COMMUNICATIONS doi.org/10.1002/adsc.202100729 Advanced Synthesis & Catalysis

Water Can Accelerate Homogeneous Gold Catalysis

Philipp M. Stein,[a] Matthias Rudolph,[a] and A. Stephen K. Hashmi[a, b,*]

[a] Organisch-Chemisches Institut, Heidelberg University, Im Neuenheimer Feld 270, 69120 Heidelberg, Germany
E-mail: hashmi@hashmi.de
[b] Chemistry Department, Faculty of Science, King Abdulaziz University, Jeddah 21589, Saudi Arabia

Manuscript received: June 11, 2021; Version of record online: ■■, ■■■

Supporting information for this article is available on the WWW under https://doi.org/10.1002/adsc.202100729

Abstract: A selection of gold-catalyzed reactions was examined in a kinetic study on the influence of water on the rate constant. Two intramolecular reactions and one intermolecular reaction, which proceed via proton transfer and/or protodeauration steps, were investigated. The kinetic data was collected by GC or ^{1}H NMR spectroscopy. The obtained rate constants provided information about the influence of water in these test reactions. On the basis of the data collected, beyond the commonly assumed tolerance against water, a *reaction-promoting* influence of water on gold catalysis was identified and kinetically quantified. The results underline that the often-mentioned water-tolerance of gold catalysis not only simplifies these reactions operationally, but in addition even provides better results than a troublesome exclusion of water.

Keywords: water; kinetic studies; reaction optimization; gold catalysis

In recent years, the transformation of organic substrates by gold catalysts has become increasingly important and numerous new gold-catalyzed reaction types and gold catalysts have been developed.[1–13] Especially, the latter are of crucial importance for the success of a reaction and can be optimized both by the choice of the ligand and by the counter anion.[14–20] The tremendous impact of the counter anion was recently demonstrated in a strategic approach for industry.[21]

Nevertheless, classic parameters such as pressure, temperature and choice of solvent, still play a decisive role in the success of a chemical reaction. In particular the choice of solvent raises the question whether technical grade solvents with small amounts of water are sufficient or whether more complex protecting gas techniques and dry solvents have to be used in order to achieve an optimal reaction rate and conversion.

However, there are only a handful of publications in literature dealing with the actual influence of water on gold catalyzed reaction systems.[22] Early work on nucleophilic additions of alcohols already indicated that hydroxyl groups are tolerated well,[23–25] and it was mentioned early that no special precautions like the exclusion of humidity or air are necessary.[1–3] This led to the ubiquitous knowledge that gold catalysis typically tolerates water, but the coordination of water was assumed to slow down the conversions by competing with the coordination of the substrate.

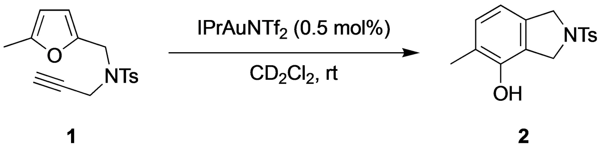
Of particular interest are reactions that include protodeauration or proton transfer steps, since these steps may be even favored by the use of non-dry solvents or the addition of water. Such an example was presented by Pernpointner in a DFT study of the nucleophilic addition of methanol to propyne. The activation barriers indicated that the simple transfer of protons via hydrogen bonds from water molecules, with even small water clusters serving as highly efficient proton shuttles, is a significant barrier-reducing factor. The water-assisted nucleophilic addition made the chemical conversion more efficient.[26] With regard to the trend towards simple conditions for sustainable chemistry, such research on the development of water-tolerant catalysts represents an important contribution to catalysis research.[27]

Here we present the first study on the influence of well-quantified amounts of water on three prototypic gold-catalyzed reactions.

We started our kinetic investigation by selecting well-known and not too complex test systems in order to precisely determine the influence of water on these gold-catalyzed processes. Therefore, the intramolecular gold-catalyzed phenol synthesis was chosen as a first potential test reaction.[1,3,28] This organic transformation is a very efficient tool which enables the rapid synthesis of highly substituted arenes from α- or β-alkynyl furans. In addition, the corresponding catalytic cycle involves cationic intermediates and a proton transfer step,[29–30] which made this substrate type a good candidate for the examination of the rate dependence on the amount of added water.

Due to the high resolution in time of NMR kinetics and the high reaction rate, this kinetic investigation was conducted by *in situ* monitoring by ^{1}H NMR spectroscopy at 25 °C, using a standardized procedure to ensure the comparability (see the Supporting Information for further details). The use of this continuous measurement method enables the recording of 512 ^{1}H NMR spectra within a period of maximum fourteen hours. For the test reactions one equivalent of the furan-yne **1** was treated with 0.5 mol% IPrAuNTf$_2$ in deuterated DCM containing varying amounts of water (Scheme 1).

