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Synthesis of Pyrazoles via Electrophilic Cyclization

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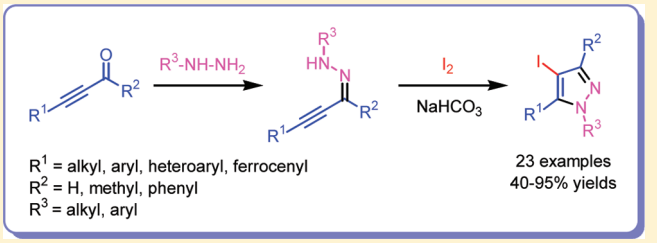
Supporting Information

ABSTRACT: Electrophilic cyclizations of α,β-alkynic hydrazones by molecular iodine were investigated for the synthesis of 4-iodopyrazoles. α,β-Alkynic hydrazones were readily prepared by the reactions of hydrazines with propargyl aldehydes and ketones. When treated with molecular iodine in the presence of sodium bicarbonate, α,β-alkynic hydrazones underwent electrophilic cyclization to afford 4-iodopyrazoles in good to high yields. Iodocyclization was general for a wide range of α,β-alkynic hydrazones and tolerated the presence of aliphatic, aromatic, heteroaromatic, and ferrocenyl moieties with electron-withdrawing and electron-donating substituents.



INTRODUCTION

Pyrazoles have occupied a unique position in the design and synthesis of novel biologically active agents that exert remarkable medicinal activities.[1] In fact, pyrazoles have been studied for over a century as an important class of heterocyclic compounds[2] and still continue to attract considerable attention due to the broad range of biological activities they possess, including analgesic,[3] antibacterial,[4] antidepressant,[5] anti-inflammatory,[6,7] antimicrobial,[6b,8] antiobesity,[9] antiviral,[10] appetite suppressant,[11] cholesterol-lowering,[12] hypoglycemic,[13] antihypertensive,[14] and anticancer[15] properties. In addition, pyrazoles are attractive building blocks for pharmaceutical and agricultural research, since they are present in the structures of a variety of leading drugs and pesticides, including Celebrex,[7] Viagra,[16] and Zometapine[17] and Cyenopyrafen,[18] Fenpyroximate,[19] and Tebufenpyrad.[20] Pyrazoles are generally synthesized by (i) the reaction of 1,3-dicarbonyl compounds with hydrazines,[21] (ii) the reaction of α,β-unsaturated or doubly unsaturated aldehydes or ketones with hydrazines,[22] and (iii) 1,3-dipolar cycloaddition of diazoalkanes or nitrilimines with alkenes or alkynes[23] and are occasionally prepared by (iv) the functionalization of unsubstituted or less substituted pyrazoles.[24] The first method often provides a mixture of regioisomers when the reactivity of the two carbonyl groups is not significantly different. The second method, which is in fact a modification of the first method where a 1,3-dicarbonyl compound is replaced by an α,β-unsaturated carbonyl compound, also furnishes a range of regioselectivities depending upon reaction conditions and substrates. The third method is often highly regioselective, but 1,3-dipolar species are relatively difficult to prepare and are potentially explosive. The fourth method generally requires multistep synthesis in a linear way. As a consequence, there is an increasing interest in developing new methods for the synthesis of substituted pyrazole derivatives. Although numerous methods have been developed and new variants continue to appear,[25] regiocontrolled synthesis of pyrazole derivatives remains a significant challenge for organic chemists.

We have recently reported the synthesis of ferrocenyl-substituted pyrazoles by the reaction of (2-formyl-1-chlorovinyl)-ferrocene (**1**) with hydrazines or hydrazinium salts (**2**) (Scheme 1).[26] Depending upon the substitution pattern of hydrazine, the reaction produces 1-alkyl/aryl-5-ferrocenylpyrazole (**3**, 1,5-isomer) and/or 1-alkyl/aryl-3-ferrocenylpyrazole (**4**, 1,3-isomer), the former being the single or the major product of the reaction in most cases. In connection with this study, we have investigated the reactions of 3-ferrocenylpropynal (**5**) with hydrazinium salts (**2**) as well (Scheme 1).[27] These reactions have afforded pyrazoles **3** and/or **4** in relatively higher yields, but in most cases, the proportion of 1,3-pyrazole isomers **4** has increased at the expense of 1,5-pyrazole isomer **3**. It is worth mentioning that in reactions with 3-ferrocenylpropynal (**5**), if hydrazines are used instead of hydrazinium salts, pyrazoles form in very low yields. As anticipated, when hydrazinium salts are employed, the reaction medium becomes slightly acidic and pyrazoles are obtained in good yields. Apparently, acid catalyzes the reaction, but in this case, the reaction leads to formation of a mixture of pyrazoles **3** and **4**, consistent with the findings of other investigators using similar systems.[22i,28] As previously noted, these reactions proceed through corresponding hydrazone and/or conjugated addition intermediates, depending upon the nature of the substituent in hydrazine derivatives **2**.[26,27]

Recently, electrophilic cyclizations have emerged as valuable tools in organic synthesis, since they often occur both under very mild reaction conditions and in a regioselective manner.[29] In particular, electrophilic cyclization of functionally substituted alkynes has been recognized as an attractive way to synthesize a variety of important heterocycles and carbocycles,[30] including furans,[31] benzofurans,[32] thiophenes,[33] benzothiophenes,[34] bicyclic β-lactams,[35] chromones,[36] cyclic carbonates,[37] isoxazoles,[38] indoles,[39] isocoumarins,[40] isochromenes,[41] isoindolinones,[42]

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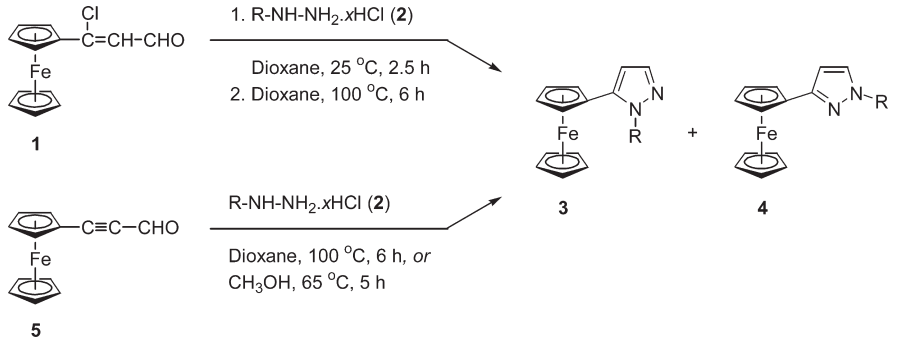
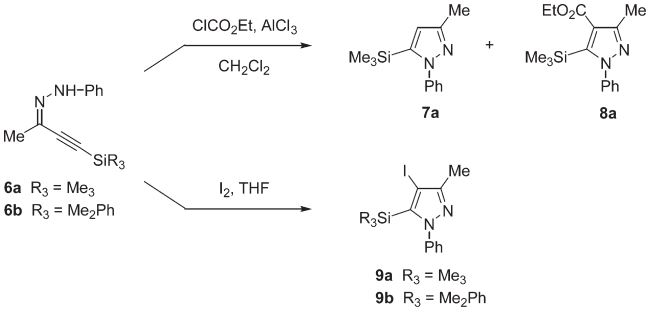
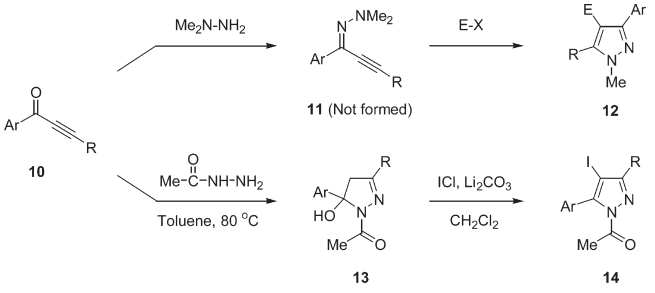
Scheme 1



Scheme 2

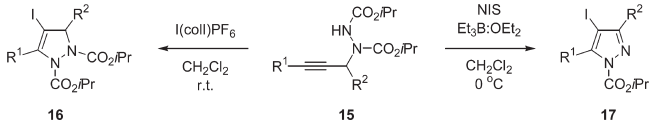


Scheme 3



naphthalenes,[43] and quinolines.[44] We reasoned that electrophilic cyclization of hydrazones of acetylenic aldehydes and ketones, which can be easily prepared from hydrazines and acetylenic aldehydes and ketones, would provide a rapid entry to a wide variety of pyrazole derivatives, particularly 4-iodopyrazoles, in a regiocontrolled manner. Surprisingly, a search of the literature revealed very few reports concerning electrophilic cyclization of such alkynes to afford pyrazoles. Gonzales-Nogal synthesized 5-silylpyrazoles **7**−**9** by electrophilic cyclization of β-silyl-substituted acetylenic hydrazones **6**, using ethyl chloroformate, aluminum chloride, and molecular iodine (Scheme 2).[45] An obstacle in this study was the preparation of intermediate hydrazones **6**, since on some occasions the condensation of silylated acetylenic ketones with hydrazines was very complicated or the desilylation of acetylenic ketones occurred in acidic medium. The Larock research group has recently aimed to study electrophilic cyclization of acetylenic *N*,*N*-dimethylhydrazones **11** to afford

Scheme 4



4-halopyrazoles **12**, but they were unable to prepare the requisite hydrazones **11** (Scheme 3).[46] Therefore, they developed an alternative route to 4-iodopyrazoles **14** through dehydration of the resulting dihydropyrazoles **13** followed by iodination, which does not involve electrophilic cyclization. Very recently, the Wada research group synthesized dihydropyrazoles **16** and pyrazoles **17** from propargylic hydrazides **15** by reagent-controlled iodocyclization (Scheme 4).[47] Interestingly, in the formation of dihydropyrazoles **16**, overoxidation to pyrazoles **17** is controlled by the conditions of iodocyclization. However, depending upon the reaction conditions, further oxidation of the in situ formed dihydropyrazoles yields pyrazole derivatives **17**.

Our continued interest in the synthesis of new pyrazole derivatives as potential pharmaceuticals has prompted us to investigate electrophilic cyclizations of acetylenic aldehydes and ketones through their hydrazones. We have found that, upon treatment with molecular iodine in the presence of sodium bicarbonate, acetylenic hydrazones, prepared readily from hydrazines and acetylenic aldehydes and ketones, undergo electrophilic cyclization to afford 4-iodopyrazole derivatives in good to excellent yields.[48] We herein report the full details of this study.

RESULTS AND DISCUSSION

The necessary α,β-acetylenic aldehydes and ketones (**5** and **19**) can be easily synthesized according to known literature procedures, as illustrated in Scheme 5. The lithiation of terminal alkynes **18a**−**f** with *n*-BuLi generates the corresponding lithium acetylides in situ, the formylation of which with DMF leads to α,β-acetylenic aldehydes **19a**−**f** in good to excellent yields.[49] Note that a reverse quench into a phosphate buffer has proved to be the key for these high-yielding formylation reactions. In particular, 3-ferrocenylpropynal (**5**) can be prepared from ethynylferrocene (**20**) by a similar formylation reaction.[50] On the other hand, the treatment of in situ generated lithium acetylide with $ZnCl_2$, followed by coupling of the resulting zinc acetylides with acetyl chloride, affords the acetylenic methyl ketone **19g** (Scheme 5).[51] The acetylenic phenyl ketone **19h** can be

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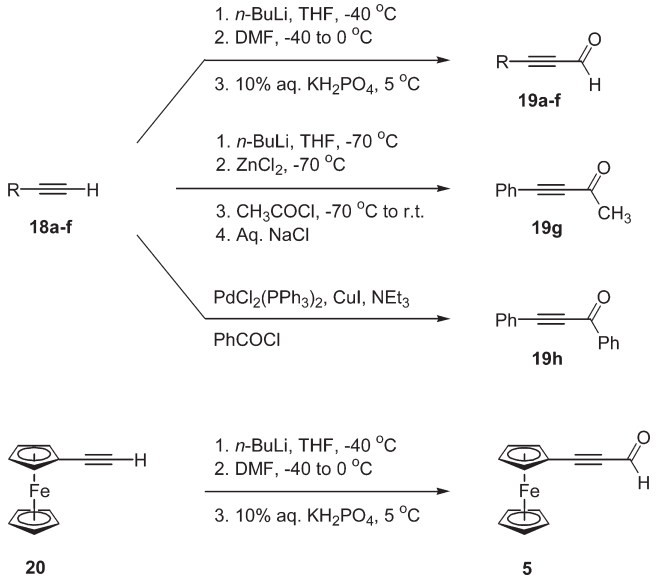
synthesized directly from benzoyl chloride and terminal alkyne via a palladium-catalyzed coupling reaction.[52]

With α,β-acetylenic aldehydes and ketones **5** and **19** in hand, we next prepared their hydrazone derivatives **22** and **23** (Scheme 6). Condensation reactions between hydrazines **21** and acetylenic aldehydes and ketones **5** and **19** were carried out in refluxing dioxane at 100 °C (condition A) or in the absence of solvent at 80 °C (condition B). The results are summarized in Tables 1 and 2. In these reactions, a variety of hydrazines and α,β-acetylenic aldehydes and ketones was employed. From the reactions of 3-alkyl or 3-aryl-substituted propargyl aldehydes and ketones **19**, *Z* isomers of acetylenic hydrazones, ***Z*-22**, were obtained as major products while *E* isomers, ***E*-22**, were formed as minor products. Under the reaction conditions, *E* isomers ***E*-22** were found not to be so stable that they partially converted into *Z* isomers ***Z*-22**. We noticed that keeping the reaction time longer minimized the formation of *E* isomers ***E*-22**, since they converted into *Z* isomers to some extent. Importantly, during flash chromatography as well as on standing at room temperature in a solvent, most derivatives of *E* isomers ***E*-22** slowly started to convert into *Z* isomers ***Z*-22**. For this reason, the isolation of *E* isomers ***E*-22** was not attempted. On the other hand, we were able to isolate most derivatives of both the *Z* and *E* isomers of ferrocenyl-substituted acetylenic hydrazones, ***Z*-23** and ***E*-23**, as shown in Table 2. Notably, ferrocenyl-substituted acetylenic hydrazones ***Z*-23** and/or ***E*-23** were quite stable to purification and the isomerization of hydrazones ***E*-23** into ***Z*-23** was very slow. However, it should be mentioned that the reaction between 3-ferrocenylpropynal (**5**) and 2-(hydroxyethyl)hydrazine (**21e**) afforded exclusively *Z*-hydrazone ***Z*-23e** (Table 2).

