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Destabilizing Predictive Copper-Catalyzed Click Reactions by Remote Interactions with a Zinc-Porphyrin Backbone

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Dedicated to Prof. Janine Cossy on the occasion of her presidency at the 55th Bürgenstock Conference 2022

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Abstract: In order to obtain new supramolecular ligands build up around a zinc-porphyrin scaffold, we envisioned to access sulfonyl triazole intermediates by well-known copper-catalyzed click reactions. Unexpectedly, these triazole intermediates do not form due to the presence of the zinc-porphyrin moiety at close proximity of the active copper species. Indeed, the copper catalyst undergoes a different chemo-selective reaction pathway reacting with traces of alcohols or water from the media that behave as effective nucleophiles leading to sulfonyl imidates or sulfonyl amides covalently-connected to the zinc-porphyrin. We show that copper-catalyzed click reactions can undergo different reaction mechanisms when the catalytic events occur at close proximity of a zinc-porphyrin unit which likely acts as a Lewis acid to stabilize otherwise inaccessible reaction intermediates.

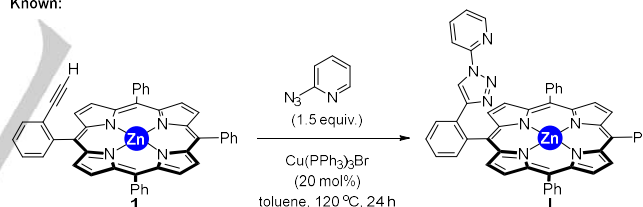
Introduction

Since the pioneering discoveries of Sharpless and Meldal, respectively,^[1-4] copper-catalyzed click reactions between azides and alkynes have found a large number of applications due to its perfect atom-economy, predictability and specificity, being compatible with many sensitive functional groups.^[5-21] In our laboratories, we have used copper-catalyzed click chemistry as a fundamental step in a reaction sequence to obtain a supramolecular ligand of formula **L** by treating the alkyne zinc-porphyrin **1** with 2-azidopyridine (**Figure 1**, top).^[22-23] Ligand **L** displays substrate-preorganization features since the zinc-porphyrin site serves for molecular recognition of nitrogen-containing substrates whereas the triazolopyridine fragment is able to coordinate by chelation catalytically active iridium sites leading to excellent levels of *meta*-selectivity when applied in iridium-catalyzed C-H bond borylation reactions.^[22-23] However, the access to 2-azidopyridine derivative reagents is not trivial due to tautomerism and many functional groups are not tolerated during the synthesis process starting from 2-bromopyridine derivatives.^[24-43] Consequently, and in view to obtain supramolecular ligands featuring different substitution patterns in the triazolopyridine site, we envisioned an alternative route that also involves copper-catalyzed click chemistry, but this time, relying on the treatment of **1** with tosyl azide and further stoichiometric reaction with pyridine *N*-oxides (**Figure 1**, bottom).^[44-46] However, as it is herein presented, the copper-catalyzed click reaction involving the alkyne zinc-porphyrin **1** with tosyl azide did not afford the expected compound **1'** but delivered products resulting from nucleophile addition such as sulfonyl

imidates or sulfonyl amides (**2**). Together with observations found in a number of control experiments, it appears that the zinc-porphyrin unit plays a key role in order to stabilize otherwise inaccessible reaction intermediates leading to the unexpected compounds.

In this context, it is relevant to note that sulfonyl imidates or sulfonyl amides may form during copper-catalyzed reactions between alkynes and tosyl azides, especially in the presence of excess water at relatively high temperatures,^[47-49] however in most examples it is observed together with the expected sulfonyl triazole compound,^[50-52] which is not the case of the present study by using zinc-porphyrins. On the other hand, the functionalization of metalloporphyrins by means of click chemistry involving alkyl and aryl azides is well known.^[53-57] Intriguingly, no examples of reacting alkyne-containing metalloporphyrins with tosyl azides have been reported to the best of our knowledge.