The obtained data confirmed the initially assumed first order reaction by using the integration method.[31–33] In addition, the rate constant was determined by standard kinetic methods using mathematical correlations (see the Supporting Information for further details). The results of the measured kinetics of the phenol synthesis are listed in Table 1 and sorted by rising amount of water. An exemplary reaction progress is shown in Figure 1. In order to simplify the comparison of the data, the relative rate constant k_{rel} of the test reaction under anhydrous conditions was normalized to $k_{rel} = 1$.



Scheme 1. Gold(I)-catalyzed phenol synthesis.

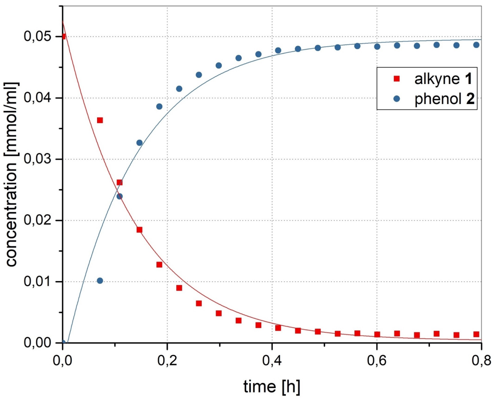
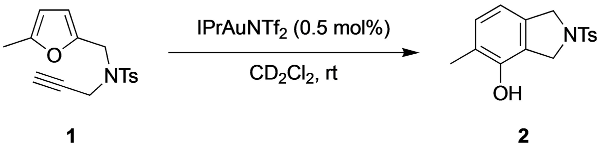


Figure 1. Reaction course of the phenol synthesis in dry CD$_2$Cl$_2$ (Table 1; Entry 1).

The choice of solvent and catalyst turned out to be a decisive parameter. While the test reactions using AuCl$_3$ in conventional acetonitrile reached a maximum conversion of 47% after 12 hours (see the Supporting Information for further details), the analogous test system with IPrAuNTf$_2$ as catalyst led to an unselective reaction and only 20% of the desired phenol. Changing the solvent to methylene chloride significantly accelerated the reaction in the case of IPrAuNTf$_2$, which is described in more detail in the following experiments. First, the course of the reaction was examined in the absence of water (Table 1; entry 1). A comparatively high-rate constant was obtained, which is also reflected by 75% conversion within the first 12 minutes with 0.5 mol% of catalyst. After 30 minutes 96% of starting material were converted.

Then the water content in the test system was gradually increased. Due to the low solubility of water in methylene chloride, kinetic studies were carried out for a 1.50 10^{-1} wt% water content and in methylene chloride saturated with water.

Table 1. Rate constants for phenol synthesis (CD$_2$Cl$_2$) depending on the water content.[a]



Entry	Water content [wt%]	Conversion [%] 0.2 h	0.5 h	k_1 [mL/(mmol*h)]	R^2	k_{rel}
1	dry	75	96	8.83 ± 0.15	0.998	1.00 ± 0.02
2	1.50 10^{-1}	85	96	12.02 ± 0.57	0.993	1.36 ± 0.07
3	Saturated	89	96	17.21 ± 0.83	0.998	1.95 ± 0.10

[a] Reaction conditions: benzenesulfonamide alkyne (50.0 μmol, 50.0 μmol/ml), IPrAuNTf$_2$ (0.5 mol%), in CD$_2$Cl$_2$ at T = 25 °C, observed by ^{1}H NMR monitoring for up to 2 h.

Furthermore, the water content of the freshly opened deuterated solvent and of the solvent saturated with water was determined using an internal standard with ^{1}H NMR spectroscopy. The freshly opened solvent showed a water content of 0.30 µl/ml and the saturated one a water content of 2.54 µl/ml.

With 1.50 10^{-1} wt% water (0.2 µl water added to 998 µl CD_2Cl_2), the reaction rate was already enhanced by 36% (Table 1; entry 2). In addition, a 10% higher conversion was observed within the first 12 minutes (see Figure 2). An even more efficient reaction was achieved by using water-saturated methylene chloride resulting in an almost doubled reaction speed compared to the dry conditions (Table 1; entry 3). Moreover, a conversion of 96% was achieved after 24 minutes instead of 30 minutes (Figure 2).

Mixtures with a higher water content led to the formation of two phases, which could not be analyzed by ^{1}H NMR spectroscopy. However, since the organic conversion takes place in the organic phase, it can be assumed that the reactions rate would be comparable to that of a saturated solution. The use of acetonitrile, which, on the other hand, is more miscible with water, did not lead to any further improvement (see the Supporting Information for further details).

