JOC The Journal of Organic Chemistry

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Ionic Diamine Rhodium Complex Catalyzed Reductive N-Heterocyclization of 2-Nitrovinylarenes

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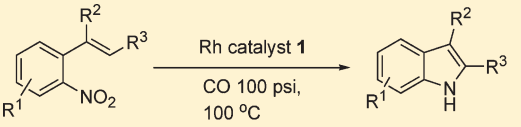
Supporting Information

ABSTRACT: Ionic diamine rhodium complex (**1**) catalyzes the reductive N-cyclization of 2-vinylnitroarenes using carbon monoxide as a reducing agent to afford functionalized indoles. The catalytic system allows direct access to indoles with ester and ketone groups at the 2- or 3-position, in good yields.



1; $[Rh(CO)_2(Me_2NCH_2CH_2NMe_2)]^+[RhCl_2(CO)_2]^-$

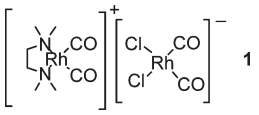
Indole derivatives are recognized as important synthetic intermediates for the design of pharmacologically active compounds.[1] Numerous synthetic methods for such compounds have been developed. Some of the well-established methods include classic organic syntheses such as the Fischer, Madelung, Reissert, Leimgruber-Batcho, and Gassman indole syntheses and others,[2−6] all of which are nonmetal-mediated approaches. Other attractive applications include the use of metal catalysts, in particular, transition metals, which allows the preparation of functionalized indoles from appropriate starting materials in a single step. Examples of straightforward pathways to construct the indole skeleton involve the Pd(II)-catalyzed intramolecular cyclization of 2-alkynylanilines[7−9] and 2-alkenylanilines.[10−14] Alternatively, reductive N-heterocyclization of 2-alkenylnitrobenzenes[15−19] catalyzed by metal complexes, where carbon monoxide can serve as a reducing agent, can produce indoles. This reductive N-heterocyclization methodology has received attention because of its avoidance of the preparation of the corresponding aniline substrates that often requires the chemoselective reduction of the nitro group when the desired substrate has functional groups sensitive to the reduction process. A stoichiometric amount of metal reducing agent such as metallic Fe, Sn, or Zn can be used for this purpose; however, the resulting metal waste originating from the metallic reducing agents often makes it difficult or problematic to isolate the aniline products effectively from the reaction mixture. Watanabe et al. have demonstrated that the Pd complex in combination with $SnCl_2$ could catalyze reductive N-cyclization of 2-vinylnitrobenzenes in the presence of carbon monoxide to afford indole derivatives.[16,17] The Pd-catalyzed reaction was applied to the synthesis of 3-indolecarboxylic acid derivatives, which are useful as pharmaceuticals or synthetic intermediates.[18] Sonoda et al. also demonstrated the use of a selenium catalyst with carbon monoxide as a reducing agent.[19]

We have previously reported the synthesis of a novel, air-stable ionic diamine rhodium complex $[Rh(CO)_2(Me_2NCH_2CH_2NMe_2)]^+[RhCl_2(CO)_2]^-$ (**1**).[20] This complex exhibits excellent catalytic activity for the highly regioselective hydroformylation of olefins[20] and the inter- or intramolecular hydroaminomethylation[21−23] of anilines containing an olefinic unit. Our interest in the catalytic behavior of complex **1** led us to examine the possibility of effecting the reductive intramolecular hydroaminomethylation of 2-nitrovinylarenes. We found that the reductive N-cyclization occurred without any additives, affording indole derivatives instead of the initially expected reductive hydroaminomethylation products. We now describe our findings using the rhodium complex **1** (Figure 1) as the reaction catalyst.

