Development of a Continuous Flow Photoisomerization Reaction Converting Isoxazoles into Diverse Oxazole Products

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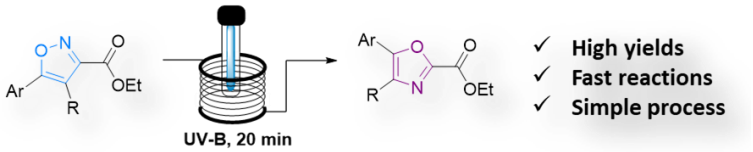
Supporting Information Placeholder



ABSTRACT: A continuous flow process is presented that directly converts isoxazoles into their oxazole counterparts via a photochemical transposition reaction. This results in the first reported exploitation of this transformation to establish its scope and synthetic utility. A series of various di- and trisubstituted oxazole products bearing different appendages including different heterocyclic moieties was realized through this rapid and mild flow process. Furthermore, the robustness of this approach was demonstrated by generating gram quantities of selected products whilst also providing insights into likely intermediates.

INTRODUCTION

Oxazoles and isoxazoles represent members of valuable and oftentimes biologically active five-membered heteroaromatic structures.[1] These can be found in both natural products as well as synthetic entities such as pharmaceutical and agrochemical agents.[2] Oxazoles are particularly prevalent in alkaloid natural products as they arise from cyclodehydration of suitable amino acid precursors, rendering a variety of small bioactive molecules including texaline (**1**), pimprinin (**2**) and annuloline (**3**, Figure 1).

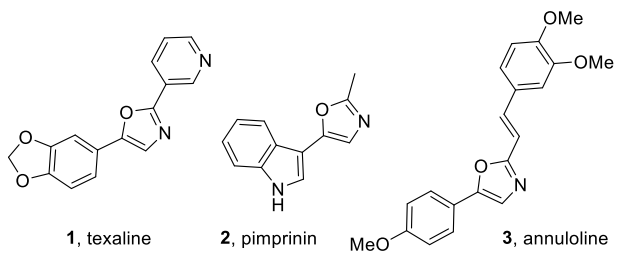
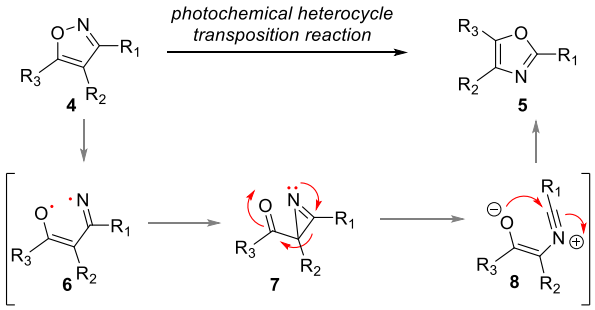


Figure 1: Selected oxazole containing natural products.

Whilst conventional synthesis strategies are in place that allow for the preparation of either isoxazole or oxazole heterocycles from suitable acyclic precursors, the direct transposition of isoxazoles into oxazoles is an overlooked alternative. Singh and coworkers reported on a photochemical transformation several decades ago providing evidence that this could be achieved.[3] More recently, Jones and co-workers reported on a thermal process based on isoxazole systems bearing crucial phenolic appendages.[4] Whilst in the latter case a mechanistic rationale based on Boulton-Katrizky as well as Neber rearrangements was put forward, extensive studies on the photochemical process are in support of a homolytic cleavage of the O–N bond, followed by generation of an acyl azirine species (**7**), which ring-opens followed by ring-closure of the resulting nitrilium enolate species (Scheme 1).[5] The latter part of this mechanism is reminiscent of the Cornforth rearrangement, which may provide further support for this pathway.[6]



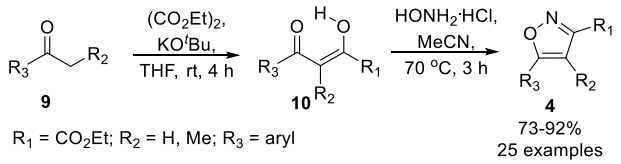
Scheme 1: Photoisomerization of isoxazoles and its proposed mechanism.

Despite a considerable amount of interest in this heterocycle transposition reaction and related processes,[7] to date no robust and generally viable means to effectively generate oxazoles from isoxazoles has been reported. This may be because in the thermal process a phenolic moiety is required, whereas the photochemical process suffers from intrinsic limitations such as long reaction time in specialized reaction glassware, formation of undesirable photodegradation products as well as limited scalability.

We therefore set out to realize such a general and scalable method that would facilitate the generation of sets of different oxazole products in a simple and effective manner. To achieve this, we opted to exploit continuous flow technology[8] in combination with a UV-photo-reactor that would impart high process control, uniform radiation profiles as well as high reproducibility as evident from many recent reports.[9] Several non-photochemical oxazole syntheses have been reported in continuous flow mode highlighting the advantageous nature of this technology.[10] Specifically, we opted to use a Vapourtec UV150 flow reactor system that provides a temperature-controlled flow coil (10 mL, PFA) unit in combination with a medium-pressure mercury lamp. The use of specific filters additionally allows to block wavelengths above 400 nm (see SI for details).

RESULTS AND DISCUSSION

We commenced our studies by devising an effective two-step preparation into a series of isoxazole substrates that was realized by a Claisen condensation between different commercially available acetophenones **9** and diethyl oxalate. The resulting 1,3-dicarbonyls (**10**) were subsequently treated with hydroxylamine hydrochloride in a thermal cyclocondensation process furnishing the desired isoxazoles in high yields. Pleasingly, this approach allowed for the rapid generation of a diverse set of isoxazole starting materials in which the nature and substitution pattern of the aryl appendage (R_3) could be varied to subsequently study the scope of this unusual heterocycle transposition process in detail (Scheme 2, see SI for full details).

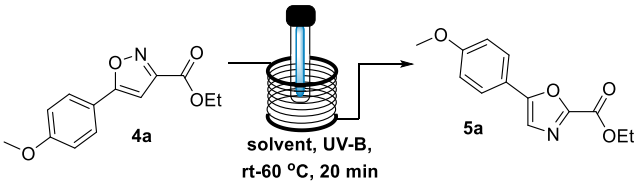


Scheme 2: General batch synthesis of isoxazole substrates (**4**).

Having secured a reliable access into the required isoxazoles we next turned to their photochemical transposition into the desired oxazole products. Using the aforementioned photo-flow reactor set-up, we were able to quickly screen a variety of different reaction conditions focusing on solvent choice, concentration and temperature. Therefore, solutions of test substrate **4a** were pumped via a peristaltic pump of the Vapourtec E-Series module at a flow rate of 0.5 mL/min. As a light source a medium-pressure Hg lamp was used that can be adjusted to operate between 75-150 W.

As outlined in Table 1, this study highlighted that acetonitrile was the best solvent with ideal concentrations at 10-15 mM. Other solvents such as DCM, acetone, THF and EtOH were tolerated however, slower reactions were observed in these cases. Temperatures ranging between 25-45 °C were well tolerated, whilst above ~50 °C impurity formation was increased. To control the temperature within the photo-reactor a stream of chilled nitrogen gas was passed into this unit that is controlled by the system's software via a pincher valve. Most notably, we established that residence times within the reactor of 20 minutes were sufficient to observe conversions greater than 90%, while most batch reports state reaction times of 4-8 h. We ascribe this improvement to the uniform radiation profile in this flow set-up that does not suffer from limitations such as the penetration depth of light into conventional reaction vessels due to the Beer-Lambert law. Additionally, we found that using a filter that blocks wavelengths greater 400 nm to be beneficial as it avoids temperature increase and thus minimizes formation of colored by-products and other side reactions.

Table 1: Optimization of reaction conditions in flow (**4a** → **5a**).



entry	solvent	concentration (mM)	Temperature[a)] (°C)	yield[b)] (%)
1	DCM	10	35	23
2	THF	10	35	40
4	acetone	10	35	34
5	EtOH	10	35	37
6	MeCN	10	35	76
7	MeCN	10	60	70
8	MeCN	15	35	81
9	MeCN	20	35	73
10	MeCN	15	35, no filter	53

Reaction conditions: residence time 20 minutes (flow rate 0.5 mL/min), lamp power 150 W; [a)] ±5 °C; [b)] ^{1}H NMR yield with 1,3,5-trimethoxybenzene as internal standard.

The optimal set of conditions (Table 1, entry 9, filter used) were subsequently applied to the continuous preparation of oxazole **5a** from its isoxazole precursor **4a** over a period of 12 hours. This experiment proved robustness of the system as well as scalability to generate 1.5 g of the desired product **5a**. In addition, we were able to crystalize both substrate and product and secure their molecular structures by single crystal X-ray diffraction experiments thus proving the anticipated photorearrangement process (Figure 2).

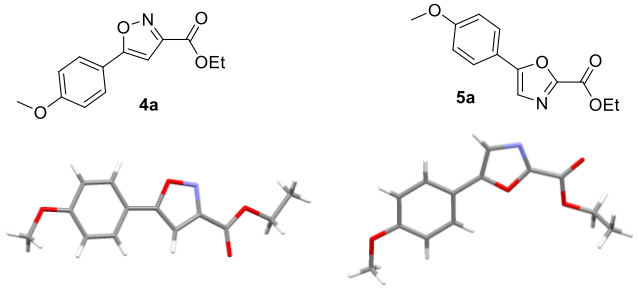
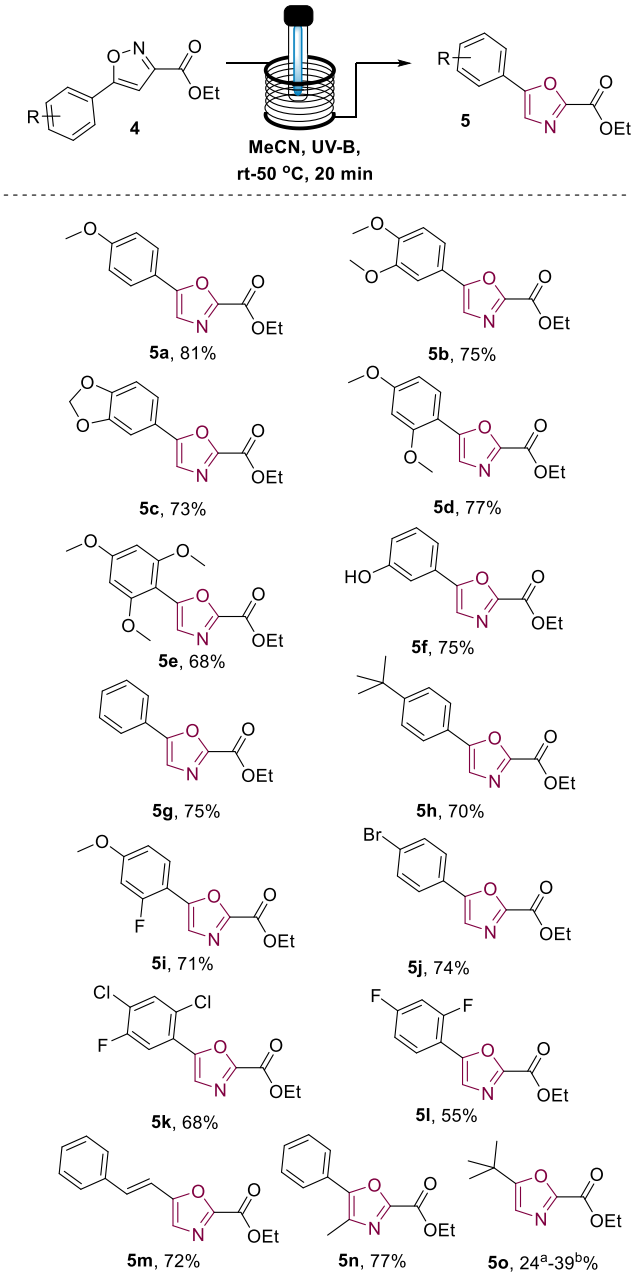


Figure 2: X-ray crystal structure substrate-product pair.

Having succeeded in generating gram quantities of desired oxazole products in a continuous manner, we next wished to explore the substrate scope of this photochemical heterocycle transposition reaction. We exploited our short entry into the isoxazole substrates (Scheme 2) that enabled rapid supply of diverse building blocks that were subjected to the optimized reaction conditions (Table 1, entry 9).

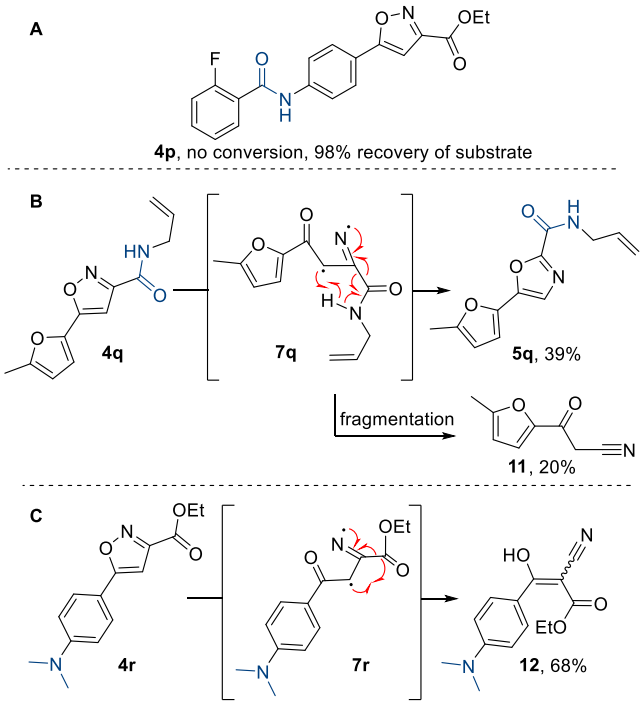
Pleasingly, it was found that a wide variety of substrates bearing different aryl moieties furnished the desired oxazole products in an effective and high yielding flow process. Different substitution patterns on the aryl moiety in the 5-position of the isoxazole ring were all well-tolerated, including methoxy and methylenedioxy groups and free phenols (Scheme 3). In addition, photo-labile bromide substituents as well as chlorides and fluorides all successfully underwent the desired transformation. It was also established that styryl moieties were competent motifs to undergo this photoisomerization process delivering the corresponding oxazole product (**5m**) in good yield.



