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Development of a Gold-Multifaceted Catalysis Approach to the Synthesis of Highly Substituted Pyrroles: Mechanistic Insights via Huisgen Cycloaddition Studies

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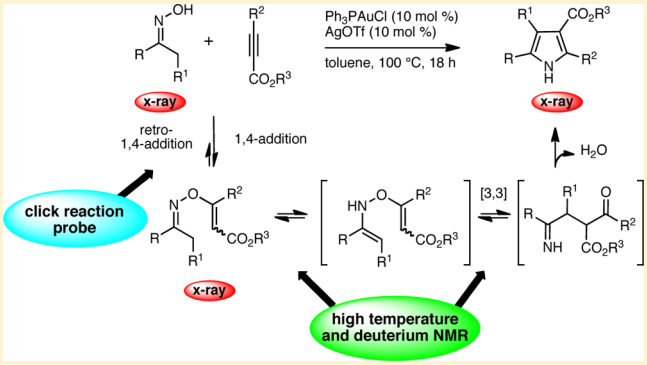
Supporting Information

ABSTRACT: A novel gold-catalyzed method for the regioselective synthesis of highly substituted pyrroles directly from oximes and alkynes was developed via independent optimization of two key steps of the process. Importantly, a cationic gold(I) species was shown to activate multiple steps along the reaction pathway and therefore act as a multifaceted catalyst. Initial gold-promoted addition of the oxime oxygen to the activated alkyne afforded the *O*-vinyloxime in situ. The *O*-vinyloxime was subsequently transformed into the pyrrole via a gold-catalyzed tautomerization, [3,3]-sigmatropic rearrangement, and cyclodehydration process. Notably, this method provides a functional group handle in the form of an ester at the 3/4-position for further exploitation. The proposed mechanistic pathway is supported by a novel application of the Huisgen cycloaddition click reaction, which was used to probe the relative stability of substituted *O*-vinyloximes. The intermediacy of *N*-alkenylhydroxylamine *O*-vinyl ethers and imino ketones or imino aldehydes along the reaction pathway were determined by high-temperature ^{1}H, $^{2}H\{^{1}H\}$, and $^{13}C\{^{1}H\}$ NMR experiments. X-ray crystallographic evidence was used to further support the mechanistic hypothesis.



INTRODUCTION

Due to the importance of pyrroles as pharmaceuticals,[1] agrochemicals[2] and in biological processes[3] as well as in polymer chemistry,[4] supramolecular chemistry,[5] bioinorganic chemistry,[6] and materials science,[7] an extensive amount of research has been conducted toward their synthesis.[8] One area in particular, the use of metal catalysis for the formation of pyrroles, has received a significant amount of interest.[9] Additionally, gold-catalyzed processes are used increasingly for the synthesis of pyrroles due to the relatively mild reaction conditions, redox neutrality, chemoselectivity, and functional group compatibility of gold catalysts.[10] Many of these methods though are multistep and require complex starting materials. Therefore, there remains a demand for increasingly efficient methods for the convergent synthesis of pyrroles from simple, readily available starting materials. An underutilized transformation that satisfies many of these criteria is the reaction of oximes with acetylenes, which is known to give pyrroles via the intermediacy of an *O*-vinyloxime (Figure 1). The reaction of an oxime with an alkyne for the formation of pyrroles is a powerful synthetic method that allows for the convergent formation of both a C−C and C−N bond. Due to the potential of this approach to the synthesis of pyrroles, a number of research groups have investigated the transformation. Some of the earliest work in this area was performed by Sheradsky who, inspired by the classical Fisher indole synthesis, sought to use a similar process for the synthesis of pyrroles.[11] Sheradsky showed in a two-step process that the *O*-vinyloxime derived from the addition of cyclohexanone oxime to dimethylacetylene dicarboxylate could be thermally converted to the corresponding pyrrole at 180 °C. The high-temperature rearrangement of *O*-vinyloximes has been exploited by a number of researchers for the synthesis of pyrroles.[12] An alternative procedure using superbasic conditions (LiOH/DMSO, pK_{aH} = 31)[13] was developed by Trofimov et al. in the late 1970s, which allowed for the synthesis of pyrroles from unactivated alkynes and oximes.[14] This method is limited by the harsh reaction conditions that can result in poor yields and low levels of chemo-/regioselectivity. In spite of these limitations, the Trofimov reaction has been used in a number of important pyrrole syntheses.[15] Research has also been undertaken on catalytic methods of pyrrole formation that go through the intermediacy of an *O*-vinyloxime in order to improve both the yield and selectivity of the process.[16] For example, Anderson et al. recently described a method for the iridium-catalyzed isomerization of allyloximes to *O*-vinyloximes, which were subsequently thermally rearranged to give either 3- or 4-methylpyrroles.[17] This methodology takes advantage of the fact that terminal allyloximes can be isomerized to the more substituted *O*-vinyloxime. Unfortunately, this limits the methodology to the synthesis of methyl-substituted pyrroles.

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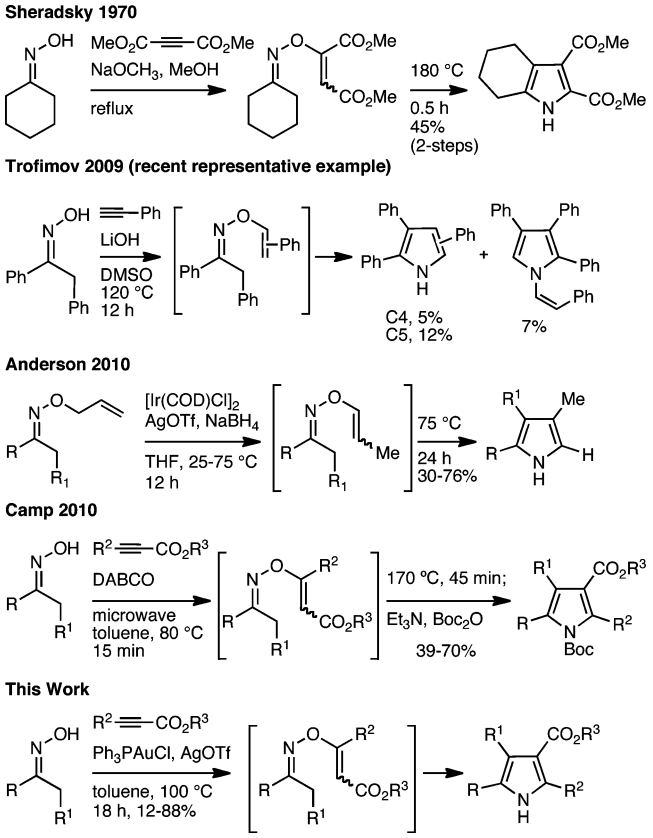


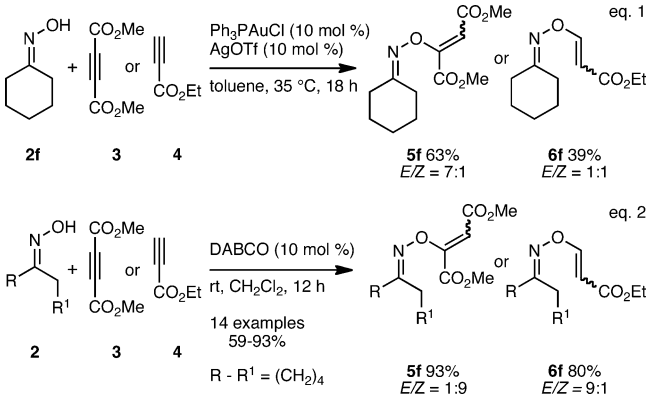
Figure 1. Synthesis of pyrroles via the intermediacy of an *O*-vinyloxime.

Recently, we reported the use of a nucleophilic catalyst to promote the in situ formation of *O*-vinyloximes from the reaction of activated alkynes and oximes, which after subjection to microwave irradiation afforded the desired pyrroles as single regioisomers and in good overall yields.[18] Herein, we report on the development and scope of a regioselective method for the direct synthesis of pyrroles from oximes and alkynes via a gold-multifaceted catalysis approach.[19] Multifaceted catalysis has been defined as the ability of one species to catalyze multiple mechanistically distinct steps in a synthetic sequence.[20,21] The equivalent terms, autotandem catalysis,[22] single-pot catalysis,[23] domino catalysis, and dual catalysis,[24] have also been used to describe this mode of catalysis. A possible mechanism, which explains the observed high levels of regioselectivity, was also investigated using a novel application of the Huisgen cycloaddition click reaction as a mechanistic probe. Additionally, high-temperature ^{1}H, $^{2}H\{^{1}H\}$ and $^{13}C\{^{1}H\}$ NMR experiments as well as X-ray crystallography were used to further support the mechanistic hypothesis.

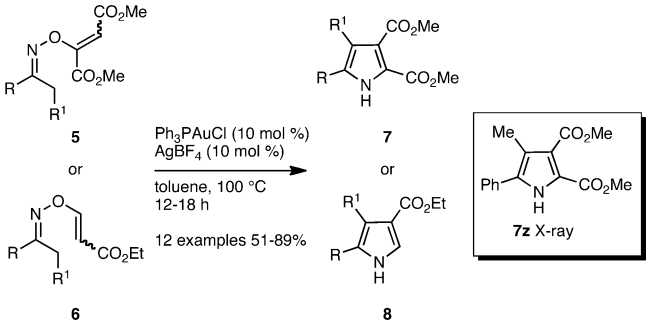
RESULTS AND DISCUSSION

In order to develop a multifaceted catalysis approach, it is important to show that multiple, mechanistically distinct processes are catalyzed by the same catalytic system.[20b] Thus, two key steps, the formation of *O*-vinyloximes **5**/**6** from oximes **2**[25,26] and alkynes **3**/**4** (Scheme 1) as well as their subsequent transformation to pyrroles **7**/**8** (Scheme 2), were investigated independently. Cationic gold(I) catalysts have been shown to activate alkynes toward intermolecular addition of a variety of heteronucleophiles.[27] To the best of our knowledge, the activation of an alkyne toward intermolecular addition of

Scheme 1. Synthesis of *O*-Vinyloximes 5/6 via Gold(I) and Nucleophilic Catalysis



Scheme 2. Gold(I)-Catalyzed Transformation of *O*-Vinyloximes to Pyrroles



ketoximes has not been previously investigated.[28] Thus, the ability of a gold(I) species to catalyze the formation of *O*-vinyloximes **5**/**6** was tested. It was found that the cationic gold(I) species derived from Ph_3PAuCl (10 mol %) and AgOTf (10 mol %) in toluene at 35 °C gave *O*-vinyloximes **5f**/**6f** from reaction of oximes **2f** with either dimethylacetylene dicarboxylate (**3**) or ethylpropiolate (**4**) (Scheme 1, eq 1). These reactions are unoptimized as their purpose was to demonstrate the ability of gold to catalyze the initial step of the process (vide infra). The olefin geometry of the *O*-vinyloximes were established by ^{1}H NMR coupling constants[29] and X-ray crystallography (see, Figure 2). Previously, we showed that the nucleophilic catalyst DABCO[18] could also catalyze this process (Scheme 1, eq 2). Interestingly, the ratio of isomers was significantly different between the two methods of *O*-vinyloxime formation. For diester **5f**, an *E*/*Z* ratio of 7:1 was observed for the gold(I)-catalyzed process, while the DABCO-catalyzed method gave an equally selective, though opposite, 1:9 mixture of isomers. Similar disparities in *E*/*Z* ratio were observed for monoester **6f**. This difference in selectivity reflects the significant difference in mechanism between the two methods (vide infra).[30] Importantly, in the absence of a catalyst no *O*-vinyloxime **5**/**6** was observed.

We were also able to show that a gold(I)-catalyzed formation of pyrroles **7**/**8** from *O*-vinyloximes **5**/**6** is feasible (Scheme 2).[19] In particular, we note the amenability of this novel method to the regioselective generation of di-, tri-, and tetrasubstituted pyrroles at a temperature significantly lower than those reported for the uncatalyzed process (100 °C vs 170 °C).[31] Importantly, the regiochemistry of the pyrrole forming

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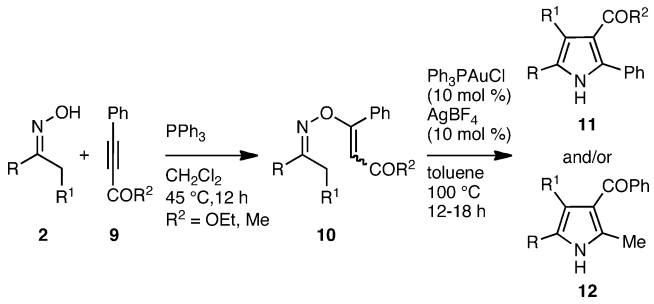
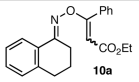
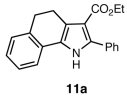
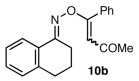
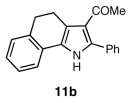
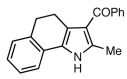
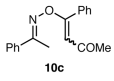
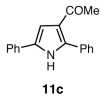
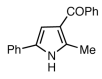
process can now be confirmed via X-ray crystallographic analysis of tetrasubstituted pyrrole **7z** (see also Figure 2).[26]

Additionally, the synthesis of pyrroles **11**/**12** from oximes **2** and aryl-substituted alkynes **9** was investigated to allow for greater substitution around the pyrrole ring (Table 1). Using a

Table 1. Use of Phenyl-Substituted Alkynes for Pyrrole Formation

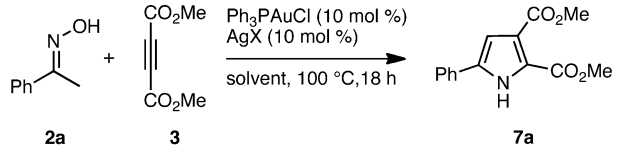


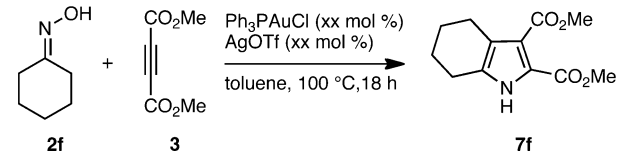
O-vinyloxime **10**	Yield (%) *E*/*Z*	Pyrrole **11**/**12**	Yield (%) **11**/**12**
 **10a**	89 1:4	 **11a**	21
 **10b**	65 0:1	 **11b**  **12b**	47 1:5
 **10c**	54 0:1	 **11c**  **12c**	57 1:5

modification of Trofimov's procedure,[32] triphenylphosphine-catalyzed addition of keto-oximes **2** to acylacetylenes **9** gave a series of ester- and keto-substituted *O*-vinyloximes **10**. Subjection of *O*-2-acylvinyloximes **10** to the standard gold(I)-catalyzed rearrangement conditions afforded the desired pyrroles **11**/**12** in moderate to good yield. Because of competing cyclization modes, ketone derivatives **10b** and **10c** gave a mixture of pyrroles **11**/**12**.[33]

Building upon our research into both the formation of *O*-vinyloximes and the subsequent rearrangement of the isolated *O*-vinyloximes to pyrroles under gold(I)-catalyzed conditions, a one-pot process that was catalyzed by the same gold catalysts was investigated. The cationic gold species should act as a multifaceted catalyst (MFC) promoting multiple mechanistically distinct steps of the reaction; the addition of the oxime to the alkyne and the subsequent transformation to the pyrrole. Previously, we had found that PPh_3AuCl was the best catalyst for the rearrangement of *O*-vinyloximes **5**/**6** to pyrroles **7**/**8**, and these results provided the basis for our investigation into a multifaceted catalysis approach.[19] Thus, the reaction of acetophenone oxime (**2a**) with dimethylacetylene dicarboxylate (**3**) to form trisubstituted pyrrole **7a** was used to screen different silver salts and solvents (Table 2). It was found that in

Table 2. Development of a Gold-Multifaceted Catalysis Process





entry	AgX	solvent	catalyst (mol %)	product yield (%)
1	AgOTf	toluene	10	**7a**, 88
2	$AgBF_4$	toluene	10	**7a**, 72
3	AgOTf	THF	10	**7a**, 36
4	$AgBF_4$	THF	10	**7a**, 27
5	AgOTf	DMSO	10	**7a**, 10
6	AgOTf	DMA	10	**7a**, 84
7	AgOTf	DMF	10	**7a**, 14
8		toluene	0	**7a**, 0
9[a]	AgOTf	toluene	10	**7a**, 0
10[a,b]		toluene	10[c]	**7a**, 0
11	AgOTf	toluene	20	**7f**, 90
12	AgOTf	toluene	10	**7f**, 83
13	AgOTf	toluene	5	**7f**, 79
14	AgOTf	toluene	2	**7f**, 52
15	AgOTf	toluene	0.5	**7f**, 14

[a]No Ph_3PAuCl was added. [b]No silver salt was added. [c]Ph_3P (10 mol %) was added.

the presence of PPh_3AuCl and either AgOTf or $AgBF_4$ the desired pyrrole **7a** was formed in low to excellent yield depending on the solvent that was employed. Several features of the optimization study are noteworthy. Toluene and DMA were shown to be the best solvents for the overall process, and AgOTf gave a slightly higher yield of pyrrole **7a** than $AgBF_4$ (Table 2, entries 1−7). Control experiments, including prolonged heating of **2a** and **3** at 100 °C or the addition of AgOTf or PPh_3 as additives at 100 °C, only afforded starting material (Table 2, entries 8−10). Next, the catalyst loading was investigated using the reaction of cyclohexanone oxime (**2f**) and dimethyl acetylenedicarboxylate (**3**) to give pyrrole **7f** (Table 2, entries 11−15). An initial test reaction using 20 mol % of the catalyst gave a promising 90% yield of the desired bicyclic pyrrole **7f**. It was found that the reaction proceeded in good yield when 5 mol % of the cationic gold(I) catalyst was used, though the yield dropped off significantly when the loading was reduced to 2 mol %. The use of 10 mol % of the in situ formed cationic gold(I) catalyst in toluene was found to be the most efficient set of conditions for the formation of pyrroles from the corresponding oximes and alkynes.