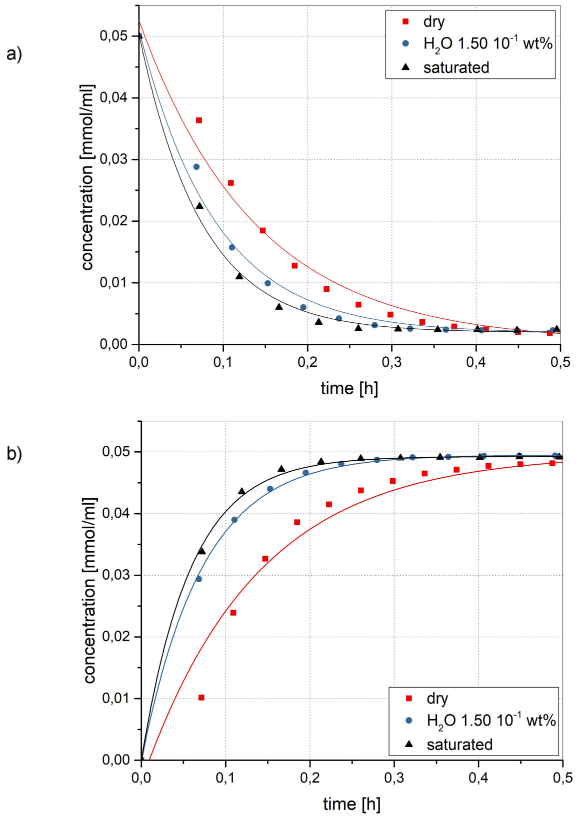


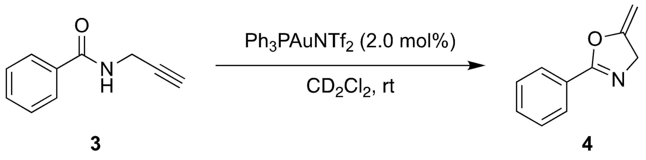
Figure 2. Reaction course of the phenol synthesis with varying water content in CD_2Cl_2: a) Decrease of reactant **1**; b) Increase of product **2**.

In order to further investigate the influence of the amount of water on the kinetics of gold-catalyzed reactions, an oxazoline synthesis was studied next. In contrast to the phenol synthesis, this reaction – which is particularly interesting for pharmaceuticals and materials science – has no proton transfer steps apart from a protodeauration.[34–40] As described above, an *in situ* monitoring with ^{1}H NMR spectroscopy was carried out according to a standardized procedure in order to compare the kinetic results (see the Supporting Information for further details). Therefore, one equivalent of *N*-(prop-2-yn-1-yl)benzamide was treated with 2.0 mol% $Ph_3PAuNTf_2$ in deuterated DCM containing varying amounts of water (Scheme 2).

The results of the mathematical regression are shown in Table 2. Dry conditions were chosen as the reference system (exemplary reaction course: see Figure 3) and the corresponding relative rate constant k_{rel} was normalized to $k_{rel} = 1$ (see Table 2). In addition, the use of the integration method confirmed a first order reaction with respect to the substrate (see the Supporting Information for further details).[31–33]

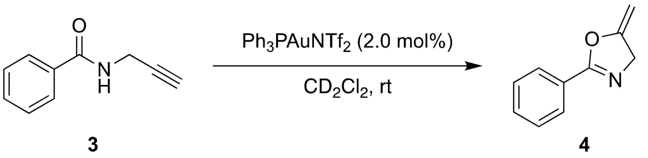
As already observed in the phenol synthesis, an increasing water content of the solvent favored the product formation in the oxazoline synthesis tested here.

First, a test reaction was examined under dry conditions (Table 2; entry 1). Within the first 30 minutes 66%, and after 60 minutes 90% conversion of



Scheme 2. Gold(I)-catalyzed oxazoline synthesis.

Table 2. Rate constants for the oxazoline synthesis (CD_2Cl_2) depending on the water content.[a]



Entry	Water content [wt%]	Conversion [%] 0.2 h	0.5 h	k_1 [mL/(mmol*h)]	R^2	k_{rel}
1	dry	66	90	2.42 ± 0.01	0.999	1.00 ± 0.01
2	1.50 10^{-1}	69	89	2.60 ± 0.09	0.996	1.07 ± 0.04
3	saturated	73	91	2.77 ± 0.02	0.999	1.14 ± 0.01

[a] Reaction conditions: *N*-(prop-2-yn-1-yl)benzamide (50 µmol, 50 µmol/ml), $Ph_3PAuNTf_2$ (2.0 mol%), in CD_2Cl_2 at T = 25 °C, observed by ^{1}H NMR monitoring for up to 2 h.

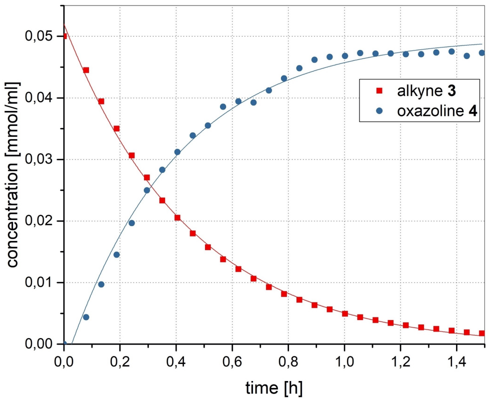


Figure 3. Reaction course of the oxazoline synthesis in dry CD_2Cl_2 (Table 2; Entry 1).

the reactant was achieved. Analogous to the considerations for the phenol synthesis, the amount of water was increased to $1.50\ 10^{-1}$ wt%. This led to a 7% higher reaction rate and 69% conversion of the starting material (Table 2; entry 2). With water-saturated methylene chloride, a further increase in the reaction rate of 7% and a reaction conversion of 73% was recorded (Table 2; entry 3). Thus, as with the phenol synthesis previously examined, a promoting influence of the water addition was also confirmed for the oxazoline synthesis. The described trends of reactant decrease, or product increase, are shown in Figure 4.

