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NIS/HFIP-Mediated Synthesis of Indene-Based β-Iodoalkenyl Sulfides from Propargylic Sulfides

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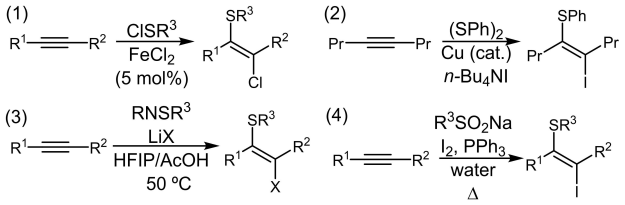
Abstract: A tandem 1,3-sulfur migration followed by iodocyclization reaction of propargylic sulfides in the presence of NIS in HFIP has been developed to synthesize indene-based β-iodoalkenyl sulfides. The choice of the reaction media is crucial to promote the reaction. The proposed mechanism involving the initial NIS activation by HFIP and favoring the sulfur migration of the starting propargylic thioether via cationic intermediates is experimentally supported. In addition, the suitability of selected indene-based β-iodoalkenyl sulfides as building blocks for subsequent C–C bond-forming reactions has been demonstrated.

Keywords: synthetic methods; sulfur; alkenes; alkynes; halogens

Alkenyl sulfide moiety is a structural motif found in biologically relevant compounds and materials.[1] Therefore, the development of methodologies for their synthesis has attracted much attention and is experiencing continuous growth.[2] Moreover, alkenyl thioethers, and particularly *β*-haloalkenyl sulfides are valuable precursors for assembling substituted alkenes.[3] Typically *β*-chloroalkenyl thioethers are obtained by the addition of sulfenyl halides to alkynes,[4] although metal catalysts are commonly required to ensure stereoselective additions (Scheme 1).[5] *β*-Chloro- and bromoalkenyl sulfides could also be accessed from alkynes and halide salts employing a disulfide combined with a copper catalyst,[6] or thiosuccinimides[7] in the absence of a catalyst. However, related strategies of iodothiolation of alkynes have proven to be more challenging and only limited to a few examples. In this sense, alternative methods to synthesize valuable *β*-iodoalkenyl thioethers were explored. Notably, iodothiolation of alkynes employing sodium sulfinates, iodine, and PPh_3 as the reductant has been reported (Scheme 1, eq 4).[8]

In parallel, sophisticated alkenyl sulfides can be easily accessed from readily available compounds by designing efficient cascade reactions generating C–S and C–C bonds.[9] In this sense, gold-catalyzed 1,2-sulfur migrations have emerged as an efficient tool to assemble alkenyl sulfides[10] since Wang and co-workers reported that propargylic sulfides activated at the alkyne by gold experienced a 1,2-sulfur shift generating a reactive gold carbene that finally evolved through



Scheme 1. Halothiolation of alkynes.

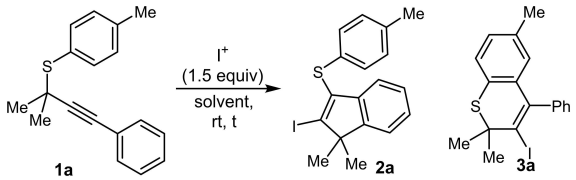
C–H bond insertion into indenes (Scheme 2a).[10a] Recently, alternative methods for synthesizing alkenyl sulfides based on transition metal-free reactions under mild conditions have arisen as effective strategies.[11] In this regard, related 2-indenyl sulfides were obtained upon the reaction of allenes with electrophilic sulfur sources like thiosuccinimides in the presence of diphenyl selenide as a catalyst.[12]

Electrophilic iodocarbocyclization reactions[13] have emerged as valuable strategies for constructing iodofuntionalizated indene scaffolds from a diverse range of starting materials.[14] Inspired by these precedents, we hypothesized that propargylic sulfides could react with a suitable iodonium source triggering sulfur migration and causing a subsequent carbocyclization giving rise to indene-containing β-iodoalkenyl sulfides which could be useful building blocks for assembling polycyclic scaffolds like indenobenzothiophene core which possess relevant applications in material science.[15]

In a previous study, we observed that *S*-aryl propargylic sulfides reacted with *N*-iodosuccinimide (NIS) in a 6-*endo-dig* cyclization affording thiochromenes (Scheme 2b).[16] To circumvent this reaction pathway, we envisioned that the choice of solvent might be crucial (Scheme 2c). Interestingly, hexafluoroisopropanol (HFIP) has been capable of modulating the reactivity of iodonium salts by hydrogen bonding,[17] as well as providing an excellent reaction media for stabilizing carbocations generated from alcohols under Brønsted acid catalysis.[18] Additionally, HFIP was also reported to activate NIS enhancing iodofunctionalization of arenes[19] and iodocyclization reactions.[20]

