Synthesis of α-Pyridone-Based Azaheteroaromatics by Intramolecular Vinylketene Cyclizations onto the C=N Bond of Nitrogen Heteroaromatics

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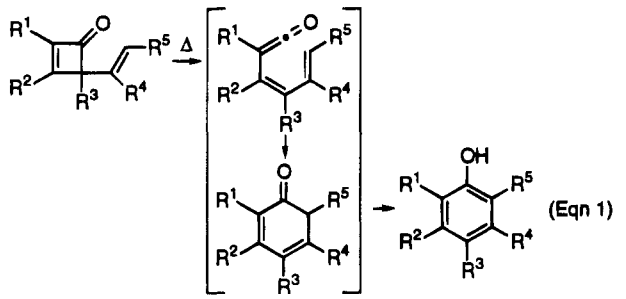
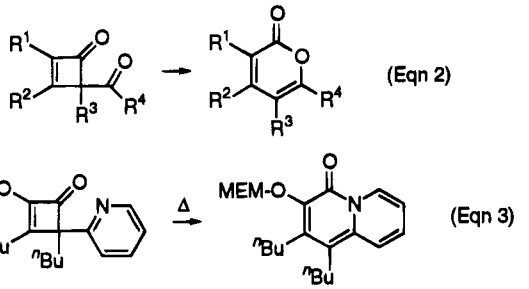
Substituted quinolizin-4-ones and ring-fused α-pyridone derivatives have been synthesized by the construction of 2,3-disubstituted-4-(2-azaheteroaryl)-2-cyclobutenones followed by thermal rearrangment. 4-(2-Azaheteroaryl)-2-cyclobutenones have been prepared regioselectively by the addition of 2-lithioazaheteroaromatics to cyclobutenediones and by palladium catalyzed cross-coupling of 4-chloro-2-cyclobutenones with 2-tri-*n*-stannylazaheteroaromatics. The thermal transformation is proposed to occur by ring-opening of the cyclobutenone followed by intramolecular cyclization of the transient vinylketene onto the carbon-nitrogen double bond of the azaheteroaromatic. A variety of quinolizin-4-ones, imidazo[1,2-*a*]pyridin-5-ones, 1-oxopyrido[2,1-*b*]benzothiazoles, and thiazolo-[3,2-*a*]pyridin-5-ones were prepared.

Introduction

The last few years have witnessed the development of a powerful new methodology for the synthesis of substituted aromatic systems and quinones proceeding through putative dienylketene intermediates (eq 1). The transient



dienylketenes can be generated by thermolysis of an appropriately substituted cyclobutenone which may be accessed through cyclobutenediones by nucleophilic addition,[1-7] through 4-chloro-2-cyclobutenones via palladium catalyzed cross couplings of organotin reagents[8-12] and through the [2+2] cycloaddition of in situ generated vinyl ketenes to electron-rich alkynes.[13-17] Variations on this basic theme are easily conceived and judicious heteroatom permutations of the dienylketene should provide direct synthetic entry to a variety of valuable heterocyclic systems. Already a new synthesis of α-pyrones has been developed (eq 2)[11] and a novel approach



to indolizine-5,8-diones was described.[18] In a previous study that focused on the regiocontrolled synthesis of 1,2-dioxygenated aromatics,[1] thermolysis of 2-alkoxy-3,4-di-*n*-butyl-4-(2-pyridyl)-2-cyclobutenone gave exclusively the quinolizinone shown in eq 3. Herein is documented a study of this new synthesis of pyridone-based substituted azaheteroaromatic ring systems, **3**, which were constructed by thermolysis of 4-(2-azaheteroaryl)cyclobutenones, **2**, generated either by addition of a 2-lithioazaheteroaromatic to a cyclobutenedione, **1**, or by palladium catalyzed cross-coupling of a 4-chlorocyclobutenone, **4**, with a 2-(tri-*n*-butylstannyl)azaheteroaromatic, **5**. The transformation apparently occurs by cyclization of a transiently generated vinylketene onto the carbon-nitrogen double bond of the azaheteroaromatic (eq 4). Specifically, this new chemistry provides access to highly fluorescent heteroaromatic ring systems of documented medicinal interest:[19-29] quinolizin-4-ones, 1-hydroxyquin-

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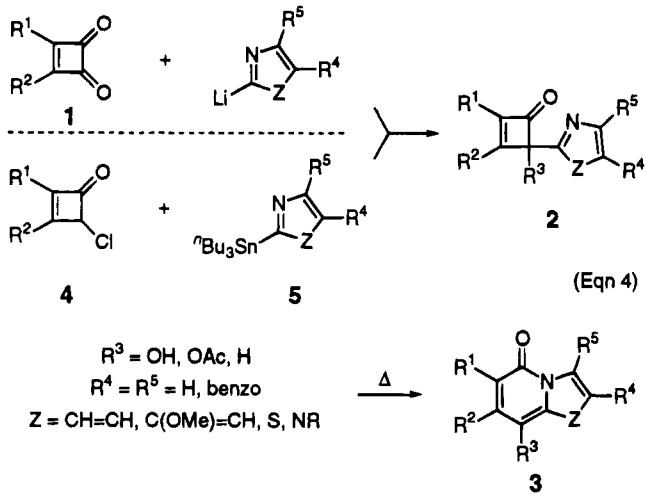


olizin-4-ones, imidazo[1,2-*a*]pyridin-5-ones, 1-oxopyrido-[2,1-*b*]benzothiazoles, and thiazolo[3,2-*a*]pyridin-5-ones.

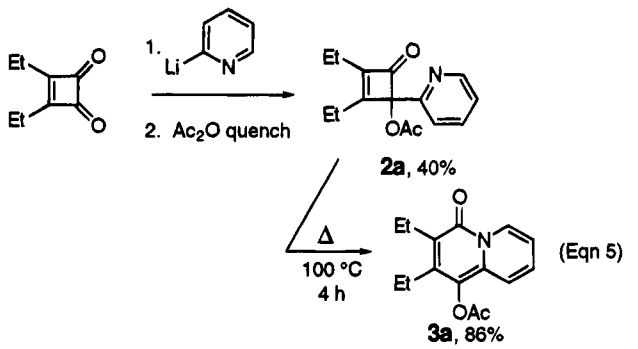
Results and Discussion

To benchmark the study, 2-lithiopyridine was added to 3,4-diethyl-3-cyclobutene-1,2-dione, and the resulting alkoxide was trapped in situ by acetylation providing in 40% yield the moderately unstable 1,2-adduct, **2a** (eq 5). Also isolated in 11% yield was the acetylated product of 1,4-addition of 2-lithiopyridine to the cyclobutenedione. The 1,2-adduct rearranged within 4 h at 100 °C in dry, argon-sparged toluene to provide 1-acetoxy-2,3-diethylquinolizin-4-one, **3a**, in 86% yield. When the procedure was repeated without purification of the intermediate **2a**, **3a** was obtained in 41% overall yield after thermolysis (Table 1, entry 1).

This proved to be a general process. A variety of substituted cyclobutenediones were treated in THF at −78 °C with preformed 2-azaheteroaryl lithiates, generated either by deprotonation with *n*-butyl or *t*-butyllithium or by lithium halogen exchange from the corresponding bromides (see Table 1).[30] Because higher yields usually resulted, the 1,2-addition products were protected *in situ* by addition of acetic anhydride to the reaction mixtures at −78 °C. The crude cyclobutenone intermediates, **2**, were isolated using an aqueous $NaHCO_3$ quench followed by extraction with EtOAc. The 1,2-adducts were moderately unstable; therefore, it proved best to transform them directly into the desired heterocycles by thermolysis (Table 1). The crude cyclobutenones were heated under an argon atmosphere between 85 and 100 °C in dry, argon-sparged toluene, dioxane, or 1,2 dichloroethane; the choice of solvent did not appear to affect the thermolysis yield.

In one case (Table 1, entry 5) the 4-hydroxycyclobutenone intermediate was studied without protection by acetylation. Addition of 2-lithiopyridine to 3-isopropoxy-4-phenylcyclobutenedione at −78 °C gave, after quenching with aqueous $NaHCO_3$ at −78 °C, a crude oil that was subjected to thermolysis in dioxane at 90 °C for 2 h and produced 1-hydroxy-2-isopropoxy-3-phenylquinolizin-4-one, **3e**, in 48% yield. Acetylation of **3e** gave, in 94% yield, a product identical to **3d**, which had been prepared directly from the 4-acetoxycyclobutenone, **2d** (Table 1, entry 4).

The following observations pertain to the results listed in Table 1. Moderate to good isolated overall yields were obtained in most cases. Because of the good yield observed in the thermolysis step documented in eq 5,



above, any diminution in yield is presumed to be due to a low yield in the formation of the 1,2-adduct. With the 5-membered ring heteroaryl lithiates (see Table 1, entries 7−12) only 1,2-addition products, **2**, were observed, while in some cases 2-lithiopyridine produced small amounts of 1,4-adducts in addition to the desired 1,2-addition products. Varying reaction conditions (addition order, reaction temperature, solvent mixture) did not significantly change the ratio of 1,2 to 1,4-addition products. 2-Lithioazaheteroaromatics added regioselectively to unsymmetrically substituted cyclobutenediones (see Table 1, entries 3−6, 11, 12), addition occurring exclusively at the more electron-deficient ketone. The isolated cyclobutenone intermediates rearranged upon thermolysis to give the expected quinolizinones and pyridinones. The formation of an unusual byproduct in one example is worth noting. Addition of 2-lithio-1-methylimidazole to 3-(*N,N*-dibenzylamino)-4-methylcyclobutene-1,2-dione followed by in situ reaction with acetic anhydride gave a mixture of the expected 1,2-addition product, **2k**, and the unacetylated 4-hydroxycyclobutenone, **2k′** (eq 6). Thermolysis of the crude mixture gave the anticipated acetoxypyridinone product, **3k**, in 33% yield along with the

