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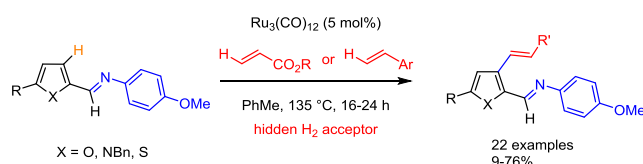
Redox Neutral Ru(0)-Catalyzed Alkenylation of 2-Carboxaldimine Heterocyclopentadienes

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ABSTRACT: A new $\text{Ru}_3(\text{CO})_{12}$ -catalyzed directed alkenylation of 2-carboxaldimine-heterocyclopentadienes has been accomplished. This process allows to couple furan, pyrrole, indole and thiophene 2-carboxaldimines with electron-poor alkenes such as acrylates, vinylsulfones, and styrenes. This regio- and chemoselective oxidative C–H coupling does not require the presence of an additional sacrificial oxidant. Density functional theory (DFT) calculations allowed to propose a mechanism and unveiled the nature of the H_2 acceptor.

INTRODUCTION

Alkenyl-substituted five-membered heteroarene scaffolds, such as furan, pyrrole, indole and thiophene derivatives, are found in many bioactive and pharmaceutical compounds (Figure 1),^{1–7} as well as in various functional organic materials.^{8–10} As a consequence, the search for safer and safer, and more atom- and step-economical methods to synthesize these motifs from simple heterocycles and alkenes is a topic of constant great interest. In this context, the formation of new C–C bonds through a transition metal (TM)-catalyzed C–H activation process has received particular attention,^{11–14} providing a rapid access to a wide range of highly functionalized heterocyclic motifs.

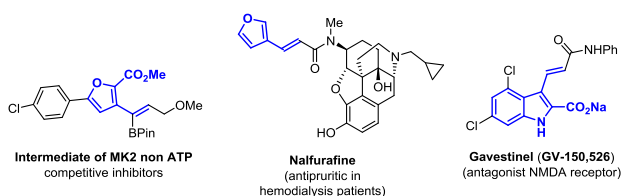


Figure 1. Some bioactive heteroarenes alkenylated at position 3.

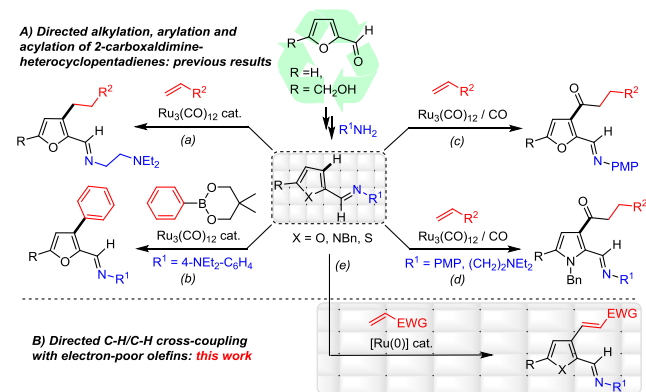
The Fujiwara-Moritani reaction, a dehydrogenative cross-coupling, is one of the earliest examples of such a TM-catalyzed C–H functionalizations.^{15–22} This type of C–H/C–H cross-coupling²³ is regarded as an ideal method to join an acrylate and an aromatic substrate, via Pd(II), Ru(II), Rh(III), Ir(III), or Co(III) catalysis.^{24–30,20} However, as these

dehydrogenative couplings are inherently endergonic, the driving force to push the transformation toward the products side often needs the addition of (super)stoichiometric amounts of an external sacrificial oxidant that accepts the two released H atoms, or the input of electrical energy,^{31–33} which drives hydrogen evolution at the cathode. In the former case, sacrificial oxidants such as quinones, Cu(II)-, Mn(IV)-, or Ag(I)-salts are required, which obviously reduces the sustainability of the coupling process. The only green terminal oxidant is molecular oxygen,³⁴ which is often used in combination with photoredox catalysis.^{35–37}

As part of a long term project directed toward the sustainable C–H functionalization of aldimine-armed heterocyclopentadienes of biomass derivation such as furan,^{38–40} pyrrole,^{41,42} as well as thiophene units, we have recently developed several directed Ru(0)-catalyzed C3-functionalizations (Scheme 1A), such as: the alkylation (*Murai reaction*)⁴³ of *N,N'*-bidentate furfurylimines with vinylsilane or styrene derivatives (*a*),⁴⁴ the arylation of electron-rich furfurylimines with arylboronates (*b*),^{45,46} and the acylation (*carbonylative Murai reaction*) of furan- (*c*) or pyrrole-based *p*-methoxyphenyl imines or *N,N'*-bidentate imines (*d*) under CO atmosphere with vinylsilane or styrene partners.⁴⁷ However, the directed C3–H alkenylation of 2-formyl-heterocyclopentadiene units, which overwhelms the natural C5 electrophilic preference of these heterocycles,⁴⁸ remains a challenge. The few reported C3–H/C–H couplings between 2-substituted heterocyclopentadienes and electron-poor alkenes make use of C2-linked directing groups belonging to the car-

boxylic acid oxidation level, such as carboxylates, amides, and esters.^{49–53} Herein, we disclose a selective, external oxidant free,^{54–58} Ru(0)-catalyzed C3-alkenylation of furfural, 5-hydroxymethylfurfural (HMF) derivatives, pyrrole-, indole-, and thiophene 2-carboxaldehydes through their corresponding aldimines (*i.e.* without modification of the formyl redox state), which act as removable directing groups (Scheme 1B, *e*).

Scheme 1. Ru-catalyzed direct functionalization of biomass-derived 2-formyl heteroaromatic compounds: *previous results and present work*



RESULTS AND DISCUSSION

In our previous studies, we established that the directed C3–H activation of 2-carboxaldehyde-heterocyclopentadienes could be successfully achieved only through a nucleophilic catalysis, which involves an initial oxidative addition step of the targeted C–H bond to the Ru(0) catalyst. In contrast, electrophilic TM-complexes, such as Ru(II) or Pd(II) catalysts, which normally involve an ambiphilic metal–ligand activation / concerted metalation deprotonation (AMLA / CMD) mechanism, appeared uneffective.¹³ Classical Fujiwara–Moritani reaction conditions [Pd(OAc)₂ cat. / *p*-benzoquinone or [RuCl₂(*p*-cymene)]₂ cat. / Cu(OAc)₂], tested in the model coupling between *p*-methoxyphenylfurfurylimine (PMP-imine) **F1** and ethyl acrylate (4 equivalents), gave no C3-alkenylated product **F2a** (Table 1, entry 1). Only traces of the C5-alkenylated product **F2a'** were observed in the case of Ru(II) catalysis (entry 2). Gratifyingly, the use of Ru₃(CO)₁₂ (5 mol%), in toluene, gave, after 24 h at 135 °C in a sealed tube under argon atmosphere, the expected dehydrogenative C3 coupling product **F2a** in 44% isolated yield, without any trace of the corresponding C5-functionalized product (entry 3).⁵⁹ This result suggests that the nature and the oxidation state of the Ru catalyst are crucial to obtain the desired imine–Ru coordination, which is in turn a *condicio sine qua non* to promote the C3-functionalization. Furthermore, pilot experiments showed that this coupling works only with electron-poor alkenes or styrenes. However, the bidentate *N,N'*-imino-amine directing group, which gave satisfactory results in the Murai reaction,⁴⁴ provided neither the desired alkenylated (Fujiwara-type) product, nor the alkylated (Murai-type) product (see Supporting Information SI). Comparable results in terms of yield were obtained carrying out the coupling under air or argon atmosphere (compare entries 3 and 4). These results clearly prove that oxygen does not act as oxidant for the ruthenium catalyst. So, how to explain our seemingly acceptorless C–H/C–H coupling? We suspected that excess acrylate acted as an endogenous sacrificial H₂ acceptor (*vide infra*).⁶⁰ In line with the above speculation, repetition of the experiment of entry 4, in the presence of only 1 equivalent of

acrylate, gave product **F2a** in a decreased yield of 7%. However, the addition of *tert*-butylethylene as a potential hydrogen acceptor,⁶¹ along with the use of only one equivalent of acrylate, was not as effective, as using an excess of the acrylate partner (entry 5).⁶² Further optimization studies varying the solvent, the temperature, as well as the reaction time did not reach better results (see SI for details).⁶³

