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Lewis Acid-Catalyzed Halonium Generation for Morpholine Synthesis and Claisen Rearrangement

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Abstract

We disclose here practical strategies toward the synthesis of morpholines and Claisen rearrangement products based on the divergent reactivity of a common halonium intermediate. These reactions employ widely available alkenes in a Lewis acid-catalyzed halo-etherification process that can then transform them into the desired products with exceptional regioselectivity for both activated and unactivated olefins. Our mechanistic probe reveals an interesting regiochemical kinetic resolution process.

Graphical Abstract

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Supporting Information

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^{1}H and ^{13}C NMR spectra of the amino alcohol starting material and the morpholine and Claisen rearrangement products (PDF)

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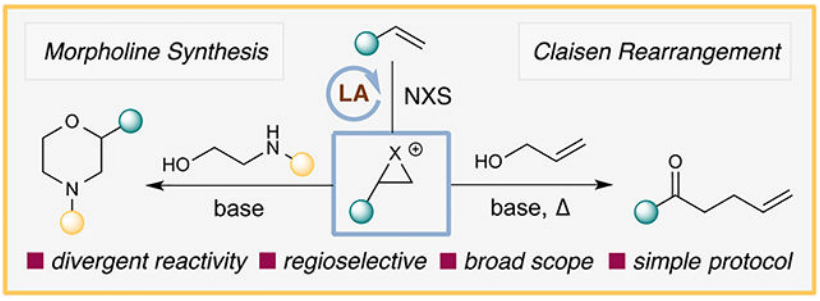

INTRODUCTION

Three-membered cyclic halonium (haliranium) is a classic intermediate that has been widely used in organic synthesis.[1] Structural elucidations of these intermediates by Olah, Wynberg, Brown, Nugent, Kochi, and others have significantly benefited our understanding of these unusual structures.[2] Variable-temperature ^{1}H NMR studies by Brown and elegant enantiospecific acetolysis experiments by Denmark further unveiled the intricacy of haloniums in olefin-to-olefin transfer processes, illuminating the challenges often encountered in asymmetric halofunctionalizations.[3] More recently, haloniums have been used as catalytic templates in olefin difunctionalizations by Muñiz[4] and Zhdankin[5] and in our recent works.[6] To aid our catalytic designs, discovering the practical synthetic utility and novel reactivity of haloniums is highly desirable.

We have long been interested in developing “-onium”-based alkene functionalization reactions that clearly benefit from the use of widely available alkene starting materials.[7] Morpholine is a highly valuable motif in bioactive molecules, and numerous synthetic strategies targeting this motif have been developed.[8] Several prominent methods, including intramolecular cyclizations,[9] the use of the memorable SnAP/SLAP reagents to couple with carbonyls,[10] and the adoption of vinyl sulfonium salts with electron-deficient olefins,[11] have been developed (Scheme 1a).[12] The Claisen rearrangement has long been recognized for its capacity to construct useful synthetic building blocks such as γ,δ-unsaturated carbonyls.[13] However, versatile synthetic access to the enol-ether precursor is rather limited.[14] An interesting recent example from the Buchwald group involves a cross-coupling strategy with allylic alcohols and vinyl iodides to access the Claisen precursor (Scheme 1b).[15] A unified strategy to access both morpholine and Claisen rearrangement products based on an alkene starting material would be an ideal alternative to the existing methods.

We envision that complementary reactivity can arise from the halonium by reacting it with either amino alcohols or allylic alcohols to generate the respective haloether intermediate prior to the morpholine synthesis or the Claisen rearrangement (Scheme 1c). We disclose here a halonium-based strategy to achieve the regioselective oxyamination of olefins for morpholine synthesis and the Claisen rearrangement couplings of allylic alcohols and alkenes. Our mechanistic investigation also unveiled an unusual kinetic resolution process that enabled even unactivated olefins to be highly regioselective in the morpholine synthesis.

RESULTS AND DISCUSSION

Our studies began with styrene **1** and 2-nitrobenzene-sulfonyl-protected amino alcohol **2** as the standard substrates. We were delighted to observe the formation of the halofunctionalized intermediate **3** when the NBS reagent was used as the halogen source (Scheme 2, entry 1). However, attempts to optimize the yield of **3** based on NBS alone proved difficult due to a lack of reactivity. To circumvent this issue, we introduced Lewis acids to facilitate the halonium formation.[16] Indeed, the introduction of several common Lewis acids significantly increased the production of **3**. $In(OTf)_3$ being the optimal Lewis acid, affording a 55% yield of **3** (Scheme 2, entry 2–4). Further tuning of the catalyst loading and the NBS stoichiometry led to the most optimal conditions shown in entry 8 (Scheme 2, entries 4–8). Under these conditions, the direct addition of DBU as a base following the optimal halogenation conditions smoothly produced the desired morpholine product **5** in a 76% isolated yield as a single regioisomer (Scheme 2, entry 9).

During our optimization, we often observed small amounts of the elimination byproduct from **3** when the base was added. While this was problematic for the morpholine synthesis, we speculated that an allylic alcohol such as 2-propen-1-ol **4** could be used instead to obtain the Claisen rearrangement precursor. With that in mind, we switched the halogen source to NIS, which was not only beneficial for the generation of intermediate **3** but also installed a better leaving group for the elimination process. Evaluation of the Lewis acid identity led to $Mg(OTf)_2$ as the optimal catalyst (Scheme 2, entries 10–12). Hence, the addition of DBU as the base at 80 °C effectively promoted both the elimination and the ensuing Claisen rearrangement to afford product **6** in a 65% isolated yield (Scheme 2, entry 13).

With these divergent synthetic applications in hand, we decided to first evaluate the substrate scopes for the morpholine synthesis. We quickly tested several electronically activated alkene substrates. In this regard, a series of cross-coupling-ready functional groups, including *p*-F, *p*-Cl, *p*-Br, and *p*-OPiv, were all well-tolerated and formed the desired products (Scheme 3, products **7**–**10**, respectively). In addition, α-methylstyrene and 2-vinylnaphthalene afforded the morpholine products **11** and **12**, respectively, as single regioisomers (Scheme 3, products **11** and **12**). Aliphatic olefins have proven to be a difficult class of substrates in the absence of directing groups for regioselective intermolecular olefin oxyamination reactions.[17] Under these conditions using NIS, a number of α-olefins containing alkyl, –OPiv, and –NPhth functional groups smoothly produced the morpholine products in excellent yields, albeit with diminished regioselectivities (Scheme 3, products **13**–**16**, respectively). Interestingly, α-olefins with slightly increased steric hindrance at the α-, β-, or even γ-positions all led to a significant boost in regioselectivity (Scheme 3, products **17**–**21**). Furthermore, several complex olefin substrates derived from estradiol, camphor, and vitamin E all proceeded to the desired products with excellent regioselectivities (Scheme 3, products **22**–**24**, respectively).

Encouraged by these findings, we then ventured to evaluate a range of amino alcohols for the morpholine synthesis. In this regard, a number of naturally derived amino alcohols effectively coupled with styrene to generate the desired morpholine products (Scheme 3, products **25**–**34**). For these cases, the stereochemistry was set during the

halofunctionalization step, resulting in a mixture of diastereomeric products. For product **32**, only the *cis*-diastereomeric product was observed due to the stereocenter next to the carbonyl group being racemized to avoid steric interactions of the *N*-nosyl group. Notably, highly sterically hindered amino alcohols could also participate in the reaction with reasonable efficiency (Scheme 3, product **28**–**31**).

With a good substrate scope in hand for the morpholine synthesis, we were intrigued by the regiochemical features observed from the unactivated olefins. (Scheme 3, examples **13**–**16** versus **17**–**21**). To understand the improved regioselectivities for products **17**–**21**, we carried out the iodoetherification process first and observed the regioselectivities from this process for both olefin substrates **35** (1-octene) and **36** (4-methyl-pent-1-ene) to be around 3:1 r.r. (Scheme 4). The regiochemical outcome here was not surprising given the stereoelectronic contrast of the terminal (sterically favored) versus that of the internal carbon (electronically favored).[18] Interestingly when the base was added to both regioisomeric mixtures, the iodoethers **37a** and **37b** of the less sterically hindered olefin led to the morpholine products in 3:1 r.r., while the iodoethers **38a** and **38b** of the more sterically hindered olefin led to highly regioselective outcomes. In this case, the cyclization process appeared to be the regio-determining step, suggesting that an apparent kinetic resolution process for the high regioselectivity was taking place.[19] Our findings here do raise the prospect that potential dynamic kinetic resolution could be developed for regiochemical purposes. Furthermore, while this may not be a concern for halide-catalyzed reactions that require the halide to be turned over, caution for rationalizing the high regioselectivity in stoichiometric halofunctionalizations must be exercised.

Satisfied with the morpholine substrate scope, we then turned our attention to the Claisen rearrangement process. Similarly, a range of styrenes bearing *para*-substitutions with –*t*-Bu, –OMe, –OPiv, and –F all proceeded smoothly to provide the rearranged products in reasonable yields (Scheme 5, products **39**–**42**, respectively). Reactions with activated olefins containing naphthalene, heteroarene, or β-methylstyrene all resulted in product formation with reasonable yields (Scheme 5, products **43**–**45**, respectively). A number of allylic alcohols also participated in the reaction with similar efficiencies (Scheme 5, products **46**–**48**). Furthermore, estradiol-derived styrene could afford the desired product with an excellent yield (Scheme 5, product **49**). Our protocol here demonstrates that simple allylic alcohols can be utilized to couple with alkenes to effect a Claisen rearrangement process to access γ,δ-unsaturated ketones, further highlighting the synthetic utility of halonium intermediates for potential catalytic chemical reaction designs.

In conclusion, we have disclosed here different synthetic utilities based on a common halonium intermediate toward both morpholine synthesis and the Claisen rearrangement. These practical protocols directly furnish useful pharmaceutical motifs and synthetic building blocks while providing interesting mechanistic insights for unexpected regiochemical features. These reaction settings and the mechanistic features will help to guide us in designing future chemical reactions involving halonium catalysis.

EXPERIMENTAL SECTION

General Information.

Commercial reagents and solvents were purchased from Sigma-Aldrich, Oakwood Chemicals, Alfa Aesar, Matrix Scientific, and Acros Organic and were used as received. Alkenes **10**,[20] **15**,[20] **16**,[21] **20**,[22] **21**,[23] **22**,[6f] **23**,[24] **24**,[6f] **39**,[20] **42**,[6f] and **44**[6f] were synthesized based on reported literature procedures. All the amino alcohol substrates were tosyl- or nosyl-protected based on a reported literature procedure.[25a] Amino alcohols **26a**, **30a**, **31a**, **32a**, **33a**, and **34a** were not known previously and are fully characterized here.[25b,c] Organic solutions were concentrated under reduced pressure on an IKA rotary evaporator using an acetone/dry ice bath. Chromatographic purification of products was accomplished using flash chromatography on 230–400 mesh silica gel. Thin-layer chromatography (TLC) was performed on Analtech 250 mm silica gel HLF UV-250 plates. Visualization of the developed plates was performed using fluorescence quenching and potassium permanganate. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker (600 and 150 MHz) or INOVA 600 (600 and 150 MHz) instrument and were internally referenced to residual protio-solvent signals (for CDCl3, 7.27 and 77.0 ppm, respectively). Data for ^{1}H NMR are reported as follows: chemicals shift (ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, h = heptet, m = multiplet, br = broad), integration, and coupling constant (Hz). ^{13}C spectra were reported as chemical shifts in ppm and multiplicity where appropriate. IR spectra were recorded on a PerkinElmer FT-IR spectrophotometer and reported in terms of the wavenumber of absorption (cm^{-1}). High-resolution mass spectra were obtained on a Waters Synapt time-of-flight (TOF) high-definition mass spectrometer (HDMS) using electrospray ionization at the University of Toledo, OH, and a Bruker MaXis TOF ultra-high-resolution ESI LC/MS at the University of Wisconsin—Madison, WI.

General Procedure for Amino Alcohol Substrate Synthesis.

To a 100 mL round-bottom flask equipped with a stir bar were added the amino alcohol substrate (5.0 mmol) and solvent (DCM, 10 mL). To the mixture was then added Et_3N (1 mL, 7.5 mmol) via syringe, followed by 2-nitrobenzenesulfonyl chloride (1.2 g, 5.5 mmol). The reaction mixture was then stirred for 16 h at room temperature. The reaction mixture was diluted with 10 mL of DCM, and the reaction was quenched with 10 mL of 0.1 N HCl. The organic layer was separated, and the aqueous layer was extracted with DCM (2 × 10 mL). The combined organic layer was concentrated under reduced pressure to give the crude product, which was purified by column chromatography on silica gel to afford the pure product.

General Procedure A for Lewis Acid-Catalyzed Morpholine Synthesis.

To an 8 mL vial equipped with a stir bar were added $In(OTf)_3$ (4 mg, 0.0075 mmol), NBS (78 mg, 0.4375 mmol), and the 2-nitrobenzenesulfonyl-protected amino alcohol (0.25 mmol). To the mixture was then added the solvent (DCM, 1.5 mL) via syringe, followed by the alkene (0.4375 mmol). The reaction mixture was then stirred for 1 h at room temperature. To the mixture was added DBU (114 μL, 0.75 mmol) after 1 h, and the mixture continued to stir for another 23 h. The reaction mixture was diluted with 2 mL of DCM, and the reaction was quenched with 2 mL of saturated $Na_2S_2O_3$ and 0.5 mL of 1 M HCl. The

organic layer was separated, and the aqueous layer was extracted with DCM (2 × 2 mL). The combined organic layer was concentrated under reduced pressure to give the crude product, which was purified by column chromatography on silica gel to afford the pure product.

General Procedure B for Lewis Acid-Catalyzed Morpholine Synthesis.

To an 8 mL vial equipped with a stir bar were added $In(OTf)_3$ (4 mg, 0.0075 mmol), NIS (98 mg, 0.4375 mmol), and *p*-toluenesulfonyl-protected amino alcohol (0.25 mmol). To the mixture was then added the solvent (DCM, 1.5 mL) via syringe, followed by the alkene (0.4375 mmol). The reaction mixture was then stirred for 1 h at room temperature. To the mixture was added DBU (114 μL, 0.75 mmol) after 1 h, and the mixture continued to stir for another 23 h. The reaction mixture was diluted with 2 mL of DCM, and the reaction was quenched with 2 mL of saturated $Na_2S_2O_3$ and 0.5 mL of 0.5 M HCl. The organic layer was separated, and the aqueous layer was extracted with DCM (2 × 2 mL). Combined organic layer was concentrated under reduced pressure to give the crude product, which was purified by column chromatography on silica gel to afford the pure product.

