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(Iminophosphorane)copper(I) Complexes as Highly Efficient Catalysts for 1,3-Dipolar Cycloaddition of Azides with Terminal and 1-Iodoalkynes in Water: One-Pot Multi-Component Reaction from Alkynes and in situ Generated Azides

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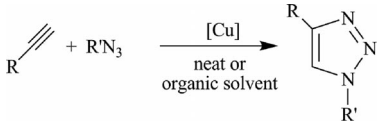
Treatment of water-soluble phosphanes PTA (**1**) and DAPTA (**2**) with an equimolecular amount of azides $(RO)_2P(=S)N_3$ (R = Et, Ph) leads to high-yield formation of the *N*-thiophosphorylated iminophosphorane derivatives **3b** and **4a**,**b**, respectively. The reaction of these new iminophosphorane ligands with $[Cu(NCCH_3)_4][PF_6]$ (in a 2:1 molar ratio) has been investigated. The resulting (iminophosphorane)copper(I) complexes **5b** and **6a**,**b** are efficient catalysts for the three-component cycloaddition reaction (organic halide, NaN_3 and terminal alkynes) in aqueous media to afford regioselectively, under mild and aerobic conditions according to "click laws", 1,4-disubstituted triazoles with a broad substrate scope and functional compatibility. The unprecedented application of the analogous (iminophosphorane)copper(I) catalyst **5a** to a one-pot three-component reaction with 1-iodoalkynes as an internal alkyne in aqueous medium is also reported. ESI-MS analysis of **5a** in water and DFT theoretical calculations [B3LYP/6-31G(d)] have been carried out providing valuable insight into the actual active species responsible for catalytic activity in water.

Introduction

During the last decade a huge amount of effort has been dedicated to the development of catalytic processes in aqueous media.[1] Regardless of the fact that water is a safe, nontoxic, eco-friendly and cheap solvent, it may give rise to a completely new reactivity, enabling a variety of highly efficient and selective synthetic approaches with both academic and industrial applications.[2] In fact, the search for new metal-mediated catalytic transformations in aqueous media has become one of the main goals in organometallic chemistry, as competitive synthetic approaches compared to traditional routes using organic solvents.

Simultaneously, the concept of click chemistry, coined by Sharpless and co-workers in 2001,[3] has emerged as a main proposal to design thermodynamically driven transformations, directed to the preparation of more complex products starting from a set of building blocks.[4,5] The most genuine example of this concept is the copper(I)-catalyzed cycloaddition of azides and terminal alkynes to yield 1,2,3-triazoles (CuAAC) reported independently in 2002 by Meldal[6] and Sharpless[7] (see Scheme 1). This achievement represents not only an outstanding synthetic tool for the regioselective synthesis of 1,4-disubstituted triazoles,[8] but also a significant target reaction, in the context of developing cleaner and more sustainable processes using an aqueous medium as an alternative benign solvent.[9]



Scheme 1. Copper-catalyzed 1,3-cycloaddition reaction (CuAAC).

Surprisingly, only a few CuAAC reactions have been performed in pure water as the reaction medium despite the strong acceleration effect and regioselectivity of many organic reactions in aqueous media.[10] Typical examples include a series of well-defined copper(I) complexes containing N-heterocyclic carbenes,[11] the complex $[CuBr(PPh_3)_3]$[12] and one further example containing a tripodal tris(triazolyl)methanol derivative as ligand.[10c,13] In this sense, we have recently reported the synthesis of the hydrosoluble iminophosphorane ligand **3a** and the corresponding

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copper(I) complex **5a** (Figure 1), which is a highly efficient catalyst for Huisgen 1,3-dipolar cycloadditions in pure water.[14] Noteworthy is that **5a** also shows chemo- and regioselective activity with 1-iodoalkynes (Scheme 2), a fact which, to the best of our knowledge, has previously been reported only for one other catalytic system in an aqueous medium.[15]

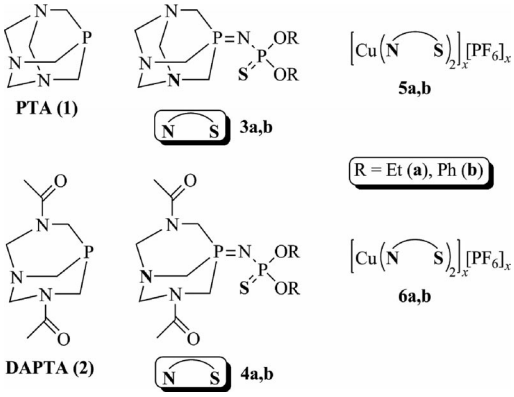
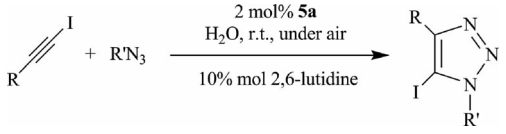


Figure 1. Structure of ligands **3**,**4a**,**b** and their copper(I) complexes **5**,**6a**,**b**.



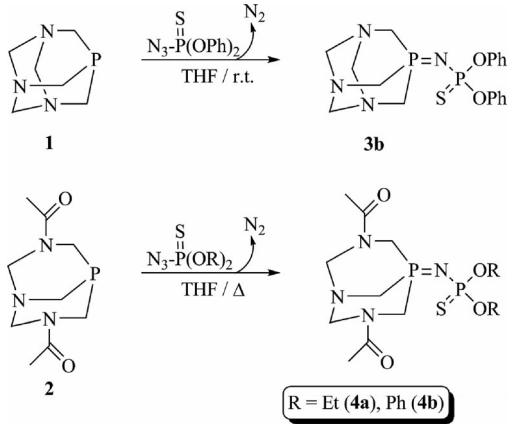
Scheme 2. (Iminophosphorane)copper(I)-catalyzed formation of 5-iodo-1,2,3-triazoles in water.

In the context of our explorations into this type of transformation in an aqueous medium, we report herein the synthesis and catalytic activity in water of a series of novel copper(I) complexes **5b**,**6a**,**b** (Figure 1) containing iminophosphorane ligands **3b**,**4a**,**b** [based on 1,3,5-triaza-7-phosphaadamantane (PTA) and 3,7-diacetyl-1,3,7-triaza-5-bicyclo[3.3.1]nonane (DAPTA)]. The following features are noteworthy: (i) all are water- and air-stable efficient catalysts and active in the three-component reaction (organic bromide, NaN_3 and terminal alkynes); (ii) complex **5a** is also active in the regio- and chemoselective synthesis of 5-iodo-1,2,3-triazoles through the one-pot 1,3-cycloaddition reaction of in situ generated azides with 1-iodoalkynes. As far as we know, this is the first example reported of an isolated copper(I) catalyst active with internal alkynes.

Results and Discussion

Synthesis and Characterization of *N*-Thiophosphorylated Iminophosphorane Ligands (PTA)=NP(=S)(OPh)$_2$ (3b) and (DAPTA)=NP(=S)(OR)$_2$ [R = Et (4a), Ph (4b)]

A large variety of water-soluble organometallic complexes have been synthesized and applied as efficient catalysts.[2,16] The most common strategy to obtain such derivatives consists of using hydrophilic P-donor ligands.[16] To date a large number of water-soluble monodentate phosphanes are available, but surprisingly their corresponding iminophosphorane derivatives $R_3P{=}NR'$ [readily accessible by Staudinger-type reactions between the phosphane and the desired azide ($R'N_3$)],[17] have barely been noticed in organometallic chemistry.[18] With this precedent in mind, and applying the procedure previously described for the synthesis of the iminophosphorane ligand **3a**,[14] we set up the synthesis of novel iminophosphoranes based on PTA (**3b**) or its acetyl derivative DAPTA (**4a**,**b**) (Figure 1) to be used as ligands for the design of new copper(I) catalysts active in CuAAC reactions in aqueous medium (**5b**,**6a**,**b**, Figure 1). Thus, using the well-known experimental procedure, through the classical Staudinger reaction,[17] the novel *N*-thiophosphorylated iminophosphorane ligands **3b** and **4a**,**b**, were readily synthesized by treatment of the water-soluble phosphane PTA (**1**) or DAPTA (**2**) with the corresponding *N*-thiophosphorylated azide $(RO)_2P(=S)N_3$ at room temperature (**3b**) or refluxing THF (**4a**,**b**) (see Scheme 3).[19] All compounds were isolated as air- and moisture-stable white solids in 79–86% yield, after a simple workup (Experimental Section).



Scheme 3. Synthesis of the iminophosphorane ligands **3b** and **4a**,**b**.