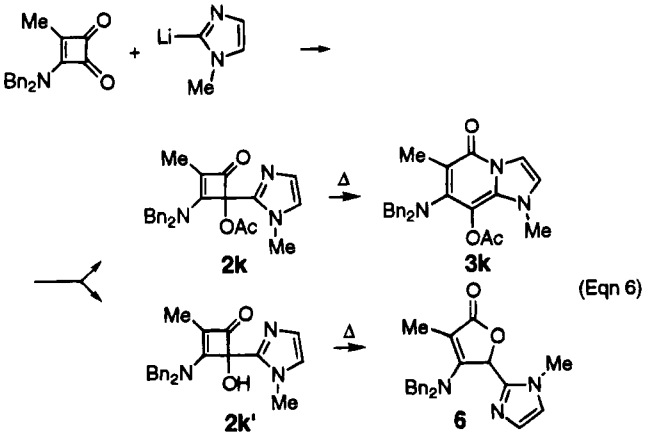


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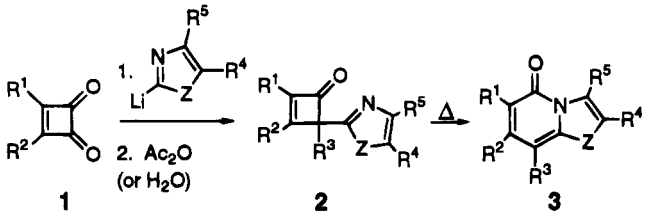
Table 1. Pyridone-Based Heteroaromatics by Addition of 2-Lithio Azaheteroaromatics to Cyclobutenediones Followed by Thermolysis



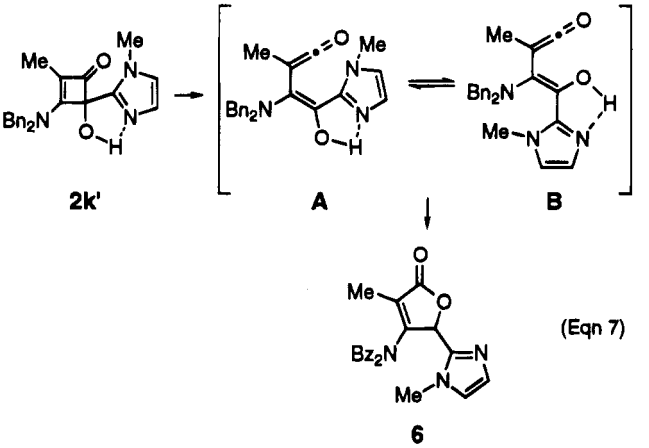
entry	R^1	R^2	lithiate	Z	R^3	R^4	R^5	compd no., overall yield (%)
1	Et	Et	2-lithiopyridine	CH=CH	OAc	H	H	**3a**,[a] 41
2	*n*-Bu	*n*-Bu	2-lithiopyridine	CH=CH	OAc	H	H	**3b**,[a] 50
3	Me	*i*-PrO	2-lithiopyridine	CH=CH	OAc	H	H	**3c**,[b] 50
4	Ph	*i*-PrO	2-lithiopyridine	CH=CH	OAc	H	H	**3d**,[b] 60
5	Ph	*i*-PrO	2-lithiopyridine	CH=CH	OH	H	H	**3e**, 48
6	Ph	*i*-PrO	2-lithio-3-methoxypyridine	C(OMe)=CH	OAc	H	H	**3f**, 29
7	Et	Et	2-lithiothiazole	S	OAc	H	H	**3g**, 44
8	Me	Me	2-lithiobenzothiazole	S	OAc	benzo		**3h**, 56
9	Et	Et	2-lithiobenzothiazole	S	OAc	benzo		**3i**, 54
10	Et	Et	2-lithio-1-methylimidazole	NMe	OAc	H	H	**3j**, 65
11	Et	Bn_2N	2-lithio-1-methylimidazole	NMe	OAc	H	H	**3k**,[c] 63
12	Ph	*i*-PrO	2-lithio-1-methoxymethylimidazole	*N*-MOM	OAc	H	H	**3l**, 38

[a] Small amounts (<11%) of a 1,4-addition product was also isolated. [b] Trace amount of an unidentified regioisomer was also isolated. [c] In situ protection performed with Ac_2O/pyridine. 15% of a lactone byproduct was also isolated.

butenolide, **6**, in 37% yield. This lactone results from the unacetylated cyclobutenone where the free hydroxyl substituent is able to attack the vinylketene intermediate formed during thermolysis. To confirm the source of the lactone byproduct a purified sample of 4-hydroxy-4-(1-methylimidazo-2-yl)-2-cyclobutenone, **2k'**, was isolated and subjected to thermolysis to yield **6** as the sole product. If the reaction mixture resulting from addition of 2-lithio-1-methylimidazole to 3-(*N,N*-dibenzylamino)-4-methylcyclobutene-1,2-dione was allowed to warm to room temperature and was then quenched with acetic anhydride and pyridine, a product mixture resulted that gave, after thermolysis, the desired pyridinone, **3k**, in 63% yield along with the butenolide byproduct, **6**, in only 18% yield (see Table 1, entry 11).

The direct formation of a butenolide on thermolysis of a 4-hydroxycyclobutenone is unusual, since other 4-hydroxycyclobutenones produce lactones on photolysis,[31] but not typically on thermolysis except in certain cases.[32-34] It is probable that the 1,2-adduct, **2k'**, exists in a stable hydrogen-bonded conformation that internally "protects" the imidazole imine nitrogen and disfavors intramolecular cyclization of the imidazole C=N bond onto the ketene intermediate (eq 7, stereoisomer **A**). Equilibration of the vinylketene stereoisomers **A** and **B** would allow closure to the butenolide **6** as observed.

The addition of aromatic, vinylic, and acetylenic organolithium nucleophiles to cyclobutenediones produces substituted cyclobutenones that can rearrange to 1,4-dioxygenated aromatics (or quinones) on thermolysis. The related palladium catalyzed cross-coupling of unsaturated organostannanes with 4-chlorocyclobutenones delivers cyclobutenones that are comparably substituted to provide phenol-based compounds when subjected to thermolysis.[1,8-12] This palladium catalyzed cross-coupling variant was studied as a means of generating the quinolizin-4-one and 1-oxopyrido[2,1-*b*]benzothiazole ring systems.



The synthesis of 2-isopropoxy-3-methylquinolizin-4-one, **3m**, is representative of the cross-coupling/rearrangement process (eq 8). A solution of 4-chloro-3-isopropoxy-2-methyl-2-cyclobutenone and 2-tri-*n*-butylstannylpyridine in dry toluene was sparged with N_2 then 2.5 mol% $Pd_2(dba)_3$ and 10 mol% tris(2-furyl)phosphine (TFP) were added. The reaction mixture was heated at 60 °C overnight to induce coupling, then refluxed for 5 h to complete rearrangement to the heterocycle. Workup and purification by SiO_2 chromatography provided **3m** in 62% yield.

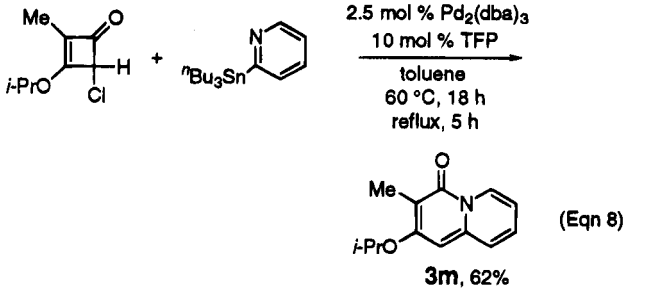


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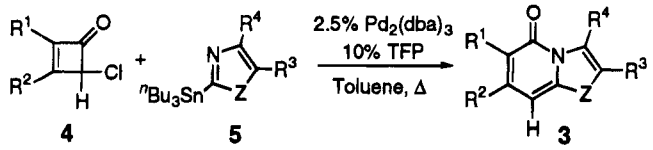
Table 2. Pyridone-Based Heteroaromatics by Pd-Catalyzed Coupling-Rearrangement with 2-(Tri-*n*-butylstannyl)azaheteroaromatics



entry	R^1	R^2	Z	R^3	R^4	compd no., yield (%)
1	Me	*i*-PrO	CH=CH	H	H	**3m**, 62
2	Me	Ph	CH=CH	H	H	**3n**, 42
3	Et	Et	CH=CH	H	H	**3o**, 34
4	*n*-Bu	Me	CH=CH	H	H	**3p**, 31
5	Ph	*i*-PrO	CH=CH	H	H	**3q**, 10
6	Me	*i*-PrO	S	benzo		**3r**, 44
7	Me	Ph	S	benzo		**3s**, 58
8	Et	Et	S	benzo		**3t**, 34

This process proved to be general for the cross-coupling and subsequent rearrangement of a variety of 4-chlorocyclobutenones with 2-(tri-*n*-butylstannyl)pyridine and provided moderate yields of the desired quinolizin-4-ones in most cases (Table 2, entries 1–5). 2,2′-Bipyridine, derived from oxidative homocoupling of 2-(tri-*n*-butylstannyl)pyridine, was formed to varying degrees (17 to 53% yield based on 2-(tri-*n*-butylstannyl)pyridine) in all of these coupling reactions.[35] In the case of 4-chloro-3-isopropoxy-2-phenyl-2-cyclobutenone the coupling did not proceed as expected, and provided only 10% of the desired 2-isopropoxy-3-phenylquinolizin-4-one, **3q**. The major products were 2,2′-bipyridine (53%), the reduction product 3-isopropoxy-2-phenyl-2-cyclobutenone (41%) and an unusual spiro compound (12%) that was first identified in another project and will be described elsewhere.

The coupling/rearrangement of 4-chlorocyclobutenones with 2-(tri-*n*-butylstannyl)benzothiazoles was performed under the same conditions used with 2-tri-*n*-butylstannylpyridine, described above, to yield 1-oxopyrido[2,1-*b*]-benzothiazoles (Table 2, entries 6–8). These transformations proceeded in acceptable yields without the complication of organostannane homocoupling observed with the pyridine system.

Conclusions

Two new methods for the construction of the quinolizin-4-one and related ring-fused pyridin-5-one systems have been developed. Palladium catalyzed cross-coupling of 2-(tri-*n*-butylstannyl)azaheteroaromatics with 4-chlorocyclobutenones allows direct access to these heterocycles, while addition of 2-lithiated heteroaromatics to cyclobutenediones provides related structures bearing a hydroxy or acetoxy substitutent situated "para" to the pyridone carbonyl group. Overall yields are modest to good and highly substituted heterocyclic ring structures are easily generated.

