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Use of the Hydantoin Directing Group in Ruthenium(II)-Catalyzed C−H Functionalization

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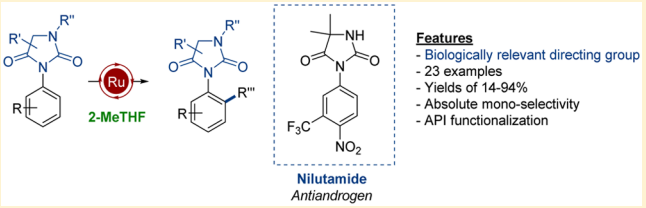
Supporting Information

ABSTRACT: Ruthenium(II)-catalyzed C−H functionalization of *N*-arylhydantoins is herein described. The biologically relevant hydantoin (imidazolidinedione) heterocycle functions as a weakly coordinating directing group in a C−H alkenylation reaction. The reaction gave a wide scope of 23 examples with yields up to 94% in the green solvent 2-MeTHF. Functionalization of API nilutamide (antiandrogen) is also reported. The use of the succinimide heterocycle as a directing group is also demonstrated in modest yields.



The hydantoin (imidazolidinedione) heterocycle (and sulfur anaologues) is prevalent in numerous medicinally and agrochemically active scaffolds. These include the hydantoin class of anticonvulsants (phenytoin, fosphenytoin, Figure 1), nonsteroidal androgen antagonists (nilutamide, enzalutamide), and fungicides (iprodione).[1]

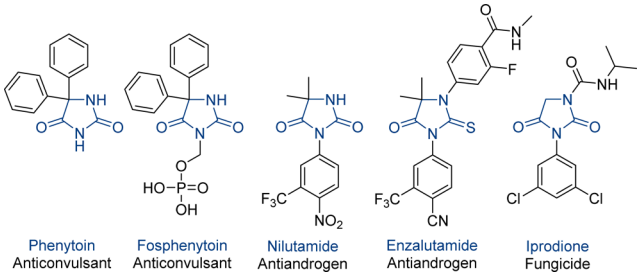
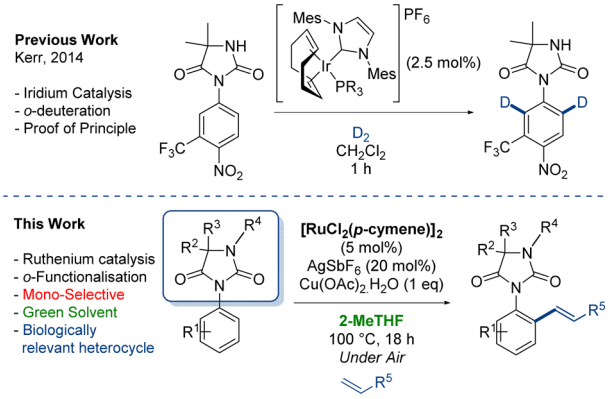


Figure 1. Biologically relevant compounds containing the hydantoin heterocycle.

Using biologically active heterocycles as directing groups in transition-metal-catalyzed C−H functionalization is a powerful synthetic tool as this can grant access to a novel library of derivatives inaccessible through other synthetic methods.[2] Direct palladium-catalyzed C−H arylation of the hydantoin heterocycle itself has been recently reported by Clayden and co-workers.[3] The hydantoin heterocycle has also been shown to form a six-membered metallacycle in elegant deuteration studies carried out by Kerr and co-workers (Scheme 1) using iridium catalysis on the antiandrogen nilutamide.[2d] This work acted as a proof of concept that this heterocycle could potentially be utilized in transition-metal-catalyzed C−H functionalization, allowing the creation of novel analogues of biologically relevant motifs.

Scheme 1. C−H Functionalization of *N*-Arylhydantoins



Ruthenium(II) catalysis has emerged as a powerful method of the formation of metallacycles and subsequent functionalization.[4] The ability of weakly coordinating directing groups to facilitate this functionalization has been brought to the forefront of C−H functionalization methodology through important contributions from Ackermann[5] and Jeganmohan[6] among others.

Preliminary reaction conditions were identified from previous work within the group and literature precedent on related alkenylation reactions.[2a,5,6] Electron-deficient alkenes are commonly used coupling partners due to their high efficiency in cross-dehydrogenative coupling reactions.[2a] Initial optimization was carried out using the nilutamide test motif (**1a**) containing the *gem*-dimethyl substituent on the hydantoin heterocycle with methyl acrylate as the coupling partner (Table 1), $[RuCl_2(p\text{-cymene})]_2$ as the ruthenium source, $AgSbF_6$ as

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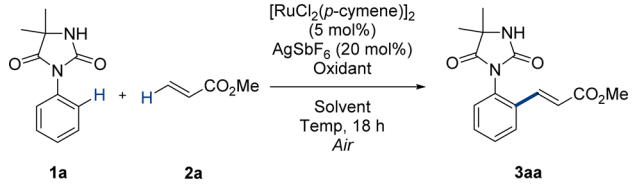
the cocatalyst, and $Cu(OAc)_2{\cdot}H_2O$ as the oxidant. Selected results will be discussed further.

Table 1. Optimization of Ruthenium(II)-Catalyzed C−H Alkenylation of *N*-Arylhydantoin[a]



entry	solvent	oxidant (1 equiv)	temp (°C)	3a[b] (%)
1	H_2O	$Cu(OAc)_2{\cdot}H_2O$	120	0
2	AcOH	$Cu(OAc)_2{\cdot}H_2O$	120	0
3	2-MeTHF	$Cu(OAc)_2{\cdot}H_2O$	120	85
4	THF	$Cu(OAc)_2{\cdot}H_2O$	120	74
5	DME	$Cu(OAc)_2{\cdot}H_2O$	120	81
6	2-MeTHF	AgOAc	120	39
7	2-MeTHF	AgO_2CCF_3	120	0
8[c]	**2-MeTHF**	**$Cu(OAc)_2{\cdot}H_2O$**	**100**	**95 (94)**[d]
9[c,e]	2-MeTHF	$Cu(OAc)_2{\cdot}H_2O$	100	70

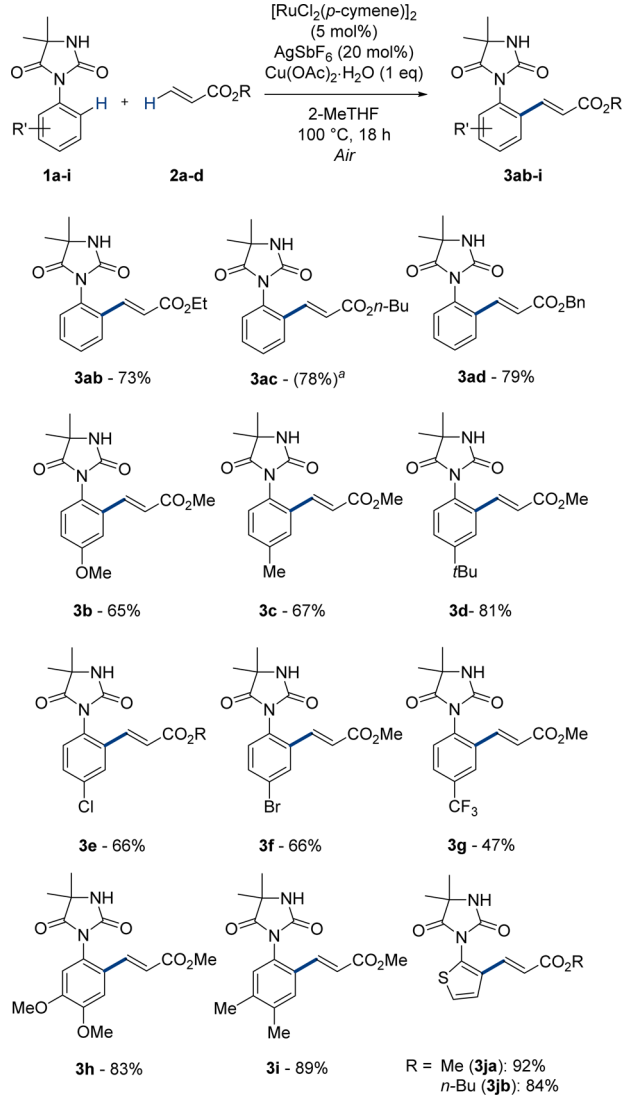
[a]Standard reaction conditions: **1a** (0.25 mmol), methyl acrylate (0.75 mmol), $[RuCl_2(p\text{-cymene})]_2$ (0.0125 mmol), $AgSbF_6$ (0.05 mmol), oxidant (0.25 mmol), solvent (1 mL). [b]^1H NMR conversions taken after silica filtration compared to 1,1,2,2-tetrachloroethane as internal standard. [c]Reaction performed at 100 °C. [d]Isolated yield. [e]Reaction performed using $[RuCl_2(p\text{-cymene})]_2$ (2.5 mol %) and $AgSbF_6$ (10 mol %).

