Concise Synthesis of Substituted Quinolizin-4-ones by Ring-Closing Metathesis

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The 4H-quinolizin-4-one scaffold is of significant pharmaceutical interest. This heterocyclic structure is predicted to have attractive physico-chemical properties and is present in a variety of biologically active molecules. Despite these interesting characteristics, 4H-quinolizin-4-ones are largely under-represented in current small molecule screening libraries, and, therefore, this scaffold has been poorly investigated. Herein, a new strategy is reported for the syntheses of these rare and biologically interesting 4H-quinolizin-4-ones. This modular route involves the regioselective N-alkylation of 6-halo-2-pyridones followed by a Stille cross-coupling, ring-closing metathesis, and palladium-catalyzed dehydrogenation reaction sequence. This method furnishes the target compounds in good yields and allows for access to unusual substitution patterns that are difficult to achieve by using other synthetic strategies.

Introduction

Heterocyclic drugs are found in all therapeutic areas of medicinal chemistry, and heterocyclic rings are also the core scaffold of numerous agrochemicals.[1,2] It is therefore not surprising that there remains intense interest in the synthesis of both new heterocyclic systems and heterocycles that have been underexploited in drug and agrochemical research. Quinolizinones are a class of heterocycles that have attracted the attention of the pharmaceutical industry in recent years. These bicyclic systems, which contain a nitrogen atom at the ring junction, are predicted to have favorable physico-chemical properties as a result of their polar zwitterionic character (see Figure 1).[2,3] The 4H-quinolizin-4-one scaffold has garnered particular attention. In addition to its predicted physico-chemical properties, this heterocyclic unit is present in a variety of molecules that have interesting biological activities (see Figure 1).[2,4] Despite these properties, 4H-quinolizin-4-ones are largely under-represented in current small molecule screening libraries. Overall, this scaffold has been poorly investigated. The relative paucity of these compounds can be attributed primarily to their synthetic intractability. General methods to construct this ring system are relatively scarce, with synthetic approaches individually tailored for a particular target. When their preparation is combined with the requirement for substitution on the ring system, the syntheses typically become unwieldy and difficult to perform. Recently, Muir et al. reported an elegant general route towards 4H-quinolizin-4-ones that proceeded through the construction of the oxygenated ring.[2] This method allowed for the introduction of substituents at the 2-position of the bicyclic ring system. However, the introduction of substituents at other positions of the scaffold was not reported. Complementary synthetic approaches that allow access to 4H-quinolizin-4-ones with alternative substitution patterns would therefore be of significant value. These would expand upon the range
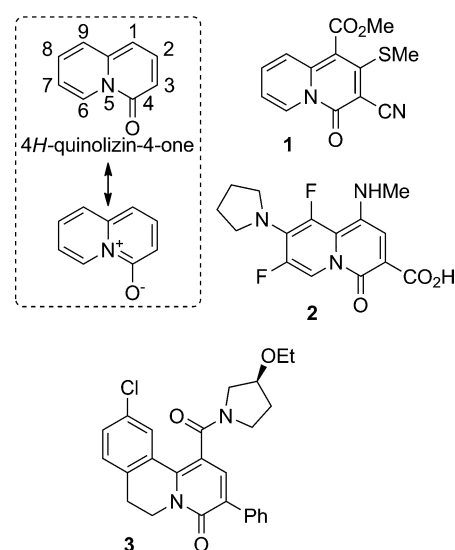

Figure 1. The 4H-quinolizinone system and its dipolar canonical form together with some examples of biologically active compounds that contain this ring system. Compound **1** is a therapeutic for immunoglobulin E related diseases.[5] Compound **2** has antibacterial activity,[6] and compound **3** is a hypnotic.[7]
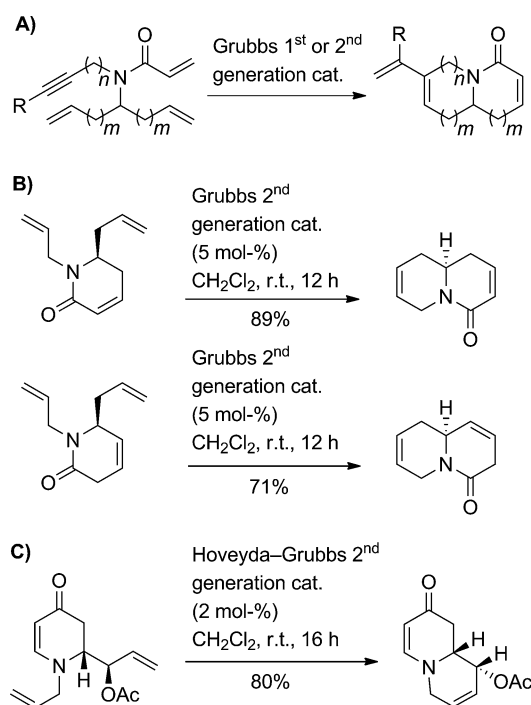
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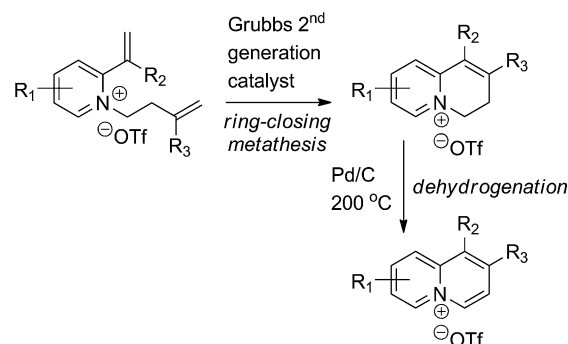   Alderly Park, Macclesfield, Cheshire, SK10, UK
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of synthetically accessible derivatives of 4*H*-quinolizin-4-ones and thus allow for further investigation of its biological usefulness.

The ring-closing metathesis (RCM) reaction has emerged as a powerful tool for the construction of a variety of heterocyclic ring systems.[8] A number of RCM-based strategies for the construction of quinolizidinones and related bicyclic heterocyclic systems that contain a nitrogen atom at the ring junction have been reported. For example, Ma et al. described the syntheses of a range of bicyclic quinolizidine alkaloid derivatives by employing a double RCM reaction with *N*-alkynyl-*N*-(1,ω)-alkadienyl acrylamides (see Scheme 1, A).[9] Nomura et al. reported the syntheses of two unsaturated quinolizidinone frameworks by carrying out the RCM reactions of two chiral unsaturated piperidine building blocks that contain propenyl substituents (see Scheme 1, B).[10] Donohoe et al. described the synthesis of a 6,6-fused ring system with a nitrogen atom at the ring junction by using a RCM reaction of a dihydropyridone (see Scheme 1, C).[11] The Alvarez-Builla group developed elegant RCM-based strategies for the syntheses of a variety of cationic bicyclic heterocyclic systems that contain a nitrogen atom at the ring junction.[12] Of particular interest, this group has reported a route for the preparation of quinolizinium salts by employing a RCM reaction with the acyclic precursors followed by the thermal dehydrogenation (oxidation) of the resultant 3,4-dihydroquinolizinium salts (see Scheme 2).[12b]

Scheme 2. RCM-based route to quinolizinium salts developed by the Alvarez-Builla group.[12b]

We envisaged that a similar approach could be used in the design of a new RCM-based strategy for the syntheses of substituted 4*H*-quinolizin-4-ones that have **4** as the general structure (see Scheme 3). By starting from readily available 2-pyridones **5**, a selective *N*-alkylation reaction would yield **6**, and a subsequent Pd-catalyzed cross-coupling reaction would furnish **7**. The RCM reaction would furnish dihydroquinolizinones **8**, and a subsequent dehydrogenation would yield the final substituted 4*H*-quinolizin-4-ones **4**. The construction of the carbocyclic ring in this fashion would represent an unprecedented approach towards the 4*H*-quinolizin-4-one scaffold. We anticipate that this route would allow for facile access to new substitution patterns at the 7- and 8-positions of the bicyclic architecture (which is difficult to achieve with existing strategies) by varying the building blocks that are used to prepare compounds **6** and **7**. Furthermore, our RCM strategy would have the added benefit of providing versatile dihydroquinolizinone intermediate **8**. In principle, this could be manipulated to generate our desired quinolizinone core **4** or reduced to provide access to tetrahydroquinolizinone moieties, which are also of interest in drug discovery efforts. Herein, we report the successful realization of the RCM-based strategy that is outlined in Scheme 3. This approach has enabled concise access to a range of new substituted 4*H*-quinolizin-4-ones from readily available starting materials. The enrichment of screening libraries with these compounds will allow for the
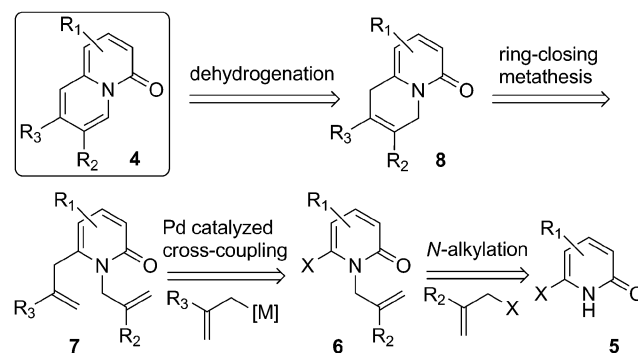

Scheme 1. Some notable examples of the syntheses of 6,6-fused bicyclic ring systems that have a nitrogen atom at the ring junction: (A) a double RCM approach by Ma et al.,[9] (B) a RCM approach that uses propenyl-substituted piperidine derivatives by Nomura et al.,[10] and (C) a RCM of a dihydropyridone by Donohoe et al.[11]


Scheme 3. Retrosynthetic strategy towards the 4*H*-quinolizin-4-one scaffold {[M] = unspecified metal, X = unspecified halide}.

sampling of attractive heterocyclic compounds that are underexploited in current drug and agrochemical discovery efforts.[13]

Results and Discussion

Our studies began with the selective *N*-alkylation of 6-bromo-2-pyridone (**9**) with a range of allylic halides to form *N*-allylated pyridones **10a**–**10d** (see Table 1).[14] In general, the reactions proceeded smoothly and with a high level of regioselectivity for the pyridone nitrogen over the pyridine oxygen atom. This approach allowed for the introduction of unsubstituted terminal alkene units as well as alkyl-, aryl-, and ester-functionalized allylic chains at the pyridone core. Alternative strategies were used to generate diester-substituted pyridone **10e** and structurally related uracil derivative **10f** (see Figure 2).[15]

Table 1. Synthesis of *N*-allylated pyridones **10a**–**10d**.[a]
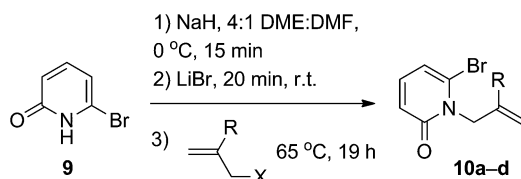
Entry	R	X	Product	Yield [%]
1	H	I	**10a**	84
2	Me	Br	**10b**	65
3	Ph	Br	**10c**	39
4	CO_2Me	Br	**10d**	87

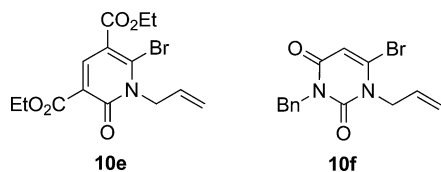[a] DME = 1,2-dimethoxyethane, DMF = *N*,*N*-dimethylformamide.

