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Metal-Free Transfer Hydroiodination of C–C Multiple Bonds

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Supporting Information Placeholder

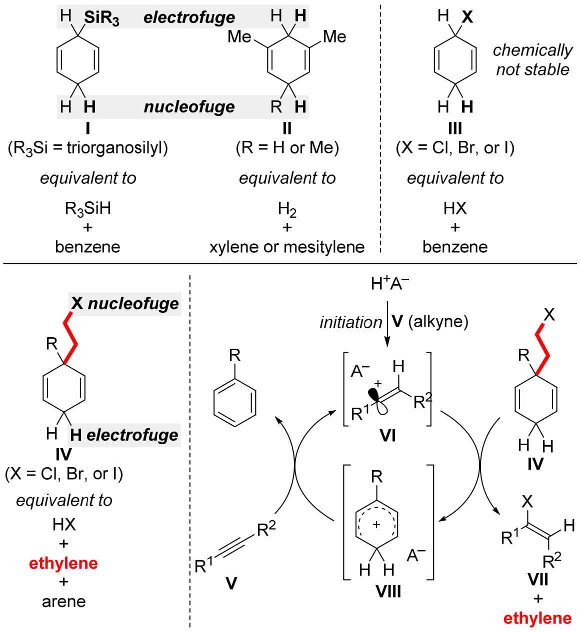
ABSTRACT: The design and a gram-scale synthesis of a bench-stable cyclohexa-1,4-diene-based surrogate of gaseous hydrogen iodide are described. By initiation with a moderately strong Brønsted acid, hydrogen iodide is transferred from the surrogate onto C–C multiple bonds such as alkynes and allenes without the involvement of free hydrogen iodide. The surrogate fragments into toluene and ethylene, easy-to-remove volatile waste. This hydroiodination reaction avoids precarious handling of hydrogen iodide or hydroiodic acid. By this, a broad range of previously unknown or difficult-to-prepare vinyl iodides can be accessed in stereocontrolled fashion.

INTRODUCTION

Hydrogen iodide (HI) is a toxic and corrosive gas that is commonly handled in the form of an equally corrosive, concentrated aqueous solution called hydroiodic acid. It can be used directly, and the Cativa™ process is an example of an industrial application,[1] but in-situ generation of hydrogen iodide is often more practical on the laboratory scale. Representative procedures make use of alkali metal iodides,[2] also together with Me_3SiCl,[3] or Me_3SiI directly,[4] as well as elemental iodine[5–10] as the iodine source; activation of Me_3SiI, I_2, and PI_3 on alumina was especially investigated.[5,6] Recently, Lautens and co-workers introduced $Et_3N{\cdot}HI$ and primary alkyl iodides as safe surrogates of HI.[11] Their elegant approach is based on oxidative addition of HI to palladium(0) or palladium(0)-catalyzed dehydrohalogenation of the alkyl iodide. Both methods arrive at the same H–Pd(II)–X intermediate that subsequently participates in the hydroiodination of 1,6-enynes. The overall process is a transition-metal-catalyzed transfer hydroiodination.[12,13]

We have been engaged in the development of metal-free transfer processes driven by aromatization of cyclohexa-1,4-dienes.[14] For example, cyclohexa-1,4-dienes **I** and **II** are surrogates of hydrosilanes and dihydrogen, respectively (Scheme 1, top). The strong boron Lewis acid $B(C_6F_5)_3$ then promotes alkene transfer hydrosilylation[14] with **I** as well as transfer hydrogenation[16] with **II**;[17] catalysis by several Brønsted acids was also demonstrated for **II**.[18] An extension of this strategy to hydrohalic acid (HX) surrogates **III** is not realistic due to their innate chemical instability (Scheme 1, top). To prevent rapid aromatization, we designed stable systems **IV** with an additional ethylene unit where we deemed controlled release of HX feasible (Scheme 1, bottom left). We hoped that this measure would simply translate into the formation of ethylene gas. However, we had to learn that derivatives of **IV** are either inert toward or do not react with $B(C_6F_5)_3$ in the planned way. Hence, we turned toward Brønsted-acid catalysis,[18] cognizant that the nucleofuge/electrofuge situation in **IV** could now be reverse to that in **I** and **II**. Halide abstraction from **IV** by an assumed carbocation intermediate **VI** by way of an iodonium ion intermediate is probably favored over hydride abstraction[18] from **IV** (Scheme 1, bottom right).

Scheme 1. Cyclohexa-1,4-diene-Based Surrogates (top) and Modified HX Surrogate and Assumed Catalytic Cycle of the Brønsted-Acid-Initiated Transfer Hydrohalogenation of Alkynes (bottom) (A^- = Counteranion)



We report here the gram-scale synthesis of an HI surrogate similar to the generic structure **IV** and its application to the Brønsted-acid-initiated transfer hydroiodination of alkynes,[19] alkenes[20] and allenes[21] (**V**→**VII** for X = I, Scheme 1, bottom right).

RESULTS AND DISCUSSION

Surrogate Identification and Preparation. Our investigation began with the identification and preparation of a robust surrogate (Figure 1). Parent compound **1**[22] seemed an obvious choice but was not sufficiently stable. Aromatization was again the problem. A quaternary carbon atom in the ring would forestall aromatization, and easy-to-access derivative **2**[22] was indeed stable. However, its high molecular weight and potential difficulties associated with removing the non-volatile biphenyl waste made it less attractive. We eventually arrived at low-molecular-weight structure **3**

that would release toluene and ethylene as waste. Its synthesis was accomplished in seven routine synthetic operations with five purifications (Scheme 2). The ethylene unit was established by Wittig homologation (**6**→**7**) after Birch alkylation and adjustment of the oxidation level (**4**→**5**→**6**). The primary alkyl iodide was installed by an Appel reaction of the corresponding alcohol (**8**→**3**). The sequence was scalable, and the four-step chain extension **5**→**8** was also possible on gram scale without purification of the intermediates (gray arrow, Scheme 2).

