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Direct C−H Alkenylation of Functionalized Pyrazoles

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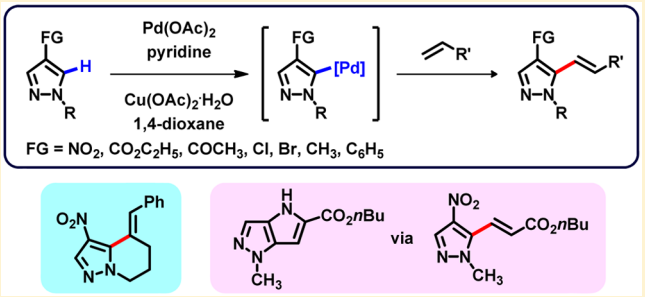
Supporting Information

ABSTRACT: We have developed inter- and intramolecular C−H alkenylation reactions of pyrazoles. The catalyst, derived from $Pd(OAc)_2$ and pyridine, enabled the oxidative alkenylation of pyrazoles containing a variety of functional groups at the C4 position. Activated alkenes, including acrylate, acrylamide, and styrene derivatives, and enamides could be installed in this process. The sequential C−H alkenylation and cyclization reactions gave rise to fused bicyclic pyrazoles, providing a new strategy to annulate readily available pyrazole compounds.



Direct C−H functionalization reactions of heteroarenes have been established as an alternative to traditional cross-coupling reactions, allowing for rapid preparation of complex heteroarenes for investigation in biological applications and functional materials.[1] Pyrazoles represent one of the most sought-after heterocycles for C−H functionalization reactions due to their importance in medicinal chemistry, agrochemical science, and organometallic chemistry.[2] For efficient synthesis of the pyrazole library, a C−H functionalization strategy is even more appealing because of the instability and high cost of prefunctionalized pyrazole building blocks.[3] Many new methods have been developed for the direct substitution of C−H bonds on the pyrazole ring, with a particular focus on arylation.[4] One strategy to promote arylation of pyrazoles utilizes electron-withdrawing groups to activate the C−H bond of the pyrazole ring.[5] Additionally, we have demonstrated that not only the acidity of the C−H bond but also the Lewis basicity of the nitrogen atom can be modulated by electron-withdrawing groups, thus preventing *N*-alkylation with alkyl halides and enabling catalytic C−H alkylation reactions of pyrazoles.[6]

In contrast to arylation and alkylation reactions, the installation of alkenyl groups onto the pyrazole ring has had limited success.[7−9] Consistent with low regioselectivity in the arylation of unsubstituted pyrazoles, an alkenylation reaction of 1-methylpyrazole gave a mixture of regioisomers (Figure 1A).[4a,8b] Furthermore, the Lewis basic nitrogen atom serves as a directing group for C−H functionalization at the neighboring arene ring, rather than the pyrazole ring (Figure 1B).[10] Lewis basicity was also attributed to the failure of pyrazole alkenylation using a directing group strategy that was successful in the regioselective C−H alkenylation of indoles.[11] While we addressed the issues of regioselectivity and high Lewis basicity of pyrazoles in C−H alkylation by taking advantage of electron-withdrawing groups, we observed that the efficiency of the catalytic system, derived from $Pd(OAc)_2$ and PPh_3, considerably decreased as the electron-withdrawing ability of the substituent decreased from nitro to carbonyl to chloride.[6b] In order to expand the scope of C−H functionalization of pyrazoles by overcoming the limitations arising from phosphine-ligated Pd complexes, we investigated a phosphine-free system to facilitate C−H metalation of pyrazoles having a wide range of electronic properties.[12] Specifically, we envisioned a catalytic cycle that involved palladation of pyrazoles prior to the generation of an aryl or alkyl palladium species, thus expanding the classes of coupling partners beyond aryl and alkyl halides. We have demonstrated the feasibility of

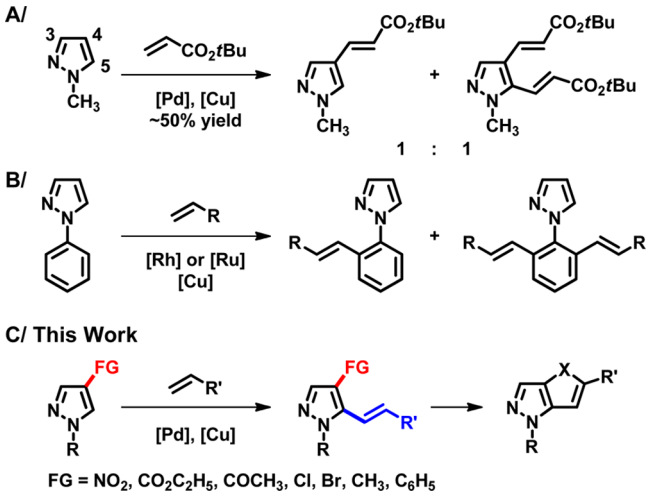


Figure 1. (A) Reactivity of an unsubstituted pyrazole in alkenylation. (B) Pyrazoles as a directing group in the alkenylation of arenes. (C) Dehydrogenative alkenylation of functionalized pyrazoles and subsequent cyclization to give fused bicyclic pyrazoles.

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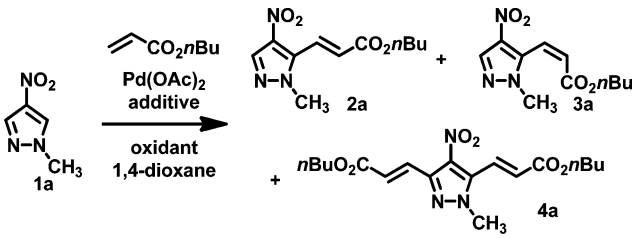
the alternative catalytic cycle by developing the dehydrogenative Heck reaction of pyrazoles (Figure 1C). In this process, pyrazoles possessing a functional group at the C4 position, including nitro, carbonyl, halo, alkyl, and aryl groups, can be subjected to C5-selective olefination reactions.[13] Subsequently, these alkenylation products can undergo interconversion of the functional groups or cyclization between the preinstalled functional groups and the newly introduced alkenes to produce fused pyrazole bicycles that are otherwise difficult to obtain.[14] Herein, we report the oxidative C−H alkenylation of functionalized pyrazoles. A variety of alkenyl groups can be incorporated in an intermolecular or intramolecular fashion, and the subsequent cyclization of the alkene products provides fused bicyclic pyrazoles.

We first examined the alkenylation reaction of 1-methyl-4-nitropyrazole (**1a**) with different oxidants, which revealed that $Cu(OAc)_2$ was superior to silver-based oxidants (Table 1, entries 1−3). Bidentate nitrogen ligands, added as ancillary ligands, only inhibited the catalytic reaction (entries 4 and 5).[15] Based on the mechanistic study of C−H alkenylation, pyridine was tested as a monodentate nitrogen ligand that can readily undergo ligand exchange, resulting in an improved reaction yield (entry 6).[16] This result showed that pyridine was a more competent ligand in oxidative alkenylation than the pyrazole substrate. A comparable result was obtained when 10 mol % of pyridine was used instead of 20 mol %, indicating that the ratio of Pd/pyridine was not critical in pyrazole alkenylation (entry 7).[17] The hydrated form of $Cu(OAc)_2$ was employed in place of the anhydrous counterpart without affecting the reaction yield (entry 8). While the amount of the copper salt could be reduced to 50 mol % when the reaction was conducted in an open flask (entry 9), microscale reactions to examine the substrate scope were performed with 2 equiv of $Cu(OAc)_2$·H_2O due to the convenience of the experimental setup. The copper salt was a necessary inclusion; in the absence of $Cu(OAc)_2$, air and oxygen were insufficient to reoxidize the Pd catalyst (entries 10 and 11). In the screening experiments, we observed small amounts of the (*Z*)-isomer and dialkenylation products, **3a** and **4a**, respectively, the latter of which offered the opportunity for application to the C3-alkenylation of indazoles using this protocol (*vide infra*).

The optimized conditions were applied to a variety of readily available olefins (Table 2). Butyl and ethyl acrylates gave **2a-c** in good yields. The reaction of butyl methacrylate gave rise to the corresponding olefin isomerization product **2d**.[18] *N*,*N*-Diethylacrylamide worked equally well to furnish **2e** in 67% yield. Styrene derivatives were also successfully coupled with the pyrazole ring (**2f−h**). Interestingly, an electron-rich alkene, 1-vinyl-2-pyrrolidinone, gave the corresponding alkenylation product **2i** in 43% yield. However, an aliphatic olefin, 3,3-dimethylbut-1-ene, was not amenable to this process (**2j**).

As anticipated from the reactivity of the Pd/pyridine system, pyrazoles substituted with a broad range of functional groups underwent C−H olefination (Table 3). The common pyrazole protecting group, 2-(trimethylsilyl)ethoxymethyl (SEM) group, was tolerated (entries 1, 6, 9, and 10), whereas protecting groups able to chelate with palladium in cooperation with the pyrazole nitrogen, such as THP and Me_2NSO_2 groups, were unsuitable for this protocol (results not shown). Carbonyl groups, including ester and ketone functionalities (entries 2−4), could be used, and it is notable that reasonable yields of **7b** and **7c** were obtained despite the presence of acidic *α*-protons in the acetyl group. Furthermore, chloro and bromo groups on the pyrazole ring were tolerated, providing opportunities for further synthetic elaboration of the resulting products (entries 5−9).[19] Most importantly, alkyl and aryl pyrazoles, represented as **13a** and **14a**, respectively, underwent alkenylation reactions under the same reaction conditions as optimized for electron-deficient pyrazoles (entries 10 and 11).[20] The alkenylation of (2*H*)-indazole **15a** could also be performed without additional