The reaction was shown to not tolerate aqueous or acidic solvent media (entries 1 and 2); however, polar aprotic etheric solvents afforded the alkenylated product in high conversions (entries 3−5). A number of silver(I) oxidants were employed in the reaction methodology (entries 6 and 7); however, none gave superior yields compared to $Cu(OAc)_2{\cdot}H_2O$. Pleasingly, the reaction performed more efficiently at lower temperatures (entry 8), giving a 95% conversion and 94% isolated yield. Despite this, when the catalyst and co-catalyst loadings were reduced the reaction conversions dropped (entry 9).

Armed with optimal C−H alkenylation conditions, the scope of this methodology was expanded, allowing access to a large number of potentially active pharmaceutical/agrochemical analogues. The nature of the coupling partners and of aromatic functionality was initially investigated (Scheme 2). Three different electron-deficient alkenes were employed in the alkenylation reaction, giving ethyl, *n*-butyl, and benzyl derivatives (**3ab**−**ac**). Despite high yields, the *n*-butyl example (**3ac**) was inseparable via standard chromatographic techniques from the starting material and was obtained in a yield of 94% as a 5:1 mixture to give a 78% NMR yield. Various aryl functionality was then introduced in order to examine electronic and steric effects on the efficiency and selectivity of the reaction.

A wide range of alkoxy, alkyl, and halogen functionalities were tolerated (**3b**−**f**) with highest yields obtained with electron-rich aromatics. The trifluoromethyl derivative (**3g**) was synthesized in reduced yield but allowed efficient functionalization of electron-poor aromatics. Compounds containing both *meta*- and *para*- functionality (**3h**−**i**) were obtained in high yields with excellent selectivity of functionalization in the least hindered *ortho*-position. A heteroaromatic variant was investigated under the conditions in order to

Scheme 2. Ruthenium(II)-Catalyzed C−H Alkenylation of *N*-Arylhydantoin Derivatives



[a]Isolated as an inseparable 5:1 mixture of **3ac**:**1a**. 78% depicts the contribution from **3ac** (94% total yield).

expand the scope of sp^2 sites that are available for functionalization. The thiophene example (**1j**) was shown to be alkenylated under the optimized conditions in excellent yields with both methyl and butyl acrylate coupling partners with no chromatographic separation issues.

The hydantoin heterocycle is commonly synthesized from naturally occurring amino acids which are a very attractive synthetic feedstock. Six examples were synthesized from natural and unnatural amino acids: glycine, valine, leucine, proline, homocycloleucine, and sarcosine (Scheme 3).[3,7] This showed that multiple hydantoin heterocycles were tolerated as directing groups; however, the bare glycine derivative (**1k**) only afforded alkenylated product in reduced yields. Bicyclic and spirocyclic directing groups derived from proline (**1n**) and cyclohomoleucine (**1o**) gave rise to good to excellent yields of C−H-alkenylated products (**3n**−**ob**), granting access to highly decorated structures. Sarcosine-derived hydantoin (**1p**) showed that compounds containing NH functionalization were also tolerated well.

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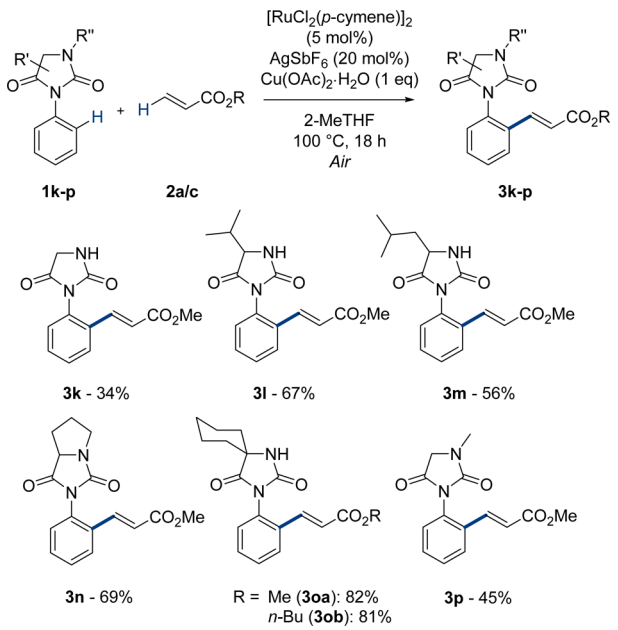
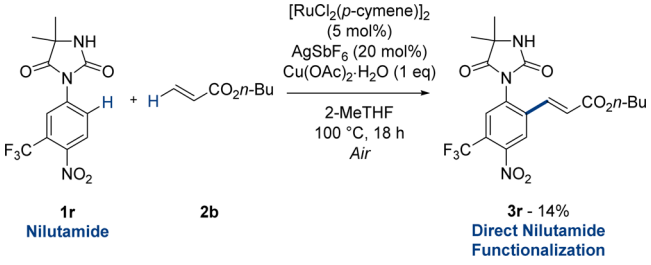
Scheme 3. Ruthenium(II)-Catalyzed C−H Alkenylation of Hydantoin Derivatives



It was now of paramount interest to submit the drug structure of nilutamide (Nilandron) to the reaction conditions in order to probe its reactivity (Scheme 4). Despite the highly

Scheme 4. Nilutamide Functionalization

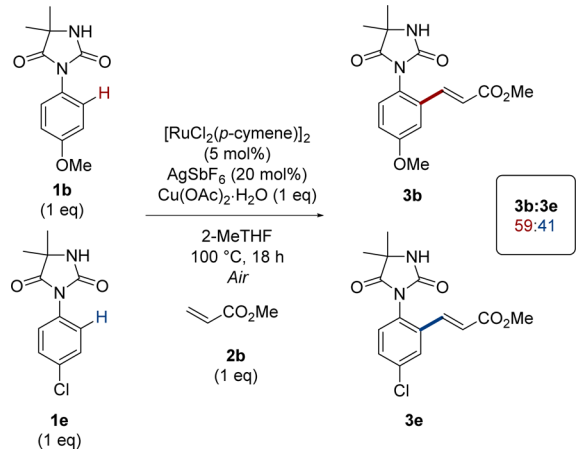


electron-poor nature of the ring (containing both CF_3 and NO_2 substituents), formation of product was observed, albeit in low isolated yield. This manifests that this methodology can be used to create direct analogues of nilutamide itself as well as a selection of structural analogues.