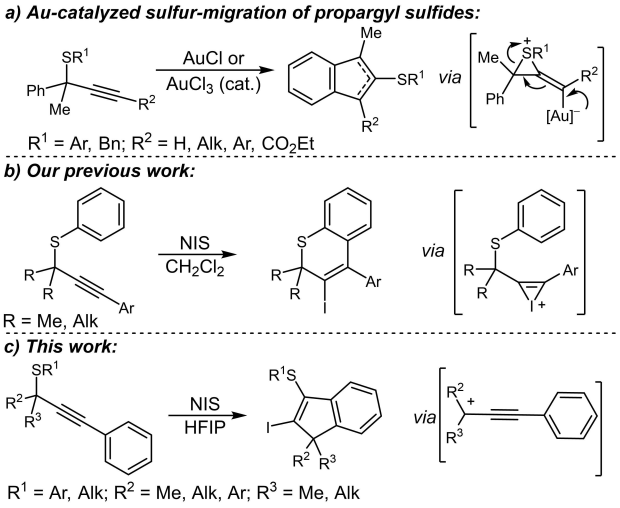
Initially, we evaluated the feasibility of the process, selecting the readily available propargylic sulfide **1a** as the model substrate (Table 1).[16] When **1a** was subjected to reaction with NIS in CH_2Cl_2 employing HFIP as a cosolvent in 1:1 ratio, the formation of the indene **2a** was observed in moderate yield at room temperature (entry 1). Under these reaction conditions, propargylic thioether **1a** experienced a formal 1,3-sulfur migration and subsequent cyclization to afford the indene core. By contrast, iodothiochromene **3a** was obtained in high yields when only CH_2Cl_2 was used as the solvent (entry 2). A higher proportion of HFIP increased notably the formation of indene **2a** (entry 3) even at lower temperatures (entry 4). Other cosolvents different from CH_2Cl_2 were also evaluated,[21] although, in several cases, **2a** was afforded in similar yields (entries 5–6). Notably, when HFIP was used in the absence of an additional solvent, indene-base β-iodoalkenyl sulfide **2a** was afforded in a considerably higher yield (entry 7). Variation of the amount of NIS

Table 1. Reaction optimization.[a]



Entry	I^+	Solvent	t (h)	Yield[b] **2a** (%)	Yield[b] **3a** (%)
1	NIS	$HFIP/CH_2Cl_2$ 1:1	0.5	40	–
2	NIS	CH_2Cl_2	24	–	80
3	NIS	$HFIP/CH_2Cl_2$ 4:1	0.5	68	–
4[c]	NIS	$HFIP/CH_2Cl_2$ 4:1	0.5	77	–
5	NIS	HFIP/MeCN 1:1	0.5	52	–
6	NIS	$HFIP/H_2O$ 1:1	0.5	47	–
7	NIS	HFIP	0.5	87 (80)	–
8[d]	NIS	HFIP	0.5	78	–
9[e]	NIS	HFIP	0.5	84	–
10[f]	NIS	*i*-PrOH	24	–	–
11[g]	NIS	CF_3CH_2OH	0.5	27	–
12[g]	NIS	$MeNO_2$	24	12	35
13[g]	I_2	HFIP	0.5	–	–
14	I_2/K_2CO_3	HFIP	15	22	–
15	I_2/Cs_2CO_3	HFIP	15	18	–
16[h]	NIP	HFIP	0.5	85	–
17[i]	DIDMH	Bn	0.5	73	–

[a] Reaction conditions: **1a** (0.4 mmol), I^+ (0.6 mmol), HFIP (4 mL), rt.
[b] Yield determined by ^1H NMR using CH_2Br_2 as internal standard, in parentheses yield of isolated product referred to sulfide **1a**.
[c] Reaction performed at −15 °C.
[d] NIS (1.3 equivalents, 0.52 mmol).
[e] NIS (2.0 equiv., 0.8 mmol).
[f] Starting material recovered unaltered.
[g] No full conversion observed.
[h] NIP *N*-iodophtalimide.
[i] DIDMH 1,3-diiodo-5,5-dimethylhydantoin.



Scheme 2. Reactivity of propargylic sulfides vs π-acids.

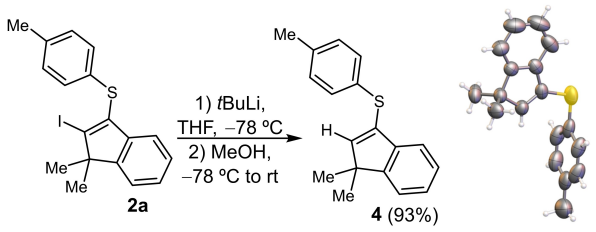
employed or the reaction time did not significantly affect the reaction outcome (entries 8–9). Other solvents such as isopropanol, 2,2,2-trifluoroethanol, or nitromethane were less effective in promoting the formation of indene **2a** (entries 10–12).

Different electrophilic iodonium sources were also tested (entries 13–17).[21] Whereas molecular iodine has proven to be inefficient in promoting the reaction, the addition of a carbonate base enables the formation of indene **2a** (entries 13–15). However, **2a** was afforded in significantly lower yields under these reaction conditions. Other iodonium sources like *N*-iodophtalimide (NIP) or 1,3-diiodo-5,5-dimethylhydantoin (DIDMH) provide access to desired product **2a** in a similar extension to the optimal conditions using NIS (entries 16–17).