Characterization of compounds **3b** and **4a**,**b** was accomplished in a straightforward fashion by analysis of their analytical and spectroscopic data (Experimental Section). In particular, imination of the phosphorus atom of both PTA (**1**) and DAPTA (**2**) phosphanes was clearly reflected in the $^{31}P\{^1H\}$ NMR spectra, showing the presence of two well-separated doublets ($^2J_{PP}$ = 6.7–24.8 Hz) at δ_P = –34.27 to –12.40 ppm for the iminophosphorane group ($R_3P{=}N$) and 52.72–62.38 ppm for the thiophosphoryl group [$(RO)_2P{=}S$]. In the ^1H and the $^{13}C\{^1H\}$ NMR spectra, the expected signals for the corresponding phosphane backbone (PTA and DAPTA, respectively) are found. It is important to note that only iminophosphorane **4a** was found to be soluble in water (312 mg/mL vs. 201 mg/mL for **3a**), with solubility values lower than for DAPTA (1696 mg/mL). The insoluble nature of derivatives **3**,**4b** in water is probably due to the enriched carbon character acquired by changing ethyl for phenyl groups in the units –P(=S)(OR)$_2$ (R = Et, Ph).[20]

Moreover, the molecular structures of compounds **3b** and **4b** have been determined by X-ray diffraction methods.

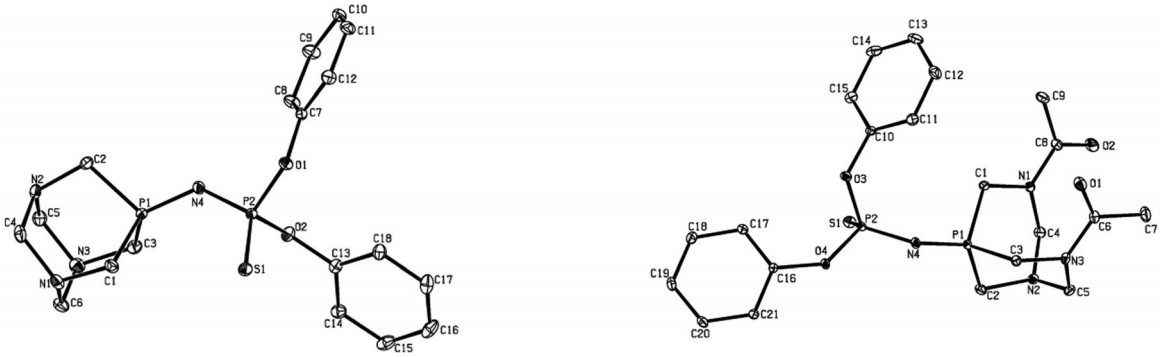
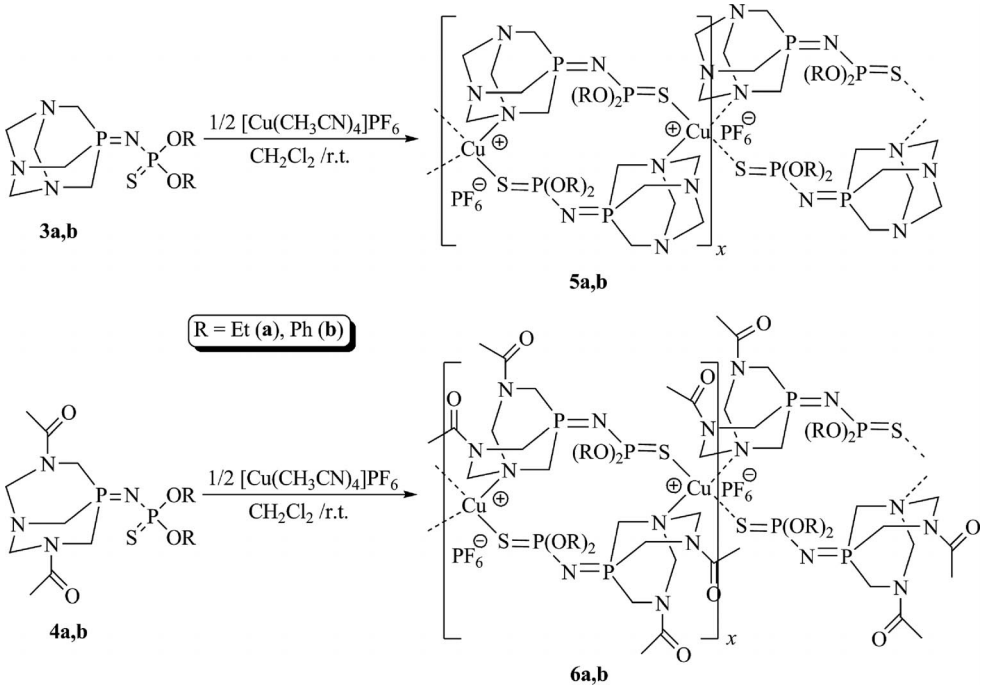


Figure 2. ORTEP-type view of the structure of compounds **3b** (left) and **4b** (right) showing the crystallographic labelling scheme. Hydrogen atoms have been omitted for clarity. Thermal ellipsoids are drawn at 10% probability level. Selected bond lengths [Å] and angles [°] for **3b**: P(1)–N(4) 1.569(3), N(4)–P(2) 1.584(3), P(2)–S(1) 1.935(1); P(1)–N(4)–P(2) 130.9(2), N(4)–P(2)–S(1) 121.5(1). Selected bond lengths [Å] and angles [°] for **4b**: P(1)–N(4) 1.572(2), N(4)–P(2) 1.592(3), P(2)–S(1) 1.935(1), C(6)–O(1) 1.218(3), C(8)–O(2) 1.225(3); P(1)–N(4)–P(2) 130.5(1), N(4)–P(2)–S(1) 118.9(1), N(1)–C(8)–O(2) 121.0(3), N(3)–C(6)–O(1) 121.0(2).

ORTEP plots of the structures are shown in Figure 2; selected bonding parameters are listed in the caption. The most noticeable features of these structures are the following: (i) the P=S bond lengths of the *N*-thiophosphorylated groups [P(2)–S(1) 1.935(1) Å for both **3b** and **4b**], which fall within the expected range for a phosphorus–sulfur double bond,[21] are in a good agreement with those previously reported for other *N*-thiophosphorylated iminophosphoranes [R_3P=N–P(=S)(OR′)$_2$],[22] and (ii) the similarity between the lengths of the formal single [N(4)–P(2) 1.584(3) (**3b**) and 1.592(3) Å (**4b**)] and double [P(1)–N(4) 1.569(3) (**3b**) and 1.572(2) Å (**4b**)] phosphorus–nitrogen bonds in the *N*-thiophosphorylated units P=NP(=S)(OPh)$_2$. This fact is probably determined by the strong π-acceptor nature of the thiophosphoryl group, which enhances the delocalization of the electron pair of the nitrogen atom along the P=N–P=S framework.[23] The two C(=O)CH_3 groups in **4b** are in an *anti* disposition as they have also been found previously in the solid-state X-ray crystal structure of DAPTA.[19]

Synthesis of (Iminophosphorane)copper(I) Complexes [Cu{μ^2-*N*,*S*-(PTA)=NP(=S)(OPh)$_2$}$_2$][PF_6] (5b) and [Cu{μ^2-*N*,*S*-(DAPTA)=NP(=S)(OR)$_2$}$_2$][PF_6] [R = Et (6a), Ph (6b)]

The new (iminophosphorane)copper(I) complexes **5b** and **6a**,**b** have been prepared by treatment of [Cu($NCCH_3$)$_4$]-[PF_6] with 2 equiv. of the corresponding iminophosphorane ligand **3b**,**4a**,**b** in dichloromethane at room temperature (see Scheme 4). All complexes were isolated as air-stable white solids in 73–79% yield. In accordance with the hydrosolu-



Scheme 4. Synthesis of the copper(I) complexes **5**,**6a**,**b**.

bility of the iminophosphorane ligand **4a**, the corresponding copper(I) complex **6a** was also found to be soluble in water (384 mg/mL vs. 219 mg/mL for **5a**) and to behave as 1:1 electrolyte in aqueous solution (Ω_M = 109 vs. 117 Ω^{-1} cm^2 mol^{-1} for **5a**). In contrast, complexes **5b** and **6b** were scarcely soluble in water. Complexes **5b**,**6a**,**b** have been characterized by means of standard spectroscopic techniques [IR and $^{31}P\{^1H\}$, ^1H, and $^{13}C\{^1H\}$ NMR] and elemental analysis, which support the proposed formulations (Experimental Section).

