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A Simple Reduction of α-Bromosulfones by cat.$(PhSe)_2$/$NaBH_4$

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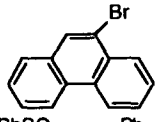
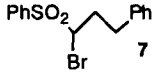
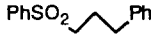
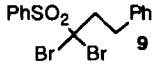
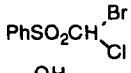
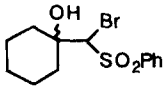
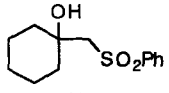
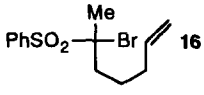
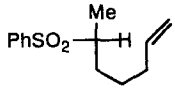
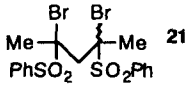
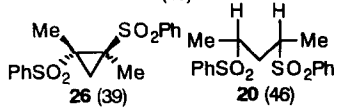
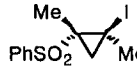
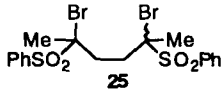
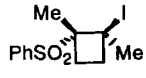
Abstract: Reduction of α-bromosulfones **1**, **5**, **13-16** by cat.$(PhSe)_2$/$NaBH_4$ occurred site-selectively in high yields. This reduction of 1,3- or 1,4-dibromobis(sulfone) **21** and **25** was applied to intramolecular coupling reactions to give the three- and four-membered carbocycles **26-28**.

The reduction of alkyl halides to the corresponding hydrocarbons, which proceeds *via* a single electron transfer (SET) process, has been studied in some detail.[1] Particularly, numerous examples have illustrated the increasing importance of free radical cyclization in synthetic chemistry.[2] Ashby *et al.* reported that $LiAlH_4$/THF[3] and 1,3-dithianyl lithium[4] can be used for the mild reduction of alkyl iodides. On the other hand, alkyl bromides have been effectively reduced by Bu_3SnH/AIBN,[5] Bu_2SnH_2,[6] $(Me_3Si)_3SiX$/$NaBH_4$.[7] Although these tin reagents are extensively used, they have several disadvantages as follows. It is difficult to remove the tin-containing by-products from the reaction mixtures.[8] Moreover, the alkyltin reagents are highly toxic.[9]

We recently reported that the reaction of *(E)*-1-bromo-5,5-dimethyl-1-phenylsulfonylhex-1-en-3-yne and PhSeNa did not give the addition-elimination product, but *(E)*-5,5-dimethyl-1-phenylsulfonylhex-1-en-3-yne was reduced by PhSeNa.[10] We examined this reduction in detail and found that $(PhSe)_2$/$NaBH_4$ can be used as a reducing agent for the Br-reduction of α-bromosulfones. Heteroatom-anions such as RO^-,[11] RS^-,[12] Me_3Sn^-,[13] RTe^-[14] have been shown to be powerful reagents for the reduction of various compounds. Especially, the reduction of alkyl halides by arene telluolate can be used for important synthetic processes.[15] On the other hand, selenolate anions can be essentially used for the substitution of halides to give the corresponding selenides; however, sometimes selenolate anions also act as reducing agents.[16] Here we report the reduction of α-bromosulfones by cat.$(PhSe)_2$/$NaBH_4$.

On treatment of bromomethyl phenyl sulfone **1** (0.5 mmol) with two equivalents of $NaBH_4$ (1.0 mmol) and $(PhSe)_2$ (0.03 mmol) in ethanol at room temperature for 10 min, methyl phenyl sulfone **2** was quantitatively obtained (Table 1, Entry 1). The reduction of **1** without the catalytic amount of $(PhSe)_2$ did not proceed at all. We performed the reduction of **1** under $NaBD_4$/EtOD (Method D), and the deuterated product **3** was obtained as colorless needles in 85% yield (Entry 2). Next, we attempted the reduction of chloromethyl phenyl sulfone **4**; however, sulfone **4** was recovered intact. Iodomethyl phenyl sulfone **5** also afforded **2** in high yield (Entry 4). Aromatic bromide **6** was treated with cat.$(PhSe)_2$/$NaBH_4$ under reflux conditions; however, the compound **6** was recovered. The reduction of 1-bromo-3-phenylpropyl phenyl sulfone **7** gave phenyl phenylpropyl sulfone **8** in 85% yield (Entry 6). Interestingly, dibromide **9** was reduced to give the mono-bromide **7** in high yield (Entry 7). The reduction of bis(phenylsulfonyl)bromomethane **10** occurred to give **11** (Entry 8). The site-selective reduction of bromochlorophenylsulfonylmethane **12** took place to give a

