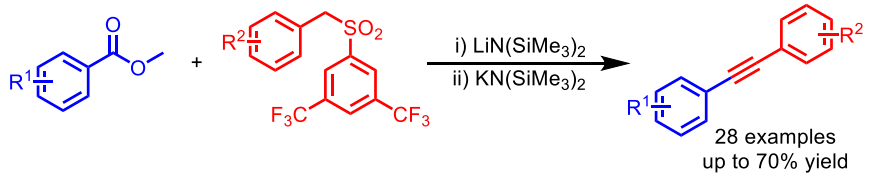
Smiles Rearrangement-based One-pot Synthesis of Diarylacetylenes from Benzylic Sulfones and Methyl Benzoates Mediated by $LiN(SiMe_3)_2/KN(SiMe_3)_2$

Mingyu Jiang,[a] Yan-En Wang,[b] Yuanyun Gu,[a] Ruyuan Ma,[a] Dan Xiong,[a] Patrick j. Walsh,*[,c] and Jianyou Mao,*[,a]

[a]*School of Chemistry and Molecular Engineering, Nanjing Tech University, 30 South Puzhu Road, Nanjing 211816, P. R. China.*

[b]*College of Science, Hebei Agricultural University, Baoding 071000, P. R. China.*

[c] *Roy and Diana Vagelos Laboratories, Department of Chemistry, University of Pennsylvania, 231 South 34th Street, Philadelphia, Pennsylvania 19104-6323, United States.*



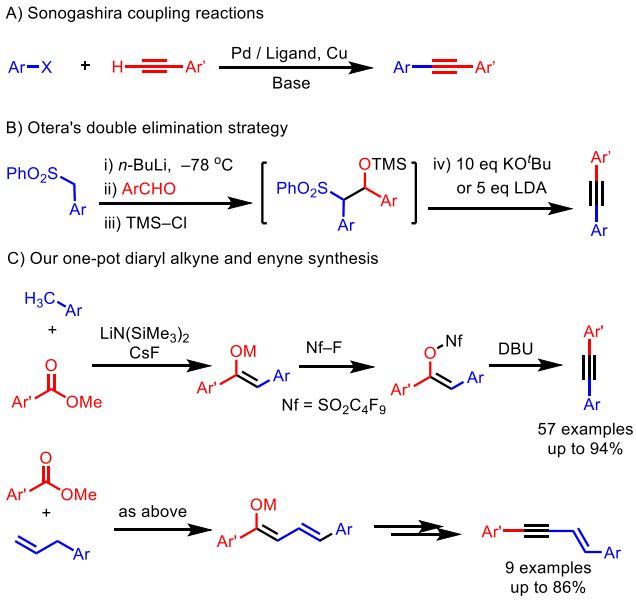
ABSTRACT: The one-pot synthesis of diphenylacetylene by the reaction of methyl benzoate with 1-(benzylsulfonyl)-3,5-di(trifluoromethyl)benzene was developed. The combination of $LiN(SiMe_3)_2$ and $KN(SiMe_3)_2$ is key to promote the reaction. Simply combining methyl benzoate, 1-(benzylsulfonyl)-3,5-di(trifluoromethyl)benzene, $LiN(SiMe_3)_2$, and $KN(SiMe_3)_2$ can produce a variety of diaryl acetylenes (28 examples, 18–70% yields).

Diarylacetylenes have emerged as an important class of unsaturated organic compounds due to their broad utility in a host of reactions.[1] These alkynes can be converted into medicinally relevant heterocycles[2] or into materials with uses in liquid crystals[3] and conducting polymers.[4] Diarylalkynes themselves are found in bioactive molecules[5] and in medicinal chemistry.[6] The demand for diarylacetylenes motivates the development of new methods for their synthesis.

The traditional approach for the synthesis of diarylacetylenes is the Sonogashira cross-coupling reaction (Scheme 1A).[7] The popularity of the palladium catalyzed and copper co-catalyzed Sonogashira is due to its reliability in the coupling of terminal alkynes with aryl halides and their derivatives. Drawbacks of this coupling reaction include use of Pd, which is expensive and Cu which is toxic, and the need to synthesize or buy terminal alkynes. Inroads have been made with use of catalysts based on iron,[8] cobalt,[9] and copper alone[10] but these processes have not achieved the utility of the Pd-based Sonogashira reaction (Scheme 1A). Of course, certain applications of alkynes require near complete removal of transition metal residues from the alkyne products, which can be challenging. In such cases, it might be better to synthesize alkynes under transition metal-free conditions.

Several groups have introduced methods to address the drawbacks of the Sonogashira approach and the need to access its precursors, terminal alkynes. Otera and coworkers employed sulfones and a double elimination strategy (Scheme 1B).[11] Deprotonation of the sulfone at –78 °C with *n*-BuLi was followed by condensation with an aldehyde and trapping of the resulting alkoxide with TMS–Cl. The elimination of $TMSO^-$ and sulfinate was conducted with either 10 equiv KO^tBu or 5 equiv LDA. Otera's method is reagent heavy and uses temperatures difficult to access on scale. Double elimination strategies using benzotriazoles have also been developed.[12] Our team has been interested in the synthesis of alkynes.[13] We have investigated the reversible deprotonation of toluene derivatives with silylamides and Cs^+ salts for use in C–C bond-forming reactions. Based on these efforts we recently advanced a method for the conversion of toluenes and methyl benzoates to diarylacetylenes.[13a] Reversible deprotonation of toluenes in the presence of methyl benzoate generates the benzylic organometallic that adds to the ester, ultimately affording an enolate. Reaction of this enolate with $F–SO_2CF_2CF_2CF_2CF_3$ (Nf–F) and elimination with DBU generates the third bond of the alkyne and furnished the diarylacetylenes. This procedure could also be employed for a one-pot synthesis of enynes from allylbenzenes (Scheme 1C).