Treatment of 2-isopropenylnitrobenzene (**2a**) with 5 mol % of **1** in THF at 100 °C under CO/H_2 (100/700 psi), optimal conditions for the hydroaminomethylation of 2-allylanilines,[23] afforded 3-methylindole (**3a**) in 27% yield (Table 1, entry 1). A dramatic increase in the yield of **3a** resulted when the partial pressure of H_2 was reduced, and the best results were obtained using 100 psi of CO (entries 2 and 3). No reaction took place at 80 °C (entry 4). Decreased CO pressure to 28 psi still induced the reaction to some extent, giving **3a** in 51% yield, with **2a** being recovered in 36% yield (entry 5). The reactions in toluene or CH_3CN were inferior to those in THF (entries 6 and 7). In order to clarify the effectiveness of complex **1**, the use of $[Rh(COD)Cl]_2$, a synthetic precursor of **1**,[20] alone or in combination with standard phosphine ligands, was evaluated. The indole **3a** was formed in only 4% yield when $[Rh(COD)Cl]_2$ was used as the catalyst. Similarly, any combined catalytic system of $[Rh(COD)Cl]_2$ and phosphines was totally ineffective, with no **3a** being formed (entries 8−14).

Our catalytic system is also versatile for reactions with functionalized 2-nitrovinylarenes under optimized conditions (Table 2). Substrates bearing an ester group on the double bond gave the corresponding indole derivatives in good to excellent yields (Table 2, entries 6−9), regardless of the position of an ester group (i.e., terminal or internal carbons). It is surprising that 2-nitrocinnamaldehyde (**2k**) also underwent the cyclization to

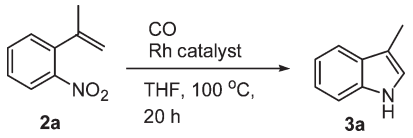
Received: March 2, 2011
Published: May 04, 2011



1

Figure 1. Structure of **1**.

Table 1. Optimization of the Ionic Diamine Complex Catalyzed N-Reductive Cyclization of 2a[a]



2a **3a**

			yield[b] (%)	
entry	catalyst system	CO/H_2 (psi)	**2a**	**3a**
1	**1**	100/700	0	27
2	**1**	100/100	0	67
3	**1**	100/0	10	81
4[c]	**1**	100/0	87	0
5	**1**	28/0	36	51
6[d]	**1**	100/0	12	59
7[e]	**1**	100/0	33	28
8	$[Rh(COD)Cl]_2$	100/100	55	4
9	$[Rh(COD)Cl]_2/2PPh_3$	100/0	100	0
10	$[Rh(COD)Cl]_2/2PCy_3$	100/0	72	0
11	$[Rh(COD)Cl]_2$/1dppe	100/0	84	0
12	$[Rh(COD)Cl]_2$/1dppp	100/0	47	0
13	$[Rh(COD)Cl]_2$/1dppb	100/0	83	0
14	$[Rh(COD)Cl]_2$/1dppf	100/0	68	0

[a] Reaction conditions: **2a** (1 mmol), Rh catalyst (0.05 mmol), monophosphine (0.20 mmol) or bisphosphine (0.1 mmol), solvent 3 mL. [b] Yield determined by ^1H NMR using *tert*-butyl acetate as an internal standard. [c] Reaction at 80 °C. [d] Reaction in toluene. [e] Reaction in acetonitrile.

produce 2-formylindole (**3k**) in 52% yield (entry 10), whereas it was reported that the palladium-catalyzed cyclization of the same substrate afforded quinoline but **3k** was not formed at al.[17] It should also be noted that α,β-unsaturated ketones can be used for the present cyclization, affording indoles substituted by acetyl or benzoyl groups in good yields, without the formation of the corresponding quinoline derivatives (entries 11−16). Along with the results for 2-nitrocinnamaldehyde (**2k**) described above, the reaction of 2-(2-methyl-1-propenyl)nitrobenzene (**2e**) gave distinct results compared to the Pd catalyst.[17] The reaction catalyzed by the Pd complex gave 2,3-dimethylindole in which [1,5]-sigmatropic rearrangement of the terminal methyl group took place during the reaction. In contrast, the current catalytic system resulted in a complex mixture, with no 2,3-dimethylindole being detected.

The reaction of 6-methoxy-2-isopropenylnitrobenzene (**2c**) did not take place, and **2c** was recovered unchanged, suggesting that the nitro group cannot access to the coordination sphere of the rhodium center because of the steric bulkiness of a methoxy group. The allylic alcohol (**2r**), allylic acetate (**2s**), and conjugated diene derivatives (**2n**) also gave unsatisfactory results (entries 17−19). The nonconjugated diene **2u** also afforded 2-(1-propenyl)indole (**3u**) in low yield.