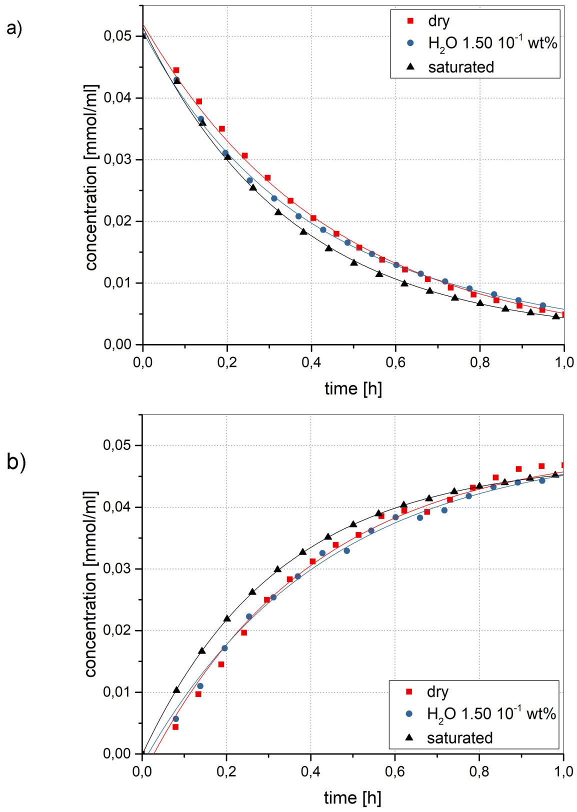
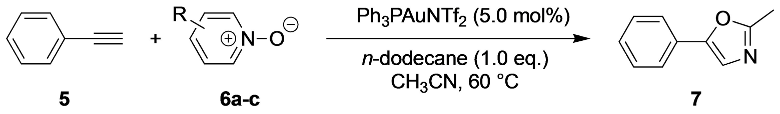


Figure 4. Reaction course of the oxazoline synthesis with varying water content in CD_2Cl_2: a) Decrease of reactant **3**; b) Increase of product **4**.

After observing the influence of water on the reaction rate of intramolecular test systems, we decided to continue our studies on an intermolecular reaction. For this purpose, an oxazole synthesis was chosen, which was developed by Zhang *et al.* and recently examined by our group to classify the reactivity of various *N*-oxides.[41] In addition to the easy accessibility of the starting materials, this reaction is also characterized by a reaction time of a few hours and is therefore of great interest for homogeneous gold catalysis.[42–43] The selection of the *N*-oxides was based on our recent work.[44] For the present study, we examined the efficient 8-methylquinoline *N*-oxide **6a** reagent, the fast-reacting 3,5-dibromopyridine *N*-oxide **6b** and pyridine *N*-oxide **6c** as reference compounds.

In contrast to the intramolecular test systems, the oxazole synthesis was analyzed by GC according to a standardized procedure to ensure comparability (see the Supporting Information for further details). For the kinetic studies, one equivalent of phenylacetylene and 1.3 equivalents of *N*-oxide **6a–c** were dissolved in 3.00 ml acetonitrile with 0.0 to 5.06 wt% of distilled water. As an internal standard, one equivalent of *n*-dodecane was added. The temperature was kept constant at 60 °C and the mixture was stirred at a speed of 400 rpm. The reaction was started by adding 5.0 mol% of the gold(I) complex $Ph_3PAuNTf_2$ (Scheme 3).

After specific time intervals, samples were taken from the reaction mixture and the catalyst was quickly removed by filtration over silica gel to stop the reaction. Afterwards the solution was analyzed by gas chromatography and the reactant and product concentrations were determined based on the method of internal standard.[45]



Scheme 3. Gold(I)-catalyzed oxazole synthesis.

Analogous to the analysis of the phenol and oxazoline synthesis, the kinetic data were evaluated, and the corresponding errors determined. The use of the unsubstituted pyridine *N*-oxide **6c** under dry conditions was chosen as the reference system and the corresponding relative rate constant k_{rel} was normalized to $k_{rel} = 1$.