General Procedure C for the Lewis Acid-Catalyzed Claisen Rearrangement Reaction.

To an 8 mL vial equipped with a stir bar were added $Mg(OTf)_2$ (8 mg, 0.025 mmol) and NIS (113 mg, 0.5 mmol). To the mixture was then added the solvent (DCM, 0.25 mL) via syringe, followed by the alkene (0.5 mmol) and the allylic alcohol (0.25 mmol). The reaction mixture was then stirred for 8 h at room temperature. To the mixture was then added DBU (114 μL, 0.75 mmol) after 8 h, and the mixture continued to stir for another 36 h at 80 °C with heating in a pie-block. The reaction mixture was diluted with 2 mL of EtOAc, and the reaction was quenched with 2 mL of saturated $Na_2S_2O_3$. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate (2 × 2 mL). Combined organic layer was concentrated under reduced pressure to give the crude product, which was purified by column chromatography on silica gel to afford the pure product.

Procedure for Large-Scale Morpholine Synthesis.

To an 10 mL round-bottom flask equipped with a stir bar waere added $In(OTf)_3$ (16 mg, 0.03 mmol), NBS (312 mg, 1.74 mmol), and 2-nitrobenzenesulfonyl-protected 2-amino-1-ethanol (248 mg, 1.0 mmol). To the mixture was then added the solvent (DCM, 6 mL) via syringe, followed by styrene (200 μL, 1.74 mmol). The reaction mixture was then stirred for 1 h at room temperature. To the mixture was added DBU (456 μL, 3.0 mmol) after 1 h, and the mixture continued to stir for another 23 h. The reaction mixture was diluted with 5 mL of DCM, and the reaction was quenched with 5 mL of saturated $Na_2S_2O_3$ and 2.0 mL of 1 M HCl. The organic layer was separated, and the aqueous layer was extracted with DCM (2 × 5 mL). The combined organic layer was concentrated under reduced pressure to give the crude product, which was purified by column chromatography on SiO_2 (10–50% EtOAc/hexanes). The title compound was isolated as a white solid (255 mg, 73% yield).

Procedure for the Large-Scale Claisen Rearrangement Reaction.

To an 8 mL vial equipped with a stir bar were added $Mg(OTf)_2$ (32 mg, 0.1 mmol) and NIS (450 mg, 2.0 mmol). To the mixture was then added the solvent (DCM, 1.0 mL) via

syringe, followed by styrene (229 μL, 2.0 mmol) and the allylic alcohol (68 μL, 1.0 mmol). The reaction mixture was then stirred for 8 h at room temperature. To the mixture was added DBU (456 μL, 3.0 mmol) after 8 h, and the mixture continued to stir for another 36 h at 80 °C in metal pie-wedge over a heating plate. The reaction mixture was diluted with 8 mL of EtOAc, and the reaction was quenched with 8 mL of saturated $Na_2S_2O_3$. The rganic layer was separated, and the aqueous layer was extracted with ethyl acetate (2 × 5 mL). The combined organic layer was concentrated under reduced pressure to give the crude product, which was purified by column chromatography on silica gel (0–2% EtOAc/hexanes). The title compound was isolated as a colorless oil (109 mg, 68% yield).

N-(1-Hydroxy-2-methylpropan-2-yl)-2-nitrobenzenesulfonamide (26a).—This compound was prepared according to the general procedure for starting materials synthesis using 2-amino-2-methylpropan-1-ol (0.5 mL, 5.0 mmol). After purification by column chromatography on SiO_2 (70–80% EtOAc/hexanes), the title compound was isolated as a white solid (1.33 g, 97% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.19 (d, J = 7.7 Hz, 1 H), 7.86 (d, J = 7.3 Hz, 1 H), 7.79−7.69 (m, 2 H), 5.65 (s, 1 H), 3.52 (d, J = 5.5 Hz, 2 H), 2.43 (t, J = 5.9 Hz, 1 H), 1.25 (s, 7 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 147.7, 136.5, 133.4, 133.0, 130.4, 125.4, 70.1, 58.9, 24.5; IR (neat) 3595, 3256, 2985, 2910, 1537, 1439, 1366, 1318, 1145, 1125, 1055, 977 cm^{-1}; HRMS (ESI) m/z calcd for $C_{10}H_{15}N_2O_5S$ [(M + H)$^+$] 275.0702, found 275.0700.

(S)-N-(1-Hydroxy-3,3-dimethylbutan-2-yl)-2-nitrobenzenesulfonamide (30a).—This compound was prepared according the general procedure for starting materials synthesis using (*S*)-2-amino-3,3-dimethylbutan-1-ol (0.59 g, 5.0 mmol). After purification by column chromatography on SiO_2 (70–80% EtOAc/hexanes), the title compound was isolated as a white solid (1.36 g, 90% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.13 (d, J = 7.3 Hz, 1 H), 7.86 (d, J = 7.3 Hz, 1 H), 7.77−7.68 (m, 2 H), 5.56 (d, J = 8.8 Hz, 1 H), 3.78−3.66 (m, 1 H), 3.58 (dd, J = 7.7, 11.4 Hz, 1 H), 3.34−3.22 (m, 1 H), 1.84 (s, 1 H), 0.91 (s, 9 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 147.5, 135.2, 133.2, 132.9, 130.5, 125.2, 65.4, 62.3, 34.0, 26.9; IR (neat) 3559, 1527, 1424, 1363, 1338, 1157, 1087, 1048, 1028 cm^{-1}; HRMS (ESI) m/z calcd for $C_{12}H_{19}N_2O_5S$ [(M + H)$^+$] 303.1015, found 303.1008.

N-((2S,3R)-1-Hydroxy-3-methylpentan-2-yl)-2-nitrobenzenesulfonamide (31a).—This compound was prepared according to the general procedure for starting materials synthesis using (2*S*,3*R*)-2-amino-3-methylpentan-1-ol (0.59 g, 5.0 mmol). After purification by column chromatography on SiO_2 (70–80% EtOAc/hexanes), the title compound was isolated as a white solid (1.29 g, 85% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.20−8.11 (m, 1 H), 7.93−7.85 (m, 1 H), 7.80−7.70 (m, 2 H), 5.53 (d, J = 8.1 Hz, 1 H), 3.69−3.58 (m, 2 H), 3.42−3.35 (m, 1 H), 1.68 (br. s., 1 H), 1.66−1.59 (m, 1 H), 1.54−1.44 (m, 1 H), 1.16−1.05 (m, 1 H), 0.92−0.78 (m, 6 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 147.6, 134.7, 133.4, 132.9, 130.6, 125.3, 62.6, 61.0, 36.4, 25.1, 15.2, 11.3; IR (neat) 3337, 3101, 2964, 2934, 1535, 1424, 1361, 1338, 1167, 1120, 1059 cm^{-1}; HRMS (ESI) m/z calcd for $C_{12}H_{19}N_2O_5S$ [(M + H)$^+$] 303.1015, found 303.1010.

Methyl ((2-Nitrophenyl)sulfonyl)-D-serinate (32a).—This compound was prepared according to the general procedure for starting materials synthesis using methyl D-serinate (0.6 g, 5.0 mmol). After purification by column chromatography on SiO_2 (70–100% EtOAc/hexanes), the title compound was isolated as a white solid (1.39 g, 91% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.18−8.05 (m, 1 H), 8.03−7.91 (m, 1 H), 7.86−7.71 (m, 2 H), 6.51 (d, J = 7.0 Hz, 1 H), 4.36−4.21 (m, 1 H), 4.09−4.01 (m, 1 H), 4.01−3.94 (m, 1 H), 3.61 (s, 3 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 169.7, 147.7, 133.9, 133.8, 133.0, 130.5, 125.7, 63.8, 58.4, 52.9; IR (neat) 3577, 3278, 3091, 2971, 2892, 1738, 1542, 1438, 1353, 1259, 1166, 1123 cm^{-1}; HRMS (ESI) m/z calcd for $C_{10}H_{13}N_2O_7S$ [(M + H)$^+$] 305.0443, found 305.0439.

Methyl (2R)-3-Hydroxy-2-((4-nitrophenyl)sulfonamido)-butanoate (33a).—This compound was prepared according to the general procedure for starting materials synthesis using methyl (2*R*)-2-amino-3-hydroxybutanoate (0.67 g, 5.0 mmol). After purification by column chromatography on SiO_2 (70–100% EtOAc/hexanes), the title compound was isolated as a white solid (1.48 g, 93% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.12−8.04 (m, 1 H), 7.99−7.92 (m, 1 H), 7.80−7.70 (m, 2 H), 6.35 (d, J = 9.5 Hz, 1 H), 4.34 (dd, J = 6.4, 2.8 Hz, 1 H), 4.11 (dd, J = 9.4, 2.8 Hz, 1 H), 3.52 (s, 3 H), 1.99 (br. s., 1 H), 1.35 (d, J = 6.2 Hz, 3 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 170.3, 147.5, 134.1, 133.7, 132.9, 130.3, 125.5, 68.1, 61.8, 52.6, 19.9; IR (neat) 3476, 3259, 1726, 1547, 1444, 1359, 1254, 1170, 1090 cm^{-1}; HRMS (ESI) m/z calcd for $C_{11}H_{15}N_2O_7S$ [(M + H)$^+$] 319.0600, found 319.0606.

N-((1R,2S)-2-Hydroxy-2,3-dihydro-1H-inden-1-yl)-2-nitrobenzenesulfonamide (34a).—This compound was prepared according to the general procedure for starting materials synthesis using (1*R*,2*S*)-1-amino-2,3-dihydro-1H-inden-2-ol (0.75 g, 5.0 mmol). After purification by column chromatography on SiO_2 (70–80% EtOAc/hexanes), the title compound was isolated as a white solid (1.37 g, 82% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.28−8.22 (m, 1 H), 7.97−7.91 (m, 1 H), 7.84−7.75 (m, 2 H), 7.29−7.22 (m, 2 H), 7.20 (d, J = 3.3 Hz, 2 H), 6.16 (d, J = 8.1 Hz, 1 H), 4.93 (dd, J = 8.4, 4.8 Hz, 1 H), 4.40 (br. s., 1 H), 3.09 (dd, J = 16.7, 5.0 Hz, 1 H), 2.93 (d, J = 16.5 Hz, 1 H), 2.07 (br. s., 1 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 147.8, 139.3, 138.9, 134.5, 133.8, 133.0, 130.7, 128.8, 127.4, 125.6, 125.5, 124.4, 77.2, 76.8, 73.0, 62.3, 39.4; IR (neat) 3527, 3321, 2938, 1535, 1413, 1344, 1161, 1113, 1077 cm^{-1}; HRMS (ESI) m/z calcd for $C_{15}H_{14}N_2O_5SNa$ [(M + Na)$^+$] 357.0516, found 357.0522.

4-((2-Nitrophenyl)sulfonyl)-2-phenylmorpholine (5).—This compound was prepared according to general procedure A using *N*-(2-hydroxyethyl)-2-nitrobenzenesulfonamide (62 mg, 0.25 mmol) and styrene (50 μL, 0.4375 mmol). After purification by column chromatography on SiO_2 (10–20% EtOAc/hexanes), the title compound was isolated as a white solid (66 mg, 76% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97 (d, J = 7.8 Hz, 1 H), 7.77−7.67 (m, 2 H), 7.64 (d, J = 7.6 Hz, 1 H), 7.40−7.35 (m, 4 H), 7.35−7.30 (m, 1 H), 4.58 (dd, J = 10.4, 2.6 Hz, 1 H), 4.13 (dd, J = 11.7, 2.7 Hz, 1 H), 3.87 (d, J = 12.5 Hz, 1 H), 3.83 (dt, J = 11.8, 2.6 Hz, 1 H), 3.74 (d, J = 12.5 Hz, 1 H), 3.08 (dt, J = 12.1, 3.3 Hz, 1 H), 2.81 (dd, J = 12.3, 10.6, Hz, 1 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 148.4, 138.3, 133.9,

131.6, 131.0, 130.9, 128.6, 128.4, 126.0, 124.2, 77.6, 66.5, 51.5, 45.3; IR (neat) 2919, 2857, 1607, 1541, 1511, 1350, 1230, 1163 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{16}H_{17}N_2O_5S$ [(M + H)$^+$] 349.0858, found 349.0861.

2-(4-Fluorophenyl)-4-((2-nitrophenyl)sulfonyl)morpholine (7).—This compound was prepared according to general procedure A using *N*-(2-hydroxyethyl)-2-nitrobenzenesulfonamide (62 mg, 0.25 mmol) and 4-fluorostyrene (52 μL, 0.4375 mmol). After purification by column chromatography on SiO_2 (10–20% EtOAc/hexanes), the title compound was isolated as a white solid (84 mg, 92% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.8 Hz, 1 H), 7.77−7.67 (m, 2 H), 7.64 (d, *J* = 7.6 Hz, 1 H), 7.34 (dd, *J* = 8.3, 5.6, Hz, 2 H), 7.05 (t, *J* = 8.7 Hz, 2 H), 4.55 (dd, *J* = 10.4, 1.8, Hz, 1 H), 4.11 (dd, *J* = 11.7, 2.4, Hz, 1 H), 3.84 (d, *J* = 12.9 Hz, 1 H), 3.81 (dt, *J* = 12.0, 3.0, Hz, 1 H), 3.72 (d, *J* = 12.5 Hz, 1 H), 3.06 (dt, *J* = 12.1, 3.2, Hz, 1 H), 2.78 (t, *J* = 12.1 Hz, 1 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 163.4, 161.7, 148.3, 134.1, 134.1, 134.0, 131.7, 130.9, 130.9, 127.8, 127.8, 124.2, 115.5, 115.4, 66.5, 51.5, 45.2; IR (neat) 2919, 2857, 1607, 1541, 1511, 1350, 1230, 1163 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{16}H_{15}FN_2NaO_5S$ [(M + Na)$^+$] 389.0583, found 389.0570.