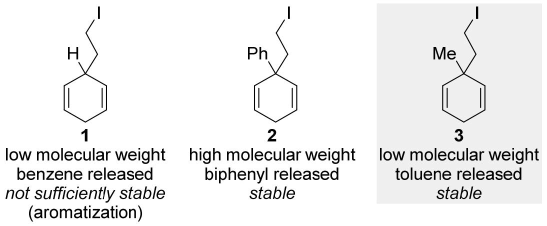
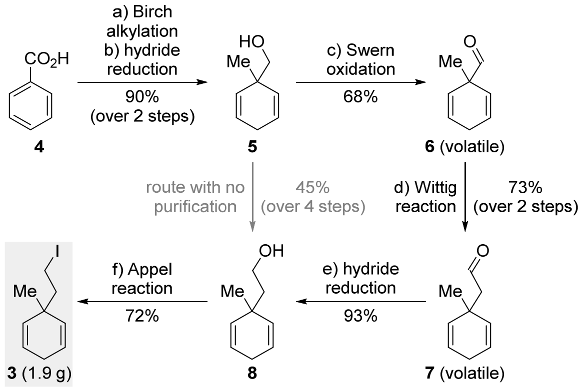


Figure 1. Potential cyclohexa-1,4-diene-based surrogates (see the Supporting Information for details).

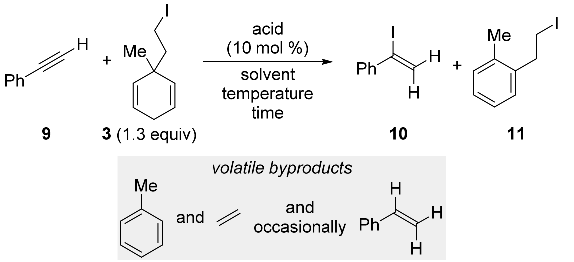
Scheme 2. Synthesis of HI Surrogate 3



Reaction conditions: a) Na (4.0 equiv), *t*BuOH (1.0 equiv), NH_3, –78 °C, 1 h; MeI (4.0 equiv), THF, –78 °C to RT, overnight; b) $LiAlH_4$ (2.0 equiv), THF, 0 °C; c) $(COCl)_2$ (1.5 equiv), DMSO (2.0 equiv), CH_2Cl_2, –78 °C, 30 min; Et_3N (excess), –78 °C to RT, 30 min; d) $[Ph_3PCH_2OMe]^+Cl^-$ (1.2 equiv), *n*BuLi (2.5 M in hexanes, 1.1 equiv), 0 °C to RT, overnight; HCl in H_2O (32%), 0 °C, 2 h; e) $NaBH_4$ (2.0 equiv), THF, 0 °C to RT, overnight; f) Ph_3P (1.3 equiv), I_2 (1.3 equiv), imidazole (1.3 equiv), CH_2Cl_2, 0 °C to RT, overnight.

Optimization and Byproduct Assignment. With gram quantities of HI surrogate **3** in hand, we tested various Brønsted acids in the transfer hydroiodination of phenylacetylene (**9**→**10**, Table 1). The outcome of this initial screening in benzene was mixed with regard to the pK_a values (entries 1–4). TfOH and $[H(OEt_2)_2]^+[BAr^F_4]^-$[23] promoted the decomposition of **9** but Tf_2NH and TsOH facilitated the desired HI transfer from **3** to **9**. The fragmentation pieces of **3**, that is toluene and ethylene, were detected in the ^1H NMR spectrum (see the Supporting Information for details). Using the relatively weak acid TsOH is already highly attractive, and the use of its monohydrate would have been even more so. $TsOH{\cdot}H_2O$ did initiate the reaction but the presence of water was detrimental (entry 5). No reaction was seen in the absence of added acid (entry 6). Substantial amounts of an unexpected compound, characterized as **11**, were found in all of the successful examples. Its proportion increased in more polar arene solvents such as chloro- and 1,2-dichlorobenzene (entries 7 and 8). Conversely, the formation of **11** was fully suppressed in cyclohexane but the yield was diminished (entry 9). By using benzene together with cyclohexane as co-solvent, that problem was overcome, and *α*-iodostyrene was obtained chemoselectively in high yield (entry 10).

Table 1. Optimization of the Brønsted-Acid-Initiated Transfer Hydroiodination of Alkynes[a]

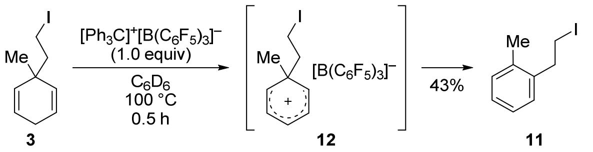


entry	acid	solvent	T (°C) for t (h)	yield of **10** (%)[b]	yield of **11** (%)[b]
1	Tf_2NH	C_6D_6	100 for 12	75	12
2[c]	TfOH	C_6D_6	100 for 6	< 1	< 1
3[c]	$[H(OEt_2)_2]^+$ $[BAr^F_4]^-$	C_6D_6	100 for 12	trace	trace
4	TsOH	C_6D_6	100 for 8	87	13
5	$TsOH{\cdot}H_2O$	C_6D_6	100 for 12	47[d]	10
6	none	C_6D_6	100 for 6	< 1	< 1
7	TsOH	C_6D_5Cl	100 for 12	59	24
8	TsOH	1,2-$C_6D_4Cl_2$	100 for 24	63	32
9	TsOH	C_6D_{12}	80 for 8	50	< 1
10	TsOH	C_6D_6/C_6D_{12}[e]	80 for 8	80	< 1
11[f]	TsOH	C_6D_6	100 for 18	trace	48