E and *Z* isomers of acetylenic hydrazone derivatives **22** and **23** can easily be differentiated on the basis of their ^{13}C NMR spectra, which were concluded from both our theoretical NMR predictions and ^{13}C NMR data of similar acetylenic hydrazones whose structures were unambiguously identified by X-ray analysis.[53] In the *E* isomer, two alkynic carbons, which we refer to as C_α and C_β carbons with respect to the carbonyl group, resonate closely, and the chemical shift difference between C_α and C_β carbons is approximately 3−12 ppm. However, in the *Z* isomer, the C_α carbon is relatively upfield while the C_β carbon is comparatively downfield, and the chemical shift difference between these carbons is around 22−30 ppm. In summary, the absolute value of chemical shift difference between C_α and C_β carbons in the *E* isomer is generally smaller than that between the respective C_α and C_β carbons in the Z isomer: i.e., $|\Delta\delta(C_\alpha-C_\beta)_{E\,\text{isomer}}| < |\Delta\delta(C_\alpha-C_\beta)_{Z\,\text{isomer}}|$. For example, in the *E* isomer of 3-ferrocenylpropynal phenylhydrazone (*E*-**23a**), C_α and C_β carbons appear around 82.0 and 92.2 ppm while, in the corresponding *Z* isomer (*Z*-**23a**), they resonate around 76.5 and 102.4 ppm, respectively.

In order to find out the relative stabilities of *E* and *Z* isomers of alkynic hydrazones, which is the matter of discussion, we calculated the relative energies of *E* and *Z* isomers of some representative acetylenic hydrazones at the density functional theory (DFT) level (B3LYP/6-31G*)[54,55] by using the Gaussian 98 program package.[56] Figure 1 depicts the B3LYP/6-31G* optimized geometries for the most stable *E* and *Z* isomers of acetylenic hydrazones **22a**, **22l**, and **22p** (see the Supporting Information for Cartesian coordinates and energy values). As can be seen in Figure 1, all hydrazones adopt almost planar structures in their most stable conformations, thus maintaining the conjugation between aromatic moieties, except that in the *E* isomer of diphenylpropynone phenylhydrazone (***E*-22p**), the phenyl

Scheme 5



Scheme 6

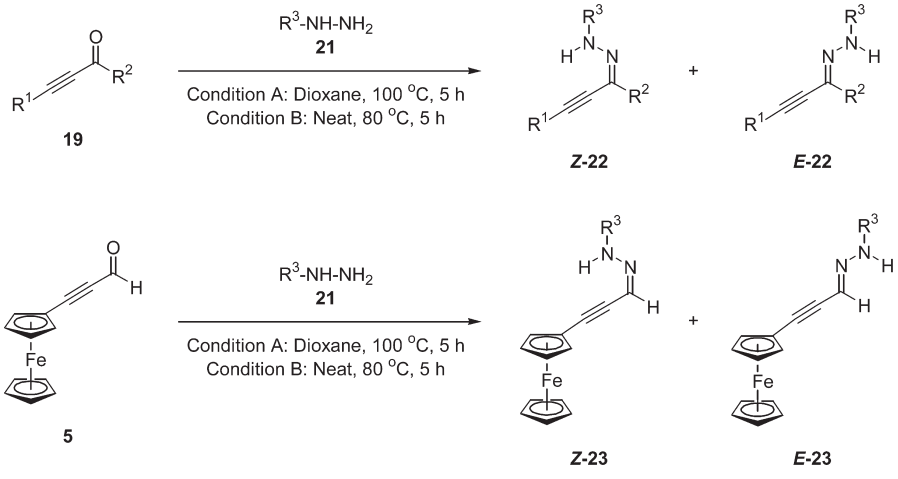


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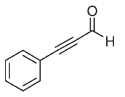
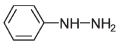
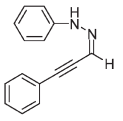
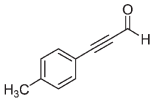
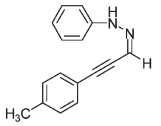
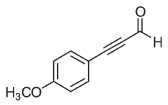
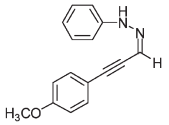
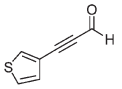
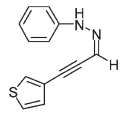
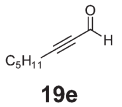
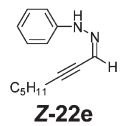
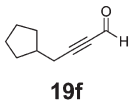
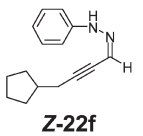
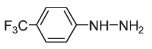
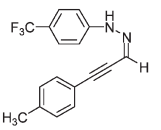
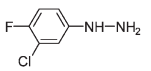
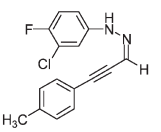
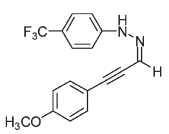
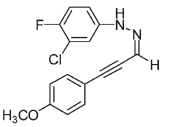
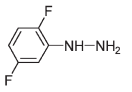
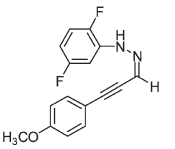
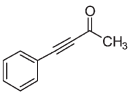
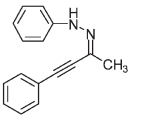
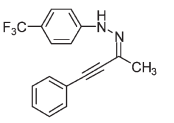
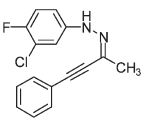
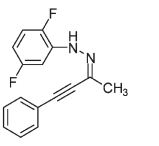
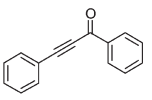
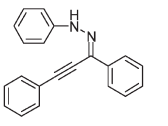
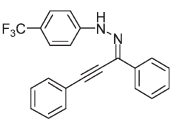
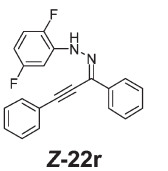
Table 1. Synthesis of Acetylenic Hydrazones 22

entry	aldehyde or ketone	hydrazine	condition[a]	hydrazone (% yield)[b]
1	 **19a**	 **21a**	A	 ***Z*-22a** (61)
2			B	(81)
3	 **19b**	**21a**	B	 ***Z*-22b** (85)
4	 **19c**	**21a**	A	 ***Z*-22c** (57)
5			B	(64)
6	 **19d**	**21a**	B	 ***Z*-22d** (54)
7	 **19e**	**21a**	B	 ***Z*-22e** (81)
8	 **19f**	**21a**	B	 ***Z*-22f** (60)
9	**19b**	 **21b**	B	 ***Z*-22g** (60)
10	**19b**	 **21c**	B	 ***Z*-22h** (77)
11	**19c**	**21b**	B	 ***Z*-22i** (52)
12	**19c**	**21c**	A	 ***Z*-22j** (63)
13			B	(82)
14	**19c**	 **21d**	B	 ***Z*-22k** (57)
15	 **19g**	**21a**	B	 ***Z*-22l** (69)
16	**19g**	**21b**	B	 ***Z*-22m** (76)
17	**19g**	**21c**	B	 ***Z*-22n** (87)
18	**19g**	**21d**	B	 ***Z*-22o** (86)
19	 **19h**	**21a**	B	 ***Z*-22p** (27)
20	**19h**	**21b**	B	 ***Z*-22q** (52)
21	**19h**	**21d**	B	 ***Z*-22r** (36)

[a] Condition A: dioxane, 100 °C, 5 h, Condition B: neat, 80 °C, 5 h. [b] Isolated yield.

group attached to the hydrazone double bond deviates from planarity by 52.4° due to its severe steric interaction with the H atom of the secondary N−H group of the hydrazone functionality. Interestingly, in the *Z* isomers of acetylenic hydrazones, the

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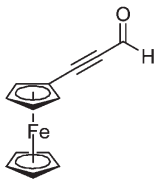
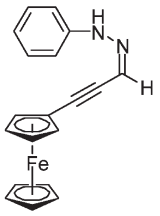
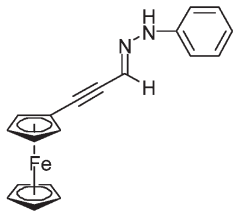
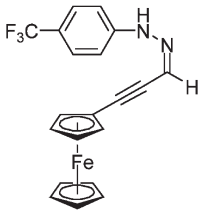
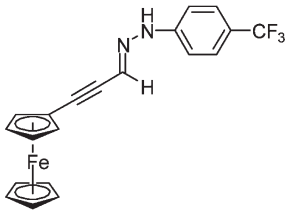
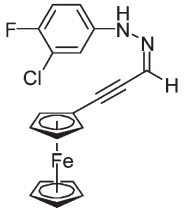
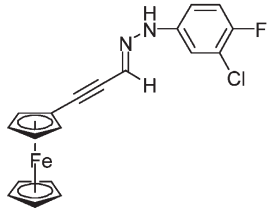
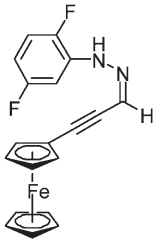
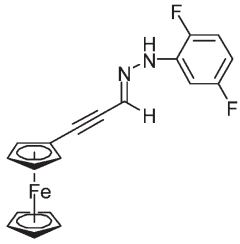
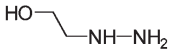
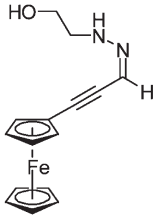
Table 2. Synthesis of Ferrocenyl-Substituted Acetylenic Hydrazones 23

entry	aldehyde or ketone	hydrazine	condition[a]	hydrazone (% yield)[b]				
1	 **5**	**21a**	A	 ***Z*-23a**	(48)	+	 ***E*-23a**	(45)
2		**21a**	B		(54)	+		(36)
3	**5**	**21b**	A	 ***Z*-23b**	(45)	+	 ***E*-23b**	(30)
4	**5**	**21b**	B		(43)	+		(50)
5	**5**	**21c**	A	 ***Z*-23c**	(47)	+	 ***E*-23c**	(52)
6	**5**	**21c**	B		(40)	+		(60)
7	**5**	**21d**	A	 ***Z*-23d**	(58)	+	 ***E*-23d**	(42)
8	**5**	**21d**	B		(56)	+		(40)
9	**5**	 **21e**	B	 ***Z*-23e**	(49)			

[a] Condition A: dioxane, 100 °C, 5 h. Condition B: neat, 80 °C, 5 h. [b] Isolated yield.

C_α carbon is in close proximity with the H atom of the secondary N−H group of the hydrazone functionality in the range of 2.312−2.387 Å (Figure 1). This might be the reason the C_α and C_β carbons in the *Z* isomers are relatively upfield and downfield, respectively, as compared to those in the *E* isomers, in the ^{13}C NMR spectra mentioned above. We found that, in the gas phase, the *Z* isomer of phenylpropynal phenylhydrazone (***Z*-22a**) is more stable than its *E* isomer (***E*-22a**) by 2.2 kcal/mol. Owing to increasing steric interactions, the *Z* isomers of α, *β*-alkynic ketone hydrazones are much more stable than the

corresponding *E* isomers, as compared with those of α,β-alkynic aldehyde hydrazones. For instance, the *Z* isomer of 4-phenyl-3-butyn-2-one phenylhydrazone (**Z-22l**) is 3.5 kcal/mol more stable than its *E* isomer (**E-22l**) while the *Z* isomer of diphenylpropynone phenylhydrazone (**Z-22p**) is 6.1 kcal/mol more stable than the corresponding *E* isomer (**E-22p**). In conclusion, our calculations at the DFT level showed that the *Z* isomers of acetylenic hydrazones are more stable than their *E* isomers.

After preparing requisite hydrazones **22** and **23**, we investigated their electrophilic cyclizations to pyrazoles. Initially, electrophilic cyclization of phenylpropynal phenylhydrazone (**Z-22a**), an alkynic aldehyde hydrazone, was examined under several conditions to find optimal reaction conditions (Table 3, entries 1−7). Since our literature search revealed that CH_2Cl_2 (DCM) and CH_3CN are among the most employed solvents and $NaHCO_3$ is one of the commonly used bases in such reactions, we performed the optimization reactions in these solvents and/or with this base. As iodination reagent, we mostly preferred to use molecular iodine, since it has gained considerable importance as a mild and nontoxic Lewis acid catalyst, which catalyzed various organic reactions with high efficiency and selectivity.[57] When hydrazone **Z-22a** was stirred in DCM for 5 h at room temperature, no conversion to pyrazole **25a** was observed (Table 3, entry 1). The same reaction with iodine monochloride afforded 4-iodopyrazole **24a** in 48% yield (Table 3, entry 2). When the same reaction was carried with molecular iodine in refluxing DCM, pyrazoles **24a** and **25a** were obtained in 72 and 24% yields, respectively (Table 3, entry 3). In this reaction, pyrazole **25a** formed in addition to 4-iodopyrazole **24a**. As anticipated, during the formation of **24a**, the reaction with iodine produces HI, which catalyzes the cyclization of hydrazone **Z-22a** to pyrazole **25a** to some extent, consistent with the earlier findings.[27,28] On the other hand, the reaction of hydrazone **Z-22a** with molecular iodine in the presence of $NaHCO_3$ provided the highest yield (80%) of iodopyrazole **24a** (Table 3, entry 4). Interestingly, iodocyclization was very fast at even room temperature and went to completion in almost 2 h. The same reaction in acetonitrile at room temperature or under reflux conditions did not improve the yield of **24a** (Table 3, entries 5−7). Surprisingly, under the optimal conditions, diphenylpropynone phenylhydrazone (**E-22p**), an alkynic ketone hydrazone, provided the corresponding 4-iodopyrazole **24p** in comparatively low yield (15%) (Table 3, entry 8). When the same reaction was carried out at relatively higher temperature such as in refluxing acetonitrile at 82 °C, pyrazole **24a** was obtained in 66% yield (Table 3, entry 9). In summary, electrophilic cyclizations were performed with 3 equiv of I_2 in the presence of 3 equiv of $NaHCO_3$ in DCM at room temperature for alkynic aldehyde hydrazones or in refluxing acetonitrile for alkynic ketone hydrazones. The results from a systematic study are given in Table 4.

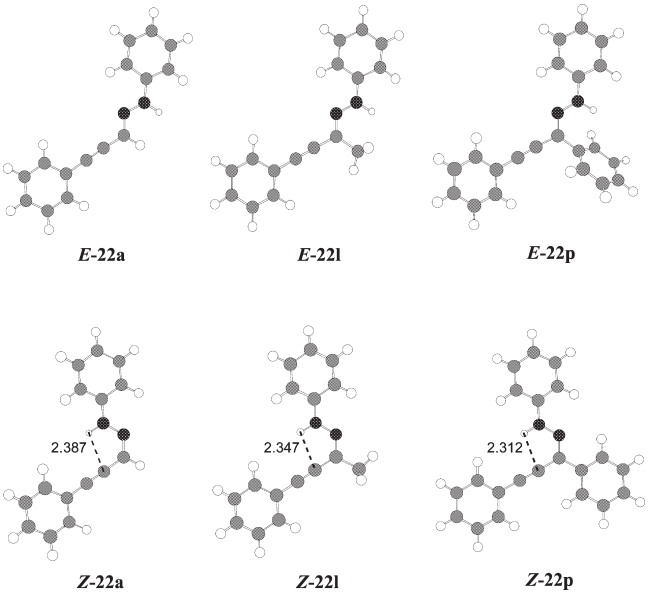
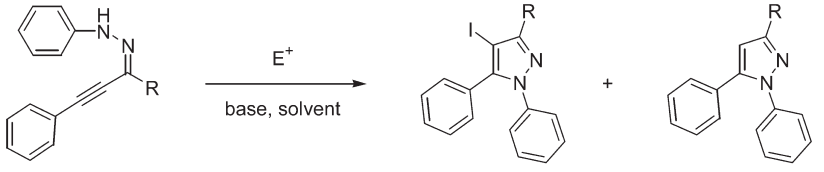


Figure 1. B3LYP/6-31G* optimized geometries for representative α,β-acetylenic hydrazones as well as selected distances in angstroms.

