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Preparation of Tetrasubstituted Olefins Using Mono or Double Aerobic Direct C−H Functionalization Strategies: Importance of Steric Effects

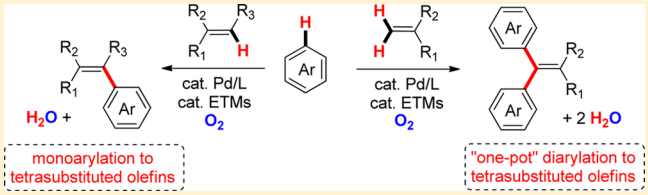
Nicolas Gigant,*[,†,‡] François Quintin,[†] and Jan-E. Bäckvall*[,†]

[†]Department of Organic Chemistry, Arrhenius Laboratory, Stockholm University, SE-106 91 Stockholm, Sweden

[‡]Equipe de Chimie des Substances Naturelles, Université Paris-Sud, UMR CNRS 8076 BioCIS, LabEx LERMIT, Faculté de Pharmacie, 5, rue Jean-Baptiste Clément, 92296 Châtenay-Malabry, France

Supporting Information

ABSTRACT: A novel protocol for the synthesis of tetrasubstituted olefins through a biomimetic approach has been explored. Both mono- and diarylations were performed under ambient oxygen pressure, giving a range of highly hindered tetrasubstituted alkenes. For diarylation of disubstituted substrates, it was demonstrated that the second arylation is the rate-limiting step of the overall transformation.



INTRODUCTION

Tetrasubstituted olefins constitute an important class of compounds since many of these olefins show significant biological activities (Figure 1). For example, (*Z*)-Tamoxifen displays effects against breast cancer[1] while Rofecoxib is a powerful nonsteroidal anti-inflammatory drug.[2] Dibenzoxapin and related compounds have been evaluated as nuclear hormone receptor modulators,[3] and finally, tetrasubstituted isocombretastatins A-4 have been recently identified as new tubulin inhibitors.[4]

Reported efficient methods for accessing such unsaturated structures are mainly based on the use of transition-metal catalysis via carbofunctionalization of alkynes,[5] olefin metathesis,[6] or cross-coupling reactions.[7] Among the latter, the oxidative Heck coupling has been frequently employed for the preparation of disubstituted alkenes.[8] However, only a few examples of successful Heck arylation have been reported regarding the synthesis of tri- or tetrasubstituted olefins.[7b−e] There are several problems associated with the oxidative Heck coupling between aromatic heterocycles and trisubstituted olefins to give tetrasubstituted olefins. The problems with the latter reaction can be rationalized by the low reactivity of the trisubstituted substrates. Due to steric hindrance around the unsaturated core, the latter alkenes are not reactive enough to undergo the required carbopalladation. Another problem is associated with the regeneration of the active catalyst. In general, the use of strong oxidants or additives—such as TEMPO (2,2,6,6-tetramethylpiperidine-*N*-oxyl radical) derivatives[7e] and/or inorganic salts[7c,d]—is required, thus reducing the applicability and sustainability of the reaction. In addition, in the dehydrogenative version of the Heck reaction—the Fujiwara−Moritani reaction[9]—the challenging metal insertion into the aromatic C−H bond makes the synthetic task even more difficult. Therefore, there is a demand for improvements of the synthesis of tetrasubstituted alkenes via the dehydrogenative Heck reaction approach.

In the past few years, we have been involved in the development of new sustainable C−C couplings via C−H activations using a biomimetic approach.[10] Following this concept, the high kinetic barrier preventing the catalyst regeneration is circumvented by the use of catalytic amounts of electron-transfer mediators (ETMs).[11] In this way, the reduced catalyst can be reoxidized by O_2 at atmospheric pressure, producing water as the sole byproduct of the reaction. On the basis of this strategy, we have previously established protocols for the dehydrogenative Heck reaction that have the following advantages: (i) relative low palladium and arene loadings, (ii) utilization of O_2 under ambient pressure as the oxidant, and (iii) extension of the scope to nonbiased olefins and heterocycles. Our continued interest in this field prompted us to explore the preparation of tetrasubstituted olefins via a biomimetic approach, and our contribution is reported herein.

RESULTS AND DISCUSSION

We first planned to prepare a trisubstituted olefin via a dehydrogenative Heck reaction that could be used as starting material for the synthesis of tetrasubstituted olefins. In our previously reported arylation of nonbiased olefins,[10a] we showed that acridine as a ligand dramatically enhances the reaction rate and totally controls the site selectivity in the coupling with veratrole. We initiated our studies with a 1:10 ratio of alkene **1a** and veratrole (**2a**) using $Pd(OAc)_2$ (5 mol %) as catalyst, acridine (5 mol %) as ligand, and benzoquinone (BQ) (10 mol %) and iron phthalocyanine Fe(Pc) (2.5 mol %) as electron-transfer mediators in a mixture of acetic acid:dioxane (1:1, v:v)

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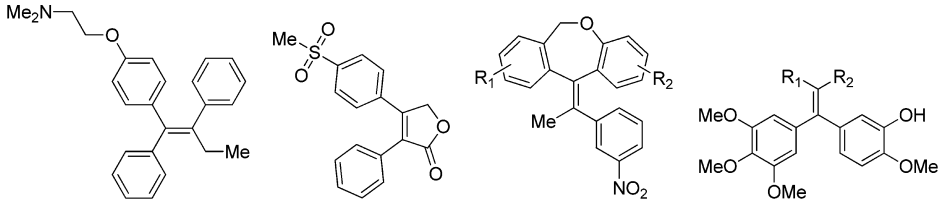
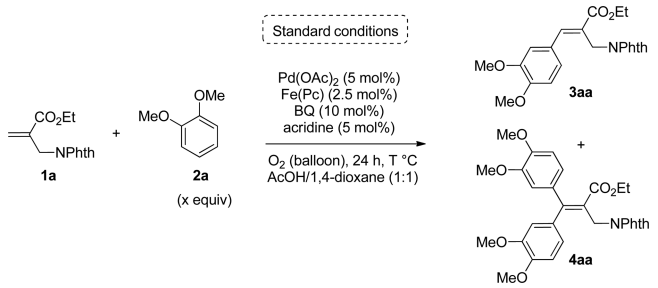


Figure 1. Representative drugs containing tetrasubstituted olefins.

Table 1. Optimization of the Synthesis of Tetrasubstituted Olefins[a]



	conditions				
entry	T (°C)	arene (equiv)	variations from standard conditions (concerning solvent and catalysts)	**3aa** (%)[b]	**4aa** (%)[b]
1	90	10	none	66	27
2	90	10	AcOH as solvent	59	17
3	100	10	none	36	35
4	110	10	none	42	3
5	100	10	BQ (20 mol %) and Fe(Pc) (5 mol %)	30	39
6	100	10	AcOH:dioxane (75:25) as solvent	57	29
7	100	10	AcOH:dioxane (25:75) as solvent	28	9
8	100	10	$Pd(OAc)_2$ (7.5 mol %)	24	66
9	100	15	none	trace	66[c]
10	100	15	AcOH:CH_3CN (8:2) as solvent	56	9
11	100	15	PivOH:dioxane (1:1) as solvent	33	7
12	100	15	C_2H_5COOH:dioxane (1:1) as solvent	18	6
13	100	15	1,4-diOMeBQ (10 mol %) instead of BQ	51	37
14	100	15	Cu(Pc) (2.5 mol %) instead of Fe(Pc)	49	37

[a]Reaction conditions: **1a** (0.30 mmol), **2a** (10 or 15 equiv) in the appropriate catalytic system for 24 h under O_2 (balloon). [b]NMR yield using an internal standard. [c]Yield after flash chromatography.

for 24 h at 90 °C under ambient oxygen pressure (Table 1, entry 1). Interestingly, we found that formation of the trisubstituted alkene **3aa** was accompanied by the tetrasubstituted alkene **4aa**. This reaction shows that the biomimetic approach is a viable strategy for providing access to tetrasubstituted olefins. Taking into account that there are not many examples in the literature for the diarylation of alkenes,[10f,12] it was highly interesting to develop a one-pot double arylation of **1a**.

