ChemPubSoc Europe

DOI: 10.1002/ejoc.201900108

EurJOC European Journal of Organic Chemistry

Full Paper

Gold Catalysis

Gold-Catalyzed Oxidation of Internal Alkynes into Benzils and its Application for One-Pot Synthesis of Five-, Six-, and Seven-Membered Azaheterocycles

Alexey Yu. Dubovtsev*[a] Dmitry V. Dar'in,[a] Mikhail Krasavin,[a] and Vadim Yu. Kukushkin*[a]

Abstract: Internal alkynes have been shown to undergo oxidation to substituted benzils (1,2-diarylethane-1,2-diones) by α-picoline *N*-oxide in the presence of $Ph_3PAuNTf_2$ (5 mol-%). In addition to the unsubstituted benzil, the method allows preparing, under markedly mild conditions (50 °C in chlorobenzene), various non-symmetrical products, including heteroaromatic versions thereof which are much more difficult to obtain otherwise. This gold(I)-catalyzed transformation was integrated into one-pot reaction sequence delivering a range of 5- to 7-membered ring systems (imidazoles, quinoxalines, 1,2,4-triazines, pyrazines, and 1,4-diazepines), thus linking these important heterocyclic motifs to the internal alkyne reagent space.

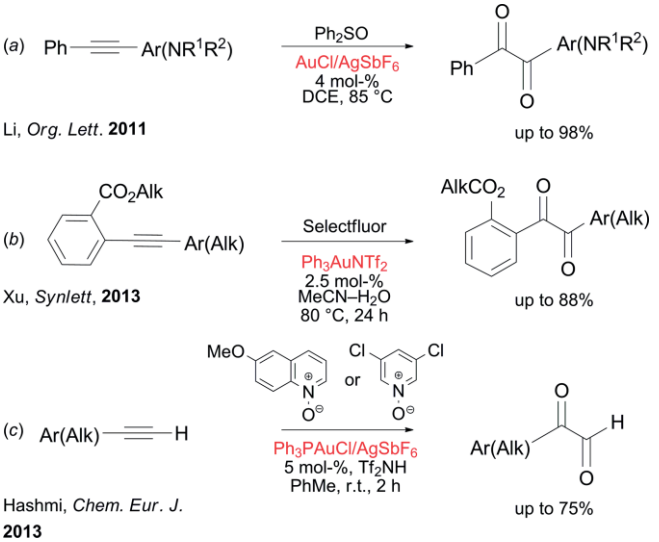
Introduction

Carbo- and heteroaromatic derivatives of the so-called benzils, $R^1C(=O)C(=O)R^2$ (IUPAC name: 1,2-diaryl(heteryl)ethane-1,2-diones; R^1/R^2 = Ar, Het), are useful synthons for design of a wide range of heterocyclic systems.[1] Benzils also found an application as precursors for syntheses of chiral 1,2-diols,[2] α-diimine ligands,[3] and *N*-heterocyclic carbenes.[4] Attractiveness of $R^1C(=O)C(=O)R^2$ is also driven by their occurrence in natural products and, in particular, natural benzils – such as scandione and calophione A – had been the goal of total synthesis.[5] Owing their carboxylesterase inhibition activity[6] as well as antimicrobial,[7] antitumor,[8] and cytotoxic[9] properties, benzils are useful species from medicinal chemistry viewpoint.

Common routes to benzils include oxidation (or, in other words, diketonization) of easily and/or commercially available acetylenes using transition-metal species as activators.[1a] These approaches to benzils are not free from substantial drawbacks that include harsh conditions, high catalyst loading, use of toxic or aggressive reagents and limited scope (see SI for detailed literature survey on synthetic methods leading to benzils).

A logical alternative to the known metal-catalyzed methods is the application of gold-based catalysts insofar as Au-involving reactions (for reviews and works on Au-catalyzed conversions of acetylenes see references[10,11]) often proceed under mild conditions, in air and in the moistures atmosphere, and the Au-catalysts are active at a very small catalyst load.[12] Considering the power of gold catalysis in achieving various synthetic goals, development of new methods for Au-catalyzed *O*- and *N*-functionalizations of alkynes with *N–O* species continues to be of great importance.[13]

In particular, Li et al. reported the Au-catalyzed synthesis of benzils and α-keto imides of limited scope from internal alkynes by their oxidation with $Ph_2S{=}O$ (Scheme 1a).[14] This method demonstrates good results for the oxidation of 4-$RC_6H_4C{\equiv}CPh$ (R = H, Me, Br, Ac; 80–98 %), but the yields drop to 74–75 % for 4-MeO- or 2-F-substituted substrates. Furthermore, the best results were obtained in refluxing 1,2-dichloroethane – a toxic and possibly carcinogenic solvent that is no longer used by the pharmaceutical industry[15] – whereas the application of safer solvents does not give satisfactory results. In a relevant Au-involving synthesis (Scheme 1b), the neighboring ester group-participated diketonization of *o*-alkynylbenzoates under the



Scheme 1. Gold-catalyzed generation of 1,2-dicarbonyl compounds from acetylenes.

[a] *Saint Petersburg State University, Universitetskaya Nab. 7/9, 199034 Saint Petersburg, Russian Federation*
E-mail: a.dubovtsev@spbu.ru (A.Yu.D.)
v.kukushkin@spbu.ru (V.Yu.K.)
http://chem.spbu.ru/ptchem.html

Supporting information and ORCID(s) from the author(s) for this article are available on the WWW under https://doi.org/10.1002/ejoc.201900108.

gold(I)/Selectfluor catalytic system[16] led to low yield of unsubstituted benzil (31 %). Noteworthy that all these methods were not applied for hetaryl-substituted internal alkynes.

Notable results, particularly in the context of this work, were obtained by Hashmi and co-workers who developed an Au-catalyzed approach to glyoxals via oxidation of terminal alkynes using pyridine *N*-oxide derivatives as convenient oxygen carriers (Scheme 1c);[17] the method was extended to one-pot synthesis of 2-substituted quinoxalines. Despite its superior efficiency for the oxidation of *terminal* alkynes, the developed method was not found suitable for *internal* acetylenes that often exhibit different reactivity (for general consideration see (*i*) Results and Discussion).

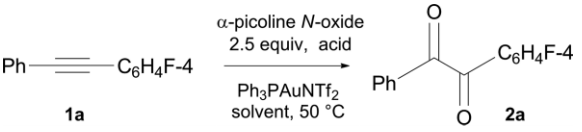
In this project, we discovered that the application of the well-established Gagosz catalyst, $Ph_3PAuNTf_2$,[18] as part of α-picoline *N*-oxide/TfOH/$Ph_3PAuNTf_2$ system can offer a facile approach to oxidation (diketonization) of internal alkynes, which complements Hashimi's oxidation of terminal alkynes. The advantages of our method for oxidation of internal alkynes include mild reaction conditions, a wide scope of obtained benzils (including non-symmetric, that are substantially more difficult-to-obtain than the symmetric), a tolerance to functional substituents, and the possibility for syntheses of heteroaromatic 1,2-diketones. An important feature of this approach is a possibility of its extension to one-pot methodology for generation of various azaheterocyclic systems. This Au^I-involving one-pot synthetic strategy was applied for molecular design of various (5-to-7)-membered heterocycles starting directly from internal acetylenes. All our results are consequently disclosed in sections that follow.

Results and Discussion

(*i*) Gold-Catalyzed Diketonization of Internal Alkynes. Both internal and terminal alkynes possess the same carbon–carbon triple bond, but in many instances, their reactivities are different. This is because some reactions with terminal alkynes proceed via intermediate generation of acetylide (e.g. nucleophilic additions) and this is not feasible for internal alkynes. On the other hand, different steric/electronic properties of internal and terminal alkynes also affect an outcome of the reaction. While terminal alkynes are most frequently employed in oxidative Au-catalyzed transformations, regioselective oxidations of internal alkynes (especially alkyl substituted) can be challenging, due to their reduced reactivity and occurrence of side reactions (e.g. facile 1,2-CH insertions).[19]

Recently we found[20] benzil (PhCOCOPh) to be a minor by-product of the reaction between diphenylacetylene and α-picoline *N*-oxide in the presence of Ph_3AuNTf_2. Considering the fact that such an oxidation has not been described for internal alkynes under gold-catalyzed conditions, we attempted to optimize this reaction to increase its utility for the preparation of substituted benzils. Oxidation of 1-fluoro-4-(phenylethynyl)-benzene (**1a**) to corresponding diketone **2a** was chosen as a model reaction as it can be easily monitored by ^{19}F NMR (Table 1).

Table 1. Optimization of the reaction conditions.[a]



1a **2a**

Entry	Catalyst, mol %	Acid, Equiv	Solvent	Time [h]	Yield,[b] %
1	5	MsOH, 1	PhCl	2	31
2	5	Tf_2NH, 1	PhCl	2	41
3	5	TfOH, 1	PhCl	2	42
4	5	None	PhCl	2	32
5	5	TfOH, 0.5	PhCl	2	33
6	5	TfOH, 1.5	PhCl	2	46
7	5	TfOH, 2	PhCl	2	87
8	5	TfOH, 2	PhCl	2	79[c]
9	5	TfOH, 2	DMSO	2	61
10	5	TfOH, 2	THF	2	77
11	5	TfOH, 2	PhMe	2	84
12	5	TfOH, 2	DCE	2	86
13	5	TfOH, 2	PhCl	1	71
14	5	TfOH, 2	PhCl	4	94
15	**5**	**TfOH, 2**	**PhCl**	**6**	**97**
16	5	TfOH, 2	PhCl	48[d]	72
17	5	TfOH, 2	PhCl	1[e]	72
18	3	TfOH, 2	PhCl	6	85
19	1.5	TfOH, 2	PhCl	6	63
20	0	TfOH, 2	PhCl	6	–

[a] All reactions were carried out on a 0.2 mmol scale (1 mL of solvent). [b] ^{19}F NMR yield. [c] Pyridine *N*-oxide was used instead α-picoline *N*-oxide. [d] Room temperature. [e] Microwave irradiation (50 W) at 50 °C.

