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Ruthenium(III) Chloride Catalyzed Efficient Synthesis of Unsymmetrical Diorganyl Selenides via Cleavage of Dibenzyl and Diphenyl Diselenides in the Presence of Zinc

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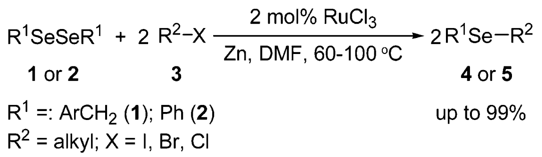

An efficient one-pot route to unsymmetrical diorganyl selenides has been developed by ruthenium(III) chloride catalyzed reactions of dibenzyl or diphenyl diselenides with alkyl halides in the presence of zinc. Organic iodides, bromides, and activated chlorides underwent the reactions efficiently. Unreactive organic chlorides also underwent the same type of selenation with sodium bromide as the additive.

Introduction

Organic selenides have been used as versatile reagents in organic synthesis and catalysis.[1] Cleavage of Se−Se bonds, especially cleavage of diphenyl or other diaryl diselenides, has recently received much effort for preparation of unsymmetrical diorganyl selenides (RSeR′). Chemical cleavage of Se−Se bonds in diaryl diselenides were realized with reducing agents such as $NaBH_4$, Na/NH_3, Bu_3SnH, $LiAlH_4$, etc.[2] However, catalytic procedures are considered more applicable for preparation of functional unsymmetrical diorganyl selenides because many functional groups cannot withstand the harsh conditions for chemical cleavage of Se−Se bonds. Direct nickel(II) bromide catalyzed coupling of a diaryl diselenide with an iodoaryl compound was realized in the presence of a polymer-supported borohydride.[3] Using a bimetallic (Sn(II)/Cu(II)) system, reactions of reactive organic bromides, i.e., allyl, propargyl, benzyl, and alkynyl bromides, with diorganyl diselenides gave unsymmetrical monoselenides.[4] Iodine-catalyzed reactions of diphenyl diselenide with organic halides in the presence of stoichiometric amount of lanthanum metal afforded unsymmetrical phenylselenides.[5] Indium(I) iodide promoted formation of diorganyl selenides was achieved by cleavage of diaryl diselenides and subsequent condensation with reactive alkyl or acyl chlorides.[6] In the presence of magnesium, copper(I)-catalyzed reactions of diphenyl diselenide with aryl iodides afforded unsymmetrical diaryl monoselenides.[7] Palladium(0)-promoted cleavage of diphenyl diselenide was also reported for phenylselenation.[8] Recently, a $Zn/AlCl_3$ (4.6/2.0 equiv ratio) system was employed to synthesize selenol esters by the reactions of diphenyl and dibenzyl diselenides with acid

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[†] Dalian Institute of Chemical Physics.

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(1) For selected recent reviews, see: (a) Nogueira, C. W.; Zeni, G.; Rocha, J. B. T. *Chem. Rev.* **2004**, *104*, 6255−6285. (b) Mugesh, G.; du Mont, W.-W.; Sies, H. *Chem. Rev.* **2001**, *101*, 2125−2179. (c) *Organoselenium Chemistry−A Practical Approach*; Back, T. G., Ed.; Oxford University Press: Oxford, 1999. (d) Krief, A. In *Comprehensive Organometallic Chemistry*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Mckillop. A., Eds.; Pergamon: Oxford, 1995; Vol. II, p 516.

(2) (a) Xu, X. H.; Huang, X. *Chin. Chem. Lett.* **2000**, *6*, 473−474. (b) Andreadou, I.; Menge, W. M. P. B.; Commandeur, J. N. M.; Worthington, E. A.; Vermeulen, N. P. E. *J. Med. Chem.* **1996**, *39*, 2040−2046. (c) Sakakibara, M.; Katsumata, K.; Watanabe, Y.; Toru, T.; Ueno, Y. *Synthesis* **1992**, 377−379. (d) Yoshimatsu, M.; Sato, T.; Shimizu, H.; Hori, M.; Kataoka, T. *J. Org. Chem.* **1994**, *59*, 1011−1019. (e) Bhasin, K. K.; Singh, N.; Kumar, R.; Deepali, D. G.; Mehta, S. K.; Klapoetke, T. M.; Crawford, M.-J. *J. Organomet. Chem.* **2004**, *689*, 3327−3334. (f) Crich, D.; Grant, D. *J. Org. Chem.* **2005**, *70*, 2384−2386.