With the optimized conditions in hand, the scope of the gold-multifaceted catalysis (gold-MFC) method was investigated to assess the effect of steric and electronic factors on the

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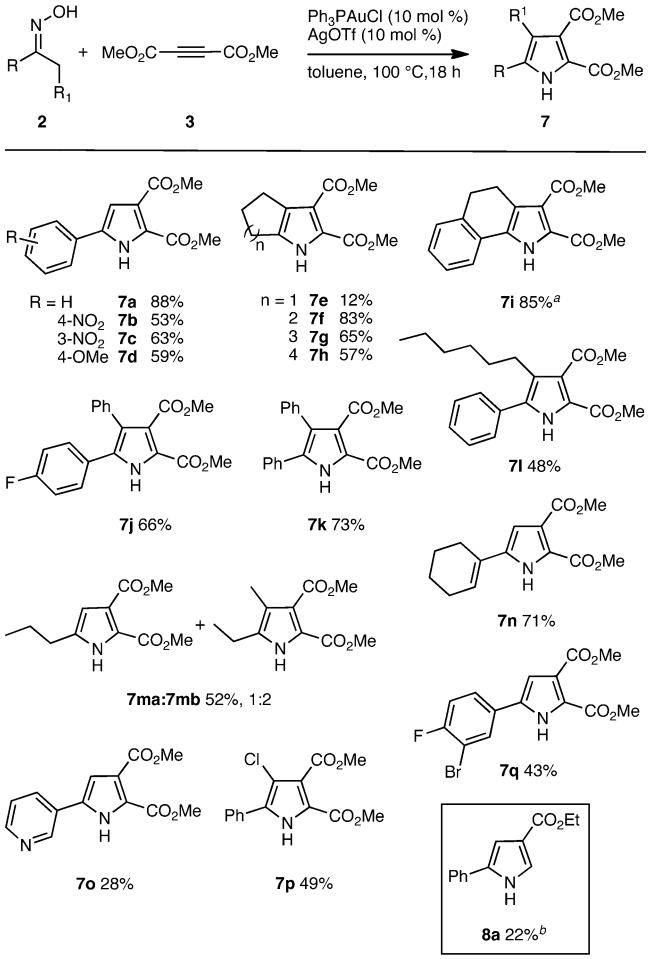
regiochemistry and yield of the process. A variety of oximes **2a–q** were reacted with dimethylacetylene dicarboxylate (**3**) under the standard conditions to give pyrroles **7a–q** (Scheme 3). Both electron-donating and -withdrawing groups on the aromatic ring were well tolerated in the process, affording pyrroles **7b–d**. Additionally, it was found that in fused pyrrole systems, such as **7e–h**, that the size of the ring had a profound effect on the yield of the desired product with fused five-membered rings, i.e., **7e**, being the lowest yielding. This is most likely due to the increase in energy required to tautomerize the five-membered ring system (vide infra) and the rapid decomposition of the fused system. α-Substituted acetophenone oximes afforded pyrroles **7i–l** as single regioisomers in moderate to good yield. The oxime of 2-pentanone, **2m**, has two possible positions for tautomerization. Subjection of **2m** to the standard gold-MFC conditions gave pyrroles **7ma** and **7mb** as a 1:2 mixture of regioisomers favoring formation of the more substituted *N*-alkenylhydroxylamine *O*-vinylether. The oxime of 1-acetyl-1-cyclohexane (**2n**) gave 5-cyclohexenepyrrole **7n** in which there is an alkene for further manipulation. In general, 5-membered ring heterocycles such as the oximes of 2-furan **2r** and 2-thiophene **2s** were not amenable to the gold-multifaceted catalysis process.[34] Pleasingly, 3-pyridyl oxime **2o** afforded the desired pyrrole **7o** in moderate yield. Additionally, pyrroles containing an aryl chloride **7p** or bromide **7q**, useful handles for further cross-coupling reactions,[35] were also synthesized via the gold-MFC process. Unfortunately, subjection of aryl-substituted alkynes **9** to the standard conditions did not afford any of the desired pyrroles **11**/**12**, and only the starting materials were recovered. Interestingly, reaction of acetophenone oxime (**2a**) with ethylpropiolate (**4**) gave the desired pyrrole **8a** in low yield. This result is in stark contrast to our previous studies, in which pyrrole **8a** was formed in good overall yield.[18,19]

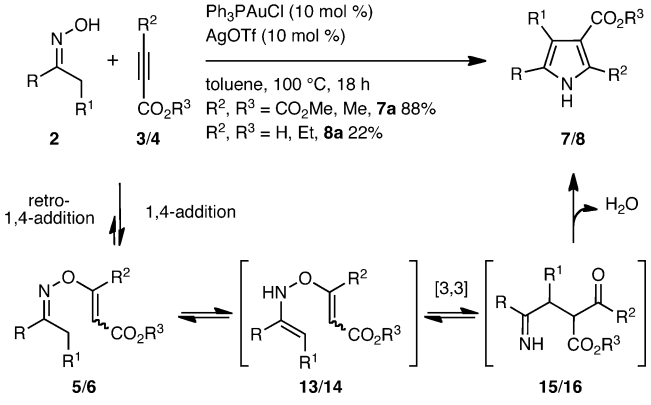
Scheme 3. Regioselective synthesis of Highly Substituted Pyrroles via a Gold-Multifaceted Catalysis Process



[a]24 h. [b]Ethyl propiolate (**4**) was used instead of dimethyl acetylenedicarboxylate (**3**).

Mechanistic Studies. To better understand the nature of the disparity in yield between the use of dimethylacetylene dicarboxylate (**3**) vs ethylpropiolate (**4**) in the formation of pyrroles **7**/**8** and to allow for the further development of the gold-MFC process, a mechanistic investigation was undertaken. At the outset of our study little research had been devoted to elucidate the mechanism of the reaction of oximes and alkynes to form pyrroles and there was none into the use of gold(I) to catalyze this process.[36] While possible roles for the gold(I) catalyst in related [3,3]-sigmatropic rearrangements[37,38] of *N*-arylhydroxylamines to 2-alkylindoles[39] and *O*-arylhydroxylamines to 3-carbonylated benzofurans have been suggested,[40] no mechanistic work was carried out. There are at least three reported mechanisms for the formation of pyrroles from *O*-vinyloximes,[41] which would give different regioisomers for monosubstituted alkynes. We offer the following mechanism for the gold-MFC process, which is based on the previously proposed mechanism for the classical anionic Trofimov reaction (Scheme 4).[14,36] Initial 1,4-addition of the oxygen of oxime **2** to gold(I)-activated alkynes **3**/**4** would give *O*-vinyloximes **5**/**6** after protodemetalation. This process most likely occurs via *syn*-addition of a coordinated oxime-gold complex,[42] as this explains the high level of stereoselectivity observed in **5f** (cf. Scheme 1). Gold-catalyzed tautomerization of *O*-vinyloximes **5**/**6** gives *N*-alkenylhydroxylamine *O*-vinylethers **13**/**14**, which subsequently undergo a gold-catalyzed [3,3]-sigmatropic rearrangement to 1,4-iminocarbonyls **15**/**16**. Cyclodehydration of imines **15**/**16** generates pyrroles **7**/**8** in a manner analogous to the Paal–Knorr pyrrole synthesis.[43]

Scheme 4. Proposed Mechanism for the Gold–MFC Approach to Pyrrole Synthesis



To probe the validity of the mechanistic hypothesis, the 1,4-addition of acetophenone oxime (**2a**) to alkynes **3**/**4** was initially investigated. In this transformation, the acetylene moiety should act as a strong σ-donor and weak π-acceptor[44] toward the highly Lewis acidic gold(I) catalyst[24] making attack of the oxime oxygen onto the intrinsically electrophilic

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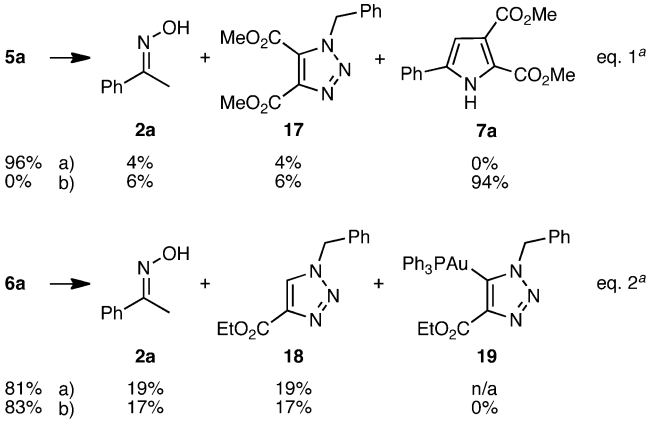
gold(I)−alkyne complex highly favorable.[45] Because of the temperatures required to convert the *O*-vinyloximes to the pyrroles and the effect that this has on the position of the equilibrium between the oximes and *O*-vinyloximes, the direct measurement of their relative stability and calculation of the equilibrium constant between the oximes and *O*-vinyloximes was untenable. Therefore, an indirect method was employed in an attempt to obtain a gross measurement of the relative stabilities of these intermediates. To accomplish this goal, a Huisgen cycloaddition[46] was used as a novel mechanistic probe to investigate the 1,4-addition step.[47] While the use of click reactions has expanded rapidly since Sharpless coined the term in 2001,[48] to the best of our knowledge, they have not been employed as a tool to probe the mechanism of an organic reaction. In particular, the Huisgen cycloaddition between an azide and an alkyne has been exploited in a number of disparate fields and its rapid and widespread use is a result of the highly efficient and chemoselective nature of the processes.[49] In our study, a click reaction will be used to trap out alkynes that are formed in situ as a consequence of a retro 1,4-addition reaction[50] and thus act as a probe of the relative stabilities of *O*-vinyloxime intermediates **5**/**6**. It was also hoped that the azide would trap any gold(I) acetylide compound formed during the reaction (vide infra). The *O*-vinyloxime derivatives of acetophenone **5a**/**6a** were used as model compounds in the study. Thus, if one of the *O*-vinyloximes has a greater propensity toward a retro 1,4-addition reaction to form alkynes **3**/**4**, then an increase in the yield of the corresponding triazole **17**/**18** would be expected.[51] *O*-vinyloximes **5a**/**6a** were reacted with benzyl azide, either in the presence or absence of the gold(I) catalyst at 100 °C for 12 h (Scheme 5). Comparison of

Scheme 5. Use of a Huisgen Cycloaddition to Probe the Relative Stability of *O*-Vinyloximes 5a/6a



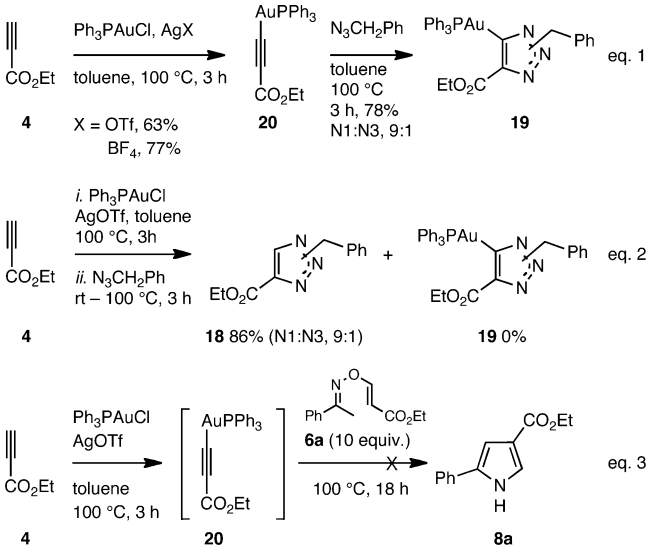
(a) N_3CH_2Ph, toluene, 100 °C, 12 h
(b) Ph_3PAuCl (10 mol %), AgOTf (10 mol %), N_3CH_2Ph, toluene, 100 °C, 12 h

[a]Percentages based on NMR conversion.

the ^1H and $^{13}C\{^1H\}$ NMR spectra to previously prepared samples allowed for determination of the relative quantities of each species,[52] with the remainder of the mass being that of the starting material *O*-vinyloxime. A number of points about this investigation are worth noting: (a) the monoester *O*-vinyloxime **6a** was more susceptible to retro 1,4-addition, (b) none of the expected gold(I) triazole **19**[53] was observed and (c) for *O*-vinyloxime **5a**, a significant amount of pyrrole **7a** was formed in contrast to **6a** in which no pyrrole was formed. The click reaction has therefore shown that *O*-vinyloxime **5a** is more stable than monoester **6a** under the reaction conditions, which helps to explain the higher isolated yield of pyrrole **7a** (see Scheme 5).

Having shown that *O*-vinyloxime **6a** is more prone to undergo a retro-1,4-addition than **5a**, we next wanted to ascertain why this minor difference in stability had such a detrimental effect on the yield of the overall process. One possible reason for the dramatic decrease in yield is the formation of gold(I) acetylide compound **20**. It has been shown that the formation of gold(I) acetylides from the reaction of terminal alkynes and gold(I) compounds is both facile and detrimental to gold-catalyzed processes.[54] Nevado et al. reported that a cationic gold species can insert into the CH bond of a terminal alkyne to form a gold(I) acetylide complex in the presence of base.[55] In our study, a trace amount of the gold(I) acetylide species **20** was observed by ^1H NMR and mass spectroscopy in the reaction of oxime **2a** with ethyl propiolate (**4**). To investigate the reactivity of this compound and its effect on our system, a novel base free method for the synthesis of gold(I) acetylide **20** was developed that is compatible with our catalytic system (Scheme 6, eq 1).