Experimental Section

Materials and Methods. All reactions were performed under an atmosphere of dry argon or nitrogen in base-washed, flame-dried glassware. Thermolyses were performed under an argon atmosphere in dried argon-sparged solvents. Solvents were dried by distillation under nitrogen from sodium-benzophenone ketyl (THF, Et_2O, toluene, dioxane) or from CaH_2 (1,2-dichloroethane). *n*-Butyllithium and *t*-butyllithium solutions were obtained from Aldrich in Sure-Seal* containers and were titrated using diphenylacetic acid as indicator. Pd_2(dibenzylideneacetone)$_3$ [$Pd_2(dba)_3$]was purchased from Aldrich and used as is.

All thin-layer chromatography was performed using Merck Kieselgel 60 F_{254} plates with visualization by UV and phosphomolybdic acid stain. Purification by flash SiO_2 column chromatography was performed using 32–63 μm SiO_2. Melting points are uncorrected and were determined either using recrystallized samples or samples which crystallized during concentration of the chromatography eluents. IR spectra were recorded in solution using KCl or NaCl cells.

Diisopropylsquarate,[36] 4-chloro-2,3-diethylcyclobutenone,[9] 4-chloro-3-isopropoxy-2-methylcyclobutenone,[12] 4-chloro-3-isopropoxy-2-phenylcyclobutenone,[9] 2-*n*-butyl-4-chloro-3-methylcyclobutenone,[9] 2-(tri-*n*-butylstannyl)pyridine,[30,37] tris(2-furyl)-phosphine,[38] dimethylcyclobutenedione,[36] dibutylcyclobutenedione,[12] 3-isopropoxy-4-phenylcyclobutenedione,[36] 3-isopropoxy-4-methylcyclobutenedione,[36] 3-(*N*,*N*-dibenzylamino)-4-methylcyclobutenedione,[12] 2-bromo-3-methoxypyridine,[39] and 1-(methoxymethyl)imidazole[40] were prepared by literature methods.

Nucleophilic Additions to Cyclobutenediones. 3,4-Diethylcyclobutene-1,2-dione. 2,3-Diethyl-4,4-dichlorocyclobutenedione was prepared by a modification of Danheiser's procedure[41] then hydrolyzed with strong acid to give the cyclobutenedione. 3-Hexyne (18.1 mL, 159 mmol, 1.00 equiv) was added to a slurry of zinc–copper couple (30.8 g, 240 mmol, 1.51 equiv) in dry Et_2O (200 mL) under argon. A solution of trichloroacetyl chloride (35.0 mL, 314 mmol, 1.97 equiv) in dry DME (100 mL) was added dropwise. The reaction was stirred overnight at room temperature to give a dark brown slurry. The slurry was filtered through Celite, rinsing with additional Et_2O. The combined Et_2O layers were washed once with 0.5 N HCl and three times with 0.5 N NaOH, then once with saturated aq NaCl. The Et_2O layer was dried ($MgSO_4$) and filtered through a pad of SiO_2, then concentrated to give a brown oil which was distilled (Kuglrohr distillation, 80 °C, 1.25 mmHg) to give a clear colorless liquid. The liquid was added dropwise to 80 mL of 95% H_2SO_4 which had been cooled to 0 °C. The reaction was stirred for 6 h while warming slowly to room temperature. The mixture was poured into ice and extracted with Et_2O, washed with saturated aq $NaHCO_3$, dried ($MgSO_4$) and concentrated to a brown oil. The crude product was distilled (Kuglrohr distillation, bp 65 °C, 0.05 mmHg) to give 10.7 g (77.4 mmol, 49%) of 3,4-diethylcyclobutene-1,2-dione as a yellow oil. IR (CH_2Cl_2, KCl, cm^{-1}): 1789 (s), 1770 (s), 1595 (s). ^1H NMR ($CDCl_3$, 300 MHz): δ 2.76 (q, J = 7.5 Hz, 4 H), 1.31 (t, J = 7.5 Hz, 6 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 203.1 (2C), 199.6 (2C), 20.0 (2C), 10.5 (2C). Anal. Calcd for $C_8H_{10}O_2$: C, 69.55; H, 7.30; O, 23.16. Found: C, 69.40; H, 7.29.

1-Acetoxy-2,3-diethylquinolizin-4-one, 3a. 2-Lithiopyridine was generated by lithium halogen exchange.[30] 2-Bromopyridine (0.25 mL, 2.62 mmol, 1.20 equiv, Aldrich) was dissolved in dry THF (5 mL) under N_2 and cooled to −78 °C. *n*-BuLi in hexane (2.1 mL, 1.24 M, 2.6 mmol, 1.19 equiv) was added dropwise and the reaction mixture was stirred at −78 °C for 1 h. 3,4-Diethylcyclobutene-1,2-dione (0.302 g, 2.19 mmol, 1.00 equiv) was dissolved in dry THF (15 mL) under N_2 and cooled to −78 °C. The pyridine reaction mixture was added to the dione solution via cannula and stirred at −78 °C

(35) 2,2-Bipyridine is formed by a process that concomitantly induces reductive homocoupling of the 4-chlorocyclobutenone. Unpublished results of Sangho Koo to be published elsewhere.

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for 25 min, then acetic anhydride (0.412 mL, 4.37 mmol, 2.00 equiv) was added and the mixture was stirred for 1.5 h. The reaction mixture was quenched with saturated aq $NaHCO_3$, extracted with EtOAc, dried ($MgSO_4$) and concentrated to a brown oil. Two products were isolated by flash chromatography (SiO_2, 3 × 15 cm column, 20% EtOAc/hexanes). The lower R_f compound, 4-acetoxy-2,3-diethyl-4-(2-pyridyl)-2-cyclobutenone, **2a**, was isolated as a brown oil (0.227 g, 0.88 mmol, 40%). TLC (SiO_2, 30% EtOAc/hexanes, $R_f = 0.20$). IR (CH_2Cl_2, KCl, cm^{-1}): 1782 (s), 1773 (s), 1647 (w), 1588 (w). ^1H NMR ($CDCl_3$, 300 MHz): δ 8.52 (d, J = 3.9 Hz, 1 H), 7.67 (d of app t, J = 1.5, 7.8 Hz, 1 H), 7.42 (d, J = 7.8 Hz, 1 H), 7.18 (m, 1 H), 2.70 (m, 2 H), 2.34 (q, J = 7.5 Hz, 2 H), 2.14 (s, 3 H), 1.19 (t, J = 7.5 Hz, 3 H), 1.16 (t, J = 7.5 Hz, 3 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 186.2, 176.3, 169.7, 157.7, 155.3, 149.1, 136.5, 122.8, 120.6, 101.0, 21.8, 21.3, 17.4, 11.4, 11.3. HRMS (EI) calcd for $C_{15}H_{17}NO_3$: 259.1208. Found: 259.1208.

In addition to the major product reported above, a higher R_f compound, identified as the 1,4-addition product 2-acetoxy-3,4-diethyl-4-(2-pyridyl)-2-cyclobutenone, **2a′**, was isolated as a yellow/brown oil (0.060 g, 0.23 mmol, 11%). TLC (SiO_2, 30% EtOAc/hexanes, $R_f = 0.35$). IR (CH_2Cl_2, KCl, cm^{-1}): 1769 (s), 1744 (s), 1629 (m), 1589 (w). ^1H NMR ($CDCl_3$, 300 MHz): δ 8.52 (d, J = 3.9 Hz, 1 H), 7.61 (d of app t, J = 1.5, 7.5 Hz, 1 H), 7.38 (d, J = 8.1 Hz, 1 H), 7.12 (m, 1 H), 2.75–2.51 (m, 2 H), 2.30–2.05 (m, 2 H), 2.18 (s, 3 H), 1.17 (t, J = 7.5 Hz, 3 H), 0.96 (t, J = 7.5 Hz, 3 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 187.3, 170.9, 166.5, 159.6, 149.2, 140.5, 136.4, 122.0, 121.3, 69.5, 24.8, 21.4, 20.2, 10.5, 9.9. HRMS (EI) calcd for $C_{15}H_{17}NO_3$: 259.1208. Found: 259.1208.

The 1,2-addition product, **2a**, was thermally rearranged to 1-acetoxy-2,3-diethylquinolizin-4-one, **3a**. A solution of **2a** (0.172 g, 0.66 mmol) in dry toluene (5 mL) was sparged with N_2 and heated at 100 °C for 4 h. The solvent was removed under vacuum and the resulting black oil was purified by flash chromatography (SiO_2, 3 × 15 cm column, 50% EtOAc/hexanes) to yield **3a** as a yellow solid (0.148 g, 0.57 mmol, 86%). TLC (SiO_2, 50% EtOAc/hexanes, $R_f = 0.32$); mp 114–115 °C (Et_2O / hexanes). IR (CH_2Cl_2, KCl, cm^{-1}): 1763 (m), 1651 (m), 1628 (s), 1549 (m). ^1H NMR ($CDCl_3$, 300 MHz): δ 9.03 (d, J = 7.2 Hz, 1 H), 7.29–7.18 (m, 2 H), 6.88 (t, J = 6.5 Hz, 1 H), 2.81 (q, J = 7.6 Hz, 2 H), 2.62 (br s, 2 H), 2.44 (s, 3 H), 1.22 (t, J = 7.6 Hz, 3 H), 1.19 (t, J = 7.6 Hz, 3 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 169.7, 156.6, 145.2, 132.4, 128.1, 126.8, 125.8, 122.3, 118.8, 113.9, 21.3, 21.0, 20.4, 13.8, 13.5. HRMS (EI) calcd for $C_{15}H_{17}NO_3$: 259.1208. Found: 259.1208. Anal. Calcd for $C_{15}H_{17}NO_3$: C, 69.48; H, 6.61; N, 5.40; O, 18.51. Found: C, 69.27; H, 6.58; N, 5.35.

Repetition of this procedure, without purification of the intermediate **2a** before thermolysis, and subsequent purification by flash silica chromatography yielded 0.230 g (41%) of **3a** and 0.036 mg (6%) of **2a′**.