Scheme 3: Photoisomerization product scope; [a] 20 min residence time, [b] 40 min residence time.

At this stage a correlation between the isolated yield and the electronic properties of the aryl moieties was noted. Namely, electron-rich systems gave consistently higher yields than electron-poor ones. While initially surprising, we surmise that this phenomenon is correlated to the specific UV-Vis absorption maximum of each substrate. This appears to best match the emission spectrum of the medium-pressure Hg lamp in case of electron-rich substrates (λ_{max} > 300 nm), whilst electron-poor ones (λ_{max} < 300 nm) are more mismatched (see SI for details). This observation was compounded when substituting the aryl moiety with a *tert*-butyl group leading to a significant decrease in conversion and isolated yield even when doubling the residence time (**5o**). It was furthermore established that substituents such as a methyl group at the 4-position of the isoxazole scaffold (R_2 = Me) are tolerated giving rise to trisubstituted oxazole products in high yield.

We furthermore subjected a selection of isoxazole substrates bearing modified substituents to this flow process. These included isoxazoles **4p** and **4q** bearing either an additional amide substituent or the amide as a replacement of the ester. Interestingly, it was observed that amide **4p** did not show any conversion (Scheme 4A), whereas amide **4q** gave the desired oxazole product (**5q**), albeit with a reduced yield (Scheme 4B). In the latter case, we also isolated a small amount of a ring opened species bearing a nitrile (**11**). Additionally, we noticed that substrate **4r** bearing a tertiary amine was converted into an alternative nitrile-bearing photoproduct (**12**) in good yield without rendering isolable amounts of the expected oxazole product (Scheme 4C). While the former nitrile product may arise from a competitive fragmentation pathway,[11] the latter nitrile appears to result from a formal 1,2-migration of the adjacent ester moiety.[12] Importantly, both cases support the intermediacy of radical species in this transformation and provide further insight into their fate.



Scheme 4: Amide and amine-based isoxazole substrates and plausible mechanistic rationales for the formation of **11** and **12**.

We next turned our attention to studying heteroaryl substituted isoxazoles in this photo-rearrangement reaction. We thus employed our general substrate synthesis (Scheme 2) to convert a small series of commercially available acylated heteroarenes to access the desired isoxazole substrates within two steps.

Subjecting these materials to our previously established flow conditions did indeed confirm that various heteroaromatic appendages are well-tolerated in this flow process. These include furans, thiophenes, indoles as well as pyrroles (Figure 3). Due to the nature of this process, no protecting groups on the nitrogen atoms of either the indole or the pyrrole substrate were required. We furthermore were able to secure a single crystal structure for pyrrole-oxazole product **5u** which confirms the

connectivity and integrity of this system. This showcases the mild and general nature of this flow process that serves as a rapid entry into interesting heterocyclic building blocks. Additionally, variations on the ester moiety were found to not impact the efficiency of the overall transformation allowing different ester products (e.g. dodecyl ester **5x** and heteroaryl ester **5y**) to be suitable replacements for the previous ethyl esters.

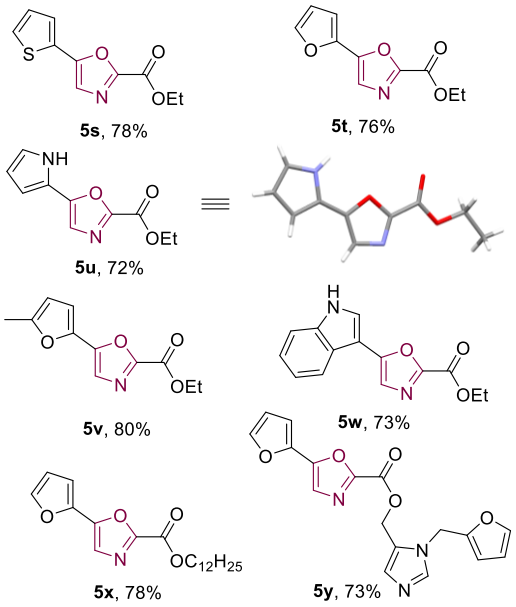


Figure 3: Product scope for heteroaromatic substrates.

The simplicity with which such scaffolds comprising of different linked heteroaryl moieties can be assembled is remarkable. Therefore, this simple and effective entry into these drug-like fragments does demonstrate their potential to inspire screening libraries in current and future medicinal chemistry campaigns.

In conclusion, we have demonstrated the feasibility of effectively performing this intriguing photoisomerization reaction to yield versatile oxazole products via a continuous photochemical process. An effective two-step preparation of various isoxazole precursors furnished a selection of substrates that allowed us to study the substrate scope of this transformation. The resulting flow process delivered the desired products in generally high yields and in a scalable manner allowing further exploitation of this unique heterocycle transposition reaction in the future.

EXPERIMENTAL SECTION

General Information

Unless otherwise stated, all solvents were purchased from Fisher Scientific and used without further purification. Substrates and reagents were purchased from Fluorochem or Sigma Aldrich and used as received.

^{1}H-NMR spectra were recorded on 400 MHz and 500 MHz instruments and are reported relative to residual solvent: $CHCl_3$ (δ 7.26 ppm), d_6-DMSO (δ 2.50 ppm). ^{13}C-NMR spectra were recorded on the same instruments (100 and 125 MHz) and are reported relative to $CHCl^3$ (δ 77.16 ppm), d_6-DMSO (δ 39.52 ppm). ^{19}F-NMR were recorded at 376 MHz. Data for ^{1}H-NMR are reported as follows: chemical shift (δ/ ppm) (integration, multiplicity, coupling constant (Hz)). Multiplicities are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet, br. s = broad singlet, app = apparent. Data for ^{13}C{1H} NMR are reported in terms of chemical shift (δ/ ppm) and multiplicity (C, CH, CH_2 or CH_3). DEPT-135, COSY, HSQC, HMBC and NOESY experiments were used in the structural assignment.

IR spectra were obtained by use of a Bruker Platinum spectrometer (neat, ATR sampling) with the intensities of the characteristic signals being reported as weak (w, <20% of tallest signal), medium (m, 21-70% of tallest signal) or strong (s, >71% of tallest signal).

High-resolution mass spectrometry was performed using the indicated techniques on a micromass LCT orthogonal time-of-flight mass spectrometer with leucine-enkephalin (Tyr-Gly-Phe-Leu) as an internal lock mass. GC-MS was performed on a Waters GCT Premier Agilent 7898 system (column Macherey-Nagel; Optima 5 MS, length 15 m, diameter: 0.25 mm).

For UV-Vis measurements a Shimadzu UV-1800 UV spectrophotometer was used. Melting points were recorded on a Stuart SMP10 melting point apparatus and are uncorrected.

Continuous flow experiments were performed on a Vapourtec E-series system equipped with the UV150 photoreactor that is based on a medium pressure Hg lamp (150 W).

Synthetic Procedures and Spectroscopic Data

Synthesis of Claisen Condensation Products 10a – 10y: General Procedure:

To a solution of the appropriate acetophenone (1.0 equiv.) in THF (1.5 M) was added diethyl oxalate (1.2 equiv.). The resulting mixture was stirred at room temperature for 10 minutes, before KO^{t}BU (1.1 equiv.) was added in small portions resulting in the formation and precipitation of the potassium salt of the Claisen adduct. After 10 hours stirring at room temperature, the resulting suspension was filtered, and the solid product was washed with further THF to remove unreacted starting materials. After treating the solid product with HCl (1 M, aqueous), the Claisen adduct typically formed a solid that was filtered and dried. In cases where no precipitation was observed an aqueous extraction with DCM was performed rendering the desired product after evaporation of the combined, dried organic layers.

Claisen condensation products derived from propiophenone and 2-acetyl pyrrole were used as crude materials directly in the subsequent step.

Ethyl (Z)-2-hydroxy-4-(4-methoxyphenyl)-4-oxobut-2-enoate, 10a:

Isolated yield: 2.30 g (9.3 mmol, 93%). Appearance: off-white solid. Melting range: 58-60 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.98 (d, *J* = 9.0 Hz, 2H) 7.03 (s, 1H) 6.98 (d, *J* = 9.0 Hz, 2H) 4.39 (q, *J* = 7.1 Hz, 2H) 1.40 (t, *J* = 7.1 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 190.3 (C), 168.1 (C), 164.3 (C), 162.5 (C), 130.3 (2CH), 127.7 (C), 114.2 (2CH), 97.7 (CH), 62.5 (CH_2), 55.6 (CH_3), 14.1 (CH_3). IR (neat) ν/cm^{-1} 2981 (w), 1719 (m), 1581 (s), 1510 (m), 1255 (s), 1165 (s), 1107 (s), 1021 (s), 825 (s), 769 (s), 583 (s). HRMS (TOF-ESI+) calculated for $C_{13}H_{15}O_5$ 251.0919, found 251.0928 (M+H+).

Ethyl (Z)-4-(3,4-dimethoxyphenyl)-2-hydroxy-4-oxobut-2-enoate, 10b:

Isolated yield: 2.57 g (9.2 mmol, 92%). Appearance: yellow solid. Melting range: 99-101 °C. ^{1}H-NMR (400 MHz, $CDCl^3$) δ/ppm 7.65 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.55 (d, *J* = 2.0 Hz, 1H), 7.05 (s, 1H), 6.94 (d, *J* = 8.4 Hz, 1H), 4.40 (q, *J* = 7.2 Hz, 2H), 3.97 (s, 3H), 3.97 (s, 3H), 1.42 (t, *J* = 7.2 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 190.8 (C), 167.2 (C), 162.5 (C), 154.1 (C), 149.3 (C), 128.1 (C), 122.9 (CH), 110.4 (CH), 109.9 (CH), 98.0 (CH), 62.5 (CH_2), 56.2 (CH_3), 56.1 (CH_3), 14.1 (CH_3). IR (neat) ν/cm^{-1} 2940 (w), 1730 (w), 1595 (m), 1518 (m), 1466 (m), 1266 (s), 1214 (m), 1021 (m), 772 (m). HRMS (TOF-ESI+) calculated for $C_{14}H_{17}O_6$ 281.1025, found 281.1021.

Ethyl (Z)-4-(benzo[d][1,3]dioxol-5-yl)-2-hydroxy-4-oxobut-2-enoate, 10c:

Isolated yield: 2.22 g (8.4 mmol, 84%). Appearance: yellow solid. Melting range: 69-71 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.61 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.46 (d, *J* = 1.7 Hz, 1H), 6.98 (s, 1H), 6.89 (d, *J* = 8.2 Hz, 1H), 6.08 (s, 2H), 4.39 (q, *J* = 7.2 Hz, 2H), 1.40 (t, *J* = 7.2 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 190.2 (C), 167.6 (C), 162.3 (C), 152.6 (C), 148.5 (C), 129.7 (C), 124.5 (CH), 108.3 (CH), 107.6 (CH), 102.1 (CH2), 97.9 (CH), 62.5 (CH_2), 14.1 (CH_3). IR (neat) ν/cm^{-1} 2985 (w), 2907 (w), 1727 (m), 1601 (m), 1504 (m), 1451 (m), 1251 (s), 1110 (m), 1036 (m), 931 (m), 814 (m). HRMS (TOF-ESI+) calculated for $C_{13}H_{13}O_6$ 265.0713, found 265.0712 (M+H+).

Ethyl (Z)-4-(2,4-dimethoxyphenyl)-2-hydroxy-4-oxobut-2-enoate, 10d:

Isolated yield: 2.26 g (8.1 mmol, 80%). Appearance: yellow solid. Melting range: 39-41 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.96 (d, *J* = 8.8 Hz, 1H), 7.32 (s, 1H), 6.58 (dd, *J* = 8.8, 2.3 Hz, 1H), 6.47 (d, *J* = 2.3 Hz, 1H), 4.37 (q, *J* = 7.2 Hz, 2H), 3.93 (s, 3H), 3.88 (s, 3H), 1.40 (t, *J* = 7.2 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 189.2 (C), 168.6 (C), 165.3 (C), 162.9 (C), 161.3 (C), 132.9 (CH), 117.5 (C), 105.7 (CH), 102.6 (CH), 98.5 (CH), 62.2 (CH_2), 55.7 (CH_3), 55.6 (CH_3), 14.1 (CH_3). IR (neat) ν/cm^{-1} 2977 (w), 1742 (m), 1725 (m), 1607 (m), 1573 (s), 1237 (s), 1115 (m), 1018 (s), 783 (m), 730 (m). HRMS (TOF-ESI+) calculated for $C_{14}H_{17}O_6$ 281.1025, found 281.1027 (M+H+).

Ethyl (Z)-2-hydroxy-4-oxo-4-(2,4,6-trimethoxyphenyl)but-2-enoate, 10e:

Isolated yield: 1.2 g (3.9 mmol, 83%). Appearance: yellow solid. Melting range: 81-83 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 6.63 (s, 1H), 6.09 (s, 2H), 4.32 (q, *J* = 7.2 Hz, 2H), 3.82 (s, 3H), 3.78 (s, 6H), 1.34 (t, *J* = 7.2 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 194.6 (C), 163.7 (C), 163.1 (C), 162.7 (C), 159.8 (C), 110.2 (C), 106.7 (CH), 90.7 (2CH), 62.2 (CH_2), 56.0 ($2CH_3$), 55.4 (CH_3), 14.1 (CH_3). IR

(neat) ν/cm^{-1} 2990 (w), 2944 (w), 2838 (w), 1741 (m), 1579 (s), 1447 (m), 1264 (s), 1185 (s). HRMS (TOF-ESI+) calculated for $C_{15}H_{18}O_7Na$ 333.0950, found 333.0959.

