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Synthesis of Functionalized 1*H*-Indenes via Copper-Catalyzed Arylative Cyclization of Arylalkynes with Aromatic Sulfonyl Chlorides

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Supporting Information

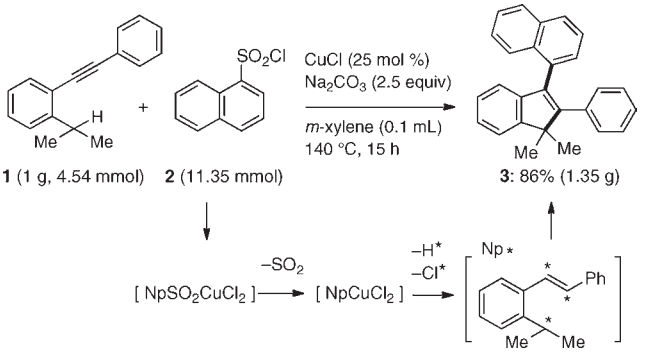
ABSTRACT: A variety of polysubstituted 1*H*-indenes can be prepared through the copper-catalyzed arylative cyclization of simple arylalkynes with commercially available aromatic sulfonyl chlorides that function as an aryl group donor. The reaction tolerates a broad range of functional groups, including bromide and iodide, nitrile, ketone, and nitro groups. The reaction allowed the synthesis of polycyclic aromatic hydrocarbons, such as a bis(indene), indacene, and fused polyarene derivatives, some of them showing strong fluorescence in solution and the solid state.

Aromatic sulfonyl chlorides, which are readily available commercially by sulfonylation of arenes, have been widely utilized for electrophilic arylsulfonylation[1] but are little known as an aryl group donor, except for some recent examples[2] of their use as an electrophilic aryl group, where SO_2Cl acts as an electrofugal group with SO_2 expulsion. Our interest in the catalytic activity of ubiquitous metals,[3,4] including copper,[5] and in organic semiconductors converged into the discovery of a new reaction. We report here a serendipitous finding of the Cu(I)-catalyzed formation of indene and indacene derivatives[6,7] by arylative cyclization[8] of an arylalkyne with an aromatic sulfonyl chloride, where the latter formally acts as a donor of an aryl radical group with loss of SO_2Cl (Scheme 1). Indene derivatives have found use in catalysis,[9] materials science,[10,11] and medicinal chemistry.[12] The present reaction tolerates a variety of functional groups, including bromide and iodide, nitrile, ketone, and nitro groups, and will be useful in obtaining functionalized indene derivatives as illustrated below (see eq 2 and Scheme 2) for organic electronic devices.[13]

A typical example performed on a gram scale illustrates the simplicity of the reaction (Scheme 1, top). A mixture of 1-isopropyl-2-(phenylethynyl)benzene (**1**; 1.00 g, 4.54 mmol), 1-naphthalenesulfonyl chloride (**2**; 2.57 g, 11.35 mmol), Na_2CO_3 (1.20 g, 11.35 mmol), and CuCl (0.11 g, 1.14 mmol) in *m*-xylene (0.1 mL) was heated under argon at 140 °C for 15 h. Aqueous workup and silica gel purification gave 1.35 g of 1,1-dimethyl-3-(1-naphthyl)-2-phenylindene (**3**; 86% yield). A small amount of starting material **1** and most of the excess **2** were recovered, and no other byproducts were detected. The reaction proceeded with 1.0 equiv of **2**, albeit more slowly. The reaction also proceeded without solvent (61% yield) and slowed down in a dilute xylene solution or in the presence of polar solvents, which destroyed the aromatic sulfonyl chloride [see the Supporting Information (SI) for details].