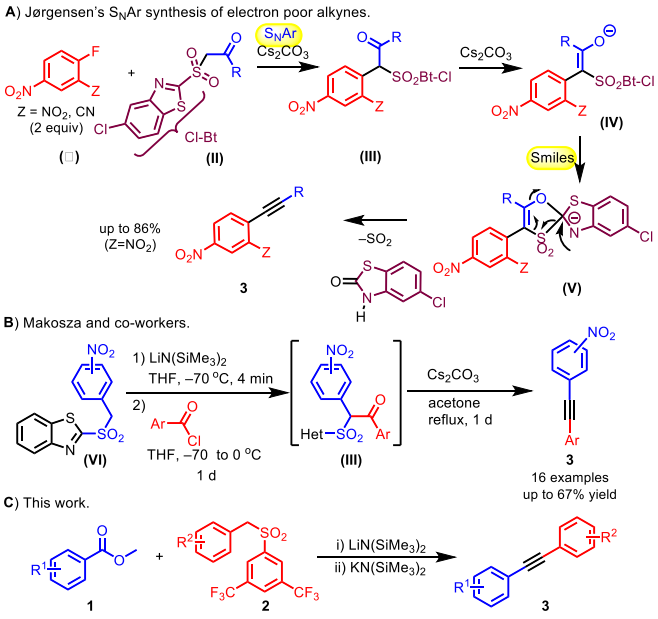
Scheme 1. Previous work for the synthesis of diarylacetylenes



Recently, the synthesis of diarylacetylenes using a Smiles rearrangement to generate a leaving group in situ has been studied. This approach is similar to the Julia-Kocienski olefination.[14] In pioneering work, Jorgensen and colleagues synthesized dinitroacetylene derivatives (**3**) by Smiles rearrangement of benzothiazolyl derivatives (**III**) (Scheme 2A).[15] Here, deprotonation of a keto sulfone (**II**) was followed by S$_N$Ar with a highly electron deficient aryl fluoride (**I**). Next, enolization and the Smiles rearrangement generated a heterocyclic leaving group (Cl-Bt–O$^-$). Although this system only works for the synthesis of electron deficient alkynes, it is conceptually interesting.

Building on this work, in 2019 Makosza reported that nitrobenzyl benzothiazol-2-yl sulfones (**VI**) reacted with benzoyl chlorides at –70 ºC to form *a*-sulfonyl ketone intermediates (**III**). Similarly, Pospíšil and Barbasiewicz presented a one-pot protocol that enabled the straightforward transformation of sulfones and acyl chlorides into ketones.[16] Those *a*-sulfonyl ketone intermediates (**III**) underwent enolization and Smiles rearrangement resulting in the formation of the corresponding nitrophenyl arylacetylenes (**3**) (Scheme 2B).[17] By using similar sulfonyl ketone intermediates (**III**), Loska and co-workers introduced a regioselective elimination process for the synthesis of allenes.[18] Like the Jorgensen approach, Makosza's method works with nitro-substituted aryl derivatives. Further, it requires low temperatures that would be difficult to scale and uses reactive benzoyl chlorides.

Scheme 2. Smiles rearrangement-based acetylene synthesis

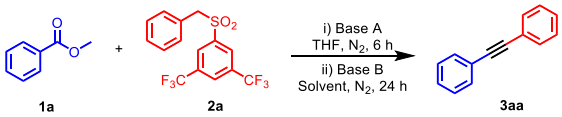


The work of Jorgensen and Makosza inspired us to explore the development of an alkyne synthesis with the Smiles rearrangement that was not limited to the synthesis of highly electron poor alkynes. Based on our experience in the synthesis of alkynes (Scheme 1C), we envisioned that the synthesis of keto-sulfonate intermediates, like those in Scheme 2A and B, could be performed with inexpensive and readily available methyl benzoates. Under basic conditions, we envisioned a reaction of the benzylic sulfone 1-(benzylsulfonyl)-3,5-di(trifluoromethyl)benzene under basic conditions with methyl benzoates would provide a more general approach to the Smiles rearrangement-based method than those in Scheme 2A and 2B.

