Peracetic Acid Mediated sp^2 C–H Selenation of Arenes

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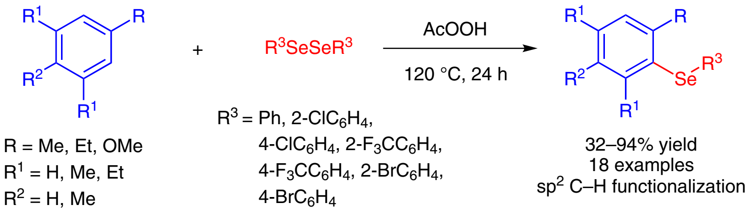

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Abstract Peracetic acid promoted C–Se coupling reaction of arenes with diselenides under metal-free and solvent-free conditions has been described. The resulting selenide ethers were obtained in good to excellent yields. Peracetic acid provided the selenide ethers via sp^2 C–H selenation whereas previously in case of DTBP sp^3 C–H selenation was observed.

Key words peracetic acid, arenes, diselenides, C–Se coupling, selenide ethers

Organoselenium compounds have received renewed interest due to their interesting applications in a variety of immune and biological functions (Figure 1) such as prevention of cardiovascular disease, antitumor, antiviral diseases, as well as anti-aging effect, and the synthesis of these organo selenium compounds is one of the emerging area in organic synthesis.[1] The organoselenium compounds have played an important role in cross-coupling reactions,[2] asymmetric catalysis,[3,4] organic synthesis,[5–7] materials science,[8] and natural products.[9] Moreover, the preparation of peptides containing selenocysteine getting attention with the discovery of an increasing number of proteins containing this amino acid.[1f,10] Traditionally, photochemical or harsh reaction conditions, such as the use of polar and toxic solvents like HMPA and high reaction temperatures or expensive and toxic reagents have been used for the formation C–Se bond.[11] Recently, several transition metals such as palladium,[12] nickel,[13] copper,[14] iron,[15] indium,[16] and zinc[17] have been used as catalytic systems for the synthesis of organoselenium molecules.

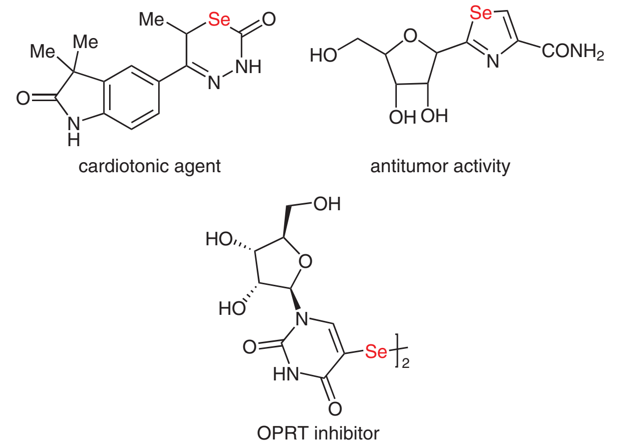
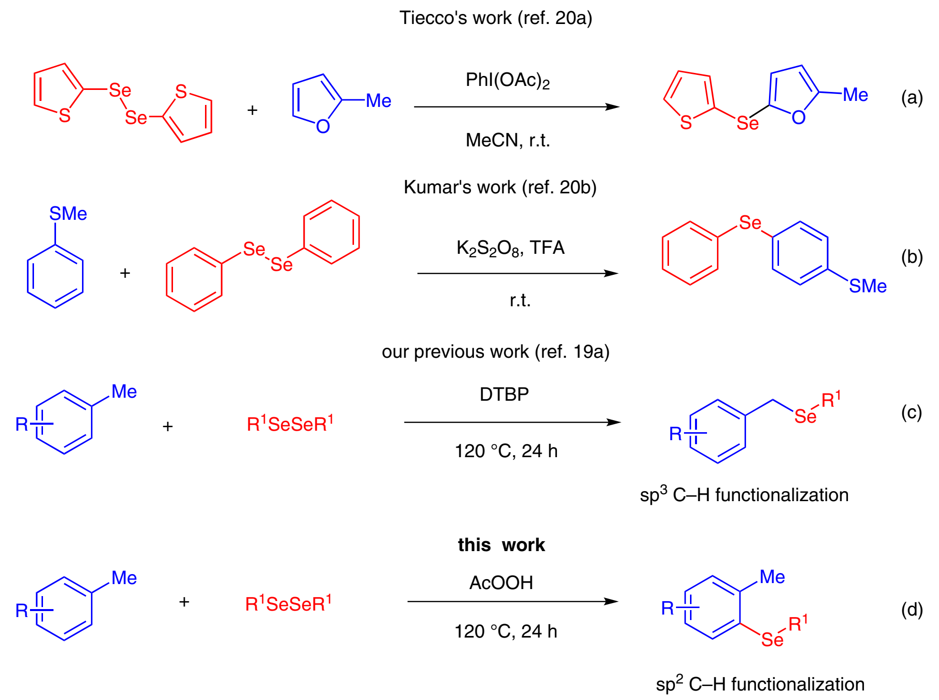