Due to the fact that acetonitrile acts both as solvent and reactant, it is legitimate to neglect its concentration when calculating the rate constants. The value k* therefore represents the rate constant taking into account the acetonitrile concentration. Furthermore, the assumed pseudo second order reaction was confirmed by using the integration method (see the Supporting Information for further details).[31–33]

Based on the evaluation of the observed reactions, the results listed in Table 3 such as reaction rate constants and conversions were obtained. In line with the previous test systems, there were also clear trends regarding water content recognizable in the examined oxazole test system. In order to clarify the trends discussed, the decrease in phenylacetylene was also shown graphically (Figure 5, Supporting Information).

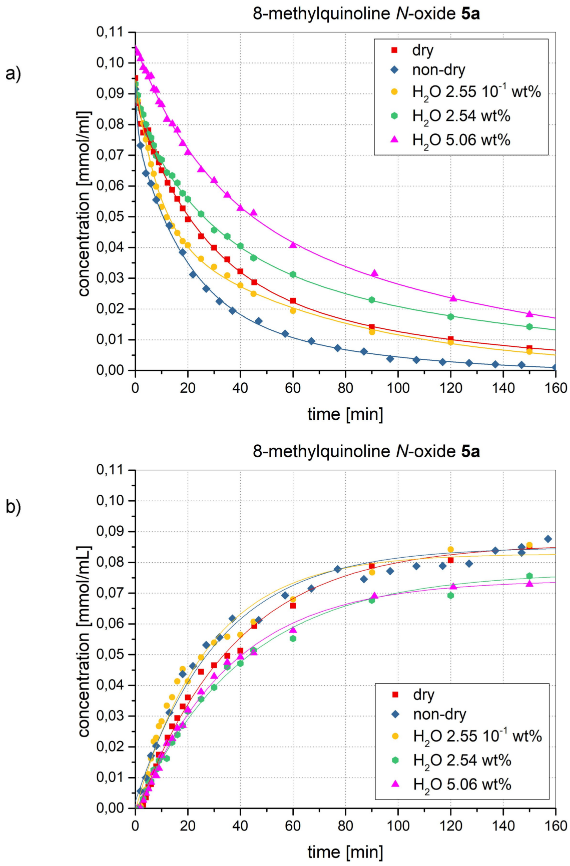


Figure 5. Reaction course of the oxazole synthesis with varying water content using **6a**: a) Decrease in phenylacetylene **5**, b) Increase in oxazole **7**.

As expected, the highest reaction rates were achieved by using 8-methylquinoline *N*-oxide **6a** and 3,5-dibromopyridine *N*-oxide **6b**. A water content of $2.55\ 10^{-1}$ wt% or the use of non-dry solvents from conventional solvent bottles proved to be ideal for high-rate constants and an efficient conversion in short time.

According to Table 3, the highest reaction rate was observed in the conversion of 8-methylquinoline *N*-oxide **6a** with a water content of $2.55\ 10^{-1}$ wt% (Table 3; entry 1). The rate of the corresponding reaction in conventional non-dry solvent (acetonitrile, ≥99.5% (GC): water content max. 0.1 wt%)[46] was slightly lower (Table 3; entry 2). In both cases, almost complete conversion was achieved within the first 150 minutes.

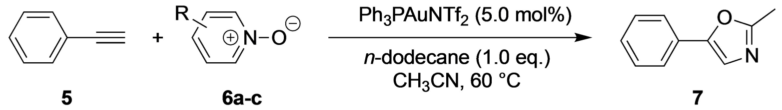
Likewise, when using 3,5-dibromopyridine *N*-oxide **6b**, a minimal amount of water was also found to promote the reaction. Thus, we obtained the highest rate constant of this *N*-oxide by using a water volume of $2.55\ 10^{-1}$ wt% in acetonitrile and the second highest rate constant by using non-dry solvent (Table 3; entry 6–7). The maximum conversion under these conditions was approximately 70% after 150 minutes and rose to 98% after 12 hours.

Using dry solvent, the reaction rate of 8-methylquinoline *N*-oxide **6a** was drastically reduced by almost 50%. At the same time, the reaction conversion achieved in the first 150 minutes dropped to 93% (Table 3; entry 3). In addition, doubling the amount of water from 2.54 wt% to 5.06 wt%, led to a significant drop in reaction speed. In the latter case, the reaction rate even dropped to only one third of the maximum value with $2.55\ 10^{-1}$ water in the solvent (Table 3; entries 4–5). In contrast, the conversion after 150 minutes did not change notably. These results are graphically depicted in Figure 5. Thus, in this test reaction we observed the maximum rate at low water concentration and a rate decrease with higher concentrations; still, the best rate was not observed under anhydrous conditions.

The trend observed was also reflected in the studies on 3,5-dibromopyridine *N*-oxide **6b**, albeit less pronounced. Thus, under dry conditions, the reaction rate dropped by 9%, while the reaction conversion remained the same (Table 3; entry 8). The rate constant, which was 30% higher than that of 8-methylquinoline *N*-oxide **6a** under analogous conditions, was particularly striking. This surprisingly greater dependence of the reaction rate on the amount of water for 8-methylquinoline *N*-oxide was also confirmed for a water content of 2.54 wt% and 5.06 wt%.