Spectroscopic data are particularly relevant for the determination of the ligands' coordination modes, which are consistent with the *S*-coordination of the thiophosphoryl fragment [$(RO)_2P{=}S$] and with the *N*-coordination of one nitrogen atom from the adamantane ring. These features are clearly reflected in their $^{31}P\{^1H\}$ NMR spectra by: (i) slight variations in the P=N ($\Delta\delta$ = 2–6 ppm) and $(RO)_2P{=}S$ ($\Delta\delta$ = 2–5 ppm) resonances, and (ii) conversion of the doublet signals of the P=N and $(RO)_2P{=}S$ groups in the free ligand into two broad singlets in complexes **5a**,**b**. As expected, ^1H and the $^{13}C\{^1H\}$ NMR spectra display the corresponding phosphane backbone signals of PTA and DAPTA. The observed preference for the *S*- vs. *N*-coordination of the iminophosphoranyl units P=N–P(=S)(OR)$_2$ in complexes **5b**,**6a**,**b** is in complete accord with the known coordination chemistry of *N*-thiophosphorylated iminophosphoranes $R_3P{=}N{-}P{=}S(OR')_2$, which is almost entirely dominated by the coordination of the sulfur atom.[24] As we have previously reported,[14] the real nature of these complexes could only be determined by single-crystal X-ray diffraction methods. These data confirmed that the coordination sphere around the copper atom consists of: (i) two *S*-coordinated $(EtO)_2P{=}S$ units, and (ii) two *N*-coordinated amino groups from the adamantane ring, displaying a distorted tetrahedral geometry. The X-ray analysis unambiguously confirmed the formation of a 14-membered ring CuSPNPCNCuSPNPCN, constructed by two Cu^I atoms bridged by two ligands in a head-to-tail conformation (see Scheme 4). The tetracoordinate copper(I) atoms allowed for connection of two 14-membered rings giving rise to a polymeric chain.

Chemical Speciation in Water: ESI Mass Spectrometry and DFT Analysis

In order to gain more information about the integrity and nature of the species present in aqueous solution, mass spectrometric measurements (ESI-MS) of a solution of **5a** in water were performed.[25] Positive ESI mass spectra recorded upon gentle ionization conditions (cone voltage U_c = 10 V) revealed a monomeric species $[Cu\{(PTA){=}NP(=S)(OEt)_2\}_2]^+$ with *m*/*z* = 711 as the base peak. Assignment was based on the *m*/*z* value as well as its characteristic isotopic pattern (see Figure SI-1 in Supporting Information). Additional ESI mass spectra were collected upon varying the ionization conditions [typically the cone voltage (U_c) in the U_c = 5–35 V range]. It is interesting to note that polynuclear or loosely solvated aquo complexes were not observed in these ESI mass spectra, thus suggesting that, unlike in the solid state, complex **5a** is dismantled in the aqueous solution to give predominantly the monomeric complex $[Cu\{(PTA){=}NP(=S)(OEt)_2\}_2]^+$. Since three coordination isomers can be proposed for these monomeric species, namely $[Cu\{\kappa^1\text{-}S\text{-}(PTA){=}NP(=S)(OEt)_2\}_2]^+$ (**I**), $[Cu\{\kappa^1\text{-}S\text{-}(PTA){=}NP(=S)(OEt)_2\}\{\kappa^1\text{-}N\text{-}(PTA){=}NP(=S)(OEt)_2\}]^+$ (**II**) and $[Cu\{\kappa^1\text{-}N\text{-}(PTA){=}NP(=S)(OEt)_2\}_2]^+$ (**III**) (see Figure 3), theoretical calculations on the relative stabi-

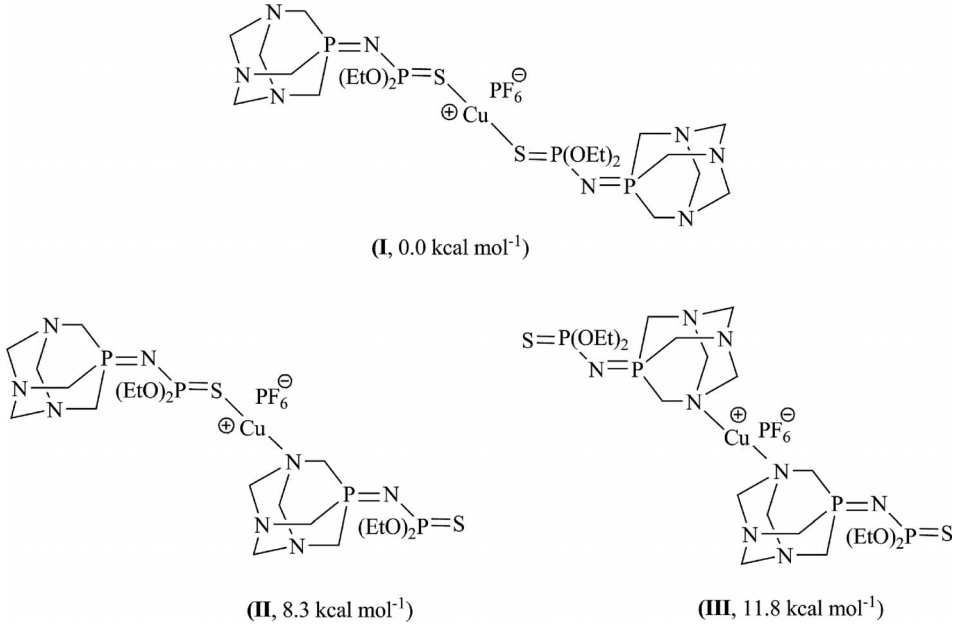


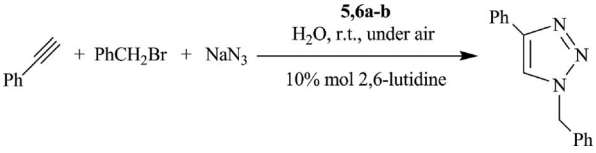
Figure 3. Structure of the three coordination isomers proposed $[Cu\{\kappa^1\text{-}S\text{-}(PTA){=}NP(=S)(OEt)_2\}_2]^+$ (**I**), $[Cu\{\kappa^1\text{-}S\text{-}(PTA){=}NP(=S)(OEt)_2\}\{\kappa^1\text{-}N\text{-}(PTA){=}NP(=S)(OEt)_2\}]^+$ (**II**) and $[Cu\{\kappa^1\text{-}N\text{-}(PTA){=}NP(=S)(OEt)_2\}_2]^+$ (**III**).

lization energies have been analyzed by B3LYP/6-31G(d) DFT studies (details are given in the Supporting Information). The theoretical data have been obtained using bond lengths and angles from the X-ray data of complex **5a**. Frequency calculations for the optimized geometries have been performed and are consistent with minima on the potential energy surface. In this theoretical study, we found that the isomer $[Cu\{\kappa^1\text{-}S\text{-}(PTA)=NP(=S)(OEt)_2\}_2]^+$ (**I**) with a selective κ^1-*S* coordination of the ligand **3a** is: (i) 8.3 kcal mol^{-1} more stable than the mixed κ^1-*S*,κ^1-*N*-monomer $[Cu\{\kappa^1\text{-}S\text{-}(PTA)=NP(=S)(OEt)_2\}\{\kappa^1\text{-}N\text{-}(PTA)=NP(=S)(OEt)_2\}]^+$ (**II**), and (ii) 11.8 kcal mol^{-1} more stable than the κ^1-*N*-monomer $[Cu\{\kappa^1\text{-}N\text{-}(PTA)=NP(=S)(OEt)_2\}_2]^+$ (**III**). This fact is in agreement with the relatively longer Cu–N bonds observed in complex **5a**, which apparently are easily cleaved in water.[14,26] It is apparent that these species are readily formed and therefore can be proposed as the active catalytic species in aqueous medium (see below).

Catalytic 1,3-Dipolar Cycloaddition of in Situ Generated Azides (Organic Halide and NaN_3) with Terminal Alkynes in Water

Due to the danger, difficulty in handling and isolation problems of low-molecular weight organic azides,[27] a number of methodologies have been developed for the synthesis of 1,4-disubstituted triazoles using [3+2] cycloadditions, avoiding the use of pre-isolated azides. In this regard, the use of a three-component reaction (organic halide, NaN_3 and terminal alkyne) catalyzed by different copper(I) species has been reported.[11a,12,13,28] Thus, inspired by these precedents, we tested the catalytic activity of complexes **5**,**6a**,**b** in three-component reactions of in situ generated azides and terminal alkynes under very mild reaction conditions (pure water as solvent, at room temperature and under aerobic conditions).[29] In a typical experiment, the multicomponent model reaction of benzyl bromide, NaN_3 and phenylacetylene was performed, using 0.5 mol-% of the complexes as catalyst loadings in the presence of 2,6-lutidine (2,6-dimethylpyridine).[30a] The course of the reaction was monitored by gas chromatography, and the results obtained are summarized in Table 1. To our satisfaction, all the complexes (Table 1, Entries 1–4) were found to be active and selective catalysts at room temperature, affording 4-phenyl-1-(phenylmethyl)-1*H*-1,2,3-triazole (**7a**) as the unique reaction product. The addition of an amine ligand to act as a base was crucial since no reaction was observed in its absence. Interestingly, the catalytic activity of complex **5a** (containing the ligand PTA-iminophosphorane) is higher than that of complex **6a** (containing the ligand DAPTA-iminophosphorane) (Table 1, Entries 1 and 3; 6 vs. 12 h, respectively). A similar catalytic trend has also been found in their water-insoluble counterpart catalysts **5b** and **6b** (Table 1, Entries 2 and 4; 15 vs. 17 h, respectively), demonstrating the influence of the iminophosphorane ligand on the reaction rate. The nature of the copper catalyst was crucial, as the efficiency of the reaction was markedly lower when complexes **5**,**6a**,**b** were replaced by other Cu^I sources such as CuI.[30b]

Table 1. One-pot multicomponent reaction of $PhCH_2Br$, NaN_3 and PhC≡CH catalyzed by complexes **5**,**6a**,**b** in water.[a]

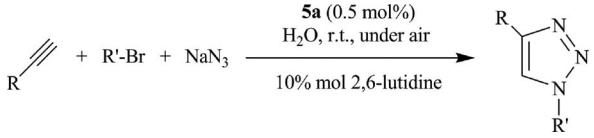


Entry	Catalyst	mol-% [Cu]	Time [h]	Yield [%][b]
1	**5a**	0.5	6	97
2	**5b**	0.5	15	99
3	**6a**	0.5	12	96
4	**6b**	0.5	17	99

[a] General conditions: 2,6-lutidine (10 mol-%), PhC≡CH (1 mmol), NaN_3 (1.1 mmol), $PhCH_2Br$ (1 mmol-%), water (2 mL), air, room temp. [b] Isolated yields.