Figure 2. Other *N*-allylated heterocycles that were prepared.[15]

Next, we sought to explore the palladium cross-coupling reactions of 2-pyridones **10a**–**10e** and uracil derivative **10f** as a mild and selective method to install the second allylic unit (see Scheme 4). The cross-coupling reaction of 2-pyridones with allylic coupling partners (such as **11**) represents an unprecedented transformation. A variety of cross-coupling methods were investigated, and it was found that the Stille cross-coupling conditions, which employ a palladium(0) source and tri(2-furyl)phosphine (TFP),[16] were the most reliable. Under these conditions, the reaction with allyltributyltin or (2-methylallyl)tributyltin coupling partners used relatively modest catalyst and ligand loadings to furnish diene compounds **12a**–**12j** in good yields (Scheme 4).[17,18] Similarly, compounds **12k** and **12l** could be accessed from **10f**.
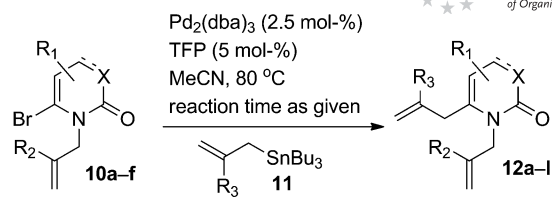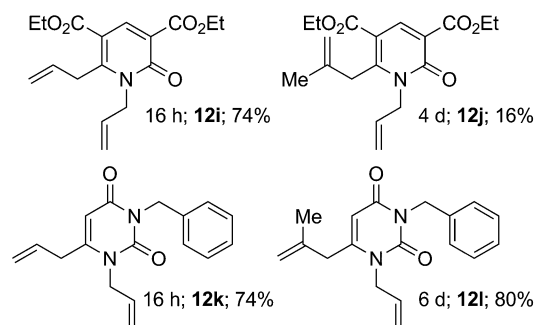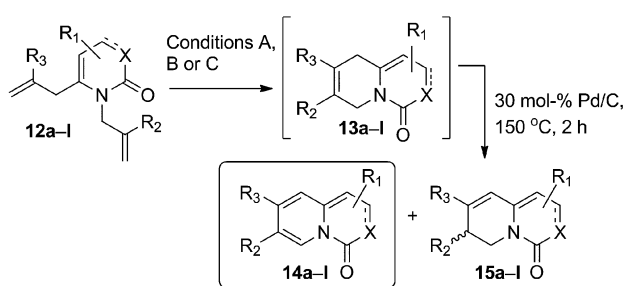

Scheme 4. Synthesis of bis(allylic) pyridones **12a**–**12j** and uracil derivatives **12k** and **12l** [dba = dibenzylideneacetone, TFP = tri(2-furyl)phosphine].

With bis(allylic) pyridones **12a**–**12j** and bis(allylic) uracil derivatives **12k** and **12l** in hand, we subjected our substrates to the RCM reaction with Grubbs second-generation catalyst in an attempt to access the corresponding dihydroquinolizinone derivatives **13** (see Scheme 5). Gratifyingly, the compounds with unsubstituted allylic groups (such as **12a**) underwent rapid ring-closure by using a catalyst loading of 5 mol-% at room temperature. Compounds with an allylic group that was monosubstituted at the 2-position (such as **12b**) required heating to 50 °C. We were also able to form sterically hindered tetrasubstituted olefin products (i.e., **13c**, **13f**, and **13h**) by increasing both the catalyst loadings and reaction times.[19] Some dihydroquinolizinones products **13** slowly degraded after isolation upon standing at room temperature.[20] For this reason, the crude metathesis mixtures were directly submitted without further purification to the dehydrogenation step. The oxidation of related quinolizinium cations has been reported by using Pd/C and heat under solvent-free conditions (see Scheme 2).[12b] A screening of conditions and reagents for the dehydrogenation step by starting from **12a** revealed that 30 mol-% Pd/C at 150 °C under solvent-free conditions gave good yields of the quinolizinone product after only 1–2 h.[20] See Supporting Information for details regarding the screening process. Pleasingly, these conditions proved to be applicable to a wide range of substrates to yield the desired 4*H*-quinolizin-4-ones **14a**–**14j** and the structurally related pyridopyrimidine derivative **14k** (see Scheme 5).[21] In the majority of cases, compound **15** was obtained after workup and detected as a

minor byproduct in the crude product mixture. This presumably resulted from the rearrangement of the alkene moiety that was generated in the RCM step.[22] In most cases, **15** could be readily separated from the desired products by column chromatography.[23] Overall, the isolated yields of the final analytically pure 4*H*-quinolizin-4-ones products **14** were typically good over the two steps. Alkyl, aryl, and carbonyl functionalities could be introduced into the 4*H*-quinolizin-4-one scaffold. Carbonyl groups are valuable, as they provide possible synthetic handles for further modifications at the 4*H*-quinolizin-4-one core. A variety of substitution patterns were accessible by using this approach, which included substitution at the 7- and 8-positions. This is rare and difficult to achieve by using other strategies.

Scheme 5. RCM and dehydrogenation steps. [a] Conditions A: Grubbs second-generation catalyst (5 mol-%), CH$_2$Cl$_2$ (substrate concentration 0.1 M), room temp., 2 h. [b] Conditions B: Grubbs second-generation catalyst (5 mol-%), CH$_2$Cl$_2$ (substrate concentration 0.1 M), 50 °C, 2 h. [c] Conditions C: Grubbs second-generation catalyst portionwise (3 × 5 mol-%), CH$_2$Cl$_2$ (substrate concentration 0.1 M), 50 °C, 2 h. [d] Ratio determined by ^{1}H NMR analysis of crude product mixture. [e] Isolated yield of pure material. [f] Ratio of **14h/15h/12h**. [g] Ratio of **14k/15k/13k**.

Conclusions

In summary, we have developed a new strategy for the synthesis of substituted 4*H*-quinolizin-4-ones from readily available pyridone precursors. This represents a valuable advance in the synthesis of this rare and biologically interesting class of compounds. We have also demonstrated that this general RCM-based approach is suitable for the preparation of the structurally related pyridopyrimidine scaffold, another synthetically challenging heterocyclic ring system of pharmaceutical interest. There are several notable features of our synthetic strategy. It is a step-efficient approach and inherently modular in nature, which renders it highly amenable to the preparation of analogues and allows for the facile introduction of a range of substituents at the 4*H*-quinolizin-4-one core (including unprecedented derivatization). In addition, the modular nature of the strategy should facilitate the systematic modification and optimization of substitution and functionality at the core scaffold to improve properties (as would be required in any hit-to-lead optimization process). Furthermore, the strategy features the cross-coupling reaction between 2-pyridones and allylic coupling partners, a previously unreported synthetic transformation that we foresee as useful in a wider synthetic context. Overall, we envisage that the research described herein will be of significant interest to medicinal chemists and the wider synthetic community. The physico-chemical properties of the 4*H*-quinolizin-4-ones that are synthesized by this method are currently being evaluated and will be reported in due course.

Experimental Section

General Methods: All nonaqueous reactions were performed under a constant stream of dry nitrogen using oven-dried glassware. Standard practices were employed when handling moisture and air-sensitive materials. Room temperature refers to ambient temperature. All temperatures below 0 °C are those of the external baths, and a temperature of 0 °C was maintained by using an ice-water bath. Temperatures below 0 °C were maintained by using an acetone-dry ice bath. All reagents and solvents were used as received, unless otherwise stated. Toluene, acetonitrile, dichloromethane, and methanol were distilled from calcium hydride. Tetrahydrofuran was dried with Na wire and distilled from a mixture of lithium aluminium hydride and calcium hydride with triphenylmethane as an indicator. Diethyl ether was distilled from a mixture of calcium hydride and lithium aluminium hydride. Petroleum ether was distilled before use. Dichloromethane and methanol were distilled from calcium hydride, yields refer to chromatographically and spectroscopically pure compounds, unless otherwise stated. When possible, reactions were monitored by thin layer chromatography, which was performed on commercially prepared glass plates that were precoated with Merck silica gel 60 F254 or aluminium oxide 60 F254. Visualization was done was by quenching with UV fluorescence ($\tilde{v}_{max}$ = 254 nm), by staining with potassium permanganate, or by using LC–MS analysis with an Agilent 1200 series LC system, an ESCi Multi-Mode Ionization Waters ZQ spectrometer, and MassLynx 4.0 software. Flash column chromatography was carried out by using slurry-packed Merck 9385 Kieselgel 60 SiO$_2$ (230–400 mesh) under a positive pressure of compressed air. Preparative