Ethyl (Z)-2-hydroxy-4-(3-hydroxyphenyl)-4-oxobut-2-enoate, 10f:

Isolated yield: 1.01 g (4.4 mmol, 88%). Appearance: beige amorphous powder. ^{1}H-NMR (400 MHz, DMSO-d_6) δ/ppm δ 9.89 (s, 1H), 7.45 (d, *J* = 7.7 Hz, 1H), 7.39 – 7.29 (m, 2H), 7.05 (d, *J* = 8.0 Hz, 1H), 6.96 (s, 1H), 4.26 (q, *J* = 7.1 Hz, 2H), 1.26 (t, *J* = 7.1 Hz, 3H). ^{13}C{1H} NMR (100 MHz, DMSO-d_6) δ/ppm 190.7 (C), 169.2 (C), 162.0 (C), 158.4 (C), 136.1 (C), 130.7 (CH), 121.8 (CH), 119.2 (CH), 114.2 (CH), 98.4 (CH), 62.6 (CH_2), 14.2 (CH_3). IR (neat) ν/cm^{-1} 3437 (s), 2980 (w), 1713 (s), 1583 (s), 1440 (m), 1284 (s), 1212 (s), 767 (s), 584 (s). HRMS (TOF-ESI+) calculated for $C_{12}H_{13}O_5$ 237.0763, found 237.0763.

Ethyl (Z)-2-hydroxy-4-oxo-4-phenylbut-2-enoate, 10g:

Isolated yield: 2.07 g (8.6 mmol, 86%). Appearance: yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 8.00 – 7.94 (m, 2H), 7.62 – 7.56 (m, 1H), 7.48 (dd, *J* = 8.4, 7.0 Hz, 2H), 7.06 (s, 1H), 4.38 (q, *J* = 7.2 Hz, 2H), 1.39 (t, *J* = 7.1 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 190.7 (C), 169.8 (C), 162.2 (C), 134.9 (C), 133.8 (CH), 128.9 (2CH), 127.9 (2CH), 97.9 (CH), 62.6 (CH_2), 14.1 (CH_3). IR (neat) ν/cm^{-1} 3065 (w), 2983 (w), 1729 (s), 1597 (s), 1450 (m), 1236 (s), 700 (s). HRMS (TOF-ESI+) calculated for $C_{12}H_{13}O_4$ 221.0814, found 221.0810.

Ethyl (Z)-4-(4-(tert-butyl)phenyl)-2-hydroxy-4-oxobut-2-enoate, 10h:

Isolated yield: 2.2 g (8.0 mmol, 80%). Appearance: yellow liquid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.92 (d, *J* = 8.4 Hz, 2H), 7.50 (d, *J* = 8.4 Hz, 2H), 7.05 (s, 1H), 4.38 (q, *J* = 7.2 Hz, 2H), 1.39 (t, *J* = 7.2 Hz, 3H), 1.33 (s, 9H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 190.6 (C), 169.4 (C), 162.3 (C), 157.9 (C), 132.2 (C), 127.9 (2CH), 125.9 (2CH), 97.9 (CH), 62.5 (CH_2), 35.2 (C), 31.0 ($3CH_3$), 14.1 (CH_3). IR (neat) ν/cm^{-1} 2963 (w), 2906 (w), 2870 (w), 1730 (m), 1602 (s), 1473 (w), 1365 (m), 1264 (s), 1242 (s). HRMS (TOF-ESI+) calculated for $C_{16}H_{21}O_4$ 277.1440, found 277.1444.

Ethyl (Z)-4-(2-fluoro-4-methoxyphenyl)-2-hydroxy-4-oxobut-2-enoate, 10i:

Isolated yield: 2.44 g (9.1 mmol, 91%). Appearance: off-white solid. Melting range: 85-88 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.95 (app t, *J* = 8.8 Hz, 1H), 7.08 (d, *J* = 1.2 Hz, 1H), 6.80 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.65 (dd, *J* = 13.6, 2.4 Hz, 1H), 4.38 (q, *J* = 7.1 Hz, 2H), 3.87 (s, 3H), 1.39 (t, *J* = 7.1 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 187.3 (C, d, *J* = 4 Hz), 168.7 (C, d, *J* = 1 Hz), 165.4 (C, d, *J* = 12 Hz), 163.4 (CF, d, *J* = 256 Hz), 162.3 (C), 131.9 (CH, d, *J* = 3 Hz), 116.2 (C, d, *J* = 11 Hz), 111.1 (CH, d, *J* = 3 Hz), 102.3 (CH), 101.9 (CH, d, *J* = 15 Hz), 62.5 (CH_2), 55.9 (CH_3), 14.0 (CH_3). ^{19}F-NMR (376 MHz, $CDCl_3$) δ/ppm -105.4. IR (neat) ν/cm^{-1} 2997 (w), 2959 (w), 1720 (m), 1617 (m), 1585 (m), 1276 (s), 1253 (s), 1231 (s), 1108 (s), 1020 (m), 956 (m), 836 (m), 780 (s), 554 (m). HRMS (GC-TOF EI+) calculated for $C_{13}H_{13}FO_5$ 268.0747, found 268.0738 (M+).

Ethyl (Z)-4-(4-bromophenyl)-2-hydroxy-4-oxobut-2-enoate, 10j:

Isolated yield: 1.17 g (3.9 mmol, 78%). Appearance: yellow powder. Melting range: 62-64 °C ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.83 (d, *J* = 8.8 Hz, 2H) 7.62 (d, *J* = 8.8 Hz, 2H) 7.0 (s, 1H) 4.38 (q, *J* = 7.1 Hz, 2H) 1.39 (t, *J* = 7.1 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$)

δ/ppm 189.4 (C), 170.1 (C), 162.0 (C), 133.6 (C), 132.2 (2CH), 129.3 (2CH), 129.0 (C), 97.7 (CH), 62.7 (CH_2), 14.1 (CH_3). IR (neat) ν/cm^{-1} 3415 (w), 2980 (w), 2934 (w), 1719 (s), 1679 (m), 1584 (s), 1478 (m), 1242 (s), 1004 (s). HRMS (TOF-ESI+) calculated for $C_{12}H_{12}O_4Br$ 298.9919, found 298.9908.

Ethyl (Z)-4-(2,4-dichloro-5-fluorophenyl)-2-hydroxy-4-oxobut-2-enoate, 10k:

Isolated yield: 2.69 g (8.8 mmol, 88%). Appearance: off-white solid. Melting range: 133-136 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.55 (d, *J* = 6.3 Hz, 1H), 7.48 (d, *J* = 8.7 Hz, 1H), 6.96 (s, 1H), 4.39 (q, *J* = 7.2 Hz, 2H), 1.40 (t, *J* = 7.2 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 189.7 (C), 168.9 (C), 161.5 (C), 156.8 (CF, d, *J* = 252 Hz), 135.2 (C, d, *J* = 6 Hz), 132.7 (CH), 127.6 (C, d, *J* = 4 Hz), 125.7 (C, d, *J* = 19 Hz), 117.9 (CH, d, *J* = 24 Hz), 102.5 (CH), 62.8 (CH_2), 14.0 (CH_3). ^{19}F-NMR (376 MHz, $CDCl_3$) δ/ppm -115.6. IR (neat) ν/cm^{-1} 3095 (w), 3040 (w), 1733 (s), 1629 (s), 1469 (m), 1378 (s), 1303 (s), 1264 (s), 1191 (s), 1088 (s), 1022 (s), 780 (s), 725 (s), 557 (m), 531 (m). HRMS (TOF-ESI+) calculated for $C_{12}H_9Cl_2FO_4Na$ 328.9760, found 328.9775.

Ethyl (Z)-4-(2,4-difluorophenyl)-2-hydroxy-4-oxobut-2-enoate, 10l:

Isolated yield: 2.02 g (7.9 mmol, 79%). Appearance: yellow solid. Melting range: 194-197 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.99 (td, *J* = 8.7, 6.5 Hz, 1H), 7.06 (d, *J* = 1.5 Hz, 1H), 7.03 – 6.97 (m, 1H), 6.90 (ddd, *J* = 11.1, 8.6, 2.4 Hz, 1H), 6.33 (br s, 1H), 4.37 (q, *J* = 7.1 Hz, 2H), 1.38 (t, *J* = 7.1 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 186.5 (d, *J* = 4 Hz, C), 169.7 (C), 166.1 (dd, *J* = 259, 13 Hz, CF), 162.4 (dd, *J* = 260, 13 Hz, CF), 161.9 (C), 132.4 (dd, *J* = 11, 3 Hz, CH), 120.2 – 120.0 (m, C), 112.5 (dd, *J* = 21, 4 Hz, CH), 105.7 – 104.6 (m, CH), 102.0 (d, *J* = 13 Hz, CH), 62.7 (CH_2), 14.0 (CH_3). ^{19}F-NMR (376 MHz, $CDCl_3$) δ/ppm -100.3 (m), -104.2 (m). IR (neat) ν/cm^{-1} 3156 (w), 3082 (w), 2994 (w), 2906 (w), 1723 (s), 1599 (s) 1260 (s), 1234 (s), 776 (s). HRMS (TOF-ESI+) calculated for $C_{12}H_{11}F_2O_4$ 257.0625, found 257.0635.

Ethyl (2Z,5E)-2-hydroxy-4-oxo-6-phenylhexa-2,5-dienoate, 10m:

Isolated yield: 1.83 g (7.5 mmol, 75%). Pale yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.72 (d, *J* = 15.8 Hz, 1H), 7.55 (dd, *J* = 6.7, 3.1 Hz, 2H), 7.45 – 7.35 (m, 3H), 6.64 (d, *J* = 15.8 Hz, 1H), 6.52 (s, 1H), 4.35 (q, *J* = 7.1 Hz, 2H), 1.38 (t, *J* = 7.1 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 185.0 (C), 174.4 (C), 162.0 (C), 143.3 (CH), 134.3 (C), 130.9 (CH), 129.0 (2CH), 128.4 (2CH), 123.0 (CH), 100.6 (CH), 62.5 (CH_2), 14.0 (CH_3). IR (neat) ν/cm^{-1} 2988 (w), 1729 (s), 1630 (m), 1579 (m), 1259 (s), 1119 (m), 977 (m), 788 (m). HRMS (TOF-ESI+) calculated for $C_{14}H_{14}O_4Na$ 269.0790, found 269.0800.

Ethyl (Z)-2-hydroxy-5,5-dimethyl-4-oxohex-2-enoate, 10o:

Isolated yield: 1.6 g (7.9 mmol, 79%). Appearance: colorless oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 6.53 – 6.51 (m, 1H), 4.38 – 4.31 (m, 2H), 1.39 – 1.33 (m, 3H), 1.21 – 1.19 (m, 9H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 209.2 (C), 167.4 (C), 162.3 (C), 97.9 (CH), 62.4 (CH_2), 41.6 (C), 26.6 ($3CH_3$), 14.0 (CH_3). IR (neat) ν/cm^{-1} 2972 (w), 1732 (m), 1633 (m), 1594 (m), 1281 (m), 1243 (s), 1109 (s), 1013 (m), 891 (m), 780 (m). HRMS (TOF-ESI+) calculated for $C_{10}H_{17}O_4$ 201.1127, found 201.1131 (M+H+).

Ethyl (Z)-4-(4-(2-fluorobenzamido)phenyl)-2-hydroxy-4-oxobut-2-enoate, 10p:

Isolated yield: 1.04 g (2.9 mmol, 81%). Appearance: pale yellow powder. ^{1}H-NMR (400 MHz, DMSO-d_6) δ/ppm 10.85 (s, 1H), 8.08 (d, *J* = 8.6 Hz, 2H), 7.90 (d, *J* = 8.6 Hz, 2H), 7.67 (td, *J* = 7.5, 1.9 Hz, 1H), 7.58 (tdd, *J* = 7.3, 5.2, 1.8 Hz, 1H), 7.35 (d, *J* = 10.5 Hz, 1H), 7.31 (d, *J* = 7.4 Hz, 1H), 7.08 (s, 1H), 4.28 (q, *J* = 7.1 Hz, 2H), 1.28 (t, *J* = 7.1 Hz, 3H). ^{13}C{1H} NMR (100 MHz, DMSO-d_6) δ/ppm 190.0 (C), 168.7 (C), 163.8 (C), 162.1 (C), 159.4 (d, *J* = 249 Hz, CF), 144.7 (C), 133.4 (d, *J* = 9 Hz, CH), 130.4 (d, *J* = 3 Hz, CH), 129.9 (2CH), 129.8 (C), 125.1 (d, *J* = 4 Hz, CH), 124.9 (d, *J* = 15 Hz, C), 119.8 (2CH), 116.7 (d, *J* = 22 Hz, CH), 98.2 (CH), 62.6 (CH_2), 14.3 (CH_3). ^{19}F-NMR (376 MHz, DMSO-d6) δ/ppm -114.5. IR (neat) ν/cm^{-1} 3335 (m), 1727 (m), 1656 (m), 1597 (m), 1519 (s), 1239 (s), 1204 (s), 853 (m), 778 (s), 751 (s), 652 (s), 499 (m). HRMS (TOF-ESI+) calculated for $C_{19}H_{17}NO_5F$ 358.1091, found 358.1094.

Ethyl (Z)-4-(4-(dimethylamino)phenyl)-2-hydroxy-4-oxobut-2-enoate, 10r:

Isolated yield: 1.41 g (5.4 mmol, 88%). Appearance: orange solid. Melting range: 100-103 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.89 (d, *J* = 9.2 Hz, 2H), 6.97 (s, 1H), 6.66 (d, *J* = 9.2 Hz, 2H), 4.36 (q, *J* = 7.2 Hz, 2H), 3.07 (s, 6H), 1.38 (t, *J* = 7.2 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 189.8 (C), 166.7 (C), 163.0 (C), 154.1 (C), 130.4 (2CH), 122.1 (C), 111.0 (2CH), 97.6 (CH), 62.2 (CH_2), 40.0 ($2CH_3$), 14.1 (CH_3). IR (neat) ν/cm^{-1} 2905 (w), 1723 (m), 1562 (m), 1523 (w), 1317 (s), 1251 (s), 1110 (s), 707 (s). HRMS (TOF-ESI+) calculated for $C_{14}H_{18}NO_4$ 264.1246, found 264.1242.