Finally, other different halonium sources were also tested. Nevertheless, no formation of related 2-haloindenes was observed when *N*-bromosuccinimide (NBS) or *N*-chlorosuccinimide (NCS) were employed. Instead, rapid degradation of **1a** was observed, detecting the formation of disulfide and multiple polyhalogenated products.

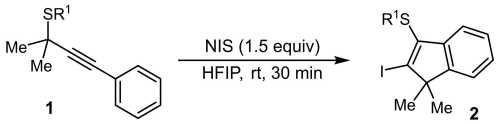
The structure of compound **2a** was unambiguously elucidated after derivatization by halogen-lithium exchange reaction (Scheme 3). Then, protonation of the generated organolithium with MeOH gave rise to deiodinated indene **4**, whose structure was determined by 2D NMR experiments and confirmed by single-crystal X-ray diffraction.[22]

With optimized reaction conditions in hand, employing HFIP at room temperature, we focused on the nature of the substituent attached to the *S*-atom that experiences the 1,3-migration (Table 2). We found that the process shows a broad variability. Aryl substituents bearing neutral, electron-withdrawing, and electron-donating groups located at different positions were well tolerated, and the desired indenes were obtained in good yields (entries 1–9). Notably, indenes **2** were selectively formed in all the examined cases, and no products derived from the 6-*endo*-*dig* cyclization were observed. Not only aryl but also alkyl substituents on the *S*-atom were tested (entries 10–11). Interestingly, both dodecyl and benzyl thioethers **1j**,**k** could be engaged in the reaction affording the indene-based β-iodoalkenyl sulfides **2j**,**k** in comparable yields to the



Scheme 3. Halogen-lithium exchange reaction of **2a**.

Table 2. Scope of the sulfur migrating group.[a]



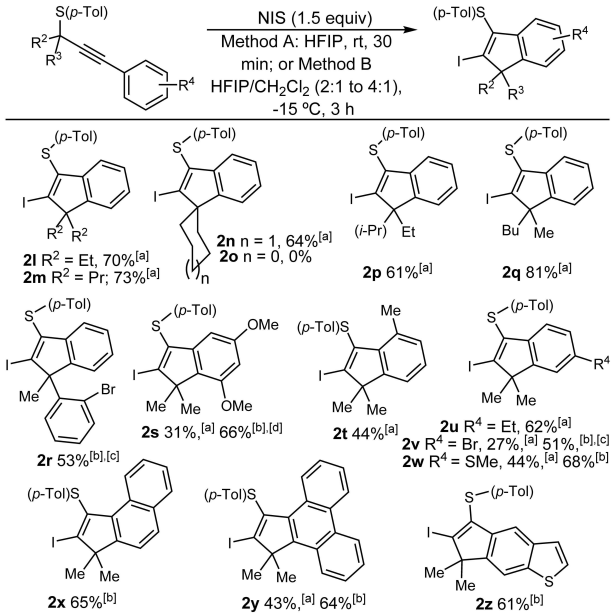
Entry	1	R^1	2	Yield (%)[b]
1	**1a**	*p*-Tol	**2a**	80
2	**1b**	Ph	**2b**	75
3	**1c**	4-BrC_6H_4	**2c**	65
4	**1d**	4-$(F_3C)C_6H_4$	**2d**	63
5	**1e**	3-$MeOC_6H_4$	**2e**	65
6	**1f**	2-BrC_6H_4	**2f**	72
7	**1g**	2-ClC_6H_4	**2g**	76
8	**1h**	2-FC_6H_4	**2h**	60
9	**1i**	2-Naphthyl	**2i**	58
10	**1j**	$(CH_2)_{11}CH_3$	**2j**	57
11	**1k**	Bn	**2k**	65

[a] Reaction conditions: **1** (0.4 mmol), NIS (0.6 mmol), HFIP (4 mL), rt, 0.5–1 h.
[b] Yield of the isolated product referred to the corresponding sulfide **1**.

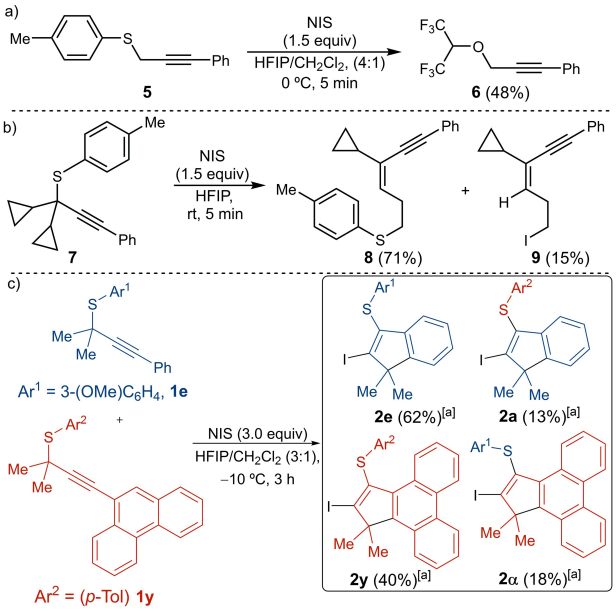
aryl counterparts. The reaction was also amenable to scale-up, affording compound **2a** in gram amounts (1.38 g, 71%).