Attempts to increase the rate of the reaction by the use of pure acetic acid as the solvent were unsuccessful and led to only 17% yield of **4aa** (Table 1, entry 2). An increase of the reaction temperature to 100 °C under the standard conditions resulted in an improvement and gave olefin **4aa** in a 35% yield, (Table 1, entry 3). However, a further increase of the reaction temperature to 110 °C decreased the amount of **4aa** to 3% (entry 4). The dramatic decrease of **4aa** may be due to decomposition at 110 °C under the acidic conditions. An increase of the catalytic amount of ETMs did not significantly affect the yield of the coupling, and modifications of the solvent ratio led to decreased yields (entries 5−7). We were pleased to find that the use of a higher catalyst loading (entry 8) or an increase of the arene loading (entry 9) improved the yield of **4aa** up to 66%. Considering the importance of the choice of solvent in the Fujiwara−Moritani reaction, we also evaluated the role of a range of cosolvents such as acetonitrile instead of dioxane,[13] or pivalic acid or propionic acid instead of acetic acid, but none of these changes increased the yield of **4aa** (entries 10−12). We chose to conclude our optimization studies with an additional screening of ETMs, but these alternative catalytic systems were not more efficient than those used in the standard conditions (entries 13−14).

The double dehydrogenative sequence for the conversion of disubstituted alkene **1a** into trisubstituted alkene **3aa** and tetrasubstituted alkene **4aa** was monitored by ^1H NMR spectroscopy (Figure 2). The reaction profile indicates that olefin **1a** is almost totally consumed after only 2 h, mostly giving **3aa** with only trace amounts of **4aa**. Then, the concentration of **3aa** is decreasing slowly with concomitant formation of **4aa**, demonstrating that the rate-limitating step of the sequence is the formation of the desired tetrasubstituted product. The steric hindrance around the double bond certainly slows down the carbopalladation.

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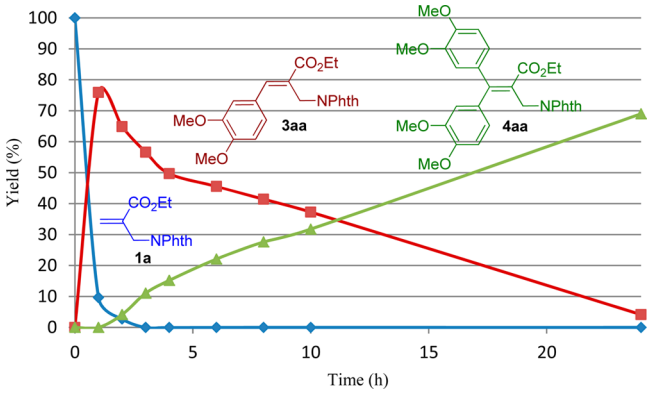
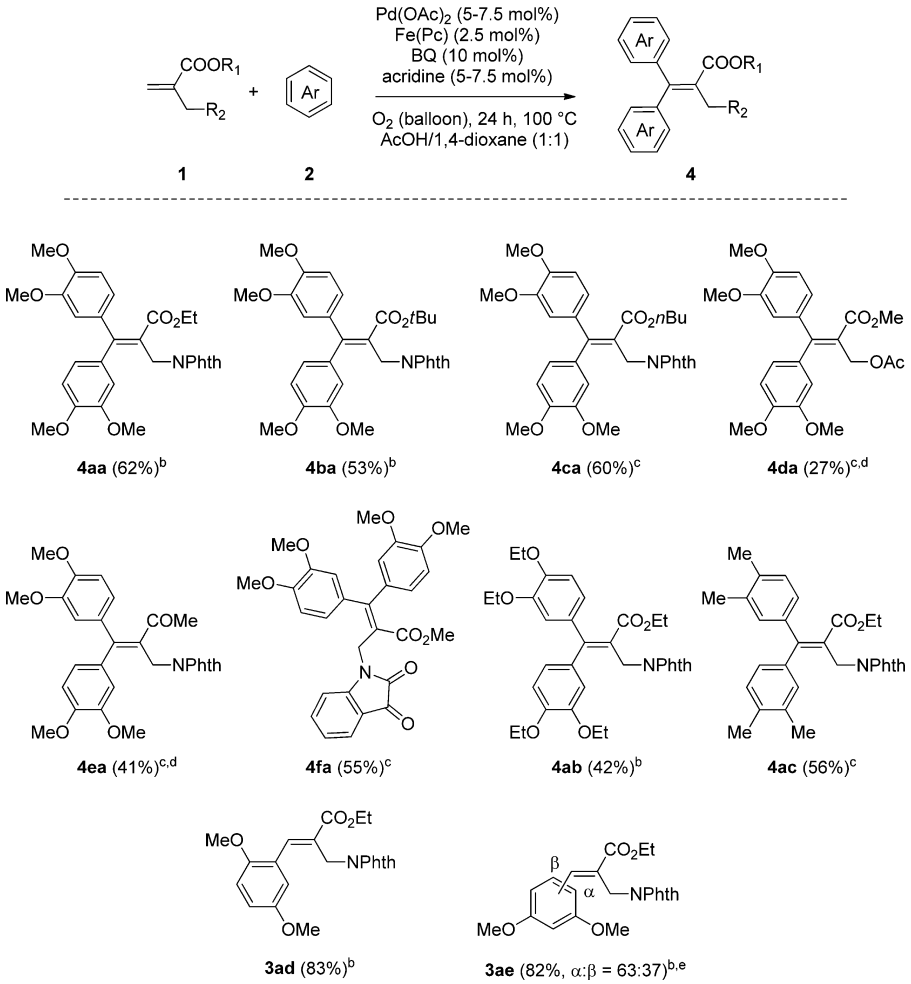


Figure 2. Reaction profile of the biomimetic double dehydrogenative sequence between alkene **1a** and arene **2a** using the reaction conditions of entry 9, Table 1.

We chose to continue our studies with a range of one-pot diarylations using the optimum conditions (Scheme 1). In most cases, the introduction of directing groups—such as acyl groups—can only be employed to partially control the regio- and the stereoselectivity of tetrasubstituted alkenes.[7d,14] Indeed, simple arenes can potentially undergo metalation at several reactive sites, generating complicated mixtures of isomers after a double cross-coupling. Usually, the site selectivity is controlled by (i) electronic factors with a preference for the most electron-rich carbon, (ii) steric factors with a preference for the less-hindered carbon. First, the influence of the substituents in 1,1-disubstituted alkene substrates was examined by reaction with veratrole **2a** as the aromatic coupling partner. We were pleased to find that a range of esters smoothly underwent the diarylation, giving **4aa**−**4ca** in good yields. An acetate and a ketone are both tolerated in the double dehydrogenative cross-coupling, albeit in lower yields (**4da** and **4ea**). An olefin substrate containing an isatin moiety underwent a smooth reaction, resulting in the formation of **4fa** in 55% yield. To our satisfaction, the site selectivity of the reaction with 1,2-diethoxybenzene and *o*-xylene was complete, leading to two highly substituted scaffolds **4ab** and **4ac**. However, no diarylated product was observed when 1,4-dimethoxybenzene **2d** was employed as coupling partner, the reaction yielding only the trisubstituted olefin **3ad** in an 83% yield. The second arylation is apparently suppressed due to steric reasons. The lack of reactivity due to steric effects was confirmed by using 1,3-dimethoxybenzene **2e** as coupling partner. Indeed, a 63:37 mixture in favor of the *ortho*-isomer **3ae-*α*** (the most reactive site) was isolated, accompanied by roughly 5% of a diarylated scaffold. In this example, due to its steric hindrance,

Scheme 1. Synthesis of Tetrasubstituted Olefins via a Double Aerobic Direct C−H Activation[a,b,c,d,e]



[a]For reaction conditions, see Table 1. [b]$Pd(OAc)_2$ (5 mol %), acridine (5 mol %). [c]$Pd(OAc)_2$ (7.5 mol %), acridine (7.5 mol %). [d]Reaction performed at 90 °C. [e]Ratio of isomers (*α*:*β*) determined by NMR spectroscopy of isolated product.