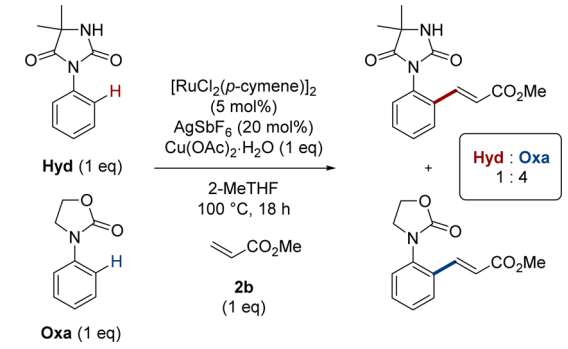
Intermolecular competition experiments were performed using electron-rich (**1b**) and electron-poor (**1e**) substrates. It was shown that the C−H alkenylation of electron-rich substituents is preferred as a ratio of ∼6:4 was observed (Scheme 5). This can be rationalized by the C−H activation occurring via an electrophilic-type activation mode by a cationic ruthenium catalyst. It is also proposed that the more electron rich and less sterically hindered urea directs the C−H functionalization (see Scheme S1).[8]

Our previous work depicts the functionalization of the biologically active oxazolidinone scaffold which bears a similar directing heterocyclic motif.[2a] Because of this, a competition experiment was carried out between the groups reacting them in equimolar quantities with 1 equiv of methyl acrylate to probe how the directing groups compete for the coupling partner (Scheme 6). The investigation showed that the oxazolidinone heterocycle competed more favorably for the acrylate as a 1:4

Scheme 5. Intermolecular Competition Studies



Scheme 6. Competition Experiment with Oxazolidinone Directing Group



mixture of hydantoin/oxazolidinone was observed in the NMR spectra.

The succinimide group is also structurally similar to the hydantoin heterocycle. Thus, it was of interest to explore whether this could also act as an efficient directing group in directed transition-metal-catalyzed C−H functionalization, as to our knowledge its utility has not yet been investigated. Our previous reports have also indicated how such subtle electronic differences can strongly affect reaction efficiency.[2a]

Four *N*-arylsuccinimide derivatives were synthesized and submitted to the optimized reactions conditions (Scheme 7). However, in this case, it was found that slightly higher temperatures were necessary to allow the reaction to proceed efficiently. The yields are modest to poor; however, this provides the first example of the use of the succinimide directing group and is in the process of being explored further.

In conclusion, we have utilized ruthenium(II)-catalyzed *ortho*-C−H alkenylation to derive a large scope of biologically relevant *N*-arylhydantoins with yields of 14−94%. The reaction methodology also favorably takes place in the green solvent 2-MeTHF, and absolute monoselectivity was observed throughout the project. This report includes the application of this methodology to hydantoin-directed C−H derivation of an antiandrogen API, nilutamide. We have also reported the first use of the succinimide directing group in directed C−H functionalization with limited but varied scope.

EXPERIMENTAL SECTION

General Information. Proton, carbon, and fluorine NMR spectra were recorded on 300, 400, and 500 MHz NMR spectrometers (^{1}H

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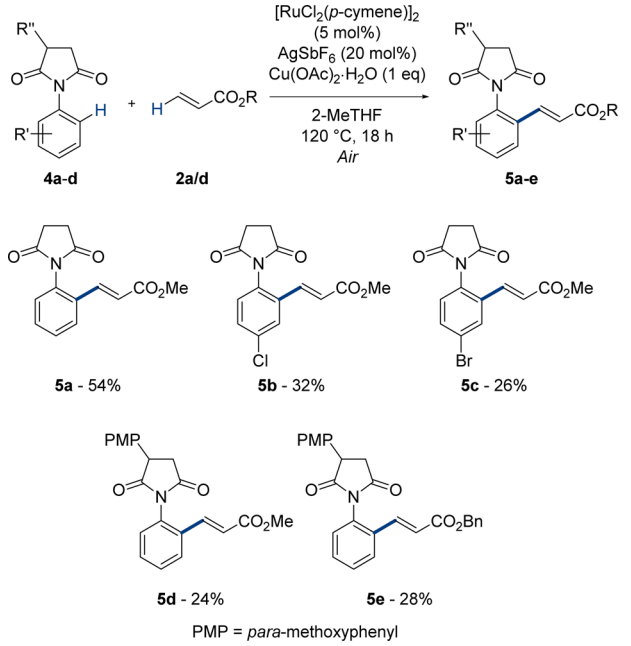
Scheme 7. Succinimide-Directed Ruthenium-Catalyzed C−H Alkenylation



NMR at 300, 400, or 500 MHz, ^{13}C NMR at 126, 100, or 75 MHz, and ^{19}F NMR at 470 MHz). Chemical shifts for protons are reported in parts per million downfield from $Si(CH_3)_4$ and are referenced to residual protium in the deuterated solvent ($CHCl_3$ at 7.26 ppm, D_2O at 4.79 and CD_3OD at 3.31). Chemical shifts for fluorines are reported in parts per million downfield from $CFCl_3$. NMR data are presented in the following format: chemical shift (number of equivalent nuclei by integration, multiplicity [app = apparent, br = broad, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, dt = doublet of triplets, dq = doublet of quartets, ddd = doublet of doublet of doublets, m = multiplet], coupling constant (Hz), assignment). HRMS data were obtained using electrospray ionization ultrahigh resolution time-of-flight mass spectrometry (ESI-UHR-TOF-MS). Infrared (IR) spectra were recorded on an IR spectrophotometer, with absorbencies quoted as wavelength (ν, cm^{-1}). Melting points were obtained on a melting point apparatus and are uncorrected. $[RuCl_2(p\text{-cymene})]_2$ was purchased from STREM chemicals. Anhydrous acetonitrile (MeCN), anhydrous dichloromethane (CH_2Cl_2), anhydrous tetrahydrofuran (THF), and anhydrous toluene (PhMe) were dried and degassed by passing through anhydrous alumina columns using a solvent purification system (SPS) and stored under an atmosphere of N_2 prior to use. Reactions were performed in oven-dried glassware and under a blanket of N_2 if not stated otherwise. Temperatures quoted are external. Solvents were removed under reduced pressure using a rotary evaporator. *N*-Arylhydantoins were synthesized using a procedure adapted from that reported by Clayden and co-workers.[3]

General Procedure for Ruthenium(II)-Catalyzed C−H Alkenylation of *N*-Arylhydantoin/*N*-Arylsuccinimide. To an oven-dried carousel tube were added *N*-arylhydantoin/*N*-arylsuccinimide (0.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (0.016 g, 0.025 mmol), $AgSbF_6$ (0.035 g, 0.1 mmol), and $Cu(OAc)_2{\cdot}H_2O$ (0.10 g, 0.5 mmol). The carousel tube was sealed with a Teflon cap with the tap left open. To the tube was added 2-MeTHF (2 mL, 0.25 M) followed by the appropriate acrylate coupling partner (1.5 mmol). The resulting mixture was stirred at 100 °C under reflux for 18 h. The mixture was quenched with EtOAc (4 mL) and allowed to return to room temperature. The crude mixture was filtered using a short plug of silica, eluting with EtOAc. The filtrate was concentrated in vacuo. The crude mixture was purified using silica gel chromatography (EtOAc/petroleum spirit 40−60 °C, 50/50−60/40 v/v) to give pure C−H alkenylated *N*-arylhydantoin/*N*-arylsuccinimide.

*Methyl (E)-3-(2-(4,4-Dimethyl-2,5-dioxoimidazolidin-1-yl)-phenyl)acrylate (**3aa**).* The above compound was synthesized using the general procedure with 5,5-dimethyl-3-phenylimidazolidine-2,4-dione (**1a**) (0.10 g, 0.5 mmol) and methyl acrylate (0.14 mL, 1.5 mmol). Silica gel chromatography gave an off-white solid, 94%, (0.135 g). Mp: (from $CHCl_3$): 188−189 °C. FT-IR (thin film): ν_{max} (cm^{-1}) = 3311.0, 1782.6, 1712.9, 1638.4. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (1H, d, J = 7.3 Hz), 7.55−7.44 (3H, m), 7.27 (1H, d, J = 7.6 Hz), 6.90 (1H, s), 6.43 (1H, d, J = 15.9 Hz), 3.76 (3H, s), 1.57 (3H, s), 1.50 (3H, s). ^{13}C NMR (126 MHz,$CDCl_3$): δ 176.6, 167.0, 155.6, 139.0, 132.9, 131.1, 130.8, 130.0, 129.5, 127.6, 120.9, 59.5, 52.0, 25.8, 24.9. HRMS (ESI): m/z calcd for $C_{15}H_{16}N_2O_4$ requires 289.1183 for $[M + H]^+$, found 289.1163.