Known:



This work:

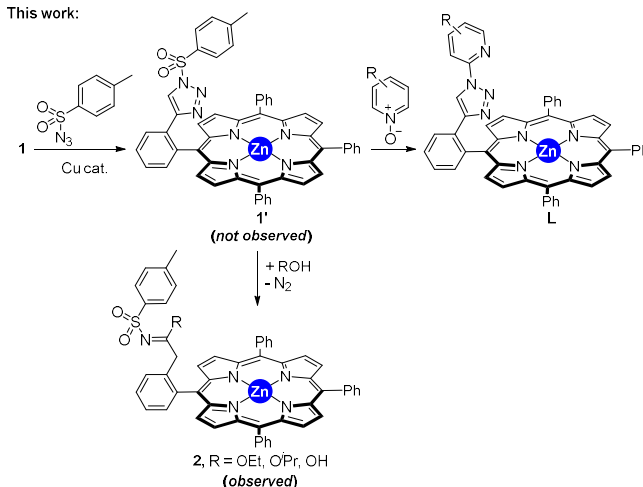
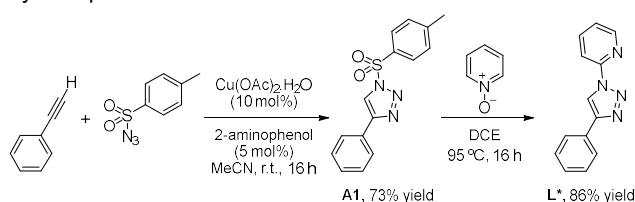


Figure 1. Previous route to access supramolecular ligand **L** (top) and newly-envisioned alternative route showing the unexpected formation of species **2** (bottom) based on a copper-catalyzed click chemistry approach.

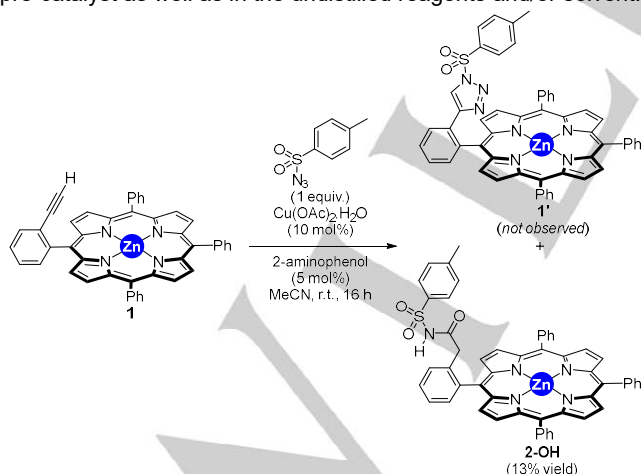
Results and Discussion

Initially, we verified the attempted strategy presented in **Figure 1** (bottom) by performing a control experiment with a system lacking a zinc-porphyrin motif (**Scheme 1**). Phenyl acetylene was reacted under known reaction conditions with tosyl azide^[58] under copper catalysis^[59] affording the expected tosyl triazole compound **A1** in a 73% isolated yield.^[60] Next, **A1** efficiently reacted with pyridine *N*-oxide affording the desired triazolopyridine **L*** in 86% isolated yield,^[25] thereby demonstrating the feasibility of such approach for systems lacking a zinc-porphyrin scaffold as similarly known in the literature.^[44] In addition, performing the synthesis of **A1** in the presence of benchmark zinc(II)-tetraphenylporphyrin (1 equivalent) led to a slight decrease in yield (50%) with absence of any side-product.



Scheme 1. Synthesis of the benchmark zinc-porphyrin-free triazolopyridine **L*** following the strategy presented in **Figure 1** (bottom). DCE = 1,2-dichloroethane.