While the mechanism for the reaction remains to be elucidated, the present reaction may conceivably involve a nitrene−rhodium intermediate, which would be formed by deoxygenation of the nitro group by carbon monoxide under the influence of the rhodium complex as proposed for the Pd-catalyzed reaction.[17] It is possible that the coordination environment around the nitrene species affects the reaction course, giving rise to the different behavior for **2e** and **2k** by the Pd-catalyzed reaction.

In summary, we have demonstrated that the reductive N-cyclization of 2-vinylnitroarenes catalyzed by the ionic diamine rhodium complex using carbon monoxide as a reducing agent affords functionalized indoles usually in good yields. This catalyst system is particularly useful for the synthesis of indoles with ester and ketone groups.

EXPERIMENTAL SECTION

Typical Procedure for the Reductive N-Heterocyclization of 2. The 2-nitrovinylarenes (1.0 mmol), complex **1**[20] (0.05 mmol, 25.6 mg), and THF (3 mL) were placed into a glass liner equipped with a magnetic stirring bar. The glass liner was then inserted into a 45 mL autoclave. The autoclave was flushed five times with carbon monoxide and pressurized to 100 psi. The autoclave was heated at 100 °C with stirring. After the reaction, the autoclave was cooled to rt prior to the release of carbon monoxide. The solvent was evaporated under reduced pressure, and the product was purified by silica gel column chromatography with *n*-hexane and diethyl ether as the eluant.

Preparation of the 2-Vinylnitroarenes 2. *2-Isopropenylnitrobenzene (**2a**).* To a suspension of methyltriphenylphosphonium bromide (72 mmol, 25.7 g) in THF (50 mL) was added dropwise NaHMDS (1.0 M THF, 72 mL) at −78 °C. The resulting solution was stirred at this temperature for 15 min, and then a solution of 2-nitrobenzaldehyde (60 mmol, 9.06 g) in THF (20 mL) was added, and the resulting reaction mixture was further stirred at rt for 14 h. The reaction was quenched using saturated NH_4Cl (aq), and the crude product was extracted twice with diethyl ether. The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by silica gel column chromatography with *n*-hexane/diethyl ether (90/10) as the eluant to obtain the product (9.28 g, 95%): ^1H NMR (400 MHz, $CDCl_3$) δ 2.07 (s, 3 H), 4.92 (d, J = 4.0 Hz, 1 H), 5.16 (d, J = 4.0 Hz, 1 H), 7.24−7.32 (m, 1 H), 7.37−7.38 (m, 1 H), 7.50−7.53 (m, 1 H), 7.83−7.85 (d, 1 H); ^{13}C NMR δ 23.3, 53.5, 115.4, 124.0, 127.9, 130.6, 132.7, 139.0, 142.8, 148.3; HRMS (EI) calcd for $C_9H_9NO_2$ 163.0633, found 163.0607.

*2-Isopropenyl-4-methoxynitrobenzene (**2b**).* A mixture of 5-hydroxy-2-nitroacetophenone (17.5 mmol, 3.16 g), K_2CO_3 (30 mmol, 4.14 g), and MeI (60 mmol, 8.46 g) in DMSO (30 mL) was stirred at rt for 20 h. The reaction mixture was poured into water, and the product was extracted three times with diethyl ether. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by column chromatography on silica gel with *n*-hexane/diethyl ether (80/20) as the eluant to give 4-methoxy-2-nitroacetophenone (2.89 g, 85%).

To a suspension of methyltriphenylphosphonium bromide (7.2 mmol, 2.57 g) in THF (30 mL) was added dropwise NaHMDS (1.0 M THF, 7.2 mL) at 0 °C, and then the solution was stirred at rt for 30 min. To the above reaction mixture was added a solution of 4-methoxy-2-nitroacetophenone (6.0 mmol, 1.17 g) in THF (30 mL) at 0 °C. Thereafter, the resulting reaction mixture was further stirred at rt for 15 h. The reaction was quenched using saturated NH_4Cl (aq), and the crude product was extracted twice with diethyl ether. The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by silica gel column chromatography with *n*-

dx.doi.org/10.1021/jo200320k |*J. Org. Chem.* 2011, 76, 4715–4720

Table 2. Results of the Ionic Diamine Rhodium Complex Catalyzed N-Heterocyclization of a Variety of 2-Nitrovinylarenes 2.[a]