Ethyl (Z)-2-hydroxy-4-oxo-4-(thiophen-2-yl)but-2-enoate, 10s:

Isolated yield: 927 mg (4.1 mmol, 81%). Appearance: yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.84 (dd, *J* = 3.9, 1.1 Hz, 1H), 7.73 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.18 (dd, *J* = 4.9, 3.8 Hz, 1H), 6.90 (s, 1H), 4.38 (q, *J* = 7.2 Hz, 2H), 1.39 (t, *J* = 7.2 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 186.0 (C), 164.8 (C), 162.2 (C), 142.1 (C), 135.2 (CH), 132.6 (CH), 128.7 (CH), 99.4 (CH), 62.6 (CH_2), 14.1 (CH_3). IR (neat) ν/cm^{-1} 3109 (w), 2984 (w), 1735 (m), 1617 (s), 1406 (m), 1274 (s), 775 (m). HRMS (ESI-TOF+) calculated for $C_{10}H_{11}O_4S$ 227.0378, found 227.0367.

Ethyl (Z)-4-(furan-2-yl)-2-hydroxy-4-oxobut-2-enoate, 10t:

Isolated yield: 1.66 g (7.9 mmol, 79%). Appearance: pale yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.64 (d, *J* = 1.9 Hz, 1H), 7.30 (d, *J* = 3.8 Hz, 1H), 6.90 (s, 1H), 6.58 (dd, *J* = 3.5, 1.6 Hz, 1H), 4.35 (q, *J* = 7.1 Hz, 2H), 1.36 (t, *J* = 7.1 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 181.0 (C), 166.0 (C), 161.9 (C), 150.8 (C), 147.7 (CH), 118.4 (CH), 113.1 (CH), 98.9 (CH), 62.5 (CH2), 14.0 (CH3). IR (neat) ν/cm^{-1} 3125 (m), 2987 (w), 1739 (m), 1612 (s), 1552 (s), 1467 (m), 1282 (s), 1246 (s), 1129 (s), 1015 (s), 771 (s). HRMS (TOF-ESI+) calculated for $C_{10}H_{11}O_5$ 211.0606, found 211.0605.

Ethyl (Z)-2-hydroxy-4-(5-methylfuran-2-yl)-4-oxobut-2-enoate, 10v:

Isolated yield: 1.91 g (8.5 mmol, 85%). Appearance: yellow solid. Melting range: 88-90 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.26 – 7.23 (m, 1H), 6.85 (s, 1H), 6.23 (dd, *J* = 3.5, 1.2 Hz, 1H), 4.37 (q, *J* = 7.2 Hz, 2H), 2.42 (s, 3H), 1.38 (t, *J* = 7.2 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 180.6 (C), 164.9 (C), 162.2 (C), 159.5 (C), 149.7 (C), 120.6 (CH), 110.1 (CH), 99.0 (CH), 62.5 (CH_2), 14.2 (CH_3). IR (neat) ν/cm^{-1} 3122 (w), 2991 (w), 1737 (s), 1606 (s), 1519 (s), 1287 (s), 1245 (s), 1209 (s), 1124 (s), 1017 (s), 822 (s), 776 (s). HRMS (TOF-ESI+) calculated for $C_{11}H_{12}O_5Na$ 247.0582, found 247.0583.

Ethyl (Z)-2-hydroxy-4-(1H-indol-3-yl)-4-oxobut-2-enoate, 10w:

Isolated yield: 2.02 g (7.9 mmol, 79%). Appearance: yellow solid. Melting range: 178-180 °C. ^{1}H-NMR (400 MHz, d_6-DMSO) δ/ppm 12.42 (s, 1H), 8.70 (s, 1H), 8.19 (d, *J* = 7.2 Hz, 1H), 7.48 (d, *J* = 7.5 Hz, 1H), 7.24 (m, 2H), 6.99 (s, 1H), 4.27 (q, *J* = 7.2 Hz, 2H), 1.28 (t, *J* = 7.2 Hz, 3H). ^{13}C{1H} NMR (100 MHz, d_6-DMSO) δ/ppm 189.7 (C), 162.8 (C), 162.4 (C), 137.6 (C), 136.5 (CH), 125.6 (C), 124.0 (CH), 123.0 (CH), 122.0 (CH), 115.2 (C), 113.1 (CH), 101.0 (CH), 62.2 (CH_2), 14.4 (CH_3). IR (neat) ν/cm^{-1} 3248 (broad), 1723 (m), 1523 (s), 1409 (s), 1242 (s), 1166 (s), 1124 (s), 994 (s), 772 (m), 740 (s), 712 (m), 626 (m). HRMS (TOF-ES+) calculated for $C_{14}H_{14}NO_4$ 260.0923, found 260.0918.

Synthesis of Isoxazole Products 4a – 4y: General Procedure:

To a solution of the appropriate Claisen adduct (**10a**-**10y**, 1.0 equiv.) in MeCN (1 M) was added hydroxylamine hydrochloride (1.1 equiv.). The resulting mixture was heated at 70 °C until complete consumption of starting material was observed by TLC (~3-6 h). After cooling to room temperature, the mixture was concentrated to ~20% of its volume and loaded onto a pad of silica (~10 g per 10 mmol product). Elution with EtOAc/hexanes (10%) yielded the desired isoxazole product after evaporation of all volatiles under reduced pressure.

Ethyl 5-(4-methoxyphenyl)isoxazole-3-carboxylate, 4a:

Isolated yield: 2.1 g (8.5 mmol, 85%). Appearance: light yellow solid. Melting range: 86-88 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.75 (d, *J* = 8.9 Hz, 2H), 7.00 (d, *J* = 8.9 Hz, 2H), 6.80 (s, 1H), 4.47 (q, *J* = 7.2 Hz, 2H), 3.87 (s, 3H), 1.44 (t, *J* = 7.2 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 171.7 (C), 161.5 (C), 160.2 (C), 156.9 (C), 127.6 (2CH), 119.4 (C), 114.5 (2CH), 98.5 (CH), 62.1 (CH_2), 55.4 (CH_3), 14.1 (CH_3). IR (neat) ν/cm^{-1} 3135 (w), 2997 (w), 1733 (s), 1618 (m), 1510 (m), 1452 (m), 1267 (s), 1188 (m), 1148 (m), 1021 (m), 827 (m), 780 (m). HRMS (TOF-EI+) calculated for $C_{13}H_{13}NO_4$ 247.0845, found 247.0849 (M+). UV-vis (λ_{max}, DCM) 289 nm. X-ray data: for $C_{13}H_{13}NO_4$; P21/c, α = 90, β = 109.660(7), γ = 90, a = 13.350(1), b = 8.1964(5), c = 11.5379(7) – CCDC1967212.

Ethyl 5-(3,4-dimethoxyphenyl)isoxazole-3-carboxylate, 4b:

Isolated yield: 2.1 g (7.7 mmol, 77%). Appearance: off-white solid. Melting range: 142-144 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.39 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.30 (d, *J* = 2.0 Hz, 1H), 6.95 (d, *J* = 8.4 Hz, 1H), 6.81 (s, 1H), 4.47 (q, *J* = 7.1 Hz, 2H), 3.96 (s, 3H), 3.94 (s, 3H), 1.44 (t, *J* = 7.1 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 171.7 (C), 160.1 (C), 156.9 (C), 151.2 (C), 149.4 (C), 119.5 (C), 119.4 (CH), 111.3 (CH), 108.6 (CH), 98.8 (CH), 62.2 (CH_2), 56.1 (CH_3), 56.0 (CH_3), 14.2 (CH_3). IR (neat) ν/cm^{-1} 2972 (w), 2901 (w), 1717 (m), 1579 (m), 1455 (m), 1276 (s), 1244 (s), 1017 (s), 856 (s), 764 (s). HRMS (TOF-EI+) calculated for $C_{14}H_{15}NO_5$ 277.0950, found 277.0950 (M+). UV-vis (λ_{max}, DCM) 308 nm.

Ethyl 5-(benzo[d][1,3]dioxol-5-yl)isoxazole-3-carboxylate; 4c:

Isolated yield: 418 mg (1.60 mmol, 70%). Appearance: pale yellow solid. Melting range: 158-160 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.34 (dd, *J* = 8.1, 1.7 Hz, 1H), 7.24 (d, *J* = 1.7 Hz, 1H), 6.90 (d, *J* = 8.1, 1H), 6.76 (s, 1H), 6.05 (s, 2H), 4.46 (q, *J* = 7.1 Hz, 2H), 1.43 (t, *J* = 7.1 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 171.4 (C), 160 (C), 156.9 (C), 149.8 (C), 148.4 (C), 120.8 (CH), 120.7 (C), 108.9

(CH), 106.1 (CH), 101.7 (CH_2), 98.9 (CH), 62.2 (CH_2), 14.1 (CH_3). IR (neat) ν/cm^{-1} 3136 (w), 1725 (s), 1504 (m), 1463 (s), 1269 (s), 1236 (m), 1023 (m), 927 (m), 779 (m). HRMS (TOF-EI+) calculated for $C_{13}H_{11}NO_5$ 261.0637, found 261.0642 (M+). UV-vis (λ_{max}, DCM) 325 nm.

Ethyl 5-(2,4-dimethoxyphenyl)isoxazole-3-carboxylate, 4d:

Isolated yield: 1.15 g (4.2 mmol, 83%). Appearance: pale yellow solid. Melting range: 123-125 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.90 (d, *J* = 8.6 Hz, 1H), 7.03 (s, 1H), 6.60 (dd, *J* = 8.6, 2.4 Hz, 1H), 6.53 (d, *J* = 2.4 Hz, 1H), 4.46 (q, *J* = 7.2 Hz, 2H), 3.94 (s, 3H), 3.86 (s, 3H), 1.43 (t, *J* = 7.2 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 167.9 (C), 162.8 (C), 160.5 (C), 157.8 (C), 156.9 (C), 128.8 (CH), 109.0 (C), 105.3 (CH), 102.1 (CH), 98.6 (CH), 62.0 (CH_2), 55.6 (CH_3), 55.5 (CH_3), 14.2 (CH_3). IR (neat) ν/cm^{-1} 3002 (w), 2942 (w), 1725 (m), 1613 (s), 1449 (s), 1292 (s), 1226 (s), 1209 (s), 1157 (m), 1111 (m), 1022 (m), 830 (m), 773 (m). HRMS (TOF-ESI+) calculated for $C_{14}H_{15}NO_5$ 277.0950, found 277.0952 (M+). UV-vis (λ_{max}, DCM) 314 nm.

Ethyl 5-(2,4,6-trimethoxyphenyl)isoxazole-3-carboxylate, 4e:

Isolated yield: 700 mg (2.3 mmol, 88%). Appearance: yellow solid. Melting range: 105-107 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 6.79 (s, 1H), 6.15 (s, 2H), 4.43 (q, *J* = 7.2 Hz, 2H), 3.84 (s, 3H), 3.79 (s, 6H), 1.40 (t, *J* = 7.2 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 167.1 (C), 163.3 (C), 160.6 (C), 159.6 (C), 155.9 (C), 105.3 (CH), 98.6 (C), 90.7 (2CH), 61.8 (CH_2), 55.9 ($2CH_3$), 55.4 (CH_3), 14.2 (CH_3). IR (neat) ν/cm^{-1} 3032 (w), 3001 (w), 2977 (w), 2838 (w), 1741 (m), 1613 (m), 1591 (s), 1224 (s), 1123 (s). HRMS (TOF-ES+) calculated for $C_{15}H_{17}NO_6$ 307.1056, found 307.1045. UV-vis (λ_{max}, DCM) 300 nm.

Ethyl (2Z,5E)-2-hydroxy-4-oxo-6-phenylhexa-2,5-dienoate, 4f:

Isolated yield: 870 mg (3.75 mmol, 75%). Appearance: off-white powder. Melting range: 191-193 °C. ^{1}H-NMR (400 MHz, DMSO-d_6) δ/ppm 9.85 (s, 1H), 7.36 (s, 1H), 7.36 – 7.29 (m, 2H), 7.26 (t, *J* = 2.0 Hz, 1H), 6.90 (dt, *J* = 7.7, 2.1 Hz, 1H), 4.35 (q, *J* = 7.1 Hz, 2H), 1.30 (t, *J* = 7.1 Hz, 3H). ^{13}C{1H} NMR (100 MHz, DMSO-d_6) δ/ppm 171.6 (C), 159.8 (C), 158.4 (C), 157.2 (C), 131.0 (CH), 127.6 (C), 118.5 (CH), 117.2 (CH), 112.6 (CH), 101.1 (CH), 62.3 (CH_2), 14.4 (CH_3). IR (neat) ν/cm^{-1} 3317 (broad), 2939 (w), 1769 (m), 1732 (s), 1577 (m), 1243 (s), 1183 (s), 1027 (m). HRMS (TOF-ESI+) calculated for $C_{12}H_{11}NO_4Na$ 256.0586, found 256.0584. UV-vis (λ_{max}, DCM) 271 nm.

