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Triptycenyl Sulfide: A Practical and Active Catalyst for Electrophilic Aromatic Halogenation using *N*-Halosuccinimides

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ABSTRACT: A Lewis base catalyst Trip-SMe (Trip = triptycenyl) for electrophilic aromatic halogenation using *N*-halosuccinimides (NXS) is introduced. In the presence of an appropriate activator (as a non-coordinating-anion source), a series of unactivated aromatic compounds were halogenated at ambient temperature using NXS. This catalytic system was applicable to transformations that are currently unachievable except for the use of Br_2 or Cl_2: e.g. multi-halogenation of naphthalene, regioselective bromination of BINOL, etc. Controlled experiments revealed that the triptycenyl substituent exerts a crucial role for the catalytic activity, and kinetic experiments implied the occurrence of a sulfonium salt [Trip-S(Me)Br][SbF_6] as an active species. Compared to simple dialkyl sulfides, Trip-SMe exhibited a significant charge-separated ion pair character within the halonium complex whose structural information was obtained by the single-crystal X-ray analysis. A preliminary computational study disclosed that the π system of the triptycenyl functionality is a key motif to consolidate the enhancement of electrophilicity.

1. INTRODUCTION

The direct halogenation of aromatic compounds is one of the most fundamental and frequently-used reactions in organic chemistry because the halide functionalities offer numerous possible transformations afterward.[1,2] Furthermore, the remarkable development of transition-metal-catalyzed coupling techniques has greatly reinforced their synthetic value over the past decades.[3,4] Halogen functionalities can widely modulate the electronic, lipophilic, and steric properties of the attached frameworks. It thus can be appreciated that the haloarenes fulfill a dichotomous function in many research fields[5] involving pharmaceuticals, agrochemicals, material science, and imaging technics. According to these aspects, halogenated aromatics have been regarded as "functional and functionalizable" molecules.[6]

Classical electrophilic halogenation using bromine (Br_2) or chlorine (Cl_2) has been a promising synthetic tool to manufacture a wide variety of haloarenes. These molecular halogen compounds have been superseded by alternative halogenating reagents, as far as possible, owing to their toxicity and handling difficulties.[2,6] *N*-Halosuccinimides (NXS: X = Cl, Br, I) are particularly useful halogen sources both in academic research and industrial production considering their stability and availability. NXS are, however, substantially less reactive reagents that yield the corresponding aryl halides only from the highly nucleophilic substrates, and harsh reaction conditions are usually required to ensure such transformations. In order to enhance the reactivity of NXS toward the electrophilic substitution, Brønsted or Lewis acid catalysts have traditionally been employed.[7,8] Here the activation is achieved through protonation or complexation of the carbonyl moiety of NXS, creating a positively charged halogen fragment (Figure 1a).

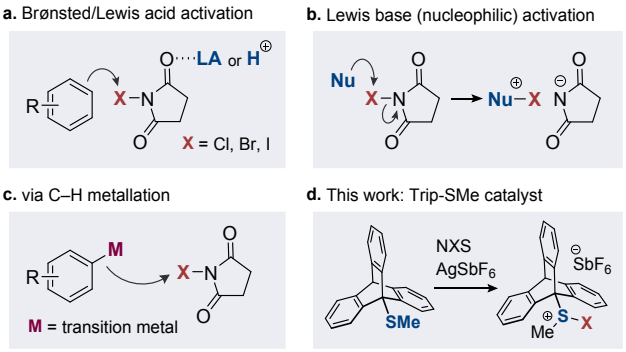


Figure 1. Aromatic electrophilic halogenation.

Meanwhile, Lewis basic reagents have also served as catalysts for the halogenation, where nucleophilic oxygen, sulfur, nitrogen, or phosphorous atoms interact with the halogenating reagents to generate catalytically active halonium complexes or, in case the nucleophile is amine (R_2NH), the corresponding halo-amine (R_2NX) (Figure 1b).[9] Although the Lewis base activation[10] is generally less powerful than the acid catalysis for the aromatic halogenation, it has been of a practical tool for manufacturing olefinic substrates. In particular, significant research interest has been paid for halonium-induced cyclization (cation-π cyclization)[11,12] to provide valuable (poly)cyclic compounds involving natural terpenoids (Figure 2). A landmark improvement in this field was achieved by developing new reagents such as [I(pyridine)$_2$][BF_4] (IPy_2BF_4) by Barluenga et al.[13] and [Et_2SBr][$SbCl_5Br$] (BDSB) as well as the analogous chlorinating/iodinating reagents (CDSC, IDSI) by Snyder et al.[14,15] Recently, Gulder et al. found that a combination of morpholine and NXS in HFIP (hexafluoroisopropanol)[16] solvent to be an effective conditions for the polyene cyclization.[17] For the catalytic variant, Denmark et al. reported that various oxygen-, sulfur-, selenium-,

and phosphorous-based Lewis base reagents promoted the halocyclization using NBS and NIS.[18] The first successful enantioselective reaction was developed by Ishihara and coworkers. who used phosphoramidites as stoichiometric chiral promoters.[19] Afterward, a catalytic enantioselective protocol was established by Samanta and Yamamoto utilizing a dual-role Lewis base/Brønsted acid catalyst.[20]

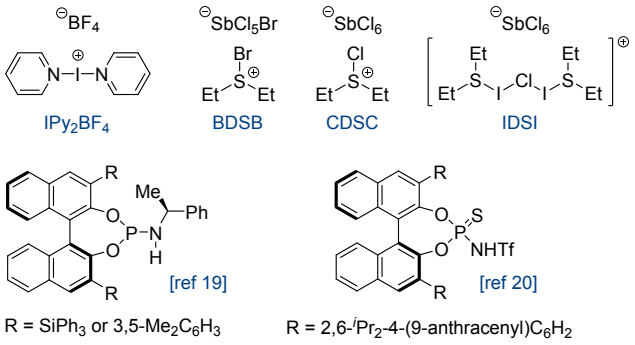


Figure 2. Lewis base reagents and catalysts for halonium-induced cyclization.