HPLC purification was performed on an Agilent 1260 Infinity system that was fitted with a Supelcosil ABZ+Plus column (250 × 21.2 mm, 5 μm) by using a linear gradient system [solvent A: 0.1% (v/v) trifluoroacetic acid (TFA) in water, solvent B: 0.05% (v/v) TFA in acetonitrile] at a flow rate of 20 mL min^{-1}. Melting points were measured on a Büchi B-545 melting point apparatus. Infrared spectra were recorded on a Perkin–Elmer Spectrum One spectrometer with internal referencing. Selected absorption maxima ($\tilde{\nu}_{max}$) are reported in wavenumbers (cm^{-1}) with the abbreviations w (weak), med (medium), str (strong), and br. (broad). The ^{1}H NMR spectroscopic data were recorded by using an internal deuterium lock at ambient probe temperatures (unless otherwise stated) with a Bruker DPX-400 (400 MHz), a Bruker Avance 400 QNP (400 MHz), or a Bruker Avance 500 Cryo Ultrashield (500 MHz) spectrometer. Chemical shifts (δ_H) are reported in ppm, to the nearest 0.01 ppm, and are referenced to the residual nondeuterated solvent peak. Coupling constants (J) are reported in Hertz to the nearest 0.1 Hz. Data are reported in the order of chemical shift, integration, multiplicity [br. (broad), s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), or a combination thereof], coupling constant(s), and assignment. The numbering/lettering systems of selected structures do not follow IUPAC nomenclature rules and are used for the assignment of the ^{1}H and ^{13}C NMR spectra. Proton assignments were determined either on the basis of unambiguous chemical shift, coupling patterns, by using patterns observed in 2D experiments [^{1}H-^{1}H COSY, HMBC, and heteronuclear multiple quantum coherence (HMQC)], or by analogy to fully interpreted spectra of related compounds. The ^{13}C NMR spectroscopic data were recorded by using broadband proton spin decoupling at ambient probe temperatures with an internal deuterium lock with a Bruker DPX-400 (100 MHz), a Bruker Avance 400 QNP (100 MHz), or a Bruker Avance 500 Cryo Ultrashield (125 MHz) spectrometer. Chemical shifts (δ_C) are reported in ppm, to the nearest 0.1 ppm, and are referenced to the residual solvent peak. Assignments were made on the basis of chemical shift, DEPT editing, and where appropriate, HMQC and HMBC experiments, or by analogy to interpreted spectra of related compounds. High resolution mass spectrometry measurements were recorded with a Bruker Bioapex 4.7e FTICR or a Micromass LCT Premier spectrometer. Mass values are reported within the error limits of ±5 ppm mass units. ToF ESI+ refers to the mass spectral ionization technique. Microwave reactions were carried out in a CEM Discover Microwave in microwave vials that were equipped with clip-on caps.

General Procedure 1 – *N*-Alkylation of 2-Pyridones: This procedure was adapted from a reported method by Liu et al.[14] To a stirred solution of the 2-pyridone (1 equiv.) in DME/DMF (4:1, 2.5 mL mmol^{-1}) at 0 °C was added NaH (60% in mineral oil, 1.1 equiv.) portionwise. The reaction was stirred at 0 °C for 15 min and then warmed to room temperature. LiBr (2 equiv.) was then added, and the reaction was stirred at room temperature for 15 min. The allylic bromide or iodide (2 equiv.) was then added, and the reaction mixture was heated to 65 °C for 16 h or until TLC indicated conversion of the starting material. The reaction mixture was then poured onto brine (30 mL), and the organic layer was separated. The aqueous layer was then extracted with EtOAc (4× 25 mL). The combined organic layers were dried with MgSO$_4$, and the solvent was removed under reduced pressure. The residue was purified by column chromatography to yield the title compounds.

General Procedure 2 – Stille Coupling Procedure: To a stirred solution of the heteroaryl bromide (1 equiv.) and tri(2-furyl)phosphine (0.05 equiv.) in anhydrous MeCN (0.1 M) at room temperature was added Pd$_2$(dba)$_3$ (0.025 equiv.). The mixture was then degassed

with N$_2$, and the allylic tin reagent (1.1 equiv.) was then added. The resulting mixture was heated to 80 °C until TLC indicated consumption of the starting material. The solvent was removed under reduced pressure, and the resulting residue was diluted with Et$_2$O (10 mL) and 10% aqueous KF (2 mL). The mixture was stirred at room temperature for 10 min. The organic layer was then separated, and the aqueous layer was extracted with Et$_2$O (20 mL). The organic layer was dried with MgSO$_4$, and the solvent was removed under reduced pressure. The resulting residue was purified by column chromatography (SiO$_2$/KF, 9:1) according to the method of Harrowven et al.[18] to yield the title compound.

General Procedure 3 – RCM and Dehydrogenation of Substrates with Unsubstituted Allyl Groups: To a stirred solution of the diene in anhydrous CH$_2$Cl$_2$ (10 mL/mmol) at room temperature was added Grubbs second-generation catalyst (0.05 equiv.). The mixture was stirred at room temperature for 1–3 h until TLC showed consumption of the starting material. Then 10% Pd/C (0.3 equiv.) was added, and the solvent was removed under reduced pressure. The mixture was heated to 150 °C for 1–3 h until ^{1}H NMR analysis showed consumption of starting material. The mixture was cooled to room temperature and then suspended in CH$_2$Cl$_2$ (10 mL). The suspension was filtered through a short pad of Celite®, and the filter cake was washed with CH$_2$Cl$_2$ (4× 20 mL). The solvent was removed under reduced pressure, and the resulting yellow residue was then purified by column chromatography (SiO$_2$) to yield the title compound.

General Procedure 4 – RCM and Dehydrogenation of Substrates with One Substituted Allyl Group: To a stirred solution of the diene (0.3 mmol) in anhydrous CH$_2$Cl$_2$ (0.1 M) at room temperature was added Grubbs second-generation catalyst (0.05 equiv.). The mixture was stirred and heated at reflux (50 °C) for 1–3 h until TLC showed consumption of the starting material. Then, 10% Pd/C (0.3 equiv.) was added, and the solvent was removed under reduced pressure. The mixture was heated to 150 °C for 1–3 h until ^{1}H NMR analysis showed consumption of the starting material. The mixture was cooled to room temperature and then suspended in CH$_2$Cl$_2$ (10 mL). The suspension was filtered through a short pad of Celite®. The filter cake was washed with CH$_2$Cl$_2$ (4× 20 mL), and the solvent was removed under reduced pressure. The resulting yellow residue was then purified by column chromatography (SiO$_2$) to yield the title compound.

General Procedure 5 – RCM and Dehydrogenation of Substrates with Two Substituted Allyl Groups: To a stirred solution of the diene (0.3 mmol) in anhydrous CH$_2$Cl$_2$ (0.1 M) at room temperature was added Grubbs second-generation catalyst (0.05 equiv.). The mixture was stirred and heated at reflux (50 °C) for 24 h. Additional portions of catalyst (0.05 equiv.) were added after 6 and 14 h or until TLC analysis showed consumption of the starting material. Then, 10% Pd/C (0.3 equiv.) was added, and the solvent was removed under reduced pressure. The mixture was then heated to 150 °C for 1–3 h until ^{1}H NMR analysis showed consumption of the starting material. The mixture was cooled to room temperature and then suspended in CH$_2$Cl$_2$ (10 mL). The suspension was filtered through a short pad of Celite®. The filter cake was washed with CH$_2$Cl$_2$ (4× 20 mL), and the solvent removed under reduced pressure. The resulting yellow residue was then purified by column chromatography (SiO$_2$) to yield the title compound.

1-Allyl-6-bromopyridin-2(1*H*)-one (10a): General procedure 1 was followed by using the allylic iodide. The crude reaction material was purified by chromatography on a silica gel column (40–60 petroleum ether/EtOAc, 4:1 then 7:3) to yield **10a** (84% yield) as a yellow solid; m.p. 54–55 °C. R_f = 0.49 (40–60 petroleum ether/

EtOAc, 1:1). IR (CDCl$_3$): $\tilde{\nu}_{max}$ = 1656 (str), 1583 (str), 1583 (med), 1431 (med) cm^{-1}. ^{1}H NMR (400 MHz, CDCl$_3$): δ_H = 7.12 (dd, J = 9.2, 7.2 Hz, 1 H), 6.50 (dd, J = 9.5, 1.1 Hz, 1 H), 6.45 (dd, J = 7.2, 1.2 Hz, 1 H), 5.96–5.86 (m, 1 H), 5.23 (ddd, J = 10.4, 2.4, 1.2 Hz, 1 H), 5.14 (ddd, J = 17.2, 2.6, 1.6 Hz, 1 H), 4.89 (ddd, J = 5.2, 3.1, 1.5 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ_C = 162.7, 139.2, 131.1, 127.2, 119.1, 118.0, 111.2, 51.1 ppm. HRMS (FTMS ESI+): calcd. for C$_8$H$_9$NO^{79}Br$^+$ [M + H]$^+$ 213.9862; found 213.9867; Δ = 2.4 ppm.

6-Bromo-1-(2-methylallyl)pyridin-2(1H)-one (10b): General procedure 1 was followed by using the allylic bromide. The crude product material was purified by chromatography on a silica gel column (40–60 petroleum ether/EtOAc, 4:1) to give **10b** (65% yield) as a cream solid; m.p. 56–57 °C. R_f = 0.37 (40–60 petroleum ether/EtOAc, 1:1). IR (neat): $\tilde{\nu}_{max}$ = 3082 (w), 2980 (w), 2936 (w), 2911 (w), 1652 (str), 1575 (med), 1502 (str), 1444 (med), 1426 (str), 1406 (med), 1380 (w), 1362 (w), 1299 (w), 1240 (w), 1215 (w), 1182 (w), 1168 (med), 1144 (med), 1130 (str) cm^{-1}. ^{1}H NMR (500 MHz, CDCl$_3$): δ_H = 7.16 (dd, J = 9.0, 7.5 Hz, 1 H), 6.54 (dd, J = 9.0, 1.0 Hz, 1 H), 6.50 (dd, J = 7.5, 1.0 Hz, 1 H), 4.91–4.86 (m, 1 H), 4.81 (s, 2 H), 4.49–4.44 (m, 1 H), 1.82 (s, 3 H) ppm. ^{13}C NMR (125 MHz, CDCl$_3$): δ_C = 162.7, 139.2, 138.9, 127.6, 119.1, 111.2, 110.4, 53.4, 20.4 ppm. HRMS (FTMS ESI+): calcd. for C$_9$H$_{11}$NO^{79}Br$^+$ [M + H]$^+$ 228.0029; found 228.0021; Δ = –3.9 ppm. This data is in accordance with that previously reported.[24]

6-Bromo-1-(2-phenylallyl)pyridin-2(1H)-one (10c): General procedure 1 was followed by using the allylic bromide. The crude reaction material was purified by chromatography on a silica gel column (40–60 petroleum ether/EtOAc, 4:1) to give **10c** (39% yield) as a red crystalline solid; m.p. 88–91 °C. R_f = 0.33 (40–60 petroleum ether/EtOAc, 4:1). IR (neat): $\tilde{\nu}_{max}$ = 3090 (w), 3060 (w), 3035 (w), 2949 (w), 1660 (str), 1648 (str), 1628 (str), 1581 (str), 1547 (w), 1508 (str), 1496 (str), 1431 (str), 1411 (med), 1393 (med), 1337 (w), 1302 (w), 1292 (w), 1268 (w), 1218 (med), 1168 (med), 1128 (str), 1105 (med) cm^{-1}. ^{1}H NMR (500 MHz, CDCl$_3$): δ_H = 7.50–7.47 (m, 2 H), 7.39–7.30 (m, 3 H), 7.20 (dd, J = 9.2, 7.2 Hz, 1 H), 6.58 (dd, J = 9.2, 1.2 Hz, 1 H), 6.53 (dd, J = 7.1, 1.3 Hz, 1 H), 5.37 (t, J = 1.8 Hz, 1 H), 5.27 (app s, 2 H), 4.64 (t, J = 2.0 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, CDCl$_3$): δ_C = 162.7, 141.9, 139.3, 138.9, 128.5 (2 C), 128.2, 127.6, 126.2 (2 C), 119.1, 111.3 (2 C), 51.8 ppm. HRMS (TOF ESI+): calcd. for C$_{14}$H$_{13}$NO^{79}Br$^+$ [M + H]$^+$ 290.0181; found 290.0190; Δ = 3.1 ppm.

