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Sulfoximine-Directed Ruthenium-Catalyzed *ortho*-C−H Alkenylation of (Hetero)Arenes: Synthesis of EP3 Receptor Antagonist Analogue

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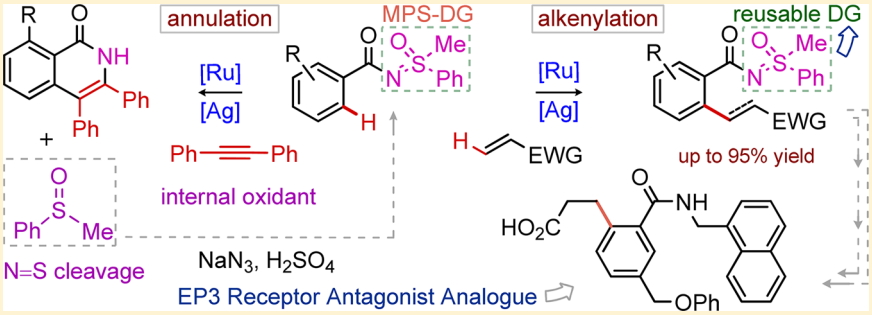
Supporting Information



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 the EP3 receptor antagonist analogue.

INTRODUCTION

The development of synthetically viable strategies for the creation of olefin units in molecules is always desirable, such as the hydrogenated acrylate derivative 3-(2-carbamoylphenyl)-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

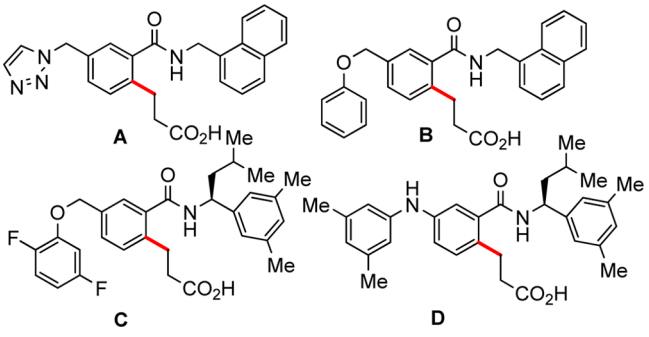


Figure 1. EP3 receptor antagonist analogues.

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 preactivated 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 nonmodifiable 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/nonmodifiable DG-assisted *o*-C−H alkenylation of arenes.[7]

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 analogue (**B**) is also shown.

RESULTS AND DISCUSSION

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, $Cu(OAc)_2 \cdot H_2O$,

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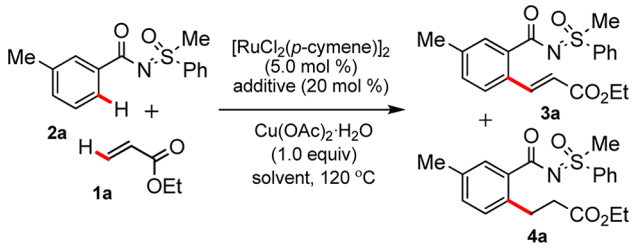
Table 1. Optimization of Reaction Conditions[a]



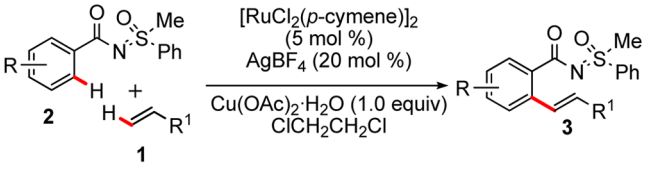
entry	additive (20 mol %)	solvent	yield (%)[b] 3a	yield (%)[b] 4a
1		$ClCH_2CH_2Cl$	<5	–
2	$AgSbF_6$	$ClCH_2CH_2Cl$	90	<10
3	$NaPF_6$	$ClCH_2CH_2Cl$	74	20
4	KPF_6	$ClCH_2CH_2Cl$	37	–
5	$NaBF_4$	$ClCH_2CH_2Cl$	22	–
6	**$AgBF_4$**	**$ClCH_2CH_2Cl$**	**92 (84)**[c]	–
7	$AgBF_4$	$ClCH_2CH_2Cl$	54[d]	–
8	$AgBF_4$	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 the ratio of starting material to product. [c]**2a** (0.5 mmol), $ClCH_2CH_2Cl$ (2.0 mL), isolated yield in parentheses. [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.

