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Article

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Sulfoximine Directed Ruthenium Catalyzed *Ortho*-C–H Alkenylation of (Hetero)Arenes: Synthesis of EP3 Receptor Antagonist Analog

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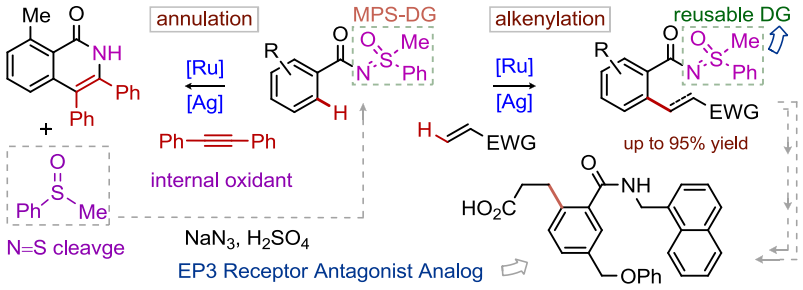
ABSTRACT



The reusable sulfoximine directing group assisted Ru(II)-catalyzed chemo and regioselective *ortho*-C–H alkenylation of arenes and heteroarenes with acrylates, and α,β-unsaturated ketones/vinyl sulfone is shown. The N-aroyl sulfoximine undergoes annulation with diphenylacetylene delivering isoquinolinones and methyl phenyl sulfoxide. The present protocol is successfully employed for the synthesis of EP3 receptor antagonist analog.

Introduction

The development of synthetically viable strategies for the creation of olefin-units in molecules is always desirable; as the hydrogenated acrylate derivative 3-(2-carbamoyl-phenyl)-propionic acid, a key structural component found in many biologically active and pharmaceutically important molecules (Figure 1).[1] The Mizoroki-Heck reaction of aryl electrophiles with alkenes and the Fujiwara-Moritani cross-dehydrogenative oxidative coupling of arenes with alkenes are reliable approaches, invariably employed for the formation of olefin moieties.[2]

The transition-metal-catalyzed, chelation assisted activation of arene C–H bonds is a straightforward method broadly useful for the functionalization of unactivated C–H bonds; one of the elegant manifestations of this strategy is expressed in the formation of chemo- and regioselective C–olefin bonds.[3,4] As these strategies do not require the pre-activated precursor, providing broad and ready access of substrate scope, their utility in the fabrication of complex molecules with step-efficiency is thus noteworthy.[5] A variety of modifiable and non-modifiable directing groups (DGs) have successfully been employed, accomplishing *o*-C–H alkenylation of arenes under the influence of Pd(II),[4] Rh(III)[6] and/or Ru(II)[7]-catalysts and oxidants. The use of inexpensive, air stable Ru(II)-catalysts under the coordination ability of reusable DGs for the *o*-C–H olefination of arene would promote widening the synthetic utility of this approach.[7] Dixneuf,[7a,c,n] Miura,[7f,o,s] Ackermann[7e,h,m,p] and Jaganmohan[7d,j,q], among others, have contributed significantly in the development of Ru-catalyzed modifiable/non-modifiable DG assisted *o*-C–H alkenylation of arenes.[7]

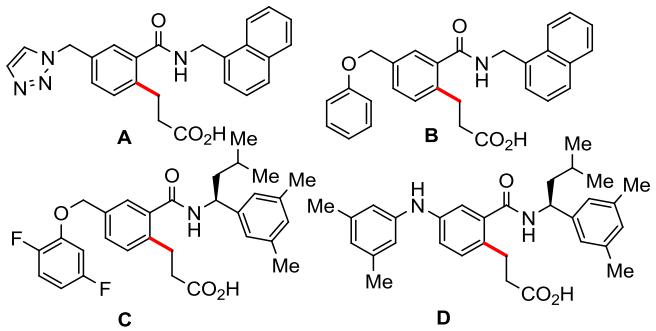
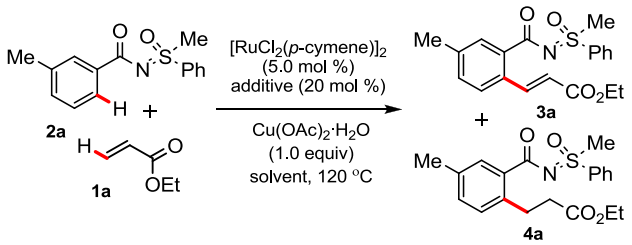


Figure 1. EP3 Receptor Antagonist Analogs

We have recently demonstrated the sp^2 C–H oxidation and amidation of arenes with the aid of the reusable S-methyl-S-phenylsulfoximine (MPS) DG.[8,9] To broaden the synthetic utility of reusable MPS-DG further, we envisioned performing alkenylation on unactivated arenes under the influence of robust Ru-catalysts; the results are detailed herewith. The application of the current method for the synthesis of an EP3 antagonist analog (**D**) is also shown.

Results and Discussion:

Table 1. Optimization of Reaction Conditions[a]



entry	additive (20 mol%)	solvent	yield (%)[b] **3a**	**4a**
1	-	$ClCH_2CH_2Cl$	<5	
2	$AgSbF_6$	$ClCH_2CH_2Cl$	90	<10
3	$NaPF_6$	$ClCH_2CH_2Cl$	74	20
4	KPF_6	$ClCH_2CH_2Cl$	37	-
5	$NaBF_4$	$ClCH_2CH_2Cl$	22	-
6	**$AgBF_4$**	**$ClCH_2CH_2Cl$**	**92 (84)**[c]	-
7	$AgBF_4$	$ClCH_2CH_2Cl$	54[d]	-
8	$AgBF_4$	CH_2Cl_2	42	14
9	$AgBF_4$	$CHCl_3$	85	-
10	$AgBF_4$	toluene	21	-
11	$AgSbF_6$	1,4-dioxane	43	25[d,e]

[a]Reaction conditions: **2a** (0.1 mmol), alkene (0.2 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5.0 mol %), $Cu(OAc)_2{\cdot}H_2O$ (1.0 equiv), solvent (0.5 mL), 24 h. [b]Crude ^1H NMR conversion based on of the ratio of starting material to product. [c]**2a** (0.5 mmol), $ClCH_2CH_2Cl$ (2.0 mL), isolated yield in parenthesis. [d]In the

absence of $Cu(OAc)_2 \cdot H_2O$. [e]AcOH (1.0 equiv) was used. The experiments in dichloromethane, chloroform, and toluene were run at 120 °C in a sealed tube.

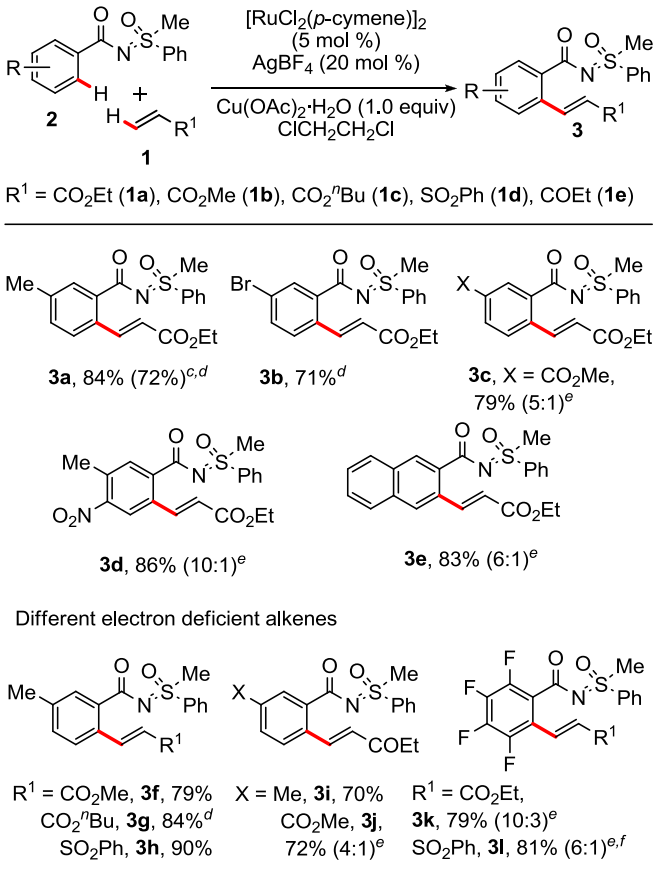
To begin with, the dehydrogenative alkenylation of *N*-(*m*-methylbenzoyl)-MPS (**2a)** with ethyl acrylate (**1a**) was investigated under the influence of Ru(II)-catalyst, silver salts, $Cu(OAc)_2 \cdot H_2O$, and solvents (Table 1). The reaction between **2a** and **1a** with 5.0 mol % $[RuCl_2(p\text{-cymene})]_2$ and $Cu(OAc)_2 \cdot H_2O$ (1.0 equiv) in 1,2-dichloroethane (DCE) at 120 °C produced a trace amount of *N*-[(*E*)-2-(3-ethoxy-3-oxoprop-1-en-1-yl)-5-methyl-benzoyl]-MP*S* (**3a**), regioselectively functionalizing the sterically less hindered *o*-C–H bond of **2a**. The yield of **3a** was enhanced to 90% when $AgSbF_6$ was employed; formation of a minor amount of hydroarylation product **4a** was also observed by ^{1}HNMR (entry 2). Screening of $NaPF_6$, KPF_6, and $NaBF_4$ salts in this reaction turned unsatisfactory (entries 3–5). The $AgBF_4$ was equally efficient, delivering **3a** in 92% yield (entry 6). To our delight, we observed the exclusive formation of *o*-C–H *E*-alkenylation products. The absence of $Cu(OAc)_2 \cdot H_2O$ led to lower yield of **3a** (entry 7). Upon careful scrutiny of various solvents, DCE was found best (entries 8–10). The reaction of **2a** with **1a** under the Miura conditions [$\{RuCl_2(p\text{-cymene})\}_2$ (5.0 mol %), $AgSbF_6$ (20 mol %), AcOH (1.0 equiv), 1,4-dioxane] led to the formation of **3a** in only 43% yield (entry 11). Thus, the condition shown in entry 6, Table 1 was realized optimum for the sulfoximine directed oxidative *o*-C–H alkenylation of arenes in **2a**. To our disappointment, **2a** did not undergo alkenylation with unactivated alkene (e.g., styrene) under the present reaction conditions.[10]

Reaction Scope:

The optimized condition was explored examining the scope and generality of *o*-C–H alkenylation of arenes **2** with activated olefins **1**. The results are summarized in scheme 1. The less hindered *o*-C–H bond in electron-rich and deficient *m*-substituted arenes selectively alkenylated, affording **3a–d** in 71–86% yield; the Br, ester, and $–NO_2$ groups did not affect the reaction outcome. The ester group did not assist the *o*-C–H alkenylation in **2c**,[7l-m] witnessing the effective directing group ability of the sulfoximine moiety. The catalytic condition is suitable for the gram scale synthesis of **3a**. The olefinated

product **3e** was exclusively obtained from β-naphthyl substrate **2e** in good yield. The alkenylation was effectively conducted between **2a** and other electron-deficient alkenes; methyl acrylate (**1b**), *n*-butyl acrylate (**1c**) and phenyl vinyl sulfone (**1d**) readily coupled with **2a**, producing the corresponding *o*-C–H alkenylation products **3f–h** in good to excellent yields. The oxidative alkenylation of *m*-substituted electron-rich and -poor substrates **2a** and **2c** with ethyl vinyl ketone (**1e**) led to **3i** and 3**j** in 70% and 72% yield, respectively. Even more electron deficient tetrafluoro substituted arene **2f** was compatible, furnishing **3k** and **3l** in 79% and 81% yield, respectively. In some cases, the formation of minor amount of hydroarylation product along with the desired alkenylation compound was observed in ^{1}H NMR; the ratio of hydroarylation and alkenylation products is shown in parenthesis.

Scheme 1. *o*-C–H Alkenylation of *meta*- and Fluoro Substituted *N*-Aroyl Derivatives[a,b]

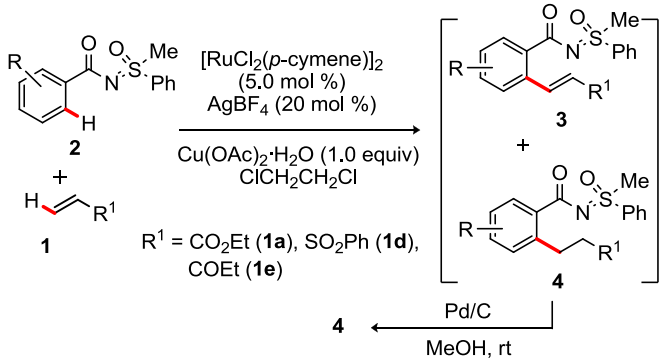


[a]Reaction conditions: **2** (0.5 mmol), alkene (1.0 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5.0 mol %), $AgBF_4$ (20 mol %), $Cu(OAc)_2{\cdot}H_2O$ (1.0 equiv), $ClCH_2CH_2Cl$ (2.0 mL), 120 °C for 24 h. [b]Isolated yields. [c]**2a** (1.0 g,

3.7 mmol), $AgSbF_6$ (20 mol %) used. [d]Minor amount of hydroarylation product (<5%) observed by ^1H NMR; the corresponding alkenylation product **3** is ~95% pure. [e]Ratio of alkenylation and hydroarylation product observed by ^1H NMR; in case of **3l**, ratio is detected by ^{19}F NMR. [f]**2f** (0.15 mmol) was employed.