Table 3. Iodocyclization of Acetylenic Hydrazones *Z*-22a and *Z*-22p



Z-22a (R = H)
Z-22p (R = Ph)

24a (R = H)
24p (R = Ph)

25a (R = H)
25p (R = Ph)

entry	hydrazone	electrophile (amt (equiv))	base (amt (equiv))	solvent	temp. (°C)	time (h)	product (% yield)[a]
1	**Z-22a**			CH_2Cl_2	room temp	5	
2	**Z-22a**	ICl (3)		CH_2Cl_2	room temp	3	**24a** (48)
3	**Z-22a**	I_2 (3)		CH_2Cl_2	40	3	**24a** (72) + **25a** (7)
4	**Z-22a**	I_2 (3)	$NaHCO_3$ (3)	CH_2Cl_2	room temp	2	**24a** (80)
5	**Z-22a**	I_2 (3)	$NaHCO_3$ (3)	CH_3CN	room temp	0.5	**24a** (30)
6	**Z-22a**	I_2 (3)	$NaHCO_3$ (3)	CH_3CN	room temp	2	**24a** (61)
7	**Z-22a**	I_2 (3)	$NaHCO_3$ (3)	CH_3CN	82	2	**24a** (66)
8	**Z-22p**	I_2 (3)	$NaHCO_3$ (3)	CH_2Cl_2	room temp	2	**24p** (15)
9	**Z-22p**	I_2 (3)	$NaHCO_3$ (3)	CH_3CN	82	2	**24p** (66)

[a] Isolated yield.

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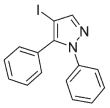
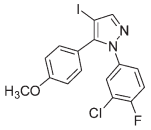
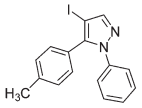
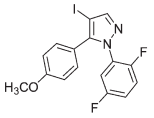
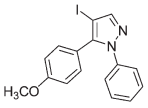
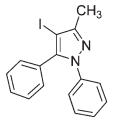
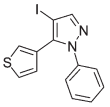
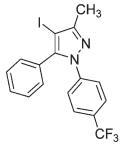
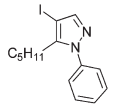
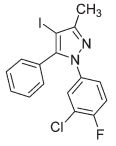
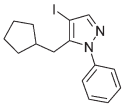
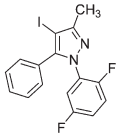
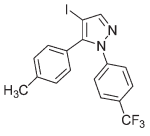
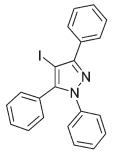
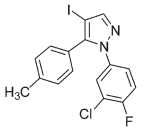
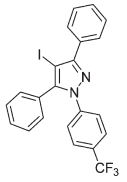
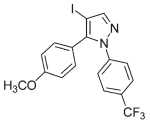
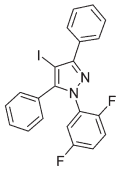
Table 4. Synthesis of Pyrazoles

entry	hydrazone	pyrazole (% yield)[a]	entry	hydrazone	pyrazole (% yield)[a]
1	***Z*-22a**	 **24a** (80)	10	***Z*-22j**	 **24j** (95)
2	***Z*-22b**	 **24b** (85)	11	***Z*-22k**	 **24k** (74)
3	***Z*-22c**	 **24c** (84)	12	***Z*-22l**	 **24l** (92)
4	***Z*-22d**	 **24d** (83)	13	***Z*-22m**	 **24m** (93)
5	***Z*-22e**	 **24e** (47)	14	***Z*-22n**	 **24n** (81)
6	***Z*-22f**	 **24f** (47)	15	***Z*-22o**	 **24o** (86)
7	***Z*-22g**	 **24g** (40)	16	***Z*-22p**	 **24p** (66)
8	***Z*-22h**	 **24h** (41)	17	***Z*-22q**	 **24q** (89)
9	***Z*-22i**	 **24i** (85)	18	***Z*-22r**	 **24r** (74)

[a] Isolated yield.

As seen in Table 4, a variety of α,β-alkynic hydrazone derivatives **Z-22a**−**r** were employed in these pyrazole-forming electrophilic cyclizations. 1,5-Dialkyl/aryl-substituted 4-iodopyrazoles **24a**−**k** were isolated in 40−95% yields (Table 4, entries 1−11), while 1,3,5-trialkyl/aryl-substituted 4-iodopyrazoles **24l**−**r** were obtained in 66−93% yields (Table 4, entries 12−18). Notably, 5-alkyl-substituted pyrazoles **24e**,**f** were obtained in moderate yield (47%) (Table 4, entries 5 and 6). Except for pyrazoles **24g**,**h** (40 and 41%, respectively), 1,5-diaryl-substituted pyrazoles were isolated in good to high yields. Similarly, 1,5-diaryl-3-alkyl/aryl-substituted pyrazole derivatives were formed in good to high yields. 5-Thiophen-3-yl-substituted pyrazole **24d** was prepared in 83% yield (Table 4, entry 4). Clearly, iodocyclizations leading to the formation of trialkyl/aryl-substituted 4-iodopyrazoles **24l**−**r** proceed well and provided them in good to high yields (Table 4, entries 12−18). In summary, iodocyclizations were found to be general for a wide range of α,β-alkynic hydrazones and tolerated the presence of aliphatic, aromatic, and heteroaromatic

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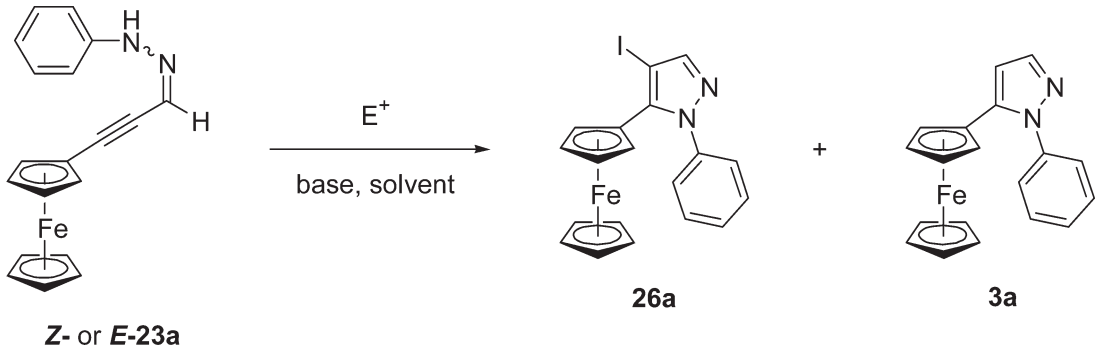
Table 5. Iodocyclization of *β*-Ferrocenyl-α,*β*-alkynic Hydrazones *Z*- and *E*-23a



***Z*- or *E*-23a** **26a** **3a**

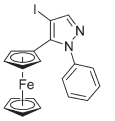
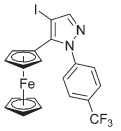
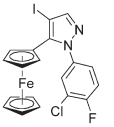
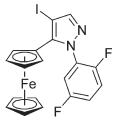
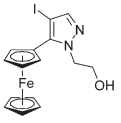
entry	hydrazone	electrophile (amt (equiv))	base (amt (equiv))	solvent	temp (°C)	time (h)	product (% yield)[a]
1	***Z*-23a**	I_2 (3)	$NaHCO_3$ (3)	CH_2Cl_2	room temp	2	**26a** (50) + **3a** (27)
2	***Z*-23a**	I_2 (3)		CH_2Cl_2	40	3	**26a** (47) + **3a** (37)
3	***E*-23a**	I_2 (3)		CH_2Cl_2	40	3	**26a** (37) + **3a** (45)
4[b]	***Z*-23a**	I_2 (3)	NEt_3 (1.5)	CH_2Cl_2	40	3	**26a** (43)
5[c]	***Z*-23a**	I_2 (3)	NEt_3 (3)	CH_2Cl_2	40	3	**26a** (59) + **3a** (7)
6	***E*-23a**	I_2 (3)	NEt_3 (3)	CH_2Cl_2	40	3	**26a** (56) + **3a** (14)
7	***Z*-23a**	I_2 (3)	$NaHCO_3$ (3)	CH_3CN	room temp	0.5	**26a** (90)
8	***Z*-23a**	I_2 (6)	$NaHCO_3$ (3)	CH_3CN	room temp	0.5	**26a** (91)
9	***E*-23a**	I_2 (3)	$NaHCO_3$ (3)	CH_3CN	room temp	0.5	**26a** (92)

[a] Isolated yield. [b] Starting hydrazone ***Z*-23a** was recovered in 23% yield. [c] Starting hydrazone ***Z*-23a** was recovered in 14% yield.

moieties with electron-withdrawing and electron-donating substituents.

Next, we examined the synthesis of 5-ferrocenylpyrazole derivatives. Unfortunately, under our optimized conditions, *β*-ferrocenyl-α,*β*-alkynic hydrazone ***Z*-23a** produced pyrazoles **26a** and **3a** in 50 and 27% yields, respectively (Table 5, entry 1). A complication in this reaction was the formation of non-iodo-substituted pyrazole **3a**, which was possibly formed by acid-catalyzed electrophilic cyclization of ***Z*-23a**, as mentioned before. For this reason, we optimized the reaction conditions again for the formation of 5-ferrocenylpyrazole derivatives (Table 5). When the same reaction of ***Z*-23a** was carried out in the absence of base, pyrazoles **26a** and **3a** were obtained in 47 and 37% yields, respectively (Table 5, entry 2). Notably, in the absence of base, the proportion of **3a** increased at the expense of **26a**. A similar trend was observed for the reaction of ***E*-23a**, and pyrazoles **26a** and **3a** were isolated (Table 5, entry 3). When the reaction of ***Z*-23a** was performed in the presence of 1.5 equiv of NEt_3, pyrazole **26a** was obtained in 43% yield as a single product (Table 5, entry 4). However, when the amount of NEt_3 was increased to 3 equiv, the reaction produced pyrazole **26a** along with pyrazole **3a** (Table 5, entry 5). A similar result was found for the reaction of hydrazone ***E*-23a**, and both pyrazole derivatives were obtained (Table 5, entry 6). When the reaction of hydrazone ***Z*-23a** was carried out in the presence of $NaHCO_3$ in CH_3CN at room temperature, it went to completion in $^1/_2$ h and afforded the expected pyrazole **23a** in 90% yield as a single product (Table 5, entry 7). The use of 6 equiv of $NaHCO_3$ did not significantly improve the yield (91%) of **26a** (Table 5, entry 8). Similarly, the reaction of hydrazone ***E*-23a** in the presence of $NaHCO_3$ in CH_3CN at room temperature produced pyrazole **26a** in 92% yield (Table 5, entry 9). In summary, electrophilic cyclizations of *β*-ferrocenyl-α,*β*-alkynic hydrazones were performed with

Table 6. Synthesis of Ferrocenyl-Substituted Pyrazoles

entry	hydrazone	pyrazole (% yield)[a]	
1	***Z*-23a**		**26a** (90)
2	***E*-23a**		**26a** (92)
3	***Z*-23b**		**26b** (95)
4	***E*-23b**		**26b** (76)
5	***Z*-23c**		**26c** (94)
6	***E*-23c**		**26c** (93)
7	***Z*-23d**		**26d** (83)
8	***E*-23d**		**26d** (89)
9	***Z*-23e**		**26e** (58)

[a] Isolated yield.

3 equiv of I_2 in the presence of 3 equiv of $NaHCO_3$ in CH_3CN at room temperature (Table 6). In most cases, both *E* and *Z* isomers of ferrocenyl-substituted hydrazones **23** worked well in these reactions and provided corresponding pyrazoles in good to high

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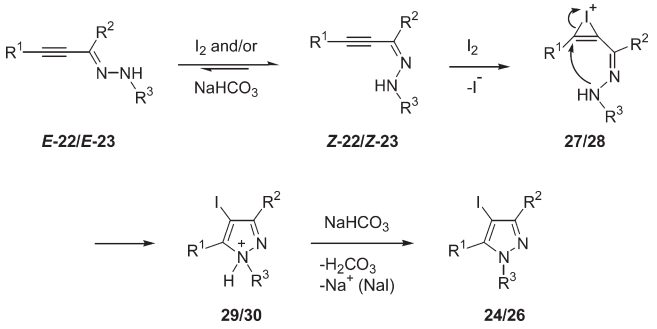
Scheme 7



yields. As concluded from the results, the stereochemical identity of starting acetylenic hydrazones did not affect the outcome of the reaction. It is noteworthy to mention that ferrocenyl-substituted pyrazoles have potential for biological and medicinal studies since, according to recent studies, the integration of a ferrocenyl group into such structures may enhance their current biological activities or generate new medicinal properties.[26,27,58]

The mechanism proposed for the formation of 4-iodopyrazoles **24** and **26** is depicted in Scheme 7. In the presence of Lewis acids such as iodine and/or in the presence of bases such as $NaHCO_3$, *E* isomers of alkynic hydrazones ***E*-22** and ***E*-23** can easily equilibrate with their *Z* isomers ***Z*-22** and ***Z*-23**, respectively, and expectedly, the equilibrium shifts to the right to a large extent, since the *Z* isomers of alkynic hydrazones are thermodynamically more stable than the corresponding *E* isomers, as mentioned before. Subsequently, the reaction with iodine yields iodonium ions **27** and **28**, which initiate electrophilic cyclization via nucleophilic attack of the secondary nitrogen atom to furnish protonated pyrazoles **29** and **30**, respectively. Finally, deprotonation with base affords 4-iodopyrazole derivatives **24** and **26**, depending upon the identity of the R groups (Scheme 7).