2-(4-Chlorophenyl)-4-((2-nitrophenyl)sulfonyl)morpholine (8).—This compound was prepared according to general procedure A using *N*-(2-hydroxyethyl)-2-nitrobenzenesulfonamide (62 mg, 0.25 mmol) and 4-chlorostyrene (52 μL, 0.4375 mmol). After purification by column chromatography on SiO_2 (10–20% EtOAc/hexanes), the title compound was isolated as a white solid (84 mg, 88% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.02−7.93 (m, 1 H), 7.79−7.68 (m, 2 H), 7.68−7.61 (m, 1 H), 7.39−7.28 (m, 4 H), 4.55 (dd, *J* = 10.5, 2.4 Hz, 1 H), 4.11 (dd, *J* = 11.7, 2.2 Hz, 1 H), 3.88−3.76 (m, 2 H), 3.72 (d, *J* = 12.5 Hz, 1 H), 3.06 (dt, *J* = 12.3, 3.3 Hz, 1 H), 2.75 (dd, *J* = 12.3, 10.5 Hz, 1 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 148.4, 136.8, 134.1, 134.0, 131.7, 131.0, 130.9, 128.7, 127.4, 124.2, 76.8, 66.5, 51.4, 45.2; IR (neat) 2914, 2874, 1587, 1547, 1376, 1359, 1165, 1121, cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{16}H_{15}ClN_2NaO_5S$ [(M + Na)$^+$] 405.0288, found 405.0287.

2-(4-Bromophenyl)-4-((2-nitrophenyl)sulfonyl)morpholine (9).—This compound was prepared according to general procedure A using *N*-(2-hydroxyethyl)-2-nitrobenzenesulfonamide (62 mg, 0.25 mmol) and 4-bromostyrene (57 μL, 0.4375 mmol). After purification by column chromatography on SiO_2 (10–20% EtOAc/hexanes), the title compound was isolated as a white solid (90 mg, 84% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.8 Hz, 1 H), 7.79−7.68 (m, 2 H), 7.65 (d, *J* = 7.6 Hz, 1 H), 7.50 (d, *J* = 8.5 Hz, 2 H), 7.25 (d, *J* = 8.3 Hz, 2 H), 4.54 (dd, *J* = 10.5, 2.2 Hz, 1 H), 4.11 (dd, *J* = 11.8, 2.3 Hz, 1 H), 3.84 (d, *J* = 12.5 Hz, 1 H), 3.80 (dt, *J* = 2.7, 11.8 Hz, 1 H), 3.72 (d, *J* = 12.5 Hz, 1 H), 3.06 (dt, *J* = 12.1, 3.2 Hz, 1 H), 2.74 (dd, *J* = 12.2, 10.7 Hz, 1 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 148.4, 137.3, 134.0, 131.7, 131.0, 130.9, 127.7, 124.2, 122.3, 76.9, 66.5, 51.4, 45.3; IR (neat) 2998, 2912, 2872, 1740, 1539, 1356, 1265, 1162, 1120, 1069 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{16}H_{15}BrN_2NaO_5S$ [(M + Na)$^+$] 448.9783, found 448.9767.

4-(4-((2-Nitrophenyl)sulfonyl)morpholin-2-yl)phenyl pivalate (10).—This compound was prepared according to general procedure A using *N*-(2-hydroxyethyl)-2-

nitrobenzenesulfonamide (62 mg, 0.25 mmol) and 4-vinylphenyl pivalate (89 mg, 0.4375 mmol). After purification by column chromatography on SiO_2 (10–30% EtOAc/hexanes), the title compound was isolated as a white solid (73 mg, 66% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.95 (d, J = 7.8 Hz, 1 H), 7.75−7.67 (m, 2 H), 7.63 (d, J = 7.8 Hz, 1 H), 7.37 (d, J = 8.5 Hz, 2 H), 7.05 (d, J = 8.5 Hz, 2 H), 4.58 (dd, J = 10.4, 2.1 Hz, 1 H), 4.12 (dd, J = 12.1, 2.1 Hz, 1 H), 3.84 (d, J = 12.5 Hz, 1 H), 3.81 (dt, J = 12.1, 3.1 Hz, 1 H), 3.73 (d, J = 12.5 Hz, 1 H), 3.06 (dt, J = 12.1, 3.1 Hz, 1 H), 2.75 (t, J = 11.4 Hz, 1 H), 1.36 (s, 9 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 177.0, 151.0, 148.4, 135.6, 134.0, 131.6, 131.0, 130.7, 127.0, 124.1, 121.6, 66.5, 51.6, 45.3, 39.0, 27.1; IR (neat) 2919, 2973, 2871, 1744, 1543, 1361, 1266, 1164 cm^{-1}; HRMS (ESI) m/z calcd for $C_{21}H_{25}N_2O_7S$ [(M + H)$^+$] 449.1382, found 449.1376.

2-Methyl-4-((2-nitrophenyl)sulfonyl)-2-phenylmorpholine (11).—This compound was prepared according to general procedure A with a slight modification using *N*-(2-hydroxyethyl)-2-nitrobenzenesulfonamide (62 mg, 0.25 mmol) and α-methylstyrene (65 μL, 0.4375 mmol). After the first step, to the mixture was added DBU (114 μL, 0.75 mmol) with DMSO (1 mL), and the mixture was stirred for 23 h. After purification by column chromatography on SiO_2 (10–20% EtOAc/hexanes), the title compound was isolated as a white solid (43 mg, 48% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.94 (d, J = 7.8 Hz, 1 H), 7.78−7.68 (m, 2 H), 7.62 (d, J = 7.6 Hz, 1 H), 7.46 (d, J = 7.8 Hz, 2 H), 7.37 (t, J = 7.7 Hz, 2 H), 7.31−7.27 (t, J = 7.8 Hz, 1 H), 3.94 (d, J = 12.5 Hz, 1 H), 3.88−3.81 (m, 1 H), 3.77−3.70 (m, 1 H), 3.40−3.31 (m, 1 H), 3.17 (d, J = 12.5 Hz, 2 H), 1.49 (s, 3 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 148.7, 142.3, 133.9, 131.4, 131.0, 130.1, 128.6, 127.4, 125.7, 124.1, 75.2, 60.7, 52.7, 45.6, 27.6; IR (neat) 2920, 2866, 1749, 1541, 1357, 1163, 1129, 1095, 1071 cm^{-1}; HRMS (ESI) m/z calcd for $C_{17}H_{18}N_2NaO_5S$ [(M + Na)$^+$] 385.0834, found 385.0823.

2-(Naphthalen-2-yl)-4-((2-nitrophenyl)sulfonyl)morpholine (12).—This compound was prepared according to general procedure A using *N*-(2-hydroxyethyl)-2-nitrobenzenesulfonamide (62 mg, 0.25 mmol) and 4-vinylnaphthalene (67 mg, 0.4375 mmol). After purification by column chromatography on SiO_2 (10–20% EtOAc/hexanes), the title compound was isolated as a white solid (44 mg, 44% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.98 (d, J = 8.1 Hz, 1 H), 7.88−7.82 (m, 4 H), 7.74 (t, J = 7.8 Hz, 1 H), 7.69 (t, J = 7.8 Hz, 1 H), 7.65 (d, J = 7.8 Hz, 1 H), 7.53−7.49 (m, 2 H), 7.47 (d, J = 8.5 Hz, 1 H), 4.76 (dd, J = 10.8, 2.4 Hz, 1 H), 4.19 (dd, J = 12.0, 2.7 Hz, 1 H), 3.96 (d, J = 12.5 Hz, 1 H), 3.90 (dt, J = 11.7, 2.7 Hz, 1 H), 3.78 (d, J = 12.5 Hz, 1 H), 3.13 (dt, J = 12.1, 3.3 Hz, 1 H), 2.88 (dd, J = 12.9, 10.5 Hz, 1 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 135.7, 133.9, 133.2, 133.1, 131.6, 131.0, 128.4, 128.0, 127.7, 126.3, 126.2, 125.1, 124.2, 123.7, 77.7, 66.6, 51.6, 45.4; IR (neat) 2920, 2855, 1592, 1541, 1439, 1509, 1358, 1271, 1164, 1100 cm^{-1}; HRMS (ESI) m/z calcd for $C_{20}H_{18}N_2NaO_5S$ [(M + Na)$^+$] 421.0834, found 421.0818.

2-Hexyl-4-tosylmorpholine (13).—This compound was prepared according to general procedure B using *N*-(2-hydroxyethyl)-4-methylbenzenesulfonamide (54 mg, 0.25 mmol) and 1-octene (69 μL, 0.4375 mmol). After purification by column chromatography on SiO_2 (10–20% EtOAc/hexanes), the title compound was isolated as a white solid (56 mg, 69% yield). Note that the reported spectral data are for the major regioisomer only. ^{1}H NMR (600

MHz, $CDCl_3$) δ 7.63 (d, J = 8.1 Hz, 2 H), 7.34 (d, J = 8.1 Hz, 2 H), 3.89 (dd, J = 11.4, 6.0 Hz, 1 H), 3.66 (dt, J = 11.5, 2.3 Hz, 1 H), 3.58−3.45 (m, 3 H), 2.45 (s, 3 H), 2.37 (dt, J = 11.4, 3.1 Hz, 1 H), 2.02 (t, J = 10.6 Hz, 1 H), 1.48−1.33 (m, 3 H), 1.33−1.21 (m, 8 H), 0.87 (t, J = 6.8 Hz, 3 H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 143.8, 132.1, 129.7, 127.8, 75.3, 65.9, 50.4, 45.5, 33.2, 31.6, 29.1, 25.0, 22.5, 21.5, 14.0; IR (neat) 2925, 2857, 1598, 1388, 1340, 1307, 1160, 1089, 1101, 1089 cm^{-1}; HRMS (ESI) m/z calcd for $C_{17}H_{28}NO_3S$ [$(M + H)^+$] 326.1790, found 326.1795.

2-Phenethyl-4-tosylmorpholine (14).—This compound was prepared according to general procedure B using *N*-(2-hydroxyethyl)-4-methylbenzenesulfonamide (54 mg, 0.25 mmol) and 4-phenyl-1-butene (66 μL, 0.4375 mmol). After purification by column chromatography on SiO_2 (10–20% EtOAc/hexanes), the title compound was isolated as a white solid (55 mg, 64% yield). For the major regioisomer: ^1H NMR (600 MHz, $CDCl_3$) δ 7.62 (d, J = 8.1 Hz, 2 H), 7.34 (d, J = 8.1 Hz, 2 H), 7.29 (t, J = 7.4 Hz, 2 H), 7.20 (t, J = 7.3 Hz, 1 H), 7.16 (d, J = 7.6 Hz, 2 H), 3.93 (dd, J = 12.0, 3.0 Hz, 1 H), 3.66 (dt, J = 11.5, 2.3 Hz, 1 H), 3.58−3.47 (m, 3 H), 2.81−2.72 (m, 1 H), 2.69−2.60 (m, 1H) 2.45 (s, 3 H), 2.41 (dt, J = 11.5, 3.3 Hz, 1 H), 2.08 (t, J = 10.5 Hz, 1 H), 1.81−1.72 (m, 1 H), 1.72−1.65 (m, 1 H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 143.8, 141.3, 132.0, 129.7, 128.4, 128.3, 127.8, 126.0, 74.3, 65.8, 50.3, 45.5, 34.7, 31.1, 21.5; IR (neat) 2979, 2916, 2849, 1597, 1497, 1446, 1340, 1160, 1103 cm^{-1}; HRMS (ESI) m/z calcd for $C_{19}H_{24}NO_3S$ [$(M + H)^+$] 346.1477, found 346.1485.

For the minor regioisomer: ^1H NMR (600 MHz, $CDCl_3$) δ 7.69 (d, J = 8.1 Hz, 2 H), 7.31 (d, J = 8.3 Hz, 3 H), 7.28 (d, J = 7.8 Hz, 2 H), 7.21 (t, J = 6.3 Hz, 1 H), 7.14 (d, J = 7.3 Hz, 2 H), 3.82 (t, J = 6.1 Hz, 1 H), 3.73 (d, J = 9.0 Hz, 1 H), 3.70 (d, J = 11.7 Hz, 1 H), 3.60 (d, J = 11.2 Hz, 1 H), 3.43 (dd, J = 11.6, 2.6 Hz, 1 H), 3.37−3.26 (m, 2 H), 2.65−2.58 (m, 2 H), 2.44 (s, 3 H), 2.05−1.96 (m, 1 H), 1.93−1.83 (m, 1 H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 143.4, 141.2, 138.0, 129.9, 128.4, 128.3, 127.0, 126.0, 68.3, 66.1, 53.2, 40.8, 32.6, 29.8, 21.5; IR (neat) 2963, 2928, 2861, 2849, 1447, 1345, 1330, 1273, 1156, 1113, 1085 cm^{-1}; HRMS (ESI) m/z calcd for $C_{19}H_{24}NO_3S$ [$(M + H)^+$] 346.1477, found 346.1456.

3-(4-Tosylmorpholin-2-yl)propyl pivalate (15).—This compound was prepared according to general procedure B using *N*-(2-hydroxyethyl)-4-methylbenzenesulfonamide (54 mg, 0.25 mmol) and pent-4-en-1-yl pivalate (74 mg, 0.4375 mmol). After purification by column chromatography on SiO_2 (20–30% EtOAc/hexanes), the title compound was isolated as a white solid (59 mg, 62% yield). Note that the reported spectral data are for the major regioisomer only. ^1H NMR (600 MHz, $CDCl_3$) δ 7.63 (d, J = 8.1 Hz, 2 H), 7.35 (d, J = 8.1 Hz, 2 H), 4.03 (t, J = 6.1 Hz, 2 H), 3.92−3.89 (dd, J = 12.1, 2.4 Hz, 1 H), 3.65 (dt, J = 12.1, 2.4 Hz, 1 H), 3.57−3.48 (m, 3 H), 2.44 (s, 3 H), 2.37 (dt, J = 11.5, 3.2 Hz, 1 H), 2.03 (t, J = 10.5 Hz, 1 H), 1.82−1.73 (m, 1 H), 1.70−1.60 (m, 1 H), 1.46 (q, J = 7.3 Hz, 2 H), 1.18 (s, 9 H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 178.5, 143.9, 132.0, 129.7, 127.8, 74.8, 65.9, 63.9, 50.3, 45.5, 38.7, 29.6, 27.1, 24.5, 21.5; IR (neat) 2957, 2865, 1721, 1447, 1479, 1344, 1287, 1162, 1098, 954 cm^{-1}; HRMS (ESI) m/z calcd for $C_{19}H_{29}NO_5S$ [$(M + Na)^+$] 406.1664, found 406.1664.