Scheme 6. Synthesis and Catalytic Activity of Gold(I)−Acetylide Complex 20



Reaction of gold(I) acetylide **20** with benzyl azide under thermal conditions afforded gold triazole **19** in good yield. In contrast, reaction of the in situ formed gold(I) acetylide **20** with benzyl azide did not give any of the expected gold triazole **19**, but instead afforded the deaurated triazole **18** (Scheme 6, eq 2). Thus, gold(I) triazole **19** is not stable under the reaction conditions, which explains why it was not observed in the click reaction stability study (cf. Scheme 5, eq 2). The difference in stability between gold(I) acetylide **20** and gold(I) triazole **19** is most likely due to increased bond strength with $C(sp^3) < C(sp^2) < C(sp)$ as demonstrated by the difference in bond lengths observed in related crystal structures.[56] Importantly, it was shown that the in situ generated gold(I) acetylide **20** does not catalyze the rearrangement of *O*-vinyloxime **6a** to pyrrole **8a** (Scheme 6, eq 3). These experiments, in combination with the click reaction study suggest that the difference in yield for the formation of pyrrole **7**/**8** from alkynes **3**/**4** is due to the in

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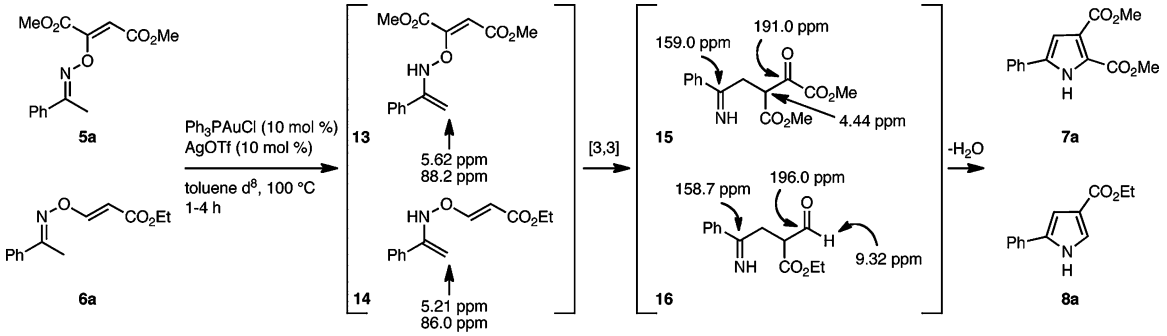
Scheme 7. High-Temperature NMR Characterization of Proposed Intermediates 13−16



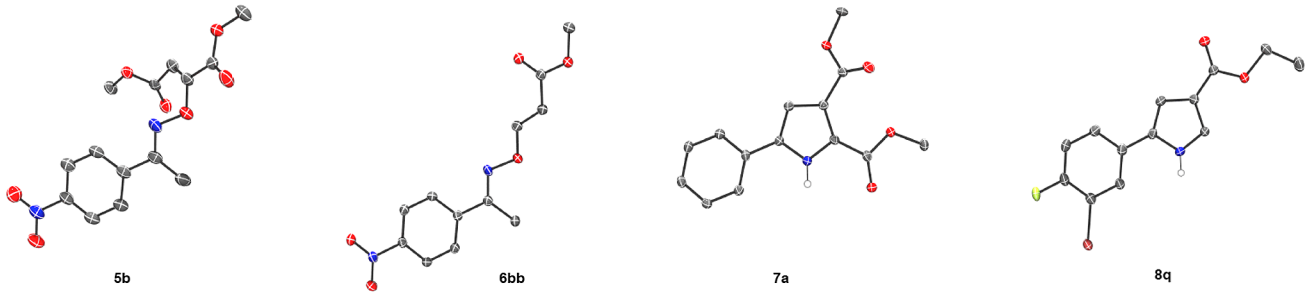


Figure 2. X-ray crystal structure of *O*-vinyloximes **5b**/**6bb**[62] and pyrroles **7a**/**8q**. Displacement ellipsoids are drawn at 50% probability. For clarity, most hydrogen atoms have been omitted.

situ formation of the noncatalytically active gold(I) acetylide **20** and the difference in relative stability of *O*-vinyloximes **5**/**6**.

Next, the second step of the proposed mechanism, the tautomerization of *O*-vinyloximes **5a**/**6a** to **13**/**14**, was investigated. *N*-Alkenylhydroxylamine *O*-vinylethers **13**/**14** that contain a methylene at the *β*-position have not previously been observed spectroscopically. The closest structural examples to **13**/**14** have an electron-withdrawing group at the *γ*-position[57] or are alkylidene isoindinone derivatives.[58] Despite this fact, a number of reports have proposed the intermediacy of these compounds in the formation of pyrroles from oximes and acetylenes.[36,39,40,59] The lack of spectroscopic evidence is not surprising as it was calculated that for the related anionic Trofimov reaction that the tautomerization to form an intermediate similar to **13**/**14** was the rate-limiting step of the overall process.[60] In order to confirm the presence of these unstable compounds, the formation of pyrroles **7a**/**8a** from *O*-vinyloximes **5a**/**6a** was monitored by high-temperature NMR (Scheme 7). The standard reaction was run in a J. Young NMR tube at 100 °C in an NMR machine for 1.5 h. The formation of *N*-alkenylhydroxylamine *O*-vinylethers **13**/**14** was directly observed in this experiment with the key ^{1}H and ^{13}C{^{1}H} NMR chemical shifts depicted in Scheme 7. In order to fully characterize these previously unobserved intermediates, the deuterated derivatives were also prepared and subjected to the experiment.[61] The key ^{1}H signals (5.62/5.21 ppm) and ^{13}C{^{1}H} NMR signals (88.2/86.0 ppm) strongly support the intermediacy of *N*-alkenylhydroxylamine *O*-vinylethers **13**/**14** along the proposed reaction pathway. Additional NMR experiments were used to probe the subsequent [3,3]-sigmatropic rearrangement of **13**/**14** to the corresponding imino ketone **15** or imino aldehyde **16**. Analysis of the crude reaction mixture confirmed the presence of both **15** and **16**. The key ^{1}H and ^{13}C{^{1}H} signals are depicted in Scheme 7. Importantly, the absolute regio- and stereochemistry of the *O*-vinyloximes and pyrroles were established by X-ray crystallography (Figure 2).[26] *O*-Vinyloximes **5b**/**6bb** were synthesized using the nucleophilic catalyst DABCO and are therefore the minor isomers of the gold-catalyzed process.[62] Establishment of the absolute configuration of pyrroles **7**/**8** is significant because it mitigates the possibility of other reaction pathways that would lead to regioisomeric pyrroles.[41]

CONCLUSION

A novel gold-multifaceted catalysis (gold-MFC) method for the regioselective synthesis of highly substituted pyrroles has been developed. This process takes advantage of the ability of a cationic gold(I) species to catalyze both the formation of an *O*-vinyloxime from the addition of an oxime to an alkyne as well as its subsequent conversion to the corresponding pyrrole. In addition, a novel mechanistic probe for organic synthesis based on a Huisgen cycloaddition reaction provided the first insights into the mechanism of the gold-MFC approach to pyrrole synthesis. Due to the utility of the novel click method we anticipate that it will be a useful tool to study the mechanism of a variety of transformations, including other retro 1,4-/1,4-addition equilibrium processes. High temperature NMR experiments provided further support for the proposed mechanism by confirming the presence of unstable intermediates, including providing the first spectroscopic evidence for *N*-alkenylhydroxylamine *O*-vinylethers **13**/**14**. Current research is centered around developing novel protocols for additional alkynes based on the mechanistic insights gained from this study.

EXPERIMENTAL SECTION

General Methods. Unless otherwise indicated, all commercially available reagents and solvents were used directly from the supplier without further purification. Anhydrous toluene was obtained by distillation from sodium/benzophenone, under dry nitrogen, or via

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filtration through a nitrogen-pressurized aluminum oxide column (58 Å, basic). Anhydrous dichloromethane was obtained by distillation from calcium hydride under dry nitrogen. Anhydrous tetrahydrofuran was obtained by distillation from sodium/benzophenone, under dry nitrogen. Unless stated otherwise, reactions requiring anhydrous conditions were conducted under an inert atmosphere of dry argon in flame-dried or oven-dried apparatus. Solvents used for column chromatography were of technical grade. Thin-layer chromatography (TLC) was performed using aluminum foil backed plates, precoated with silica gel 60 UVF254. Visualization was effected via UV fluorescence quenching (λ_{max} = 254 nm) and staining with potassium permanganate (3.00 g, $KMnO_4$, 12.0 g, in 5 mL 5% aq sodium hydroxide and 300 mL water) followed by rapid heating. Flash column chromatography was performed on silica gel mesh (60−120). ^1H NMR, $^2H\{^1H\}$ NMR, $^{13}C\{^1H\}$ NMR, $^{19}F\{^1H\}$ NMR, and $^{31}P\{^1H\}$ NMR were recorded on 300−500 MHz spectometers at ambient temperature, unless otherwise stated. Proton magnetic resonance chemical shifts (δ_H) were recorded in parts per million (ppm), referenced relative to the residual solvent peak (chloroform-d_1 = 7.27 ppm, methanol-d_4 = 3.31 ppm, toluene-d_8 = 2.09 ppm), and are recorded to two decimal places. Coupling constants (J) are recorded to the nearest 0.1 Hz. The multiplicity of each signal is designated by the following abbreviations; s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sxt (sextet), m (multiplet), and br s (broad singlet), or combination. Carbon magnetic resonance chemical shifts (δ_C) were recorded in parts per million (ppm), referenced relative to the residual solvent peak (cholroform-d_1 = 77.1 ppm, methanol-d_4 = 49.1 ppm, toluene-d_8 = 20.4 ppm) and are recorded to one decimal place. Infrared spectra were recorded as diluted solutions, in spectroscopic grade chloroform unless otherwise stated. Absorption maxima (λ max) of major peaks are reported in wavenumbers (cm^{-1}), quoted to the nearest integral wavenumber. High resolution electrospray ionization mass spectra were obtained using a TOF method, running in an open-access mode. Melting points were measured to the nearest °C and are uncorrected. Microwave reactions were run in a sealed reaction vessel and the temperature of the reaction was monitored by IR. The synthesis of oxime **2y**, *O*-vinyloxime **5b** and pyrrole **7z** were prepared by previously reported procedures.[18,19]

General Procedures for the Preparation of *O*-Vinyl Oximes 5f, 6bb, 6f, and 6q (Scheme 1) and 10a−c (Table 1). *General Procedure A for the Preparation of O-Vinyl Oximes.* To a stirred solution of DABCO (0.1 equiv) and oxime (1 equiv) in dichloromethane (0.12 M) at −10 °C was added dropwise a mixture of alkyne (1 equiv) in dichloromethane (0.35 M) over 15 min. The reaction mixture was stirred at rt for 12 h. The mixture was concentrated under reduced pressure and the residue purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate).

General Procedure B for the Preparation of O-Vinyl Oximes. To a stirred solution of oxime (1 equiv) and alkyne (1 equiv) in toluene (0.1 M) were added [Au(PPh_3)Cl] (0.1 equiv) and AgOTf (0.1 equiv). The reaction mixture was stirred at 35 °C for 18 h in a sealed microwave vial. The mixture was concentrated under reduced pressure and the residue purified by flash column chromatography on silica gel (petroleum ether: ethyl acetate).

General Procedure C for the Preparation of O-Vinyl Oximes . To a stirred solution of PPh_3 (0.1 equiv) and oxime (1 equiv) in dichloromethane (0.62 M) at −10 °C was added dropwise a mixture of alkyne (1 equiv) in dichloromethane (1.55 M) over 15 min. The reaction mixture was stirred at 45 °C for 12 h. The mixture was concentrated under reduced pressure and the residue purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate).

*O-Vinyl Oxime **5f**.[19] General Procedure B.* To a stirred solution of cyclohexanone oxime (**2f**, 50 mg, 0.44 mmol) and dimethyl acetylenedicarboxylate (**3**, 55 μL, 0.44 mmol) in toluene (0.44 mL) were added [Au(PPh_3)Cl] (22 mg, 0.044 mmol) and AgOTf (11 mg, 0.044 mmol). The reaction mixture was stirred at 35 °C for 18 h and the residue purified by flash column chromatography on silica gel (10:1 petroleum ether: ethyl acetate) to afford dimethyl 2-((cyclohexylideneamino)oxy)maleate (**5f**, 70 mg, 63%) as a colorless oil that is an inseparable *E*:*Z* mixture (7:1): IR ($CHCl_3$) ν (cm^{-1}) 1722, 1638, 1272, 1026, 928; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{12}H_{17}NNaO_5$ 278.0999, found 278.1004. *(E)-Isomer:* ^1H NMR (300 MHz, $CDCl_3$) δ_H 5.77 (s, 1H), 3.91 (s, 3H), 3.70 (s, 3H), 2.54−2.51 (m, 2H), 2.28−2.25 (m, 2H), 1.64−1.62 (m, 6H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ_C 165.6, 164.7, 162.3, 152.3, 104.7, 52.9, 51.4, 32.1, 27.0, 25.3, 23.4, 18.8. *(Z)-Isomer:* ^1H NMR (300 MHz, $CDCl_3$) δ_H 5.88 (s, 1H), 3.84 (s, 3H), 3.73 (s, 3H), 2.67−2.64 (m, 2H), 2.24−2.21 (m, 2H), 1.73−1.70 (m, 6H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ_C 165.9, 165.1, 163.3, 154.3, 104.2, 52.7, 51.5, 31.5, 26.7, 26.2, 25.6, 25.4.

*O-Vinyl Oxime **6bb**. General Procedure A.* To a stirred solution of DABCO (19 mg, 0.167 mmol) and (*E*)-1-(4-nitrophenyl)ethanone oxime (**2b**, 300 mg, 1.67 mmol) in dichloromethane (14 mL) was added methyl propiolate (**4a**, 148 μL, 1.67 mmol) in dichloromethane (5 mL). The resultant mixture was stirred at rt for 12 h and the residue purified by flash column chromatography on silica gel (10:1 petroleum ether/ethyl acetate) to afford (*E*)-methyl 3-(((*E*)-(1-(4-nitrophenyl)-ethylidene)amino)oxy)acrylate (**6bb**, 419 mg, 95%) as an orange solid: mp 76−77 °C; IR ($CHCl_3$) ν (cm^{-1}) 3690, 3042, 2953, 1709, 1649, 1638, 1620, 1600, 1524, 1437, 1347, 1319, 1290, 1190, 1190, 1190, 1171, 1132, 1079, 950, 855 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 8.28 (d, J = 7.8 Hz, 2 H), 8.10 (d, J = 12.6 Hz, 1H), 7.90 (d, J = 7.8 Hz, 2H), 5.72 (d, J = 12.6 Hz, 1H), 3.76 (s, 3H), 2.43 (s, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ_C 167.7, 161.6, 158.4, 148.7, 140.5, 127.5 (2C), 123.8 (2C), 97.9, 51.4, 13.6. HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{12}H_{12}N_2NaO_5$ 287.0639, found 287.0636.

*O-Vinyl Oxime **6f**.[19] General Procedure B.* To a stirred solution of cyclohexanone oxime (**2f**, 100 mg, 0.88 mmol) and ethyl propiolate (**4**, 89 μL, 0.88 mmol) in toluene (0.5 mL) were added [Au(PPh_3)Cl] (43 mg, 0.088 mmol) and AgOTf (22 mg, 0.088 mmol). The reaction mixture was stirred at 35 °C for 18 h and the residue purified by flash column chromatography on silica gel (7:1 petroleum ether/ethyl acetate) to afford ethyl 3-((cyclohexylideneamino)oxy)acrylate (**6f**, 75 mg, 39%) as a colorless oil that is an inseparable *E*/*Z* mixture (1:1): IR ($CHCl_3$) ν (cm^{-1}) 1701, 1654, 1316, 1071, 862 cm^{-1}; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{11}H_{17}NNaO_3$ 234.1101, found 234.1106. *(E)-isomer:* ^1H NMR (300 MHz, $CDCl_3$) δ_H 7.93 (d, J = 12.6 Hz, 1H), 5.54 (d, J = 12.6 Hz, 1H), 4.23 (q, J = 7.1 Hz, 2H), 2.54−2.51 (m, 2H), 2.34−2.30 (m, 2H), 1.65−1.62 (m, 6H), 1.37 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ_C 167.8, 166.4, 162.1, 96.1, 59.7, 31.7, 26.8, 26.2, 25.7, 25.4, 14.3. *(Z)-isomer:* ^1H NMR (300 MHz, $CDCl_3$) δ_H 7.34 (d, J = 7.5 Hz, 1H), 4.82 (d, J = 7.5 Hz, 1H), 4.22 (q, J = 7.1 Hz, 2H), 2.75−2.72 (m, 2H), 2.37−2.33 (m, 2H), 1.75−1.72 (m, 6H), 1.36 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ_C 165.9, 165.5, 159.5, 93.2, 59.5, 31.4, 26.8, 26.6, 25.7, 25.4, 14.8.