While the successive increase in water content in reactions with 3,5-dibromopyridine *N*-oxide **6b** hardly influenced the reaction conversion, the rate constant decreased by 44% at 2.54 wt% (Table 3; entry 9) and by 53% at 5.06 wt% water content (Table 3; entry 10).

Table 3. Rate constants of varying *N*-oxides depending on the water content.[a]



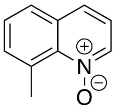
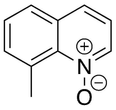
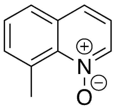
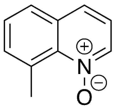
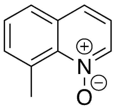
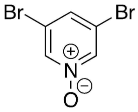
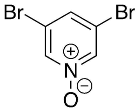
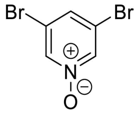
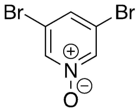
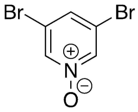
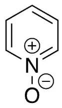
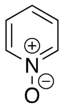
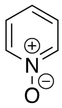
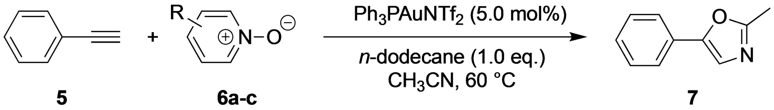
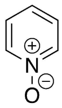
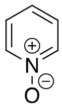
Entry	*N*-oxide	Water content [wt%]	Conversion [%] 2.5 h	Conversion [%] 24 h	k_1 [mL/(mmol*h)]	k* [$mL^2/(mmol^2*h)$]	R^2	k_{rel}
1		2.55 10^{-1}	94	100	33.16 ± 2.31	1.79 ± 0.12	0.99	6.73 ± 0.47
2[b,c]		non-dry	100	100	31.94 ± 2.08	1.72 ± 0.11	0.99	6.48 ± 0.42
3		abs.	93	100	18.52 ± 1.28	1.00 ± 0.07	0.99	3.76 ± 0.26
4		2.54	85	100	13.97 ± 0.96	0.77 ± 0.05	0.99	2.84 ± 0.19
5		5.06	83	100	10.70 ± 1.06	0.64 ± 0.08	0.99	2.17 ± 0.22
6		2.55 10^{-1}	71	98	28.86 ± 1.87	1.56 ± 0.10	0.99	5.85 ± 0.38
7[b,c]		non-dry	68	96	27.12 ± 2.04	1.46 ± 0.11	0.99	5.51 ± 0.41
8		abs.	74	97	26.28 ± 2.72	1.42 ± 0.15	0.98	5.34 ± 0.55
9		2.54	69	96	16.06 ± 1.41	0.88 ± 0.08	0.98	3.26 ± 0.29
10		5.06	73	95	13.76 ± 1.56	0.77 ± 0.09	0.97	2.79 ± 0.32
11		2.55 10^{-1}	51	100	7.89 ± 0.55	0.43 ± 0.03	0.99	1.60 ± 0.11
12		2.54	41	88	7.27 ± 0.64	0.40 ± 0.04	0.98	1.48 ± 0.13
13[b,c]		non-dry	60	100	6.19 ± 0.51	0.33 ± 0.03	0.98	1.26 ± 0.10

Table 3. continued



Entry	*N*-oxide	Water content [wt%]	Conversion [%] 2.5 h	24 h	k_1 [mL/(mmol*h)]	k* [mL^2/($mmol^2$*h)]	R^2	k_{rel}
14		5.06	45	75	5.49 ± 0.58	0.31 ± 0.03	0.98	1.12 ± 0.12
15		abs.	49	91	4.92 ± 0.39	0.27 ± 0.02	0.99	1.00 ± 0.08

[a] Reaction conditions: benzenesulfonamide alkyne (50 µmol, 50 µmol/ml), IPrAuNTf$_2$ (5.0 mol%), in CD_2Cl_2 at T = 25 °C, observed by ^{1}H NMR monitoring for up to 2 h.
[b] In order to compare, data were taken from reference[39].
[c] conventional solvent.[46]

Finally, further experiments with pyridine *N*-oxide **6c** were carried out. Using 2.55 10^{-1} wt% water content the reaction rate was increased by approximately 63% compared to dry solvent, almost reaching the reaction rate of 8-methylquinoline *N*-oxide with 5.06 wt% of water. After 12 hours the phenylacetylene was completely converted (Table 3; entry 11, 5). Increasing the water content to 2.54 wt% or the use of non-dry solvents led to a decrease in the corresponding rate constants (Table 3; entries 12–13). Nevertheless, in contrast to the other pyridine *N*-oxide **6c** test series, complete conversion was achieved after 24 hours under the latter conditions. The increase in the amount of water to 5.06 wt%, as well as the use of dry solvents resulted in the lowest measured conversions and time constants (Table 3; entries 14–15).