Table 1 **Reduction of Halides by cat. $(PhSe)_2/NaBH_4$**

Entry	Halides	Conditions	Products (%yields)
1	$PhSO_2CH_2Br$ **1**	Method A/rt	$PhSO_2CH_3$ **2** (quant.)
2	**1**	Method D/rt	$PhSO_2CH_2D$ **3** (85)
3	$PhSO_2CH_2Cl$ **4**	Method A/rt	-
4	$PhSO_2CH_2I$ **5**	Method A/rt	**2** (95)
5	 **6**	Method A/reflux	-
6	 **7**	Method A/rt	 **8** (85)
7	 **9**	Method A/rt	**7** (93)
8	$(PhSO_2)_2CHBr$ **10**	Method A/rt	$(PhSO_2)_2CH_2$ **11** (91)
9	 **12**	Method A/rt	**4** (99)
10	 **13**	Method A/rt	 **14** (78)
11	 **16**	Method A/rt	 **17** (26)
12	**16**	Method A/reflux	**17** (49)
13	**16**	Method B/rt	complex mixture
14	**16**	Method C/rt	**17** (65)
15	 **21**	Method A/rt	 **26** (39) **20** (46)
16	**21**	Method A/reflux	**26** (42) **20** (52)
17	**21**	Method C/rt	 **27** (61) **26** (39)*1
18	 **25**	Method C/reflux	 **28** (quant.)

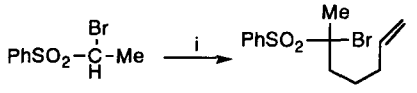
Method A: cat. $(PhSe)_2/NaBH_4$(2eq.)/THF-EtOH/rt; Method B: $LiAlH_4$(2eq.)/THF/reflux;
Method C: SmI_2 (2eq.)/THF/rt; Method D: cat. $(PhSe)_2/NaBD_4$(2eq.)/EtOD

*1 The ratio of products **27** and **26** (61:39) was determined by the intensities of CH_2 in the ^1H NMR spectrum.

chloride **4** (Entry 9). β-Hydroxy derivative **13** gave the reduced product **14** (Entry 10). Next, we applied this reduction to radical cyclization reactions. We synthesized 6-bromo-6-phenylsulfonyl-1-heptene (**16**) as shown in Scheme 1. The reaction of **16** under the same conditions afforded the reduced product in low yield instead of the cyclized product (Entries 11, 12). Therefore, we examined the reduction of **16** by the usual SET reductant, SmI_2, but, no cyclized product was obtained (Entry 14).[17]

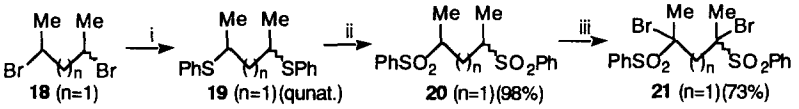
Next, we performed the intramolecular coupling reaction of 1,3-dibromobis(sulfone) **21**. The syn-

thetic procedure for the bis(sulfone) is shown in Scheme 2.[18] The 1,3- or 1,4-dibromobis(sulfone) **21** (49:51), **25** (42:58) was obtained as diastereo isomeric mixtures. The reduction of **21** by cat.$(PhSe)_2$/$NaBH_4$ gave the coupling product **26** (39%), accompanied by bis(sulfone) **20** (46%). The yield of the coupling product **26** could not be increased under reflux conditions (Entry 16). Therefore, we performed this coupling reaction using SmI_2[17] to give the coupling product **26** accompanied by 2-iodo-1,2-dimethyl-1-phenylsulfonylcyclopropane (**27**). The ratio of products **26** and **27** was determined by the intensities of the methylene protons of the cyclopropanes (**26**:**27**=61:39). The recrystallization of the mixture afforded the sole product **27**. The cyclopropanes **26** and **27** have been fully characterized by IR, ^1H and ^{13}C NMR, Mass and elemental analysis.[19] The stereochemistry of the cyclopropanes was determined according to Makosza's method.[20] The stereochemistry of **26** is obviously *trans* because in the NMR spectrum only two singlets are present at δ 1.85 and 2.09 ppm in a 3:1 ratio. We also examined the coupling reaction for the construction of the four-membered ring system. The reaction of **25** with SmI_2 gave *trans*-2-iodo-1,2-dimethyl-1-phenylsulfonylcyclobutane (**28**) quantitatively (Entry 18). The structure of **28** was also determined by IR, ^1H and ^{13}C NMR, MS, and elemental analysis.[21] The ^{13}C NMR spectrum exhibited six carbons at δ 25.91 (q), 25.92 (q), 34.17 (t), 34.43 (t), 78.37 (s), 78.58 (s) due to the cyclobutane ring, respectively. The MS and the elemental analysis of the iodide **28** also satisfied the molecular formula $C_{12}H_{15}IO_2S$.