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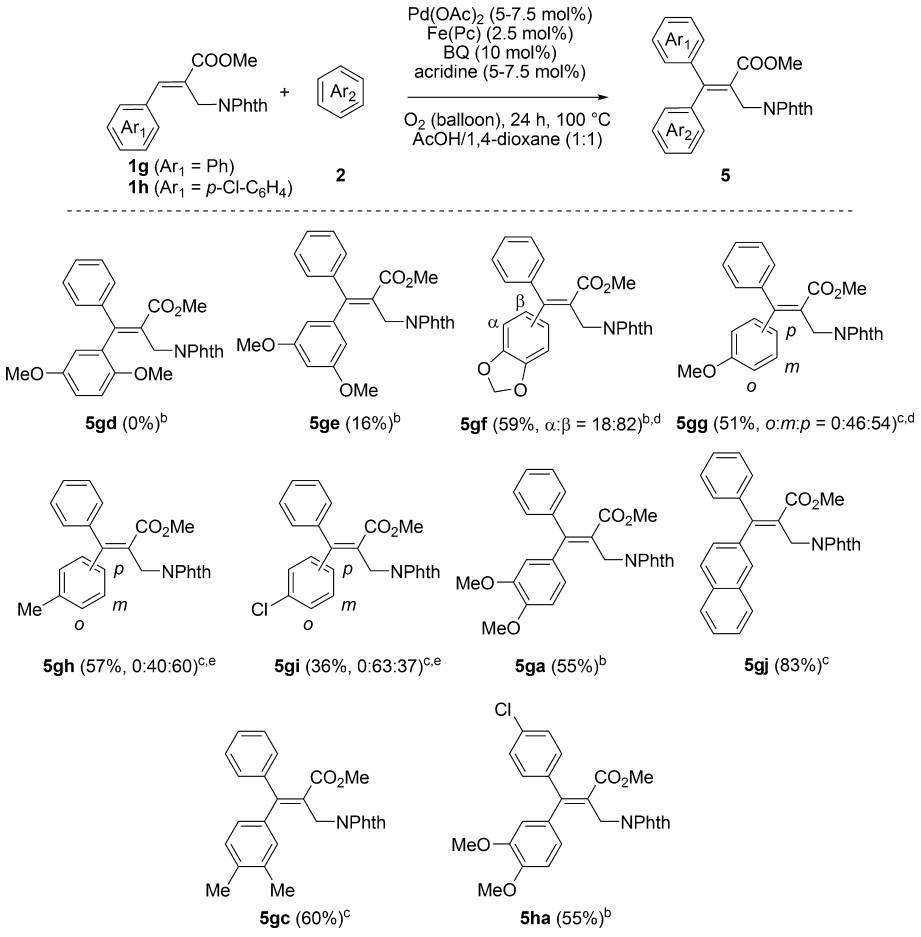
Scheme 2. Synthesis of Tetrasubstituted Olefins via a Mono Aerobic Direct C−H Activation[a,b,c,d,e]



[a]For reaction conditions, see Table 1. [b]$Pd(OAc)_2$ (5 mol %), acridine (5 mol %). [c]$Pd(OAc)_2$ (7.5 mol %), acridine (7.5 mol %). [d]Ratio of isomers (α:β or *o*:*m*:*p*) determined by NMR spectroscopy of isolated product. [e]Ratio of regioisomers, which could not be assigned and are thus given in no particular order (determined by NMR of isolated product).

3ae-*α* is already too crowded to perform a second arylation with **2e**. In addition, **3ae-*β*** can only react with the β position of **2e**, which is unfortunately the less reactive carbon of the arene.

We also confirmed the influence of steric hindrance starting from trisubstituted alkenes **1g** and **1h** (Scheme 2). Reaction of **1g** with arene **2d** did not deliver the desired product **5gd**, the starting materials being mostly recovered and no identifiable byproduct being detected. Furthermore, with arene **2e**, only one isomer **5ge** was obtained in a 16% yield, whereas 57% of olefin **1g** remained intact. These systematic studies on these sterically hindered substrates led to some instructive results: *ortho*-C−H functionalization of simple arenes is very slow with trisubstituted olefins, illustrating the influence of steric effects on the rate. The reaction was also conducted with 1,3-benzodioxole (**1f**) as coupling partner, and surprisingly, the selectivity of the coupling was not complete. The desired alkenes **5gf** were isolated as a mixture of isomers in a 18:82 ratio in favor of the β-alkenylated scaffold. In light of these results, it was of interest to establish the selectivity of anisole as coupling partner. Anisole is known to mainly undergo palladium insertion at (i) *para*, (ii) *ortho*, (iii) *meta* positions.[10a−c,13] As expected, no coupling occurred at the *ortho* position of anisole, and **5gg** was isolated as a mixture of isomers in a 0:46:54 (*o*:*m*:*p*) ratio. Similarly, toluene and chlorobenzene were also successfully employed and only two regioisomers were detected in each case (**5gh** and **5gi**). To further explore the scope of this transformation, the coupling reaction with **1g** (or **1h**) was conducted with difunctionalized arenes such as veratrole, naphtalene, or *o*-xylene, which furnished a range of densely substituted alkenes **5ga**, **5gj**, **5gc**, and **5ha** with synthetically useful yields and complete selectivity.[15]

CONCLUSION

In summary, we have developed an operationally simple protocol for the synthesis of tetrasubstituted olefins via mono or double aerobic dehydrogenative Heck couplings through a biomimetic approach. It was shown that the steric hindrance around the unsaturated core plays a key role in the selectivity of the reaction, and a range of highly substituted alkenes were isolated with complete chemoselectivity around the double bond and with partial to complete regioselectivity depending on the arene. Remarkably, the reaction involves readily available nonfunctionalized reagents and proceeds at ambient oxygen pressure.

EXPERIMENTAL SECTION

General Information. Reactions were monitored by thin-layer chromatography (TLC) analysis using silica gel (60 F254) plates. Compounds were visualized by UV irradiation and/or spraying with a solution of potassium permanganate, followed by charring at 150 °C. Flash column chromatography was performed on silica gel 60 (230−400 mesh, 0.040−0.063 mm). ^1H and ^{13}C NMR spectra were recorded on a spectrometer at 400 MHz (^{13}C, 100 MHz). Chemical shifts are given in

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parts per million from tetramethylsilane (TMS) as internal standard. The following abbreviations are used for the proton spectra multiplicities: s: singulet, d: doublet, t: triplet, q: quartet, qu: quintuplet, sex:sextet, m: multiplet. Coupling constants (J) are reported in hertz (Hz). HRMS were recorded using ESI-TOF techniques. Dry solvents were obtained from a VAC solvent purifier. All reagents were obtained from commercial suppliers unless otherwise stated.

Protecting alkenes **1** were prepared following a two-step sequence Baylis–Hillman reaction (giving products **6**)/Mitsunobu reaction as described below.