CONCLUSION

In summary, we have prepared α,β-alkynic hydrazone derivatives and investigated their electrophilic cyclizations with molecular iodine. Hydrazone derivatives were synthesized by condensation reactions of hydrazines with acetylenic aldehydes and ketones in refluxing dioxane or under neat conditions at 80 °C. We found that *Z* isomers of acetylenic hydrazones are more stable than their *E* isomers, as supported by theoretical calculations as well. Subsequently, we carried out electrophilic cyclization of acetylenic hydrazones with molecular iodine, which provided a rapid entry into 4-iodopyrazole derivatives. In general, electrophilic cyclizations were quite fast even at room temperature and afforded corresponding pyrazoles in good to high yields. We also synthesized 5-ferrocenyl-substituted 4-iodopyrazoles in high yields from both *E* and *Z* isomers of corresponding acetylenic hydrazones. The resulting iodine-containing products can be further elaborated to a wide range of functionally substituted pyrazoles using subsequent palladium-catalyzed processes,[59] which will be reported in due course.[60]

EXPERIMENTAL SECTION

General Information. ^1H and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively. Chemical shifts are reported in parts per million (ppm) downfield from an internal TMS (trimethylsilane) reference. Coupling constants (*J*) are reported in hertz (Hz), and spin multiplicities are represented by the symbols s (singlet), br s (broad singlet), d (doublet), t (triplet), q (quartet), p (pentet), and m (multiplet). DEPT ^{13}C NMR information is given in parentheses as C, CH, CH_2, and CH_3. Infrared spectra (IR) were recorded by using attenuated total reflection (ATR). Band positions are reported in reciprocal centimeters (cm^{-1}). Band intensities are indicated relative to the most intense band, and are listed as br (broad), vs (very strong), s (strong), m (medium), w (weak), and vw (very weak). Mass spectra (MS) were obtained by using electrospray ionization (ESI) with MICRO-TOF; *m*/*z* values are reported (for each measurement, the mass scale was recalibrated with sodium formiate clusters, and samples were dissolved and measured in MeOH). High-resolution mass spectra (HRMS) were also obtained by using electrospray ionization (ESI) with MICRO-TOF. Flash chromatography was performed using thick-walled glass columns and "flash grade" silica (230−400 mesh). Thin-layer chromatography (TLC) was performed by using commercially prepared 0.25 mm silica gel plates, and visualization was effected with a short-wavelength UV lamp (254 nm). The relative proportions of solvents in chromatography solvent mixtures refer to the volume to volume ratio. All commercially available reagents were used directly without purification unless otherwise stated. All the solvents used in the reactions were distilled for purity. The inert atmosphere was created by a slight positive pressure (ca. 0.1 psi) of argon. All glassware was dried in an oven prior to use. 3-Ferrocenylpropynal (**5**),[49,50] 3-phenyl-2-propynal (3-phenylpropiolaldehyde; **19a**),[49,61] 3-(*p*-tolyl)propiolaldehyde (**19b**),[49,61] 3-(4-methoxyphenyl)propiolaldehyde (**19c**),[49,62] 3-(thiophen-3-yl)propiolaldehyde (**19d**),[49,63] oct-2-ynal (**19e**),[49,64] 4-cyclopentylbut-2-ynal (**19f**),[49] 4-phenylbut-3-yn-2-one (**19g**),[51] and 1,3-diphenylprop-2-yn-1-one (**19h**)[52] were prepared according to literature procedures.

General Procedures for the Synthesis of Acetylenic Hydrazones (22a−r and 23a−e). *Condition A.* A mixture of arylhydrazine (2 mmol) and propargyl aldehyde or ketone (2 mmol) in dioxane (8 mL) was heated at 100 °C in a round-bottom flask equipped with a condenser under argon for 5 h. After the reaction was over, dioxane was removed under reduced pressure. The residue was purified by flash column chromatography on silica gel using hexane/ethyl acetate (9/1) as the eluent to afford the desired product.

Condition B. A mixture of arylhydrazine (2 mmol) and propargyl aldehyde or ketone (2 mmol) in a round-bottom flask was heated at 80 °C under argon for 5 h. After the reaction was over, the residue was purified by flash column chromatography on silica gel using hexane/ethyl acetate (9/1) as the eluent to afford the desired product.

*(Z)-1-Phenyl-2-(3-phenylprop-2-yn-1-ylidene)hydrazine (**Z-22a**).* 3-Phenyl-2-propynal (phenylpropiolaldehyde; 200 mg, 1.55 mmol) and phenylhydrazine (167 mg, 1.55 mmol) were employed to afford 207 mg (61%) and 275 mg (81%) of the indicated product for conditions A and B, respectively. ^1H NMR (400 MHz, $CDCl_3$): δ 8.67 (br s, 1H, NH), 7.53 (m, 2H), 7.40 (m, 3H), 7.29 (m, 2H), 7.10 (m, 2H), 6.92 (m, 1H), 6.62 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.5 (C), 131.8 (CH), 129.5 (CH), 129.4 (CH), 128.6 (CH), 121.6 (C), 121.2 (CH), 114.7 (CH), 113.3 (CH), 101.9 (C), 79.6 (C). IR (neat): 3307, 3051, 3028, 2185, 1596, 1523, 1500, 1438, 1342, 1309, 1255, 1124, 1068, 764, 682 cm^{-1}. MS (ESI, *m*/*z*): 243.09 $[M + Na]^+$. HRMS (ESI): calcd for $C_{15}H_{12}N_2Na$ 243.0897 $[M + Na]^+$, found 243.0893.

*(Z)-1-Phenyl-2-(3-(p-tolyl)prop-2-yn-1-ylidene)hydrazine (**Z-22b**).* 3-*p*-Tolylpropiolaldehyde (200 mg, 1.39 mmol) and phenylhydrazine (150 mg, 1.39 mmol) were employed to afford 276 mg (85%) of the indicated product for condition B. ^1H NMR (400 MHz, $CDCl_3$): δ 8.68 (br s, 1H), 7.45 (d, *J* = 7.99 Hz, 2H), 7.31 (t, *J* = 7.7 Hz, 2H), 7.22 (d, *J* = 7.9 Hz, 2H), 7.13 (d, *J* = 8.2 Hz, 2H), 6.94 (t, *J* = 7.2 Hz, 1H), 2.41 (s, 3H). ^{13}C NMR (400 MHz, $CDCl_3$): δ 143.6 (C), 139.9 (C), 131.7 (CH), 129.4 (CH), 129.3 (CH), 121.0 (CH), 118.5 (C), 114.9 (CH), 113.3 (CH), 102.3 (C), 79.1 (C), 21.6 (CH_3). IR (neat): 3317, 3053,

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3029, 2918, 2189, 1598, 1531, 1508, 1348, 1253, 1122, 1068, 885, 810, 750, 688 cm^{-1}. MS (ESI, *m/z*): 257.11 $[M + Na]^+$. HRMS (ESI): calcd for $C_{16}H_{14}N_2Na$ 257.1054 $[M + Na]^+$, found 257.1049.

(Z)-1-(3-(4-Methoxyphenyl)prop-2-yn-1-ylidene)-2-phenylhydrazine (***Z-22c***). 3-(4-Methoxyphenyl)propiolaldehyde (200 mg, 1.25 mmol) and phenylhydrazine (136 mg, 1.25 mmol) were employed to afford 178 mg (57%) and 200 mg (64%) of the indicated product for conditions A and B, respectively. ^1H NMR (400 MHz, $CDCl_3$): δ 8.64 (br s, 1H, NH), 7.48 (d, *J* = 8.7 Hz, 2H), 7.29 (t, *J* = 7.5 Hz, 2H), 7.11 (d, *J* = 8.2 Hz, 2H), 6.93 (m, 3H), 6.62 (s, 1H), 3.86 (s, 3H). ^{13}C NMR (400 MHz, $CDCl_3$): δ 160.6 (C), 143.6 (C), 133.4 (CH), 129.3 (CH), 121.0 (CH), 115.2 (C), 114.3 (CH), 113.6 (C), 113.2 (C), 102.2 (C), 78.6 (C), 55.4 (CH_3). IR (neat): 3290, 3055, 2839, 2192, 1598, 1542, 1504, 1346, 1290, 1240, 1172, 1105, 1026, 885, 827, 748, 690 cm^{-1}. MS (ESI, *m/z*): 273.10 $[M + Na]^+$. HRMS (ESI): calcd for $C_{16}H_{14}N_2ONa$ 273.1003 $[M + Na]^+$, found 273.0998.

(Z)-1-Phenyl-2-(3-(thiophen-3-yl)prop-2-yn-1-ylidene)hydrazine (***Z-22d***). 3-(Thiophen-3-yl)propiolaldehyde (200 mg, 1.47 mmol) and phenylhydrazine (159 mg, 1.47 mmol) were employed to afford 179 mg (54%) of the indicated product for condition B. ^1H NMR (400 MHz, $CDCl_3$): δ 8.55 (br s, 1H, NH), 7.51 (d, *J* = 1.9 Hz, 1H), 7.26 (m, 1H), 7.20 (m, 2H), 7.12 (d, *J* = 5.4 Hz, 1H), 7.02 (d, *J* = 8.3 Hz, 2H), 6.84 (t, *J* = 7.2 Hz, 1H), 6.51 (s, 1H). ^{13}C NMR (400 MHz, $CDCl_3$): δ 143.5 (C), 130.2 (CH), 129.7 (CH), 129.4 (CH), 126.1 (CH), 121.1 (CH), 120.7 (C), 114.7 (CH), 113.3 (CH), 97.0 (C), 79.3 (C). IR (neat): 3305, 3105, 3053, 2181, 1598, 1498, 1342, 1521, 1120, 1068, 856, 779, 748, 688 cm^{-1}. MS (ESI, *m/z*): 249.05 $[M + Na]^+$. HRMS (ESI): calcd for $C_{13}H_{10}N_2SNa$ 249.0462 $[M + Na]^+$, found 249.0457.

(Z)-1-(Oct-2-yn-1-ylidene)-2-phenylhydrazine (***Z-22e***). Oct-2-ynal (200 mg, 1.61 mmol) and phenylhydrazine (174 mg, 1.61 mmol) were employed to afford 280 mg (81%) of the indicated product for condition B. ^1H NMR (400 MHz, $CDCl_3$): δ 8.46 (br s, 1H, NH), 7.19 (t, *J* = 7.7 Hz, 2H), 7.03 (d, *J* = 7.9 Hz, 2H), 6.81 (t, *J* = 7.2 Hz, 1H), 6.32 (s, 1H), 2.40 (t, *J* = 6.9 Hz, 2H), 1.55 (p, *J* = 7.1 Hz, 2H), 1.33 (m, 4H), 0.87 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (400 MHz, $CDCl_3$): δ 143.8 (C), 129.3 (CH), 120.8 (CH), 115.8 (CH), 113.1 (CH), 104.3 (C), 71.9 (C), 31.2 (CH_2), 28.2 (CH_2), 22.2 (CH_2), 19.7 (CH_2), 14.0 (CH_3). IR (neat): 3307, 2954, 2929, 2858, 2196, 1600, 1535,1502, 1344, 1253, 1151, 1114, 1066, 883, 810, 746, 690 cm^{-1}. MS (ESI, *m/z*): 237.14 $[M + Na]^+$. HRMS (ESI): calcd for $C_{14}H_{18}N_2Na$ 237.1367 $[M + Na]^+$, found 237.1362.

(Z)-1-(4-Cyclopentylbut-2-yn-1-ylidene)-2-phenylhydrazine (***Z-22f***). 4-Cyclopentylbut-2-ynal (200 mg, 1.47 mmol) and phenylhydrazine (160 mg, 1.47 mmol) were employed to afford 200 mg (60%) of the indicated product for condition B. ^1H NMR (400 MHz, $CDCl_3$): δ 8.58 (s, 1H), 7.31 (m, 2H), 7.08 (d, *J* = 7.5 Hz, 2H), 7.0 (t, *J* = 7.3 Hz, 1H), 6.43 (s, 1H), 2.55 (d, *J* = 6.8 Hz, 2H), 2.16−2.27 (m, 1H), 1.95−1.88 (m, 2H), 1.77−1.61 (m, 4H), 1.43−1.35 (m, 2H). IR (neat): 3307, 2947, 2864, 2194, 1600, 1533, 1502, 1344, 1307, 1523, 1151, 114, 1066, 810, 764, 690 cm^{-1}. MS (ESI, *m/z*): 249.14 $[M + Na]^+$. HRMS (ESI): calcd for $C_{15}H_{18}N_2Na$ 249.1367 $[M + Na]^+$, found 249.1362.

(Z)-1-(3-(p-Tolyl)prop-2-yn-1-ylidene)-2-(4-(trifluoromethyl)phenyl)hydrazine (***Z-22g***). 3-*p*-Tolylpropiolaldehyde (166 mg, 1.15 mmol) and (4-(trifluoromethyl)phenyl)hydrazine (203 mg, 1.15 mmol) were employed to afford 208 mg (60%) of the indicated product for condition B. ^1H NMR (400 MHz, $CDCl_3$): δ 8.74 (br s, 1H), 7.51 (d, *J* = 8.5 Hz, 2H), 7.42 (d, *J* = 8.0 Hz, 2H), 7.20 (d, *J* = 7.9 Hz, 2H), 7.14 (d, *J* = 8.5 Hz, 2H), 6.67 (s, 1H), 2.38 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.1 (C), 140.3 (C), 131.8 (CH), 129.5 (CH), 126.7 (m, CH), 124.6 (d, *J* = 268 Hz, C), 122.6 (q, *J* = 32.5 Hz, C), 118.1 (C), 117.174 (CH), 112.80 (CH), 102.9 (C), 78.6 (C), 21.6 (CH_3). IR (neat): 3313, 3033, 2925, 2181, 1614, 1537, 1321, 1261, 1159, 1099, 1064, 840, 815 cm^{-1}. MS (ESI, *m/z*): 325.09 $[M + Na]^+$. HRMS (ESI): calcd for $C_{17}H_{13}F_3N_2Na$ 325.0929 $[M + Na]^+$, found 325.0924.

(Z)-1-(3-Chloro-4-fluorophenyl)-2-(3-(p-tolyl)prop-2-yn-1-ylidene)hydrazine (***Z-22h***). 3-*p*-Tolylpropiolaldehyde (153 mg, 1.06 mmol) and (3-chloro-4-fluorophenyl)hydrazine (170 mg, 1.06 mmol) were employed to afford 234 mg (77%) of the indicated product for condition B. ^1H NMR (400 MHz, $CDCl_3$): δ 8.52 (br s, 1H), 7.45 (d, *J* = 7.9 Hz, 2H), 7.18 (d, *J* = 7.9 Hz, 2H), 7.15 (m, 1H), 7.03 (t, *J* = 8.7 Hz, 1H), 6.90 (m, 1H), 6.61 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.5 (d, *J* = 18.9 Hz, C), 140.0 (C), 139.7 (C), 131.2 (CH), 128.9 (CH), 121.1 (d, *J* = 18.9 Hz, C), 117.7 (C), 116.4 (d, *J* = 22.1 Hz, CH), 115.7 (CH), 114.4 (CH), 111.8 (d, *J* = 6.9 Hz, CH), 102.2 (C), 78.2 (C), 21.1 (CH_3). IR (neat): 3301, 2918, 2858, 2177, 1604, 1531, 1500, 1342, 1251, 1205, 1101, 810, 740 cm^{-1}. MS (ESI, *m/z*): 309.06 $[M + Na]^+$. HRMS (ESI): calcd for $C_{16}H_{12}ClFN_2Na$ 309.0571 $[M + Na]^+$, found 309.0565.

