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Selectfluor-mediated mild oxidative halogenation and thiocyanation of 1-aryl-allenes with TMSX (X = Cl, Br, I, NCS) and NH_4SCN

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ABSTRACT

Presence of TMSX (X = Cl, Br, I) unleashes the oxidative character of *Selectfluor* and provides a mild dihalogenation method for 1-arylallenes. Preference for 2,3-addition was observed with TMSCl in MeCN irrespective of the nature of the substituent on the aryl moiety, whereas 1,2-addition was preferred in [BMIM][BF_4]. With TMSBr and TMSI only products corresponding to 2,3-addition were observed. Reactions carried out with TMSBr in IL solvents gave the corresponding monobromoalkenes as a major product along with the isomeric dibromo-alkenes. Reaction with NH_4SCN provided convenient access to dithiocyanate derivatives. The same products were formed via TMS-NCS/*Selectfluor*. Formation of common products via TMSNCS and NH_4SCN points to the formation and interplay of SCN^+/NCS^+ as incipient electrophiles.

In a recent study[1] we reported on the reaction of 1-aryl-allenes with propargylic alcohols in the presence of metallic triflates and TMSX (X = Cl, Br, N_3) and formation of isomeric enzymes by attack of propargyl cation at the central carbon of allenes and subsequent trapping of the resulting allyl cations with TMSX. Inspired by a report on fluorohydroxylation of aryl-allenes with *Selectfluor* in MeCN/H_2O,[2] we sought to develop a fluorohalogenation approach for allenes employing TMSX/*Selectfluor*, but product analysis with TMSCl/*Selectfluor* showed no fluorine incorporation, instead isomeric dichloroalkenes were formed. We report here on the efficacy of this *Selectfluor*-mediated approach for dihalofunctionalization and dithiocyanation of 1-aryl-allenes.

Whereas *Selectfluor* is widely employed for fluoro functionalization of organic compounds,[3,4] its ability to act as mediator and catalyst for oxidative transformations without fluorination is relatively less explored. Generation of electrophile equivalents Cl^+, Br^+, SCN^+, and NO_2^+ mediated by *Selectfluor* and their in situ reactions with aromatics, and bromination of representative alkenes with *Selectfluor*/KBr have previously been reported.[5a,b] *Selectfluor*-mediated thiocyanation of representative heteroarenes and ketones with NH_4SCN have also been demonstrated,[6a,b] and the progress in *Selectfluor*-mediated synthesis has been reviewed.[7] More recently, oxyarylation of alkenes[8a] and hydroxylation of arenes[8b]were reported by a combined use of transition metals and *Selectfluor*.

Reactions of 1-aryl-allenes **1a**–**1d** with TMSX (X = Cl, Br, I) (2 equiv) were investigated at room temperature in the presence of 1 equiv of *Selectfluor*. Acetonitrile and imidazolium-ILs were selected as solvents for this study because *Selectfluor* can be dissolved in these media.[4a,7a] Reaction with TMSCl resulted in the formation of isomeric dichloroalkenes **2** and **3** as major and **4** as minor products, in combined isolated yields ranging from 55% to 78% (Scheme 1 and Table 1).[9] Product ratios observed for **1a** in the present study using TMSCl/*Selectfluor* differ from those reported using TMSCl/[$PhCH_2NMe_3$][Cl]/$KMnO_4$, where the dichloroalkene **4a** was a major product (**2a**:**3a**:**4a** = 3:1:6).[10] In an early study of halogenation of aryl-allenes with X_2 (Cl_2, Br_2, IBr)[11] the 1,2-addition products were found to be major in MeOH at 0 °C, and 2,3-addition was predominant (>0 °C) in nonpolar media (CS_2, CH_2Cl_2, CCl_4). Rearrangement of the 1,2-adducts to 2,3-adducts was observed in an NMR tube experiment on increasing temperature (−70 °C to >0 °C).

Products formed with TMSCl/*Selectfluor* implies oxidative transformation of Cl^- to >Cl^+,[12] followed by an electrophilic attack at the central carbon of the allenyl moiety generating an incipient haloallyl cation, and nucleophilic trapping by Cl^- at the unsubstituted and substituted termini of the haloallyl moiety.[13] The observed product distributions (Table 1) indicate a clear preference for nucleophilic attack at the less substituted terminus of the allylic moiety leading to 2,3-addition, but there is no clear correlation

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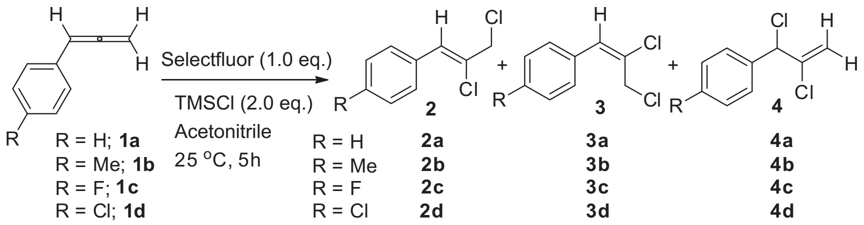


Scheme 1. Oxidative dichlorination of 1-aryl-allenes with TMSCl/*Selectfluor* in MeCN.