In conclusion, the comparison of the results for some representative key reactions of gold catalysis showed clear trends with regard to the influence of water on a given reaction system. Particularly interesting results were obtained for the reactions executed in methylene chloride; the phenol synthesis and the oxazoline synthesis. For the furan-yne reaction, a remarkable proportionality was discovered: the higher the water content, the higher the reaction rate. However, the maximum amount of water was limited by the low miscibility of water and methylene chloride which hinders from an even higher increase in the reaction rate.

Comparable relations were also obtained for the intermolecular oxazole synthesis examined. Reactions with a small amount of 2.55 10^{-1} wt% of water achieved higher rate constants than those under completely dry conditions. The use of conventional solvents is therefore optimal for an efficient product synthesis. Though, this effect cannot be increased arbitrarily by further increasing the amount of water. Decreasing rate constants were observed from a water content of over 2.54 wt% with respect to the solvent.

Based on the kinetic data found, small amounts of water proved to promote the reaction and led to increased reaction rates in combination with good yields. Probably many reactions in the field behave similarly, thus complex protective gas techniques and the use of dry solvents is not beneficial, time and money can be saved and the increased rate in applications significantly improves the important space time yield. Since some of the test reactions involved protodeauration, but others did not, it is beyond the scope of this manuscript to provide a detailed mechanistic model for the role of the water in the different reactions; ongoing studies focus on this.

Acknowledgements

P.M.S. and A.S.K.H. gratefully acknowledge the Hector Fellow Academy for the generous provision of funding.

References

[1] A. S. K. Hashmi, T. M. Frost, J. W. Bats, *J. Am. Chem. Soc.* **2000**, *122*, 11553–11554.
[2] A. S. K. Hashmi, L. Schwarz, J.-H. Choi, T. M. Frost, *Angew. Chem. Int. Ed.* **2000**, *39*, 2285–2288; *Angew. Chem.* **2000**, *39*, 2285–2288.
[3] A. S. K. Hashmi, T. M. Frost, J. W. Bats, *Org. Lett.* **2001**, *3*, 3769–3771.
[4] A. S. K. Hashmi, G. J. Hutchings, *Angew. Chem. Int. Ed.* **2006**, *45*, 7896–7936; *Angew. Chem.* **2006**, *45*, 7896–7936.
[5] A. S. K. Hashmi, *Chem. Rev.* **2007**, *107*, 3180–3211.