(Z)-1-(3-(4-Methoxyphenyl)prop-2-yn-1-ylidene)-2-(4-(trifluoromethyl)phenyl) hydrazine (***Z-22i***). 3-(4-Methoxyphenyl)propiolaldehyde (160 mg, 1 mmol) and (4-(trifluoromethyl)phenyl)hydrazine (176 mg, 1 mmol) were employed to afford 165 mg (52%) of the indicated product for condition B. ^1H NMR (400 MHz, $CDCl_3$): δ 8.71 (br s, 1H, NH), 7.50 (d, *J* = 8.5 Hz, 2H), 7.46 (d, *J* = 8.8 Hz, 2H), 7.13 (d, *J* = 8.5 Hz, 2H), 6.91 (d, *J* = 8.8 Hz, 2H), 6.67 (s, 1H), 3.84 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.8 (C), 146.2 (C), 133.5 (CH), 126.6 (m, CH), 124.6 (d, *J* = 271 Hz, C), 122.5 (q, *J* = 31.9 Hz, C), 117.4 (CH), 114.4 (CH), 113.2 (C), 112.8 (CH), 102.9 (C), 78.8 (C), 55.4 (CH_3). IR (neat): 3321, 2970, 2840, 2177, 1600, 1506, 1328, 1296, 1251, 1095, 1060, 1033, 823 cm^{-1}. MS (ESI, *m/z*): 341.09 $[M + Na]^+$. HRMS (ESI): calcd for $C_{17}H_{13}F_3N_2ONa$ 341.0877 $[M + Na]^+$, found 341.0872.

(Z)-1-(3-Chloro-4-fluorophenyl)-2-(3-(4-methoxyphenyl)prop-2-yn-1-ylidene) hydrazine (***Z-22j***). 3-(4-Methoxyphenyl)propiolaldehyde (200 mg, 1.25 mmol) and (3-chloro-4-fluorophenyl)hydrazine (201 mg, 1.25 mmol) were employed to afford 237 mg (63%) and 309 mg (82%) of the indicated product for conditions A and B, respectively. ^1H NMR (400 MHz, $CDCl_3$): δ 8.71 (br s, 1H, NH), 7.50 (d, *J* = 8.5 Hz, 2H), 7.46 (d, *J* = 8.8 Hz, 2H), 7.13 (d, *J* = 8.5 Hz, 2H), 6.91 (d, *J* = 8.8 Hz, 2H), 6.67 (s, 1H), 3.84 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.8 (C), 146.2 (C), 133.5 (CH), 126.6 (m, CH), 124.6 (d, *J* = 271 Hz, C), 122.5 (q, *J* = 31.9 Hz, C), 117.4 (CH), 114.4 (CH), 113.2 (C), 112.8 (CH), 102.9 (C), 78.8 (C), 55.4 (CH_3). IR (neat): 3321, 2970, 2840, 2177, 1600, 1506, 1328, 1296, 1251, 1095, 1060, 1033, 823 cm^{-1}. MS (ESI, *m/z*): 341.09 $[M + Na]^+$. HRMS (ESI): calcd for $C_{16}H_{12}ClFN_2ONa$ 325.0520 $[M + Na]^+$, found 325.0514.

(Z)-1-(2,5-Difluorophenyl)-2-(3-(4-methoxyphenyl)prop-2-yn-1-ylidene) hydrazine (***Z-22k***). 3-(4-Methoxyphenyl)propiolaldehyde (68 mg, 0.42 mmol) and (2,5-difluorophenyl)hydrazine (61 mg, 0.42 mmol) were employed to afford 69.5 mg (57%) of the indicated product for condition B. ^1H NMR (400 MHz, $CDCl_3$): δ 8.80 (br s, 1H, NH), 7.46 (d, *J* = 8.6 Hz, 2H), 7.20 (m, 1H), 6.96 (m, 1H), 6.89 (d, *J* = 8.6 Hz, 2H), 6.70 (s, 1H), 6.47 (m,1H), 3.82 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.8 (C), 159.8 (d, *J* = 239 Hz, C), 145.8 (d, *J* = 235.8 Hz,C), 133.6 (CH), 133.5 (t, *J* = 11.3 Hz, C), 118.5 (CH), 115.5 (dd, *J* = 20, 10 Hz, CH), 114.4 (CH), 113.2 (C), 105.8 (dd, *J* = 24.5, 7.4 Hz, CH), 103.5 (C), 101.9 (dd, *J* = 29, 2.5 Hz, CH), 78.3 (C), 55.4 (CH_3). IR (neat): 3338, 2844, 2183, 1633, 1600, 1517, 1556, 1299, 1251, 1176, 1151, 1107, 1031, 852, 827, 800, 777, 756 cm^{-1}. MS (ESI, *m/z*): 309.08 $[M + Na]^+$. HRMS (ESI): calcd for $C_{16}H_{12}F_2N_2ONa$ 309.0815 $[M + Na]^+$, found 309.0810.

(Z)-1-Phenyl-2-(4-phenylbut-3-yn-2-ylidene)hydrazine (***Z-22l***). 4-Phenylbut-3-yn-2-one (179 mg, 1.25 mmol) and phenylhydrazine (135 mg, 1.25 mmol) were employed to afford 201 mg (69%) of the indicated product for condition B. ^1H NMR (400 MHz, $CDCl_3$): δ 8.33 (br s, 1H), 7.57 (m, 2H), 7.43 (m, 3H), 7.30 (t, *J* = 8.0 Hz, 2H), 7.13 (d, *J* = 7.6 Hz, 2H), 6.91 (t, *J* = 7.3 Hz, 2H), 2.28 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.2 (C), 131.8 (CH), 129.5 (CH), 129.3 (CH), 128.6

(CH), 123.7 (C), 121.6 (C), 120.3 (CH), 113.0 (CH), 101.2 (C), 81.0 (C), 22.2 (CH_3). IR (neat): 3056, 2923, 2200, 1670, 1598, 1504, 1442, 1363, 1253, 1155, 1072, 970, 758, 690 cm^{-1}. MS (ESI, *m/z*): 257.11 $[M + Na]^+$. HRMS (ESI): calcd for $C_{16}H_{14}N_2Na$ 257.1055 $[M + Na]^+$, found 257.1049. The spectral data were in agreement with those reported previously for this compound.[65]

*(Z)-1-(4-Phenylbut-3-yn-2-ylidene)-2-(4-(trifluoromethyl)phenyl)-hydrazine (**Z-22m**).* 4-Phenylbut-3-yn-2-one (125 mg, 0.87 mmol) and (4-(trifluoromethyl)phenyl)hydrazine (153 mg, 0.87 mmol) were employed to afford 200 mg (76%) of the indicated product for condition B. ^1H NMR (400 MHz, $CDCl_3$): δ 8.31 (br s, 1H), 7.45 (d, J = 7.6 Hz, 2H), 7.39 (d, J = 8.5 Hz, 2H), 7.32 (m, 3H), 7.02 (d, J = 8.4 Hz, 2H), 2.16 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.6 (C), 131.9 (CH), 129.7 (CH), 128.7 (CH), 126.6 (m, CH), 125.9 (C), 124.7 (d, J = 269.8 Hz, C), 121.8 (q, J = 32.9 Hz, C), 121.2 (C), 112.5 (CH), 101.7 (C), 80.4 (C), 22.3 (CH_3). IR (neat): 3313, 3082, 2989, 2918, 2360, 2177, 2162, 1612, 1527, 1488, 1325, 1311, 1267, 1153, 1099, 1062, 821, 748, 684 cm^{-1}. MS (ESI, *m/z*): 303.11 $[M + H]^+$. HRMS (ESI): calcd for $C_{17}H_{14}F_3N_2$ 303.1109 $[M + Na]^+$, found 303.1104.

*(Z)-1-(3-Chloro-4-fluorophenyl)-2-(4-phenylbut-3-yn-2-ylidene)-hydrazine (**Z-22n**).* 4-Phenylbut-3-yn-2-one (114 mg, 0.79 mmol) and (3-chloro-4-fluorophenyl)hydrazine (127 mg, 0.79 mmol) were employed to afford 198 mg (87%) of the indicated product for condition B. ^1H NMR (400 MHz, $CDCl_3$): δ 8.18 (br s, 1H), 7.54 (m, 2H), 7.42 (m, 3H), 7.17 (dd, J = 6.3, 2.5 Hz, 1H), 7.03 (t, J = 8.7 Hz, 1H), 6.88 (m, 1H), 2.24 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.5 (d, J = 18.4 Hz, C), 141.0 (C), 131.8 (CH), 129.6 (CH), 128.7 (CH), 125.0 (C), 121.5 (d, J = 18.4 Hz, C), 121.3 (C), 116.8 (d, J = 21.8 Hz, CH), 114.5 (CH), 112.0 (d, J = 6.2 Hz, CH), 101.6 (C), 80.6(C), 22.2 (CH_3). IR (neat): 3309, 3055, 2916, 2360, 2165, 1606, 1556, 1506, 1442, 1259, 1209, 1186, 1153, 862, 804, 746, 680 cm^{-1}. MS (ESI, *m/z*): 309.06 $[M + Na]^+$. HRMS (ESI): calcd for $C_{16}H_{12}ClFN_2Na$ 309.0571 $[M + Na]^+$, found 309.0565.

*(Z)-1-(2,5-Difluorophenyl)-2-(4-phenylbut-3-yn-2-ylidene)hydrazine (**Z-22o**).* 4-Phenylbut-3-yn-2-one (151 mg, 1.05 mmol) and (2,5-difluorophenyl)hydrazine (152 mg, 1.05 mmol) were employed to afford 245 mg (86%) the indicated product for condition B. ^1H NMR (400 MHz, $CDCl_3$): δ 8.54 (br s, 1H), 7.57 (m, 2H), 7.44 (m, 3H), 7.25 (m, 1H), 6.98 (m, 1H), 6.47 (m, 1H), 2.28 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.8 (d, J = 239.8 Hz, C), 145.7 (d, J = 233.4 Hz, C), 133.7 (t, J = 12 Hz, C), 131.9 (CH), 129.7 (CH), 128.7 (CH), 127.2 (C), 121.2 (C), 115.3 (dd, J = 20, 9.7 Hz, CH), 105.0 (dd, J = 24.8, 7 Hz, CH), 102.2 (C), 101.6 (dd, J = 30.4, 2.5 Hz, CH), 80.4 (C), 22.1 (CH_3). IR (neat): 3327, 3066, 3045, 2921, 2173, 1633, 1521, 1460, 1247, 1151, 1130, 977, 854, 808, 754, 732, 684 cm^{-1}. MS (ESI, *m/z*): 293.09 $[M + Na]^+$. HRMS (ESI): calcd for $C_{16}H_{12}F_2N_2Na$ 293.0868 $[M + Na]^+$, found 293.0861.

*(Z)-1-(1,3-Diphenylprop-2-yn-1-ylidene)-2-phenylhydrazine (**Z-22p**).* 1,3-Diphenylprop-2-yn-1-one (206 mg, 1.0 mmol) and phenylhydrazine (115 mg, 1.0 mmol) were employed to afford 80 mg (27%) of the indicated product for condition B. ^1H NMR (400 MHz, $CDCl_3$): δ 8.79 (br s, 1H), 8.06 (d, J = 7.9 Hz, 2H), 7.69 (m, 2H), 7.49 (m, 5H), 7.39 (m, 3H), 7.30 (d, J = 7.9 Hz, 2H), 7.0 (t, J = 7.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.6 (C), 135.9 (C), 132.0 (CH), 129.7 (CH), 129.4 (CH), 128.8 (CH), 128.5 (CH), 128.2 (CH), 125.7 (C), 125.6 (CH), 121.6 (CH), 121.1 (C), 113.6 (CH), 103.8 (C), 78.9 (C). IR (neat): 3298, 2928, 2360, 2160, 1600, 1517, 1490, 1442, 1259, 1168, 1072, 885, 748, 686 cm^{-1}. MS (ESI, *m/z*): 319.12 $[M + Na]^+$. HRMS (ESI): calcd for $C_{21}H_{16}N_2Na$ 319.1211 $[M + Na]^+$, found 319.1206.

*(Z)-1-(1,3-Diphenylprop-2-yn-1-ylidene)-2-(4-(trifluoromethyl)-phenyl)hydrazine (**Z-22q**).* 1,3-Diphenyl-prop-2-yn-1-one (206 mg, 1.0 mmol) and (4-(trifluoromethyl)phenyl)hydrazine (176 mg, 1.0 mmol) was employed to afford 189 mg (52%) of the indicated product for condition B. ^1H NMR (400 MHz, $CDCl_3$): δ 8.83 (br s, 1H), 8.02 (d, J = 7.5 Hz, 2H), 7.67 (d, J = 7.6 Hz, 2H), 7.58 (d, J = 8.4 Hz, 2H), 7.49 (m, 5H), 7.39 (d, J = 7.3 Hz, 1H), 7.29 (d, J = 8.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.8 (C) 135.4 (C), 132.0 (CH), 129. (CH), 128.8 (CH), 128.5 (CH), 127.9 (C), 126.7 (m, CH), 125.9 (CH), 125.8 (CH), 123.8 (d, J = 175 Hz, (C), 122.6 (q, J = 32.2 Hz, C), 121.2 (C), 113.1 (CH), 104.2 (C), 78.5 (C). IR (neat): 3303, 3064, 3029, 2360, 2187, 1612, 1533, 1488, 1419, 1321, 1267, 1551, 1095, 1060, 829, 752, 682 cm^{-1}. MS (ESI, *m/z*): 387.11 $[M + Na]^+$. HRMS (ESI): calcd for $C_{22}H_{15}F_3N_2Na$ 387.1085 $[M + Na]^+$, found 387.1080.

*(Z)-1-(2,5-Difluorophenyl)-2-(1,3-diphenylprop-2-yn-1-ylidene)-hydrazine (**Z-22r**).* 1,3-Diphenylprop-2-yn-1-one (220 mg, 1.06 mmol) and (2,5-difluorophenyl)hydrazine (154 mg, 1.06 mmol) were employed to afford 139 mg (36%) of the indicated product for condition B. ^1H NMR (400 MHz, $CDCl_3$): δ 8.93 (br s, 1H), 8.01 (d, J = 7.5 Hz, 2H), 7.65 (m, 2H), 7.45 (m, 5H), 7.40 (m, 2H), 7.02 (m, 1H), 6.52 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.4 (d, J = 239 Hz, C), 145.7 (d, J = 235.5 Hz, C), 134.7 (C), 132.8 (t, J = 11.5 Hz, C), 131.6 (CH), 129.4 (CH), 128.6 (C),128.4 (CH), 128.3 (CH), 128.0 (CH), 125.3 (CH), 120.7 (C), 115.0 (dd, J = 20, 9.4 Hz, CH), 105.3 (dd, J = 24.6, 7.5 Hz, CH), 104.3 (C), 101.6 (d, J = 29.1 Hz, CH), 78.0 (C). IR (neat): 3317, 3056, 2920, 2360, 2185, 1633, 1529, 1496, 1461, 1436, 1346, 1288 1247, 1182, 1157, 839, 785, 752, 729, 686 cm^{-1}. MS (ESI, *m/z*): 355.10 $[M + Na]^+$. HRMS (ESI): calcd for $C_{21}H_{14}F_2N_2Na$ 355.1023 $[M + Na]^+$, found 355.1017.