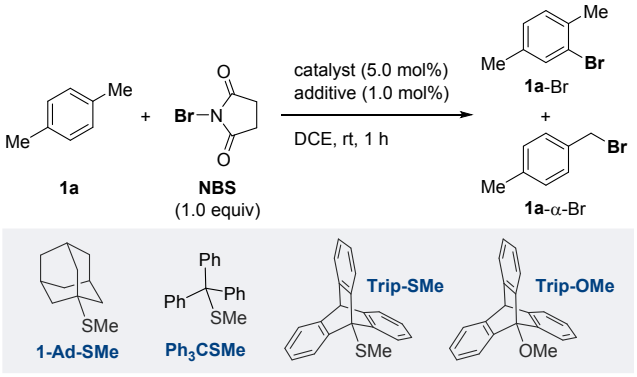
Apart from the activation of NXS, in situ formation of reactive organometallic species through the direct metalation of aromatic C–H bonds has been considered as well (Figure 1c).[21] As an elegant work in this category, Wang and coworkers reported that $AuCl_3$ exhibited excellent catalytic performance for the halogenation using NXS.[11a] The system afforded a series of halogenated products from unactivated aromatic substrates under mild reaction conditions (rt to 80 °C) with low catalyst loadings (0.01 to 5.0 mol%). Additionally, if appropriate directing groups are provided, regioselective halogenation is possible using various transition-metal complexes (Co, Cu, Ni, Pd, Ru, Rh).[22]

As described above, much effort has been directed toward the development of catalytic systems that function under relatively mild reaction conditions. However, it should be pointed out that many halogenation processes still need to rely on the use of Br_2 or Cl_2 due to the inherently lower reactivity of user-friendly halogenating reagents. In order that NXS actually replace the molecular halogens, there still have been a great demand for developing further effective catalytic protocols. In this work, we report the invention of a Lewis base Trip-SMe (Trip = triptycenyl) catalyst for the aromatic halogenation using *N*-halosuccinimides (Figure 1d). Trip-SMe could easily be prepared in one step from the commercially available starting materials and exhibited exceptional high activity. Mechanistic studies revealed that the occurrence of amplified electrophilic character within a halonium intermediate plays a central role in the catalysis.

2. RESULTS & DISCUSSION

We first investigated the catalytic activity of various thioethers for the bromination of *p*-xylene (**1a**) with *N*-bromosuccinimide (NBS) in the presence of an additive (Table 1). To our delight, **1a** was smoothly brominated at room temperature within 1 h to give **1a**-Br (81% yield) using 5.0 mol% of Trip-SMe catalyst together with 10 mol% of TfOH co-catalyst (entry 1 vs 2). Remarkable acceleration of the reaction rate was also achieved with 1.0 mol% of $In(OTf)_3$ (88% yield) or $AgSbF_6$ (82% yield) (entries 3 and 4). AgOTf gave a lower yield (entry 5), and AgOAc was totally inactive (entry 6). While the use of TfOH is preferable to establish a metal-free system with lower cost, $AgSbF_6$ was selected as a representative activator for the following experiments because of its ease of handling ($In(OTf)_3$ is considerably hygroscopic). The reaction did not proceed in the absence of Trip-SMe catalyst (entry 7).[23] We then examined the effect of substituents on the sulfur atom of the catalyst. Replacement of the triptycenyl group with a linear alkyl group resulted in the exclusive benzylic bromination (entry 8). 1-Ad-SMe (Ad = adamantyl) and Ph_3C-SMe gave **1a**-Br in low to moderate yields, but the competing benzylic bromination was ineluctable (entries 9 and 10). Trip-OMe did not show any catalytic activity, indicating that the triptycene fragment itself is not an active center in the catalysis (entry 11). A significant drop of the productivity was observed in case the benzene rings of the triptycenyl group was brominated (see Scheme 6) (entry 12).

Table 1. Optimization study [a]



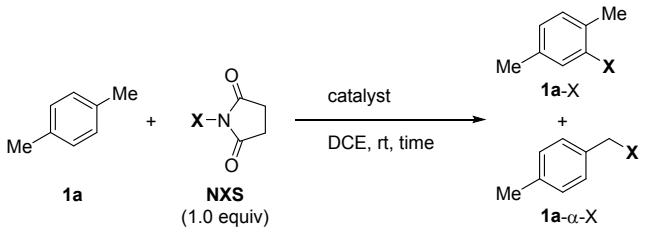
entry	catalyst	additive	**1a**-Br [b]	**1a**-α-Br [b]
1	Trip-SMe	--	trace	n.d.
2 [c]	Trip-SMe	TfOH	81%	n.d.
3	Trip-SMe	$In(OTf)_3$	88%	n.d.
4	Trip-SMe	$AgSbF_6$	82%	n.d.
5	Trip-SMe	AgOTf	29%	n.d.
6	Trip-SMe	AgOAc	trace	n.d.
7	--	$AgSbF_6$	trace	n.d.
8	^{n}Octyl-SMe	$AgSbF_6$	trace	60%
9	1-Ad-SMe	$AgSbF_6$	50%	20%
10	Ph_3C-SMe	$AgSbF_6$	13%	7%
11	Trip-OMe	$AgSbF_6$	trace	n.d.
12	Trip-SMe-Br_3	$AgSbF_6$	18% 44% (5 h)	n.d. n.d.