Methyl 2-{[6-Bromo-2-oxopyridin-1(2H)-yl]methyl}acrylate (10d): General procedure 1 was followed by using the allylic bromide. The crude reaction material was purified by chromatography on a silica gel column (40–60 petroleum ether/EtOAc, 4:1) to give **10d** (87% yield) as a brown solid; m.p. 69–70 °C. R_f = 0.10 (40–60 petroleum ether/EtOAc, 4:1). IR (CDCl$_3$): $\tilde{\nu}_{max}$ = 3113 (w), 2953 (w), 1718 (str), 1665 (str), 1589 (med), 1510 (str) cm^{-1}. ^{1}H NMR (500 MHz, CDCl$_3$): δ_H = 7.21 (dd, J = 9.3, 7.2 Hz, 1 H), 6.57 (dd, J = 9.3, 1.2 Hz, 1 H), 6.53 (dd, J = 7.2, 1.2 Hz, 1 H), 6.30 (t, J = 1.9 Hz, 1 H), 5.20 (t, J = 1.9 Hz, 1 H), 5.16 (t, J = 1.9 Hz, 2 H), 3.83 (s, 3 H) ppm. ^{13}C NMR (125 MHz, CDCl$_3$): δ_C = 165.6, 162.6, 139.5, 134.1, 127.2, 124.3, 119.2, 111.4, 52.1, 49.0 ppm. HRMS (FTMS ESI+): calcd. for C$_{10}$H$_{10}$NO$_3$^{79}BrNa$^+$ [M + Na]$^+$ 293.9742; found 293.9750; Δ = 2.7 ppm.

Diethyl 1-Allyl-6-bromo-2-oxo-1,2-dihydropyridine-3,5-dicarboxylate (10e): To a stirred solution of diethyl 1-allyl-6-hydroxy-2-oxo-1,2-dihydropyridine-3,5-dicarboxylate (1.00 g, 3.15 mmol) in anhydrous DMF (47.3 mL) at 0 °C was added PBr$_3$ (0.50 mL, 4.73 mmol) dropwise. The mixture was stirred at 0 °C for 1 h and then warmed to room temperature over 8 h. The reaction was mon-

itored by LC–MS analysis. Additional PBr$_3$ (0.1 mL) was added every hour until no starting material was observed. The reaction was then quenched at 0 °C by the addition of water. The organic solvent was removed under reduced pressure, and the residue was again dissolved in water (100 mL) and Et$_2$O (50 mL). The organic layer was separated, and the aqueous layer was washed with Et$_2$O (2 × 50 mL). The combined organic layers were dried with MgSO$_4$, and the solvent was removed under reduced pressure to yield a pale yellow solid, which was purified by column chromatography (SiO$_2$, 50 g; 40–60 petroleum/EtOAc, 9:1 then 4:1) to give **10e** (0.91 g, 2.53 mmol, 80%) as a pale yellow solid; m.p. 82–85 °C. R_f = 0.42 (40–60 petroleum ether/EtOAc, 1:1). IR (neat): $\tilde{\nu}_{max}$ = 2968 (med), 2918 (med), 2850 (w), 1721 (med), 1697 (str), 1676 (str), 1596 (med), 1484 (med), 1424 (med), 1395 (w), 1365 (med), 1306 (med), 1268 (w), 1229 (str), 1155 (str), 1113 (med) cm^{-1}. ^{1}H NMR (500 MHz, CDCl$_3$): δ_H = 8.62 (s, 1 H), 5.92 (ddt, J = 17.1, 10.4, 5.6 Hz, 1 H), 5.34–5.24 (m, 2 H), 5.10 (d, J = 5.6 Hz, 2 H), 4.38 (q, J = 7.1 Hz, 2 H), 4.35 (q, J = 7.2 Hz, 2 H), 1.38 (app t, J = 7.2 Hz, 6 H) ppm. ^{13}C NMR (125 MHz, CDCl$_3$): δ_C = 164.1, 163.3, 158.3, 144.4, 137.6, 130.0, 119.6, 117.8, 111.8, 62.0, 61.7, 52.5, 14.2 (2 C) ppm. HRMS (TOF ESI+): calcd. for C$_{14}$H$_{17}$NO$_5$^{79}Br$^+$ [M + H]$^+$ 358.0290; found 358.0306; Δ = 4.5 ppm.

1-Allyl-3-benzyl-6-bromopyrimidine-2,4(1H,3H)-dione (10f): To a stirred solution of 3-benzyl-6-bromopyrimidine-2,4(1H,3H)-dione (0.30 g, 1.07 mmol) in CH$_2$Cl$_2$ (2.0 mL) at room temperature was added 10% aqueous NaOH (2 mL) followed by tetrabutylammonium bromide (0.14 g, 0.43 mmol) and allyl iodide (0.29 mL, 3.20 mmol). The mixture was then heated to 40 °C for 19 h. TLC (40–60 petroleum ether/EtOAc, 7:3) showed consumption of starting material. The mixture was then cooled to room temperature and diluted with H$_2$O (20 mL). The organic layer was separated, and the aqueous layer was extracted with CH$_2$Cl$_2$ (2 × 20 mL). The combined organic layers were dried with MgSO$_4$, and the solvent was removed under reduced pressure to yield an orange oil, which was purified by column chromatography (SiO$_2$, 20 g; 40–60 petroleum ether/EtOAc, 4:1) to give **10f** (0.31 g, 0.98 mmol, 91%) as a white solid; m.p. 103–104 °C. R_f = 0.39 (40–60 petroleum ether/EtOAc, 7:3). IR (neat): $\tilde{\nu}_{max}$ = 3095 (w), 3065 (w), 3028 (w), 2961 (w), 1704 (str), 1647 (str), 1597 (str), 1526 (w), 1496 (w), 1425 (str), 1385 (med), 1351 (med), 1336 (med), 1284 (med), 1205 (w), 1178 (w), 1158 (w), 1129 (w), 1105 (w) cm^{-1}. ^{1}H NMR (400 MHz, CDCl$_3$): δ_H = 7.43 (dt, J = 8.2, 1.3 Hz, 2 H), 7.32–7.21 (m, 3 H), 6.14 (s, 1 H), 5.86 (ddt, J = 17.2, 10.4, 5.1 Hz, 1 H), 5.30–5.19 (m, 2 H), 5.08 (s, 2 H), 4.68 (dt, J = 5.5, 1.5 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ_C = 160.6, 150.3, 136.3 (2 C), 130.9, 129.0 (2 C), 128.5 (2 C), 127.8, 118.7, 106.7, 51.5, 44.9 ppm. HRMS (TOF ESI+): calcd. for C$_{14}$H$_{14}$N$_2$O$_2$^{79}Br$^+$ [M + H]$^+$ 321.0239; found 321.0246; Δ = 2.2 ppm.

1,6-Diallylpyridin-2(1H)-one (12a): General procedure 2 was followed by using 1-allyl-6-bromopyridin-2(1H)-one (**10a**) and allyltributyltin. The crude reaction material was purified by column chromatography (silica/KF, 9:1; 40–60 petroleum ether/EtOAc, 7:3 then 6:4) to yield **12a** (91% yield) as a yellow solid; m.p. 38–41 °C. R_f = 0.25 (40–60 petroleum ether/EtOAc, 1:1). IR (neat): $\tilde{\nu}_{max}$ = 2960 (w), 1657 (str), 1582 (str), 1550 (str), 1429 (med), 1146 (med) cm^{-1}. ^{1}H NMR (400 MHz, CDCl$_3$): δ_H = 7.24 (dd, J = 9.1, 6.9 Hz, 1 H), 6.49 (dd, J = 9.2, 1.1 Hz, 1 H), 6.03 (app dt, J = 6.9, 0.6 Hz, 1 H), 5.98–5.80 (m, 2 H), 5.21 (app dq, J = 10.2, 1.4 Hz, 1 H), 5.18–5.11 (m, 1 H), 5.07 (app dq, J = 17.2, 1.4 Hz, 1 H), 4.98–4.90 (m, 1 H), 4.69 (ddd, J = 4.7, 2.0, 1.8 Hz, 2 H), 3.33 (d, J = 6.0 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ_C = 163.4, 147.6, 138.9, 133.1, 132.6, 118.5, 118.3, 116.2, 106.6, 45.6, 36.8 ppm.

HRMS (TOF ESI+): calcd. for $C_{11}H_{14}NO^+$ [M + H]$^+$ 176.1075; found 176.1070; Δ = –2.8 ppm.

1-Allyl-6-(2-methylallyl)pyridin-2(1H)-one (12b): General procedure 2 was followed by using 1-allyl-6-bromopyridin-2(1H)-one (**10a**) and 2-methylallyltributyltin. The crude reaction material was purified by column chromatography (silica/KF, 9:1; 40–60 petroleum ether/EtOAc, 7:3 then 6:4) to give **12b** (72% yield) as a pale yellow oil; R_f = 0.17 (40–60 petroleum ether/EtOAc, 1:1). IR (CH$_2$Cl$_2$): $\tilde{\nu}_{max}$ = 3082 (w), 2926 (w), 1656 (str), 1582 (str), 1549 (str), 1430 (med), 1377 (w), 1336 (w), 1291 (w), 1242 (w), 1146 (med) cm^{-1}. ^{1}H NMR (400 MHz, CDCl$_3$): δ_H = 7.20 (dd, J = 9.1, 6.8 Hz, 1 H), 6.43 (dd, J = 9.1, 1.3 Hz, 1 H), 5.98 (dd, J = 6.8, 1.3 Hz, 1 H), 5.87 (ddt, J = 17.2, 10.4, 4.8 Hz, 1 H), 5.09 (dq, J = 10.5, 1.7 Hz, 1 H), 4.89 (dq, J = 17.2, 1.6 Hz, 1 H), 4.87 (m, 1 H), 4.60 (dt, J = 4.8, 1.8 Hz, 2 H), 4.56 (m, 1 H), 3.20 (s, 2 H), 1.70 (d, J = 0.5 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ_C = 163.5, 147.2, 142.3, 138.8, 132.8, 118.3, 116.0, 113.5, 107.6, 45.6, 41.1, 22.6 ppm. HRMS (FTMS ESI+): calcd. for $C_{12}H_{16}ON^+$ [M + H]$^+$ 190.1226; found 190.1222; Δ = –2.2 ppm.