***tert*-Butyl 2-(Hydroxymethyl)acrylate (6b).** The title compound was prepared via Baylis–Hillman reaction according to a literature procedure.[16] Experimental data were in accordance with those reported in the previous literature.[16] ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.15 (m, 1H), 5.74 (m, 1H), 4.28 (m, 2H), 1.51 (s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 165.8, 140.9, 125.0, 81.5, 63.0, 28.2.

***tert*-Butyl 2-(Hydroxymethyl)acrylate (6c).** The title compound was prepared via Baylis–Hillman reaction according to a literature procedure.[16] Experimental data were in accordance with those reported in the previous literature.[17] ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.25 (q, J = 1.3 Hz, 1H), 5.82 (q, J = 1.4 Hz, 1H), 4.33 (m, 2H), 4.20 (t, J = 6.6 Hz, 2H), 1.67 (qu, J = 7.4 Hz, 2H), 1.40 (sex, J = 7.4 Hz, 2H), 0.95 (t, J = 7.4 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 166.5, 139.6, 125.7, 64.9, 62.8, 30.7, 19.2, 13.8.

Methyl 2-(Hydroxymethyl)acrylate (6d). The title compound was prepared via Baylis–Hillman reaction according to a literature procedure.[16] Experimental data were in accordance with those reported in the previous literature.[16] ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.23 (q, J = 0.9 Hz, 1H), 5.83 (q, J = 1.3 Hz, 1H), 4.36 (m, 2H), 3.80 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 166.8, 139.4, 125.9, 62.4, 52.0.

3-(Hydroxymethyl)but-3-en-2-one (6e). The title compound was prepared via a Baylis–Hillman reaction according to a literature procedure.[18] Experimental data were in accordance with those reported in the previous literature.[18] ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.11 (s, 1H), 6.03 (t, J = 1.4 Hz, 1H), 4.29 (q, J = 0.8 Hz, 2H), 2.35 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 200.5, 147.3, 126.2, 62.3, 26.0.

Methyl 2-(Hydroxy(phenyl)methyl)acrylate (6g). The title compound was prepared via Baylis–Hillman reaction according to a literature procedure.[19] Experimental data were in accordance with those reported in the previous literature.[19] ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.39–7.28 (m, 5H), 6.34 (q, J = 0.8 Hz, 1H), 5.83 (t, J = 1.2 Hz, 1H), 5.57 (s, 1H), 3.73 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 166.9, 142.1, 141.4, 128.6, 128.0, 126.7, 126.3, 73.4, 52.1.

Methyl 2-((4-Chlorophenyl)(hydroxy)methyl)acrylate (6h). The title compound was prepared via Baylis–Hillman reaction according to a literature procedure.[19] Experimental data were in accordance with those reported in the previous literature.[19] ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.30 (m, 4H), 6.33 (t, J = 0.8 Hz, 1H), 5.83 (t, J = 1.2 Hz, 1H), 5.51 (m, 1H), 3.70 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 166.7, 141.7, 139.9, 133.6, 128.6, 128.1, 126.4, 72.7, 52.1.

Ethyl 2-((1,3-Dioxoisoindolin-2-yl)methyl)acrylate (1a). Compound **1a** was prepared via a Mitsunobu reaction according to a literature procedure.[20] Experimental data were in accordance with those reported in the previous literature.[21] ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.88 (dd, J = 5.5, 3.1 Hz, 2H), 7.74 (dd, J = 5.6, 3.1 Hz, 2H), 6.33 (t, J = 1.4 Hz, 1H), 5.57 (t, J = 3.3 Hz, 1H), 4.57 (t, J = 3.1 Hz, 2H), 4.25 (q, J = 7.1 Hz, 2H), 1.31 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.8, 165.4, 134.7, 134.2, 132.1, 125.9, 123.5, 61.2, 38.4, 14.2.

***tert*-Butyl 2-((1,3-Dioxoisoindolin-2-yl)methyl)acrylate (1b).** Compound **1b** was prepared via a Mitsunobu reaction according to a literature procedure.[20] Experimental data were in accordance with those reported in the previous literature.[20] ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.88 (dd, J = 5.6, 3.1 Hz, 2H), 7.74 (dd, J = 5.5, 3.0 Hz, 2H), 6.21 (td, J = 1.4, 0.5 Hz, 1H), 5.44 (t, J = 1.7, 0.5 Hz, 1H), 4.52 (t, J = 1.6 Hz, 2H), 1.50 (s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.9, 164.6, 136.1, 134.2, 132.1, 124.6, 123.6, 81.6, 38.5, 28.2.

Butyl 2-((1,3-Dioxoisoindolin-2-yl)methyl)acrylate (1c). Compound **1c** was prepared via a Mitsunobu reaction according to a literature procedure.[20] ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.87 (dd, J = 5.6, 3.1 Hz, 2H), 7.74 (dd, J = 5.5, 3.0 Hz, 2H), 6.31 (td, J = 1.4, 0.4 Hz, 1H), 5.56 (t, J = 1.7, 0.4 Hz, 1H), 4.56 (t, J = 1.5 Hz, 2H), 4.18 (t, J = 6.7 Hz, 2H), 1.69–1.62 (m, 2H), 1.44–1.34 (m, 2H), 0.93 (t, J = 7.4 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.8, 165.5, 134.8, 134.3, 132.1, 125.9, 123.6, 65.1, 38.4, 30.7, 19.3, 13.8.

Methyl 2-(Acetoxymethyl)acrylate (1d). Compound **1d** was prepared according to a literature procedure.[22] ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.34 (q, J = 1.3 Hz, 1H), 5.83 (q, J = 1.3 Hz, 1H), 4.79 (t, J = 1.5 Hz, 2H), 3.77 (s, 3H), 2.08 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 170.4, 165.7, 135.3, 127.6, 62.5, 52.1, 20.9.

2-(2-Methylene-3-oxobutyl)isoindoline-1,3-dione (1e). Compound **1e** was prepared via a Mitsunobu reaction according to a literature procedure.[20] Experimental data were in accordance with those reported in the previous literature. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.87 (dd, J = 5.6, 3.1 Hz, 2H), 7.74 (dd, J = 5.5, 3.1 Hz, 2H), 6.13 (m, 1H), 5.70 (m, 1H), 4.54 (t, J = 1.5 Hz, 2H), 2.37 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.2, 168.0, 142.6, 134.4, 134.3, 123.7, 123.6, 37.7, 26.0.

Methyl 2-((2,3-Dioxoindolin-1-yl)methyl)acrylate (1f). To a solution of (hydroxymethyl)acrylate **6d** (600 mg, 5.17 mmol, 1 equiv) in diethyl ether (25 mL) was added dropwise phosphorus tribromide (535 μL, 5.68 mmol, 1.1 equiv) at 0 °C under argon. After 1 h at 25 °C, $NaHCO_3$ was added and the reaction mixture was extracted with diethyl ether (3 × 30 mL). The combined organic layers were washed with brine (50 mL) and dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting allylic bromide (270 mg, 1.51 mmol, equiv) was dissolved in acetonitrile (15 mL) in the presence of indoline-2,3-dione (260 mg, 1.81 mol, 1.2 equiv) and K_2CO_3 (250 mg, 1.81 mmol, 1.2 equiv). The resulting solution was stirred for 20 h at 25 °C. H_2O was then added, and the mixture was extracted with ethyl acetate (3 × 30 mL). The organic phase was washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The desired product **1f** was purified by flash chromatography (petroleum ether/ethyl acetate = 6:4 to 5:5) and isolated as an orange solid in 26% yield over two steps (327 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.58 (ddd, J = 7.5, 1.3, 0.6 Hz, 1H), 7.54 (dd, J = 7.8, 1.4 Hz, 1H), 7.11 (td, J = 7.5, 0.7 Hz, 1H), 6.89 (d, J = 7.9 Hz, 1H), 6.35 (t, J = 1.3 Hz, 1H), 5.73 (t, J = 1.5 Hz, 1H), 4.58 (s, 2H), 3.79 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 182.9, 165.9, 158.3, 150.5, 138.6, 133.1, 127.5, 125.5, 124.1, 117.7, 111.1, 52.4, 40.7. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{13}H_{11}NNaO_4$ 268.0586, found 268.0589.