We started the reaction development and optimization by using methyl benzoate (**1a**) and 1-(benzylsulfonyl)-3,5-di(trifluoromethyl)benzene (**2a**) as model substrates and THF as the solvent (Table 1, see SI for full details on the optimization). We explored three different bases [LiN(SiMe$_3$)$_2$, NaN(SiMe$_3$)$_2$, and KN(SiMe$_3$)$_2$] at 80 °C for 6 h (Table 1, entries 1–3). Unfortunately, these conditions only gave traces of the alkyne product. Considering the possible synergistic effect between Li, Na, and K,[19] we examined the combination between LiN(SiMe$_3$)$_2$ and KN(SiMe$_3$)$_2$ which generated the target product **3aa** in 19% yield. We next screened temperatures with the bases LiN(SiMe$_3$)$_2$ and KN(SiMe$_3$)$_2$ (Table 1, entries 4–6). When LiN(SiMe$_3$)$_2$ and KN(SiMe$_3$)$_2$ were added at 0 °C for 6 h, then heated at 80 °C for 24 h, the desired product was generated in 20% yield (Table 1, entry 6). These studies indicated that temperature is important because the byproducts benzonitrile (formed from methyl benzoate reacting with the silylamide base) and stilbene (from self-coupling of 1-(benzylsulfonyl)-3,5-di(trifluoromethyl)benzene) were formed in different amounts at different temperatures. These results inspired us to hypothesize that these two bases might have different roles in the tandem reaction. We assumed that LiN(SiMe$_3$)$_2$ mainly promotes the condensation of 1-(benzylsulfonyl)-3,5-

di(trifluoromethyl)benzene with methyl benzoate to generate the key intermediate ketosulfones and their enolates. In contrast, $KN(SiMe_3)_2$ mainly facilitates the Smiles rearrangement. Based on this hypothesis, we changed the experimental procedure by adding the $LiN(SiMe_3)_2$ first to the mixture of methyl benzoate (**1a**) and 1-(benzylsulfonyl)-3,5-di(trifluoromethyl)benzene (**2a**) with stirring for 6 h at 0 °C. After that, $KN(SiMe_3)_2$ was added with continued stirring for 24 h at 80 °C. After extensive optimization, the desired alkyne product was generated in 37% yield in a one-pot two-step process (Table 1, entry 7). Under the conditions of entry 7, we observed the byproduct of the unreacted keto sulfones. The intermediate keto sulfone was isolated, and we screened different solvents for the Smiles rearrangement. The results showed that DME and 1,4-dioxane solvents gave acceptable results (conditions listed in SI Table S2). To facilitate

Table 1. Optimization of Reaction Conditions



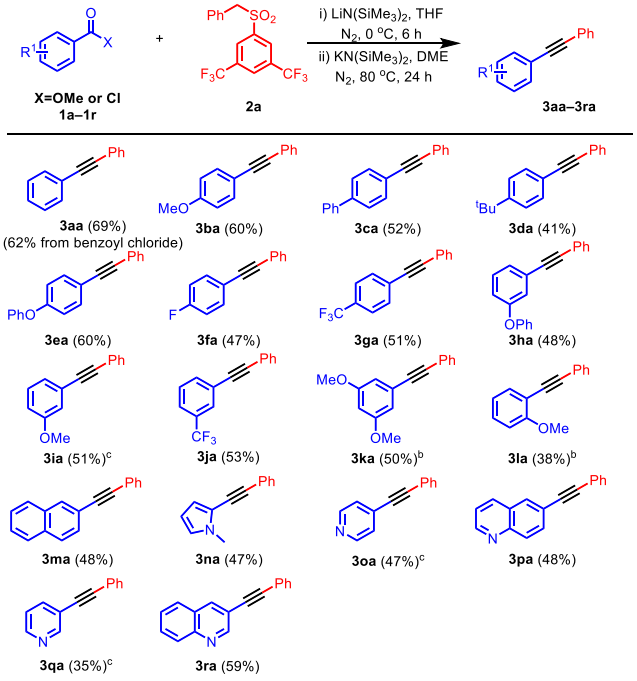
Entry[a]	Base A	Base B	Solvent	T (°C)	AY[b](%)
1	$LiN(SiMe_3)_2$		THF	80	trace
2	$NaN(SiMe_3)_2$		THF	80	trace
3	$KN(SiMe_3)_2$		THF	80	trace
4	$LiN(SiMe_3)_2$	$KN(SiMe_3)_2$	THF	80	19
5	$LiN(SiMe_3)_2$	$KN(SiMe_3)_2$	THF	25-80	11
6	$LiN(SiMe_3)_2$	$KN(SiMe_3)_2$	THF	0-80	20
7[c]	$LiN(SiMe_3)_2$	$KN(SiMe_3)_2$	THF	0-80	37
8[d]	**$LiN(SiMe_3)_2$**	**$KN(SiMe_3)_2$**	**THF/ DME**	**0-80**	**67/69[e]**

[a]Reactions conducted under nitrogen on 0.1 mmol scale. [b]Assay yield determined by GC integration with *n*-tetradecane as an internal standard. [c]$LiN(SiMe_3)_2$ (0.4 mmol) at 0 °C for 6 h, then addition $KN(SiMe_3)_2$ (0.6 mmol) at 80 °C for 24 h. [d]$LiN(SiMe_3)_2$ (0.4 mmol) and THF (1.0 mL) at 0 °C for 6 h, then addition $KN(SiMe_3)_2$ (0.6 mmol) and DME (0.6 mL) at 80 °C for 24 h. [e]Isolated yield.

the operation, we added DME to the reaction mixture prior to the Smiles rearrangement. Under these conditions, the mixture of THF and DME was superior to THF alone (Table 1, entry 8). Ultimately, our optimized conditions are 2.5 equiv of methyl benzoate (**1a**), 1.0 equiv of 1-(benzylsulfonyl)-3,5-di(trifluoromethyl)benzene (**2a**), 4.0 equiv of $LiN(SiMe_3)_2$ and 1.0 mL of THF at 0 °C for 6 h, then addition of 6.0 equiv of $KN(SiMe_3)_2$ and 0.6 mL of DME to the reaction solution at 80 °C for 24 h.