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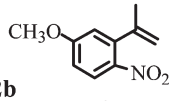
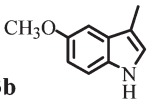
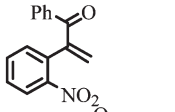
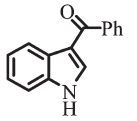
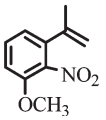
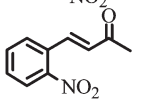
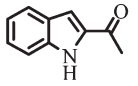
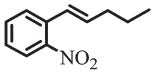
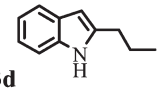
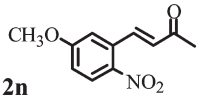
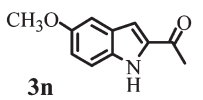
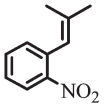
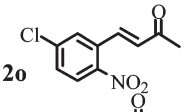
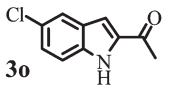
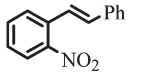
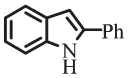
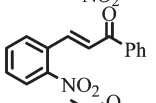
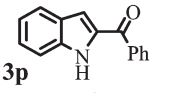
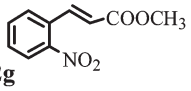
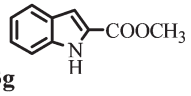
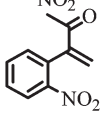
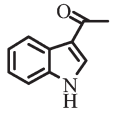
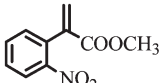
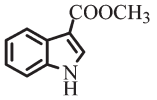
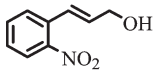
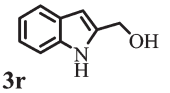
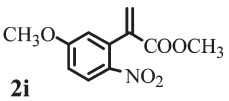
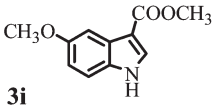
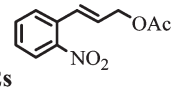
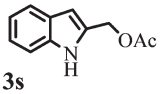
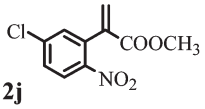
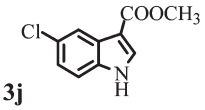
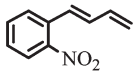
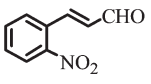
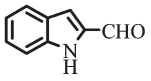
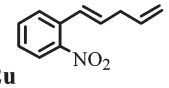
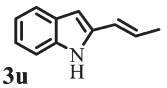
1	 **2b**	 **3b**	75	11	 **2l**	 **3l**	85
2	 **2c**		0[c]	12	 **2m**	 **3m**	80
3	 **2d**	 **3d**	77	13	 **2n**	 **3n**	82
4	 **2e**		complex mixture	14	 **2o**	 **3o**	77
5	 **2f**	 **3f**	100	15	 **2p**	 **3p**	92
6	 **2g**	 **3g**	83	16	 **2q**	 **3q**	94
7	 **2h**	 **3h**	96	17	 **2r**	 **3r**	11
8	 **2i**	 **3i**	79	18	 **2s**	 **3s**	26
9	 **2j**	 **3j**	83	19	 **2t**		complex mixture
10	 **2k**	 **3k**	52	20	 **2u**	 **3u**	23

[a] Reaction conditions: **2** (1.0 mmol), **1** (0.05 mmol), THF 3 mL, CO 100 psi, 100 °C, 20 h. [b] Isolated yield after column chromatography. [c] The starting material **2c** was completely recovered.

hexane/diethyl ether (80/20) as the eluant to obtain the product (1.06 g, 92%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.05 (d, J = 1.2 Hz, 3 H), 3.86 (s, 3 H), 4.89 (dd, J = 1.2, 1.5 Hz, 1 H), 5.12 (d, J = 1.5 Hz, 1 H), 6.72 (d, J = 2.8 Hz, 1 H), 6.83 (dd, J = 2.8, 9.1 Hz, 1 H), 7.97 (d, J = 9.1 Hz, 1 H); ^{13}C NMR δ 23.3, 55.9, 112.8, 114.6, 115.7, 127.0, 140.9, 142.4, 144.0, 163.0; HRMS (EI) calcd for $C_{10}H_{11}NO_3$ 193.0739, found 193.0726.