Both the copper catalyst and the mild inorganic base are essential for this reaction, and in the absence of either, no reaction took place. The high temperature was also essential to achieve conversion of the starting materials. The catalyst loading could be decreased at the expense of a lower reaction rate (71% yield with 5 mol % catalyst, 5 h of reaction). In the presence of other metal salts, this reaction did not proceed at all ($FeCl_2$, $CoBr_2$, $NiCl_2$, and $PtCl_2$) or gave a trace (4% yield) of the indene product **3** [$PdCl_2(PPh_3)_2$]. Other copper(I) catalysts (CuBr and CuI) gave **3** in good yield (69 and 60%, respectively), whereas copper(II) salts such as $CuCl_2$ and $Cu(OTf)_2$ performed poorly (30 and 26%, respectively). Na_2CO_3 was found to be the best base, and other inorganic or organic bases gave inferior results, in some cases destroying the aromatic sulfonyl chloride (see the SI for details). In the absence of the base, even when a stoichiometric amount of copper was used, the indene product was formed in a trace amount.

Scheme 1. Copper-Catalyzed Cyclization of Arylalkyne 1 with Naphthalenesulfonyl Chloride (2)



To gain insight into the mechanism, we examined the reaction of tolane under the same reaction conditions and found that 1-naphthalenesulfonyl chloride undergoes desulfitative addition to diphenylacetylene to give a triarylvinyl chloride as a mixture of stereoisomers through loss of the SO_2 group (eq 1). This result contradicts some previous results that an organic sulfonyl chloride adds across an alkyne to form arylvinylsulfones in the presence of a copper catalyst.[14] In light of the thermal behavior of related palladium catalysis,[2] we may consider that the first step of the reaction is insertion of the metal into the SO_2–Cl bond, and the thermal conditions employed here promote the loss of the SO_2 group from a SO_2–Cu–Cl intermediate, as illustrated at the bottom of Scheme 1. On the other hand, a radical scavenger (TEMPO) shut off the reaction, suggesting the involvement of

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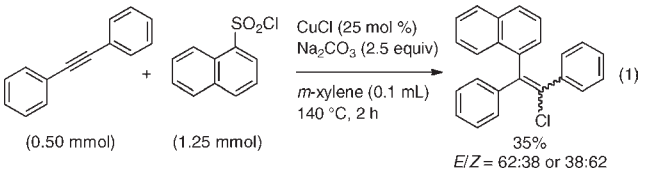
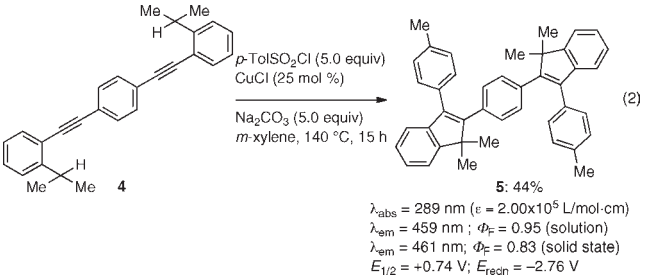
radical species.[14] We defer a mechanistic discussion until we obtain further relevant experimental results.



As illustrated in Table 1, a variety of aromatic sulfonyl chlorides reacted smoothly with 1-isopropyl-2-[(4-methoxyphenyl)ethynyl]-benzene under the optimized conditions. Both electron-rich and electron-deficient aromatic sulfonyl chlorides (entries 2−10) gave the corresponding indene products in good yield. Ortho-substituted aromatic sulfonyl chlorides (entries 9, 11, 12) reacted cleanly, suggesting that steric effects do not significantly affect the reaction. An important feature of this reaction is the functional group tolerance in spite of the high-temperature conditions, as illustrated by the tolerance of nitrile (entry 4), nitro (entry 10), ketone (entry 5), fluoride (entry 6), chloride (entries 7 and 10), bromide (entry 9), and even iodide (entry 8) groups. 2,3-Dehydrobenzo[1,4]dioxine and thiophene molecules (entries 12 and 13) could also be introduced with good yield. Aliphatic sulfonyl chlorides did not react under these conditions, suggesting that the C−S bond cleavage is a difficult step.