1,6-Bis(2-methylallyl)pyridin-2(1H)-one (12c): General procedure 2 was followed by using 6-bromo-1-(2-phenylallyl)pyridin-2(1H)-one (**10c**) and 2-methylallyltributyltin. The crude reaction material was purified by column chromatography (silica/KF, 9:1; 40–60 petroleum ether/EtOAc, 7:3 then 6:4) to yield **12c** (75% yield) as an orange oil; R_f = 0.13 (40–60 petroleum ether/EtOAc, 1:1). IR (neat): $\tilde{\nu}_{max}$ = 3080 (w), 2973 (w), 2937 (w), 1656 (str), 1582 (str), 1549 (str), 1432 (med), 1403 (w), 1377 (w), 1309 (w), 1260 (w), 1239 (w), 1142 (med) cm^{-1}. ^{1}H NMR (400 MHz, CDCl$_3$): δ_H = 7.22 (dd, J = 9.2, 6.8 Hz, 1 H), 6.46 (dd, J = 9.1, 1.0 Hz, 1 H), 6.01 (dd, J = 6.8, 1.0 Hz, 1 H), 4.89 (t, J = 1.2 Hz, 1 H), 4.78 (t, J = 1.2 Hz, 1 H), 4.58 (s, 1 H), 4.55 (app s, 2 H), 4.33 (s, 1 H), 3.18 (s, 2 H), 1.75 (s, 3 H), 1.71 (s, 3 H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ_C = 163.6, 147.4, 141.4, 140.3, 138.8, 118.3, 113.5, 109.5, 107.5, 48.0, 41.2, 22.6, 20.5 ppm. HRMS (FTMS ESI+): calcd. for $C_{13}H_{18}ON^+$ [M + H]$^+$ 204.1383; found 204.1382; Δ = –0.5 ppm.

6-Allyl-1-(2-methylallyl)pyridin-2(1H)-one (12d): General procedure 2 was followed by using 6-bromo-1-(2-methylallyl)pyridin-2(1H)-one (**10b**) and allyltributyltin. The crude reaction material was purified by column chromatography (silica/KF, 9:1; 40–60 petroleum ether/EtOAc, 7:3 then 6:4) to yield **12d** (92% yield) as a yellow oil; R_f = 0.24 (40–60 petroleum ether/EtOAc, 1:1). IR (neat): $\tilde{\nu}_{max}$ = 3085 (w), 2938 (w), 1655 (str), 1580 (med), 1548 (str), 1431 (br. med), 1377 (w), 1311 (w), 1235 (w), 1142 (med) cm^{-1}. ^{1}H NMR (400 MHz, CDCl$_3$): δ_H = 7.25 (dd, J = 9.1, 6.9 Hz, 1 H), 6.51 (d, J = 9.0 Hz, 1 H), 6.03 (d, J = 6.8 Hz, 1 H), 5.86 (ddt, J = 17.1, 10.2, 6.1 Hz, 1 H), 5.20 (dd, J = 10.2, 1.3 Hz, 1 H), 5.07 (dd, J = 17.2, 1.5 Hz, 1 H), 4.82 (t, J = 0.9 Hz, 1 H), 4.61 (app s, 2 H), 4.36 (t, J = 0.7 Hz, 1 H), 3.29 (d, J = 6.1 Hz, 2 H), 1.78 (s, 3 H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ_C = 163.4, 147.8, 140.0, 138.9, 133.2, 118.4, 118.2, 109.7, 106.6, 48.0, 36.8, 20.4 ppm. HRMS (TOF ESI+): calcd for $C_{12}H_{16}NO^+$ [M + H]$^+$ 190.1232; found 190.1238; Δ = 3.2 ppm.

6-Allyl-1-(2-phenylallyl)pyridin-2(1H)-one (12e): General procedure 2 was followed by using 6-bromo-1-(2-phenylallyl)pyridin-2(1H)-one (**10c**) and allyltributyltin. The crude reaction material was purified by column chromatography (silica/KF, 9:1; 40–60 petroleum ether/EtOAc, 4:1 then 7:3) to give **12e** (88% yield) as a yellow oil; R_f = 0.21 (40–60 petroleum ether/EtOAc, 1:1). IR (neat): $\tilde{\nu}_{max}$ = 2951 (w), 1658 (str), 1581 (med), 1548 (str), 1495 (w), 1429 (med), 1290 (w), 1238 (w), 1165 (w), 1143 (med) cm^{-1}. ^{1}H NMR (400 MHz, CDCl$_3$): δ_H = 7.52–7.42 (m, 2 H), 7.40–7.22 (m, 4 H), 6.54 (d, J = 9.1 Hz, 1 H), 6.08 (d, J = 6.8 Hz, 1 H), 5.87 (ddt, J =

17.1, 10.3, 6.0 Hz, 1 H), 5.34 (t, J = 1.6 Hz, 1 H), 5.19 (dd, J = 10.3, 1.3 Hz, 1 H), 5.14–5.00 (m, 3 H), 4.56 (t, J = 1.9 Hz, 1 H), 3.32 (app d, J = 6.1 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ_C = 163.5, 147.8, 142.7, 139.0, 138.8, 133.2, 128.6 (2 C), 128.3, 126.0 (2 C), 118.5, 118.4, 110.9, 106.8, 46.2, 37.0 ppm. HRMS (TOF ESI+): calcd. for $C_{17}H_{18}NO^+$ [M + H]$^+$ 252.1388; found 252.1396; Δ = 3.2 ppm.

6-(2-Methylallyl)-1-(2-phenylallyl)pyridin-2(1H)-one (12f): General procedure 2 was followed by using 6-bromo-1-(2-phenylallyl)pyridin-2(1H)-one (**10c**) and 2-methylallyltributyltin. The crude reaction material was purified by column chromatography (silica/KF, 9:1; 40–60 petroleum ether/EtOAc, 4:1 then 3:1) to give **12f** (52% yield) as a yellow oil; R_f = 0.10 (40–60 petroleum ether/EtOAc, 1:1). IR (neat): $\tilde{\nu}_{max}$ = 3067 (w), 2967 (w), 2945 (w), 1653 (str), 1575 (str), 1545 (str), 1493 (w), 1443 (w), 1426 (med), 1399 (w), 1377 (w), 1353 (w), 1320 (w), 1304 (w), 1251 (w), 1169 (w), 1143 (med) cm^{-1}. ^{1}H NMR (400 MHz, CDCl$_3$): δ_H = 7.48–7.26 (m, 2 H), 7.40–7.26 (m, 4 H), 6.54 (dd, J = 9.2, 1.1 Hz, 1 H), 6.08 (dd, J = 6.8, 1.4 Hz, 1 H), 5.34 (t, J = 1.7 Hz, 1 H), 5.05 (br. s, 2 H), 4.91 (t, J = 1.2 Hz, 1 H), 4.60 (app s, 1 H), 4.57 (t, J = 1.9 Hz, 1 H), 3.23 (s, 2 H), 1.71 (s, 3 H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ_C = 163.6, 147.4, 143.0, 141.4, 139.0, 138.4, 128.6 (2 C), 128.2, 126 (2 C), 118.5, 113.6, 110.8, 107.7, 46.2, 41.4, 22.6 ppm. HRMS (FTMS ESI+): calcd. for $C_{18}H_{20}ON^+$ [M + H]$^+$ 266.1539; found 266.1538; Δ = –0.6 ppm.

Methyl 2-{[6-Allyl-2-oxopyridin-1(2H)-yl]methyl}acrylate (12g): General procedure 2 was followed by using methyl 2-{[6-bromo-2-oxopyridin-1(2H)-yl]methyl}acrylate (**10d**) and allyltributyltin. The crude reaction material was purified by column chromatography (silica/KF, 9:1; 40–60 petroleum ether/EtOAc, 3:2) to give **12g** (82% yield) as a yellow oil; R_f = 0.30 (EtOAc). IR (neat): $\tilde{\nu}_{max}$ = 2953 (w), 1717 (med), 1659 (str), 1583 (med), 1548 (str), 1435 (med), 1369 (w), 1299 (med), 1268 (med), 1195 (med), 1134 (str) cm^{-1}. ^{1}H NMR (400 MHz, CDCl$_3$): δ_H = 7.29 (dd, J = 9.1, 6.9 Hz, 1 H), 6.52 (dd, J = 9.0 Hz, 1 H), 6.08 (dd, J = 6.8 Hz, 1 H), 5.84 (ddt, J = 17.1, 10.2, 6.1 Hz, 1 H), 6.23 (t, J = 1.6 Hz, 1 H), 5.20 (app dq, J = 10.2, 6.1 Hz, 1 H), 5.13 (t, J = 1.9 Hz, 1 H), 5.08 (app dq, J = 17.1, 1.2 Hz, 1 H), 4.93 (dd, J = 1.9, 1.6 Hz, 2 H), 3.78 (s, 3 H), 3.24 (d, J = 6.1 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ_C = 165.8, 163.3, 147.4, 139.1, 134.9, 132.8, 124.3, 118.7, 118.4, 106.9, 52.2, 43.6, 37.0 ppm. HRMS (FTMS ESI+): calcd. for $C_{13}H_{16}O_3N^+$ [M + H]$^+$ 234.1136; found 234.1127; Δ = –3.9 ppm.