We next investigated the coupling of *o*-substituted *N*-aroyl-MPS with **1** (Table 2). The reaction between *N*-(*o*-methylbenzoyl)-MPS (**2g**) and **1a** surprisingly produced a major amount of *o*-hydroarylation product **4b** over the desired alkenylation compound **3m** (by ^1H NMR), suggesting the occurrence of proto-demetalation over β-hydride elimination.[11] The inseparable hydroarylation and alkenylation products render the purification extremely difficult. To validate product isolation ease, the non-purified mixture of compounds was subjected to hydrogenation with Pd/C in methanol, converting the alkenylation product to the hydroarylation compound with the survival of MPS-DG.[12] Following these procedures, a wide variety of *o*,*o*′-disubstituted *N*-aroyl MPS products **4b–j** were synthesized in overall good yields (Table 2). The *o*-alkenylation followed by hydrogenation of *o*-Me/Ph/OPh substituted compounds **2g–i** with **1a** furnished **4b–d** in 74–87% yield. The fluoro-bearing product **4e** was isolated in 70% yield. The desired 2-alkyl-4,6-dimethyl derivative **4f** was obtained from **2k** in good yield. The α-naphthyl substrate **2l** reacted well, affording 73% of product **4g**. The alkenylation and hydrogenation sequence on **2h** with phenyl vinyl sulfone delivered **4h** in 82% yield. The α,β-unsaturated ketones smoothly participated, and the desired products **4i** and **4j** were prepared in moderate yields.

Table 2. Alkylation of *o*-Substituted Arenes[a,b]



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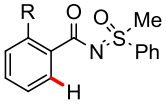
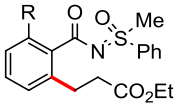
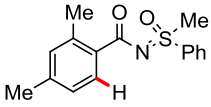
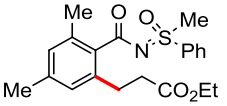
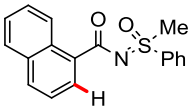
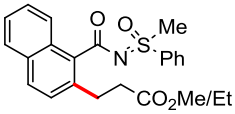
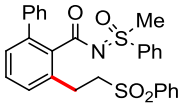
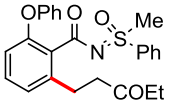
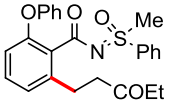
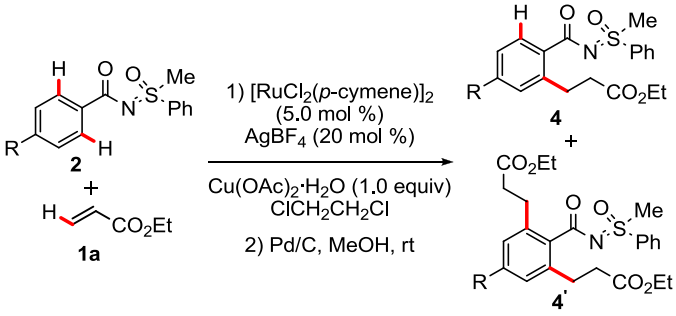
			
1	R = Me (**2g**)	1:2	**4b**, 80%
2	Ph (**2h**)	2:1	**4c**, 87%
3	OPh (**2i**)	2:1	**4d**, 74%
4	F (**2j**)	2:3	**4e**, 70%
			
5	**2k**	1:3	**4f**, 78%
			
6	**2l**	1:2	**4g**, 73% (14:3)[c]
7	**2h**	4:3	 **4h**, 82%
8	**2i**	2:1	 **4i**, 61%
9	**2j**	3:1	 **4j**, 64%

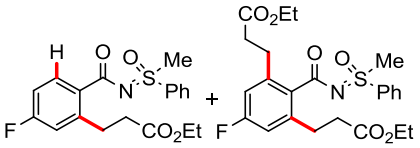
[a]Reaction conditions: **2** (0.5 mmol), alkene (1.0 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5.0 mol %), $AgBF_4$ (20 mol %), $Cu(OAc)_2{\cdot}H_2O$ (1.0 equiv), $ClCH_2CH_2Cl$ (2.0 mL), 120 °C for 24 h and Pd/C (50 mg, 20 wt%).[b]Isolated yields. [c]**2l** (0.32 mmol) was employed.

In contrast, the reaction of electron neutral **2m** or *p*-Me/F substituted *N*-aroylated sulfoximines **2n/2o** with **1a** showed a complex mixture (by ^{1}H NMR), displaying the possible formation of a non-separable mixture of *o*-C–H mono-, di-alkenylation, and their corresponding hydroarylation products; subsequent hydrogenation of the non-purified mixture of compounds exhibited the corresponding mono-(**4k–m**) and di-hydroarylation (**4'k–m**) products in overall good yields (Table 3). The formation of di-hydroarylation product enables accessing highly peripheral decorated benzoic acid derivatives.

Table 3. *o*-C–H Alkylation of Unsubstituted and *p*-Substituted Arene Derivatives[a,b]



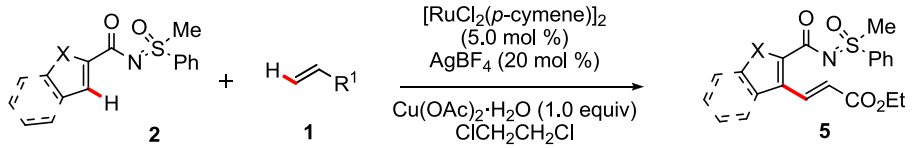
entry	2	4/4′
1	R = H, **2m**	**4k** 69% (1:1)[b] **4′k**
2	R = Me, **2n**	**4l** 71% (1:1)[b] **4′l**

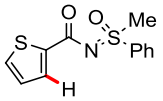
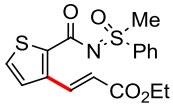
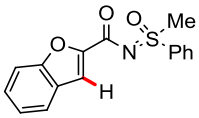
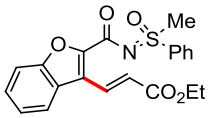
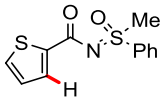
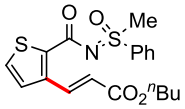
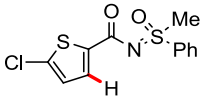
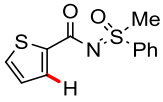
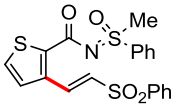
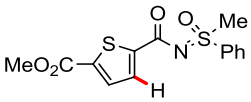
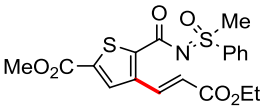
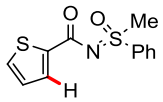
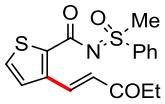
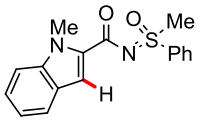
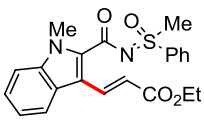
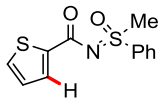
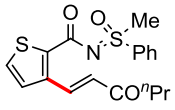
3	R = F, **2o**		**4m** 83% (9:4)[b] **4′m**

[a]Reaction conditions: **2** (0.5 mmol), **1a** (3.5 equiv), $[RuCl_2(p\text{-cymene})]_2$ (5.0 mol %), $AgBF_4$ (20 mol %), $Cu(OAc)_2 \cdot H_2O$ (1.0 equiv), $ClCH_2CH_2Cl$ (2.0 mL), 120 °C for 24 h and Pd/C (50 mg, 20 wt%). [b]Combined yield of isolated mono- and dialkylation products (the mono/di ratio is indicated in the parentheses).

The utility of the catalytic conditions to the introduction of an olefin moiety on heteroarenes is further examined (Table 4). The unsubstituted and 5-substituted thienyl derivatives **2p–s** smoothly underwent oxidative alkenylation, affording the desired products **5a–d** in excellent yields; the chloro and ester functional groups did not interfere with the reaction efficiency. However, the *N*-methyl indole derivative **2t** furnished a mixture of alkenylation **5e** and hydroarylation **5′e** at the electron rich C3 position in a 2:3 ratio; while, the reaction of benzofuran derivative **2u** with **1a** exclusively produced **5f**. Other activated alkenes **1c** and **1d** were effective coupling partners and the C–C coupled products **5g** and **5h** were isolated good to excellent yields. The reaction of **2p** with activated ketones (**1e** and **1f)** is no exception, providing **5i** and **5j** in 91% and 86% yield, respectively. The inseparable mixture of alkenylation and hydroarylation products in **5j** is observed 3:1 ratio.

Table 4. Alkenylation of Heteroarene Derivatives[a,b]

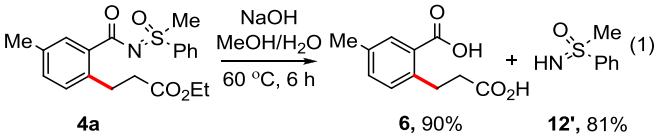


entry	2	5	entry	2	5
1	 **2p**	 **5a**, 88%	6	 **2u**	 **5f**, 88%
2	 **2q**	 **5b**, 90%	7	 **2p**	 **5g**, 82%
3	 **2r**	 **5c**, 85%	8	 **2p**	 **5h**, 95%
4	 **2s**	 **5d**, 84%	9	 **2p**	 **5i**, 91%
5	 **2t**	 **5e**, 60% (2:3)[c]	10	 **2p**	 **5j**, 86% (3:1)[c]

[a]Reaction conditions: **2** (0.5 mmol), alkene (1.0 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5.0 mol %), $AgBF_4$ (20 mol %), $Cu(OAc)_2 \cdot H_2O$ (1.0 equiv), $ClCH_2CH_2Cl$ (2.0 mL), 120 °C for 24 h. [b]Isolated yields. [c]Ratio of alkenylation and hydroarylation product observed by ^1H NMR.

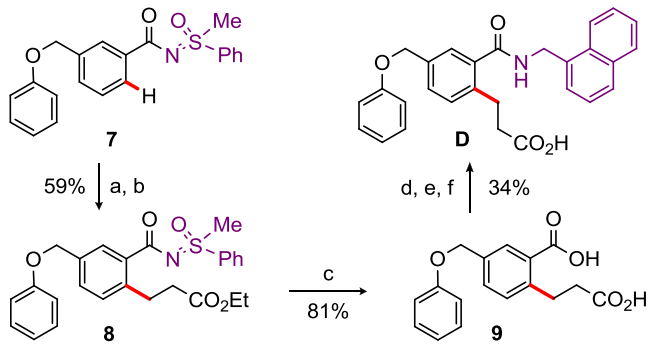
The practical utility of the present protocol is demonstrated with the ready cleavage amide-linkage and recovery of methyl phenyl sulfoximine. Gratifyingly, the base promoted (NaOH in

MeOH/H_2O solvent at 60 °C for 6 h) saponification of **4a** yielded **6** (90%) with recovery of 81% of methyl phenyl sulfoximine **12′**(eq 1).



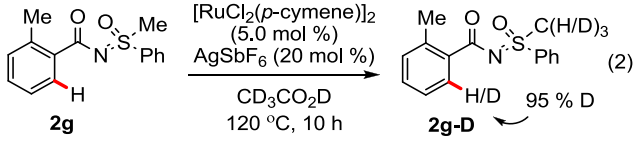
The current protocol has successfully been applied in the synthesis of EP3 antagonist analog 3-(2-(naphthalen-1-ylmethylcarbamoyl)-4-(phenoxymethyl)phenyl)propanoic acid (**D**) (Scheme 2).[1] The synthesis is begun by reacting **7** and **1a** under the optimized conditions shown in entry 6, Table 1, producing the *o*-C–H alkenylation product **8′** along with a minor amount hydroarylation compound **8** (4:1 ratio by ^{1}H NMR). The reduction of activated olefin with $NiCl_2 \cdot 6H_2O/NaBH_4$ in MeOH/THF gave the hydrogenated product **8** in 59% overall yield from **7**. Base mediated hydrolysis of **8** led to the dicarboxylic acid derivative **9** with the recovery of methyl phenyl sulfoximine. The selective esterification of aliphatic acid, EDC-mediated amide formation between naphthalen-1-ylmethanamine and benzoic acid moiety, and finally hydrolysis of ester group delivered the desired EP3 antagonist molecule **D** in 34% overall yield from **9**.

Scheme 2. Synthesis of EP3 Antagonist Analog



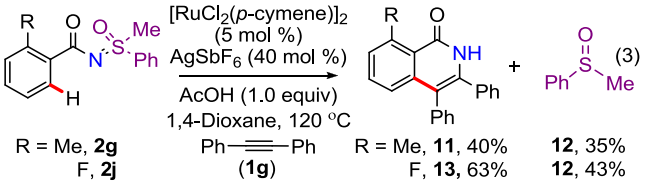
Reaction conditions: a) **7** (2.5 g, 6.8 mmol), **1a** (13.7 mmol), $[RuCl_2(p\text{-cymene})]_2$ (10 mol %), $AgSbF_6$ (40 mol %), $Cu(OAc)_2 \cdot H_2O$ (1.0 equiv), $ClCH_2CH_2Cl$ (10.0 mL), 120 °C for 24 h; 66%. b) $NiCl_2 \cdot 6H_2O$, $NaBH_4$, MeOH/THF, 0 ^oC to rt, overnight; 89%. c) NaOH, MeOH/H_2O, 60 °C, 4h. d) cat. H_2SO_4, MeOH (1.0 equiv), 20 min; 85%. e) EDC·HCl, HOBt, naphthalen-1-ylmethanamine, DMF, rt, 24 h; 64%. f) $LiOH \cdot H_2O$, MeOH/THF, 60 °C, 4h; 62%.

To understand the mechanistic insights, a deuterium labelling experiment was performed on **2g** (eq 2). Gratifyingly, 95% deuterium incorporation at the *ortho*-C–H in **2g** occurred,[13] when **2g** exposed to Ru(II)-catalyst, $AgSbF_6$ in CD_3COOD at 120 °C for 10 h. In addition, the acidic s-methyl protons underwent deuterium exchange. These results presumably suggest that the insertion of Ru to the *o*-C–H bond is reversible.



