Advanced Synthesis & Catalysis

DOI: 10.1002/adsc.201400742

Intermolecular [3+2] Annulation of Cyclopropylanilines with Alkynes, Enynes, and Diynes *via* Visible Light Photocatalysis

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Received: July 29, 2014; Published online: ■■ ■■, 0000

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.201400742.

Abstract: One-step syntheses of carbocycles substituted with amines from simple starting materials remain rare. We recently developed an intermolecular [3+2] annulation of cyclopropylanilines with alkenes and alkynes that enables this one-step synthesis. Herein, we report our findings for a full-scale study of the annulation. Significant expansion of the substrate scope for both cyclopropylanilines and alkynes has been achieved. A range of structurally diverse carbocycles substituted with amines is prepared.

Keywords: alkynes; [3+2] annulation; cyclopropylanilines; diynes; enynes; intermolecular annulation; photocatalysis; visible light

Introduction

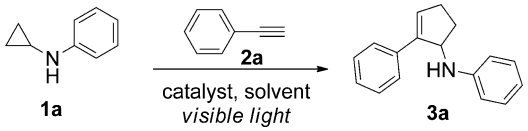
Cycloaddition or annulation reactions have been primarily used to construct carbo- or heterocycles with various sizes.[1] These types of reactions have gained increasing prominence in diversity-oriented synthesis (DOS) because it can efficiently increase the structural diversity and complexity of small molecules.[2] Both features are critical for the success of small molecule libraries as they enable small molecules to occupy more chemical space. Recently, the renaissance of visible light photocatalysis has brought new life to some existing reactions, including cycloaddition or annulation reactions.[3] Since the interaction of photoexcited catalysts and small molecules is often specific,[4] the photocatalyzed transformations are usually highly chemoselective and thus tolerate a variety of functional groups. Therefore, in principle, photocatalyzed cycloaddition or annulation reactions are ideal reactions for making small molecule libraries. We have recently developed a [3+2] annulation of cyclopropylanilines with alkenes and alkynes.[5] Although our preliminary results in these reactions gave a glimpse of their potential in DOS, constraints with respect to both reacting partners, cyclopropylanilines and alkenes or alkynes, existed. An aryl group was required on the cyclopropylamine moiety while only terminal alkenes and alkynes were reactive.[5] We intended to address both limitations with the ultimate goal of thoroughly investigating the scope of the [3+2] annulation. Herein we report our findings towards expansion of these reactions.

Results and Discussion

Reaction Optimization

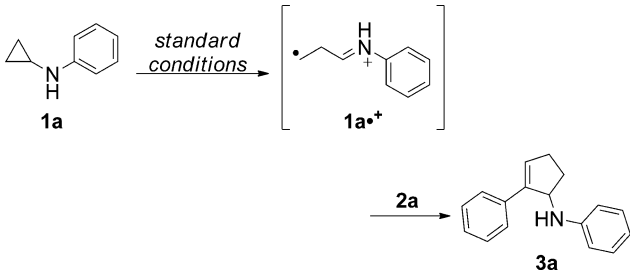
Although we previously optimized the conditions for the [3+2] annulation of cyclopropylanilines with alkynes using ruthenium polypyridyl complexes, the desired annulation products were obtained in only modest yields.[5b] We were motived to examine more conditions in order to improve the yields, as shown in Table 1. Using the [3+2] annulation of cyclopropylaniline **1a** with phenylacetylene **2a** as the model reaction, we first investigated the annulation in a continuous flow format[6] (entry 2). To our surprise, comparing against the batch format (entry 1), although the reaction time was shortened from 8 h to 3 h as expected, the yield did not improve. We also examined the use of cyclometalated iridium complexes to catalyze the annulation. These complexes are another important class of photocatalysts that finds rising numbers of synthetic applications in photochemistry.[7] Two iridium complexes were examined and neither provided a better yield than $Ru(bpz)_3(PF_6)_2$ (entries 3 and 4). Lastly, we performed the reaction in the presence of TEMPO (entry 5). We previously proposed distonic ion $\mathbf{1a}^{\bullet+}$ as one of the key intermediates in the