Methyl 2-{[6-(2-Methylallyl)-2-oxopyridin-1(2H)-yl]methyl}acrylate (12h): General procedure 2 was followed by using methyl 2-{[6-bromo-2-oxopyridin-1(2H)-yl]methyl}acrylate (**10d**) and methylallyltributyltin. The crude reaction material was purified by column chromatography (silica/KF, 9:1; 40–60 petroleum ether/EtOAc, 3:2) to give **12h** (62% yield) as an orange oil; R_f = 0.16 (40–60 petroleum ether/EtOAc, 1:1). IR (CH$_2$Cl$_2$): $\tilde{\nu}_{max}$ = 2922 (w), 2850 (w), 1724 (str), 1663 (str), 1583 (str), 1553 (str), 1435 (med), 1408 (w), 1392 (w), 1298 (w), 1268 (str), 1197 (w), 1170 (w), 1147 (str) cm^{-1}. ^{1}H NMR (500 MHz, CDCl$_3$): δ_H = 7.30 (dd, J = 9.2, 6.8 Hz, 1 H), 6.53 (dd, J = 9.2, 1.2 Hz, 1 H), 6.24 (t, J = 1.8 Hz, 1 H), 6.08 (dd, J = 6.7, 1.2 Hz, 1 H), 5.15 (t, J = 1.9 Hz, 1 H), 4.95 (s, 1 H), 4.92 (t, J = 1.8 Hz, 2 H), 4.65 (s, 1 H), 3.81 (s, 3 H), 3.17 (s, 2 H), 1.74 (s, 3 H) ppm. ^{13}C NMR (125 MHz, CDCl$_3$): δ_C = 165.8, 163.5, 147.0, 141.0, 139.0, 135.1, 124.2, 118.5, 113.9, 107.8, 52.1, 43.7, 41.4, 22.5 ppm. HRMS (TOF ESI+): calcd. for $C_{14}H_{17}NO_3Na^+$ [M + Na]$^+$ 270.1106; found 270.1119; Δ = 4.8 ppm.

Diethyl 1,6-Diallyl-2-oxo-1,2-dihydropyridine-3,5-dicarboxylate (12i): General procedure 2 was followed by using diethyl 1-allyl-6-bromo-2-oxo-1,2-dihydropyridine-3,5-dicarboxylate (**10e**) and allyl-

tributyltin. The crude reaction material was purified by column chromatography (silica/KF, 9:1; 40–60 petroleum ether/EtOAc, 85:15, 82:18, and then 80:20) to give **12i** (74% yield) as a white crystalline solid; m.p. 37–38 °C. R_f = 0.33 (40–60 petroleum ether/ EtOAc, 1:1). IR (neat): $\tilde{\nu}_{max}$ = 3248 (w), 3082 (w), 2979 (w), 2923 (w), 1742 (med), 1703 (str), 1672 (str), 1603 (w), 1528 (med), 1432 (med), 1413 (med), 1399 (med), 1380 (med), 1365 (med), 1309 (med), 1290 (med), 1229 (str), 1199 (med), 1172 (med), 1144 (med) cm^{-1}. ^{1}H NMR (400 MHz, CDCl$_3$): δ_H = 8.71 (s, 1 H), 5.99–5.89 (m, 2 H), 5.23 (app d, J = 11.0 Hz, 1 H), 5.20 (dd, J = 11.3, 0.8 Hz, 1 H), 5.04 (d, J = 17.3 Hz, 1 H), 4.98 (dd, J = 17.4, 0.7 Hz, 1 H), 4.82 (d, J = 4.7 Hz, 2 H), 4.38 (q, J = 7.1 Hz, 2 H), 4.31 (q, J = 7.1 Hz, 2 H), 4.02 (d, J = 5.2 Hz, 2 H), 1.38 (t, J = 7.1 Hz, 3 H), 1.36 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ_C = 164.8, 164.4, 159.2, 158.6, 144.9, 132.4, 131.7, 117.7, 117.6, 117.3, 108.8, 61.4, 61.3, 46.7, 34.2, 14.3, 14.2 ppm. HRMS (TOF ESI+): calcd. for C$_{17}$H$_{22}$NO$_5{}^+$ [M + H]$^+$ 320.1498; found 320.1511; Δ = 4.1 ppm.

Diethyl 1-Allyl-6-(2-methylallyl)-2-oxo-1,2-dihydropyridine-3,5-dicarboxylate (12j): General procedure 2 was followed by using diethyl 1-allyl-6-bromo-2-oxo-1,2-dihydropyridine-3,5-dicarboxylate (**10e**) and methylallyltributyltin. The crude reaction material was purified by column chromatography (silica/KF, 9:1; 40–60 petroleum ether/EtOAc, 17:3 then 4:1) to give **12j** (16% yield) as a yellow oil; R_f = 0.38 (40–60 petroleum ether/EtOAc, 1:1). IR (neat): $\tilde{\nu}_{max}$ = 2980 (w), 2931 (w), 1742 (med), 1709 (str), 1672 (str), 1603 (w), 1530 (str), 1434 (w), 1407 (w), 1377 (w), 1367 (w), 1307 (med), 1278 (w), 1228 (str), 1143 (str) cm^{-1}. ^{1}H NMR (500 MHz, CDCl$_3$): δ_H = 8.73 (s, 1 H), 5.94 (ddt, J = 17.4, 10.5, 4.9 Hz, 1 H), 5.22 (dq, J = 10.4, 0.6 Hz, 1 H), 5.04 (dq, J = 17.4, 0.6 Hz, 1 H), 4.86 (s, 1 H), 4.74 (d, J = 4.8 Hz, 2 H), 4.38 (q, J = 7.0 Hz, 2 H), 4.32–4.27 (m, 3 H), 3.95 (s, 2 H), 1.87 (s, 3 H), 1.39 (t, J = 7.0 Hz, 3 H), 1.35 (t, J = 7.0 Hz, 3 H) ppm. ^{13}C NMR (125 MHz, CDCl$_3$): δ_C = 164.8, 164.4, 159.2, 158.8, 144.9, 141.0, 131.9, 117.6, 117.2, 111.5, 109.1, 61.4, 61.2, 47.1, 37.6, 23.5, 14.3, 14.2 ppm. HRMS (TOF ESI+): calcd. for C$_{18}$H$_{23}$NO$_5$Na$^+$ [M + Na]$^+$ 356.1474; found 356.1474; Δ = 0.0 ppm.

1,6-Diallyl-3-benzylpyrimidine-2,4(1H,3H)-dione (12k): General procedure 2 was followed by using 1-allyl-3-benzyl-6-bromopyrimidine-2,4(1H,3H)-dione (**10f**) and allyltributyltin. The crude reaction material was purified by column chromatography (silica/KF, 9:1; 40–60 petroleum ether/EtOAc, 9:1 then 4:1) to give **12k** (74% yield) as a yellow oil; R_f = 0.23 (40–60 petroleum ether/EtOAc, 7:3). IR (neat): $\tilde{\nu}_{max}$ = 2983 (w), 1702 (med), 1655 (str), 1619 (med), 1586 (w), 1496 (w), 1444 (str), 1393 (med), 1341 (med), 1292 (w), 1267 (w), 1211 (w), 1197 (w), 1157 (w), 1107 (w) cm^{-1}. ^{1}H NMR (500 MHz, CDCl$_3$): δ_H = 7.45 (dd, J = 7.2, 3.5 Hz, 2 H), 7.31–7.21 (m, 3 H), 5.92–5.76 (m, 2 H), 5.66 (s, 1 H), 5.29 (dq, J = 9.0, 1.3 Hz, 1 H), 5.24–5.16 (m, 2 H), 5.15 (s, 2 H), 5.08 (dq, J = 17.3, 0.7 Hz, 1 H), 4.49 (dt, J = 4.9, 1.8 Hz, 2 H), 3.21 (ddd, J = 6.3, 2.2, 1.4 Hz, 2 H) ppm. ^{13}C NMR (125 MHz, CDCl$_3$): δ_C = 162.2, 152.1, 152.1, 136.9, 132.3, 131.2, 128.9 (2 C), 128.4 (2 C), 127.5, 120.0, 116.8, 110.7, 46.3, 44.7, 35.9 ppm. HRMS (FTMS ESI+): calcd. for C$_{17}$H$_{11}$O$_2$N$_2{}^+$ [M + H]$^+$ 283.1452; found 283.1444; Δ = –2.8 ppm.

1-Allyl-3-benzyl-6-(2-methylallyl)pyrimidine-2,4(1H,3H)-dione (12l): General procedure 2 was followed by using 1-allyl-3-benzyl-6-bromopyrimidine-2,4(1H,3H)-dione (**10f**) and methylallyltributyltin. The crude reaction mixture was purified by column chromatography (silica/KF, 9:1; 40–60 petroleum ether/EtOAc, 4:1) to give **12l** (80% yield) as a colorless oil; R_f = 0.54 (40–60 petroleum ether/EtOAc, 1:1). IR (neat): $\tilde{\nu}_{max}$ = 3083 (w), 3031 (w), 2967 (w), 1703 (med), 1655 (str), 1620 (med), 1496 (w), 1444 (str), 1391 (med), 1342 (med), 1292 (w), 1212 (w) cm^{-1}. ^{1}H NMR (400 MHz, CDCl$_3$): δ_H = 7.48–7.42 (m, 2 H), 7.31–7.20 (m, 3 H), 5.86 (ddt, J = 17.2, 10.4, 4.9 Hz, 1 H), 5.64 (s, 1 H), 5.19 (dq, J = 10.4, 0.7 Hz, 1 H), 5.12 (s, 2 H), 5.06 (dq, J = 17.2, 0.7 Hz, 1 H), 4.99 (t, J = 1.2 Hz, 1 H), 4.77 (t, J = 1.2 Hz, 1 H), 4.43 (dt, J = 4.8, 1.7 Hz, 2 H), 3.12 (s, 2 H), 1.76 (s, 3 H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ_C = 162.3, 152.6, 152.2, 139.4, 136.9, 132.5, 128.9 (2 C), 128.4 (2 C), 127.5, 116.7, 115.0, 102.5, 46.5, 44.5, 40.4, 22.5 ppm. HRMS (TOF ESI+): calcd. for C$_{18}$H$_{20}$O$_2$N$_2$Na$^+$ [M + Na]$^+$ 319.1422; found 319.1438; Δ = 5.0 ppm.