Table 1
Yields and product distributions in oxidative dichlorination of 1-aryl-allenes with TMSCl/*Selectfluor* in MeCN

Entry	Allene	Yield[a] (%)	**2**[b]:**3**[c]:**4**[c]
1	**1a**	68	44:40:16
2	**1b**	55	53:47:0
3	**1c**	70	40:33:27
4	**1d**	78	27:30:33

[a] Total isolated yield.
[b] Isolated yield.
[c] Compounds **3** and **4** were isolated as a mixture and NMR ratios were used to determine their respective isolated yields.

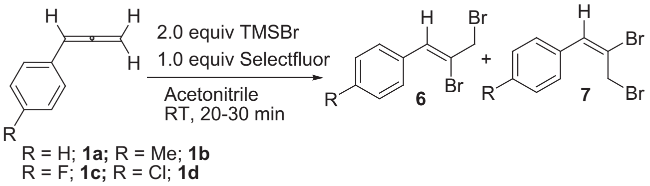
with regard to substituent effects (**1a**–**1d**). Interestingly when the same reactions were carried out in [BMIM][BF_4] as solvent significantly increased formation of the dichloroalkenes **4** was observed, and in addition the monochloroalkene **5** was formed as a minor product with allenes **1b** and **1c** (Scheme 2 and Table 2). Increased formation of compound **4** may be attributed to differences in ion-pairing and solvation effect between IL and MeCN, and increased haloallylic cation character in the IL solvent.[14]

Focusing on oxidative bromination, 1-aryl-allenes **1a**–**1d** were reacted with TMSBr/*Selectfluor* in MeCN to give the isomeric dibromoalkenes **6** and **7** in roughly 1:1 ratio, and typically in better than 70% combined yields (Scheme 3 and Table 3). In this case the 1,2-addition products were not detected. A different product distribution was observed in [BMIM][BF_4] as solvent. Apart from isomeric **6** and **7** the corresponding monobromoalkene **8** was formed as major product (Scheme 4 and Table 4). The cinnamyl bromides **8** were quickly transformed into cinnamyl alcohols during silica-gel chromatography. Products **8** and **5** correspond to formal addition of HX, and were only observed when ILs were used as solvent. Formation of **8** as a major product was also observed in [BMIM][PF_6] and [BMIM][NTf_2] in control experiments using aryl-allene **1a**. Product ratios (**6b**:**7b**:**8b**) in [BMIM][PF_6] and in [BMIM][NTf_2] were 9:7:85 and 3:2:95, respectively. Competing formation of **8** may be attributed to possible presence of H_3O^+ or HBF_4 in [BMIM][BF_4] but this seems less likely given that the same results were observed in two other freshly prepared ILs and it seems more plausible that HX originated from hydrolysis of TMSX by adventitious moisture.

Table 2
Yields and product distributions in oxidative dichlorination of 1-aryl-allenes with TMSCl/*Selectfluor* in [BMIM][BF_4]

Entry	Allene	Yield[a] (%)	**2**:**3**:**4**:**5**
1	**1a**	55	13:19:68:0
2	**1b**	52	25:13:26:26
3	**1c**	58	16:17:51:16
4	**1d**	61	16 16:66:0

[a] Total yield of crude reaction mixture; product ratios were estimated by NMR.



Scheme 3. Oxidative dibromination of allenes with TMSBr/*Selectfluor* in MeCN.