A common feature of the oxidation reactions involving *N*-oxides is the formation of the respective free base in the reaction mixture,[21] which leads to deactivation of the gold catalyst.[22] Thus, it was shown that using acid to scavenge the base formed upon the transfer of oxygen from the *N*-oxide is critical for gold-catalyzed oxidation of acetylenes with pyridine *N*-oxides.[17] Therefore, we first screened for the optimal acid component (1 equiv.) which would scavenge the pyridine base and reactivate the catalyst. Between triflic acid and triflic imide which gave the best results, triflic acid (TfOH) was selected as more readily available. It was further found that the acid/acetylene ratio substantially affected the yield of the product. The yield of the benzil product steadily increased from 32 to 87 % when 0, 0.5, 1.5, and 2 equiv. of TfOH were employed in the reaction.

Next, we tested the possibility of using a cheaper oxidizing agent in this reaction and found that unsubstituted pyridine *N*-oxide also exhibited a high oxidative efficiency (79 %). The effect of the solvent was also examined and the best synthetic results were obtained in non-polar solvents (chlorobenzene, DCE, toluene). Chlorobenzene was chosen due to its lower toxicity compared to 1,2-dichloroethane[23] and the possibility of carrying out reactions over a wide range of temperatures in this solvent. The yield was further improved (up to 97 %) by increasing the reaction time to 6 h. The reaction at r.t. was much slower and the yield obtained after 48 h was somewhat lower (72 %). The reaction conducted under microwave irradiation (50 °C, 50 W, 1 h) gave a similar result (Entry 17).

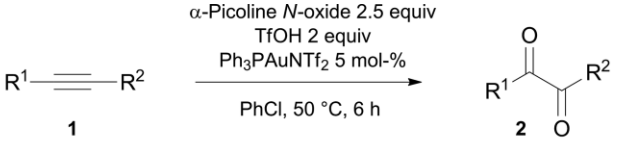
Finally, we tested different catalyst loadings and found that using 3 mol-% of the catalyst was sufficient for achieving a

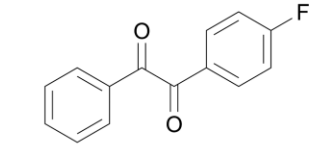
good product yield (85 %) whereas reducing the amount of the catalyst to 1.5 mol-% led to a significant reduction of the yield. Thus, the optimal results were obtained in the model reaction conducted in PhCl with 2 equiv. of TfOH, 2.5 equiv of α-picoline *N*-oxide and 5 mol-% of $Ph_3PAuNTf_2$ at 50 °C for 6 h.

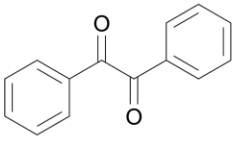
***(ii)* Scope of the Gold-catalyzed Oxidation.** With the optimal conditions at hand, the substrate scope and limitations of the developed approach were examined (Table 2). Excellent yields of substituted benzils **2** were obtained from unsubstituted diphenylacetylene and diarylacetylenes bearing either electron-donating (Me, OMe) or electron-withdrawing (F, Br) groups. Strong electron-withdrawing groups (CN, Ac) slightly reduced the product yields. In the case of acetylene featuring a nitro group, the yield decreased significantly (44 %), most likely due to the lower electron density on the alkyne triple bond. The decreased reactivity of electron-deficient substrates is documented in the literature as a common limitation of alkyne oxidation methods.[1a] However, by increasing both the catalyst loading (10 mol-%) and the reaction time (24 h), we succeeded to increase the yield of 1-(4-nitrophenyl)-2-phenylethane-1,2-dione (**2j**) to 72 %. While moving from *para*- (**1e**) to *meta*- (**1f**), and then to *ortho*-methoxy-4-(phenylethynyl)benzene (**1g**) as substrates for the oxidation, the yield of the corresponding benzils slightly decreased. The reaction conditions were also found applicable to the oxidation of heteroaryl substituted acetylenes **1l–o**. However, all attempts to employ alkyl-substituted internal acetylenes or 1-trimethylsilyl-2-phenylacetylene in the reaction failed and the desired diketones were not obtained. This fact is probably related to the facile 1,2-CH insertions in gold carbene intermediates.[19b–19d] The method is inapplicable for the oxidation of terminal alkynes and, e.g., phenylacetylene under the optimized conditions gave phenylglyoxal in only 22 % ^{1}H NMR yield.

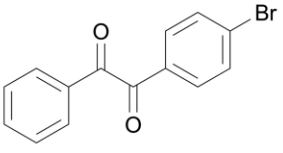
It has been reported that a carbonyl group in the *ortho*-position of a phenylacetylene moiety can participate in the diketonization.[16,24] We observed such a neighbouring group participation when methyl 2-(phenylethynyl) benzoate (**1p**) was reacted under the optimized reaction conditions and 3-phenyl-

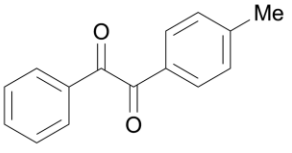
Table 2. Gold-catalyzed oxidation of internal alkynes into benzils.[a,b]

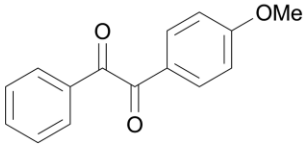


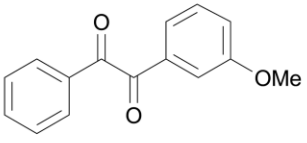

2a, 94%

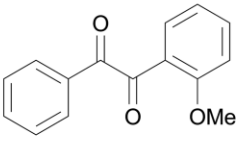

2b, 96%

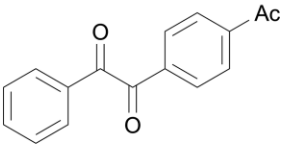

2c, 93%

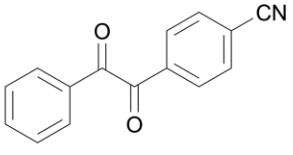

2d, 98%

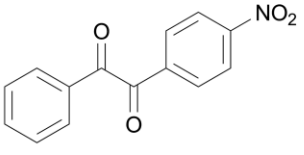

2e, 97%

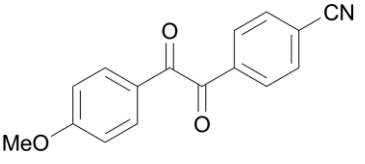

2f, 83%

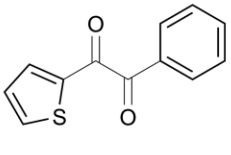

2g, 79%

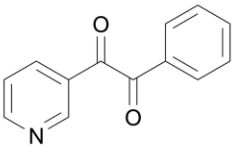

2h, 81%

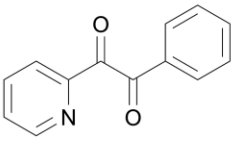

2i, 74%

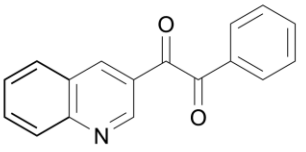

2j, 44(72[c])%


2k, 75%


2l, 80%

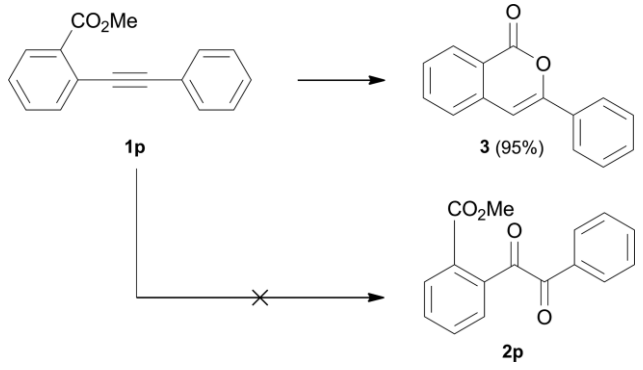

2m, 56%


2n, 53%


2o, 76%

[a] All reactions were carried out on a 0.5 mmol scale (2 mL of PhCl). [b] Isolated yield. [c] Ph_3AuNTf_2 10 mol-%, 16 h.

1*H*-isochromen-1-one (**3**) – and not diketone **2p** – was obtained as the major product (Scheme 2). Control experiments indicated that in the absence of both the *N*-oxide and TfOH, 1*H*-isochromen-1-one **3** was formed in 31 % yield. However, using only 1 equiv. TfOH (without added $Ph_3PAuNTf_2$ and the *N*-oxide), the yield of **3** increased to 95 %. Similar 6-*endo-dig* gold-catalyzed and silver/*p*-TsA co-catalyzed cyclizations of ester **1p** to isocoumarin **3** had been previously reported.[25]