[a] Unless otherwise noted, reactions on a 0.030 mmol scale in 0.5 mL of the indicated solvent. [b] Determined by ^1H NMR spectroscopy by the addition of 1,4-dioxane as internal standard after the indicated time. [c] Decomposition of **9**. [d] Styrene detected in significant amounts (14% yield). [e] 2:1 ratio. [f] Addition of **9** after full consumption of **3**.

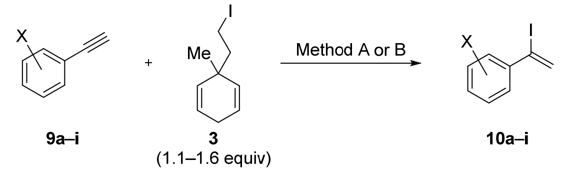
Exclusive formation of **11** was achieved when substrate **9** was added to the reaction after full consumption of surrogate **3** (entry 11). This experiment supports the notion that no free HI is involved in the transfer process. New compound **11** apparently originates from the HI surrogate **3**. We assume that it is formed by alkene protonation followed by Wagner–Meerwein rearrangement of either alkyl group; evidence for subsequent aromatization came from the detection of trace amounts of H_2 in the ^1H NMR spectrum (see the Supporting Information for details). An alternative way of the formation of **11** could be by hydride abstraction, that is one of the endocyclic methylene hydrogen atoms becoming the nucleofuge (see Scheme 1). Treatment of **3** with the trityl cation as hydride acceptor rapidly furnished **11**, here through the intermediacy of Wheland complex **12** that again undergoes a 1,2-alkyl shift[24] (Scheme 3). Finally, under the palladium(0)-catalyzed conditions reported by Lautens and co-workers for the dehydrohalogenation of alkyl iodides,[11a] no productive reactivity occurred with only isomerization of HI surrogate **3** to the corresponding cyclohexa-1,3-diene observed (not shown).

Scheme 3. Rearrangement of the HI Surrogate Initiated by Hydride Abstraction



Substrate Scope. The scope of the TsOH-initiated transfer hydroiodination of C–C triple bonds was then examined. It quickly became clear though that purification of the obtained products is challenging. Its success was dependent on the procedure employed for the individual substrate as different procedures caused slightly different compositions of byproducts. We therefore continued with C_6H_6 at 100 °C (Method A as in Table 1, entry 4) and C_6H_6/C_6H_{12} at 80 °C (Method B as in Table 1, entry 10) to simplify product isolation. Nine terminal (Table 2) and four internal alkynes (Figure 2) were brought to reaction with HI surrogate **3**. Yields were generally good for the synthesis of *α*-iodostyrenes and the functional-group tolerance acceptable. It is noteworthy that the reaction even works with electron-withdrawing substituents present at the aryl group as in **10f–h** (entries 6–8). A delicate CHO group as in **10g** was compatible (entry 7), as was a CN group as in **10h**, albeit in lower yield (entry 8). The borylated derivative **10i** was obtained in decent yield in view of the fact the reaction mixture is heated at 80 °C for 24 h (entry 9). Routes to formylated *α*-iodostyrenes are rare[25] and to the best of our knowledge this is the first reported preparation of a borylated *α*-iodostyrene.[26] This methodology therefore offers valuable access to these versatile building blocks.

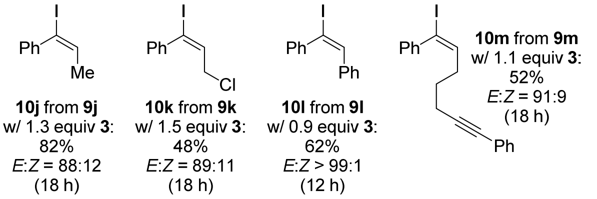
Table 2. Scope of the Brønsted-Acid-Initiated Transfer Hydroiodination of Terminal Alkynes[a]



entry	**9** with X	method	time (h)	yield of **10** (%)[b]
1	**9a** (X = H)	A	8	81 (**10a**)
2[c]	**9b** (X = 4-Me)	B	24	65 (**10b**)
3[c]	**9c** (X = 3-Me)	B	12	61 (**10c**)
4	**9d** (X = 2-Me)	B	24	46 (**10d**)
5	**9e** (X = 4-Cl)	A	8	86 (**10e**)
6	**9f** (X = 4-F)	A	8	70 (**10f**)
7	**9g** (X = 4-CHO)	B	24	59 (**10g**)
8	**9h** (X = 4-CN)	A	24	23 (**10h**)
9	**9i** (X = 4-Bpin)	B	24	44 (**10i**)

[a]Reaction conditions: Method A: TsOH (10 mol %), C_6H_6, 100 °C; Method B: TsOH (10 mol %), C_6H_6/C_6H_{12} 2:1, 80 °C. [b]Isolated yield after flash chromatography on silica gel.