Once the nature of the migrating sulfur group was studied, we evaluated the influence of the substituents at both the propargylic position and the arene linked to the alkyne (Scheme 4). Considering the relevancy of 1,1-disubstituted 1*H*-indenes,[23] we initially focused on tertiary propargylic sulfides, and indenes **2l**,**m**,**q** with different alkyl chains at C-1 were obtained in high yields.

Even spiro compounds like **2n** (R^2, $R^3 = -(CH_2)_5-$) could be easily accessed. Surprisingly when the thioether **1o** (R^2,$R^3 = -(CH_2)_4-$) was tested, no desired cyclization product **2o** was obtained, affording a complex mixture of byproducts instead even at lower temperatures. More sterically demanding substrates bearing branched alkyl chains (**2p**) proved to be more challenging than those substituted with linear groups (**2l**,**m**,**q**), affording the corresponding indenes in slightly lower yields. Thioethers aryl-substituted at the propargylic position required modified reaction conditions using CH_2Cl_2 as cosolvent (method B) to enable the 1,3-sulfur-migration/cyclization process, likely due to the poor solubility shown in HFIP (**2r**). Additionally, to minimize alternative reaction pathways, the temperature was lowered to −15 °C, and NIP was employed instead of NIS. Similar behavior was observed when the nature of the aryl group attached to the acetylene and involved in the cyclization was modified ($R^4 \neq H$). Thus, the transformation generally proceeds in a higher extension under alternative reaction conditions (method B). Interestingly, *ortho* or



Scheme 4. Synthesis of (2-iodo-1,1-disubstituted-(1*H*)-inden-3-yl) (*p*-tolyl) sulfides.[a] Method A: **1** (0.4 mmol), NIS (0.6 mmol), HFIP (4 mL), rt, 0.5–1 h.[b] Method B: **1** (0.4 mmol), NIS or NIP (0.6 mmol), HFIP/CH_2Cl_2 (4:1, 4 mL), −15 °C. Yield of the isolated products referred to starting material **1**.[c] NIP (0.6 mmol) was used instead of NIS.[d] Stoichiometric amount of NIS was employed.



Scheme 5. Control experiments.[a] Yield of isolated products referred to starting product **1e** and **1y**.

para substituents comprising electron-donating, neutral, and moderate electron-withdrawing groups at position R^4 were well-tolerated (**2t–w**).

Not surprisingly, when two strong electron-donating substituents were present, additional iodination at the activated arene was also observed when NIS (1.5 equiv.) was used at room temperature. Lower reaction temperature employing stoichiometric amounts of NIS in an HFIP/CH_2Cl_2 mixture (4:1) at −15 °C increased the selectivity and produced the desired indene **2s** in higher yield. Furthermore, the preparation of (hetero)polycyclic structure was also accomplished by reaction of propargylic thioethers bearing other (hetero)arenes attached to the alkyne different from phenyl. Thus, benzo- and thiophene fused indenes (**2x–z**) were obtained in good yields.

Next, we proceed to evaluate the performance of primary propargylic sulfide **5**, which is demonstrated to be highly reactive (Scheme 5a). After 5 min at 0 °C in an HFIP/CH_2Cl_2 mixture, thioether **5** is fully converted, affording compound **6** derived from a substitution of thioaryl moiety by a hexafluoroisopropoxy group as the major product. Similar results were observed employing secondary thioethers bearing a methyl group at the propargylic position that reacted even at lower temperatures affording multiple by-products. Nevertheless, the corresponding 1-monosubstituted indenes were not obtained. When secondary sulfides bearing a phenyl group at the propargylic position were tested, enones derived from a C–S cleavage were afforded after aqueous work-up.[21] Considering these findings, we hypothesized that 1,3-sulfur migration might proceed through C–S cleavage, generating a tertiary propargylic cation after sulfur atom activation by the iodonium instead of a competitive alkyne activation. Recently, Moran and co-workers have reported an interesting cyclopropane ring-opening reaction in HFIP through cationic intermediates.[24] Inspired by these results, we envisioned that thioethers bearing a cyclopropyl substituent at the propargylic position might provide valuable information. Thus, when thioether **7** was subjected to the reaction conditions in HFIP, and after NIS addition, full conversion was observed after 5 min (Scheme 5b). Notably, no indene derived from the 1,3-sulfur migration was formed, and only two 1,3-enynes **8** and **9** resulting from cyclopropane ring opening were obtained instead. Interestingly, similar results were observed in the presence of TEMPO or BHT, suggesting that no radical mechanism is operating. In addition, no reaction was detected in the absence of NIS, and the starting material was recovered. These results support an initial activation of the sulfur atom by the iodonium, which could experience nucleophilic substitution[25] or alternatively facilitate a C–S cleavage and the subsequent formation of a propargylic cation. Then, this carbocationic intermediate undergoes nucleophilic attack by a sulfide or an iodide generated during the reaction, affording the enynes **8** or **9**.