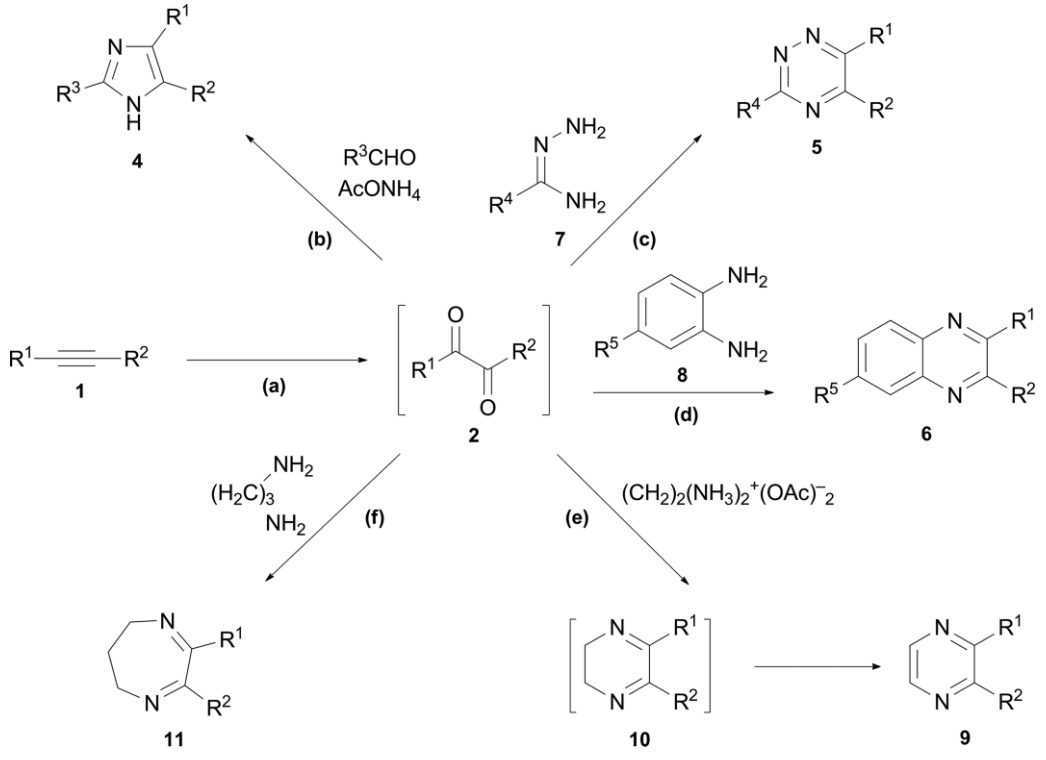


Scheme 2. Generation of 3-phenyl-1*H*-isochromen-1-one (**3**).

To summarize sections (*i*) and (*ii*) one should indicate that if the Hashmi method, considered in Introduction, of the ($Ph_3PAuCl/AgSbF_6$)-catalyzed oxidation of alkynes is useful for terminal alkynes, but unsuccessful for internal alkynes, our approach utilizing the Gagosz catalyst ($Ph_3PAuNTf_2$) is, on the contrary, useful for internal alkynes but not for the terminal species. However, altogether these two gold-involving methods comprise a unified approach to the oxidation of both internal- and terminal alkynes. Application of these two approaches to the oxidation of internal- or terminal alkynes clearly illustrates how seemingly small modifications of the catalytic system (usage of $Ph_3PAuNTf_2/H^+$ instead of in situ generated Ph_3PAu^+ species) and the nature of nucleophilic oxygenation[26] agent (replacement of quinoline- or Cl_2-pyridine oxides with more nucleophilic α-picoline oxide) lead to remarkable consequences and allow the selective syntheses of different type 1,2-dicarbonyl compounds.

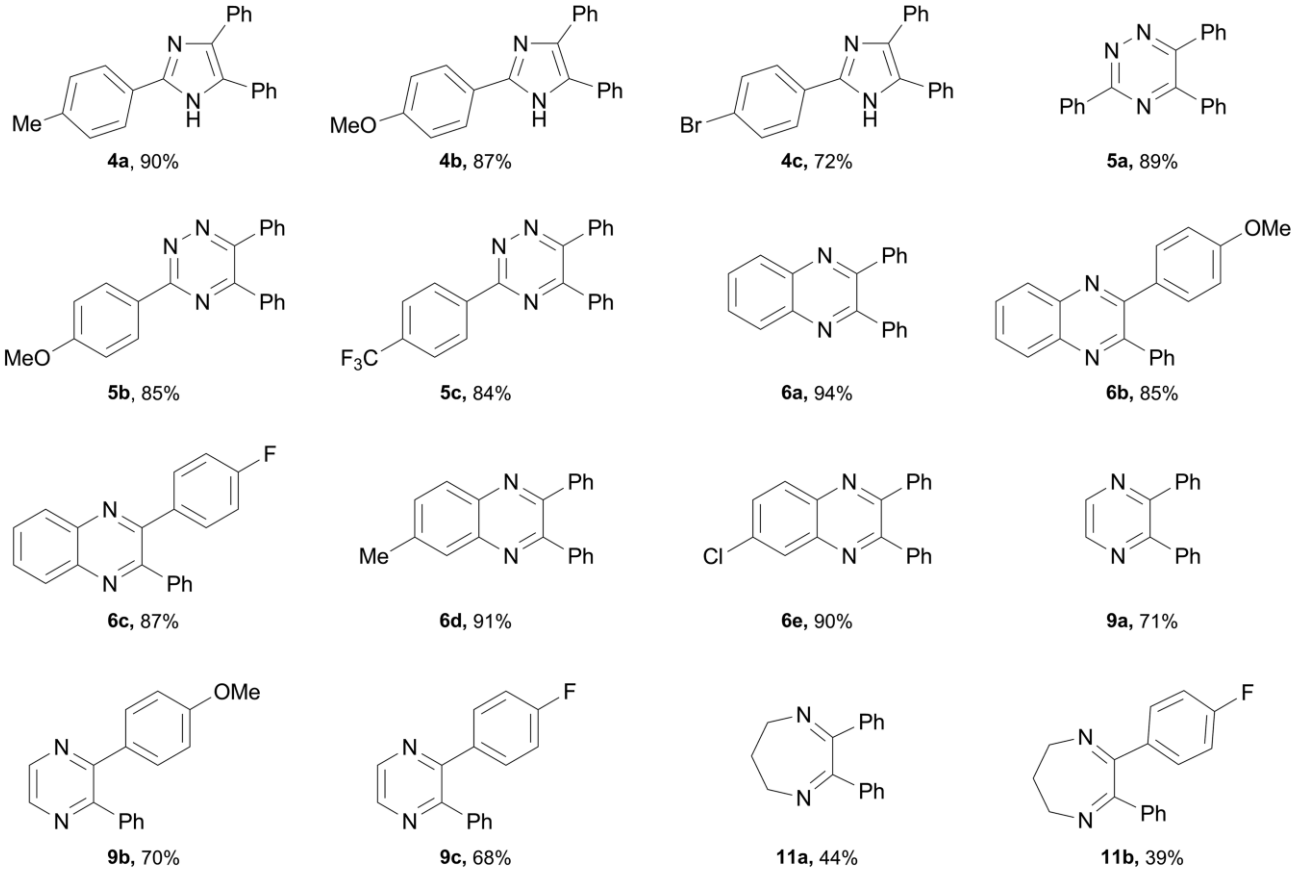
(*iv*) Application of the Gold-catalyzed Diketonization for One-pot Heterocycle Synthesis. With the Au-catalyzed protocol for oxidation of internal akynes at hand, we aimed to develop a one-pot methodology toward various medicinally important azaheterocycles (such as imidazole,[27] quinoxaline,[28] 1,2,4-triazine,[29] pyrazine,[30] and 1,4-diazepine[31]). To this end, 1,2-diaryl-1,2-ethandiones **2** (obtained by diketonization of internal alkynes **1**) were not isolated and further reacted with various mono- and bis-nucleophiles to give these heterocyclic cores (Scheme 3).

The one-pot synthesis of imidazoles **4a –c** was carried out in a sequential way by diketonization of diarylacetylenes **1** under the optimized conditions followed by the addition of an aldehyde (1.2 equiv) with an excess amount of $AcONH_4$ while increasing the reaction temperature in the second step. Thus, 2,4,5-triaryl-1*H*-imidazoles **4a–c** were obtained in good yields (Table 3). A similar one-pot approach was applied to the synthe-



Scheme 3. One-pot Synthesis of (5-to-7)-Membered Azaheterocycles. All reactions were carried out on a 0.25 mmol scale (2 mL of PhCl as solvent). Reaction conditions: (a) α-picoline *N*-oxide (2.5 equiv.), TfOH (2 equiv.), $Ph_3PAuNTf_2$ (5 mol-%), 50 °C, 6 h; (b) R^3CHO (1.2 equiv), $AcONH_4$ (5 equiv.), 120 °C, 24 h; (c) **7** (1.1 equiv.), 110 °C, 18 h; (d) **8** (1.1 equiv), 90 °C, 10 h; (e) ethylenediamine diacetate (1.5 equiv.), α-picoline *N*-oxide (1.5 equiv), 110 °C, 24 h; (f) $NH_2(CH_2)_3NH_2$ (1.5 equiv.), 110 °C, 24 h.

Table 3. The scope of the one-pot azaheterocycle synthesis developed in this work.



sis of 3,5,6- triaryl-1,2,4-triazines **5a**–**c** and 2,3-diarylquinoxalines **6a**–**e** starting from amidrazones **7** and *o*-phenylenediamines **8**, respectively. 2,3-Diarylpyrazines **9a**–**c** were obtained analogously starting from ethylenediamine diacetate, but yields were lower (68–71 %). In this case, an additional 1.5 equiv. of α-picoline *N*-oxide was required to oxidize intermediate 5,6-dihydropyrazines **10**. For preparation of 7-membered azaheterocycles the method proved to be less efficient and 2,3-diaryl-6,7-dihydro-5*H*-1,4-diazepines **11a**–**b** were obtained in only moderate yields (39–44 %). Overall, the above examples demonstrated the applicability of this tandem one-pot route to the synthesis of a broad variety of useful azaheterocycles.

Conclusions

We have developed a facile gold-catalyzed method for the transformation of internal aryl- and heteroaryl-substituted alkynes into the respective benzil (1,2-diaryl-1,2-ethandione) derivatives. The protocol carries a number of advantages over the previously described methods of the diketonization due to significantly milder reaction conditions, higher product yields, and a good substituent tolerance.

We also found that our oxidation method can be applied for syntheses of heteroaromatic benzils. The strongest point of our synthetic scheme is its ability to construct a wide range of important five-, six-, and seven-membered azaheterocyclic motifs from broadly available starting materials and, consequently, the method can be useful for combinatorial medicinal chemistry.