2-(3-(4-Tosylmorpholin-2-yl)propyl)isoindoline-1,3-dione (16).—This compound was prepared according to general procedure B using *N*-(2-hydroxyethyl)-4-methylbenzenesulfonamide (54 mg, 0.25 mmol) and 2-(pent-4-en-1-yl)isoindoline-1,3-dione (94 mg, 0.4375 mmol). After purification by column chromatography on SiO_2 (10–30% EtOAc/hexanes), the title compound was isolated as a white solid (63 mg, 59% yield). Note that the reported spectral data are for the major regioisomer only. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.86−7.81 (m, 2 H), 7.74−7.70 (m, 2 H), 7.62 (d, J = 8.1 Hz, 2 H), 7.34 (d, J = 8.1 Hz, 2 H), 3.85 (dd, J = 11.7, 2.0 Hz, 1 H), 3.68 (dt, J = 7.0, 2.9 Hz, 2 H), 3.63 (dt, J = 11.5, 2.3 Hz, 1 H), 3.56−3.46 (m, 3 H), 2.45 (s, 3 H), 2.34 (dt, J = 11.5, 3.2 Hz, 1 H), 2.01 (t, J = 11.1 Hz, 1 H), 1.91−1.79 (m, 1 H), 1.77−1.66 (m, 1 H), 1.50−1.37 (m, 2 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 168.4, 143.9, 133.9, 132.0, 129.7, 127.8, 123.2, 74.8, 65.8, 50.2, 45.5, 37.7, 30.4, 24.5, 21.5; IR (neat) 2922, 2871, 1771, 1708, 1432, 1465, 1455, 1400, 1331, 1163, 1111 cm^{-1}; HRMS (ESI) m/z calcd for $C_{22}H_{24}N_2O_5S$ [(M + Na)$^+$] 451.1304, found 451.1302.

2-Isobutyl-4-tosylmorpholine (17).—This compound was prepared according to general procedure B using *N*-(2-hydroxyethyl)-4-methylbenzenesulfonamide (54 mg, 0.25 mmol) and 4-methyl-1-pentene (56 μL, 0.4375 mmol). After purification by column chromatography on SiO_2 (10% EtOAc/hexanes), the title compound was isolated as a white solid (52 mg, 70% yield). The spectral data of this compound matched those from previously reported literature.[8] ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.63 (d, J = 8.4 Hz, 2 H), 7.34 (d, J = 8.1 Hz, 2 H), 3.88 (dd, J = 11.6, 2.0 Hz, 1 H), 3.65 (dt, J = 11.5, 2.4 Hz, 1 H), 3.59−3.54 (m, 1 H), 3.52 (d, J = 11.7 Hz, 2 H), 2.44 (s, 3 H), 2.37 (dt, J = 11.6, 3.3 Hz, 1 H), 2.01 (t, J = 10.6 Hz, 1 H), 1.79−1.70 (m, 1 H), 1.40−1.32 (m, 1 H), 1.16−1.09 (m, 1 H), 0.90 (d, J = 3.3 Hz, 3 H), 0.89 (d, J = 3.3 Hz, 3 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 143.8, 132.0, 129.7, 127.8, 73.5, 65.8, 50.6, 45.5, 42.1, 24.0, 23.1, 22.1, 21.5; IR (neat) 2953, 2865, 1706, 1597, 1454, 1346, 1336, 1160, 1102, 1086 cm^{-1}.

2-Benzyl-4-tosylmorpholine (18).—This compound was prepared according to general procedure B using *N*-(2-hydroxyethyl)-4-methylbenzenesulfonamide (54 mg, 0.25 mmol) and allylbenzene (59 μL, 0.4375 mmol). After purification by column chromatography on SiO_2 (10% EtOAc/hexanes), the title compound was isolated as a white solid (44 mg, 53% yield). The spectral data of this compound matched those from previously reported literature.[26] ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.62 (d, J = 8.1 Hz, 2 H), 7.36 (d, J = 7.8 Hz, 2 H), 7.31 (t, J = 7.4 Hz, 2 H), 7.24 (t, J = 7.2 Hz, 1 H), 7.17 (d, J = 7.3 Hz, 2 H), 3.90 (d, J = 11.5 Hz, 1 H), 3.81−3.73 (m, 1 H), 3.64 (dt, J = 11.5, 2.2 Hz, 1 H), 3.56 (d, J = 11.5 Hz, 1 H), 3.50 (d, J = 11.5 Hz, 1 H), 2.79 (dd, J = 13.9, 7.3 Hz, 1 H), 2.67 (dd, J = 13.9, 5.6 Hz, 1 H), 2.46 (s, 3 H), 2.42 (dt, J = 11.4, 2.8 Hz, 1 H), 2.14 (t, J = 10.6 Hz, 1 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 143.9, 136.9, 132.1, 129.7, 129.1, 128.5, 127.8, 126.6, 75.9, 65.9, 49.9, 45.4, 39.6, 21.5; IR (neat) 2967, 2858, 1724, 1596, 1445, 1345, 1164, 1117, 1097, 1068 cm^{-1}.

2-Cyclohexyl-4-tosylmorpholine (19).—This compound was prepared according to general procedure B using *N*-(2-hydroxyethyl)-4-methylbenzenesulfonamide (54 mg, 0.25 mmol) and vinylcyclohexane (60 μL, 0.4375 mmol). After purification by column

chromatography on SiO_2 (10–20% EtOAc/hexanes), the title compound was isolated as a white solid (20 mg, 25% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.64 (d, J = 8.1 Hz, 2 H), 7.35 (d, J = 7.8 Hz, 2 H), 3.92−3.86 (dd, J = 12.1, 1.8 Hz, 1 H), 3.67−3.57 (m, 2 H), 3.51 (d, J = 11.5 Hz, 1 H), 3.28−3.22 (m, 1 H), 2.45 (s, 3 H), 2.35 (dt, J = 11.4, 3.3 Hz, 1 H), 2.08 (t, J = 10.7 Hz, 1 H), 1.83 (d, J = 12.9 Hz, 1 H), 1.77−1.68 (m, 2 H), 1.67−1.56 (m, 2 H), 1.39−1.29 (m, 1 H), 1.23−1.10 (m, 3 H), 1.07−0.91 (m, 2 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 143.8, 132.2, 129.7, 127.8, 79.4, 65.9, 48.3, 45.6, 40.8, 28.7, 28.5, 26.3, 25.9, 25.8, 21.5; IR (neat) 2921, 2846, 1600, 1441, 1338, 1308, 1162, 1101, 1092, 1063 cm^{-1}; HRMS (ESI) m/z calcd for $C_{17}H_{26}NO_3S$ [(M + H)$^+$] 324.1633, found 324.1613.

N, 4-Dimethyl-N-((4-tosylmorpholin-2-yl)methyl)-benzenesulfonamide (20).— This compound was prepared according to general procedure B using *N*-(2-hydroxyethyl)-4-methylbenzenesulfonamide (54 mg, 0.25 mmol) and *N*-allyl-*N*,4-dimethylbenzenesulfonamide (99 mg, 0.4375 mmol). After purification by column chromatography on SiO_2 (10–30% EtOAc/hexanes), the title compound was isolated as a white solid (37 mg, 34% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.64 (d, J = 8.1 Hz, 2 H), 7.35 (d, J = 7.8 Hz, 2 H), 3.92−3.86 (dd, J = 12.1, 1.8 Hz, 1 H), 3.67−3.57 (m, 2 H), 3.51 (d, J = 11.5 Hz, 1 H), 3.28−3.22 (m, 1 H), 2.45 (s, 3 H), 2.35 (dt, J = 11.4, 3.3 Hz, 1 H), 2.08 (t, J = 10.7 Hz, 1 H), 1.83 (d, J = 12.9 Hz, 1 H), 1.77−1.68 (m, 2 H), 1.67−1.56 (m, 2 H), 1.39−1.29 (m, 1 H), 1.23−1.10 (m, 3 H), 1.07−0.91 (m, 2 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 143.8, 132.2, 129.7, 127.8, 79.4, 65.9, 48.3, 45.6, 40.8, 28.7, 28.5, 26.3, 25.9, 25.8, 21.5; IR (neat) 2920, 2844, 1596, 1453, 1345, 1329, 1153, 1108, 1087 cm^{-1}; HRMS (ESI) m/z calcd for $C_{20}H_{27}N_2O_5S_2$ [(M + H)$^+$] 439.1361, found 439.1364.

2-(2-((tert-Butyldimethylsilyl)oxy)ethyl)-4-tosylmorpholine (21).—This compound was prepared according to general procedure B using *N*-(2-hydroxyethyl)-4-methylbenzenesulfonamide (54 mg, 0.25 mmol) and *tert*-butyldimethylsilyl-protected homoallylic alcohol (82 mg, 0.4375 mmol). After purification by column chromatography on SiO_2 (10–20% EtOAc/hexanes), the title compound was isolated as a white solid (53 mg, 53% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.64 (d, J = 7.8 Hz, 2 H), 7.35 (d, J = 8.1 Hz, 2 H), 3.88 (d, J = 10.3 Hz, 1 H), 3.73−3.63 (m, 4 H), 3.60 (d, J = 11.2 Hz, 1 H), 3.53 (d, J = 11.2 Hz, 1 H), 2.45 (s, 3 H), 2.42−2.35 (m, 1 H), 2.09 (t, J = 10.7 Hz, 1 H), 1.67−1.53 (m, 2 H), 0.90 (s, 9 H), 0.05 (s, 3 H), 0.04 (s, 3 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 143.8, 132.2, 129.7, 127.8, 72.5, 65.8, 58.7, 50.5, 45.5, 36.2, 25.9, 21.5, 18.3, −5.4; IR (neat) 2953, 2929, 2887, 2857, 1597, 1454, 1349, 1250, 1161, 1110 cm^{-1}; HRMS (ESI) m/z calcd for $C_{19}H_{34}NO_4SSi$ [(M + H)$^+$] 400.1978, found 400.1958.

(8R,9S,13S,14S,17S)-13-Methyl-3-(4-((2-nitrophenyl)sulfonyl)-morpholin-2-yl)-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-17-yl Pivalate (22).—This compound was prepared according to general procedure A using *N*-(2-hydroxyethyl)-2-nitrobenzenesulfonamide (62 mg, 0.25 mmol) and (8*R*,9*S*,13*S*,14*S*,17*S*)-13-methyl-3-vinyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-17-yl pivalate (160 mg, 0.4375 mmol). After purification by column chromatography on SiO_2 (10–20%EtOAc/hexanes), the title compound was isolated as a white solid (94 mg, 62% yield). ^{1}H NMR (600 MHz, $CDCl_3$)

δ 7.94 (d, *J* = 7.8 Hz, 1 H), 7.71 (t, *J* = 7.6 Hz, 1 H), 7.67 (t, *J* = 7.6 Hz, 1 H), 7.62 (d, *J* = 7.8 Hz, 1 H), 7.25 (s, 1 H), 7.10 (d, *J* = 7.8 Hz, 1 H), 7.06 (br. s., 1 H), 4.65 (t, *J* = 8.3 Hz, 1 H), 4.49 (d, *J* = 9.8 Hz, 1 H), 4.09 (d, *J* = 11.5 Hz, 1 H), 3.85−3.75 (m, 2 H), 3.71 (d, *J* = 12.5 Hz, 1 H), 3.05 (t, *J* = 12.0 Hz, 1 H), 2.86 (d, *J* = 5.1 Hz, 2 H), 2.79 (t, *J* = 11.5 Hz, 1 H), 2.29−2.17 (m, 3 H), 1.94−1.86 (m, 2 H), 1.80−1.70 (m, 1 H), 1.53−1.33 (m, 8 H), 1.20 (s, 9 H), 0.83 (s, 3 H); $^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$) δ 178.6, 148.4, 140.5, 137.0, 135.5, 133.9, 131.6, 131.0, 130.9, 130.9, 126.6, 126.6, 125.6, 124.1, 123.4, 123.3, 82.2, 77.6, 77.5, 66.5, 51.5, 51.5, 49.8, 45.3, 44.2, 43.0, 38.9, 38.2, 36.9, 29.5, 29.4, 27.5, 27.2, 27.1, 25.9, 23.3, 12.1; IR (neat) 2970, 1725, 1544, 1479, 1438, 1370, 1289, 1161, 1130, 1100 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{33}H_{43}N_2O_7S$ $[(M + H)^+]$ 611.2791, found 611.2795.

4-Tosyl-2-(((1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl)oxy)-methyl)morpholine (23).—This compound was prepared according to general procedure B using *N*-(2-hydroxyethyl)-4-methylbenzenesulfonamide (54 mg, 0.25 mmol) and 2-(allyloxy)-1,7,7-trimethylbicyclo[2.2.1]heptane (85 mg, 0.4375 mmol). After purification by column chromatography on SiO_2 (10–30% EtOAc/hexanes), the title compound was isolated as a white solid (38 mg, 36% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.73 (d, *J* = 9.2 Hz, 2 H_{Min}), 7.65 (d, *J* = 7.8 Hz, 2 H_{Maj}), 7.35 (d, *J* = 8.1 Hz, 2 H_{Maj}), 7.32 (d, *J* = 7.2 Hz, 2 H_{Min}) 3.98 (dd, *J* = 11.7, 4.2 Hz, 1 H_{Min}), 3.91 (d, *J* = 11.7 Hz, 1 H_{Maj}), 3.89−3.85 (m, 1 H_{Min}), 3.82−3.64 (m, 3 H_{Maj} + 3 H_{Min}), 3.57−3.47 (m, 3 H_{Maj}), 3.21 (t, *J* = 12.0 Hz, 1 H_{Min}), 2.45 (s, 3 H_{Maj}), 2.44 (s, 3 H_{Min}), 2.43−2.37 (m, 1 H_{Maj}), 2.20 (q, *J* = 12.5 Hz, 1 H_{Maj}), 2.12−2.0 (m, 1 H_{Maj} + 1 H_{Min}), 1.94−1.84 (m, 1 H_{Maj} + 1 H_{Min}), 1.75−1.65 (m, 1 H_{Maj} + 1 H_{Min}), 1.65−1.57 (m, 2 H_{Maj}), 1.23−1.12 (m, 2 H_{Maj} + 2 H_{Min}), 1.00−0.90 (m, 1 H_{Maj} + 2 H_{Min}), 0.88−0.77 (6 singlets, 9 H_{Maj} + 9 H_{Min}); $^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$) δ 143.9, 143.5, 137.79, 137.76, 132.1, 132.0, 129.8, 129.7, 127.9, 127.0, 85.7, 85.64, 85.57, 85.1, 74.4, 74.2, 70.6, 70.4, 66.3, 66.2, 66.02, 66.04, 65.9, 65.8, 65.6, 65.1, 52.5, 52.1, 49.2, 48.2, 47.89, 47.86, 47.8, 47.7, 45.58, 45.57, 45.0, 44.9, 41.59, 41.56, 36.08, 36.05, 36.0, 28.2, 26.6, 26.51, 26.48, 21.6, 21.5, 19.7, 18.8, 14.03, 14.01, 14.98, 13.9; IR (neat) 2949, 2872, 1598, 1453, 1388, 1349, 1306, 1164, 1095, 1019 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{22}H_{33}NNaO_4S$ $[(M + Na)^+]$ 430.2028, found 430.2012.