Next, to gain further insights into the mechanism, we designed a cross experiment employing two differ-

ent propargylic sulfides (**1e** and **1y**). If the reaction proceeds through C–S cleavage and subsequent propargyl cation intermediates, the formation of four different indenes could be expected. When **1e** and **1y** (1:1 ratio) were treated with NIS in HFIP/CH_2Cl_2 mixture at −10 °C (Scheme 5c), indenes **2a**,**e**,**y**,**α** were observed, although those indenes (**2e** and **2y**) in which the two fragments belong to the same propargylic thioether precursor were preferentially formed. This observation could be reasoned by the tendency of HFIP molecules to generate networks and the solvation of ions in this solvent.

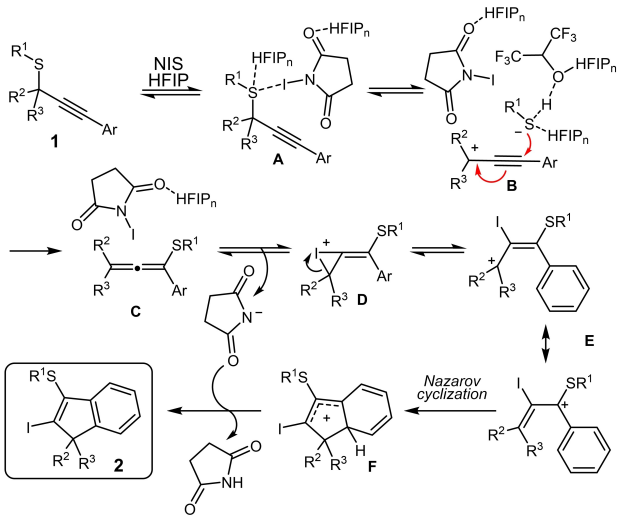
Based on these findings, a plausible mechanistic pathway to the selective formation of functionalized indenes **2** from propargylic thioethers **1** is depicted in Scheme 6. Initially, the propargylic thioether **1** could be solvated by hydrogen bonding with HFIP molecules.[26] In this sense, ^{1}H-NMR experiments employing equimolar amounts of HFIP and thioether **1a** in $CDCl_3$ showed that the proton at OH group of the alcohol is shifted around 0.35 ppm when **1a** is added, which supports this interaction between the thioether and the HFIP molecules.[27] Then, activation of the NIS reagent by hydrogen bonding with the solvent enables the interaction of the *I*-atom with the *S*-atom of the propargylic thioether, obtaining intermediate **A**. The combination of sulfur-iodine interaction (halogen bonding) and hydrogen bonding between the sulfur atom and HFIP causes the cleavage of the C–S bond, affording a tertiary propargylic cation **B** and the solvated sulfide or thiol. This intermediate, bearing two substituents at the propargylic position, evolves through a S_N' nucleophilic attack by the sulfur atom, which belongs to the other fragment of the initial propargylic thioether.[28] As a result, an allenyl thioether **C** is generated. This species could react with electrophiles[12,15] similarly to related carbon-substituted allenes generating the iodonium **D**. Further evolution of **D** generates a pentadienyl-type carbocation **E** stabilized by the S-atom. Finally, a Nazarov cyclization accounts for the indene **2** formation through an intermediate species such as **F**.

The presence of Csp^2–I bond in the indenes **2** provides multiple derivatization alternatives (Scheme 7). For instance, Pd-catalyzed cross-coupling reactions, like Sonogashira coupling (Scheme 7, eq 1), could be performed over that position affording indene **10**. More remarkably, indenobenzothiophene *S*-based polyaromatic cores,[15] which possess relevant optoelectronic properties, like 10*H*-benzo[*b*]indeno[2,1-*d*]thiophene **11**, could be accessed through Pd-catalyzed cyclization processes, involving C–H bond activation at the *ortho* position of the thioarene moiety (Scheme 7, eq 2).

