, 1490, 1447, 1303, 1143 cm^{-1}.

Polymer **3** (3.1 g) was swollen in THF (35 mL) at 0 °C, and acetic anhydride (1.1 g, 1 mL, 11 mmol) and DBU (2.5 g, 2.5 mL, 16.6 mmol) were added. The reaction was stirred at room temperature for 1 day at which time the resin was collected by filtration using a medium sintered glass fritted Buchner funnel, washed with H_2O (2 × 15 mL), THF/H_2O (1:1, 2 × 20 mL), THF (2 × 20 mL), and ether (2 × 10 mL), and dried, affording polymer **4** as yellow beads: IR (KBr) 1598, 1491, 1449, 1314, 1142 cm^{-1}.

Polymer **4** (3 g) was swollen in CH_2Cl_2 (60 mL), and benzaldehyde oxime (0.64 g, 5.3 mmol) was added. Aqueous NaOCl (19 g, 13.2 mmol) was added dropwise over 30 min at 0 °C, and the reaction was allowed to warmed to room temperature for 12 h. The resin was collected by filtration using a medium sintered glass fritted Buchner funnel, washed with H_2O (2 × 15 mL), THF/H_2O (1:1, 2 × 20 mL), THF (2 × 20 mL), CH_2Cl_2 (2 × 15 mL), and ether (2 × 10 mL), and dried overnight, affording polymer **5** as yellow beads: IR (KBr) 1604, 1496, 1446, 1304, 1142 cm^{-1}.

1,1,1,3,3,3-Hexamethyldisilazane (1.3 g, 8 mmol) was added to a suspension of NaH (0.32 g, 8 mmol, 60% in mineral oil) in THF (10 mL) and stirred for 10 min. This mixture was added dropwise to a suspension of polymer **4** (3 g) and ethyl isocyanoacetate (0.66 g, 5.8 mmol) in dry THF (17 mL) at 0 °C. DMSO (2.8 mL, 40 mmol) was added, and the reaction mixture was stirred at room temperature for 1 day. The reaction was quenched by addition of saturated aqueous NH_4Cl, and the polymer was removed by filtration and washed with ethyl acetate (3 × 30 mL). The combined organic filtrate and washings were washed with H_2O, and the resulting organic layer was dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (20% EtOAc in *n*-hexane) to give **6a** (80 mg, 14% overall yield from polymer **1**; 25% overall yield from PS/1%-DVB **1**) as a white solid (CH_2Cl_2/Et_2O): mp 87 °C; IR (neat) 3295, 1676 cm^{-1}; ^{1}H NMR δ 9.07 (br s, 1H), 7.72−7.66 (m, 2H), 7.42−7.37 (m, 3H), 6.88 (t, J = 2.75 Hz, 1H), 6.40 (t, J = 2.75 Hz, 1H), 6.28 (dd, J = 10.85 and 7.8 Hz, 1H), 4.36 (q, J = 7.14 Hz, 2H), 3.81 (dd, J = 16.6 and 10.9 Hz, 1H), 3.27 (dd, J = 16.6 and 7.8 Hz, 1H), 1.38 (t, J = 7.14 Hz, 3H); ^{13}C NMR δ 160.77, 156.36, 132.00, 129.98, 129.73, 128.68, 126.71, 122.21, 118.31, 108.95, 77.13, 60.66, 43.13, 14.70. Anal. Calcd for $C_{16}H_{16}N_2O_3$: C, 67.59; H, 5.67; N, 9.85. Found: C, 67.78; H, 5.63; N, 9.89.

3-(3-(4-Methoxyphenyl)-4,5-dihydro-isoxazol-5-yl)-1*H*-pyrrole-2-carboxylic Acid Ethyl Ester (6b). White solid in 17% overall yield (CH_2Cl_2/ Et_2O): mp 109.3 °C; IR (neat) 3321, 1681 cm^{-1}; ^{1}H NMR δ 9.03 (br s, 1H), 7.65−7.61 (m, 2H), 6.94−6.89 (m, 2H), 6.87 (t, J = 2.8 Hz, 1H), 6.40 (t, J = 2.8 Hz, 1H), 6.25 (dd, J = 11 and 7.69 Hz, 1H), 4.35 (q, J = 7.1 Hz, 2H), 3.84 (s, 3H), 3.78 (dd, J = 17 and 11 Hz, 1H), 3.23 (dd, J = 17 and 7.7 Hz, 1H), 1.38 (t, J = 7.1 Hz, 3H); ^{13}C NMR δ 160.93, 160.72, 155.94, 132.27, 128.28, 122.39, 122.05, 118.35, 114.14, 109.12, 76.99, 60.67, 55.53, 43.44, 14.75. Anal. Calcd for $C_{17}H_{18}N_2O_4$: C, 64.96; H, 5.77; N, 8.91. Found: C, 65.20; H, 5.70; N, 8.83.