1-Acetoxy-2,3-di-*n*-butylquinolizin-4-one, 3b. 2-Lithiopyridine was generated from 2-bromopyridine (0.383 mL, 4.02 mmol, 1.10 equiv, Aldrich) in dry THF (10 mL) under argon at −78 °C for 1.5 h using *n*-BuLi in hexanes (3.09 mL, 1.30 M, 4.02 mmol, 1.10 equiv). This solution was cannulated into 3,4-di-*n*-butylcyclobutene-1,2-dione (0.709 g, 3.65 mmol, 1.00 equiv) in dry THF (20 mL) at −78 °C and after 45 min acetic anhydride (0.689 mL, 7.30 mmol, 2.00 equiv) was added. The mixture was stirred for 10 min at −78 °C and 10 min at room temperature, then subjected to workup as for **2a**. The crude oil was dissolved in dry dioxane (5 mL), sparged with argon and heated at 90 °C for 7.5 h. The solvent was removed under vacuum and the crude material was purified by flash chromatography (SiO_2, 2 × 15 cm column, gradient 30% EtOAc/hexanes to EtOAc) to yield **3b** as a green solid (0.574 g, 1.82 mmol, 50%). TLC (SiO_2, 30% EtOAc/hexanes, $R_f = 0.45$); mp 90–92 °C (Et_2O / hexanes). IR (CH_2Cl_2, KCl, cm^{-1}): 1763 (m), 1652 (m), 1627 (s), 1550 (m). ^1H NMR ($CDCl_3$, 360 MHz): δ 9.13 (d, J = 7.6 Hz, 1 H), 7.26–7.18 (m, 2 H), 6.87 (d of app t, J = 1.5, 6.1 Hz, 1 H), 2.78 (m, 2 H), 2.56 (br s, 2 H), 2.15 (s, 3 H), 1.63–1.40 (m, 8 H), 0.98 (t, J = 7.2 Hz, 3 H), 0.96 (t, J = 7.2 Hz, 3 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 169.5, 156.6, 144.2, 132.2, 127.9, 126.6, 125.9, 121.2, 118.8, 113.8, 31.4, 31.1, 27.8, 27.7, 23.0, 22.9, 20.3, 13.8, 13.6. Anal. Calcd for $C_{19}H_{25}O_3N$: C, 72.35; H, 7.99; O, 15.22; N, 4.44. Found: C, 72.46; H, 7.96; N, 4.38.

Two regioisomeric products were isolated during chromatography. 2-Acetoxy-3,4-di-*n*-butyl-4-(2-pyridyl)-2-cyclobutenone, **2b′**, the cyclobutenone intermediate formed by 1,4-addition of 2-lithiopyridine to the dione, was isolated as a brown oil (78 mg, 0.25 mmol, 7%). TLC (SiO_2, 30% EtOAc/hexanes, $R_f = 0.66$). IR (CH_2Cl_2, KCl, cm^{-1}): 1778 (s), 1648 (m). ^1H NMR ($CDCl_3$, 300 MHz): δ 8.56 (d, J = 5.2 Hz, 1 H), 7.63 (ddd, J = 7.7, 7.2, 1.4 Hz, 1 H), 7.42 (d, J = 7.7 Hz, 1 H), 7.16 (dd, J = 7.2, 5.2 Hz, 1 H), 2.73–2.50 (m, 2 H), 2.21 (s, 3 H), 2.28–2.15 (m, 1 H), 2.11–1.98 (m, 1 H), 1.66–1.51 (m, 4 H), 1.33–1.27 (m, 4 H), 0.89 (t, J = 7.2 Hz, 3 H), 0.88 (t, J = 7.2 Hz, 3 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 170.9, 166.5, 159.2, 148.8, 148.6, 140.7, 137.1, 122.2, 121.6, 69.4, 24.8 (2C), 21.4 (2C), 20.2, 10.5 (2C), 10.0 (2C).

Additionally, 3-acetoxy-1,2-di-*n*-butylquinolizin-4-one, **3b′**, the quinolizinone regioisomer formed by thermal rearrangement of the 1,4-addition product, was isolated as a green solid (15 mg, 0.05 mmol, 1%). TLC (SiO_2, 30% EtOAc/hexanes, R_f = 0.08). ^1H NMR (dioxane-d_8, 300 MHz): δ 8.96 (d, J = 7.3 Hz, 1 H), 7.61 (d, J = 9.3 Hz, 1 H), 7.20 (d of app t, J = 1.1, 6.7 Hz, 1 H), 6.86 (app t, J = 6.7 Hz, 1 H), 2.77–2.72 (m, 2 H), 2.62–2.56 (m, 2 H), 2.25 (s, 3 H), 1.53–1.37 (m, 8 H), 0.94 (t, J = 6.9 Hz, 3 H), 0.93 (t, J = 6.9 Hz, 3 H).

To further confirm the identification of the regioisomeric products a sample of 2-acetoxy-3,4-di-*n*-butyl-4-(2-pyridyl)-2-cyclobutenone, **2b′**, was subjected to thermolysis in dioxane in a sealed NMR tube (140 °C, 7 h) to give 3-acetoxy-1,2-di-*n*-butylquinolizin-4-one, **3b′**, as the only product detectable by ^1H NMR.

1-Acetoxy-2-isopropoxy-3-methylquinolizin-4-one, 3c. Following the procedure for **3b**, 2-bromopyridine (0.204 mL, 2.14 mmol, 1.10 equiv, Aldrich) in Et_2O (5 mL) was treated dropwise with *n*-BuLi in pentane (1.53 mL, 1.40 M, 2.14 mmol, 1.10 equiv) at −78 °C. After 1.2 h, the solution was cannulated into 3-isopropoxy-4-methylcyclobutene-1,2-dione (0.30 g, 1.95 mmol, 1.00 equiv) in THF (30 mL) at −78 °C. After 25 min, acetic anhydride (0.275 mL, 2.92 mmol, 1.50 equiv) was added, and after 30 min workup gave a black oil that was dissolved in dry dioxane (8 mL), sparged with argon and heated at 90 °C for 3 h. Removal of solvent and flash chromatography (SiO_2, 2 × 15 cm column, 70% EtOAc/hexanes) gave **3c** as a dark green solid (0.267 g, 0.97 mmol, 50%). TLC (SiO_2, 70% EtOAc/hexanes, $R_f = 0.50$); mp 93–94 °C (Et_2O). IR (CH_2Cl_2, KCl, cm^{-1}): 1778 (m), 1653 (s), 1627 (s). ^1H NMR ($CDCl_3$, 300 MHz): δ 9.00 (d, J = 7.5 Hz, 1 H), 7.34 (d, J = 9.0 Hz, 1 H), 7.22 (dd, J = 7.0, 9.0 Hz, 1 H), 6.86 (ddd, J = 1.0, 7.0, 7.5 Hz, 1 H), 4.49 (sept, J = 6.3 Hz, 1 H), 2.41 (s, 3 H), 2.28 (s, 3 H), 1.32 (d, J = 6.3 Hz, 6 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 168.7, 158.4, 156.2, 133.1, 128.4, 126.7, 122.1, 118.4, 113.5, 111.5, 77.4, 22.6 (2C), 20.4, 11.5. Anal. Calcd for $C_{15}H_{17}O_4N$: C, 65.44; H, 6.22; O, 23.25; N, 5.09. Found: C, 65.39; H, 6.19.

A trace amount of a second regioisomer was isolated during chromatography (<1% yield). Though isolated in an amount too small to allow rigorous identification, this compound might be the quinolizinone product formed by 1,4-addition of 2-lithiopyridine to the cyclobutenedione followed by thermal rearrangement. TLC (SiO_2, 70% EtOAc/hexanes, $R_f = 0.20$). IR (CH_2Cl_2, KCl, cm^{-1}): 1765 (m), 1657 (s), 1633 (s), 1566 (m); ^1H NMR ($CDCl_3$, 300 MHz) δ 9.02 (d, J = 7.2 Hz, 1H), 7.79 (d, J = 9.3 Hz, 1H), 7.21–7.27 (m, 1H), 6.93 (d of appar t, J = 6.9 and 1.2 Hz, 1H), 4.14 (hept, J = 6.2 Hz, 1H), 2.42 (s, 3H), 2.30 (s, 3H), 1.33 (d, J = 6.2 Hz, 6H).

1-Acetoxy-2-isopropoxy-3-phenylquinolizin-4-one, 3d. Following the procedure for **3b**, 2-bromopyridine (0.146 mL, 1.53 mmol, 1.10 equiv, Aldrich) in Et_2O (5 mL) was treated dropwise with *n*-BuLi in pentane (1.41 mL, 1.08 M, 1.52 mmol, 1.09 equiv) at −78 °C. After 1.5 h, the solution was cannulated into 3-isopropoxy-4-phenylcyclobutene-1,2-dione (0.30 g, 1.39 mmol, 1.00 equiv) in THF (30 mL) at −78 °C. After 20 min, acetic anhydride (0.196 mL, 2.08 mmol, 1.50 equiv) was added, and after 20 min workup gave a brown oil that was dissolved in dry dioxane (5 mL), sparged with argon and heated at 90 °C for 5 h. Removal of solvent and flash chromatography (SiO_2, 2 × 15 cm column, 70% EtOAc/hexanes) gave **3d** as a

yellow solid (0.279 g, 0.83 mmol, 60%). TLC (SiO_2, 70% EtOAc/hexanes, R_f = 0.50); mp 116–118 °C (Et_2O/hexanes). IR (CH_2Cl_2, KCl, cm^{-1}): 1773 (m), 1653 (s), 1626 (s), 1548 (m). ^1H NMR ($CDCl_3$, 360 MHz): δ 9.08 (d, J = 7.6 Hz, 1 H), 7.58 (d, J = 7.6 Hz, 2 H), 7.42 (app t, J = 7.7 Hz, 3 H), 7.31 (app t, J = 7.6 Hz, 2 H), 6.90 (d of app t, J = 1.1, 6.8 Hz, 1 H), 3.96 (sept, J = 6.1 Hz, 1 H), 2.42 (s, 3 H), 1.00 (d, J = 6.1 Hz, 6 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 169.0, 157.6, 156.2, 134.8, 134.0, 130.9 (2C), 129.9, 128.0 (2C), 127.6, 127.3, 122.5, 118.7, 113.8, 113.4, 76.1, 22.2 (2C), 20.4. Anal. Calcd for $C_{20}H_{19}O_4N$: C, 71.20; H, 5.68; O, 18.97; N, 4.15. Found: C, 71.04; H, 5.75; N, 4.13.