Ethyl 5-phenylisoxazole-3-carboxylate, 4g:

Isolated yield: 333 mg (1.53 mmol, 90%). Appearance: colorless solid. Melting range: 54-57 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.81 – 7.76 (m, 2H), 7.46 (m, 3H), 6.90 (s, 1H), 4.45 (q, *J* = 7.2 Hz, 2H), 1.42 (t, *J* = 7.2 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 171.7 (C), 160.0 (C), 156.9 (C), 130.8 (CH), 129.1 (2CH), 126.6 (C), 125.9 (2CH), 99.9 (CH), 62.2 (CH_2), 14.1 (CH_3). IR (neat) ν/cm^{-1} 3147 (w), 3131 (w), 2986 (w), 2940 (w), 1729 (s), 1389 (s), 1247 (s), 1148 (s). HRMS (TOF-ESI+) calculated for $C_{12}H_{12}NO_3$ 218.0817, found 218.0827. UV-vis (λ_{max}, DCM) 272 nm.

Ethyl 5-(4-(tert-butyl)phenyl)isoxazole-3-carboxylate, 4h:

Isolated yield: 294 mg (1.1 mmol, 82%). Appearance: yellow solid. Melting range: 57-59 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.72 (d, *J* = 8.6 Hz, 2H), 7.49 (d, *J* = 8.6 Hz, 2H), 6.86 (s, 1H), 4.45 (q, *J* = 7.2 Hz, 2H), 1.42 (t, *J* = 7.2 Hz, 3H), 1.33 (s, 9H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 171.9 (C), 160.1 (C), 156.9 (C), 154.3 (C), 126.1 (2CH), 125.7 (2CH), 123.9 (C), 99.4 (CH), 62.2 (CH_2), 35.0 (C), 31.1 ($3CH_3$), 14.1 (CH_3). IR (neat) ν/cm^{-1} 2962 (m), 2904 (w), 2868 (w), 1712 (s), 1613 (m), 1444 (m), 1244 (m), 1143 (m). HRMS (TOF-ESI+) calculated for $C_{16}H_{20}NO_3$ 274.1443, found 274.1440. UV-vis (λ_{max}, DCM) 279 nm.

Ethyl 5-(2-fluoro-4-methoxyphenyl)isoxazole-3-carboxylate, 4i:

Isolated yield: 1.2 g (4.5 mmol, 90%). Appearance: off-white solid. Melting range: 102-104 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.87 (app t, *J* = 8.6 Hz, 1H), 6.95 (d, *J* = 3.8 Hz, 1H), 6.81 (dd, *J* = 8.6, 2.5 Hz, 1H), 6.73 (dd, *J* = 12.7, 2.5 Hz, 1H), 4.46 (q, *J* = 7.2 Hz, 2H), 3.85 (s, 3H), 1.43 (t, *J* = 7.2 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 165.8 (C, d, *J* = 3 Hz), 162.9 (C), 160.2 (CF, d, *J* = 252 Hz), 160.0 (C), 157.1 (C), 128.3 (CH, d, *J* = 4 Hz), 110.9 (CH, d, *J* = 2 Hz), 107.8 (C, d, *J* = 13 Hz), 102.2 (CH, d, *J* = 24 Hz), 102.1 (CH, d, *J* = 10 Hz), 62.1 (CH_2), 55.8 (CH_3), 14.1 (CH_3). ^{19}F-NMR (376 MHz, $CDCl_3$) δ/ppm -109.1. IR (neat) ν/cm^{-1} 2987 (w), 1731 (m), 1624 (m), 1335 (m), 1269 (m), 1224 (s), 1103 (m), 1014 (s), 842 (s), 809 (s), 772 (s), 632 (m). HRMS (TOF-EI+) calculated for $C_{13}H_{12}NO_4F$ 265.0750, found 265.0744 (M+). UV-vis (λ_{max}, DCM) 297 nm.

Ethyl 5-(4-bromophenyl)isoxazole-3-carboxylate, 4j:

Isolated yield: 866 mg (2.92 mmol, 77%). Appearance: colorless solid. Melting range: 130-132 °C. ^{1}H-NMR (500 MHz, $CDCl_3$) δ/ppm 7.68 (d, *J* = 8.7 Hz, 2H), 7.63 (d, *J* = 8.7 Hz, 2H), 6.93 (s, 1H), 4.48 (q, *J* = 7.2 Hz, 2H), 1.45 (t, *J* = 7.2 Hz, 3H). ^{13}C{1H} NMR (125 MHz, $CDCl_3$) δ/ppm 170.6 (C), 159.8 (C), 157.1 (C), 132.5 (2CH), 127.3 (2CH), 125.5 (C), 125.3 (C), 100.3 (CH), 62.3 (CH_2), 14.2 (CH_3). IR (neat) ν/cm^{-1} 2984 (w), 1724 (s), 1606 (m), 1445 (m), 1248 (s), 1150 (m), 996 (m), 944 (s), 829 (s), 780 (s), 499 (s). HRMS (TOF-ESI+) calculated for $C_{12}H_{11}NO_3Br$ 295.9922, found 295.9930. UV-vis (λ_{max}, DCM) 278 nm.

Ethyl 5-(2,4-dichloro-5-fluorophenyl)isoxazole-3-carboxylate, 4k:

Isolated yield: 1.2 g (4.0 mmol, 80%). Appearance: off-white solid. Melting range: 76-79 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.78 (d, *J* = 9.4 Hz, 1H), 7.59 (d, *J* = 6.7 Hz, 1H), 7.38 (s, 1H), 4.48 (q, *J* = 7.2 Hz, 2H), 1.44 (t, *J* = 7.2 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 165.9 (C), 159.5 (C), 157.1 (C), 156.9 (CF, d, *J* = 250 Hz), 133 (CH), 127.1 (C, d, *J* = 4 Hz), 125.1 (C, d, *J* = 7 Hz), 124.2 (C, d, *J* = 19 Hz), 116.7 (CH, d, *J* = 25 Hz), 105.3 (CH), 62.4 (CH_2), 14.1 (CH_3). ^{19}F-NMR (376 MHz, $CDCl_3$) δ/ppm -115.3. IR (neat) ν/cm^{-1} 2985 (w), 1720 (s), 1474 (m), 1447 (m), 1287 (s), 1134 (w), 1023 (w), 780 (m), 734 (m). HRMS (TOF-EI+) calculated for $C_{12}H_8NO_3FCl_2$ 302.9865, found 302.9874 (M+). UV-vis (λ_{max}, DCM) 269 nm.

Ethyl 5-(2,4-difluorophenyl)isoxazole-3-carboxylate, 4l:

Isolated yield: 393 mg (1.55 mmol, 97%). Appearance: colorless solid. Melting range: 113-115 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.97 (td, *J* = 8.5, 6.2 Hz, 1H), 7.06 – 7.00 (m, 2H), 6.96 (ddd, *J* = 10.9, 8.6, 2.5 Hz, 1H), 4.46 (q, *J* = 7.2 Hz, 2H), 1.42 (t, *J* = 7.2 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 164.7 (d, *J* = 3 Hz, C), 163.8 (dd, *J* = 254, 14 Hz, CF), 159.8 (C), 159.5 (dd, *J* = 255, 14 Hz, CF), 157.2 (C), 128.9 (dd, *J* = 10, 3 Hz, CH), 112.5 (dd, *J* = 22, 4 Hz, CH), 112.0 – 111.6 (m, C), 105.3 – 104.7 (m, CH), 103.4 (d, *J* = 11 Hz, CH),

62.30 (CH_2), 14.12 (CH_3). ^{19}F-NMR (376 MHz, $CDCl_3$) δ/ppm -104.6 (m), -107.0 (m). IR (neat) ν/cm^{-1} 3186 (w), 3079 (w), 2996 (w), 1727 (s), 1618 (m), 1602 (m), 1504 (s), 823 (s). HRMS (TOF-ESI+) calculated for $C_{12}H_{10}NO_3F_2$ 254.0629, found 254.0640. UV-vis (λ_{max}, DCM) 260 nm.

Ethyl (E)-5-styrylisoxazole-3-carboxylate, 4m:

Isolated yield: 632 mg (2.6 mmol, 85%). Appearance: beige solid. Melting range: 116-118 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.54 – 7.48 (m, 2H), 7.42 – 7.30 (m, 4H), 6.95 (d, *J* = 16.5 Hz, 1H), 6.65 (s, 1H), 4.44 (q, *J* = 7.1 Hz, 2H), 1.41 (t, *J* = 7.1 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 170.3 (C), 160.0 (C), 156.7 (C), 136.1 (CH), 135.1 (C), 129.5 (CH), 128.9 (2CH), 127.3 (2CH), 112.3 (CH), 101.5 (CH), 62.2 (CH_2), 14.1 (CH_3). IR (neat) ν/cm^{-1} 2978 (m), 1733 (s), 1639 (m), 1499 (m), 1391 (m), 1292 (m), 1232 (s), 1029 (m), 970 (m), 834 (m), 694 (m). HRMS (TOF-ESI+) calculated for $C_{14}H_{14}NO_3$ 244.0974, found 244.0962. UV-vis (λ_{max}, DCM) 312 nm.

Ethyl 4-methyl-5-phenylisoxazole-3-carboxylate, 4n:

Isolated yield: 721 mg (3.1 mmol, 78%). Appearance: pale yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.72 (dd, *J* = 8.2, 1.6 Hz, 2H), 7.54 – 7.43 (m, 3H), 4.47 (q, *J* = 7.2 Hz, 2H), 2.43 (s, 3H), 1.45 (t, *J* = 7.2 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 167.4 (C), 160.8 (C), 155.6 (C), 130.0 (CH), 128.9 (2CH), 127.6 (C), 127.0 (2CH), 111.4 (C), 61.8 (CH_2), 14.2 (CH_3), 8.5 (CH_3). IR (neat) ν/cm^{-1} 2983 (w), 1728 (s), 1499 (s), 1303 (m), 1223 (s), 1097 (s), 1017 (m), 769 (m), 693 (s). HRMS (TOF- EI+) calculated for $C_{13}H_{13}NO_3$ (M+) 231.0895, found 231.0901. UV-vis (λ_{max}, DCM) 274 nm.

Ethyl 5-(tert-butyl)isoxazole-3-carboxylate, 4o:

Isolated yield: 1.8 g (9.1 mmol, 91%). Appearance: colorless oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 6.35 (s, 1H), 4.41 (q, *J* = 7.2 Hz, 3H), 1.39 (t, *J* = 7.2 Hz, 3H), 1.35 (s, 9H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 183.1 (C), 160.3 (C), 156.1 (C), 99.1 (CH), 61.9 (CH_2), 32.9 (C), 28.7 ($3CH_3$), 14.1 (CH_3). IR (neat) ν/cm^{-1} 2970 (w), 1731 (s), 1585 (w), 1454 (m), 1240 (s), 1211 (s), 1154 (s), 1020 (m), 777 (s). HRMS (TOF-EI+) calculated for $C_{10}H_{15}NO_3$ 197.1052, found 197.1059 (M+). UV-vis (λ_{max}, DCM) 238 nm.

Ethyl 5-(4-(2-fluorobenzamido)phenyl)isoxazole-3-carboxylate, 4p:

Isolated yield: 517 mg (1.46 mmol, 73%). Appearance: off-white powder. Melting range: 184-186 °C. ^{1}H-NMR (400 MHz, DMSO-d_6) δ/ppm 10.68 (s, 1H), 7.92 (d, *J* = 8.9 Hz, 2H), 7.88 (d, *J* = 8.9 Hz, 2H), 7.67 (td, *J* = 7.6, 1.7 Hz, 1H), 7.61 – 7.51 (m, 1H), 7.37 – 7.32 (m, 2H), 7.32 – 7.28 (m, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 1.31 (t, *J* = 7.1 Hz, 3H). ^{13}C{1H} NMR (100 MHz, DMSO-d_6) δ/ppm 171.3 (C), 163.6 (C), 159.9 (C), 159.4 (d, *J* = 250 Hz, CF), 157.2 (C), 141.6 (C), 133.2 (d, *J* = 8 Hz, CH), 130.4 (d, *J* = 3 Hz, CH), 127.1 (2CH), 125.2 (C), 125.0 (d, *J* = 4 Hz, CH), 121.8 (C), 120.3 (2CH), 116.7 (d, *J* = 22 Hz, CH), 100.3 (CH), 62.3 (CH_2), 14.4 (CH_3). ^{19}F-NMR (376 MHz, DMSO-d_6) δ/ppm -114.5. IR (neat) ν/cm^{-1} 3327 (w), 2986 (w), 1727 (s), 1651 (s), 1527 (s), 1443 (m), 1237 (s), 1132 (s), 781 (m), 751 (s), 512 (m). HRMS (TOF-ESI+) calculated for $C_{19}H_{16}N_2O_4F$ 355.1094, found 355.1102. UV-vis (λ_{max}, DCM) 308 nm.

N-Allyl-5-(5-methylfuran-2-yl)isoxazole-3-carboxamide, 4q:

Isolated yield: 415 mg (1.8 mmol, 90%). Appearance: waxy yellow solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 6.93 (br s, 1H), 6.83 (d, *J* = 3.3 Hz, 1H), 6.78 (s, 1H), 6.16 – 6.12 (m, 1H), 5.91 (ddt, *J* = 17.2, 10.2, 5.7 Hz, 1H), 5.28 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.20 (dt, *J* = 10.2, 1.3 Hz, 1H), 4.08 (tt, *J* = 5.9, 1.6 Hz, 2H), 2.38 (s, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 163.3 (C), 158.6 (C), 158.5 (C), 155.2 (C), 140.9 (C), 133.3 (CH), 117.1 (CH2), 112.4 (CH), 108.3 (CH), 97.7 (CH), 41.8 (CH_2), 13.7 (CH_3). IR (neat) ν/cm^{-1} 3324 (m), 3126 (w), 1676 (s), 1626 (m), 1551 (s), 1436 (s), 1275 (s), 939 (m), 838 (m), 784 (s), 656 (m), 598 (m). HRMS (TOF-EI+) calculated for $C_{12}H_{12}N_2O_3$ 232.0848, found 232.0855 (M+).