Figure 1 Some biologically active organoselenium compounds

Transition-metal-free C–H functionalization is an emerging approach for constructing carbon–carbon and carbon–heteroatom bonds in recent years[18] and in this regard the peroxide chemistry have emerged as suitable substitute for traditional transition-metal catalysis.[19] Tiecco and co-workers[20a] demonstrated that the diselenides can be conveniently employed to produce electrophilic 2-thienylselenenylating agents which easily effect substitution reactions on furan derivatives (Scheme 1, a). Kumar et al.[20b] reported the synthesis of selenide ethers via $K_2S_2O_8$-catalyzed reaction between arenes and diselenides. Their methodology required trifluoroacetic acid as strong acid for this transformation (Scheme 1, b). Very recently, we have reported a di-*tert*-butyl peroxide (DTBP) promoted syntheses of selenide ethers and thioesters from methyl arenes via metal-free sp^3 C–H functionalization (Scheme 1, c).[19a] Now, we have observed an interesting oxidant-dependent C–H selenation of methyl arenes, and herein we report the peracetic acid (AcOOH) mediated sp^2 C–H selenation of methyl arenes under metal-free and solvent-free conditions (Scheme 1, d).

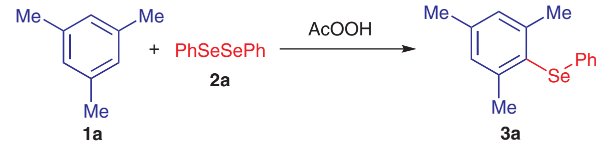


Scheme 1 Metal-free synthesis of organoselenium compound

Our study began by selecting mesitylene (**1a**) as the model and treated with diphenyl diselenide (**2a**) under the influence of AcOOH at room temperature for 24 hours (Table 1, entry 1); unfortunately no product was obtained instead only starting materials were detected using GC–MS. Enhancement in temperature (Table 1, entries 2–5) provided better results as 120 °C after 24 hours provided the corresponding selenide ether **3a** in 94% yield (Table 1, entry 5). Decrease in the reaction time diminished the product formation (Table 1, entries 6–9). The spectroscopic analysis (^{1}H NMR and ^{13}C NMR) of the product **3a** were varied from that of the earlier data (when the same reaction was carried out using DTBP as oxidant).[19] Then careful analysis of spectroscopic data confirm that the reaction underwent via sp^2 C–H functionalization instead of sp^3 C–H functionalization, and the structure of compound **3a** was then established as shown in Table 1.

Once we have optimized conditions in our hand, we then turned our attention towards generalization of this interesting sp^2 C–H selenation strategy. In this regard, we have carried out the reaction of mesitylene (**1a**) with a variety of diaryl diselenides using AcOOH under optimized reaction conditions (Table 2, entries 1–6). The resultant selenide ethers **3b**–**g** were obtained in good to excellent yields. Different methyl arenes **1b**–**d** were also employed for this C–H selenation with various diselenides under the same reaction conditions and afforded the resulting selenide ethers in good yields (Table 2, entries 7–15). Not only methyl arenes but also ethyl arenes were tested in this reaction,

Table 1 Optimization of Reaction Conditions[a]



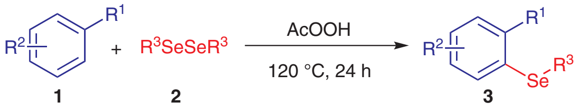
Entry	Temp (°C)	Time (h)	Yield (%)[b]
1	r.t.	24	n.r.
2	60	24	11
3	80	24	15
4	100	24	91
5	120	24	94
6	120	12	88
7	120	6	24
8	120	3	22
9	120	1	12
10	120	24	91[c]

[a] Reaction conditions: mesitylene (**1a**, 1.0 mL), diphenyl diselenide (**2a**, 0.5 mmol), AcOOH (1.0 mmol).
[b] Isolated yield.
[c] 4 Å MS was used.

and we could obtain the selenide ethers via sp^2 C–H selenation only (Table 2, entries 16 and 17). The system shows good functional-group tolerance as chloro, bromo, trifluoromethyl, and methoxy groups were all tolerated by the reaction conditions employed.