(3) Millois, C.; Diaz, P. *Org. Lett.* **2000**, *2*, 1705−1708.

(4) Kundu, A.; Roy, S. *Organometallics* **2000**, *19*, 105−107.

(5) Nishino, T.; Okada, M.; Kuroki, T.; Watanabe, T.; Nishiyama, Y.; Sonoda, N. *J. Org. Chem.* **2002**, *67*, 8696−8698.

(6) (a) Ranu, B. C.; Mandal, T.; Samanta, S. *Org. Lett.* **2003**, *5*, 1439−1441. (b) Ranu, B. C.; Mandal, T. *J. Org. Chem.* **2004**, *69*, 5793−5795.

(7) Taniguchi, N.; Onami, T. *J. Org. Chem.* **2004**, *69*, 915−920.

(8) Knapton, D. J.; Meyer, T. Y. *J. Org. Chem.* **2005**, *70*, 785−796.

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chlorides.[9a] A modified $Zn/AlCl_3$ system was applied for preparation of unsymmetrical diorganyl selenides from the reactions of dibenzyl diselenide with reactive bromides, i.e., benzyl bromide and ethyl α-bromoacetate, in moderate yields.[9b] Cleavage of Se−Se bonds in diaryl diselenides has received more attention than that of dialkyl diselenides in the literature because diaryl diselenides are more reactive, and only a few examples involving reactions of dialkyl diselenides with reactive organic bromides were reported.[4]

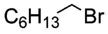
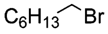
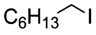
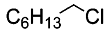
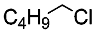
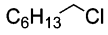
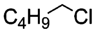
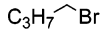
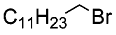
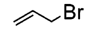
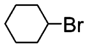
During our ongoing investigation on catalytic selenation, we have recently developed two very efficient procedures to synthesize symmetrical dibenzyl diselenides from the reactions of aldehydes[10a] or imines of aldehydes and ketones[10b] with elemental selenium in the presence of CO and water. Development of efficient catalytic procedures to cleave these diorganyl diselenides to unsymmetrical benzylselenides was one of our goals. Herein, we report the ruthenium(III) chloride catalyzed synthesis of unsymmetrical diorganyl selenides from the reactions of dibenzyl and diphenyl diselenides with organic halides including unreactive bromides and chlorides in the presence of zinc. To the best of our knowledge, catalytic reactions of dibenzyl and other di(substituted benzyl) diselenides with organic iodides, unreactive organic bromides, and chlorides have never been reported.

Results and Discussion

To cleave the Se−Se bond in dibenzyl diselenide (**1a**), the reaction of **1a** and 1-bromoheptane (**3a**) was initially carried out in the presence of zinc (1.6 equiv) in DMF at 100 °C for 4 h, and only less than 5% of the desired product, i.e., heptyl benzyl selenide (**4a**) was obtained (Table 1, entry 1). When 2 mol % of $RuCl_3{\cdot}3H_2O$ was used as the catalyst, **4a** was obtained in 85% isolated yield (eq 1, Table 1, entry 2). At ambient temperature the catalytic reaction gave **4a** in <10% yield. Without using zinc the same catalytic reaction did not undergo in DMF at 100 °C for 4 h. These results reveal that both the Ru(III) catalyst and zinc are necessary for the described benzylselenation to undergo. A variety of organic halides underwent the same type of reactions to afford unsymmetrical diorganyl diselenides in good to excellent yields (Table 1). 1-Iodoheptane (**3b**), organic bromides except 1-bromocyclohexane (**3j**), and reactive benzyl chloride (**3h**) efficiently underwent the reaction to form **4**. Unreactive chlorides, i.e., 1-heptyl chloride (**3c**) and 1-pentyl chloride (**3d**), did not undergo the same type of benzylselenation (Table 1, entries 4 and 5). Surprisingly, sodium bromide remarkably promoted the reactions of the unreactive organic chlorides with **1a** to afford the desired unsymmetrical selenides (Table 1, entries 6 and 7). In the cases using benzyl bromide (**3g**) and chloride (**3h**) as the organic halides, the desired product, i.e., dibenzyl selenide (**4e**), was obtained in 98% and 95% yields, respectively (Table 1, entries 10 and 11). The corresponding reaction of allyl bromide afforded the product in a low yield (28%) as a result of the high volatility of allyl bromide under the reaction conditions (Table 1, entry 12). It is unclear why 1-bromocyclohexane (**3j**) hardly underwent the reaction (Table 1, entry 13). When the present methodology was applied to the analogues of **1a**, i.e., di(substituted benzyl) diselenides (**1b**−**f**), the corresponding unsymmetrical diorganyl selenides were obtained with organic bromides and benzyl chloride as the halides in good to excellent yields (Table 2). Organic iodides and unreactive organic chlorides in the presence of sodium bromide underwent the same type of benzylselenation, and the relevant results will be published in a separate paper.