Experimental Section

Materials and methods

NMR spectra were recorded at ambient temperature with a Bruker Avance III 400 instrument at 400.13 MHz (^{1}H NMR), 376.50 MHz (^{19}F), and 100.61 MHz (^{13}C NMR) in $CDCl_3$ or [D_6]DMSO. Chemical shifts (δ) are given in ppm relative to resonances of solvents (^{1}H: δ = 7.26 for residual $CHCl_3$ peak, δ = 2.50 for residual DMSO peak; ^{13}C: δ = 77.2 for $CDCl_3$, δ = 39.5 for [D_6]DMSO). Mass-spectra were recorded on Bruker MicroTOF (ESI) and Bruker maXis HRMS-ESI-QTOF instruments. Chromatographic separation was carried out on Macherey–Nagel silica gel 60 M (0.04–0.063 mm). Analytical TLC was performed on unmodified Merck ready-to-use plates (TLC silica gel 60 F254); detection was achieved with a UV lamp. Melting points were measured with Stuart smp30 apparatus. $Ph_3PAuNTf_2$ was synthesized accordingly to our previously published protocol.[20] Amidrazones **7** were prepared by the literature procedure.[32] The solvents, diphenylacetylene, and other reagents were purchased from commercial vendors and were used as received. Internal alkynes **2** were prepared by the Sonogashira coupling between aryl alkynes and aryl halides. Details of the syntheses and characterization of compounds **2** is provided in the SI.

General Procedure A. Preparation of Benzil Derivatives 2: A solution of trifluoromethanesulfonic acid (150 mg, 1.0 mmol, 2.0 equiv) in chlorobenzene (1.0 mL) was added to reaction flask containing a solution of internal alkyne **1** (500 μmol, 1.0 equiv), α-picoline *N*-oxide (136.4 mg, 1.25 mmol, 2.5 equiv) and $Ph_3PAuNTf_2$ (18.5 mg, 25 μmol, 5 mol-%) in chlorobenzene (1.0 mL). The resulting mixture was stirred at 50 °C for 6 h. After cooling, the solvent was then removed in vacuo. The residue was purified by silica gel chromatography eluting with EtOAc/hexane (gradient from 1:12 to 1:4) to afford target benzils **2**.

1-(4-Fluorophenyl)-2-phenylethane-1,2-dione (**2a**):[33] yellow crystals (107 mg, 94 %); mp 62.5–63.5 °C (hexane/ethyl acetate); R_f 0.65 (hexane/ethyl acetate, 8:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03–8.00 (m, 2H, Ar), 7.97 (d, *J* = 7.2 Hz, 2H, Ar), 7.65 (t, *J* = 7.4 Hz, 1H, Ar), 7.51 (t, *J* = 7.8 Hz, 2H, Ar), 7.18 (t, *J* = 8.6 Hz, 2H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.2, 192.8, 166.7 (d, J_F = 258.2 Hz, CF), 135.1, 133.0, 132.8 (d, J_F = 9.8 Hz, CH), 130.0, 129.6 (d, J_F = 2.9 Hz, C), 129.2, 116.5 (d, J_F = 22.2 Hz, CH); ^{19}F NMR (376.5 MHz, $CDCl_3$) δ –101.2; HRMS (ESI): *m/z* $[M + Na]^+$ calcd. for $C_{14}H_9FNaO_2^+$: 251.0479, found 251.0471.

1,2-Diphenylethane-1,2-dione (**2b**):[33] yellow crystals (101 mg, 96 %); mp 94.5–95.5 °C (hexane/ethyl acetate); R_f 0.30 (hexane/ethyl acetate, 12:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99–7.97 (m, 4H, Ar), 7.66 (t, *J* = 7.4 Hz, 2H, Ar), 7.51 (t, *J* = 7.8 Hz, 4H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.7, 135.0, 133.2, 130.0, 129.2; HRMS (ESI): *m/z* $[M + Na]^+$ calcd. for $C_{14}H_{10}NaO_2^+$: 233.0573, found 233.0578.

1-(4-Bromophenyl)-2-phenylethane-1,2-dione (**2c**):[33] yellow crystals (134 mg, 93 %); mp 85.0–86.5 °C (hexane/ethyl acetate); R_f 0.60 (hexane/ethyl acetate, 8:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 7.2 Hz, 2H, Ar), 7.85 (d, *J* = 8.6 Hz, 2H, Ar), 7.69–7.65 (m, 3H, Ar), 7.52 (t, *J* = 7.8 Hz, 2H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.0, 193.4, 135.2, 132.9, 132.6, 131.9, 131.4, 130.6, 130.1, 129.2; HRMS (ESI): *m/z* $[M + Na]^+$ calcd. for $C_{14}H_9BrNaO_2^+$: 310.9678, found 310.9682.

1-Phenyl-2-(4-tolyl)ethane-1,2-dione (**2d**):[34] yellow crystals (110 mg, 98 %); mp 30.0–30.5 °C (hexane/ethyl acetate); R_f 0.65 (hexane/ethyl acetate, 8:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.3 Hz, 2H, Ar), 7.87 (d, *J* = 8.2 Hz, 2H, Ar), 7.64 (t, *J* = 7.4 Hz, 1H, Ar), 7.50 (t, *J* = 7.7 Hz, 2H, Ar), 7.31 (d, *J* = 8.0 Hz, 2H, Ar), 2.43 (s, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.9, 194.4, 146.3, 134.9, 133.2, 130.7, 130.1, 130.0, 129.9, 129.1, 22.0; HRMS (ESI): *m/z* $[M + Na]^+$ calcd. for $C_{15}H_{12}NaO_2^+$: 247.0730, found 247.0742.

1-(4-Methoxyphenyl)-2-phenylethane-1,2-dione (**2e**):[34] yellow crystals (117 mg, 97 %); mp 62.0–63.0 °C (hexane/ethyl acetate); R_f 0.35 (hexane/ethyl acetate, 4:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98–7.93 (m, 4H, Ar), 7.64 (t, *J* = 7.4 Hz, 1H, Ar), 7.50 (t, *J* = 7.7 Hz, 2H, Ar), 6.97 (d, *J* = 8.9 Hz, 2H, Ar), 3.88 (s, 3H, OMe); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.0, 193.3, 165.1, 134.8, 133.3, 132.5, 130.0, 129.1, 126.2, 114.5, 55.8; HRMS (ESI): *m/z* $[M + Na]^+$ calcd. for $C_{15}H_{12}NaO_3^+$: 263.0679, found 263.0676.

1-(3-Methoxyphenyl)-2-phenylethane-1,2-dione (**2f**):[34] yellow crystals (100 mg, 83 %); mp 90.5–91.5 °C (hexane/ethyl acetate); R_f 0.45 (hexane/ethyl acetate, 8:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.9 Hz, 2H, Ar), 7.66 (t, *J* = 7.4 Hz, 1H, Ar), 7.55–7.47 (m, 4H, Ar), 7.39 (t, *J* = 7.9 Hz, 1H, Ar), 7.20 (d, *J* = 10.7 Hz, 1H, Ar), 3.86 (s, 3H, OMe); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.6 (×2), 160.2, 135.0, 134.4, 133.2, 130.2, 130.0, 129.2, 123.4, 122.0, 113.0, 55.7; HRMS (ESI): *m/z* $[M + Na]^+$ calcd. for $C_{15}H_{12}NaO_3^+$: 263.0679, found 263.0691.

1-(2-Methoxyphenyl)-2-phenylethane-1,2-dione (**2g**):[34] yellow crystals (94.9 mg, 79 %), mp 70.5–71.5 °C (hexane/ethyl acetate); R_f 0.30 (hexane/ethyl acetate, 4:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 9.4 Hz, 1H, Ar), 7.92 (d, *J* = 7.2 Hz, 2H, Ar), 7.63–7.57 (m, 2H, Ar), 7.49 (t, *J* = 7.6 Hz, 2H, Ar), 7.12 (t, *J* = 7.5 Hz, 1H, Ar), 6.93 (d, *J* = 8.4 Hz, 1H, Ar), 3.55 (s, 3H, OMe); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.8, 193.6, 160.5, 136.6, 133.9, 133.1, 130.6, 129.4, 128.8, 124.0, 121.7, 112.5, 55.8; HRMS (ESI): *m/z* $[M + Na]^+$ calcd. for $C_{15}H_{12}NaO_3^+$: 263.0679, found 263.0673.

1-(4-Acetylphenyl)-2-phenylethane-1,2-dione (**2h**):[35] yellow crystals (102 mg, 81 %); mp 77.0–78.0 °C (hexane/ethyl acetate); R_f 0.30 (hexane/ethyl acetate, 4:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 4H, Ar), 7.97 (d, *J* = 7.2 Hz, 2H, Ar), 7.68 (t, *J* = 7.5 Hz, 1H, Ar), 7.53 (t, *J* = 7.8 Hz, 2H, Ar), 2.65 (s, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.3, 193.9, 193.7, 141.5, 136.1, 135.3, 132.9, 130.2, 130.1, 129.3, 128.8, 27.1; HRMS (ESI): *m/z* $[M + Na]^+$ calcd. for $C_{16}H_{12}NaO_3^+$: 275.0679, found 275.0677.

4-(2-Oxo-2-phenylacetyl)benzonitrile (**2i**):[34] yellow crystals (87.0 mg, 74 %); mp 108.0–109.0 °C (hexane/ethyl acetate); R_f 0.40 (hexane/ethyl acetate, 4:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 8.5 Hz, 2H, Ar), 7.97 (d, *J* = 7.2 Hz, 2H, Ar), 7.81 (d, *J* = 8.5 Hz, 2H, Ar), 7.70 (t, *J* = 7.5 Hz, 1H, Ar), 7.54 (t, *J* = 7.8 Hz, 2H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.1, 192.5, 136.0, 135.5, 132.9, 132.6, 130.3, 130.2, 129.3, 118.0, 117.7; HRMS (ESI): *m/z* $[M + Na]^+$ calcd. for $C_{15}H_9NNaO_2^+$: 258.0525, found 258.0516.