The plausible mechanism of this reaction can be depicted by choosing mesitylene (**1a**) and diphenyl diselenide (**2a**) as reacting partners as shown in Scheme 2. Initially, diphenyl diselenide (**2a**) will react with AcOOH to form PhSeOH and phenylselenylacetate as transient species. Phenylselenylacetate and PhSeOH undergo electrophilic substitution with mesitylene to afford mesityl(phenyl)selane (**3a**).

Table 2 Reactions of Various Alkyl Arenes **1** with Diaryldiselenides **2**^{a}



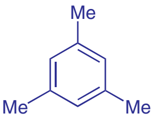
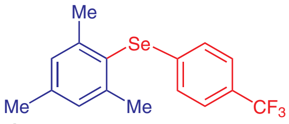
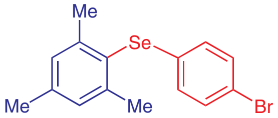
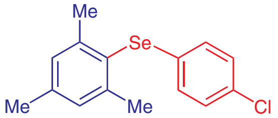
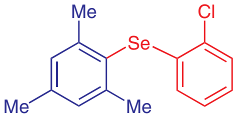
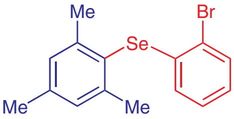
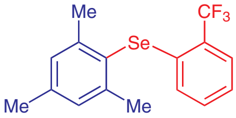
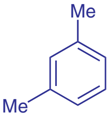
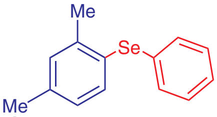
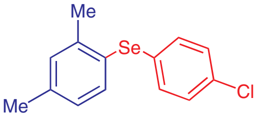
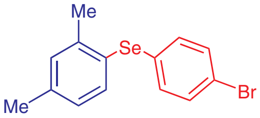
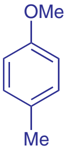
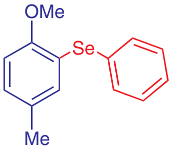
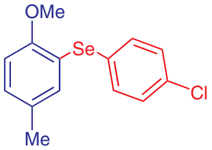
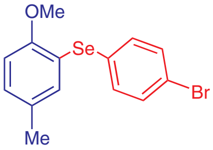
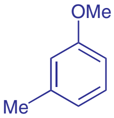
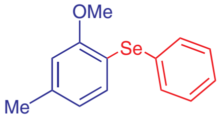
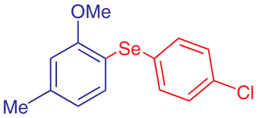
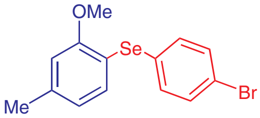
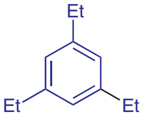
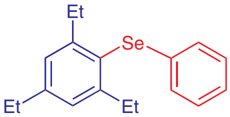
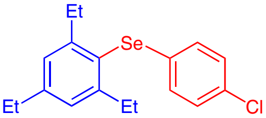
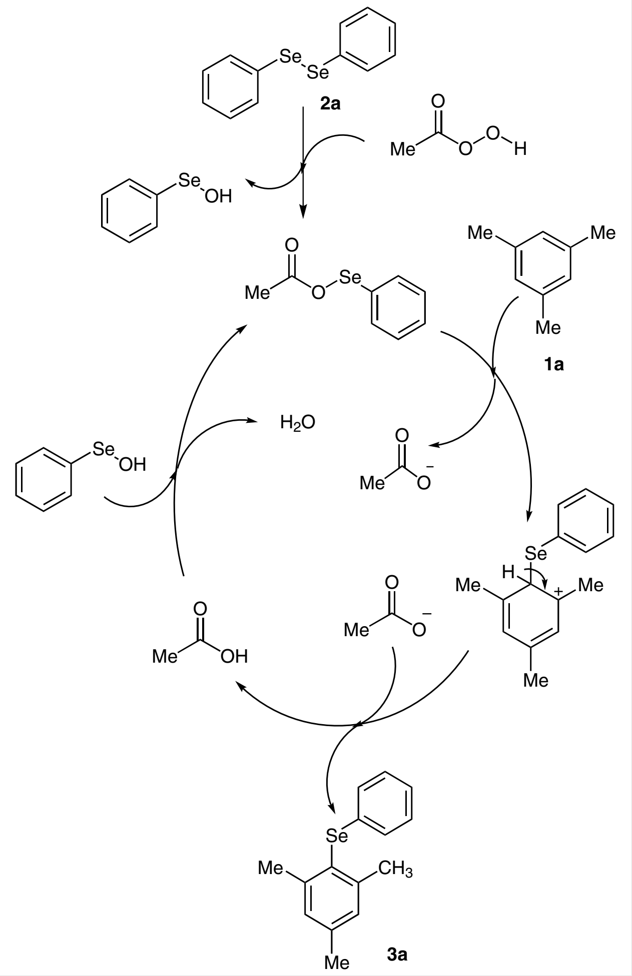
Entry	1	R^3	Product	Yield (%)^b
1	 **1a**	4-$F_3CC_6H_4$	 **3b**	40
2	**1a**	4-BrC_6H_4	 **3c**	81
3	**1a**	4-ClC_6H_4	 **3d**	88
4	**1a**	2-ClC_6H_4	 **3e**	79
5	**1a**	4-BrC_6H_4	 **3f**	73
6	**1a**	2-$F_3CC_6H_4$	 **3g**	59
7	 **1b**	Ph	 **3h**	65