Ethyl 5-(4-(dimethylamino)phenyl)isoxazole-3-carboxylate, 4r:

Isolated yield: 396 mg (1.52 mmol, 95%). Appearance: light orange solid. Melting range: 120-122 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.64 (d, *J* = 9.0 Hz, 2H), 6.71 (d, *J* = 9.0 Hz, 2H), 6.67 (s, 1H), 4.43 (q, *J* = 7.2 Hz, 2H), 3.01 (s, 6H), 1.41 (t, *J* = 7.2 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 172.5 (C), 160.4 (C), 156.7 (C), 151.6 (C), 127.2 (2CH), 114.5 (C), 111.8 (2CH), 97.0 (CH), 62.0 (CH_2), 40.1 ($2CH_3$), 14.2 (CH_3). IR (neat) ν/cm^{-1} 3298 (w), 2996 (w), 2982 (w), 2901 (w), 1717 (s), 1605 (s), 1518 (s), 1436 (s), 1253 (s). HRMS (TOF-ESI+) calculated for $C_{14}H_{17}N_2O_3$ 261.1239, found 261.1229. UV-vis (λ_{max}, DCM) 340 nm.

Ethyl 5-(thiophen-2-yl)isoxazole-3-carboxylate, 4s:

Isolated yield: 2.0 g (9.0 mmol, 90%). Appearance: pale yellow solid. Melting range: 48-50 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.56 (dd, *J* = 3.8, 1.2 Hz, 1H), 7.50 (dd, *J* = 5.0, 1.2 Hz, 1H), 7.15 (dd, *J* = 5.0, 3.8 Hz, 1H), 6.78 (s, 1H), 4.46 (q, *J* = 7.1 Hz, 2H), 1.43 (t, *J* = 7.1 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 166.7 (C), 159.8 (C), 156.9 (C), 128.8 (CH), 128.2 (CH), 128.2 (C), 127.8 (CH), 99.5 (CH), 62.3 (CH_2), 14.1 (CH_3). IR (neat) ν/cm^{-1} 2986 (w), 1727 (s), 1592 (m), 1453 (s), 1237 (s), 1189 (s), 1113 (s), 1014 (s), 829 (m), 778 (s), 727 (s). HRMS (TOF-EI+) calculated for $C_{10}H_9NO_3S$ 223.0303, found 223.0310 (M+). UV-vis (λ_{max}, DCM) 298 nm. X-ray data: for $C_{10}H_9NO_3S$; P21/n, α = 90, β = 93.837(2), γ = 90, a = 5.29000(9), b = 16.4483(2), c = 12.6312(2) – CCDC1967213.

Ethyl 5-(furan-2-yl)isoxazole-3-carboxylate, 4t:

Isolated yield: 373 mg (1.8 mmol, 90%). Appearance: beige powder. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.54 (d, *J* = 1.8 Hz, 1H), 6.95 (d, *J* = 3.6 Hz, 1H), 6.79 (s, 1H), 6.53 (dd, *J* = 3.6, 1.8 Hz, 1H), 4.43 (q, *J* = 7.1 Hz, 2H), 1.40 (t, *J* = 7.1 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 163.2 (C), 159.7 (C), 156.6 (C), 144.7 (CH), 142.4 (C), 112.0 (CH), 111.4 (CH), 99.4 (CH), 62.3 (CH_2), 14.1 (CH_3). IR (neat) ν/cm^{-1} 3127 (w), 2992 (w), 1722 (s), 1642 (s), 1432 (m), 1247 (s), 1225 (s), 1012 (s), 768 (s). HRMS (TOF-ESI+) calculated for $C_{10}H_{10}NO_4$ 208.0610, found 208.0614. UV-vis (λ_{max}, DCM) 291 nm.

Ethyl 5-(1H-pyrrol-2-yl)isoxazole-3-carboxylate, 4u:

Isolated yield: 330 mg (1.6 mmol, 81%). Appearance: yellow solid. Melting range: 117-119 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 9.23 (s, 1H), 7.00 (td, *J* = 2.6, 1.4 Hz, 1H), 6.74 (ddd, *J* = 3.8, 2.6, 1.4 Hz, 1H), 6.69 (s, 1H), 6.34 (dt, *J* = 3.8, 2.6 Hz, 1H), 4.46 (q, *J* = 7.1 Hz, 2H), 1.43 (t, *J* = 7.1 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 165.3 (C), 160.1 (C), 156.8 (C), 121.8 (CH), 119.4 (C), 110.9 (CH), 110.7 (CH), 96.9 (CH), 62.2 (CH_2), 14.1 (CH_3). IR (neat) ν/cm^{-1} 3226 (m), 3154 (w), 1731 (m), 1627 (m), 1473 (m), 1450 (m), 1242 (s), 1155 (m), 1022 (m), 772 (s), 739 (s). HRMS (TOF-EI+) calculated for $C_{10}H_{10}N_2O_3$ 206.0691, found 206.0693 (M+). UV-vis (λ_{max}, DCM) 307 nm.

Ethyl 5-(5-methylfuran-2-yl)isoxazole-3-carboxylate, 4v:

Isolated yield: 886 mg (4.0 mmol, 80%). Appearance: yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 6.85 (d, *J* = 3.4 Hz, 1H), 6.73 (s, 1H), 6.18 – 6.10 (m, 1H), 4.44 (q, *J* = 7.2 Hz, 2H), 2.37 (d, *J* = 0.8 Hz, 3H), 1.41 (t, *J* = 7.2 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 163.4 (C), 159.8 (C), 156.6 (C), 155.3 (C), 140.8 (C), 112.6 (CH), 108.3 (CH), 98.4 (CH), 62.2 (CH_2), 14.1 (CH_3), 13.7 (CH_3). IR (neat) ν/cm^{-1} 2985 (w), 1731 (s), 1644 (m), 1579 (m), 1439 (m), 1235 (s), 1143 (s), 1021 (s), 771 (s). HRMS (TOF-ESI+) calculated for $C_{11}H_{12}NO_4$ 222.0766, found 222.0759. UV-vis (λ_{max}, DCM) 303 nm.

Ethyl 5-(1H-indol-3-yl)isoxazole-3-carboxylate, 4w:

Isolated yield: 1.0 g (4.1 mmol, 82%). Appearance: grey solid. Melting range: 176-178 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 8.66 (s, 1H), 8.00 – 7.93 (m, 1H), 7.81 (d, *J* = 2.8 Hz, 1H), 7.53 – 7.44 (m, 1H), 7.36 – 7.29 (m, 2H), 6.86 (s, 1H), 4.49 (q, *J* = 7.2 Hz, 2H), 1.46 (t, *J* = 7.2 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 168.4 (C), 160.4 (C), 156.7 (C), 136.1 (C), 124.7 (CH), 123.9 (C), 123.5 (CH), 121.8 (CH), 119.9 (CH), 111.8 (CH), 105.0 (C), 98.0 (CH), 62.1 (CH_2), 14.2 (CH_3). IR (neat) ν/cm^{-1} 3172 (broad), 2984 (w), 1731 (m), 1603 (s), 1462 (s), 1239 (s), 1106 (s), 754 (s), 689 (s). HRMS (TOF-EI+) calculated for $C_{14}H_{12}N_2O_3$ 256.0848, found 256.0845 (M+). UV-vis (λ_{max}, DCM) 309 nm.

Dodecyl 5-(furan-2-yl)isoxazole-3-carboxylate, 4x:

Isolated yield: 519 mg (1.5 mmol, 75%). Appearance: off-white powder. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.57 (d, *J* = 1.9 Hz, 1H), 6.98 (d, *J* = 3.5 Hz, 1H), 6.81 (s, 1H), 6.56 (dd, *J* = 3.5, 1.9 Hz, 1H), 4.39 (t, *J* = 6.8 Hz, 2H), 1.79 (dt, *J* = 15.0, 6.8 Hz, 2H), 1.49 – 1.38 (m, 2H), 1.37 – 1.21 (m, 16H), 0.93 – 0.84 (m, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 163.2 (C), 159.8 (C), 156.7 (C), 144.7 (CH), 142.4 (C), 112.1 (CH), 111.4 (CH), 99.4 (CH), 66.4 (CH_2), 31.9 (CH_2), 29.6 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.5 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 28.5 (CH_2), 25.8 (CH_2), 22.7 (CH_2), 14.1 (CH_3). IR (neat) ν/cm^{-1} 2922 (m), 2853 (m), 1736 (s), 1516 (m), 1286 (s), 1157 (s), 1010 (m), 888 (m), 739 (m), 652 (m). HRMS (TOF-EI+) calculated for $C_{20}H_{29}NO_4$ 347.2097, found 347.2101 (M+).

(1-(Furan-2-ylmethyl)-1H-imidazol-5-yl)methyl 5-(furan-2-yl)isoxazole-3-carboxylate, 4y:

Isolated yield: 455 mg (1.34 mmol, 82%). Appearance: beige waxy solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.56 (s, 1H), 7.55 (d, *J* = 2.0 Hz, 1H), 7.33 (dd, *J* = 2.0, 1.1 Hz, 1H), 7.19 (s, 1H), 6.95 (d, *J* = 3.5 Hz, 1H), 6.75 (s, 1H), 6.53 (dd, *J* = 3.5, 2.0 Hz, 1H), 6.30 (d, *J* = 3.5 Hz, 1H), 6.29 (dd, *J* = 3.5, 2.0 Hz, 1H), 5.40 (s, 2H), 5.18 (s, 2H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 163.4 (C), 159.2 (C), 156.1 (C), 148.5 (C), 144.8 (CH), 143.3 (CH), 142.2 (C), 139.5 (CH), 132.2 (CH), 125.0 (C), 112.1 (CH), 111.6 (CH), 110.6 (CH), 109.1 (CH), 99.4 (CH), 56.6 (CH_2), 42.0 (CH_2). IR (neat) ν/cm^{-1} 3126 (w), 1738 (s), 1644 (m), 1490 (m), 1438 (m), 1239 (s), 1218 (s), 1113 (m), 1012 (m), 767 (s), 745 (s). HRMS (TOF-ESI+) calculated for $C_{17}H_{14}N_3O_5$ 340.0933, found 340.0921. X-ray data: for $C_{34}H_{28}N_6O_{11}$; C2/c, α = 90, β = 105.039(3), γ = 90, a = 19.0650(5), b = 8.0448(2), c = 21.6927(5) – CCDC1967210.

Synthesis of Oxazole Products 5a – 5y and Derivatives 11 and 12: General Procedure:

A solution of the corresponding isoxazole precursor (**4a-y**) in MeCN (10-20 mM) was pumped at a flow rate of 0.5 mL/min (for 20-minute residence time, reactor volume: 10 mL) through the UV150 photoreactor of a Vapourtec E-series flow reactor. The medium-pressure Hg lamp was used at 90-100% power setting (equivalent to 135-150 W) in combination with a suitable broadband filter. The temperature within the reactor was controlled via a stream of chilled air resulting in a temperature of 25-40 °C. The crude reaction products were evaporated under reduced pressure and purified by silica column chromatography (EtOAc/ hexane 5-25%) yielding the desired photoisomerization products.

Ethyl 5-(4-methoxyphenyl)oxazole-2-carboxylate, 5a:

Isolated yield: 200 mg (0.81 mmol, 81%). Appearance: pale yellow solid. Melting range: 75-78 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.68 (d, *J* = 8.9 Hz, 2H), 7.38 (s, 1H), 6.96 (d, *J* = 8.9 Hz, 2H), 4.47 (q, *J* = 7.2 Hz, 2H), 3.84 (s, 3H), 1.44 (t, *J* = 7.2 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 160.8 (C), 155.8 (C), 154.5 (C), 151.1 (C), 126.7 (2CH), 122.5 (CH), 119.4 (C), 114.5 (2CH), 62.5 (CH_2), 55.4 (CH_3), 14.2 (CH_3). IR (neat) ν/cm^{-1} 2981 (w), 1733 (s), 1614 (m), 1490 (s), 1302 (m), 1261 (s), 1173 (s), 1024 (m), 832 (m). HRMS (TOF-ESI+) calculated for $C_{13}H_{14}NO_4$ 248.0923, found 248.0933. UV-vis (λ_{max}, DCM) 315 nm. X-ray data: for $C_{13}H_{13}NO_4$; P21/n, α = 90, β = 92.793(2), γ = 90, a = 6.7593(2), b = 13.8328(3), c = 12.7123(3) – CCDC1967211.

Ethyl 5-(3,4-dimethoxyphenyl)oxazole-2-carboxylate, 5b:

Isolated yield: 207 mg (0.75 mmol, 75%). Appearance: yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.41 (s, 1H), 7.34 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.22 (d, *J* = 2.0 Hz, 1H), 6.93 (d, *J* = 8.4 Hz, 1H), 4.49 (q, *J* = 7.2 Hz, 2H), 3.96 (s, 3H), 3.93 (s, 3H), 1.46 (t, *J* = 7.2 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 155.8 (C), 154.5 (C), 151.1 (C), 150.5 (C), 149.4 (C), 122.7 (CH), 119.6 (C), 118.5 (CH), 111.4 (CH), 108.0 (CH), 62.5 (CH_2), 56.1 (CH_3), 56.0 (CH_3), 14.2 (CH_3). IR (neat) ν/cm^{-1} 2940 (w), 1733 (s), 1495 (s), 1252 (s), 1176 (s), 1145 (s), 1023 (m), 857 (m). HRMS (TOF-EI+) calculated for $C_{14}H_{15}NO_5$ 277.0950, found 277.0940 (M+).