[a] Reaction conditions: **1a** (0.5 mmol), NBS (0.5 mmol), DCE (2.0 mL). [b] Determined by GC analysis. [c] 10 mol% of TfOH was used as an additive.

Subsequently, we evaluated the efficiency of the developed reaction system in comparison with existing methods for the halogenation of **1a** using NBS and NCS (Table 2). Under the standard conditions with 1.0 mol% catalyst loading, chlorination of **1a** was also successful to afford **1a**-Cl in 90% yield (entry 2). In general, chlorination of unactivated aromatic systems has been of highly challenging task. As demonstrated in the previous reports,[21a,21b] $AuCl_3$ has been one of the most powerful catalysts for the halogenation of unactivated arenes; however, only small amounts of the halogenated products were obtained under identical reaction conditions (entries 3 and 4). With an increased catalyst loading and a longer reaction time, $FeCl_3$ gave **1a**-Br in 33% yield along with the benzyl bromide, but was not suitable for the chlorination (entries 5 and 6).[24] $ZrCl_4$ and $AlCl_3$ failed to trigger the aromatic halogenation (entries 7 and 8).[25] Interestingly, some sulfur-based catalysts were prone to induce the benzylic bromination, whereas the sulfonium reagent BDSB itself was inert under the conditions (entries 10–13).[9b,9c,9g] An ammonium salt

NH_4NO_3 was also not an active catalyst (entry 14). HFIP solvent was a suitable promotor for the bromination to achieve a good yield within 1 h (entry 15). In contrast, it was not competent in the chlorination (entry 16). We also tested some reactive chlorinating reagents in HFIP solvent and found that trichloroisocyanuric acid (TCCA) afforded **1a**-Cl in 61% yield (entry 17). The amount of the Trip-SMe catalyst could be decreased to 0.1 mol% without affecting the chemical yield (Scheme 1). These results clearly highlight the exceptional activity of the Trip-SMe/$AgSbF_6$ system.

Table 2. Bromination and chlorination of 1a with NXS using various catalysts [a]

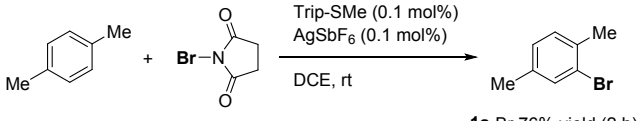


entry	X	catalyst	time	yield [b]
1	Br	Trip-SMe/$AgSbF_6$ (1.0 mol% each)	1 h	79%
2	Cl	Trip-SMe/$AgSbF_6$ (1.0 mol% each)	1 h	90%
3	Br	$AuCl_3$ (1.0 mol%)	1 h	14 %
4	Cl	$AuCl_3$ (1.0 mol%)	1 h	trace
5	Br	$FeCl_3$ (10 mol%)	18 h	33% (α-Br 5%)
6	Cl	$FeCl_3$ (10 mol%)	18 h	7%
7	Br	$ZrCl_4$ (10 mol%)	18 h	trace (α-Br 63%)
8	Cl	$ZrCl_4$ (10 mol%)	18 h	trace
9	Br	$AlCl_3$ (10 mol%)	18 h	trace (α-Br 66%)
10	Br	S=PPh_3 (20 mol%)	18 h	trace (α-Br 39%)
11	Br	thiourea (20 mol%)	18 h	trace (α-Br 60%)
12	Br	BDSB (5.0 mol%)	1 h	4% (α-Br 59%)
13	--	BDSB (1.0 equiv)	1 h	trace
14	Br	NH_4NO_3 (20 mol%)	18 h	trace
15 [c]	Br	HFIP	1 h	71%
16 [c]	Cl	HFIP	18 h	trace
17 [c,d]	Cl	HFIP using TCCA	18 h	63%

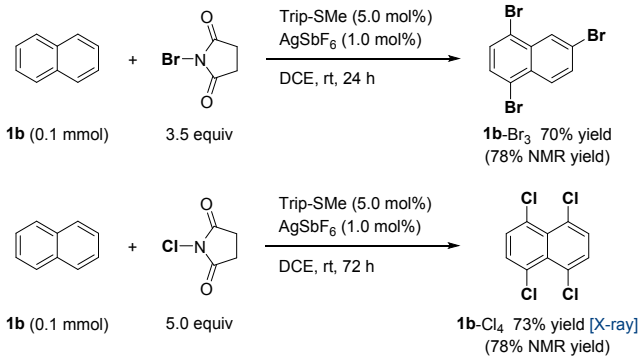
[a] Reaction conditions: **1a** (0.5 mmol), NXS (0.5 mmol), DCE (2.0 mL). [b] Determined by GC analysis. [c] HFIP (2.0 mL) was used as solvent instead of DCE. [d] TCCA (trichloroisocyanuric acid, 0.17 mmol) was used instead of NCS.