With the optimized reaction conditions in hand, the substrate scope of methyl benzoate derivatives was explored (Scheme 3). The product from use of methyl benzoate provided the isolated alkyne in 69% yield (**3aa**). When using benzoyl chloride as a substrate instead of methyl benzoate, the target product **3aa** could also be obtained in 62% yield. Methyl benzoate derivatives with electron-donating groups, including 4-OMe (**1b**), 4-Ph (**1c**), 4-^{t}Bu (**1d**) and 4-OPh (**1e**), showed good reactivity, producing alkynes **3ba**-**3ea** in 41–60% yields. Methyl benzoates possessing electronegative or electron-withdrawing groups exhibited compatibility with the procedure. Methyl 4-fluorobenzoate (**1f**) and methyl 4-trifluoromethylbenzoate (**1g**) afforded **3fa** and **3ga** in 47% and 51% yields, respectively. Methyl benzoates bearing *meta* substituents 3-OPh (**1h**), 3-OMe (**1i**), 3-CF_3 (**1j**) and 3,5-OMe (**1k**) were also good coupling partners, giving the target products **3ha**-**3ka** in 48–53% yields. A sterically hindered methyl benzoate with a 2-OMe group (**1l**) was used to obtain the corresponding product **3la** in 38% yield. π-Extended 2-naphthyl derivative (**1m**) was a viable substrate, providing **3ma** in 48% yield. Heterocyclic diaryl alkynes could be prepared by using *N*-methylpyrrole, pyridine and quinoline as substrates, producing **3na**-**3ra** in 35–59% yields. Unfortunately, alkyl-substituted acid chlorides and esters were not viable. (See SI for details).

Scheme 3. Substrate Scope of Methyl Benzoates and Benzoyl Chloride



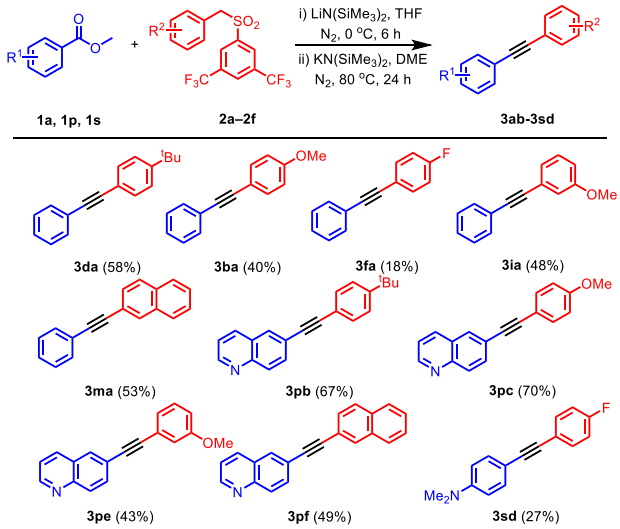
[a]Conditions: **1a** (0.25 mmol), **2a** (0.1 mmol), $LiN(SiMe_3)_2$ (0.4 mmol), 1 mL THF, N_2, 0 °C, and 6 h, then add $KN(SiMe_3)_2$ (0.6 mmol), 0.6 mL DME, 80 °C, 24 h. [b]$NaN(SiMe_3)_2$ (0.6 mmol), 130 °C were used. [c]130 °C was used.

Next, we explored the substrate scope by using 1-(benzylsulfonyl)-3,5-di(trifluoromethyl)benzene substituted with various groups (Scheme 4). Using the 4-*tert*-butyl benzyl derivative **2b,** the alkyne product **3da** was isolated in 58% yield. With a benzyl substituted with an electron-donating 4-OMe (**2c**), the corresponding alkyne **3ba** was isolated in 40% yield. A substrate containing 4-F (**2d**) underwent the transformation, but furnished **3fa** in only 18% yield. The sulfone containing 3-OMe (**2e**) produced **3ia** in 48% yield while the π-extended 2-naphthalene derivative reacted to furnish the product **3ma** in 53% yield.