Similar results were seen with internal alkyl/aryl-substituted triple bonds, and even a propargyl chloride was converted into the corresponding allylic system **10k** in moderate yield. A tethered triple bond as in **10m** remained untouched. Also, aryl/aryl-substituted **10l** formed in moderate yield. However, the reaction of purely alkyl-substituted substrates was not clean; e.g., oct-4-yne yielded the desired vinyl iodide in 28% NMR yield but could not be further purified (not shown). This is presumably due to the presence of an aliphatic rather than aromatic group at R^1 of vinyl cation **VI** (cf. Scheme 1), leading to both poorer stabilization of the cation and the availability of alternative reaction pathways.



10j from **9j** w/ 1.3 equiv **3**: 82% *E*:*Z* = 88:12 (18 h)

10k from **9k** w/ 1.5 equiv **3**: 48% *E*:*Z* = 89:11 (18 h)

10l from **9l** w/ 0.9 equiv **3**: 62% *E*:*Z* > 99:1 (12 h)

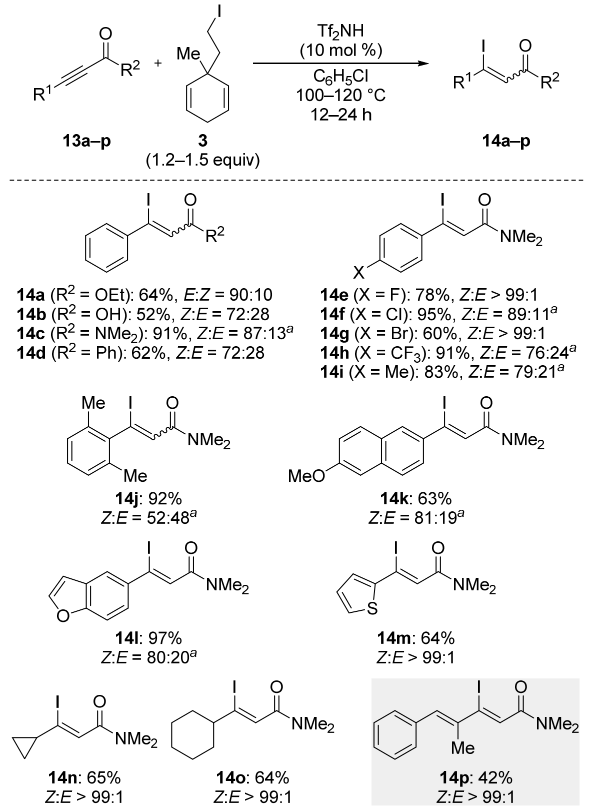
10m from **9m** w/ 1.1 equiv **3**: 52% *E*:*Z* = 91:9 (18 h)

Figure 2. Examples of the Brønsted-acid-initiated transfer hydroiodination of internal alkynes. [a]Reaction conditions: Method A: TsOH (10 mol %), C_6H_6, 100 °C.

The transfer hydroiodination of cycloalkenes to give secondary alkyl iodides was possible when using the stronger Brønsted-acid Tf_2NH but the results were rather poor. Iodocyclopentane (20%), iodocyclohexane (40%), and iodocycloheptane (38%) were all formed in low to moderate yield (see the Supporting Information for details). The rearrangement of the HI surrogate (**3**→**11**; cf. Table 1, entry 11 and Scheme 3) outrivaled the transfer process in these reactions. We explain this by similar reactivity of the double bonds in the substrate and the surrogate.

Interestingly, *α*,*β*-unsaturated acceptors were particularly successful participants in the transfer hydroiodination (Scheme 4). Despite their intrinsically electron-poor nature, the use of the stronger acid Tf_2NH overcame their lack of reactivity, and **14a** was predominantly isolated as its *E* isomer. Methods for the *E* selective preparation of *β*-iodo acrylates are rare.[27] Use of conditions previously reported by Piers and co-workers (NaI/AcOH)[28] produced the *Z* isomer in 85% yield (see the Supporting Information for details), highlighting the novel reactivity of HI surrogate **3**. A variety of carbonyl functionalities were tolerated to produce carboxylic acid, amide, and ketone derivatives **14b–d** in good to excellent yields predominantly with *Z* configuration. Routes to *β*-iodo acrylamides are scarce,[29] and variation of the *β*-alkyne substitution revealed this to be a general route to this class of compounds. In all cases, the two geometrical isomers were either separable by flash column chromatography on silica gel or the *Z* isomer was formed exclusively. As before, electron-withdrawing substitutents such as those in **14e–h** were tolerated but in this case electron-donating substituents as in **14i–j** also demonstrated excellent reactivity. Heteroaromatic substituents as in **14l** and **14m** were also amenable to the reaction and, importantly, aryl substitution was not a requirement for reactivity, allowing for the formation of acrylamides bearing aliphatic substituents as in **14n** and **14o**. We were also able to prepare diene **14p** from the corresponding enyne **13p** (gray box). In this case, no reaction at the alkene site was observed.