*(Z)-1-Phenyl-2-(3-ferrocenylprop-2-yn-1-ylidene)hydrazine (**Z-23a**).* 3-Ferrocenylpropynal (200 mg, 0.84 mmol) and phenylhydrazine (91 mg, 0.84 mmol) were employed to afford 132 mg (48%) and 149 mg (54%) of the indicated product for conditions A and B, respectively. ^1H NMR (400 MHz, $CDCl_3$): δ 8.64 (br s, 1H, NH), 7.32 (t, J = 7.3 Hz, 2H), 7.13 (d, J = 7.6 Hz, 2H), 6.94 (t, J = 7.3 Hz, 1H), 6.55 (s, 1H), 4.57 (s, 2H), 4.35 (s, 2H), 4.29 (s, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.7 (C), 129.4 (CH), 120.4 (CH), 115.7 (CH), 113.2 (CH), 102.4 (C), 76.5 (C), 71.8 (CH), 70.3 (CH), 69.7 (CH), 62.9 (C). IR (neat): 3303, 2360, 2204, 2160, 1602, 1560, 1519, 1488, 1259, 1147, 1105, 1018, 999, 875, 810, 750, 692 cm^{-1}. MS (ESI, *m/z*): 351.06 $[M + Na]^+$. HRMS (ESI): calcd for $C_{19}H_{16}FeN_2Na$ 351.0559 $[M + Na]^+$, found 351.0555.

*(E)-1-Phenyl-2-(3-ferrocenylprop-2-yn-1-ylidene)hydrazine (**E-23a**).* 3-Ferrocenylpropynal (200 mg, 0.84 mmol) and phenylhydrazine (91 mg, 0.84 mmol) were employed to afford 124 mg (45%) and 99 mg (36%) of the indicated product for conditions A and B, respectively. ^1H NMR (400 MHz, $CDCl_3$): δ 7.95 (br s, 1H, NH), 7.27 (t, J = 7.9 Hz, 2H), 7.08 (d, J = 7.9 Hz, 2H), 7.03 (s, 1H), 6.90 (t, J = 7.3 Hz, 1H), 4.51 (s, 2H), 4.27 (s, 2H), 4.25 (s, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.7 (C), 129.3 (CH), 120.8 (CH), 120.4 (C), 113.12 (CH), 92.2 (C), 82.0 (C), 71.6 (CH), 70.1 (CH), 69.2 (CH), 64.3 (C). IR (neat): 3305, 2204, 2160, 1602, 1560, 1519, 1490, 1348, 1261, 1147, 1105, 1018, 999, 875, 810, 750, 692 cm^{-1}. MS (ESI, *m/z*): 351.06 $[M + Na]^+$. HRMS (ESI): calcd for $C_{19}H_{16}FeN_2Na$ 351.0559 $[M + Na]^+$, found 351.0555.

*(Z)-1-(3-(Ferrocenyl)prop-2-yn-1-ylidene)-2-(4-(trifluoromethyl)phenyl) hydrazine (**Z-23b**).* 3-Ferrocenylpropynal (200 mg, 0.84 mmol) and (4-(trifluoromethyl)phenyl)hydrazine (148 mg, 0.84 mmol) were employed to afford 150 mg (45%) and 143 mg (43%) of the indicated product for conditions A and B, respectively. ^1H NMR (400 MHz, $CDCl_3$): δ 8.72 (br s, 1H, NH), 7.54 (d, J = 7.5 Hz, 2H), 7.16 (d, J = 7.6 Hz, 2H), 6.60 (s, 1H), 4.57 (s, 2H), 4.37 (s, 2H), 4.28 (s, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.2 (C), 126.7 (m, CH), 124.6 (d, J = 269.5 Hz, C), 122.5 (q, J = 32.3 Hz, C), 117.8 (CH), 112.8 (CH), 103.2 (C), 76.0 (C), 71.9 (CH), 70.4 (CH), 69.9 (CH), 62.4 (C). IR (neat): 3325, 2187, 1614, 1542, 1523, 1323, 1263, 1091, 1058, 1001, 821 cm^{-1}. MS (ESI, *m/z*): 419.04 $[M + Na]^+$. HRMS (ESI): calcd for $C_{20}H_{15}F_3FeN_2Na$ 419.0433 $[M + Na]^+$, found 419.0429.

*(E)-1-(3-(Ferrocenyl)prop-2-yn-1-ylidene)-2-(4-(trifluoromethyl)-phenyl) hydrazine (**E-23b**).* 3-Ferrocenylpropynal (200 mg, 0.84 mmol)

and (4-(trifluoromethyl)phenyl)hydrazine (148 mg, 0.84 mmol) were employed to afford 100 mg (30%) and 166 mg (50%) of the indicated product for conditions A and B, respectively. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09 (br s, 1H, NH), 7.51 (d, J = 7.2 Hz, 2H), 7.13 (d, J = 7.4 Hz, 2H), 7.09 (s, 1H), 4.53 (s, 2H), 4.29 (s, 2H), 4.26 (s, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.2 (C), 126.6 (m, CH), 124.6 (d, J = 268.8 Hz, C), 122.4 (d, J = 33 Hz, C), 122.3 (CH), 112.6 (CH), 93.5 (C), 81.6 (C), 71.7 (CH), 70.2 (CH), 69.4 (CH), 63.6 (C). IR (neat): 3315, 2202, 1616, 1533, 1326, 1661, 1155, 1103, 1064, 894, 813 cm^{-1}. MS (ESI, m/z): 419.04 [M + Na]$^+$. HRMS (ESI): calcd for $C_{20}H_{15}F_3FeN_2Na$ 419.0433 [M + Na]$^+$, found 419.0429.

*(Z)-1-(3-Chloro-4-fluorophenyl)-2-(3-ferrocenylprop-2-yn-1-ylidene)hydrazine (**Z-23c**).* 3-Ferrocenylpropynal (200 mg, 0.84 mmol) and (3-chloro-4-fluorophenyl)hydrazine (135 mg, 0.84 mmol) were employed to afford 150 mg (47%) and 128 mg (40%) of the indicated product for conditions A and B, respectively. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.50 (br s, 1H), 7.20 (m, 1H), 7.06 (t, J = 8.6 Hz, 1H), 6.92 (m, 1H), 6.55 (s, 2H), 4.56 (s, 2H), 4.36 (s, 2H), 4.28 (s, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.6 (d, J = 239.5 Hz, C), 140.6 (C), 121.6 (d, J = 18.5 Hz, C), 117.1 C, 116.8 (CH), 114.8 (CH), 112.2 (d, J = 6.2 Hz, CH), 103.1 (C), 76.2 (C), 71.8 (CH), 70.3 (CH), 69.9 (CH), 62.5 (C). IR (neat): 3303, 3093, 2181, 1606, 1492, 1411, 1330, 1251, 1207, 1143, 1105, 1047, 1001, 812, 732 cm^{-1}. MS (ESI, m/z): 403.01 [M + Na]$^+$. HRMS (ESI): calcd for $C_{19}H_{14}ClFFeN_2Na$ 403.0076 [M + Na]$^+$, found 403.0072.

*(E)-1-(3-Chloro-4-fluorophenyl)-2-(3-ferrocenylprop-2-yn-1-ylidene)hydrazine (**E-23c**).* 3-Ferrocenylpropynal (200 mg, 0.84 mmol) and (3-chloro-4-fluorophenyl)hydrazine (135 mg, 0.84 mmol) were employed to afford 166 mg (52%) and 192 mg (60%) of the indicated product for conditions A and B, respectively. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (br s, 1H), 7.19 (m, 1H), 7.03 (m 2H), 6.86 (m, 1H), 4.52 (s, 2H), 4.28 (s, 2H), 4.26 (s, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.6 (d, J = 239.5 Hz, C), 140.6 (C), 121.6 (d, J = 18.5 Hz, C), 117.1 (C), 116.8 (CH), 114.8 (CH), 112.2 (d, J = 6.2 Hz, CH), 103.1 (C), 76.2 (C), 71.8 (CH), 70.3 (CH), 69.9 (CH), 62.5 (C). MS (ESI, m/z): 403.01 [M + Na]$^+$. HRMS (ESI): calcd for $C_{19}H_{14}ClFFeN_2Na$ 403.0076 [M + Na]$^+$, found 403.0072.

*(Z)-1-(2,5-Difluorophenyl)-2-(3-ferrocenylprop-2-yn-1-ylidene)-hydrazine (**Z-23d**).* 3-Ferrocenylpropynal (200 mg, 0.84 mmol) and (2,5-difluorophenyl)hydrazine (121 mg, 0.84 mmol) were employed to afford 177 mg (58%) and 171 mg (56%) of the indicated product for conditions A and B, respectively. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.81 (br s, 1H), 7.23 (m, 1H), 7.00 (m, 1H), 6.64 (s, 1H), 6.50 (m, 1H), 4.57 (s, 2H), 4.36 (s, 2H), 4.28 (s, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.8 (d, J = 239 Hz, C), 145.9 (d, J = 235.5 Hz, C), 133.3 (t, J = 11.3 Hz, C), 118.9 (CH), 115.5 (dd, J = 20, 10 Hz, CH), 105.7 (dd, J = 24.5, 7.5 Hz, CH), 103.8 (C), 101.9 (dd, J = 28.4, 2.3 Hz, CH), 76.0 (C), 71.9 (CH), 70.4 (CH), 69.9 (CH), 62.2 (C). IR (neat): 3325, 3093, 2189, 1633, 1521, 1452, 1342, 1247, 1182, 1153, 1118, 1004, 817, 754 cm^{-1}. MS (ESI, m/z): 387.04 [M + Na]$^+$. HRMS (ESI): calcd for $C_{19}H_{14}F_2FeN_2Na$ 387.0371 [M + Na]$^+$, found 387.0367.

*(E)-1-(2,5-Difluorophenyl)-2-(3-ferrocenylprop-2-yn-1-ylidene)-hydrazine (**E-23d**).* 3-Ferrocenylpropynal (200 mg, 0.84 mmol) and (2,5-difluorophenyl)hydrazine (121 mg, 0.84 mmol) were employed to afford 129 mg (42%) and 122 mg (40%) of the indicated product for conditions A and B, respectively. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01 (br s, 1H), 7.27 (m, 1H), 7.13 (s, 1H), 6.95 (m, 1H), 6.47 (m, 1H), 4.59 (s, 2H), 4.32 (s, 7H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.7 (d, J = 239 Hz, C), 145.6 (d, J = 233 Hz, C), 133.0 (t, J = 11.9 Hz, C), 126.2 (CH), 115.4 (dd, J = 20, 9.5 Hz, CH), 105.7 (dd, J = 25, 7.5 Hz, CH), 102.2 (d, J = 31 Hz, CH), 93.7 (C), 81.4 (C), 71.7 (CH), 70.2 (CH), 69.5 (CH), 63.8 (C). IR (neat): 3321, 3087, 2185, 1631, 1517, 1450, 1338, 1290, 1244, 1184, 1157, 1107, 1001, 977, 815, 734 cm^{-1}. MS (ESI, m/z): 387.04 [M + Na]$^+$. HRMS (ESI): calcd for $C_{19}H_{14}F_2FeN_2Na$ 387.0371 [M + Na]$^+$, found 387.0367.

*(Z)-2-(2-(3-Ferrocenylprop-2-yn-1-ylidene)hydrazinyl)ethanol (**Z-23e**).* 3-Ferrocenylpropynal (200 mg, 0.84 mmol) and 2-hydrazinylethanol (167 mg, 0.84 mmol) were employed to afford 122 mg (49%) of the indicated product for condition B. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.42 (s, 1H), 4.49 (s, 2H), 4.29 (s, 2H), 4.23 (s, 5H), 3.85 (t, 2H), 3.47 (t, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 116.9 (CH), 101.5 (C), 71.7 (CH), 70.2 (CH), 70.0 (C), 69.5 (CH), 63.1 (C), 62.3 (CH_2), 51.9 (CH_2). IR (neat): 3253 b, 2185, 1529, 1467, 1409, 1340, 1164, 1105, 1058, 1022, 1001, 815 cm^{-1}. MS (ESI, m/z): 319.05 [M + Na]$^+$. HRMS (ESI): calcd for $C_{15}H_{16}FeN_2ONa$ 319.0509 [M + Na]$^+$, found 319.0504.

General Procedure for the Synthesis of 1,5-Diaryl/alkyl-4-iodo-1*H*-pyrazoles (24a−k). To a stirred solution of iodine (0.75 mmol) and $NaHCO_3$ (0.75 mmol) in CH_2Cl_2 (5 mL) was added the appropriate acetylenic hydrazone (0.25 mmol) in CH_2Cl_2 (2 mL), and the resulting solution was stirred at room temperature under argon for 2 h. After the reaction was over, the excess I_2 was removed by washing with a saturated aqueous solution of $Na_2S_2O_3$. The aqueous solution was then extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under a vacuum to afford the crude product, which was purified by flash chromatography on silica gel using hexane/ethyl acetate (9/1) as the eluent to afford the desired product.

*4-Iodo-1,5-diphenyl-1H-pyrazole (**24a**).* Hydrazone **Z-22a** (50 mg, 0.23 mmol), iodine (173 mg, 0.69 mmol), and $NaHCO_3$ (58 mg, 0.69 mmol) were employed to afford 64 mg (80%) of the indicated product. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (s, 1H), 7.29 (m, 3H), 7.19 (m, 5H), 7.13 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.5, 143.5, 139.9, 130.3, 129.6, 129.0, 128.8, 128.5, 127.6, 124.7, 62.3. IR (neat): 3029, 2923, 2852, 1595, 1492, 1444, 1377, 1066, 943, 844, 758 cm-1. MS (ESI, m/z): 368.98 [M + Na]$^+$. HRMS (ESI): calcd for $C_{15}H_{11}IN_2Na$ 368.9865 [M + Na]$^+$, found 368.9859.

*4-Iodo-1-phenyl-5-(p-tolyl)-1H-pyrazole (**24b**).* Hydrazone **Z-22b** (55 mg, 0.23 mmol), iodine (173 mg, 0.69 mmol), and $NaHCO_3$ (58 mg, 0.69 mmol) were employed to afford 71 mg (85%) of the indicated product. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72 (s, 1H), 7.23 (m, 3H), 7.14 (m, 4H), 6.83 (d, J = 8.3 Hz, 2H), 3.77 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.9 (C), 145.3 (CH), 143.4 (C), 140.0 (C), 131.6 (CH), 128.8 (CH), 127.5 (CH), 124.7 (CH), 121.7 (C), 113.9 (CH), 62.2 (C), 55.2 (CH_3). IR (neat): 3101, 2914, 2852, 1595, 1496, 1434, 1380, 1315, 1068, 943, 914, 858, 815, 761 cm^{-1}. MS (ESI, m/z): 383.00 [M + Na]$^+$. HRMS (ESI): calcd for $C_{16}H_{13}IN_2Na$ 383.0021 [M + Na]$^+$, found 383.0016.