TABLE 1. Catalytic Cleavage of $(PhCH_2Se)_2$ (1a) to $PhCH_2SeR^2$ (4)[d]

$$\underset{\mathbf{1}\text{ or }\mathbf{2}}{R^1SeSeR^1} + \underset{\mathbf{3}}{2\,R^2{-}X} \xrightarrow[\text{Zn, DMF, 60-100 }^\circ\text{C}]{\text{2 mol\% RuCl}_3} \underset{\mathbf{4}\text{ or }\mathbf{5}}{2\,R^1Se{-}R^2} \qquad (1)$$

Entry	Halide R^2X (**3**)		Temp. (°)	Time (h)		Yield[a] (%)
1[b]		**3a**	100	4	**4a**	<5
2		**3a**	100	1	**4a**	85
3		**3b**	100	4	**4a**	75
4		**3c**	100	4	**4a**	0
5		**3d**	100	4	**4b**	0
6[c]		**3c**	100	2	**4a**	85
7[c]		**3d**	100	2	**4b**	71
8		**3e**	80	4	**4c**[13]	82
9		**3f**	100	4	**4d**[13]	82
10	$PhCH_2Br$	**3g**	100	1	**4e**[12]	98
11	$PhCH_2Cl$	**3h**	100	1	**4e**[12]	95
12		**3i**	60	8	**4f**	28
13		**3j**	100	24	**4g**	<1

[a] Isolated yield based on **1a**. [b] No catalyst. [c] Additive NaBr (1.2 mmol) was added. [d] Reaction conditions: diselenide **1a**, 0.5 mmol; halide, 1.2 mmol; Zn, 0.8 mmol; catalyst $RuCl_3{\cdot}3H_2O$, 2.6 mg (0.01 mmol); solvent DMF, 3 mL.

Diphenyl diselenide (**2**) is more reactive than **1** and is much more easily cleaved.[4,9] Usually, organic iodides, bromides, and reactive chlorides such as benzyl, allyl, and acid chlorides and *tert*-butyl chloride were used in the cleavage reactions of **2**. The only exception is that an unreactive organic chloride, i.e., dodecyl chloride, was used as the organic halide in the iodine-catalyzed cleavage of **2** with stoichiometric amount of lanthanum metal.[5] The results for catalytic cleavage of **2** using the present methodology are summarized in Table 3. Organic iodide, bromides, and reactive chloride (i.e., $PhCH_2Cl$) efficiently

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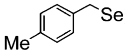
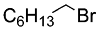
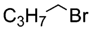
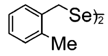
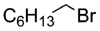
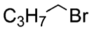
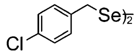
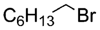
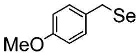
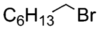
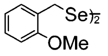
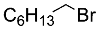
(9) (a) Movassaghi, B.; Mirshojaei, F. *Monatsh. Chem.* **2003**, *134*, 831−835. (b) Movassagh, B.; Shamsipoor, M. *Synlett* **2005**, *1*, 121−122.