With this promising findings and considering the compatibility of *ortho*-substitution patterns in the aromatic ring of phenylacetylene derivatives in copper-catalyzed click chemistry,^[61-67] we applied the same copper-catalyzed protocol from **Scheme 1** to the reaction between the alkyne-containing porphyrin **1** and tosyl azide (**Scheme 2**). Unfortunately, the expected porphyrin product **1'** did not form according to TLC, NMR and HRMS studies. In fact, the side-product **2-OH** was isolated in 13% isolated yield (**Scheme 2**). **2-OH** likely results from a nucleophilic water attack onto an open-form of a triazole intermediate followed by dinitrogen release and amide-hemiaminal tautomerism. Note that water is present in the copper pre-catalyst as well as in the undistilled reagents and/or solvent.



Scheme 2. Attempts to synthesize compound **1'** starting from **1** under copper catalysis and identification of undesired side-product **2-OH**.

Next, we searched for an alternative copper-catalyzed protocol. In 2007, Fokin, Chang and co-workers reported the most general method known to date for the preparation of *N*-sulfonyltriazoles structurally similar to **1'** by reacting terminal alkynes with tosyl azides under copper catalysis.^[68] The reactions

were identified to take place at 0 °C using CuI as the pre-catalyst in the presence of stoichiometric amounts of 2,6-lutidine and chloroform as the solvent.^[68] Consequently, we applied such reaction conditions to the alkyne porphyrin **1** (**Table 1**, entry 1). Although full conversion of starting material was observed after 24 hours, the targeted tosyl triazole porphyrin **1'** did not form so far. However, a major porphyrin compound was formed and isolated in 67% yield corresponding to amidate species **2-OEt** according to HRMS and NMR spectroscopy studies, besides minor formation of **2-OH**. **2-OEt** likely originates in a similar manner as **2-OH** but with ethanol (stabilizer of chloroform) as the nucleophile and release of dinitrogen.^[69-70] Variations of the reaction conditions were explored as well. For instance, performing the reaction at room temperature proceeded with full conversion of **1**, but still affording **2-OEt** in a similar 70% yield whereas the yield of **2-OH** raised to 13% (**Table 1**, entry 2). Using molecular sieves as well as decreasing the reaction temperature to -20 °C and -70 °C led to 70% and 30% conversions of **1**, respectively, and the yield of **2-OEt** was significantly reduced to 43% and 16%, respectively (**Table 1**, entries 3 and 4). Under these conditions, the side-product **2-OH** was formed only in trace amounts. Replacing chloroform stabilized with ethanol for chloroform stabilized with amylene or THF led to no formation of **2-OEt** (**Table 1**, entries 5 and 6), further demonstrating that the ethanol that reacts is the one found as stabilizer in the chloroform solvent. Note that applying the reaction conditions developed previously with Cu(PPh₃)₃Br as the pre-catalyst (**Figure 1**, top)^[22-23] did not yield the targeted porphyrin **1'** neither. In the presence of one equivalent of water, the reaction was selective towards the formation of **2-OH** in 90% yield (**Table 1**, entry 7).

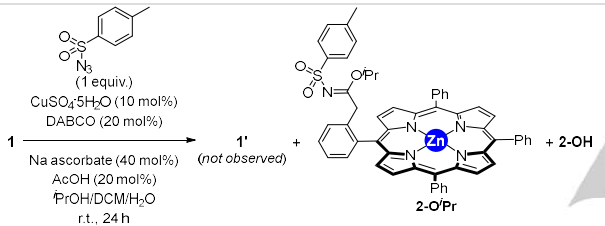
Table 1. Attempts to synthesize compound **1'** starting from **1** with CuI pre-catalyst and identification of undesired side-products **2-OEt** and **2-OH**.^[a]

Entry	Deviation from above conditions	Conv. 1 (%) ^[b]	Yield 2-OEt (%) ^[b]	Yield 2-OH (%) ^[b]
1	none	>99	67	5
2	20 °C instead of 0 °C	>99	70	13
3 ^[c]	-20 °C instead of 0 °C	70	43	<5
4 ^[c]	-70 °C instead of 0 °C	30	16	<5
5 ^[c]	CHCl ₃ stabilized with amylene	30	0	10
6 ^[c]	THF instead of CHCl ₃	50	0	10
7	with H ₂ O (1 equiv.)	>99	0	90

[a] Reaction conditions: **1** (0.100 g, 0.14 mmol), tosyl azide (0.027 g, 0.14 mmol), CuI (0.003 g, 0.014 mmol), 2,6-lutidine (0.015 g, 0.016 mL, 0.14 mmol), chloroform stabilized with ethanol (10 mL), 0 °C, 24 h. [b] Conversion and yields estimated by ¹H NMR spectroscopy studies. [c] Reaction performed in the presence of molecular sieves.