(*E*)-Methyl 2-((1,3-Dioxoisoindolin-2-yl)methyl)-3-phenyl Acrylate (1g). Compound **1g** was prepared via a Mitsunobu reaction according to a literature procedure.[20] Experimental data were in accordance with those reported in the previous literature.[21] Experimental data were in accordance with those reported in the previous literature. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.95 (s, 1H), 7.78 (dd, J = 5.5, 3.1 Hz, 2H), 7.67 (dd, J = 5.5, 3.0 Hz, 2H), 7.46 (d, J = 7.7 Hz, 2H), 7.35 (t, J = 7.5 Hz, 2H), 7.27 (t, J = 7.5 Hz, 1H), 4.75 (s, 2H), 3.75 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.0, 167.1, 143.4, 134.8, 133.9, 132.1, 129.1, 128.8, 128.6, 126.5, 123.5, 52.1, 35.9.

(*E*)-Methyl 3-(4-Chlorophenyl)-2-((1,3-dioxoisoindolin-2-yl)-methyl)acrylate (1h). Compound **1h** was prepared via a Mitsunobu reaction according to a literature procedure.[20] Experimental data were in accordance with those reported in the previous literature.[21] ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.90 (s, 1H) 7.81 (dd, J = 5.6, 3.1 Hz, 2H), 7.71 (dd, J = 5.5, 3.0 Hz, 2H), 7.45 (d, J = 8.1 Hz, 2H), 7.35 (d, J = 8.0 Hz, 2H), 4.74 (d, J = 1.1 Hz, 2H), 3.78 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.0, 166.9, 142.0, 134.1, 133.2, 132.0, 130.4, 128.9, 127.1, 123.7, 123.3, 52.4, 35.8.

General Procedure for the Synthesis of Functionalized Olefins 3, 4, or 5. $Pd(OAc)_2$ (5 mol %), acridine (5 mol %), *p*-benzoquinone (10 mol %), iron phtalocyanine (2.5 mol %), olefin **1** (1 equiv), arene **2** (15 equiv), and AcOH:dioxane (1:1, 1.0 mL) were charged in a Schlenk tube. The resulting mixture was degassed three times under reduced pressure before introducing oxygen gas with a balloon. After vigorous stirring at 100 °C for 24 h, the reaction mixture was cooled to room temperature, diluted with AcOEt, filtered through Celite, rinsed with AcOEt, and concentrated under vacuum. Products were purified by flash chromatography with hexane/ethyl acetate to yield the desired functionalized olefins **3**, **4**, or **5**.

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Ethyl 3,3-Bis(3,4-dimethoxyphenyl)-2-((1,3-dioxoisoindolin-2-yl)methyl)acrylate (4aa). Prepared following the general procedure. Compound **4aa** was obtained as a red solid in 62% yield (66 mg) after flash chromatography (SiO_2, petroleum ether/ethyl acetate, 7:3 to 5:5). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.79 (dd, J = 5.6, 3.0 Hz, 2H), 7.67 (dd, J = 5.6, 3.0 Hz, 2H), 7.04 (d, J = 1.8 Hz, 1H), 6.87−6.80 (m, 2H), 6.73 (d, J = 0.9 Hz, 2H), 6.67 (s, 1H), 4.68 (s, 2H), 3.88 (q, J = 7.2 Hz, 2H), 3.85 (s, 6H), 3.84 (s, 3H), 3.75 (s, 3H), 0.85 (t, J = 7.1 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.2, 167.9, 149.1, 149.0, 148.9, 148.7, 148.4, 134.6, 133.9, 132.5, 132.1, 125.5, 123.2, 122.4, 121.7, 112.8, 112.1, 110.9, 110.5, 60.8, 56.1, 55.9, 55.9, 55.9, 39.4, 13.7. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{30}H_{29}NNaO_8$ 554.1785, found 554.1782 (0.6 ppm).

(*E*)-Ethyl 3-(3,4-Dimethoxyphenyl)-2-((1,3-dioxoisoindolin-2-yl)methyl)acrylate (3aa). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.88 (s, 1H), 7.77 (dd, J = 5.6, 3.1 Hz, 2H), 7.66 (dd, J = 5.5, 3.2 Hz, 2H), 7.14 (d, J = 1.9 Hz, 1H), 7.06 (ddd, J = 8.3, 2.0, 0.7 Hz, 1H), 7.14 (d, J = 8.4 Hz, 1H), 4.79 (d, J = 1.1 Hz, 2H), 4.18 (q, J = 7.1 Hz, 2H), 3.88 (s, 3H), 3.84 (s, 3H), 1.23 (t, J = 7.0 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.0, 166.9, 149.6, 148.9, 143.0, 133.9, 132.1, 127.5, 125.2, 123.2, 122.7, 112.4, 111.0, 61.1, 56.0, 55.9, 36.0, 14.2. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{22}H_{21}NNaO_6$ 418.1261, found 418.1241 (4.8 ppm).

***tert*-Butyl 3,3-Bis(3,4-dimethoxyphenyl)-2-((1,3-dioxoisoindolin-2-yl)methyl)acrylate (4ba).** Prepared following the general procedure. Compound **4ba** was obtained as a red solid in 53% yield (59 mg) after flash chromatography (SiO_2, petroleum ether/ethyl acetate, 7:3 to 6:4). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.82 (dd, J = 5.5, 3.0 Hz, 2H), 7.70 (dd, J = 5.5, 3.1 Hz, 2H), 7.11 (d, J = 1.9 Hz, 1H), 6.89 (dd, J = 8.2, 2.0 Hz, 1H), 6.84−6.75 (m, 3H), 6.70 (d, J = 1.8 Hz, 1H), 4.68 (s, 2H), 3.89 (s, 3H), 3.87 (s, 3H), 3.86 (s, 3H), 3.79 (s, 3H), 1.09 (s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.9, 167.8, 148.8, 148.6, 148.6, 148.3, 147.0, 134.8, 133.9, 132.6, 132.1, 127.3, 123.1, 122.2, 121.7, 112.6, 112.2, 101.8, 110.4, 81.1, 56.0, 55.9, 55.8, 55.8, 39.3, 27.4. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{32}H_{33}NNaO_8$ 582.2098, found 582.2122 (−4.0 ppm).

Butyl 3,3-Bis(3,4-dimethoxyphenyl)-2-((1,3-dioxoisoindolin-2-yl)methyl)acrylate (4ca). Prepared following the general procedure, except that $Pd(OAc)_2$ (7.5 mol %) and acridine (7.5 mol %) were used. Compound **4ca** was obtained as a red solid in 60% yield (67 mg) after flash chromatography (SiO_2, petroleum ether/ethyl acetate, 7:3 to 5:5). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.80 (dd, J = 5.6, 3.1 Hz, 2H), 7.68 (dd, J = 5.5, 3.0 Hz, 2H), 7.03 (d, J = 1.8 Hz, 1H), 6.86 (dd, J = 8.2, 1.9 Hz, 1H), 6.81 (d, J = 8.3 Hz, 1H), 6.74 (m, 2H), 6.67 (s, 1H), 4.68 (s, 2H), 3.86 (s, 3H), 3.86 (s, 3H), 3.85 (s, 3H), 3.81 (t, J = 6.6 Hz, 2H), 3.76 (s, 3H), 1.19 (m, 2H), 0.96 (m, 2H), 0.67 (t, J = 7.3 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.5, 167.9, 149.1, 149.0, 148.9, 148.7, 148.5, 134.7, 134.0, 132.5, 132.2, 125.5, 123.3, 122.5, 121.8, 112.8, 112.1, 110.9, 110.5, 64.9, 56.1, 55.9, 55.9, 55.9, 39.5, 30.3, 18.9, 13.6. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{32}H_{33}NNaO_8$ 582.2098, found 582.2093 (0.8 ppm).