Ethyl 5-(benzo[d][1,3]dioxol-5-yl)oxazole-2-carboxylate; 5c:

Isolated yield: 190 mg (0.73 mmol, 73%). Appearance: yellow solid. Melting range: 135-138 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.38 (s, 1H), 7.20 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.20 (d, *J* = 1.8 Hz, 1H), 6.89 (d, *J* = 8.1 Hz, 1H), 6.03 (s, 2H), 4.48 (q, *J* = 7.1 Hz, 2H), 1.45 (t, *J* = 7.1 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 155.6 (C), 154.2 (C), 150.9 (C), 149.2 (C), 148.3 (C), 123.1 (CH), 120.7 (C), 119.6 (CH), 108.8 (CH), 105.3 (CH), 101.3 (CH_2), 62.3 (CH_2), 14.4 (CH_3). IR (neat) ν/cm^{-1} 2992 (w), 1729 (s), 1612 (s), 1488 (s), 1452 (m), 1374 (m), 1308 (m), 1266 (m), 1209 (s), 1158 (s), 1056 (s), 1032 (s). HRMS (TOF-EI+) calculated for $C_{13}H_{11}NO_5$ 261.0637, found 261.0630 (M+). UV-vis (λ_{max}, DCM) 314 nm.

Ethyl 5-(2,4-dimethoxyphenyl)oxazole-2-carboxylate, 5d:

Isolated yield: 213 mg (0.77 mmol, 77%). Appearance: yellow solid. Melting range: 115-118 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.84 (d, *J* = 8.7 Hz, 1H), 7.58 (s, 1H), 6.60 (dd, *J* = 8.7, 2.3 Hz, 1H), 6.53 (d, *J* = 2.3 Hz, 1H), 4.48 (q, *J* = 7.1 Hz, 2H), 3.95 (s, 3H), 3.86 (s, 3H), 1.45 (t, *J* = 7.1 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 161.9 (C), 157.7 (C), 156.0 (C), 151.3 (C), 150.0 (C), 128.0 (CH), 126.1 (CH), 109.3 (C), 105.2 (CH), 98.5 (CH), 62.3 (CH_2), 55.5 (2xCH_3), 14.2 (CH_3). IR (neat) ν/cm^{-1} 2992 (w), 1945 (w), 1731 (s), 1614 (s),

1489 (s), 1461 (m), 1350 (m), 1210 (s), 1159 (s), 1057 (m), 831 (m). HRMS (TOF-EI+) calculated for $C_{14}H_{16}NO_5$ 278.1028, found 278.1030 (M+H+). UV-vis (λ_{max}, DCM) 325 nm.

Ethyl 5-(2,4,6-trimethoxyphenyl)oxazole-2-carboxylate, 5e:

Isolated yield: 208 mg (0.7 mmol, 68%). Appearance: yellow solid. Melting range: 89-91 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.35 (s, 1H), 6.14 (s, 2H), 4.44 (q, *J* = 7.2 Hz, 2H), 3.83 (s, 3H), 3.80 (s, 6H), 1.41 (t, *J* = 7.2 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 162.8 (C), 159.6 (C), 156.1 (C), 151.0 (C), 148.8 (C), 128.9 (CH), 98.4 (C), 90.7 (2CH), 62.2 (CH_2), 55.9 ($2CH_3$), 55.4 (CH_3), 14.2 (CH_3). IR (neat) ν/cm^{-1} 3013 (w), 2965 (w), 2840 (w), 1722 (m), 1603 (m), 1586 (s), 1453 (s), 1429 (s). HRMS (TOF-ESI+) calculated for $C_{15}H_{18}NO_6$ 308.1141, found 308.1134.

Ethyl 5-(3-hydroxyphenyl)oxazole-2-carboxylate, 5f:

Isolated yield: 175 mg (0.75 mmol, 75%). Appearance: colourless waxy solid. ^{1}H-NMR (400 MHz, d_4-MeOD) δ/ppm 7.64 (s, 1H), 7.31 – 7.22 (m, 2H), 7.18 (t, *J* = 1.9 Hz, 1H), 6.86 – 6.82 (m, 1H), 4.44 (q, *J* = 7.1 Hz, 2H), 1.41 (t, *J* = 7.1 Hz, 3H). ^{13}C{1H} NMR (100 MHz, d_4-MeOD) δ/ppm 157.9 (C), 155.3 (C), 154.4 (C), 151.6 (C), 130.0 (CH), 127.6 (C), 123.3 (CH), 116.7 (CH), 115.9 (CH), 111.2 (CH), 62.2 (CH_2), 13.0 (CH_3). IR (neat) ν/cm^{-1} 3207 (broad), 2907 (w), 1727 (s), 1524 (m), 1479 (m), 1448 (m), 1298 (m), 1241 (s), 1195 (m). HRMS (TOF-ESI+) calculated for $C_{12}H_{11}NO_4Na$ 256.0586, found 256.0576.

Ethyl 5-phenyloxazole-2-carboxylate, 5g:

Isolated yield: 109 mg (0.5 mmol, 75%). Appearance: yellow solid. Melting range: 56-58 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm δ 7.75 – 7.71 (m, 2H), 7.49 (s, 1H), 7.46 – 7.41 (m, 2H), 7.40 – 7.36 (m, 1H), 4.47 (q, *J* = 7.2 Hz, 2H), 1.43 (t, *J* = 7.2 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 155.7 (C), 154.3 (C), 151.6 (C), 129.8 (CH), 129.1 (2CH), 126.7 (C), 125.1 (2CH), 123.9 (CH), 62.6 (CH_2), 14.2 (CH_3). IR (neat) ν/cm^{-1} 3115 (w), 3065 (w), 2979 (w), 2906 (w), 1717 (s), 1597 (s), 1515 (s), 1474 (s), 1446 (s), 1172 (s). HRMS (TOF-ESI+) calculated for $C_{12}H_{12}NO_3$ 218.0817, found 218.0807.

Ethyl 5-(4-(tert-butyl)phenyl)oxazole-2-carboxylate, 5h:

Isolated yield: 184 mg (0.7 mmol, 70%). Appearance: yellow solid. Melting range: 79-82 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.67 (d, *J* = 8.5 Hz, 2H), 7.49 – 7.43 (m, 3H), 4.48 (q, *J* = 7.1 Hz, 2H), 1.44 (t, *J* = 7.1 Hz, 3H), 1.33 (s, 9H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 155.8 (C), 154.6 (C), 153.3 (C), 151.4 (C), 126.0 (2CH), 124.9 (2CH), 123.9 (C), 123.4 (CH), 62.5 (CH_2), 34.9 (C), 31.1 ($3CH_3$), 14.2 (CH_3). IR (neat) ν/cm^{-1} 2962 (m), 2905 (w), 2869 (w), 1733 (s), 1614 (w), 1488 (s), 1174 (s), 1154 (s). HRMS (TOF-ESI+) calculated for $C_{16}H_{20}NO_3$ 274.1443, found 274.1447.

Ethyl 5-(2-fluoro-4-methoxyphenyl)oxazole-2-carboxylate, 5i:

Isolated yield: 187 mg (0.71 mmol, 71%). Appearance: off-white solid. Melting range: 107-109 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.82 (t, *J* = 8.7 Hz, 1H), 7.53 (d, *J* = 3.9 Hz, 1H), 6.81 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.73 (dd, *J* = 12.7, 2.5 Hz, 1H), 4.49 (q, *J* = 7.2 Hz, 2H), 3.86 (s, 3H), 1.46 (t, *J* = 7.2 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 161.9 (C, d, *J* = 11 Hz), 160.3 (CF, d, *J* = 251 Hz), 155.7 (C), 150.8

(C), 149.1 (C), 127.7 (CH, d, J = 5 Hz), 126.2 (CH, d, J = 12 Hz), 110.8 (CH, d, J = 2 Hz), 108.0 (C, d, J = 14 Hz), 102.1 (CH, d, J = 24 Hz), 62.6 (CH_3), 55.8 (CH_3), 14.2 (CH_3). ^{19}F-NMR (376 MHz, $CDCl_3$) δ/ppm -109.2. IR (neat) ν/cm^{-1} 2980 (w), 1737 (s), 1626 (s), 1489 (s), 1264 (m), 1181 (s), 1117 (m), 1060 (m), 1024 (m), 871 (m), 815 (m). HRMS (TOF-EI+) calculated for $C_{13}H_{12}NO_4F$ 265.0750, found 265.0742 (M+).

Ethyl 5-(4-bromophenyl)oxazole-2-carboxylate, 5j:

Isolated yield: 354 mg (1.2 mmol, 74%). Appearance: colorless solid. Melting range: 104-106 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.61 (d, J = 8.8 Hz, 2H), 7.57 (d, J = 8.8 Hz, 1H), 7.50 (s, 1H), 4.48 (q, J = 7.2 Hz, 2H), 1.44 (t, J = 7.2 Hz 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 155.6 (C), 153.3 (C), 151.8 (C), 132.3 (2CH), 126.5 (2CH), 125.6 (C), 124.2 (CH), 124.0 (C), 62.7 (CH_2), 14.2 (CH_3). IR (neat) ν/cm^{-1} 2981 (w), 1721 (s), 1475 (m), 1409 (m), 1183 (m), 941 (m), 830 (m). HRMS (TOF-ESI+) calculated for $C_{12}H_{10}NO_3BrNa$ 317.9742, found 317.9748.

Ethyl 5-(2,4-dichloro-5-fluorophenyl)oxazole-2-carboxylate, 5k:

Isolated yield: 205 mg (0.68 mmol, 68%). Appearance: off-white solid. Melting range: 108-111 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.99 (s, 1H), 7.76 (d, J = 9.4 Hz, 1H), 7.58 (d, J = 6.6 Hz, 1H), 4.52 (q, J = 7.2 Hz, 2H), 1.47 (t, J = 7.2 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 156.8 (CF, d, J = 290 Hz), 155.8 (C), 151.7 (C), 148.9 (C), 132.4 (CH), 129.2 (CH), 126.4 (C, d, J = 4 Hz), 125.6 (C, d, J = 8 Hz), 122.8 (C, d, J = 19 Hz), 115.9 (CH, d, J = 25 Hz), 63.0 (CH_2), 14.1 (CH_3). ^{19}F-NMR (376 MHz, $CDCl_3$) δ/ppm -115.7. IR (neat) ν/cm^{-1} 2985 (w), 1738 (s), 1522 (m), 1471 (s), 1378 (m), 1257 (s), 1208 (s), 885 (m), 732 (m). HRMS (TOF-EI+) calculated for $C_{12}H_8NO_3FCl_2$ 302.9865, found 302.9873 (M+). UV-vis (λ_{max}, DCM) 294 nm.

Ethyl 5-(2,4-difluorophenyl)oxazole-2-carboxylate, 5l:

Isolated yield: 177 mg (0.7 mmol, 55%). Appearance: yellow solid. Melting range: 70-72 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.90 (td, J = 8.5, 6.2 Hz, 1H), 7.59 (d, J = 4.0 Hz, 1H), 7.04 – 6.98 (m, 1H), 6.95 (ddd, J = 10.9, 8.5, 2.5 Hz, 1H), 4.48 (q, J = 7.2 Hz, 2H), 1.44 (t, J = 7.2 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 163.4 (dd, J = 253, 12 Hz, CF), 158.4 (dd, J = 254, 12 Hz, CF), 155.6 (C), 151.3 (C), 148.0 (m, C), 128.1 (dd, J = 10, 4. Hz, CH), 127.3 (d, J = 13 Hz, CH), 112.4 (dd, J = 22, 4 Hz, CH), 111.8 (m, C), 105.3 – 104.4 (m, CH), 62.8 (CH_2), 14.2 (CH_3). ^{19}F-NMR (376 MHz, $CDCl_3$) δ/ppm -106.5 (m), -107.2 (m). IR (neat) ν/cm^{-1} 3063 (w), 3038 (w), 2920 (s), 2851 (s), 1731 (m), 1620 (m), 1488 (m), 1272 (s), 1178 (m). HRMS (TOF-ESI+) calculated for $C_{12}H_{10}NO_3F_2$ 254.0629, found 254.0637.

Ethyl (E)-5-styryloxazole-2-carboxylate, 5m:

Isolated yield: 267 mg (1.1 mmol, 72%). Appearance: yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.35 (m, 5H), 6.94 (d, J = 12.5 Hz, 1H), 6.51 (d, J = 12.5 Hz, 1H), 6.40 (s, 1H), 4.38 (q, J = 7.1 Hz, 2H), 1.37 (t, J = 7.1 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 169.3 (C), 159.9 (C), 156.3 (C), 137.2 (CH), 135.5 (C), 128.8 (CH), 128.6 (2CH), 128.3 (2CH), 114.6 (CH), 103.0 (CH), 62.1 (CH_2), 14.1 (CH_3). IR (neat) ν/cm^{-1} 2984 (w), 1730 (s), 1443 (m), 1258 (s), 1230 (s), 1156 (m), 1096 (m), 1021 (m), 778 (s), 698 (s). HRMS (TOF-ESI+) calculated for $C_{14}H_{13}O_3NNa$ 266.0793, found 266.0802.

Ethyl 4-methyl-5-phenyloxazole-2-carboxylate, 5n:

Isolated yield: 176 mg (0.77 mmol, 77%). Appearance: pale yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.73 – 7.68 (m, 2H), 7.50 – 7.44 (m, 2H), 7.42 – 7.37 (m, 1H), 4.49 (q, *J* = 7.1 Hz, 2H), 2.51 (s, 3H), 1.45 (t, *J* = 7.1 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 155.8 (C), 149.8 (C), 148.9 (C), 134.2 (C), 128.9 (2CH), 128.9 (CH), 127.8 (C), 126.1 (2CH), 62.5 (CH_2), 14.2 (CH_3), 13.5 (CH_3). IR (neat) ν/cm^{-1} 2982 (w), 1733 (s), 1529 (m), 1447 (m), 1327 (m), 1314 (m), 1187 (s), 1016 (m), 766 (m), 692 (m). HRMS (TOF-EI+) calculated for $C_{13}H_{13}NO_3$ 231.0895, found 231.0905. UV-vis (λ_{max}, DCM) 304 nm.