Table 1. Reaction optimization.[a]



Entry	Catalyst	Solvent	Light	GC Yield [%][b]
1	$Ru(bpz)_3(PF_6)_2$	CH_3NO_2	18 W LED	69 (68)[c]
2	$Ru(bpz)_3(PF_6)_2$	CH_3NO_2	flow[d]	60
3	$Ir(ppy)_2(dtb\text{-}bpy)(PF_6)$	CF_3CH_2OH	18 W LED	60
4	$Ir[dF(CF_3)ppy]_2(dtb\text{-}bpy)(PF_6)$	CF_3CH_2OH	18 W LED	36
5[e,f]	$Ru(bpz)_3(PF_6)_2$	CH_3NO_2	18 W LED	7

[a] A solution of **1a** (0.2 mmol), catalyst (2 mol%), and **2a** (5 equiv.) in 2 mL of solvent was degassed *via* freeze-pump-thaw cycles. The resulting solution was irradiated using an 18 W white LED for 8 h.
[b] Using dodecane as an internal standard.
[c] Isolated yield.
[d] Flow reaction time of 3 h.
[e] 19 hour reaction.
[f] Using 1 equiv. of TEMPO.



Scheme 1. Proposed intermediate distonic ion in the [3+2] annulations.

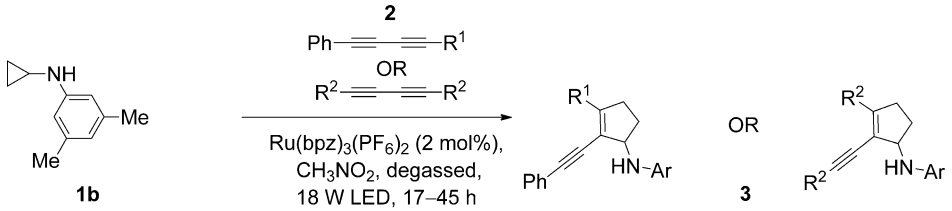
[3+2] annulation of cyclopropylanilines with alkenes and alkynes (Scheme 1). This ion presumably results from ring opening of cyclopropylanilines that is induced by one-electron oxidation of the parent amine by the excited state of $Ru(bpz)_3(PF_6)_2$.[5a] The use of TEMPO was designed to intercept the radical moiety of the ion and thereby perturb the annulation. Indeed, the annulation product was isolated in a negligible yield, which lent credence to our argument for the involvement of distonic ion $\mathbf{1a}^{\bullet+}$. Since no improvement in the yield was achieved using the flow or the Ir catalysts, we settled for the previously optimized conditions (entry 1, Table 1) as the standard conditions for the scope studies.

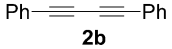
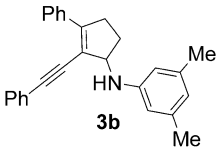
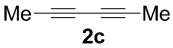
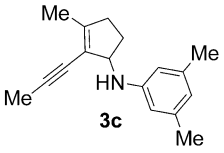
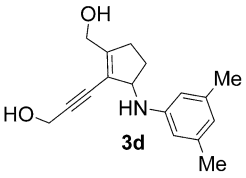
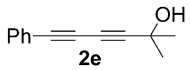
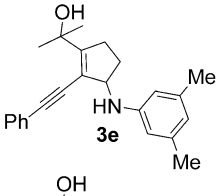
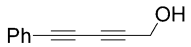
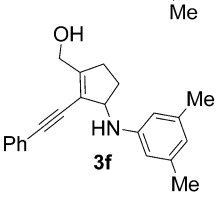
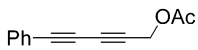
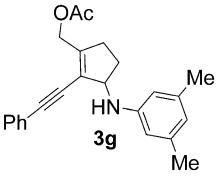
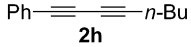
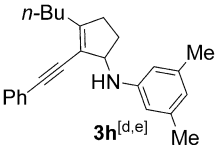
Diyne and Enyne Studies