2-((((2S)-2,5,7,8-Tetramethyl-2-(4,8,12-trimethyltridecyl)-chroman-6-yl)oxy)methyl)-4-tosylmorpholine (24).—This compound was prepared according to general procedure B using *N*-(2-hydroxyethyl)-4-methylbenzenesulfonamide (54 mg, 0.25 mmol) and (*S*)-6-(allyloxy)-2,5,7,8-tetramethyl-2-(4-methylpentyl)chromane (145 mg, 0.4375 mmol). After purification by column chromatography on SiO_2 (10–30% EtOAc/hexanes), the title compound was isolated as a white solid (49 mg, 29% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.1 Hz, 2 H), 7.36 (d, *J* = 7.8 Hz, 2 H), 4.01 (d, *J* = 11.5 Hz, 1 H), 3.97−3.89 (m, 1 H), 3.82−3.73 (m, 2 H), 3.66 (d, *J* = 3.0 Hz, 2 H), 3.57 (d, *J* = 11.2 Hz, 1 H), 2.56 (t, *J* = 6.6 Hz, 2 H), 2.52−2.40 (m, 5 H), 2.13 (s, 3 H), 2.09 (s, 3 H), 2.07 (s, 3 H), 1.86−1.70 (m, 2 H), 1.63−1.50 (m, 3 H), 1.50−1.41 (m, 2 H), 1.41−1.34 (m, 3 H), 1.34−1.24 (m, 8 H), 1.23 (s, 3 H), 1.19−1.01 (m, 7 H), 0.93−0.80 (4ds, 3*4 = 12 H); $^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$) δ 148.0, 147.4, 144.0, 131.9, 129.8, 127.9, 127.5, 125.6, 123.0, 117.6, 74.8, 74.3, 72.8, 66.0, 47.5, 45.5, 40.0, 39.3, 37.5, 37.4, 37.4, 37.4, 37.3, 37.3, 32.8, 32.7, 32.7, 31.2, 31.1,

28.0, 24.8, 24.8, 24.4, 23.8, 22.7, 22.6, 21.5, 21.0, 21.0, 20.6, 19.7, 19.7, 19.6, 19.6, 19.6, 12.6, 11.8; IR (neat) 2923, 2865, 1598, 1455, 1350, 1377, 1350, 1257, 1167, 1087, 1060 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{41}H_{65}NNaO_5S$ [(M + Na)$^+$] 706.4481, found 706.4471.

(5S)-5-Methyl-4-((2-nitrophenyl)sulfonyl)-2-phenylmorpholine (25).—This compound was prepared according to general procedure A using 2-nitrobenzenesulfonamide-protected (*S*)-alaninol (65 mg, 0.25 mmol) and styrene (50 μL, 0.4375 mmol). After purification by column chromatography on SiO_2 (10–20% EtOAc/hexanes), the title compound was isolated as a white solid (65 mg, 72% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.13 (d, *J* = 7.8 Hz, 1 H_{Maj}), 8.09 (d, 7.8 Hz, 1 H_{Min}), 7.79−7.66 (m, 3 H_{Maj} + 3 H_{Min}), 7.44−7.29 (m, 5 H_{Maj} + 5 H_{Min}), 4.68 (dd, *J* = 8.5, 2.4 Hz, 1 H_{maj}), 4.47 (dd, *J* = 11.0, 2.7 Hz, 1 H_{Min}), 4.09−4.02 (m, 1 H_{Min}), 3.97 (dd, *J* = 12.8, 2.8 Hz, 1 H_{Maj}), 3.89 (dd, *J* = 12.0, 3.2 Hz, 1 H_{Maj}), 3.86 (m, 2 H_{Min}), 3.71 (dd, *J* = 13.6, 2.6 Hz, 1 H_{Min}), 3.61 (m, 1 H_{Maj}), 3.41 (dd, *J* = 11.7, 8.8 Hz, 1 H_{Maj}), 3.27 (dd, *J* = 13.4, 11.0 Hz, 1 H_{Min}), 3.18 (dd, *J* = 12.9, 8.8 Hz, 1 H_{Maj}), 1.41 (d, *J* = 6.8 Hz, 3 H_{Min}), 1.11 (d, *J* = 6.3 Hz, 3 H_{Maj}); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 147.8, 147.7, 138.5, 138.1, 134.6, 133.8, 133.7, 133.5, 132.0, 131.9, 130.9, 130.2, 128.5, 128.5, 128.4, 128.1, 126.3, 126.0, 124.4, 124.3, 78.0, 76.5, 71.2, 70.7, 52.9, 50.2, 48.8, 46.3, 15.1, 15.0; IR (neat) 2979, 2920, 2864, 1540, 1441, 1386, 1349, 1265, 1162, 1125 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{17}H_{19}N_2O_5S$ [(M + H)$^+$] 363.1015, found 363.1016.

5,5-Dimethyl-4-((2-nitrophenyl)sulfonyl)-2-phenylmorpholine (26).—This compound was prepared according to general procedure A using 2-nitrobenzenesulfonamide-protected 2-amino-2-methylpropan-1-ol (67 mg, 0.25 mmol) and styrene (50 μL, 0.4375 mmol). After purification by column chromatography on SiO_2 (10–20% EtOAc/hexanes), the title compound was isolated as a white solid (61 mg, 65% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.25−8.19 (m, 1 H), 7.77−7.68 (m, 3 H), 7.47 (d, *J* = 7.3 Hz, 2 H), 7.40 (t, *J* = 7.6 Hz, 2 H), 7.37−7.32 (m, 1 H), 4.64 (dd, *J* = 10.9, 2.6 Hz, 1 H), 3.88 (dd, *J* = 13.3, 2.8 Hz, 1 H), 3.51 (d, *J* = 11.7 Hz, 1 H), 3.46 (d, *J* = 11.5 Hz, 1 H), 3.20 (dd, *J* = 13.2, 11.0 Hz, 1 H), 1.59 (s, 3 H), 1.14 (s, 3 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 147.5, 138.5, 136.3, 133.5, 132.2, 130.4, 128.5, 128.2, 126.1, 124.5, 77.9, 77.3, 57.7, 48.8, 23.2, 21.2; IR (neat) 2922, 2862, 1725, 1536, 1463, 1366, 1333, 1304, 1159, 1088 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{18}H_{20}N_2NaO_5S$ [(M + Na)$^+$] 399.0991, found 399.0967.

(5S)-5-Benzyl-4-((2-nitrophenyl)sulfonyl)-2-phenylmorpholine (27).—This compound was prepared according to general procedure A using 2-nitrobenzenesulfonamide-protected (*S*)-phenylalaninol (84 mg, 0.25 mmol) and styrene (50 μL, 0.4375 mmol). After purification by column chromatography on SiO_2 (10–20% EtOAc/hexanes), the title compound was isolated as a white solid (78 mg, 71% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.07 (d, *J* = 7.3 Hz, 1 H_{Maj}), 7.93 (d, *J* = 7.8 Hz, 1 H_{Min}), 7.75−7.56 (m, 3 H_{Maj} + 3 H_{Min}), 7.46−7.41 (m, 1 H_{Maj}), 7.39 (t, *J* = 7.3 Hz, 1 H_{Maj}), 7.36−7.31 (m, 1 H_{Min}), 7.31−7.12 (m, 8 H_{Maj} + 8 H_{Min}), 4.90 (t, *J* = 3.8 Hz, 1 H_{Maj}), 4.51 (dd, *J* = 10.8, 2.4 Hz, 1 H_{Min}) 4.00 (dd, *J* = 13.4, 3.7 Hz, 1 H_{Maj} + 1 H_{Min}), 3.91 (d, *J* = 11.7 Hz, 1 H_{Min}), 3.88−3.80 (m, 1 H_{Maj} + 1 H_{Min}), 3.76 (dd, *J* = 13.4, 4.6 Hz, 1 H_{Maj}), 3.73−3.66 (m, 1 H_{Maj} + 1 H_{Min}), 3.46 (dd, *J* = 12.0, 4.2 Hz, 1 H_{Maj}), 3.38 (dd, *J* = 13.7, 11.2 Hz,

1 H_{Min}), 3.26 (dd, J = 13.1, 9.9 Hz, 1 H_{Min}), 3.05−2.97 (m, 1 H_{Maj} + 1 H_{Min}), 2.97−2.92 (m, 1 H_{Maj}); $^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$) δ 147.7, 147.5, 138.5, 137.7, 137.4, 137.0, 133.82, 133.78, 133.63, 133.56, 132.0, 131.9, 130.8, 130.7, 129.5, 129.3, 128.7, 128.59, 128.57, 128.43, 128.40, 127.8, 126.83, 126.76, 126.5, 126.0, 124.49, 124.45, 78.1, 74.0, 67.8, 63.4, 56.9, 55.0, 47.1, 45.7, 35.2; IR (neat) 3029, 2927, 1059, 1539, 1496, 1453, 1345, 1163, 1124, 1085 cm^{-1}; HRMS (ESI) m/z calcd for $C_{23}H_{23}N_2O_5S$ [$(M + H)^+$] 439.1328, found 439.1303.

(5S)-5-Isopropyl-4-((2-nitrophenyl)sulfonyl)-2-phenylmorpholine (28).—This compound was prepared according to general procedure A using 2-nitrobenzenesulfonamide-protected (*S*)-valinol (72 mg, 0.25 mmol) and styrene (50 μL, 0.4375 mmol). After purification by column chromatography on SiO_2 (10–20% EtOAc/hexanes), the title compound was isolated as a colorless oil (52 mg, 53% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.08−8.10 (m, 1 H_{Min}) 7.95 (d, J = 8.1 Hz, 1 H_{Maj}), 7.765−7.71 (m, 2 H_{Min}), 7.70−7.66 (m, 1 H_{Min}), 7.76 (d, J = 7.5 Hz, 1 H_{Maj}), 7.59 (d, J = 8.3 Hz, 2 H_{Maj}), 7.40−7.35 (m, 1 H_{Maj} + 1 H_{Min}), 7.34−7.30 (m, 1 H_{Min}) 7.26−7.21 (m, 2 H_{Maj}), 7.20−7.14 (m, 2 H_{Maj} + 2 H_{Min}), 4.87 (t, J = 3.3 Hz, 1 H_{Maj}), 4.07 (dd, J = 12.0, 3.4 Hz, 1 H_{Min}), 4.18 (d, J = 11.4 Hz, 1H_{Min}) 4.07 (dd, J = 12.1, 3.3 Hz, 1 H_{Maj}), 4.02−4.94 (m, 1 H_{Maj} + 1 H_{Min}), 3.87−3.79 (m, 2 H_{Maj}) 3.74 (dd, J = 6.2, 3.0 Hz, 1 H_{Min}) 3.45−3.39 (m, 1 H_{Maj} + 1 H_{Min}), 3.18 (dd, J = 15.2, 11.1 Hz, 1 H_{Min}) 2.56−2.48 (m, 1 H_{Maj}), 2.47−2.41 (m, 1 H_{Min}), 1.06 (d, J = 6.9 Hz, 3 H_{Min}) 0.99 (d, J = 6.6 Hz, 3 H_{Maj}), 0.89 (d, J = 6.8 Hz, 3 H_{Maj}), 0.80 (d, J = 6.8 Hz, 1 H_{Maj}); $^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$) δ 147.5, 138.5, 137.9, 134.6, 134.0, 133.5, 133.4, 131.8, 131.7, 131.2, 130.7, 128.5, 128.3, 127.3, 126.1, 125.9, 124.4, 124.3, 77.9, 72.7, 67.5, 62.4, 60.5, 60.0, 47.5, 44.2, 29.7, 26.3, 25.4, 20.1, 19.6, 19.6, 19.3; IR (neat) 2595, 1591, 1539, 1496, 1454, 1344, 1269, 1158, 1125, 1091, 1073 cm^{-1}; HRMS (ESI) m/z calcd for $C_{19}H_{23}N_2O_5S$ [$(M + H)^+$] 391.1328, found 391.1319.

(5S)-5-Isobutyl-4-((2-nitrophenyl)sulfonyl)-2-phenylmorpholine (29).—This compound was prepared according to general procedure A using 2-nitrobenzenesulfonamide-protected (*S*)-leucenol (76 mg, 0.25 mmol) and styrene (50 μL, 0.4375 mmol). After purification by column chromatography on SiO_2 (10–20% EtOAc/hexanes), the title compound was isolated as a white solid (65 mg, 72% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.08 (dd, J = 7.4, 1.3 Hz, 1 H_{Min}), 8.02 (d, J = 8.1 Hz, 1 H_{Maj}), 7.73−7.66 (m, 1 H_{Maj} + 3 H_{Min}), 7.64 (t, J = 9.6 Hz, 2 H_{Maj}), 7.34 (d, J = 4.2 Hz, 2 H_{Maj}), 7.32−7.27 (m, 1 H_{Maj} + 3 H_{Min}), 7.27−7.20 (m, 2 H_{Maj} + 2 H_{Min}), 4.79 (t, J = 4.2 Hz, 1 H_{Maj}), 4.39 (dd, J = 11.1, 2.8 Hz, 1 H_{Min}), 3.91 (dd, J = 13.6, 3.5 Hz, 2 H_{Min}), 3.89−3.83 (m, 1 H_{Min}), 3.80−3.74 (m, 2 H_{Min}), 3.66 (dd, J = 13.6, 4.8 Hz, 2 H_{Maj}), 3.52 (dd, J = 12.0, 4.6 Hz, 1 H_{Maj}), 3.22 (dd, J = 14.0, 11.1 Hz, 1 H_{Min}), 1.88−1.84 (m, 1 H_{Min}), 1.77−1.68 (m, 1 H_{Maj}), 1.62−1.43 (m, 2 H_{Maj} + 1 H_{Min}), 1.29−1.22 (m, 2 H_{Min}), 0.88 (2ds, J = 4.5 Hz, 6 H_{Min}), 0.81 (d, J = 6.6 Hz, 6 H_{maj}); $^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$) δ 147.8, 147.7, 138.5, 137.8, 134.3, 134.0, 133.7, 133.6, 131.84, 131.77, 131.0, 130.8, 128.6, 128.5, 128.3, 127.8, 126.5, 126.0, 124.5, 124.4, 77.9, 74.3, 68.9, 65.1, 54.3, 51.6, 46.8, 46.3, 37.7, 37.3, 25.1, 24.8, 23.6, 22.9, 22.2, 21.4; IR (neat) 2957, 2928, 2869, 1541, 1453, 1367, 1349, 1298, 1159, 1098 cm^{-1}; HRMS (ESI) m/z calcd for $C_{20}H_{25}N_2O_5S$ [$(M + H)^+$] 405.1484, found 405.1500.