*Ethyl (E)-3-(2-(4,4-Dimethyl-2,5-dioxoimidazolidin-1-yl)phenyl)-acrylate (**3ab**).* The above compound was synthesized using the general procedure using *N*-arylhydantoin **1a** (0.10 g, 0.5 mmol) and ethyl acrylate (0.17 mL, 1.5 mmol). Silica gel chromatography gave an amorphous solid, 73% (0.192 g). Mp: (from $CHCl_3$): 105−107 °C. FT-IR (thin film): ν_{max} (cm^{-1}) = 3305.4, 2980.6, 1783.2, 1708.0, 1638.0. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.79−7.68 (1H, m), 7.53−7.43 (3H, m), 7.28 (1H, dd, J = 10.3, 8.8 Hz), 6.97 (1H, s), 6.43 (1H, d, J = 15.9 Hz), 4.22 (1H, qd, J = 7.1, 2.3 Hz), 1.56 (3H, s), 1.49 (3H, s), 1.29 (3H, t, J = 7.1 Hz). ^{13}C NMR (126 MHz, $CDCl_3$): δ 176.6, 166.5, 155.6, 138.6, 133.0, 131.0, 130.8, 129.9, 129.5, 127.5, 121.3, 60.8, 59.5, 25.8, 24.8, 14.4. HRMS (ESI): m/z calcd for $C_{16}H_{18}N_2O_4$ requires 303.1300 for $[M + H]^+$, found 303.1312.

*Butyl (E)-3-(2-(4,4-Dimethyl-2,5-dioxoimidazolidin-1-yl)phenyl)-acrylate (**3ac**).* The above compound was synthesized using the general procedure using *N*-arylhydantoin **1a** (0.10 g, 0.5 mmol) and butyl acrylate (0.22 mL, 1.5 mmol). Silica gel chromatography gave a thick oil, 94% (inseparable mixture of 6:1 **3ac**/**1a**) (0.154 g). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.73 (1H, dd, J = 7.6, 1.8 Hz), 7.55−7.43 (3H, m), 7.28−7.24 (1H, m), 7.11 (1H, s), 6.42 (1H, d, J = 15.9 Hz), 4.16 (2H, td, J = 6.7, 3.9 Hz), 1.69−1.58 (2H, m), 1.54 (3H, s), 1.47 (3H, s), 1.44−1.34 (2H, m), 0.92 (3H, t, J = 7.4 Hz). ^{13}C NMR (126 MHz, $CDCl_3$): δ 176.6, 166.5, 155.5, 138.5, 132.9, 130.9, 130.7, 129.8, 129.4, 129.1, 127.4, 126.3, 121.2, 64.6, 59.3, 30.7, 25.6,, 24.7, 19.2, 13.7.

*Benzyl (E)-3-(2-(4,4-Dimethyl-2,5-dioxoimidazolidin-1-yl)phenyl)-acrylate (**3ad**).* The above compound was synthesized using the general procedure using *N*-arylhydantoin **1a** (0.10 g, 0.5 mmol) and benzyl acrylate (0.20 mL, 1.5 mmol). Silica gel chromatography gave an amorphous solid, 79% (0.144 g). Mp: (from $CHCl_3$): 143−145 °C. FT-IR (thin film): ν_{max} (cm^{-1}) = 3312.7, 2978.9, 1782.4, 1713.8, 1638.2. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.75 (1H, dd, J = 7.3, 1.7 Hz), 7.56 (d, J = 15.9 Hz), 7.53−7.24 (10H, m), 7.21 (1H, s), 6.51 (1H, d, J = 15.9 Hz), 5.30−5.11 (2H, m), 1.46 (3H, s), 1.45 (3H, s). ^{13}C NMR (75 MHz, $CDCl_3$): δ 176.7, 166.2, 155.6, 139.1, 135.8, 132.7, 131.2, 130.8, 129.9, 129.4, 129.2, 128.7, 128.4, 127.4, 126.3, 120.8, 66.7, 59.4, 25.5, 24.7. HRMS (ESI): m/z calcd for $C_{21}H_{20}N_2O_4$ requires 365.1501 for $[M + H]^+$, found 365.1484.

*Methyl (E)-3-(2-(4,4-Dimethyl-2,5-dioxoimidazolidin-1-yl)-5-methoxyphenyl)acrylate (**3b**).* The above compound was synthesized using the general procedure using *N*-arylhydantoin **1b** (0.081 g, 0.5 mmol) and methyl acrylate (0.14 mL, 1.5 mmol). Silica gel chromatography gave an off-white solid, 65% (0.101 g). Mp: (from $CHCl_3$): 167−169 °C. FT-IR (thin film): ν_{max} (cm^{-1}) = 3317.2, 1779.2, 1711.1, 1642.8. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.45 (1H, d, J = 15.9 Hz), 7.19 (1H, d, J = 2.8 Hz), 7.17 (2H, d, J = 8.7 Hz), 7.02 (2H, m) 6.40 (1H, d, J = 15.9 Hz), 3.83 (3H, s), 3.76 (3H, s), 1.55 (3H, s), 1.48 (3H, s). ^{13}C NMR (126 MHz, $CDCl_3$): δ 177.0, 166.9, 160.4, 156.0, 139.0, 134.0, 130.6, 123.5, 121.0, 117.0, 112.2, 59.4, 55.8, 52.0, 25.7, 24.8. HRMS (ESI): m/z calcd for $C_{16}H_{18}N_2O_5$ requires 341.1112 for $[M + Na]^+$, found 341.1099.

*Methyl (E)-3-(2-(4,4-Dimethyl-2,5-dioxoimidazolidin-1-yl)-5-methylphenyl)acrylate (**3c**).* The above compound was synthesized using the general procedure using *N*-arylhydantoin **1c** (0.109 g, 0.5 mmol) and methyl acrylate (0.14 mL, 1.5 mmol). Silica gel chromatography gave an off-white solid, 52% (0.079 g). Mp: (from $CHCl_3$): 191−193 °C. FT-IR (thin film): ν_{max} (cm^{-1}) = 3313.6, 1778.9, 1707.6, 1641.8. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.53 (1H, s),

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7.49 (1H, d, J = 15.9 Hz), 7.31 (1H, d, J = 7.5 Hz), 7.15 (1H, d, J = 8.0 Hz), 6.99 (1H, s), 6.41 (1H, d, J = 15.9 Hz), 3.76 (3H, s), 2.40 (3H, s,), 1.56 (3H, s), 1.49 (3H, s). ^{13}C NMR (126 MHz, $CDCl_3$): δ 176.7, 167.0, 155.8, 140.1, 139.1, 132.5, 132.0, 129.2, 128.3, 128.1, 120.6, 59.4, 51.9, 25.7, 24.9, 21.4. HRMS (ESI): m/z calcd for $C_{16}H_{18}N_2O_4$ requires 325.1159 for $[M + Na]^+$, found 325.1154.