*2-Isopropenyl-6-methoxynitrobenzene (**2c**).* A mixture of 3-hydroxy-2-nitroacetophenone (1.8 mmol, 0.33 g), K_2CO_3 (10 mmol, 1.38 g), and MeI (20 mmol, 2.84 g) in DMSO (30 mL) was stirred at 50 °C for 20 h. The reaction mixture was poured into water, and the product was extracted three times with diethyl ether. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by silica gel column chromatography with *n*-hexane/diethyl ether (75/25) as the eluant to give 3-methoxy-2-nitroacetophenone (0.32 g, 91%).

To a suspension of methyltriphenylphosphonium bromide (1.9 mmol, 0.69 g) in THF (10 mL) was added dropwise NaHMDS (1.0 M THF, 1.9 mL) at 0 °C, and then the solution was stirred at rt for 30 min. To the above reaction mixture was added a solution of 4-methoxy-2-nitroacetophenone (1.6 mmol, 0.32 g) in THF (10 mL) at 0 °C. Thereafter, the resulting reaction mixture was further stirred at rt for 15 h. The reaction was quenched using saturated NH_4Cl (aq), and the crude product was extracted twice with diethyl ether. The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by silica gel column chromatography with *n*-hexane/diethyl ether (80/20) as the eluant to give 0.24 g (64%) of **2c**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.04 (d, J = 1.0 Hz, 3H), 3.87 (s, 3 H), 5.00 (dd, J = 1.0, 1.6 Hz, 1 H), 5.17 (d, J = 1.6 Hz, 1 H), 6.85−6.87 (m, 2 H), 7.32−7.36 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.5, 56.4, 111.0, 117.0, 120.4, 130.6, 137.4, 140.5, 150.6; HRMS (EI) calcd for $C_{10}H_{11}NO_3$ 193.0739, found 193.0741.

*2-(1-Pentenyl)nitrobenzene (**2d**).* A mixture of 2-nitrobenzyl bromide (20 mmol, 4.32 g) and triphenylphosphine (20 mmol, 5.24 g) in toluene (50 mL) was heated at 100 °C for 24 h. The precipitated (2-nitrobenzyl)triphenylphosphonium bromide was collected by filtration (9.44 g, 99%).

A mixture of (2-nitrobenzyl)triphenylphosphonium bromide (10 mmol, 4.78 g) and K_2CO_3 (20 mmol, 2.76 g) in DMSO (30 mL)

dx.doi.org/10.1021/jo200320k |*J. Org. Chem.* 2011, 76, 4715–4720

was stirred at rt for 2 h, and then butyraldehyde (20 mmol, 1.40 g) was added. The resulting mixture was further stirred at rt for 18 h. The mixture was poured into water, and the product was extracted three times with diethyl ether. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by silica gel column chromatography with *n*-hexane/diethyl ether (90/10) as the eluant to give 1.67 g (88%) of **2d**. The ^1H and ^{13}C NMR spectra were in accordance with literature data.[24]

*2-(2-Methyl-1-propenyl)nitrobenzene (**2e**).* To a solution of isopropyltriphenylphosphonium iodide (18 mmol, 7.78 g) in THF (30 mL) was added *n*-BuLi (2.5 M in hexane, 7.2 mL) at 0 °C, and then the resulting solution was further stirred at this temperature for 30 min. A solution of 2-nitrobenzaldehyde (15 mmol, 2.27 g) in THF (10 mL) was then added to the above solution, and the resulting mixture was stirred again at 0 °C for 3 h. The reaction was quenched using saturated NH_4Cl (aq), and the crude product was extracted twice with diethyl ether. The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by silica gel column chromatography with *n*-hexane/diethyl ether (90/10) as the eluant to form 1.27 g (48%) of **2e**. The ^1H and ^{13}C NMR spectra were in accordance with literature data.[25]

*2-Nitrostilbene (**2f**).* The product was prepared from 2-nitrobenzyltriphenylphosphonium bromide and benzaldehyde in a manner similar to that for **2d** (100%). The ^1H and ^{13}C NMR spectra were in accordance with literature data.[26]