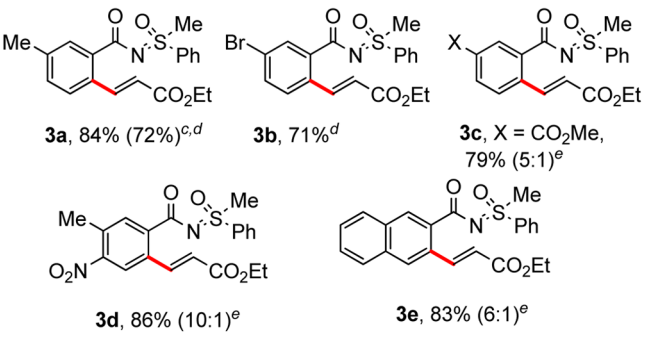
and solvents (Table 1). The reaction between **2a** and **1a** with 5.0 mol % of $[RuCl_2(p\text{-cymene})]_2$ and $Cu(OAc)_2{\cdot}H_2O$ (1.0 equiv) in 1,2-dichloroethane (DCE) at 120 °C produced a trace amount of *N*-[(*E*)-2-(3-ethoxy-3-oxoprop-1-en-1-yl)-5-methylbenzoyl]-MPS (**3a**), regioselectively 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 ^1H NMR (entry 2). Screening of $NaPF_6$, KPF_6, and $NaBF_4$ salts in this reaction was unsatisfactory (entries 3−5). The $AgBF_4$ was equally efficient, delivering **3a** in 92% yield (entry 6). To our delight, we observed the 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 to be the 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 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 by 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 electron-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**,[7p,q] demonstrating the effective directing group ability of the sulfoximine moiety. The

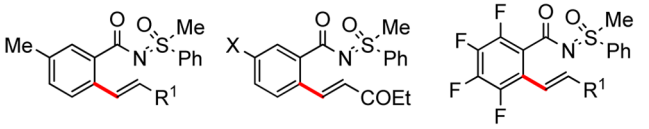
Scheme 1. *o*-C−H Alkenylation of *meta*- and Fluoro-Substituted *N*-Aroyl Derivatives[a,b]



R^1 = CO_2Et (**1a**), CO_2Me (**1b**), $CO_2{}^nBu$ (**1c**), SO_2Ph (**1d**), COEt (**1e**)



Different electron deficient alkenes



[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 the case of **3l**, ratio is detected by ^{19}F NMR. [f]**2f** (0.15 mmol) was employed.

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 electron-poor substrates **2a** and **2c** with ethyl vinyl ketone (**1e**) led to **3i** and **3j** 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 a minor amount of hydroarylation product along with the desired alkenylation compound was observed in ^1H NMR; the ratio of alkenylation and hydroarylation products is shown in parentheses.

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

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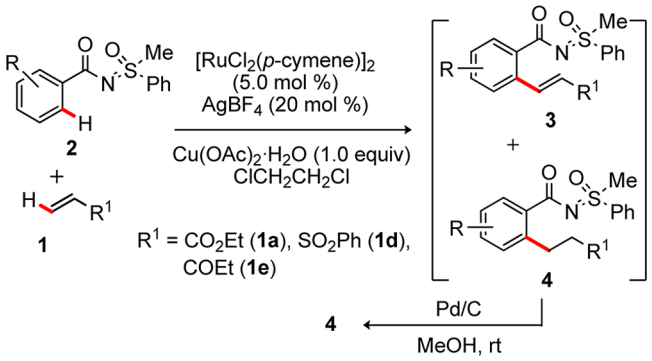
Table 2. Alkylation of *o*-Substituted Arenes[a,b]