Table 1. Fujiwara–Moritani reaction on PMP-imine **F1**

entry	conditions	results ^[a]
1	Pd(OAc) ₂ (5 mol%), <i>p</i> -benzoquinone (1 equiv.), PTSA (1 equiv.), AcOH/PhMe, 60 °C, 24 h	NR /hydrolysis
2	[RuCl ₂ (<i>p</i> -cymene)] ₂ (5 mol%), Cu(OAc) ₂ (2 equiv.), PhMe, 135 °C, 24 h	F2a' 22%
3	Ru ₃ (CO) ₁₂ (5 mol%), PhMe, 135 °C, 24 h (argon atmosphere)	F2a (47%), 44%
4	Ru ₃ (CO) ₁₂ (5 mol%), PhMe, 135 °C, 24 h (air atmosphere)	F2a (50%), 46%
5 ^[b]	Ru ₃ (CO) ₁₂ (5 mol%), 3 equiv. of TBE, PhMe, 135 °C, 24 h (air atmosphere)	F2a (13%)

^[a] In parentheses, ¹H-NMR yield, determined using *p*-dinitrobenzene as internal standard. Isolated yield from silica gel chromatography deactivated with 1% of Et₃N.

^[b] With 1.1 equiv. of ethyl acrylate. TBE = *tert*-butylethylene

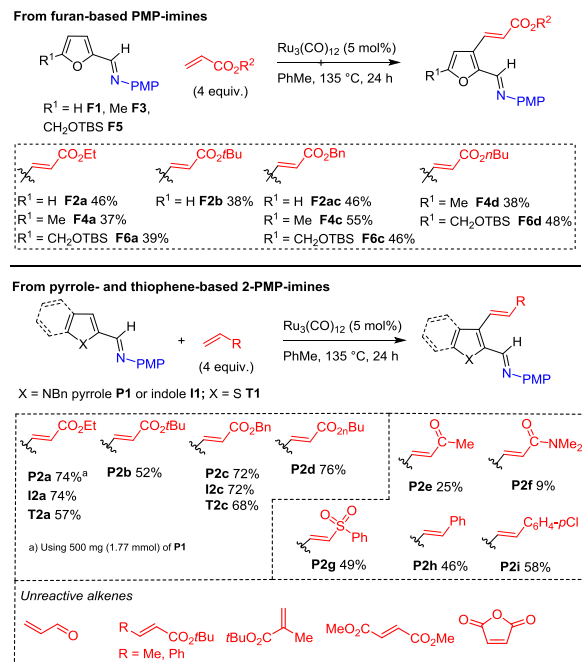
With the optimal conditions in hand [5 mol% Ru₃(CO)₁₂, acrylate (4 equiv.), PhMe, 135 °C, 24 h (air)], the scope of this C3–H alkenylation was subsequently studied in the coupling between the PMP-imines of furfural (**F1**), 5-methylfurfural (**F3**), *O*-TBS-protected HMF (**F5**), and ethyl-, *n*-butyl-, *t*-butyl-, and benzyl acrylates (Scheme 2, top). The nature of the C5 substituent in the starting furfurylimines did not sensibly affect the couplings, which led to the expected coupled products **F2a**, **F4a**, and **F6a** from ethyl acrylate, **F2b** from *t*-butyl acrylate, **F4d** and **F6d** from *n*-butyl acrylate, and **F2c**, **F4c**, and **F6c** from benzyl-acrylate, in moderate yields.

Following these encouraging results, we decided to extend our study to pyrrol- and thiophene-based 2-imino heterocyclopentadienes (Scheme 2, bottom). First, pyrrole 2-carboxaldehyde was considered as a suitable starting substrate,⁶⁴ given its direct availability from furfural via the Paal–Knorr synthesis,⁶⁵ or via a three-step sequence (carbonyl reduction / Achmatowicz rearrangement / Maillard condensation).⁶⁶ Indole and thiophene 2-carboxaldehydes were also included, to assess the scope of the coupling within the heterocyclopentadiene family. The couplings of these *N*-based heterocycles were found to be much more efficient and selective than those of the previously studied more fragile furfural derivatives. Accordingly, the coupling between *N*-benzylpyrrole 2-PMP-imine **P1** and ethyl-, *t*-butyl-, *n*-butyl-, and benzyl acrylates led to the expected products (**P2a–d**) in fair to good yields. Similarly, this C–H/C–H coupling could be extended to the 2-PMP-imines of *N*-benzylindole (**I1**), and thiophene (**T1**), which reacted efficiently with ethyl- and benzyl-acrylates to afford the coupled products **I2a**, **I2c**, **T2a**, **T2c**. Further variations at the electron-poor alkene partner were also considered. However α - and β -substituted acrylates, as well as acrolein did not allow the coupling, even under more forcing reaction conditions.

Other monosubstituted electron-poor alkenes were considered as coupling partners for imine **P1** (Scheme 2, bottom).

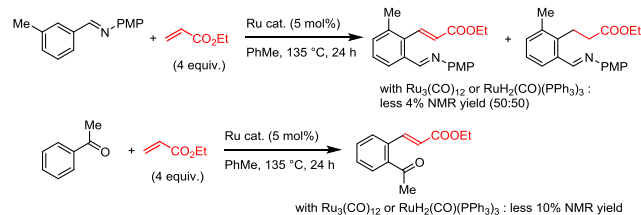
Methyl vinyl ketone gave the expected adduct **P2e** in 25% yield, whereas *N,N'*-dimethyl acrylamide gave **P2f** in only 9% yield. Better results were obtained with phenyl vinyl sulfone, which afforded the coupled product **P2g** in 49% yield. Styrene, and 4-chlorostyrene gave the corresponding coupled products **P2h** and **P2i** in 46% and 58% yield, respectively. Thus, in the case of styrenes, by playing with the CO atmosphere, it is possible to switch from a carbonylative Murai coupling⁴⁷ to a Fujiwara-Moritani type alkenylation. This feature renders the Ru(0)-catalyzed C3–H functionalization of five-membered heteroarene scaffolds quite general and versatile.

Scheme 2. Ru(0)-catalyzed alkenylation of furan- (top) and pyrrole- and thiophene-based 2-PMP-imines (bottom)



Finally, we wished to verify if the presently developed Ru(0)-catalyzed protocol could also enable the directed Fujiwara-Moritani coupling between simple aryl PMP-imines (or aryl ketones) and electron-poor alkenes. To this purpose, *N*-PMP-(*m*-tolyl)methanimine was synthesized and then submitted to our standard protocol in the presence of ethyl acrylate. A second experiment was repeated replacing the imine with acetophenone (Scheme 3).