We were pleased to find that sulfones containing 4-^{t}Bu (**2b**), 4-OMe (**2c**), 3-OMe (**2e**) and 2-naphthalene (**2f**) coupled with methyl quinoline carboxylate (**1p**) providing the corresponding products **3pb**-**3pf** in 43-70% yields. Similarly, substrate **2d** reacted with methyl 4-*N,N*-dimethylamino benzoate **1s** to provide the alkyne product **3sd** in 27%

yield. It is worth noting that **3sd** can repress c-myc expression in cancer cells.[5c]

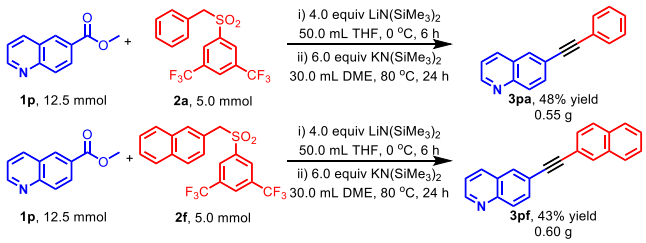
Scheme 4. Substrate Scope of 1-(benzylsulfonyl)-3,5-di(trifluoromethyl)benzene



[a]Reactions conducted under nitrogen on 0.1 mmol scale, 1 mL THF, **1a** (0.25 mmol), **2a** (0.1 mmol), 4 equiv $LiN(SiMe_3)_2$, 0 °C, and 6 h, then add 6 equiv $KN(SiMe_3)_2$, 0.6 mL DME, 80 °C, 24 h.

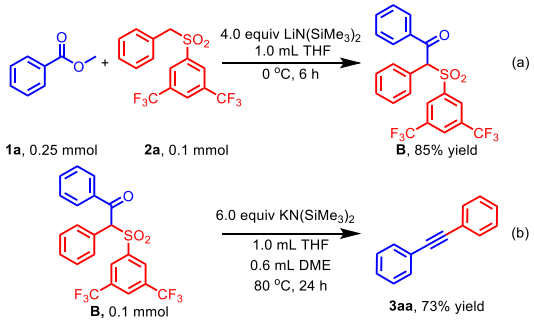
To test the scalability of this alkyne synthesis, 5 mmol of 1-(benzylsulfonyl)-3,5-di(trifluoromethyl)benzene (**2a**) and 3,5-bis(trifluoromethyl)phenyl 2-naphthylmethyl sulfone (**2f**) were reacted with methyl quinoline-6-carboxylate (**1p**) (Scheme 5). A 48% yield of **3pa** and a 43% yield of **3pf** were obtained.

Scheme 5. Scale up Synthesis



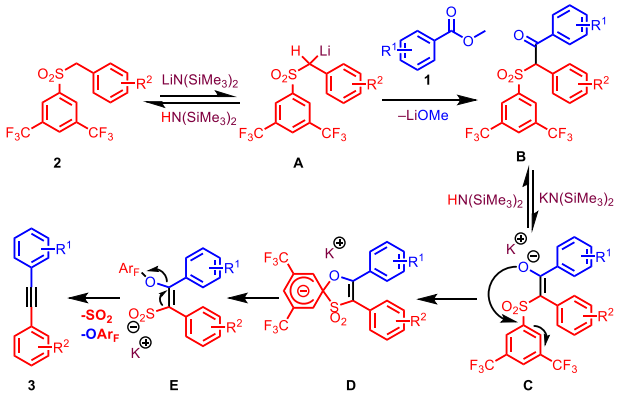
To explore the mechanism of this one-pot synthesis of diaryl acetylenes, the following reactions were conducted (Scheme 6). The result of entry 1 in Table 1 showed that intermediate **B** was first formed with the help of $LiN(SiMe_3)_2$. Using 4 equiv $LiN(SiMe_3)_2$ with methyl benzoate at 0 °C formed intermediate **B** in 85% yield (Scheme 6a). Under standard conditions, no intermediate keto sulfone was observed. Next, the pre-prepared intermediate **B** was reacted with $KN(SiMe_3)_2$ giving the corresponding product **3aa** in 73% yield (Scheme 6b). The combined yield in Scheme 6 (62%) is similar to the one-pot procedure (67%) and suggests that neither step is high yielding.

Scheme 6. Isolation and Examination of Intermediates.



On the basis of these studies, we proposed a mechanism in Scheme 7. Reversible deprotonation of **2** generates **A**. Reaction of **A** with methyl benzoate **1** forms intermediate ketosulfonates **B**, which is deprotonated to give enolate **C**. In the presence of the K^+ salt, which should exhibit greater solvent separation, the Smiles rearrangement ensues with loss of SO_2 and the leaving aryloxide, $MOC_6H_3(CF_3)_2$.

Scheme 7. Proposed Reaction Pathway



In summary, we developed a transition metal-free diarylacetylene synthesis mediated by $LiN(SiMe_3)_2$ and $KN(SiMe_3)_2$. It is possible that the need for the K^+ salt stems from the higher expected solvent separation in the enolate, which may contribute to the nucleophilicity of the enolate and favor the first step in the Smiles rearrangement. The carbon-carbon triple bond was successfully constructed by Smiles rearrangement, albeit with low conversions in some cases. By simple combination of methyl benzoate, 1-(benzylsulfonyl)-3,5-di(trifluoromethyl)benzene, $LiN(SiMe_3)_2$ and $KN(SiMe_3)_2$, a variety of diphenylacetylenes were produced. It is hoped that this chemistry draws increased attention to the use of the Smiles rearrangement in the one-pot synthesis of alkynes and leads to further development in this area.

ASSOCIATED CONTENT

Data Availability Statement

The data underlying this study are available in the published article and its Supporting Information.