1-(4-Nitrophenyl)-2-phenylethane-1,2-dione (**2j**):[34] yellow crystals (56.2 mg, 44 %); mp 138.5–139.5 °C (hexane/ethyl acetate); R_f 0.40 (hexane/ethyl acetate, 4:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 8.8 Hz, 2H, Ar), 8.17 (d, *J* = 8.8 Hz, 2H, Ar), 7.99 (d, *J* = 7.2 Hz, 2H, Ar), 7.71 (t, *J* = 7.5 Hz, 1H, Ar), 7.55 (t, *J* = 7.8 Hz, 2H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.0, 192.2, 151.3, 137.5, 135.6, 132.5, 131.1, 130.2, 129.4, 124.3; HRMS (ESI): *m/z* $[M + H]^+$ calcd. for $C_{14}H_{10}NO_4^+$: 256.0604, found 256.0603.

4-(2-(4-Methoxyphenyl)-2-oxoacetyl)benzonitrile (**2k**):[36] yellow crystals (99.5 mg, 75 %); mp 134.5–136.0 °C (hexane/ethyl acetate); R_f 0.50 (hexane/ethyl acetate, 2:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 8.4 Hz, 2H, Ar), 7.95 (d, *J* = 8.9 Hz, 2H, Ar), 7.80 (d, *J* = 8.4 Hz, 2H, Ar), 7.00 (d, *J* = 8.9 Hz, 2H, Ar), 3.90 (s, 3H, OMe); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.8, 191.6, 165.6, 136.3, 132.8, 132.7, 130.4, 125.7, 117.9, 117.8, 114.7, 55.9; HRMS (ESI): *m/z* $[M + Na]^+$ calcd. for $C_{16}H_{11}NNaO_3^+$: 288.0631, found 288.0637.

1-Phenyl-2-(thiophen-2-yl)ethane-1,2-dione (**2l**):[37] brown crystals (86.5 mg, 80 %), mp 61.5–62.5 °C (hexane/ethyl acetate); R_f 0.30 (hexane/ethyl acetate, 8:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 7.3 Hz, 2H, Ar), 7.83–7.79 (m, 2H, Ar), 7.65 (t, *J* = 7.4 Hz, 1H, Ar), 7.50 (t, *J* = 7.8 Hz, 2H, Ar), 7.18–7.16 (m, 1H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.2, 185.7, 139.9, 137.0, 136.8, 135.0, 132.7, 130.3, 129.0, 128.9; HRMS (ESI): *m/z* $[M + Na]^+$ calcd. for $C_{12}H_8NaO_2S^+$: 239.0137, found 239.0142.

1-Phenyl-2-(pyridin-3-yl)ethane-1,2-dione (**2m**):[37] yellow crystals (59.1 mg, 56 %); mp 48.0–49.5 °C (hexane/ethyl acetate); R_f 0.30 (hexane/ethyl acetate, 2:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.16 (s, 1H, Ar), 8.86 (d, *J* = 6.0 Hz, 1H, Ar), 8.29 (d, *J* = 8.0 Hz, 1H, Ar), 7.99 (d, *J* = 7.2 Hz, 2H, Ar), 7.68 (t, *J* = 7.4 Hz, 1H, Ar), 7.53 (t, *J* = 7.8 Hz, 2H, Ar), 7.45–7.49 (m, 1H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.0, 192.9, 155.0, 151.5, 137.0, 135.4, 132.6, 130.2, 129.3, 128.8, 124.0; HRMS (ESI): *m/z* $[M + H]^+$ calcd. for $C_{13}H_{10}NO_2^+$: 212.0706, found 212.0697.

1-Phenyl-2-(pyridin-2-yl)ethane-1,2-dione (**2n**):[37] yellow crystals (55.9 mg, 53 %); mp 72.0–73.5 °C (hexane/ethyl acetate); R_f 0.40 (hexane/ethyl acetate, 2:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (d, *J* = 4.7 Hz, 1H, Ar), 8.20 (d, *J* = 7.9 Hz, 1H, Ar), 7.96–7.91 (m, 3H, Ar), 7.63 (t, *J* = 7.5 Hz, 1H, Ar), 7.53–7.48 (m, 3H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.2, 195.2, 151.8, 150.0, 137.4, 134.7, 133.3, 129.7, 129.0,

128.2, 123.3; HRMS (ESI): *m/z* [M + H]$^+$ calcd. for $C_{13}H_{10}NO_2^+$: 212.0706, found 212.0705.

1-Phenyl-2-(quinolin-3-yl)ethane-1,2-dione (**2o**):[36] yellow crystals (99.2 mg, 76 %); mp 127.0–128.0 °C (hexane/ethyl acetate); R_f 0.45 (hexane/ethyl acetate, 4:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.48 (d, J = 2.2 Hz, 1H, Ar), 8.72 (d, J = 1.5 Hz, 1H, Ar), 8.17 (d, J = 7.4 Hz, 1H, Ar), 8.05–8.03 (m, 2H, Ar), 7.91–7.85 (m, 2H, Ar), 7.68 (t, J = 7.4 Hz, 1H, Ar), 7.62 (t, J = 7.5 Hz, 1H, Ar), 7.53 (t, J = 7.8 Hz, 2H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.2, 192.9, 150.5, 149.3, 140.3, 135.3, 133.1, 132.8, 130.2, 129.82, 129.78. 129.3, 128.0, 126.7, 125.5; HRMS (ESI): *m/z* [M + H]$^+$ calcd. for $C_{17}H_{12}NO_2^+$: 262.0863, found 262.0869.

3-Phenyl-1*H*-isochromen-1-one (**3**)[25] was obtained from methyl 2-(phenylethynyl) benzoate (**1n**) according to **General Procedure A** as colorless crystals (106 mg, 95 %); mp 88.0–89.0 °C (hexane/ethyl acetate); R_f 0.45 (hexane/ethyl acetate, 4:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, J = 8.2 Hz, 1H, Ar), 7.85 (d, J = 6.5 Hz, 2H, Ar), 7.69 (t, J = 8.1 Hz, 1H, Ar), 7.48–7.38 (m, 5H, Ar), 6.92 (s, 1H, CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3, 153.7, 137.6, 134.9, 132.0, 130.0, 129.7, 128.9, 128.2, 126.1, 125.3, 120.6, 101.9; HRMS (ESI): *m/z* [M + H]$^+$ calcd. for $C_{15}H_{11}O_2^+$: 223.0754, found 223.0746.

General Procedure B. Preparation of Imidazoles 4: A solution of trifluoromethanesulfonic acid (75.0 mg, 500 µmol, 2.0 equiv) in chlorobenzene (0.5 mL) was added to a flask containing a solution of diphenylacetylene (**1b**) (44.6 mg, 250 µmol, 1.0 equiv), α-picoline *N*-oxide (68.2 mg, 625 µmol, 2.5 equiv) and $Ph_3PAuNTf_2$ (9.24 mg, 12.5 µmol, 5 mol-%) in chlorobenzene (0.5 mL). The resulting mixture was stirred at 50 °C for 6 h. Then a benzaldehyde (300 µmol, 1.2 equiv), ammonium acetate (96.4 mg, 125 µmol, 5.0 equiv) and chlorobenzene (1.0 mL) were added. The mixture was stirred at 120 °C for 24 h. After cooling, the solvent was then removed in vacuo. The residue was purified by silica gel chromatography eluted by EtOAc/hexane (1:4) to afford target imidazoles **4**.

4,5-Diphenyl-2-(4-tolyl)-1*H*-imidazole (**4a**):[38] colorless crystals (69.8 mg, 90 %); mp 231.5–232.0 °C (hexane/ethyl acetate); R_f 0.60 (hexane/ethyl acetate, 2:1); ^{1}H NMR (400 MHz, [D$_6$]DMSO) δ 12.59 (br. s, 1H, NH), 7.98 (d, J = 8.1 Hz, 2H, Ar), 7.54–7.52 (m, 4H, Ar), 7.37–7.28 (m, 8H, Ar), 2.35 (s, 3H, Me); ^{13}C NMR (100 MHz, [D$_6$]DMSO) δ 145.6, 137.6, 129.2, 128.3, 127.7, 125.1, 20.9; HRMS (ESI): *m/z* [M + H]$^+$ calcd. for $C_{22}H_{19}N_2^+$: 311.1543, found 311.1549.

2-(4-Methoxyphenyl)-4,5-diphenyl-1*H*-imidazole (**4b**):[38] colorless crystals (71.0 mg, 87 %); mp 233.0–234.0 °C (hexane/ethyl acetate); R_f 0.35 (hexane/ethyl acetate, 2:1); ^{1}H NMR (400 MHz, [D$_6$]DMSO) δ 12.51 (br. s, 1H, NH), 8.02 (d, J = 8.8 Hz, 2H, Ar), 7.53–7.51 (m, 4H, Ar), 7.36–7.29 (m, 6H, Ar), 7.04 (d, J = 8.8 Hz, 2H, Ar), 3.82 (s, 3H, OMe); ^{13}C NMR (100 MHz, [D$_6$]DMSO) δ 159.4, 145.6, 128.4, 127.7, 126.7, 123.1, 114.1, 55.2; HRMS (ESI): *m/z* [M + H]$^+$ calcd. for $C_{22}H_{19}N_2O^+$: 327.1492, found 327.1478.