Considering the unexpected reactivity of alkyne porphyrin **1** with respect to its counterpart lacking the zinc-porphyrin and with the aim to further generalize such reactivity, we envisioned to react **1** with tosyl azide under copper-catalyzed click conditions in the presence of another alcohol reagent. For that, we adapted some reaction conditions from the literature which utilized $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ as the pre-catalyst in a mixture of solvents comprising *iso*-propanol and additives such as DABCO (DABCO = 1,4-diazabicyclo[2.2.2]octane), acetic acid and sodium ascorbate in catalytic amounts (Table 2).^[71] In this manner, full conversion of **1** and 81% isolated yield of the corresponding amidate product **2-OⁱPr** was obtained with trace amounts formation of **2-OH** (Table 2, entry 1). Performing the reaction in pure DCM or pure water inhibited the copper-catalyzed process leading to no formation of products (Table 2, entries 2 and 3), thereby indicating the key role of *iso*-propanol for enabling the formation of **2-OⁱPr** under copper-catalyzed click chemistry conditions.

Table 2. Attempts to synthesize compound **1'** starting from **1** with $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ pre-catalyst and identification of undesired side-products **2-OⁱPr** and **2-OH**.^[a]

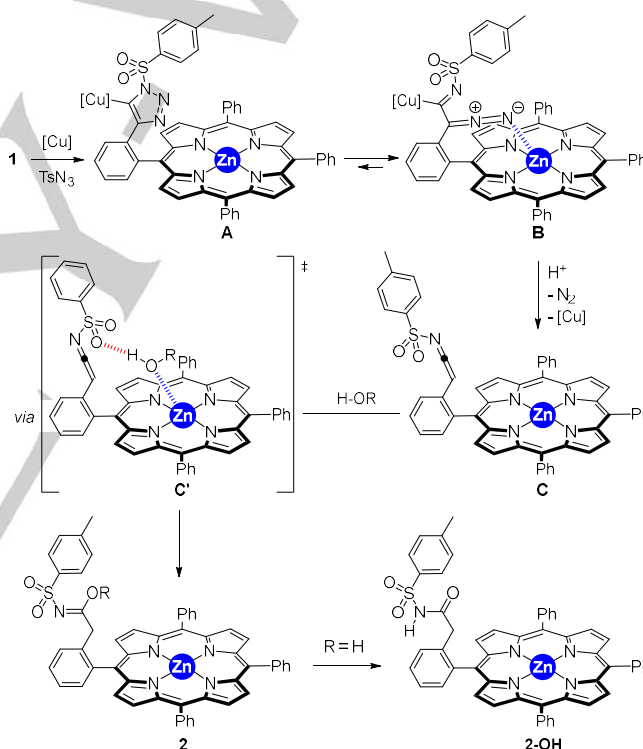


Entry	Deviation from above conditions	Conv. 1 (%) ^[b]	Yield 2-OⁱPr (%) ^[b]	Yield 2-OH (%) ^[b]
1	none	>99	81	5
2	only DCM as the solvent ^[c]	<10	0	0
3	only H ₂ O as the solvent	0	0	0

[a] Reaction conditions: **1** (0.100 g, 0.14 mmol), tosyl azide (0.027 g, 0.14 mmol), $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ (0.003 g, 0.014 mmol), DABCO (0.003 g, 0.03 mmol), sodium ascorbate (0.011 g, 0.056 mmol) acetic acid (0.0017 g, 0.0016 mL, 0.028 mmol), PrOH/DCM/H₂O (amylene stabilized, 10 mL, v/v 1:1:1), 20 °C, 24 h. [b] Conversion and yields estimated by ¹H NMR spectroscopy studies. [c] DCM stabilized with amylene.