3-(3-(4-Cyanophenyl)-4,5-dihydro-isoxazol-5-yl)-1*H*-pyrrole-2-carboxylic Acid Ethyl Ester (6c). White solid in 24% overall yield (CH_2Cl_2/ Et_2O): mp 173.3 °C; IR (neat) 3292, 2227, 1672 cm^{-1}; ^{1}H NMR δ 9.07 (br s, 1H), 7.80−7.67 (m, 4H), 6.89 (t, J = 2.8 Hz, 1H), 6.38−6.31 (m, 2H), 4.36 (q, J = 7.1 Hz, 2H), 3.80 (dd, J = 16.6 and 11 Hz, 1H), 3.25 (dd, J = 16.6 and 8 Hz, 1H), 1.38 (t, J = 7.1 Hz, 3H); ^{13}C NMR δ 160.56, 155.13, 134.09, 132.47, 131.28, 127.14, 122.21, 118.44, 118.41, 113.22, 108.85, 78.10, 60.75, 42.37, 14.71. ESI MS *m*/*z* calcd for $C_{17}H_{15}N_3O_3Na$ (M + Na) 332.10, found 331.75. Anal. Calcd for $C_{17}H_{15}N_3O_3$: C, 66.01; H, 4.89; N, 13.58. Found: C, 65.88; H, 5.00; N, 13.46.

3-(3-Pyridin-2-yl-4,5-dihydro-isoxazol-5-yl)-1*H*-pyrrole-2-carboxylic Acid Ethyl Ester (6d). White solid in 19% overall yield (CH_2Cl_2/ Et_2O): mp 122.5 °C; IR (neat) 3176.4, 1683.6 cm^{-1}; ^{1}H NMR δ 9.08 (br s, 1H), 8.59 (ddd, J = 4.94, 1.65, and 1.1 Hz, 1H), 8.06 (dt, J = 7.97 and 1.1 Hz, 1H), 7.73 (dt, J = 8 and 1.8 Hz, 1H), 7.31−7.26 (m, 1H), 6.88 (t, J = 2.8 Hz, 1H), 6.38 (dt, J = 2.75 and 0.55 Hz, 1H), 6.33 (dd, J = 11.1 and 7.9 Hz, 1H), 4.35 (q, J = 7.14 Hz, 2H), 3.92 (dd, J = 17.6 and 10.99 Hz, 1H), 3.45 (dd, J = 17.6 and 7.69 Hz, 1H), 1.38 (t, J = 7.14 Hz, 3H); ^{13}C NMR δ 160.81, 158.21, 149.59, 149.28, 136.38, 131.51, 124.16, 122.09, 121.80, 118.58, 108.94, 77.91, 60.71, 42.64, 14.68. Anal. Calcd for $C_{15}H_{15}N_3O_3$: C, 63.15; H, 5.30; N, 14.73. Found: C, 63.08; H, 5.41; N, 14.63.

3-(3-*n*-Hexyl-4,5-dihydro-isoxazol-5-yl)-1*H*-pyrrole-2-carboxylic Acid Ethyl Ester (6e). Colorless oil in 13% overall yield: IR (neat) 3320, 1695 cm^{-1}; ^{1}H NMR δ 9.05 (br s, 1H), 6.86 (t, J = 2.75 Hz, 1H), 6.35 (t, J = 2.75 Hz, 1H), 6.06 (dd, J = 10.71 and 7.42 Hz, 1H), 4.33 (q, J = 7.14 Hz, 2H), 3.38 (dd, J = 17.03 and 10.71 Hz, 1H), 2.80 (dd, J = 17.04 and 7.42 Hz,

1H), 2.36 (t, J = 7.69 Hz, 2H), 1.57−1.50 (m, 2H), 1.39−1.25 (m, 6H), 1.36 (t, J = 7.14 Hz, 3H), 0.90−0.85 (m, 3H); ^{13}C NMR δ 160.77, 158.89, 132.65, 122.09, 118.08, 108.83, 75.77, 60.54, 45.30, 31.61, 29.05, 27.91, 26.55, 22.69, 14.67, 14.23. Anal. Calcd for $C_{16}H_{24}N_2O_3$: C, 65.73; H, 8.27; N, 9.58. Found: C, 65.63; H, 8.05; N, 9.32.