The scope of applications for catalyst **5a** in the three-component reaction was investigated under the optimized reaction conditions (see Table 2). Thus, satisfactory catalytic activities have been found for a wide variety of alkynes containing a plethora of functional groups such as, alkyl (**7b**), hydroxy (**7c**), halide (**7d**), and ester (**7e**) substituents, which react with in situ generated benzyl azide leading with almost quantitative yields to the corresponding triazoles in 5–7 h. This catalytic methodology is also feasible for the synthesis of triazoles with different in situ generated azides. Satisfyingly, an array of activated organic bromides (Table 2, Entries 6–9) were tested leading nicely to the formation of corresponding triazoles in near quantitative yields bearing either electron-withdrawing (Table 2, Entry 7) or electron-donating groups (Table 2, Entries 8 and 9).

Table 2. One-pot multicomponent synthesis of 1,2,3-triazoles catalyzed by complex **5a** in water.[a]



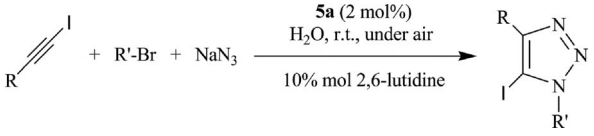
Entry	R	R′		Time [h]	Yield [%][b]
1	Ph	CH_2Ph	**7a**	6	97
2	*n*Bu	CH_2Ph	**7b**	7	95
3	$C(OH)Ph_2$	CH_2Ph	**7c**	7	97
4	*p*-FC_6H_4	CH_2Ph	**7d**	6	96
5	CO_2Et	CH_2Ph	**7e**	5	95
6	Ph	allyl	**7f**	4	96
7	Ph	3-Cl-$C_6H_4CH_2$	**7g**	8	94
8	Ph	3-Me-$C_6H_4CH_2$	**7h**	5	92
9	Ph	3-MeO-$C_6H_4CH_2$	**7i**	4	97

[a] General conditions: 2,6-lutidine (10 mol-%), alkyne (1 mmol), NaN_3 (1.1 mmol), R′–Br (1 mmol), H_2O (2 mL), air, room temp. [b] Isolated yields.

Catalytic 1,3-Dipolar Cycloaddition of in Situ Generated Azides (Organic Halide and NaN_3) with Internal 1-Iodoalkynes in Water

The formation of intermediates based on copper(I) acetylide species is postulated as the first step in CuAAC reactions.[31] In accordance with this proposed mechanism, internal alkynes are not able to undergo the required cycloaddition, a limitation generally observed with conventional copper catalysts.[32] As a matter of fact, only one example of an efficient catalytic system for chemo- and regioselective cycloaddition of azides with 1-iodoalkynes in an aqueous medium, namely the equimolar mixture of CuI and TTTA {TTTA = tris[(1-*tert*-butyl-1*H*-1,2,3-triazolyl)methyl]-amine},[15,33] has been described to date.[34] 5-Iodo-1,2,3-triazoles synthesized by application of this click reaction[35] are versatile synthetic intermediates amenable to further functionalization providing an appealing synthetic approach to different substituted 1,2,3-triazoles.[36] Taking into account the efficiency of **5a** in the three-component reaction of in situ generated azides and terminal alkynes, and our previously gained experience in the CuAAC of azides and 1-iodoalkynes in an aqueous medium,[14] we decided to focus our attention on the three-component reaction with iodoalkynes; as far as we are aware, such systems have not been previously reported. The reaction of benzyl bromide ($PhCH_2Br$), sodium azide (NaN_3) and PhC≡CI, in pure water, in air and at room temperature, was used as a model reaction. To our delight, this new process was catalyzed by **5a** (2 mol-%) affording chemoselectively (no by-products or products derived from reductive dehalogenation were detected by GC, i.e. 5-*H*-1,2,3-triazoles) the corresponding 5-iodo-1,2,3-triazole in excellent yield (Table 3, Entry 1). As in the aforementioned three-component reaction with terminal alkynes catalyzed by **5a**, the reaction tolerates a diverse array of functional groups in the 1-iodoalkyne (Table 3), including alkyl (**8b**), hydroxy (**8c**), fluoride (**8d**) and ester (**8e**) groups. Moreover, this catalytic system can also promote the cycloaddition reaction using different organic bromides (Table 3, Entries 6–9). Again, reactions proceeded to completion in water with both electron-withdrawing (Table 3, Entry 7) and electron-donating groups (Table 3, Entries 8 and 9), although longer reaction times were required, relative to their terminal counterparts. At this point, it is important to note that, as far as we are aware, no precedent for a multicomponent reaction using 1-iodoalkynes has been previously reported.

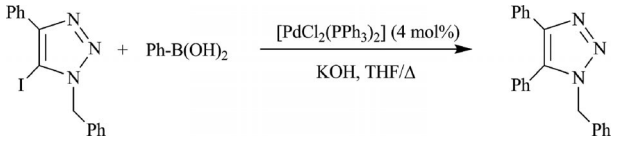
Table 3. One-pot multicomponent synthesis of 5-iodo-1,2,3-triazoles catalyzed by complex **5a** in water.[a]



Entry	R	R′		Time [h]	Yield [%][b]
1	Ph	CH_2Ph	**8a**	10	94
2	*n*Bu	CH_2Ph	**8b**	9	96
3	$C(OH)Ph_2$	CH_2Ph	**8c**	9	98
4	*p*-FC_6H_4	CH_2Ph	**8d**	8	93
5	CO_2Et	CH_2Ph	**8e**	7	95
6	Ph	allyl	**8f**	7	98
7	Ph	3-$ClC_6H_4CH_2$	**8g**	12	96
8	Ph	3-$MeC_6H_4CH_2$	**8h**	9	93
9	Ph	3-$MeOC_6H_4CH_2$	**8i**	9	94

[a] General conditions: 2,6-lutidine (10 mol-%), 1-iodoalkyne (1 mmol), NaN_3 (1.1 mmol), R′–Br (1 mmol), H_2O (2 mL), air, room temp. [b] Isolated yields.

As expected, the 5-iodo-1,2,3-triazole **8a** was subsequently functionalized easily using a Suzuki cross-coupling reaction with the organoboronic acid $PhB(OH)_2$; the corresponding 1-benzyl-4,5-diphenyl-1*H*-1,2,3-triazole was generated in almost quantitative yield (95%) (Scheme 5). This result clearly shows that 5-iodo-1,2,3-triazoles can be readily functionalized by cross-coupling reactions and confirms their utility for construction of new organic derivatives.[37]



Scheme 5. Suzuki cross coupling of 5-iodotriazole **8a** with $PhB(OH)_2$.

Conclusions

In the present work we have described a high-yielding synthesis of new *N*-thiophosphorylated iminophosphorane ligands **3b**,**4a**,**b** and their corresponding copper(I) complexes **5b**,**6a**,**b** in which these heterodifunctional ligands adopt a bridging μ^2-(*N*,*S*) coordination mode giving rise to a polymeric structure in the solid state. These complexes, along with partner complex **5a**, are efficient catalysts in multicomponent one-pot CuAAC reactions in water of in situ generated azides with alkynes to selectively afford 1,2,3-triazoles. The following features are noteworthy. (i) The high stability of these copper(I) complexes precludes their oxidation or disproportionation, which allows the catalytic reactions to be performed in the presence of air and in aqueous media. This property represents an important contribution to click chemistry, since these processes are generally associated with most polyamine copper(I) catalysts in CuAAC reactions. (ii) Complex **5a** is a highly efficient catalyst for one-pot three-component reactions in aqueous media (organic halide, NaN_3 and alkynes) under mild and aerobic conditions displaying broad substrate scope and functional compatibility. (iii) Complex **5a** is the first example of an isolated and crystallographically characterized copper(I) pre-catalyst active in the multicomponent CuAAC reactions of 1-iodoalkynes in water in a one-pot manner to give exclusively 5-iodo-1,2,3-triazoles according to "click" laws. (iv) 5-Iodo-1,2,3-triazole **8a** was successfully used in a palladium-catalyzed cross-coupling reaction with an organo-

boronic acid, demonstrating that this methodology is amenable to further functionalizations of synthetic interest.