*Methyl 2-Nitrocinnamate (**2g**).* The product was prepared by acid (concd H_2SO_4)-catalyzed esterification of commercially available 2-nitrocinnamic acid in MeOH (92%). The ^1H and ^{13}C NMR spectra were in accordance with literature data.[27]

*Methyl 2-(2-Nitrophenyl)acrylate (**2h**).* The product was prepared according to the literature method.[28]

*Methyl 2-(5-Methoxy-2-nitrophenyl)acrylate (**2i**).* The product was prepared according to the literature method.[29]

*Methyl 2-(5-Chloro-2-nitrophenyl)acrylate (**2j**).* A solution of *tert*-butyl 2-(5-chloro-2-nitrophenyl)acetic acid (8 mmol, 2.2 g) prepared by the literature method[18] was heated in the presence of concd H_2SO_4 (a few drops) for 20 h. The solution was evaporated in vacuo, and the resulting crude methyl 2-(5-chloro-2-nitrophenyl)acetate was further transformed by the literature method[28] to obtain the product (82%): mp 61−63 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 3.67 (s, 3 H), 5.85 (d, J = 0.6 Hz, 1 H), 6.50 (d, J = 0.6 Hz, 1 H), 7.33 (dd, J = 2.3, 8.7 Hz, 1 H), 7.44 (dd, J = 0.2, 8.7 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 52.4, 126.1, 128.1, 129.4, 132.0, 134.6, 138.8, 139.9, 146.1, 164.8; HRMS (EI) calcd for $C_{10}H_8ClNO_4$ 241.0142, found 241.0112.

*2-(2-Nitrophenyl)-1-phenylpropen-1-one (**2l**).* To a solution of 2-nitrophenylacetic acid (15 mmol, 2.72 g) in CH_2Cl_2 (30 mL) were added DMF (a few drops) and oxalyl chloride (30 mmol, 3.81 g), and the resulting solution was stirred at rt for 20 h. The organic solvent was removed under reduced pressure, and then benzene (30 mL) and $AlCl_3$ (22 mmol, 2.94 g) were added to the residue. The mixture was allowed to react at rt for 45 min. The reaction was quenched using cold 10% HCl (20 mL), and the organic layer was separated, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by silica gel column chromatography with *n*-hexane/diethyl ether (80/20) as the eluant to give 2-nitrobenzyl phenyl ketone (1.91 g, 53%).

A mixture of 2-nitrobenzyl phenyl ketone (4.0 mmol, 0.359 g), 37% HCHO (aq) (62 mmol, 5 mL), and morpholine (4.0 mmol, 0.35 g) in AcOH (20 mL) was refluxed for 20 h. After being cooled to rt, water was added, and the product was extracted three times with diethyl ether. The combined organic layers were washed with water, dried over Na_2SO_4, and concentrated in vacuo to give the crude product, which was purified by silica gel column chromatography with *n*-hexane/diethyl ether (80/20) as the eluant to obtain the product (0.95 g, 48%): mp 122−123 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 5.99 (s, 1 H), 6.19 (s, 1 H), 7.46−7.48 (m, 3 H), 7.54−7.56 (m, 2 H), 7.66−7.70 (m, 1 H), 7.91−7.93 (m, 2 H), 8.13−8.15 (m, 1 H); ^{13}C NMR δ 124.9, 127.9, 128.3, 129.49, 123.0, 132.5, 132.9, 134.0, 134.2, 137.2, 146.8, 147.2, 195.0; HRMS (EI) calcd for $C_{15}H_{11}NO_3$ 253.0739, found 253.0696.

*1-(Nitrophenyl)-buten-3-one (**2m**).* The product was prepared according to the literature method.[30]