We were intrigued by the possibility of using 1,3-conjugated diynes and enynes in the [3+2] annulation as they offer the potential to further enhance the value of the annulation in diversity-oriented synthesis (DOS). The expected annulation products would possess a 1,3-conjugated enyne moiety from 1,3-conjugated diynes or a 1,3-conjugated diene moiety from 1,3-conjugated enynes. Both moieties can be further engaged in cycloaddition reactions such as the Diels–Alder reaction, and thereby enable cycloaddition cascades to rapidly assembly complex fused carbocycles or heterocycles. However, 1,3-conjugated diynes and enynes present more challenges than simple alkynes in the annulation. We previously reported that the annulation was sensitive to substitution on alkynes as well as their electronic characters. For example, alkyl-substituted terminal alkynes and internal alkynes were found to be unreactive.[5b] It was not clear to us whether addition of one more π bond would enhance the original π bond's reactivity enough to take part in the annulation. Moreover, prediction of regiochemistry in 1,3-conjugated diynes and enynes could be challenging. Finally, for unsymmetric diynes and enynes, since there are two different π bonds, the issue of chemoselectivity may arise as addition to either or both π bonds can occur.

To our delight, under the standard conditions, symmetrical and asymmetrical 1,3-conjugated diynes successfully underwent the intermolecular [3+2] annulation with monocyclic cyclopropylaniline **1b** to afford the conjugated cyclopentene adducts (Table 2). Symmetrical diynes bearing phenyl **2b**, methyl **2c**, and hydroxymethyl **2d** groups proceeded in fair yields (entries 1–3). Asymmetrical diynes also produced the annulation products in similar yields (entries 4–7). These diynes **2e**–**h** all bore a phenyl group on one end, while a variety of moieties, such as *n*-Bu and hydroxymethyl groups, were tolerated on the other end. A quaternary center adjacent to the reactive carbon center of diyne

Table 2. Scope studies using symmetrical and unsymmetrical diynes.[a]



Entry	Substrate	Diyne **2**	Product[b]	Yield [%][c]
1	**1b**	 **2b**	 **3b**	20
2	**1b**	 **2c**	 **3c**	35
3	**1b**	 **2d**	 **3d**	45
4	**1b**	 **2e**	 **3e**	43
5	**1b**	 **2f**	 **3f**	40
6	**1b**	 **2g**	 **3g**	54
7	**1b**	 **2h**	 **3h**[d,e]	20

[a] A solution of **1b** (0.2 mmol), $Ru(bpz)_3(PF_6)_2$ (2 mol%), and **2** (5 equiv.) in 2 mL of solvent was degassed *via* freeze-pump-thaw cycles. The resulting solution was irradiated using an 18 W white LED.
[b] Ratio >20:1, determined using GC.
[c] Isolated yields.
[d] Ratio 12:1, determined using GC.
[e] Unidentified minor isomer.

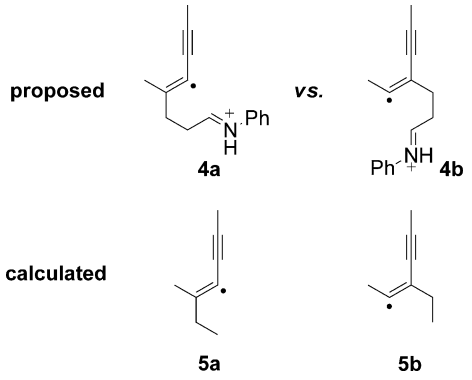


Figure 1. Rationale for the observed selectivity using DFT calculations.

2e was also well tolerated. Although the yields for the annulation products were modest, complete regiocontrol was observed universally in all but one example (entry 7). Even with the exception **3h**, the regioselectivity was excellent (12:1). We rationalized the observed excellent regioselectivity based on the stability of radicals generated after the first C–C bond formation. DFT calculations on two regioisomeric radicals (**5a** and **5b**) that model the proposed regioisomeric radicals (**4a** and **4b**) in the annulation supported this argument (Figure 1). Radical **5a** was found to be 44 kJ mol^{-1} more stable than radical **5b** due to resonance. The stability trend of the two regioisomeric radicals was also observed in diyne **2b** (see the Supporting Information).