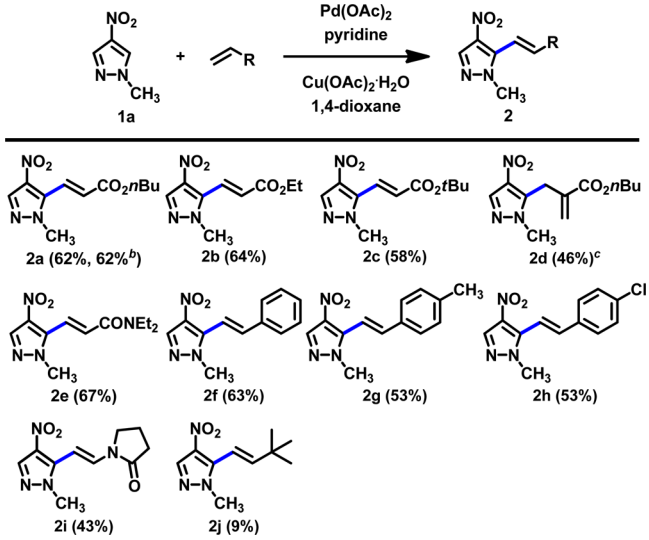
Table 1. Alkenylation of 1-Methyl-4-nitropyrazole[a]



entry	additive	oxidant	yield (%)[b] 2a	3a	4a
1	–	Ag_2CO_3	15	0	0
2	–	AgOAc	30	3	3
3	–	$Cu(OAc)_2$	47	6	6
4[c]	2,2′-bipyridine	$Cu(OAc)_2$	–	–	–
5[c]	1,10-phenanthroline	$Cu(OAc)_2$	–	–	–
6	pyridine	$Cu(OAc)_2$	62	7	7
7[c]	pyridine	$Cu(OAc)_2$	57	8	8
8	**pyridine**	**$Cu(OAc)_2$·H_2O**	**65**	**8**	**7**
9[d]	**pyridine**	**$Cu(OAc)_2$**	**66**	**8**	**5**
10	pyridine	O_2	15	2	1
11	pyridine	air	7	–	–

[a]Reaction conditions: pyrazole (0.50 mmol), butyl acrylate (0.50 mmol), $Pd(OAc)_2$ (0.050 mmol), additive (0.10 mmol), oxidant (1.0 mmol), 1,4-dioxane (0.50 M), 120 °C. [b]^{1}H NMR yield. [c]The amount of additive was reduced to 10 mol %. [d]The reaction was carried out with 0.50 equiv of $Cu(OAc)_2$ in an open flask.

Table 2. Alkene Substrate Scope[a]



[a]Reaction conditions: pyrazole (0.50 mmol), alkene (0.50 mmol), $Pd(OAc)_2$ (0.050 mmol), pyridine (0.10 mmol), $Cu(OAc)_2$·H_2O (1.0 mmol), 1,4-dioxane (0.50 M), 120 °C. [b]Yield of a 1-g-scale reaction. [c]The reaction was performed in the absence of pyridine.

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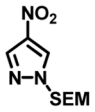
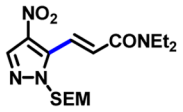
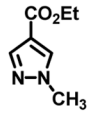
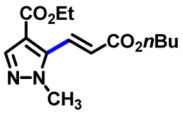
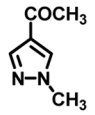
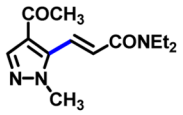
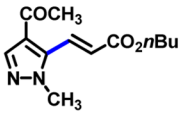
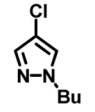
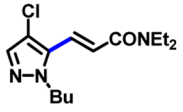
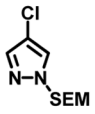
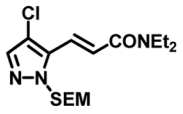
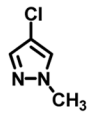
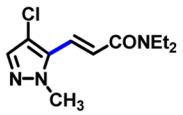
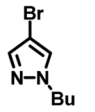
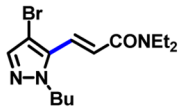
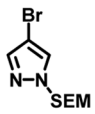
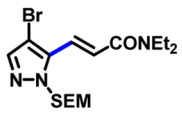
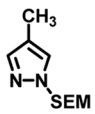
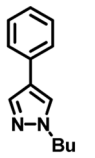
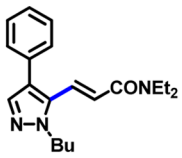
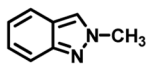
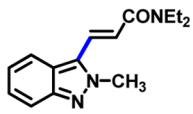
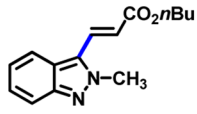
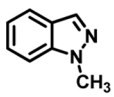
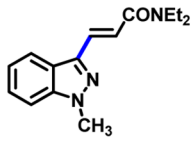
Table 3. Pyrazole Substrate Scope[a]

entry	reactant		product		yield
1		5a		5b	74%
2		6a		6b	51%
3		7a		7b	43%
4	7a			7c	49%
5		8a		8b	67%
6		9a		9b	64%
7		10a		10b	55%
8		11a		11b	57%
9		12a		12b	41%
10		13a		13b	69%
11		14a		14b	53%
12		15a		15b	64%
13	15a			15c	72%
14		16a		16b	42%

[a]Reaction conditions: pyrazole (0.50 mmol), alkene (0.50 mmol), $Pd(OAc)_2$ (0.050 mmol), pyridine (0.10 mmol), $Cu(OAc)_2·H_2O$ (1.0 mmol), 1,4-dioxane (0.50 M), 120 °C.

optimization (entries 12 and 13). Just as the C3 position of pyrazoles was vulnerable to C−H alkenylation, the C3 position of (1*H*)-indazole **16a** was alkenylated in this method (entry 14).

Both intermolecular alkenylation and the intramolecular variant could be carried out with pyrazole heterocycles (Table 4). Five-, six-, and seven-membered rings were readily constructed by Pd/Cu catalysis. In the reactions with pendant styryl groups (entries 1−3), the major products were *exo*-(*E*)-alkenes: the structures of **17b** and **19b** were confirmed by X-ray crystallographic analysis (see Supporting Information).[21] Presumably, syn-addition of the palladated pyrazole followed by syn-*β*-hydride elimination was responsible for the stereochemical outcome, similar to other Heck-type reactions.[22] The formation of the exocyclic alkenes represents a rare example of intramolecular alkenylation with a styryl group. In addition, nonactivated olefins could be used to prepare six- and seven-membered rings, as exemplified in the formation of **20b** and **21b**, respectively (entries 4 and 5).

In order to demonstrate the utility of the C−H alkenylation of pyrazoles in complex pyrazole synthesis, we pursued the preparation of fused pyrazole rings from the resultant alkenylation products. A modified protocol for the Cadogan reaction was readily applied to the synthesis of pyrrolopyrazoles **22** and **23** from alkenyl nitropyrazoles **2a** and **2f**, respectively (Scheme 1).[23] In addition, the corresponding cyclopentapyrazolidene was generated by palladium-catalyzed annulation with an internal alkyne, favoring formation of the (*Z*)-isomer (**24**).[24]

In conclusion, we have developed a new approach to prepare C5-alkenylated pyrazoles. The catalyst, derived from $Pd(OAc)_2$ and pyridine, in combination with $Cu(OAc)_2·H_2O$ oxidant, enabled inter- and intramolecular alkenylation reactions of electronically varied pyrazoles, as well as indazoles. No special directing groups were required, but directing groups that were able to accompany the Lewis basic nitrogen atom of pyrazole to form a bidentate ligand had an inhibitory effect. Lewis basicity of pyrazoles was not detrimental to olefination. In fact, the addition of pyridine, a better Lewis base than pyrazole, was advantageous to oxidative alkenylation. Many synthetically versatile functional groups were tolerated in this process, including nitro, ester, ketone, chloro, bromo, methyl, and

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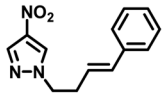
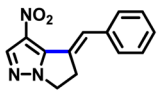
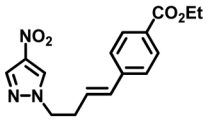
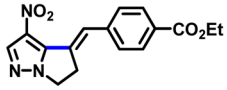
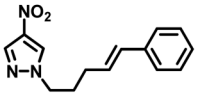
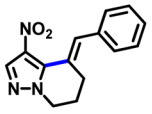
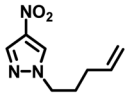
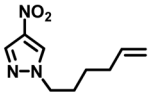
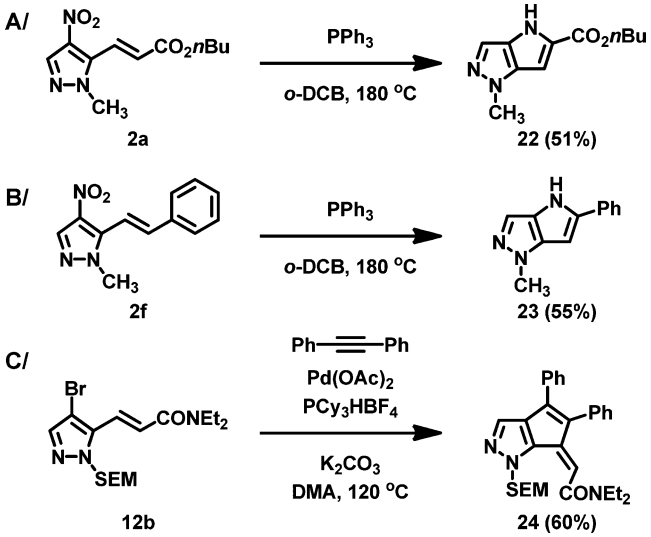
Table 4. Intramolecular C−H Alkenylation of Pyrazoles

entry	reactant		product	yield
1		17a		17b (47%)
2		18a		18b (56%)
3		19a		19b (56%)
4		20a		20b (45%)[a]
5		21a		21b (58%)

[a]Obtained as a mixture of the alkenylation product and the corresponding olefin isomerization product (6:1).

Scheme 1. Synthesis of Fused Pyrazoles from Alkenylation Products



phenyl groups in the pyrazole ring, and acrylates, acrylamides, styrenes, and an enamide in the olefin. Preinstalled functional groups at the pyrazole C4 position allowed for efficient alkenylation of pyrazoles and led to the formation of fused pyrazole bicycles that were challenging to access with conventional methods. The construction of fused pyrazole rings by the sequential addition of functional groups and alkenyl moieties to the parent pyrazole ring shows potential for the development of new strategies for pyrazole annulation, which are currently underway in our laboratory.