As regards of the previous observations, the copper-catalyzed click reaction with porphyrin alkyne **1** and tosyl azide does not deliver the expected tosyl triazole **1'**, but a series of side-products resulting from nucleophile (alcohol or water) addition towards tosyl amidates (**2-OEt**, **2-OⁱPr**) and tosyl amides (**2-OH**). Such findings are in stark contrast with simple phenylacetylene that does deliver the expected tosyl triazole **A1** (Scheme 1). As such, the presence of the zinc-porphyrin backbone appears to play an important role to explain the formation of tosyl amidates and tosyl amides products. From a mechanistic point of view, and based on previous literature,^[72-75] we propose the following considerations depicted in Scheme 3. The alkyne porphyrin **1** reacts with tosyl azide under copper catalysis affording the well-known cuprated triazole intermediate **A** which is in equilibria towards the formation of intermediate **B**. We postulated that the equilibria is shifted towards **B** due to a eventual intramolecular

binding of the diazo fragment to the zinc center of the porphyrin backbone that would promote the release of dinitrogen leading to ketenimine species **C**. A final step could involve the nucleophilic addition of an alcohol reagent leading to the final tosyl amidate products **2-OEt** or **2-OⁱPr**. In the case of water addition, a last amide/hemiaminal tautomerism is at play to provide the amide product **2-OH**. The nucleophilic attack could be also enhanced by initial coordination of the nucleophile to the zinc center and hydrogen bonding to the sulfone (formation of species **C'**).^[76-78] Although this is unlikely considering that he higher yield is obtained with the less nucleophilic *iso*-propanol reagent, this event cannot be rule out at this stage. Preliminary CPK modelling strongly suggests the feasibility of intermediates **B** and **C'** in which the remotely-located zinc-porphyrin plays an activator role. The fact that sulfonyl amidates or sulfonyl amides do not form when the zinc(II)-porphyrin scaffold is not covalently connected to the alkyne fragment (see discussion related to Scheme 1) strongly indicates that the observed reactivity in copper-catalyzed click chemistry arises for an intramolecular effect as herein discussed and shown in Scheme 3.



Scheme 3. Postulated reaction mechanism accounting for the formation of sulfonyl amidates **2** starting from **1** under copper catalysis highlighting the role of the zinc-porphyrin scaffold in several intermediates.

Conclusion

In summary, we have disclosed that the usually highly predictable copper-catalyzed click reactions do not provide the desired tosyl triazole product in the case of the herein discussed zinc-porphyrin compounds upon reaction with tosyl azide besides having explored different set of copper catalysts under different reaction conditions. The selectivity in this case is directed towards the exclusive formation of sulfonyl amidates in the presence of alcohols or to sulfonyl amide in the presence of water. By means of several control experiments, it appears that the zinc-porphyrin motif could play a relevant role by enhancing dinitrogen release and/or nucleophilic addition, which are key selective-determining

steps in the reaction mechanism, *via* remote non-covalent interactions. Overall, the reactivity of metalloporphyrins encountered when using copper-catalyzed click reactions may be quite different than what one could expect or anticipate, which is reminiscent of observations found when employing organolithium reagents with some metalloporphyrins or free-base porphyrins.^[79-87] Future research will be devoted to the use of ruthenium complexes or other metal complexes as alternative catalysts to copper in azide-alkyne cycloaddition reactions with (metallo)porphyrins.