The annulation with enynes was expected to be more complicated than with diynes. In addition to regioselectivity, chemoselectivity has to be dealt with because of the competition between the alkene and alkyne moiety in the annulation. We found that in our previous work, alkenes are more reactive than alkynes in general.[5b] However, because of steric effects, this reactivity trend can be reversed if the alkene is more substituted than the alkyne. Furthermore, if the alkene moiety is more reactive than the alkyne moiety, the diastereoselectivity also needs to be addressed.

Indeed, 1,3-conjugated enynes **2i–l** produced a mixture of isomeric products in the annulation (Table 3). Commercially available enyne **2i**, possessing both a terminal alkyne and a terminal alkene, underwent the [3+2] annulation predominately on the alkene moiety to provide the annulation products in 50% combined yields (entry 1), with the minor isomer being identified as the annulation on the alkyne. The chemoselectivity was 10 to 1, favoring the alkene moiety. Another commercially available enyne, **2j**, bearing a terminal alkyne and a trisubstituted alkene, was subjected to the annulation with cyclopropylanilines **1b** and **1c**, respectively, to afford the corresponding conjugated 1,3-dienes **6b** and **6c** in moderate yields (entries 2 and 3). In both cases, the annulation favored the terminal alkyne moiety of enyne **2j**. It is worth noting that for these two enynes (**2i** and **2j**), the catalyst system composed of $Ir(ppy)_2(dtb\text{-}bpy)(PF_6)$ in a 1:1 mixture of CH_3NO_2 and CF_3CH_2OH proved to be more effective than the standard catalyst system [$Ru(bpz)_3(PF_6)_2$ in CH_3NO_2]. Likewise for synthetically prepared enyne **2k**[8] bearing a terminal alkyne and a 1,2-disubstituted alkene, the furnished annulated product **6d** was isolated in 59% combined yields, with the 1,3-diene as the major isomer (entry 4). Lastly, enyne **2l**, possessing both an internal alkyne and a 1,2-disubstituted alkene, was prepared according to a literature protocol[9] and then treated with cyclopropylaniline **1b** under the standard conditions. The major products **6e**, composed of four diastereomers derived from the annulation on the alkene moiety, was obtained in 66% combined yields (entry 5).

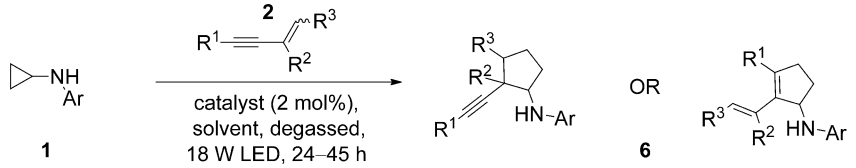
Substituted Cyclopropanes

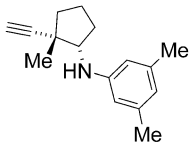
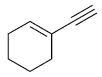
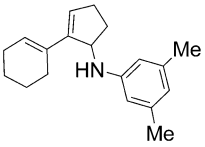
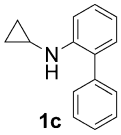
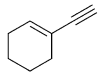
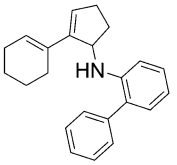
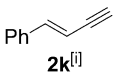
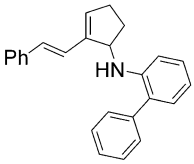
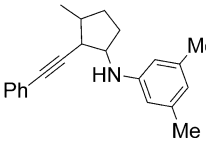
Next, we shifted our attention to focus on the scope of cyclopropylanilines. To maximize the potential of the [3+2] annulation, it was imperative for us to examine substituents on the nitrogen atom and the cyclopropyl ring. Particularly for the latter, if succeeded, it would allow us to decorate the cyclopentene ring of the annulation products. Using phenylacetylene **2a** as the model alkyne, we first investigated the annulation of *N*-cyclopropyl-*N*-methylaniline **1d** to form **7a** and no reaction was observed (entry 1, Table 4). This is in accordance with the result reported by Tanko and coworkers in which the ring opening of the amine radical cation derived from **1d** was found to be very sluggish.[10] Despite this observation, substitution on the cyclopropyl ring was generally tolerated. *N*-(1-methylcyclopropyl)aniline **1e** provided the annulation product **7b** bearing a quaternary carbon center in 33% yield when subjected to the standard conditions (entry 2). The [3+2] annulation was also effective using 2-substituted cyclopropyl rings, as demonstrated with methyl **1f** and phenyl **1g** substituents (entries 3 and 4). In both examples, the ring opening was completely regioselective, presumably forming the more substituted carbon radical. Modest diastereoselectivity was observed, providing the *cis* isomer as the major product in both cases.