EXPERIMENTAL SECTION

Flash column chromatography was performed on silica gel (40−63 μm) using the indicated solvent system. NMR spectra were recorded in $CDCl_3$ at 300 K on a 300 MHz Fourier transform NMR spectrometer. Proton chemical shifts are expressed in parts per million (ppm, δ scale) and are referenced to residual protium in the NMR solvent ($CDCl_3$, δ 7.26). Carbon chemical shifts are expressed in parts per million (ppm, δ scale) and are referenced to the carbon resonance of the NMR solvent ($CDCl_3$, δ 77.16). Infrared (IR) spectra are reported as absorption wavenumbers (cm^{-1}). High-resolution mass spectra (HRMS) were acquired on high-resolution mass spectrometers: Q-TOF (ionization mode: ESI) and magnetic sector−electric sector double focusing mass analyzer (ionization mode: EI).

General Procedure for C−H Alkenylation of Pyrazoles. To a solution of the pyrazole substrate (0.50 mmol) and 1,4-dioxane (1.0 mL, 0.50 M) in an 8 mL glass vial were added the alkene (0.50 mmol), $Cu(OAc)_2·H_2O$ (200 mg, 1.0 mmol), pyridine (8.1 μL, 0.10 mmol), and $Pd(OAc)_2$ (11 mg, 0.050 mmol). The reaction mixture was stirred at 120 °C for 12 h, then cooled to 25 °C, and concentrated. The residue was then purified by flash column chromatography to furnish the desired product.

*1-Methyl-4-nitro-1H-pyrazole (**1a**).*[5d] To a stirred solution of 4-nitro-1*H*-pyrazole (3.00 g, 26.5 mmol) in DMF (15.0 mL) at 25 °C were added K_2CO_3 (4.40 g, 31.8 mmol) and iodomethane (1.98 mL, 31.8 mmol). After stirring for 14 h at 25 °C, the reaction mixture was treated with water (20 mL) and EtOAc (20 mL) and transferred to a 125 mL separatory funnel. The organic layer was collected and the aqueous layer was extracted with EtOAc (20 mL × 2). The combined organic layers were washed with brine (20 mL), dried over sodium sulfate and filtered. The filtrate was concentrated, and the residue was purified by flash column chromatography (hexanes/EtOAc = 1:3) to provide pyrazole **1a** as a white solid (3.30 g, 98% yield). ^1H NMR (300 MHz, $CDCl_3$) δ 8.12 (s, 1H), 8.06 (s, 1H), 3.97 (s, 3H).

*(E)-Butyl 3-(1-methyl-4-nitro-1H-pyrazol-5-yl)acrylate (**2a**).* Purification by flash column chromatography (hexanes/EtOAc = 9:2) provided alkenylated pyrazole **2a** as a yellow oil (78 mg, 62% yield). A 1-g-scale reaction was conducted with **1a** (1.00 g, 7.90 mmol), *n*-butyl acrylate (1.13 mL, 7.90 mmol), $Cu(OAc)_2$ (727 mg, 4.00 mmol), pyridine (129 μL, 1.60 mmol), $Pd(OAc)_2$ (177 mg, 0.790 mmol), and 1,4-dioxane (10.0 mL, 0.790 M) in an open flask to give **2a** (1.24 g, 62%). IR (film) 3127, 2958, 2874, 1714, 1651, 1538, 1393 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.89 (d, *J* = 16.5 Hz, 1H), 6.67 (d, *J* = 16.5 Hz, 1H), 4.26 (t, *J* = 6.7 Hz, 2H), 4.02 (s, 3H), 1.77−1.65 (m, 2H), 1.50−1.37 (m, 2H), 0.97 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.3, 136.5, 135.3, 134.0, 128.5, 127.4, 65.4, 39.6, 30.6, 19.1, 13.7; HRMS (ESI) calcd for $C_{11}H_{16}N_3O_4$ $[M + H]^+$ 254.1135, found 254.1137.

*(Z)-Butyl 3-(1-Methyl-4-nitro-1H-pyrazol-5-yl)acrylate (**3a**).* Yellow oil. IR (film) 2960, 2874, 1723, 1501, 1402, 1318 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.10 (s, 1H), 6.98 (d, *J* = 11.8 Hz, 1H), 6.45 (d, *J* = 11.9 Hz, 1H), 4.08 (t, *J* = 6.7 Hz, 2H), 3.77 (s, 3H), 1.61−1.50 (m, 2H), 1.35−1.26 (m, 2H), 0.90 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.2, 136.6, 135.8, 129.0, 128.5, 110.1, 65.3, 38.2, 30.5, 19.1, 13.8; HRMS (ESI) calcd for $C_{11}H_{16}N_3O_4$ $[M + H]^+$ 254.1135, found 254.1145.

*(2E,2′E)-Dibutyl 3,3′-(1-Methyl-4-nitro-1H-pyrazole-3,5-diyl)-diacrylate (**4a**).* Yellow solid. Mp 74−76 °C; IR (film) 2961, 2934, 2874, 1717, 1547, 1455, 1360 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.07 (d, *J* = 16.2 Hz, 1H), 7.88 (d, *J* = 16.0 Hz, 1H), 6.83 (d, *J* = 15.9 Hz, 1H), 6.53 (d, *J* = 15.9 Hz, 1H), 4.32−4.18 (m, 4H), 4.02 (s, 3H), 1.76−1.66 (m, 4H), 1.50−1.37 (m, 4H), 1.02−0.92 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.2, 165.1, 142.5, 137.2, 131.5, 131.2, 128.7, 128.0, 124.5, 65.6, 64.9, 40.0, 30.7, 30.6, 19.3, 19.2, 13.8, 13.8; HRMS (ESI) calcd for $C_{18}H_{26}N_3O_6$ $[M + H]^+$ 380.1816, found 380.1813.

*(E)-Ethyl 3-(1-methyl-4-nitro-1H-pyrazol-5-yl)acrylate (**2b**).* The ^1H NMR of the reaction mixture showed the formation of the corresponding (*E*)- and (*Z*)-olefination products and dialkenylation product (63%, 7%, and 5%, respectively). Purification by flash column chromatography (hexanes/EtOAc = 3:1) provided alkenylated pyrazole **2b** as a yellow oil (72 mg, 64% yield). IR (film) 3128, 2984, 1717, 1650, 1538, 1503 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.89 (d, *J* = 16.5 Hz, 1H), 6.67 (d, *J* = 16.5 Hz, 1H), 4.32 (q, *J* = 7.1 Hz, 2H), 4.02 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.2, 136.5, 135.3, 133.9, 128.5, 127.4, 61.5,

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39.6, 14.2; HRMS (ESI) calcd for $C_9H_{12}N_3O_4$ $[M + H]^+$ 226.0822, found 226.0827.

*(E)-tert-Butyl 3-(1-Methyl-4-nitro-1H-pyrazol-5-yl)acrylate (**2c**).* The ^1H NMR of the reaction mixture showed the formation of the corresponding (*E*)- and (*Z*)-olefination products and dialkenylation product (64%, 9%, and 7%, respectively). Purification by flash column chromatography (hexanes/EtOAc = 9:2) provided alkenylated pyrazole **2c** as a yellow solid (74 mg, 58% yield). Mp 64−66 °C; IR (film) 3129, 2980, 2932, 1714, 1645, 1505, 1370 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.80 (d, J = 16.5 Hz, 1H), 6.59 (d, J = 16.5 Hz, 1H), 4.01 (s, 3H), 1.55 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.4, 136.5, 135.6, 133.9, 130.4, 126.5, 82.1, 39.6, 28.1; HRMS (ESI) calcd for $C_{11}H_{16}N_3O_4$ $[M + H]^+$ 254.1135, found 254.1137.

*Butyl 2-((1-Methyl-4-nitro-1H-pyrazol-5-yl)methyl)acrylate (**2d**).* Purification by flash column chromatography (hexanes/EtOAc = 5:1) provided alkenylated pyrazole **2d** as a yellow oil (62 mg, 46% yield). IR (film) 2960, 2931, 2874, 1716, 1552, 1427 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.11 (s, 1H), 6.31 (s, 1H), 5.44 (s, 1H), 4.18 (t, J = 6.6 Hz, 2H), 4.08 (s, 2H), 3.88 (s, 3H), 1.71−1.61 (m, 2H), 1.46−1.33 (m, 2H), 0.95 (t, J = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.0, 139.3, 136.3, 134.3, 133.5, 127.5, 65.4, 37.7, 30.6, 27.0, 19.3, 13.8; HRMS (ESI) calcd for $C_{12}H_{18}N_3O_4$ $[M + H]^+$ 268.1292, found 268.1291.

*(E)-N,N-Diethyl-3-(1-methyl-4-nitro-1H-pyrazol-5-yl)acrylamide (**2e**).* The GC analysis of the reaction mixture showed the formation of the corresponding (*E*)-olefination and dialkenylation products (area percentage: >50:1). Purification by flash column chromatography (hexanes/EtOAc = 1:2) provided alkenylated pyrazole **2e** as a yellow oil (84 mg, 67% yield). IR (film) 2977, 2934, 1658, 1618, 1362, 1217 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.61 (d, J = 15.6 Hz, 1H), 7.54 (d, J = 15.6 Hz, 1H), 3.99 (s, 3H), 3.58−3.43 (m, 4H), 1.31−1.18 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.3, 137.4, 136.3, 129.8, 123.6, 42.7, 41.6, 38.9, 15.3, 13.2; HRMS (ESI) calcd for $C_{11}H_{17}N_4O_3$ $[M + H]^+$ 253.1295, found 253.1298.

*(E)-1-Methyl-4-nitro-5-styryl-1H-pyrazole (**2f**).* Purification by flash column chromatography (hexanes/EtOAc = 7:1) provided alkenylated pyrazole **2f** as a yellow solid (72 mg, 63% yield). Mp 91−93 °C; IR (film) 3060, 1731, 1694, 1681, 1579, 1446 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.62−7.56 (m, 2H), 7.48−7.37 (m, 4H), 7.21 (d, J = 16.9 Hz, 1H), 4.05 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.7, 138.5, 136.3, 135.2, 132.7, 129.8, 129.0, 127.3, 112.8, 39.4; HRMS (ESI) calcd for $C_{12}H_{12}N_3O_2$ $[M + H]^+$ 230.0924, found 230.0925.