*4-Iodo-5-(4-methoxyphenyl)-1-phenyl-1H-pyrazole (**24c**).* Hydrazone **Z-22c** (56 mg, 0.23 mmol), iodine (173 mg, 0.69 mmol), and $NaHCO_3$ (58 mg, 0.69 mmol) were employed to afford 73 mg (84%) of the indicated product. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72 (s, 1H), 7.23 (m, 3H), 7.14 (m, 4H), 6.83 (d, J = 8.3 Hz, 2H), 3.77 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.9 (C), 145.3 (CH), 143.4 (C), 140.0 (C), 131,6 (CH), 128.8 (CH), 127.5 (CH), 124.7 (CH), 121.7 (C), 113.9 (CH), 62.2 (C), 55.2 (CH_3). IR (neat): 2912, 1595, 1496, 1434, 1380, 1315, 1068, 943, 914, 858, 815, 761 cm^{-1}. MS (ESI, m/z): 399.00 [M + Na]$^+$. HRMS (ESI): calcd for $C_{16}H_{13}IN_2ONa$ 398.9970 [M + Na]$^+$, found 398.6665.

*4-Iodo-1-phenyl-5-(thiophen-3-yl)-1H-pyrazole (**24d**).* Hydrazone **Z-22d** (75 mg, 0.33 mmol), iodine (251 mg, 0.99 mmol), and $NaHCO_3$ (83 mg, 0.99 mmol) were employed to afford 96 mg (83%) of the indicated product. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (s, 1H), 7.29 (dd, J = 2.9, 1.0 Hz, 1H), 7.22 (m, 2H), 7.19 (m, 2H), 7.16 (d, J = 1.7 Hz, 1H), 7.14 (m, 1H), 6.79 (d, J = 4.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.6 (CH), 139.9 (C), 139.4 (C), 129.3 (C), 128.9 (CH), 128.2 (CH), 127.9 (CH), 126.8 (CH), 125.8 (CH), 124.8 (CH), 62.2

(C). IR (neat): 3091, 2954, 2921, 2852, 1593, 1498, 1444, 1375, 1182, 1066, 943, 854, 786, 761 cm^{-1}. MS (ESI, *m/z*): 374.94 $[M + Na]^+$. HRMS (ESI): calcd for $C_{13}H_9IN_2SNa$ 374.9429 $[M + Na]^+$, found 374.9423.

*4-Iodo-5-pentyl-1-phenyl-1H-pyrazole (**24e**).* Hydrazone ***Z*-22e** (100 mg, 0.46 mmol), iodine (356 mg, 1.38 mmol), and $NaHCO_3$ (116 mg, 1.38 mmol) were employed to afford 73.5 mg (47%) of the indicated product. ^1H NMR (400 MHz, $CDCl_3$): δ 7.59 (s, 1H), 7.44 (m, 3H), 7.35 (d, J = 7.6 Hz, 2H), 2.67 (t, J = 8 Hz, 2H), 1.44 (p, J = 7.39 Hz, 2H), 1.23 (m, 4H), 0.8 (t, J= 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.6 (C), 144.5 (CH), 139.9 (C), 129.2 (CH), 128.5 (CH), 125.5 (CH), 60.6 (C), 31.2 (CH_2), 28.2 (CH_2), 25.7 (CH_2), 22.0 (CH_2), 13.8 (CH_3). IR (neat): 2954, 2925, 2858, 1596, 1500, 1456, 1390, 1174, 933, 846, 761 cm^{-1}. MS (ESI, *m/z*): 363.03 $[M + Na]^+$. HRMS (ESI): calcd for $C_{14}H_{17}IN_2Na$ 363.0334 $[M + Na]^+$, found 363.0329.

*5-(Cyclopentylmethyl)-4-iodo-1-phenyl-1H-pyrazole (**24f**).* Hydrazone ***Z*-22f** (41 mg, 0.18 mmol), iodine (137 mg, 0.54 mmol), and $NaHCO_3$ (46 mg, 0.54 mmol) were employed to afford 30 mg (47%) of the indicated product. ^1H NMR (400 MHz, $CDCl_3$): δ 7.59 (s, 1H), 7.43 (m, 3H), 7.36 (m, 2H), 2.74 (d, J = 7.6 Hz, 2H), 1.91 (p, 1H), 1.49 (m, 4H), 1.38 (m, 2H), 1.01 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.6 (CH), 144.3 (C), 140.2 (C), 129.2 (CH), 128.9 (CH), 125.8 (CH), 61.3 (C), 39.6 (CH), 32.7 (CH_2), 31.0 (CH_2), 24.6 (CH_2). MS (ESI, *m/z*): 375.03 $[M + Na]^+$. HRMS (ESI): calcd for $C_{15}H_{17}IN_2Na$ 375.0334 $[M + Na]^+$, found 375.0329.

*4-Iodo-5-(p-tolyl)-1-(4-(trifluoromethyl)phenyl)-1H-pyrazole (**24g**).* Hydrazone ***Z*-22g** (65 mg, 0.22 mmol), iodine (168 mg, 0.66 mmol), and $NaHCO_3$ (55 mg, 0.66 mmol) were employed to afford 38 mg (40%) of the indicated product. ^1H NMR (400 MHz, $CDCl_3$): δ 7.81 (s, 1H), 7.56 (d, J = 8.4 Hz, 2H), 7.36 (d, J = 8.4 Hz, 2H), 7.21 (d, J = 7.9 Hz, 2H), 7.15 (d, J = 7.9 Hz, 2H), 2.41 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.1 (CH), 143.9 (C), 142.5 (C), 139.5 (C), 130.0 (CH), 129.4 (CH), 129.2 (q, J = 32.5 Hz, C), 126.2 (C), 126.0 (m, CH), 124.3 (CH), 123.7 (d, J = 271 Hz, C), 63.6 (C), 21.4 (CH_3). MS (ESI, *m/z*): 450.99 $[M + Na]^+$. HRMS (ESI): calcd for $C_{17}H_{12}F_3IN_2Na$ 450.9895 $[M + Na]^+$, found 450.9889.

*1-(3-Chloro-4-fluorophenyl)-4-iodo-5-(p-tolyl)-1H-pyrazole (**24h**).* Hydrazone ***Z*-22 h** (50 mg, 0.17 mmol), iodine (130 mg, 0.51 mmol), and $NaHCO_3$ (43 mg, 0.51 mmol) were employed to afford 29 mg (41%) of the indicated product. ^1H NMR (400 MHz, $CDCl_3$): δ 7.74 (s, 1H), 7.40 (dd, J = 2.30, 6.4 Hz), 7.18 (d, J = 7.9, 2H), 7.11 (d, J = 7.9 Hz, 2H), 6.99 (t, J = 8.7 Hz, 1H), 6.94 (m, 1H), 2.37 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.0 (d, J = 249.5 Hz, C), 145.8 (CH), 143.8 (C), 139.5 (C), 136.4 (C), 130.0 (CH), 129.5 (CH), 126.9 (CH), 125.9 (C), 124.3 (d, J = 7.5 Hz, CH), 121.4 (d, J = 19.5 Hz, C), 116.5 (d, J = 22.5 Hz, CH), 62.9 (C), 21.5 (CH_3). IR (neat): 2921, 2850, 1598, 1498, 1438, 1406, 1384, 1259, 1230, 1053, 952, 867, 844, 813, 717 cm^{-1}. MS (ESI, *m/z*): 434.95 $[M + Na]^+$. HRMS (ESI): calcd for $C_{16}H_{11}ClFIN_2Na$ 434.9537 $[M + Na]^+$, found 434.9532.

*4-Iodo-5-(4-methoxyphenyl)-1-(4-(trifluoromethyl)phenyl)-1H-pyrazole (**24i**).* Hydrazone ***Z*-22i** (50 mg, 0.16 mmol), iodine (122 mg, 0.48 mmol), and $NaHCO_3$ (23 mg, 0.48 mmol) were employed to afford 60 mg (85%) of the indicated product. ^1H NMR (400 MHz, $CDCl_3$): δ 7.77 (s, 1H), 7.53 (d, J = 8.3 Hz, 2H), 7.33 (d, J = 8.3 Hz, 2H), 7.16 (d, J = 8.5 Hz, 2H), 6.90 (d, J = 8.5 Hz, 2H), 3.82 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.3 (C), 146.1 (CH), 143.7 (C), 142.6 (C), 131.5 (CH), 129.2 (q, J = 33.3 Hz, C), 126.0 (CH), 124.3 (CH), 123.7 (d, J = 271 Hz, C), 121,3 (C), 114.3 (CH), 63.6 (C), 55.3 (CH_3). IR (neat): 2966, 2939, 2839, 1612, 1544, 1519, 1490, 1377, 1323, 1249, 1166, 1109, 1058, 1028, 941, 831 cm^{-1}. MS (ESI, *m/z*): 466.98 $[M + Na]^+$. HRMS (ESI): calcd for $C_{17}H_{12}F_3IN_2ONa$ 466.9844 $[M + Na]^+$, found 466.9839.

*1-(3-Chloro-4-fluorophenyl)-4-iodo-5-(4-methoxyphenyl)-1H-pyrazole (**24j**).* Hydrazone ***Z*-22j** (74 mg, 0.25 mmol), iodine (191 mg, 0.75 mmol), and $NaHCO_3$ (63 mg, 0.75 mmol) were employed to afford 102 mg (95%) of the indicated product. ^1H NMR (400 MHz, $CDCl_3$): δ 7.76 (s, 1H), 7.42 (m, 1H), 7.18 (d, J = 8.5 Hz, 2H), 7.01 (m, 2H), 6.93 (d, J = 8.5 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.3 (C), 157.0 (d, J = 248.5 Hz, C), 145.8 (CH), 143.7 (CH), 136.5 (C), 131.5 (CH), 126.9 (CH), 124.2 (CH), 121.4 (d, J = 18.4 Hz, C), 121.0 (C), 116.5 (d, J = 22.1 Hz, CH), 114.3 (CH), 62.9 (C), 55.3 (CH_3);. IR (neat): 2933, 2837, 1612, 1542, 1498, 1434, 1375, 1249, 1176, 1029, 948, 831, 719 cm^{-1}. MS (ESI, *m/z*): 450.94 $[M + Na]^+$. HRMS (ESI): calcd for $C_{16}H_{11}ClFIN_2ONa$ 450.9486 $[M + Na]^+$, found 450.9481.

*1-(2,5-Difluorophenyl)-4-iodo-5-(4-methoxyphenyl)-1H-pyrazole (**24k**).* Hydrazone ***Z*-22k** (70 mg, 0.24 mmol), iodine (183 mg, 0.72 mmol), and $NaHCO_3$ (60.5 mg, 0.72 mmol) were employed to afford 73 mg (74%) of the indicated product. ^1H NMR (400 MHz, $CDCl_3$): δ 7.78 (s, 1H), 7.17 (d, J = 8.6 Hz, 2H), 7.12 (m, 1H), 6.99 (m, 2H), 6.84 (d, J = 8.6 Hz, 2H), 3.78 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.2 (C), 158.0 (d, J = 244, C), 152.6 (d, J = 248.5 Hz, C), 146.5 (CH), 145.4 (CH), 130.9 (CH), 128.5 (C), 120.8 (C), 117.4 (dd, J = 22.8, 9.1 Hz, CH), 116.9 (dd, J = 23.8, 7.5 Hz, CH), 115.8 (d, J = 25.7 Hz, CH), 113.9 (CH), 61.5 (C), 55.2 (CH_3). IR (neat): 2981, 2943, 1616, 1542, 1508, 1488, 1461, 1425, 1365, 1288, 1249, 1205, 1178, 1110, 1026, 952, 867, 815, 767 cm^{-1}. MS (ESI, *m/z*): 434.97 $[M + Na]^+$. HRMS (ESI): calcd for $C_{16}H_{11}F_2IN_2ONa$ 434.9782 $[M + Na]^+$, found 434.9776.

General Procedure for the Synthesis of 4-Iodo-1,3,5-triaryl/alkyl-1*H*-pyrazoles (24l−r). To a stirred solution of iodine (0.75 mmol) and $NaHCO_3$ (0.75 mmol) in CH_3CN (5 mL) was added an appropriate amount of acetylenic hydrazone (0.25 mmol) in CH_3CN (2 mL), and the resulting solution was stirred for 80 °C under argon for 2 h. After the reaction was over, the excess I_2 was removed by washing with a saturated aqueous solution of $Na_2S_2O_3$. The aqueous solution was then extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under vacuum to afford the crude product, which was purified by flash chromatography on silica gel using hexane/ethyl acetate (9/1) as the eluent to afford the desired product.

*4-Iodo-3-methyl-1,5-diphenyl-1H-pyrazole (**24l**).* Hydrazone ***Z*-22l** (50 mg, 0.21 mmol), iodine (160 mg, 0.63 mmol), and $NaHCO_3$ (53 mg, 0.63 mmol) were employed to afford 69.5 mg (92%) of the indicated product. ^1H NMR (400 MHz, $CDCl_3$): δ 7.37 (m, 3H), 7.28 (m, 5H), 7.21 (d, J = 8.4 Hz, 2H), 2.44 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.7 (C), 144.1 (C), 139.9 (C), 130.3 (C), 130.2 (CH), 128.8 (CH), 128.7 (CH), 128.4 (CH), 127.3 (CH), 124.7 (CH), 66.2 (C), 14.4 (CH_3). IR (neat): 2921, 2852, 1596, 1504, 1440, 1407, 1379, 1357, 1047, 966, 916, 840, 767 cm^{-1}. MS (ESI, *m/z*): 383.00 $[M + Na]^+$. HRMS (ESI): calcd for $C_{16}H_{13}IN_2Na$ 383.0021 $[M + Na]^+$, found 383.0016. The spectral data were in agreement with those reported previously for this compound.[66]

*4-Iodo-3-methyl-5-phenyl-1-(4-(trifluoromethyl)phenyl)-1H-pyrazole (**24m**).* Hydrazone ***Z*-22m** (72 mg, 0.23 mmol), iodine (173 mg, 0.69 mmol), and $NaHCO_3$ (57 mg, 0.69 mmol) were employed to afford 92 mg (93%) of the indicated product. ^1H NMR (400 MHz, $CDCl_3$): δ 7.54 (d, J = 8.4, 2H), 7.43 (m, 3H), 7.34 (d, J = 8.4 Hz, 2H), 7.30 (m, 2H), 2.44 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.5 (C), 144.3 (C), 142.6 (C), 130.1 (CH), 129.9 (C), 129.3 (CH), 128.9 (q, J = 32.5 Hz, C), 128.8 (CH), 126.0 (m, CH), 124.1 (CH), 123.7 (d, J = 271.3 Hz, C), 67.7 (C), 14.4 (CH_3). IR (neat): 2958, 2925, 1614, 1519, 1492, 1444, 1402, 1357, 1319, 1164, 1124, 1064, 1045, 964, 844, 752 cm^{-1}. MS (ESI, *m/z*): 450.99 $[M + Na]^+$. HRMS (ESI): calcd for $C_{17}H_{12}F_3IN_2Na$ 450.9895 $[M + Na]^+$, found 450.9889.