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Supporting Information. (Experimental details, characterization data and NMR spectra)

AUTHOR INFORMATION

Corresponding Author

Patrick J. Walsh – *Roy and Diana Vagelos Laboratories, Department of Chemistry, University of Pennsylvania, Philadelphia, Pennsylvania 19104-6323, United States;* https://orcid.org/0000-0001-8392-4150; Email: pwalsh@ sas.upenn.edu

Jianyou Mao – *Technical Institute of Fluorochemistry (TIF), State Key Laboratory of Materials Oriented Chemical Engineering (MCE),School of Chemistry and Molecular Engineering, Nanjing Tech University, 30 South Puzhu Road, Nanjing 211816, P. R. China;* https://orcid.org/0000-0003-0581-3978; Email: ias_jymao@njtech.edu.cn

Authors

Mingyu Jiang – *Technical Institute of Fluorochemistry (TIF), State Key Laboratory of Materials Oriented Chemical Engineering (MCE), School of Chemistry and Molecular Engineering, Nanjing Tech University, 30 South Puzhu Road, Nanjing 211816, P. R. China;*

Yan-En Wang – *College of Science, Hebei Agricultural University, Baoding 071000, P. R. China;*

Yuanyun Gu – *Technical Institute of Fluorochemistry (TIF), State Key Laboratory of Materials Oriented Chemical Engineering (MCE), School of Chemistry and Molecular Engineering, Nanjing Tech University, 30 South Puzhu Road, Nanjing 211816, P. R. China;*

Ruyuan Ma – *Technical Institute of Fluorochemistry (TIF), State Key Laboratory of Materials Oriented Chemical Engineering (MCE), School of Chemistry and Molecular Engineering, Nanjing Tech University, 30 South Puzhu Road, Nanjing 211816, P. R. China;*

Dan Xiong – *Technical Institute of Fluorochemistry (TIF), State Key Laboratory of Materials Oriented Chemical Engineering (MCE), School of Chemistry and Molecular Engineering, Nanjing Tech University, 30 South Puzhu Road, Nanjing 211816, P. R. China;*

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENT

The authors acknowledge the National Natural Science Foundation of China (22071107), the Natural Science Foundation of Jiangsu Province, China (BK20211588), and the Provincial Key Research and Development Program of Jiangsu (Modern Agriculture) (No. BE2023333). PJW thanks the US National Science Foundation (CHE-2154593) and the Petroleum Research Fund (67280-ND1) for financial support

REFERENCES

(1) Fürstner, A.; Davies, P. W. Heterocycles by $PtCl_2$-Catalyzed Intramolecular Carboalkoxylation or Carboamination of Alkynes. *J. Am. Chem. Soc* **2005,** *127*, 15024-15025.

(2) (a) Stuart, D. R.; Bertrand-Laperle, M..; Burgess, K. M. N.; Fagnou, K.; Indole Synthesis via Rhodium Catalyzed Oxidative Coupling of Acetanilides and Internal Alkynes. *J. Am. Chem. Soc* **2008,** *130*, 16474-16475; (b) Li, B.; Ju, Z.; Zhou, M.; Su, K.; Yuan, D. A Reusable MOF-Supported Single-Site Zinc(II) Catalyst for Efficient Intramolecular Hydroamination of o-Alkynylanilines. *Angew.Chem. Int.Ed.* **2019,** *58*, 7687-7691; (c) Wang, H.; Li, Y.; Jiang, L.; Zhang, R.; Jin, K.; Zhao, D.; Duan, C. Ready synthesis of free N-H 2-arylindoles via the copper-catalyzed amination of 2-bromo-arylacetylenes with aqueous ammonia and sequential intramolecular cyclization. *Org. Biomol. Chem.* **2011,** *9*, 4983-4986; (d) Phetrak, N.; Rukkijakan, T.; Sirijaraensre, J.; Prabpai, S.; Kongsaeree, P.; Klinchan, C.; Chuawong, P. Regioselectivity of Larock Heteroannulation: A Contribution from Electronic Properties of Diarylacetylenes. *J. Org. Chem.* **2013,** *78*, 12703-12709; (e) Alonso, F.; Moglie, Y.; Radivoy, G., Copper Nanoparticles in Click Chemistry. *Acc. Chem. Res.* **2015,** *48*, 2516-2528; (f) Jarosław Kalisiak, K. B. S., and Valery V. Fokin, Efficient Synthesis of 2-Substituted-1,2,3-triazoles. *Org. Lett.* **2008,** *10*, 3171-3174.

(3) (a) Li, Y.; Liu, T.; Ambrogi, V.; Rios, O.; Xia, M.; He, W.; Yang, Z. Liquid Crystalline Elastomers Based on Click Chemistry. *ACS Appl. Mater. Interfaces* **2022,** *14*, 14842-14858; (b) García-Frutos, E. M.; Pandey, U. K.; Termine, R.; Omenat, A.; Barberá, J.; Serrano, J. L.; Golemme, A.; Gómez-Lor, B. High Charge Mobility in Discotic Liquid-Crystalline Triindoles: Just a Core Business? *Angew. Chem. Int. Ed.* **2011,** *50*, 7399-7402; (c) Kitamura, T.; Lee, C. H.; Taniguchi, H.; Matsumoto, M.; Sanot, Y. Preparation and Coupling Reactions of Alkynyl(phenyl)iodonium Salts Bearing Long Alkoxy Chains. Formation of Liquid-Crystalline Diacetylenes. *J. Org. Chem.* **1994,** *59*, 8053-8057.