*(E)-1-Methyl-5-(4-methylstyryl)-4-nitro-1H-pyrazole (**2g**).* The GC analysis of the reaction mixture showed the formation of the corresponding (*E*)-olefination and dialkenylation products (area percentage: >50:1). Purification by flash column chromatography (hexanes/EtOAc = 9:2) provided alkenylated pyrazole **2g** as a yellow solid (65 mg, 53% yield). Mp 80−81 °C; IR (film) 3585, 3116, 3026, 2922, 1608, 1573, 1225 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.13 (s, 1H), 7.48 (d, J = 8.1 Hz, 2H), 7.35 (d, J = 16.9 Hz, 1H), 7.26−7.22 (m, 2H), 7.18 (d, J = 16.9 Hz, 1H), 4.03 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.2, 139.7, 138.8, 136.4, 132.6, 132.5, 129.8, 127.3, 111.8, 39.5, 21.5; HRMS (ESI) calcd for $C_{13}H_{14}N_3O_2$ $[M + H]^+$ 244.1081, found 244.1080.

*(E)-5-(4-Chlorostyryl)-1-methyl-4-nitro-1H-pyrazole (**2h**).* Purification by flash column chromatography (hexanes/EtOAc = 9:2) provided alkenylated pyrazole **2h** as a yellow solid (70 mg, 53% yield). Mp 113−115 °C; IR (film) 3130, 3026, 2925, 1643, 1451, 1319 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.52 (d, J = 8.5 Hz, 2H), 7.43−7.32 (m, 3H), 7.17 (d, J = 16.8 Hz, 1H), 4.04 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.3, 138.2, 136.4, 135.6, 133.8, 132.8, 129.2, 128.5, 113.4, 39.5; HRMS (ESI) calcd for $C_{12}H_{11}ClN_3O_2$ $[M + H]^+$ 264.0534, found 264.0535.

*(E)-1-(2-(1-Methyl-4-nitro-1H-pyrazol-5-yl)vinyl)pyrrolidin-2-one (**2i**).* Purification by flash column chromatography (hexanes/EtOAc = 1:3) provided alkenylated pyrazole **2i** as a yellow solid (51 mg, 43% yield). Mp 128−130 °C; IR (film) 3114, 2926, 1716, 1637, 1533, 1490 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.69 (d, J = 15.3 Hz, 1H), 6.29 (d, J = 15.3 Hz, 1H), 3.97 (s, 3H), 3.75 (t, J = 7.2 Hz, 2H), 2.60 (t, J = 8.2 Hz, 2H), 2.25 (p, J = 7.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.2, 138.1, 136.3, 132.1, 95.9, 44.9, 39.6, 31.1, 17.5; HRMS (ESI) calcd for $C_{10}H_{13}N_4O_3$ $[M + H]^+$ 237.0982, found 237.0986.

*(E)-5-(3,3-Dimethylbut-1-en-1-yl)-1-methyl-4-nitro-1H-pyrazole (**2j**).* Purification by flash column chromatography (hexanes/EtOAc = 5:1) provided alkenylated pyrazole **2j** as a light yellow solid (9 mg, 9% yield). Mp 56−57 °C; IR (film) 2962, 2906, 2869, 1653, 1472, 1365, 1207 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.07 (s, 1H), 6.57 (d, J = 16.8 Hz, 1H), 6.33 (d, J = 16.8 Hz, 1H), 3.90 (s, 3H), 1.19 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.2, 139.4, 136.2, 132.4, 110.8, 38.9, 34.7, 29.0; HRMS (ESI) calcd for $C_{10}H_{16}N_3O_2$ $[M + H]^+$ 210.1237, found 210.1229.

*4-Nitro-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrazole (**5a**).*[5c] To a stirred solution of 4-nitro-1*H*-pyrazole (1.00 g, 8.84 mmol) in THF (10.0 mL) at 0 °C was added sodium hydride 60% in oil (456 mg, 11.4 mmol). After stirring for 30 min at 0 °C, 2-(chloromethoxy)ethyltrimethylsilane (1.70 mL, 9.60 mmol) was added. Stirring was continued for 12 h at 25 °C, and the reaction mixture was treated with water (15 mL) and EtOAc (20 mL) and transferred to a 125 mL separatory funnel. The organic layer was collected, and the aqueous layer was extracted with EtOAc (25 mL × 2). The combined organic layers were washed with brine (20 mL), dried over sodium sulfate, and filtered. The filtrate was concentrated, and the residue was purified by flash column chromatography (hexanes/EtOAc = 9:1) to provide pyrazole **5a** as a white solid (1.40 g, 65% yield). ^1H NMR (300 MHz, $CDCl_3$) δ 8.31 (s, 1H), 8.10 (s, 1H), 5.45 (s, 2H), 3.62 (t, J = 8.3 Hz, 2H), 0.94 (t, J = 8.3, 2H), 0.01 (s, 9H).

*(E)-N,N-Diethyl-3-(4-nitro-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrazol-5-yl)acrylamide (**5b**).* Purification by flash column chromatography (hexanes/EtOAc = 5:2) provided alkenylated pyrazole **5b** as a yellow oil (136 mg, 74% yield). IR (film) 2955, 1659, 1622, 1541, 1504, 1463 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.94 (d, J = 15.8 Hz, 1H), 7.50 (d, J = 15.8 Hz, 1H), 5.50 (s, 2H), 3.71 (t, J = 8.5 Hz, 2H), 3.57−3.38 (m, 4H), 1.31−1.17 (m, 6H), 0.93 (t, J = 8.5 Hz, 2H), 0.00 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.0, 138.0, 136.5, 134.0, 130.2, 124.7, 79.9, 67.6, 42.5, 41.3, 17.9, 15.1, 13.0, −1.5; HRMS (ESI) calcd for $C_{16}H_{29}N_4O_4Si$ $[M + H]^+$ 369.1953, found 369.1968.

*Ethyl 1-Methyl-1H-pyrazole-4-carboxylate (**6a**).*[25] Similar to the synthesis of **1a**, **6a** was prepared from a reaction of ethyl 1*H*-pyrazole-4-carboxylate (1.00 g, 7.14 mmol), K_2CO_3 (1.08 g, 7.85 mmol), iodomethane (0.67 mL, 10.7 mmol), and acetonitrile (10.0 mL). Purification by flash column chromatography (hexanes/EtOAc = 3:1) provided pyrazole **6a** as a colorless oil (677 mg, 62% yield). ^1H NMR (300 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.86 (s, 1H), 4.28 (q, J = 7.1 Hz, 2H), 3.92 (s, 3H), 1.34 (t, J = 7.1 Hz, 3H).

*(E)-Ethyl 5-(3-Butoxy-3-oxoprop-1-en-1-yl)-1-methyl-1H-pyrazole-4-carboxylate (**6b**).* Purification by flash column chromatography (hexanes/EtOAc = 6:1) provided alkenylated pyrazole **6b** as a brown oil (72 mg, 51% yield). IR (film) 2961, 2874, 1645, 1533, 1467, 1375 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.97−7.81 (m, 2H), 6.85 (d, J = 16.4 Hz, 1H), 4.31 (q, J = 7.1 Hz, 2H), 4.23 (t, J = 6.7 Hz, 2H), 4.00 (s, 3H), 1.74−1.65 (m, 2H), 1.50−1.34 (m, 5H), 0.96 (t, J = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.4, 162.9, 141.6, 139.3, 129.0, 125.6, 114.3, 64.9, 60.5, 38.8, 30.7, 19.2, 14.3, 13.7; HRMS (ESI) calcd for $C_{14}H_{21}N_2O_4$ $[M + H]^+$ 281.1496, found 281.1503.

*1-(1-Methyl-1H-pyrazol-4-yl)ethanone (**7a**).*[26] To a stirred solution of 1*H*-pyrazole (2.00 g, 24.3 mmol) at 25 °C were added acetic anhydride (4.00 mL, 42.5 mmol) and conc. H_2SO_4 (0.020 mL). After heating at 160 °C for 20 h, the reaction mixture was neutralized by 20% aqueous NaOH, treated by water (15 mL) and EtOAc (20 mL) and transferred to a 125 mL separatory funnel. The organic layer was collected, and the aqueous layer was extracted with EtOAc (25 mL × 2). The combined organic layers were washed with brine (20 mL), dried over sodium sulfate, and filtered. The filtrate was concentrated, and the residue was purified by flash column chromatography (hexanes/EtOAc = 2:1) to provide pyrazole **7a** as a white solid (1.47 g, 49% yield). ^1H NMR (300 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.84 (s, 1H), 3.91 (s, 3H), 2.40 (s, 3H).

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*(E)-3-(4-Acetyl-1-methyl-1H-pyrazol-5-yl)-N,N-diethylacrylamide (**7b**).* Purification by flash column chromatography (EtOAc only) provided alkenylated pyrazole **7b** as a brown solid (54 mg, 43% yield). Mp 91−93 °C; IR (film) 3102, 2983, 2937, 1651, 1400, 1313, 1222 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.17 (d, J = 15.2 Hz, 1H), 7.93 (s, 1H), 7.60 (d, J = 15.2 Hz, 1H), 3.99 (s, 3H), 3.60−3.47 (m, 4H), 2.52 (s, 3H), 1.31 (t, J = 7.1 Hz, 3H), 1.20 (t, J = 7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 192.6, 165.3, 142.4, 139.9, 127.1, 125.1, 121.4, 42.5, 41.2, 38.0, 29.1, 15.0, 13.1; HRMS (ESI) calcd for $C_{13}H_{20}N_3O_2$ $[M + H]^+$ 250.1550, found 250.1550.