*1-(3-Chloro-4-fluorophenyl)-4-iodo-3-methyl-5-phenyl-1H-pyrazole (**24n**).* Hydrazone ***Z*-22n** (80 mg, 0.28 mmol), iodine (213 mg, 0.84 mmol), and $NaHCO_3$ (70.5 mg, 0.84 mmol) were employed to afford 93 mg (81%) of the indicated product. ^1H NMR (400 MHz, $CDCl_3$): δ 7.30 (m, 4H), 7.17 (m, 2H), 6.87 (m, 2H), 2.30 (s, 3H). ^{13}C NMR (100

MHz, $CDCl_3$): δ 156.9 (d, J = 248.5 Hz, C), 152.2 (C), 144.3 (C), 136.5 (C), 130.1 (CH), 129.7 (C), 129.3 (CH), 128.7 (CH), 126.8 (CH), 124.1 (d, J = 7.5 Hz, CH), 121.4 (d, J = 19 Hz, C), 116.4 (d, J = 21.8 Hz, CH), 66.8 (C), 14.3 (CH_3);. IR (neat): 3041, 2920, 2850, 1596, 1502, 1444, 1400, 1380, 1359, 1263, 1230, 1172, 1134, 1047, 974, 869, 829, 771 cm^{-1}. MS (ESI, m/z): 412.97 $[M + H]^+$. HRMS (ESI): calcd for $C_{16}H_{12}ClFIN_2$: 412.9718 $[M + H]^+$, found 412.9712.

*1-(2,5-Difluorophenyl)-4-iodo-3-methyl-5-phenyl-1H-pyrazole (**24o**).* Hydrazone ***Z*-22o** (70 mg, 0.26 mmol), iodine (198 mg, 0.78 mmol), and $NaHCO_3$ (65.5 mg, 0.78 mmol) were employed to afford 88.5 mg (86%) of the indicated product. ^1H NMR (400 MHz, $CDCl_3$): δ 7.35 (m, 3H), 7.30 (m, 2H), 7.16 (m, 2H), 6.99 (m, 2H), 2.42 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 158. (d, J = 244 Hz, C), 152.8 (C), 152.6 (d, J = 250 Hz, C), 146.0 (C), 129.4 (CH), 129.3 (C), 129.1 (CH), 128.9 (C), 128.4 (t, J = 10.7 Hz, C), 128.4 (CH), 117.4 (dd, J = 22.5, 9.2 Hz, CH), 116.7 (dd, J = 24.1, 7.5 Hz, CH), 115.7 (d, J = 25.5 Hz, CH), 65.6 (C), 14.5 (CH_3). IR (neat): 3080, 2923, 1623, 1508, 1488, 1434, 1394, 1352, 1251, 1195, 1166, 1043, 871, 819, 761, 750 cm^{-1}. MS (ESI, m/z): 418.98 $[M + Na]^+$. HRMS (ESI): calcd for $C_{16}H_{11}F_2IN_2Na$ 418.9833 $[M + Na]^+$, found 418.9837.

*4-Iodo-1,3,5-triphenyl-1H-pyrazole (**24p**).* Hydrazone ***Z*-22p** (50 mg, 0.17 mmol), iodine (130 mg, 0.51 mmol), and $NaHCO_3$ (43 mg, 0.51 mmol) were employed to afford 47 mg (66%) of the indicated product. ^1H NMR (400 MHz, $CDCl_3$): δ 8.00 (d, J = 7.3 Hz, 2H), 7.5 (m, 2H), 7.40 (m, 4H), 7.37 (m, 2H), 7.29 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.0 (C), 145.4 (C), 139.9 (C), 132.9 (C), 130.6 (CH), 130.3 (C), 129.1 (CH), 128.8 (CH), 128.6 (CH), 128.5 (CH), 128.4 (CH), 128.3 (CH), 127.5 (CH), 124.8 (CH), 63.6 (C). IR (neat): 3066, 2923, 1591, 1490, 1450, 1396, 1350, 1147, 1072, 1028, 960, 912, 758 cm^{-1}. MS (ESI, m/z): 445.02 $[M + Na]^+$. HRMS (ESI): calcd for $C_{21}H_{15}IN_2Na$ 445.0178 $[M + Na]^+$, found 445.0172. The spectral data were in agreement with those reported previously for this compound.[67]

*4-Iodo-3,5-diphenyl-1-(4-(trifluoromethyl)phenyl)-1H-pyrazole (**24q**).* Hydrazone ***Z*-22q** (53 mg, 0.15 mmol), iodine (115 mg, 0.45 mmol), and $NaHCO_3$ (38 mg, 0.45 mmol) were employed to afford 66 mg (89%) of the indicated product. ^1H NMR (400 MHz, $CDCl_3$): δ 7.86 (d, J = 7.2 Hz, 2H), 7.44 (d, J = 8.5 Hz, 2H), 7.33 (m, 8H), 7.24 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.7 (C), 145.6 (C), 142.5 (C), 132.4 (C), 130.5 (CH), 130.0 (C), 129.5 (CH), 159.2 (q, J = 32.5 Hz, C), 128.9 (CH), 128.7 (CH), 128.6 (CH), 128.4 (CH), 126.0 (m, CH), 124.3 (CH), 123.7 (d, J = 270.5 Hz, C), 65.0 (C). IR (neat): 3056, 2925, 1614, 1523, 1436, 1321, 1151, 1119, 1062, 1018, 960, 839, 761 cm^{-1}. MS (ESI, m/z): 513.01 $[M + Na]^+$. HRMS (ESI): calcd for $C_{22}H_{14}F_3IN_2Na$ 513.0051 $[M + Na]^+$, found 513.0046.

*1-(2,5-Difluorophenyl)-4-iodo-3,5-diphenyl-1H-pyrazole (**24r**).* Hydrazone ***Z*-22r** (68 mg, 0.20 mmol), iodine (153 mg, 0.60 mmol), and $NaHCO_3$ (50.5 mg, 0.60 mmol) were employed to afford 68 mg (74%) of the indicated product. ^1H NMR (400 MHz, $CDCl_3$): δ 7.98 (d, J = 7.4 Hz, 2H), 7.5 (m, 3H), 7.40 (m, 5H), 7.28 (m, 1H), 7.04 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.01 (d, J = 244.3 Hz, C), 154.2 (C), 152.6 (d, J = 244.5 Hz, C), 147.4 (C), 132.5 (C), 129.9 (CH), 129.3 (CH), 128.71 (C), 128.7 (C), 128.65 (CH), 128.6 (CH), 128.4 (CH), 128.3 (CH), 117.4 (dd, J = 22.4, 9.2 Hz, CH), 117.0 (dd, J = 23.6, 7.5 Hz, CH), 115.9 (d, J = 25.7 Hz, CH), 62.9 (C). IR (neat): 2921, 2852, 1620, 1498, 1473, 1442, 1344, 1251, 1195, 1147, 1112, 1029, 972, 867, 812, 763 cm^{-1}. MS (ESI, m/z): 481.00 $[M + Na]^+$. HRMS (ESI): calcd for $C_{21}H_{13}F_2IN_2Na$ 480.9989 $[M + Na]^+$, found 480.9984.

General Procedure for the Synthesis of 1-Aryl-5-ferrocenyl-4-iodo-1*H*-pyrazoles (26a−e). To a stirred solution of iodine (0.90 mmol) and $NaHCO_3$ (0.90 mmol) in CH_3CN (6 mL) was added an appropriate amount of acetylenic hydrazone (0.30 mmol) in CH_3CN (2.4 mL), and the resulting solution was stirred at room temperature under argon for 30 min. After the reaction was over, the excess I_2 was removed by washing with a saturated aqueous solution of $Na_2S_2O_3$. The aqueous solution was then extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under vacuum to yield the crude product, which was purified by flash chromatography on silica gel using hexane/ethyl acetate (9/1) as the eluent to afford the desired product.

*5-Ferrocenyl-4-iodo-1-phenyl-1H-pyrazole (**26a**).* Hydrazone **23a** (100 mg, 0.30 mmol), iodine (228 mg, 0.90 mmol), and $NaHCO_3$ (75 mg, 0.90 mmol) was employed to afford 123 mg (90%) of the indicated product from ***Z*-23a** and 125 mg (92%) of the indicated product from ***E*-23a**. ^1H NMR (400 MHz, $CDCl_3$): δ 7.61 (s, 1H), 7.30 (m, 3H), 7.17 (m, 2H), 4.31 (s, 2H), 4.15 (s, 2H), 4.11 (s, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.7 (C), 141.1 (C), 140.8 (C), 128.2 (CH), 128.4 (CH), 126.4 (CH), 74.1 (C), 70.2 (CH), 69.2 (CH), 68.7 (CH), 59.6 (C). IR (neat): 3080, 2921, 2850, 1595, 1496, 1394, 1377, 1213, 1103, 1029, 995, 943, 840, 813, 767 cm^{-1}. MS (ESI, m/z): 476.95 $[M + Na]^+$. HRMS (ESI): calcd for $C_{19}H_{15}FeIN_2Na$ 476.9527 $[M + Na]^+$, found 476.9522.

*5-Ferrocenyl-4-iodo-1-(4-(trifluoromethyl)phenyl)-1H-pyrazole (**26b**).* Hydrazone **23b** (100 mg, 0.25 mmol), iodine (191 mg, 0.75 mmol), and $NaHCO_3$ (63 mg, 0.75 mmol) were employed to afford 124 mg (95%) of the indicated product from ***Z*-23b** and 99 mg (76%) of the indicated product from ***E*-23b**. ^1H NMR (400 MHz, $CDCl_3$): δ 7.74 (s, 1H), 7.65 (d, J = 8.4 Hz, 2H), 7.37 (d, J = 8.4 Hz, 2H), 4.36 (s, 2H), 4.29 (s, 2H), 4.22 (s, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.5 (CH), 143.2 (C), 141.3 (C), 130.0 (q, J = 32 Hz, C), 126.2 (CH), 126,2 (m, CH), 123.7 (d, J = 271 Hz, C), 73.95 (C), 70.0 (CH), 69.1 (CH), 68.7 (CH), 60.8 (C). IR (neat): 3116, 2921, 1614, 1519, 1377, 1321, 1163, 1141, 1122, 1107, 1064, 941, 848, 823 cm^{-1}. MS (ESI, m/z): 544.94 $[M + Na]^+$. HRMS (ESI): calcd for $C_{20}H_{14}F_3FeIN_2Na$ 544.9401 $[M + Na]^+$, found 544.9396.

*1-(3-Chloro-4-fluorophenyl)-5-ferrocenyl-4-iodo-1H-pyrazole (**26c**).* Hydrazone **23c** (100 mg, 0.26 mmol), iodine (198 mg, 0.78 mmol), and $NaHCO_3$ (66 mg, 0.78 mmol) were employed to afford 125 mg (94%) of the indicated product from ***Z*-23c** and 122.5 mg (93%) of the indicated product from ***E*-23c**. ^1H NMR (400 MHz, $CDCl_3$): δ 7.69 (s, 1H), 7.41 (d, J = 4.8 Hz, 1H), 7.14 (m, 1H), 7.08 (s, 1H), 4.38 (s, 2H), 4.29 (s, 2H), 4.23 (s, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.1 (d, J = 249.3 Hz), 146.7, 140.9, 136.6, 128.0, 125.6 (d, J = 7.5 Hz), 120.9 (d, J = 19 Hz), 116.0 (d, J = 22.3 Hz), 72.9, 69.6, 68.5, 68.3, 59.6. MS (ESI, m/z): 528.90 $[M + Na]^+$. HRMS (ESI): calcd for $C_{28}H_{13}ClFFeIN_2Na$ 528.9043 $[M + Na]^+$, found 528.9038.

*1-(2,5-Difluorophenyl)-5-ferrocenyl-4-iodo-1H-pyrazole (**26d**).* Hydrazone **23d** (100 mg, 0.27 mmol), iodine (206 mg, 0.81 mmol), and $NaHCO_3$ (68 mg, 0.81 mmol) were employed to afford 110 mg (83%) of the indicated product from ***Z*-23d** and 118 mg (89%) of the indicated product from ***E*-23d**. ^1H NMR (400 MHz, $CDCl_3$): δ 7.70 (s, 1H), 7.17 (m, 3H), 6.51 (s, 1H), 4.24 (s, 4H), 4.11 (s, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.1 (d, J = 244.6 Hz, C), 153.9 (d, J = 250.9 Hz, C), 143.6 (C), 141.2 (CH), 129.0 (C), 117.3 (m, 2 x CH), 116.6 (d, J = 25.2 Hz, CH), 105.9 (CH), 74.1 (C), 69.9 (CH), 69.0 (CH), 67.7 (CH). IR (neat): 3083, 2989, 2869, 1625, 1508, 1473, 1415, 1371, 1253, 1180, 1141, 1103, 999, 925, 879, 819, 794, 765 cm^{-1}. MS (ESI, m/z): 512.93 $[M + Na]^+$. HRMS (ESI): calcd for $C_{19}H_{13}F_2FeIN_2Na$ 512.9339 $[M + Na]^+$, found 512.9333.

*2-(5-Ferrocenyl-4-iodo-1H-pyrazol-1-yl)ethanol (**26e**).* Hydrazone ***Z*-23e** (50 mg, 0.17 mmol), iodine (130 mg, 0.51 mmol), and $NaHCO_3$ (43 mg, 0.51 mmol) were employed to afford 42.5 mg (58%) of the indicated product. ^1H NMR (400 MHz, $CDCl_3$): δ 7.52 (s, 1H), 4.74 (s, 2H), 4.57 (m, 2H), 4.42 (s, 2H), 4.25 (s, 5H), 4.07 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.4 (CH), 141.4 (C), 73.7 (C), 69.8 (CH), 69.2 (CH), 68.8 (CH), 61.7 (CH_2), 58.9 (C), 52.2 (CH_2). IR (neat): 3095, 2927, 2871, 1542, 1398, 1369, 1284, 1232, 1105, 1060, 1001, 960,

871, 819, 729 cm^{-1}. MS (ESI, *m/z*): 444.95 $[M + Na]^+$. HRMS (ESI): calcd for $C_{15}H_{15}FeIN_2ONa$ 444.9476 $[M + Na]^+$, found 444.9471.

■ ASSOCIATED CONTENT

Supporting Information. Figures giving ^1H and ^{13}C NMR spectra of all acetylenic hydrazones and 4-iodopyrazole products as well as tables giving B3LYP/6-31G* optimized Cartesian coordinates and all energy values for model structures. This material is available free of charge via the Internet at http://pubs.acs.org.

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