To further demonstrate the catalytic performance of the Trip-SMe/$AgSbF_6$ system, we examined the multi-halogenation of naphthalene (**1b**) (Scheme 2). The reaction of **1b** with 3.5 equiv of NBS at room temperature produced 1,4,6-tribromonaphthalene (**1b**-Br_3) in 70% isolated yield. In a similar manner, 1,4,5,8-tetrachloronaphthalene (**1b**-Cl_4) was readily obtained in 73% isolated yield from **1b** upon treatment with 5.0 equiv of NCS. The difference of the outcome is presumably dictated by the steric effect of halogen atoms. Single crystal diffraction analysis of **1b**-Cl_4 found a twist of 5.8° within the naphthalene ring due to the steric repulsion between the chloro substituents.[26] This was not a case for the bromination where the proximal positions could not be occupied. These multi-halogenated compounds have not been available except via cumbersome multi-step processes adopting Br_2 under UV irradiation[27] and the Sandmeyer conditions.[28] Notably, $AuCl_3$, $FeCl_3$, and $ZrCl_4$ catalysts as well as a reaction in HFIP solvent all failed to produce **1b**-Br_3 and **1b**-Cl_4 because of their insufficient activity and selectivity (see the Supporting Information).

Scheme 1. Bromination and chlorination of 1a with 0.1 mol% catalyst loading.



Scheme 2. Multi-halogenation of naphthalene.

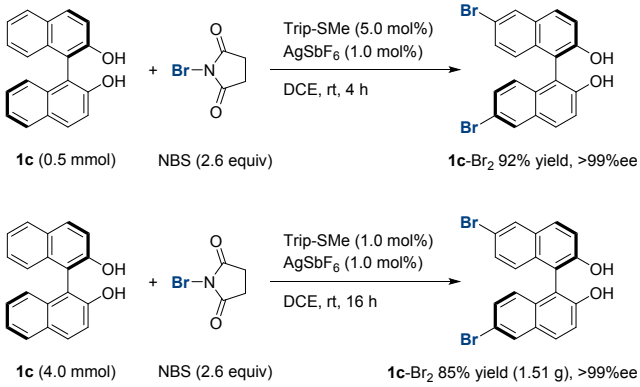


For another synthetic application, we examined a halogenation of BINOL (Scheme 3). Regioselective bromination of BINOL at the C6 and C6' positions has been an "opening" for the construction of various binaphthyl-based functional molecules.[29,30] To achieve this transformation, one needs to use Br_2 under cryogenic conditions, and the addition rate must be controlled properly to suppress the formation of regioisomers. In our catalysis, (*R*)-(+)-BINOL **1c** was converted cleanly into the desired product **1c**-Br_2 in 92% isolated yield after 4 h using 2.6 equiv of NBS at ambient temperature, without any loss of its optical purity. This reaction could be conducted in a gram scale with 1.0 mol% catalyst loading to produce **1c**-Br_2 in 85% isolated yield as optically pure form. We also examined the BINOL bromination using other promotors (see the Supporting Information); however, the target compound **1c**-Br_2 was obtained in low to moderate yields (6%~53%) and was inseparable from the reaction mixture due to the formation of various isomers.

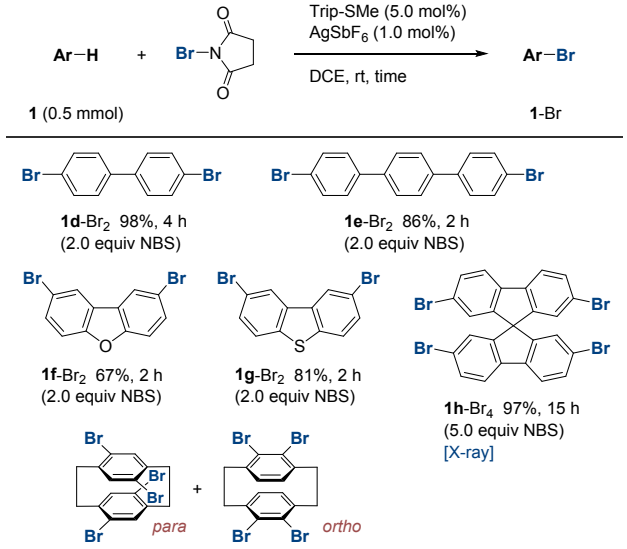
As exemplified in these reactions, the developed protocol is highly useful for the site-selective multi-halogenation of unactivated aromatic substrates. Additional examples are showcased in Scheme 4. Biphenyl (**1d**) and terphenyl (**1e**) were selectively di- brominated to give the corresponding "linear" compounds in high yields. Dibenzofuran (**1f**) dibenzothiophene (**1g**) were also successfully converted into the target products. Similarly, reaction of 9,9'-spirobi[fluorene] (**1h**) with NBS

produced 2,2',7,7'-tetrabromo-9,9'-spirobi[fluorene] (**1h**-Br_4) as a sole product. Note that the synthesis of these bromoarenes is currently not achievable except using Br_2.[31] For the bromination of [2.2]paracyclophane (**1i**), two tetrabromo isomers **1i**-*para*-Br_4 and **1i**-*ortho*-Br_4 were obtained in 33% and 30% yields after 21 h upon treatment with 5.0 equiv of NBS. Conventional methods have required the continuous addition of a large excess Br_2 (ca. 20 equiv in total) over 8 days in the presence of I_2 catalyst.[32]

Scheme 3. Bromination of BINOL using NBS.