Methyl 2-(Acetoxymethyl)-3,3-bis(3,4-dimethoxyphenyl)-acrylate (4da). Prepared following the general procedure, except that $Pd(OAc)_2$ (7.5 mol %) and acridine (7.5 mol %) at 90 °C were used. Compound **4da** was obtained as a red solid in 27% yield (23 mg) after flash chromatography (SiO_2, petroleum ether/ethyl acetate, 6:4 to 4:6). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.83−6.71 (m, 5H), 6.63 (d, J = 2.0 Hz, 1H), 4.85 (s, 2H), 3.89 (s, 3H), 3.88 (s, 3H), 3.79 (s, 3H), 3.77 (s, 3H), 3.54 (s, 3H), 2.09 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 170.7, 170.3, 153.4, 150.0, 150.0, 148.6, 148.6, 134.2, 132.3, 125.0, 123.0, 122.1, 113.1, 112.3, 110.8, 110.5, 60.0, 56.0, 56.0, 56.0, 55.9, 52.0, 21.1. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{23}H_{26}NaO_8$ 453.1520, found 453.1524 (−0.9 ppm).

2-(2-(Bis(3,4-dimethoxyphenyl)methylene)-3-oxobutyl)-isoindoline-1,3-dione (4ea). Prepared following the general procedure, except that $Pd(OAc)_2$ (7.5 mol %) and acridine (7.5 mol %) at 90 °C were used. Compound **4ea** was obtained as a brown solid in 41% yield (41 mg) after flash chromatography (SiO_2, petroleum ether/ethyl acetate, 5:5 to 4:6). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.77 (dd, J = 5.5, 3.1 Hz, 2H), 7.67 (dd, J = 5.5, 2.9 Hz, 2H), 7.01 (d, J = 2.0 Hz, 1H), 6.84 (dd, J = 8.2, 2.0 Hz, 1H), 6.78 (m, 2H), 6.73 (dd, J = 8.2, 2.0 Hz, 1H), 6.60 (d, J = 2.0 Hz, 1H), 4.66 (s, 2H), 3.88 (s, 3H), 3.85 (s, 3H), 3.80 (s, 3H), 3.76 (s, 3H), 1.77 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 205.3, 168.2, 150.1, 149.1, 149.0, 148.9, 148.8, 134.4, 134.1, 134.0, 132.9, 132.1, 123.5, 123.3, 122.7, 112.9, 112.8, 111.0, 110.8, 56.1, 56.1, 56.0, 56.0, 40.4, 30.6. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{29}H_{27}NNaO_7$ 524.1680, found 524.1682 (−0.5 ppm).

Methyl 3,3-Bis(3,4-dimethoxyphenyl)-2-((2,3-dioxoindolin-1-yl)methyl)acrylate (4fa). Prepared following the general procedure, except that $Pd(OAc)_2$ (7.5 mol %) and acridine (7.5 mol %) were used. Compound **4fa** was obtained as a red solid in 55% yield (57 mg) after flash chromatography (SiO_2, petroleum ether/ethyl acetate, 6:4 to 4:6). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.53−7.49 (m, 2H), 7.06 (td, J = 7.5, 0.8 Hz, 1H), 6.92 (m, 1H), 6.80 (d, J = 8.2 Hz, 1H), 6.73 (d, J = 8.4 Hz, 1H), 6.70−6.76 (m, 3H), 6.55 (d, J = 2.0 Hz, 1H), 4.74 (s, 2H), 3.88 (s, 3H), 3.85 (s, 3H), 3.75 (s, 3H), 3.73 (s, 3H), 3.44 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 183.0, 170.2, 157.9, 150.8, 150.8, 149.6, 149.5, 148.9, 148.6, 137.9. 134.2, 131.7, 125.1, 123.6, 123.1, 122.2, 121.7, 117.9, 112.3, 112.0, 111.3, 111.2, 110.5, 56.1, 56.1, 55.9, 55.9, 52.3, 41.2. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{29}H_{27}NNaO_8$ 540.1629, found 540.1637 (−1.5 ppm).

Ethyl 3,3-Bis(3,4-diethoxyphenyl)-2-((1,3-dioxoisoindolin-2-yl)methyl)acrylate (4ab). Prepared following the general procedure. Compound **4ab** was obtained as a yellow solid in 42% yield (49 mg) after flash chromatography (SiO_2, petroleum ether/ethyl acetate, 7:3 to 5:5). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.80 (dd, J = 5.5, 3.1 Hz, 2H), 7.67 (dd, J = 5.4, 3.1 Hz, 2H), 6.96 (d, J = 1.7 Hz, 1H), 6.83 (m, 2H), 6.71 (m, 2H), 6.65 (d, J = 1.8 Hz, 1H), 4.67 (s, 2H), 4.10−4.01 (m, 6H), 3.94 (q, J = 7.0 Hz, 2H), 3.85 (q, J = 7.1 Hz, 2H), 1.45−1.34 (m, 12H), 0.83 (t, J = 7.1 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.4, 168.0, 149.5, 148.8, 148.7, 148.3, 148.1, 134.8, 133.9, 132.6, 132.2, 125.0, 123.3, 122.6, 121.9, 114.9, 114.3, 112.8, 112.5, 64.6, 64.6, 64.5, 64.5, 60.8, 39.5, 14.9, 14.9, 14.9, 14.8, 13.7. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{34}H_{37}NNaO_8$ 610.2411, found 610.2438 (−4.4 ppm).

Ethyl 3,3-Bis(3,4-dimethylphenyl)-2-((1,3-dioxoisoindolin-2-yl)methyl)acrylate (4ac). Prepared following the general procedure, except that $Pd(OAc)_2$ (7.5 mol %) and acridine (7.5 mol %) were used. Compound **4ac** was obtained as a yellow solid in 56% yield (52 mg) after flash chromatography (SiO_2, petroleum ether/ethyl acetate, 6:4). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.80 (dd, J = 5.5, 3.0 Hz, 2H), 7.66 (dd, J = 5.5, 3.0 Hz, 2H), 7.07 (m, 3H), 6.99 (d, J = 7.8 Hz, 1H), 6.96 (s, 1H), 6.88 (dd, J = 7.7, 1.9 Hz, 1H), 4.64 (s, 2H), 3.87 (q, J = 7.1 Hz, 2H), 2.21 (s, 6H), 2.20 (s, 3H), 2.17 (s, 3H), 0.81 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.1, 167.9, 150.6, 139.6, 137.6, 136.6, 136.5, 136.4, 136.0, 133.9, 132.3, 130.5, 129.8, 129.6, 129.3, 126.9, 126.2, 125.3, 123.2, 60.7, 39.1, 19.8, 19.8, 19.7, 19.6, 13.5. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{30}H_{29}NNaO_4$ 490.1989, found 490.1994 (−1.0 ppm).

(*E*)-Ethyl 3-(2,5-Dimethoxyphenyl)-2-((1,3-dioxoisoindolin-2-yl)methyl)acrylate (3ad). Prepared following the general procedure. Compound **3ad** was obtained as a brown solid in 83% yield (66 mg) after flash chromatography (SiO_2, petroleum ether/ethyl acetate, 7:3 to 6:4). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.95 (s, 1H), 7.75 (dd, J = 5.5, 3.0 Hz, 2H), 7.65 (dd, J = 5.5, 3.2 Hz, 2H), 7.15 (m, 1H), 6.76 (m, 2H), 4.69 (d, J = 1.2 Hz, 2H), 4.17 (q, J = 7.1 Hz, 2H), 3.78 (s, 3H), 3.74 (s, 3H), 1.22 (t, J = 7.1 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.9, 166.5, 153.3, 151.6, 139.5, 133.8, 132.2, 127.3, 124.5, 123.2, 115.4, 115.3, 111.9, 61.1, 56.2, 55.9, 36.1, 14.2. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{22}H_{21}NNaO_6$ 418.1261, found 418.1254 (1.7 ppm).