Experimental Section

General methods. Solvents were purified with an MB SPS-800 purification system. Pyrrole was dried with CaH₂ and distilled prior to use. CDCl₃ was filtered through alumina and stored under argon over molecular sieves. All the other employed chemicals were purchased from commercial sources and used as received. Unless otherwise specified, reactions were carried out under argon atmosphere by employing standard Schlenk and vacuum-line techniques. ¹H and ¹³C NMR spectra were recorded with a Bruker GPX (400 MHz) spectrometer. ¹H NMR spectra were referenced to residual protiated solvent (δ = 7.26 ppm for CDCl₃). ¹³C NMR spectra were referenced to CDCl₃ (δ = 77.16 ppm). Abbreviations for signal couplings are: br, broad; s, singlet; d, doublet; t, triplet; m, multiplet; dd, doublet of doublets; dt, triplet of doublets; td, doublet of triplets; tt, triplet of triplets; tdd, doublet of doublet of triplets. Coupling constants, *J*, were reported in hertz unit (Hz). The reactions were monitored by using a Shimadzu 2014 gas chromatograph equipped with an EquityTM-1 Fused Silica capillary column (30 m x 0.25 mm x 0.25 μ m) and an FID detector; conversion and selectivity were determined by using dodecane as internal standard. UV/Vis absorption spectra were recorded with a Specord 205 UV/Vis/NIR spectrophotometer and quartz cuvettes of 1 cm path length. Mass spectroscopy and microanalysis were performed in the laboratories of the Centre Regional de Mesures Physiques de l'Ouest (CRMPO, Université de Rennes 1, Rennes, France). Alkyne porphyrin **1**^[22] and tosyl azide^[58] were prepared according to literature protocols.

Synthesis and characterization of A1: Cu(OAc)₂·H₂O (0.010 g, 0.05 mmol, 0.1 equiv.), 2-aminophenol (0.003 g, 0.025 mmol, 0.05 equiv.), tosylazide (0.100 g, 0.5 mmol, 1 equiv.) acetonitrile (5 mL) and phenylacetylene (0.51 g, 0.055 mL, 0.5 mmol, 1 equiv.) were introduced in a round bottom flask equipped with a stirring bar. The reaction mixture was stirred for 16 hours at room temperature. Then the solvent was evaporated and the crude mixture was purified by column chromatography (SiO₂, heptane:EtOAc, v/v 1:0 to 7:3) affording analytically pure **A1** (0.109 g, 73% yield) as a white solid. ¹H NMR (400 MHz, CDCl₃): δ = 8.07 (s, 1H), 8.00 (d, *J* = 8.3 Hz, 2H), 7.85-7.80 (m, 2H), 7.48-7.40 (m, 3H), 7.34 (d, *J* = 8.3 Hz, 2H), 2.41 (s, 3H) ppm. The spectral data match those found in the literature.^[60]

Synthesis and characterization of L*: **A1** (0.100 g, 0.33 mmol, 0.0 equiv.), DCE (10 mL) and pyridine oxide (0.032 g, 0.33 mmol, 1 equiv.) were introduced in a round bottom flask equipped with a stirring bar. The reaction mixture was heated at 95 °C for 16 hours. Back at room temperature, the solvent was evaporated and the crude mixture was purified by column chromatography (SiO₂, heptane:EtOAc, v/v 9:1 to 1:9) affording analytically pure **L*** (0.063 g, 86% yield) as a white solid. ¹H NMR (400 MHz, CDCl₃): δ = 8.82 (s, 1H), 8.54 (d, *J* = 3.9 Hz, 1H), 8.26 (d, *J* = 8.2 Hz, H_{pyr}, 1H), 7.95-7.93 (m, 3H), 7.47 (t, *J* = 7.5 Hz, 2H), 7.40-7.35 (m, 2H) ppm. The spectral data match those found in the literature.^[25]

General procedure for the copper-catalyzed reactions: **1** (0.100 g, 0.14 mmol, 1 equiv.), copper catalyst (0.014 mmol, 0.1 equiv.), TsN₃ (0.028 g, 0.14 mmol, 1 equiv.), sodium ascorbate (0 to 0.2 equiv.), 2-aminophenol (0 to 0.05 equiv.), DABCO (0 to 0.2 equiv.), solvent (10 mL), base (0 to 1

equiv.) and AcOH (0 to 0.2 equiv.) were added to an oven dried Schlenk flask. The reaction mixture was stirred at a given temperature under Argon atmosphere for 24 hours. Conversion is an estimated value determined by ¹H NMR analysis of the crude reaction mixture. Isolated yields of **2** are reported after purification of the crude mixture by column chromatography (SiO₂, heptane:DCM, v/v 1:0 to 0:1).