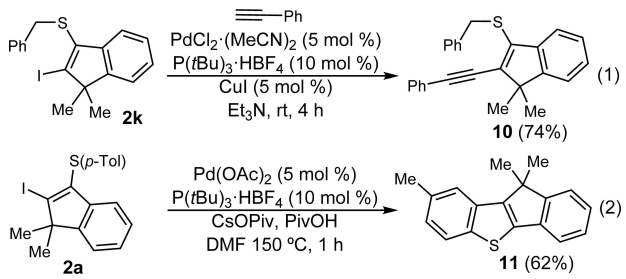
In summary, we have developed a new, efficient, metal-free protocol of alkyne iodothiolation, which enables the synthesis of (2-iodo-1*H*-inden-3-yl)sulfides involving a tandem 1,3-sulfur migration and iodocyclization by reaction of readily available propargylic sulfides with an iodonium source in HFIP. The solvent plays a crucial role in enabling the transformation. HFIP modulates the reactivity of the NIS reagent, activates the thioether, and contributes to stabilize key carbocationic intermediates. Mechanistic studies suggest an initial activation of the sulfur atom, which debilitates the C–S bond, leading to its cleavage. The tertiary propargylic cation generated evolves through a more favorable nucleophilic addition in an overall S_N' process, thus allowing the synthesis of reactive *S*-substituted allenes through 1,3-sulfur migration. Then, an iodonium-promoted cyclization afforded the indene-based β-alkenyl sulfides in a formal process of alkyne iodothiolation. Moreover, these 2-iodo-1*H*-inden-3-yl sulfides proved to be efficient precursors for further derivatizations affording different indene derivatives or indenobenzothiophene polyaromatic scaffolds.

Experimental Section

N-Iodosuccinimide (135 mg, 1.5 equiv., 0.6 mmol) was added in portions to a solution of propargyl thioether **1** (1 equiv., 0.4 mmol) in HFIP (4 mL, 0.1 M) in the dark. The reaction



Scheme 6. Mechanistic proposal.



Scheme 7. Derivatization reactions of indenes **2**.

mixture was allowed to stir (0.5 h) until full depletion of the propargylic sulfide was determined by GC–MS and TLC (the spots were visualized using *p*-anisaldehyde in ethanol solution and heat as the staining agent). Then, the reaction was quenched by the addition of aqueous $Na_2S_2O_3$ (saturated solution, 10 mL). Afterward, HFIP was evaporated under reduced pressure. Then, the aqueous phase was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure affording crude 2-iodo-1*H*-inden-3-yl sulfides **2**, which were purified by column chromatography on silica gel (eluent: mixtures of hexane/EtOAc or hexane/CH_2Cl_2 as specified) to obtain the corresponding pure 2-iodo-1*H*-inden-3-yl sulfide **2**.

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References

[1] a) A. Lavecchia, S. Cosconati, V. Limongelli, V. Novellino, *ChemMedChem* **2006**, *1*, 540–550; b) P. Johannesson, G. Lindeberg, A. Johansson, G. V. Nikiforovich, A. Gogoll, B. Synnergren, M. Le Grèves, F. Nyberg, A. Karlén, A. Hallberg, *J. Med. Chem.* **2002**, *45*, 1767–1777; c) A. Kausar, S. Zulfiqar, M. I. Sarwar, *Polym. Rev.* **2014**, *54*, 185–267. For a perspective review in organosulfur chemistry, see: d) M. Wang, X. Jiang, *ACS Sustainable Chem. Eng.* **2022**, *10*, 671–677.

[2] For a review, see: a) C.-F. Lee, Y.-C. Liu, S. S. Badsara, *Chem. Asian J.* **2014**, *9*, 706–722. For selected recent examples, see: b) E. S. Degtyareva, J. V. Burykina, A. N. Fakhrutdinov, E. G. Gordeev, V. N. Khrustalev, V. P. Ananikov, *ACS Catal.* **2015**, *5*, 7208–7213; c) I. Strydom, G. Guisado-Barrios, I. Fernández, D. C. Liles, E. Peris, D. I. A. Bezuidenhout, *Chem. Eur. J.* **2017**, *23*, 1393–1401; d) N. Velasco, C. Virumbrales, R. Sanz, S. Suárez-Pantiga, M. A. Fernández-Rodríguez, *Org. Lett.* **2018**, *20*, 2848–2852.

[3] J. Lou, Q. Wang, P. Wu, H. Wang, Y.-G. Zhou, Z. Yu, *Chem. Soc. Rev.* **2020**, *49*, 4307–4359.

[4] V. Calo, G. Scorrano, G. Modena, *J. Org. Chem.* **1969**, *34*, 2020–2022.

[5] a) M. Iwasaki, T. Fujii, K. Nakajima, Y. Nishihara, *Angew. Chem. Int. Ed.* **2014**, *53*, 13880–13884; *Angew. Chem.* **2014**, *126*, 14100–14104; b) M. Iwasaki, T. Fujii, A. Yamamoto, K. Nakajima, Y. Nishihara, *Chem. Asian J.* **2014**, *9*, 58–62.

[6] a) N. Taniguchi, *Synlett* **2008**, 849–852; b) N. Taniguchi, *Tetrahedron* **2009**, *65*, 2782–2790.

[7] S. Liu, X. Zeng, B. Xu, *Org. Chem. Front.* **2020**, *7*, 1690–1695.

[8] a) Y.-M. Lin, G.-P. Lu, C. Cai, W.-B. Yi, *Org. Lett.* **2015**, *17*, 3310–3313. See also:; b) S. Liang, L. Jiang, W.-B. Yi, J. Wei, *Org. Lett.* **2018**, *20*, 7024–7028.