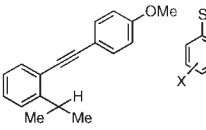
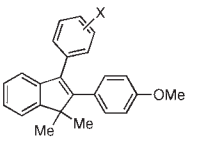
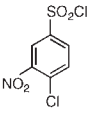
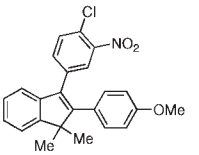
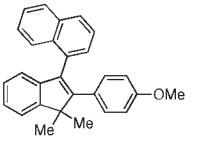
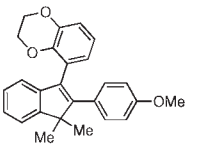
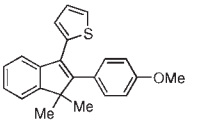
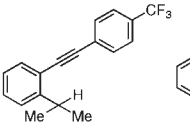
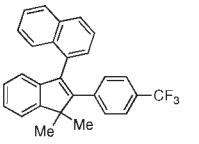
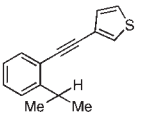
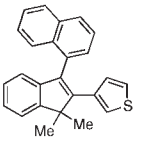
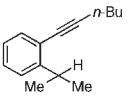
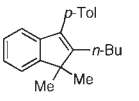
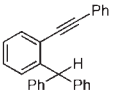
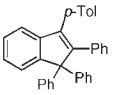
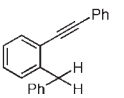
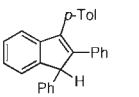
Various 2-(alkynyl)alkylbenzene derivatives could also be utilized. Both electron-rich (entries 1−13) and electron-deficient alkynes (entry 14) reacted well, although the reaction was slightly slower for the latter. A heteroaromatic alkyne substrate (entry 15) and an aliphatic alkyne (entry 16) could also be employed to produce the corresponding indenes. The isopropyl group on the benzene ring could be replaced with a diphenylmethyl group (entry 17) or a benzyl group (entry 18) but not with a methyl group (data not shown). These data indicate that the cleaving C−H bond must be labile, and combined with the high functional group tolerance, they may be taken as support for a radical, cation, or carbene mechanism for the ring-forming reaction.

A double cyclization reaction of diacetylenic compounds creates four new C−C bonds to produce a bisindene (e.g., **5** in eq 2) or a dibromoindacene (e.g., **7** in Scheme 2), both of which are of considerable interest for the promising properties of structurally related polybenzoheterole molecules.[15] Indacene derivatives have recently received attention as metal ligands[16] and ambipolar organic semiconductors,[11] and therefore, we examined the cyclization of diyne **6** with 2-bromobenzenesulfonyl chloride to obtain dibromo-1,7-dihydro-*s*-indacene **7** (Scheme 2). Utilizing the two bromine groups, we could form two additional rings in excellent yield to obtain nonacyclic compound **8** through formation of six new C−C bonds in two steps.



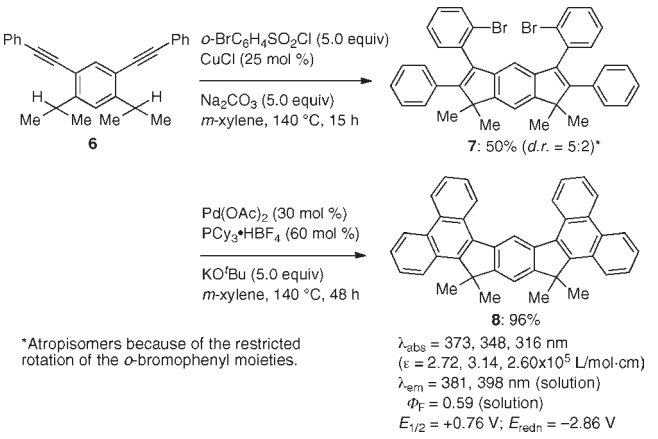
Interestingly, compounds **5** and **8** showed strong blue fluorescence both in solution and in the solid state. Compound **5** showed especially strong blue (458 nm) fluorescence both in solution ($\Phi_F = 0.95$) and in the solid state ($\Phi_F = 0.83$). A study

Table 1. Copper-Catalyzed Reaction of 2-(Alkynyl)alkylbenzenes with Various Aromatic Sulfonyl Chlorides[a]

entry	arylalkyne	$ArSO_2Cl$	product	yield (%)[b]
1				66 (X = H)
2				73 (X = *p*-Me)
3				54 (X = *p*-OMe)
4				85 (X = *p*-CN)
5				73 (X = *p*-COMe)
6				60 (X = *p*-F)
7				66 (X = *p*-Cl)
8				65 (X = *p*-I)
9				73 (X = *o*-Br)
10				36
11				85
12				80
13				70
14				74
15				71
16		*p*-$TolSO_2Cl$		54
17				49
18				41

[a] Reaction conditions: 2-(alkynyl)alkylbenzene (0.50 mmol), aromatic sulfonyl chloride (1.25 mmol), CuCl (0.125 mmol), Na_2CO_3 (1.25 mmol), *m*-xylene (0.1 mL), 140 °C; see the SI for details. [b] Isolated yields.