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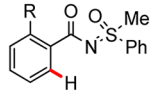
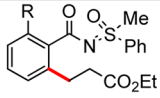
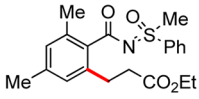
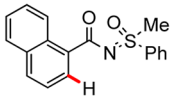
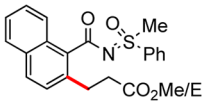
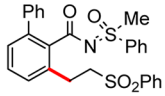
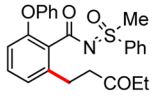
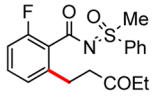
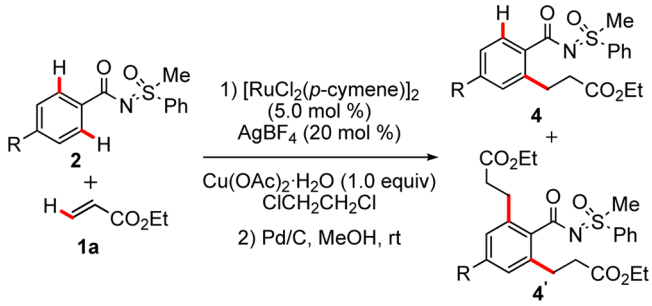
			
1	R = Me (**2g**)	1:2	**4b**, 80%
2	Ph (**2h**)	2:1	**4c**, 87%
3	OPh (**2i**)	2:1	**4d**, 74%
4	F (**2j**)	2:3	**4e**, 70%
			
5	**2k**	1:3	**4f**, 78%
			
6	**2l**	1:2	**4g**, 73% (14:3)[c]
7	**2h**	4:3	 **4h**, 82%
8	**2i**	2:1	 **4i**, 61%
9	**2j**	3:1	 **4j**, 64%

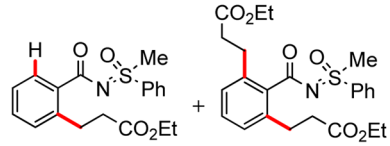
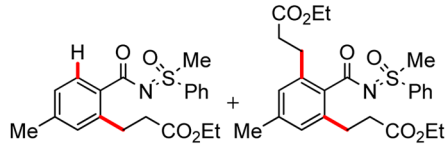
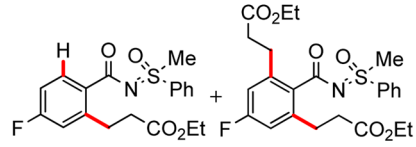
[a]Reaction conditions: **2** (0.5 mmol), alkene (1.0 mmol), [$RuCl_2$(*p*-cymene)]$_2$ (5.0 mol %), $AgBF_4$ (20 mol %), $Cu(OAc)_2{\cdot}H_2O$ (1.0 equiv), $ClCH_2CH_2Cl$ (2.0 mL), 120 °C for 24 h and Pd/C (50 mg, 20 wt %). [b]Isolated yields. [c]**2l** (0.32 mmol) was employed.

proto-demetalation over *β*-hydride elimination.[11] The inseparable hydroarylation and alkenylation products render the purification extremely difficult. To validate product isolation ease, the nonpurified 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.

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 ^1H NMR), displaying the possible formation of a nonseparable mixture of *o*-C–H mono-, dialkenylation, and their corresponding hydroarylation products; subsequent hydrogenation of the nonpurified mixture of compounds exhibited the corresponding mono- (**4k–m**) and dihydroarylation (**4′k–m**) products in overall good yields (Table 3). The formation of dihydroarylation product enables accessing highly peripheral decorated benzoic acid derivatives.