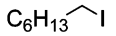
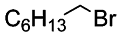
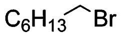
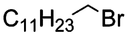
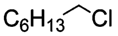
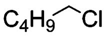
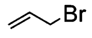
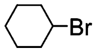
(10) (a) Tian, F. S.; Yu, Z. K.; Lu, S. W. *J. Org. Chem.* **2004**, *69*, 4520−4523. (b) Zhao, X. D.; Yu, Z. K.; Zeng, F. L.; Chen, J. Z.; Wu, X. W.; Wu, S. Z.; Xiao, W.-J.; Zheng, Z. Y. *Adv. Synth. Catal.* **2005**, *347*, 877−882.

TABLE 2. Catalytic Cleavage of $(ArCH_2Se)_2$ (1) to $ArCH_2SeR^2$ (4)[b]

Entry	$(ArCH_2Se)_2$ (1)	Halide R^2X (3)	Temp. (°)	Time (h)	Yield[a] (%)
1	 **1b**		100	4	**4h** 81
2	**1b**		80	8	**4i** 81
3	**1b**	$PhCH_2Br$	100	4	**4j**[2d] 93
4	**1b**	$PhCH_2Cl$	100	4	**4j**[2d] 91
5	 **1c**		100	4	**4k** 71
6	**1c**		80	20	**4l** 58
7	**1c**	$PhCH_2Br$	100	4	**4m**[2d] 94
8	**1c**	$PhCH_2Cl$	100	4	**4m**[2d] 90
9	 **1d**		100	4	**4n** 84
10	 **1e**		100	4	**4o** 72
11	 **1f**		100	4	**4p** 71

[a] Isolated yield based on **1**. [b] Reaction conditions: diselenide **1**, 0.5 mmol; halide, 1.2 mmol; Zn, 0.8 mmol; catalyst, $RuCl_3{\cdot}3H_2O$, 2.6 mg (0.01 mmol); solvent DMF, 3 mL.

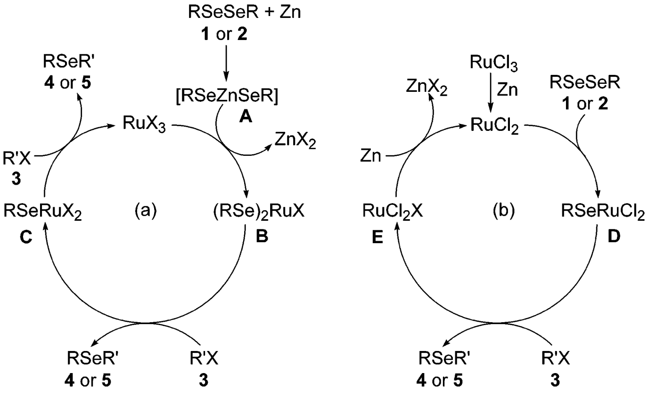
TABLE 3. Catalytic Cleavage of $(PhSe)_2$ (2) to $PhSeR^2$ (5)[c]

Entry	Halide R^2X (3)	Temp. (°)	Time (h)	Yield[a] (%)
1		100	0.5	**5a**[2c] 99
2		100	1	**5a**[2c] 97
3		100	2	**5a**[2c] 88
4		100	1	**5b**[5] 98
5[b]		100	1	**5a**[2c] 93
6[b]		100	1	**5c**[6] 95
7	$PhCH_2Br$	100	0.5	**5d**[2d] 95
8	$PhCH_2Cl$	100	1	**5d**[2d] 98
9		60	2	**5e**[5] 77
10		100	24	**5f**[5] 57

[a] Isolated yield based on **2**. [b] Additive NaBr (1.2 mmol) was added. [c] Reaction conditions: diselenide **2**, 0.5 mmol; halide, 1.2 mmol; Zn, 0.8 mmol; catalyst $RuCl_3{\cdot}3H_2O$, 2.6 mg (0.01 mmol); solvent, DMF, 3 mL.

underwent phenylselenation to afford unsymmetrical diorganyl monoselenides **5** in excellent yields (Table 3).