Scheme 3. Attempted Ru(0)-catalyzed alkenylations of benzenic derivatives

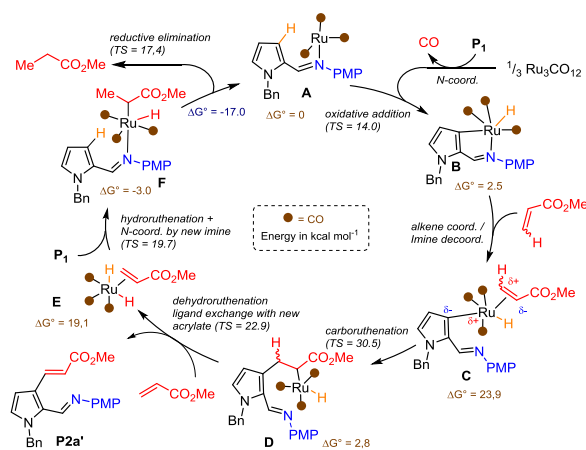


The former experiment gave only traces of a mixture of the alkylated (Murai type) and the alkenylated products (Fujiwara-Moritani type), while the second experiment gave only 10% of the alkenylated one. These results unambiguously demonstrate that our Ru(0)-catalyzed protocol selectively enables the coupling between carboxaldehyde-heterocyclopentadienes and

electron-poor alkenes. Such a selective and unprecedented reactivity is likely due to the combination of the electron richness of the Ru(0) pre-catalyst and of the heterocyclopentadienes with the electron poor nature of the acrylate derivative.

The mechanism of the C3-alkenylation between pyrrole **P1** and methyl acrylate was also studied via DFT calculations.⁶⁷ As in our previous mechanistic studies concerning Ru-catalyzed C–H functionalizations,^{44,47} we anticipate the conversion of the trimeric Ru₃(CO)₁₂ pre-catalyst into a mononuclear ruthenium carbonyl by Ru–Ru breaking and CO release.^{68,69} However, the simplicity of the model used may limit the scope of the calculations. The simplified calculated catalytic cycle is shown in Scheme 4, while the complete reaction free energy profile is presented in the SI.

Scheme 4. Proposed mechanism for the Ru(0)-catalyzed alkenylative coupling between N-based PMP-imine **P1** and methyl acrylate. Free energy (kcal/mol) relative to **A**.



The proposed mechanism starts with complex **A**, wherein the imine function of substrate **P1** coordinates Ru(CO)₃. Oxidative addition of the C3–H bond to the metal affords the corresponding Ru(II) hydride intermediate **B**. This is a slightly endergonic step ($\Delta G = 2.5$ kcal/mol) with a barrier of 14.0 kcal/mol. The reaction proceeds with olefin η^2 -coordination, which occurs with simultaneous break of imine coordination to give intermediate **C**. This is followed by the regioselective carboration of the acrylate to generate intermediate **D**, which overcomes a barrier of 30.5 kcal/mol.⁷⁰ This is the highest energy transition state along the path and corresponds to the TOF determining transition state (TDTS) of the process. Decoordination of the imine ligand followed by β -elimination produces the product, **P2a'**, η^2 -coordinated through the C=C double bond (**D'**, Figure S1 in the SI). A new acrylate molecule replaces **P2a'** in the metal coordination sphere resulting in the Ru(II)-dihydride **E**. Hydroruthenation of **E** followed by metal coordination by the imine function of a new entering molecule of imine **P1** gives intermediate **F**. Finally, passing through a barrier of 17 kcal/mol, a reductive elimination generates methyl propionate and regenerates the starting Ru(0) complex. So, overall, in the catalytic cycle one molecule of imine reacts with two molecules of acrylate to generate one molecule of alkenylated coupling product and one molecule of methyl propionate.

CONCLUSION

In summary, we have developed a novel Ru(0)-catalyzed method for the selective C3-alkenylation of oxygen-, nitrogen-

and sulfur-based heterocyclopentadiene 2-PMP-imines, in the presence of acrylic acid derivatives. In the case of the pyrrole ring, the coupling could be extended to a variety of electron-poor alkene partners with good results. This method does not need the presence of an additional external sacrificial oxidant, as a second unit of the acrylic acid derivative enters the catalytic cycle, accepting the two H atoms expelled in the C–H/C–H coupling. This hidden acceptor part of the cycle is key, as it renders the process thermodynamically favorable, allowing the closure of the catalytic cycle.

This protocol is not only regioselective for the C3–H functionalization, but also chemoselective, as it does not touch carbocyclic arylimines. In particular, in the case of styrenes, by playing with the CO atmosphere, one can switch from a carbonylative Murai coupling to a Fujiwara-Moritani type alkenylation. Finally, DFT computations allowed to propose a plausible mechanism for this process, and unveiled the hidden acceptor.

EXPERIMENTAL SECTION

General Information. All reactions were carried out under an argon by standard syringe and septa techniques. Reagents and solvents were purchased from commercial sources and generally used as received. CH₂Cl₂, Et₂O, THF, CH₃CN and DMF were dried on a Mbraun purification system MB SPS-800. NMR spectra (¹H, ¹³C{¹H}) were recorded on a Bruker AM 300 MHz or on a Bruker AVANCE 400 MHz spectrophotometer. NMR experiments were carried out at room temperature in CDCl₃. Chemical shifts are given in parts per million (ppm) using the CDCl₃ residual non-deuterated signals as reference (δ ¹H = 7.26 ppm; δ ¹³C{¹H} = 77.16 ppm). The terms m, s, d, t, q and br s represent multiplet, singlet, doublet, triplet, quartet and broad singlet, respectively. Coupling constants (*J*) are given in Hertz (Hz). For previously unknown compounds, a combination of ¹³C{¹H}, DEPT and 2D experiments (COSY, HSQC, HMBC) were used. IR spectra were recorded with a Tensor 27 (ATR Diamond) Bruker spectrophotometer. IR spectra were reported as characteristic bands (cm⁻¹). High-resolution mass spectra (HRMS) were recorded using a mass spectrometer MicroTOF from Bruker with an electron spray ion source (ESI) and a TOF detector or using a mass spectrometer from Thermo Fisher Scientific with an electron spray ion source (ESI) and a LTQ Orbitrap as detector at Institut Parisien de Chimie Moléculaire. Melting points were measured in capillary tubes on a Stuart Scientific SMP3 apparatus and are uncorrected. For the synthesis and characterization of 2-carboxaldimine heteroaromatic starting materials, see the Supporting Information.

General procedure for the ruthenium vinylation Fujiwara-Moritani type reaction. To a pressure tube, dried under vacuum, was added the Ru₃(CO)₁₂ (16 mg, 0.025 mmol, 0.05 equiv.). The aldimine (0.5 mmol, 1 equiv.) dissolved in toluene (0.5 M), was then added followed by the acrylate partner (2 mmol, 4 equiv.). The solution was heated at 135 °C for 16–24 h. The mixture was filtered over celite and washed with CH₂Cl₂. The volatiles were removed under reduced pressure and the crude was then purified by silica column chromatography affording the corresponding product.