2-(4-Bromophenyl)-4,5-diphenyl-1*H*-imidazole (**4c**):[38] colorless crystals (67.5 mg, 72 %), mp 243.0–244.5 °C (hexane/ethyl acetate); R_f 0.60 (hexane/ethyl acetate, 2:1); ^{1}H NMR (400 MHz, [D$_6$]DMSO) δ 12.77 (br. s, 1H, NH), 8.04 (d, J = 8.6 Hz, 2H, Ar), 7.68 (d, J = 8.6 Hz, 2H, Ar), 7.55 (d, J = 7.2 Hz, 2H, Ar), 7.50 (d, J = 7.1 Hz, 2H, Ar), 7.44 (t, J = 7.4 Hz, 2H, Ar), 7.38 (t, J = 7.2 Hz, 1H, Ar), 7.30 (t, J = 7.4 Hz, 2H, Ar), 7.23 (t, J = 7.3 Hz, 1H, Ar); ^{13}C NMR (100 MHz, [D$_6$]DMSO) δ 144.4, 137.3, 135.0, 131.6, 130.9, 129.5, 128.6 (×2), 128.4, 128.2, 127.9, 127.1, 127.0, 126.6, 121.4; HRMS (ESI): *m/z* [M + H]$^+$ calcd. for $C_{21}H_{16}BrN_2^+$: 375.0491, found 375.0496.

General Procedure C. Preparation of Triazines 5: A solution of trifluoromethanesulfonic acid (75.0 mg, 500 µmol, 2.0 equiv) in chlorobenzene (0.5 mL) was added to a flask containing a solution of diphenylacetylene (**1b**) (44.6 mg, 250 µmol, 1.0 equiv), α-picoline *N*-oxide (68.2 mg, 625 µmol, 2.5 equiv) and $Ph_3PAuNTf_2$ (9.24 mg, 12.5 µmol, 5 mol-%) in chlorobenzene (0.5 mL). The resulting mixture was stirred at 50 °C for 6 h. Then amidrazone **7** (275 µmol, 1.1 equiv) and chlorobenzene (1.0 mL) were added. The resulted mixture was stirred at 110 °C for 18 h. Upon cooling to r.t., the solvent was removed in vacuo. The residue was purified by silica gel chromatography eluted by EtOAc/hexane (gradient from 1:12 to 1:4) to afford target triazines **5**.

3,5,6-Triphenyl-1,2,4-triazine (**5a**):[39] yellow crystals (68.8 mg, 89 %); mp 144.0–145.0 °C (hexane/ethyl acetate); R_f 0.50 (hexane/ethyl acetate, 4:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69–8.67 (m, 2H, Ar), 7.69 (d, J = 7.2 Hz, 2H, Ar), 7.63 (d, J = 6.6 Hz, 2H, Ar), 7.58–7.56 (m, 3H, Ar), 7.48–7.36 (m, 6H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 155.7, 155.6, 136.1, 135.7, 135.0, 131.7, 130.8, 130.0, 129.7, 129.6, 129.0, 128.7 (×2), 128.5; HRMS (ESI): *m/z* [M + H]$^+$ calcd. for $C_{21}H_{16}N_3^+$: 310.1339, found 310.1339.

3-(4-Methoxyphenyl)-5,6-diphenyl-1,2,4-triazine (**5b**): yellow crystals (72.1 mg, 85 %); mp 161.0–162.0 °C (hexane/ethyl acetate); R_f 0.40 (hexane/ethyl acetate, 4:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (d, J = 9.0 Hz, 2H, Ar), 7.67 (d, J = 7.1 Hz, 2H, Ar), 7.61 (d, J = 6.4 Hz, 2H, Ar), 7.44–7.34 (m, 6H, Ar), 7.07 (d, J = 9.0 Hz, 2H, Ar), 3.90 (s, 3H, OMe); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.7, 161.2, 155.5, 155.0, 136.2, 135.8, 130.7, 130.2, 129.9, 129.5 (×2), 128.6 (×2), 127.4, 114.3, 55.5; HRMS (ESI): *m/z* [M + H]$^+$ calcd. for $C_{22}H_{18}N_3O^+$: 340.1444, found 340.1469.

5,6-Diphenyl-3-(4-(trifluoromethyl)phenyl)-1,2,4-triazine (**5c**): yellow crystals (79.2 mg, 84 %); mp 151.0–152.0 °C (hexane/ethyl acetate); R_f 0.50 (hexane/ethyl acetate, 4:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (d, J = 8.2 Hz, 2H, Ar), 7.83 (d, J = 8.3 Hz, 2H, Ar), 7.69 (d, J = 7.3 Hz, 2H, Ar), 7.64 (d, J = 6.8 Hz, 2H, Ar), 7.48–7.38 (m, 6H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.3, 156.3, 155.9, 138.3, 135.7, 135.4, 133.2 (q, J_F = 32.5 Hz, C), 130.0 (×2), 129.6, 128.8 (×2), 128.7, 125.9 (q, J_F = 3.7 Hz, CH), 125.5, 122.8; ^{19}F NMR (376.5 MHz, $CDCl_3$) δ –62.8; HRMS (ESI): *m/z* [M + H]$^+$ calcd. for $C_{22}H_{15}F_3N_3^+$: 378.1213, found 378.1223.

General Procedure D. Preparation of Quinoxalines 6: A solution of trifluoromethanesulfonic acid (75.0 mg, 500 µmol, 2.0 equiv) in chlorobenzene (0.5 mL) was added to a flask containing a solution of internal alkyne **1** (250 µmol, 1.0 equiv), α-picoline *N*-oxide (68.2 mg, 625 µmol, 2.5 equiv) and $Ph_3PAuNTf_2$ (9.24 mg, 12.5 mmol, 5 mol-%) in chlorobenzene (0.5 mL). The resulting mixture was stirred at 50 °C for 6 h. Then *o*-phenylenediamine **8** (275 µmol, 1.1 equiv) and chlorobenzene (1.0 mL) were added. The mixture was stirred at 90 °C for 10 h. Upon cooling to r.t., the solvent was removed in vacuo. The residue was purified by silica gel chromatography eluting with EtOAc/hexane (gradient from 1:12 to 1:8) to afford target quinoxalines **6**.

2,3-Diphenylquinoxaline (**6a**):[40] colorless crystals (66.4 mg, 94 %); mp 129.5–130.5 °C (hexane/ethyl acetate); R_f 0.30 (hexane/ethyl acetate, 8:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20–8.18 (m, 2H, Ar), 7.79–7.76 (m, 2H, Ar), 7.54–7.52 (m, 4H, Ar), 7.39–7.32 (m, 6H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.6, 141.4, 139.3, 130.1, 130.0, 129.4, 128.9, 128.4; HRMS (ESI): *m/z* [M + H]$^+$ calcd. for $C_{20}H_{15}N_2^+$: 283.1230, found 283.1231.

2-(4-Methoxyphenyl)-3-phenylquinoxaline (**6b**):[40] yellow crystals (66.4 mg, 85 %); mp 105.5–106.5 °C (hexane/ethyl acetate); R_f 0.45 (hexane/ethyl acetate, 4:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17–8.14 (m, 2H, Ar), 7.77–7.72 (m, 2H, Ar), 7.55–7.53 (m, 2H, Ar), 7.48 (d, J = 8.8 Hz, 2H, Ar), 7.37–7.36 (m, 3H, Ar), 6.86 (d, J = 8.8 Hz, 2H, Ar), 3.82 (s, 3H, OMe); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.4, 153.6,

153.2, 141.5, 141.2, 139.6, 131.6, 131.5, 130.0, 129.9, 129.7, 129.3, 129.2, 128.9, 128.5, 113.9, 55.4; HRMS (ESI): *m/z* [M + H]$^+$ calcd. for $C_{21}H_{17}N_2O^+$: 313.1335, found 313.1343.

2-(4-Fluorophenyl)-3-phenylquinoxaline (**6c**):[40] yellow crystals (65.3 mg, 87 %); mp 109.5–111.0 °C (hexane/ethyl acetate); R_f 0.30 (hexane/ethyl acetate, 8:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19–8.15 (m, 2H, Ar), 7.80–7.76 (m, 2H, Ar), 7.54–7.50 (m, 4H, Ar), 7.41–7.34 (m, 3H, Ar), 7.03 (t, J = 8.7 Hz, 2H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3 (d, J_F = 249.3 Hz, CF), 153.5, 152.5, 141.4, 141.3, 139.1, 135.3 (d, J_F = 3.4 Hz, C), 132.0 (d, J_F = 8.4 Hz, CH), 130.2 (×2), 129.9, 129.4, 129.3, 129.1, 128.5, 115.6 (d, J_F = 21.7 Hz, CH); ^{19}F NMR (376.5 MHz, $CDCl_3$) δ –112.3; HRMS (ESI): *m/z* [M + H]$^+$ calcd. for $C_{20}H_{14}FN_2^+$: 301.1136, found 301.1129.

6-Methyl-2,3-diphenylquinoxaline (**6d**):[36] yellow crystals (67.4 mg, 91 %); mp 116.5–117.5 °C (hexane/ethyl acetate); R_f 0.30 (hexane/ethyl acetate, 8:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 8.5 Hz, 1H, Ar), 7.96 (s, 1H, Ar), 7.60 (dd, J = 8.6, 1.7 Hz, 1H, Ar), 7.53–7.51 (m, 4H, Ar), 7.37–7.30 (m, 6H, Ar), 2.62 (s, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.4, 152.7, 141.4, 140.6, 139.8, 139.4 (×2), 132.4, 130.0 (×2), 128.8 (×2), 128.7, 128.3 (×2), 128.1, 22.0; HRMS (ESI): *m/z* [M + H]$^+$ calcd. for $C_{21}H_{17}N_2^+$: 297.1386, found 297.1377.

6-Chloro-2,3-diphenylquinoxaline (**6e**):[41] yellow crystals (71.2 mg, 90 %), mp 120.0–121.0 °C (hexane/ethyl acetate); R_f 0.40 (hexane/ethyl acetate, 8:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, J = 2.2 Hz, 1H, Ar), 8.11 (d, J = 8.9 Hz, 1H, Ar), 7.70 (dd, J = 8.9, 2.3 Hz, 1H, Ar), 7.52 (d, J = 7.1 Hz, 4H, Ar), 7.40–7.32 (m, 6H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.4, 153.7, 141.6, 139.8, 138.9, 138.8, 135.8, 131.0, 130.5, 130.0, 129.9, 129.2, 129.1, 128.4 (×2), 128.2; HRMS (ESI): *m/z* [M + H]$^+$ calcd. for $C_{20}H_{14}ClN_2^+$: 317.0840, found 317.0843.