*4-(5-Methoxy-2-nitrophenyl)buten-2-one (**2n**).* A mixture of 4-(5-hydroxy-2-nitrophenyl)buten-3-one (6 mmol, 1.24 g), which was prepared from 4-hydroxy-2-nitrobenzaldehyde with 1-(triphenylphosphoranylidene)-2-propanone in a similar manner to **2m** (77%),[30] KOH (24 mmol, 1.34 g), and MeI (24 mmol, 3.40 g) in DMSO was stirred at rt for 16 h. The resulting solution was poured into water, and the product was extracted three times with diethyl ether. The combined organic layers were washed with water, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by silica gel column chromatography with *n*-hexane/diethyl ether (80/20) as the eluant to give 0.90 g (68%) of **2n**: mp 118−121 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 2.42 (s, 3 H), 3.90 (s, 3 H), 6.48 (d, J = 16.0 Hz, 1 H), 6.96−6.99 (m, 2 H), 8.07 (d, J = 16.0 Hz, 1 H), 8.13 (m, 1 H); ^{13}C NMR δ 26.9, 56.1, 114.0, 115.2, 127.9, 131.9, 134.0, 140.4, 163.6, 198.4; HRMS (EI) calcd for $C_9H_8NO_3$ [M − Ac] 178.0504, found 178.0500.

*1-(5-Chloro-2-nitrophenyl)buten-2-one (**2o**).* The product was prepared from 5-chloro-2-nitrobenzaldehyde in a manner similar to that for the synthesis of **2m** (81%):[30] mp 147−148 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 2.41 (s, 3 H), 6.54 (d, J = 16.0 Hz, 1 H), 7.24−7.51 (m, 1 H), 7.58−7.59 (m, 1H), 7.93 (d, J = 16.0 Hz, 1 H), 8.04−8.06 (m, 1 H); ^{13}C NMR δ 27.4, 126.6, 126.7, 129.1, 129.1, 130.3, 132.6, 137.8, 140.3, 197.6; HRMS (EI) calcd for $C_8H_5NO_2$ [M − Ac] 182.0009, found 182.0015.

*3-(2-Nitrophenyl)buten-2-one (**2q**).* To a solution of 2-nitrophenylacetic acid (50 mmol, 9.08 g) in Ac_2O (25 mL) was added 1-methylimidazole (25 mmol, 2.0 mL). After the mixture was allowed to react for 12 h, it was poured into water. The crude product was extracted three times with diethyl ether. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The crude 2-nitrophenylacetone thus obtained was used for the next step without purification.

A mixture of crude 2-nitrophenylacetone, morpholine (12.5 mmol, 1.09 g), and 37% HCHO (aq) (12.5 mL) in AcOH (50 mL) was heated at 100 °C for 20 h. After the solvent was removed under reduced pressure, diethyl ether and water were added. The organic layer was separated, dried over Na_2SO_4, and evaporated in vacuo. The residue was purified by silica gel column chromatography with *n*-hexane/diethyl ether (80/20) as the eluant, giving 3.20 g (67%) of **2q**: ^1H NMR (400 MHz, $CDCl_3$) δ 2.45 (s, 3 H), 6.00 (s, 1 H), 6.27 (s, 1 H), 7.28−7.31 (m, 1 H), 7.46−7.50 (m, 1 H), 7.59−7.63 (m, 1 H), 8.05−8.09 (m, 1 H); ^{13}C NMR δ 26.3, 124.5, 125.6, 129.3, 129.3, 132.1, 133.4, 133.7, 148.3, 197.3; HRMS (EI) calcd for $C_8H_6NO_2$ [M − Ac] 148.0399, found 148.0376.

*3-(2-Nitrophenyl)buten-1-ol (**2r**).* To a solution of 2-nitrocinnamaldehyde (30 mmol, 5.31 g) in MeOH (30 mL) was added $NaBH_4$ (15 mmol, 0.57 g) in one portion at rt, and the mixture was stirred for 10 min. The reaction mixture was poured into water, and the crude product was extracted with diethyl ether. After the organic layer was dried over Na_2SO_4 and concentrated in vacuo, the crude product was recrystallized from *n*-hexane/AcOEt (1/1, v/v) to form 1.3 g (24%) of **2r**. The ^1H and ^{13}C NMR spectra were in accordance with literature data.[31]

*1-Acetoxy-3-(2-nitrophenyl)-2-butene (**2s**).* To a solution of **2u** (15 mmol, 2.69 g) and dimethylaminopyridine (15 mg) in pyridine (10 mL) was added Ac_2O (20 mmol, 2.04 g) at 0 °C, and the resulting mixture was stirred at rt for 15 h. The reaction solution was poured into water, and the product was extracted three times with diethyl ether. After the combined organic layers were washed with 10% HCl and then water, the organic layer was dried (Na_2SO_4) and concentrated in vacuo. The

residue was purified by silica gel column chromatography with *n*-hexane/diethyl ether (85/15) as the eluant to obtain 3.13 g (95%) of **2s**. The ^{1}H and ^{13}C NMR spectra were in accord with literature data.[32]