1-Hydroxy-2-isopropoxy-3-phenylquinolizin-4-one, 3e. Following the procedure for **3b**, 2-bromopyridine (0.147 mL, 1.54 mmol, 1.11 equiv, Aldrich) in THF (5 mL) was treated dropwise with t-BuLi in pentane (1.62 mL, 1.90 M, 3.08 mmol, 2.22 equiv) at −78 °C. After 1.5 h, the solution was cannulated into 3-isopropoxy-4-phenylcyclobutene-1,2-dione (0.30 g, 1.39 mmol, 1.00 equiv) in THF (5 mL) at −78 °C. After 20 min, saturated aq $NaHCO_3$ was added and workup as for **3b**, above, gave a brown oil that was dissolved in dry dioxane (5 mL), sparged with argon and heated at 90 °C for 2 h. Removal of solvent gave a crude brown solid that was purified by recrystallization from EtOAc/hexanes to yield **3e** as a gold solid (0.197 g, 0.67 mmol, 48%). TLC (SiO_2, 30% EtOAc/hexanes, R_f = 0.08); mp 160 °C w/decomp (EtOAc / hexanes). IR (CH_2Cl_2, KCl, cm^{-1}): 1650 (s), 1624 (s), 1560 (m). ^1H NMR (CD_2Cl_2, 360 MHz): δ 8.85 (br s, 1 H), 7.90–7.25 (m, 7 H), 6.85 (br s, 1 H), 5.58 (br s, 1 H), 3.87 (br s, 1 H), 1.05 (d, J = 6.1 Hz, 6 H). Anal. Calcd for $C_{18}H_{17}O_3N$: C, 73.20; H, 5.80; O, 16.25; N, 4.74. Found: C, 73.00; H, 5.91; N, 4.71.

The structure identification was confirmed by acetylation. 1-Hydroxy-2-isopropoxy-3-phenylquinolizin-4-one, **3e** (60 mg, 0.20 mmol, 1.0 equiv) was dissolved in dry Et_2O (10 mL) with Et_3N (0.845 mL, 0.61 mmol, 3.0 equiv) and acetic anhydride (0.383 mL, 0.41 mmol, 2.0 equiv) and stirred at room temperature for 4 h. The reaction mixture was quenched with water and extracted with Et_2O, then dried ($MgSO_4$) and concentrated to a brown oil. The crude material was purified by flash chromatography (SiO_2, 2 × 15 cm column, 50% EtOAc/hexanes) to give 65 mg (94%) of **3d** as a yellow solid, fully characterized above.

1-Acetoxy-2-isopropoxy-9-methoxy-3-phenylquinolizin-4-one, 3f. 2-Bromo-3-methoxypyridine[39] (0.483 g, 2.57 mmol, 1.11 equiv) in THF (8 mL) was treated dropwise with t-BuLi in pentane (2.71 mL, 1.90 M, 5.15 mmol, 2.23 equiv) at −78 °C. After 1 h, this solution was added via cannula to 3-isopropoxy-4-phenylcyclobutene-1,2-dione (0.50 g, 2.31 mmol, 1.00 equiv) in THF (12 mL) at −78 °C. After 30 min, acetic anhydride (0.485 mL, 5.14 mmol, 2.23 equiv) was added, and after 30 min workup as for **3b**, above, gave a brown oil that was dissolved in dry dioxane (8 mL), sparged with argon and heated at 100 °C for 20 min. Removal of solvent and flash chromatography (SiO_2, 2 × 15 cm column, 80% EtOAc/hexanes) gave **3f** as a yellow solid (0.250 g, 0.68 mmol, 29%). TLC (SiO_2, 80% EtOAc/hexanes, R_f = 0.49); mp 172–174 °C (EtOAc/hexanes). IR (CH_2Cl_2, KCl, cm^{-1}): 1765 (m), 1649 (m), 1633 (s), 1572 (w). ^1H NMR ($CDCl_3$, 360 MHz): δ 8.80 (d, J = 7.5 Hz, 1 H), 7.58 (d, J = 7.9 Hz, 2 H), 7.40 (app t, J = 7.4 Hz, 2 H), 7.30 (app t, J = 7.4 Hz, 1 H), 6.76 (app t, J = 7.4 Hz, 1 H), 6.56 (d, J = 7.6 Hz, 1 H), 3.96 (sept, J = 6.1 Hz, 1 H), 3.88 (s, 3 H), 2.34 (s, 3 H), 0.99 (br s, 6 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 169.4, 157.5, 156.5, 152.4, 133.8, 130.7 (2C), 129.5, 127.8 (2C), 127.3, 122.9, 120.5, 114.5, 112.6, 106.2, 76.2, 56.6, 22.2 (2C), 20.3. HRMS (EI) calcd for $C_{21}H_{21}O_5N$: 367.1419. Found: 367.1419. Anal. Calcd for $C_{21}H_{21}O_5N$: C, 68.65; H, 5.76; O, 21.77; N, 3.81. Found: C, 68.49; H, 5.78.

8-Acetoxy-6,7-diethylthiazolo[3,2-*a*]pyridin-5-one, 3g. 2-Bromothiazole (0.215 mL, 2.39 mmol, 1.10 equiv, Aldrich) in THF (5 mL) at −78 °C was treated dropwise with n-BuLi in hexane (1.59 mL, 1.50 M, 2.39 mmol, 1.10 equiv) at −78 °C. After 1.5 h, the black heterogeneous reaction mixture was added via cannula to 3,4-diethylcyclobutene-1,2-dione (0.30 g, 2.17 mmol, 1.00 equiv) in THF (20 mL) at −78 °C. After 40 min, acetic anhydride (0.410 mL, 4.34 mmol, 2.0 equiv) was added, and after 1 h workup as for **3b**, above, gave a brown oil that was dissolved in dry dioxane (5 mL), sparged with argon and heated at 90 °C for 4 h. Removal of solvent and flash chromatography (SiO_2, 2 × 15 cm column, 50% EtOAc/hexanes) gave **3g** as a brown solid (0.254 g, 0.96 mmol, 44%). TLC (SiO_2, 50% EtOAc/hexanes, R_f = 0.26); mp 63–66 °C (EtOAc/hexanes). IR (CH_2Cl_2, KCl, cm^{-1}): 1771 (m), 1645 (m), 1582 (m). ^1H NMR ($CDCl_3$, 360 MHz): δ 8.08 (d, J = 4.5 Hz, 1 H), 6.85 (d, J = 4.5 Hz, 1 H), 2.71 (q, J = 7.5 Hz, 2 H), 2.55 (q, J = 7.5 Hz, 2 H), 2.37 (s, 3 H), 1.18 (t, J = 7.5 Hz, 3 H), 1.16 (t, J = 7.5 Hz, 3 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 168.1, 158.1, 145.3, 136.4, 126.7, 124.8, 122.7, 110.5, 21.0, 20.3 (2C), 13.7, 13.6. HRMS (EI) calcd for $C_{13}H_{15}NSO_3$: 265.0772. Found: 265.0772.

4-Acetoxy-2,3-dimethyl-1-oxopyrido[2,1-*b*]benzothiazole, 3h. Benzothiazole (0.331 mL, 3.03 mmol, 1.11 equiv, Aldrich) in THF (7 mL) at −78 °C was treated dropwise with n-BuLi in pentane (2.01 mL, 1.51 M, 3.04 mmol, 1.12 equiv) at −78 °C. After 1.2 h, this solution was added via cannula to 3,4-dimethylcyclobutene-1,2-dione (0.30 g, 2.72 mmol, 1.00 equiv) in THF (5 mL) at −78 °C. After 25 min, acetic anhydride (0.571 mL, 6.05 mmol, 2.22 equiv) was added and after 30 min workup as for **3b**, above, gave a yellow solid that was dissolved in dry dioxane (8 mL), sparged with argon and heated to 95 °C for 3 h. Removal of solvent gave a crude brown solid that was purified by recrystallization from EtOAc/hexanes to yield **3h** as a tan solid (0.439 g, 1.53 mmol, 56%). TLC (SiO_2, 50% EtOAc/hexanes, R_f = 0.47); mp 185–187 °C (EtOAc/hexanes). IR (CH_2Cl_2, KCl, cm^{-1}): 1772 (m), 1653 (s), 1597 (s). ^1H NMR ($CDCl_3$, 300 MHz): δ 9.25 (dd, J = 1.1, 8.5 Hz, 1 H), 7.55 (dd, J = 1.1, 7.9 Hz, 1 H), 7.43 (d of app t, J = 1.1, 7.6 Hz, 1 H), 7.36 (d of app t, J = 1.1, 7.6 Hz, 1 H), 2.36 (s, 3 H), 2.22 (s, 3 H), 2.10 (s, 3 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 168.4, 161.2, 140.0, 139.2, 127.3, 126.4 (2C), 125.8, 121.4 (2C), 120.6, 120.5, 20.3, 13.9, 12.9. HRMS (EI) calcd for $C_{15}H_{13}O_3NS$: 287.0615. Found: 287.0616.

4-Acetoxy-2,3-diethyl-1-oxopyrido[2,1-*b*]benzothiazole, 3i. Benzothiazole (0.261 mL, 2.39 mmol, 1.10 equiv, Aldrich) in THF (7 mL) at −78 °C was treated with n-BuLi in pentane (1.71 mL, 1.40 M, 2.39 mmol, 1.10 equiv) at −78 °C. After 1.2 h, this solution was added via cannula to 3,4-diethylcyclobutene-1,2-dione (0.30 g, 2.17 mmol, 1.00 equiv) in THF (10 mL) at −78 °C. After 25 min, acetic anhydride (0.307 mL, 3.25 mmol, 1.50 equiv) was added, and after 20 min workup as for **3b**, above, gave an orange oil that was dissolved in dry dioxane (5 mL), sparged with argon and heated at 90 °C for 3 h. Removal of solvent gave a crude brown solid that was purified by recrystallization from Et_2O/hexanes to yield **3i** as a brown solid (0.368 g, 1.17 mmol, 54%). TLC (SiO_2, 30% EtOAc/hexanes, R_f = 0.55); mp 163–165 °C (Et_2O/hexanes). IR (CH_2Cl_2, KCl, cm^{-1}): 1771 (s), 1653 (s), 1595 (s). ^1H NMR ($CDCl_3$, 360 MHz): δ 9.27 (d, J = 8.3 Hz, 1 H), 7.56 (d, J = 7.6 Hz, 1 H), 7.44 (dd, J = 7.0, 8.3 Hz, 1 H), 7.38 (dd, J = 7.0, 7.6 Hz, 1 H), 2.73 (q, J = 7.6 Hz, 2 H), 2.53 (q, J = 7.6 Hz, 2 H), 2.39 (s, 3 H), 1.20 (t, J = 7.6 Hz, 3 H), 1.17 (t, J = 7.6 Hz, 3 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 168.3, 161.1, 145.0, 139.0, 134.8, 126.8, 126.2, 125.9, 125.7, 121.3, 121.2, 120.4, 21.2, 20.4, 20.3, 13.7, 13.6. Anal. Calcd for $C_{17}H_{17}O_3NS$: C, 64.74; H, 5.43; O, 15.22; N, 4.44; S, 10.17. Found: C, 64.49; H, 5.48; N, 4.40.