*(E)-Butyl 3-(4-Acetyl-1-methyl-1H-pyrazol-5-yl)acrylate (**7c**).* Purification by flash column chromatography (hexanes/EtOAc = 3:1) provided alkenylated pyrazole **7c** as a brown oil (61 mg, 49% yield). IR (film) 2960, 2874, 1716, 1670, 1643, 1400, 1222 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.98−7.79 (m, 2H), 6.91 (d, J = 16.4 Hz, 1H), 4.23 (t, J = 6.7 Hz, 2H), 4.00 (s, 3H), 2.49 (s, 3H), 1.74−1.65 (m, 2H), 1.50−1.37 (m, 2H), 0.96 (t, J = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 192.7, 166.4, 141.5, 138.7, 129.3, 126.1, 122.4, 65.0, 38.8, 30.7, 28.9, 19.2, 13.8; HRMS (ESI) calcd for $C_{13}H_{19}N_2O_3$ $[M + H]^+$ 251.1390, found 251.1393.

*1-Butyl-4-chloro-1H-pyrazole (**8a**).* To a stirred solution of 4-chloro-1*H*-pyrazole (1.00 g, 9.75 mmol) in DMF (10.0 mL) at 25 °C were added K_2CO_3 (1.62 g, 11.7 mmol) and 1-bromobutane (1.26 mL, 11.7 mmol). After stirring for 18 h at 25 °C, the reaction mixture was treated with water (15 mL) and EtOAc (20 mL) and transferred to a 125 mL separatory funnel. The organic layer was collected, and the aqueous layer was extracted with EtOAc (25 mL × 2). The organic layers were combined, washed with brine (20 mL), dried over sodium sulfate, and filtered. The filtrate was concentrated, and the residue was purified by flash column chromatography (hexanes/EtOAc = 7:1) to provide pyrazole **8a** as a colorless oil (745 mg, 48% yield). IR (film) 3118, 2961, 2934, 2874, 1450, 1434, 1385 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.40 (s, 1H), 7.35 (s, 1H), 4.06 (t, J = 7.1 Hz, 2H), 1.81 (pentet, J = 7.4 Hz, 2H), 1.31 (sextet, J = 7.4 Hz, 2H), 0.93 (t, J = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.4, 127.0, 109.5, 52.7, 32.3, 19.8, 13.6; HRMS (ESI) calcd for $C_7H_{12}ClN_2$ $[M + H]^+$ 159.0684, found 159.0687.

*(E)-3-(1-Butyl-4-chloro-1H-pyrazol-5-yl)-N,N-diethylacrylamide (**8b**).* The reaction was conducted for 3 h. Purification by flash column chromatography (hexanes/EtOAc = 2:1) provided alkenylated pyrazole **8b** as a yellow oil (95 mg, 67% yield). IR (film) 3104, 2963, 2874, 1651, 1249, 1219 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.57 (d, J = 15.5 Hz, 1H), 7.45 (s, 1H), 7.34 (d, J = 15.4 Hz, 1H), 4.20 (t, J = 7.3 Hz, 2H), 3.55−3.42 (m, 4H), 1.78 (pentet, J = 7.4 Hz, 2H), 1.39−1.24 (m, 5H), 1.20 (t, J = 7.1 Hz, 3H), 0.92 (t, J = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.0, 137.6, 133.3, 125.6, 121.4, 109.7, 50.6, 42.5, 41.3, 32.5, 19.7, 15.0, 13.6, 13.2; HRMS (ESI) calcd for $C_{14}H_{23}ClN_3O$ $[M + H]^+$ 284.1524, found 284.1523.

*4-Chloro-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrazole (**9a**).*[6a] Similar to the synthesis of **5a**, **9a** was prepared from a reaction of 4-chloro-1*H*-pyrazole (3.80 g, 37.1 mmol), sodium hydride 60% in oil (2.20 g, 55.5 mmol), 2-(chloromethoxy)ethyltrimethylsilane (7.20 mL, 40.7 mmol), and THF (18.0 mL). Purification by flash column chromatography (hexanes/EtOAc = 13:1) provided pyrazole **9a** as a colorless oil (8.00 g, 99% yield). ^1H NMR (300 MHz, $CDCl_3$) δ 7.56 (s, 1H), 7.46 (s, 1H), 5.37 (s, 2H), 3.54 (t, J = 8.3 Hz, 2H), 0.90 (t, J = 8.3 Hz, 2H), −0.02 (s, 9H).

*(E)-3-(4-Chloro-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrazol-5-yl)-N,N-diethylacrylamide (**9b**).* Purification by flash column chromatography (hexanes/EtOAc = 3:1) provided alkenylated pyrazole **9b** as a yellow liquid (114 mg, 64% yield). IR (film) 2954, 1655, 1615, 1483, 1462, 1428 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.67 (d, J = 15.7 Hz, 1H), 7.48 (s, 1H), 7.33 (d, J = 15.6 Hz, 1H), 5.49 (s, 2H), 3.60−3.42 (m, 6H), 1.26 (t, J = 7.1 Hz, 3H), 1.19 (t, J = 7.1 Hz, 3H), 0.89 (t, J = 8.3 Hz, 2H), −0.03 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.9, 138.1, 134.9, 125.3, 122.7, 112.0, 79.3, 66.7, 42.5, 41.3, 17.7, 15.1, 13.2, −1.5; HRMS (ESI) calcd for $C_{16}H_{29}ClN_3O_2Si$ $[M + H]^+$ 358.1712, found 358.1714.

*4-Chloro-1-methyl-1H-pyrazole (**10a**).*[27] Similar to the synthesis of **1a**, **10a** was prepared from a reaction of 4-chloro-1*H*-pyrazole (500 mg, 4.88 mmol), K_2CO_3 (1.01 g, 7.32 mmol), iodomethane (0.304 mL, 4.88 mmol), and DMF (8.00 mL). Purification by flash column chromatography (hexanes/EtOAc = 3:1) provided pyrazole **10a** as a colorless oil (392 mg, 69% yield). ^1H NMR (300 MHz, $CDCl_3$) δ 7.40 (s, 1H), 7.34 (s, 1H), 3.86 (s, 3H).

*(E)-3-(4-Chloro-1-methyl-1H-pyrazol-5-yl)-N,N-diethylacrylamide (**10b**).* Purification by flash column chromatography (hexanes/EtOAc = 2:3) provided alkenylated pyrazole **10b** as a yellow solid (66 mg, 55% yield). Mp 101−103 °C; IR (film) 2976, 2935, 1609, 1382, 1328, 1217 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.57 (d, J = 15.9 Hz, 1H), 7.44 (s, 1H), 7.33 (d, J = 15.5 Hz, 1H), 3.93 (s, 3H), 3.55−3.43 (m, 4H), 1.28 (t, J = 7.1 Hz, 3H), 1.20 (t, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.9, 137.5, 134.0, 125.5, 121.5, 110.1, 42.5, 41.3, 38.0, 15.0, 13.2; HRMS (ESI) calcd for $C_{11}H_{17}ClN_3O$ $[M + H]^+$ 242.1055, found 242.1052.

*4-Bromo-1-butyl-1H-pyrazole (**11a**).* To a stirred solution of 4-boromo-1*H*-pyrazole (3.00 g, 20.0 mmol) in DMF (18.0 mL) at 25 °C were added K_2CO_3 (6.90 g, 50.0 mmol) and 1-iodobutane (3.40 mL, 30.0 mmol). After stirring for 13 h at 25 °C, the reaction mixture was treated with water (20 mL) and EtOAc (20 mL) and transferred to a 125 mL separatory funnel. The organic layer was collected, and the aqueous layer was extracted with EtOAc (30 mL × 3). The combined organic layers were washed with brine (20 mL), dried over sodium sulfate, and filtered. The filtrate was concentrated, and the residue was purified by flash column chromatography (hexanes/EtOAc = 7:1) to provide pyrazole **11a** as a colorless oil (3.90 g, 96% yield). IR (film) 3118, 2960, 2934, 2873, 1433, 1380 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.44 (s, 1H), 7.39 (s, 1H), 4.09 (t, J = 7.1 Hz, 2H), 1.82 (pentet, J = 7.4 Hz, 2H), 1.31 (sextet, J = 7.4 Hz, 2H), 0.93 (t, J = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.9, 128.7, 92.1, 52.1, 31.9, 19.3, 13.2; HRMS (ESI) calcd for $C_7H_{12}BrN_2$ $[M + H]^+$ 203.0178, found 203.0167.

*(E)-3-(4-Bromo-1-butyl-1H-pyrazol-5-yl)-N,N-diethylacrylamide (**11b**).* The reaction was conducted for 1 h. Purification by flash column chromatography (hexanes/EtOAc = 5:2) provided alkenylated pyrazole **11b** as a yellow liquid (94 mg, 57% yield). IR (film) 2963, 2933, 2873, 1653, 1611, 1483, 1461 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.56 (d, J = 15.4 Hz, 1H), 7.49 (s, 1H), 7.42 (d, J = 15.5 Hz, 1H), 4.21 (t, J = 7.3 Hz, 2H), 3.57−3.41 (m, 4H), 1.79 (pentet, J = 7.5 Hz, 2H), 1.39−1.24 (m, 5H), 1.20 (t, J = 7.1 Hz, 3H), 0.92 (t, J = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.8, 139.8, 134.4, 125.8, 121.7, 93.8, 50.5, 42.4, 41.3, 32.4, 19.7, 15.0, 13.5, 13.1; HRMS (ESI) calcd for $C_{14}H_{23}BrN_3O$ $[M + H]^+$ 328.1019, found 328.1015.

*4-Bromo-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrazole (**12a**).*[4a] Similar to the synthesis of **5a**, **12a** was prepared from a reaction of 4-bromo-1*H*-pyrazole (1.00 g, 6.80 mmol), sodium hydride 60% in oil (408 mg, 10.2 mmol), 2-(chloromethoxy)ethyltrimethylsilane (1.26 mL, 7.14 mmol), and THF (10.0 mL). Purification by flash column chromatography (hexanes/EtOAc = 20:1) provided pyrazole **12a** as a colorless oil (1.50 g, 80% yield). ^1H NMR (300 MHz, $CDCl_3$) δ 7.59 (s, 1H), 7.50 (s, 1H), 5.39 (s, 2H), 3.54 (t, J = 8.3 Hz, 2H), 0.90 (t, J = 8.3 Hz, 2H), −0.02 (s, 9H).