(2)

The hydroarylation outcome from *o*-substituted N-benzoylated sulfoximine and the activated olefin (Table 2) prompted us to examine the reaction between *N*-(*o*-methylbenzoyl)-MPS (**2g)** and internal unactivated alkyne, as this would result in the trisubstituted olefin. To our surprise, we noticed the formation of isoquinolinone **11** (40%) and 35% of methyl phenyl sulfoxide (**12**) from **2g** and diphenylacetylene (**1g**) under the Miura conditions (eq 3).[14,15,16] Furthermore, the annulation between **2j** and **1g** gave product **13** in 63% yield (eq 3). The compound **12** is useful for the synthesis of MPS-DG.



Conclusion: In summary, we report Ru(II)-catalyzed *o*-C–H alkenylation and hydroarylation of (hetero)arenes with activated olefins: acrylates, vinyl sulfones, and ketones with the aid of *reusable methyl phenyl sulfoximine directing group*. Isoquinolinone derivatives are synthesized from N-aroylated sulfoximines and diphenylacetylene. The isolation of MPS and the methyl phenyl sulfoxide make these strategies synthetically viable and useful. The utility of this transformation enables the synthesis of EP3 receptor antagonist analog.

Experimental Section

General Information:

All the reactions were performed in an oven-dried Schlenk flask. Commercial grade solvents were distilled prior to use. Column chromatography was performed using either 100-200 Mesh or 230-400 Mesh silica gel. Thin layer chromatography (TLC) was performed on silica gel GF254 plates. Visualization of spots on TLC plate was accomplished with UV light (254 nm) and staining over I_2 chamber.

Proton, carbon, and fluorine nuclear magnetic resonance spectra (^{1}H NMR, ^{13}C NMR and ^{19}F NMR) were recorded based on the resonating frequencies as follows: (^{1}H NMR, 400 MHz; ^{13}C NMR, 101 MHz; ^{19}F NMR, 376 MHz) and (^{1}H NMR, 500 MHz; ^{13}C NMR, 126 MHz; ^{19}F NMR, 470 MHz) having the solvent resonance as internal standard (^{1}H NMR, $CHCl_3$ at 7.26 ppm; ^{13}C NMR, $CDCl_3$ at 77.0 ppm). Few cases tetramethylsilane (TMS) at 0.00 ppm was used as

reference standard. Data for ^{1}H NMR are reported as follows: chemical shift (ppm), multiplicity (s = singlet; bs = broad singlet; d = doublet; bd = broad doublet, t = triplet; bt = broad triplet; q = quartet; m = multiplet), coupling constants, *J*, in (Hz), and integration. Data for ^{13}C NMR, ^{19}F NMR were reported in terms of chemical shift (ppm). IR spectra were reported in cm^{-1}. High resolution mass spectra were obtained in (ESI-TOF analyzer) equipment. Melting points were determined by electro-thermal heating and are uncorrected.

Materials: Unless otherwise noted, all the reagents and intermediates were obtained commercially and used without purification. Dichloromethane (DCM) and 1, 2-dichloroethane (DCE) were distilled over CaH_2. $[RuCl_2(p\text{-cymene})]_2$, $AgSbF_6$, $AgBF_4$, $AgPF_6$ and KPF_6 were purchased from Sigma Aldrich Ltd, and used as received. Analytical and spectral data of all the known compounds are exactly matching with the reported values.

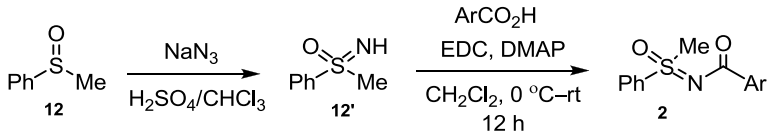
Following the known procedure, compounds **2a**, **2c, 2d, 2e, 2g, 2h, 2j, 2k, 2l, 2m**, **2n**, **2o**, and **2p** are prepared.[8a-b] Analytical and spectral data of these compounds are exactly matching with the reported values.

Experimental Procedures:

Preparation of *N*-Aroyl *S*-methyl-*S*-phenylsulfoximines:

Synthesis of methyl phenyl sulfoximine from sulfoxide is well established. [8a]

Scheme 3



General procedure (GP-1); EDC-coupling:[8a]

A solution of *N*'-(3-dimethylaminopropyl)-*N*-ethylcarbodimide, hydrochloride salt (EDC·HCl) (2.0 equiv), 4-*N*,*N*-dimethylaminopyridine (DMAP) (2.2 equiv) and benzoic acids (**1**; 1.1 equiv)

in CH_2Cl_2 (5.0 mL, for 1 mmol of sulfoximine) was stirred under an argon atmosphere. Sulfoximine (**12′**; 1.0 equiv) was introduced drop wise at 0 °C. The resulting reaction mixture was stirred for about 1 h at 0 °C, and warmed to ambient temperature and continued for overnight. Upon complete consumption of sulfoximine, the reaction mixture was acidified with hydrochloric acid (HCl, 1N). The organic layer was separated; the aqueous layer was extracted with CH_2Cl_2 (3 times).The combined extracts were washed with 10% aqueous $NaHCO_3$ and brine. The organic layer was dried over Na_2SO_4. Solvent was filtered and evaporated under reduced pressure. The crude residue was purified using column chromatography on silica gel using hexane/ ethyl acetate (3:2).

***N*-[3-Bromobenzoyl]-*S*-methyl-*S*-phenylsulfoximine (2b):** 0.76 g, 70% yield; colorless solid; m.p. = 99–100 ^{o}C; R_f = 0.34 (1:1 hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (s, 1H), 8.07 (d, J = 7.6, 1H), 8.03 (d, J = 7.6, 2H), 7.69 (bt, J = 7.2 Hz, 1H), 7.65–7.58 (m, 3H), 7.28 (t, J = 7.8 Hz, 1H), 3.46 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.6, 138.5, 137.5, 134.9, 133.9, 129.7, 129.6, 127.9 (2C), 127.0 (3C), 122.1, 44.3; IR (Neat) ν_{max} 3028, 2922, 1635, 1215 cm^{-1}; HRMS (ESI) for $C_{14}H_{12}BrNO_2S$ $(M+H)^+$: calcd. 337.985, found 337.9850.

***N*-[2,3,4,5-Tetrafluorobenzoyl]-*S*-methyl-*S*-phenylsulfoximine (2f):** 0.42 g, 40% yield, colorless crystalline solid; m.p. = 104–106 ^{o}C; R_f = 0.50 (3:2 hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 7.6 Hz, 2H), 7.72 (bt, J = 7.4 Hz, 1H), 7.68–7.60 (m, 3H), 3.48 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.9, 147.5 (dd, J = 260, 11 Hz), 146.1 (dd, J = 248, 11 Hz), 142.6 (dt, J = 261, 14 Hz), 141.0 (dt, J = 255, 14 Hz), 137.9, 134.2, 129.8 (2C), 127.1 (2C), 120.5, 112.9 (d, J = 20 Hz), 44.3; ^{19}F (376 MHz, $CDCl_3$) δ –135.90 (m), –139.01 (m),–149.81

(m), –154.61 (m); IR (KBr) ν_{max} 3030, 2936, 1649, 1632, 1468, 1216 cm^{-1}; HRMS (ESI) for $C_{14}H_9F_4NO_2S$ $(M+Na)^+$: calcd. 354.0188, found 354.0189.

***N*-[2-Phenoxybenzoyl]-*S*-methyl-*S*-phenylsulfoximine (2i):** 0.73 g, 65% yield; colorless crystalline solid; m.p. = 120–122 ^oC; R_f = 0.42 (3:2 hexane/EtOAc); ^1H NMR (400 MHz, $CDCl_3$)δ7.94 (d, J = 7.6 Hz, 1H), 7.78 (d, J = 7.6 Hz, 2H), 7.60 (t, J = 7.2 Hz, 1H), 7.50–7.40 (m, 3H), 7.29 (t, J = 7.6 Hz, 2H), 7.21 (t, J = 7.6 Hz, 1H), 7.07–7.00 (m, 2H), 6.96 (d, J = 8.0 Hz, 2H), 3.15 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ173.8, 158.7, 154.1, 138.3, 133.6, 132.4, 131.5, 130.2 (2C), 129.6 (2C), 129.4, 127.1 (2C), 124.2, 122.1, 121.8, 117.0 (2C), 43.9; IR (KBr) ν_{max} 3063, 2926, 1621, 1309, 1232 cm^{-1}; HRMS (ESI) for $C_{20}H_{17}NO_3S$ $(M+Na)^+$: calcd. 374.0827, found 374.0820.

***N*-[5-Methylthenoyl]-*S*-methyl-*S*-phenylsulfoximine (2q):** 0.65 g, 72% yield, colorless crystalline solid; m.p. = 129–131 ^oC; R_f = 0.30 (2:3hexane/EtOAc); ^1H NMR (400 MHz, $CDCl_3$)δ8.04 (d, J = 7.6 Hz, 2H), 7.68 (t, J = 7.4 Hz, 1H), 7.64–7.56 (m, 3H), 6.73 (d, J = 3.2 Hz, 1H), 3.44 (s, 3H), 2.50 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$)δ168.7, 146.9, 138.7, 138.4, 133.7, 132.4, 129.5 (2C), 127.0 (2C), 126.2, 44.3, 15.7; IR (KBr) ν_{max} 3030, 2926, 1610, 1282 cm^{-1}; HRMS (ESI) for $C_{13}H_{13}NO_2S_2$ $(M+Na)^+$: calcd. 302.0286, found 302.0282.

***N*-[5-Chlorothenoyl]-*S*-methyl-*S*-phenylsulfoximine (2r):** 0.80 g, 82% yield; colorless crystalline solid; m.p. = 120–121 ^oC; R_f = 0.35 (3:2 hexane/EtOAc); ^1H NMR (400 MHz, $CDCl_3$)δ8.03 (d, J = 7.6 Hz, 2H), 7.71 (bt, J = 7.4 Hz, 1H), 7.63 (bt, J = 7.6 Hz, 2H), 7.57 (d, J = 4.0 Hz, 1H), 6.90 (d, J = 3.6 Hz, 1H), 3.45 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$)δ167.7,

139.2, 138.5, 136.1, 134.0, 131.4, 129.7 (2C), 127.2, 127.1 (2C), 44.4; IR (KBr) ν_{max} 3024, 2931, 1610, 1435, 1221 cm^{-1}; HRMS (ESI) for $C_{12}H_{10}ClNO_2S_2$ $(M+Na)^+$: calcd. 321.9739, found 321.9740.

***N*-[5-Methoxycarbonylthenoyl]-*S*-methyl-*S*-phenylsulfoximine (2s):** 0.71g, 68% yield; colorless crystalline solid; m.p. = 152–154 ^oC; R_f = 0.32 (3:2 hexane/EtOAc); ^1H NMR (400 MHz, $CDCl_3$)δ 8.05 (d, J = 7.6 Hz, 2H), 7.75–7.68 (m, 3H), 7.64 (t, J = 7.6 Hz, 2H), 3.90 (s, 3H), 3.47 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$)δ 168.2, 162.5, 146.5, 138.3, 137.6, 134.1, 133.2, 131.6, 129.8 (2C), 127.2 (2C), 52.4, 44.4; IR (KBr) ν_{max} 3024, 2926, 1720, 1610, 1254 cm^{-1}; HRMS (ESI) for $C_{14}H_{13}NO_4S_2$ $(M+Na)^+$: calcd. 346.0184, found 346.0187.

***N*-[N-Methyl-2-indoloyl]-*S*-methyl-*S*-phenylsulfoximine (2t):** 0.73 g, 73% yield; colorless crystalline solid; m.p. = 153–155 ^oC; R_f = 0.38(3:2 hexane/EtOAc); ^1H NMR (400 MHz, $CDCl_3$)δ 8.08 (d, J = 7.2 Hz, 2H), 7.73–7.65 (m, 2H), 7.63 (t, J = 7.4 Hz, 2H), 7.45 (s, 1H), 7.39–7.28 (m, 2H), 7.13 (t, J = 7.2 Hz, 1H), 4.07 (s, 3H), 3.44 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$)δ 169.7, 139.8, 139.0, 133.8, 133.3, 129.7 (2C), 127.2 (2C), 125.9, 124.5, 122.4, 120.2, 110.3, 110.1, 44.8, 31.7; IR (KBr) ν_{max} 3008, 2920, 1616, 1468, 1260 cm^{-1}; HRMS (ESI) for $C_{17}H_{16}N_2O_2S$ $(M+Na)^+$: calcd. 335.0830, found 335.0829.

***N*-[2-benzofuronoyl]-*S*-methyl-*S*-phenylsulfoximine (2u):** 1.51 g, 79% yield; colorless crystalline solid; m.p. = 130–131 ^oC; R_f = 0.31 (3:2 hexane/EtOAc); ^1H NMR (400 MHz, $CDCl_3$)δ 8.08 (d, J = 7.6 Hz, 2H), 7.72–7.57 (m, 5H), 7.53 (s, 1H), 7.41 (t, J = 7.8 Hz, 1H), 7.31–7.25 (m, 1H), 3.52 (s, 3H);^{13}C NMR (101 MHz, $CDCl_3$)δ 166.0, 155.4, 150.7, 138.2,

133.9, 129.6 (2C), 127.3, 127.0 (2C), 126.8, 123.3, 122.5, 112.5, 112.2, 44.3; IR (KBr) ν_{max} 3024, 2920, 1643, 1616, 1572, 1216 cm^{-1}; HRMS (ESI) for $C_{16}H_{13}NO_3S$ $(M+H)^+$: calcd. 300.0694, found 300.0697.