8-Acetoxy-6,7-diethyl-1-methylimidazo[1,2-*a*]pyridin-5-one, 3j. 1-Methylimidazole (0.32 mL, 4.01 mmol, 1.11 equiv, Aldrich) in THF (10 mL) was treated dropwise with n-BuLi in pentane (2.96 mL, 1.36 M, 4.03 mmol, 1.11 equiv) at −78 °C. After 1.7 h, this solution was added via cannula to 3,4-diethylcyclobutene-1,2-dione (0.50 g, 3.62 mmol, 1.00 equiv) in THF (20 mL) at −78 °C. After 1 h, acetic anhydride (0.759 mL, 8.04 mmol, 2.22 equiv) was added, and after 30 min workup as for **3b**, above, gave an orange oil that was dissolved in dry 1,2-dichloroethane (5 mL), sparged with argon and refluxed at 85 °C for 4 h. Removal of solvent and flash chromatography (SiO_2, 3 × 15 cm column, 15% MeOH/EtOAc) gave **3j** as a brown solid (0.616 g, 2.35 mmol, 65%). TLC (SiO_2, 15% MeOH/EtOAc, R_f = 0.40); mp 111–114 °C (Et_2O/hexanes). IR (CH_2Cl_2, KCl, cm^{-1}): 1769 (m), 1656 (s), 1583 (s), 1554 (s), 1521 (s). ^1H NMR ($CDCl_3$, 360 MHz): δ 7.65 (d, J = 2.2 Hz, 1 H), 6.74 (d, J = 2.2 Hz, 1 H), 3.69 (s, 3 H), 2.66 (q, J = 7.2

Hz, 2 H), 2.60 (br s, 2 H), 2.36 (s, 3 H), 1.14 (t, J = 7.2 Hz, 3 H), 1.11 (t, J = 7.6 Hz, 3 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 171.1, 154.5, 144.4, 133.3, 121.6, 114.3, 112.1, 108.4, 34.4, 20.9, 20.5, 19.9, 14.2 (2C). Anal. Calcd for $C_{14}H_{18}O_3N_2$: C, 64.11; H, 6.92; O, 18.30; N, 10.68. Found: C, 63.85; H, 6.81; N, 10.47.

8-Acetoxy-7-(*N*,*N*-dibenzylamino)-1,6-dimethylimidazo-[1,2-*a*]pyridin-5-one, 3k. 1-Methylimidazole (0.093 mL, 1.17 mmol, 1.89 equiv, Aldrich) in THF (5 mL) was treated dropwise with *n*-BuLi in pentane (0.755 mL, 1.55 M, 1.17 mmol, 1.89 equiv) at −78 °C. After 1.25 h, this solution was added to 3-(*N*,*N*-dibenzylamino)-4-methylcyclobutene-1,2-dione (0.18 g, 0.62 mmol, 1.00 equiv) in THF (20 mL) at −78 °C. After 45 min, acetic anhydride (0.170 mL, 1.80 mmol, 2.90 equiv) and pyridine (0.160 mL, 1.98 mmol, 3.19 equiv) were added, and after 1 h at −78 °C and 10 min at room temperature workup as for **3b**, above, gave a brown oil that was dissolved in dry dioxane (5 mL), sparged with argon and heated at 90 °C for 4 h. Removal of solvent and flash chromatography (SiO_2, 2 × 15 cm column, gradient EtOAc to 10% MeOH/EtOAc) gave **3k** as a tan solid (0.164 g, 0.39 mmol, 63%). TLC (SiO_2, 10% MeOH/EtOAc, R_f = 0.24); mp 151−153 °C (Et_2O). IR (CH_2Cl_2, KCl, cm^{-1}): 1770 (m), 1652 (s), 1582 (s), 1549 (s). ^{1}H NMR ($CDCl_3$, 360 MHz): δ 7.68 (d, J = 2.2 Hz, 1 H), 7.34−7.20 (m, 10 H), 6.74 (d, J = 2.2 Hz, 1 H), 4.22 (B of AB quartet, J = 14.0 Hz, 2 H), 4.04 (A of AB quartet, J = 14.0 Hz, 2 H), 3.65 (s, 3 H), 2.11 (s, 3 H), 2.00 (s, 3 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 170.7, 155.4, 151.6, 138.3 (2C), 136.1 (4C), 128.9 (4C), 128.2 (2C), 127.2, 121.8, 113.1, 108.1, 103.8, 55.4 (2C), 34.3, 20.4, 13.3. Anal. Calcd for $C_{25}H_{25}O_3N_3$: C, 72.27; H, 6.06; O, 11.55; N, 10.11. Found: C, 72.13; H, 6.12; N, 10.09.

Also isolated by chromatography was 39 mg (0.11 mmol, 18%) of a tan solid with a higher R_f which was identified as 2-methyl-3-(dibenzylamino)-4-(1-methylimidazol-2-yl)-4-hydroxybutyric acid γ-lactone, **6**. This compound resulted from thermal rearrangement of the unprotected 4-hydroxy-4-(1-methylimidazol-2-yl)-3-(dibenzylamino)-2-methyl cyclobutenedione, **2k′**. This was confirmed by isolating a sample of **2k′** and subjecting it to thermolysis at 90 °C in dioxane for 4 h, producing exclusively the 5-membered ring lactone product, **6**. TLC (SiO_2, 10% MeOH/EtOAc, R_f = 0.67); mp 149−150 °C (Et_2O). IR (CH_2Cl_2, KCl, cm^{-1}): 1746 (w), 1593 (s), 1570 (s). ^{1}H NMR ($CDCl_3$, 360 MHz): δ 7.39−7.23 (m, 10 H), 6.98 (d, J = 1.1 Hz, 1 H), 6.85 (d, J = 1.1 Hz, 1 H), 5.45 (br s, 1 H), 4.71−4.51 (m, 4 H), 3.89 (s, 3 H), 1.71 (s, 3 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 172.0, 144.6, 135.7 (2C), 135.0, 129.0 (2C), 128.9 (2C), 128.5 (4C), 127.9, 127.7, 126.9 (2C), 123.0, 88.7, 54.6, 51.3, 34.2, 7.5. Anal. Calcd for $C_{23}H_{23}O_2N_3$: C, 73.97; H, 6.21; O, 8.57; N, 11.25. Found: C, 73.73; H, 6.22.

8-Acetoxy-7-isopropoxy-6-phenyl-1-(methoxymethyl)-imidazo[1,2-*a*]pyridin-5-one, 3l. 1-(Methoxymethyl)imidazole[40] (0.20 g, 2.08 mmol, 1.10 equiv) in THF (5 mL) was treated dropwise with *n*-BuLi in pentane (1.83 mL, 1.14 M, 2.09 mmol, 1.11 equiv) at −78 °C. After 1.2 h, this solution was added via cannula to 3-isopropoxy-4-phenylcyclobutene-1,2-dione (0.409 g, 1.89 mmol, 1.00 equiv) in THF (15 mL) at −78 °C. After 45 min, acetic anhydride (0.268 mL, 2.84 mmol, 1.50 equiv) was added and after 45 min workup as for **3b**, above, gave a yellow oil that was dissolved in dry dioxane (5 mL), sparged with argon and heated at 90 °C for 4 h. Removal of solvent gave a crude brown solid that was recrystallized from EtOAc/hexanes to give **3l** as an off white solid (0.265 g, 0.72 mmol, 38%): mp 186 °C w/decomp (EtOAc/hexanes). IR (CH_2Cl_2, KCl, cm^{-1}): 1778 (m), 1661 (m), 1591 (m). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.76 (d, J = 2.3 Hz, 1 H), 7.53 (d, J = 7.5 Hz, 2 H), 7.34 (app t, J = 7.5 Hz, 2 H), 7.22 (app t, J = 7.5 Hz, 1 H), 6.96 (d, J = 2.3 Hz, 1 H), 5.34 (br s, 2 H), 3.85 (sept, J = 6.1 Hz, 1 H), 3.30 (s, 3 H), 2.31 (s, 3 H), 0.94 (d, J = 6.1 Hz, 6 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 169.0, 157.3, 154.6, 134.4, 134.1, 131.2 (2C), 127.7 (2C), 126.4, 121.1, 112.2, 109.4, 107.2, 78.8, 76.0, 56.1, 22.2 (2C), 20.6. Anal. Calcd for $C_{20}H_{22}O_5N_2$: C, 64.85; H, 5.99; O, 21.60; N, 7.56. Found: C, 64.74; H, 6.02; N, 7.58.

Stannylazaheteroaromatic Cross-Couplings with 4-Chlorocyclobutenones. 4-Chloro-2-methyl-3-phenyl-2-cyclobutenone. A 250-mL, three-necked, round-bottomed flask was equipped with a magnetic stirring bar, two glass stoppers, and a 125-mL pressure-equalizing addition funnel fitted with a N_2 inlet adapter. The flask was charged with Zn−Cu couple (5.11 g, 78.17 mmol, 3.00 equiv), 40 mL of Et_2O and 1-phenyl-1-propyne (3.029 g, 26.08 mmol, 1.00 equiv). The dropping funnel was charged with a solution of dichloroacetyl chloride (7.68 g, 52.10 mmol, 2.00 equiv) in 15 mL of distilled DME, and this solution was then added dropwise to the reaction mixture over 1 h. After 48 h, the resulting brown mixture was filtered through a sintered-glass Buchner funnel and the black solid was washed with 100 mL of CH_2Cl_2. The filtrate was washed successively with 50 mL each of ice-cold 0.5 N HCl, ice-cold 5% NaOH and saturated NaCl solution, dried over $MgSO_4$ (20 g) and then concentrated to a heterogeneous mixture which was purified by flash chromatography (SiO_2, 5 × 20 cm column, 9% EtOAc/hexanes) to afford 4-chloro-2-methyl-3-phenylcyclobutenone as a white solid (2.074 g, 10.77 mmol, 41%). TLC (SiO_2, 90% EtOAc/hexanes, R_f = 0.15); mp 80−81 °C (CH_2Cl_2/hexanes). IR (CH_2Cl_2, NaCl, cm^{-1}): 1767, 1616, 1569. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.77−7.72 (m, 2 H), 7.56−7.54 (m, 3 H), 5.62 (d, J = 1.0 Hz, 1 H), 2.12 (d, J = 1.0 Hz, 3 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 184.4, 165.8, 145.3, 132.0, 129.6, 129.4, 129.2, 67.2, 9.7. Anal. Calcd for $C_{11}H_9OCl$: C, 68.58; H, 4.71; O, 8.31; Cl, 18.40. Found: C, 68.24; H, 4.63.