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



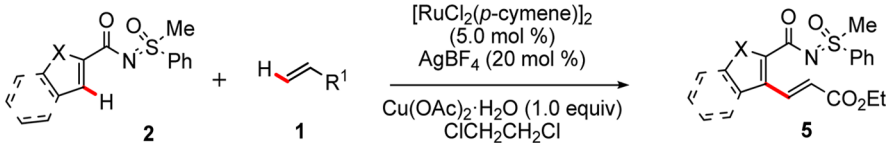
entry	2	4/4′
1	R = H, **2m**	 **4k** 69% (1:1)[b] **4′k**
2	R = Me, **2n**	 **4l** 71% (1:1)[b] **4′l**
3	R = F, **2o**	 **4m** 83% (9:4)[b] **4′m**

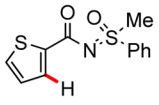
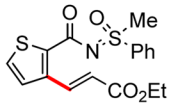
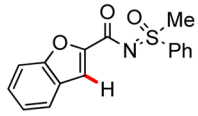
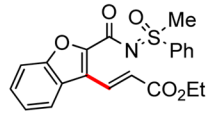
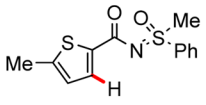
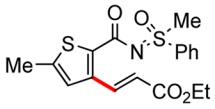
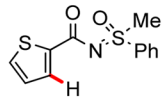
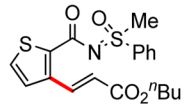
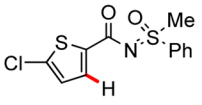
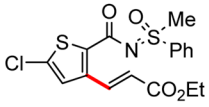
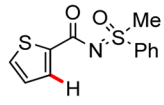
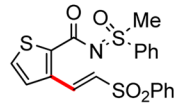
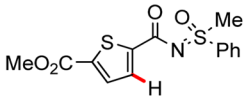
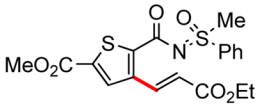
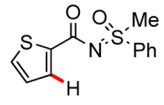
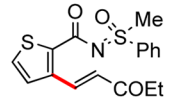
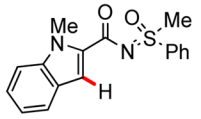
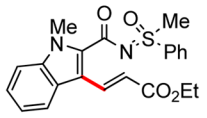
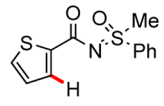
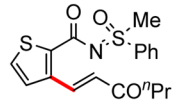
[a]Reaction conditions: **2** (0.5 mmol), **1a** (3.5 equiv), [$RuCl_2$(*p*-cymene)]$_2$ (5.0 mol %), $AgBF_4$ (20 mol %), $Cu(OAc)_2{\cdot}H_2O$ (1.0 equiv), $ClCH_2CH_2Cl$ (2.0 mL), 120 °C for 24 h, and Pd/C (50 mg, 20 wt %). [b]Combined yield of isolated mono- and dialkylation products (the mono/di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

dx.doi.org/10.1021/jo5008465 | J. Org. Chem. 2014, 79, 6123–6134

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

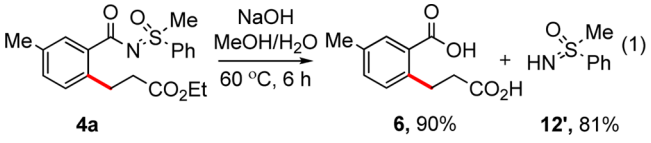


entry	2	5	entry	2	5
1	 **2p**	 **5a**, 88%	6	 **2u**	 **5f**, 88%
2	 **2q**	 **5b**, 90%	7	 **2p**	 **5g**, 82%
3	 **2r**	 **5c**, 85%	8	 **2p**	 **5h**, 95%
4	 **2s**	 **5d**, 84%	9	 **2p**	 **5i**, 91%
5	 **2t**	 **5e**, 60% (2:3)[c]	10	 **2p**	 **5j**, 86% (3:1)[c]

[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.

desired products **5a–d** in excellent yields; the chloro and ester functional groups did not interfere with the reaction efficiency. However, the *N*-methylindole 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 in 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 in a 3:1 ratio.

The practical utility of the present protocol is demonstrated with the ready cleavage of 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 analogue 3-(2-(naphthalen-1-ylmethylcarbamoyl)-4-(phenoxymethyl)phenyl)propanoic acid (**B**) (Scheme 2).[1] The synthesis begins 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 ^1H 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 the ester group delivered the desired EP3 antagonist molecule **B** in 34% overall yield from **9**.