Experimental Section

General Methods: Synthetic procedures were performed under dry nitrogen using vacuum-line and standard Schlenk techniques. Solvents were dried by standard methods and distilled under nitrogen before use. All reagents were obtained from commercial suppliers and used without further purification with the exception of compounds DAPTA[19] and $N_3P(=S)(OR)_2$ (R = Et, Ph),[38] which were prepared by applying the method reported in the literature. Infrared spectra were recorded with a Perkin–Elmer 1720-XFT spectrometer. The conductivities were measured at room temp., in ca. 10^{-3} mol dm^{-3} acetone or water solutions, with a Jenway PCM3 conductimeter. The C, H and N analyses were carried out with a Perkin–Elmer 2400 microanalyzer. NMR spectra were recorded using a Bruker DPX300 instrument at 300 MHz (^{1}H), 121.5 MHz (^{31}P) or 75.4 MHz (^{13}C) using $SiMe_4$ or 85% H_3PO_4 as standards. DEPT experiments have been carried out for all the compounds reported in this paper. For electrospray ionization mass spectrometry (ESI-MS) studies, a QTOF Premier instrument with an orthogonal Z-spray-electrospray interface (Waters, Manchester, UK) was used operating in the W-mode at a resolution of ca. 15000 (FWHM). The drying and cone gas was nitrogen set to flow rates of 300 and 30 L/h, respectively. A capillary voltage of 3.5 kV was used in the positive scan mode, and the cone voltage varied in the U_c = 5–35 V range. CCDC-891690 (for **3b**), and -891691 (for **4b**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

General Procedure for the Synthesis of the *N*-Thiophosphorylated Iminophosphorane Ligands (PTA)=NP(=S)(OPh)$_2$ (3b) and (DAPTA)=NP(=S)(OR)$_2$ [R = Et (4a), Ph (4b)]: For **3b**, a solution of the water-soluble phosphane ligand PTA (0.314 g, 2 mmol) in THF (40 mL) was treated with the thiophosphorylated azide $N_3P=S(OPh)_2$ (2.1 mmol) at room temp. for 4 h. Then, the solvent was evaporated to dryness to give a colourless oil, which was dissolved in CH_2Cl_2 (ca. 5 mL). The addition of diethyl ether (ca. 50 mL) precipitated a white microcrystalline solid, which was washed with diethyl ether (3 × 10 mL) and dried in vacuo. For **4a**,**b**, a solution of the phosphane ligand DAPTA (0.458 g, 2 mmol) in THF (40 mL) was refluxed in the presence of the corresponding thiophosphorylated azide $N_3P=S(OR)_2$ (R = Et, Ph) (2.1 mmol) for 6 h. Again, the solvent was removed under vacuum to yield a colourless oil, which was dissolved in CH_2Cl_2 (ca. 5 mL). The addition of diethyl ether (ca. 50 mL) precipitated a white microcrystalline solid, which was washed with diethyl ether (3 × 10 mL), and dried in vacuo. **3b**: Yield 79% (0.664 g). $C_{18}H_{22}N_4O_2P_2S$ (420.40): calcd. C 51.42, H 5.27, N 13.33; found C 51.51, H 5.20, N 13.39. IR (KBr): $\tilde{\nu}$ = 461, 494, 539, 565, 581, 607, 631, 668, 692, 736, 759, 768, 782, 816, 840, 898, 921, 971, 1009, 1032, 1071, 1090, 1167, 1194, 1233, 1248, 1271, 1286, 1359, 1409, 1440, 1452, 1488, 1590, 1653, 1749, 1816, 1869, 1941, 2874, 2912, 2931, 2951, 3057 cm^{-1}. ^{31}P{^{1}H} NMR (121.5 MHz, CD_2Cl_2): δ = –34.27 (d, $^2J_{PP}$ = 14.7 Hz, P=N), 55.64 [d, $^2J_{PP}$ = 14.7 Hz, $(PhO)_2P=S$] ppm. ^{1}H NMR (300 MHz, CD_2Cl_2): δ = 3.97 (d, $^2J_{HP}$ = 9.2 Hz, 6 H, PCH_2N), 4.12 and 4.30 (AB spin system, $J_{HA,HB}$ = 13.4 Hz, 3 H each, NCH_2N), 7.16–7.38 (m, 10 H, CH_{arom}) ppm. ^{13}C{^{1}H} NMR (75.4 MHz, CD_2Cl_2): δ = 53.92 (dd, $^1J_{CP}$ = 51.9, $^3J_{CP}$ = 3.7 Hz, PCH_2N), 72.25 (d, $^3J_{CP}$ = 9.5 Hz, NCH_2N), 120.25–129.81 (m, CH_{arom}), 151.76 (d, $^2J_{CP}$ = 9.5 Hz, C_{ipso} of OPh) ppm. **4a**: Yield 86% (0.681 g). $C_{13}H_{26}N_4O_4P_2S$ (396.38): calcd. C 39.39, H 6.61, N 14.13; found C 39.30, H 6.57, N 14.15. IR (KBr): $\tilde{\nu}$ = 464, 483, 518, 560, 592, 624, 668, 702, 780, 838, 894, 951, 990, 1042, 1094, 1123, 1161, 1223, 1258, 1300, 1332, 1355, 1422, 1651, 2140, 2360, 2898, 2931, 2978 cm^{-1}. ^{31}P{^{1}H} NMR (121.5 MHz, D_2O): δ = –12.40 (d, $^2J_{PP}$ = 6.7 Hz, P=N), 60.58 [d, $^2J_{PP}$ = 6.7 Hz, $(EtO)_2P=S$] ppm. ^{1}H NMR (300 MHz, D_2O): δ = 1.36 (t, $^3J_{HH}$ = 7.0 Hz, 6 H, OCH_2CH_3), 2.18 and 2.19 (s, 3 H each, $COCH_3$), 3.84 (m, 1 H, NCH_2N), 4.22 (m, 8 H, 4 H for OCH_2CH_3 and 4 H for PCH_2NCO), 4.67, 5.16, 5.64 (d, J_{HH} = 14.3 Hz, 1 H, each, NCH_2N), 4.91 and 5.57 (m, 1 H, each, PCH_2N) ppm. ^{13}C{^{1}H} NMR (75.4 MHz, D_2O): δ = 14.91 (d, $^3J_{CP}$ = 8.2 Hz, OCH_2CH_3), 20.47 and 20.27 (s, $COCH_3$), 39.49 (dd, $^1J_{CP}$ = 70.0, $^3J_{CP}$ = 4.3 Hz, PCH_2N), 44.63 (dd, $^1J_{CP}$ = 68.4, $^3J_{CP}$ = 4.5 Hz, PCH_2N), 49.14 (dd, $^1J_{CP}$ = 60.7, $^3J_{CP}$ = 3.5 Hz, PCH_2N), 61.20 (d, $^3J_{CP}$ = 7.1 Hz, NCH_2N), 63.41 (d, $^2J_{CP}$ = 6.4 Hz, OCH_2CH_3), 66.22 (d, $^3J_{CP}$ = 6.7 Hz, NCH_2N), 171.81 and 172.46 (d, $^3J_{CP}$ = 2.5 Hz, $COCH_3$) ppm. **4b**: Yield 83% (0.817 g). $C_{21}H_{26}N_4O_4P_2S$ (492.47): calcd. C 51.22, H 5.32, N 11.38; found C 51.26, H 5.37, N 11.34. IR (KBr): $\tilde{\nu}$ = 464, 488, 517, 555, 575, 599, 618, 690, 705, 743, 782, 839, 878, 891, 907, 931, 945, 988, 1022, 1041, 1070, 1095, 1123, 1162, 1200, 1243, 1267, 1306, 1320, 1349, 1378, 1397, 1421, 1460, 1484, 1585, 1633, 1652, 1898, 1965, 2893, 2989, 3008, 3066 cm^{-1}. ^{31}P{^{1}H} NMR (121.5 MHz, CD_2Cl_2): δ = –18.66 (d, $^2J_{PP}$ = 24.8 Hz, P=N), 52.72 [d, $^2J_{PP}$ = 24.8 Hz, $(PhO)_2P=S$] ppm. ^{1}H NMR (300 MHz, CD_2Cl_2): δ = 2.01 and 2.06 (s, 3 H each, $COCH_3$), 3.38, 4.83 and 5.63 (d, J_{HH} = 14.0 Hz, 1 H, each, NCH_2N), 4.34 (m, 2 H, 1 H, for NCH_2N and 1 H, for PCH_2N), 3.88 (m, 4 H, PCH_2NCO), 5.47 (m, 1 H, PCH_2N), 6.86–7.40 (m, 10 H, CH_{arom}) ppm. ^{13}C{^{1}H} NMR (75.4 MHz, CD_2Cl_2): δ = 21.00 and 21.36 (s, $COCH_3$), 40.02 (dd, $^1J_{CP}$ = 73.5, $^3J_{CP}$ = 5.6 Hz, PCH_2N), 45.02 (dd, $^1J_{CP}$ = 68.6, $^3J_{CP}$ = 5.2 Hz, PCH_2N), 51.01 (d, $^1J_{CP}$ = 58.3 Hz, PCH_2N), 61.60 (d, $^3J_{CP}$ = 7.2 Hz, NCH_2N), 66.66 (d, $^3J_{CP}$ = 6.4 Hz, NCH_2N), 115.32–129.53 (m, CH_{arom}), 151.50 (d, $^2J_{CP}$ = 8.8 Hz, C_{ipso} of OPh), 151.56 (d, $^2J_{CP}$ = 5.9 Hz, C_{ipso} of OPh), 169.32 and 169.82 (s, $COCH_3$) ppm.