SCHEME 1



In the presence of sodium bromide, phenylselenation of unreactive organic chlorides also gave **5** in excellent yields (Table 3, entries 5 and 6). Allyl bromide afforded the corresponding phenylselenide in 77% yield (Table 3, entry 9), demonstrating a yield much higher than 28% for its corresponding benzylselenation (Table 1). 1-Bromocyclohexane underwent phenylselenation to afford its corresponding phenylselenide in 57% yield (Table 3, entry 10), whereas no reaction occurred for **1a** under the same conditions (Table 1, entry 13).

As mentioned in the introduction session zinc directly causes cleavage of reactive diaryl diselenides, i.e., **2**, in the presence of a limited number of reactive organic bromides and chlorides to form unsymmetrical diorganyl selenides. With reactive organic bromides, i.e., benzyl bromide and ethyl α-bromoacetate, zinc also causes cleavage of **1a** in the presence of $AlCl_3$. Ruthenium(III) chloride hydrate is easy to manipulate as a catalyst in organic synthesis.[11] For ruthenium(III) chloride catalyzed cleavage of Se−Se bonds in **1** and **2** or their analogues, a mechanism with two paths is proposed as shown in Scheme 1. In path a, elemental zinc initially reacts with diorganyl diselenide **1** or **2** to form di(benzylselenyl)zinc or di(phenylselenyl)zinc **A**. The Ru(III) catalyst then reacts with **A** to afford Ru(III) species **B**, which undergoes coupling with organic halide R′X (**3**), giving unsymmetrical diorganyl selenide **4** or **5** and species **C**. Further reaction of **C** with **3** affords **4** or **5** and regenerates the catalytic species RuX_3 ($X_3 = Cl_3$, $ClBr_2$, or ClI_2 depending on the starting organic halides). In path b, elemental zinc reduces Ru(III) chloride to Ru(II) species $RuCl_2$, which reacts with **1** or **2** to form **D** by oxidative addition. Further reaction of **D** with organic halide **3** to afford diorganyl monoselenide **4** or **5** and generate Ru(III) species **E**. Reduction of **E** with zinc regenerates the catalytic species $RuCl_2$. Detailed study of the reaction mechanism is under way.

Conclusion

In conclusion, we have developed an efficient one-pot method for the synthesis of unsymmetrical diorganyl

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selenides via cleavage of dibenzyl and diphenyl diselenides using ruthenium(III) chloride as the catalyst in the presence of zinc. Organic iodides, reactive or unreactive organic bromides, or chlorides can be used for the benzyl- and phenylselenation under relatively mild conditions.

Experimental Section

General Procedure for Preparation of Unsymmetrical Diorganyl Selenides. Synthesis of Heptyl Benzyl Selenide (4a). Under nitrogen atmosphere, to a mixture of dibenzyl diselenide (**1a**) (170 mg, 0.5 mmol), zinc (52.3 mg, 0.8 mmol), and ruthenium(III) chloride hydrate (2.6 mg, 0.01 mmol) were successively added DMF (3 mL) and 1-bromoheptane (215 mg, 1.2 mmol). The mixture was stirred at 100 °C for 1 h. After the mixture was cooled to ambient temperature, 10 mL of water was added, and the resultant mixture was extracted with diethyl ether (3 × 20 mL). The combined organic phase was washed with brine, dried over anhydrous $MgSO_4$, and filtered through Celite. All volatiles were removed under reduced pressure, and the crude product was purified by silica gel column chromatography using petroleum ether (30−60 °C) or petroleum ether (30−60 °C)/CH_2Cl_2 (ca 10:1, v/v) as the eluent. In most cases, the products were originally colorless liquids or oils, but they usually became slightly yellow when they were isolated or kept in air for a while.

The products were characterized by NMR and compared with the authentic samples for known compounds or further analyzed by elemental analysis for new compounds. No satisfactory elemental analysis results were obtained for **4b** and **4f** because of decomposition of the compounds. For all other products ≥98% purity was obtained by ^{1}H NMR measurements.

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Supporting Information Available: General experimental procedures, analytic data, and copies of ^{1}H, and ^{13}C NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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