Scheme 4. Scope of the Brønsted-Acid-Initiated Transfer Hydroiodination of Activated Alkynes[a]

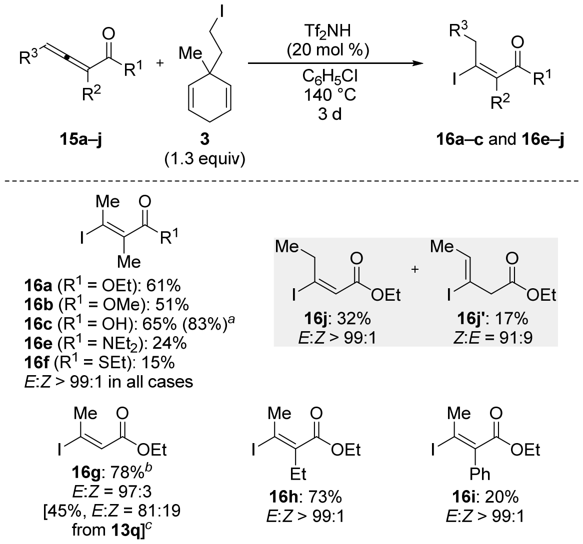


[a] The geometrical isomers were separable by flash column chromatography and were isolated individually.

Interestingly, individual resubjection of the isolated *Z* and *E* isomers of amide **14i** to the acidic conditions led to no observable isomerization. This suggests that the reaction operates under kinetic rather than thermodynamic control, and that prolonged heating would not result in changes to the isomer ratio. The reason for the varying quantities of *E* and *Z* isomers is, however, unclear at this stage.

HI surrogate **3** also proved proficient at the transfer hydroiodination of allene derivatives (Scheme 5). Previous work by Ma and co-workers had demonstrated the use of HI generated *in situ* from NaI and AcOH to form primarily β-iodo-β,γ-unsaturated esters from allenes.[21f] Under our reaction conditions, we instead formed β-iodo-α,β-unsaturated ester **16a** exclusively in 61% yield from allene **15a**, and with excellent control of the double bond geometry.[30] Alternative routes to tetrasubstituted β-iodo-α,β-unsaturated carbonyl species either give the *Z* isomer as the major product[31] or rely on specially designed substrates to deliver the *E* isomer.[32,33] Exploring the scope of the reaction, a number of carbonyl derivatives were tolerated to provide a small collection of tetrasubstituted *E*-alkenes **16b–f**. Interestingly, the isopropyl ester moiety was cleaved *in situ* to give carboxylic acid **16c** in 83% yield. No hydrolysis was seen for ethyl or methyl ester derivatives **16a** or **16b**, suggesting that the transformation occurred via cleavage of the alkyl C–O bond and formation of the secondary isopropyl cation.[34] Ester **16g**, which lacks substitution at the α-position, was formed in high yield and as almost exclusively the *E* isomer. Starting from the corresponding alkyne using the method outlined in Scheme 4 led to the same product but in lower yield and poorer stereoselectivity. Extended aliphatic or aromatic substitution at the α-position as in **16h** and **16i** was also tolerated, although the latter only in low yield. Adding substitution at the γ-position of the allene led to the formation of product mixtures as seen in the ca. 2:1 formation of **16j** and **16j'** (gray box). Allenes lacking the electron-withdrawing carbonyl functionality such as those bearing only aromatic substitution were not suitable substrates and decomposed under the reaction conditions.

Scheme 5. Scope of the Brønsted-Acid-Initiated Transfer Hydroiodination of Activated Allenes[a]



[a] Obtained from **15d** (R^1 = O*i*Pr). [b] Tf_2NH (10 mol %), 140 °C, 5 d. [c] Tf_2NH (10 mol %), 100 °C, 24 h.

CONCLUSION

To summarize, we introduced here a new transfer process that avoids handling of gaseous hydrogen iodide or its aqueous solution. Free HI is not even formed in this proton-initiated transfer hydroiodination of alkynes as well as allenes. Iodide abstraction, probably by way of an iodonium ion intermediate, from the ethylene tether of the cyclohexa-1,4-diene-based surrogate leads to its almost traceless fragmentation into toluene and ethylene accompanied by release of a proton. The method provides access to a wide range of hydroiodinated species, many of which have either not be accessed previously or were difficult to prepare. Further investigations into the mechanistic details of the reaction and the extension of this strategy to other HX transfer reactions are currently underway in our laboratory.[35]

ASSOCIATED CONTENT

Supporting Information

Experimental procedures and spectral data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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REFERENCES

(1) Sunley, G. J.; Watson, D. J. High productivity methanol carbonylation catalysis using iridium: The Cativa™ process for the manufacture of acetic acid. *Catal. Today* **2000**, *58*, 293–307.

(2) Ma, S.; Lu, X.; Li, Z. A novel regio- and stereospecific hydrohalogenation reaction of 2-propynoic acid and its derivatives. *J. Org. Chem.* **1992**, *57*, 709–713.

(3) Irifune, S.; Kibayashi, T.; Ishii, Y.; Ogawa, M. A Facile Synthesis of Alkyl Iodides and Deuterated Alkyl Iodides by Hydroiodination and Deuterioiodination of Olefins. *Synthesis* **1988**, 366–369.

(4) Yu, W.; Jin, Z. A Highly Stereoselective Synthesis of *α*-Halo Vinyl Ethers and Their Applications in Organic Synthesis. *J. Am. Chem. Soc.* **2000**, *122*, 9840–9841.

(5) (a) Kropp, P. J.; Daus, K. A.; Tubergen, M. W.; Kepler, K. D.; Wilson, V. P.; Craig, S. L.; Baillargeon, M. M.; Breton, G. W. Surface-mediated reactions. 3. Hydrohalogenation of alkenes. *J. Am. Chem. Soc.* **1993**, *115*, 3071–3079. (b) Kropp, P. J.; Crawford, S. D. Surface-Mediated Reactions. 4. Hydrohalogenation of Alkynes. *J. Org. Chem.* **1994**, *59*, 3102–3112.