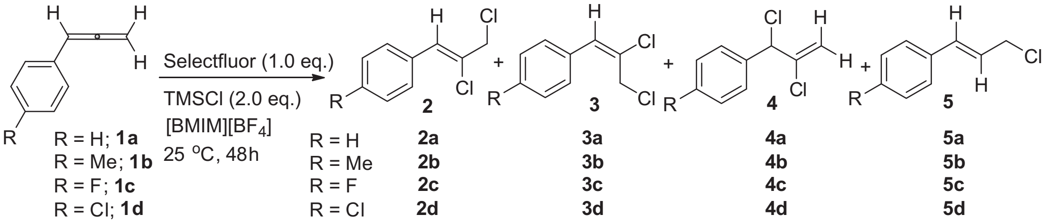
Table 3
Yields and product distributions in oxidative dibromination of 1-aryl-allenes with TMSBr/*Selectfluor* in MeCN

Entry	Allene	Yield[a] (%)	
		6	**7**
1	**1a**	34 (**6a**)	37 (**7a**)
2	**2a**	31 (**6b**)	27 (**7b**)
3	**3a**	34 (**6c**)	38 (**7c**)
4	**4a**	35 (**6d**)	38 (**7d**)

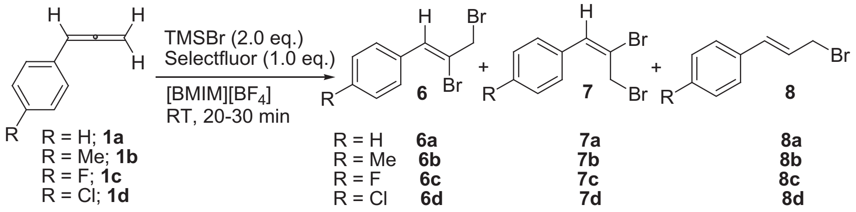
[a] Isolated yield.

Moving onto oxidative iodination, 1-aryl-allenes **1a**–**1d** reacted with TMSI/*Selectfluor* in MeCN to give the isomeric di-iodoalkenes **9** and **10** in 1:1 ratio in respectable isolated yields (Scheme 5a and Table 5a). Interconversion of the diiodo isomers **9** and **10** was observed during silica gel chromatography. These isomers also underwent aerial oxidation to the alcohol **11** and the aldehyde **12** (Scheme 5b).

There have been only limited earlier studies on *Selectfluor*-mediated thiocyanation,[6a,b,7b] and the potential of this method for



Scheme 2. Oxidative dichlorination of 1-aryl-allenes with TMSCl/*Selectfluor* in [BMIM][BF_4].

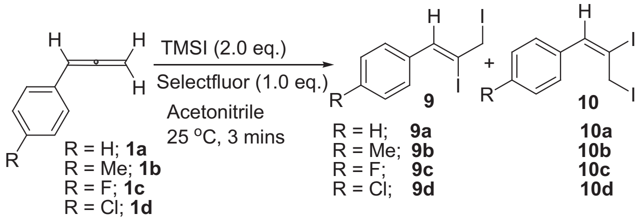


Scheme 4. Oxidative dibromination of 1-aryl allenes with TMSBr/*Selectfluor* in [BMIM][BF$_4$].

Table 4
Yields and product distributions in oxidative dibromination of 1-aryl-allenes with TMSBr/*Selectfluor* in [BMIM][BF$_4$]

Entry	Allene	Yield[a] (%)	**6:7:8**
1	**1a**	94	9:12:79
2	**1b**	95	4:3:93
3	**1c**	98	2:2:96
4	**1d**	93	18:18:64

[a] Total yield of crude reaction mixture; product ratios were determined by NMR.



Scheme 5a. Oxidative diiodination of 1-aryl-allenes with TMSI/*Selectfluor* in MeCN.

Table 5a
Yields and product distributions in oxidative diiodination of 1-aryl-allenes with TMSI/*Selectfluor* in MeCN

Entry	Allene (**1**)	Yield[a] (%)	**9:10**
1	**1a**	68	1:1
2	**1b**	63	1:1
3	**1c**	70	54:46
4	**1d**	67	56:44

[a] Isolated yields for **9**+**10**; isomers ratios from NMR.

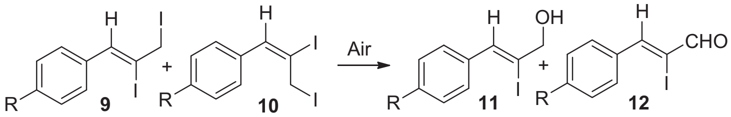
oxidative dithiocyanation of allenes has not been explored. Reaction of 1-aryl-allenes **1a**–**1d** with NH$_4$SCN/*Selectfluor* in MeCN at room temperature resulted in slow formation of two isomeric 2,3-disubstituted derivatives in relatively modest isolated yields (only trace amounts in the cases of **1d**). Prolonged mixing at room temperature followed by stirring at 50 °C did not improve the conversions. Further studies, aided in particular by differences in their ^{13}C NMR and IR spectra (Supplemental data) showed that whereas the major isomer was the dithiocyanate derivative **13**, the minor isomer was a mixed NCS/SCN disubstituted compound **14** (Scheme 6 and Table 6). Relative stereochemistry of **13** as *E* and **14** as *Z* was decided based on NOE data.