(*E*)-Ethyl 3-(3,5-Dimethoxyphenyl)-2-((1,3-dioxoisoindolin-2-yl)methyl)acrylate (3ae-*β*). Prepared following the general procedure. Compounds **3ae-*α*** and **3ae-*β*** were obtained and separated as brown solids in 82% yield (66 mg, α:β = 63:37) after flash chromatography (SiO_2, petroleum ether/ethyl acetate, 7:3 to 6:4). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.87 (s, 1H), 7.76 (dd, J = 5.7, 3.0 Hz, 2H), 7.66 (dd, J = 5.4, 3.0 Hz, 2H), 6.59 (dd, J = 2.3, 0.7 Hz, 2H), 6.28 (d, J = 2.2 Hz, 1H), 4.74 (d, J = 1.3 Hz, 2H), 4.19 (q, J = 7.1 Hz, 2H), 3.75 (s, 6H), 1.23 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.9, 166.5, 160.8, 142.8, 136.7, 134.4, 133.9, 132.1, 127.3, 123.7, 123.1, 106.6, 100.8, 62.2, 55.5, 55.5, 36.0, 14.2. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{22}H_{21}NNaO_6$ 418.1261, found 418.1256 (1.1 ppm).

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(*E*)-Ethyl 3-(2,4-Dimethoxyphenyl)-2-((1,3-dioxoisoindolin-2-yl)methyl)acrylate (3ae-*α*). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.98 (s, 1H), 7.77 (dd, J = 5.6, 3.1 Hz, 2H), 7.65 (dd, J = 5.5, 2.9 Hz, 2H), 7.48 (dd, J = 8.4, 0.6 Hz, 1H), 6.46 (dd, J = 8.4, 2.4 Hz, 1H), 6.42 (d, J = 2.5 Hz, 1H), 4.70 (d, J = 1.1 Hz, 2H), (q, J = 7.1 Hz, 2H), 3.82 (s, 3H), 3.78 (s, 3H), 1.20 (t, J = 7.1 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.0, 166.9, 161.8, 158.9, 139.4, 133.8, 132.2, 131.1, 125.2, 123.1, 116.7, 104.5, 98.5, 60.9, 55.6, 55.5, 36.3, 14.2. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{22}H_{21}NNaO_6$ 418.1261, found 418.1281 (−4.7 ppm).

(*E*)-Methyl 3-(3,5-Dimethoxyphenyl)-2-((1,3-dioxoisoindolin-2-yl)methyl)-3-phenyl Acrylate (5ge). Prepared following the general procedure. Compound **5ge** was obtained as an orange solid in 16% yield (15 mg) after flash chromatography (SiO_2, petroleum ether/ethyl acetate/toluene, 5:3:2). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.80 (dd, J = 5.6, 3.1 Hz, 2H), 7.68 (dd, J = 5.5, 3.0 Hz, 2H), 7.25 (m, 3H), 7.18 (m, 2H), 6.52 (d, J = 2.3 Hz, 2H), 6.34 (t, J = 2.3 Hz, 1H), 4.66 (s, 2H), 3.74 (s, 6H), 3.39 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.1, 167.8, 160.8, 149.8, 141.5, 141.2, 134.4, 134.0, 132.1, 128.3, 128.1, 123.7, 123.3, 107.2, 100.3, 55.5, 51.9, 39.2. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{27}H_{23}NNaO_6$ 480.1418, found 480.1430 (−2.6 ppm).

(*E*)-Methyl 3-(Benzo[*d*][1,3]dioxol-4-yl)-2-((1,3-dioxoisoindolin-2-yl)methyl)-3-phenyl Acrylate (5gf-*α*) and (*E*)-Methyl 3-(3,4-Dimethoxyphenyl)-2-((1,3-dioxoisoindolin-2-yl)methyl)-3-phenyl Acrylate (5gf-*β*). Prepared following the general procedure. Compounds **5gf-*α*** and **5gf-*β*** were obtained as an inseparable mixture of isomers as a red solid in 59% yield (52 mg, α:β = 18:82) after flash chromatography (SiO_2, petroleum ether/ethyl acetate, 75:25 to 6:4). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.82 (m, 2.44H), 7.69 (m, 2.44H), 7.26 (m, 3.66H), 7.14 (m, 2.44H), 6.86 (dd, J = 7.8, 2.0 Hz, 1H), 6.79 (m, 2H), 6.74 (m, 0.44H), 6.65 (dd, J = 5.4, 3.7 Hz, 0.22H), 5.93 (s, 2H), 5.89 (s, 0.44H), 4.67 (s, 2H), 4.62 (s, 0.44H), 3.41 (s, 0.66H), 3.36 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.2, 169.2, 167.9, 167.8, 150.2, 147.8, 147.7, 147.6, 141.7, 140.5, 134.0, 133.9, 133.5, 132.2, 132.1, 129.2, 128.6, 128.4, 128.2, 128.2, 128.1, 128.1, 127.8, 123.9, 123.4, 123.4, 123.3, 122.6, 121.9, 121.2, 110.0, 109.8, 108.5, 108.3, 101.3, 101.2, 52.0, 51.8, 39.2, 38.7. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{26}H_{19}NNaO_6$ 464.1105, found 464.1102 (0.5 ppm).

(*E*)-Methyl 2-((1,3-Dioxoisoindolin-2-yl)methyl)-3-(3-methoxyphenyl)-3-phenyl Acrylate (5gg-*m*) and (*E*)-Methyl 2-((1,3-Dioxoisoindolin-2-yl)methyl)-3-(4-methoxyphenyl)-3-phenyl Acrylate (5gg-*p*). Prepared following the general procedure, except that $Pd(OAc)_2$ (7.5 mol %) and acridine (7.5 mol %) were used. Compounds **5gg-*m*** and **5gg-*p*** were obtained as an inseparable mixture of isomers as a yellow solid in 51% yield (44 mg, o:m:p = 0:46:54) after flash chromatography (SiO_2, petroleum ether/ethyl acetate, 75:25). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.82 (m, 3.70H), 7.68 (m, 3.70H), 7.28−7.13 (m, 12.45H), 6.98 (dd, J = 2.6, 1.5 Hz, 0.85H), 6.90 (m, 2.85H), 6.81 (ddd, J = 8.3, 2.6, 1.0 Hz, 0.85H), 4.67 (s, 2H), 4.64 (s, 1.7H), 3.79 (s, 3H), 3.78 (s, 2.55H), 3.39 (s, 2.55H), 3.36 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.4, 169.1, 168.0, 167.8, 159.7, 159.6, 150.6, 150.0, 142.1, 141.4, 141.0, 134.0, 134.0, 132.2, 132.2, 132.2, 131.0, 129.6, 129.1, 128.7, 128.4, 128.1, 128.1, 128.1, 128.1, 126.4, 125.4, 123.3, 121.6, 114.6, 114.0, 113.9, 55.4, 55.3, 51.9, 51.8, 39.3, 39.2. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{26}H_{21}NNaO_5$ 450.1312, found 450.1331 (−4.9 ppm).