[9] a) J. F. Hooper, A. B. Chaplin, C. González-Rodríguez, A. L. Thompson, A. S. Weller, M. C. Willis, *J. Am. Chem. Soc.* **2012**, *134*, 2906–2909; b) H. Li, S. Liu, Y. Huang, X.-H. Xu, F.-L. Qing, *Chem. Commun.* **2017**, *53*, 10136–10139; c) F. Martínez-Lara, A. Suárez, N. Velasco, S. Suárez-Pantiga, R. Sanz, *Adv. Synth. Catal.* **2022**, *364*, 132–138.

[10] a) L. Peng, X. Zhang, S. Zhang, J. Wang, *J. Org. Chem.* **2007**, *72*, 1192–1197; b) X. Zhao, Z. Zhong, L. Peng, W. Zhang, J. Wang, *Chem. Commun.* **2009**, 2535–2537; c) S. B. Wagh, R. R. Sing, R. L. Sahani, R.-S. Liu, *Org. Lett.* **2019**, *21*, 2755–2758; d) H. Tashiro, M. Terada, I. Nakamura, *Angew. Chem. Int. Ed.* **2021**, *60*, 12248–12252; *Angew. Chem.* **2021**, *133*, 12356–12360; e) T. Yuan, B. Ryckaert, K. Van Hecke, J. Hullaert, J. M. Winne, *Angew. Chem. Int. Ed.* **2021**, *60*, 4070–4074; *Angew. Chem.* **2021**, *133*, 4116–4120.

[11] For selected examples employing iodonium salts, see: a) L. Castoldi, E. M. Di Tommaso, M. Reitti, B. Gräfen, B. Olofsson, *Angew. Chem. Int. Ed.* **2020**, *59*, 15512–15516; *Angew. Chem.* **2020**, *132*, 15642–15646; b) B. Liu, J. V. Alegre-Requena, R. S. Paton, G. M. Miyake, *Chem. Eur. J.* **2020**, *26*, 2386–2394.

[12] Q. Jiang, H. Li, X. Zhao, *Org. Lett.* **2021**, *23*, 8777–8782.

[13] a) A. Palisse, S. F. Kirsch, *Org. Biomol. Chem.* **2012**, *10*, 8041–8047; b) T. Khan, S. Yaragorla, *Eur. J. Org. Chem.* **2019**, 3989–4012.

[14] From ethynyl malonates, see: a) Z. A. Khan, T. Wirth, *Org. Lett.* **2009**, *11*, 229–231. From *o*-alkynylstyrenes, see: b) R. Sanz, A. Martínez, P. García-García, M. A. Fernández-Rodríguez, M. A. Rashid, F. Rodríguez, *Chem. Commun.* **2010**, *46*, 7427–7429; c) P. García-García, A. M. Sanjuán, M. A. Rashid, A. Martínez-Cuezva, M. A. Fernández-Rodríguez, F. Rodríguez, R. Sanz, *J. Org. Chem.* **2017**, *82*, 1155–1165. From propargylic alcohols, see: d) H.-T. Zhu, K.-G. Ji, F. Yang, L.-J. Wang, S.-C. Zhao, S. Ali, X.-Y. Liu, Y.-M. Liang, *Org. Lett.* **2011**, *13*, 684–687; e) Y. Zhu, G. Yin, D. Hong, P. Lu, Y. Wang, *Org. Lett.* **2011**, *13*, 1024–1027; f) H.-T. Zhu, X. Dong, L.-J. Wang, M.-J. Zhong, X.-Y. Liu, Y.-M. Liang, *Chem. Commun.* **2012**, *48*, 10748–10750; g) L. Sun, Y. Zhu, J. Wang, P. Lu, Y. Wang, *Org. Lett.* **2015**, *17*, 242–245. From allenes, see: h) C. Grandclaudon, V. Michelet, P. Y. Toullec, *Org. Lett.* **2016**, *18*, 676–679. From diynes, see: i) F. Xu, L. Peng, A. Orita, J. Otera, *Org. Lett.* **2012**, *14*, 3970–3973; j) P. Nösel, T. Lauterbach, M. Rudolph, F. Rominger, A. S. K. Hashmi, *Chem. Eur. J.* **2013**, *19*, 8634–8641.

[15] a) K. Takase, K. Noguchi, K. Nakano, *Org. Lett.* **2017**, *19*, 5082–5085; b) M. Xiao, A. Sadhanala, M. Abdi-Jalebi, T. H. Thomas, X. Ren, T. Zhao, H. Chen, R. L. Carey, Q. Wang, S. P. Senanayak, C. Jellet, A. Onwubi-

ko, M. Moser, H. Liao, W. Yue, I. McCulloch, M. Nikolka, H. Sirringhaus, *Adv. Funct. Mater.* **2021**, *31*, 2007359. See also the following link: https://doi.org/10.1002/adfm.202007359; c) S. Yoon, G. S. Lee, K. M. Sim, M.-J. Kim, Y.-H. Kim, D. S. Chung, *Adv. Funct. Mater.* **2021**, *31*, 2006448.