(6) (a) Stewart, L. J.; Gray, D.; Pagni, R. M.; Kabalka, G. W. A convenient method for the addition of HI to unsaturated hydrocarbons using I_2 on Al_2O_3. *Tetrahedron Lett.* **1987**, *28*, 4497–4498. (b) Pagni, R. M.; Kabalka, G. W.; Boothe, R.; Gaetano, K.; Stewart, L. J.; Conaway, R.; Dial, C.; Gray, D.; Larson, S.; Luidhardt, T. Reactions of unsaturated compounds with iodine and bromine on *γ* alumina. *J. Org. Chem.* **1988**, *53*, 4477–4482.

(7) (a) Kawaguchi, S.-i.; Ogawa, A. Highly Selective Hydroiodation of Alkynes Using an Iodine−Hydrophosphine Binary System. *Org. Lett.* **2010**, *12*, 1893–1895. (b) Kawaguchi, S.-I.; Gonda, Y.; Masuno, H.; Thị Vũ, M.; Yamaguchi, K.; Shinohara, H.; Sonoda, M.; Ogawa, A. A convenient hydroiodination of alkynes using $I_2/PPh_3/H_2O$ and its application to the one-pot synthesis of trisubstituted alkenes via iodoalkenes using Pd-catalyzed cross-coupling reactions. *Tetrahedron Lett.* **2014**, *55*, 6779–6783.

(8) Reddy, C. K.; Periasamy, M. A new, simple procedure for the generation and addition of HI to alkenes and alkynes using BI_3:N,N-diethylaniline complex and acetic acid. *Tetrahedron Lett.* **1990**, *31*, 1919–1920.

(9) Chervin, S. M.; Abada, P.; Koreeda, M. Convenient, in Situ Generation of Anhydrous Hydrogen Iodide for the Preparation of α-Glycosyl Iodides and Vicinal Iodohydrins and for the Catalysis of Ferrier Glycosylation. *Org. Lett.* **2000**, *2*, 369–372.

(10) Zeng, C.; Shen, G.; Yang, F.; Chen, J.; Zhang, X.; Gu, C.; Zhou, Y.; Fan, B. Rhodium-Catalyzed Generation of Anhydrous Hydrogen Iodide: An Effective Method for the Preparation of Iodoalkanes. *Org. Lett.* **2018**, *20*, 6859–6862.

(11) (a) Petrone, D. A.; Franzoni, I.; Ye, J.; Rodríguez, J. F.; Poblador-Bahamonde, A. I.; Lautens, M. Palladium-Catalyzed Hydrohalogenation of 1,6-Enynes: Hydrogen Halide Salts and Alkyl Halides as Convenient HX Surrogates. *J. Am. Chem. Soc.* **2017**, *139*, 3546–3557. For a related hydroiodination with $BnEt_3NI$/camphorsulfonic acid catalyzed by ruthenium, see: (b) Dérien, S.; Klein, H.; Bruneau, C. Selective Ruthenium ‐ Catalyzed Hydrochlorination of Alkynes: One-Step Synthesis of Vinylchlorides. *Angew. Chem., Int. Ed.* **2015**, *54*, 12112–12115.

(12) For recent reviews of transition-metal-catalyzed transfer processes, see: (a) Bhawal, B. N.; Morandi, B. Shuttle Catalysis—New Strategies in Organic Synthesis. *Chem. Eur. J.* **2017**, *23*, 12004–12013. (b) Bhawal, B. N.; Morandi, B. Catalytic Transfer Functionalization through Shuttle Catalysis. *ACS Catal.* **2016**, *6*, 7528–7535.

(13) (a) Fang, X.; Yu, P.; Morandi, B. Catalytic reversible alkene-nitrile interconversion through controllable transfer hydrocyanation. *Science* **2016**, *351*, 832–836. (b) Fang, X.; Cacherat, B.; Morandi, B. CO- and HCl-free synthesis of acid chlorides from unsaturated hydrocarbons via shuttle catalysis. *Nat. Chem.* **2017**, *9*, 1105–1109.

(14) For a review, see: Keess, S.; Oestreich, M. Cyclohexa-1,4-dienes in transition-metal-free ionic transfer processes. *Chem. Sci.* **2017**, *8*, 4688–4695.

(15) For a review of transfer hydrosilylation, see: (a) Oestreich, M. Transfer Hydrosilylation. *Angew. Chem., Int. Ed.* **2016**, *55*, 494–499. (b) Simonneau, A.; Oestreich, M. 3-Silylated Cyclohexa-1,4-dienes as Precursors for Gaseous Hydrosilanes: The $B(C_6F_5)_3$-Catalyzed Transfer Hydrosilylation of Alkenes. *Angew. Chem., Int. Ed.* **2013**, *52*, 11905–11907. (c) Simonneau, A.; Oestreich, M. Formal SiH_4 chemistry using stable and easy-to-handle surrogates. *Nat. Chem.* **2015**, *7*, 816–822.

(16) Chatterjee, I.; Qu, Z.-W.; Grimme, S.; Oestreich, M. $B(C_6F_5)_3$-Catalyzed Transfer of Dihydrogen from One Unsaturated Hydrocarbon to Another. *Angew. Chem., Int. Ed.* **2015**, *54*, 12158–12162.

(17) For related transfer processes using cyclohexa-1,3-diene-based surrogates, see: Yuan, W.; Orecchia, P.; Oestreich, M. Cyclohexa-1,3-diene-based dihydrogen and hydrosilane surrogates in $B(C_6F_5)_3$-catalysed transfer processes. *Chem. Commun.* **2017**, *53*, 10390–10393.