[6] A. S. K. Hashmi, M. Rudolph, *Chem. Soc. Rev.* **2008**, *37*, 1766–1775.
[7] N. Marion, S. P. Nolan, *Chem. Soc. Rev.* **2008**, *37*, 1776–1782.
[8] A. Arcadi, *Chem. Rev.* **2008**, *108*, 3266–3325.
[9] S. Sengupta, X. Shi, *ChemCatChem* **2010**, *2*, 609–619.
[10] P. Garcia, M. Malacria, C. Aubert, V. Gandon, L. Fensterbank, *ChemCatChem* **2010**, *2*, 493–497.
[11] M. Rudolph, A. S. K. Hashmi, *Chem. Commun.* **2011**, *47*, 6536–6544.
[12] D.-H. Zhang, X.-Y. Tang, M. Shi, *Acc. Chem. Res.* **2014**, *47*, 913–924.
[13] D. Pflästerer, A. S. K. Hashmi, *Chem. Soc. Rev.* **2016**, *45*, 1331–1367.
[14] Z. Zhang, R. A. Widenhoefer, *Org. Lett.* **2008**, *10*, 2079–2081.
[15] P. W. Davies, N. Martin, *Org. Lett.* **2009**, *11*, 2293–2296.
[16] W. Wang, G. B. Hammond, B. Xu, *J. Am. Chem. Soc.* **2012**, *134*, 5697–5705.
[17] Z. Lu, J. Han, G. B. Hammond, B. Xu, *Org. Lett.* **2015**, *17*, 4534–4537.
[18] F. Jaroschik, A. Simonneau, G. Lemière, K. Cariou, N. Agenet, H. Amouri, C. Aubert, J.-P. Goddard, D. Lesage, M. Malacria, Y. Gimbert, V. Gandon, L. Fensterbank, *ACS Catal.* **2016**, *6*, 5146–5160.
[19] Z. Lu, J. Han, O. E. Okoromoba, N. Shimizu, H. Amii, C. F. Tormena, G. B. Hammond, B. Xu, *Org. Lett.* **2017**, *19*, 5848–5851.
[20] Z. Lu, T. Li, S. R. Mudshinge, B. Xu, G. B. Hammond, *Chem. Rev.* **2021**, *121*, doi.org/10.1021/acs.chemrev.0c00713.
[21] J. Schießl, J. Schulmeister, A. Doppiu, E. Wörner, M. Rudolph, R. Karch, A. S. K. Hashmi, *Adv. Synth. Catal.* **2018**, *360*, 2493–2502.
[22] C. Wei, C.-J. Li, *J. Am. Chem. Soc.* **2003**, *125*, 9584–9585.
[23] Y. Fukuda, K. Utimoto, *J. Org. Chem.* **1991**, *56*, 3729–3731.
[24] J. H. Teles, S. Brode, M. Chabanas, *Angew. Chem. Int. Ed.* **1998**, *37*, 1415–1418; *Angew. Chem.* **1998**, *37*, 1415–1418.
[25] E. Mizushima, K. Sato, T. Hayashi, M. Tanaka, *Angew. Chem. Int. Ed.* **2002**, *41*, 4563–4565; *Angew. Chem.* **2002**, *41*, 4563–4565.
[26] C. M. Krauter, A. S. K. Hashmi, M. Pernpointner, *ChemCatChem* **2010**, *2*, 1226–1230.
[27] A. S. K. Hashmi, *Catal. Today* **2007**, *122*, 211–214.
[28] A. S. K. Hashmi, R. Salathé, W. Frey, *Chem. Eur. J.* **2006**, *12*, 6991–6996.
[29] A. S. K. Hashmi, M. Rudolph, J. P. Weyrauch, M. Wölfle, W. Frey, J. W. Bats, *Angew. Chem. Int. Ed.* **2005**, *44*, 2798–2801; *Angew. Chem.* **2005**, *44*, 2798–2801.
[30] A. S. K. Hashmi, M. Rudolph, H.-U. Siehl, M. Tanaka, J. W. Bats, W. Frey, *Chem. Eur. J.* **2008**, *14*, 3703–3708.
[31] W. Bechmann, J. Schmidt, *Einstieg in die Physikalische Chemie für Nebenfächler*, Vieweg Teubner, Wiesbaden, **2001**.
[32] P. W. Atkins, J. Paula, *Physikalische Chemie, 4th edn.*, Wiley-VCH, Weinheim, **2006**.
[33] P. L. Houston, *Chemical Kinetics and Reaction Dynamics*, Dover Publications, Inc., Minola, New York, **2012**.
[34] A. S. K. Hashmi, J. P. Weyrauch, W. Frey, J. W. Bats, *Org. Lett.* **2004**, *6*, 4391–4394.
[35] A. S. K. Hashmi, A. M. Schuster, F. Rominger, *Angew. Chem. Int. Ed.* **2009**, *48*, 8247–8249; *Angew. Chem.* **2009**, *48*, 8247–8249.
[36] J.-I. Kuroyanagi, K. Kanai, Y. Sugimoto, T. Horiuchi, I. Achiwa, H. Takeshita, K. Kawakami, *Bioorg. Med. Chem.* **2010**, *18*, 7593–7606.
[37] C.-Y. Chen, T. Andreani, H. Li, *Org. Lett.* **2011**, *13*, 6300–6303.
[38] A. J. Morrison, J. M. Adam, J. A. Baker, R. A. Campbell, J. K. Clark, J. E. Cottney, M. Deehan, A.-M. Easson, R. Fields, S. Francis, F. Jeremiah, N. Keddie, T. Kiyoi, D. R. McArthur, K. Meyer, P. D. Ratcliffe, J. Schulz, G. Wishart, K. Yoshiizumi, *Bioorg. Med. Chem. Lett.* **2011**, *21*, 506–509.
[39] F. Hamon, E. Largy, A. Guédin-Beaurepaire, M. Rouchon-Dagois, A. Sidibe, D. Monchaud, J.-L. Mergny, J.-F. Riou, C.-H. Nguyen, M.-P. Teulade-Fichou, *Angew. Chem. Int. Ed.* **2011**, *50*, 8745–8749; *Angew. Chem.* **2011**, *50*, 8745–8749.
[40] A. S. K. Hashmi, A. Littmann, *Chem. Asian J.* **2012**, *7*, 1435–1442.
[41] W. Yang, R. Zhang, F. Yi, M. Cai, *J. Org. Chem.* **2017**, *82*, 5204–5211.
[42] D. Azarifar, B. Mahmoudi, *J. Iran. Chem. Soc.* **2016**, *13*, 645–651.
[43] A. Biswas, U. Karmakar, A. Pal, R. Samanta, *Chem. Eur. J.* **2016**, *22*, 13826–13830.
[44] J. Schießl, P. M. Stein, J. Stirn, K. Emler, M. Rudolph, F. Rominger, A. S. K. Hashmi, *Adv. Synth. Catal.* **2019**, *361*, 725–738.
[45] R. L. Grob, E. F. Barry, *Modern Practice of Gas Chromatography, 4th edn.*, Wiley Interscience, Hoboken, NJ, **2005**.
[46] *Honeywell International Inc; Acetonitril 99.5% (GC)* **2020**.

Water Can Accelerate Homogeneous Gold Catalysis

Adv. Synth. Catal. **2021**, *363*, 1–9

P. M. Stein, Dr. M. Rudolph, Prof. Dr. A. S. K. Hashmi*