Scheme 2. Applications of the Copper-Catalyzed Arylative Cyclization to the Synthesis of Indacene Derivative 7 and Nonacyclic Fused Hydrocarbon 8



of the origin of the high efficiency of fluorescence in the solid state needs crystallographic information, which we have not yet been able to obtain. Cyclic voltammetry showed reversible oxidation waves for **5** and **8** at +0.74 and +0.76 V (vs ferrocene), respectively, and an irreversible reduction wave at −2.76 V for **5** and at −2.86 V for **8**.

In summary, we have developed a new synthesis of polysubstituted indene derivatives by exploiting aromatic sulfonyl chlorides as an aryl group donor. Several new indene derivatives are accessible from alkynylarenes[17] that can be synthesized in a few steps from commercially available compounds by the Sonogashira reaction and commercially available aromatic sulfonyl chlorides. The new dibromide **7** provided access to the new nonacyclic compound **8**. Given the variety of accessible indene derivatives and the high functional group tolerance, we anticipate that the present reaction will serve as a useful tool in the development of functional materials.[18]

■ ASSOCIATED CONTENT

Supporting Information. Experimental procedures, optimization of the reaction conditions, and physical properties of the compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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■ REFERENCES

(1) Morrison, R. T.; Boyd, R. N. *Organic Chemistry*, 5th ed.; Allyn and Bacon, Boston, 1987.

(2) (a) Kasahara, A.; Izumi, T.; Kudou, N.; Azami, H.; Yamamoto, S. *Chem. Ind.* **1988**, 51–52. (b) Miura, M.; Hashimoto, H.; Itoh, K.; Nomura, M. *Tetrahedron Lett.* **1989**, *30*, 975–976. (c) Dubbaka, S. R.; Vogel, P. *Angew. Chem., Int. Ed.* **2005**, *44*, 7674–7684 and references therein. (d) Volla, C. M. R.; Vogel, P. *Angew. Chem., Int. Ed.* **2008**, *47*, 1305–1307.

(3) Nakamura, E.; Sato, K. *Nat. Mater.* **2011**, *10*, 158–161.

(4) Nakamura, E.; Yoshikai, N. *J. Org. Chem.* **2010**, *75*, 6061–6067.

(5) (a) Nakamura, E.; Mori, S. *Angew. Chem., Int. Ed.* **2000**, *39*, 3750–3771. (b) Xiao, Z.; Matsuo, Y.; Nakamura, E. *J. Am. Chem. Soc.* **2010**, *132*, 12234–12236. (c) Zhang, Y.; Matsuo, Y.; Li, C.-Z.; Tanaka, H.; Nakamura, E. *J. Am. Chem. Soc.* **2011**, *133*, 8086–8089.

(6) Selected examples: (a) Quan, L. G.; Gevorgyan, V.; Yamamoto, Y. *J. Am. Chem. Soc.* **1999**, *121*, 3545–3546. (b) Xi, Z.; Guo, R.; Mito, S.; Yan, H.; Kanno, K.; Nakajima, K.; Takahashi, T. *J. Org. Chem.* **2003**, *68*, 1252–1257. (b) Lautens, M.; Marquardt, T. *J. Org. Chem.* **2004**, *69*, 4607–4614. (c) Tobisu, M.; Nakai, H.; Chatani, N. *J. Org. Chem.* **2009**, *74*, 5471–5475. (d) Liu, C.-R.; Yang, F.-L.; Jin, Y.-Z.; Ma, X.-T.; Cheng, D.-J.; Li, N.; Tian, S.-K. *Org. Lett.* **2010**, *12*, 3832–3835.