Cleavage of *N*-Aryl Groups

The requirement of an aniline moiety has been a limitation to the [3+2] annulation, as it lowers the generality of the reaction. To circumvent this limitation, we were interested in installing a removable aryl or het-

Table 3. Scope studies using enynes.[a]

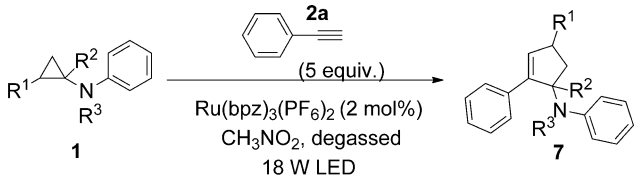


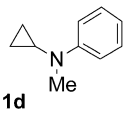
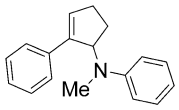
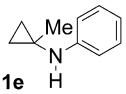
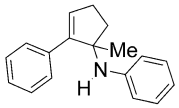
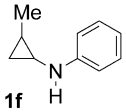
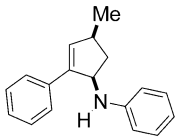
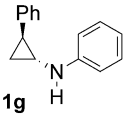
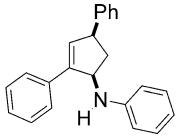
Entry	Substrate	Enyne **2**	Product[b]	Yield [%][c,d]
1	**1b**	 **2i**	 **6a**[e]	50 (10:1)
2	**1b**	 **2j**	 **6b**	43 (11:2[f]:1[f])
3	 **1c**	 **2j**	 **6c**	53 (8:1[f]:1[f])
4[g]	**1c**	 **2k**[i]	 **6d**	59 (4:1[h]:1[f])
5[g]	**1b**	 **2l**	 **6e**	66 (2:1:2:2)[j]

[a] A solution of cyclopropylaniline (0.2 mmol), $Ir(ppy)_2(dtb\text{-}bpy)(PF_6)$ (2 mol%), and enyne (5 equiv.) in 2 mL CH_3NO_2:CF_3CH_2OH (1:1), was degassed *via* freeze-pump-thaw cycles. The resulting solution was irradiated using an 18 W white LED.
[b] Major isomer shown.
[c] Isolated yields.
[d] Isomer ratios (determined by GC-MS) shown in parentheses.
[e] 7:3 *dr*.
[f] Unidentified minor isomers.
[g] Using $Ru(bpz)_3(PF_6)_2$.
[h] Identified as the *cis*-alkene of **6d**.
[i] Ratio 10:1 *trans*:*cis*.
[j] All identified as diastereomers of **6e**. See the Supporting Information for details.