Ethyl (E)-3-(2-((E)-((4-methoxyphenyl)imino) methyl)furan-3-yl)acrylate (F2a). Prepared according to general procedure from the reaction of **F1** (100 mg, 0.5 mmol, 1 equiv.) with ethyl acrylate (225 μL, 2 mmol, 4 equiv.). The crude mixture was purified by flash column chromatography on deactivated silica gel eluting with pentane/Et₂O (75/25) to afford 68 mg (46% yield) of **F2a** as yellow oil. ¹H-NMR (400

MHz, CDCl₃): δ 8.46 (s, 1H), 7.96 (d, *J* = 15.8 Hz, 1H), 7.45 (d, *J* = 1.3 Hz, 1H), 7.24 (d, *J* = 8.9 Hz, 2H), 6.86 (d, *J* = 8.9 Hz, 2H), 6.63 (d, *J* = 1.6 Hz, 1H), 6.23 (d, *J* = 15.8 Hz, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 3.75 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 3H). ¹³C{¹H}-NMR (101 MHz, CDCl₃): δ 166.6, 159.0, 150.7, 145.4, 143.9, 143.4, 133.1, 125.7, 122.6, 120.8, 114.5, 109.5, 60.6, 55.5, 14.3. IR (cm⁻¹): ν 2928, 1685, 1508, 1247, 1179, 1031, 762. HRMS: *m/z* calculated for C₁₇H₁₈NO₄ [M+H]⁺: 300.1230; found: 300.1231.

Tert-butyl (E)-3-(2-((E)-((4-methoxyphenyl)imino) methyl)furan-3-yl)acrylate (F2b). Prepared according to general procedure from the reaction of **F1** (100 mg, 0.5 mmol, 1 equiv.) with *t*-butyl acrylate (290 μL, 2 mmol, 4 equiv.). The crude mixture was purified by flash column chromatography on deactivated silica gel eluting with pentane/Et₂O (80/20) to afford 63 mg (38% yield) of **F2b** as brown solid. **M.p.:** 103–105 °C. ¹H-NMR (400 MHz, CDCl₃): δ 8.53 (s, 1H), 7.95 (d, *J* = 15.8 Hz, 1H), 7.55 (s, 1H), 7.33 (d, *J* = 8.8 Hz, 2H), 6.95 (dd, *J* = 8.5, 6.6 Hz, 2H), 6.71 (s, 1H), 6.26 (d, *J* = 15.7 Hz, 1H), 3.84 (s, 3H), 1.54 (s, 9H). ¹³C{¹H}-NMR (101 MHz, CDCl₃): δ 166.0, 159.0, 150.4, 145.7, 143.9, 132.0, 126.0, 122.6, 122.3, 114.5, 112.2, 109.5, 110.8, 55.5, 28.2. IR (cm⁻¹): ν 2928, 1695, 1631, 1506, 1244, 1445, 854. HRMS: *m/z* calculated for C₁₉H₂₁NNaO₄ [M+Na]⁺: 350.1368; found: 350.1368.

Benzyl (E)-3-(2-((E)-((4-methoxyphenyl)imino) methyl)furan-3-yl)acrylate (F2c). Prepared according to general procedure from the reaction of **F1** (100 mg, 0.5 mmol, 1 equiv.) with benzyl acrylate (300 μL, 2 mmol, 4 equiv.), under nitrogen atmosphere. The crude mixture was purified by flash column chromatography on deactivated silica gel eluting with hexane/Et₂O (85/15) to afford 115 mg (46% yield) of **F2c** as yellow oil. ¹H-NMR (400 MHz, CDCl₃): δ 8.44 (s, 1H), 8.05 (d, *J* = 15.8 Hz, 1H), 7.44 (s, 1H), 7.34–7.20 (m, 7H), 6.84 (d, *J* = 8.7 Hz, 2H), 6.61 (s, 1H), 6.27 (d, *J* = 15.8 Hz, 1H), 5.17 (s, 2H), 3.74 (s, 3H). ¹³C{¹H}-NMR (101 MHz, CDCl₃): δ 166.4, 159.1, 150.8, 145.4, 143.8, 143.5, 136.0, 133.9, 128.6, 128.3, 128.3, 125.5, 122.6, 120.3, 114.5, 109.5, 66.5, 55.5. IR (cm⁻¹): ν 2918, 1708, 1614, 1493, 1247, 1142. HRMS: *m/z* calculated for C₂₂H₁₉NNaO₄ [M+Na]⁺: 384.1212; found: 384.1213.

Ethyl (E)-3-(2-((E)-((4-methoxyphenyl)imino) methyl)-5-methylfuran-3-yl)acrylate (F4a). Prepared according to general procedure from the reaction of **F3** (107 mg, 0.5 mmol, 1 equiv.) with ethyl acrylate (225 μL, 2 mmol, 4 equiv.). The crude mixture was purified by flash column chromatography on deactivated silica gel eluting with pentane/Et₂O (80/20) to afford 51 mg (37% yield) of **F4a** as yellow oil. ¹H-NMR (300 MHz, CDCl₃): δ 8.45 (s, 1H), 7.91 (d, *J* = 15.7 Hz, 1H), 7.28 (d, *J* = 8.8 Hz, 2H), 6.92 (d, *J* = 8.8 Hz, 2H), 6.32 (s, 1H), 6.23 (d, *J* = 15.7 Hz, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 3.82 (s, 3H), 2.40 (s, 3H), 1.32 (t, *J* = 7.1 Hz, 3H). ¹³C{¹H}-NMR (101 MHz, CDCl₃): δ 166.7, 158.7, 156.6, 129.6, 144.3, 143.2, 133.0, 127.5, 122.5, 120.3, 144.4, 105.8, 60.6, 55.5, 14.3, 13.9. IR (cm⁻¹): ν 2980, 1704, 1614, 1500, 1295, 1242, 1174, 1031, 831. HRMS: *m/z* calculated for C₁₈H₁₉NNaO₄ [M+Na]⁺: 336.1206; found: 336.1207.

Butyl (E)-3-(2-((E)-((4-methoxyphenyl)imino) methyl)-5-methylfuran-3-yl)acrylate (F4d). Prepared according to general procedure from the reaction of **F3** (107 mg, 0.5 mmol, 1 equiv.) with butyl acrylate (287 μL, 2 mmol, 4 equiv.). The crude mixture was purified by flash column chromatography on deactivated silica gel eluting with hexane/AcOEt (70/30) to afford 64 mg (38% yield) of **F4d** as yellow oil. ¹H-NMR (400 MHz, CDCl₃): δ 8.47 (s, 1H), 7.92 (d, *J* = 15.7 Hz, 1H), 7.30

(d, $J = 8.6$ Hz, 2H), 6.94 (d, $J = 8.5$ Hz, 2H), 6.34 (s, 1H), 6.25 (d, $J = 15.7$ Hz, 1H), 4.21 (t, $J = 6.6$ Hz, 2H), 3.84 (s, 3H), 2.42 (s, 3H), 1.72-1.66 (m, 2H), 1.47-1.41 (m, 2H), 0.97 (t, $J = 7.3$ Hz, 3H). $^{13}\text{C}\{^1\text{H}\}$ -NMR (101 MHz, CDCl_3): δ 166.8, 158.8, 156.5, 149.7, 144.3, 143.2, 133.1, 127.5, 122.5, 120.4, 114.4, 105.9, 64.5, 55.5, 30.8, 19.2, 13.9, 13.7. IR (cm^{-1}): ν 2958, 1706, 1629, 1501, 1244, 1175, 1033. HRMS: m/z calculated for $\text{C}_{20}\text{H}_{24}\text{NO}_4$ $[\text{M}+\text{H}]^+$: 342.1705; found: 342.1706.