*Methyl (E)-3-(2-(4,4-Dimethyl-2,5-dioxoimidazolidin-1-yl)-5-tert-butylphenyl)acrylate (**3d**).* The above compound was synthesized using the general procedure using *N*-arylhydantoin **1d** (0.130 g, 0.5 mmol) and methyl acrylate (0.14 mL, 1.5 mmol). Silica gel chromatography gave an off-white solid, 81% (0.140 g). Mp: (from $CHCl_3$): 161−164 °C. FT-IR (thin film): ν_{max} (cm^{-1}) = 3310.5, 1780.0, 1709.9, 1640.9. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.71 (1H, s), 7.59−7.47 (2H, m), 7.19 (1H, d, J = 8.2 Hz), 7.08 (1H, s), 6.43 (1H, d, J = 15.9 Hz), 3.76 (3H, s), 1.54 (3H, s), 1.47 (3H, s), 1.33 (9H, s). ^{13}C NMR (126 MHz, $CDCl_3$): δ 176.8, 167.0, 155.8, 152.9, 139.6, 132.1, 128.9, 128.6, 128.1, 124.5, 120.3, 59.4, 51.9, 35.0, 31.2, 25.7, 24.8. HRMS (ESI): m/z calcd for $C_{19}H_{24}N_2O_4$ requires 345.1809 for $[M + H]^+$, found 345.1783.

*Methyl (E)-3-(2-(4,4-Dimethyl-2,5-dioxoimidazolidin-1-yl)-5-chlorophenyl)acrylate (**3e**).* The above compound was synthesized using the general procedure using *N*-arylhydantoin **1e** (0.119 g, 0.5 mmol) and methyl acrylate (0.14 mL, 1.5 mmol). Silica gel chromatography gave an off-white solid, 66% (0.106 g). Mp: (from $CHCl_3$): 193−195 °C. FT-IR (thin film): ν_{max} (cm^{-1}) = 3317.3, 1782.8, 1714.0, 1641.6. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.69 (1H, d, J = 2.1 Hz), 7.49−7.38 (2H. m), 7.22 (1H, d, J = 8.5 Hz), 7.03 (1H, s), 6.42 (1H, d, J = 15.9 Hz), 3.76 (3H, s), 1.56 (3H, s), 1.49 (3H, s). ^{13}C NMR (126 MHz, $CDCl_3$): δ 176.4, 166.5, 155.2, 137.7, 136.0, 134.5, 131.0, 130.8, 129.2, 127.6, 122.1, 59.6, 52.1, 25.7, 24.8. HRMS (ESI): m/z calcd for $C_{15}H_{15}N_2O_4Cl_1$ requires 323.0799 for $[M + H]^+$, found 323.0770.

*Methyl (E)-3-(2-(4,4-Dimethyl-2,5-dioxoimidazolidin-1-yl)-5-bromophenyl)acrylate (**3f**).* The above compound was synthesized using the general procedure using *N*-arylhydantoin **1f** (0.142 g, 0.5 mmol) and methyl acrylate (0.14 mL, 1.5 mmol). Silica gel chromatography gave an off-white solid, 66% (0.122 g). Mp: (from $CHCl_3$): 181−183 °C. FT-IR (thin film): ν_{max} (cm^{-1}) = 3314.2, 1783.1, 1709.7, 1640.1. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.85 (1H, d, J = 2.2 Hz), 7.60 (1H, dd, J = 8.4, 2.2 Hz), 7.41 (1H, d, J = 15.9 Hz), 7.15 (1H, d, J = 8.4 Hz), 7.06 (1H, s), 6.42 (1H, d, J = 15.9 Hz), 3.76 (3H, s), 1.55 (3H, s), 1.48 (3H, s_2). ^{13}C NMR (126 MHz, $CDCl_3$): δ 176.3, 166.6, 155.3, 137.7, 134.8, 134.0, 131.0, 130.5, 129.7, 124.0, 122.1, 59.6, 52.1, 25.7, 24.8. HRMS (ESI): m/z calcd for $C_{15}H_{15}N_2O_4Br_1$ requires 367.0293 for $[M + H]^+$, found 367.0275.

*Methyl (E)-3-(2-(4,4-Dimethyl-2,5-dioxoimidazolidin-1-yl)-5-trifluoromethylphenyl)acrylate (**3g**).* The above compound was synthesized using the general procedure using *N*-arylhydantoin **1g** (0.136 g, 0.5 mmol) and methyl acrylate (0.14 mL, 1.5 mmol). Silica gel chromatography gave an off-white solid, 47% (0.084 g). Mp (from $CHCl_3$): 175−178 °C. FT-IR (thin film): ν_{max} (cm^{-1}) = 3300.5, 1785.6, 1713.4, 1644.4. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.97 (1H, s), 7.75 (1H, d, J = 8.4 Hz), 7.51 (1H, d, J = 15.9 Hz), 7.43 (1H, d, J = 8.2 Hz), 6.89 (1H, s), 6.50 (1H, d, J = 15.9 Hz), 3.79 (3H, s), 1.60 (3H, s), 1.53 (3H, s). ^{13}C NMR (126 MHz, $CDCl_3$): δ 176.1, 166.5, 154.9, 137.8, 133.8 (d, J = 26.9 Hz), 132.2 (q, J = 33.2 Hz), 130.2, 127.6 (d, J = 3.5 Hz), 124.8 (d, J = 3.8 Hz), 123.3 (q, J = 272.7 Hz).122.6, 59.8, 52.2, 25.8, 24.9. ^{19}F NMR (470 MHz, $CDCl_3$): δ −63.03 (s). HRMS (ESI): m/z calcd for $C_{16}H_{15}N_2O_4F_3$ requires 379.0882 for $[M + Na]^+$, found 379.0870.

*Methyl (E)-3-(2-(4,4-Dimethyl-2,5-dioxoimidazolidin-1-yl)-4,5-dimethoxyphenyl)acrylate (**3h**).* The above compound was synthesized using the general procedure using *N*-arylhydantoin **1h** (0.132 g, 0.5 mmol) and methyl acrylate (0.14 mL, 1.5 mmol). Silica gel chromatography gave an off-white solid, 83% (0.145 g). Mp: (from $CHCl_3$): 196−198 °C. FT-IR (thin film): ν_{max} (cm^{-1}) = 3328.4, 1779.6, 1712.5, 1634.3. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.41 (1H, d, J = 15.8 Hz), 7.15 (1H, s), 7.00 (1H, s), 6.70 (1H, s), 6.33 (1H, d, J = 15.8 Hz), 3.92−3.88 (6H, m), 3.74 (3H, s), 1.58 (3H, s), 1.50 (3H, s). ^{13}C NMR (126 MHz, $CDCl_3$): δ 176.9, 167.2, 155.8, 151.6, 150.1, 138.6, 125.3, 124.4, 118.4, 111.7, 108.7, 59.4, 56.4, 56.3, 51.9, 25.8, 24.8. HRMS (ESI): m/z calcd for $C_{17}H_{20}N_2O_6$ requires 349.1355 for $[M + H]^+$, found 349.1374.

*Methyl (E)-3-(2-(4,4-Dimethyl-2,5-dioxoimidazolidin-1-yl)-4,5-dimethylphenyl)acrylate (**3i**).* The above compound was synthesized using the general procedure using *N*-arylhydantoin **1i** (0.116 g, 0.5 mmol) and methyl acrylate (0.14 mL, 1.5 mmol). Silica gel chromatography gave an off-white solid, 89%, (0.141 g). Mp: (from $CHCl_3$): 232−234 °C. FT-IR (thin film): ν_{max} (cm^{-1}) = 3327.5, 1783.6, 1728.0, 1636.1. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.51 (1H, s), 7.46 (1H, d, J = 15.9 Hz), 7.04 (1H, s), 6.79 (1H, s), 6.39 (1H, d, J = 15.9 Hz), 3.76 (3H, s), 2.31−2.29 (6H, m), 1.59 (3H, s), 1.52 (3H, s). ^{13}C NMR (126 MHz, $CDCl_3$): δ 176.8, 167.2, 155.9, 140.8, 139.0, 130.3, 130.1, 128.5, 128.4, 119.6, 59.5, 51.9, 25.8, 25.0, 20.0, 19.8. HRMS (ESI): m/z calcd for $C_{17}H_{20}N_2O_4$ requires 317.1496 for $[M + H]^+$, found 317.1462.