(4) Sakaguchi, T.; Hayakawa, Y.; Ishima, R.; Hashimoto, T. Synthesis and photoluminescence properties of poly(1-hexyl-2-aryl acetylene)s, poly(1-phenyl-2-fluorenylacetylene), and poly(1-fluorenyl-2-fluorenlacetylene). *Synth. Met.* **2012,** *162*, 64-69.

(5) (a) Chen, Q.-H.; Praveen Rao, P. N.; Knaus, E. E. Design, synthesis, and biological evaluation of linear 1-(4-, 3- or 2-methylsulfonylphenyl)-2-phenylacetylenes: A novel class of cyclooxygenase-2 inhibitors. *Biorg. Med. Chem.* **2005,** *13*, 6425-6434; (b) Kordik, C. P.; Luo, C.; Gutherman, M.; Vaidya, A. H.; Rosenthal, D. I.; Crooke, J. J.; McKenney, S. L.; Plata-Salaman, C. R.; Reitz, A. B. Diarylacetylene piperidinyl amides as novel anxiolytics. *Bioorg. Med. Chem. Lett.* **2006,** *16*, 3065-3067; (c) Sviripa, V. M.; Zhang, W.; Kril, L. M.;, Liu, A. X.; Yuan, Y.; Zhan, C.; Liu, C.; Watt, D. S. Halogenated diarylacetylenes repress c-myc expression in cancer cells. *Bioorg. Med. Chem. Lett.* **2014,** *24*, 3638-3640.

(6) (a) Talele, T. T. Acetylene Group, Friend or Foe in Medicinal Chemistry. *J. Med. Chem.* **2020,** *63*, 5625-5663; (b) Tron, G. C.; Pirali, T.; Billington, R. A.; Canonico, P. L.; Sorba, G.; Genazzani, A. A. Click chemistry reactions in medicinal chemistry: Applications of the 1,3-dipolar cycloaddition between azides and alkynes. *Med. Res. Rev.* **2007,** *28*, 278-308.

(7) (a) Sapegin, A.; Krasavin, M. One-Pot Conversion of Aldehydes and Aryl Halides to Disubstituted Alkynes via Tandem Seyferth-Gilbert Homologation/Copper-Free Sonogashira Coupling. *J. Org. Chem.* **2019,** *84*, 8788-8795; (b) Sonogashira, K.; Tohda, Y.; Hagihara, N. A convenient synthesis of acetylenes: catalytic substitutions of acetylenic hydrogen with bromoalkenes, iodoarenes and bro-mopyridines. *Tetrahedron Lett.* **1975,** *50*, 4467-4470; (c) Johansson Seechurn, C. C. C.; Kitching, M. O.; Colacot, T. J.; Snieckus, V., Palladium-Catalyzed Cross-Coupling: A Historical Contextual Perspective to the 2010 Nobel Prize. *Angew. Chem., Int. Ed.* **2012,** *51*, 5062-5085; (d) Karak, M.; Barbosa, L. C. A.; Hargaden, G. C. Recent mechanistic developments and next generation catalysts for the Sonogashira coupling reaction. *RSC Adv.* **2014,** *4*, 53442-53466.

(8) (a) Sindhu, K. S.; Thankachan, A. P.; Thomas, A. M.; Anilkumar, G. Iron-Catalyzed Sonogashira Type Cross-Coupling Reaction of Aryl Iodides with Terminal Alkynes in Water under Aerobic Conditions. *ChemistrySelect* **2016,** *1*, 556-559; (b) Handa, S.; Jin, B.; Bora, P. P.; Wang, Y.; Zhang, X.; Gallou, F.; Reilly, J.; Lipshutz, B. H. Sonogashira Couplings Catalyzed by Fe Nanoparticles Containing ppm Levels of Reusable Pd, under Mild Aqueous Micellar Conditions. *ACS Catal.* **2019,** *9*, 2423-2431; (c) Hung, T.; Huang, C.; Tsai, F. Y., Sonogashira-Hagihara Coupling towards Diaryl Alkynes Catalyzed by $FeCl_3{\cdot}6H_2O$/Cationic 2,2'-Bipyridyl. *ChemCatChem* **2012,** *4*, 540-545.

(9) (a) Hajipour, A. R.; Rezaei, F.; Khorsandi, Z. Pd/Cu-free Heck and Sonogashira cross-coupling reaction by Co nanoparticles immobilized on magnetic chitosan as reusable catalyst. *Green Chem*. **2017,** *19*, 1353-1361; (b) Hajipour, A. R.; Khorsandi, Z.; Abeshtian, Z. Pd/Cu-free Heck and Sonogashira reactions using cobalt immobilized on in situ magnetic cross-linked chitosan fibers: A highly efficient and reusable catalyst. *Inorg. Chem. Commun*. **2019,** *107*, 107470.

(10) (a) Xu, W.; Yu, B.; Sun, H.; Zhang, G.; Zhang, W.; Gao, Z. Copper-catalyzed C(sp^2)─C(sp) Sonogashira-type cross-coupling reactions accelerated by polycyclic aromatic hydrocarbons. *Appl. Organomet. Chem*. **2015,** *29*, 353-356; (b) Wang, X.; Wang, Z.; Xie, Z.; Zhang, G.; Zhang, W.; Gao, Z. Functionalized *α,β*-ynones: efficient ligand for Cu catalyzed Sonogashira-type cross-coupling reaction. *RSC Adv*. **2016,** *6*, 109296-109300.