Benzyl (E)-3-(2-((E)-((4-methoxyphenyl)imino)methyl)-5-methylfuran-3-yl)acrylate (F4c). Prepared according to general procedure from the reaction of **F3** (107 mg, 0.5 mmol, 1 equiv.) with benzyl acrylate (287 μL , 2 mmol, 4 equiv.). The crude mixture was purified by flash column chromatography on deactivated silica gel eluting with hexane/ Et_2O (70/30) to afford 103 mg (55% yield) of **F4c** as yellow oil. ^1H -NMR (400 MHz, CDCl_3): δ 8.37 (s, 1H), 7.92 (d, $J = 15.7$ Hz, 1H), 7.33-7.24 (m, 5H), 7.20 (d, $J = 8.8$ Hz, 2H), 6.84 (d, $J = 8.8$ Hz, 2H), 6.30-6.16 (m, 2H), 5.17 (s, 2H), 3.74 (s, 3H), 2.31 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ -NMR (101 MHz, CDCl_3): δ 166.5, 158.8, 156.6, 149.8, 144.3, 143.2, 136.0, 133.8, 128.6, 128.3 (2C), 127.3, 122.5, 119.9, 114.5, 105.8, 66.5, 55.5, 13.9. IR (cm^{-1}): ν 2937, 1704, 1608, 1257, 1169, 1055. HRMS: m/z calculated for $\text{C}_{23}\text{H}_{22}\text{NO}_4$ $[\text{M}+\text{H}]^+$: 376.1549; found: 376.1552.

Ethyl (E)-3-(5-(((tert-butyl)dimethylsilyloxy)methyl)-2-((E)-((4-methoxyphenyl)imino)methyl)furan-3-yl)acrylate (F6a). Prepared according to general procedure from the reaction of **F5** (174 mg, 0.5 mmol, 1 equiv.) with ethyl acrylate (225 μL , 2 mmol, 4 equiv.). The crude mixture was purified by flash column chromatography on deactivated silica gel eluting with pentane/ Et_2O (90/10) to afford 86 mg (39% yield) of **F6a** as yellow oil. ^1H -NMR (300 MHz, CDCl_3): δ 8.49 (s, 1H), 8.02 (d, $J = 15.8$ Hz, 1H), 7.29 (d, $J = 8.8$ Hz, 2H), 6.93 (d, $J = 8.8$ Hz, 2H), 6.57 (s, 1H), 6.30 (d, $J = 15.8$ Hz, 1H), 4.74 (s, 2H), 4.26 (q, $J = 7.1$ Hz, 2H), 3.83 (s, 3H), 1.33 (t, $J = 7.1$ Hz, 3H), 0.93 (s, 9H), 0.12 (s, 6H). $^{13}\text{C}\{^1\text{H}\}$ -NMR (101 MHz, CDCl_3): δ 166.7, 158.9, 158.5, 150.0, 144.1, 143.7, 133.3, 126.7, 122.5, 120.6, 114.4, 106.0, 60.6, 58.6, 55.5, 25.8, 18.4, 14.3, -5.3. IR (cm^{-1}): ν 2954, 2930, 1708, 1616, 1501, 1246, 1176, 1033, 834. HRMS: m/z calculated for $\text{C}_{24}\text{H}_{34}\text{NO}_5\text{Si}$ $[\text{M}+\text{H}]^+$: 444.2199; found: 444.2201.

Benzyl (E)-3-(5-(((tert-butyl)dimethylsilyloxy)methyl)-2-((E)-((4-methoxyphenyl)imino)methyl)furan-3-yl)acrylate (F6c). Prepared according to general procedure from the reaction of **F5** (174 mg, 0.5 mmol, 1 equiv.) with benzyl acrylate (300 μL , 2 mmol, 4 equiv.). The crude mixture was purified by flash column chromatography on deactivated silica gel eluting with hexane/ Et_2O (85/15) to afford 115 mg (46% yield) of **F6c** as yellow oil. ^1H -NMR (400 MHz, CDCl_3): δ 8.50 (s, 1H), 8.14 (d, $J = 15.8$ Hz, 1H), 7.44-7.34 (m, 5H), 7.29 (d, $J = 8.7$ Hz, 2H), 6.93 (d, $J = 8.6$ Hz, 2H), 6.58 (s, 1H), 6.36 (d, $J = 15.8$ Hz, 1H), 5.26 (s, 2H), 4.75 (s, 2H), 3.84 (s, 3H), 0.94 (s, 9H), 0.13 (s, 6H). $^{13}\text{C}\{^1\text{H}\}$ -NMR (101 MHz, CDCl_3): δ 166.5, 158.9, 158.5, 150.2, 144.1, 143.8, 136.0, 134.1, 128.6, 128.3, 126.5, 122.6, 122.3, 120.2, 114.5, 106.0, 66.5, 58.6, 55.5, 25.9, 18.4, -5.3. IR (cm^{-1}): ν 2954, 2929, 1712, 1632, 1617, 1502, 1248, 1164, 836. HRMS: m/z calculated for $\text{C}_{29}\text{H}_{36}\text{NO}_5\text{Si}$ $[\text{M}+\text{H}]^+$: 506.2363; found: 506.2365.

Butyl (E)-3-(5-(((tert-butyl)dimethylsilyloxy)methyl)-2-((E)-((4-methoxyphenyl)imino)methyl)furan-3-yl)acrylate (F6d). Prepared according to general procedure from the reaction of **F5** (174 mg, 0.5 mmol, 1 equiv.) with butyl acrylate (287 μL , 2 mmol, 4 equiv.). The crude mixture was purified by flash column chromatography on deactivated silica gel eluting with pentane/ Et_2O (90/10) to afford 114 mg (48%

yield) of **F6d** as yellow oil. ^1H -NMR (400 MHz, CDCl_3): δ 8.49 (s, 1H), 8.04 (d, $J = 15.8$ Hz, 1H), 7.31 (d, $J = 8.7$ Hz, 2H), 6.93 (d, $J = 8.7$ Hz, 2H), 6.58 (s, 1H), 6.31 (d, $J = 15.8$ Hz, 1H), 4.75 (s, 2H), 4.22 (t, $J = 6.6$ Hz, 2H), 3.84 (s, 3H), 1.69 (d, $J = 7.0$ Hz, 2H), 1.44 (sext, $J = 7.4$ Hz, 2H), 0.99-0.93 (m, 12H), 0.12 (s, 6H). $^{13}\text{C}\{^1\text{H}\}$ -NMR (101 MHz, CDCl_3): δ 166.8, 158.9, 158.6, 149.9, 144.1, 143.7, 133.3, 126.8, 122.5, 120.7, 114.5, 106.0, 64.6, 58.6, 55.5, 30.8, 25.8, 19.2, 18.4, 13.7, -5.3. IR (cm^{-1}): ν 2928, 1695, 1631, 1506, 1244, 1145, 1034, 854. HRMS: m/z calculated for $\text{C}_{26}\text{H}_{38}\text{NO}_5\text{Si}$ $[\text{M}+\text{H}]^+$: 472.2519; found: 472.2520.