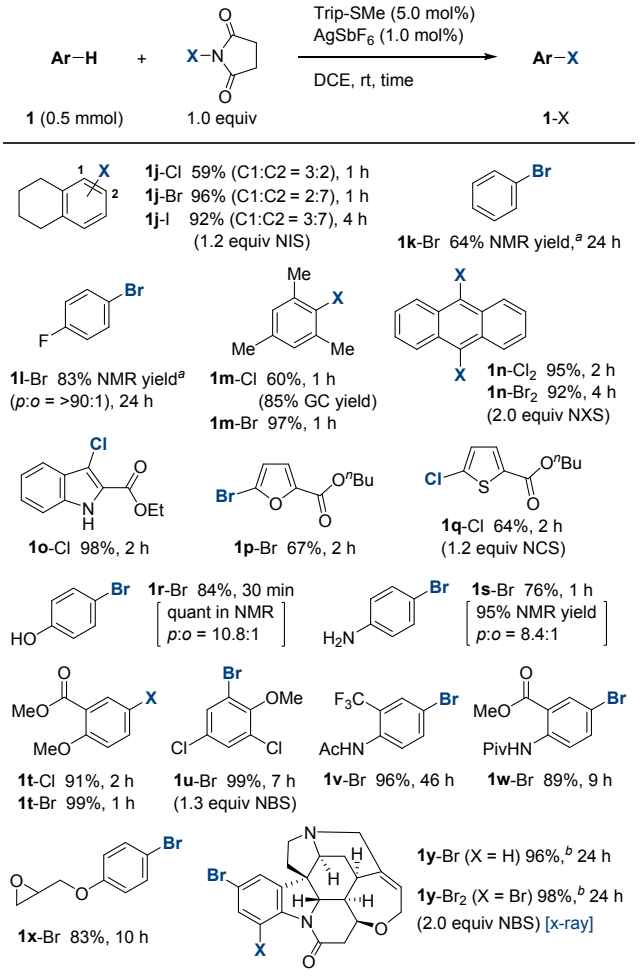


Scheme 4. Substrate scope of the aromatic halogenation catalyzed by the Trip-SMe/$AgSbF_6$ system.



Next, we examined the functional group compatibility of the Trip-SMe/$AgSbF_6$ catalyst with a range of aromatic substrates (Scheme 5). For the reaction of tetrahydronaphthalene (**1j**), the bromination was found to take place preferentially at a more sterically accessible C2 position, whereas the chlorination produced the C1 adduct as a major isomer. This system was also applicable for the iodination using 1.2 equiv of NIS to afford **1j**-I in an excellent yield. Benzene (**1k**) required a longer reaction time and produced a mixture of bromobenzene **1k**-Br and *p*-dibromobenzene **1k**-Br_2 in 64% and 8% yields, respectively. The bromination of fluorobenzene (**1l**) resulted in a selective conversion where the para isomer formed exclusively in 83% yield. For mesitylene (**1m**), both the chlorination and the bromination proceeded smoothly to give the corresponding haloarenes in high yields. Competing benzylic bromination was not observed for these substrates. Anthracene (**1n**) was smoothly converted into the doubly halogenated compounds. For heteroaromatic substrates, indole (**1o**), furan (**1p**), and thiophene (**1q**) were tolerated, whereas pyridine derivatives (involving quinolines and isoquinolines) were not suitable for the present system due to their electron deficient nature as well as strong Lewis basicity (not shown). With activated aromatic compounds such as phenol (**1r**) and aniline (**1s**), the products were obtained with considerably high para-selectivities. Anisole and anilide derivatives **1t**–**1w** bearing electron withdrawing groups gave the desired products with satisfactory yields. The terminal epoxide functionality of a glycidyl ether **1x**, which is hardly tolerated under acidic conditions, remained intact to give the desired product in 83% yield. The reaction of strychnine (**1y**) bearing a tri-substituted strained alkene moiety within the polycyclic skeleton proceeded very cleanly,[33] and both mono- and di-brominated products (**1q**-Br and **1q**-Br_2)[26] were obtained almost quantitatively. In this case, the tertiary amine group was protected throughout the reaction by protonation with a slight excess amount of TfOH (1.2 equiv) (TfOH can be used as the co-catalyst; see Table 1). It is of interest to note that the halogenation of strychnine has not been sufficient via a Sandmeyer sequence (15% total yield)[34a] or a radical reaction (34% yield).[34b]

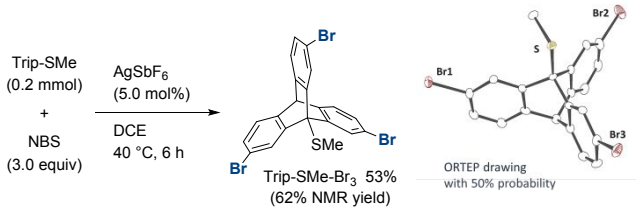
Scheme 5. Substrate scope of the aromatic halogenation catalyzed by the Trip-SMe/$AgSbF_6$ system.



[a] Not isolated due to the volatility of the product: 0.2 mmol scale, NBS (1.2 equiv), Trip-SMe/$AgSbF_6$ (2.5 mol% each). [b] TfOH (1.2 equiv) was used instead of $AgSbF_6$.

On the other hand, the developed catalytic system was not readily applicable to electron deficient aromatics such as benzonitrile, nitrobenzene, *tert*-butylbenzoate, and 1,3,5-trichlorobenzene even under forceful reaction conditions (higher temperature up to 80 °C and longer reaction time, not shown). In these cases, the benzenoid core of the catalyst was preferentially halogenated. Interestingly, bromination of Trip-SMe proceeded with considerable regioselectivity to give Trip-SMe-Br_3 as a major isomer in 53% yield (Scheme 6). This compound was isolated by the regular silica-gel column chromatography, and the structure was ambiguously determined by the X-ray crystallographic analysis.[26] Considering the recent achievements in transformation of the thioether functionality,[35] this compound appears to be a potentially useful building block for the construction of triptycene-based three-dimensional π-conjugated architectures.[36]

Scheme 6. Bromination of Trip-SMe mediated by $AgSbF_6$.