Ethyl 5-(tert-butyl)oxazole-2-carboxylate, 5o:

Isolated yield: 95 mg (0.48 mmol, 24%). Appearance: light brown oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 6.89 (s, 1H), 4.42 (q, *J* = 7.2 Hz, 2H), 1.40 (t, *J* = 7.2 Hz, 3H), 1.32 (s, 9H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 164.6 (C), 155.9 (C), 151.5 (C), 122.3 (CH), 62.3 (CH_2), 31.8 (C), 28.5 ($3CH_3$), 14.2 (CH_3). IR (neat) ν/cm^{-1} 2970 (m), 1738 (s), 1523 (s), 1368 (m), 1336 (m), 1269 (s), 1178 (s), 1136 (m), 1018 (m), 977 (m), 705 (m). HRMS (TOF-ESI+) calculated for $C_{10}H_{16}NO_3$ 198.1125, found 198.1120.

N-Allyl-5-(5-methylfuran-2-yl)oxazole-2-carboxamide, 5q:

Isolated yield: 91 mg (0.39 mmol, 39%). Appearance: pale yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.22 (s, 1H), 7.08 (br s, 1H), 6.74 (d, *J* = 3.4 Hz, 1H), 6.11 (d, *J* = 3.4 Hz, 1H), 5.91 (ddt, *J* = 17.4, 11.0, 5.7 Hz, 1H), 5.33 – 5.25 (m, 1H), 5.21 (dd, *J* = 10.3, 1.4 Hz, 1H), 4.11 – 4.04 (m, 2H), 2.36 (s, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 154.9 (C), 154.1 (C), 153.1 (C), 146.6 (C), 140.9 (C), 133.2 (CH), 121.3 (CH), 117.2 (CH2), 110.6 (CH), 108.1 (CH), 41.9 (CH_2), 13.6 (CH_3). IR (neat) ν/cm^{-1} 3305 (broad), 1759 (w), 1679 (s), 1582 (m), 1546 (s), 1516 (m), 1200 (m), 1022 (s), 788 (m). HRMS (TOF-EI+) calculated for $C_{12}H_{12}N_2O_3$ 232.0848, found 232.0840 (M+).

3-(5-Methylfuran-2-yl)-3-oxopropanenitrile, 11:

Isolated yield: 30 mg (0.20 mmol, 20%). Appearance: yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.28 (d, *J* = 3.6 Hz, 1H), 6.27 – 6.22 (m, 1H), 3.87 (s, 2H), 2.41 (s, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 174.7 (C), 159.5 (C), 149.2 (C), 121.3 (CH), 113.6 (C), 110.2 (CH), 28.4 (CH_2), 14.1 (CH_3). IR (neat) ν/cm^{-1} 2948 (w), 2917 (w), 2361 (m), 1678 (m), 1668 (s), 1517 (s), 1382 (m), 1370 (m), 1262 (m), 1056 (m), 1036 (m), 799 (m). HRMS (TOF-ESI+) calculated for $C_8H_7NO_2Na$ 172.0374, found 172.0379.

Ethyl 2-cyano-3-(4-(dimethylamino)phenyl)-3-hydroxyacrylate, 12:

Isolated yield: 128 mg (0.5 mmol, 68%). Appearance: yellow solid. Melting range: 113-116 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 8.07 (d, *J* = 9.3 Hz, 2H), 6.67 (d, *J* = 9.3 Hz, 2H), 4.35 (q, *J* = 7.2 Hz, 2H), 3.06 (s, 6H), 1.38 (t, *J* = 7.2 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 181.6 (C), 172.3 (C), 153.6 (C), 130.9 (2CH), 117.71 (C), 117.67 (C), 110.8 (2CH), 74.2 (C), 62.2 (CH_2), 39.9 ($2CH_3$), 14.2 (CH_3). IR (neat) ν/cm^{-1} 2980 (w), 2924 (w), 2212 (m), 1709 (s), 1577 (s), 1518 (s), 1166 (s), 1128 (s), 820 (s). HRMS (TOF-ESI+) calculated for $C_{14}H_{16}N_2O_3Na$ 283.1059, found 283.1059.

Ethyl 5-(thiophen-2-yl)oxazole-2-carboxylate, 5s:

Isolated yield: 176 mg (0.80 mmol, 78%). Appearance: dark yellow oil. ^{1}H-NMR (500 MHz, $CDCl_3$) δ/ppm 7.49 (dd, *J* = 3.9, 1.4 Hz, 1H), 7.44 – 7.41 (m, 1H), 7.37 (s, 1H), 7.12 (dd, *J* = 5.3, 3.5 Hz, 1H), 4.49 (q, *J* = 7.1 Hz, 3H), 1.45 (t, *J* = 7.1 Hz, 3H). ^{13}C{1H} NMR (126 MHz, $CDCl_3$) δ/ppm 155.5 (C), 151.0 (C), 149.8 (C), 128.4 (C), 128.1 (CH), 127.6 (CH), 126.5 (CH), 123.4 (CH), 62.7 (CH_2), 14.2 (CH_3). IR (neat) ν/cm^{-1} 3111 (w), 2984 (w), 1735 (s), 1530 (m), 1487 (m), 1376 (m), 1276 (m), 1176 (s), 1155 (m), 1019 (m), 850 (m), 707 (m). HRMS (TOF-EI+) calculated for $C_{10}H_9NO_3S$ 223.0303, found 223.0297 (M+).

Ethyl 5-(furan-2-yl)oxazole-2-carboxylate, 5t:

Isolated yield: 355 mg (1.71 mmol, 76%). Appearance: pale waxy solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.52 (d, *J* = 1.7 Hz, 1H), 7.41 (s, 1H), 6.86 (d, *J* = 3.4 Hz, 1H), 6.53 (dd, *J* = 3.4, 1.7 Hz, 1H), 4.48 (q, *J* = 7.2 Hz, 2H), 1.44 (t, *J* = 7.2 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 155.5 (C), 151.0 (C), 146.4 (C), 144.0 (CH), 142.4 (C), 123.5 (CH), 111.9 (CH), 109.9 (CH), 62.7 (CH_2), 14.1 (CH_3). IR (neat) ν/cm^{-1} 3131 (w), 2984 (w), 1732 (s), 1515 (s), 1447 (m), 1286 (s), 1174 (s), 1152 (s), 1115 (m), 1010 (s), 966 (m), 888 (m), 742 (s), 651 (m), 591 (m). HRMS (TOF-EI+) calculated for $C_{10}H_9NO_4$ 207.0532, found 207.0540 (M+). UV-vis (λ_{max}, DCM) 312 nm.

Ethyl 5-(1H-pyrrol-2-yl)oxazole-2-carboxylate, 5u:

Isolated yield: 170 mg (0.83 mmol, 72%). Appearance: yellow solid. Melting range: 148-150 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 9.02 (br s, 1H), 7.30 (s, 1H), 6.95 (td, *J* = 2.7, 1.5 Hz, 1H), 6.67 (ddd, *J* = 3.9, 2.7, 1.5 Hz, 1H), 6.32 (dt, *J* = 3.9, 2.7 Hz, 1H), 4.47 (q, *J* = 7.1 Hz, 2H), 1.44 (t, *J* = 7.1 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 155.8 (C), 149.7 (C), 148.7 (C), 121.1 (CH), 121.0 (CH), 119.1 (C), 110.7 (CH), 109.5 (CH), 62.5 (CH_2), 14.2 (CH_3). IR (neat) ν/cm^{-1} 3220 (broad), 3132 (w), 1716 (s), 1617 (s), 1500 (s), 1376 (m), 1344 (m), 1279 (m), 1251 (s), 1168 (s), 738 (m). HRMS (TOF-EI+) calculated for $C_{10}H_{10}N_2O_3$ 206.0691, found 206.0706 (M+). UV-vis (λ_{max}, DCM) 338 nm. X-ray data: for $C_{10}H_{10}N_2O_3$; P21/c, α = 90, β = 115.800(3), γ = 90, a = 9.6285(2), b = 11.3962(2), c = 9.9019(3) – CCDC1967214.

Ethyl 5-(5-methylfuran-2-yl)oxazole-2-carboxylate, 5v:

Isolated yield: 884 mg (4.0 mmol, 80%). Appearance: waxy yellow solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.32 (s, 1H), 6.73 (d, *J* = 3.4 Hz, 1H), 6.10 (dd, *J* = 3.4, 1.0 Hz, 1H), 4.46 (q, *J* = 7.2 Hz, 2H), 2.35 (s, 3H), 1.42 (t, *J* = 7.2 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 155.6 (C), 154.5 (C), 150.6 (C), 146.8 (C), 140.8 (C), 122.6 (CH), 111.1 (CH), 108.2 (CH), 62.6 (CH_2), 14.2 (CH_3), 13.6 (CH_3). IR (neat) ν/cm^{-1} 2985 (w), 1736 (s), 1641 (m), 1581 (m), 1535 (m), 1467 (m), 1292 (s), 1176 (s), 1021 (s), 788 (m). HRMS (TOF-ESI+) calculated for $C_{11}H_{12}NO_4$ 222.0766, found 222.0757.

Ethyl 5-(1H-indol-3-yl)oxazole-2-carboxylate, 5w:

Isolated yield: 193 mg (0.76 mmol, 73%). Appearance: yellow solid. Melting range: 180-182 °C. ^{1}H-NMR (400 MHz, DMSO-d_6) δ/ppm 11.79 (s, 1H), 7.97 (d, *J* = 2.8 Hz, 1H), 7.91 (dd, *J* = 7.5, 1.4 Hz, 1H), 7.71 (s, 1H), 7.47 (dd, *J* = 7.5, 1.4 Hz, 1H), 7.21 (ddd, *J* = 8.1, 7.1, 1.4 Hz, 1H), 7.16 (td, *J* = 7.5, 1.4 Hz, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 1.32 (t, *J* = 7.1 Hz, 3H). ^{13}C{1H} NMR (100 MHz, DMSO-d_6) δ/ppm 155.7 (C), 151.8 (C), 149.6 (C), 136.9 (C), 125.9 (CH), 123.9 (C), 123.0 (CH), 122.0 (CH), 121.2 (CH), 119.8 (CH), 112.8 (CH), 103.0 (C), 62.2 (CH_2), 14.5 (CH_3). IR (neat) ν/cm^{-1} 3294 (br), 1720 (s), 1623 (s), 1609 (s), 1540 (s), 1480 (m), 1355 (s), 1258 (s), 1232 (m), 1120 (m), 787 (m), 746 (s), 734 (s), 643 (m). HRMS (TOF-EI+) calculated for $C_{14}H_{12}N_2O_3$ 256.0848, found 256.0840 (M+). UV-vis (λ_{max}, DCM) 333 nm.

Dodecyl 5-(furan-2-yl)oxazole-2-carboxylate, 5x:

Isolated yield: 271 mg (0.78 mmol, 78%). Appearance: waxy solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.52 (d, *J* = 1.7 Hz, 1H), 7.41 (s, 1H), 6.86 (d, *J* = 3.5 Hz, 1H), 6.53 (dd, *J* = 3.5, 1.7 Hz, 1H), 4.41 (t, *J* = 6.8 Hz, 2H), 1.81 (app p, *J* = 6.9 Hz, 2H), 1.42 (td, *J* = 6.8, 6.4, 2.4 Hz, 2H), 1.38 – 1.21 (m, 16H), 0.91 – 0.83 (m, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 155.6 (C), 151.0 (C), 146.4 (C), 144.0 (CH), 142.5 (C), 123.5 (CH), 111.9 (CH), 109.9 (CH), 66.8 (CH_2), 31.9 (CH_2), 29.6 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 28.5 (CH_2), 25.8 (CH_2), 22.6 (CH_2), 14.1 (CH_3). IR (neat) ν/cm^{-1} 2923 (s), 2853 (m), 1736 (s), 1544 (m), 1466 (m), 1349 (m), 1287 (s), 1158 (s), 1011 (m), 888 (m), 732 (s), 651 (m), 591 (m). HRMS (TOF-EI+) calculated for $C_{20}H_{29}NO_4$ 347.2097, found 347.2088 (M+). UV-vis (λ_{max}, DCM) 314 nm.

(1-(Furan-2-ylmethyl)-1H-imidazol-5-yl)methyl 5-(furan-2-yl)oxazole-2-carboxylate; 5y:

Isolated yield: 366 mg (1.08 mmol, 73%). Appearance: waxy solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.58 (d, *J* = 1.1 Hz, 1H), 7.53 (d, *J* = 1.8 Hz, 1H), 7.42 (s, 1H), 7.35 (d, *J* = 2.2 Hz, 1H), 7.24 (s, 1H), 6.86 (d, *J* = 3.4 Hz, 1H), 6.55 (dd, *J* = 3.4, 1.8 Hz, 1H), 6.34 (d, *J* = 3.4 Hz, 1H), 6.30 (dd, *J* = 3.4, 1.8 Hz, 1H), 5.45 (s, 2H), 5.22 (s, 2H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ/ppm 155.0 (C), 150.3 (C), 148.4 (C), 146.7 (C), 144.2 (CH), 143.3 (CH), 142.3 (C), 139.4 (CH), 132.4 (CH), 124.9 (C), 123.7 (CH), 112.0 (CH), 110.6 (CH), 110.2 (CH), 109.1 (CH), 56.9 (CH_2), 42.1 (CH_2). IR (neat) ν/cm^{-1} 3126 (w), 1735 (s), 1515 (s), 1288 (s), 1166 (s), 1112 (m), 1013 (m), 889 (m), 707 (m). HRMS (TOF-ESI+) calculated for $C_{17}H_{14}N_3O_5$ 340.0933, found 340.0940. UV-vis (λ_{max}, DCM) 320 nm.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Copies of ^{1}H and ^{13}C NMR spectra, representative UV-vis spectra of substrates and Hg-lamp emission spectra (pdf).

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ACKNOWLEDGMENT

We gratefully acknowledge support from the School of Chemistry at University College Dublin for a Research Demonstratorship (to CB) and general support (to MB). We are thankful to Dr Helge Müller-Bunz for solving the X-ray crystal structures reported herein. We are furthermore grateful to UCD for providing seed funding (SF1606 and SF1609) and SSPC for supporting our work through PharM5.

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