Ethyl (E)-3-(1-benzyl-2-((E)-((4-methoxyphenyl)imino)methyl)-1H-pyrrol-3-yl)acrylate (P2a). Prepared according to general procedure from the reaction of **P1** (141 mg, 0.5 mmol, 1 equiv.) with ethyl acrylate (225 μL , 2 mmol, 4 equiv.). The crude mixture was purified by flash column chromatography on deactivated silica gel eluting with pentane/ Et_2O (70/30) to afford 139 mg (74% yield) of **P2a** as yellow solid. M.p.: 84-85 $^\circ\text{C}$. (From 500 mg of **P1** (1.77 mmol), 490 mg of **P2a** were isolated (74%)). ^1H -NMR (400 MHz, CDCl_3): δ 8.53 (s, 1H), 7.92 (d, $J = 15.6$ Hz, 1H), 7.25-7.15 (m, 3H), 7.08 (d, $J = 6.9$ Hz, 2H), 7.01 (d, $J = 8.8$ Hz, 2H), 6.81 (d, $J = 8.9$ Hz, 2H), 6.76 (d, $J = 2.9$ Hz, 1H), 6.43 (d, $J = 2.9$ Hz, 1H), 6.17 (d, $J = 15.6$ Hz, 1H), 5.69 (s, 2H), 4.17 (q, $J = 7.1$ Hz, 2H), 3.74 (s, 3H), 1.25 (t, $J = 7.1$ Hz, 3H). $^{13}\text{C}\{^1\text{H}\}$ -NMR (101 MHz, CDCl_3): δ 167.5, 158.1, 146.1, 145.1, 138.1, 135.7, 129.2, 128.8, 128.6, 127.4, 127.1, 126.6, 121.9, 116.2, 114.4, 106.8, 60.2, 55.5, 52.6, 14.4. IR (cm^{-1}): ν 2979, 1696, 1613, 1502, 1438, 1242, 1151, 1035, 831. HRMS: m/z calculated for $\text{C}_{24}\text{H}_{24}\text{N}_2\text{O}_3\text{Na}$ $[\text{M}+\text{Na}]^+$: 411.1679; found: 411.1679.

tert-Butyl (E)-3-(1-benzyl-2-((E)-((4-methoxyphenyl)imino)methyl)-1H-pyrrol-3-yl)acrylate (P2b). Prepared according to general procedure from the reaction of **P1** (141 mg, 0.5 mmol, 1 equiv.) with *tert*-butyl acrylate (290 μL , 2 mmol, 4 equiv.). The crude mixture was purified by flash column chromatography on deactivated silica gel eluting with pentane/ Et_2O (90/10) to afford 109 mg (52% yield) of **P2b** as yellow oil. ^1H -NMR (400 MHz, CDCl_3): δ 8.64 (s, 1H), 7.98 (d, $J = 15.6$ Hz, 1H), 7.33 (t, $J = 7.2$ Hz, 2H), 7.27 (dd, $J = 9.9, 4.5$ Hz, 1H), 7.18 (d, $J = 7.0$ Hz, 2H), 7.12 (d, $J = 8.8$ Hz, 2H), 6.92 (d, $J = 8.9$ Hz, 2H), 6.85 (d, $J = 2.9$ Hz, 1H), 6.53 (d, $J = 2.9$ Hz, 1H), 6.23 (d, $J = 15.6$ Hz, 1H), 5.78 (s, 2H), 3.84 (s, 3H), 1.57 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ -NMR (101 MHz, CDCl_3): δ 167.0, 158.1, 146.1, 145.1, 138.2, 134.8, 129.0, 128.7, 128.6, 127.4, 127.1, 126.8, 121.9, 118.1, 114.4, 106.8, 80.1, 55.5, 52.6, 28.3. IR (cm^{-1}): ν 2976, 2931, 1697, 1615, 1503, 1244, 1140, 1033, 831. HRMS: m/z calculated for $\text{C}_{26}\text{H}_{28}\text{N}_2\text{NaO}_3$ $[\text{M}+\text{Na}]^+$: 439.1992; found: 439.1993.

Butyl (E)-3-(1-benzyl-2-((E)-((4-methoxyphenyl)imino)methyl)-1H-pyrrol-3-yl)acrylate (P2d). Prepared according to general procedure from the reaction of **P1** (141 mg, 0.5 mmol, 1 equiv.) with butyl acrylate (288 μL , 2 mmol, 4 equiv.). The crude mixture was purified by flash column chromatography on deactivated silica gel eluting with Pentane/ Et_2O (80/20) to afford 154 mg (76% yield) of **P2d** as yellow solid. M.p.: 88-89 $^\circ\text{C}$. ^1H -NMR (400 MHz, CDCl_3): δ 8.63 (s, 1H), 8.04 (d, $J = 15.6$ Hz, 1H), 7.36-7.29 (m, 2H), 7.29-7.25 (m, 1H), 7.18 (d, $J = 7.1$ Hz, 2H), 7.12 (d, $J = 8.8$ Hz, 2H), 6.91 (d, $J = 8.8$ Hz, 2H), 6.86 (d, $J = 2.8$ Hz, 1H), 6.53 (d, $J = 2.8$ Hz, 1H), 6.27 (d, $J = 15.6$ Hz, 1H), 5.78 (s, 2H), 4.22 (t, $J = 6.7$ Hz, 2H), 3.83 (s, 3H), 1.70 (quint, $J = 7.2$ Hz, 2H), 1.46 (sext, $J = 1.5$ Hz, 2H), 0.99 (t, $J = 7.4$ Hz, 3H). $^{13}\text{C}\{^1\text{H}\}$ -NMR (101 MHz, CDCl_3): δ 167.6, 158.2, 146.1,

145.1, 138.14, 135.7, 129.2, 128.8, 128.6, 127.5, 127.1, 126.6, 121.9, 116.2, 114.4, 106.9, 64.2, 55.5, 52.6, 30.9, 19.2, 13.8. IR (cm⁻¹): ν 2957, 1701, 1615, 1503, 1439, 1245, 1173, 1153, 831. HRMS: m/z calculated for C₂₆H₂₈N₂NaO₃ [M+H]⁺: 439.1992; found: 439.1995.

Benzyl (E)-3-(1-benzyl-2-((E)-(4-methoxyphenyl)imino)methyl)-1H-pyrrol-3-yl)acrylate (P2c). Prepared according to general procedure **GP3** from the reaction of **P1** (141 mg, 0.5 mmol, 1 equiv.) with benzyl cinnamate (306 μ L, 2 mmol, 4 equiv.). The crude mixture was purified by flash column chromatography on deactivated silica gel eluting with pentane/Et₂O (80/20) to afford 172 mg (72% yield) of **P2c** as yellow solid. M.p.: 117-119 °C. ¹H-NMR (400 MHz, CDCl₃): δ 8.49 (s, 1H), 7.98 (t, J = 15.7 Hz, 1H), 7.32-7.13 (m, 8H), 7.05 (d, J = 7.1 Hz, 2H), 6.98 (d, J = 8.7 Hz, 2H), 6.78 (d, J = 8.8 Hz, 2H), 6.72 (d, J = 2.7 Hz, 1H), 6.40 (d, J = 2.7 Hz, 1H), 6.20 (d, J = 15.6 Hz, 1H), 5.61 (d, J = 18.4 Hz, 2H), 5.14 (s, 2H), 3.70 (s, 3H). ¹³C{¹H}-NMR (101 MHz, CDCl₃): δ 167.4, 158.2, 146.0, 145.0, 138.1, 136.5, 136.4, 129.4, 128.8, 128.7, 128.6, 128.2, 128.1, 127.5, 127.1, 126.5, 122.0, 115.7, 114.4, 106.9, 66.1, 55.5, 52.6. IR (cm⁻¹): ν 2955, 1702, 1614, 1502, 1439, 1244, 1149, 1029, 730. HRMS: m/z calculated for C₂₉H₂₆N₂NaO₃ [M+H]⁺: 473.1836; found: 473.1842.