(7) Khan, Z. A.; Wirth, T. *Org. Lett.* **2009**, *11*, 229–231.

(8) (a) Zhang, D.; Yum, E. K.; Liu, Z.; Larock, R. C. *Org. Lett.* **2005**, *7*, 4963–4966. (b) Guo, L.-N.; Duan, X.-H.; Bi, H.-P.; Liu, X.-Y.; Liang, Y.-M. *J. Org. Chem.* **2006**, *71*, 3325–3327. (c) Zhang, D.; Liu, Z.; Yum, E. K.; Larock, R. C. *J. Org. Chem.* **2007**, *72*, 251–262.

(9) (a) Cadierno, V.; Diez, J.; Gamasa, M. P.; Gimeno, H.; Lastra, E. *Coord. Chem. Rev.* **1999**, *193−195*, 147–205. (b) Stradiotto, M.; McGlinchey, M. J. *Coord. Chem. Rev.* **2001**, *219−221*, 311–378. (c) Zargarian, D. *Coord. Chem. Rev.* **2002**, *233−234*, 157–276.

(10) Grimsdale, A. C.; Müllen, K. *Angew. Chem., Int. Ed.* **2005**, *44*, 5592–5629.

(11) (a) Zhu, X.; Mitsui, C.; Tsuji, H.; Nakamura, E. *J. Am. Chem. Soc.* **2009**, *131*, 13596–13597. (b) Zhu, X.; Tsuji, H.; Nakabayashi, K.; Ohkoshi, S.-i.; Nakamura, E. *J. Am. Chem. Soc.* **2011**, *133*, 16342–16345.

(12) For example, see: (a) Karaguni, I.-M.; Glüsenkamp, K.-H.; Langerak, A.; Geisen, C.; Ullrich, V.; Winde, G.; Möröy, T.; Müller, O. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 709–713. (b) Watanabe, N.; Nakagawa, H.; Ikeno, A.; Minato, H.; Kohayakawa, C.; Tsuji, J. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 4317–4320. (c) Alcalde, E.; Mesquida, N.; López-Pérez, S.; Frigola, J.; Mercè, R. *J. Med. Chem.* **2009**, *52*, 675–687.

(13) (a) Watson, M. D.; Fechtenkötter, A.; Müllen, K. *Chem. Rev.* **2001**, *101*, 1267–1300. (b) Feng, X.; Pisula, W.; Müllen, K. *Pure Appl. Chem.* **2009**, *81*, 2203–2224.

(14) (a) Amiel, Y. *J. Org. Chem.* **1971**, *36*, 3691–3696. (b) Amiel, Y. *J. Org. Chem.* **1971**, *36*, 3697–3702. (c) Amiel, Y. *Tetrahedron Lett.* **1971**, *12*, 661–663. (d) Liu, X.; Duan, X.; Pan, Z.; Han, Y.; Liang, Y. *Synlett* **2005**, 1752–1754.

(15) (a) Ilies, L.; Tsuji, H.; Sato, Y.; Nakamura, E. *J. Am. Chem. Soc.* **2008**, *130*, 4240–4241. (b) Tsuji, H.; Mitsui, C.; Sato, Y.; Nakamura, E. *Adv. Mater.* **2009**, *21*, 3776–3779. (c) Ilies, L.; Sato, Y.; Mitsui, C.; Tsuji, H.; Nakamura, E. *Chem.—Asian J.* **2010**, *5*, 1376–1381.

(16) Adams, C.; Morales-Verdejo, C.; Morales, V.; MacLeod-Carey, D.; Manríquez, M.; Chávez, I.; Muñoz-Castro, A.; Delpech, F.; Castel, A.; Gornitzka, H.; Rivière-Baudet, M.; Rivière, P.; Molins, E. *Eur. J. Inorg. Chem.* **2009**, 784–791.

(17) Yang, S.; Li, Z.; Jian, X.; He, C. *Angew. Chem., Int. Ed.* **2009**, *48*, 3999–4001.

(18) Matsuo, Y.; Sato, Y.; Niinomi, T.; Soga, I.; Tanaka, H.; Nakamura, E. *J. Am. Chem. Soc.* **2009**, *131*, 16048–16050.