*(E)-3-(4-Bromo-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrazol-5-yl)-N,N-diethylacrylamide (**12b**).* Purification by flash column chromatography (hexanes/EtOAc = 3:1) provided alkenylated pyrazole **12b** as a yellow oil (82 mg, 41% yield). IR (film) 2954, 2932, 1656, 1615, 1482, 1460 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.64 (d, J = 15.6 Hz, 1H), 7.49 (s, 1H), 7.37 (d, J = 15.6 Hz, 1H), 5.49 (s, 2H), 3.59−3.40 (m, 6H), 1.25 (t, J = 7.0 Hz, 3H), 1.17 (t, J = 7.1 Hz, 3H), 0.88 (t, J = 8.3 Hz, 2H), −0.05 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.0, 140.4, 136.5, 125.9, 123.3, 96.8, 79.4, 66.8, 42.6, 41.4, 17.8, 15.2, 13.3, −1.4; HRMS (ESI) calcd for $C_{16}H_{29}BrN_3O_2Si$ $[M + H]^+$ 402.1207, found 402.1202.

*4-Methyl-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrazole (**13a**).*[28] Similar to the synthesis of **5a**, **13a** was prepared from a reaction of 4-methyl-1*H*-pyrazole (500 mg, 6.09 mmol), sodium hydride 60% in oil (400 mg, 10.0 mmol), 2-(chloromethoxy)ethyltrimethylsilane (1.27 mL, 7.20 mmol), and THF (10.0 mL). Purification by flash column chromatography (hexanes/EtOAc = 12:1) provided pyrazole **13a** as a colorless oil (1.04 g, 80% yield). ^1H

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NMR (300 MHz, $CDCl_3$) δ 7.35 (s, 1H), 7.33 (s, 1H), 5.36 (s, 2H), 3.53 (t, J = 8.3 Hz, 2H), 2.09 (s, 3H), 0.90 (t, J = 8.3 Hz, 2H), −0.03 (s, 3H).

(E)-N,N-Diethyl-3-(4-methyl-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrazol-5-yl)acrylamide (**13b**). Purification by flash column chromatography (hexanes/EtOAc = 2:1) provided alkenylated pyrazole **13b** as a yellow oil (117 mg, 69% yield). IR (film) 2954, 1653, 1612, 1484, 1459, 1427 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.69 (d, J = 15.7 Hz, 1H), 7.34 (s, 1H), 6.93 (d, J = 15.6 Hz, 1H), 5.48 (s, 2H), 3.59 (t, J = 8.3 Hz, 2H), 3.55−3.41 (m, 4H), 2.18 (s, 3H), 1.28−1.16 (m, 6H), 0.89 (t, J = 8.3 Hz, 2H), −0.04 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.4, 140.0, 136.2, 127.5, 120.8, 118.9, 78.7, 66.2, 42.4, 41.2, 17.8, 15.1, 13.2, 10.0, −1.5; HRMS (ESI) calcd for $C_{17}H_{32}N_3O_2Si$ $[M + H]^+$ 338.2258, found 338.2255.

1-Butyl-4-phenyl-1H-pyrazole (**14a**). To an 8 mL glass vial equipped with a magnetic bar were sequentially added Cs_2CO_3 (320 mg, 0.98 mmol), *N*-butyl-4-bromopyrazole **11a** (100 mg, 0.49 mmol), 1,4-dioxane (1.0 mL, 0.50 M), phenylboronic acid (66 mg, 0.54 mmol), $Pd(OAc)_2$ (5.5 mg, 0.0245 mmol), and PCy_3HBF_4 (18 mg, 0.049 mmol). The reaction mixture was purged with nitrogen through a Teflon-lined cap. Then the cap was replaced with a new Teflon-lined solid cap. After moving the reaction vial to a preheated reaction block, the reaction mixture was stirred at 100 °C. After 12 h, the reaction mixture was cooled to 25 °C and concentrated. The residue was purified by flash column chromatography (hexanes/EtOAC = 10:1) to provide pyrazole **14a** as a colorless oil (183 mg, 91% yield). IR (film) 3035, 2959, 2933, 2873, 1608, 1565, 1460 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.78 (s, 1H), 7.63 (s, 1H), 7.48 (d, J = 7.6 Hz, 2H), 7.36 (t, J = 7.6 Hz, 2H), 7.22 (t, J = 7.2 Hz, 1H), 4.15 (t, J = 7.1 Hz, 2H), 1.89 (pentet, J = 7.3 Hz, 2H), 1.36 (sextet, J = 7.5 Hz, 2H), 0.96 (t, J = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.5, 132.7, 128.9, 126.3, 125.9, 125.5, 122.7, 52.2, 32.5, 19.9, 13.7; HRMS (ESI) calcd for $C_{13}H_{17}N_2$ $[M + H]^+$ 201.1386, found 201.1376.

(E)-3-(1-Butyl-4-phenyl-1H-pyrazol-5-yl)-N,N-diethylacrylamide (**14b**). Purification by flash column chromatography (hexanes/EtOAc = 3:2) provided alkenylated pyrazole **14b** as a yellow oil (86 mg, 53% yield). IR (film) 2962, 2932, 2873, 1651, 1609, 1486, 1462 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.63 (d, J = 15.4 Hz, 1H), 7.48 (s, 1H), 7.43−7.34 (m, 4H), 7.33−7.28 (m, 1H), 6.48 (d, J = 15.5 Hz 1H), 4.25 (t, J = 7.3 Hz, 2H), 3.39 (q, J = 7.1 Hz, 2H), 3.01 (q, J = 7.0 Hz, 2H), 1.86, (pentet, J = 7.5 Hz, 2H), 1.39 (sextet, J = 7.5 Hz, 2H), 1.12 (t, J = 7.1 Hz, 3H), 0.96 (t, J = 7.3 Hz, 3H), 0.88 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.1, 138.7, 134.4, 133.8, 129.2, 128.8, 127.4, 127.2, 122.9, 121.2, 50.0, 42.1, 41.2, 32.8, 20.0, 14.9, 13.8, 13.2; HRMS (ESI) calcd for $C_{20}H_{28}N_3O$ $[M + H]^+$ 326.2227, found 326.2221.

2-Methyl-2H-indazole (**15a**).[29] To a stirred solution of 1*H*-indazole (1.00 g, 8.47 mmol) in acetone (10.0 mL) at 0 °C was added potassium hydroxide (1.41 g, 25.2 mmol). After stirring for 1 h at 0 °C, iodomethane (0.98 mL, 15.7 mmol) was added to the flask, and the mixture was stirred for 15 h at 25 °C. The potassium hydroxide was removed by filtration and the filtrate was concentrated, and the residue was purified by flash column chromatography (hexanes/EtOAc = 1:1) provided indazole **15a** as a brown oil (421 mg, 38% yield) and indazole **16a** as a yellow solid (619 mg, 55% yield). ^1H NMR (300 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.73−7.60 (m, 2H), 7.36−7.26 (m, 1H), 7.14−7.04 (m, 1H), 4.23 (s, 3H).

1-Methyl-1H-indazole (**16a**).[29] ^1H NMR (300 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.74 (d, J = 8.1 Hz, 1H), 7.41 (d, J = 3.7 Hz, 2H), 7.22−7.09 (m, 1H), 4.10 (s, 3H).

(E)-N,N-Diethyl-3-(2-methyl-2H-indazol-3-yl)acrylamide (**15b**). Purification by flash column chromatography (hexanes/EtOAc = 1:3) provided alkenylated indazole **15b** as an orange oil (83 mg, 64% yield). IR (film) 2975, 2933, 1642, 1594, 1487, 1447 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.94 (d, J = 15.3 Hz, 1H), 7.74 (t, J = 9.7 Hz, 2H), 7.32 (t, J = 7.6 Hz, 1H), 7.19 (t, J = 7.5 Hz, 1H), 7.06 (d, J = 15.3 Hz, 1H), 4.24 (s, 3H), 3.60−3.43 (m, 4H), 1.31 (t, J = 7.0 Hz, 3H), 1.20 (t, J = 7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.1, 147.9, 131.1, 127.6, 126.1, 123.4, 120.7, 119.7, 118.6, 118.1, 42.4, 41.3, 38.5, 15.1, 13.2; HRMS (ESI) calcd for $C_{15}H_{20}N_3O$ $[M + H]^+$ 258.1601, found 258.1603.

(E)-Butyl 3-(2-Methyl-2H-indazol-3-yl)acrylate (**15c**).[9] Purification by flash column chromatography (hexanes/EtOAc = 4:1) provided alkenylated indazole **15c** (93 mg, 72% yield). ^1H NMR (300 MHz, $CDCl_3$) δ 7.93 (d, J = 15.9 Hz, 1H), 7.87 (d, J = 8.4 Hz, 1H), 7.75 (d, J = 8.6, 1H), 7.40−7.32 (m, 1H), 7.28−7.22 (m, 2H), 6.67 (d, J = 15.9 Hz, 1H), 4.35−4.19 (m, 5H), 1.78−1.67 (m, 2H), 1.54−1.40 (m, 2H), 0.99 (t, J = 7.3 Hz, 3H).

(E)-N,N-Diethyl-3-(1-methyl-1H-indazol-3-yl)acrylamide (**16b**). Purification by flash column chromatography (hexanes/EtOAc = 5:1) provided alkenylated indazole **16b** as a yellow oil (54 mg, 42% yield). Mp 103−105 °C; IR (film) 2974, 2932, 1650, 1602, 1490, 1449 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.03 (d, J = 15.4 Hz, 1H), 7.90 (d, J = 8.1 Hz, 1H), 7.57−7.41 (m, 2H), 7.35−7.14 (m, 2H), 4.13 (s, 3H), 3.65−3.49 (m, 4H), 1.32 (t, J = 6.8 Hz, 3H) 1.23 (t, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.8, 141.1, 140.3, 132.4, 126.6, 123.0, 121.6, 120.3, 118.2, 109.4, 42.4, 41.1, 35.8, 15.2, 13.3; HRMS (ESI) calcd for $C_{15}H_{20}N_3O$ $[M + H]^+$ 258.1601, found 258.1603.