Optimization for *ortho*-C–H Alkenylation:

The C–H alkenylation reaction was conducted in a 50 mL Schlenk tube with high pressure valve and side arm. The tube was charged with *N*-(*m*-methylbenzoyl)-MPS (**2a**, 27.3 mg, 0.1 mmol), ethyl acrylate (**1a**, 21 μL, 0.2 mmol), $[RuCl_2(p\text{-cymene})]_2$ (3.1 mg, 5.0 mol %), $Cu(OAc)_2 \cdot H_2O$ (20 mg, 0.1 mmol). Subsequently, the reaction tube was taken to the glove box and the additives were introduced. The corresponding solvent (0.5 mL) was added to the mixture and the resulting mixture was stirred at 120 ^oC for 24 h. The reaction mixture was cooled to ambient temperature, filtered through a plug of Celite and then washed with CH_2Cl_2 (3 × 5 mL). The solvents were evaporated under reduced pressure and the crude material was analyzed based on ^1H NMR spectroscopy.

General Procedure for *ortho*-C–H Alkenylation Reaction (GP-2):

The C–H alkenylation reactions were carried out in a 50 mL Schlenk tube with high pressure valve and side arm. The tube was charged with *N*-aroylated sulfoximine (**2a–2u**, 0.5 mmol), alkene (**1a–f**, 1.0 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.0 mg, 5.0 mol %), and $Cu(OAc)_2 \cdot H_2O$ (100 mg, 1.0 mmol). Subsequently, the reaction tube was taken to the glove box and $AgSbF_6/AgBF_4$ (20 mol %) was introduced. The solvent 1,2–dichloroethane (DCE, 2.0 mL) was added to the mixture and the resulting mixture was stirred at 120 ^oC for 24 h. The reaction mixture was cooled to ambient temperature, filtered through a small plug of Celite and then washed with

CH_2Cl_2 (3 × 10 mL). The solvents were evaporated under reduced pressure and the crude material was purified using column chromatography on silica gel (30–40% *n*-hexane/EtOAc as an eluent) to give the desired product.

***N*-[(*E*)-2-(3-Ethoxy-3-oxoprop-1-en-1-yl)-5-methylbenzoyl]-*S*-methyl-*S*-phenylsulfoximine (3a):** 156 mg, 84% yield; colorless crystalline solid; m.p. = 95–97 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$)δ 8.56 (d, *J* = 15.2 Hz, 1H), 8.09 (d, *J* = 8.4 Hz, 2H), 7.83 (s, 1H), 7.69 (bt, *J* = 7.4 Hz, 1H), 7.62 (bt, *J* = 7.8 Hz, 2H), 7.47 (d, *J* = 7.6 Hz, 1H), 7.27 (bd, *J* = 7.6 Hz, 1H), 6.26 (d, *J* = 15.6 Hz, 1H), 4.24 (q, *J* = 6.9 Hz, 2H), 3.50 (s, 3H), 2.39 (s, 3H), 1.30 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$)δ175.4, 167.1, 144.9, 139.6, 138.4, 136.2, 133.9, 132.3, 132.0, 131.0, 129.7 (2C), 127.5, 127.2 (2C), 118.7, 60.3, 44.4, 21.2, 14.3; IR (KBr) ν_{max} 2980, 2931, 1719, 1615, 1308, 1210 cm^{-1}; HRMS (ESI) for $C_{20}H_{21}NO_4S$ $(M+H)^+$: calcd. 372.1269, found 372.1269.

The same reaction was carried out in bulk scale using **2a** (1.0 g, 3.7 mmol), ethyl acrylate (**1a**, 5.55 mmol), $[RuCl_2(p\text{-cymene})]_2$ (113 mg, 5.0 mol %), $Cu(OAc)_2{\cdot}H_2O$ (736 mg, 3.7 mmol), $AgSbF_6$ (254 mg, 0.74 mmol) in 1,2-DCE (10.0 mL) at 120 ^{o}C for 24 h. The product **3a** (0.98 g) was obtained in 72% yield.

***N*-[(*E*)-2-(3-Ethoxy-3-oxoprop-1-en-1-yl)-5-bromobenzoyl]-*S*-methyl-*S*-phenylsulfoximine (3b):** 155 mg, 71% yield; colorless crystalline solid; m.p. = 110–112 °C; ^{1}H NMR (400 MHz, $CDCl_3$)δ8.48 (d, *J* = 15.6 Hz, 1H), 8.19 (d, *J* = 2.0 Hz, 1H), 8.06 (d, *J* = 7.2 Hz, 2H), 7.70 (t, *J* = 7.4 Hz, 1H), 7.63 (t, *J* = 7.4 Hz, 2H), 7.58 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.40 (d, *J* = 8.4 Hz, 1H), 6.25 (d, *J* = 16.0 Hz, 1H), 4.23 (q, *J* = 7.2 Hz, 2H), 3.48 (s, 3H), 1.29 (t, *J* = 7.2 Hz, 3H); ^{13}C

NMR (101 MHz, $CDCl_3$) δ 173.5, 166.6, 143.8, 138.1, 137.5, 134.2, 134.1, 134.0, 133.5, 129.7 (2C), 129.1, 127.1 (2C), 123.3, 120.1, 60.4, 44.3, 14.2; IR (KBr) ν_{max} 3018, 2980, 2936, 1719, 1621, 1100 cm^{-1}; HRMS (ESI) for $C_{19}H_{18}BrNO_4S$ $(M+H)^+$: calcd. 436.0218, found 436.0223.

***N*-[3-Methoxycarbonyl-(*E*)-6-(3-ethoxy-3-oxoprop-1-en-1-yl)-benzoyl]-*S*-methyl-*S*-phenyl sulfoximine (3c):** 164 mg, 79% yield; colorless crystalline solid; m.p. = 126–128 ^oC; ^1H NMR (400 MHz, $CDCl_3$) δ 8.70 (s, 1H), 8.54 (d, J = 16.0 Hz, 1H), 8.13–8.05 (m, 3H), 7.70 (t, J = 7.2 Hz, 1H), 7.67–7.57 (m, 3H), 6.32 (d, J = 16.0 Hz, 1H), 4.24 (q, J = 7.1 Hz, 2H), 3.93 (s, 3H), 3.49 (s, 3H), 1.30 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.1, 166.4, 165.9, 143.8, 139.5, 138.0, 136.1, 133.9, 131.8 (2C), 130.5, 129.6 (2C), 127.8, 127.0 (2C), 121.3, 60.4, 52.2, 44.2, 14.1; IR (KBr) ν_{max} 3019, 2926, 1704, 1632, 1200 cm^{-1}; HRMS (ESI) for $C_{21}H_{21}NO_6S$ $(M+Na)^+$: calcd. 438.0988, found 438.1006.

***N*-[(*E*)-2-(3-Ethoxy-3-oxoprop-1-en-1-yl)-5-methyl-4-nitrobenzoyl]-*S*-methyl-*S*-phenyl sulfoximine (3d):** 180 mg, 86% yield; yellow crystalline solid; m.p. = 145–147 ^oC; ^1H NMR (400 MHz, $CDCl_3$) δ 8.45 (d, J = 16.0 Hz, 1H), 8.12 (s, 1H), 8.06 (d, J = 7.6 Hz, 2H), 7.96 (s, 1H), 7.71 (t, J = 7.4 Hz, 1H), 7.64 (t, J = 7.6 Hz, 2H), 6.34 (d, J = 16.0 Hz, 1H), 4.24 (q, J = 7.1 Hz, 2H), 3.50 (s, 3H), 2.61 (s, 3H),1.30 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 166.3, 149.9, 142.2, 139.6, 137.8, 134.9, 134.1 (2C), 133.9, 129.8 (2C), 127.0 (2C), 123.5, 121.1, 60.6, 44.2, 20.1, 14.2; IR (KBr) ν_{max} 2997, 2931, 1715, 1638, 1523, 1221, 1189 cm^{-1}; HRMS (ESI) for $C_{20}H_{20}N_2O_6S$ $(M+H)^+$: calcd. 417.1120, found 417.1121.

***N*-[(*E*)-2-(3-Ethoxy-3-oxoprop-1-en-1-yl)-*β*-naptholoyl]-*S*-methyl-*S*-phenyl sulfoximine (3e):** 170 mg, 83% yield; viscous liquid; ^{1}H NMR (400 MHz, $CDCl_3$)δ 8.64 (bd, J = 15.6 Hz, 1H), 8.61 (bs,1H), 8.09 (d, J = 7.6 Hz, 2H), 7.97 (s, 1H), 7.88 (d, J = 7.6 Hz, 1H), 7.82 (d, J = 7.6 Hz, 1H), 7.66 (bt, J = 7.2 Hz, 1H), 7.59 (t, J = 7.2 Hz, 2H), 7.57–7.46 (m, 2H), 6.36 (d, J = 15.6 Hz, 1H), 4.24 (q, J = 7.1 Hz, 2H), 3.50 (s, 3H), 1.30 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$)δ 174.9, 166.9, 145.7, 138.4, 134.1, 133.8, 133.2, 132.8, 132.5, 131.6, 129.6 (2C), 128.7, 128.0, 127.9, 127.5, 127.1 (3C), 119.0, 60.3, 44.3, 14.2; IR (Neat) ν_{max} 3063, 2980, 1709, 1638, 1282, 1221 cm^{-1}; HRMS (ESI) for $C_{23}H_{21}NO_4S$ $(M+Na)^+$: calcd. 430.1089, found 430.1090.

***N*-[(*E*)-2-(3-Methoxy-3-oxoprop-1-en-1-yl)-5-methylbenzoyl]-*S*-methyl-*S*-phenylsulfoximine (3f):** 141 mg, 79% yield; colorless crystalline solid; m.p. = 123–125 °C; ^{1}H NMR (400 MHz, $CDCl_3$)δ 8.55 (d, J = 16.0 Hz, 1H), 8.07 (d, J = 7.6 Hz, 2H), 7.84 (s, 1H), 7.68 (t, J = 7.4 Hz, 1H), 7.61 (t, J = 7.6 Hz, 2H), 7.45 (d, J = 8.0 Hz, 1H), 7.26 (d, J = 8.0 Hz, 1H), 6.25 (d, J = 16.0 Hz, 1H), 3.75 (s, 3H), 3.47 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$)δ 175.3, 167.4, 145.1, 139.6, 138.3, 136.0, 133.8, 132.2, 131.9, 131.0, 129.6 (2C), 127.4, 127.1 (2C), 118.2, 51.5, 44.3, 21.2; IR (Neat) ν_{max} 3013, 2947, 1704, 1627, 1210 cm^{-1}; HRMS (ESI) for $C_{19}H_{19}NO_4S$ $(M+Na)^+$: calcd. 380.0933, found 380.0937.

***N*-[(*E*)-2-(3-*n*-Butoxy-3-oxoprop-1-en-1-yl)-5-methylbenzoyl]-*S*-methyl-*S*-phenylsulfoximine (3g):** 167 mg, 84% yield; viscous liquid; ^{1}H NMR (400 MHz, $CDCl_3$)δ 8.55 (d, J = 15.6 Hz, 1H), 8.09 (d, J = 8.0 Hz, 2H), 7.82 (s, 1H), 7.69 (t, J = 7.4 Hz, 1H), 7.62 (t, J = 7.6 Hz, 2H),

7.47 (d, *J* = 8.0 Hz, 1H), 7.25 (bd, *J* = 5.2 Hz, 1H), 6.27 (d, *J* = 16.0 Hz, 1H), 4.17 (t, *J* = 6.6 Hz, 2H), 3.49 (s, 3H), 2.38 (s, 3H), 1.70–1.59 (m, 2H), 1.47–1.36 (m, 2H), 0.94 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.5, 167.3, 145.0, 139.7, 138.5, 136.3, 133.9, 132.3, 132.0, 131.1, 129.7 (2C), 127.5, 127.2 (2C), 118.7, 64.3, 44.4, 30.8, 21.3, 19.2, 13.8; IR (Neat) ν_{max} 2964, 2926, 1704, 1627, 1315, 1210 cm^{-1}; HRMS (ESI) for $C_{22}H_{25}NO_4S$ $(M+H)^+$: calcd. 400.1582, found 400.1583.

_N_-[(_E_)-2-(2-(Phenylsulfonyl)vinyl)-5-methylbenzoyl]-_S_-methyl-_S_-phenylsulfoximine (3h):

198 mg, 90% yield; colorless crystalline solid; m.p. = 157–159 ^oC; ^{1}H NMR (400 MHz, $CDCl_3$)δ8.71 (d, *J* = 15.2 Hz, 1H), 8.09 (d, *J* = 7.6 Hz, 2H), 7.91 (d, *J* = 7.6 Hz, 2H), 7.82 (s, 1H), 7.70–7.53 (m, 4H), 7.49 (t, *J* = 7.6 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 1H), 7.22 (d, *J* = 7.6 Hz, 1H), 6.67 (d, *J* = 15.2 Hz, 1H), 3.50 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$)δ174.6, 143.4, 140.7, 138.1, 136.4, 133.8, 133.1, 131.9, 131.2, 129.8, 129.7 (2C), 129.1(2C), 127.5, 127.4 (2C), 127.0 (2C), 126.9, 44.2, 21.1 (one 13C–value is merged with other peak); IR (KBr) ν_{max} 3052, 2920, 1621, 1221 cm^{-1}; HRMS (ESI) for $C_{23}H_{21}NO_4S_2$ $(M+H)^+$: calcd. 440.0990, found 440.0990.

_N_-[(_E_)-2-(3-Oxopent-1-enyl)-5-methylbenzoyl]-_S_-methyl-_S_-phenylsulfoximine (3i):

124 mg, 70% yield; colorless viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$)δ8.45 (d, *J* = 17.2 Hz, 1H), 8.08 (d, *J* = 8.4 Hz, 2H), 7.89 (s, 1H), 7.71 (t, *J* = 7.8 Hz, 1H), 7.63 (bt, *J* = 7.6 Hz, 2H), 7.49 (d, *J* = 8.4 Hz , 1H), 7.32–7.26 (m, 1H), 6.53 (d, *J* = 16.4 Hz , 1H), 3.49 (s, 3H), 2.72–2.61 (m, 2H), 2.41 (s, 3H), 1.11 (t, *J* = 7.2 Hz , 3H); ^{13}C NMR (101 MHz, $CDCl_3$)δ201.7, 175.5, 142.8, 139.7, 138.4, 136.0, 133.9, 132.7, 132.1, 131.2, 129.7 (2C), 127.4, 127.1 (3C), 44.4, 33.2,

21.2, 8.2; IR (KBr) ν_{max} 3013, 2920, 1665, 1621, 1276, 1210 cm^{-1}; HRMS (ESI) for $C_{20}H_{21}NO_3S$ $(M+H)^+$: calcd. 356.1320, found 356.1322.