Synthesis of [Cu{μ^2-*N*,*S*-(PTA)=NP(=S)(OPh)$_2$}][SbF$_6$] (5b) and [Cu{μ^2-*N*,*S*-(DAPTA)=NP(=S)(OR)$_2$}][SbF$_6$] [R = Et (6a), Ph (6b)]: A solution of the corresponding iminophosphorane ligand **3b** or **4a**,**b** (2 mmol) in CH_2Cl_2 (30 mL) was treated with $[Cu(NCCH_3)_4][PF_6]$ (0.343 g, 1 mmol) and stirred for 1 h to yield a pale-yellow clear solution. The mixture was then concentrated (ca. 1 mL) in vacuo and the addition of diethyl ether (ca. 50 mL) precipitated a white solid, which washed with diethyl ether (3 × 10 mL) and dried in vacuo. **5b**: Yield 75% (0.786 g). $CuC_{36}H_{44}F_6N_8O_4P_5S_2$ (1049.32): calcd. C 41.21, H 4.23, N 10.68; found C 41.31, H 4.27, N 10.61. Conductivity (acetone, 20 °C): 109 Ω^{-1} cm^2 mol^{-1}. IR (KBr): $\tilde{\nu}$ = 454, 484, 495, 559, 578, 607, 628, 631, 669, 691, 736, 769, 838, 899, 921, 1009, 1024, 1071, 1097, 1167, 1196, 1229, 1250, 1271, 1288, 1359, 1409, 1453, 1488, 1590, 1629, 2872, 2934, 2959, 3059 cm^{-1}. ^{31}P{^{1}H} NMR [121.5 MHz, $(CD_3)_2C=O$]: δ = –143.88 (sept, J_{PF} = 707.2 Hz, PF_6), –32.80 (br. s, P=N), 50.88 [br. s, $(PhO)_2P=S$] ppm. ^{1}H NMR [300 MHz, $(CD_3)_2C=O$]: δ = 4.10 (br. s, 6 H, PCH_2N), 4.16 and 4.37 (AB spin system, $J_{HA,HB}$ = 10.7 Hz, 3 H each, NCH_2N), 7.20–7.43 (m, 10 H, CH_{arom}) ppm. ^{13}C{^{1}H} NMR [75.4 MHz, $(CD_3)_2C=O$]: δ = 53.29 (br. s, PCH_2N), 71.70 (br. s, NCH_2N), 122.00–129.96 (m, CH_{arom}), 152.14 (d, $^2J_{CP}$ = 9.5 Hz, C_{ipso} of OPh) ppm. **6a**: Yield 79% (0.791 g). $CuC_{26}H_{52}F_6N_8O_8P_5S_2$ (1001.27): calcd. C 31.19, H 5.23, N 11.19; found C 31.24, H 5.30, N 11.24. Conductivity (water, 20 °C): 115 Ω^{-1} cm^2 mol^{-1}. IR (KBr): $\tilde{\nu}$ = 474, 483, 500, 529, 557, 603, 625, 706, 743, 786, 804, 841, 877, 904, 960, 991, 1022, 1096, 1124, 1161, 1192, 1234, 1263, 1301, 1343,

1364, 1431, 1651, 1718, 2905, 2933, 2985 cm^{-1}. $^{31}P\{^1H\}$ NMR [121.5 MHz, $(CD_3)_2C=O$]: δ = –144.30 (sept, J_{PF} = 707.5 Hz, PF_6), –16.65 (d, $^2J_{PP}$ = 9.9 Hz, P=N), 54.80 [d, $^2J_{PP}$ = 9.9 Hz, $(EtO)_2P=S$] ppm. ^1H NMR [300 MHz, $(CD_3)_2C=O$]: δ = 1.30 (t, $^3J_{HH}$ = 6.8 Hz, 6 H, OCH_2CH_3), 2.06 and 2.09 (s, 3 H each, $COCH_3$), 3.85 (m, 1 H, NCH_2N), 4.07 (m, 4 H, OCH_2CH_3), 4.33 (m, 4 H, PCH_2NCO), 4.67 and 5.06 (d, J_{HH} = 13.7 Hz, 1 H, each, NCH_2N), 4.84 (m, 1 H, PCH_2N), 5.63 (m, 2 H, 1 H, for NCH_2N and 1 H, for PCH_2N) ppm. $^{13}C\{^1H\}$ NMR [75.4 MHz, $(CD_3)_2C=O$]: δ = 17.48 (d, $^3J_{CP}$ = 8.5 Hz, OCH_2CH_3), 22.64 and 23.07 (s, $COCH_3$), 42.10 (dd, $^1J_{CP}$ = 70.5, $^3J_{CP}$ = 2.7 Hz, PCH_2N), 47.37 (dd, $^1J_{CP}$ = 70.5, $^3J_{CP}$ = 4.3 Hz, PCH_2N), 52.43 (dd, $^1J_{CP}$ = 59.3, $^3J_{CP}$ = 1.6 Hz, PCH_2N), 63.00 (d, $^3J_{CP}$ = 7 Hz, NCH_2N), 65.09 (d, $^2J_{CP}$ = 6.9 Hz, OCH_2CH_3), 68.26 (d, $^3J_{CP}$ = 6.9 Hz, NCH_2N), 170.88 (s, $COCH_3$), 171.28 (d, $^3J_{CP}$ = 2.1 Hz, $COCH_3$) ppm. **6b**: Yield 73% (0.871 g). $CuC_{42}H_{52}F_6N_8O_8P_5S_2$ (1193.44): calcd. C 42.27, H 4.39, N 9.39; found C 42.35, H 4.42, N 9.43. Conductivity (acetone, 20 °C): 109 $\Omega^{-1}cm^2mol^{-1}$. IR (KBr): $\tilde{\nu}$ = 462, 499, 558, 617, 691, 739, 778, 843, 896, 921, 993, 1024, 1043, 1070, 1091, 1124, 1160, 1193, 1228, 1261, 1303, 1335, 1349, 1407, 1429, 1488, 1652, 2925, 2960 cm^{-1}. $^{31}P\{^1H\}$ NMR [121.5 MHz, $(CD_3)_2C=O$]: δ = –144.16 (sept, J_{PF} = 707.1 Hz, PF_6), –14.89 (d, $^2J_{PP}$ = 9.8 Hz, P=N), 54.42 [d, $^2J_{PP}$ = 9.8 Hz, $(RO)_2P=S$] ppm. ^1H NMR [300 MHz, $(CD_3)_2C=O$]: δ = 1.99 and 2.02 (s, 3 H each, $COCH_3$), 3.52 (m, 1 H, NCH_2N), 4.07 (m, 4 H, PCH_2NCO), 4.58 (m, 2 H, 1 H, for NCH_2N and 1 H, for PCH_2N), 4.99 and 5.59 (d, J_{HH} = 14.1 Hz, 1 H, NCH_2N), 5.47 (m, 1 H, PCH_2N), 7.18–7.40 (m, 10 H, CH_{arom}) ppm. $^{13}C\{^1H\}$ NMR [75.4 MHz, $(CD_3)_2C=O$]: δ = 21.04 and 21.42 (s, $COCH_3$), 40.04 (dd, $^1J_{CP}$ = 70.5, $^3J_{CP}$ = 3.2 Hz, PCH_2N), 45.23 (dd, $^1J_{CP}$ = 69.1, $^3J_{CP}$ = 4.0 Hz, PCH_2N), 50.81 (dd, $^1J_{CP}$ = 60.4, $^3J_{CP}$ = 2.7 Hz, PCH_2N), 61.54 and 66.77 (d, $^3J_{CP}$ = 7.4 Hz, NCH_2N), 122.04–129.80 (m, CH_{arom}), 152.32 (d, $^2J_{CP}$ = 7.9 Hz, C_{ipso} of OPh), 152.37 (d, $^2J_{CP}$ = 8.5 Hz, C_{ipso} of OPh), 169.29 (d, $^3J_{CP}$ = 2.1 Hz, $COCH_3$), 169.71 (d, $^3J_{CP}$ = 1.6 Hz, $COCH_3$) ppm.