3. MECHANISTIC CONSIDERATION

In order to gain insight into the reaction mechanism, a kinetic study was carried out with the variable-time normalized analysis (VTNA)[37] graphical method for the concentration profiles.[38] We investigated the bromination of *p*-xylene as a model reaction (Figure 3). Here the concentration of catalyst was assumed to be constant because any catalyst deactivation was not observed under the standard conditions (for details, see the Supporting Information), thereby the time integral $\Sigma[\text{cat}]^x\Delta t$ becomes $t[\text{cat}]^x$. An order of 1.0 was obtained for xylene (Figure 3a), suggesting that the electrophilic addition of Br^+ species onto the aromatic system is rate limiting. On the other hand, an order of zero was obtained for NBS (Figure 3b). This result implied the existence of a pre-equilibrium before the formation of catalytically active species.

As illustrated in Scheme 7, if the equilibrium constant for the Trip-SMe/NBS adduct formation step is considerably small, concentration of the adduct **A** can be approximated as a constant at loadings examined in this study, and the formation of a possible active species **B** would be expressed solely as a function of $AgSbF_6$ concentration. Indeed, an equilibrium constant K_{obs} of 1.69×10^{-3} was obtained when NBS and a catalytic amount of Trip-SMe were mixed in DCM-d_2. An order of zero in Trip-SMe and an order of 1.0 in $AgSbF_6$ provided a further support for this speculation (Figure 3c and 3d). We cannot rule out the possibility that $AgSbF_6$ acted as a Lewis acid to directly activate NBS and facilitate the formation of the intermediate **B**, whereas other common Lewis acids such as $Al(OTf)_3$, $Zn(OTf)_2$, $Cu(OTf)_2$, and $Ni(OTf)_2$ did not promote the reaction (see the Supporting Information). An arenium ion intermediate **C** forms passing through the turnover limiting step, and subsequent deprotonation by succinimide anion liberates the brominated product and $AgSbF_6$.

For the present we assume that a sulfonium salt consists of Trip-S(Me)Br and a weakly coordinating SbF_6 counter anion is an active species for the electrophilic halogenation (see Scheme 7, **B**). Since this sulfonium salt is a transient and self-reactive species, we investigated the reactivity of a relevant sulfonium salt derived from the "pre-brominated" Trip-SMe (see Scheme 6). Trip-SMe-Br_3 was sequentially treated with Br_2 and $SbCl_5$ to produce the corresponding adduct **2** in 75% yield (Scheme 8). This complex was rather stable under an inert atmosphere at low temperature (below -20 °C) and could be recrystallized to elucidate its structure by X-ray crystallographic analysis.[26]

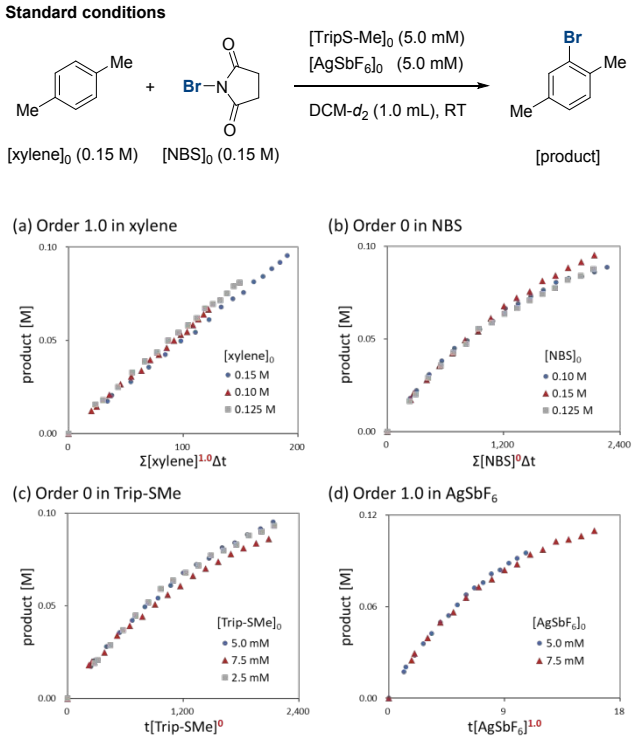
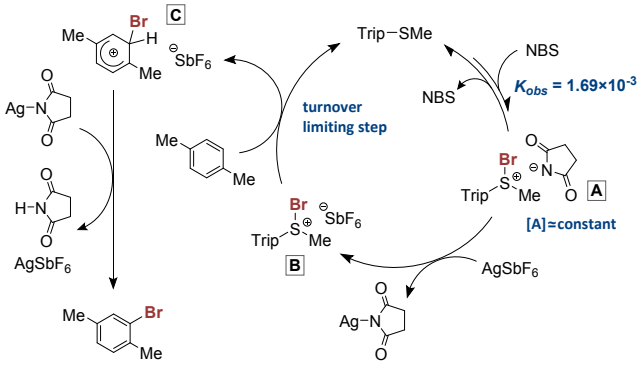
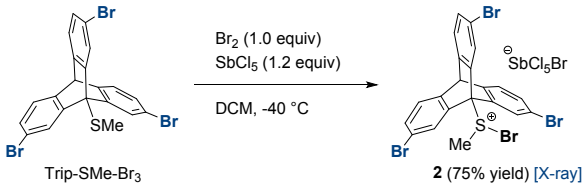


Figure 3. Variable-time normalized analysis for the estimation of the order in (a) xylene, (b) NBS, (c) Trip-SMe, and (d) $AgSbF_6$.