eroaryl group that is also capable of mediating the annulation. Some of these potential candidates include pyrimidine **1h**,[11] pyridine **1i**,[12] and *para*-methoxyphenyl (PMP, **1k**)[13] groups. With this in mind, we synthesized *N*-arylcyclopropylamines **1h–k** bearing these groups and subjected them under the standard conditions to reaction with phenylacetylene **2a**. The results are summarized in Table 5. No reaction was observed with 2-pyrimidyl-substituted cyclopropylamine **1h** (entry 1). Surprisingly, 2-pyridyl-substituted cyclopropylamine **1i** afforded the annulation product in a low yield (13%), which was not synthetically useful (entry 2). In comparison, a much higher yield (48%) was obtained with 3-pyridyl-substituted cyclopropylamine **1j** (entry 3). Unfortunately, the 3-pyridyl group was not cleavable. A similar yield (47%) was achieved with PMP-substituted cyclopropylamine **1k**

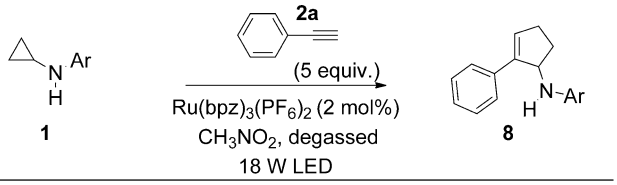
Table 4. [3+2] Annulation of substituted cyclopropylanilines.[a]

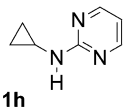
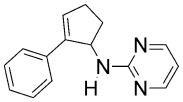
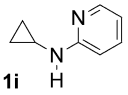
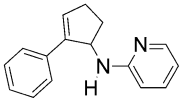
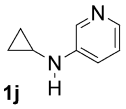
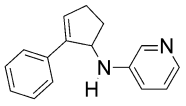
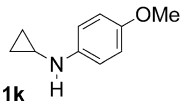
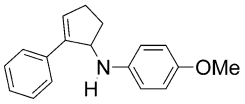


Entry	Substrate	Time [h]	Product		Yield [%][b]
1	 **1d**	16		**7a**	0[c]
2	 **1e**	15		**7b**	33
3	 **1f**	18		**7c**[d]	46[e]
4	 **1g**	36		**7d**[d]	30[f]

[a] A solution of **1** (0.2 mmol), $Ru(bpz)_3(PF_6)_2$ (2 mol%), and **2a** (5 equiv.) in 2 mL of CH_3NO_2 was degassed *via* freeze-pump-thaw cycles. The resulting solution was irradiated using an 18 W white LED.
[b] Isolated yields.
[c] Determined using GC-MS.
[d] Major isomer shown.
[e] Ratio 2:1 *cis:trans*, determined by GC-MS.
[f] Ratio 4:1 *cis:trans*, determined by GC-MS.

Table 5. [3+2] Annulation of various arylamines.[a]

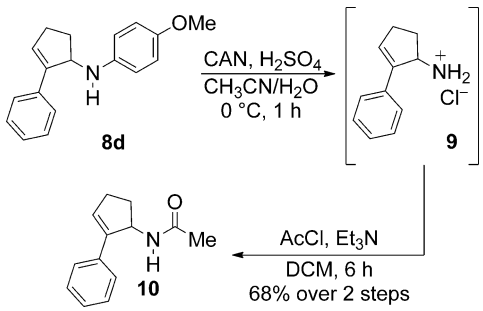


Entry	Substrate	Time [h][b]	Product		Yield [%][c]
1	 **1h**	48		**8a**	0[d]
2	 **1i**	16		**8b**	13
3	 **1j**	21		**8c**	48
4	 **1k**	18		**8d**	47

[a] A solution of **1** (0.2 mmol), $Ru(bpz)_3(PF_6)_2$ (2 mol%), and **2a** (5 equiv.) in 2 mL CH_3NO_2 was degassed *via* freeze-pump-thaw cycles. The resulting solution was irradiated using an 18 W white LED.
[b] Monitored by TLC.
[c] Isolated yields.
[d] Determined using GC-MS.

(entry 4). Therefore, we opted to focus on studying the cleavage of the PMP group in **8d**.