General Procedure E. Preparation of Pyrazines 9: A solution of trifluoromethanesulfonic acid (75.0 mg, 500 µmol, 2.0 equiv) in chlorobenzene (0.5 mL) was added to a flask containing a solution of internal alkyne **1** (250 µmol, 1.0 equiv), α-picoline *N*-oxide (109 mg, 1.0 mmol, 4.0 equiv) and $Ph_3PAuNTf_2$ (9.24 mg, 12.5 µmol, 5 mol-%) in chlorobenzene (0.5 mL). The resulting mixture was stirred at 50 °C for 6 h. Ethylenediamine diacetate (67.6 mg, 375 µmol, 1.5 equiv) and chlorobenzene (1.0 mL) were added. The resulting mixture was stirred at 110 °C for 24 h. Upon cooling to r.t., the solvent was removed in vacuo. The residue was purified by silica gel chromatography eluting with EtOAc/hexane (gradient from 1:8 to 1:4) to afford target pyrazines **9**.

2,3-Diphenylpyrazine (**9a**):[42] orange crystals (41.2 mg, 71 %); mp 116.5–117.5 °C (hexane/ethyl acetate); R_f 0.50 (hexane/ethyl acetate, 2:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (s, 2H, Ar), 7.48–7.44 (m, 4H, Ar), 7.35–7.28 (m, 6H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.0, 142.2, 138.7, 129.8, 128.8, 128.4; HRMS (ESI): *m/z* [M + H]$^+$ calcd. for $C_{16}H_{13}N_2^+$: 233.1073, found 233.1063.

2-(4-Methoxyphenyl)-3-phenylpyrazine (**9b**): orange oil (45.9 mg, 70 %); R_f 0.35 (hexane/ethyl acetate, 2:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (dd, J = 6.4, 2.4 Hz, 2H, Ar), 7.49–7.46 (m, 2H, Ar), 7.41 (d, J = 8.8 Hz, 2H, Ar), 7.33–7.30 (m, 3H, Ar), 6.82 (d, J = 8.8 Hz, 2H, Ar), 3.79 (s, 3H, OMe); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.2, 152.6, 152.5, 142.1, 141.6, 139.0, 131.2, 131.0, 129.6, 128.7, 128.4, 113.8, 55.3; HRMS (ESI): *m/z* [M + H]$^+$ calcd. for $C_{17}H_{15}N_2O^+$: 263.1179, found 263.1174.

2-(4-Fluorophenyl)-3-phenylpyrazine (**9c**): orange oil (42.5 mg, 68 %); R_f 0.45 (hexane/ethyl acetate, 2:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (dd, J = 6.1, 2.4 Hz, 2H, Ar), 7.45–7.42 (m, 4H, Ar), 7.34–7.29 (m, 3H, Ar), 6.99 (t, J = 8.7 Hz, 2H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.1 (d, J_F = 249.1 Hz, CF), 152.8, 151.8, 142.3, 142.2, 138.5, 134.7 (d, J_F = 3.4 Hz, C), 131.7 (d, J_F = 8.4 Hz, CH), 129.7, 128.9, 128.5, 115.5 (d, J_F = 21.7 Hz, CH); ^{19}F NMR (376.5 MHz, $CDCl_3$) δ –112.4; HRMS (ESI): *m/z* [M + H]$^+$ calcd. for $C_{16}H_{12}FN_2^+$: 251.0979, found 251.0984.

General Procedure F. Preparation of Diazepines 11: A solution of trifluoromethanesulfonic acid (75.0 mg, 500 µmol, 2.0 equiv) in chlorobenzene (0.5 mL) was added to a flask containing a solution of internal alkyne **1** (250 µmol, 1.0 equiv), α-picoline *N*-oxide (68.2 mg, 625 mmol, 2.5 equiv) and $Ph_3PAuNTf_2$ (9.24 mg, 12.5 mmol, 5 mol-%) in chlorobenzene (0.5 mL). The resulting mixture was stirred at 50 °C for 6 h. 1,3-Diaminopropane (27.8 mg, 375 µmol, 1.5 equiv) and chlorobenzene (1.0 mL) were added. The mixture was stirred at 110 °C for 24 h. Upon cooling to r.t., the solvent was removed in vacuo. The residue was purified by silica gel chromatography eluting with EtOAc/hexane (gradient from 1:4 to 1:2) to afford target diazepines **11**.

2,3-Diphenyl-6,7-dihydro-5*H*-1,4-diazepine (**11a**):[43] yellow crystals (27.3 mg, 44 %); mp 114.5–116.0 °C (hexane/ethyl acetate); R_f 0.35 (hexane/ethyl acetate, 2:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62–7.60 (m, 4H, Ar), 7.38–7.29 (m, 6H, Ar), 3.54 (br. s, 4H, CH_2), 2.36 (p, J = 6.8 Hz, 2H, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 136.3, 130.6, 128.7, 127.6, 49.1, 32.1; HRMS (ESI): *m/z* [M + H]$^+$ calcd. for $C_{17}H_{17}N_2^+$: 249.1386, found 249.1375.

2-(4-Fluorophenyl)-3-phenyl-6,7-dihydro-5*H*-1,4-diazepine (**11b**):[43] yellow crystals (25.9 mg, 39 %); mp 76.5–78.0 °C (hexane/ethyl acetate); R_f 0.35 (hexane/ethyl acetate, 2:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62–7.58 (m, 4H, Ar), 7.39–7.30 (m, 3H, Ar), 6.99 (t, J = 8.6 Hz, 2H, Ar), 3.52 (br. s, 4H, CH_2), 2.35 (p, J = 6.7 Hz, 2H, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 165.6, 164.2 (d, J_F = 251.2 Hz, CF), 136.2, 132.5 (d, J_F = 3.2 Hz, C), 130.8, 129.7 (d, J_F = 8.7 Hz, CH), 128.8, 127.5, 115.8 (d, J_F = 21.9 Hz, CF), 49.1, 49.0, 32.1; ^{19}F NMR (376.5 MHz, $CDCl_3$) δ –109.5; HRMS (ESI): *m/z* [M + H]$^+$ calcd. for $C_{17}H_{16}FN_2^+$: 267.1292, found 267.1288.

For compounds **2a–n**, **3**, **4a–c**, **5a**, **6a–e**, **9a**, and **11a,b** the ^{1}H, ^{13}C spectra and melting points are identical to those reported in the literature.

Acknowledgments

AYuD thanks the Russian Science Foundation for support of these studies (grant 18-73-00026). We are much obliged to the Center for Magnetic Resonance, Center for Chemical Analysis and Material Research (both belonging to Saint Petersburg State University) for physicochemical measurements.

Keywords: Homogeneous catalysis · Heterocycles · Oxidation · Gold · Synthetic methods

[1] a) L. Z. Yuan, A. Hamze, M. Alami, O. Provot, *Synthesis* **2017**, *49*, 504–525; b) P. Zhou, Y. Li, Y. Fan, Z. Wang, R. Chopra, A. Olland, Y. Hu, R. L. Magolda, M. Pangalos, P. H. Reinhart, *Bioorg. Med. Chem. Lett.* **2010**, *20*, 2326–2329; c) R. Ramajayam, R. Giridhar, M. R. Yadav, R. Balaraman, H. Djaballah, D. Shum, C. Radu, *Eur. J. Med. Chem.* **2008**, *43*, 2004–2010.

[2] a) L. De Luca, A. Mezzetti, *Angew. Chem. Int. Ed.* **2017**, *56*, 11949–11953; *Angew. Chem.* **2017**, *129*, 12111; b) T. Touge, T. Hakamata, H. Nara, T. Kobayashi, N. Sayo, T. Saito, Y. Kayaki, T. Ikariya, *J. Am. Chem. Soc.* **2011**, *133*, 14960–14963.

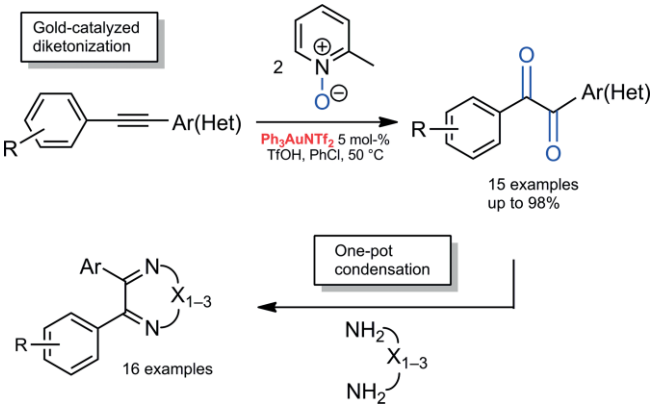
[3] L. Guo, H. Gao, Q. Guan, H. Hu, J. Deng, J. Liu, F. Liu, Q. Wu, *Organometallics* **2012**, *31*, 6054–6062.

[4] a) F. Ullah, M. K. Kindermann, P. G. Jones, J. Heinicke, *Organometallics* **2009**, *28*, 2441–2449; b) A. P. Dove, H. Li, R. C. Pratt, B. G. G. Lohmeijer, D. A. Culkin, R. M. Waymouth, J. L. Hedrick, *Chem. Commun.* **2006**, *0*, 2881–2883.