Scheme 7. Proposed reaction mechanism for the Trip-SMe catalyzed bromination of xylene.



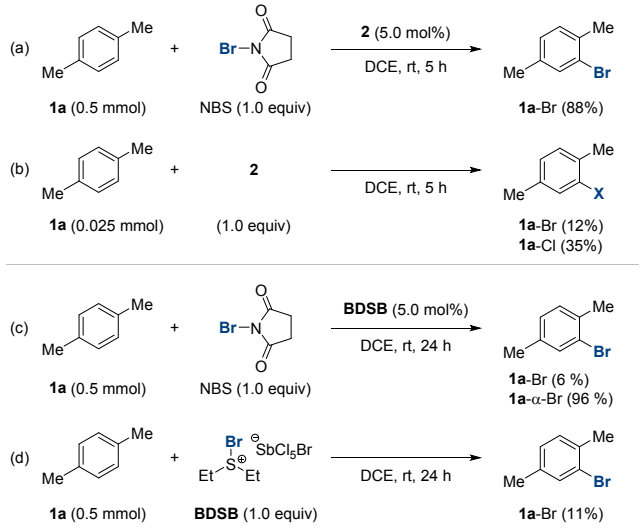
Scheme 8. Preparation of sulfonium complex 2.



When the bromination of **1a** was conducted using a catalytic amount of **2**, the product **1a**-Br was obtained in a reasonably high yield of 88% without any additive (Scheme 9a). On the other hand, stoichiometric use of **2** produced considerable amount of **1a**-Cl (35%) along with **1a**-Br (12%) probably via the halogen atom

scrambling over the counter anion (Scheme 9b). A sulfonium salt derived from diethyl sulfide (BDSB)[14b] were insufficiently reactive to trigger the aromatic halogenation both in catalytic and stoichiometric conditions even with a longer reaction time (Scheme 9c and 9d). These results provided further proof that the triptycenyl substituent exerted a decisive influence on the catalytic activity.

Scheme 9. Bromination of 1a in the presence of 2 and BDSB.



A comprehensive mechanistic rationale for the Lewis basic activation of electrophiles was provided by Denmark et al.[10b] The binding of the Lewis base to the halogen center will induce a redistribution of electron density via n-σ* interaction (Figure 3). Accordingly, this interaction leads to a polarization of the adjacent bonds to create an electron positive center within the complex. Here the length of peripheral bonds are elongated as the Lewis base interacts with the halogen atom and shortens the D–X distance. If the polarization effect is strong enough to eventually form a charge-separated ion pair species, the electrophilicity of the halogen atom is highly amplified. Basically, much information on a degree of the polarization can be obtained from their solid state structures.

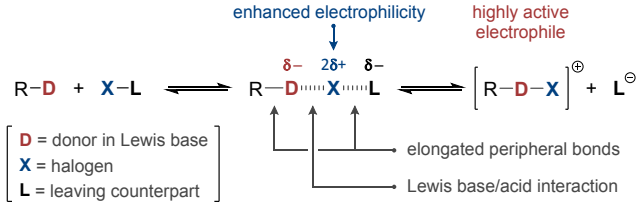


Figure 3. Schematic representation of the formation of halonium adduct via the n–σ* mode of interaction.

With this picture in mind, we looked into the bond length in the crystal structure of **2** (Figure 4). The S–Br length of 2.10 Å indicated a strong donor/accepter interaction between these atoms. No significant bonding interaction was found between the Br atom and the counter anion, whose distance was not shorter than 3.45 Å.[39] Moreover, the Trip–S bond was considerably elongated by 2.0 pm (1.827 Å) as compared to the parent Trip-SMe-Br_3 (1.807 Å). These results are consistent with the idea that **2** retains a significant separated ion pair character. The SbX_6 (X = F, Cl, Br) anion is generally considered as a non-coordinating species; however, an X-ray analysis of BDSB[14b] showed a Br–Br short contact of 3.17 Å and slightly longer S–Br distance of 2.17 Å. As compared to a typical bromide complex **3** (2.72 Å for Br–Br, 2.32 Å for S–Br),[40] BDSB does have more polarized bonds and enhanced electrophilic character, but yet in the state of a tight ion pair. Considering these facts, we concluded that the superb activity of the Trip-SMe catalyst can be attributed to the occurrence of a highly positive halogen center through the formation of the charge-separated halonium complex.

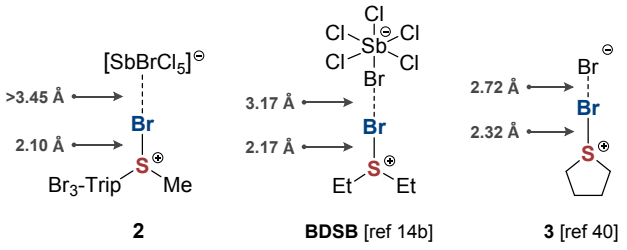


Figure 4. Comparison of the bond lengths of sulfonium complexes.