*O-Vinyl Oxime **6q**. General procedure A.* To a stirred solution of DABCO (25 mg, 0.22 mmol) and (*E*)-1-(3-bromo-4-fluorophenyl)-ethanone oxime (**2q**, 500 mg, 2.20 mmol) in dichloromethane (18 mL) was added ethyl propiolate (**4**, 220 μL, 2.20 mmol) in dichloromethane (6 mL). The resultant mixture was stirred at rtor 12 h,and the residue purified by flash column chromatography on silica gel (10:1 petroleum ether/thyl acetate) to afford (*E*)-ethyl 3-(((*E*)-(1-(3-bromo-4-fluorophenyl)ethylidene)amino)oxy)acrylate (**6q**, 675 mg, 93%) as a pale yellow solid: m52−54 °C; IR ($CHCl_3$) ν (cm^{-1}) 3692, 3606, 3086, 2984, 1704, 1637, 1617, 1501, 1393, 1393, 1394, 1370, 1313, 1283, 1268, 1177, 1125, 1086, 1048, 995, 956, 909, 823 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 8.05 (d, J = 12.5 Hz, 1H), 7.93 (dd, J = 6.6, 2.3 Hz, 1H), 7.62−7.68 (m, 1H), 7.16 (t, J = 8.4 Hz, 1H), 5.68 (d, J = 12.5 Hz, 1H), 4.21 (q, J = 7.2 Hz, 2H), 2.34 (s, 3H), 1.31 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ_C 167.4, 161.6, 160.3 (d, $^1J_{C-F}$ = 258.8 Hz), 158.1, 131.9, 127.4, 127.3, 116.6, 109.6, 97.7, 60.0, 14.3, 13.5; $^{19}F\{^1H\}$ NMR (282 MHz, $CDCl_3$) δ_F 104.2; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{13}H_{13}BrFNNaO_3$, 351.9956; found, 351.9948. *(Z)-isomer:* ^1H NMR (300 MHz, $CDCl_3$) δ_H 7.84 (d, J = 7.8 Hz, 1H), 7.50 (d, J = 7.6 Hz, 1H), 6.94 (d, J = 7.6 Hz, 1H), 5.51 (d, J = 7.8 Hz, 1H), 4.20 (q, J = 7.0 Hz, 2H), 2.26 (s, 3H), 1.26 (t, J = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ_C 167.3, 161.0, 158.4, 156.3 (d, $^1J_{C-F}$ = 247.6 Hz), 133.7, 131.4, 126.0, 122.6, 115.5, 97.6, 59.9, 20.7, 14.3; $^{19}F\{^1H\}$ NMR (282 MHz, $CDCl_3$) δ_F 116.0.

*O-Vinyl Oime **10a**. General Procedure C.* To a stirred solution of PPh_3 (81 mg, 0.31 mmol) and (*E*/*Z*)-3,4-dihydronaphthalen-1(2*H*)-one oxime (**2i**, 500 mg, 3.10 mmol) in dichloromethane (5 mL) was added ethyl 3-phenylpropiolate (**9a**, 537 μL, 3.10 mmol) in dichloromethane (2 mL). The resultant mixture was stirred at 45 °C for 12 h and the residue purified by flash column chromatography on silica gel (10:1 petroleum ether/thyl acetate) to afford (*E*/*Z*)-ethyl 3-(((*E*)-(3,4-dihydronaphthalen-1(2*H*)-ylidene)amino)oxy)-3-phenylacrylate (**10a**, 883 mg, 89%) as a dark brown oil that is an inseparable *E*/*Z* mixture (4:1): IR ($CHCl_3$) ν (cm^{-1}) 1707, 1635, 1260, 1078, 949 cm^{-1}; HRMS (ESI) *m*/*z* $[M + Na]^+$ calcd for $C_{21}H_{21}NNaO_3$ 358.1414, found 358.1415. *(E)-isomer:* ^1H NMR (400 MHz, $CDCl_3$) δ_H 7.91 (d, *J* = 7.8 Hz, 1H), 7.89 (d, *J* = 7.8 Hz, 1H), 7.58−7.55 (m, 1H), 7.48−7.46 (m, 1H), 7.46−7.44 (m, 2H), 7.43−7.41 (m, 1H), 7.32−7.26 (m, 1H), 7.20−7.16 (m, 1H), 6.22 (s, 1H), 4.09 (q, *J* = 7.1 Hz, 2H), 2.87 (t, *J* = 6.4 Hz, 2H), 2.80 (t, *J* = 6.4 Hz, 2H), 1.91 (quin, *J* = 6.4 Hz, 2H), 1.19 (t, *J* = 7.1 Hz, 3H); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ_C 168.7, 167.1, 155.3, 139.7, 130.5, 129.8, 129.2, 129.1 (2C), 128.6, 127.7 (2C), 126.5, 126.4, 124.0, 95.2, 59.6, 29.8, 25.4, 21.3, 14.2. *(Z)-isomer:* ^1H NMR (400 MHz, $CDCl_3$) δ_H 8.19 (d, *J* = 7.8 Hz, 2H) 8.17, (d, *J* = 7.8 Hz, 2H), 7.74−7.70 (m, 1H), 7.54−7.51 (m, 1H), 7.50−7.46 (m, 2H), 7.48−7.43 (m, 1H), 7.41−7.36 (m, 1H), 7.14−7.09 (m, 1H), 5.58 (s, 1H), 4.21 (q, *J* = 7.2 Hz, 2H), 3.13 (t, *J* = 6.7 Hz, 2H), 2.91−2.88 (m, 2H), 1.96 (quin, *J* = 6.4 Hz, 2H), 1.29 (t, *J* = 7.2 Hz, 3H); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ_C 166.3, 165.7, 157.8, 140.3, 134.9, 133.3, 129.8 (2C), 129.4, 129.2, 128.0 (2C), 126.6, 126.3, 124.9, 99.4, 59.9, 29.6, 25.2, 21.3, 14.3.

*O-Vinyl Oxime **10b**. General Procedure C.* To a stirred solution of PPh_3 (73 mg, 0.278 mmol) and (*E*/*Z*)-3,4-dihydronaphthalen-1(2*H*)-one oxime (**2i**, 447 mg, 2.78 mmol) in dichloromethane (4.5 mL) was added 4-phenylbut-3-yn-2-one (**9b**, 400 μL, 2.78 mmol) in dichloromethane (2 mL). The resultant mixture was stirred at 45 °C for 12 h and the residue purified by flash column chromatography on silica gel (8:1 petroleum ether/ethyl acetate) to afford (*E*)-4-(((*E*)-(3,4-dihydronaphthalen-1(2*H*)-ylidene)amino)oxy)-4-phenylbut-3-en-2-one (**10b**, 542 mg, 65%) as a brown oil: IR ($CHCl_3$) ν (cm^{-1}) 1760, 1679, 1288, 1003, 908 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ_H 8.18 (d, *J* = 7.8 Hz, 1H), 7.56 (d, *J* = 7.8 Hz, 1H), 7.54 (d, *J* = 7.6 Hz, 1H), 7.51−7.44 (m, 1H), 7.38−7.34 (m, 1H), 7.32−7.29 (m, 1H), 7.28−7.24 (m, 2H), 7.21 (d, *J* = 7.8 Hz, 1H), 6.56 (s, 1H), 2.88 (t, *J* = 6.5 Hz, 2H), 2.80 (t, *J* = 6.5 Hz, 2H), 2.04 (s, 3H), 1.89 (dt, *J* = 6.5, 6.4 Hz, 2H); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ_C 197.9, 167.8, 160.0, 140.8, 130.5, 130.2, 129.4 (2C), 129.0, 128.8, 128.2, 128.0 (2C), 126.5, 125.1, 105.6, 31.0, 29.4, 25.4, 21.2; HRMS (ESI) *m*/*z* $[M + Na]^+$ calcd for $C_{20}H_{19}NNaO_2$ 328.1308, found 328.1303.

*O-Vinyl Oxime **10c**. General Procedure C.* To a stirred solution of PPh_3 (37 mg, 0.15 mmol) and (*E*)-acetophenone oxime (**2a**, 200 mg, 1.5 mmol) in dichloromethane (2.5 mL) was added 4-phenylbut-3-yn-2-one (**9b**, 220 μL, 1.5 mmol) in dichloromethane (1 mL). The resultant mixture was stirred at 45 °C for 12 h and the residue purified by flash column chromatography on silica gel (8:1 petroleum ether/ethyl acetate) to afford (*E*)-4-phenyl-4-(((*E*)-(1-phenylethylidene)-amino)oxy)but-3-en-2-one (**10c**, 330 mg, 54%) as a brown oil: IR ($CHCl_3$) ν (cm^{-1}) 1761, 1684, 1240; 1016 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ_H 7.80 (d, *J* = 7.2 Hz, 1H), 7.78 (d, *J* = 7.2 Hz, 1H), 7.56 (d, *J* = 7.4 Hz, 1H), 7.54 (d, *J* = 7.4 Hz, 1H), 7.43−7.51 (m, 6H), 6.51 (s, 1H), 2.40 (s, 3H), 2.02 (s, 3H); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ_C 198.0, 167.6, 161.1, 135.0, 130.5, 130.3, 130.1, 129.4 (2C), 128.6 (2C), 128.2 (2C), 126.8 (2C), 105.7, 31.1, 14.0; HRMS (ESI) *m*/*z* $[M + Na]^+$ calcd for $C_{18}H_{17}NNaO_2$ 302.1152, found 302.1151.

General Procedures for the Preparation of Pyrroles 7o, 8c, 8cc, and 8q (Scheme 3), 11a−c and 12b,c (Table 1), and 7a−q (Scheme 4). *General Procedure D for the Preparation of Pyrroles.* To a stirred solution of oxime (1.0 equiv) and alkyne (1.0 equiv) in toluene (1.0 M) were added $[Au(PPh_3)Cl]$ (0.1 equiv) and AgOTf (0.1 equiv), and the resultant mixture was heated to 100 °C for 18−24 h in a sealed microwave vial (2−5 mL). The mixture was concentrated under reduced pressure and the residue purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate).

General Procedure E for the Preparation of Pyrroles. A mixture of *O*-vinyl oxime (1.0 equiv), $[Au(PPh_3)Cl]$ (0.1 equiv), and $AgBF_4$ (0.1 equiv) in toluene (0.1−0.2 M) was heated to 100 °C for 18 h in a sealed microwave vial. The mixture was concentrated under reduced pressure and the residue purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate).

*Pyrrole **7a**.* [19]*General Procedure D.* To a stirred solution of acetophenone oxime (**2a**, 80 mg, 0.60 mmol) and dimethyl acetylenedicarboxylate (**3**, 70 μL, 0.60 mmol) in toluene (0.6 mL) were added $[Au(PPh_3)Cl]$ (29 mg, 0.06 mmol) and AgOTf (15 mg, 0.06 mmol), and the resultant mixture was heated to 100 °C for 18 h. The residue was purified by flash column chromatography on silica gel (9:1 petroleum ether/ethyl acetate) to afford dimethyl 5-phenyl-1*H*-pyrrole-2,3-dicarboxylate (**7a**, 137 mg, 88%) as a white solid: mp 142−144; IR ($CHCl_3$) ν (cm^{-1}) 3479, 1781, 1459, 1398, 1112, 987 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ_H 9.63 (br s, 1H), 7.57 (d, *J* = 7.4 Hz, 2H), 7.44 (t, *J* = 7.4 Hz, 2H), 7.36 (t, *J* = 7.4 Hz, 1H), 6.94 (d, *J* = 3.1 Hz, 1H), 3.94 (s, 3H), 3.91 (s, 3H); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ_c 164.2, 160.6, 134.8, 130.2, 129.2 (2C), 128.4, 124.8 (2C), 122.7, 121.5, 110.7, 52.3, 51.9. HRMS (ESI) *m*/*z* $[M + Na]^+$ calcd for $C_{14}H_{13}NNaO_4$ 282.0737, found 282.0741.

*Pyrrole **7b**. General Procedure D.* To a stirred solution of (*E*)-1-(4-nitrophenyl)ethanone oxime (**2b**, 100 mg, 0.56 mmol) and dimethyl acetylenedicarboxylate (**3**, 69 μL, 0.56 mmol) in toluene (0.56 mL) were added $[Au(PPh_3)Cl]$ (28 mg, 0.056 mmol) and $AgOTf_4$ (14 mg, 0.056 mmol), and the resultant mixture was heated to 100 °C for 18 h. The residue was purified by flash column chromatography on silica gel (4:1 petroleum ether: ethyl acetate) to afford dimethyl 5-(4-nitrophenyl)-1*H*-pyrrole-2,3-dicarboxylate (**7b**, 85 mg, 53%) as a pale yellow solid: mp 98−101 °C; IR ($CHCl_3$) ν (cm^{-1}) 3411, 1791, 1611, 1578, 1302, 1189, 985 cm^{-1}; ^1H NMR (400 MHz,$CDCl_3$) δ_H 9.81 (br s, 1H), 8.34 (d, *J* = 8.9 Hz, 2H), 7.73 (d, *J* = 8.9 Hz, 2H), 7.13 (d, *J* = 3.1 Hz, 1H), 4.07 (s, 3H), 3.94 (s, 3H); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ_c 163.7, 160.4, 147.1, 136.1, 132.0, 125.1 (2C), 124.7 (2C), 124.6, 121.8, 113.0, 52.5, 52.0; HRMS (ESI) *m*/*z* $[M + Na]^+$ calcd for $C_{14}H_{12}N_2NaO_6$ 327.0588, found 327.0591.

*Pyrrole **7c**. General Procedure D.* To a stirred solution of (*E*)-1-(3-nitrophenyl)ethanone oxime (**2c**, 80 mg, 0.44 mmol) and dimethyl acetylenedicarboxylate (**3**, 54 μL, 0.44 mmol) in toluene (0.44 mL) were added $[Au(PPh_3)Cl]$ (22 mg, 0.044 mmol) and AgOTf (11 mg, 0.044 mmol), and the resultant mixture was heated to 100 °C for 18 h. The residue was purified by flash column chromatography on silica gel (6:1 petroleum ether: ethyl acetate) to afford dimethyl 5-(3-nitrophenyl)-1*H*-pyrrole-2,3-dicarboxylate (**7c**, 85 mg, 63%) as a pale yellow solid: mp 96−97 °C °C; IR ($CHCl_3$) ν (cm^{-1}) 3631, 3465, 3008, 2945, 2838, 2460, 2019, 1734, 1603, 1535, 1463, 1333, 1240, 1073, 1014, 918, 660 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 9.72 (br s, 1H), 8.45−8.37 (m, 1H), 8.19 (d, *J* = 8.2 Hz, 1 H), 7.90 (d, *J* = 8.2 Hz, 1 H), 7.64 (t, *J* = 8.2 Hz, 1H), 7.08 (d, *J* = 3.1 Hz, 1H), 3.97 (s, 3H), 3.93 (s, 3H); ^{13}C {^1H} NMR (75 MHz, $CDCl_3$) δ_c 163.8, 160.4, 148.9, 132.0, 130.4, 130.3, 124.1, 122.7, 121.7, 121.6, 119.5, 112.1, 53.4, 52.0; HRMS (ESI) *m*/*z* $[M + Na]^+$ calcd for $C_{14}H_{12}N_2NaO_6$ 327.0587, found 327.0587.