4H-Quinolizin-4-one (14a): General procedure 3 was followed by using 1,6-diallylpyridin-2(1H)-one (**12a**). The crude reaction mixture was purified by chromatography on a silica gel column (40–60 petroleum ether/EtOAc, 2:3) to give **14a** (68% yield over 2 steps) as a yellow solid, m.p. 54–56 °C (Et$_2$O/hexane); ref.[2] m.p. 71–72 °C. R_f = 0.22 (EtOAc/40–60 petroleum ether, 4:1). IR (CDCl$_3$): $\tilde{\nu}_{max}$ = 1663 (med), 1633 (med), 1546 (med), 1475 (str) cm^{-1}. ^{1}H NMR (500 MHz, CDCl$_3$): δ_H = 9.13 (dd, J = 7.6, 0.6 Hz, 1 H), 7.64 (app dd, J = 8.5, 7.6 Hz, 1 H), 7.47 (app d, J = 8.9 Hz, 1 H), 7.35–7.31 (m, 1 H), 7.00 (dd, J = 6.7, 1.1 Hz, 1 H), 6.68–6.63 (m, 2 H) ppm. ^{13}C NMR (125 MHz, CDCl$_3$): δ_c = 158.7, 142.6, 138.1, 129.3, 127.3, 125.4, 115.1, 109.1, 103.5 ppm. HRMS (FTMS ESI+): calcd. for C$_9$H$_8$NO$^+$ [M + H]$^+$ 146.0600; found 146.0600; Δ = 0.1 ppm. This data is in accordance with that previously reported.[25]

8-Methyl-4H-quinolizin-4-one (14b): General procedure 4 was followed by using 1-allyl-6-(2-methylallyl)pyridin-2(1H)-one (**12b**). The crude product material was purified by chromatography on a silica gel column (40–60 petroleum ether/EtOAc, 2:3) to give **14b** (33% yield over 2 steps) as a yellow/brown crystalline solid, m.p. 132–133 °C; ref.[26] m.p. 135 °C. R_f = 0.11 (40–60 petroleum ether/ EtOAc, 3:7). IR (neat): $\tilde{\nu}_{max}$ = 3044 (w), 2918 (w), 1660 (med), 1634 (str), 1529 (med), 1481 (str), 1451 (med), 1431 (med), 1367 (w), 1342 (med), 1260 (w), 1179 (w), 1165 (med), 1144 (med) cm^{-1}. ^{1}H NMR (500 MHz, CDCl$_3$): δ_H = 9.01 (d, 1 H, J = 7.6 Hz), 7.58 (dd, J = 8.5, 7.6 Hz, 1 H), 7.21 (s, 1 H), 6.82 (app dd, J = 7.6, 1.8 Hz, 1 H), 6.51 (d, J = 7.6 Hz, 1 H), 6.50 (d, J = 8.6 Hz, 1 H), 2.38 (s, 3 H) ppm. ^{13}C NMR (125 MHz, CDCl$_3$): δ_C = 158.6, 142.9, 140.6, 138.2, 126.8, 123.3, 117.8, 107.5, 102.1, 21.1 ppm. HRMS (FTMS ESI+): calcd. for C$_{10}$H$_{10}$ON$^+$ [M + H]$^+$ 160.0757; found 160.0756; Δ = –0.6 ppm. This data is in accordance with that previously reported.[26]

7,8-Dimethyl-4H-quinolizin-4-one (14c): General procedure 5 was followed by using 1,6-bis(2-methylallyl)pyridin-2(1H)-one (**12c**). The crude product material was purified by chromatography on a silica gel column (40–60 petroleum ether/EtOAc, 1:3) to yield **14c** (75% yield over 2 steps) as a green/brown crystalline solid; m.p. 126–129 °C. R_f = 0.23 (EtOAc). IR (neat): $\tilde{\nu}_{max}$ = 2957 (w), 2924 (w), 1731 (w), 1656 (str), 1637 (str), 1566 (w), 1529 (str), 1504 (w), 1482 (str), 1441 (med), 1420 (med), 1402 (med), 1389 (w), 1372 (med), 1322 (med), 1220 (w), 1180 (med), 1149 (med), 1130 (med) cm^{-1}. ^{1}H NMR (500 MHz, CDCl$_3$): δ_H = 8.88 (s, 1 H), 7.52 (dd, J = 8.7, 7.7 Hz, 1 H), 7.19 (s, 1 H), 6.48 (d, J = 7.6 Hz, 1 H), 6.45 (d, J = 8.8 Hz, 1 H), 2.30 (s, 3 H), 2.24 (s, 3 H) ppm. ^{13}C NMR (125 MHz, CDCl$_3$): δ_C = 158.2, 142.1, 141.8, 137.4, 125.9, 124.6, 123.5, 106.9, 101.8, 19.2, 16.9 ppm. HRMS (FTMS ESI+): calcd. for C$_{11}$H$_{12}$ON$^+$ [M + H]$^+$ 174.0913; found 174.0912; Δ = –0.7 ppm.

7-Methyl-4H-quinolizin-4-one (14d): General procedure 4 was followed by using 6-allyl-1-(2-methylallyl)pyridin-2(1H)-one (**12d**). The crude reaction material was purified by chromatography on a

silica gel column (40–60 petroleum ether/EtOAc, 2:3) to give **14d** (62% yield over 2 steps) as a yellow crystalline solid; m.p. 93–94 °C. $R_f = 0.19$ (40–60 petroleum ether/EtOAc, 1:3). IR (neat): $\tilde{v}_{max} = 3090$ (w), 3066 (w), 2921 (w), 2858 (w), 1656 (str), 1634 (str), 1536 (str), 1505 (w), 1476 (str), 1458 (str), 1394 (med), 1378 (med), 1328 (w), 1264 (w), 1244 (w), 1209 (w), 1175 (w), 1151 (med), 1122 (med) cm^{-1}. ^{1}H NMR (500 MHz, CDCl$_3$): $\delta_H = 8.94$ (s, 1 H), 7.58 (dd, $J = 8.7$, 7.7 Hz, 1 H), 7.38 (d, $J = 9.0$ Hz, 1 H), 7.18 (app dd, $J = 9.0$, 1.6 Hz, 1 H), 6.60 (d, $J = 7.6$ Hz, 1 H), 6.58 (app dd, $J = 8.8$, 1.0 Hz, 1 H), 2.36 (app d, $J = 1.1$ Hz, 3 H) ppm. ^{13}C NMR (125 MHz, CDCl$_3$): $\delta_C = 158.4$, 141.4, 137.3, 132.4, 125.0, 124.9, 124.6, 108.7, 103.1, 18.6 ppm. HRMS (FTMS ESI+): calcd. for C$_{10}$H$_{10}$ON$^+$ [M + H]$^+$ 160.0757; found 160.0760; $\Delta = 1.8$ ppm.

7-Phenyl-4H-quinolizin-4-one (14e): General procedure 4 was followed by using 6-allyl-1-(2-phenylallyl)pyridin-2(1H)-one (**12e**). The crude reaction material was purified by chromatography on a silica gel column (40–60 petroleum ether/EtOAc, 2:3) to yield **14e** (72% yield over 2 steps) as a yellow crystalline solid; m.p. 99–101 °C. $R_f = 0.33$ (40–60 petroleum ether/EtOAc, 1:3). IR (neat): $\tilde{v}_{max} = 3059$ (w), 2926 (w), 1664 (str), 1616 (str), 1543 (str), 1501 (w), 1457 (str), 1392 (str), 1336 (w), 1290 (w), 1266 (w), 1245 (w), 1180 (w), 1156 (med), 1132 (med) cm^{-1}. ^{1}H NMR (500 MHz, CDCl$_3$): $\delta_H = 9.34$ (d, $J = 0.7$ Hz, 1 H), 7.66–7.58 (m, 4 H), 7.52 (d, $J = 9.1$ Hz, 1 H), 7.46 (dd, $J = 7.9$, 7.3 Hz, 2 H), 7.39 (tt, $J = 7.3$, 1.0 Hz, 1 H), 6.65 (d, $J = 7.6$ Hz, 1 H), 6.62 (app dd, $J = 8.8$, 0.8 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, CDCl$_3$): $\delta_C = 158.7$, 141.5, 137.8, 136.2, 129.4, 129.2 (2 C), 128.8, 128.5, 126.8 (2 C), 125.6, 124.4, 109.2, 103.1 ppm. HRMS (FTMS ESI+): calcd. for C$_{15}$H$_{12}$ON$^+$ [M + H]$^+$ 222.0913; found 222.0912; $\Delta = -0.8$ ppm.

8-Methyl-7-phenyl-4H-quinolizin-4-one (14f): General procedure 5 was followed by using 6-(2-methylallyl)-1-(2-phenylallyl)pyridin-2(1H)-one (**12f**). The crude reaction mixture was purified by chromatography on a silica gel column (40–60 petroleum ether/EtOAc, 3:2 then 1:1) to give **14f** (36% yield over 2 steps) as a yellow wax; $R_f = 0.50$ (EtOAc). IR (neat): $\tilde{v}_{max} = 3057$ (w), 2958 (w), 2925 (w), 2854 (w), 1719 (w), 1659 (med), 1626 (str), 1603 (w), 1540 (med), 1498 (w), 1475 (str), 1419 (w), 1401 (med), 1378 (w), 1319 (w), 1260 (w), 1181 (w), 1154 (str) cm^{-1}. ^{1}H NMR (500 MHz, CDCl$_3$): $\delta_H = 9.02$ (s, 1 H), 7.63 (dd, $J = 8.8$, 7.7 Hz, 1 H), 7.49–7.37 (m, 6 H), 6.58 (d, $J = 7.6$ Hz, 1 H), 6.54 (d, $J = 8.8$ Hz, 1 H), 2.30 (s, 3 H) ppm. ^{13}C NMR (125 MHz, CDCl$_3$): $\delta_C = 158.6$, 142.1, 140.3, 138.0, 136.3, 131.6, 129.4 (2 C), 128.5 (2 C), 128.2, 126.2, 124.4, 107.6, 101.7, 20.3 ppm. HRMS (TOF ESI+): calcd. for C$_{16}$H$_{14}$ON$^+$ [M + H]$^+$ 236.1075; found 236.1082; $\Delta = 3.0$ ppm.

Methyl 4-Oxo-4H-quinolizine-7-carboxylate (14g): General procedure 4 was followed by using methyl 2-{[6-allyl-2-oxopyridin-1(2H)-yl]methyl}acrylate (**12g**). The crude reaction mixture was purified by chromatography on a silica gel column (40–60 petroleum ether/EtOAc, 2:3) to give **14g** (40% yield over 2 steps) as a yellow solid; m.p. 121–122 °C. $R_f = 0.53$ (EtOAc). IR (neat): $\tilde{v}_{max} = 3078$ (w), 2924 (w), 2850 (w), 1718 (str), 1664 (str), 1630 (str), 1619 (str), 1554 (str), 1489 (str), 1451 (str), 1438 (str), 1397 (str), 1369 (med), 1327 (med), 1293 (str), 1261 (str), 1240 (str), 1197 (med), 1179 (med), 1145 (med), 1116 (str) cm^{-1}. ^{1}H NMR (500 MHz, CDCl$_3$): $\delta_H = 9.76$ (s, 1 H), 7.74 (app dd, $J = 9.0$, 1.0 Hz, 1 H), 7.68 (dd, $J = 9.0$, 7.5 Hz, 1 H), 7.42 (d, $J = 9.0$ Hz, 1 H), 6.65 (d, $J = 9.0$ Hz, 1 H), 6.62 (d, $J = 7.5$ Hz, 1 H), 3.97 (s, 3 H) ppm. ^{13}C NMR (125 MHz, CDCl$_3$): $\delta_C = 164.8$, 158.8, 142.5, 139.5, 131.8, 127.5, 125.3, 118.3, 110.7, 103.3, 52.5 ppm. HRMS (FTMS ESI+): calcd. for C$_{11}$H$_{10}$O$_3$N$^+$ [M + H]$^+$ 204.0655; found 204.0655; $\Delta = -0.1$ ppm.