*Methyl (E)-3-(2-(4,4-Dimethyl-2,5-dioxoimidazolidin-1-yl)-thiophene-3-yl)acrylate (**3ja**).* The above compound was synthesized using the general procedure using *N*-arylhydantoin **1j** (0.105 g, 0.5 mmol) and methyl acrylate (0.14 mL, 1.5 mmol). Silica gel chromatography gave an off-white solid, 92% (0.135 g). Mp: (from $CHCl_3$): 172−174 °C. FT-IR (thin film): ν_{max} (cm^{-1}) = 3327.5, 1783.6, 1723.0, 1636.1. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.33 (1H, d, J = 5.8 Hz), 7.24−7.14 (3H. m), 6.25 (1H, d, J = 15.9 Hz), 3.72 (3H, s), 1.48 (6H, s). ^{13}C NMR (126 MHz, $CDCl_3$): δ 176.3, 167.3, 154.6, 134.3, 134.2, 131.7, 126.1, 124.4, 119.6, 59.5, 51.9, 25.2. HRMS (ESI): m/z calcd for $C_{13}H_{14}N_2O_4S_1$ requires 295.0708 for $[M + H]^+$, found 295.0706.

*Butyl (E)-3-(2-(4,4-Dimethyl-2,5-dioxoimidazolidin-1-yl)-thiophene-3-yl)acrylate (**3jb**).* The above compound was synthesized using the general procedure using *N*-arylhydantoin **1j** (0.105 g, 0.5 mmol) and butyl acrylate (0.22 mL, 1.5 mmol). Silica gel chromatography gave an amorphous solid, 84% (0.140 g). FT-IR (thin film): ν_{max} (cm^{-1}) = 3317.5, 1788.6, 1728.0, 1634.1. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.37−7.22 (3H, m), 6.99 (1H, s), 6.27 (1H, d, J = 15.9 Hz), 4.15 (2H, t, J = 6.6 Hz), 1.63 (2H, dt, J = 14.5, 6.7 Hz), 1.52 (6H, s), 1.38 (2H, dd, J = 15.0, 7.5 Hz), 0.92 (3H, t, J = 7.4 Hz). ^{13}C NMR (126 MHz, $CDCl_3$): δ 176.2, 167.0, 154.7, 134.5, 133.9, 131.5, 126.2, 124.4, 120.2, 64.7, 59.5, 30.8, 25.4, 19.3, 13.9. HRMS (ESI): m/z calcd for $C_{16}H_{20}N_2O_4S_1$ requires 337.1177 for $[M + H]^+$, found 337.1179.

*Methyl (E)-3-(2-(2,5-Dioxoimidazolidin-1-yl)phenyl)acrylate (**3k**).* The above compound was synthesized using the general procedure using *N*-arylhydantoin **1k** (0.088 g, 0.5 mmol) and methyl acrylate (0.14 mL, 1.5 mmol). Silica gel chromatography gave a white solid, 35% (0.045 g). Mp: (from $CHCl_3$): 154−157 °C FT-IR (thin film): ν_{max} (cm^{-1}) = 3301.9, 1778.4, 1708.4, 1638.3. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.76 (1H, d, J = 7.5 Hz), 7.59−7.45 (3H, m), 7.27 (1H, d, J = 7.9 Hz), 6.81 (1H, s), 6.47 (1H, d, J = 15.9 Hz), 4.18 (1H, d, J = 17.8 Hz), 4.09 (1H, d, J = 17.8 Hz), 3.78 (3H, s). ^{13}C NMR (126 MHz, $CDCl_3$): δ 170.5, 167.1, 157.5, 139.1, 132.9, 131.2, 130.7, 130.1, 129.4, 127.7, 121.0, 52.1, 47.0. HRMS (ESI): m/z calcd for $C_{13}H_{12}N_2O_4$ requires 283.0697 for $[M + Na]^+$, found 283.0674.

*Methyl (E)-3-(2-(4-Isopropyl-2,5-dioxoimidazolidin-1-yl)phenyl)-acrylate (**3l**).* The above compound was synthesized using the general procedure using *N*-arylhydantoin **1l** (0.109 g, 0.5 mmol) and methyl acrylate (0.14 mL, 1.5 mmol). Silica gel chromatography gave a white solid, 67% (0.101 g). Mp: (from $CHCl_3$): 178−180 °C. FT-IR (thin film): ν_{max} (cm^{-1}) = 3301.9, 1778.4, 1708.4, 1638.3. ^{1}H NMR (400 MHz, DMSO-d_6, 368 K): δ 8.22 (1H, d, J = 25.3 Hz), 7.93−7.86 (1H, m), 7.57−7.45 (3H, m), 7.28 (1H, s), 6.53 (1H, d, J = 16.0 Hz), 4.20 (1H, d, J = 2.7 Hz), 3.73 (3H, s), 2.20 (1H, dtd, J = 13.7, 6.9, 3.9 Hz), 1.10 (3H, d, J = 7.0 Hz), 1.03 (3H, d, J = 6.8 Hz). ^{13}C NMR (101 MHz, DMSO-d_6, 368 K) 172.2, 165.5, 155.3, 138.4, 132.0, 131.1, 130.1, 129.0, 128.7, 126.7, 112.0, 50.7, 29.4, 17.7, 15.8. HRMS (ESI): m/z calcd for $C_{16}H_{18}N_2O_4$ requires 325.1167 for $[M + Na]^+$, found 325.1146.

*Methyl (E)-3-(2-(4-Isobutyl-2,5-dioxoimidazolidin-1-yl)phenyl)-acrylate (**3m**).* The above compound was synthesized using the general procedure on half scale using *N*-arylhydantoin **1m** (0.63 g,

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0.25 mmol) and methyl acrylate (0.07 mL, 0.75 mmol). Silica gel chromatography gave a white solid, 56% (0.044 g). FT-IR (thin film): ν_{max} (cm^{-1}) = 3298.62, 2957.1, 1780.9, 1716.5, 1638.7. ^1H NMR (400 MHz, DMSO-d_6, 368 K): δ 8.41−8.29 (s, 1H), 7.89 (1H, dd, J = 7.5, 1.9 Hz), 7.59−7.41 (3H, m), 7.34−7.26 (1H, m), 6.52 (1H, d, J = 16.0 Hz), 4.31 (1H, app s), 3.74 (3H, s), 3.14−2.85 (2H, m), 1.94 (1H, ddt, J = 14.6, 13.0, 6.6 Hz), 1.00 (6H, app d). ^{13}C NMR (101 MHz, DMSO-d_6, 368 K): δ 173.2, 165.5, 154.9, 138.3, 132.0, 131.1, 130.1, 128.7, 126.8, 125.8, 120.0, 55.1, 50.7, 23.6, 22.3, 21.3. HRMS (ESI): m/z calcd for $C_{17}H_{20}N_2O_4$ requires 317.1501 for $[M + H]^+$, found 317.1493.

*Methyl (E)-3-(2-(1,3-Dioxotetrahydro-1H-pyrrolo[1,2-c]imidazol-2(3H)-yl)phenyl)acrylate (**3n**).* The above compound was synthesized using the general procedure using *N*-arylhydantoin **1n** (0.108 g, 0.5 mmol) and methyl acrylate (0.14 mL, 1.5 mmol). Silica gel chromatography gave an amorphous solid, 69% (0.103 g). FT-IR (thin film): ν_{max} (cm^{-1}) = 2953.6, 1777.9, 1710.6, 1637.6. ^1H NMR (500 MHz, DMSO-d_6, 368 K): δ 7.90 (1H, dd, J = 7.6, 1.8 Hz), 7.60−7.48 (2H, m), 7.37 (1H, app s), 7.39−7.34 (1H, m), 6.53 (1H, d, J = 15.9 Hz), 4.44 (1H, t, J = 8.3 Hz), 3.74 (3H, s), 3.69 (1H, q, J = 7.9 Hz), 3.27 (1H, ddd, J = 11.1, 7.5, 5.7 Hz), 2.50 (1H, p, J = 1.9 Hz), 2.29 (1H, app s), 2.11 (2H, m), 1.89 (1H, app s). ^{13}C NMR (126 MHz, DMSO): δ 172.3, 165.6, 158.4, 138.0, 131.8, 130.9, 130.2, 129.0, 126.9, 120.2, 62.6, 50.9, 45.2, 26.7, 25.8. HRMS (ESI): m/z calcd for $C_{16}H_{16}N_2O_4$ requires 323.1010 for $[M + Na]^+$, found 323.1022.