(E)-4-(1-benzyl-2-((E)-(4-methoxyphenyl)imino)methyl)-1H-pyrrol-3-yl)but-3-en-2-one (P2e). Prepared according to general procedure from the reaction of **P1** (141 mg, 0.5 mmol, 1 equiv.) with but-3-en-2-one (162 μ L, 2 mmol, 4 equiv.). The crude mixture was purified by flash column chromatography on deactivated silica gel eluting with pentane/Et₂O (60/40) to afford 44 mg (25% yield) of **P2e** as yellow oil. ¹H-NMR (400 MHz, CDCl₃): δ 8.61 (s, 1H), 8.01 (d, J = 15.9 Hz, 1H), 7.35-7.28 (m, 3H), 7.17 (d, J = 7.2 Hz, 2H), 7.11 (d, J = 8.8 Hz, 2H), 6.92 (d, J = 8.8 Hz, 2H), 6.88 (d, J = 2.8 Hz, 1H), 6.59 (d, J = 15.1 Hz, 2H), 5.73 (s, 2H), 3.84 (s, 3H), 2.37 (s, 3H). ¹³C{¹H}-NMR (101 MHz, CDCl₃): δ 198.4, 158.3, 146.0, 145.0, 137.9, 135.1, 129.8, 128.7, 128.7, 127.6, 127.0, 126.3, 125.5, 121.9, 114.4, 107.0, 55.5, 52.5, 27.6. IR (cm⁻¹): ν 2933, 1611, 1502, 1438, 1244, 1032, 832. HRMS: m/z calculated for C₂₃H₂₂N₂NaO₂ [M+Na]⁺: 381.1573; found: 381.1573.

(E)-3-(1-benzyl-2-((E)-(4-methoxyphenyl)imino)methyl)-1H-pyrrol-3-yl)-N,N-dimethylacrylamide (P2f). Prepared according to general procedure from the reaction of **P1** (141 mg, 0.5 mmol, 1 equiv.) *N,N*-dimethylacrylamide (206 μ L, 2 mmol, 4 equiv.). The crude mixture was purified by flash column chromatography on deactivated silica gel eluting with pentane/Et₂O (20/80) to afford 17 mg (9% yield) of **P2f** as yellow oil. M.p.: 105-107 °C. ¹H-NMR (400 MHz, CDCl₃): δ 8.67 (s, 1H), 7.98 (d, J = 15.0 Hz, 1H), 7.33-7.24 (m, 3H), 7.17 (d, J = 7.1 Hz, 2H), 7.10 (d, J = 8.9 Hz, 2H), 6.90-6.86 (m, 2H), 6.84 (d, J = 2.9 Hz, 1H), 6.71 (d, J = 15.0 Hz, 1H), 6.50 (d, J = 2.8 Hz, 1H), 5.80 (s, 2H), 3.82 (s, 3H), 3.16 (s, 3H), 3.07 (s, 3H). ¹³C{¹H}-NMR (101 MHz, CDCl₃): δ 167.1, 158.0, 146.4, 145.1, 138.4, 133.4, 128.9, 128.6, 128.5, 127.6, 127.4, 127.2, 122.0, 115.5, 114.3, 106.4, 55.5, 52.6, 37.3, 35.9. IR (cm⁻¹): ν 2928, 2012, 1940, 1643, 1614, 1502, 1439, 1391, 1244, 1139, 1032. HRMS: m/z calculated for C₂₄H₂₆N₂O₂ [M+H]⁺: 388.2020; found: 388.2024.

(E)-1-(1-benzyl-3-((E)-2-(phenylsulfonyl)vinyl)-1H-pyrrol-2-yl)-N-(4-methoxyphenyl)methanimine (P2g). Prepared according to general procedure from the reaction of **P1** (141 mg, 0.5 mmol, 1 equiv.) with phenylvinylsulphone (336 mg, 2 mmol, 4 equiv.). The crude mixture was purified by flash column chromatography on deactivated silica gel eluting with pentane/Et₂O (70/30) to afford 112 mg (49% yield) of **P2g** as yellow solid. M.p.: 113-115 °C. ¹H-NMR (400 MHz, CDCl₃):

δ 8.59 (s, 1H), 8.03 (d, J = 15.0 Hz, 1H), 7.94 (d, J = 7.5 Hz, 2H), 7.58 (d, J = 6.8 Hz, 1H), 7.56-7.50 (m, 2H), 7.33-7.27 (m, 3H), 7.12 (t, J = 7.8 Hz, 4H), 6.91 (d, J = 8.7 Hz, 2H), 6.83 (d, J = 2.7 Hz, 1H), 6.64 (d, J = 15.0 Hz, 1H), 6.41 (d, J = 2.7 Hz, 1H), 5.73 (s, 2H), 3.83 (s, 3H). ¹³C{¹H}-NMR (101 MHz, CDCl₃): δ 158.5, 145.4, 144.6, 141.4, 137.7, 134.3, 133.0, 130.1, 129.2, 128.8, 128.7, 127.6, 127.5, 127.1, 124.4, 123.8, 122.1, 114.5, 107.3, 55.6, 52.6. IR (cm⁻¹): ν 1608, 1502, 1443, 1314, 1243, 1143, 1031, 761, 726. HRMS: m/z calculated for C₂₇H₂₄N₂NaO₃S [M+Na]⁺: 479.1405; found: 479.1408.

(E)-1-(1-benzyl-3-((E)-4-chlorostyryl)-1H-pyrrol-2-yl)-N-(4-methoxyphenyl)methanimine (P2i). Prepared according to general procedure from the reaction of **P1** (141 mg, 0.5 mmol, 1 equiv.) with chlorostyrene (254 μ L, 2 mmol, 4 equiv.). The crude mixture was purified by flash column chromatography on deactivated silica gel eluting with hexane/Et₂O (90/10) to afford 123 mg (58% yield) of **P2i** as yellow oil. ¹H-NMR (400 MHz, CDCl₃): δ 8.50 (s, 1H), 7.36-7.23 (m, 3H), 7.24-7.20 (m, 5H), 7.10 (d, J = 7.5 Hz, 2H), 7.01 (d, J = 8.7 Hz, 2H), 6.85-6.78 (m, 4H), 6.47 (d, J = 2.6 Hz, 1H), 5.66 (s, 2H), 3.75 (s, 3H). ¹³C{¹H}-NMR (101 MHz, CDCl₃): δ 157.8, 146.8, 145.9, 138.56 (2C), 136.4, 132.6, 129.7, 128.8, 128.6, 128.6, 127.4, 127.3, 127.1, 126.7, 121.8, 120.6, 114.4, 55.6, 52.4. IR (cm⁻¹): ν 2918, 1696, 1615, 1506, 1245, 1176. HRMS: m/z calculated for C₂₇H₂₃ClN₂NaO [M+Na]⁺: 449.1397; found: 449.1396.

(E)-1-(1-benzyl-3-((E)-styryl)-1H-pyrrol-2-yl)-N-(4-methoxyphenyl)methanimine (P2h). Prepared according to general procedure from the reaction of **P1** (141 mg, 0.5 mmol, 1 equiv.) with styrene (230 μ L, 2 mmol, 4 equiv.). The crude mixture was purified by flash column chromatography on deactivated silica gel eluting with hexane/Et₂O (90/10) to afford 90 mg (46% yield) of **P2h** as brown solid. M.p.: 90-91 °C. ¹H-NMR (400 MHz, CDCl₃): δ 8.48 (s, 1H), 7.41-7.32 (m, 3H), 7.25-7.19 (m, 4H), 7.16-7.13 (m, 2H), 7.08 (d, J = 7.1 Hz, 2H), 6.99 (d, J = 8.4 Hz, 2H), 6.85 (d, J = 16.0 Hz, 1H), 6.82-6.77 (m, 3H), 6.45 (d, J = 2.0 Hz, 1H), 5.66 (s, 2H), 3.72 (s, 3H). ¹³C{¹H}-NMR (101 MHz, CDCl₃): δ 158.8, 146.9, 145.7, 138.6, 137.9, 137.1, 128.8, 128.6, 128.6, 128.3, 127.3, 127.2, 127.1, 126.8, 126.2, 121.8, 119.8, 114.4, 115.9, 55.5, 52.5. IR (cm⁻¹): ν 2927, 1613, 1502, 1438, 1243, 1033, 734. HRMS: m/z calculated for C₂₇H₂₄N₂NaO [M+Na]⁺: 415.1787; found: 415.1791.