(5S)-5-Isobutyl-4-((2-nitrophenyl)sulfonyl)-2-phenylmorpholine (30).—This compound was prepared according to general procedure A using (S)-*N*-(1-hydroxy-3,3-dimethylbutan-2-yl)-4-nitrobenzenesulfonamide (76 mg, 0.25 mmol) and styrene (50 μL, 0.4375 mmol). After purification by column chromatography on SiO_2 (10–20% EtOAc/hexanes), the title compound was isolated as a white solid (46 mg, 45% yield). Note that the reported spectral data are for the major diastereomer only. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.84 (d, J = 8.1 Hz, 1 H), 7.60 (t, J = 7.7 Hz, 1 H), 7.53 (d, J = 7.8 Hz, 1 H), 7.43 (t, J = 7.7 Hz, 1 H), 7.15−7.07 (m, 3 H), 7.00 (d, J = 6.1 Hz, 2 H), 4.73 (t, J = 4.5 Hz, 1 H), 4.32−4.23 (m, 1 H), 4.08−3.96 (m, 2 H), 3.87−3.77 (m, 2 H), 1.11 (s, 9 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 147.8, 139.4, 133.6, 133.3, 131.9, 131.4, 128.2, 127.0, 125.2, 124.3, 72.2, 62.0, 59.5, 45.4, 36.2, 28.3; IR (neat) 2968, 2875, 1541, 1497, 1368, 1347, 1166, 1123, 1095, 1058 cm^{-1}; HRMS (ESI) m/z calcd for $C_{20}H_{25}N_2O_5S$ [(M + H)$^+$] 405.1484, found 405.1477.

((5S)-5-((S)-sec-Butyl)-4-((2-nitrophenyl)sulfonyl)-2-phenylmorpholine (31).—This compound was prepared according to general procedure A using 2-nitrobenzenesulfonamide-protected (*S*)-isoleucenol (76 mg, 0.25 mmol) and styrene (50 μL, 0.4375 mmol). After purification by column chromatography on SiO_2 (10–20% EtOAc/hexanes), the title compound was isolated as a white solid (56 mg, 53% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.11−8.05 (m, 1 H_{Min}) 7.94 (d, J = 7.8 Hz, 1 H_{Maj}), 7.77−7.70 (m, 2 H_{Min}), 7.66−7.62 (m, 1 H_{Min}) 7.61 (d, J = 7.8 Hz, 1 H_{Maj}), 7.56 (d, J = 7.8 Hz, 1 H_{Maj}), 7.54 (t, J = 7.2 Hz, 1 H_{Maj}), 7.36−7.31 (m, 1 H_{Maj}), 7.31−7.26 (m, 1 H_{Min}), 7.24−7.19 (m, 2 H_{Maj} + 2 H_{Min}), 7.19−7.13 (m, 2 H_{Maj} + 2 H_{Min}), 4.80 (t, J = 4.0 Hz, 1 H_{Maj}), 4.35 (dd, J = 10.8, 3.0 Hz, 1 H_{Min}), 4.15 (d, J = 12.0 Hz, 1 H_{Min}), 4.03 (dd, J = 12.0, 3.4 Hz, 1 H_{Maj}), 3.94 (dd, J = 15.0, 3.0 Hz, 1 H_{Min}), 3.81 (d, J = 4.2 Hz, 2 H_{Maj}), 3.78 (dd, J = 12.0, 3.9 Hz, 1 H_{Maj}), 3.69 (dd, J = 12.0, 2.4 Hz, 1 H_{Min}), 3.50−3.45 (m, 1 H_{Maj}), 3.13 (dd, J = 15.0, 11.4 Hz, 1 H_{Min}), 2.24−2.07 (m, 1 H_{Maj} + 1 H_{Min}), 1.53−1.46 (m, 1 H_{Maj}), 0.99 (d, J = 6.6 Hz, 3 H_{Min}), 0.98−0.89 (m, 1 H_{Maj} + 1 H_{Min}) 0.88 (d, J = 6.6 Hz, 3 H_{Maj}), 0.84 (t, J = 7.2 Hz, 3 H_{Maj}), 0.80 (t, J = 6.0 Hz, 3 H_{Min}); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 147.68, 147.66, 138.5, 138.2, 134.6, 134.0, 133.5, 133.4, 131.8, 131.6, 131.1, 130.8, 128.6, 128.4, 128.3, 127.5, 126.1, 125.8, 124.4, 124.3, 77.7, 73.4, 67.5, 63.0, 59.9, 58.9, 47.5, 45.7, 33.2, 31.8, 25.8, 24.9, 16.0, 15.4, 11.8, 11.4; IR (neat) 2972, 2933, 2876, 1544, 1372, 1348, 1061 cm^{-1}; HRMS (ESI) m/z calcd for $C_{20}H_{24}N_2NaO_5S$ [(M + Na)$^+$] 427.1304, found 427.1316.

(±)-Methyl (3R,6S)-4-((2-Nitrophenyl)sulfonyl)-6-phenylmorpholine-3-carboxylate (32).—This compound was prepared according to general procedure A using 2-nitrobenzenesulfonamide-protected (D)-serine methyl ester (76 mg, 0.25 mmol) and styrene (50 μL, 0.4375 mmol). After purification by column chromatography on SiO_2 (10–30% EtOAc/hexanes), the title compound was isolated as a white solid (54 mg, 53% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.01 (dd, J = 7.8, 1.5 Hz, 1 H), 7.77−7.67 (m, 2 H), 7.65 (dd, J = 7.6, 1.2 Hz, 1 H), 7.39−7.29 (m, 5 H), 4.68−4.63 (m, 1 H), 4.59 (d, J = 11.7 Hz, 1 H), 4.54 (dd, J = 11.0, 2.9 Hz, 1 H), 4.01 (dd, J = 11.8, 3.5 Hz, 1 H), 3.83 (dd, J = 12.8, 2.3 Hz, 1 H), 3.72 (s, 3 H), 3.53 (dd, J = 12.7, 11.0 Hz, 1 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 169.3, 147.7, 137.9, 133.7, 132.7, 131.8, 130.7, 128.6, 128.6, 126.2, 124.2, 78.2, 68.8, 55.4,

52.6, 48.3; IR (neat) 2923, 1745, 1591, 1541, 1497, 1439, 1352, 1292, 1259, 1218, 1165 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{18}H_{19}N_2O_7S$ [(M + H)$^+$] 407.0913, found 407.0924.

Methyl (2R)-2-Methyl-4-((2-nitrophenyl)sulfonyl)-6-phenylmorpholine-3-carboxylate (33).—This compound was prepared according to general procedure A using methyl ((4-nitrophenyl)sulfonyl)-D-allothreoninate (80 mg, 0.25 mmol) and styrene (50 μL, 0.4375 mmol). After purification by column chromatography on SiO_2 (10–30% EtOAc/hexanes), the title compound was isolated as a colorless oil (43 mg, 41% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.01 (d, *J* = 7.8 Hz, 1 H_{Maj}), 7.97 (d, *J* = 8.1 Hz, 1 H_{Min}), 7.76−7.64 (m, 3 H_{Maj} + 2 H_{Min}), 7.62 (d, *J* = 7.6 Hz, 1 H_{Min}), 7.41−7.29 (m, 5 H_{Maj} + 5 H_{Min}), 4.98 (dd, *J* = 11.2, 3.4 Hz, 1 H_{Min}), 4.81 (q, *J* = 6.8 Hz, 1 H_{Min}), 4.64 (dd, *J* = 10.7, 3.4 Hz, 1 H_{Maj}), 4.49−4.43 (m, 1 H_{Maj} + 1 H_{Min}), 4.09 (m, 1 H_{Maj}), 3.92 (dd, *J* = 12.8, 2.8 Hz, 1 H_{Min}), 3.84 (t, *J* = 11.4 Hz, 1 H_{Maj}), 3.78 (dd, *J* = 12.9, 3.6 Hz, 1 H_{Min}), 3.68 (s, 3 H_{Maj}), 3.67 (s, 3 H_{Min}), 3.49 (t, *J* = 12.1 Hz, 1 H_{Min}), 1.58 (d, *J* = 6.8 Hz, 3 H_{Min}), 1.40 (d, *J* = 6.6 Hz, 3 H_{Maj}); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 169.5, 168.7, 147.8, 147.7, 138.3, 138.2, 133.8, 133.6, 132.7, 132.4, 131.8, 131.7, 130.9, 130.4, 128.6, 128.5, 126.5, 126.4, 124.3, 124.1, 78.6, 74.3, 70.6, 70.5, 69.4, 58.7, 58.1, 52.5, 51.9, 48.1, 47.4, 18.3, 16.4; IR (neat) 2954, 1743, 1541, 1497, 1439, 1355, 1248, 1165, 1100, 1070 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{19}H_{21}N_2O_7S$ [(M + H)$^+$] 421.1069, found 421.1071.

2-Nitro-4-((4aR,9aS)-2-phenyl-2,3,9,9a-tetrahydroindeno[2,1-b]-[1,4]oxazin-4(4aH)-yl)benzenesulfonic acid (34).—This compound was prepared according to general procedure A using *N*-((1*R*,2*S*)-2-hydroxy-2,3-dihydro-1*H*-inden-1-yl)-2-nitrobenzenesulfonamide (84 mg, 0.25 mmol) and styrene (50 μL, 0.4375 mmol). After purification by column chromatography on SiO_2 (10–30% EtOAc/hexanes), the title compound was isolated as a white solid (52 mg, 46% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.02 (d, *J* = 7.8 Hz, 1 H), 7.75−7.65 (m, 2 H), 7.62 (t, *J* = 8.4 Hz, 1 H), 7.31−7.19 (m, 8 H), 7.18 (t, *J* = 6.8 Hz, 1 H), 5.19 (d, *J* = 4.6 Hz, 1 H), 4.86−4.76 (m, 2 H), 3.84−3.69 (m, 2 H), 3.17−3.02 (m, 2 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 147.5, 141.0, 137.9, 133.8, 133.5, 131.9, 131.3, 128.5, 128.4, 127.6, 126.9, 126.2, 125.3, 125.2, 124.7, 73.7, 71.2, 60.3, 44.5, 36.8; IR (neat) 2988, 2972, 1740, 1539, 1441, 1365, 1351, 1342, 1161, 1062 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{23}H_{20}N_2NaO_5S$ [(M + Na)$^+$] 459.0991, found 459.0982.

1-Phenylpent-4-en-1-one (6).—This compound was prepared according to general procedure C using allylic alcohol (17 μL, 0.25 mmol) and styrene (58 μL, 0.5 mmol). After purification by column chromatography on SiO_2 (0–2% EtOAc/hexanes), the title compound was isolated as a colorless oil (26 mg, 65% yield). The spectral data of this compound matched those from previously reported literature.[27] ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.98 (d, *J* = 7.3 Hz, 2 H), 7.57 (t, *J* = 7.2 Hz, 1 H), 7.48 (t, *J* = 7.7 Hz, 2 H), 5.96−5.88 (m, 1 H), 5.10 (dd, *J* = 17.1, 1.5 Hz, 1 H), 5.03 (dd, *J* = 10.2, 0.6 Hz, 1 H) 3.09 (t, *J* = 7.3 Hz, 2 H), 2.51 (q, *J* = 7.1 Hz, 2 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 199.4, 137.3, 136.9, 133.0, 128.6, 128.0, 115.3, 37.7, 28.1; IR (neat) 2925, 1732, 1683, 1598, 1449, 1362, 1270, 1206, 1108, 984 cm^{-1}.

1-(4-(tert-Butyl)phenyl)pent-4-en-1-one (39).—This compound was prepared according to general procedure C using allylic alcohol (17 μL, 0.25 mmol) and *p*-(*tert*-butyl)styrene (91 μL, 0.5 mmol). After purification by column chromatography on SiO_2 (0–2% EtOAc/hexanes), the title compound was isolated as a colorless oil (41 mg, 76% yield). The spectral data of this compound matched those from previously reported literature.[28] ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.92 (d, J = 8.3 Hz, 2 H), 7.49 (d, J = 8.3 Hz, 2 H), 5.96−5.87 (m, 1 H), 5.10 (dd, J = 17.4, 0.9 Hz, 1 H), 5.02 (d, J = 10.3 Hz, 1 H), 3.06 (t, J = 7.4 Hz, 2 H), 2.51 (q, J = 7.0 Hz, 2 H), 1.35 (s, 9 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 199.1, 156.7, 137.4, 134.3, 128.0, 125.5, 115.2, 37.6, 35.1, 31.1, 28.2; IR (neat) 3078, 2963, 2869, 1682, 1605, 1463, 1406, 1270, 1190, 1107 cm^{-1}.

1-(4-Methoxyphenyl)pent-4-en-1-one (40).—This compound was prepared according to general procedure C using allylic alcohol (17 μL, 0.25 mmol) and *p*-methoxy styrene (67 μL, 0.5 mmol). After purification by column chromatography on SiO_2 (5–10% EtOAc/hexanes), the title compound was isolated as a white solid (26 mg, 55% yield). The spectral data of this compound matched those from previously reported literature.[28] ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.96 (d, J = 8.8 Hz, 2 H), 6.94 (d, J = 8.8 Hz, 2 H), 5.96−5.87 (m, 1 H), 5.09 (dd, J = 17.4, 1.5 Hz, 1 H), 5.01 (d, J = 10.3 Hz, 1 H), 3.88 (s, 3 H), 3.03 (t, J = 7.4 Hz, 2 H), 2.49 (q, J = 7.0 Hz, 2 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 198.0, 163.4, 137.5, 130.3, 130.0, 115.1, 113.7, 55.4, 37.4, 28.3; IR (neat) 3060, 3013, 2978, 2838, 1667, 1639, 1599, 1576, 1509, 1419, 1250, 1178, 1029 cm^{-1}.