To understand the mechanistic insights, a deuterium labeling experiment was performed on **2g** (eq 2). Gratifyingly, 95% deuterium incorporation at the *ortho*-C–H in **2g** occurred[13] when **2g** was 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.

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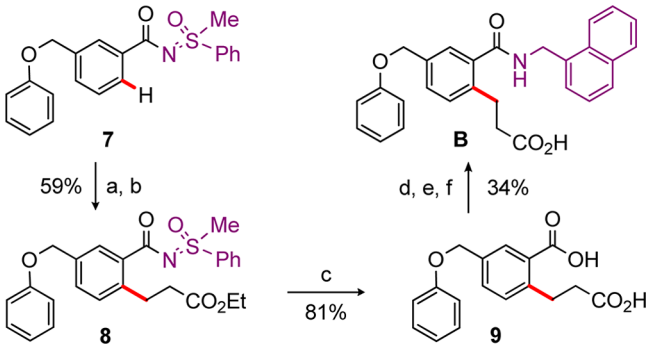
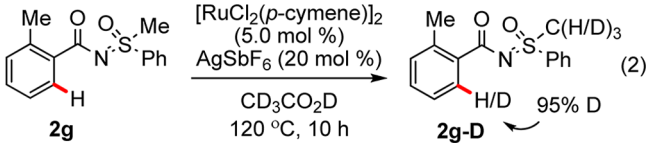
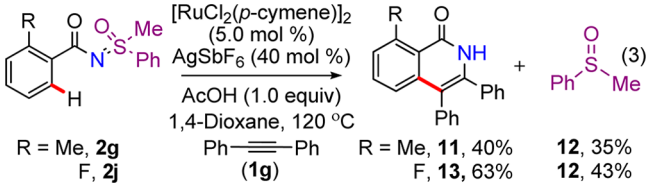
Scheme 2. Synthesis of EP3 Antagonist Analogue[a]



[a]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 °C to rt, overnight, 89%; (c) NaOH, MeOH/H_2O, 60 °C, 4 h; (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·H_2O, MeOH/THF, 60 °C, 4 h, 62%.



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 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).[14−16] 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 analogue.

EXPERIMENTAL SECTION

General Information. All 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 the TLC plate was accomplished with UV light (254 nm) and staining over an 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 the internal standard (^{1}H NMR, $CHCl_3$ at 7.26 ppm; ^{13}C NMR, $CDCl_3$ at 77.0 ppm). In a few instances, tetramethylsilane (TMS) at 0.00 ppm was used as the reference standard. Data for ^{1}H NMR are reported as follows: chemical shift (ppm), multiplicity (s = singlet; br s = broad singlet; d = doublet; br d = broad doublet, t = triplet; br t = broad triplet; q = quartet; m = multiplet), coupling constants, *J* (Hz), and integration. Data for ^{13}C NMR and ^{19}F NMR were reported in terms of chemical shift (ppm). IR spectra were reported in cm^{-1}. High-resolution mass spectra were obtained with ESI-TOF analyzer equipment. Melting points were determined by electrothermal heating and are uncorrected.

Materials. Unless otherwise noted, all 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 exactly match the reported values.

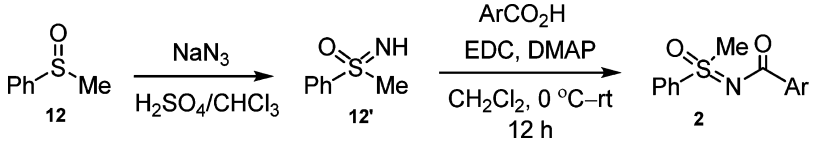
Following the known procedure, compounds **2a**, **2c**, **2d**, **2e**, **2g**, **2h**, **2j**, **2k**, **2l**, **2m**, **2n**, **2o**, and **2p** were prepared.[8a,b] Analytical and spectral data of these compounds exactly match the reported values.