Typical Procedure for the Synthesis of 1,2,3-Triazoles Using a Three-Component Reaction; Synthesis of 1-Benzyl-4-phenyl-1*H*-1,2,3-triazole (7a): Catalyst **5a** (0.0042 g, 0.5 mol-%) was dissolved in H_2O (2 mL) in air. Phenylacetylene (1 mmol, 0.110 mL), NaN_3 (1.1 mmol, 0.0072 g) and benzyl bromide (1 mmol, 0.119 mL) were added in the presence of 2,6-lutidine (0.012 mL, 10 mol-%). The course of the reaction was monitored by regular sampling and analysis by NMR spectroscopy and GC. The mixture was stirred at room temp. for 6 h, after which time a yellow oil had formed. The crude of the reaction was washed with CH_2Cl_2 (3 × 10 mL), and the combined organic fractions were concentrated by solvent evaporation to give **7a** as a yellow oil (0.228 g, 97%).

Typical Procedure for the Synthesis of 5-Iodo-1,2,3-triazoles Using a Three-Component Reaction; Synthesis of 5-Iodo-4-phenyl-1-(phenylmethyl)-1*H*-1,2,3-triazole (8a): Catalyst **5a** (0.0168 g, 2 mol-%) was dissolved in H_2O (2 mL) in air. 1-Iodo-2-phenylacetylene (1 mmol, 0.228 g), NaN_3 (1.1 mmol, 0.0072 g) and benzyl bromide (1 mmol, 0.119 mL) were added in the presence of 2,6-lutidine (0.012 mL, 10 mol-%). The mixture was stirred at room temp. for 10 h, after which time a yellow powder had formed. The crude of the reaction was washed with CH_2Cl_2 (3 × 10 mL), and the combined organic fractions were concentrated by solvent evaporation to give **8a** as a white solid (0.339 g, 94%).

Supporting Information (see footnote on the first page of this article): ESI mass spectrum of aqueous solutions of **5a**; Cartesian coordinates, total electronic energies and figures of coordination isomers **I**, **II** and **III** for $[Cu\{(PTA)=NP(=S)(OEt)_2\}_2]^+$; crystallographic data for **3b** and **4b**.

Acknowledgments

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[1] Catalytic processes in water are genuine examples of green chemistry. For fundamental principles see, for example: a) P. T. Anastas, J. C. Warner in *Green Chemistry: Theory and Practice*, Oxford University Press, Oxford, **1998**; b) A. S. Matlack in *Introduction to Green Chemistry*, Marcel Dekker, New York, **2001**; c) M. Lancaster in *Green Chemistry: An Introductory Text*, RSC Editions, London, **2002**.

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[4] Click chemistry has found wide chemical applications in many fields like synthetic and medicinal chemistry, bioconjugations, materials science and polymer chemistry. For reviews in this field, see for example: a) *Macromol. Rapid Commun.* **2008**, *29*, 943, special thematic issue; b) *QSAR Comb. Sci.* **2007**, *26*, 1110, special thematic issue; c) Y. L. Angell, K. Burgess, *Chem. Soc. Rev.* **2007**, *36*, 1674–1689; d) J. E. Moses, A. D. Moorhouse, *Chem. Soc. Rev.* **2007**, *36*, 1249–1262; e) J.-F. Lutz, *Angew. Chem.* **2007**, *119*, 1036; *Angew. Chem. Int. Ed.* **2007**, *46*, 1018–1025; f) P. Wu, V. V. Fokin, *Aldrichim. Acta* **2007**, *40*, 7–17; g) J. Broggi, S. Díez-González, J. L. Petersen, S. Berteina-Raboin, S. P. Nolan, L. Agrofoglio, *Synthesis* **2008**, 141–148; h) C. O. Kappe, E. Van der Eicken, *Chem. Soc. Rev.* **2010**, *39*, 1325–1337; i) C. Spiteri, J. E. Moses, *Angew. Chem.* **2010**, *122*, 33; *Angew. Chem. Int. Ed.* **2010**, *49*, 31–33; j) J. E. Hein, V. V. Fokin, *Chem. Soc. Rev.* **2010**, *39*, 1302–1315; k) *Chem. Asian J.* **2011**, *6*, special thematic issue.

[5] For reactions to be considered "click" they must fulfill a number of basic requirements: (i) they must demonstrate no sensitivity towards moisture or oxygen, (ii) they must afford products in high yields and with stereospecificity, and (iii) they must proceed in the absence of solvent (or use of a benign one) and lend themselves to simple product isolation.

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[8] In contrast to the classical 1,3-dipolar cycloadditions (Huisgen reactions), displaying a strong thermodynamic driving force, which leads to mixtures of regioisomers usually obtained under

thermal conditions; a) R. Huisgen, *Proc. Chem. Soc.* **1961**, 357–369; b) *1,3-Dipolar Cycloaddition Chemistry* (Eds.: R. Huisgen, A. Pawda), Wiley, New York, **1984**, p. 1; c) R. Huisgen, *Pure Appl. Chem.* **1989**, *61*, 613–628.

[9] In regards to this consideration, the application of the concept of atom economy (term used to describe the complete transformations of all atoms of the reactants into the final product) has become one of the most desirable goals in chemical reactions. See, for example: a) B. M. Trost, *Science* **1991**, *254*, 1471–1477; b) B. M. Trost, *Angew. Chem.* **1995**, *107*, 285; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 259–281; c) R. A. Sheldon, *Pure Appl. Chem.* **2000**, *72*, 1233–1246; d) B. M. Trost, *Acc. Chem. Res.* **2002**, *35*, 695–705; e) B. M. Trost, M. U. Frederiksen, M. T. Rudd, *Angew. Chem.* **2005**, *117*, 6788; *Angew. Chem. Int. Ed.* **2005**, *44*, 6630–6666; f) R. A. Sheldon, *Green Chem.* **2007**, *9*, 1273–1283.

[10] Most of the reactions proceed either in organic solvents or mixtures with water (i.e. water/*t*BuOH) using catalytic active species generated in situ (traditionally a mixture of $CuSO_4$ and sodium ascorbate is used) with concomitant addition of an excess of *N*-polydentate ligands, usually necessary to achieve optimal catalytic performances. See, for example: a) V. O. Rodionov, S. I. Preloski, S. Gardinier, Y.-H. Lim, M. G. Finn, *J. Am. Chem. Soc.* **2007**, *129*, 12696–12704; b) V. O. Rodionov, S. I. Preloski, D. Díaz Díaz, V. V. Fokin, M. G. Finn, *J. Am. Chem. Soc.* **2007**, *129*, 12705–12712. For an isolated complex of this type, see: c) N. Candelon, D. Lastérouères, A. K. Diallo, J. Ruiz Aranzanes, D. Astruc, J.-M. Vincent, *Chem. Commun.* **2008**, 741–743. For isolated complexes containing the ligand Tpm*Br [tris(3,5-dimethyl-4-bromopyrazolyl)methane], see: d) I. Cano, M. C. Nicasio, P. J. Perez, *Org. Biomol. Chem.* **2010**, *8*, 536–538; e) I. Cano, E. Alvarez, M. C. Nicasio, P. J. Perez, *J. Am. Chem. Soc.* **2011**, *133*, 191–193. For a recent review on well-defined copper(I) catalysts see: f) S. Díez-González, *Catal. Sci. Technol.* **2011**, *1*, 166–178.

[11] a) S. Díez-González, A. Correa, L. Cavallo, S. P. Nolan, *Chem. Eur. J.* **2006**, *12*, 7558–7564; b) S. Díez-González, S. P. Nolan, *Angew. Chem.* **2008**, *120*, 9013; *Angew. Chem. Int. Ed.* **2008**, *47*, 8881–8884; c) S. Díez-González, E. D. Stevens, S. P. Nolan, *Chem. Commun.* **2008**, 4747–4749; d) W. Wang, J. Wu, C. Xia, F. Li, *Green Chem.* **2011**, *13*, 3440–3445.

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[15] a) J. E. Hein, J. C. Tripp, L. B. Krasnova, K. B. Sharpless, V. V. Fokin, *Angew. Chem.* **2009**, *121*, 8162; *Angew. Chem. Int. Ed.* **2009**, *48*, 8018–8021; b) E. Schwartz, K. Breitenkamp, V. V. Fokin, *Macromolecules* **2011**, *44*, 4735–4741; c) B. R. Buckley, S. E. Dann, H. Heaney, E. C. Stubbs, *Eur. J. Org. Chem.* **2011**, 770–776.