Finally, we conducted a computational study to investigate a correlation between structural feature of the thioether and electrophilicity of the Br nucleus. NPA charges on Br atom and S atom were calculated for bromosulfonium complexes of Trip-SMe and SMe_2 changing the S–Br distance from 2.00 Å to 2.50 Å. In each case, cationic character of the Br atom was amplified as the S–Br distance was shortened (Figure 5a), being consistent with the description in Figure 3. More importantly, the triptycenyl substituent was found to place an increased positive charge on the Br atom, whereas there was no significant difference in the charge on the S atom (Figure 5b).

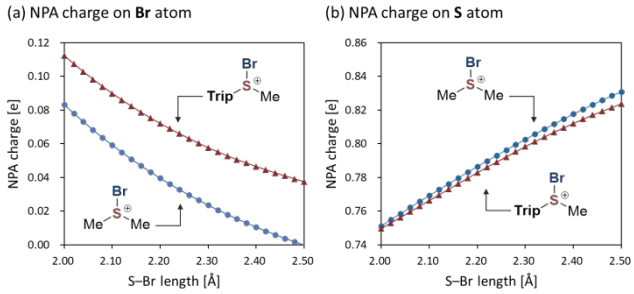


Figure 5. Plots of the calculated NPA charge on (a) Br atom and (b) S atom against the S–Br bond length.

In order to elucidate which fragment of the triptycenyl functionality is responsible for its catalytic activity, NPA charge on the Br atom was calculated for various sulfonium salts (Figure 6). Here all the S–Br distances fall within the range of 2.186–2.191 Å. When the benzene rings of the Trip-SMe was partially replaced by saturated bonds, the cationic character of the Br nucleus was gradually decreased from +0.074 to +0.051 (**a**→**b**,**c**,**d**). Notably, the charge on Br atom of a barrelenyl (bicyclo[2.2.2]octatrienyl) sulfide (**e**) was commensurate with that of **d**, suggesting that the steric bulkiness of the triptycenyl moiety exerts a minimal impact on the catalytic activity. In stark contrast, bicyclo[2.2.2]octyl sulfide (**f**) exhibited a much weak cationic character. 1-Adamantyl sulfide (**g**) and triphenylmethyl sulfide (**h**), which were ineffective catalysts for the aromatic halogenation (see Table 1), gave similar values. These results imply that the existence of the π system that is located perpendicularly to the C–S linkage is a key motif to consolidate the enhancement of electrophilicity. The largest positive charge within the complex of Trip-SMe presumably reflected the highest reactivity toward the electrophilic substitution.

4. CONCLUSION

In conclusion, we have introduced a highly active Trip-SMe catalyst for the aromatic electrophilic halogenation using *N*-

halosuccinimides. This protocol was applicable to a variety of unactivated compounds and yielded the corresponding haloarenes under mild reaction conditions. Kinetic analysis and controlled experiments revealed that the triptycenyl substituent exerts a crucial role for the catalytic activity. X-ray crystallographic analysis enabled us to elucidate the occurrence of a highly electrophilic halogen atom through the formation of the charge-separated complex. The effect of substituents on the sulfur atom was systematically investigated by a computational method to find a trend between their structural feature and the cationic character of the Br atom. Although we have not yet found a convincing rationale for the role of the π system in reinforcing the electrophilicity, calculations for NPA charge would be a proper mean to predict the activity of Lewis base catalysts, and furthermore, to create more efficient catalytic systems.

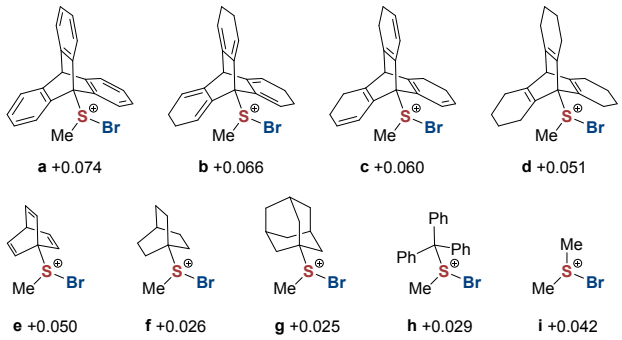


Figure 6. Calculated NPA charge on Br atom for sulfonium salts.

ASSOCIATED CONTENT

Supporting Information

Experimental procedures, kinetic experiments, computational data, and copy of ^{1}H and ^{13}C NMR spectra (PDF). Atomic coordinates of all calculated molecules (XYZ). Crystallographic data for **1b**-Cl_4, **1h**-Br_4, **1y**-Br_2, Trip-SMe-Br_3, and **2** (CIF). 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 interests.

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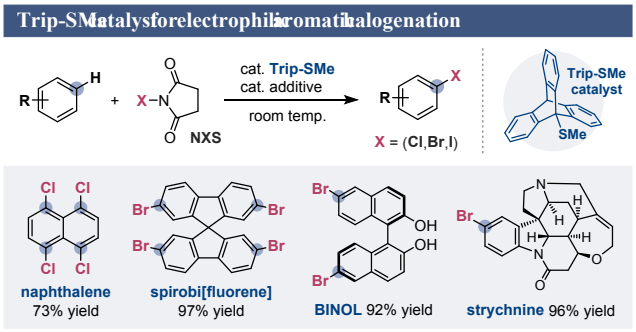
Trip-SMe catalysforelectrophilaromatihalogenation
cat. Trip-SMe
cat. additive
room temp.
NXS
X = (Cl,Br,I)
Trip-SMe catalyst
SMe
naphthalene 73% yield
spirobi[fluorene] 97% yield
BINOL 92% yield
strychnine 96% yield