*Methyl (E)-3-(2-(2,4-Dioxo-1,3-diazaspiro[4.5]decan-3-yl)-phenyl)acrylate (**3oa**).* The above compound was synthesized using the general procedure using *N*-arylhydantoin **1o** (0.122 g, 0.5 mmol) and methyl acrylate (0.14 mL, 1.5 mmol). Silica gel chromatography gave a white solid, 82% (0.135 g). Mp: (from $CHCl_3$): 228−229 °C FT-IR (thin film): ν_{max} (cm^{-1}) = 3288.9, 1777.8, 1708.3, 1638.1. ^1H NMR (500 MHz, $CDCl_3$): δ 7.72 (1H, d, J = 7.4 Hz), 7.61−7.42 (4H, m), 7.25 (1H, d, J = 7.3 Hz), 6.42 (1H, d, J = 15.9 Hz), 3.75 (3H, s), 2.07−1.67 (6H, m), 1.61−1.23 (2H, m). ^{13}C NMR (126 MHz, $CDCl_3$): δ 176.2, 166.9, 156.0, 139.2, 132.9, 131.0, 130.9, 129.7, 129.5, 127.4, 120.6, 62.5, 51.9, 34.3, 33.4, 24.6, 21.7, 21.6. HRMS (ESI): m/z calcd for $C_{18}H_{20}N_2O_4$ requires 329.1496 for $[M + H]^+$, found 329.1475.

*Methyl (E)-3-(2-(2,4-Dioxo-1,3-diazaspiro[4.5]decan-3-yl)-phenyl)acrylate (**3ob**).* The above compound was synthesized using the general procedure using *N*-arylhydantoin, **1o**, (0.122 g, 0.5 mmol) and butyl acrylate (0.14 mL, 1.5 mmol). Silica gel chromatography gave a white solid, 81% (0.150 g). Mp: (from $CHCl_3$): 157−159 °C FT-IR (thin film): ν_{max} (cm^{-1}) = 3284.3, 1778.3, 1707.8, 1638.0. ^1H NMR (500 MHz, $CDCl_3$): δ 7.72 (1H, d, J = 7.3 Hz), 7.68 (1H, s), 7.53−7.37 (4H, m), 7.25 (1H, d, J = 7.7 Hz), 6.41 (1H, d, J = 15.9 Hz), 4.22−4.09 (2H, m,), 2.00−1.85 (2H, m,), 1.83−1.53 (8H, m), 1.46−1.30 (5H, m), 0.92 (3H, t, J = 7.4 Hz). ^{13}C NMR (126 MHz, $CDCl_3$): δ 176.2, 166.5, 156.0, 138.7, 132.9, 130.9, 130.8, 129.7, 129.5, 129.1, 127.4, 126.3, 121.1, 64.7, 62.5, 34.3, 33.8, 33.4, 30.8, 24.6, 21.7, 21.6, 21.6, 19.3, 13.9. HRMS (ESI): m/z calcd for $C_{21}H_{26}N_2O_4$ requires 393.1793 for $[M + Na]^+$, found 393.1825.

*Methyl (E)-3-(2-(3-methyl-2,5-dioxoimidazolidin-1-yl)phenyl)-acrylate (**3p**).* The above compound was synthesized using the general procedure using *N*-arylhydantoin **1p** (0.095 g, 0.5 mmol) and methyl acrylate (0.14 mL, 1.5 mmol). Silica gel chromatography gave an amorphous solid, 45% (0.062 g). FT-IR (thin film): ν_{max} (cm^{-1}) = 1778.0, 1710.0, 1636.7. ^1H NMR (500 MHz, $CDCl_3$): δ 7.73 (1H, dd, J = 7.6, 1.8 Hz), 7.52 (1H, d, J = 15.9, 7.0 Hz), 7.25−7.20 (2H, m), 6.44 (1H. d, J = 15.9 Hz), 4.15 (1H, d, J = 17.7 Hz), 4.03 (1H, d, J = 17.7 Hz), 3.76 (3H, s), 3.06 (3H, s). ^{13}C NMR (126 MHz,$CDCl_3$): δ 168.9, 167.1, 155.7, 139.3, 132.9, 131.2, 131.1, 129.8, 129.3, 127.5, 120.7, 52.0, 52.0, 30.2. HRMS (ESI): m/z calcd for $C_{14}H_{14}N_2O_4$ requires 275.1032 for $[M + H]^+$, found 275.1018.

*Butyl (E)-3-(2-(4,4-Dimethyl-2,5-dioxoimidazolidin-1-yl)-5-nitro-4-(trifluoromethyl)phenyl)acrylate (**3r**).* The above compound was synthesized using the general procedure using *N*-arylhydantoin **1r** (0.159 g, 0.5 mmol) and butyl acrylate (0.22 mL, 1.5 mmol). Silica gel chromatography gave an off white anorphous solid, 14%, (0.030 g). FT-IR (thin film): ν_{max} (cm^{-1}) = 3310.8, 2964.6, 1789.8, 1722.1, 1643.8, 1546.1, 1387.0. ^1H NMR (500 MHz, $CDCl_3$): δ 8.21 (1H, s), 7.77 (1H, s), 7.44 (1H, d, J = 15.9 Hz), 6.57 (1H, d, J = 15.9 Hz), 5.98 (1H, s), 4.21 (2H, t, J = 6.6 Hz), 1.70−1.57 (8H, m), 1.42 (2H, dq, J = 14.5, 7.3 Hz), 0.95 (2H, t, J = 7.4 Hz). ^{13}C NMR (126 MHz, $CDCl_3$): δ 175.2, 165.4, 153.5, 148.3, 138.4, 135.3, 133.8, 129.7 (q, J = 5.3 Hz), 126.0, 125.3 (d, J = 35.3 Hz), 124.5, 122.5, 120.3, 65.5, 60.0, 30.8, 26.0, 25.1, 19.3, 13.9. ^{19}F NMR (470 MHz, $CDCl_3$): δ −60.06 (s). HRMS (ESI): m/z calcd for $C_{19}H_{20}N_3O_6F_3$ requires 444.1377 for $[M + H]^+$, found 444.1355.

*Methyl (E)-3-(2-(2,5-Dioxopyrrolidin-1-yl)phenyl)acrylate (**5a**).* The general procedure was followed using the following compounds: *N*-phenylsuccinimide **4a** (0.088 g, 0.5 mmol), methyl acrylate (0.14 mL, 0.13 g, 1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (0.016 g, 0.025 mmol), $AgSbF_6$ (0.035 g, 0.1 mmol), and $Cu(OAc)_2{\cdot}H_2O$ (0.10 g, 0.5 mmol). The solvent was removed in vacuo, and the crude mixture was purified using column chromatography (EtOAc/hexanes) to yield a white solid, **5a**, 54% (0.14 g). Mp: (from $CHCl_3$) = 108−110 °C. FT-IR (thin film): ν_{max} (cm^{-1}) = 1708.6, 1638.1. ^1H NMR (500 MHz, $CDCl_3$): δ 7.75 (1H, dd, J = 7.5, 1.8 Hz), 7.53−7.47 (2H, m), 7.41 (1H, d, J = 15.9 Hz), 7.16 (1H, dd, J = 7.6, 1.5 Hz), 6.44 (1H, d, J = 15.9 Hz), 3.78 (3H, s), 3.07−2.91 (4H, m). ^{13}C NMR (126 MHz, $CDCl_3$): δ 176.2, 167.0, 138.9, 132.5, 131.2, 130.0, 129.0, 127.7, 126.7, 121.1, 52.0, 28.9. HRMS (ESI): m/z calcd for $C_{14}H_{13}N_1O_4$ requires 282.0743 for $[M + Na]^+$, found 282.0713.