(11) Mandai, T.; Yanagi, T.; Araki, K.; Morisaki, Y.; Kawada, M.; Otera, J. Novel Synthesis of Acetylenes and Polyenes via Desulfonylation Reaction. *J. Am. Chem. Soc*. **1984,** *106*, 3670-3672.

(12) (a) Katritzky, A. R.; Gordeev, M. F. New Synthesis of Diarylalkynes from 1 -(Arylrnethyl)benzotriazoles and arylideneamines. *J. Chem. Soc., Perkin Trans*. **1992**, 1295-1298; (b) Katritzky, A. R.; Rogovoy, B. V.; Mitrokhin, A. Y. The preparation of diarylacetylenes via diphenyl (benzotriazol-1-yl)(aryl)methylphosphonates. *ARKIVOC* **2003,** *2002*, 17-27; (c) Katritzky, A. R.; Wang, J.; Karodia, N.; Li, J. A Novel Transformation of Esters to Alkynes with 1-Substituted Benzotriazoles. *J. Org. Chem*. **1997,** *62*, 4142-4147; (d) Paventi, M.; Elce, E.; Jackman, R. J.; Hay, A. S. A novel synthesis of diarylacetylenes from N-arylmethylheteroarenes and *N*-arylmethyleneanilines. *Tetrahedron Lett*. **1992,** *33*, 6405-6406; (e) Chen, J.; Zhang, X.; Wu, J.; Wang, R.; Lei, C.; An, Y. Facile one-pot synthesis of diarylacetylenes from arylaldehydes via an addition-double elimination process. *Org. Biomol. Chem*. **2021,** *19*, 4701-4705.

(13) (a) Gu, Y.; Wu, Y.; Wang, Y.-E.; Phadnis, N.; Xiong, D.; Mao, J.; Walsh, P. J. One-pot transition-metal-free synthesis of alkynes and enynes. *Cell Rep. Phys. Sci*. **2024,** DOI: 10.1016/j.xcrp.2024.102132. (b) Zhang, M.; Jia, T.; Wang, C. Y.; Walsh, P. J. Organocatalytic Synthesis of Alkynes. *J. Am. Chem. Soc* **2015,** *137*, 10346-10350. (c) Wu, Y.; Sátiro, B. G.; Mao, J. ; Walsh, P. J. One-Pot Transition-Metal-Free Synthesis of Alkynyl Amides. *Angew. Chem., Int. Ed*. **2024**, DOI: 10.1002/anie.202415472.

(14) Alonso, D. A.; Fuensanta, M.; Nájera, C.; Varea, M. 3,5-Bis(trifluoromethyl)phenyl Sulfones in the Direct Julia-Kocienski Olefination. *J. Org. Chem*. **2005,** *70*, 6404-6416.

(15) Prüger, B.; Hofmeister, G. E.; Jacobsen, C. B.; Alberg, D. G.; Nielsen, M.; Jørgensen, K. A. Transition-Metal-Free Formal Sonogashira Coupling and *α*-Carbonyl Arylation Reactions. *Chem. Eur. J*. **2010,** *16*, 3783-3790.

(16) (a) Bon, D. J. Y. D.; Chrenko, D.; Kováč, O.; Ferugová, V.; Lasák, P.; Fuksová, M.; Zálešák, F.; Pospíšil, J. Julia-Kocienski-Like Connective C−C and C=C Bond-Forming Reaction. *Adv. Synth. Catal*. **2024**, *366*, 480–487; (b) Pospíšil, J.; Sato, H. Practical Synthesis of *β*-Acyl and *β*-Alkoxycarbonyl Heterocyclic Sulfones. *J. Org. Chem*. **2011,** *76*, 2269-2272; (c) Pospíšil, J.; Robiette, R.; Sato, H.; Debrus, K. Practical synthesis of β-oxo benzo[d]thiazolyl sulfones: Scope and limitations. *Org. Biomol. Chem*. **2012,** *10*, 1225-1234; (d) Górski, B.; Basiak, D.; Grzesiński, Ł.; Barbasiewicz, M. Stereodivergent synthesis of alkenes by controllable syn-/anti-fragmentation of *β*-hydroxysulfonyl intermediates. *Org. Biomol. Chem*. **2019,** *17*, 7660-7663.

(17) Bujok, R.; Mąkosza, M. Synthesis of Diarylacetylenes Bearing Electron-Withdrawing Groups via the Smiles Rearrangement. *Synth*. **2019,** *51*, 3109-3116.

(18) Wasilewska-Rosa, A.; Kisiel, K.; Tkaczyk, A.; Loska, R. Stereospecific Synthesis of Allenes from β-Ketosulfones. *Adv. Synth. Catal*. **2023,** *365*, 704-708.

(19) Robertson, S. D.; Uzelac, M.; Mulvey, R. E. Alkali-Metal-Mediated Synergistic Effects in Polar Main Group Organometallic Chemistry. *Chem. Rev*. **2019,** *119*, 8332-8405.