*Pyrrole **7d**.*[18] *General Procedure D.* To a stirred solution of (*E*)-1-(4-methoxyphenyl)ethanone oxime (**2d**, 80 mg, 0.48 mmol) and dimethyl acetylenedicarboxylate (**3**, 60 μL, 0.48 mmol) in toluene (0.48 mL) were added $[Au(PPh_3)Cl]$ (24 mg, 0.048 mmol) and AgOTf (12 mg, 0.048 mmol), and the resultant mixture was heated to 100 °C for 18 h. The residue was purified by flash column chromatography on silica gel (10:1 petroleum ether: ethyl acetate) to afford dimethyl 5-(4-methoxyphenyl)-1*H*-pyrrole-2,3-dicarboxylate (**7d**, 82 mg, 59%) as an orange oil: IR ($CHCl_3$) ν (cm^{-1}) 3656, 3613, 3442, 3034, 2989, 2876, 2049, 1777, 1676, 1545, 1445, 1387, 1187, 989, 843, 638 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ_H 9.44 (br s, 1H), 7.49 (d, *J* = 8.9 Hz, 2H), 6.97 (d, *J* = 8.9 Hz, 2H), 6.84 (s, 1H), 3.94 (s, 3H), 3.90, (s, 3H), 3.87 (s, 3H); ^{13}C {^1H} NMR (400 MHz, $CDCl_3$) δ_C 164.3, 160.6, 159.8, 134.8, 126.2 (2C), 122.9, 122.0, 121.5, 114.6 (2C), 109.8, 55.3, 52.1, 51.8; HRMS (ESI) *m*/*z* $[M + Na]^+$ calcd for $C_{15}H_{15}NNaO_5$ 312.0843, found 312.0845.

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Pyrrole ***7e****. General Procedure D.*[63] To a stirred solution of cyclopentanone oxime (**3e**, 100 mg, 0.72 mmol) and dimethyl acetylenedicarboxylate (**3**, 90 μL, 0.72 mmol) in toluene (0.72 mL) were added [Au(PPh$_3$)Cl] (36 mg, 0.07 mmol) and AgOTf (18 mg, 0.07 mmol), and the resultant mixture was heated to 100 °C for 18 h. The residue was purified by flash column chromatography on silica gel (5:1 petroleum ether/ethyl acetate) to afford dimethyl 1,4,5,6-tetrahydrocyclopentapyrrole-2,3-dicarboxylate (**7e**, 19 mg, 12%) as an orange oil: IR ($CHCl_3$) ν (cm^{-1}) 3439, 1725, 1691, 1506, 1071 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 9.15 (br s, 1H), 3.89 (s, 3H), 3.85 (s, 3H), 2.78 (t, J = 6.8 Hz, 2H), 2.73 (t, J = 6.8 Hz, 2H), 2.49−2.41 (m, 2H); ^{13}C {^1H} NMR (75 MHz, $CDCl_3$) δ_c 166.0, 160.3, 132.2, 122.1, 120.4, 119.7, 51.9, 51.6, 28.7, 25.9, 25.1; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{11}H_{13}NNaO_4$ 246.0737, found 246.0733.

Pyrrole ***7f****.* [19]*General Procedure D.* To a stirred solution of cyclohexanone oxime (**2f**, 80 mg, 0.71 mmol) and dimethyl acetylenedicarboxylate (**3**, 87 μL, 0.71 mmol) in toluene (0.7 mL) were added [Au(PPh$_3$)Cl] (35 mg, 0.071 mmol) and AgOTf (17.5 mg, 0.071 mmol), and the resultant mixture was heated to 100 °C for 18 h. The residue was purified by flash column chromatography on silica gel (6:1 petroleum ether/ethyl acetate) to afford dimethyl 4,5,6,7-tetrahydro-1*H*-indole-2,3-dicarboxylate (**7f**, 139 mg, 83%) as a pale yellow solid: mp 138−140 °C; IR ($CHCl_3$) ν (cm^{-1}) 3435, 1769, 1480, 1047, 898 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ_H 9.02 (br s, 1H), 3.86 (s, 3H), 3.82 (s, 3H), 2.62 (t, J = 6.1 Hz, 1H), 2.59 (t, J = 6.1 Hz, 2H), 1.79−1.77 (m, 4H); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ_C 165.6, 160.8, 132.1, 121.6, 119.8, 118.7, 51.8, 51.6, 22.9, 22.6, 22.4, 22.3; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{12}H_{15}NNaO_4$ 260.0894, found 260.0899.

Pyrrole ***7g****. General Procedure D.*[64] To a stirred solution of cycloheptanone oxime (**2g**, 60 mg, 0.48 mmol) and dimethyl acetylenedicarboxylate (**3**, 54 μL, 0.48 mmol) in toluene (0.48 mL) were added [Au(PPh$_3$)Cl] (24 mg, 0.048 mmol) and AgOTf (12 mg, 0.048 mmol), and the resultant mixture was heated to 100 °C for 18 h. The residue was purified by flash column chromatography on silica gel (5:1 petroleum ether/ethyl acetate) to afford dimethyl 1,4,5,6,7,8-hexahydrocyclohepta[*b*]pyrrole-2,3-dicarboxylate (**7g**, 78 mg, 65%) as a pale yellow solid: mp 112−114 °C; IR ($CHCl_3$) ν (cm^{-1}) 3631, 3438, 3006, 2930, 2845, 1730, 1502, 1445, 1416, 1374, 1246, 1062, 1046, 1016, 909, 634 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 8.92 (br s, 1H), 3.88 (s, 3H), 3.82 (s, 3H), 2.68 (t, J = 6.0 Hz, 2 H), 2.62 (t, J = 6.0 Hz, 2H), 1.95−1.75 (m, 2 H), 1.75−1.58 (m, 4H); ^{13}C {^1H} NMR (75 MHz, $CDCl_3$) δ_c 166.5, 160.6, 136.7, 124.7, 121.5, 116.7, 51.9, 51.6, 31.8, 29.0, 28.3, 27.0, 25.7; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{13}H_{17}NNaO_4$ 274.1050, found 274.1055.

Pyrrole ***7h****. General Procedure D.*[64] To a stirred solution of cyclooctanone oxime (**2h**, 80 mg, 0.57 mmol) and dimethyl acetylenedicarboxylate (**3**, 71 μL, 0.57 mmol) in toluene (0.57 mL) were added [Au(PPh$_3$)Cl] (28 mg, 0.06 mmol) and AgOTf (14 mg, 0.06 mmol), and the resultant mixture was heated to 100 °C for 18 h. The residue was purified by flash column chromatography on silica gel (8:1 petroleum ether/ethyl acetate) to afford dimethyl 4,5,6,7,8,9-hexahydro-1*H*-cycloocta-pyrrole-2,3-dicarboxylate (**7h**, 86 mg, 57%) as a pale yellow solid: mp 117−118 °C; IR ($CHCl_3$) ν (cm^{-1}) 3443, 1723, 1501, 1016 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 8.90 (br s, 1H), 3.88 (s, 3H), 3.85 (s, 3H), 2.71 (t, J = 6.2 Hz, 2H), 2.63 (t, J = 6.2 Hz, 2H), 1.69−1.62 (m, 4H), 1.50−1.43 (m, 2H), 1.41−1.34 (m, 2H); ^{13}C {^1H} NMR (75 MHz, $CDCl_3$) δ_c 166.2, 160.6, 134.8, 123.1, 120.5, 118.4, 51.8, 51.7, 30.0, 30.0, 25.7 (s, 2C), 25.5, 22.7; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{14}H_{19}NNaO_4$ 288.1207, found 288.1200.

Pyrrole ***7i****. General Procedure D.* To a stirred solution of (*E*/*Z*)-3,4-dihydronaphthalen-1(2*H*)-one oxime (**2i**, 80 mg, 0.50 mmol) and dimethyl acetylenedicarboxylate (**3**, 60 μL, 0.50 mmol) in toluene (0.5 mL) were added [Au(PPh$_3$)Cl] (25 mg, 0.05 mmol) and AgOTf (13 mg, 0.05 mmol), and the resultant mixture was heated to 100 °C for 24 h. The residue was purified by flash column chromatography on silica gel (6:1 petroleum ether: ethyl acetate) to afford dimethyl 4,5-dihydro-1*H*-benzo[*g*]indole-2,3-dicarboxylate (**7i**, 78 mg, 85%) as a white solid: mp 177−179 °C; IR ($CHCl_3$) ν (cm^{-1}) 3425, 1768, 1479, 1048, 898 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ_H 9.65 (br s, 1H), 7.40 (d, J = 6.8 Hz, 1H), 7.26−7.23 (m, 2H), 7.22−7.17 (m, 1H), 3.92 (s, 3H), 3.91 (s, 3H), 2.96 (t, J = 7.6 Hz, 2H), 2.91 (t, J = 7.6 Hz, 2H); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ_C 165.2, 160.9, 136.33, 131.34, 128.6, 127.60, 127.59, 127.0, 126.7, 123.2, 121.4, 120.2, 52.1, 51.8, 29.2, 20.6; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{16}H_{15}NNaO_4$ 308.0894, found 308.0895.

Pyrrole ***7j****. General Procedure D.* To a stirred solution of (*E*)-1-(4-fluorophenyl)-2-phenylethanone oxime (**2j**, 100 mg, 0.44 mmol) and dimethyl acetylenedicarboxylate (**3**, 54 μL, 0.44 mmol) in toluene (0.44 mL) were added [Au(PPh$_3$)Cl] (22 mg, 0.044 mmol) and AgOTf (11 mg, 0.044 mmol) and the resultant mixture was heated to 100 °C for 18 h The residue was purified by flash column chromatography on silica gel (9:1 petroleum ether: ethyl acetate) to afford dimethyl 5-(4-fluorophenyl)-4-phenyl-1*H*-pyrrole-2,3-dicarboxylate (**7j**, 103 mg, 66%) as a light orange solid: mp 112−114 °C; IR ($CHCl_3$) ν (cm^{-1}) 3630, 3459, 3004, 2945, 2838, 2461, 2019, 1729, 1463, 1333, 1240, 1072, 1019, 918, 839, 659 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 9.27 (br s, 1 H), 7.32−7.28 (m, 2 H), 7.26−7.19 (m, 5H), 7.00 (dd, J = 8.6, 8.5 Hz, 2H), 3.90 (s, 3H), 3.76 (s, 3H); ^{13}C {^1H} NMR (75 MHz, $CDCl_3$) δ_c 166.2, 161.9 (d, $^1J_{C-F}$ = 247.3 Hz), 160.4, 133.1, 131.9, 129.7 (2C), 129.7, 129.6 (2C), 128.4 (2C), 127.3, 123.2, 122.9, 116.1, 115.8 (2C), 52.3, 52.2; ^{19}F {^1H} NMR (282 MHz, $CDCl_3$) δ_F 112.41; HRMS (ESI) m/z [M] calcd for $C_{20}H_{16}FNO_4$ 353.1063, found 353.1052.

Pyrrole ***7k****.* [19]*General Procedure D.* To a stirred solution of (*E*)-1,2-diphenylethanone oxime (**2k**, 80 mg, 0.38 mmol) and dimethyl acetylenedicarboxylate (**3**, 50 μL, 0.038 mmol) in toluene (0.38 mL) were added [Au(PPh$_3$)Cl] (18 mg, 0.038 mmol) and AgOTf (9 mg, 0.038 mmol), and the resultant mixture was heated to 100 °C for 18 h. The residue was purified by flash column chromatography on silica gel (6:1 petroleum ether/ethyl acetate) to afford dimethyl 4,5-diphenyl-1*H*-pyrrole-2,3-dicarboxylate (**7k**, 94 mg, 73%) as a pale yellow solid: mp 190−192 °C; IR ($CHCl_3$) ν (cm^{-1}) 3433, 1732, 1476, 1096, 908 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ_H 9.50 (br s, 1H), 7.33−7.22 (m, 10H), 3.83 (s, 3H), 3.76 (s, 3H); ^{13}C {^1H} NMR (400 MHz, $CDCl_3$) δ_C 166.3, 160.6, 133.3, 133.0, 130.8, 129.8 (2C), 128.8 (2C), 128.4 (2C), 127.8 (2C), 127.2 (2C), 123.2, 122.9, 119.9, 52.3, 52.2; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{20}H_{17}NO_4Na$ 358.1050, found 358.1059.

Pyrrole ***7l****. General Procedure D.* To a stirred solution of (*E*)-1-phenylheptan-1-one oxime (**2l**, 100 mg, 0.46 mmol) and dimethyl acetylenedicarboxylate (**3**, 57 μL, 0.46 mmol) in toluene (0.46 mL) were added [Au(PPh$_3$)Cl] (23 mg, 0.046 mmol) and AgOTf (12 mg, 0.046 mmol), and the resultant mixture was heated to 100 °C for 18 h. The residue was purified by flash column chromatography on silica gel (8:1 petroleum ether/ethyl acetate) to afford dimethyl 4-pentyl-5-phenyl-1*H*-pyrrole-2,3-dicarboxylate (**7l**, 72 mg, 48%) as an orange oil: IR ($CHCl_3$) ν (cm^{-1}) 3691, 3436, 3006, 2955, 2929, 2857, 1727, 1604, 1568, 1482, 1448, 1420, 1354, 1286, 1239, 1106, 1038, 970 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 9.10 (br s, 1H), 7.49−7.35 (m, 5H), 3.92 (s, 3H), 3.87 (s, 3H), 2.65 (t, J = 7.3 Hz, 2H), 1.50 (dt, J = 7.6, 7.3 Hz, 2H), 1.34−1.15 (m, 6H), 0.85 (t, J = 6.8 Hz, 3H); ^{13}C {^1H} NMR (75 MHz, $CDCl_3$) δ_c 166.4, 160.5, 133.1, 131.5, 128.9 (2C), 128.2, 127.8 (2C), 124.0, 121.9, 120.2, 52.0, 51.9, 31.4, 31.2, 29.1, 24.7, 22.5, 14.0; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{20}H_{25}NNaO_4$ 366.1676, found 366.1673.

Pyrrole ***7ma:mb****. General Procedure D.*[19] To a stirred solution of pentan-2-one oxime (**2m**, 80 mg, 0.78 mmol) and dimethyl acetylenedicarboxylate (**3**, 100 μL, 0.78 mmol) in toluene (0.78 mL) were added [Au(PPh$_3$)Cl] (38 mg, 0.078 mmol) and AgOTf (20 mg, 0.078 mmol), and the resultant mixture was heated to 100 °C for 18 h. The residue was purified by flash column chromatography on silica gel (8:1 petroleum ether/ethyl acetate) to afford to afford an inseparable (1:2) mixture of dimethyl 5-ethyl-4-methyl-1*H*-pyrrole-2,3-dicarboxylate/dimethyl 5-propyl-1*H*-pyrrole-2,3-dicarboxylate (**7ma:mb**, 92 mg, 52%) as an orange oil: IR ($CHCl_3$) ν (cm^{-1}) 3712, 1798, 1478, 1061, 997 cm^{-1}; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{11}H_{15}NNaO_4$ 248.0894, found 248.0897. *Dimethyl 5-ethyl-4-methyl-1H-pyrrole-2,3-dicarboxylate (****7ma****):* ^1H NMR (400 MHz, $CDCl_3$) δ_H

9.07 (br s, 1H), 3.88 (s, 3H), 3.84 (s, 3H), 2.50 (q, J = 7.5 Hz, 2H), 2.22 (s, 3H), 1.09 (t, J = 7.5 Hz, 3H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ_C 166.4, 160.5, 129.3, 128.6, 124.9, 118.4, 51.9, 51.7, 18.0, 15.5, 11.0. *Dimethyl 5-propyl-1H-pyrrole-2,3-dicarboxylate(**7mb**):* ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 9.36 (br s, 1H), 6.43 (d, J = 3.1 Hz, 1H), 3.97 (s, 3H), 3.93 (s, 3H), 2.6 (t, J = 7.5 Hz, 2H), 1.73 (sxt, J = 7.5 Hz, 2H), 1.04 (t, J = 7.5 Hz, 3H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ_C 164.6, 160.8, 134.4, 120.7, 120.5, 111.1, 52.0, 51.9, 29.7, 22.3, 13.6.