Synthesis and characterization of 2-OEt: Following the general procedure, **1** (0.100 g, 0.14 mmol, 1 equiv.), CuI (0.003 g, 0.014 mmol, 0.1 equiv.), TsN₃ (0.027 g, 0.14 mmol, 1 equiv.), DCM (EtOH stabilized, 10 mL) 2,6-lutidine (0.015 g, 0.016 mL, 0.14 mmol, 1 equiv.) were stirred at room temperature under Argon atmosphere during 24 hours. Then, after solvents evaporation, the crude mixture was purified by column chromatography (SiO₂, heptane:DCM, v/v 1:0 to 1:1) affording analytically pure **2-OEt** (90 mg, 70% yield). m.p. dec. ¹H NMR (400 MHz, CDCl₃): δ = 8.93 (s, 4H), 8.79 (AB, *J* = 5.6, 4H), 8.27-8.14 (m, 7H), 7.81-7.70 (m, 10H), 7.67 (t, *J* = 7.4 Hz, 2H), 6.38 (d, *J* = 0.9 Hz, 4H), 3.91 (s, 2H), 3.70 (q, *J* = 7.1 Hz, 2H), 1.86 (s, 3H), 1.01 (t, *J* = 7.1 Hz, 3H) ppm. ¹³C{¹H} NMR (101 MHz, CDCl₃): δ = 172.64, 150.26, 150.16, 149.78, 143.00, 142.95, 142.67, 142.34, 137.76, 136.18, 134.51, 134.47, 133.67, 132.06, 131.95, 131.89, 131.28, 129.77, 128.52, 128.36, 127.40, 127.38, 126.48, 126.48, 125.58, 125.44, 121.21, 121.01, 117.80, 64.63, 38.88, 20.93, 13.3 ppm. HRMS (ESI, CHCl₃) calcd. for [M]⁺ C₅₅H₄₁N₅O₃S⁶⁴Zn 915.22161; found: 915.2206 (1 ppm).

Synthesis and characterization of 2-OPr: Following the general procedure, **1** (0.100 g, 0.14 mmol, 1 equiv.), CuSO₄·5H₂O (0.004 g, 0.014 mmol, 0.1 equiv.), DABCO (0.003 g, 0.03 mmol, 0.2 equiv.), TsN₃ (0.027 g, 0.14 mmol, 1 equiv.), ⁱPrOH/ H₂O/DCM (amylene stabilized, v/v/v 1:1:1, 10 mL), sodium ascorbate (0.011 g, 0.056 mmol, 0.4 equiv.) and acetic acid (0.0017 g, 0.0016 mL, 0.028 mmol, 0.2 equiv.) were stirred at room temperature under Argon atmosphere during 24 hours. Then, after solvents evaporation, the crude mixture was purified by column chromatography (SiO₂, heptane:DCM, v/v 1:0 to 1:1) affording analytically pure **2-OPr** (106 mg, 81% yield). m.p. dec. ¹H NMR (400 MHz, CDCl₃): δ = 8.93 (s, 4H), 8.82 (AB, *J* = 6.5 Hz, 4H), 8.30-8.11 (m, 7H), 7.84-7.70 (m, 10H), 7.70-7.57 (m, 2H), 6.76 (d, *J* = 8.3 Hz, 2H), 6.54 (d, *J* = 8.3 Hz, 2H), 4.69 (hept, *J* = 6.2 Hz, 1H), 3.92 (s, 2H), 1.91 (s, 3H), 1.00 (d, *J* = 6.2 Hz, 6H) ppm. ¹³C{¹H} NMR (101 MHz, CDCl₃): δ = 172.42, 150.30, 150.22, 149.93, 142.95, 142.90, 142.53, 142.39, 138.28, 136.18, 134.50, 134.45, 133.94, 132.17, 131.98, 131.93, 131.54, 129.29, 128.58, 128.35, 127.44, 127.42, 126.49, 125.71, 125.32, 121.27, 121.08, 118.06, 72.52, 38.79, 20.98, 20.93 ppm. HRMS (MALDI, DCTB) calcd. for [M]⁺ C₅₆H₄₃N₅O₃S⁶⁴Zn 929.23726; found: 929.235 (2 ppm).