***N*-[3-Methoxycarbonyl-(*E*)-6-(3-oxopent-1-enyl)-5-methylbenzoyl]-*S*-methyl-*S*-phenyl sulfoximine (3j):** Following GP-2, reaction between **2c** and **1e** gave the inseparable alkenylation **3j** and hydroarylation products (4:1 by ^1H NMR; 144 mg, 72% yield) as colorless crystalline solid. ^1H NMR (400 MHz, $CDCl_3$)δ 8.76 (s, 1H), 8.45 (d, J = 16.4 Hz, 1H), 8.15–8.03 (m, 3H), 7.72 (bt, J = 7.6 Hz, 1H), 7.64 (bt, J = 8.4 Hz, 3H), 6.57 (d, J = 16.4 Hz, 1H), 3.95 (s, 3H), 3.49 (s, 3H), 2.70–2.65 (m, 2H), 1.12 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$)δ 201.3, 174.4, 166.1, 141.7, 140.1, 138.2, 136.1, 134.0, 132.0, 130.6, 129.8 (2C), 129.4, 127.8, 127.1 (3C), 52.3, 44.4, 28.8, 8.0; IR (Neat) ν_{max} 2926, 1720, 1671, 1627, 1315 cm^{-1}; HRMS (ESI) for $C_{21}H_{21}NO_5S$ $(M+H)^+$: calcd. 400.1218, found 400.1223.

***N*-[(*E*)-2-(3-Ethoxy-3-oxoprop-1-en-1-yl)-tetrafluorobenzoyl]-*S*-methyl-*S*-phenylsulfoximine (3k):** Following GP-2, reaction between **2f** and **1a** gave the inseparable alkenylation **3k** and hydroarylation products (3.3:1 by ^1H NMR; 170 mg, 79% yield) as pale yellow solid. ^1H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J = 8.4 Hz, 2H), 7.77–7.62 (m, 4H), 6.60 (d, J = 16.0 Hz, 1H), 4.25 (q, J = 7.1 Hz, 2H), 3.49 (s, 3H), 1.32 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$)δ 172.1, 169.7, 166.2, 137.4, 134.4, 133.5, 130.0 (2C), 127.2 (2C), 60.9, 44.2, 14.1 (*The large number of less-intense 13C values arise from ^{19}F and C coupling are omitted due to lack of clarity*); ^{19}F (470 MHz, $CDCl_3$)δ −137.46, −141.04, −152.26, −154.52; IR (KBr) ν_{max} 3013, 2926, 1715, 1632, 1512, 1473, 1232 cm^{-1}; HRMS (ESI) for $C_{19}H_{15}F_4NO_4S$ $(M+Na)^+$: calcd. 452.0556, found 452.0556.

***N*-[(*E*)-2-(2-(Phenylsulfonyl)vinyl)-tetrafluorobenzoyl]-*S*-methyl-*S*-phenylsulfoximine (3l):**

Following GP-2, reaction between **2f** and **1d** gave the inseparable alkenylation **3l** and hydroarylation products (6:1 by ^{19}F NMR; 60 mg, 81% yield) as yellow viscous liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (bd, J = 7.2 Hz, 2H), 7.89 (bd, J = 7.6 Hz, 2H), 7.80 (bd, J = 15.6 Hz, 1H), 7.76–7.60 (m, 4H), 7.55 (bt, J = 7.4 Hz, 2H), 7.10 (d, J = 16.0 Hz, 1H), 3.54 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.0, 139.5, 137.2, 134.5, 133.8, 131.5, 130.0 (2C), 129.5 (2C), 127.8 (2C), 127.1 (3C), 44.0 (*The large number of less-intense 13C values arise from ^{19}F and C coupling are omitted due to lack of clarity*); ^{19}F (470 MHz, $CDCl_3$) δ –136.13, –139.85, –149.83, –153.74; IR (Neat) ν_{max} 3079, 2926, 1627, 1506, 1369, 1238 cm^{-1}; HRMS (ESI) for $C_{22}H_{15}F_4NO_4S_2$ $(M+H)^+$: calcd. 498.0457, found 498.0457.

General Procedure for *ortho*-C–H Alkenylation and Hydrogenation on *ortho* and *para*-Substituted *N*-Aroyl-MPS Derivatives (GP-3):

Following GP-2, the C–H alkenylation on *ortho*-substituted-*N*-aroyl-MPS derivatives gave non-separable mixture of alkenylation and hydroarylation products. To make the purification ease, the non-purified mixture of compounds were subjected to hydrogenation.

Accordingly, a solution of non-purified mixture of compounds in methanol was subjected to hydrogenation in the presence of Pd/C (50 mg, 20 wt%) under hydrogen balloon for overnight at room temperature. The solvent was evaporated under reduced pressure and the crude material was purified using column chromatography on silica gel (30–40% *n*-hexane/EtOAc as eluent) to give the desired hydroarylation product.

***N*-[2-(3-Ethoxy-3-oxopropyl)-6-methylbenzoyl]-*S*-methyl-*S*-phenylsulfoximine(4b):** 150 mg, 80% yield; colorless crystalline solid; m.p. = 95–97 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$)δ 8.05 (d, *J* = 7.2 Hz, 2H), 7.66 (bt, *J* = 7.2 Hz, 1H), 7.59 (t, *J* = 7.4 Hz, 2H), 7.13 (t, *J* = 7.6 Hz, 1H), 7.01 (d, *J* = 7.6 Hz, 2H), 4.10 (q, *J* = 7.1 Hz, 2H), 3.47 (s, 3H), 3.06–2.96 (m, 2H), 2.70–2.60 (m, 2H), 2.35 (s, 3H), 1.21 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$)δ 178.7, 173.1, 139.0, 138.4, 135.9, 134.0, 133.8, 129.6 (2C), 128.24, 128.18, 127.0 (2C), 126.3, 60.3, 43.9, 36.1, 29.0, 19.4, 14.1; IR (KBr) ν_{max} 3030, 2926, 1731, 1632, 1293,1216 cm^{-1}; HRMS (ESI) for $C_{20}H_{23}NO_4S$ $(M+H)^+$: calcd. 374.1426, found 374.1426.

***N*-[2-(3-Ethoxy-3-oxopropyl)-6-phenylbenzoyl]-*S*-methyl-*S*-phenylsulfoximine (4c):** 190 mg, 87% yield; colorless viscous liquid; ^{1}H NMR (400 MHz, $CDCl_3$)δ 7.60–7.50 (m, 3H), 7.45–7.28 (m, 8H), 7.28–7.22 (m, 1H), 7.21 (d, *J* = 7.2 Hz, 1H), 4.11 (q, *J* = 7.1 Hz, 2H), 3.21 (s, 3H), 3.20–3.01 (m, 2H), 2.78–2.69 (m, 2H), 1.22 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$)δ 178.2, 173.0, 141.9, 138.8, 138.4, 138.0, 137.4, 133.6, 129.2 (2C), 129.1(2C), 128.6, 128.4, 128.0 (2C), 127.8, 127.0, 126.9 (2C), 60.2, 42.8, 35.8, 28.8, 14.1; IR (Neat) ν_{max} 3063, 2980, 1726, 1627, 1221 cm^{-1}; HRMS (ESI) for $C_{25}H_{25}NO_4S$ $(M+H)^+$: calcd. 436.1582, found 436.1581.

***N*-[2-(3-Ethoxy-3-oxopropyl)-6-phenoxybenzoyl]-*S*-methyl-*S*-phenylsulfoximine (4d):** 166 mg, 74% yield; colorless crystalline solid; m.p. = 146–148 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$)δ 7.86 (d, *J* = 8.0 Hz, 2H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.8 Hz, 2H), 7.31 (t, *J* = 7.8 Hz, 2H), 7.21 (t, *J* = 7.8 Hz, 1H), 7.10–7.00 (m, 4H), 6.82 (d, *J* = 8.4 Hz, 1H), 4.11 (q, *J* = 7.1 Hz, 2H), 3.23 (s, 3H), 3.09 (t, *J* = 7.8 Hz, 2H), 2.71 (t, *J* = 8.0 Hz, 2H), 1.22 (t, *J* = 7.0 Hz,

3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.6, 172.9, 157.9, 152.7, 139.4, 138.0, 133.7, 132.1, 129.6 (2C), 129.5, 129.4 (2C), 127.2 (2C), 124.9, 122.7, 117.9 (2C), 117.8, 60.2, 43.9, 35.7, 28.5, 14.1; IR (KBr) ν_{max} 3024, 2926, 1736, 1638, 1216 cm^{-1}; HRMS (ESI) for $C_{25}H_{25}NO_5S$ $(M+H)^+$: calcd. 452.1531, found 452.1532.

***N*-[2-(3-Ethoxy-3-oxopropyl)-6-fluorobenzoyl]-*S*-methyl-*S*-phenylsulfoximine (4e):** 132 mg, 70% yield; colorless crystalline solid; m.p. = 64–66 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 7.6 Hz, 2H), 7.68 (bt, *J* = 7.4 Hz, 1H), 7.61 (bt, *J* = 7.4 Hz, 2H), 7.29–7.18 (m, 1H), 7.00 (d, *J* = 7.6 Hz, 1H), 6.93 (t, *J* = 9.0 Hz, 1H), 4.09 (q, *J* = 7.2 Hz, 2H), 3.43 (s, 3H), 3.06 (t, *J* = 7.8 Hz, 2H), 2.65 (td, *J* = 2.2, 7.8 Hz, 2H), 1.20 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.8, 172.7, 159.3 (d, *J* = 248 Hz, 1C), 140.2, 138.0, 134.0, 129.9 (d, *J* = 9.1 Hz, 1C), 129.7 (2C), 127.2 (2C), 127.0, 125.0, 113.6 (d, *J* = 22 Hz, 1C), 60.3, 44.2, 35.7, 28.4, 14.1; ^{19}F(470 MHz, $CDCl_3$) δ –115.82; IR (Neat) ν_{max} 2975, 2936, 1731, 1627, 1287, 1227 cm^{-1}; HRMS (ESI) for $C_{19}H_{20}FNO_4S$ $(M+H)^+$: calcd. 378.1175, found 378.1178.

***N*-[2-(3-Ethoxy-3-oxopropyl)-4,6-dimethylbenzoyl]-*S*-methyl-*S*-phenylsulfoximine (4f):** 151 mg, 78% yield; colorless crystalline solid; m.p. = 113–115 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 7.6 Hz, 2H), 7.68 (bt, *J* = 6.8 Hz, 1H), 7.61 (bt, *J* = 7.6 Hz, 2H), 6.85 (bd, *J* = 2.4 Hz,, 2H), 4.12 (q, *J* = 7.2 Hz, 2H), 3.48 (s, 3H), 3.07–2.91 (m, 2H), 2.70–2.61 (m, 2H), 2.35 (s, 3H), 2.26 (s, 3H), 1.24 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.9, 173.3, 138.7, 138.0, 136.3, 136.2, 134.2, 133.8, 129.6 (2C), 129.1, 127.2 (2C), 127.1, 60.3, 44.0, 36.3,

29.1, 21.1, 19.5, 14.2; IR (Neat) ν_{max} 3019, 2931, 1715, 1605, 1287, 1216 cm^{-1}; HRMS (ESI) for $C_{21}H_{25}NO_4S$ $(M+H)^+$: calcd. 388.1582, found 388.1577.

***N*-[2-(3-Ethoxy-3-oxopropyl)-*α*-naphtholoyl]-*S*-methyl-*S*-phenylsulfoximine and *N*-[2-(3-Methoxy-3-oxopropyl)-*α*-naphtholoyl]-*S*-methyl-*S*-phenylsulfoximine (4g & 4'g):**

Following GP-3, reaction between **2l** (100 mg, 0.32 mmol) and ethyl acrylate (**1a**, 69 μL, 0.65 mmol) under the optimized conditions followed by hydrogenation in MeOH afforded the inseparable mixture of products **4g & 4′g** (94 mg, 4.6:1; ^{1}H NMR) in 73% yield. ^{1}H NMR (400 MHz, $CDCl_3$)δ 8.11 (d, J = 7.6 Hz, 2H), 7.98 (d, J = 8.4 Hz, 1H), 7.81–7.73 (m, 2H), 7.69 (t, J = 7.4 Hz, 1H), 7.62 (t, J = 7.6 Hz, 2H), 7.51–7.38 (m, 2H), 7.36–7.29 (m, 1H), 4.14 (q, J = 7.1 Hz, 0.5 H), 3.68 (s, 2.3H), 3.53 (s, 3H), 3.25–3.16 (m, 2H), 2.80–2.72 (m, 2H), 1.24 (t, J = 7.2 Hz, 0.75H); ^{13}C NMR (101 MHz, $CDCl_3$)δ178.3, 173.5, 173.1, 138.4, 135.7, 133.9, 133.5, 132.1, 129.8, 129.7, 128.8, 127.8, 127.1, 126.6, 125.5, 125.1, 60.4, 51.6, 44.2, 36.1, 35.9, 29.4, 14.2.