4-(Pent-4-enoyl)phenyl Pivalate (41).—This compound was prepared according to general procedure C using allylic alcohol (17 μL, 0.25 mmol) and 4-vinylphenyl pivalate (102 mg, 0.5 mmol). After purification by column chromatography on SiO_2 (2–5% EtOAc/hexanes), the title compound was isolated as a white solid (33 mg, 51% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.01 (d, J = 8.5 Hz, 2 H), 7.16 (d, J = 8.5 Hz, 2 H), 5.95−5.86 (m, 1 H), 5.01 (dd, J = 17.1, 1.2 Hz, 1 H), 5.02 (d, J = 10.3 Hz, 1 H), 3.07 (t, J = 7.4 Hz, 2 H), 2.50 (q, J = 7.0 Hz, 2 H), 1.37 (s, 9 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 198.2, 176.5, 154.8, 137.2, 134.3, 129.6, 121.7, 115.3, 39.2, 37.7, 28.1, 27.0; IR (neat) 3078, 2974, 2933, 1747, 1682, 1643, 1594, 1478, 1411, 1276, 1201, 1164, 1106 cm^{-1}; HRMS (ESI) m/z calcd for $C_{16}H_{21}O_3$ $[(M + H)^+]$ 261.1491, found 261.1477.

1-(4-Fluorophenyl)pent-4-en-1-one (42).—This compound was prepared according to general procedure C using allylic alcohol (17 μL, 0.25 mmol) and *p*-fluorostyrene (60 μL, 0.5 mmol). After purification by column chromatography on SiO_2 (0–2% EtOAc/hexanes), the title compound was isolated as a colorless oil (28 mg, 63% yield). The spectral data of this compound matched those from previously reported literature.[29] ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.04−7.96 (m, 2 H), 7.14 (t, J = 8.5 Hz, 2 H), 5.95−5.85 (m, 1 H), 5.10 (dd, J = 17.4, 1.5 Hz, 1 H), 5.03 (d, J = 10.3 Hz, 1 H), 3.06 (t, J = 7.3 Hz, 2 H), 2.50 (q, J = 6.8 Hz, 2 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 197.8, 165.7 (d, $J_{C,F}$ = 252.0 Hz), 137.1, 133.3, 130.6 (d, $J_{C,F}$ = 9.0 Hz), 115.7 (d, $J_{C,F}$ = 21.0 Hz), 115.4, 37.6, 28.1; IR (neat) 2933, 1685, 1599, 1507, 1468, 1410, 1314, 1237, 1156, 1031 cm^{-1}.

1-(Naphthalen-2-yl)pent-4-en-1-one (43).—This compound was prepared according to general procedure C using allylic alcohol (17 μL, 0.25 mmol) and 2-vinylnaphthalene (77 mg, 0.5 mmol). After purification by column chromatography on SiO_2 (0–2% EtOAc/hexanes), the title compound was isolated as a colorless oil (30 mg, 57% yield). The spectral data of this compound matched those from previously reported literature.[27] ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.49 (s, 1 H), 8.05 (d, J = 8.5 Hz, 1 H), 7.98 (d, J = 8.1 Hz, 1 H), 7.89 (d, J = 8.3 Hz, 1 H), 7.91 (d, J = 8.8 Hz, 1 H), 7.66−7.53 (m, 2 H), 6.02−5.92 (m, 1 H), 5.14 (d, J = 17.1 Hz, 1 H), 5.06 (d, J = 10.3 Hz, 1 H), 3.23 (t, J = 7.4 Hz, 2 H), 2.58 (q, J = 7.1 Hz, 2 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 199.4, 137.3, 135.5, 134.2, 132.5, 129.6, 129.5, 128.4, 128.4, 127.7, 126.7, 123.8, 115.3, 37.8, 28.3; IR (neat) 3059, 2917, 1677, 1627, 1468, 1359, 1276, 1171, 1123, 985 cm^{-1}.

1-(1-Tosyl-1H-indol-3-yl)pent-4-en-1-one (44).—This compound was prepared according to general procedure C using allylic alcohol (17 μL, 0.25 mmol) and 1-tosyl-3-vinyl-1*H*-indole (149 mg, 0.5 mmol). After purification by column chromatography on SiO_2 (5–10% EtOAc/hexanes), the title compound was isolated as a white solid (55 mg, 71% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.31 (d, J = 7.6 Hz, 1 H), 8.22 (s, 1 H), 7.90 (d, J = 8.1 Hz, 1 H), 7.81 (d, J = 8.1 Hz, 2 H), 7.38−7.28 (m, 2 H), 7.25 (d, J = 8.1 Hz, 2 H), 5.94−5.84 (m, 1 H), 5.09 (d, J = 17.3 Hz, 1 H), 5.00 (d, J = 10.0 Hz, 1 H), 2.99 (t, J = 7.4 Hz, 2 H), 2.50 (q, J = 6.8 Hz, 2 H), 2.33 (s, 3 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 199.4, 137.3, 135.5, 134.2, 132.5, 129.6, 129.5, 128.4, 128.4, 127.7, 126.7, 123.8, 115.3, 37.8, 28.3; IR (neat) 3134, 3072, 2920, 1663, 1643, 1596, 1537, 1447, 1384, 1368, 1169 cm^{-1}; HRMS (ESI) m/z calcd for $C_{20}H_{20}NO_3S$ [(M + H)$^+$] 354.1164, found 354.1142.

2-Methyl-1-phenylpent-4-en-1-one (45).—This compound was prepared according to general procedure C using allylic alcohol (17 μL, 0.25 mmol) and *trans*-β-methylstyrene (65 μL, 0.5 mmol). After purification by column chromatography on SiO_2 (0–2% EtOAc/hexanes), the title compound was isolated as a colorless oil (23 mg, 53% yield). The spectral data of this compound matched those from previously reported literature.[30] ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97 (d, J = 7.6 Hz, 2 H), 7.57 (t, J = 7.4 Hz, 1 H), 7.48 (t, J = 7.7 Hz, 2 H), 5.84−5.75 (m, 1 H), 5.07 (dd, J = 18 Hz, 1.8 Hz, 1 H), 5.02 (d, J = 10.0 Hz, 1 H), 3.59−3.51 (m, 1 H), 2.62−2.52 (m, 1 H), 2.25−2.17 (m, 1 H), 1.22 (d, J = 7.1 Hz, 3 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 203.6, 136.4, 135.8, 132.9, 128.6, 128.3, 116.7, 40.4, 37.6, 17.0; IR (neat) 2962, 1747, 1682, 1605, 1546, 1364, 1270, 1171, 1107, 998 cm^{-1}.

1-(4-(tert-Butyl)phenyl)-4-methylpent-4-en-1-one (46).—This compound was prepared according to general procedure C using 2-methylprop-2-en-1-ol (21 μL, 0.25 mmol) and *p*-(*tert*-butyl)styrene (91 μL, 0.5 mmol). After purification by column chromatography on SiO_2 (0–2% EtOAc/hexanes), the title compound was isolated as a colorless oil (25 mg, 44% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97 (d, J = 7.6 Hz, 2 H), 7.57 (t, J = 7.4 Hz, 1 H), 7.48 (t, J = 7.7 Hz, 2 H), 5.84−5.75 (m, 1 H), 5.07 (dd, J = 18 Hz, 1.8 Hz, 1 H), 5.02 (d, J = 10.0 Hz, 1 H), 3.59−3.51 (m, 1 H), 2.62−2.52 (m, 1 H), 2.25−2.17 (m, 1 H), 1.22 (d, J = 7.1 Hz, 3 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 199.4, 156.7, 144.8, 134.3, 128.0, 125.5, 110.1, 36.7, 35.1, 31.9, 31.1, 22.8; IR (neat) 2963, 2870, 1716,

1683, 1606, 1462, 1408, 1368, 1269, 1188, 1109 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{16}H_{23}O$ [$(M + H)^+$] 231.1749, found 231.1734.

1-(4-(tert-Butyl)phenyl)-3-methylpent-4-en-1-one (47).—This compound was prepared according to general procedure C using 2-buten-1-ol (21 μL, 0.25 mmol) and *p*-(*tert*-butyl)styrene (91 μL, 0.5 mmol). After purification by column chromatography on SiO_2 (0–2% EtOAc/hexanes), the title compound was isolated as a colorless oil (44 mg, 77% yield). ^1H NMR (600 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.3 Hz, 2 H), 7.49 (d, *J* = 8.5 Hz, 2 H), 5.90−5.83 (m, 1 H), 5.04 (d, *J* = 17.1 Hz, 1 H), 4.96 (d, *J* = 10.3 Hz, 1 H), 3.06−2.98 (m, 1 H), 2.96−2.84 (m, 2 H), 1.35 (s, 9 H), 1.10 (d, *J* = 6.6 Hz, 3 H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 199.0, 156.7, 143.2, 134.7, 128.1, 125.5, 112.9, 45.0, 35.1, 33.6, 31.1, 19.7; IR (neat) 2962, 1680, 1641, 1605, 11544, 1461, 1406, 1363, 1270, 1191 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{16}H_{23}O$ [$(M + H)^+$] 231.1749, found 231.1737.

1-(4-(tert-Butyl)phenyl)-3-phenylpent-4-en-1-one (48).—This compound was prepared according to general procedure C using (*E*)-3-phenylprop-2-en-1-ol (34 mg, 0.25 mmol) and *p*-(*tert*-butyl)-styrene (91 μL, 0.5 mmol). After purification by column chromatography on SiO_2 (0–2% EtOAc/hexanes), the title compound was isolated as a colorless oil (42 mg, 57% yield). ^1H NMR (600 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.5 Hz, 2 H), 7.48 (m, *J* = 8.3 Hz, 2 H), 7.35−7.27 (m, 4 H), 7.22 (t, *J* = 7.2 Hz, 1 H), 6.11−6.03 (m, 1 H), 5.08 (d, *J* = 10.3 Hz, 1 H), 5.05 (d, *J* = 17.3 Hz, 1 H), 4.17 (q, *J* = 6.7 Hz, 1 H), 3.44 (dd, *J* = 16.5, 7.7 Hz, 1 H), 3.36 (dd, *J* = 16.6, 6.3 Hz, 1 H), 1.36 (s, 9 H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 197.8, 156.7, 143.2, 140.7, 134.5, 128.5, 128.0, 127.7, 126.5, 125.5, 114.6, 44.5, 44.4, 43.9, 35.1, 31.1; IR (neat) 2962, 1681, 1637, 1604, 1492, 1452, 1406, 1363, 1266, 1107 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{21}H_{25}O$ [$(M + H)^+$] 293.1905, found 293.1903.

(8R, 9S, 13S, 14S)-13-Methyl-3-(pent-4-enoyl)-6,7,8,9,11,12,13,14,15,16-decahydro-17H-cyclopenta[a]-phenanthren-17-one (49).—This compound was prepared according to general procedure C using allylic alcohol (17 μL, 0.25 mmol) and (8*R*,9*S*,13*S*,14*S*)-13-methyl-3-vinyl-6,7,8,9,11,12,13,14,15,16-decahydro-17*H*-cyclopenta[*a*]phenanthren-17-one (140 mg, 0.5 mmol). After purification by column chromatography on SiO_2 (2–5% EtOAc/hexanes), the title compound was isolated as a white solid (60 mg, 77% yield). ^1H NMR (600 MHz, $CDCl_3$) 7.74 (d, *J* = 8.1 Hz, 1 H), 7.71 (s, 1 H), 7.38 (d, *J* = 8.3 Hz, 1 H), 5.95−5.85 (m, 1 H), 5.09 (dd, *J* = 17.1, 1.5 Hz, 1 H), 5.01 (d, *J* = 10.3 Hz, 1 H), 3.05 (t, *J* = 7.3 Hz, 2 H), 3.03−2.91 (m, 2 H), 2.56−2.43 (m, 4 H), 2.34 (dt, *J* = 3.5, 10.8 Hz, 1 H), 2.21−2.12 (m, 1 H), 2.12−2.03 (m, 2 H), 2.02−1.96 (m, 1 H), 1.70−1.60 (m, 2 H), 1.59−1.43 (m, 4 H), 0.92 (s, 3 H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 199.3, 145.3, 137.3, 136.9, 134.5, 128.6, 125.5, 125.5, 115.2, 50.4, 47.8, 44.6, 37.8, 37.6, 35.8, 31.5, 29.3, 28.2, 26.2, 25.5, 21.5, 13.7, −18.4; IR (neat) 2925, 2882, 1730, 1666, 1599, 1539, 1453, 1416, 1370, 1257, 1154 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{23}H_{29}O_2$ [$(M + H)^+$] 337.2168, found 337.2151.