*1-(2-Nitrophenyl)-1,3-butadiene (**2t**).* To a suspension of allyltriphenylphosphonium bromide (22 mmol, 8.43 g) in diethyl ether (120 mL) was added *t*-BuOK (24 mmol, 2.69 g) at rt, and the resulting solution was stirred for 15 min. Thereafter, a solution of 2-nitrobenzaldehyde (20 mmol, 3.02 g) in diethyl ether (20 mL) was added, and the solution was allowed to react for 7 h. The reaction was quenched using saturated NH_4Cl (aq), and the crude product was extracted twice with diethyl ether. The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by silica gel column chromatography with *n*-hexane/diethyl ether (90/10) as the eluant to form 0.66 g (19%) of **2t**. The ^{1}H and ^{13}C NMR spectra were in accord with literature data.[33]

*1-(2-Nitrophenyl)-1,4-pentadiene (**2u**).* A mixture of 3-butenylphosphonium bromide (12 mmol, 4.79 g), K_2CO_3 (12 mmol, 1.66 g), and 18-crown-6 (21 mg) in CH_2Cl_2 (40 mL) was stirred at rt for 20 h. Thereafter, a solution of 2-nitrobenzaldehyde (8.0 mmol, 1.21 g) was added, and the resulting solution was further stirred for 15 h. The reaction was quenched using saturated NH_4Cl (aq), and the organic layer was separated. The organic layers were dried over Na_2SO_4 and concentrated in vacuo, and the residue was purified by silica gel column chromatography with *n*-hexane/diethyl ether (90/10) as the eluant to form 1.37 g (91%) of **2u**: ^{1}H NMR (400 MHz, $CDCl_3$) (a mixture of a trans and cis isomer) the major isomer δ 2.79−2.83 (m, 2 H), 5.01−5.09 (m, 2 H), 5.82−5.86 (m, 2 H), 6.77−6.78 (m, 1 H), 7.36−7.39 (m, 2 H), 7.54−7.56 (m, 1 H), 7.98−8.00 (m, 1H), the minor isome δ 2.99−3.00 (m, 1 H), 5.01−5.09 (m, 2 H), 5.01−5.09 (m, 2 H), 6.23−6.24 (m, 2 H), 6.80−6.81 (m, 1 H), 7.36−7.39 (m, 2 H), 7.54−7.56 (m, 1 H), 7.81−7.83 (m, 1 H); ^{13}C NMR (a mixture of a trans and cis isomer) δ 32.6, 37.1, 115.7, 116.4, 124.4, 124.6, 126.1, 126.5, 127.6, 128.0, 128.5, 131.2, 131.6, 132.8, 132.9, 136.0, 148.3; HRMS (EI) calcd for $C_{11}H_{11}NO_2$ 189.0790, found 189.0728.

*Products **3**.* The N-heterocyclization products, **3a**,[34] **3b**,[35] **3d**,[36] **3f**,[37] **3g**,[38] **3h**,[39] **3i**,[40] **3j**,[41] **3k**,[42] **3l**,[43] **3m**,[44] **3n**,[45] **3p**,[46] **3q**,[47] **3r**,[48] **3s**,[49] and **3u**[50] are known compounds, and the ^{1}H NMR spectra were in accordance with literature data.

*2-Acetyl-5-chloroindole (**3o**):* mp 205 °C dec; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.58 (s, 3 H), 7.11 (s, 1 H), 7.24−7.29 (m, 2 H), 7.67 (s, 1 H), 9.23 (brs, 1 H); ^{13}C NMR δ 25.9, 108.9, 113.3, 122.2, 126.6, 126.9, 128.5, 135.5, 136.4, 190.4; HRMS (EI) calcd for $C_{10}H_8ClNO$ 193.0294, found 193.0293.

■ ASSOCIATED CONTENT

Supporting Information. General procedures and ^{1}H and/or ^{13}C NMR spectra for obtained compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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■ ACKNOWLEDGMENT

We are grateful to the Natural Sciences and Engineering Research Council of Canada (NSERC) for financial support of this research.

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