[16] a) N. Pinault, D. W. Bruce, *Coord. Chem. Rev.* **2003**, *241*, 1–25; b) A. D. Phillips, L. Gonsalvi, A. Romerosa, F. Vizza, M. Peruzzini, *Coord. Chem. Rev.* **2004**, *248*, 955–993; c) K. H. Shaughnessy, *Chem. Rev.* **2009**, *109*, 643–710; d) C. I. Herrerias, X. Yao, Z. Li, C.-J. Li, *Chem. Rev.* **2007**, *106*, 2546–2562; e) V. Cadierno, P. Crochet, *Advances in Organometallic Chemistry Research* (Ed.: K. Yamamoto), Nova Science Publishers, New York, **2007**, pp. 37–65.

[17] a) H. Staudinger, J. Meyer, *Helv. Chim. Acta* **1919**, *2*, 635–646. For reviews on the Staudinger reaction see: b) Y. G. Gololobov, I. N. Zhamurova, L. F. Kasukhin, *Tetrahedron* **1981**, *37*, 437–445; c) Y. G. Gololobov, L. F. Kasukhin, *Tetrahedron* **1992**, *48*, 1353–1406; d) A. W. Johnson in *Ylides and Imines of Phosphorous*, Wiley, New York, **1999**, p. 403.

[18] To the best of our knowledge, only one example, namely RN=PTA (R = Et, Ph), has been reported, and as far as we are aware, the coordination chemistry of this type of hydrosoluble ligands still remains unknown. M. Benhammou, R. Kraemer, H. Germa, J.-P. Majoral, J. Navech, *Phosphorus Sulfur Relat. Elem.* **1982**, *14*, 105.

[19] Iminophosphoranes derived from DAPTA are, to the best of our knowledge, unknown. The synthesis of its corresponding oxide [O=(DAPTA)] has been previously reported but, organometallic complexes containing this oxide ligand appear to be unpublished. D. J. Darensbourg, C. G. Ortiz, J. W. Kamplain, *Organometallics* **2004**, *23*, 1747–1754.

[20] A similar solubility trend has been previously reported in (η^6-arene)Ru^{II} complexes containing monodentate phosphanes or phosphites, as the reported ruthenium(II) complexes containing alkylphosphanes were soluble in water, whereas their aryl analogues were completely insoluble; a) B. Lastra-Barreira, P. Crochet, *Green Chem.* **2010**, *12*, 1311–1314; b) B. Lastra-Barreira, J. Francos, P. Crochet, V. Cadierno, *Green Chem.* **2011**, *13*, 307–313.

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[22] We have described a series of: (i) iminophosphorane–phosphane ligands $Ph_2PCH_2P\{=NP(=S)(OR)_2\}Ph_2$ (R = Et, Ph); (ii) bis(iminophosphorane)methane ligands $CH_2[P\{=NP(=S)(OR)_2\}Ph_2]_2$ (R = Et, Ph), and (iii) mixed (iminophosphoranyl)(thio- or selenaphosphoranyl)methane ligands $Ph_2P(=X)CH_2P\{=NP(=S)(OR)_2\}Ph_2$ (X = S, Se; R = Et, Ph) in: a) V. Cadierno, P. Crochet, J. Díez, J. García-Álvarez, S.-E. García-Garrido, S. García-Granda, J. Gimeno, M. A. Rodriguez, *Dalton Trans.* **2003**, 3240–3249; b) V. Cadierno, J. Díez, J. García-Álvarez, J. Gimeno, *Organometallics* **2004**, *23*, 3425–3436; c) V. Cadierno, J. Díez, J. García-Álvarez, J. Gimeno, *J. Organomet. Chem.* **2005**, *690*, 2087–2096; d) V. Cadierno, J. Díez, J. García-Álvarez, J. Gimeno, *Organometallics* **2008**, *27*, 1809–1822; e) V. Cadierno, J. Díez, J. García-Álvarez, J. Gimeno, *Dalton Trans.* **2010**, *39*, 941–956.

[23] Extensive electronic delocalization is a classical feature of *N*-thiophosphorylated iminophosphorane units $–P=N–P(=S)(OR)_2$. See, for example: a) V. Maraval, R. Laurent, B. Donnadieu, M. Mauzac, A.-M. Caminade, J.-P. Majoral, *J. Am. Chem. Soc.* **2000**, *122*, 2499–2511; b) G. Magro, B. Donnadieu, A.-M. Caminade, J.-P. Majoral, *Chem. Eur. J.* **2003**, *9*, 2151–2159. See also ref.[22]

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[25] ESI-MS has become an important technique in solution speciation studies related analysis of catalytic processes. See, for example: a) P. Chen, *Angew. Chem.* **2003**, *115*, 2938; *Angew. Chem. Int. Ed.* **2003**, *42*, 2832–2847; b) L. S. Santos, L. Knaack, J. O. Metzger, *Int. J. Mass Spectrom.* **2005**, *246*, 84–104; c) M. N. Eberlin, *Eur. J. Mass Spectrom.* **2007**, *13*, 19–28; d) L. S. Santos, *Eur. J. Org. Chem.* **2008**, 235–253; e) R. Jirasko, M. Holcapek, *Mass Spectrom. Rev.* **2011**, *30*, 1013–1036.

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[27] E. F. V. Scriven, K. Turnbull, *Chem. Rev.* **1988**, *88*, 297–368.

[28] a) S. Kamijo, T. Jin, Z. Huo, Y. Yamamoto, *J. Am. Chem. Soc.* **2003**, *125*, 7786–7787; b) S. Kamijo, T. Jin, Y. Yamamoto, *Tetrahedron Lett.* **2004**, *45*, 689–691; c) S. Kamijo, T. Jin, Z. Huo, Y. Yamamoto, *J. Org. Chem.* **2004**, *69*, 2386–2393; d) P. Appukkuttan, W. Dehaen, V. V. Fokin, E. Van der Eycken, *Org. Lett.* **2004**, *6*, 4223–4225; e) K. Kacpraz, *Synlett* **2005**, 943–946; f) S.-Q. Bai, L. Koh, T. S. A. Hor, *Inorg. Chem.* **2009**, *48*, 1207–1213; g) F. Li, T. S. A. Hor, *Chem. Eur. J.* **2009**, *15*, 10585–10592; h) T. Miao, L. Wang, *Synthesis* **2008**, 363–368; i) Z.-Y. Yan, L. Wang, *Synthesis* **2010**, 447–452.

[29] Water has been found previously to be the best solvent for this three-component transformation using the copper(I) complex $[CuBr(PPh_3)_3]$ as a catalyst (ref.[12]).

[30] a) The same reaction with benzyl chloride as an azide precursor also took place but requiring longer reaction times (99% yield, 24 h); b) using CuI in a 0.5 mol-% catalyst loading in water required longer reaction time (24 h) and yielded desired 1,4-disubstituted triazole **7a** in only 48% yield.

[31] a) F. Himo, T. Lovell, R. Hilgraf, V. V. Rostovtsev, L. Noodleman, K. B. Sharpless, V. V. Fokin, *J. Am. Chem. Soc.* **2005**, *127*, 210–216; b) V. D. Bock, H. Hiemstra, H. van Maarseveen, *Eur. J. Org. Chem.* **2006**, 51–68; c) B. R. Buckley, S. E. Dann, H. Heaney, *Chem. Eur. J.* **2010**, *16*, 6278–6284.

[32] Nevertheless, it has been reported that Cu catalyst can mediate the reaction of benzyl azide and 3-hexyne (see ref.[10c,11a]).

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[35] 5-Iodotriazoles can be also accessed through one-pot cycloaddition/iodination using stoichiometric amounts of copper derivatives and reactive electrophilic iodinating reagents: a) Y. Wu, M. J. Deng, Y. Li, Q.-Y. Chen, *Synthesis* **2005**, 1314–1318; b) L. Li, G. Zhang, A. Zhu, L. Zhang, *J. Org. Chem.* **2008**, *73*, 3630–3633; c) N. W. Smith, B. P. Polenz, S. B. Johnson, S. V. Dzyuba, *Tetrahedron Lett.* **2010**, *51*, 550–553; d) L. Li, Y. Li, R. Li, A. Zhu, G. Zhang, *Aust. J. Chem.* **2011**, *64*, 1383–1389.

[36] a) N. Chernyak, A. S. Dudnik, V. Gevorgyan, *Org. Lett.* **2007**, *9*, 2333–2336; b) S.-I. Fukuzawa, E. Shimizu, K. Ogata, *Heterocycles* **2009**, *78*, 645–655; c) M. Iwasaki, H. Yorimitsu, K. Oshima, *Chem. Asian J.* **2007**, *2*, 1430–1435; d) L. Ackermann, R. Vicente, R. Born, *Adv. Synth. Catal.* **2008**, *350*, 741–748; e) L. Ackermann, H. K. Potukuchi, D. Landsberg, R. Vicente, *Org. Lett.* **2008**, *10*, 3081–3084; f) L. Ackermann, H. K. Potukuchi, *Org. Biomol. Chem.* **2010**, *8*, 4503–4513; g) J. M. Schulman, A. A. Friedman, J. Panteleev, M. Lautens, *Chem. Commun.* **2012**, *48*, 55–57.

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