The PMP group is generally cleaved under oxidative conditions, and a number of oxidants are suitable for the cleavage.[13] We subjected **8d** to these oxidants, including ceric ammonium nitrate (CAN), periodic acid (H_5IO_6), trichloroisocyanuric acid (TCCA), and CAN/$Fe(bpy)_3(PF_6)_2$.[14] Among the conditions examined, CAN in sulfuric acid gave the highest yield. The cleavage product was initially isolated as the HCl salt **9** and then immediately acylated in the presence of Et_3N and acetyl chloride to give the corresponding acetamide **10** in 68% isolated yield over 2 steps (Scheme 2). The successful removal of the PMP group circumvents the previous limitation of our chemistry and allows for more structural diversification of the [3+2] annulation products.



Scheme 2. Removal of the *para*-methoxyphenyl (PMP) group.

Conclusions

In summary, we have significantly expanded our studies on the [3+2] annulation of cyclopropylanilines with alkynes. These studies were conducted on multiple fronts including catalyst optimization, mechanistic studies, expansion of the substrate scope for both cyclopropylanilines and alkynes, and identification of a removable *N*-aryl group for cyclopropylamines. Using simple building blocks, the [3+2] annulation enables rapid assembly of diverse cyclic allylic amine

derivatives. Most of these amines possess embedded functional groups that allow for further structural diversification. We anticipate that this method will find usage particularly in diversity-oriented synthesis (DOS).

Experimental Section

General Procedure for the [3+2] Annulation of Cyclopropylanilines with Alkyne, Enyne, and Diyne

An oven-dried test tube (16×125 mm) equipped with a stir bar was charged with catalyst (2 mol%), cyclopropylaniline (0.2 mmol), alkyne, enyne, or diyne (1.0 mmol), and dry solvent (2 mL). The test tube was sealed with a Teflon screw cap. The reaction mixture was degassed by freeze-pump-thaw cycles and then irradiated at room temperature with one white LED (18 W) positioned 8 cm from the test tube. After the reaction was complete as monitored by TLC, the mixture was diluted with diethyl ether and filtered through a short pad of silica gel. The filtrate was concentrated under vacuum and purified by silica gel flash chromatography to afford the desired product.

Procedure for the Deprotection of the PMP Group

To a pre-cooled solution of *para*-methoxyphenylamine (51 mg, 0.2 mmol) in 3:1 CH_3CN:H_2O (2 mL) was slowly added concentrated H_2SO_4 (22 μL, 0.385 mmol) at 0 °C. Ceric ammonium nitrate (220 mg, 0.4 mmol) was then added in one portion, and the mixture was stirred for one hour at 0 °C. The resulting mixture was then diluted with water (2 mL) and separated. The aqueous phase was then washed with Et_2O (3×5 mL). The combined organic phase was then extracted with 0.1 N HCl (1×15 mL), and the obtained aqueous phase was added to the previous aqueous mixture, which was immediately basified to pH 14 using 5 N KOH. The basic aqueous layer was then extracted with Et_2O (2× 30 mL). The combined organic layer was then acidified to pH 1 using hydrogen chloride (2 M in Et_2O). The resulting solution was then dried over $MgSO_4$ and concentrated to give the HCl salt as a dark brown oil. The crude HCl salt was used in the next step without further purification.

To a solution of the HCl salt (35 mg, 0.18 mmol) in dry CH_2Cl_2 (5 mL) was added Et_3N (56 μL, 0.4 mmol) dropwise at room temperature. Acetyl chloride (16 μL, 0.22 mmol) was slowly added and the reaction mixture was stirred for 6 h at room temperature. The reaction was quenched with water (10 mL) and the layers were separated. The aqueous phase was extracted with CH_2Cl_2 (3×10 mL). The combined organic layers were dried over $MgSO_4$ and concentrated to give the crude product. Purification using silica gel chromatography (1:1 hexanes:EtOAc) provided the desired acylated product; yield; 26.5 mg (68% over 2 steps).

Acknowledgements

This publication was supported by the University of Arkansas, Arkansas Bioscience Institute, National Institute of General Medical Sciences of the National Institutes of Health (NIH) (Grant Number P30 GM103450), NSF Career Award under Award Number CHE-1255539. We thank Jiang Wang, Soumitra Maity, and Mingzhao Zhu for early experimental assistance of this work as well as Derrel Walters and Professor Peter Pulay for the DFT calculations.