*Methyl (E)-3-(5-Chloro-2-(2,5-dioxopyrrolidin-1-yl)phenyl)-acrylate (**5b**).* The general procedure was followed using the following compounds: *N*-(4-chlorophenyl)succinimide **4b** (0.105 g, 0.5 mmol), methyl acrylate (0.14 mL, 0.13 g, 1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (0.016 g, 0.025 mmol), $AgSbF_6$ (0.035 g, 0.1 mmol), $Cu(OAc)_2{\cdot}H_2O$ (0.10 g, 0.5 mmol). Column chromatography gave a pale orange amorphous solid, **5c**, 32% (0.047 g). Mp: (from $CHCl_3$) = 101−103 °C. FT-IR: (thin film): ν_{max} (cm^{-1}) = 3066.8, 2993.1, 1700.9, 1639.4, 1610.2. ^1H NMR: (500 MHz, $CDCl_3$): δ 7.70 (1H, d, J = 2.1 Hz), 7.45 (1H, dd, J = 8.4, 2.2 Hz), 7.31 (1H, d, J = 15.9 Hz), 7.10 (1H, d, J = 8.5 Hz), 6.42 (1H, d, J = 15.9 Hz), 3.77 (3H, s), 3.03−2.86 (4H, m). ^{13}C NMR: (126 MHz, $CDCl_3$): δ 175.8, 166.4, 137.5, 135.8, 133.9, 130.9, 130.1, 129.8, 127.4, 122.1, 51.9, 28.6. HRMS: (ESI): m/z calcd for $C_{14}H_{12}Cl_1N_1Na_1O_4$ requires 316.0352 for $[M + Na]^+$, found 316.0327.

*Methyl (E)-3-(5-Bromo-2-(2,5-dioxopyrrolidin-1-yl)phenyl)-acrylate (**5c**).* The general procedure was followed using the following compounds: *N*-(4-bromophenyl)succinimide **4c** (0.127 g, 0.5 mmol), methyl acrylate (0.14 mL, 0.13 g, 1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (0.016 g, 0.025 mmol), $AgSbF_6$ (0.035 g, 0.1 mmol), and $Cu(OAc)_2{\cdot}H_2O$ (0.10 g, 0.5 mmol). Column chromatography gave an off-white amorphous solid, **25**, 26% (0.044 g). Mp: (from $CHCl_3$) = 98−101 °C. FT-IR: (thin film): ν_{max} (cm^{-1}) = 3073.5, 2996.4, 1701.3, 1643.4, 1609.1. ^1H NMR: (500 MHz, $CDCl_3$): δ 7.86 (1H, d, J = 1.9 Hz), 7.60 (1H, dd, J = 8.4, 2.0 Hz), 7.30 (1H, d, J = 15.9 Hz), 7.03 (1H, d, J = 8.4 Hz), 6.42 (1H, d, J = 15.8 Hz), 3.78 (3H, s), 3.03−2.87 (4H, m). ^{13}C NMR: (126 MHz, $CDCl_3$): δ 175.7, 166.4, 137.4, 134.2, 133.8, 130.4, 130.3, 123.9, 122.1, 52.0, 28.6. HRMS: (ESI): m/z calcd for $C_{14}H_{12}Br_1N_1O_4$ requires 338.0004 for $[M + H]^+$, found 338.0028.

*Methyl (E)-3-(2-(3-(4-Methoxyphenyl)-2,5-dioxopyrrolidin-1-yl)-phenyl)acrylate (**5d**).* The general procedure was followed using the following compounds: *N*-phenyl(4-methoxy)succinimide **4d** (0.141 g, 0.5 mmol), methyl acrylate (0.14 mL, 0.13 g, 1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (0.016 g, 0.025 mmol), $AgSbF_6$ (0.035 g, 0.1 mmol), and $Cu(OAc)_2{\cdot}H_2O$ (0.10 g, 0.5 mmol). Column chromatography gave an off-white amorphous solid, **33**, 24% (0.043 g). Mp: (from $CHCl_3$) = 92−94 °C. FT-IR: (thin film): ν_{max} (cm^{-1}) = 3065.1, 2995.1, 2835.5, 1701.5, 1644.3, 1608.8. ^1H NMR: (400 MHz, DMSO-d_6, 368 K): δ 7.90 (1H, d, J = 7.8 Hz), 7.60−7.38 (4H, m), 7.37−7.26 (2H, m), 6.99−6.94 (2H, m), 6.53 (1H, d, J = 15.9 Hz), 4.39−4.26 (1H, m), 3.80 (3H, s), 3.76 (3H, s), 3.02−2.96 (1H, m), 2.93−2.86 (1H, m). ^{13}C NMR: (126 MHz, $CDCl_3$): δ 176.8, 175.2, 175.1, 166.8, 166.5, 159.4, 138.7, 138.6, 132.5, 132.3, 131.4, 131.0, 129.9, 129.9, 129.2, 128.9, 128.9, 128.8, 128.8, 128.7, 128.4, 127.5, 127.4, 126.4, 121.3, 121.0, 114.9, 114.7, 114.7, 55.3, 55.3, 51.9, 51.8, 45.9, 45.4, 45.2, 37.8, 37.4, 37.3, 28.4. (Mixture of peaks observed due to presence of

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rotamers). HRMS: (ESI): m/z calcd for $C_{21}H_{19}N_1O_5$ requires 388.1155 for $[M + Na]^+$, found 388.1143.

*Benzyl (E)-3-(2-(3-(4-Methoxyphenyl)-2,5-dioxopyrrolidin-1-yl)-phenyl)acrylate (**5e**).* The general procedure was followed using the following compounds: *N*-phenyl(4-methoxy)succinimide **4d** (0.141 g, 0.5 mmol), benzyl acrylate (0.22 mL, 0.24 g, 1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (0.016 g, 0.025 mmol), $AgSbF_6$ (0.035 g, 0.1 mmol), $Cu(OAc)_2{\cdot}H_2O$ (0.10 g, 0.5 mmol). Column chromatography gave an off-white amorphous solid, **34**, 28% (0.061 g). Mp: (from $CHCl_3$) = 88−91 °C. FT-IR: (thin film): ν_{max} (cm^{-1}) = 3074.0, 2996.4, 2837.5, 1700.9, 1643.4, 1608.8. ^1H NMR: (400 MHz, DMSO-d_6, 368 K): δ 7.93 (1H, d, J = 7.4 Hz), 7.62−7.45 (4H, m), 7.44−7.31 (7H, m), 6.96 (2H, dt, J = 9.8, 5.4 Hz), 6.61 (1H, d, J = 15.9 Hz), 5.26 (2H, d, J = 1.9 Hz), 4.33 (1H, ddd, J = 27.2, 9.3, 5.1 Hz), 3.77 (3H, s), 2.98−2.87 (2H, m). ^{13}C NMR: (126 MHz, $CDCl_3$): δ 138.9, 131.0, 129.9, 128.8, 128.6, 128.6, 128.4, 128.1, 127.4, 126.4, 121.3, 114.9, 114.7, 77.3, 77.0, 76.8, 66.4, 55.3, 45.9, 45.4, 37.8. (Mixture of peaks observed due to presence of rotamers.) HRMS: (ESI): m/z calcd for $C_{27}H_{23}N_1O_5$ requires 464.1470 for $[M + Na]^+$, found 464.1484.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02073.

NMR spectra for novel compounds and supporting spectra for competition experiments (PDF)

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Notes

The authors declare no competing financial interest.

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