***N*-[2-(2-(Phenylsulfonyl)ethyl)-6-phenylbenzoyl]-*S*-methyl-*S*-phenylsulfoximine (4h):** 206 mg, 82% yield; colorless viscous liquid; ^{1}H NMR (400 MHz, $CDCl_3$)δ 7.95 (d, J = 7.6 Hz, 2H), 7.68–7.59 (m, 2H), 7.55 (bt, J = 7.2 Hz, 2H), 7.50–7.28 (m, 10H), 7.21 (bt, J = 8.6 Hz, 2H), 3.55 (bt, J = 8.0 Hz, 2H), 3.33–3.19 (m, 4H), 3.18–3.08 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ177.5, 141.2, 139.1, 138.6, 138.3, 137.7, 134.1, 133.6, 133.4, 129.2 (2C), 129.0 (2C), 128.72 (3C), 128.68, 128.5, 128.0 (2C), 127.8 (2C), 127.1, 126.7 (2C), 56.8, 42.6, 27.1; IR (neat) ν_{max} 3068, 2920, 1626, 1451, 1308, 1150 cm^{-1}; HRMS (ESI) for $C_{28}H_{25}NO_4S_2$ $(M+Na)^+$: calcd. 526.1123, found 526.1125.

***N*-[2-(3-Oxopentyl)-6-phenoxybenzoyl]-*S*-methyl-*S*-phenylsulfoximine (4i):** 134 mg, 61% yield; colorless viscous liquid; ^{1}H NMR (400 MHz, $CDCl_3$)δ 7.83 (bd, J = 7.6 Hz, 2H), 7.58 (t, J = 7.2 Hz, 1H), 7.44 (t, J = 7.8 Hz, 2H), 7.31 (t, J = 7.8 Hz, 2H), 7.19 (t, J = 8.0 Hz, 1H), 7.12–6.97 (m, 4H), 6.80 (d, J = 8.0 Hz, 1H), 3.21 (s, 3H), 3.06–2.97 (m, 2H), 2.90–2.77 (m, 2H), 2.37 (q, J = 6.9 Hz, 2H), 1.00 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$)δ 210.8, 175.9, 157.9, 152.6, 140.0, 137.9, 133.7, 132.0, 129.6 (2C), 129.4 (3C), 127.2 (2C), 125.2, 122.6, 117.9 (2C), 117.6, 43.9, 43.8, 35.8, 27.6, 7.6; IR (neat) ν_{max} 3057, 2931, 1709, 1632, 1451, 1226 cm^{-1}; HRMS (ESI) for $C_{25}H_{25}NO_4S$ $(M+Na)^+$: calcd. 458.1402, found 458.1402.

***N*-[2-(3-Oxopentyl)-6-fluorobenzoyl]-*S*-methyl-*S*-phenylsulfoximine (4j):** 117 mg, 64% yield; colorless viscous liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (bd, J = 8.0 Hz, 2H), 7.68 (bt, J = 7.0 Hz, 1H), 7.62 (bt, J = 7.2 Hz, 2H), 7.25–7.16 (m, 1H), 6.98 (bd, J = 7.6 Hz, 1H), 6.91 (t, J = 8.8 Hz, 1H), 3.42 (s, 3H), 3.05–2.95 (m, 2H), 2.75 (bt, J = 7.6 Hz, 2H), 2.35 (q, J = 7.2 Hz, 2H), 0.98 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 210.6, 174.1, 159.2 (d, J = 247 Hz), 140.8, 137.9, 134.0, 130.0 (d, J = 9.1 Hz), 129.7 (2C), 127.2 (2C), 127.0 (d, J = 17 Hz), 125.3, 113.5 (d, J = 22 Hz),44.3, 43.7, 35.8, 27.5, 7.6; ^{19}F (470 MHz, $CDCl_3$)δ –116.0; IR (Neat) ν_{max} 3018, 2975, 2931, 1709, 1637, 1287, 1226, 1133 cm^{-1}; HRMS (ESI) for $C_{19}H_{20}FNO_3S$ $(M+Na)^+$: calcd. 384.1046, found 384.1051.

***N*-[2-(3-Ethoxy-3-oxopropyl)-benzoyl]-*S*-methyl-*S*-phenylsulfoximine (4k):**

Following GP-3, reaction between **2m** (129 mg, 0.5 mmol) and **1a** (0.19 mL, 1.75 mmol) under the optimized conditions followed by flash column chromatography purification of crude material on silica gel eluting with 1–10% $CHCl_3$/THF gave **4k** (61 mg, 34%) and **4′k** (80 mg,

35%) as pale brown viscous oil. ^{1}H NMR (400 MHz, $CDCl_3$)δ 8.07 (bd, J = 7.6 Hz, 2H), 8.04 (bd, J = 7.6 Hz, 1H), 7.70 (bt, J = 7.4 Hz, 1H), 7.63 (bt, J = 7.2 Hz, 2H), 7.37 (t, J = 7.4 Hz, 1H), 7.30–7.22 (m, 2H), 4.09 (q, J = 7.2 Hz, 2H), 3.44 (s, 3H), 3.39–3.22 (m, 2H), 2.77–2.60 (m, 2H),1.21 (t, J = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$)δ 176.2, 173.4, 141.4, 138.8, 135.4, 133.8, 131.1, 130.9, 129.7, 127.1, 126.2, 60.2, 44.4, 36.1, 29.9, 14.2; IR (Neat) ν_{max} 3063, 2931, 1726, 1632, 1260 cm^{-1}; HRMS (ESI) for $C_{19}H_{21}NO_4S$ $(M+H)^+$: calcd. 360.1269, found 360.1269.

***N*-[2,6-Di(3-ethoxy-3-oxopropyl)-benzoyl]-*S*-methyl-*S*-phenylsulfoximine (4′k):** ^{1}H NMR (400 MHz, $CDCl_3$)δ 8.09 (d, J = 7.6 Hz, 2H), 7.68 (bt, J = 7.4 Hz, 1H), 7.62 (bt, J = 7.4 Hz, 2H), 7.19 (t, J = 7.6 Hz, 1H), 7.08 (bd, J = 7.6 Hz, 2H), 4.11 (q, J = 7.1 Hz, 4H), 3.52 (s, 3H), 3.08–2.97 (m, 4H), 2.72–2.60 (m, 4H), 1.22 (t, J = 7.2 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$)δ 178.4, 173.1, 139.0, 138.5, 136.6, 133.8, 129.7, 128.5, 127.3, 127.0, 60.3, 43.8, 36.0, 29.0, 14.2; IR (Neat) ν_{max} 3068, 2980, 2926, 1726, 1627, 1293, 1221 cm^{-1}; HRMS (ESI) for $C_{24}H_{29}NO_6S$ $(M+H)^+$: calcd. 460.1794, found 460.1796.

***N*-[2-(3-Ethoxy-3-oxopropyl)-4-methylbenzoyl]-*S*-methyl-*S*-phenylsulfoximine (4l):**

Following GP-3, reaction between **2n** (136 mg, 0.5 mmol) and **1a** (0.19 mL, 1.75 mmol) under the optimized conditions followed by flash column chromatography purification of crude material on silica gel eluting with 1–10% $CHCl_3$/THF gave **4l** (66 mg, 35%) and **4′l** (85 mg, 36%) as pale brown viscous oil. ^{1}H NMR (400 MHz, $CDCl_3$)δ 8.05 (d, J = 7.6 Hz, 2H), 7.97 (d, J = 8.0 Hz, 1H), 7.68 (bt, J = 7.2 Hz, 1H), 7.60 (bt, J = 7.6 Hz, 2H), 7.08–7.02 (m, 2H), 4.08 (q, J = 7.2 Hz, 2H), 3.42 (s, 3H), 3.34–3.20 (m, 2H), 2.69–2.60 (m, 2H), 2.33 (s, 3H), 1.20 (t, J =

7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$)δ176.0, 173.5, 141.7, 141.5, 138.9, 133.7, 132.2, 131.7, 131.3, 129.7, 127.1, 126.8, 60.1, 44.4, 36.1, 30.0, 21.3, 14.2; IR (Neat) ν_{max} 3063, 2920, 2854, 1726, 10627, 1446, 1221 cm^{-1}; HRMS (ESI) for $C_{20}H_{23}NO_4S$ $(M+H)^+$: calcd. 374.1426, found 374.1427.

***N*-[2,6-Di(3-ethoxy-3-oxopropyl)-4-methylbenzoyl]-*S*-methyl-*S*-phenylsulfoximine (4′l):** ^{1}H NMR (400 MHz, $CDCl_3$)δ8.09 (d, J = 7.6 Hz, 2H), 7.67 (bt, J = 7.2 Hz, 1H), 7.61 (bt, J =7.4 Hz, 2H), 6.89 (s, 2H), 4.11 (q, J = 6.9 Hz, 4H), 3.50 (s, 3H), 3.05–2.90 (m, 4H), 2.67–2.60 (m, 4H), 2.27 (s, 3H), 1.22 (t, J = 7.0 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$)δ178.5, 173.1, 138.5, 138.2, 136.2, 133.7, 129.6, 128.0, 127.0, 60.2, 43.8, 36.1, 29.0, 21.1, 14.1; IR (Neat) ν_{max} 3057, 2931, 2854, 1731, 1627, 1106 cm^{-1}; HRMS (ESI) for $C_{25}H_{31}NO_6S$ $(M+H)^+$: calcd. 474.1950, found 474.1950.

***N*-[2-(3-Ethoxy-3-oxopropyl)-4-fluorobenzoyl]-*S*-methyl-*S*-phenylsulfoximine (4m):**

Following GP-3, reaction between **2o** (139 mg, 0.5 mmol) and **1a** (0.19 mL, 1.75 mmol) under the optimized conditions followed by flash column chromatography purification of crude material on silica gel eluting with 1–10% $CHCl_3$/THF gave **4m** (107 mg, 57%) and **4′m** (63 mg, 26%) as pale brown viscous oil. ^{1}H NMR (400 MHz, $CDCl_3$)δ8.09 (dd, J = 6.4, 2.4 Hz, 1H), 8.03 (d, J = 7.6 Hz, 2H), 7.68 (bt, J = 7.4 Hz, 1H), 7.60 (bt, J = 7.6 Hz, 2H), 6.97–6.86 (m, 2H), 4.07 (q, J = 7.2 Hz, 2H), 3.41 (s, 3H), 3.37–3.23 (m, 2H), 2.71–2.59 (m, 2H), 1.20 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$)δ174.9, 173.0, 163.9 (d, J = 252 Hz, 1C), 144.9 (d, J = 8 Hz, 1C), 138.6, 133.7, 133.6 (d, J = 9.1 Hz, 1C), 131.2, 129.6 (2C), 127.0 (3C), 117.5 (d, J = 21.2 Hz, 1C), 112.9 (d, J = 21.2 Hz, 1C), 60.2, 44.3, 35.6, 29.8, 14.1; ^{19}F (470 MHz, $CDCl_3$)δ –109.0;

IR (Neat) ν_{max} 2931, 2854, 1720, 1627, 1221 cm^{-1}; HRMS (ESI) for $C_{19}H_{20}FNO_4S$ $(M+H)^+$: calcd. 378.1175, found 378.1175.

***N*-[2,6-Di(3-ethoxy-3-oxopropyl)-4-fluorobenzoyl]-*S*-methyl-*S*-phenylsulfoxi-mine (4′m):** ^1H NMR (400 MHz, $CDCl_3$)δ 8.09 (d, J = 8.0 Hz, 2H), 7.69 (bt, J = 6.8 Hz, 1H), 7.63 (bt, J = 7.4 Hz, 2H), 6.79 (d, J = 9.6 Hz, 2H), 4.12 (q, J = 7.1 Hz, 4H), 3.51 (s, 3H), 3.08–2.97 (m, 4H), 2.69–2.60 (m, 4H), 1.23 (t, J = 7.2 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$)δ 177.7, 172.8 (2CO-), 162.2 (d, J = 247.4 Hz, 1C), 139.6 (d, J = 8.1 Hz, 1C), 138.4, 135.2, 133.9, 129.7 (2C), 127.0 (3C), 114.0 (d, J = 21.2 Hz, 2C), 60.4 (2C), 43.8, 35.6 (2C), 28.9 (2C), 14.2 (2C); ^{19}F (470 MHz, $CDCl_3$)δ −113.0; IR (Neat) ν_{max} 2924, 1727, 1626, 1290, 1140 cm^{-1}; HRMS (ESI) for $C_{24}H_{28}FNO_6S$ $(M+H)^+$: calcd. 478.1699, found 478.1699.

***N*-[(*E*)-3-(3-Ethoxy-3-oxoprop-1-en-1-yl)-thenoyl]-*S*-methyl-*S*-phenylsulfoximine (5a):** Following GP-2, **5a** (160 mg) was obatined in 88% yield as colorless crystalline solid. m.p. = 143–145 ^oC; ^1H NMR (400 MHz, $CDCl_3$) δ 8.73 (d, J = 16.4 Hz, 1H), 8.06 (bd, J = 7.6 Hz, 2H), 7.69 (bt, J = 7.2 Hz, 1H), 7.62 (bt, J = 7.4 Hz, 2H), 7.38 (d, J = 5.2 Hz, 1H), 7.31 (d, J = 5.2 Hz, 1H), 6.31 (d, J = 16.4 Hz, 1H), 4.21 (q, J = 6.9 Hz, 2H), 3.47 (s, 3H), 1.28 (t, J = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.8, 166.9, 140.0, 139.0, 138.3, 137.6, 134.0, 129.8 (2C), 129.7, 127.2 (2C), 126.7, 120.8, 60.4, 44.5, 14.2; IR (KBr) ν_{max} 3101, 2931, 1698, 1627, 1282 cm^{-1}; HRMS (ESI) for $C_{17}H_{17}NO_4S_2$ $(M+Na)^+$: calcd. 386.0497, found 386.0499.