2-(Tri-*n*-butylstannyl)benzothiazole. An ether solution (30 mL) of *n*-BuLi in hexanes (4.84 mL, 2.40 M, 11.62 mmol, 1.00 equiv) under N_2 was cooled to −78 °C and treated dropwise with an ether solution (5 mL) of benzothiazole (1.57 g, 11.61 mmol, 1.00 equiv). After 8 h the reaction mixture was treated slowly with *n*-Bu_3SnCl (3.78 g, 11.61 mmol, 1.00 equiv). After 90 min, the solution was warmed to room temperature and the solvent was evaporated under vacuum. Methylcyclohexane (80 mL) was added to this mixture and the precipitate was filtered immediately. The eluent was concentrated to a orange oil and distilled (standard distillation, bp 159−162 °C, 0.07 mmHg) to give 2-(tri-*n*-butylstannyl)benzothiazole as a yellow oil (4.04 g, 9.52 mmol, 82%). IR (CH_2Cl_2, NaCl, cm^{-1}): 1466, 1377. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.16 (d, J = 8.1 Hz, 1 H), 7.95 (d, J = 7.5 Hz, 1 H), 7.46 (dd, J = 7.8, 6.6 Hz, 1 H), 7.36 (dd, J = 7.5, 6.9 Hz, 1 H), 1.64−1.56 (m, 6 H), 1.38−1.24 (m, 12 H), 0.90−0.85 (t, J = 7.2 Hz, 9 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 177.4, 156.2, 136.4, 125.3, 124.4, 122.9, 121.3, 28.9 (3C), 27.3 (3C), 13.6 (3C), 11.3 (3C). Anal. Calcd for $C_{19}H_{31}NSSn$: C, 53.80; H, 7.37; N, 3.30; S, 7.56; Sn, 27.98. Found: C, 53.74; H, 7.41.

2-Isopropoxy-3-methylquinolizin-4-one, 3m. A N_2 sparged toluene (8 mL) solution of 4-chloro-3-isopropoxy-2-methyl-2-cyclobutenone,[12] (175 mg, 1.00 mmol, 1.00 equiv) and 2-(tri-*n*-butylstannyl)pyridine (442 mg, 1.20 mmol, 1.20 equiv) with $Pd_2(dba)_3$ (22.9 mg, 0.03 mmol, 2.5 mol%) and tris(2-furyl)phosphine (23.2 mg, 0.10 mmol, 0.10 equiv) was heated under N_2 at 60 °C overnight followed by refluxing for 6 h. The mixture was cooled to room temperature and 5% aq KF was added to remove *n*-Bu_3SnCl. The solution was extracted with 2:1 Et_2O/CH_2Cl_2 (35 mL × 3). The combined organic phases were washed with water (30 mL × 2) and brine (30 mL), dried over 10 g of $MgSO_4$ and concentrated. The resulting yellow-brown oil was purified by flash chromatography (SiO_2, 2 × 20 cm column) eluting with CH_2Cl_2 first to remove dba, then with 50% EtOAc/hexanes to give **3m** as a yellow-green oil (134 mg, 0.62 mmol, 62%). TLC (SiO_2, 50% EtOAc/hexanes, R_f = 0.19). IR (CH_2Cl_2, NaCl, cm^{-1}): 1651, 1627, 1561. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.96 (d, J = 7.2 Hz, 1 H), 7.24 (d, J = 9.0 Hz, 1 H), 7.14 (dd, J = 8.7, 6.6 Hz, 1 H), 6.76 (app t, J = 6.9 Hz, 1 H), 6.25 (s, 1 H), 4.67−4.56 (sept, J = 6.0 Hz, 1 H), 2.15 (s, 3 H), 1.35 (d, J = 6.0 Hz, 6 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 162.3, 159.1, 140.3, 128.4, 127.0, 124.2, 113.0, 105.0, 90.3, 70.7, 22.2 (2C), 9.7. Anal. Calcd for $C_{13}H_{15}NO_2$: C, 71.87; H, 6.96; N, 6.45; O, 14.73. Found: C, 71.51; H, 7.21; N, 6.73. Also isolated was 28% of 2,2′-bipyridine, mp 71−73 °C (lit.[42,43] 69.5 °C) identified by comparison with literature spectroscopic data.

(42) *Handbook of Data on Organic Compounds*; 2nd ed.; Weast, R. C.; Grasselli, J. G., Eds.; CRC Press: 1989; Vol. III, pp 11339.

(43) Pouchert, C. J. *The Aldrich Library of NMR Spectra;* II ed.; Aldrich Chemical Company, Inc.: 1983; Vol. 2, pp 612.

3-Methyl-2-phenylquinolizin-4-one, 3n. Following the procedure for **3m**, a solution of 4-chloro-2-methyl-3-phenyl-2-cyclobutenone (116 mg, 0.60 mmol, 1.00 equiv) and 2-(tri-*n*-butylstannyl)pyridine (243 mg, 0.66 mmol, 1.10 equiv) in toluene (8 mL) with $Pd_2(dba)_3$ (13.7 mg, 0.01 mmol, 2.5 mol%) and tris(2-furyl)phosphine (13.9 mg, 0.06 mmol, 0.10 equiv) at 60 °C overnight and 10 h at reflux gave after workup a red oil that was purified by flash chromatography (SiO_2, 2 × 20 cm column) eluting with CH_2Cl_2 first to remove dba, then 50% EtOAc/hexanes to give **3n** as a yellow-green oil (59 mg, 0.25 mmol, 42%). TLC (SiO_2, 50% EtOAc/hexanes, R_f = 0.33). IR (CH_2Cl_2, NaCl, cm^{-1}): 1652, 1626, 1567. ^1H NMR ($CDCl_3$, 300 MHz): δ 9.06 (d, J = 7.5 Hz, 1 H), 7.46–7.33 (m, 6 H), 7.20 (dd, J = 8.7, 6.6 Hz, 1 H), 6.92 (d of app t, J = 6.9, 1.1 Hz, 1 H), 6.58 (s, 1 H), 2.25 (s, 3 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 158.7, 149.8, 140.1, 139.0, 128.5 (2C), 128.3 (2C), 127.9, 127.7, 126.7, 125.3, 116.5, 114.4, 104.6, 14.9. Anal. Calcd for $C_{16}H_{13}NO$: C, 81.68; H, 5.57; N, 5.95; O, 6.80. Found: C, 81.58; H, 5.61; N, 5.90. Also isolated was 17% of 2,2′-bipyridine.

2,3-Diethylquinolizin-4-one, 3o. Following the procedure for **3m**, a solution of 4-chloro-2,3-diethyl-2-cyclobutenone[9] (159 mg, 1.00 mmol, 1.00 equiv) and 2-(tri-*n*-butylstannyl)pyridine (442 mg, 1.20 mmol, 1.20 equiv) in toluene (8 mL) with $Pd_2(dba)_3$ (22.9 mg, 0.03 mmol, 2.5 mol%) and tris(2-furyl)-phosphine (23.2 mg, 0.10 mmol, 0.10 equiv) at 60 °C overnight then 8 h at reflux gave after workup a solid that was purified by flash chromatography (SiO_2, 2 × 20 cm column) eluting with CH_2Cl_2 first to remove dba, then 50% EtOAc/hexanes to give **3o** as a yellow solid (68 mg, 0.34 mmol, 34%). TLC (SiO_2, 50% EtOAc/hexanes, R_f = 0.40); mp 86–87 °C (Et_2O/hexane). IR (CH_2Cl_2, NaCl, cm^{-1}): 1650, 1624, 1563. ^1H NMR ($CDCl_3$, 300 MHz): δ 8.99 (d, J = 7.5 Hz, 1 H), 7.30 (d, J = 9.0 Hz, 1 H), 7.14 (dd, J = 8.7, 6.9 Hz, 1 H), 6.84 (d of app t, J = 1.2, 6.9 Hz, 1 H), 6.47 (s, 1 H), 2.82 (q, J = 7.5 Hz, 2 H), 2.73 (q, J = 7.5 Hz, 2 H), 1.27 (t, J = 7.5 Hz, 3 H), 1.19 (t, J = 7.5 Hz, 3 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 158.1, 151.4, 139.4, 127.3, 126.7, 124.8, 122.5, 113.8, 103.6, 26.3, 20.5, 14.7, 13.4. Anal. Calcd for $C_{13}H_{15}NO$: C, 77.58; H, 7.51; N, 6.96; O, 7.95. Found: C, 77.89; H, 7.57; N, 6.56. Also isolated was 22% of 2,2′-bipyridine.