[5] R. Worayuthakarn, S. Boonya-Udtayan, S. Ruchirawat, N. Thasana, *Eur. J. Org. Chem.* **2014**, *2014*, 2496–2507.
[6] a) L. D. Hicks, J. L. Hyatt, T. Moak, C. C. Edwards, L. Tsurkan, M. Wierdl, A. M. Ferreira, R. M. Wadkins, P. M. Potter, *Bioorg. Med. Chem.* **2007**, *15*, 3801–3817; b) J. L. Hyatt, V. Stacy, R. M. Wadkins, K. J. P. Yoon, M. Wierdl, C. C. Edwards, M. Zeller, A. D. Hunter, M. K. Danks, G. Crundwell, *J. Med. Chem.* **2005**, *48*, 5543–5550.
[7] W. Li, Y. Asada, T. Yoshikawa, *Planta Med.* **1998**, *64*, 746–747.
[8] C. Mousset, A. Giraud, O. Provot, A. Hamze, J. Bignon, J. M. Liu, S. Thoret, J. Dubois, J. D. Brion, M. Alami, *Bioorg. Med. Chem. Lett.* **2008**, *18*, 3266–3271.
[9] S. Ganapaty, G. V. K. Srilakshmi, S. T. Pannakal, H. Rahman, H. Laatsch, R. Brun, *Phytochemistry* **2009**, *70*, 95–99.
[10] a) S. B. Alyabyev, I. P. Beletskaya, *Russ. Chem. Rev.* **2017**, *86*, 689–749; b) R. Dorel, A. M. Echavarren, *Chem. Rev.* **2015**, *115*, 9028–9072; c) Z. Li, C. Brouwer, C. He, *Technology* **2008**, *108*, 3239–3265; d) A. S. K. Hashmi, *Chem. Rev.* **2007**, *107*, 3180–3211; e) A. S. K. Hashmi, G. J. Hutchings, *Angew. Chem. Int. Ed.* **2006**, *45*, 7896–7936; *Angew. Chem.* **2006**, *118*, 8064; f) Y. Li, W. Li, J. Zhang, *Chem. Eur. J.* **2017**, *23*, 467–512; g) R. Quach, D. P. Furkert, M. A. Brimble, *Org. Biomol. Chem.* **2017**, *15*, 3098–3104; h) M. Rudolph, A. S. K. Hashmi, *Chem. Soc. Rev.* **2012**, *41*, 2448–2462.
[11] a) B. Yu, *Acc. Chem. Res.* **2018**, *51*, 507–516; b) A. Fuerstner, *Angew. Chem. Int. Ed.* **2018**, *57*, 4215–4233; *Angew. Chem.* **2018**, *130*, 4289–4308; c) J. Cai, B. Wu, G. Rong, C. Zhang, L. Qui, X. Xu, *Org. Lett.* **2018**, *20*, 2733–2736; d) C. Virumbrales, S. Suarez-Pantiga, M. Solas, M. A. Fernandez-Rodriguez, R. Sanz, *Org. Biomol. Chem.* **2018**, *16*, 2623–2628; e) J. M. Yang, Y. T. Zhao, Z. Q. Li, X. S. Gu, S. F. Zhu, Q. L. Zhou, *ACS Catal.* **2018**, *8*, 7351–7355.
[12] A. Arcadi, *Chem. Rev.* **2008**, *108*, 3266–3325.
[13] D. B. Huple, S. Ghorpade, R. S. Liu, *Adv. Synth. Catal.* **2016**, *358*, 1348–1367.
[14] C. F. Xu, M. Xu, Y. X. Jia, C. Y. Li, *Org. Lett.* **2011**, *13*, 1556–1559.
[15] a) R. K. Henderson, C. Jiménez-González, D. J. C. Constable, S. R. Alston, G. G. A. Inglis, G. Fisher, J. Sherwood, S. P. Binks, A. D. Curzons, *Green Chem.* **2011**, *13*, 854–862; b) K. Alfonsi, J. Colberg, P. J. Dunn, T. Fevig, S. Jennings, T. A. Johnson, H. P. Kleine, C. Knight, M. A. Nagy, D. A. Perry, *Green Chem.* **2008**, *10*, 31–36.
[16] Y. Liu, X. Chen, J. Zhang, Z. Xu, *Synlett* **2013**, *24*, 1371–1376.
[17] S. Shi, T. Wang, W. Yang, M. Rudolph, A. S. K. Hashmi, *Chem. Eur. J.* **2013**, *19*, 6576–6580.
[18] N. Mézailles, L. Ricard, F. Gagosz, *Org. Lett.* **2005**, *7*, 4133–4136.
[19] a) M. Chen, Y. Chen, N. Sun, J. Zhao, Y. Liu, Y. Li, *Angew. Chem. Int. Ed.* **2015**, *54*, 1200–1204; *Angew. Chem.* **2015**, *127*, 1216; b) B. Lu, C. Li, L. Zhang, *J. Am. Chem. Soc.* **2010**, *132*, 14070–14072; c) H. Chen, L. Zhang, *Angew. Chem. Int. Ed.* **2015**, *54*, 11775–11779; *Angew. Chem.* **2015**, *127*, 11941; d) S. Nejrotti, G. P. Cerai, A. Oppedisano, A. Maranzana, E. G. Occhiato, D. Scarpi, A. Deagostino, C. Prandi, *Eur. J. Org. Chem.* **2017**, *2017*, 6228–6238.
[20] V. A. Rassadin, V. P. Boyarskiy, V. Y. Kukushkin, *Org. Lett.* **2015**, *17*, 3502–3505.
[21] A. Albini, *Synthesis* **1993**, *3*, 263–277.
[22] M. Kumar, G. B. Hammond, B. Xu, *Org. Lett.* **2014**, *16*, 3452–3455.
[23] M. Tobiszewski, J. Namieśnik, *Ecotoxicol. Environ. Saf.* **2015**, *120*, 169–173.
[24] a) S.-T. Yuan, Y.-H. Wang, J.-B. Liu, G. Qiu, *Adv. Synth. Catal.* **2017**, *359*, 1981–1989; b) S.-T. Yuan, H. Zhou, L. Zhang, J.-B. Liu, G. Qiu, *Org. Biomol. Chem.* **2017**, *15*, 4867–4874; c) K. Sakthivel, K. Srinivasan, *Eur. J. Org. Chem.* **2013**, *2013*, 3386–3396.
[25] a) E. Marchal, P. Uriac, B. Legouin, L. Toupet, P. van de Weghe, *Tetrahedron* **2007**, *63*, 9979–9990; b) J. Gianni, V. Pirovano, G. Abbiati, *Org. Biomol. Chem.* **2018**, *16*, 3213–3219.
[26] J. Schulz, L. Jašíková, A. Škríba, J. Roithová, *J. Am. Chem. Soc.* **2014**, *136*, 11513–11523.
[27] a) Y. L. Fan, X. H. Jin, Z. P. Huang, H. F. Yu, Z. G. Zeng, T. Gao, L. S. Feng, *Eur. J. Med. Chem.* **2018**, *150*, 347–365; b) L. Zhang, X.-M. Peng, G. L. V. Damu, R.-X. Geng, C.-H. Zhou, *Med. Res. Rev.* **2014**, *34*, 340–437.
[28] a) J. Jampilek, *Curr. Med. Chem.* **2014**, *21*, 4347–4373; b) I. Balderas-Renteria, P. Gonzalez-Barranco, A. Garcia, B. K. Banik, G. Rivera, *Curr. Med. Chem.* **2012**, *19*, 4377–4398.
[29] a) S. Cascioferro, B. Parrino, V. Spanò, A. Carbone, A. Montalbano, P. Barraja, P. Diana, G. Cirrincione, *Eur. J. Med. Chem.* **2017**, *142*, 328–375; b) R. Kumar, T. S. Sirohi, H. Singh, R. Yadav, R. K. Roy, A. Chaudhary, S. N. Pandeya, *Mini-Rev. Med. Chem.* **2014**, *14*, 168–207.
[30] a) P. Miniyar, P. Murumkar, P. Patil, M. Barmade, K. Bothara, *Mini-Rev. Med. Chem.* **2013**, *13*, 1607–1625; b) R. Goel, V. Luxami, K. Paul, *Org. Biomol. Chem.* **2015**, *13*, 3525–3555.
[31] R. Ramajayam, R. Giridhar, M. R. Yadav, *Mini-Rev. Med. Chem.* **2007**, *7*, 793–812.
[32] I. Akritopoulou-Zanze, Y. Wang, H. Zhao, S. W. Djuric, *Tetrahedron Lett.* **2009**, *50*, 5773–5776.
[33] W. Ren, J. Liu, L. Chen, X. Wan, *Adv. Synth. Catal.* **2010**, *352*, 1424–1428.
[34] S. Mori, M. Takubo, T. Yanase, T. Maegawa, Y. Monguchi, H. Sajiki, *Adv. Synth. Catal.* **2010**, *352*, 1630–1634.
[35] Y. Miao, A. Dupé, C. Bruneau, C. Fischmeister, *Eur. J. Org. Chem.* **2014**, *2014*, 5071–5077.
[36] C. Mousset, O. Provot, A. Hamze, J. Bignon, J. D. Brion, M. Alami, *Tetrahedron* **2008**, *64*, 4287–4294.
[37] S. W. Kim, T. W. Um, S. Shin, *J. Org. Chem.* **2018**, *83*, 4703–4711.
[38] A. Shaabani, A. Maleki, M. Behnam, *Synth. Commun.* **2008**, *39*, 102–110.
[39] J. Nagy, J. Nyitrai, P. Kolonits, K. Lempert, A. Gergely, L. Parkanyi, A. Kalman, *J. Chem. Soc., Perkin Trans. 1* **1988**, *0*, 3267–3274.
[40] Y. Xu, X. Wan, *Tetrahedron Lett.* **2013**, *54*, 642–645.
[41] C. Qi, H. Jiang, L. Huang, Z. Chen, H. Chen, *Synthesis* **2011**, *3*, 387–396.
[42] P. J. Steel, G. B. Caygill, *J. Organomet. Chem.* **1990**, *395*, 359–373.
[43] M. E. Jung, G. Deng, *Org. Lett.* **2014**, *16*, 2142–2145.

Received: January 23, 2019

Gold Catalysis



Internal alkynes have been shown to undergo oxidation to substituted benzils (1,2-diarylethane-1,2-diones) by α-picoline *N*-oxide in the presence of $Ph_3PAuNTf_2$ (5 mol-%).

DOI: 10.1002/ejoc.201900108