(*E*)-Methyl 2-((1,3-Dioxoisoindolin-2-yl)methyl)-3-phenyl-3-(*m*-tolyl)acrylate and (*E*)-Methyl 2-((1,3-Dioxoisoindolin-2-yl)methyl)-3-phenyl-3-(*p*-tolyl)acrylate (5gh). Prepared following the general procedure, except that $Pd(OAc)_2$ (7.5 mol %) and acridine (7.5 mol %) were used. Compounds **5gh** were obtained as an inseparable mixture of isomers as a yellow solid in 57% yield (47 mg, ratio that could not be assigned and is thus given in no particular order = 0:40:60) after flash chromatography (SiO_2, petroleum ether/ethyl acetate/toluene, 5:3:2). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.80 (m, 3.4H), 7.68 (m, 3.4H), 7.27−7.07 (m, 14.3H), 4.65 (s, 1.4H), 4.63 (s, 2H), 3.39 (s, 3H), 3.38 (s, 2.1H), 2.33 (s, 2.1H), 2.30 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.3, 169.3, 167.9, 167.8, 150.7, 150.7, 141.9, 141.7, 139.7, 138.2, 138.2, 136.9, 134.0, 132.2, 132.2, 129.8, 129.4, 129.2, 129.1, 129.0, 128.6, 128.5, 128.4, 128.3, 128.1, 128.1, 126.3, 126.0, 125.7, 125.4, 123.3, 123.3, 51.9, 51.9, 39.2, 39.1, 21.5, 21.4. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{26}H_{21}NNaO_4$ 434.1363, found 434.1372 (−2.2 ppm).

(*E*)-Methyl 3-(3-Chlorophenyl)-2-((1,3-dioxoisoindolin-2-yl)methyl)-3-phenyl Acrylate and (*E*)-Methyl 3-(4-Chlorophenyl)-2-((1,3-dioxoisoindolin-2-yl)methyl)-3-phenyl Acrylate (5gi). Prepared following the general procedure, except that $Pd(OAc)_2$ (7.5 mol %) and acridine (7.5 mol %) were used. Compounds **5gi** were obtained as an inseparable mixture of isomers as a yellow solid in 36% yield (31 mg, ratio which could not be assigned and is thus given in no particular order = 0:63:37) after flash chromatography (SiO_2, petroleum ether/ethyl acetate/toluene, 5:3:2). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.81 (m, 3.16H), 7.69 (m, 3.16H), 7.35−7.11 (m, 14.22H), 4.61 (s, 2H), 4.60 (s, 1.16H), 3.39 (s, 1.74 H), 3.38 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.9, 168.8, 167.8, 167.8, 148.9, 148.5, 141.4, 141.2, 140.9, 138.1, 134.5, 134.4, 134.1, 134.1, 132.1, 132.1, 130.8, 129.9, 129.3, 128.8, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 127.5, 127.2, 126.7, 123.4, 123.4, 52.0, 52.0, 39.0, 39.0. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{25}H_{18}ClNNaO_4$ 454.0817, found 454.0827 (−2.2 ppm).

(*E*)-Methyl 3-(3,4-Dimethoxyphenyl)-2-((1,3-dioxoisoindolin-2-yl)methyl)-3-phenyl Acrylate (5ga). Prepared following the general procedure. Compound **5ga** was obtained as a red solid in 55% yield (50 mg) after flash chromatography (SiO_2, petroleum ether/ethyl acetate, 7:3). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.80 (dd, J = 5.5, 3.1 Hz, 2H), 7.68 (dd, J = 5.5, 3.0 Hz, 2H), 7.25 (m, 3H), 7.15 (m, 2H), 6.99 (d, J = 1.7 Hz, 1H), 6.82 (m, 2H), 4.69 (s, 2H), 3.84 (s, 3H), 3.84 (s, 3H), 3.37 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.3, 167.9, 150.2, 149.0, 148.7, 141.9, 134.0, 132.4, 132.1, 128.6, 128.1, 128.1, 125.8, 123.3, 122.2, 112.7, 110.9, 56.1, 55.9, 51.8, 39.4. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{27}H_{23}NNaO_6$ 480.1418, found 480.1433 (−3.3 ppm).

(*E*)-Methyl 2-((1,3-Dioxoisoindolin-2-yl)methyl)-3-(naphthalen-2-yl)-3-phenyl Acrylate (5gj). Prepared following the general procedure, except that $Pd(OAc)_2$ (7.5 mol %) and acridine (7.5 mol %) were used. Compound **5gj** was obtained as a brown solid in 83% yield (74 mg) after flash chromatography (SiO_2, petroleum ether/ethyl acetate/toluene, 7:3:2). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.91 (d, J = 1.1 Hz, 1H), 7.85−7.76 (m, 5H), 7.64 (dd, J = 5.5, 3.1 Hz, 2H), 7.48 (m, 2H), 7.39 (dd, J = 8.5, 1.7 Hz, 1H), 7.28−7.16 (m, 5H), 4.70 (s, 2H), 3.43 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.2, 167.9, 150.2, 141.6, 137.1, 134.0, 133.1, 133.0, 132.1, 128.7, 128.7, 128.4, 128.3, 128.2, 128.2, 127.8, 127.1, 126.6, 126.6, 126.5, 123.2, 51.9, 39.2. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{29}H_{21}NNaO_4$ 470.1363, found 470.1343 (4.2 ppm).

(*E*)-Methyl 3-(3,4-Dimethylphenyl)-2-((1,3-dioxoisoindolin-2-yl)methyl)-3-phenyl Acrylate (5gc). Prepared following the general procedure, except that $Pd(OAc)_2$ (7.5 mol %) and acridine (7.5 mol %) were used. Compound **5gc** was obtained as a yellow solid in 60% yield (51 mg) after flash chromatography (SiO_2, petroleum ether/ethyl acetate/toluene, 7:3:2). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.80 (dd, J = 5.5, 3.0 Hz, 2H), 7.68 (dd, J = 5.5, 3.2 Hz, 2H), 7.25 (m, 3H), 7.16 (m, 2H), 7.10−7.04 (m, 3H), 4.67 (s, 2H), 3.89 (s, 3H), 2.22 (s, 3H), 2.20 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.4, 167.8, 150.8, 142.0, 137.2, 136.8, 136.6, 133.9, 132.2, 130.4, 129.7, 128.5, 128.0, 127.9, 126.8, 125.5, 123.2, 51.7, 39.2, 19.8, 19.8. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{27}H_{23}NNaO_4$ 448.1519, found 448.1537 (−4.0 ppm).

(*Z*)-Methyl 3-(4-Chlorophenyl)-3-(3,4-dimethoxyphenyl)-2-((1,3-dioxoisoindolin-2-yl)methyl)acrylate (5ha). Prepared following the general procedure. Compound **5ha** was obtained as a red solid in 55% yield (54 mg) after flash chromatography (SiO_2, petroleum ether/ethyl acetate, 7:3). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.80 (dd, J = 5.4, 2.9 Hz, 2H), 7.70 (dd, J = 5.4, 3.0 Hz, 2H), 7.23 (d, J = 8.6 Hz, 2H), 7.09 (d, J = 8.7 Hz, 2H), 6.95 (m, 1H), 6.80 (m, 2H), 4.68 (s, 2H), 3.85 (s, 3H), 3.84 (s, 3H), 3.41 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.0, 167.9, 149.2, 149.0, 148.9, 140.4, 134.2, 134.1, 132.1, 132.0, 130.0, 128.4, 126.3, 123.3, 122.3, 112.6, 111.0, 56.1, 56.0, 52.0, 39.4. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{27}H_{22}ClNNaO_6$ 514.1028, found 514.1021 (1.3 ppm).

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra of alkenes **1f**, **3**, **4**, and **5**. This material is available free of charge via the Internet at http://pubs.acs.org.

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AUTHOR INFORMATION

Corresponding Authors

*E-mail: jeb@organ.su.se (J.-E.B.).
*E-mail: nicolas.gigant@u-psud.fr (N.G.).

Notes

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