Surprisingly, the same products were formed when allenes **1a**–**1d** were allowed to react with TMS-NCS/*Selectfluor* (Scheme 7 and Table 7). The TMS-NCS reactions proved more efficient and resulted in better isolated yields. It is noteworthy that similar to reactions with TMSBr and TMSI a product corresponding to nucleophilic attack by SCN$^-$ at the substituted terminus of the allylic moiety was not observed. Crystals suitable for X-ray analysis were obtained from **13b** and **13c** from CH$_2$Cl$_2$/hexane at −20 °C. Thermal ellipsoid plots for **13b** and **13C** (Figs. 1a and 1b) confirm the *E* configuration at the double-bond, in agreement with the NOE-based correlations.[9] Unfortunately the SCN/NCS derivatives **14b**, **14c**, and **14d** were oils and would not crystallize. Compound **14a** was obtained as solid but did not produce good crystals.

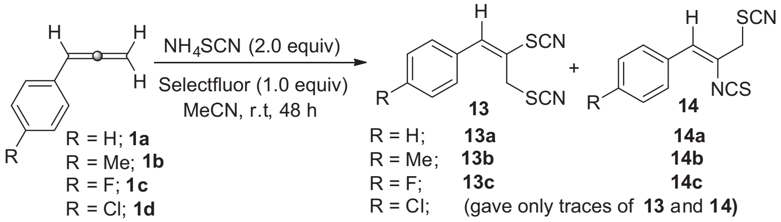
Table 6
Yields and product distributions in reaction of 1-arylallenes with NH$_4$SCN/*Selectfluor*

Entry	Allene	Yield[a] (%)	
		13	**14**
1	**1a**	27	11
2	**2a**	26	19
3	**3a**	22	8
4	**4a**	tr	tr

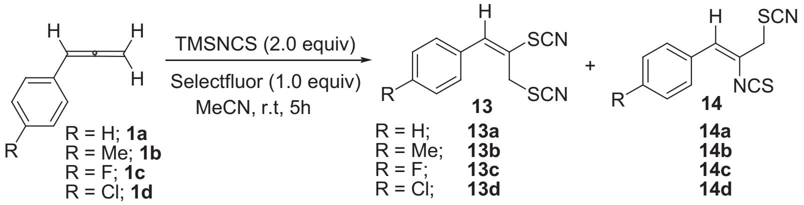
[a] Isolated yield; tr: trace.



Scheme 5b. Aerial oxidation of the diiodo compounds.



Scheme 6. Reaction of 1-arylallenes with NH$_4$SCN/*Selectfluor*.



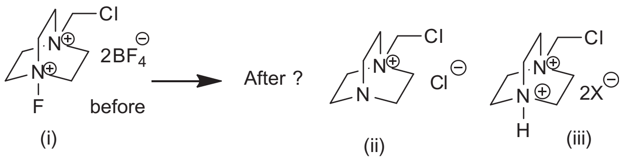
Scheme 7. Reaction of 1-arylallenes with TMS-NCS/*Selectfluor*.

Table 7
Yields and product distributions in reaction of 1-arylallenes with TMSNCS/*Selectfluor*

Entry	Allene	Yield[a] (%)	
		13	**14**
1	**1a**	41	22
2	**1b**	39	19
3	**1c**	40	23
4	**1d**	29	15

[a] Isolated yield.

Finally in an effort to understand how *Selectfluor* is transformed in these reactions (Scheme 8 and Supplementary data) NMR spectra of 'spent' *Selectfluor* (the solid formed in the reaction upon addition of TMSX and collected after completion of the reaction) (see Supplemental file) were compared with: (a) an authentic sample of *Selectfluor* (**i**); (b) an authentic sample of the monocation salt (**ii**) synthesized by refluxing DABCO in CH_2Cl_2; and (c) the dication (**iii**) generated by protonation of (**ii**) with TFAH (X = $CF_3CO_2^-$). Based on this comparison (Suppl. data) it may be concluded that *Selectfluor* (**i**) is transformed into dication salt **iii** (the source of H^+ is likely hydrolysis of TMSX).



Scheme 8. Insight into the structure of 'spent' *Selectfluor*.