Methyl 8-Methyl-4-oxo-4H-quinolizine-7-carboxylate (14h): General procedure 5 was followed by using methyl 2-{[6-(2-methylallyl)-

2-oxopyridin-1(2H)-yl]methyl}acrylate (**12h**). The crude reaction material was purified by chromatography on a silica gel column (40–60 petroleum ether/EtOAc, 4:1 then 3:2) to give **14h** (25% yield over 2 steps) as a yellow solid; m.p. 144–146 °C. $R_f = 0.50$ (EtOAc). IR (neat): $\tilde{v}_{max} = 2954$ (w), 2926 (w), 1723 (str), 1666 (str), 1624 (med), 1543 (med), 1451 (str), 1456 (med), 1444 (med), 1419 (med), 1402 (med), 1380 (med), 1315 (w), 1280 (str), 1247 (med), 1200 (w), 1187 (w), 1163 (med), 1109 (med) cm^{-1}. ^{1}H NMR (500 MHz, CDCl$_3$): $\delta_H = 9.71$ (s, 1 H), 7.64 (dd, $J = 8.9$, 7.6 Hz, 1 H), 7.21 (s, 1 H), 6.54 (app dd, $J = 9.0$, 1.1 Hz, 1 H), 6.50 (d, $J = 7.6$ Hz, 1 H), 3.93 (s, 3 H), 2.62 (app d, $J = 0.7$ Hz, 3 H) ppm. ^{13}C NMR (125 MHz, CDCl$_3$): $\delta_C = 165.2$, 158.5, 142.5, 139.9, 139.7, 132.6, 125.4, 119.0, 108.9, 101.7, 52.3, 21.1 ppm. HRMS (FTMS ESI+): calcd. for C$_{12}$H$_{12}$O$_3$N$^+$ [M + H]$^+$ 218.0812; found 218.0808; $\Delta = -1.7$ ppm.

Diethyl 4-Oxo-4H-quinolizine-1,3-dicarboxylate (14i): General procedure 3 was followed by using diethyl 1,6-diallyl-2-oxo-1,2-dihydropyridine-3,5-dicarboxylate (**12i**). The crude reaction material was purified by chromatography on a silica gel column (40–60 petroleum ether/EtOAc, 1:1 then 2:3) to give **14i** (81% yield over 2 steps) as a yellow solid, m.p. 122–124 °C; ref.[27,28] m.p. 131–132 and 135–138 °C. $R_f = 0.34$ (40–60 petroleum ether/EtOAc, 1:3). IR (neat): $\tilde{v}_{max} = 3139$ (w), 2984 (w), 2905 (w), 1713 (med), 1674 (str), 1622 (str), 1582 (str), 1518 (med), 1494 (str), 1437 (med), 1390 (w), 1373 (med), 1350 (med), 1324 (w), 1295 (med), 1255 (w), 1203 (str), 1169 (med), 1149 (str), 1110 (med) cm^{-1}. ^{1}H NMR (500 MHz, CDCl$_3$): $\delta_H = 9.52$ (d, $J = 7.1$ Hz, 1 H), 9.36 (d, $J = 9.1$ Hz, 1 H), 9.15 (s, 1 H), 7.87 (app ddd, $J = 9.1$, 6.8, 1.4 Hz, 1 H), 7.35 (app td, $J = 7.0$, 1.3 Hz, 1 H), 4.43 (q, $J = 7.1$ Hz, 2 H), 4.38 (q, $J = 7.1$ Hz, 2 H), 1.45–1.38 (m, 6 H) ppm. ^{13}C NMR (125 MHz, CDCl$_3$): $\delta_C = 165.4$, 164.8, 155.5, 147.0, 144.4, 136.8, 130.3, 124.4, 117.6, 105.6, 101.9, 61.3, 61.2, 14.4 (2 C) ppm. HRMS (TOF ESI+): calcd. for C$_{15}$H$_{16}$NO$_5^+$ [M + H]$^+$ 290.1028; found 290.1035; $\Delta = 2.4$ ppm. This data is consistent with that previously reported.[28]

Diethyl 8-Methyl-4-oxo-4H-quinolizine-1,3-dicarboxylate (14j): General procedure 4 was followed by using diethyl 1-allyl-6-(2-methylallyl)-2-oxo-1,2-dihydropyridine-3,5-dicarboxylate (**12j**). The crude reaction material was purified by chromatography on a silica gel column (40–60 petroleum ether/EtOAc, 3:2 then 1:1) to give **14j** (22% yield over 2 steps) as a yellow wax; $R_f = 0.25$ (40–60 petroleum ether/EtOAc, 1:1). IR (neat): $\tilde{v}_{max} = 3084$ (w), 2979 (w), 2926 (w), 2854 (w, C–H), 1739 (med), 1691 (str), 1670 (str), 1634 (med), 1584 (med), 1517 (med), 1501 (str), 1461 (med), 1390 (w), 1367 (med), 1320 (med), 1294 (med), 1259 (w), 1215 (str), 1174 (med), 1140 (med), 1108 (med) cm^{-1}. ^{1}H NMR (500 MHz, CDCl$_3$): $\delta_H = 9.44$ (d, $J = 7.0$ Hz, 1 H), 9.19 (s, 1 H), 9.15 (s, 1 H), 7.21 (dd, $J = 7.0$, 0.9 Hz, 1 H), 4.44 (q, $J = 7.3$ Hz, 2 H), 4.39 (q, $J = 7.3$ Hz, 2 H), 2.58 (s, $J = 0.9$ Hz, 3 H, d), 1.45–1.40 (m, 6 H) ppm. ^{13}C NMR (125 MHz, CDCl$_3$): $\delta_C = 165.6$, 165.0, 155.6, 149.7, 146.8, 144.6, 129.9, 123.1, 120.0, 104.4, 101.0, 61.1, 60.9, 22.1, 14.5, 14.4 ppm. HRMS (TOF ESI+): calcd. for C$_{16}$H$_{18}$O$_5$N$^+$ [M + H]$^+$ 304.1185; found 304.1199, $\Delta = 4.6$ ppm; calcd. for C$_{16}$H$_{17}$O$_5$NNa$^+$ [M + Na]$^+$ 326.1004; found 326.1018, $\Delta = 4.3$ ppm.

2-Benzyl-1H-pyrido[1,2-c]pyrimidine-1,3(2H)-dione (14k): General procedure 3 was followed by using 1,6-diallyl-3-benzylpyrimidine-2,4(1H,3H)-dione (**12k**). The crude reaction material was purified by HPLC (30–45% solvent B, 20 min, 200 µL injections of 30 mg mL^{-1} sample) to give **14k** (30% yield) as a crystalline yellow solid; m.p. 158–160 °C. $R_f = 0.18$ (40–60 petroleum ether/EtOAc, 1:1). IR (neat): $\tilde{v}_{max} = 3081$ (w), 2926 (w), 1704 (med), 1662 (str), 1639 (str), 1579 (str), 1543 (str), 1493 (med), 1455 (w), 1424 (med),

1407 (med), 1385 (med), 1362 (w), 1336 (med), 1265 (med), 1207 (w), 1161 (w), 1137 (w), 1116 (w) cm^{-1}. ^{1}H NMR (500 MHz, CDCl$_3$): δ_H = 8.19 (d, J = 7.5 Hz, 1 H), 7.51 (d, J = 8.3 Hz, 2 H), 7.33–7.22 (m, 3 H), 6.97 (app ddd, J = 9.1, 7.5, 1.0 Hz, 1 H), 6.79 (d, J = 9.2 Hz, 1 H), 6.33 (app dt, J = 1.2, 7.6 Hz, 1 H), 5.70 (s, 1 H), 5.26 (s, 2 H) ppm. ^{13}C NMR (125 MHz, CDCl$_3$): δ_C = 160.9, 149.3, 146.3, 136.5, 132.9, 129.1 (2 C), 128.4 (2 C), 127.9, 127.7, 122.7, 110.8, 92.0, 45.0 ppm. HRMS (FTMS ESI+): calcd. for C$_{15}$H$_{13}$O$_2$N$_2$$^+$ [M + H]$^+$ 253.0972; found 253.0968; Δ = –1.4 ppm.

Supporting Information (see footnote on the first page of this article): ^{1}H and ^{13}C NMR spectra, synthetic routes towards pyridone **10e** and uracil derivative **10f**, and optimization studies for the RCM and dehydrogenation steps.

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[17] The allyltributyltin resulted in a high conversion of starting material after 16 h, whereas the more sterically demanding 2-methylallyltin coupling partner required significantly longer reaction times (4 to 6 days) to give acceptable yields.

[18] Tin residues were effectively removed from products **12** by aqueous extraction with KF solution (10% w/v) and chromatography on SiO$_2$/KF (9:1) as the stationary phase. For details, see: D. C. Harrowven, I. L. Guy, *Chem. Commun.* **2004**, *17*, 1968–1969.

[19] The use of microwave irradiation conditions for the RCM process was also briefly examined, but the results were comparable to those obtained by thermal heating.

[20] For example, it was found that the alkene of **13a** rearranged after a short period of time to afford a product (i.e., **15a**) that proved inert to dehydrogenation.

[21] The reaction of **12l** afforded **15l** as the major product.

[22] The majority of the rearrangements (i.e., compound **13** into **15**) was found to occur in the dehydrogenation step (the Pd presumably acted as a Lewis acid). In general, the ^{1}H NMR analysis of the crude reaction mixtures of the metathesis step indicated only trace amounts of rearranged products. The use of known ruthenium hydride scavengers (e.g., AcOH and quinones) did not prevent the isomerization from occurring. The rearranged dihydroquinolizinones **15** were found to be stable to oxidation. Hydride abstraction appears to occur only at the allylic/benzylic position away from the N atom. Nunez et al. have reported that this is not the case for quinolizinium cations, see ref.[12b]

[23] In the case of pyrido-pyrimidine derivative **14k**, purification by HPLC was required.

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