(18) Chatterjee, I.; Oestreich, M. Brønsted Acid-Catalyzed Transfer Hydrogenation of Imines and Alkenes Using Cyclohexa-1,4-dienes as Dihydrogen Surrogates. *Org. Lett.* **2016**, *18*, 2463–2466.

(19) (a) See References [2,5b,6,7,8]. (b) Campos, P. J.; García, B.; Rodríguez, M. A. A simple and versatile method for the hydroiodination of alkenes and alkynes using I_2 and Et_3SiH in the presence of copper(II). *Tetrahedron Lett.* **2002**, *43*, 6111–6112. (c) Bartoli, G.; Cipolletti, R.; Di Antonio, G.; Giovannini, R.; Lanari, S.; Marcolini, M.; Marcantoni, E. A convergent approach to (*R*)-Tiagabine by a regio- and stereocontrolled hydroiodination of alkynes. *Org. Biomol. Chem.* **2010**, *8*, 3509–3517. (d) Kawaguchi, S.-i.; Masuno, H.; Sonoda, M.; Nomoto, A.; Ogawa, A. Highly regioselective hydroiodination of terminal alkynes and silylalkynes with iodine and phosphorus reagents leading to internal iodoalkenes. *Tetrahedron* **2012**, *68*, 9818–9825.

(20) (a) See References 3, 5a, 6, 8, and 18b. (b) Landini, D.; Rolla, F. Addition of hydrohalogenic acids to alkenes in aqueous-organic, two-phase systems in the presence of catalytic amounts of onium salts. *J. Org. Chem.* **1980**, *45*, 3527–3529. (c) Shimizu, M.; Toyoda, T.; Baba, T. An Intriguing Hydroiodination of Alkenes and Alkynes with Titanium Tetraiodide. *Synlett* **2005**, 2516–2518. (d) Ma, X.; Herzon, S. B. Non-classical selectivities in the reduction of alkenes by cobalt-mediated hydrogen atom transfer. *Chem. Sci.* **2015**, *6*, 6250–6255.

(21) (a) Ma, S.; Shi, Z.; Li, L. Efficient Synthesis of 4-Halo-4-penten-2-ones and 3-Halo-3-butenoic Acids/Esters via Hydrohalogenation Reaction of 3,4-Pentadien-2-one and 2,3-Butadienoic Acid/Methyl Ester. *J. Org. Chem.* **1998**, *63*, 4522–4523. (b) Ma, S.; Wei, Q. Hydrohalogenation Reactions of 1,2-Allenic Sulfones. A Novel Synthesis of 2-Haloallylic Sulfones. *J. Org. Chem.* **1999**, *64*, 1026–1028. (c) Ma, S.; Li, L.; Xie, H. Hydrohalogenation Reaction of 1,2-Allenyl Ketones Revisited. Efficient and Highly Stereoselective Synthesis of β,γ-Unsaturated β-Haloketones. *J. Org. Chem.* **1999**, *64*, 5325–5328. (d) Ma, S.; Wang, G. Highly selective hydrohalogenation reaction of substituted 23-allenoates. *Chin. J. Chem.* **1999**, *17*, 545–549. (e) Ma, S.; Wei, Q. Hydrohalogenation Reaction of 1,2-Allenic Sulfoxides with AlX_3 and H_2O: Efficient Synthesis of 2-Haloallyl Sulfoxides. *Eur. J. Org. Chem.* **2000**, 1939–1943. (f) Ma, S.; Xie, H.; Wang, G.; Zhang, J.; Shi, Z. Hydrohalogenation Reaction of Substituted 1,2-Allenic Carboxylic Acids, Esters, Amides, Nitriles, and Diphenyl Phosphine Oxides. *Synthesis* **2001**, 713–730. (g) Reddy, A. S.; Laali, K. K. Reaction of allene esters with Selectfluor/TMSX (X = I, Br, Cl) and Selectfluor/NH_4SCN: Competing oxidative/electrophilic dihalogenation and nucleophilic/conjugate addition. *Beilstein J. Org. Chem.* **2015**, *11*, 1641–1648.

(22) The syntheses of surrogates **1** and **2** are described in the Supporting Information.

(23) Brookhart, M.; Grant, B.; Volpe, Jr., A. F. $[(3,5\text{-}(CF_3)_2C_6H_3)_4B]^-[H(OEt_2)_2]^+$: a convenient reagent for generation and stabilization of cationic, highly electrophilic organometallic complexes. *Organometallics* **1992**, *11*, 3920–3922.

(24) Vitullo, V. P.; Cashen, M. J. Mechanistic aspects of the dienol-benzene rearrangement. *Tetrahedron Lett.* **1973**, 4823–4826.

(25) (a) Che, C.; Zheng, H.; Zhu, G. Copper-Catalyzed *trans*-Carbohalogenation of Terminal Alkynes with Functionalized Tertiary Alkyl Halides. *Org. Lett.* **2015**, *17*, 1617–1620. (b) Zhong, J.-J.; Yang, C.; Chang, X.-Y.; Zou, C.; Lu, W.; Che, C.-M. Platinum(II) photo-catalysis for highly selective difluoroalkylation reactions. *Chem. Comm.* **2017**, *53*, 8948–8951.

(26) A SciFinder substructure search of *α*-iodostyrenes with boron at any of the *ortho*-, *meta*-, or *para*-positions yielded no results.