Experimental Procedures. *Preparation of N-Aroyl S-Methyl-S-phenylsulfoximines.* Synthesis of methyl phenyl sulfoximine from sulfoxide is well established (Scheme 3).[8a]

General Procedure (GP-1): EDC Coupling.[8a] A solution of *N*′-(3-(dimethylamino)propyl)-*N*-ethylcarbodiimide, hydrochloride salt (EDC·HCl) (2.0 equiv), 4-*N*,*N*-dimethylaminopyridine (DMAP) (2.2 equiv), and benzoic acids (1.1 equiv) in CH_2Cl_2 (5.0 mL, for 1.0 mmol of sulfoximine) was stirred under an argon atmosphere. Sulfoximine (**12**′; 1.0 equiv) was introduced dropwise at 0 °C. The resulting reaction mixture was stirred for about 1 h at 0 °C and warmed to ambient temperature and continued overnight. Upon complete consumption of sulfoximine, the reaction mixture was acidified with hydrochloric acid (1 N). 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; mp = 99−100 °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 Hz, 1H), 8.03 (d, *J* = 7.6 Hz, 2H), 7.69 (br t, *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,

Scheme 3



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$CDCl_3$) 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 337.9850, found 337.9850.

*N-[2,3,4,5-Tetrafluorobenzoyl]-S-methyl-S-phenylsulfoximine (**2f**):* 0.42 g, 40% yield, colorless crystalline solid; mp = 104−106 °C; R_f = 0.50 (3:2 hexane/EtOAc); ^1H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 7.6 Hz, 2H), 7.72 (br t, 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; mp = 120−122 °C; R_f = 0.42 (3:2 hexane/EtOAc); ^1H NMR (400 MHz, $CDCl_3$) δ 7.94 (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, $CDCl_3$) δ 173.8, 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; mp = 129−131 °C; R_f = 0.30 (2:3 hexane/EtOAc); ^1H NMR (400 MHz, $CDCl_3$) δ 8.04 (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, $CDCl_3$) δ 168.7, 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; mp = 120−121 °C; R_f = 0.35 (3:2 hexane/EtOAc); ^1H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J = 7.6 Hz, 2H), 7.71 (br t, J = 7.4 Hz, 1H), 7.63 (br t, 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, $CDCl_3$) δ 167.7, 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; mp = 152−154 °C; 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; mp = 153−155 °C; 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; mp = 130−131 °C; 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 %), and $Cu(OAc)_2{\cdot}H_2O$ (20 mg, 0.1 mmol). Subsequently, the reaction tube was taken to the glovebox and the additives were introduced. The corresponding solvent (0.5 mL) was added to the mixture, and the resulting mixture was stirred at 120 °C 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 glovebox, 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 °C 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; mp = 95−97 °C; ^1H 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 (br t, J = 7.4 Hz, 1H), 7.62 (br t, J = 7.8 Hz, 2H), 7.47 (d, J = 7.6 Hz, 1H), 7.27 (br d, 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, $CDCl_3$) δ 175.4, 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**, 0.55 g, 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), and $AgSbF_6$ (254 mg, 0.74 mmol) in 1,2-DCE (10.0 mL) at 120 °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; mp = 110−112 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.48 (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-phenylsulfoximine (**3c**):* 164 mg, 79% yield; colorless crystalline solid; mp = 126−128 °C; ^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-nitro-benzoyl]-S-methyl-S-phenylsulfoximine (**3d**):* 180 mg, 86% yield;