4-Methyl-3-(3-Phenyl-4,5-dihydro-isoxazol-5-yl)-1*H*-pyrrole-2-carboxylic Acid Ethyl Ester (6f). White solid in 12% overall yield (CH_2Cl_2/ Et_2O): mp 129.5 °C; IR (neat) 3299, 1664 cm^{-1}; ^{1}H NMR δ 9.00 (br s, 1H), 7.73−7.69 (m, 2H), 7.42−7.40 (m, 3H), 6.70 (d, J = 2.5 Hz, 1H), 6.49 (dd, J = 11.5 and 10.4 Hz, 1H), 4.31 (q, J = 7.1 Hz, 2H), 3.70 (dd, J = 16.8 and 11.5 Hz, 1H), 3.34 (dd, J = 16.8 and 10.4 Hz, 1H), 2.09 (s, 3H), 1.33 (t, J = 7.1 Hz, 3H); ^{13}C NMR δ 160.87, 156.20, 129.94, 129.83, 128.74, 127.52, 126.66, 121.57, 120.38, 119.80, 76.77, 60.63, 41.84, 14.69, 11.36. Anal. Calcd for $C_{17}H_{18}N_2O_3$: C, 68.44; H, 6.08; N, 9.39. Found: C, 68.59; H, 6.10; N, 9.34.

3-(5-Methyl-3-phenyl-4,5-dihydro-isoxazol-5-yl)-1*H*-pyrrole-2-carboxylic Acid Ethyl Ester (6g). White solid in 24% overall yield (Et_2O/*n*-hexane): mp 79.8 °C; IR (neat) 3321, 1688 cm^{-1}; ^{1}H NMR δ 9.12 (br s, 1H), 7.68−7.65 (m, 2H), 7.38−7.34 (m, 3H), 6.82 (t, J = 2.7 Hz, 1H), 6.57 (t, J = 2.7 Hz, 1H), 4.35 (q, J = 7.1 Hz, 2H), 3.63 (dd, J = 19.2 and 17.0 Hz, 2H), 1.85 (s, 3H), 1.39 (t, J = 7.1 Hz, 3H); ^{13}C NMR δ 159.98, 157.03, 137.73, 130.20, 129.77, 128.60, 126.58, 121.05, 116.53, 110.02, 86.34, 60.53, 48.61, 27.57, 14.73. Anal. Calcd for $C_{17}H_{18}N_2O_3$: C, 68.44; H, 6.08; N, 9.39. Found: C, 68.33; H, 6.04; N, 9.33.

3-(3-Phenyl-4,5-dihydro-isoxazol-5-yl)-1*H*-pyrrole-2-carboxylic Acid Benzyl Ester (6h). White solid in 6% overall yield (Et_2O/*n*-hexane): mp 113.2 °C; IR 3252, 1696 cm^{-1}; ^{1}H NMR δ 9.1 (br s, 1H), 7.67−7.62 (m, 2H), 7.52−7.37 (m, 8H), 6.86 (t, J = 3 Hz, 1H), 6.40 (t, J = 3 Hz, 1H), 6.25 (dd, J = 10.9 and 8 Hz, 1H), 5.33 (q, J = 12 Hz, 2H), 3.68 (dd, J = 16.71 and 11 Hz, 1H), 3.20 (dd, J = 16.71 and 7.7 Hz, 1H); ^{13}C NMR δ 160.48, 156.37, 135.73, 132.68, 130.00, 129.71, 128.88, 128.76, 128.68, 128.55, 128.51, 122.49, 117.89, 109.15, 77.16, 66.54, 43.19. Anal. Calcd for $C_{21}H_{18}N_2O_3$: C, 72.82; H, 5.24; N, 8.09. Found: C, 72.70; H, 5.19; N, 8.06.

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