(27) (a) Ma, S.; Lu, X. A novel stereospecific hydrohalogenation reaction of propiolates and propiolic acid. *J. Chem. Soc., Chem. Commun.* **1990**, 1643–1644. (b) Feutrill, J. T.; Lilly, M. J.; Rizzacasa, M. A. Total Synthesis of (+)-Crocacin C. *Org. Lett.* **2000**, *2*, 3365–3367. (c) Wang, B.; Lu, C.; Zhang, S.-Y.; He, G.; Nack, W. A.; Chen, G. Palladium-Catalyzed Stereoretentive Olefination of Unactivated C(sp^3)–H Bonds with Vinyl Iodides at Room Temperature: Synthesis of β-Vinyl α-Amino Acids. *Org. Lett.* **2014**, *16*, 6260–6263.

(28) Piers, E.; Wong, T.; Coish, P. D.; Rogers, C. A convenient procedure for the efficient preparation of alkyl (*Z*)-3-iodo-2-alkenoates. *Can. J. Chem.* **1994**, *72*, 1816–1819.

(29) For examples, see: (a) Luo, F.-T.; Hsieh, L.-C. Stereoselective Hydroiodination of 3-Substituted Derivatives of Propynoic Acid. *J. Chin. Chem. Soc.* **1994**, *41*, 871–873. (b) Feray, L.; Perfetti, P.; Bertrand, M. $AlCl_3$–NaI(NaBr)–*t*-BuOH: mild, chemo- and stereoselective reagents for hydrohalogenation of propiolic derivatives. *Tetrahedron* **2009**, *65*, 8733–8737. (c) Kuhl, N.; Schröder, N.; Glorius, F. Rh(III)-Catalyzed Halogenation of Vinylic C–H Bonds: Rapid and General Access to *Z*-Halo Acrylamides. *Org. Lett.* **2013**, *15*, 3860–3863. (d) Yu, D.-G.; Gensch, T.; de Azambuja, F.; Vásquez-Céspedes, S.; Glorius, F. Co(III)-Catalyzed C–H Activation/Formal SN-Type Reactions: Selective and Efficient Cyanation, Halogenation, and Allylation. *J. Am. Chem. Soc.* **2014**, *136*, 17722–17725.

(30) Similar (*E*)-*β*-iodo-*α*,*β*-unsaturated esters have previously been formed from allenes under aprotic conditions but only in small quantities and together with the corresponding *β*,*γ*-unsaturated ester and dihalogenated products. See Reference 20g.

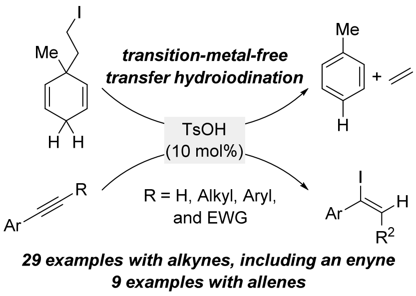
(31) (a) See Reference 25c. (b) Chen, J.-M.; Huang, X. Poly[styrene(iodosodiacetate)]-Promoted Ring Expansion Reaction of 1-Alkynylcycloalkanols: A Novel Synthesis of (*Z*)-2-(1-Iodo-1-organyl)methylenecycloalkanones. *Synthesis* **2004**, 2459–2462.

(32) Yashiro, K.; Ito, S.; Kayaki, S.; Sakata, K.; Mizota, I.; Hachiya, I. Titanium tetraiodide-mediated diastereoselective iodo-aldol and Mannich reactions of γ-alkoxy-α,β-alkynyl ketone derivatives. *Tetrahedron* **2016**, *72*, 6875–6885.

(33) Other preparations of these compounds typically involve metalation followed by quenching of the organometallic species with I_2 to deliver the *Z* isomer, see: (a) Takahashi, T.; Xi, C.; Ura, Y.; Nakajima, K. Metallo-Esterification of Alkynes: Reaction of Alkynes with Cp_2ZrEt_2 and Chloroformate. *J. Am. Chem. Soc.* **2000**, *122*, 3228–3229. (b) Six, Y. Titanium ‑ Mediated Carboxylation of Alkynes With Carbon Dioxide. *Eur. J. Org. Chem.* **2003**, 1157–1171. (c) Wolan, A.; Carodet, F.; Six, Y. A convenient titanium-mediated intermolecular alkyne–carbonate coupling reaction. *Tetrahedron* **2009**, *65*, 7429–7439. (d) Silwal, S.; Rahaim, R. J. Regioselective Synthesis of Enones via a Titanium-Promoted Coupling of Unsymmetrical Alkynes with Weinreb Amides. *J. Org. Chem.* **2014**, *79*, 8469–8476. (e) Nogi, K.; Fujihara, T.; Terao, J.; Tsuji, Y. Carboxyzincation Employing Carbon Dioxide and Zinc Powder: Cobalt-Catalyzed Multicomponent Coupling Reactions with Alkynes. *J. Am. Chem. Soc.* **2016**, *138*, 5547–5550.

(34) Kirby, A. J. Hydrolysis and Formation of Esters of Organic Acids. In *Ester Formation and Hydrolysis and Related Reactions*; Compton, R. G.; Bamford, C. H.; Tipper, C. F. H., Eds.; Elsevier: Amsterdam, 1972; Vol. 10, pp 71–124.

(35) HBr and HCl surrogates with the same platform as HI surrogate **3** are chemically more robust and will require further modification.


transition-metal-free
transfer hydroiodination
Me
I
H H
Me
H
+
TsOH
(10 mol%)
R
Ar
R = H, Alkyl, Aryl,
and EWG
I
Ar
H
R2
29 examples with alkynes, including an enyne
9 examples with allenes