[16] N. Velasco, A. Suárez, F. Martínez-Lara, M. A. Fernández-Rodríguez, R. Sanz, S. Suárez-Pantiga, *J. Org. Chem.* **2021**, *86*, 7078–7091.

[17] I. Colomer, C. Batchelor-McAuley, B. Odell, T. J. Donohoe, R. G. Compton, *J. Am. Chem. Soc.* **2016**, *138*, 8855–8861.

[18] a) I. Colomer, A. E. R. Chamberlain, M. B. Haughey, T. J. Donohoe, *Nat. Chem. Rev.* **2017**, *1*, 0088; b) V. Pozhydaiev, M. Power, V. Gandon, J. Moran, D. Lebœuf, *Chem. Commun.* **2020**, *56*, 11548–11564; c) V. D. Vuković, E. Richmond, E. Wolf, J. Moran, *Angew. Chem. Int. Ed.* **2017**, *56*, 3085–3089; *Angew. Chem.* **2017**, *129*, 3131–3135; d) F. Noël, V. D. Vuković, J. Yi, E. Richmond, P. Kravljanac, J. Moran, *J. Org. Chem.* **2019**, *84*, 15926–15947.

[19] R.-J. Tang, T. Milcent, B. Crousse, *J. Org. Chem.* **2018**, *83*, 930–938.

[20] a) A. M. Arnold, A. Pöthig, M. Drees, T. J. Gulder, *J. Am. Chem. Soc.* **2018**, *140*, 4344–4353; b) C. Qi, G. Force, V. Gandon, D. Lebœuf, *Angew. Chem. Int. Ed.* **2021**, *60*, 946–953; *Angew. Chem.* **2021**, *133*, 959–966.

[21] For further details, see Supporting Information.

[22] The X-ray structure for compound **2 a** was deposited in CCDC2173852, which contains the supplementary crystallographic data for this paper. These data are provided free of charge by The Cambridge Crystallographic Data Centre.

[23] a) Z. Zeng, X. Shi, C. Chi, J. T. López Navarrete, J. Casado, J. Wu, *Chem. Soc. Rev.* **2015**, *44*, 6578–6596; b) B. Gabriele, R. Mancuso, L. Veltri, *Chem. Eur. J.* **2016**, *22*, 5056–5094.

[24] E. Richmond, J. Yi, V. D. Vuković, F. Sajadi, C. N. Rowley, J. Moran, *Chem. Sci.* **2018**, *9*, 6411–6416.

[25] a) T. Hiramitsu, Y. Maki, S. Senda, *J. Chem. Soc. Perkin Trans. 1* **1978**, 716–721; b) D. Canestrari, C. Cioffi, I. Biancofiore, S. Lancianesi, L. Ghisu, M. Ruether, J. O'Brien, M. F. A. Adamo, H. Ibrahim, *Chem. Sci.* **2019**, *10*, 9042–9050.

[26] The ability of the *S*-atom of thioethers to act as a hydrogen bond acceptor is well-documented, and various adducts of thioethers with HFIP, and TFE alcohols have been studied, see: a) K. F. Purcell, J. A. Stikeleather, S. D. Brunk, *J. Mol. Spectrosc.* **1969**, *32*, 202–213; b) K. F. Purcell, J. A. Stikeleather, S. D. Brunk, *J. Am. Chem. Soc.* **1969**, *91*, 4019–4027; c) A. D. Sherry, K. F. Purcell, *J. Am. Chem. Soc.* **1972**, *94*, 1848–1853. For hydrogen bonding between phenols and thioethers, see: d) R. West, D. L. Powell, M. K. T. Lee, L. S. Whatley, *J. Am. Chem. Soc.* **1964**, *86*, 3227–3229; e) G. C. Vogel, R. S. Drago, *J. Am. Chem. Soc.* **1970**, *92*, 5347–5352.

[27] In addition, when thioethers **1** are dissolved in HFIP, appreciable bathochromic shift is observed compared to conventional solvents. The UV-Vis spectrum of **1 a** is red-shifted in HFIP compared to the spectra recorded in isopropanol (IPA) which supports the activation of thioethers **1** by HFIP. For additional details, see Supporting Information.

[28] a) R. Sanz, D. Miguel, A. Martínez, J. M. Álvarez-Gutiérrez, F. Rodríguez, *Org. Lett.* **2007**, *9*, 727–730; b) T. Haven, G. Kubik, S. Haubenreisser, M. Niggemann, *Angew. Chem. Int. Ed.* **2013**, *52*, 4016–4019; *Angew. Chem.* **2013**, *125*, 4108–4111; c) N. Cabrera-Lobera, N. Velasco, R. Sanz, M. A. Fernández-Rodríguez, *Tetrahedron* **2019**, *75*, 4071–4080.