*Pyrrole **7n**. General Procedure D.* To a stirred solution of (*E*)-1-(cyclohex-1-en-1-yl)ethanone oxime (**2n**, 100 mg, 0.72 mmol) and dimethyl acetylenedicarboxylate (**3**, 90 μL, 0.72 mmol) in toluene (0.72 mL) were added [Au(PPh_3)Cl] (36 mg, 0.072 mmol) and AgOTf (18 mg, 0.072 mmol), and the resultant mixture was heated to 100 °C for 18 h. The residue was purified by flash column chromatography on silica gel (5:1 petroleum ether: ethyl acetate) to afford dimethyl 5-(cyclohex-1-en-1-yl)-1*H*-pyrrole-2,3-dicarboxylate (**7n**, 134 mg, 71%) as a light brown oil: IR ($CHCl_3$) ν (cm^{-1}) 3451, 1728, 1461, 1020, 909 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 9.18 (br s, 1H), 6.59 (d, J = 3.1 Hz, 1H), 6.15 (s, 1H), 3.91 (s, 3H), 3.86 (s, 3H), 2.36−2.29 (m, 2H), 2.24−2.17 (m, 2H), 1.82−1.71 (m, 2H), 1.70−1.62 (m, 2H); ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$) δ_c 164.6, 161.0, 136.7, 127.7, 124.6, 121.7, 120.9, 109.5, 52.1, 51.9, 25.9, 25.4, 22.4, 22.0; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{14}H_{17}NNaO_4$ 286.1050, found 286.1046.

*Pyrrole **7o**. Method 1. General Procedure D.* To a stirred solution of 1-(pyridin-3-yl)ethanone oxime (**2o**, 50 mg, 0.37 mmol) and dimethyl acetylenedicarboxylate (**3**, 60 μL, 0.37 mmol) in toluene (0.37 mL) were added [Au(PPh_3)Cl] (18 mg, 0.037 mmol) and AgOTf (9 mg, 0.037 mmol), and the resultant mixture was heated to 100 °C for 18 h. The residue was purified by flash column chromatography on silica gel (5:1 petroleum ether: ethyl acetate) to afford dimethyl 5-(pyridin-3-yl)-1*H*-pyrrole-2,3-dicarboxylate (**7o**, 27 mg, 28%) as light brown oil. *Method 2. General Procedure E.* Pyrrole **7o** was synthesized according to general procedure E. Dimethyl 2-(((*E*/*Z*)-(1-(pyridin-3-yl)ethylidene)amino)oxy)maleate (**5o**, 100 mg, 0.36 mmol), [Au(PPh_3)Cl] (18 mg, 0.036 mmol) and $AgBF_4$ (7 mg, 0.036 mmol) in toluene (0.36 mL) were heated to 100 °C for 18 h. The residue was purified by flash column chromatography on silica gel (5:1 petroleum ether: ethyl acetate) to afford dimethyl 5-(pyridin-3-yl)-1*H*-pyrrole-2,3-dicarboxylate (**7o**, 50 mg, 54%) as a light brown oil: IR ($CHCl_3$) ν (cm^{-1}) 3689, 3424, 3053, 3008, 2954, 1741,1699, 1596, 1568, 1511, 1438, 1292, 1261, 1159, 1073, 971 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 10.52 (br s, 1H), 8.52−8.49 (m, 1H), 7.74 (d, J = 4.9 Hz, 1H), 7.64 (d, J = 8.2 Hz, 1H), 7.21 (dd, J = 8.2, 4.9 Hz, 1H), 7.13 (s, 1H), 3.95 (s, 3H), 3.91 (s, 3H); ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$) δ_c 164.2, 159.9, 149.0, 148.0, 137.1, 135.0, 133.0, 122.6, 121.4, 119.4, 111.3, 52.2, 51.9; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{13}H_{12}N_2NaO_4$, 283.0690; found 283.0690.

*Pyrrole **7p**. General Procedure D.* To a stirred solution of (*Z*)-2-chloro-1-phenylethanone oxime (**2p**, 80 mg, 0.47 mmol) and dimethyl acetylenedicarboxylate (**3**, 57 μL, 0.47 mmol) in toluene (0.47 mL) were added [Au(PPh_3)Cl] (23 mg, 0.047 mmol) and AgOTf (12 mg, 0.047 mmol), and the resultant mixture was heated to 100 °C for 18 h. The residue was purified by flash column chromatography on silica gel (10:1) petroleum ether: ethyl acetate) to afford dimethyl 4-chloro-5-phenyl-1*H*-pyrrole-2,3-dicarboxylate (**7p**, 67 mg, 49%) as a colorless solid: mp 92−94 °C; IR ($CHCl_3$) ν (cm^{-1}) 3691, 3427, 3043, 2955, 1733, 1602, 1569, 1521, 1480, 1449, 1352, 1289, 1248, 1175, 1072, 1032, 998, 964 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 9.43 (br s, 1H), 7.69−64 (m, 2H), 7.52−7.39 (m, 3H), 3.96 (s, 3H), 3.88 (s, 3H); ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$) δ_c 163.8, 159.9, 134.1, 131.6, 129.3, 129.0, 127.2 (s, 2C), 121.3, 119.7, 110.8, 52.5, 52.4; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{14}H_{12}ClNO_4$ 294.0528, found 294.0523.

*Pyrrole **7q**. General Procedure D.* To a stirred solution of (*E*)-1-(3-bromo-4-fluorophenyl)ethanone oxime (**2q**, 80 mg, 0.34 mmol) and dimethyl acetylenedicarboxylate (**3**, 42 μL, 0.34 mmol) in toluene (0.34 mL) were added [Au(PPh_3)Cl] (17 mg, 0.034 mmol) and AgOTf (8.4 mg, 0.034 mmol), and the resultant mixture was heated to 100 °C for 18 h. The residue was purified by flash column chromatography on silica gel (12:1 petroleum ether: ethyl acetate) to afford dimethyl 5-(3-bromo-4-fluorophenyl)-1*H*-pyrrole-2,3-dicarboxylate (**7q**, 46 mg, 43%) as a brown solid: mp 113−115 °C; IR ($CHCl_3$) ν (cm^{-1}) 3690, 3430, 3009, 2954, 2853, 1737, 1586, 1475, 1450, 1347, 1260, 1156, 1070, 1047, 1017, 973, 882, 821 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 9.58 (br s, 1H), 7.76 (dd, J = 6.2, 2.3 Hz, 1H), 7.51−7.44 (m, 1H), 7.19 (t, J = 8.4 Hz, 1H), 6.89 (d, J = 3.1 Hz, 1H), 3.95 (s, 3H), 3.91 (s, 3H); ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$) δ_c 163.9, 160.5 d, ($^1J_{C-F}$ = 258.8 Hz), 157.3, 132.4, 130.1, 125.6, 125.4, 123.2, 121.5, 117.3, 111.1, 110.0, 52.4, 52.0; ^{19}F {^{1}H} NMR (282 MHz, $CDCl_3$) δ_F 107.1; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{14}H_{11}BrFNNaO_4$ 377.9748, found 377.9750.

*Pyrrole **8a**. General Procedure D.*[18] To a stirred solution of acetophenone oxime (**2a**, 80 mg, 0.60 mmol) and ethyl propiolate (**4**, 56 μL, 0.60 mmol) in toluene (2 mL) were added [Au(PPh_3)Cl] (29 mg, 0.06 mmol) and AgOTf (15 mg, 0.06 mmol), and the resultant mixture was heated to 100 °C for 12 h. The residue was purified by flash column chromatography on silica gel (9:1 petroleum ether/ethyl acetate) to afford ethyl 5-phenyl-1*H*-pyrrole-3-carboxylate (**8a**, 37 mg, 22%) as an orange oil: IR ($CHCl_3$) ν (cm^{-1}) 3631, 1708, 1486, 1073, 891 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 8.77 (br s, 1H), 7.52−7.46 (m, 3H, H), 7.43−7.36 (m, 2H), 7.31−7.28 (m, 1H), 6.92 (dd, J = 2.7, 1.3 Hz, 1H), 4.32 (q, J = 7.1 Hz, 2H), 1.37 (t, J = 7.1 Hz, 3H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ_c 164.9, 133.0, 131.7, 129.0 (2C), 127.0 (2C), 124.1 (2C), 118.1, 106.7, 59.9, 14.5; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{13}H_{13}NNaO_2$ 238.0839, found 238.0845.

*Pyrrole **8q**. General Procedure E.* (*E*)-Ethyl 3-(((*E*)-(1-(3-bromo-4-fluorophenyl)ethylidene)amino)oxy)acrylate (**6q**, 150 mg, 0.45 mmol), [Au(PPh_3)Cl] (23 mg, 0.045 mmol), and $AgBF_4$ (9 mg, 0.045 mmol) in toluene (2.5 mL) were heated to 100 °C for 18 h. The residue was purified by flash column chromatography on silica gel (12:1 petroleum ether/ethyl acetate) to afford ethyl 5-(3-bromo-4-fluorophenyl)-1*H*-pyrrole-3-carboxylate (**8q**, 74 mg, 53%) as a light brown solid: mp 135−137 °C; IR ($CHCl_3$) ν (cm^{-1}) 3693, 3461, 3052, 2984, 2928, 2854, 1704, 1602, 1520, 1483, 1427, 1375, 1337, 1268, 1240, 1140, 1119, 968, 823 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 8.86 (br s, 1H), 7.68 (dd, J = 8.4, 2.3 Hz, 1H), 7.51−7.45 (m, 1H), 7.43−7.36 (m, 1H), 7.14 (t, J = 8.4 Hz, 1H), 6.89−6.84 (m, 1H), 4.32 (q, J = 7.2 Hz, 2H), 1.38 (t, J = 7.2 Hz, 3H); ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$) δ_c 164.8, 158.1 (d, $^1J_{C-F}$ = 258.8 Hz), 130.8, 129.6, 129.1, 124.8, 124.6, 117.2, 116.9, 109.7, 107.4, 60.0, 14.4; ^{19}F {^{1}H} NMR (282 MHz, $CDCl_3$) δ_F 109.4; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{13}H_{11}BrFNO_2$ 310.9957, found 310.9946.

*Pyrrole **11a**. General Procedure E.* (*E*/*Z*)-Ethyl 3-(((*E*)-(3,4-dihydronaphthalen-1(2*H*)-ylidene)amino)oxy)-3-phenylacrylate (**10a**, 100 mg, 0.30 mmol), [Au(PPh_3)Cl] (14.8 mg, 0.3 mmol), and $AgBF_4$ (6 mg, 0.03 mmol) in toluene (2 mL) were heated to 100 °C for 12 h. The residue was purified by flash column chromatography on silica gel (9:1 petroleum ether/ethyl acetate) to afford ethyl 2-phenyl-4,5-dihydro-1*H*-benzo[g]indole-3-carboxylate (**11a**, 20 mg, 21%) as a brown oil: IR ($CHCl_3$) ν (cm^{-1}) 3455, 1628, 1465, 1017 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 9.34 (br s 1H), 7.42 (d, J = 6.8 Hz, 1H), 7.39−7.37 (m, 1H), 7.37−7.33 (m, 2H), 7.32−7.29 (m, 2H), 7.27−7.23 (m, 2H), 7.23−7.19 (m, 1H), 4.25 (q, J = 7.1 Hz, 2H), 2.93 (t, J = 7.8 Hz, 2H), 2.70 (t, J = 7.8 Hz, 2H), 1.21 (t, J = 7.2 Hz, 3H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ_C 161.4, 136.5, 134.1, 131.2, 130.2 (2C), 128.6, 128.2, 127.8, 127.5 (2C), 127.2, 126.9, 126.8, 121.4, 120.0, 118.5, 60.2, 29.7, 20.3, 14.2; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{21}H_{19}NNaO_2$ 340.1308, found 340.1303.

*Pyrroles **11b:12b**. General Procedure E.* (*E*)-4-(((*E*)-(3,4-Dihydronaphthalen-1(2*H*)-ylidene)amino)oxy)-4-phenylbut-3-en-2-one (**10b**, 60 mg, 0.20 mmol), [Au(PPh_3)Cl] (10 mg, 0.02 mmol), and $AgBF_4$ (4 mg, 0.02 mmol) in toluene (1 mL) were heated to 100 °C for 18 h. The residue was purified by flash column chromatography on silica gel (4:1 petroleum ether/ethyl acetate) to afford an inseparable (1:5) mixture of 1-(2-phenyl-4,5-dihydro-1*H*-benzoindol-3-yl)-ethanone and (2-methyl-4,5-dihydro-1*H*-benzoindol-3-yl)(phenyl)-methanone (**11b**:**12b**, 26 mg, 47%) as a brown oil: IR ($CHCl_3$) ν (cm^{-1}) 3441, 1731, 1573, 939 cm^{-1}; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{20}H_{17}NNaO$ 310.1203, found 310.1202. *1-(2-Phenyl-4,5-dihydro-1H-benzoindol-3-yl)ethanone (**11b**):* ^{1}H NMR (400 MHz,

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$CDCl_3$) δ_H 9.75 (br s, 1H), 7.56 (d, J = 6.8 Hz, 1H), 7.56−7.51 (m, 3H), 7.48 (dd, J = 7.6, 7.3 Hz, 1H), 7.50−7.47 (m, 1H), 7.29−7.19 (m, 3H), 2.95 (t, J = 7.4 Hz, 2H), 2.61 (t, J = 7.4 Hz, 2H), 2.06 (s, 3H). ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ_C 176.9, 139.9, 136.9, 133.3, 130.9, 128.6 (2C), 128.4, 127.9, 127.6, 127.5 (2C), 126.9 (2C), 126.9, 122.3, 119.8, 27.5, 19.9, 16.2. *(2-Methyl-4,5-dihydro-1H-benzoindol-3-yl)(phenyl)methanone (**12b**):* ^1H NMR (400 MHz, $CDCl_3$) δ_H 9.60 (br s, 1H), 7.68 (d, J = 6.8 Hz, 1H), 7.56−7.54 (m, 3H), 7.50 (dd, J = 7.5, 7.4 Hz, 1H), 7.48−7.45 (m, 1H), 7.26−7.17 (m, 3H), 2.98 (t, J = 7.5 Hz, 2H), 2.68 (t, J = 7.5 Hz, 2H), 1.94 (s, 3H); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ_C 186.1, 140.2, 137.0, 133.8, 131.0, 130.1, 129.0, 128.6, 128.3, 128.3 (2C), 127.6, 127.5, 127.5, 126.9, 122.8, 120.8, 29.7, 19.6, 11.7.

*Pyrrole **11c:12c**. General Procedure E.* (*E*)-4-phenyl-4-(((*E*)-(1-phenylethylidene)amino)oxy)but-3-en-2-one (**10c**, 100 mg, 0.36 mmol), [Au(PPh_3)Cl] (18 mg, 0.036 mmol), and $AgBF_4$ (7 mg, 0.036 mmol) in toluene (2 mL) were heated to 100 °C for 18 h. The residue was purified by flash column chromatography on silica gel (15:1 petroleum ether/ethyl acetate) to afford an inseparable (1:5) mixture of 1-(2,5-diphenyl-1*H*-pyrrol-3-yl)ethanone and (2-methyl-5-phenyl-1*H*-pyrrol-3-yl)(phenyl)methanone (**11c:12c**, 54 mg, 57%) as a brown oil: IR ($CHCl_3$) ν (cm^{-1}) 3441, 1730, 1448, 1110, 934 cm^{-1}; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{18}H_{15}NNa$, 284.1046, found 284.1037. *1-(2,5-Diphenyl-1H-pyrrol-3-yl)ethanone (**11c**):* ^1H NMR (400 MHz, $CDCl_3$) δ_H 9.69 (br s, 1H), 7.72 (dd, J = 7.6, 7.8 Hz, 2H), 7.63−7.59 (m, 2H), 7.54−7.50 (m, 2H), 7.42−7.40 (m, 2H), 7.35−7.31 (m, 2H), 6.57 (d, J = 3.0 Hz, 1H), 2.10 (s, 3H); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ_C 186.4, 183.8, 136.1, 129.7 (2C), 129.3 (2C), 129.1 (2C), 128.7, 128.6, 128.3, 128.2 (2C), 128.0, 127.7, 110.8, 29.7. *(2-Methyl-5-phenyl-1H-pyrrol-3-yl)(phenyl)methanone (**12c**):* ^1H NMR (400 MHz, $CDCl_3$) δ_H 9.52 (br s, 1H), 7.70 (dd, J = 7.4, 7.2 Hz, 2H), 7.61 (d, J = 7.6, 7.2 Hz, 2H), 7.52−7.48 (m, 4H), 7.45−7.42 (m, 2H), 6.47 (d, J = 2.9 Hz, 1H), 2.03 (s, 3H); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ_C 188.6, 139.9, 137.4, 131.2, 130.9, 130.7, 129.1 (2C), 128.4 (s, 2C), 128.3, 128.2 (2C), 128.2, 125.0 (2C), 111.5, 14.1.