***N*-[5-Methyl-(*E*)-3-(3-ethoxy-3-oxoprop-1-en-1-yl)-thenoyl]-*S*-methyl-*S*-phenylsulfoximine (5b):** Following GP-2, **5b** (169 mg) was obtained in 90% yield as colorless crystalline solid. m.p. = 121–123 ^oC; ^1H NMR (400 MHz, $CDCl_3$)δ 8.64 (b, J = 16.0 Hz, 1H), 8.00 (d, J = 8.0 Hz, 2H),

7.63 (bt, *J* = 7.0 Hz, 1H), 7.56 (t, *J* = 7.6 Hz, 2H), 6.95 (s, 1H), 6.20 (d, *J* = 16.4 Hz, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 3.41 (s, 3H), 2.41 (s, 3H), 1.23 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$)δ 168.6, 166.8, 144.5, 140.1, 138.2, 137.5, 136.7, 133.8, 129.5 (2C), 127.0 (2C), 124.9, 120.4, 60.1, 44.3, 15.4, 14.1; IR (KBr) ν_{max} 3063, 2931, 1709, 1610, 1463, 1276 cm^{-1}; HRMS (ESI) for $C_{18}H_{19}NO_4S_2$ $(M+H)^+$: calcd. 378.0833, found 378.0828.

***N*-[(*E*)-3-(3-*n*Butoxy-3-oxoprop-1-en-1-yl)-thenoyl]-*S*-methyl-*S*-phenylsulfoximine (5c):** Following GP-2, **5c** (169 mg) was obtained in 85% yield as colorless crystalline solid. m.p. = 162–164 °C; ^{1}H NMR (400 MHz, $CDCl_3$)δ 8.64 (d, *J* = 16.0 Hz, 1H), 8.04 (d, *J* = 7.6 Hz, 2H), 7.71 (bt, *J* = 7.2 Hz, 1H), 7.64 (bt, *J* = 7.4 Hz, 2H), 7.13 (s, 1H), 6.23 (d, *J* = 16.4 Hz, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.46 (s, 3H), 1.28 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$)δ 167.8, 166.7, 139.8, 138.1, 137.3, 136.5, 135.2, 134.2, 129.8(2C), 127.2(2C), 125.8, 121.8, 60.6, 44.6, 14.3; IR (KBr) ν_{max} 3035, 2931, 1698, 1605, 1435, 1293 cm^{-1}; HRMS (ESI) for $C_{17}H_{16}ClNO_4S_2$ $(M+H)^+$: calcd. 398.0287, found 398.0285.

***N*-[2-Methoxycarbonyl-(*E*)-4-(3-ethoxy-3-oxoprop-1-en-1-yl)-thenoyl]-*S*-methyl-*S*-phenylsulfoximine (5d):** Following GP-2, **5d** (178 mg) was obtained in 84% yield as colorless crystalline solid. m.p. = 185–187 °C; ^{1}H NMR (400 MHz, $CDCl_3$)δ 8.63 (d, *J* = 16.4 Hz, 1H), 8.06 (d, *J* = 8.0 Hz, 2H), 7.94 (s, 1H), 7.72 (bt, *J* = 7.0 Hz, 1H), 7.64 (bt, *J* = 7.4 Hz, 2H), 6.34 (d, *J* = 16.4 Hz, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.90 (s, 3H), 3.48 (s, 3H), 1.28 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$)δ 168.2, 166.6, 162.0, 143.4, 139.8, 138.0, 136.8, 135.6, 134.2, 131.9, 129.9 (2C), 127.2 (2C), 121.8, 60.5, 52.6, 44.5, 14.3; IR (KBr) ν_{max} 3019, 2931, 1704, 1632, 1221 cm^{-1}; HRMS (ESI) for $C_{19}H_{19}NO_6S_2$ $(M+H)^+$: calcd. 422.0732, found 422.0734.

***N*-[1-Methyl-(*E*)-3-(3-ethoxy-3-oxoprop-1-en-1-yl)-2-indoloyl]-*S*-methyl-*S*-phenylsulfoximine (5e) and *N*-[1-Methyl-3-(3-ethoxy-3-oxopropyl)-2-indoloyl]-*S*-methyl-*S*-phenyl sulfoximine (5′e):**

Following the GP-2, reaction between **2t** and **1a** gave the inseparable mixture of alkenylation **5e** and hydroarylation products (2:3 by ^{1}H NMR; 122 mg, 60%) as colorless crystalline solid.

Data for **5e** and **5′e:** ^{1}H NMR (400 MHz, $CDCl_3$)δ 9.02 (d, J = 16.4 Hz, 0.65H), 8.15 (d, J = 7.6 Hz, 1.4H), 8.07 (d, J = 6.8 Hz, 2H), 8.02 (d, J = 8.4 Hz, 0.73H), 7.74–7.59 (m, 6.3H), 7.41–7.36 (m, 1.4H), 7.35–7.30 (m, 2H), 7.18–7.10 (m, 1H), 6.60 (d, J = 16.4 Hz, 0.65H), 4.28 (q, J = 6.8 Hz, 1.4H), 4.12 (q, J = 7.1 Hz, 2H), 4.00 (s, 2H), 3.99 (s, 3H), 3.65–3.53 (m, 2H), 3.52 (s, 2H), 3.44 (s, 3H), 2.86–2.64 (m, 2H), 1.34 (t, J = 7.0 Hz, 2H), 1.23 (t, J = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$)δ 173.7, 169.6, 168.9, 168.3, 139.6, 138.74, 138.69, 138.4, 137.9, 134.8, 134.0, 133.7, 130.0, 129.9, 129.7, 127.3, 127.1, 126.3, 125.0, 124.8, 124.6, 121.9, 121.6, 120.2, 119.6, 116.2, 115.5, 110.6, 110.0, 60.2, 60.1, 44.8, 36.0, 32.2, 32.1, 21.7, 14.4, 14.2.

***N*-[(*E*)-3-(3-ethoxy-3-oxoprop-1-en-1-yl)-benzofuranoyl]-*S*-methyl-*S*-phenylsulfoximine (5f):** Following GP-2, **5f** (175 mg) was obtained in 88% yield as light brown liquid. ^{1}H NMR (400 MHz, $CDCl_3$)δ 8.74 (d, J = 16.4 Hz, 1H), 8.08 (d, J = 7.6 Hz, 2H), 7.89 (d, J = 8.0 Hz, 1H), 7.68 (bt, J = 7.4 Hz, 1H), 7.65–7.54 (m, 3H), 7.43 (t, J = 7.8 Hz, 1H), 7.33 (t, J = 7.4 Hz, 1H), 6.67 (d, J = 16.8 Hz, 1H), 4.28–4.19 (m, 2H), 3.52 (s, 3H), 1.28 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$)δ 166.6, 166.0, 154.2, 148.5, 137.9, 136.0, 134.1, 129.7 (2C), 127.5, 127.1 (2C), 125.5, 124.1, 122.1, 121.9, 121.0, 112.5, 60.4, 44.5, 14.2; IR (KBr) ν_{max} 3063, 2926, 1709, 1627, 1271 cm^{-1}; HRMS (ESI) for $C_{21}H_{19}NO_5S(M+Na)^+$: calcd. 420.0882, found 420.0881.

***N*-[(*E*)-3-(3-^{n}Butoxy-3-oxoprop-1-en-1-yl)-thenoyl]-*S*-methyl-*S*-phenylsulfoximine (5g):** Following GP-2, **5g** (161 mg) was obtained in 82% yield as light brown liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (d, J = 16.4 Hz, 1H), 8.07 (d, J = 7.6 Hz, 2H), 7.70 (bt, J = 7.2 Hz, 1H), 7.63 (t, J = 7.4 Hz, 2H), 7.38 (d, J = 5.2 Hz, 1H), 7.32 (d, J = 4.4 Hz, 1H), 6.32 (d, J = 16.0 Hz, 1H), 4.22–4.12 (m, 2H), 3.47 (s, 3H), 1.70–1.59 (m, 2H), 1.46–1.35 (m, 2H), 0.93 (t, J = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.6, 166.9, 139.8, 138.9, 138.1, 137.5, 133.9, 129.7, 129.6 (2C), 127.0 (2C), 126.6, 120.7, 64.2, 44.3, 30.5, 18.9, 13.6; IR (neat) ν_{max} 3013, 2947, 1704, 1638, 1424, 1232 cm^{-1}; HRMS (ESI) for $C_{19}H_{21}NO_4S_2$ $(M+Na)^+$: calcd. 414.0810, found 414.0819.

***N*-[(*E*)-3-(2-(Phenylsulfonyl)vinyl)-thenoyl]-*S*-methyl-*S*-phenylsulfoximine (5h):** Following GP-2, **5h** (206 mg) was obtained in 95% yield as colorless crystalline solid. m.p. = 128–130 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$)δ 8.88 (d, J = 15.6 Hz, 1H), 8.08 (bd, J = 7.2 Hz, 2H), 7.89 (bd, J = 7.2 Hz, 2H), 7.71 (bt, J = 7.0 Hz, 1H), 7.65 (bt, J = 7.4 Hz, 2H), 7.58 (bt, J = 7.2 Hz, 1H), 7.50 (bt, J = 7.6 Hz, 2H), 7.37 (d, J = 5.2 Hz, 1H), 7.19 (d, J = 5.2 Hz, 1H), 6.77 (d, J = 15.6 Hz, 1H), 3.51 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$)δ 168.5, 141.5, 140.8, 138.1, 136.9, 136.0, 134.2, 133.3, 130.2, 130.0 (2C), 129.3 (3C), 127.7 (2C), 127.3 (2C), 126.7, 44.7; IR (KBr) ν_{max} 3052, 2920, 1638, 1260, 1221 cm^{-1}; HRMS (ESI) for $C_{20}H_{17}NO_4S_3$ $(M+H)^+$: calcd. 432.0398, found 432.0399.

***N*-[(*E*)-3-(3-Oxopent-1-enyl)-thenoyl]-*S*-methyl-*S*-phenylsulfoximine (5i):** Following GP-2, **5i** (159 mg) was obtained in 91% yield as light brown liquid. ^{1}H NMR (400 MHz, $CDCl_3$)δ 8.62

(d, J = 16.8 Hz, 1H), 8.04 (d, J = 7.6 Hz, 2H), 7.68 (bt, J = 7.4 Hz, 1H), 7.61 (t, J = 7.4 Hz, 2H), 7.37 (d, J = 5.2 Hz, 1H), 7.31 (d, J = 5.2 Hz, 1H), 6.51 (d, J = 16.8 Hz, 1H), 3.46 (s, 3H), 2.67 (q, J = 7.2 Hz, 2H), 1.07 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$)δ 202.2, 168.9, 140.6, 138.7, 138.2, 135.8, 134.0, 129.8, 129.7 (2C), 129.2, 127.1 (2C), 126.5, 44.5, 32.2, 8.1; IR (KBr) ν_{max} 3084, 3024, 2926, 1676, 1616, 1419, 1287 cm^{-1}; HRMS (ESI) for $C_{17}H_{17}NO_3S_2$ $(M+H)^+$: calcd. 348.0728, found 348.0730.

_N_-[(_E_)-3-(3-Oxohex-1-enyl)-thenoyl]-_S_-methyl-_S_-phenylsulfoximine (5j):

Following GP-2, reaction between **2p** and **1f** gave the inseparable mixture of alkenylation **5j** and hydroarylation products (3:1 by ^{1}H NMR; 156 mg, 86%) as colorless crystalline solid.

Data for **5j:** ^{1}H NMR (400 MHz, $CDCl_3$)δ 8.62 (d, J = 16.4 Hz, 1H), 8.05 (d, J = 7.6 Hz, 2H), 7.70 (bt, J = 7.4 Hz, 1H), 7.62 (bt, J = 7.4 Hz, 2H), 7.38 (d, J = 5.2 Hz, 1H), 7.32 (d, J = 5.2 Hz, 1H), 6.52 (d, J = 16.4 Hz, 1H), 3.47 (s, 3H), 2.64 (t, J = 7.4 Hz, 2H), 1.68–1.58 (m, 2H), 0.90 (t, J = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.8, 168.9, 140.6, 138.8, 138.2, 135.9, 134.0, 129.8, 129.7, 127.1, 126.5, 44.5, 40.8, 17.6, 13.7.

General Procedure for the Hydrolysis of Hydroarylation Product (GP-4):

A solution of **4a** (0.3 mmol) in MeOH (2.0 mL) was added aq. NaOH (5.0 M, 2.0 mL). The reaction mixture was heated at 60 ^{o}C for 6 h. The crude mixture was extracted with CH_2Cl_2 (5 × 10 mL), and the combined extracts were dried over Na_2SO_4. The solvent was filtered and evaporated under vacuum to give the methyl phenyl sulfoximine.

The aqueous layer was acidified with 1N HCl and extracted with CH_2Cl_2 (7 × 10 mL). The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated under vacuum to give the corresponding benzoic acid derivatives.

***N*-[2-(3-Ethoxy-3-oxopropyl)-5-methylbenzoyl]-*S*-methyl-*S*-phenylsulfoximine (4a):** Following GP-3, hydrogenation of **3a** (1.0 g, 2.7 mmol) with Pd/C in MeOH gave **4a** (830 mg, 83%) as colorless viscous liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 8.4 Hz, 2H), 7.81 (s, 1H), 7.67 (bt, J = 7.6 Hz, 1H), 7.60 (t, J = 7.6 Hz, 2H), 7.16 (d, J = 8.0 Hz, 1H), 7.11 (d, J = 8.0 Hz, 1H), 4.07 (q, J = 7.2 Hz, 2H), 3.41 (s, 3H), 3.28–3.19 (m, 2H), 2.67–2.58 (m, 2H), 2.33 (s, 3H), 1.39 (t, J = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ176.4, 173.5, 138.9, 138.3, 135.7, 135.2, 133.8, 131.8, 131.2, 130.9, 129.7 (2C), 127.1 (2C), 60.2, 44.4, 36.3, 29.5, 20.9, 14.2; IR (Neat) ν_{max} 2975, 2926, 1726, 1632, 1298, 1221 cm^{-1}; HRMS (ESI) for $C_{20}H_{23}NO_4S$ $(M+Na)^+$: calcd. 396.1246, found 396.1249.