References

[1] *Comprehensive Organic Synthesis*, 2ednnd ednVol. 5, (Eds.: P. Knochel, G. A. Molander), Elsevier, Amsterdam, **2014**.

[2] For selected recent reviews: a) G. Muncipinto, in: *Diversity-Oriented Synthesis: Basics and Applications in Organic Synthesis Drug Discovery, and Chemical Biology*, (Ed.: A. Trabocchi), John Wiley & Sons, Hoboken, **2013**, p 59–95; b) C. J. O'Connor, H. S. G. Beckmann, D. R. Spring, *Chem. Soc. Rev.* **2012**, *41*, 4444–4456.

[3] For selected recent reviews: a) J. J. Douglas, J. D. Nguyen, K. P. Cole, C. R. J. Stephenson, *Aldrichimica Acta* **2014**, *47*, 15–25; b) T. P. Yoon, *ACS Catal.* **2013**, *3*, 895–902; c) C. K. Prier, D. A. Rankic, D. W. C. MacMillan, *Chem. Rev.* **2013**, *113*, 5322–5363; d) J. Xuan, L.-Q. Lu, J.-R. Chen, W.-J. Xiao, *Eur. J. Org. Chem.* **2013**, 6755–6770.

[4] a) K. Kalyanasundaram, *Coord. Chem. Rev.* **1982**, *46*, 1159–1244; b) L. Flamigni, A. Barbieri, C. Sabatini, B. Ventura, F. Barigelletti, *Top. Curr. Chem.* **2007**, *281*, 143–203.

[5] a) S. Maity, M. Zhu, R. S. Shinabery, N. Zheng, *Angew. Chem.* **2012**, *124*, 226–230; *Angew. Chem. Int. Ed.* **2012**, *51*, 222–226; b) T. H. Nguyen, S. Maity, N. Zheng, *Beilstein J. Org. Chem. Beilstein. J. Org. Chem.* **2014**, *10*, 975–980.

[6] J. D. Nguyen, B. Reiss, C. Dai, C. R. J. Stephenson, *Chem. Commun.* **2013**, *49*, 4352–4354.

[7] M. S. Lowry, S. Bernhard, *Chem. Eur. J.* **2006**, *12*, 7970–7977.

[8] M. Charpenay, A. Boudhar, C. Hulot, G. Blond, J. Suffert, *Tetrahedron* **2013**, *69*, 7568–7591.

[9] H. Zhou, C. Moberg, *J. Am. Chem. Soc.* **2012**, *134*, 15992–15999.

[10] X. Li, M. L. Grimm, K. Igarashi, N. Castagnoli Jr, J. M. Tanko, *Chem. Commun.* **2007**, 2648–2650.

[11] a) L. Ackermann, A. V. Lygin, *Org. Lett.* **2011**, *13*, 3332–3335; b) L. Ackermann, A. V. Lygin, *Org. Lett.* **2012**, *14*, 764–767.

[12] a) C. K. Jana, S. Grimme, A. Studer, *Chem. Eur. J.* **2009**, *15*, 9078–9084; b) N. Dastbaravardeh, M. Schnürch, M. D. Mihovilovic, *Org. Lett.* **2012**, *14*, 1930–1933; c) Z. Wang, B. J. Reinus, G. Dong, *Chem. Commun.* **2014**, *50*, 5230–5232.

[13] a) J. M. M. Verkade, L. J. C. van Hemert, P. J. L. M. Quaedflieg, P. L. Alsters, F. L. van Delft, F. P. J. T. Rutjes, *Tetrahedron Lett.* **2006**, *47*, 8109–8113; b) S. De Lamo Marin, T. Martens, C. Mioskowski, J. Royer, *J. Org. Chem.* **2005**, *70*, 10592–10595.

[14] G. Bergonzini, C. S. Schindler, C.-J. Wallentin, E. N. Jacobsen, C. R. J. Stephenson, *Chem. Sci.* **2014**, *5*, 112–116.