*Pyrrole **21**.* To a stirred solution of DABCO (9 mg, 0.07 mmol) and (*E*/*Z*)-1-(furan-2-yl)ethanone oxime (**2r**, 100 mg, 0.80 mmol) in toluene (1.30 mL) was added dimethyl acetylenedicarboxylate (**3**, 98 μL, 0.80 mmol), and the resultant mixture was subjected to a two-stage microwave irradiation sequence (stage 1, 80 °C, 10 min; stage 2, 170 °C, 45 min). Ditert-butyl dicarbonate (262 mg, 1.20 mmol), DMAP (10 mg, 0.08 mmol), and triethylamine (111 μL, 0.80 mmol) were added and the resultant mixture was stirred at rt for 30 min. The mixture was concentrated under reduced pressure, and the residue was purified by flash column chromatography on silica gel (9:1 petroleum ether/ethyl acetate) to afford 1-*tert*-butyl 2,3-dimethyl 5-(furan-2-yl)-1*H*-pyrrole-1,2,3-tricarboxylate (**21**, 143 mg, 51%) as a dark brown oil: IR ($CHCl_3$) ν (cm^{-1}) 3631, 3458, 3008, 2945, 2838, 2460, 2337, 2010, 1741, 1603, 1515, 1445, 1371, 1252, 1155, 1125, 1016, 908, 848, 660 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 7.49 (d, J = 5.0 Hz, 1H), 6.71 (s, 1H), 6.53 (d, J = 3.8 Hz, 1H), 6.44 (dd, J = 5.0, 3.8 Hz, 1H), 3.97 (s, 3H), 3.84 (s, 3H), 1.45 (s, 9H); ^{13}C {^1H} NMR (75 MHz, $CDCl_3$) δ_c 163.1, 162.4, 147.5, 144.7, 142.6, 132.4, 125.3, 117.4, 114.0, 111.0, 110.3, 86.3, 53.0, 51.9, 27.5; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{17}H_{19}NO_7$ 350.1235, found 350.1218.

*Mechanistic Study: Synthesis of starting materials and other intermediates. (E)-Acetophenone Oxime (**2a**).*[18] A stirred solution of pyridine (0.66 mL, 8.3 mmol), acetophenone (1.0 g, 8.3 mmol), and hydroxylamine·HCl (0.87 g, 8.3 mmol) were refluxed in ethanol (50 mL) for 12 h. The solvent was removed under reduced pressure and water (30 mL) and EtOAc (30 mL) were added. The organic layer was dried over sodium sulfate and the solvente removed under reduced pressure to afford (*E*) acetophenone oxime (**2a**, 1.02 g, 91%) as a white solid: mp 56−58 °C (lit.[18] mp 55−60 °C); IR ($CHCl_3$) ν (cm^{-1}) 3250, 3112, 3060, 3035, 2930, 1490, 1371, 1302, 1082, 1005, 927, 754, 690 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 8.59 (br s, 1H), 7.71−7.59 (m, 2H), 7.44−7.34 (m, 3H), 2.32 (s, 3H); ^{13}C {^1H} NMR (75 MHz, $CDCl_3$) δ_C 155.9, 136.4, 129.2, 128.4 (2C), 126.0 (2C), 12.4; HRMS (ESI) m/z $[M + Na]^+$ calcd for C_8H_9NONa 158.0577, found 158.0581.

*Dimethyl 2-(((E/Z)-(1-Phenylethylidene)amino)oxy)maleate (**5a**).*[19] *General Procedure A.* To a stirred solution of DABCO (45 mg, 0.37 mmol) and (*E*)-acetophenone oxime (**2a**, 500 mg, 3.7 mmol) in dichloromethane (32 mL) was added dropwise a mixture of dimethylacetylene dicarbonate (**3**, 455 μL, 3.7 mmol) in dichloromethane (12 mL). The mixture was concentrated under reduced pressure and the residue purified by flash column chromatography on silica gel (6:1 petroleum ether/ethyl acetate) to afford dimethyl 2-(((*E*/*Z*)-(1-phenylethylidene)amino)oxy)maleate (**5a**, 762 mg, 79%) as a colorless oil that is an inseparable *E*/*Z* mixture (1:8): IR ($CHCl_3$) ν (cm^{-1}), 3435, 3086, 2953, 2888, 2494, 1956, 1722, 1642, 1573, 1437, 1308, 1274, 1135, 1026, 946, 844, 637 cm^{-1}; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{14}H_{15}NO_5Na$ 300.0843, found 300.0849. *(E)-isomer:* ^1H NMR (400 MHz, $CDCl_3$) δ_H 7.72−7.64 (m, 2H), 7.47−7.41 (m, 3H), 5.93 (s, 1H), 3.95 (s, 3H), 3.72 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 166.4, 163.0, 161.7, 160.6, 134.2, 130.7, 128.6 (2C), 126.7 (2C), 96.0, 52.9, 51.5, 13.8 *(Z)-isomer:* ^1H NMR (400 MHz, $CDCl_3$) δ_H 7.66−7.60 (m, 2H), 7.43−7.37 (m, 3H), 6.04 (s, 1H), 3.87 (s, 3H), 3.69 (s, 3H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 165.0, 162.9, 160.1, 153.4, 134.6, 130.2, 128.4 (2C), 126.6 (2C), 105.5, 52.7, 51.7, 13.6.

*Ethyl 3-(((E/Z)-(1-Phenylethylidene)amino)oxy)acrylate (**6a**).*[19] *General Procedure A.* To a stirred solution of DABCO (36 mg, 0.3 mmol) and (*E*)-acetophenone oxime (**2a**, 400 mg, 3.0 mmol) in dichloromethane (24 mL) was added dropwise a mixture of ethyl propiolate (303 μL, 3.0 mmol) in dichloromethane (9 mL). The mixture was concentrated under reduced pressure and the residue purified by flash column chromatography on silica gel (4:1 petroleum ether/ethyl acetate) to afford ethyl 3-(((*E*/*Z*)-(1-phenylethylidene)-amino)oxy)acrylate (**6a**, 503 mg, 72%) as a colorless oil that is an inseparable *E*/*Z* mixture (8:1): IR ($CHCl_3$) ν (cm^{-1}) 3180, 2961, 2872, 2728, 1701, 1615, 1573, 1465, 1312, 1129, 1048, 896, 840, 640; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{13}H_{15}NO_3Na$ 256.0945, found 256.0949. *(E)-Isomer:* ^1H NMR (400 MHz, $CDCl_3$) δ_H 8.11 (d, J = 12.6 Hz, 1H), 7.74−7.67 (m, 2H), 7.46−7.37 (m, 3H), 5.71 (d, J = 12.6 Hz, 1H), 4.22 (q, J = 7.1 Hz, 2H), 2.37 (s, 3H), 1.31 (t, J = 7.1, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 167.6, 161.9, 160.3, 134.6, 130.4, 128.6 (2C), 126.9 (2C), 97.3, 59.8, 14.3, 13.6. *(Z)-Isomer*: ^1H NMR (400 MHz, $CDCl_3$) δ_H 7.77−7.68 (m, 2H), 7.49 (d, J = 7.5 Hz, 1H), 7.49−7.45 (m, 3H), 4.94 (d, J = 7.5 Hz, 1H), 4.24 (q, J = 7.1 Hz, 2H), 1.31 (t, J = 7.1 Hz, 3H), 2.48 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 165.2, 159.9, 159.2, 134.6, 130.2, 128.3 (2C), 125.9 (2C), 94.3, 59.7, 14.1, 13.6.

*Dimethyl 1-Benzyl-1H-1,2,3-triazole-4,5-dicarboxylate (**17**).*[65] To a stirred solution of dimethyl acetylenedicarboxylate (**3**, 60 μL, 0.5 mmol) in toluene (0.5 mL) at rt was added benzyl azide (73 μL, 0.55 mmol). The reaction mixture was stirred at 100 °C for 3 h and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (3:1 petroleum ether/ethyl acetate) to afford dimethyl 1-benzyl-1*H*-1,2,3-triazole-4,5-dicarboxylate (**17**, 0.13 g, 93%) as a white solid: mp 65−67 °C (lit.[65] mp 64−66 °C); IR ($CHCl_3$) ν (cm^{-1}) 2255, 1734, 1497, 1061, 825 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ_H 7.33−7.15 (m, 5H, H), 5.41 (s, 2H), 3.92 (s, 3H), 3.84 (s, 3H); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ_c 159.9, 158.3, 139.7, 133.4, 129.3, 128.5, 128.4, 127.5, 53.5, 52.8, 52.2; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{13}H_{13}$ N_3NaO_4 298.0799, found 298.0802.

*Ethyl 1-Benzyl-1H-1,2,3-triazole-4-carboxylate/Ethyl 1-Benzyl-1H-1,2,3-triazole-5-carboxylate (**18a:18b**).*[66] To a stirred solution of ethyl propiolate (**4**, 51 μL, 0.50 mmol) in toluene (0.5 mL) at rt was added benzyl azide (73 μL, 0.55 mmol). The reaction mixture was stirred at 100 °C for 3 h and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (4:1 petroleum ether/ethyl acetate) to afford a separable mixture of regioisomers (6:1) ethyl 1-benzyl-1*H*-1,2,3-triazole-4-carboxylate/ethyl 1-benzyl-1*H*-1,2,3-triazole-5-carboxylate (**18a:18b**, 97 mg, 94%) as white solids: mp 81−83 °C (lit.[66] mp 82−83 °C); IR ($CHCl_3$) ν (cm^{-1}) 3630, 3458, 3154, 3008, 2945, 2838, 2461, 2019, 1721, 1603, 1549, 1463, 1376, 1334, 1240, 1073, 1014, 909, 840, 660 cm^{-1}; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{12}H_{13}$ N_3NaO_2

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254.0900, found 254.0892. *Ethyl 1-benzyl-1H-1,2,3-triazole-4-carboxylate (**18a**):* ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.97 (s, 1H), 7.40−7.25 (m, 5H), 5.60 (s, 2H), 4.37 (q, J = 7.2 Hz, 2H), 1.35 (t, J = 7.2 Hz, 3H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ_c 160.2, 140.0, 133.7, 128.8 (2C), 128.5, 127.8 (2C), 127.2, 60.8, 53.9, 13.9. *Ethyl 1-benzyl-1H-1,2,3-triazole-5-carboxylate (**18b**):* ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 8.15 (s, 1H), 7.42−7.29 (m, 5H), 5.93 (s, 2H), 4.35 (q, J = 7.2 Hz, 2H), 1.36 (t, J = 7.2 Hz, 3H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ_c 158.5, 138.1 (2C), 135.1, 128.7 (2C), 128.4, 128.0 (2C), 61.8, 53.4, 29.6, 14.1.

*Gold(I) Acetylide **20**.[67] Method 1.* To a stirred solution of ethyl propiolate (**4**, 5.2 μL, 0.05 mmol) and toluene (0.2 mL) at rt were added [Au(PPh_3)Cl] (25 mg, 0.05 mmol) and AgOTf (13 mg, 0.05 mmol). The reaction mixture was heated to 100 °C for 3 h and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (5:1 petroleum ether/ethyl acetate) to afford gold(I) acetylide **20** (18 mg, 63%) as a pale yellow solid. *Method 2.* To a stirred solution of ethyl propiolate (**4**, 5.2 μL, 0.05 mmol) in toluene (0.2 mL) at rt were added [Au(PPh_3)Cl] (25 mg, 0.05 mmol) and $AgBF_4$ (10 mg, 0.05 mmol). The reaction mixture was heated to 100 °C for 3 h and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (5:1 petroleum ether/ethyl acetate) to afford gold(I) acetylide **20** (21 mg, 77%) as a pale yellow solid: IR ($CHCl_3$) ν (cm^{-1}) 2253, 2131, 1694, 1240, 1102, 909 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.66−7.35 (m, 15H), 4.21 (q, J = 7.2 Hz, 2H), 1.30 (t, J = 7.2 Hz, 3H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ_c 153.5, 134.0 (d, J = 18.8 Hz, 6C), 132.0 (d, J = 22.5, 3C), 130.7 (d, J = 0.7, 3C), 128.9 (d, J = 7.5 Hz, 6C), 93.6, 68.1, 61.1, 14.2; ^{31}P {^{1}H} NMR (100 MHz, $CDCl_3$) δ_p 41.3; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{23}H_{21}AuO_2P$ 557.0932, found 557.0945; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{23}H_{20}AuO_2PNa$ 579.0759, found 579.0764.

*Gold(I) Triazole **19a:19b**.* To a stirred solution of gold acetylide **20** (35 mg, 0.06 mmol) in toluene (0.2 mL) at rt was added benzyl azide (7 μL, 0.06 mmol). The reaction mixture was stirred at 100 °C for 3 h and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (3:1 petroleum ether/ethyl acetate) to afford an inseparable mixture of regioisomers (9:1) of gold(I) triazole **19a:19b** (32 mg, 78%) as a white solid: IR ($CHCl_3$) ν (cm^{-1}) 3690, 3632, 3063, 3009, 1712, 1602, 1497, 1482, 1456, 1437, 1407, 1386, 1340, 1192, 1120, 1102, 1073, 1048, 1016, 846, 657 cm^{-1}; ^{31}P {^{1}H} NMR (100 MHz, $CDCl_3$) δ_p 42.3; HRMS (ESI) [M + H]$^+$ m/z calcd for $C_{30}H_{28}N_3O_2PAu$, 690.1580; found 690.1580; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{30}H_{27}N_3O_2PAuNa$ 712.1399, found 712.1403. *Gold(I) triazole **19a**:* ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.58−7.43 (m, 15H), 7.23−7.12 (m, 3H), 5.64 (s, 2H), 4.40 (q, J = 7.2 Hz, 2H), 1.35 (t, J = 7.2 Hz, 3H); ^{1}H NMR (400 MHz, $CDCl_3$) δ_c 163.8, 137.6, 134.3 (d, J = 13.8 Hz, 5C), 132.1 (d, J = 10.0 Hz, 5C), 129.9 (2C), 129.4 (2C), 129.2 (d, J = 12.2 Hz, 5C), 128.5 (d, J = 8.4 Hz, 3C), 128.4, 127.8, 127.6, 60.2, 55.8, 14.5. *Gold(I) triazole **19b**:* ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.77−7.63 (m, 3H), 7.57−7.42 (m, 14H), 7.33−7.29 (m, 3H), 5.74 (s, 2H), 4.26 (q, J = 7.4 Hz, 2H), 1.18 (t, J = 7.4 Hz, 3H).