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yellow crystalline solid; mp = 145−147 °C; ^{1}H 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-phenylsulfoximine (**3e**):* 170 mg, 83% yield; viscous liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (br d, J = 15.6 Hz, 1H), 8.61 (br s,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 (br t, 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; mp = 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 (br d, 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; mp = 157−159 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (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, $CDCl_3$) δ 174.6, 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 ^{13}C value is merged with another 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, $CDCl_3$) δ 8.45 (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 (br t, 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, $CDCl_3$) δ 201.7, 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-phenylsulfoximine (**3j**):* Following GP-2, reaction between **2c** and **1e** gave the inseparable alkenylation **3j** and hydroarylation products (4:1 by ^{1}H NMR; 144 mg, 72% yield) as colorless crystalline solid. ^{1}H 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 (br t, J = 7.6 Hz, 1H), 7.64 (br t, 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 ^{1}H NMR; 170 mg, 79% yield) as a pale yellow solid. ^{1}H 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 ^{13}C values that 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 a yellow viscous liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (br d, J = 7.2 Hz, 2H), 7.89 (br d, J = 7.6 Hz, 2H), 7.80 (br d, J = 15.6 Hz, 1H), 7.76−7.60 (m, 4H), 7.55 (br t, 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 ^{13}C values that 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 of *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 nonseparable mixture of alkenylation and hydroarylation products. To make the purification easy, the nonpurified mixture of compounds was subjected to hydrogenation.

Accordingly, a solution of nonpurified mixture of compounds in methanol was subjected to hydrogenation in the presence of Pd/C (50 mg, 20 wt %) under a 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; mp = 95−97 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 7.2 Hz, 2H), 7.66 (br t, 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

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(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; mp = 146−148 °C; ^1H 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; mp = 64−66 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 7.6 Hz, 2H), 7.68 (br t, J = 7.4 Hz, 1H), 7.61 (br t, 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; mp = 113−115 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 7.6 Hz, 2H), 7.68 (br t, J = 6.8 Hz, 1H), 7.61 (br t, J = 7.6 Hz, 2H), 6.85 (br d, 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** and **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** and **4′g** (94 mg, 4.6:1; ^1H NMR) in 73% yield. ^1H 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, $CDCl_3$) δ 178.3, 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; ^1H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 7.6 Hz, 2H), 7.68−7.59 (m, 2H), 7.55 (br t, J = 7.2 Hz, 2H), 7.50−7.28 (m, 10H), 7.21 (br t, J = 8.6 Hz, 2H), 3.55 (br t, J = 8.0 Hz, 2H), 3.33−3.19 (m, 4H), 3.18−3.08 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.5, 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; ^1H NMR (400 MHz, $CDCl_3$) δ 7.83 (br d, 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; ^1H NMR (400 MHz, $CDCl_3$) δ 8.07 (br d, J = 8.0 Hz, 2H), 7.68 (br t, J = 7.0 Hz, 1H), 7.62 (br t, J = 7.2 Hz, 2H), 7.25−7.16 (m, 1H), 6.98 (br d, 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 (br t, 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. ^1H NMR (400 MHz, $CDCl_3$) δ 8.07 (br d, J = 7.6 Hz, 2H), 8.04 (br d, J = 7.6 Hz, 1H), 7.70 (br t, J = 7.4 Hz, 1H), 7.63 (br t, 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**):* ^1H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, J = 7.6 Hz, 2H), 7.68 (br t, J = 7.4 Hz, 1H), 7.62 (br t, J = 7.4 Hz, 2H), 7.19 (t, J = 7.6 Hz, 1H), 7.08 (br d, 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. ^1H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 7.6 Hz, 2H), 7.97 (d, J = 8.0 Hz, 1H), 7.68 (br t, J = 7.2 Hz, 1H), 7.60 (br t, 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, $CDCl_3$) δ 176.0, 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**):* ^1H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, J = 7.6 Hz, 2H), 7.67 (br t, J = 7.2 Hz, 1H), 7.61 (br t, 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, $CDCl_3$) δ 178.5, 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. ^1H NMR (400 MHz, $CDCl_3$) δ 8.09 (dd, J = 6.4, 2.4 Hz, 1H), 8.03 (d, J = 7.6 Hz, 2H), 7.68 (br t, J = 7.4 Hz, 1H), 7.60 (br t, J = 7.6 Hz, 2H),