3-*n*-Butyl-2-methylquinolizin-4-one, 3p. Following the procedure for **3m**, a solution of 2-butyl-4-chloro-3-methyl-2-cyclobutenone[9] (173 mg, 1.00 mmol, 1.00 equiv) and 2-(tri-*n*-butylstannyl)pyridine (442 mg, 1.20 mmol, 1.20 equiv) in toluene (8 mL) with $Pd_2(dba)_3$ (22.9 mg, 0.03 mmol, 2.5 mol%) and tris(2-furyl)phosphine (23.2 mg, 0.10 mmol, 0.10 equiv) at 60 °C overnight and 8 h at reflux gave after workup a brown oil that was purified by flash chromatography (SiO_2, 2 × 20 cm column) eluting with CH_2Cl_2 first to remove dba, then 50% EtOAc/hexanes to give **3p** as a yellow-green oil (67 mg, 0.31 mmol, 31%). TLC (SiO_2, 50% EtOAc/hexanes, R_f = 0.39). IR (CH_2Cl_2, NaCl, cm^{-1}): 1651, 1628, 1565. ^1H NMR ($CDCl_3$, 300 MHz): δ 9.00 (d, J = 7.2 Hz, 1 H), 7.29 (d, J = 8.4 Hz, 1 H), 7.16 (dd, J = 8.4, 6.9 Hz, 1 H), 6.86 (d of app t, J = 1.2, 6.9 Hz, 1 H), 6.47 (s, 1 H), 2.78 (t, J = 7.2 Hz, 2 H), 2.37 (s, 3 H), 1.56–1.40 (m, 4 H), 0.97 (t, J = 7.2 Hz, 3 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 157.9, 145.9, 138.9, 127.4, 126.7, 124.5, 121.8, 113.8, 105.3, 30.6, 27.5, 23.0, 20.0, 14.0. Anal. Calcd for $C_{14}H_{17}NO$: C, 78.10; H, 7.96; N, 6.51; O, 7.43. Found: C, 78.40; H, 8.02; N, 6.71. Also isolated was 41% of 2,2′-bipyridine.

2-Isopropoxy-3-phenylquinolizin-4-one, 3q. Following the procedure for **3m**, a solution of 4-chloro-3-isopropoxy-2-phenyl-2-cyclobutenone[9] (101 mg, 0.43 mmol, 1.00 equiv) and 2-(tri-*n*-butylstannyl)pyridine (189 mg, 0.51 mmol, 1.19 equiv) in toluene (5 mL) with of $Pd_2(dba)_3$ (9.8 mg, 0.01 mmol, 2.5 mol%) and tris(2-furyl)phosphine (9.9 mg, 0.04 mmol, 0.10 equiv) at 60 °C overnight and 3 h a reflux gave after workup an oil that was purified by flash chromatography (SiO_2, 2 × 20 cm column) eluting with a gradient from 25% to 50% EtOAc/hexanes to give 2,2′-bipyridine (21 mg, 53%, R_f = 0.35 in 25% EtOAc/hexanes), then 3-isopropoxy-2-phenyl-2-cyclobutenone as a white solid (35 mg, 0.17 mmol, 41%). TLC (SiO_2, 50% EtOAc/hexanes, R_f = 0.53); mp 66–67 °C (Et_2O/hexane). IR (CH_2Cl_2, NaCl, cm^{-1}): 1749, 1635, 1599. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.68 (d, J = 7.5 Hz, 2 H), 7.30 (app t, J = 7.5 Hz, 2 H), 7.18 (app t, J = 7.5 Hz, 1 H), 4.59 (sept, J = 6.3 Hz, 1 H), 3.42 (s, 2 H), 1.47 (d, J = 6.3 Hz, 6 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 181.6, 174.2, 129.5, 128.3 (2C), 126.9, 126.1 (2C), 120.3, 78.9, 47.6, 23.1 (2C). Anal. Calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98; O, 15.82. Found: C, 77.52; H, 7.05. After elution of a small amount of another reaction product (12 mg, 0.03 mmol, 14%; TLC: SiO_2, 50% EtOAc/hexanes, R_f = 0.32) that was identified as part of another project and will be described in detail elsewhere, **3q** was eluted as a yellow-green solid (12 mg, 0.04 mmol, 10%). TLC (SiO_2, 50% EtOAc/hexanes, R_f = 0.23); mp 118–119 °C (Et_2O/hexane). IR (CH_2Cl_2, NaCl, cm^{-1}): 1652, 1629. ^1H NMR ($CDCl_3$, 300 MHz): δ 9.09 (d, J = 7.5 Hz, 1 H), 7.53 (d, J = 7.2 Hz, 2 H), 7.39–7.22 (m, 5 H), 6.83 (d of app t, J = 1.2, 6.6 Hz, 1 H), 6.35 (s, 1 H), 4.66 (sept, J = 6.0 Hz, 1 H), 1.31 (d, J = 6.0 Hz, 6 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 161.9, 158.5, 141.9, 134.0, 131.1 (2C), 129.8, 127.9, 127.5 (2C), 126.5, 124.2, 113.2, 108.9, 90.4, 71.1, 29.7, 22.0. Anal. Calcd for $C_{18}H_{17}NO_2$: C, 77.40; H, 6.13; N, 5.01; O, 11.46. Found: C, 77.32; H, 5.96; N, 5.19.

3-Isopropoxy-2-methyl-1-oxopyrido[2,1-*b*]benzothiazole, 3r. Following the procedure for **3m**, a solution of 4-chloro-3-isopropoxy-2-methyl-2-cyclobutenone,[12] (87 mg, 0.50 mmol, 1.00 equiv) and 2-(tri-*n*-butylstannyl)benzothiazole (318 mg, 0.75 mmol, 1.50 equiv) in toluene (8 mL) with $Pd_2(dba)_3$ (11.4 mg, 0.01 mmol, 2.5 mol%) and tris(2-furyl)phosphine (11.6 mg, 0.05 mmol, 0.10 equiv) at 60 °C overnight and 6 h at reflux gave after workup a solid that was purified by flash chromatography (SiO_2, 2 × 20 cm column) eluting with CH_2Cl_2 first to remove dba, then 14% EtOAc/hexanes to give **3r** as a white solid (60 mg, 0.22 mmol, 44%). TLC (SiO_2, 14% EtOAc/hexanes, R_f = 0.23); mp 140–142 °C (EtOAc/hexane). IR (CH_2Cl_2, NaCl, cm^{-1}): 1644, 1592. ^1H NMR ($CDCl_3$, 300 MHz): δ 9.29 (d, J = 8.1 Hz, 1 H), 7.53 (d, J = 7.8 Hz, 1 H), 7.43–7.30 (m, 2 H), 6.41 (s, 1 H), 4.63–4.50 (sept, J = 6.0 Hz, 1 H), 2.09 (s, 3 H), 1.37 (d, J = 6.0 Hz, 6 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 163.6, 161.8, 143.6, 138.8, 126.2, 125.9, 125.6, 121.1, 120.3, 106.5, 89.8, 71.3, 22.4 (2C), 8.9. Anal. Calcd for $C_{15}H_{15}NSO_2$: C, 65.91; H, 5.53; N, 5.12; S, 11.73; O, 11.71. Found: C, 65.76; H, 5.56; N, 5.05.

2-Methyl-3-phenyl-1-oxopyrido[2,1-*b*]benzothiazole, 3s. Following the procedure for **3m**, a solution of 4-chloro-2-methyl-3-phenyl-2-cyclobutenone (96 mg, 0.50 mmol, 1.00 equiv) and 2-(tri-*n*-butylstannyl)benzothiazole (255 mg, 0.60 mmol, 1.20 equiv) in toluene (8 mL) with $Pd_2(dba)_3$ (11.4 mg, 0.01 mmol, 2.5 mol%) and tris(2-furyl)phosphine (11.6 mg, 0.05 mmol, 0.10 equiv) at 60 °C overnight and 8 h at reflux gave after workup a solid that was purified by flash chromatography (SiO_2, 2 × 20 cm column) eluting with CH_2Cl_2 first to remove dba, then 14% EtOAc/hexanes to give **3s** as a white solid (84 mg, 0.29 mmol, 58%). TLC (SiO_2, 14% EtOAc/hexanes, R_f = 0.29); mp 152–154 °C (EtOAc/hexane). IR (CH_2Cl_2, NaCl, cm^{-1}): 1644, 1592. ^1H NMR ($CDCl_3$, 300 MHz): δ 9.34 (d, J = 8.1 Hz, 1 H), 7.57 (d, J = 7.5 Hz, 1 H), 7.47–7.32 (m, 7 H), 6.56 (s, 1 H), 2.18 (s, 3 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 163.3, 148.6, 141.4, 139.5, 138.6, 128.4 (4C), 128.1, 126.4, 126.2, 126.1, 121.3, 120.5, 119.6, 101.9, 14.0. Anal. Calcd for $C_{18}H_{13}NSO$: C, 74.20; H, 4.50; N, 4.81; S, 11.00; O, 5.49. Found: C, 74.09; H, 4.51; N, 4.86.

2,3-Diethyl-1-oxopyrido[2,1-*b*]benzothiazole, 3t. Following the procedure for **3m**, a solution of 4-chloro-2,3-diethyl-2-cyclobutenone[9] (79 mg, 0.50 mmol, 1.00 equiv) and 2-(tri-*n*-butylstannyl)benzothiazole (255 mg, 0.60 mmol, 1.20 equiv) in toluene (8 mL) with $Pd_2(dba)_3$ (11.4 mg, 0.01 mmol, 2.5 mol%) and tris(2-furyl)phosphine (11.6 mg, 0.05 mmol, 0.10 equiv) at 60 °C overnight and 8 h at reflux gave after workup a solid that was purified by flash chromatography (SiO_2, 2 × 20 cm column) eluting with CH_2Cl_2 first to remove dba, then 14% EtOAc/hexanes to give **3t** as a white solid (44 mg, 0.17 mmol, 34%). TLC (SiO_2, 14% EtOAc/hexanes, R_f = 0.42); mp 146–148 °C (EtOAc/hexane). IR (CH_2Cl_2, NaCl, cm^{-1}): 1638, 1590. ^1H NMR ($CDCl_3$, 300 MHz): δ 9.30 (d, J = 8.1 Hz, 1 H), 7.54 (d, J = 7.5 Hz, 1 H), 7.43–7.32 (m, 2 H), 6.45 (s, 1 H), 2.74 (q, J = 7.5 Hz, 2 H), 2.64 (q, J = 7.5 Hz, 2 H), 1.25 (t, J = 7.5 Hz, 3 H), 1.19 (t, J = 7.5 Hz, 3 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 162.8, 150.4, 141.5, 138.8, 126.2, 126.0, 125.9,

125.1, 121.2, 120.4, 101.0, 26.2, 19.7, 14.4, 13.6. Anal. Calcd for $C_{15}H_{15}NSO$: C, 70.01; H, 5.87; N, 5.44; S, 12.46; O, 6.22. Found: C, 69.81; H, 5.98; N, 5.19.

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Supplementary Material Available: Copies of ^1H and ^{13}C NMR spectra of **2a**, **2a'**, **2b**, **2b'**, **3c**, **3e**, **3g**, and **3h** (24 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.