*2,2,2-Trideuterio-1-phenylethanone Oxime (**2aa**).[68]* A stirred solution of pyridine (0.992 mL, 12.3 mmol), acetophenone-ß,ß,ß-d^3 (**1aa**, 1.42 mL, 12.3 mmol) and hydroxylamine·HCl (845 mg, 12.3 mmol) were refluxed in ethanol (75 mL) for 12 h. The solvent was removed under reduced pressure and water (20 mL) and EtOAc (20 mL) were added. The organic layer was dried over sodium sulfate and the solvent removed under reduced pressure to afford 2,2,2-trideuterio-1-phenylethanone oxime (**2aa**, 1.65 g, 98%) as a white solid: mp 56−58 °C; IR ($CHCl_3$) ν (cm^{-1}) 3585, 3299, 3085, 3062, 3009, 2221, 1954, 1724, 1626, 1577, 1496, 1576, 1496, 1443, 1362, 1318, 1296, 1281, 1240, 1117, 935, 834, 623 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 9.92 (br s, 1H), 7.70−7.62 (m, 2H), 7.45−7.36 (m, 3H); ^{2}H {^{1}H} NMR (400 MHz, toluene) δ_D 2.36 (s, 3D); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ_C 155.9, 136.43, 129.2, 128.5 (2C), 126.0 (2C), 11.8 (spt, J = 19.4 Hz, C); HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_8H_7D_3NO$ 139.0946, found 139.0926.

*Dimethyl 2-(((E/Z)-(2,2,2-Trideuterio-1-phenylethylidene)amino)-oxy)maleate (**5aa**).* *O*-Vinyl oxime **5aa** was synthesized according to general procedure A. To a stirred solution of DABCO (41 mg, 0.365 mmol) and 2,2,2-trideuterio-1-phenylethanone oxime (**2aa**, 500 mg, 3.65 mmol) in dichloromethane (30 mL) was added ethyl propiolate (**4**, 370 μL, 3.65 mmol) in dichloromethane (10 mL). The resultant mixture was stirred at rt for 12 h and the residue purified by flash column chromatography on silica gel (6:1 petroleum ether/ethyl acetate) to afford dimethyl 2-(((*E*/*Z*)-(2,2,2-trideuterio-1-phenylethylidene)amino)oxy)maleate (0.94 g, 93%) as a colorless oil: IR ($CHCl_3$) ν (cm^{-1}) 3690, 3009, 2954, 2849, 1724, 1652, 1612, 1495, 1437, 1362, 1309, 1275, 1179, 1130, 1026, 976, 949, 889 cm^{-1}; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{14}H_{12}D_3NNaO_5$ 303.1031, found 3031021. *(E)-Isomer:* ^{1}H NMR (500 MHz, $CDCl_3$) δ_H ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.71−7.67 (m, 2H), 7.48−7.36 (m, 3H), 5.94 (s, 1H), 3.95 (s, 3H), 3.73 (s, 3H); ^{2}H {^{1}H} NMR (500 MHz, toluene) δ_D 2.35 (s, 3D); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ_C 166.5, 163.1, 161.7, 160.6, 134.2, 130.7, 128.6 (2C), 126.7 (2C), 95.9, 53.0, 51.6, 13.2 (spt, J = 19.5 Hz, C). *(Z)-Isomer:* ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.66−7.61 (m, 2H), 7.41−7.36(m, 3H), 6.05 (s, 1H), 3.88 (s, 3H), 3.69 (s, 3H); ^{2}H {^{1}H} NMR (500 MHz, toluene) δ_D 2.42 (s, 3D); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ_C 165.1, 163.0, 160.1, 153.4, 134.5, 130.2, 128.5 (2C), 126.6 (2C), 105.4, 52.8, 51.7, 13.1 (spt, J = 19.3 Hz, C).

*(E)-Ethyl 3-(((E)-(2,2,2-Trideuterio-1-phenylethylidene)amino)-oxy)acrylate (**6aa**).* *O*-Vinyl oxime **6aa** was synthesized according to general procedure A. To a stirred solution of DABCO (41 mg, 0.365 mmol) and 2,2,2-trideuterio-1-phenylethanone oxime (**2aa**, 500 mg, 3.65 mmol) in dichloromethane (30 mL) was added ethyl propiolate (**4**, 370 μL, 3.65 mmol) in dichloromethane (10 mL). The resultant mixture was stirred at rt for 12 h and the residue purified by flash column chromatography on silica gel (6:1 petroleum ether/ethyl acetate) to afford (*E*)-ethyl 3-(((*E*)-(2,2,2-trideuterio-1-phenylethylidene)amino)oxy)acrylate (**6aa**, 0.77 g, 91%) as a colorless oil: IR ($CHCl_3$) ν (cm^{-1}) 3009, 2985, 1701, 1636, 1612, 1573, 1445, 1370, 1313, 1283, 1180, 1129, 1048, 998, 958, 866, 842 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.10 (d, J = 12.6 Hz, 1H), 7.76−7.69 (m, 2H), 7.47−7.39 (m, 3H), 5.69 (d, J = 12.6 Hz, 1H), 4.20 (q, J = 7.1 Hz, 2H), 1.31 (t, J = 7.1 Hz, 3H); ^{2}H {^{1}H} NMR (500 MHz, toluene) δ_D 2.31 (s, 3D); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ_C 167.6, 161.9, 160.3, 134.5, 130.4, 128.6 (2C), 126.5 (2C), 59.8, 14.3, 13.0 (spt, J = 19.6 Hz, C); HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{13}H_{12}D_3NNaO_5$ 259.1133, found 259.1127.

*Dimethyl 3-Deuterio-5-phenyl-1H-pyrrole-2,3-dicarboxylate and Dimethyl 5-Phenyl-1H-pyrrole-2,3-dicarboxylate (**7aa:7a**).* Pyrroles **7aa:7a** were synthesized according to general procedure E. Dimethyl 2-(((*E*)-(2,2,2-trideuterio-1-phenylethylidene)amino)oxy)but-2-enedioate (**5aa**, 80 mg, 0.29 mmol), [Au(PPh_3)Cl] (14 mg, 0.029 mmol), and $AgBF_4$ (6 mg, 0.029 mmol) in toluene (2.5 mL) were heated to 100 °C for 18 h. The residue was purified by flash column chromatography on silica gel (6:1 petroleum ether/ethyl acetate) to afford an inseparable mixture (5:2) of dimethyl 3-deuterio-5-phenyl-1*H*-pyrrole-2,3-dicarboxylate and dimethyl 5-phenyl-1*H*-pyrrole-2,3-dicarboxylate (**7aa:7a**, 49 mg, 66%) as an orange solid: mp 144−146 °C; IR ($CHCl_3$) ν (cm^{-1}) 3855, 3840, 3822, 3808, 3690, 3608, 3096, 3050, 3042, 2855, 2373, 2345, 1725, 1602, 1509, 1459, 1375, 1375, 1239, 1120, 1028, 918, 660, 644 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 9.75 (br s, 1H), 7.58 (d, J = 7.8 Hz, 2H), 7.43 (dt, J = 7.8, 7.4 Hz, 2H), 7.36 (t, J = 7.4 Hz, 1H), 6.94 (d, J = 3.2 Hz, 1H), 3.93 (s, 3H), 3.90 (s, 3H); ^{2}H {^{1}H} NMR (500 MHz, toluene) δ_D 6.98 (s, 1D); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ_C 164.1, 160.7, 134.8, 130.3, 129.1 (2C), 128.3, 124.8 (2C), 122.6, 121.4, 110.7, 110.6 (t, J = 34.1 Hz, C), 52.3, 51.9; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{14}H_{12}DNNaO_4$ 283.0800, found 283.0791.

*Ethyl 3-Deuterio-5-phenyl-1H-pyrrole-3-carboxylate and Ethyl 5-Phenyl-1H-pyrrole-3-carboxylate (**8aa:8a**).* Pyrroles **8aa:8a** were synthesized according to general procedure E. (*E*)-Ethyl 3-(((*E*)-(2,2,2-trideuterio-1-phenylethylidene)amino)oxy)acrylate (**6aa**, 80 mg, 0.34 mmol), [Au(PPh_3)Cl] (17 mg, 0.034 mmol), and $AgBF_4$ (7 mg, 0.034 mmol) in toluene (2.5 mL) were heated to 100 °C for 18 h. The

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residue was purified by flash column chromatography on silica gel (8:1 petroleum ether/ethyl acetate) to afford an inseparable mixture (5:2) of ethyl 3-deuterio-5-phenyl-1*H*-pyrrole-3-carboxylate and ethyl 5-phenyl-1*H*-pyrrole-3-carboxylate (**8aa:8a**, 31 mg, 43%) as an orange oil: IR ($CHCl_3$) ν (cm^{-1}) 3936, 3905, 3855, 3822, 3771, 3691, 3631, 3607, 3231, 3081, 3068, 3043, 3006, 2927, 2856, 2420, 1720, 1602, 1560, 1446, 1239, 1174, 1028, 933, 832, 660, 644 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ_H 8.85 (br s, 1H), 7.52−7.47 (m, 3H), 7.42−7.36 (m, 2H), 7.31−7.28 (m, 1H), 6.93 (d, J = 2.3 Hz, 1H), 4.32 (q, J = 7.2 Hz, 2H), 1.37 (t, J = 7.1 Hz, 3H); ^2H {^1H} NMR (500 MHz, toluene) δ_D 7.25 (s, 1D); ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ_C 164.9, 132.9, 131.8, 129.0 (2C), 128.4 (t, J = 32.1 Hz, C), 127.0, 124.1 (2C), 118.1, 106.6, 59.9, 14.5; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{13}H_{12}DNNaO_2$ 216.1004, found 216.0990.

Mechanistic Study: Experimental Details. *Investigations into the Relative Stability of O-Vinyl Oxime **5a**. Method a.* To a stirred solution of dimethyl 2-(((*E*/*Z*)-(1-phenylethylidene)amino)oxy)-maleate (**5a**, 80 mg, 0.29 mmol) and toluene (2 mL) at rt was added benzyl azide (36 μL, 0.29 mmol). The mixture was heated to 100 °C for 12 h in a sealed 5 mL microwave vial. The mixture was concentrated under reduced pressure and the crude contents were analyzed by ^1H and ^{13}C {^1H} NMR spectroscopy. Relative concentrations of the products were calculated via integration of the ^1H NMR and comparison of the spectra with the previously synthesized pure compounds.

Method b. To a stirred solution of dimethyl 2-(((*E*/*Z*)-(1-phenylethylidene)amino)oxy)maleate (**5a**, 100 mg, 0.36 mmol) and toluene (2 mL) at rt were added benzyl azide (45 μL, 0.36 mmol), [Au(PPh_3)Cl] (18 mg, 0.036 mmol), and AgOTf (9 mg, 0.036 mmol). The mixture was heated to 100 °C for 12 h in a sealed 5 mL microwave vial. The mixture was concentrated under reduced pressure and the crude contents was analyzed by ^1H and ^{13}C {^1H} NMR spectroscopy. Relative concentrations of the products were calculated via integration of the ^1H NMR and comparison of the spectra with the previously synthesized pure compounds.

*Investigations into the Relative Stability of O-Vinyl Oxime **6a**. Method a.* To a stirred solution of ethyl 3-(((*E*)-(1-phenylethylidene)amino)oxy)acrylate (**6a**, 100 mg, 0.43 mmol) and toluene (2 mL) at rt was added benzyl azide (54 μL, 0.43 mmol). The mixture was heated to 100 °C for 12 h in a sealed 5 mL microwave vial. The mixture was concentrated under reduced pressure and the crude contents was analyzed by H and ^{13}C {^1H} NMR spectroscopy. Relative concentrations of the products were calculated via integration of the ^1H NMR and comparison of the spectra with the previously synthesized pure compounds.

Method b. To a stirred solution of ethyl 3-(((*E*)-(1-phenylethylidene)amino)oxy)acrylate (**6a**, 100 mg, 0.43 mmol) and toluene (2 mL) at rt were added benzyl azide (54 μL, 0.43 mmol), [Au(PPh_3)Cl] (21 mg, 0.043 mmol) and AgOTf (11 mg, 0.043 mmol). The mixture was heated to 100 °C for 12 h in a sealed 5 mL microwave vial. The mixture was concentrated under reduced pressure and the crude contents was analyzed by H and ^{13}C {^1H} NMR spectroscopy. Relative concentrations of the products were calculated via integration of the ^1H NMR and comparison of the spectra with the previously synthesized pure compounds.

*Characterization of Proposed Intermediates **13**−**15**. Dimethyl 2-(((1-Phenylvinyl)amino)oxy)maleate/Dimethyl 2-(2-Imino-2-phenylethyl)-3-oxosuccinate (**13/15**).* To a stirred solution of dimethyl 2-(((*E*)-(1-phenylethylidene)amino)oxy)-but-2-enedioate (**5a**, 80 mg, 0.29 mmol) and toluene-d_8 (0.4 mL) at rt were added [Au(PPh_3)Cl] (14 mg, 0.029 mmol) and AgOTf (7 mg, 0.029 mmol). The mixture was heated to 100 °C for 1−4 h in a sealed 5 mL microwave vial. The crude mixture was transferred to a NMR tube under argon and the crude contents were analyzed by ^1H, ^{13}C {^1H} and HMQC NMR spectroscopy.

*Characterization of Proposed Intermediates **14**−**16**. (E/Z)-Ethyl 3-(((1-Phenylvinyl)amino)oxy)acrylate/ethyl 2-formyl-4-imino-4-phenylbutanoate (**14/16**).* To a stirred solution of ethyl 3-(((*E*)-(1-phenylethylidene)amino)oxy)acrylate (**6a**, 100 mg, 0.43 mmol) and toluene-d_8 (0.4 mL) at rt were added [Au(PPh_3)Cl] (21 mg, 0.043 mmol) and AgOTf (11 mg, 0.043 mmol). The mixture was heated to 100 °C for 4 h in a sealed 5 mL microwave vial. The crude mixture was transferred to a NMR tube under argon and the crude contents were analyzed by ^1H and ^{13}C {^1H} NMR spectroscopy.

*Characterization of Proposed Intermediates **13-d**−**15-d**. Deuteriodimethyl 2-(((1-Phenylvinyl)amino)oxy)maleate/Deuteriodimethyl 2-(2-imino-2-phenylethyl)-3-oxosuccinate (**13/15**).* A 5 mL microwave vial was charged with dimethyl 2-(((*E*/*Z*)-(2,2,2-trideuterio-1-phenylethylidene)-amino)oxy)maleate (**5aa**, 30 mg, 0.11 mmol), toluene (0.4 mL), [Au(PPh_3)Cl] (5.4 mg, 0.011 mmol), and AgOTf (2.8 mg, 0.011 mmol). The crude mixture was transferred into a J. Young tube under argon and the mixture was heated in a NMR machine (Bruker AV400) to 100 °C for 1.5 h. ^2H {^1H} NMR were taken at 2 min intervals.

*Characterization of Proposed Intermediates **14-d**−**16-d**. Deuterio-(E/Z)-ethyl 3-(((1-Phenylvinyl)amino)oxy)acrylate/Deuterioethyl 2-Formyl-4-imino-4-phenylbutanoate (**14-d/16-d**).* To a stirred solution of (*E*)-ethyl 3-(((*E*)-(2,2,2-trideuterio-1-phenylethylidene)-amino)oxy)acrylate (**6aa**, 40 mg, 0.17 mmol) and toluene (0.4 mL) at rt were added [Au(PPh_3)Cl] (8.4 mg, 0.017 mmol) and AgOTf (4.3 mg, 0.017 mmol). The mixture was heated to 100 °C for 18 h in a sealed 5 mL microwave vial. The crude mixture was transferred to a NMR tube under argon and analyzed by ^2H {^1H} NMR spectroscopy.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of NMR spectra, microwave data, and further information regarding the X-ray crystal structures. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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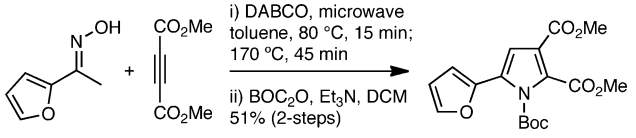

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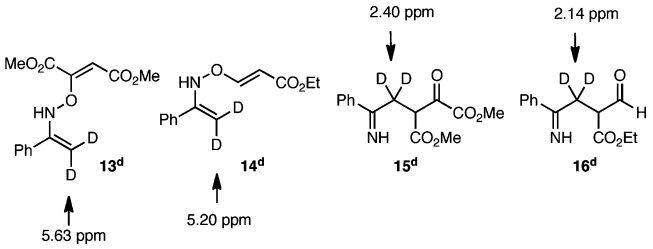

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