2-(2-Carboxyethyl)-5-methylbenzoic acid (6): Following GP-4, hydrolysis of **4a** (124 mg, 0.33 mmol) with aq. NaOH afforded **6** (62 mg, 90%) and sulfoximine (42 mg, 81%). ^{1}H NMR (400 MHz, DMSO-D_6)δ12.45 (bs, 2H), 7.60 (s, 1H), 7.26 (d, J = 7.2 Hz, 1H), 7.20 (d, J = 7.6 Hz, 1H), 3.06 (bt, J = 7.6 Hz, 2H), 2.48–2.42 (m, 2H), 2.28 (s, 3H); ^{13}C NMR (101 MHz, DMSO-D_6)δ174.3, 169.2, 139.3, 135.9, 132.8, 131.2 (2C), 130.6, 35.9, 29.2, 20.8; IR (KBr) ν_{max} 3030, 2920, 1693, 1309, 1276 cm^{-1}; HRMS (ESI) for $C_{11}H_{12}O_4$ $(M+Na)^+$: calcd. 231.0634, found 231.0636.

Synthesis of *N*-[3-(phenoxymethyl)benzoyl]-*S*-methyl-*S*-phenylsulfoximine (7):

Following GP-1, **7** (4.6 g) was prepared in 65% yield as viscous liquid. R_f = 0.38 (3:2 hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$)δ 8.24 (s, 1H), 8.14 (d, J = 7.6 Hz, 1H), 8.06 (d, J = 7.6 Hz, 2H), 7.69 (t, J = 7.4 Hz, 1H), 7.66–7.58 (m, 3H),7.45 (t, J = 7.6 Hz, 1H), 7.30 (t, J = 7.8 Hz, 2H), 7.02–6.93 (m, 3H), 5.11 (s, 2H), 3.47 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.0, 158.6, 138.8, 137.0, 135.8, 133.8, 131.2, 129.7 (2C), 129.4 (2C), 129.0, 128.43, 128.37, 127.1 (2C), 121.0, 114.8(2C), 69.5, 44.3; IR (Neat) ν_{max} 3057, 2926, 1632, 1594, 1287, 1227 cm^{-1}; HRMS (ESI) for $C_{21}H_{19}NO_3S$ $(M+H)^+$: calcd. 366.1164, found 366.1161.

***N*-[2-(3-Ethoxy-3-oxopropyl)-5-(phenoxymethyl)benzoyl]-*S*-methyl-*S*-phenylsulfoximine (8):** Following GP-2, the reaction of **7** (2.5 g, 6.8 mmol) with **1a** (1.46 mL, 13.7 mmol) was conducted in the presence of $[RuCl_2(p\text{-cymene})]_2$ (416.0 mg, 10 mol %), $Cu(OAc)_2{\cdot}H_2O$ (1.35 g, 6.8 mmol), $AgSbF_6$ (933 mg, 2.72 mmol) in 1,2-DCE (10.0 mL) at 120 ^{o}C for 24 h. Upon completion, the inseparable regioisomeric mixture of alkenylation **8′** (major) and hydroarylation **8** (minor) products were isolated [2.1 g (4:1), 66%] as yellow viscous oil. This mixture of compounds was subsequently used for the hydrogenation reaction.

To a solution of **8′**and **8** (2.0 g, 4.3 mmol) in THF (15 mL) and MeOH (10 mL) was added $NiCl_2{\cdot}6H_2O$ (2.0 g, 8.6 mmol) and $NaBH_4$ (0.82 g, 21.5 mmol) at 0 ^{o}C under an argon atmosphere. The resulting mixture was stirred overnight and then quenched with acetone (5.0 mL) and water (5.0 mL). The crude mixture was diluted with Et_2O and filtered through a pad of Celite. The filtrate was separated and the organic layer was washed with water and brine, and dried over $NaSO_4$. The solvent was evaporated and the crude mixture was purified by column chromatography eluting with 3:2 hexane/EtOAc to afford **8** (1.78 g, 89%) as colorless oil.

For product **8**: ^{1}H NMR (400 MHz, $CDCl_3$)δ 8.10 (s, 1H), 8.05 (d, J = 7.6 Hz, 2H), 7.69 (bt, J = 7.2 Hz, 1H), 7.61 (bt, J = 7.6 Hz, 2H), 7.46 (d, J = 7.6 Hz, 1H), 7.33–7.26 (m, 3H), 7.02–6.93 (m, 3H), 5.06 (s, 2H), 4.09 (q, J = 7.1 Hz, 2H), 3.43 (s, 3H), 3.37–3.24 (m, 2H), 2.71–2.62 (m, 2H), 1.21 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.8, 173.3, 158.6, 141.1, 138.6, 135.4, 134.9, 133.7, 131.3, 130.1, 130.0, 129.7 (2C), 129.4 (2C), 127.0 (2C), 120.9, 114.7 (2C), 69.3, 60.2, 44.3, 36.0, 29.6, 14.1; IR (Neat) ν_{max} 3452, 3347, 2986, 2926, 1736, 1627, 1594, 1490, 1227 cm^{-1}; HRMS (ESI) for $C_{26}H_{27}NO_5S$ $(M+Na)^+$: calcd. 488.1508, found 488.1509.

2-(2-Carboxyethyl)-5-(phenoxymethyl)benzoic acid (9): Following GP-4, hydrolysis of **8** (1.5 g, 3.2 mmol) afforded **9** (0.79 g) in 81% yield as colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$/DMSO-D_6)δ 11.86 (bs, 2H), 7.90 (s, 1H), 7.40 (bd, J = 7.6 Hz, 1H), 7.28–7.14 (m, 3H), 6.91–6.83 (m, 3H), 4.95 (s, 2H), 3.18 (bt, J = 7.4 Hz, 2H), 2.62–2.45 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$/DMSO-D_6) δ 174.9, 169.0, 158.5, 142.3, 135.1, 131.3, 130.9, 130.5, 130.2, 129.5 (2C), 121.0, 114.7 (2C), 69.1, 35.7, 29.5; IR (KBr) ν_{max} 2964, 2926, 1726, 1687, 1238 cm^{-1}; HRMS (ESI) for $C_{17}H_{16}O_5$ $(M+Na)^+$: calcd. 323.0896, found 323.0898.

The reaction of **9** (300 mg) with catalytic amount of H_2SO_4 (0.15 mL) in methanol (1.2 mL) in 30 min afforded the mono-esterification product 2-(3-methoxy-3-oxopropyl)-5-(phenoxymethyl) benzoic acid (**9′**, 85%) and the di-esterification compound (**9″**, 10%). The mixture of crude compounds was subjected to the EDC-coupling for the amide formations in the next step.

Methyl-3-(2-(naphthalen-1-ylmethylcarbamoyl)-4-(phenoxymethyl)phenyl)propanoate (10):

A solution of *N*'-(3-dimethylaminopropyl)-*N*-ethylcarbodimide, hydrochloride salt (EDC.HCl) (99 mg, 0.64 mmol), hydroxybenzotriazole (HOBt) (98 mg, 0.64 mmol) and **9′+9″** (100 mg, 0.32 mmol) in DMF (15 mL) was stirred under an argon atmosphere. The naphthalen-1-ylmethanamine (56 μL, 0.38 mmol) was introduced drop wise at 0 °C. The resulting reaction mixture was stirred for about 1 h at 0 °C, and warmed to ambient temperature and continued for overnight. Upon completion, the reaction mixture was acidified with HCl (1N). The organic layer was separated; the aqueous layer was extracted with CH_2Cl_2 (3 × 5.0 mL). The combined extracts were washed with 10% aqueous $NaHCO_3$ and brine. The organic layer was dried over Na_2SO_4. Solvent was filtered and evaporated under reduced pressure. The crude residue was purified using column chromatography on silica gel furnishing **10** (92 mg, 64%) as colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$)δ 8.15 (d, *J* = 8.0 Hz, 1H), 7.90 (d, *J* = 7.6 Hz, 1H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.62–7.51 (m, 3H), 7.49–7.36 (m, 3H), 7.31–7.23 (m, 3H), 6.99–6.88 (m, 3H), 6.53 (bs, 1H), 5.10 (bd, *J* = 5.2 Hz, 2H), 4.97 (s, 2H), 3.60 (s, 3H), 3.09 (t, *J* = 7.4 Hz, 2H), 2.71 (t, *J* = 7.4 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.5, 169.2, 158.5, 138.4, 136.6, 135.4, 133.9, 133.3, 131.4, 130.2 (2C), 129.5, 129.2, 128.8 (2C), 127.0, 126.7, 126.3, 126.1, 125.4, 123.6, 121.1, 114.8 (2C), 69.1, 51.7, 42.3, 35.3, 27.9; IR (KBr) ν_{max} 3293, 2947, 2920, 1753, 1632, 1517, 1249 cm^{-1}; HRMS (ESI) for $C_{29}H_{27}NO_4$ $(M+H)^+$: calcd. 454.2018, found 454.2017.

3-(2-(Naphthalen-1-ylmethylcarbamoyl)-4-(phenoxymethyl)phenyl)propanoic acid (D):[1]

A solution of **10** (50 mg, 0.11 mmol), $LiOH{\cdot}H_2O$ (5 mg, 0.11 mmol) in THF/MeOH (4.0 mL, 1:1) was heated at 60 ^{o}C for about 4 h. The solvent was evaporated. The crude mixture was diluted with CH_2Cl_2 (10 mL) and acidified with 1N HCl; the mixture was extracted with CH_2Cl_2 (5 × 5.0 mL). The combined organic layers were dried over Na_2SO_4, and concentrated to give **D**

(30 mg, 62%) as colorless solid. ^{1}H NMR (500 MHz, DMSO-D_6)δ 12.15 (bs, 1H, OH), 8.99 (bt, J = 5.7 Hz, 1H), 8.19 (d, J = 8.0 Hz, 1H), 7.96 (d, J = 8.0 Hz, 1H), 7.87 (d, J = 8.0 Hz, 1H), 7.62–7.40 (m, 6H), 7.35–7.25 (m, 3H), 6.99 (d, J = 8.5 Hz, 2H), 6.94 (t, J = 7.2 Hz, 1H), 5.07 (s, 2H), 4.92 (bd, J = 6.0 Hz, 2H), 2.94 (bt, J = 8.0 Hz, 2H), 2.54 (bt, J = 8.0 Hz, 2H); ^{13}C NMR (125 MHz, DMSO-D_6) δ174.2, 169.2, 158.7, 138.7, 137.4, 135.3, 135.0, 133.8, 131.4, 130.2, 130.0 (2C), 129.1, 129.0, 128.0, 127.0, 126.7, 126.3, 126.0, 125.9, 124.0, 121.2, 115.2 (2C), 69.0, 41.1, 35.8, 28.4; HRMS (ESI) for $C_{28}H_{25}NO_4$ $(M+H)^+$: calcd. 440.1862, found 440.1861.

General procedure for annulation of *N*-benzoylated MPS with diphenyl acetylene (GP-5).

A mixture of *N*-protected sulfoximine (0.5 mmol), diphenylacetylene (178 mg, 1.0 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.0 mg, 5.0 mol %), and $AgSbF_6$ (69 mg, 40 mol %) in AcOH (28.0 µL, 1.0 equiv) & 1,4-dioxane (2.0 mL) was taken in a Schelenk tube under an argon atmosphere. The resulting mixture was stirred at 120 ^{o}C for 24 h. Subsequently, the reaction mixture was cooled to ambient temperature, filtered through a small plug of Celite and then washed with CH_2Cl_2 (3 × 10 mL). The solvents were evaporated under reduced pressure and the crude material was purified using column chromatography on silica gel (10-40% *n*-hexane/EtOAc) as an eluent.

8-Methyl-3,4-diphenylisoquinolin-1(2H)-one (11):[17] 63 mg, 40% yield; colorless crystalline solid; ^{1}H NMR (400 MHz, DMSO-D_6)δ 11.27 (s, 1H, NH), 7.43 (t, J = 7.2 Hz, 1H), 7.32–7.19 (m, 9H), 7.14–7.08 (m, 2H), 6.93 (d, J = 7.6 Hz, 1H), 2.88 (s, 3H); ^{13}C NMR (101 MHz, DMSO-D_6)δ 163.2, 141.1, 140.4, 139.0, 137.0, 135.0, 132.3, 132.0, 130.2, 129.6, 128.7, 128.6, 128.1, 127.4, 123.8, 116.0, 24.1 (one peak is missing due to overlap).

8-Fluoro-3,4-diphenylisoquinolin-1(2H)-one (**13**): Following GP-5, reaction between **2j** (55.4 mg, 0.2 mmol) and diphenylacetylene (71 mg, 0.4 mmol), in the presence of $[RuCl_2(p\text{-cymene})]_2$ (6.0 mg, 5.0 mol %), and $AgSbF_6$ (14 mg, 40 mol %) in AcOH (11.0 μL) & 1,4-dioxane (1.0 mL) at 120 ^oC for 24 h afforded **13 (**40 mg) in 63% yield as yellow crystalline solid.^{1}H NMR (400 MHz, $CDCl_3$)δ 9.37 (s, 1H, NH), 7.54–7.46 (m, 1H), 7.36–7.29 (m, 3H), 7.28–7.22 (m, 5H), 7.20–7.14 (m, 2H), 7.14–7.10 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$)δ 164.0, 160.8 (d, J = 108 Hz, 1C), 141.5, 138.4, 135.6, 134.4, 133.4 (d, J = 9 Hz, 1C), 131.8, 129.1, 128.9, 128.5, 128.4, 127.5, 121.6 (d, J = 4 Hz, 1C), 116.5, 113.4 (d, J = 21 Hz, 1C); ^{19}F (470 MHz, $CDCl_3$)δ −110.4;IR (KBr) ν_{max} 3183, 3035, 1649, 1473 cm^{-1}; HRMS (ESI) for $C_{21}H_{14}FNO$ $(M+H)^+$: calcd. 316.1137, found 316.1138.

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Supporting Information Available: Figures giving the ^{1}H and ^{13}C spectra of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org

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