Synthesis and characterization of 2-OH: Following the general procedure, **1** (0.100 g, 0.14 mmol, 1 equiv.), CuI (0.003 g, 0.014 mmol, 0.1 equiv.), TsN₃ (0.027 g, 0.14 mmol, 1 equiv.), DCM (amylene stabilized, 10 mL), 2,6-lutidine (0.015 g, 0.016 mL, 0.14 mmol, 1 equiv.) and water (0.0025 g, 2.52 μ L, 0.14 mmol, 1 equiv.) were stirred at room temperature under Argon atmosphere 24 hours. Then, after solvents evaporation, the crude mixture was purified by column chromatography (SiO₂, heptane:DCM, v/v 1:0 to 0:1) affording analytically pure **2-OH** (110.8 mg, 90% yield). m.p. dec. ¹H NMR (400 MHz, CDCl₃): δ = 8.94 (s, 4H), 8.79 (AB, *J* = 7.0, 4H), 8.33-8.13 (m, 7H), 7.82-7.67 (m, 11H), 7.59 (d, *J* = 7.7 Hz, 1H), 7.46 (br, 1H), 7.12 (d, *J* = 8.0 Hz, 2H), 6.66 (d, *J* = 8.0 Hz, 2H), 3.21 (s, 2H), 2.00 (s, 3H) ppm. ¹³C{¹H} NMR (101 MHz, CDCl₃): δ = 167.66, 150.45, 150.42, 150.19, 149.51, 144.31, 142.81, 142.69, 142.32, 134.55, 134.45, 134.40, 134.20, 132.97, 132.21, 130.60, 129.40, 128.84, 127.70, 127.54, 126.63, 126.58, 126.52, 125.99, 121.59, 121.40, 117.11, 41.46, 21.24 ppm. HRMS (ESI, DCM) calcd. for [M]⁺ C₅₃H₃₇N₅O₃S⁶⁴Zn 887.19031; found: 887.1903 (0 ppm).

Supplementary Material

Supporting information for this article is available on the WWW under <http://dx.doi.org/10.1002/MS-number>. Supplementary data includes NMR spectra.

Acknowledgements

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Author Contribution Statement

J.T. performed the experiments. J.T. and R.G.-D. conceived and designed the experiments, analyzed the data and wrote the manuscript. R.G.-D. acquired funding for this research.

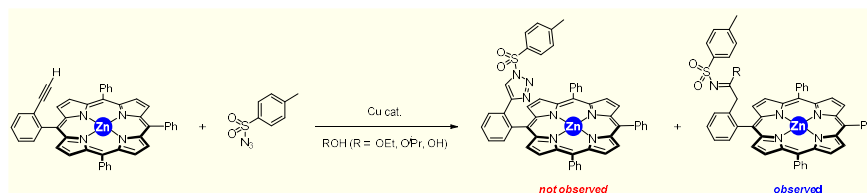
Keywords: click chemistry • porphyrins • zinc • water • alcohols

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Copper-catalyzed click reactions taking place nearby to zinc-porphyrin scaffolds lead exclusively to sulfonyl imidates and sulfonyl amides. The expected triazole-containing counterparts did not form as a result of an intermolecular nucleophilic addition of alcohols or water, respectively. These findings demonstrate the unique reactivity encountered in metalloporphyrins that strongly contrasts with systems lacking such skeleton.

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