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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, $CDCl_3$) δ 174.9, 173.0, 163.9 (d, J = 252 Hz, 1C), 144.9 (d, J = 8.0 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-phenylsulfoximine (**4′m**):* ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, J = 8.0 Hz, 2H), 7.69 (br t, J = 6.8 Hz, 1H), 7.63 (br t, 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 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. mp = 143−145 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (d, J = 16.4 Hz, 1H), 8.06 (br d, J = 7.6 Hz, 2H), 7.69 (br t, J = 7.2 Hz, 1H), 7.62 (br t, 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. mp = 121−123 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (b, J = 16.0 Hz, 1H), 8.00 (d, J = 8.0 Hz, 2H), 7.63 (br t, 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. mp = 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 (br t, J = 7.2 Hz, 1H), 7.64 (br t, 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. mp = 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 (br t, J = 7.0 Hz, 1H), 7.64 (br t, 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-phenylsulfoximine (**5′e**):* Following 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 (br t, 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 (br t, 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. mp = 128−130 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (d, J = 15.6 Hz, 1H), 8.08 (br d, J = 7.2 Hz, 2H), 7.89 (br d, J = 7.2 Hz, 2H), 7.71 (br t, J = 7.0 Hz, 1H), 7.65 (br t, J = 7.4 Hz, 2H), 7.58 (br t, J = 7.2 Hz, 1H), 7.50 (br t, 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 (br t, 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 (br t, J = 7.4 Hz, 1H), 7.62 (br t, 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.

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General Procedure for the Hydrolysis of Hydroarylation Product (GP-4). To a solution of **4a** (0.3 mmol) in MeOH (2.0 mL) was added aqueous NaOH (5.0 M, 2.0 mL). The reaction mixture was heated at 60 °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 1 N 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 (270 mg) 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 (br t, 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, $CDCl_3$) δ 176.4, 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 aqueous NaOH afforded **6** (62 mg, 90%) and sulfoximine (42 mg, 81%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.45 (br s, 2H), 7.60 (s, 1H), 7.26 (d, J = 7.2 Hz, 1H), 7.20 (d, J = 7.6 Hz, 1H), 3.06 (br t, J = 7.6 Hz, 2H), 2.48−2.42 (m, 2H), 2.28 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 174.3, 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 °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) were added $NiCl_2 \cdot 6H_2O$ (2.0 g, 8.6 mmol) and $NaBH_4$ (0.82 g, 21.5 mmol) at 0 °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 Na_2SO_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.

Data 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 (br t, J = 7.2 Hz, 1H), 7.61 (br t, 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 (br s, 2H), 7.90 (s, 1H), 7.40 (br d, J = 7.6 Hz, 1H), 7.28−7.14 (m, 3H), 6.91−6.83 (m, 3H), 4.95 (s, 2H), 3.18 (br t, 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 monoesterification product 2-(3-methoxy-3-oxopropyl)-5-(phenoxymethyl)-benzoic acid (**9′**, 85%) and the diesterification 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-(dimethylamino)propyl)-*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 dropwise 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 (1 N). 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 (br s, 1H), 5.10 (br d, 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 (**B**):*[7] A solution of **10** (50 mg, 0.11 mmol) and LiOH·H_2O (5.0 mg, 0.11 mmol) in THF/MeOH (4.0 mL, 1:1) was heated at 60 °C for about 4 h. The solvent was evaporated. The crude mixture was diluted with CH_2Cl_2 (10 mL) and acidified with 1 N 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 **B** (30 mg, 62%) as colorless solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.15 (br s, 1H, OH), 8.99 (br t, 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 (br d, J = 6.0 Hz, 2H), 2.94 (br t, J = 8.0 Hz, 2H), 2.54 (br t, J = 8.0 Hz, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 174.2, 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) and 1,4-dioxane (2.0 mL) was taken in a Schlenk tube under an argon atmosphere. The resulting mixture was stirred at 120 °C for 24 h. Subsequently, the reaction mixture was cooled to ambient temperature, filtered through a small

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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) and 1,4-dioxane (1.0 mL) at 120 °C 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 = 9.0 Hz, 1C), 131.8, 129.1, 128.9, 128.5, 128.4, 127.5, 121.6 (d, J = 4.0 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.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

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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Notes

The authors declare no competing financial interest.

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