Supplementary Material

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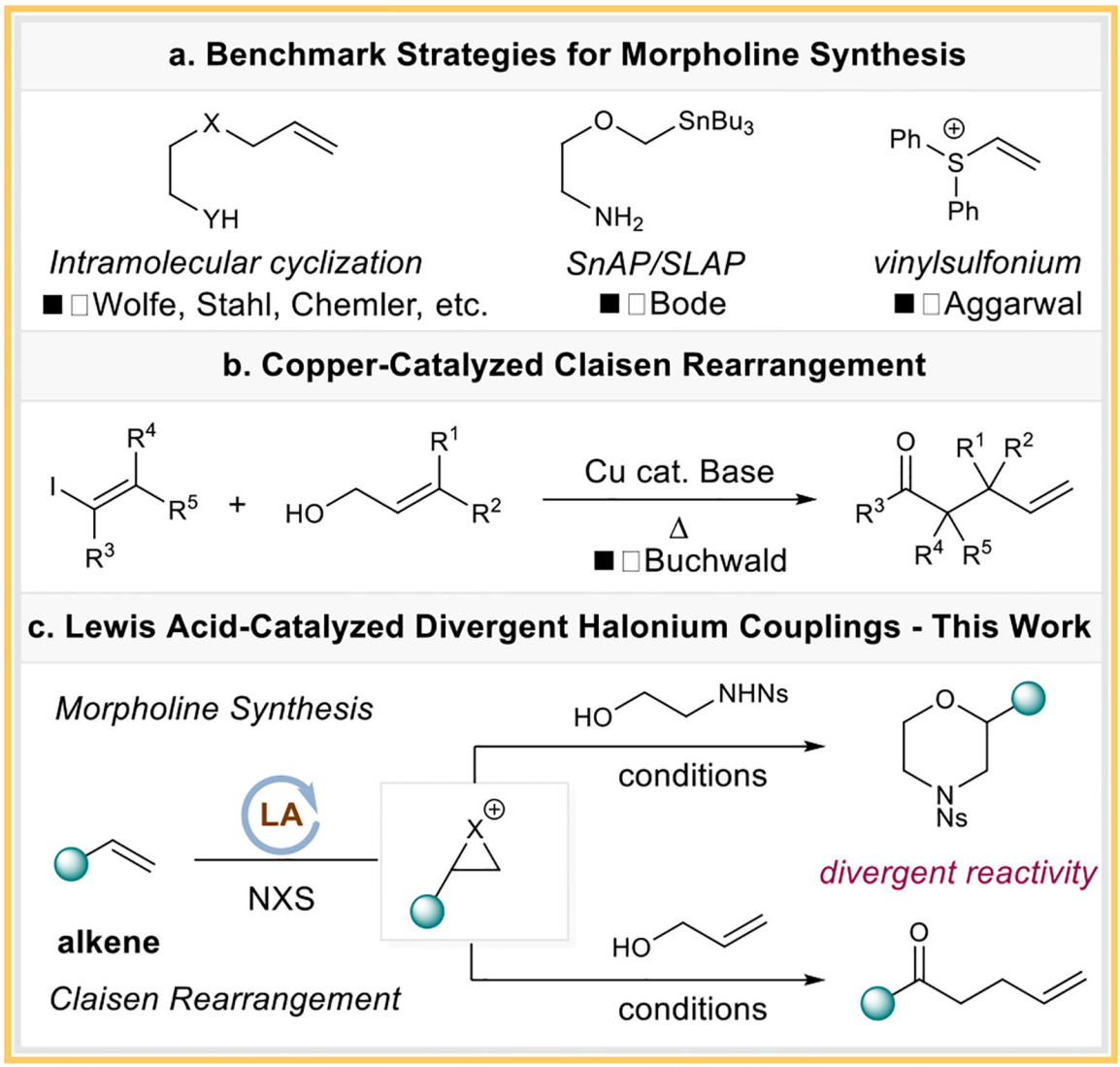
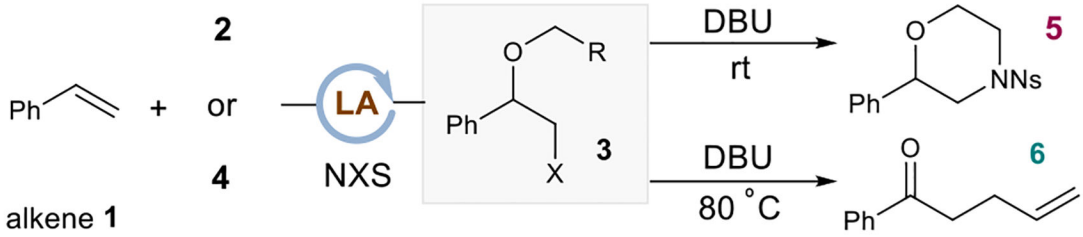


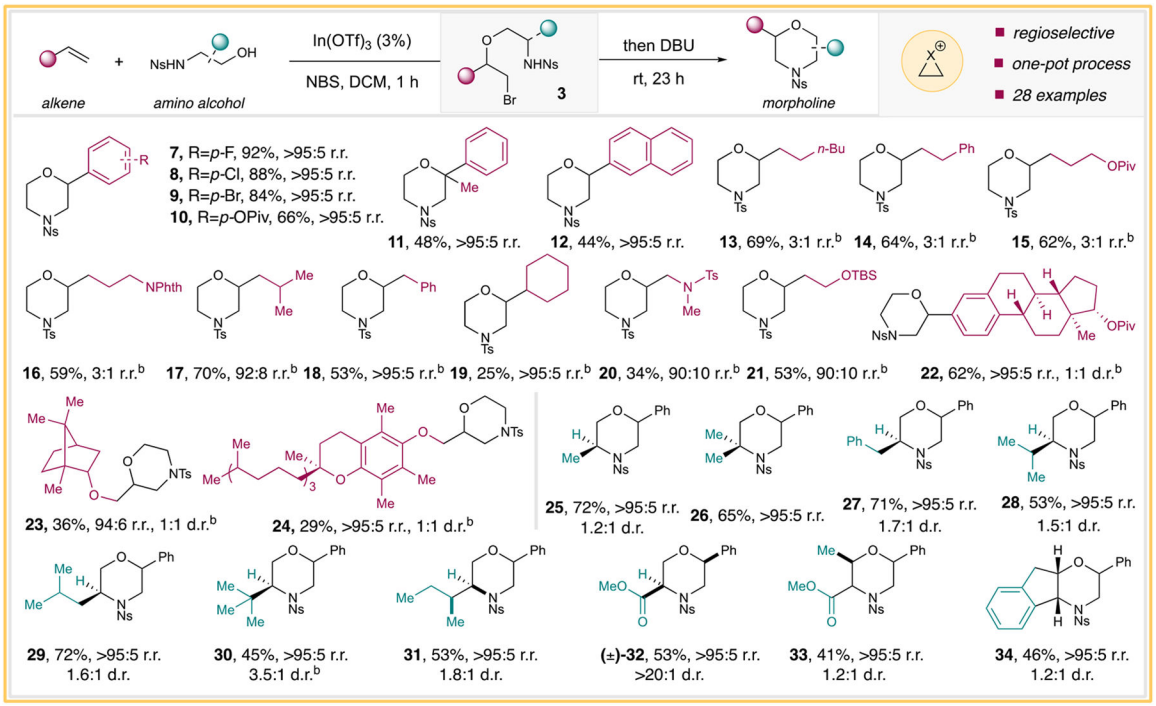
Scheme 1.
Background on Morpholine Synthesis and Claisen Rearrangement



entry	LA (%)	halide (%)	base (%)	**3** (%)[b]	**5** (%)[b]	**6** (%)[b]
1	-	NBS (200)	-	17	-	-
2	$Mg(OTf)_2$ (10)	NBS (200)	-	44	-	-
3	$Sc(OTf)_3$ (10)	NBS (200)	-	38	-	-
4	$In(OTf)_3$ (10)	NBS (200)	-	55	-	-
5	$In(OTf)_3$ (5)	NBS (200)	-	65	-	-
6	$In(OTf)_3$ (3)	NBS (200)	-	76	-	-
7	$In(OTf)_3$ (1)	NBS (200)	-	36	-	-
8	$In(OTf)_3$ (3)	NBS (175)	-	86	-	-
9	$In(OTf)_3$ (3)	NBS (175)	DBU (300)	-	79(76)	-
10	$In(OTf)_3$ (10)	NIS (200)	-	47	-	-
11	$Sc(OTf)_3$ (10)	NIS (200)	-	36	-	-
12	$Mg(OTf)_2$ (10)	NIS (200)	-	79	-	-
13	$Mg(OTf)_2$ (10)	NIS (200)	DBU (300)	-	-	67(65)

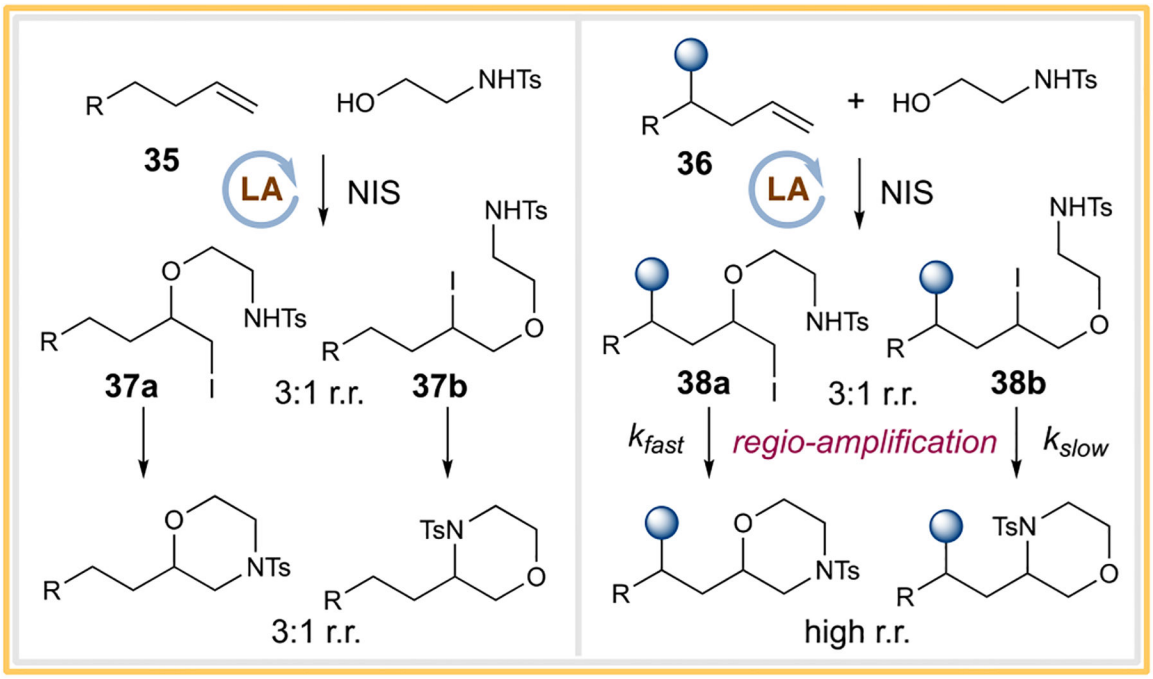
Scheme 2. Optimization Studies[a]

[a]Reaction conditions are as follows: For **5**, **1** (0.4375 mmol), **2** (0.25 mmol), $In(OTf)_3$ (3 mol %), NBS (175 mol %), and DCM (1.5 mL), at rt for 1 h, then DBU (0.75 mmol) at rt for 23 h. For **6**, **1** (0.5 mmol), **4** (0.25 mmol), $Mg(OTf)_2$ (10 mol %), NIS (200 mol %), and DCM (0.25 mL) at rt for 8 h, then DBU (0.75 mmol) at 80 °C for 36 h. [b]Yields were determined by crude ^1H NMR using 1,3-benzodioxole as the internal standard. The yield shown in parentheses was the isolated yield.

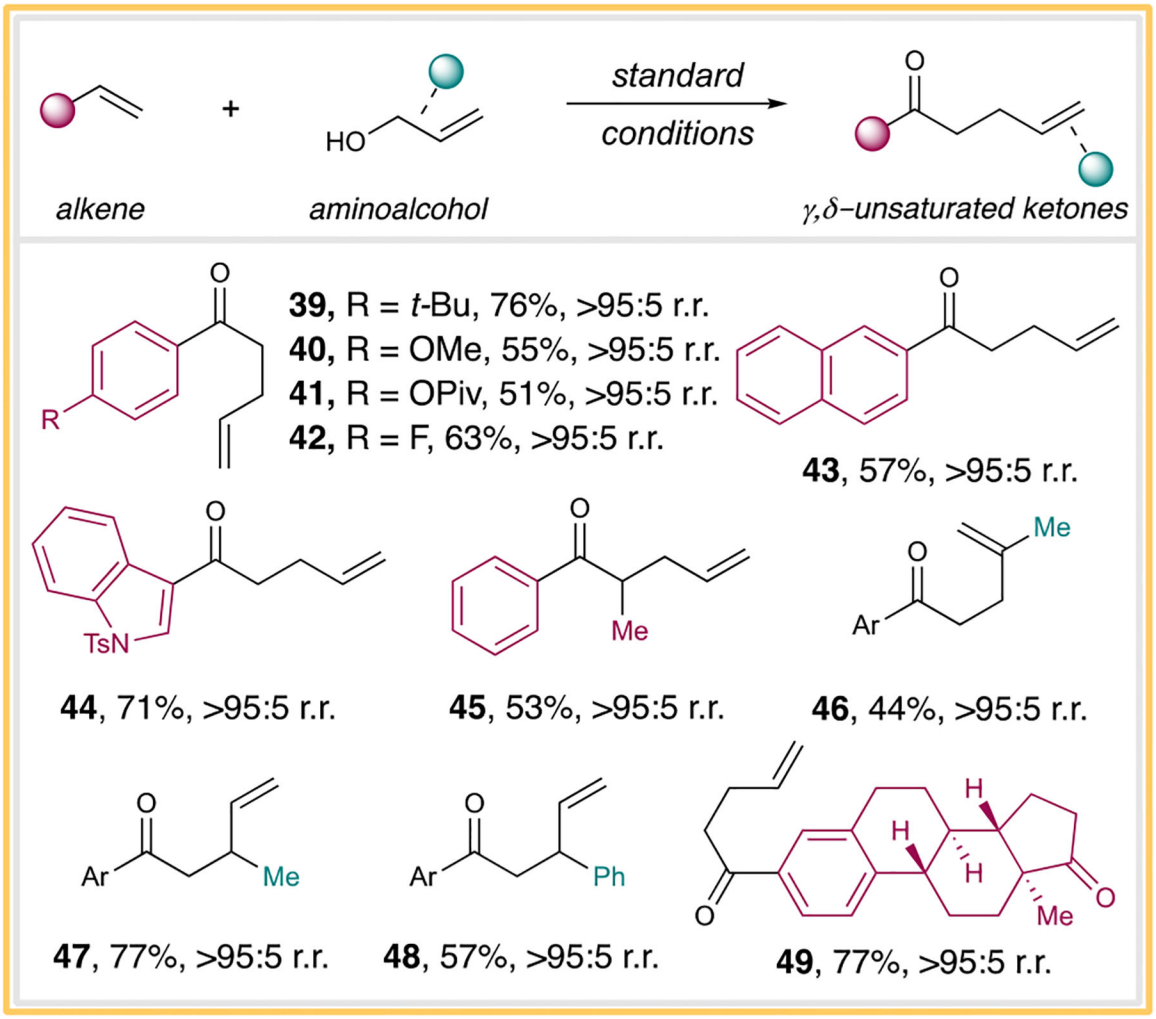


Scheme 3. Morpholine Substrate Scope[a]

[a]For specific reaction conditions, please refer to the Supporting Information. Yields were isolated, and r.r. was assigned by crude ^{1}H NMR using 1,3-benzodioxole as the internal standard. [b]NIS was used, and isolated yields were for the major regioisomer or stereoisomer.



Scheme 4.
Regiochemical Probe



Scheme 5. Claisen Rearrangement Scope[a]

[a]Standard reaction conditions for the Claisen rearrangement. Ar = *para*-*t*-butylphenyl.