In summary the potential of *Selectfluor* to act as mediator and oxidant for mild dihalogenation and dithiocyanation of 1-arylallenes in the presence of TMSX (X = Cl, Br, I, NCS) and NH_4SCN is demonstrated. The observed products may be rationalized by electrophilic attack of 'X^+' and 'SCN^+' at the central carbon of allenes to form incipient allylic cations that are preferentially quenched at the unsubstituted (less sterically crowded) terminus of the allylic moiety to furnish the 2,3-adducts. The 1,2-addition products were only observed with TMSCl. These products increased when $[BMIM][BF_4]$ was used as solvent. Quenching at the substituted terminus of the allylic moiety and/or halonium ion formation could account for the 1,2-adducts. The observed regioselectivity differences in MeCN and in IL may be due to differences in solvation and ion pairing effects. Formation of common dithiocyanate derivatives **13** and **14** via TMSNCS/*Selectfluor* and NH_4SCN/*Selectfluor* implies the formation and interplay of SCN^+/NCS^+ as incipient electrophiles. Comparative NMR study suggests that 'spent' *Selectfluor* is an N-protonated dication salt.[15] Further studies

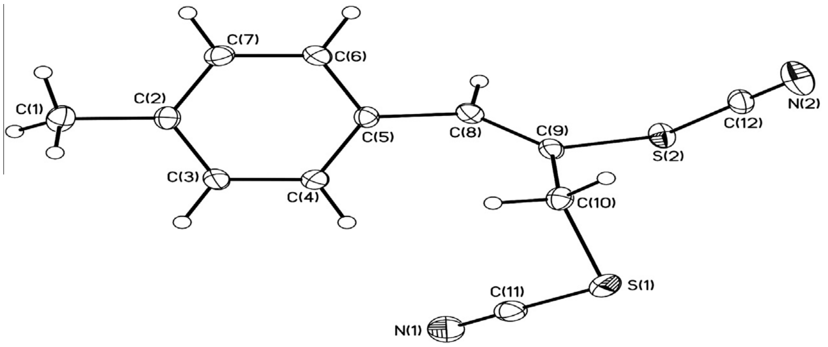


Figure 1a. Thermal ellipsoid plot for **13b**.

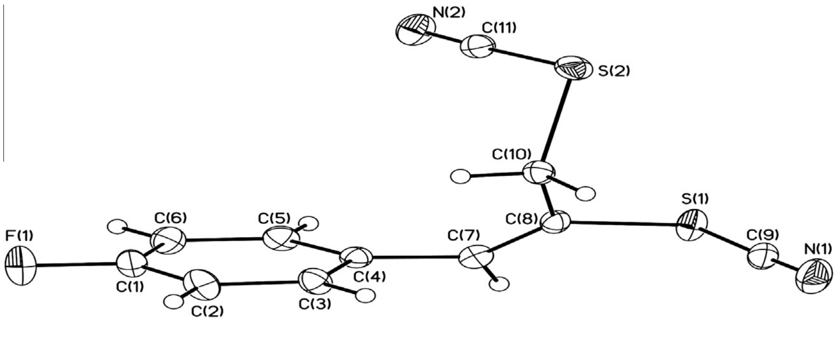


Figure 1b. Thermal ellipsoid plot for **13c**.

aimed at gaining deeper understanding of the mechanistic aspects of these transformations are called for.[16]

Acknowledgment

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Supplementary data

Supplementary data (experimental section and selected ^{1}H, ^{13}C{^{1}H}, and ^{19}F (as applicable) NMR and IR spectra for the products. CCDC 954949-954950 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif) associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2014.02.110.

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9. The *E* and *Z* assignments were based on magnitude of allylic coupling and were verified in selected cases by NOE (see Experimental).
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12. The $E_{1/2}$ (V, SCE) for *Selectfluor* is 0.33 (see Ref. 7a) as compared to −1.33 for Cl^- to >Cl_2.
13. It is conceivable that the 1,2-adduct is also formed via a cyclic halonium ion (as suggested in Ref. 11).
14. Alternatively this could stem from increased lifetime of the halonium ion intermediate in IL solvent.
15. These observations imply that recycling and reuse of *Selectfluor* may be feasible in large scale operations by recovery of the dication salt (**iii**) and subsequent deprotonation/N-fluorination.
16. Reaction of **1c** with *Selectfluor*/TMSCl was performed in an NMR scale experiment in CD_3CN in an effort to determine if **4C** is formed first and subsequently rearranges to **3c**/**2c**. Signals due to all 3 products were detected in the spectra after 1 h (suggesting that 1,2- and 2,3-addition products might have been formed concurrently) but due to multicomponent nature and complexity of the reaction mixture and slow conversion of the allene these observation were at best inconclusive. Attempts at monitoring the reaction progress via GC were also unsuccessful because the allenes underwent thermal decomposition in the GC.