(E)-4-Nitro-1-(4-phenylbut-3-en-1-yl)-1H-pyrazole (**17a**). To a stirred solution of 4-nitro-1*H*-pyrazole (1.00 g, 8.84 mmol) in DMF (5.00 mL) at 25 °C were added K_2CO_3 (1.47 g, 10.6 mmol) and 4-bromo-1-butene (1.08 mL, 10.61 mmol). After 14 h, the reaction mixture was treated with water (15 mL) and EtOAc (20 mL). After shaking in a 125 mL separatory funnel, the separated aqueous phase was extracted with EtOAc (20 mL × 2). The combined organic layers were washed with brine (20 mL), dried over sodium sulfate, and filtered. The filtrate was concentrated, and the residue was purified by flash column chromatography (hexane/EtOAc = 4:1) to provide 1-(but-3-en-1-yl)-4-nitro-1*H*-pyrazole as a white solid (1.47 mg, 99% yield). ^1H NMR (300 MHz, $CDCl_3$) δ 8.10 (s, 1H), 8.08 (s, 1H), 5.85−5.62 (m, 1H), 5.19−4.98 (m, 2H), 4.22 (t, J = 6.9 Hz, 2H), 2.65 (q, J = 6.9 Hz, 2H). Following a reported procedure, the Heck reaction was carried out.[30] To an 8 mL glass vial equipped with a magnetic bar were sequentially added 1-(but-3-en-1-yl)-4-nitro-1*H*-pyrazole (167 mg, 1.0 mmol), *N,N*-diisopropylethylamine (281 μL, 2.0 mmol), acetonitrile (2.00 mL, 0.50 M), bromobenzene (105 μL, 1.0 mmol), $Pd(OAc)_2$ (11.2 mg, 0.050 mmol), and P(*o*-tolyl)$_3$ (45.6 mg, 0.15 mmol). The reaction mixture was purged with nitrogen through a Teflon-lined cap followed by replacement with a new Teflon-lined solid cap. After the reaction vial was moved to a preheated reaction block, the reaction mixture was stirred at 90 °C. After 6 h, the reaction mixture was cooled to 25 °C and concentrated. The residue was purified by flash column chromatography (hexanes/EtOAc = 11:2) to provide pyrazole **17a** as a yellow solid (143 mg, 59% yield). Mp 123−124 °C; IR (film) 3131, 3027, 1530, 1509, 1408, 1301 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.13 (s, 1H), 8.10 (s, 1H), 7.39−7.14 (m, 5H), 6.43 (d, J = 15.8 Hz, 1H), 6.18−5.98 (m, 1H), 4.28 (t, J = 6.9 Hz, 2H), 2.82 (q, J = 6.9 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.6, 135.9, 135.6, 133.8, 128.7, 128.6, 127.8, 126.2, 124.1, 53.2, 33.3; HRMS (EI) calcd for $C_{13}H_{13}N_3O_2$ $[M]^+$ 243.1008, found 243.1010.

(E)-4-Benzylidene-3-nitro-5,6-dihydro-4H-pyrrolo[1,2-b]pyrazole (**17b**). For the intramolecular alkenylation reaction, **17a** (73 mg, 0.30 mmol), 1,4-dioxane (3.0 mL, 0.10 M), $Cu(OAc)_2{\cdot}H_2O$ (120 mg, 0.60 mmol), pyridine (4.8 μL, 0.060 mmol), and $Pd(OAc)_2$ (6.7 mg, 0.030 mmol) were used. Purification by flash column chromatography (hexanes/EtOAc = 3:1) provided alkenylated pyrazole **17b** as a yellow solid (34 mg, 47% yield). Mp 144−146 °C. IR (film) 2924, 1539, 1495, 1427, 1388, 1304 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.16 (s, 2H), 7.58−7.30 (m, 5H), 4.39 (t, J = 6.7 Hz, 2H), 3.69−3.55 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.0, 131.8, 129.5, 128.9, 128.7, 125.7, 48.3, 32.4, 29.8; HRMS (ESI) calcd for $C_{13}H_{12}N_3O_2$ $[M + H]^+$ 242.0924, found 242.0928.

(E)-Ethyl 4-(4-(4-Nitro-1H-pyrazol-1-yl)but-1-en-1-yl)benzoate (**18a**). To an 8 mL glass vial equipped with a magnetic bar were sequentially added 1-(but-3-en-1-yl)-4-nitro-1*H*-pyrazole, the intermediate in the preparation of **17a** (134 mg, 0.80 mmol), *N,N*-diisopropylethylamine (279 μL, 1.6 mmol), acetonitrile (1.60 mL, 0.50 M), ethyl-4-bromobenzoate (131 μL, 0.80 mmol), $Pd(OAc)_2$ (18.0 mg, 0.080 mmol), and P(*o*-tolyl)$_3$ (73.0 mg, 0.24 mmol). The reaction

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mixture was purged with nitrogen through a Teflon-lined cap followed by replacement with a new Teflon-lined solid cap. After the reaction vial was moved to a preheated reaction block, the reaction mixture was stirred at 90 °C. After 6 h, the reaction mixture was cooled to 25 °C and concentrated. The residue was purified by flash column chromatography (hexanes/EtOAc = 5:2) to provide pyrazole **18a** as a white solid (152 mg, 60% yield). Mp 99−100 °C; IR (film) 3130, 2982, 1711, 1607,1531, 1510, 1408, 1302 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.13 (s, 1H), 8.10 (s, 1H), 7.98 (d, J = 8.3 Hz, 2H), 7.35 (d, J = 8.3 Hz, 2H), 6.46 (d, J = 15.5 Hz, 1H), 6.29−6.13 (m, 1H), 4.45−4.25 (m, 4H), 2.85 (q, J = 7.2 Hz, 2H), 1.39 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.3, 140.9, 135.9, 135.6, 132.9, 129.9, 129.5, 128.6, 126.9, 126.0, 61.0, 52.9, 33.4, 14.4; HRMS (ESI) calcd for $C_{16}H_{18}N_3O_4$ $[M + H]^+$ 316.1292, found 316.1299.

*(E)-Ethyl 4-((3-Nitro-5,6-dihydro-4H-pyrrolo[1,2-b]pyrazol-4-ylidene)methyl)benzoate (**18b**).* For the intramolecular alkenylation reaction, **18a** (79 mg, 0.25 mmol), 1,4-dioxane (2.5 mL, 0.10 M), $Cu(OAc)_2{\cdot}H_2O$ (100 mg, 0.50 mmol), pyridine (4.0 μL, 0.050 mmol), and $Pd(OAc)_2$ (5.6 mg, 0.025 mmol) were used. Purification by flash column chromatography (hexanes/EtOAc = 9:4) provided alkenylated pyrazole **18b** as a yellow solid (44 mg, 56% yield). Mp 161−163 °C. IR (film) 3101, 2979, 1715, 1605, 1538, 1411, 1387 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.20 (s, 2H), 8.10 (d, J = 7.4 Hz, 2H), 7.54 (d, J = 7.8 Hz, 2H), 4.48−4.35 (m, 4H), 3.66 (t, J = 5.1 Hz, 2H), 1.42 (t, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.1, 146.2, 143.4, 142.0, 140.2, 130.4, 130.1, 130.0, 129.2, 127.8, 61.3, 48.3, 32.5, 14.4; HRMS (ESI) calcd for $C_{16}H_{15}N_3O_4Na$ $[M + Na]^+$ 336.0955, found 336.0959.

*(E)-4-Nitro-1-(5-phenylpent-4-en-1-yl)-1H-pyrazole (**19a**).* Following a reported procedure, the Heck reaction was carried out.[30] To an 8 mL glass vial equipped with a magnetic stir bar were sequentially added **20a** (181 mg, 1.0 mmol), *N*,*N*-diisopropylethylamine (0.350 μL, 2.0 mmol), acetonitrile (2.00 mL, 0.50 M), bromobenzene (105 μL, 1.0 mmol), $Pd(OAc)_2$ (11.2 mg, 0.050 mmol), and P(*o*-tolyl)$_3$ (45.7 mg, 0.15 mmol). The reaction mixture was purged with argon through a Teflon-lined cap followed by replacement with a new Teflon-lined solid cap. After the reaction vial was moved to a preheated reaction block, the reaction mixture was stirred at 90 °C. After 12 h, the reaction mixture was cooled to 25 °C and concentrated. The residue was purified by recrystallization with EtOAc and hexanes to provide pyrazole **19a** as a white solid (57 mg, 22% yield). Mp 66−67 °C; IR (film) 3131, 3024, 2922, 1529, 1480, 1369 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.13 (s, 1H), 8.09 (s, 1H), 7.37−7.27 (m, 4H), 7.24−7.18 (m, 1H), 6.41 (d, J = 16.2 Hz, 1H), 6.22−6.06 (m, 1H), 4.20 (t, J = 6.7 Hz, 2H), 2.26 (q, J = 7.2 Hz, 2H), 2.11 (d, J = 7.3 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.1, 136.0, 131.8, 128.7, 128.6, 128.0, 127.5, 126.1, 52.8, 29.8, 29.2; HRMS (EI) calcd for $C_{14}H_{15}N_3O_2$ $[M]^+$ 257.1164, found 257.1163.

*(E)-4-Benzylidene-3-nitro-4,5,6,7-tetrahydropyrazolo[1,5-a]pyridine (**19b**).* For the intramolecular alkenylation reaction, **19a** (38 mg, 0.15 mmol), 1,4-dioxane (1.5 mL, 0.10 M), $Cu(OAc)_2{\cdot}H_2O$ (60 mg, 0.30 mmol), pyridine (2.4 μL, 0.030 mmol), and $Pd(OAc)_2$ (3.4 mg, 0.015 mmol) were used. Purification by flash column chromatography (hexanes/EtOAc = 7:2) provided alkenylated pyrazole **19b** as a yellow solid (21 mg, 56% yield). Mp 77−78 °C; IR (film) 2929, 1523, 1426, 1343, 1254 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.20 (s, 1H), 8.09 (s, 1H), 7.48−7.28 (m, 5H), 4.29 (t, J = 6.2 Hz, 2H), 2.89 (t, J = 5.5 Hz, 2H), 2.10 (pentet, J = 6.3 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.8, 138.2, 136.2, 135.9, 129.5, 128.5, 128.1, 123.4, 49.6, 25.2, 22.7; HRMS (ESI) calcd for $C_{14}H_{14}N_3O_2$ $[M + H]^+$ 256.1081, found 256.1073.