Table 2 (continued)

Entry	1	R^3	Product	Yield (%)[b]
8	**1b**	4-ClC_6H_4	 **3i**	60
9	**1b**	4-BrC_6H_4	 **3j**	63
10	 **1c**	Ph	 **3k**	67
11	**1c**	4-ClC_6H_4	 **3l**	75
12	**1c**	4-BrC_6H_4	 **3m**	89
13	 **1d**	Ph	 **3n**	54
14	**1d**	4-ClC_6H_4	 **3o**	72
15	**1d**	4-BrC_6H_4	 **3p**	88
16	 **1e**	Ph	 **3q**	40
17	**1e**	4-ClC_6H_4	 **3r**	32

[a] Reaction conditions: various methyl arenes (1.0 mL), diaryl diselenide (0.5 mmol), AcOOH (1.0 mmol), 120 °C, 24 h.
[b] Isolated yield.



Scheme 2 Plausible mechanism

In conclusion, we have developed an interesting transition-metal-free peracetic acid promoted C–Se coupling reaction of arenes with diselenides under solvent-free conditions,[21] and the resulting selenide ethers were obtained in good to excellent yields. Peracetic acid provided the selenide ethers via sp^2 C–H selenation. The system shows good functional-group tolerance.

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Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0035-1561408.

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(21) **General Procedure for a Representative Example: Mesityl(phenyl)selane (3a)**

A Schlenk tube equipped with a magnetic stir bar was charged with diphenyl diselenide (0.5 mmol, 0.157 g), mesitylene (1.0 mL), and AcOOH (1.0 mmol), then heated at 120 °C in an oil bath under N_2 atmosphere. After stirring at this temperature for 24 h, the reaction mixture was cooled to r.t. and diluted with EtOAc (20 mL). The resulting solution was directly filtered through a pad of Celite then washed with EtOAc (20 mL) and concentrated to give the crude material which was then purified by column chromatography (SiO_2, hexane) to provide **3a** as a yellow oil (248 mg, 94% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.30 (s, 3 H), 2.43 (s, 6 H), 6.99 (s, 2 H), 7.06–7.13 (m, 5 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.0, 24.2, 125.3, 128.4, 128.8, 128.9, 129.1, 133.4, 139.0, 143.6 ppm. ^{77}Se NMR (114.45 MHz, $CDCl_3$): δ = 286.3 ppm. HRMS (EI): *m/z* calcd for $C_{15}H_{16}Se$: 276.0417; found: 276.0407.