15 **16** (45%)

Scheme 1 Reagent: i, LDA/5-bromo-1-pentene/-78°C



18 (n=1) **19** (n=1)(qunat.) **20** (n=1)(98%) **21** (n=1)(73%)
22 (n=2) **23** (n=2)(80%) **24** (n=2)(78%) **25** (n=2)(36%)

Scheme 2 Reagents: i, PhSH/NaOEt; ii, H_2O_2/AcOH; iii, *n*-BuLi/CBr_4/-78°C

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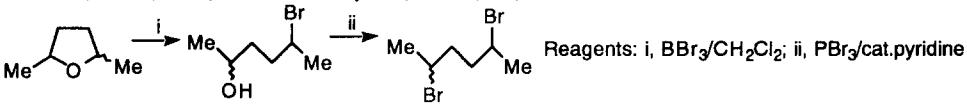

19. *trans*-1,2-Dimethyl-1,2-bis(phenylsulfonyl)cyclopropane (**26**): colorless prisms, mp 147-151 °C, IR ν 1320, 1150 (SO_2); ^1H NMR δ 1.85 (6H, s, Mex2), 2.09 (2H, s, 3-Hx2), 7.54-7.58 (4H, m, ArH), 7.65-7.69 (2H, m, ArH), 7.84 (4H, dd, *J*=1 and 9 Hz, ArH); ^{13}C NMR δ 15.16 (qx2), 22.74 (t), 48.21 (sx2), 128.45 (dx4), 129.27 (dx4), 133.91 (dx2), 138.42 (sx2). FABMS calcd for $C_{17}H_{19}O_4S_2$ *m/z* 351.0713, found *m/z* 351.0719. *trans*-2-Iodo-1,2-dimethyl-1-phenylsulfonylcyclopropane (**27**): colorless plates, mp 124 -126 °C, IR ν 1310, 1140 (SO_2); ^1H NMR δ 1.85 (3H, s, Me), 2.08 (1H, s, CH_2), 2.26 (3H, s, Me), 3.21 (1H, s, CH_2), 7.54-7.58 (2H, m, ArH), 7.65-7.69 (1H, m, ArH), 7.84 (2H, dd, *J*=1 and 9 Hz, ArH); ^{13}C NMR δ 15.10 (q), 22.72 (t), 24.86 (q), 43.00 (s), 48.21 (s), 128.45 (dx2), 129.27 (dx2), 133.91 (d), 138.42 (s); MS *m/z* 209 (M^+-I). Anal. Calcd for $C_{11}H_{13}IO_2S$: C, 39.30; H, 3.90. Fonud: C, 39.07; H, 3.70.
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21. *trans*-2-Iodo-1,2-dimethyl-1-phenylsulfonylcyclobutane (**28**): colorless needles, mp 299-233 °C, IR ν 2300, 1290 (SO_2), 1130 (SO_2); ^1H NMR δ 1.94 (3H, s, Me), 1.97 (3H, s, Me), 2.41-2.63 (4H, m, CH_2x2), 7.58-7.63 (2H, m, ArH), 7.71-7.75 (1H, m, ArH), 7.98-8.03 (2H, m, ArH); ^{13}C NMR δ 25.73 (q), 25.92 (q), 34.17 (t), 34.43 (t), 78.37 (s), 78.58 (s), 128.83 (dx2), 131.66 (dx2), 133.35 (s), 134.68 (d); MS *m/z* 223 (M^+-I). Anal. Calcd for $C_{12}H_{15}IO_2S$: C, 41.16; H, 4.32. Found: C, 41.18; H, 3.99.

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