*4-Nitro-1-(pent-4-en-1-yl)-1H-pyrazole (**20a**).* To a stirred solution of 4-nitro-1*H*-pyrazole (500 mg, 4.42 mmol) in DMF (3.00 mL) at 25 °C were added K_2CO_3 (732 mg, 5.30 mmol) and 5-bromo-1-pentene (0.630 mL, 5.30 mmol). After 13 h, the reaction mixture was treated with water (15 mL) and EtOAc (20 mL). After shaking in a 125 mL separatory funnel, the separated aqueous phase was extracted with EtOAc (20 mL × 2). The combined organic layers were washed with brine (20 mL), dried over sodium sulfate, and filtered. The filtrate was concentrated, and the residue was purified by flash column chromatography (hexanes/EtOAc = 6:1) to provide pyrazole **20a** as a yellow oil (757 mg, 94% yield). IR (film) 3133, 3079, 2978, 2940, 2852, 1506, 1407, 1302 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.11 (s, 1H), 8.08 (s, 1H), 5.89−5.63 (m, 1H), 5.16−4.94 (m, 2H), 4.16 (t, J = 6.6 Hz, 2H), 2.13−1.96 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.4, 135.8, 135.6, 128.5, 116.5, 52.7, 30.3, 28.7; HRMS (ESI) calcd for $C_8H_{12}N_3O_2$ $[M + H]^+$ 182.0924, found 182.0914.

*4-Methylene-3-nitro-4,5,6,7-tetrahydropyrazolo[1,5-a]pyridine (**20b**).* For the intramolecular alkenylation reaction, **20a** (91 mg, 0.50 mmol), 1,4-dioxane (5.0 mL, 0.10 M), $Cu(OAc)_2{\cdot}H_2O$ (200 mg, 1.0 mmol), pyridine (8.1 μL, 0.10 mmol), and $Pd(OAc)_2$ (11 mg, 0.050 mmol) were used. Purification by flash column chromatography (hexanes/EtOAc = 4:1) provided alkenylated pyrazole **20b** as a yellow solid (40 mg, 45% yield). Mp 44−47 °C; IR (film) 3129, 2966, 2855, 1531, 1504, 1417 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.17 (s, 1H), 6.61 (s, 1H), 5.65 (s, 1H), 4.28 (t, J = 6.2 Hz, 2H), 2.71−2.54 (m, 2H), 2.21−2.07 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.4, 136.7, 130.0, 128.8, 122.1, 49.7, 31.0, 22.7; HRMS (ESI) calcd for $C_8H_{10}N_3O_2$ $[M + H]^+$ 180.0768, found 180.0767.

*1-(Hex-5-en-1-yl)-4-nitro-1H-pyrazole (**21a**).* Similar to the synthesis of **20a**, **21a** was prepared from a reaction of 4-nitro-1*H*-pyrazole (599 mg, 5.30 mmol), K_2CO_3 (879 mg, 6.36 mmol), 6-bromo-1-hexene (0.850 mL, 6.36 mmol), and DMF (8.00 mL). Purification by flash column chromatography (hexanes/EtOAc = 5:1) provided pyrazole **21a** as a white solid (1.01 g, 98% yield). Mp 27−29 °C; IR (film) 3134, 3077, 2933, 2860, 1530, 1510 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.12 (s, 1H), 8.07 (s, 1H), 5.85−5.67 (m, 1H), 5.12−4.87 (m, 2H), 4.15 (t, J = 7.1 Hz, 2H), 2.16−2.04 (m, 2H), 1.99−1.87 (m, 2H), 1.48−1.35 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.6, 135.5, 128.4, 115.2, 53.2, 32.9, 29.0, 25.4; HRMS (ESI) calcd for $C_9H_{14}N_3O_2$ $[M + H]^+$ 196.1081, found 196.1074.

*4-Methylene-3-nitro-5,6,7,8-tetrahydro-4H-pyrazolo[1,5-a]-azepine (**21b**).* For the intramolecular alkenylation reaction, **21a** (98 mg, 0.50 mmol), 1,4-dioxane (5.0 mL, 0.10 M), $Cu(OAc)_2{\cdot}H_2O$ (200 mg, 1.0 mmol), pyridine (8.1 μL, 0.10 mmol), and $Pd(OAc)_2$ (11 mg, 0.050 mmol) were used. Purification by flash column chromatography (hexanes/EtOAc = 4:1) provided alkenylated pyrazole **21b** as a white solid (56 mg, 58% yield). Mp 58−60 °C; IR (film) 3126, 2937, 2857, 1549, 1504, 1466 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.01 (s, 1H), 5.73 (s, 1H), 5.52 (s, 1H), 4.26 (t, J = 4.9 Hz, 2H), 2.47 (t, J = 5.6 Hz, 3H), 1.98−1.86 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.5, 135.9, 134.2, 124.6, 54.8, 35.4, 30.6, 26.8; HRMS (ESI) calcd for $C_9H_{12}N_3O_2$ $[M + H]^+$ 194.0924, found 194.0925.

*Butyl 1-Methyl-1,4-dihydropyrrolo[3,2-c]pyrazole-5-carboxylate (**22**).* To an 8 mL glass vial equipped with a magnetic bar were sequentially added **2a** (121 mg, 0.48 mmol), PPh_3 (315 mg, 1.20 mmol), and *o*-dichlorobenzene (2.00 mL, 0.24 M). The reaction mixture was stirred at 180 °C. After 24 h, the reaction mixture was cooled to 25 °C. The residue was purified by flash column chromatography (hexanes/EtOAC = 3:1) to provide pyrazole **22** as a brown solid (54 mg, 51% yield). Mp 89−90 °C; IR (film) 3227, 2954, 2869, 1694, 1528, 1455 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.44 (br s, 1H), 7.37 (s, 1H), 6.70 (s, 1H), 4.32 (t, J = 6.6 Hz, 2H), 3.96 (s, 3H), 1.74 (pentet, J = 7.0 Hz, 2H), 1.47 (sextet, J = 7.4 Hz, 2H), 0.98 (t, J = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.4, 138.6, 130.4, 129.5, 119.3, 93.7, 64.9, 37.3, 30.8, 19.3, 13.8; HRMS (ESI) calcd for $C_{11}H_{16}N_3O_2$ $[M + H]^+$ 222.1237, found 222.1231.

*1-Methyl-5-phenyl-1,4-dihydropyrrolo[3,2-c]pyrazole (**23**).* To an 8 mL glass vial equipped with a magnetic bar were sequentially added **2f** (115 mg, 0.50 mmol), PPh_3 (328 mg, 1.25 mmol), and *o*-dichlorobenzene (2.00 mL, 0.25 M). The reaction mixture was stirred at 180 °C. After 36 h, The reaction mixture was cooled to 25 °C. The residue was purified by flash column chromatography (hexanes/EtOAc = 2:3) to provide pyrazole **23** as a brown solid (54 mg, 55% yield). Mp 185−186 °C; IR (film) 3177, 3062, 2931, 2854, 1602, 1503 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.83 (br s, 1H), 7.58−7.56 (m, 2H), 7.42 (t, J = 7.7 Hz, 2H), 7.34−7.31 (m, 2H), 6.34 (s, 1H), 3.97 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.7, 140.4, 133.2, 129.1, 128.3, 127.7, 124.9, 118.9, 86.7, 37.3; HRMS (ESI) calcd for $C_{12}H_{12}N_3$ $[M + H]^+$ 198.1026, found 198.1026.

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*(Z)-2-(4,5-Diphenyl-1-((2-(trimethylsilyl)ethoxy)methyl)cyclopenta[c]pyrazol-6(1H)-ylidene)-N,N-diethylacetamide (**24**).* To an 8 mL glass vial equipped with a magnetic bar were sequentially added K_2CO_3 (116 mg, 0.84 mmol), **12b** (170 mg, 0.42 mmol), *N,N*-dimethylacetamide (1.0 mL, 0.42 M), 1.2-diphenylacetylene (75 mg, 0.42 mmol), $Pd(OAc)_2$ (4.7 mg, 0.021 mmol), and PCy_3HBF_4 (23 mg, 0.063 mmol). The reaction mixture was purged with nitrogen through a Teflon-lined cap. Then the cap was replaced with a new Teflon-lined solid cap. After moving the reaction vial to a preheated reaction block, the reaction mixture was stirred at 120 °C. After 14 h, the reaction mixture was cooled to 25 °C and concentrated. The residue was purified by flash column chromatography (hexanes/EtOAc = 9:2) to provide pyrazole **24** as a red oil (125 mg, 60% yield). IR (film) 2952, 2895, 1625, 1488, 1458, 1432 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.49 (s, 1H), 7.39−7.27 (m, 6H), 7.26−7.19 (m, 4H), 6.38 (s, 1H), 5.64 (s, 2H), 3.54−3.41 (m, 4H), 3.30 (q, J = 7.1 Hz, 2H), 1.21 (t, J = 7.2 Hz, 3H), 1.11 (t, J = 7.1, 3H), 0.84 (t, J = 8.5 Hz, 2H), −0.04 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.6, 140.5, 135.9, 135.0, 134.7, 134.5, 134.3, 133.9, 131.0, 130.2, 128.6, 128.5, 128.2, 127.9, 127.6, 126.0, 80.4, 66.1, 43.1, 40.0, 17.8, 14.0, 13.1, −1.4; HRMS (ESI) calcd for $C_{30}H_{38}N_3O_2Si$ $[M + H]^+$ 500.2728, found 500.2739.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02398.

^1H and ^{13}C spectra for all new compounds (PDF)

Crystallographic data for **17b** (CIF)

Crystallographic data for **19b** (CIF)

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Notes

The authors declare no competing financial interest.

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