Ethyl (E)-3-(1-benzyl-2-((E)-(4-methoxyphenyl)imino)methyl)-1H-indole-3-yl)acrylate (I2A). Prepared according to general procedure from the reaction of **I1** (171 mg, 0.5 mmol, 1 equiv.) with ethyl acrylate (225 μ L, 2 mmol, 4 equiv.). The crude mixture was purified by flash column chromatography on deactivated silica gel eluting with pentane/Et₂O (80/20) to afford 164 mg (74% yield) of **I2a** as yellow solid. M.p.: 139-141 °C. ¹H-NMR (400 MHz, CDCl₃): δ 8.93 (s, 1H), 8.32 (d, J = 15.9 Hz, 1H), 8.03 (d, J = 8.0 Hz, 1H), 7.41-7.32 (m, 2H), 7.29-7.21 (m, 4H), 7.21-7.17 (m, 2H), 7.12 (d, J = 6.9 Hz, 2H), 6.97-6.87 (m, 2H), 6.63 (d, J = 15.8 Hz, 1H), 6.11 (s, 2H), 4.31 (q, J = 7.1 Hz, 2H), 3.84 (s, 3H), 1.37 (t, J = 7.1 Hz, 3H). ¹³C{¹H}-NMR (101 MHz, CDCl₃): δ 167.8, 158.9, 146.6, 144.3, 139.7, 137.9, 135.7, 135.0, 128.5, 127.1, 126.6, 125.5, 125.3, 122.3, 122.1, 121.6, 117.8, 116.9, 114.5, 111.0, 60.4, 55.5, 48.4, 14.4. IR (cm⁻¹): ν 2980, 2904, 1702, 1614, 1492, 1465, 1247, 1175, 1030, 831. HRMS: m/z calculated for C₂₈H₂₆N₂NaO₃ [M+Na]⁺: 461.1836; found: 461.1836.

Benzyl (E)-3-(1-benzyl-2-((E)-(4-methoxyphenyl)imino)methyl)-1H-indole-3-yl)acrylate (I2c). Prepared according to general procedure from the reaction of **I1** (171 mg, 0.5

mmol, 1 equiv.) with benzyl cinnamate (306 μ L, 2 mmol, 4 equiv.). The crude mixture was purified by flash column chromatography on deactivated silica gel eluting with pentane/Et₂O (90/10) to afford 172 mg (72% yield) of **12c** as yellow solid. M.p.: 142–143 °C. ¹H-NMR (400 MHz, CDCl₃): δ 8.92 (s, 1H), 8.39 (d, J = 15.9 Hz, 1H), 8.01 (d, J = 8.0 Hz, 1H), 7.45 (d, J = 6.8 Hz, 2H), 7.39–7.33 (m, 7H), 7.18 (d, J = 8.9 Hz, 2H), 7.12 (d, J = 6.7 Hz, 2H), 6.91 (d, J = 8.9 Hz, 2H), 6.78 (d, J = 8.9 Hz, 1H), 6.68 (d, J = 15.9 Hz, 1H), 6.58 (d, J = 8.9 Hz, 1H), 6.10 (s, 2H), 5.30 (s, 2H), 3.84 (s, 3H). ¹³C{¹H}-NMR (75 MHz, CDCl₃): δ 167.7, 158.9, 146.5, 144.3, 139.7, 137.9 (2C), 136.4, 135.2, 128.6, 128.3, 127.2, 126.6, 125.6, 125.3, 122.4, 122.2, 121.6, 117.6, 116.3, 115.0, 114.7, 114.5, 111.0, 66.2, 55.6, 48.4. IR (cm⁻¹): ν 3034, 2953, 1708, 1618, 1497, 1249, 1167, 1031. HRMS: m/z calculated for C₃₃H₂₈N₂NaO₃ [M+Na]⁺: 523.1992; found: 523.1995.

Ethyl (E)-3-(2-((E)-(4-methoxyphenyl) imino) methyl)-5-methylthiophen-3-yl)acrylate (T2a). Prepared according to general procedure from the reaction of **T1** (115 mg, 0.5 mmol, 1 equiv.) with ethyl acrylate (225 μ L, 2 mmol, 4 equiv.). The crude mixture was purified by flash column chromatography on deactivated silica gel eluting with pentane/Et₂O (80/20) to afford 94 mg (57% yield) of **T2a** as yellow solid. M.p.: 89–90 °C. ¹H-NMR (300 MHz, CDCl₃): δ 8.67 (s, 1H), 7.87 (d, J = 15.7 Hz, 1H), 7.19–7.12 (m, 2H), 6.88 (s, 1H), 6.87–6.80 (m, 2H), 6.20 (d, J = 15.7 Hz, 1H), 4.18 (q, J = 7.1 Hz, 2H), 3.74 (s, 3H), 2.41 (s, 3H), 1.25 (t, J = 7.1 Hz, 3H). ¹³C{¹H}-NMR (75 MHz, CDCl₃): δ 167.0, 158.6, 148.1, 144.8, 144.2, 141.5, 138.7, 134.8, 124.3, 122.5, 119.8, 114.4, 60.7, 55.5, 15.9, 14.3. IR (cm⁻¹): ν 2978, 2934, 1705, 1609, 1471, 1291, 1245, 1173, 1034, 831. HRMS: m/z calculated for C₁₈H₁₉NNaO₃S [M+Na]⁺: 352.0978; found: 352.0978.

Benzyl (E)-3-(2-((E)-(4-methoxyphenyl) imino)methyl)-5-methylthiophen-3-yl)acrylate (T2c). Prepared according to general procedure from the reaction of **T1** (115 mg, 0.5 mmol, 1 equiv.) with benzyl acrylate (306 μ L, 2 mmol, 4 equiv.). The crude mixture was purified by flash column chromatography on deactivated silica gel eluting with Pentane/Et₂O (80/20) to afford 134 mg (68 % yield) of **T2c** as yellow solid. ¹H-NMR (400 MHz, CDCl₃): δ 8.65 (s, 1H), 7.92 (d, J = 15.7 Hz, 1H), 7.27 (m, 5H), 7.13 (d, J = 8.6 Hz, 2H), 6.85 (s, 1H), 6.81 (d, J = 8.6 Hz, 2H), 6.24 (d, J = 15.7 Hz, 1H), 5.15 (s, 2H), 3.72 (s, 3H), 2.37 (s, 3H). ¹³C{¹H}-NMR (101 MHz, CDCl₃): δ 165.8, 157.6, 146.9, 143.8, 143.1, 140.7, 137.5, 135.0, 134.4, 127.6, 127.2, 127.2, 123.2, 121.5, 118.3, 113.4, 65.4, 54.4, 14.8. IR (cm⁻¹): ν 2924, 1710, 1609, 1506, 1472, 1214, 1163, 1033. HRMS: m/z calculated for C₂₃H₂₁NNaO₃S [M+Na]⁺: 414.1140; found: 414.1146.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website. Further optimizations, DFT study details, atomic coordinates of all optimized species, experimental procedures, compound characterization (PDF).

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Notes

Any additional relevant notes should be placed here.

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