



Synthetic Communications An International Journal for Rapid Communication of Synthetic Organic Chemistry

ISSN: 0039-7911 (Print) 1532-2432 (Online) Journal homepage: http://www.tandfonline.com/loi/lsyc20

A simple method for the preparation of arylselanyl anilines

Zhongshi Zhou & Xuehan He

To cite this article: Zhongshi Zhou & Xuehan He (2018): A simple method for the preparation of arylselanyl anilines, Synthetic Communications, DOI: <u>10.1080/00397911.2018.1513531</u>

To link to this article: <u>https://doi.org/10.1080/00397911.2018.1513531</u>



View supplementary material 🕝



Published online: 12 Oct 2018.



🖉 Submit your article to this journal 🕑



View Crossmark data 🗹



Check for updates

A simple method for the preparation of arylselanyl anilines

Zhongshi Zhou^a and Xuehan He^b

^aCollege of Biological and Environmental Sciences, Zhejiang Shuren University, Hangzhou, P. R. China; ^bZhejiang Institute of Geology and Mineral Resource, Hangzhou, P. R. China

ABSTRACT

In the presence of l_{2r} a simple method for the preparation of arylselanyl anilines from anilines and diselenides is developed. This metalfree iodine-promoted procedure proceeds efficiently under mild reaction conditions, providing a series of arylselanyl anilines with high regioselectivity, and mostly in moderate to good yields.

GRAPHICAL ABSTRACT

A Simple Method for the Preparation of Arylselanyl Anilines



ARTICLE HISTORY Received 10 February 2018

KEYWORDS

Aniline; arylselanyl aniline; diselenide; I2-promoted

Introduction

Arylselanyl anilines are important organoselenium compounds, they can be prepared by a traditional selenenylation of electron-rich aromatic compounds with some pre-prepared selenenylating reagents, such as N-phenylselenosaccharin (NPSSac) and (phenylseleno)dimethylsulfonium tetrafluoroborate.^[1-2] They were also synthesized by the palladium catalyzed reaction of aryl iodide or triflate with Bu₃SnSePh.^[3-4] Using PhSeCl as selenenylating reagent in glycerol, Lenardão and coworkers reported a green procedure to access arylselanyl anilines.^[5] However, this method should be done in inert gas due to the moisturesensitive nature of PhSeCl. An alternative method is the use of cheaper and more stable diaryl diselenides. Under conventional heating or microwave heating, the CuI-catalyzed reaction of anilines or haloaromatics with diaryl diselenides can provide arylselanyl anilines.^[6-7] Recently, using DMSO as oxidant, Braga's group developed a metal-free and solvent-free iodine-catalyzed protocol for the preparation of arylselanyl anilines under microwave irradiation.^[8] In this reaction, the *in situ* generated active electrophilic selenium species ArSeI, which was formed by the reaction of I_2 with diaryl diselenide, played a key role. However, this greener methodology needed a special reactor (Microwave monomode CEM reactor) and was not effective at room temperature. Similarly, near the same time,

CONTACT Zhongshi Zhou 😒 zhoushanzsu@163.com 🗈 College of Biological and Environmental Sciences, Zhejiang Shuren University, Hangzhou 310015, P. R. China.

^{© 2018} Taylor & Francis Group, LLC

Yan's group demonstrated another way of using KI as catalyst and H_2O_2 as oxidant for obtaining arylselanyl anilines.^[9] This protocol was suitable for the selenation of *N*,*N*-disubstituted anilines and *N*-substituted anilines, but when the unsubstituted aniline was used as substrate, it was difficult to get the desired product. More recently, the Rose Bengal-catalyzed photo-induced synthesis of arylselanyl anilines was reported by Braga's group.^[10] The above approaches, though effective for obtaining arylselanyl aniline, have some limitations such as the use of special reactors, pre-functionalized reagents and metal catalysts, as well as, long reaction times and high reaction temperatures. Consequently, the development of simple and general methods for the preparation of arylselanyl aniline is still desired.

Recently, iodine-catalyzed or iodine-promoted reactions have been increasingly explored due to its eco-friendly and metal-like behaviors.^[11–17] Considering ArSeI is the key intermediate for the preparation of arylselanyl aniline^[8,9] and that it can be prepared from the reaction of diaryl diselenide with molecular iodine,^[18] we have investigated the reaction of anilines with diaryl diselenides in the presence of I₂. Although the Braga's study has disclosed the iodine-promoted conditions, this reaction needs DMSO as oxidant and has to be carried out under microwave heating.^[8] Compared with it, our protocol is effective at room temperature, which is simple and mild.

Results and discussion

The Optimization study on the reaction was initiated by using *N*,*N*-dimethylaniline **1a** with diphenyl diselenide **2a** in the presence of I_2 at room temperature. As depicted in Table 1, the effect of solvent was first examined. The reaction can be carried out in several solvents, and afford the desired product *N*,*N*-dimethyl-4-(phenylselanyl)aniline **3a** in 11–62% yields, showing that EtOH was the most suitable solvent for the reaction (Table 1, entries 1–8). Then, the amount of I_2 was optimized, and 1.0 equiv proved to be the best choice (entries 2, 10–15). However, in the absence of I_2 , **3a** was not formed (entry 9). As a control experiment, when HI took the place of I_2 , the reaction gave 23% yield of **3a** (entry 16). Finally, both the optimal amount of **1a** and the suitable reaction time were determined: 1.2 equiv of **1a** was suitable for the reaction and in 6 h the reaction was completed (entries 2, 17–23).

Having established the optimal conditions, the selenation of 1.2 equiv of anilines **1** with 1.0 equiv of diselenides **2** and I_2 in EtOH at room temperature for 6 h was investigated, and as a result, a series of arylselanyl anilines **3** were afforded. As shown from Table 2, several *N*,*N*-disubstituted anilines can react with **2a** easily, resulting in the corresponding 4-arylselanyl anilines **3a-3d** in good yields (Table 2, entries 1-4). However, *N*,*N*-dibenzylaniline **1e** let only to 21% yield of desired product **3e** due to the sterically hindered structure (entry 5). To extend the scope of our methodology, two unsubstituted anilines **1f**, **1g** and two *N*-substituded anilines **1h**, **1i** were chosen as representatives to treat with **2a**, and obtained the corresponding products **3f-3i** in moderate to good yields (entries 6–9), indicating that this protocol is suitable for a wide variety of anilines. Other diaryl diselenides such as **2 b** and **2c**, whether having an electron-donating group or an electron-withdrawing group on benzene ring, usually had no significant influence on their reactivity and provided the corresponding products **31** in 75% yield

	N +	PhSeSePh Solv	I ₂ rent, r.t.	h	
	1a	2a	3a		
Entry	N,N-Dimethylaniline (equiv.)	l ₂ (equiv.)	Solvent	Time (h)	Yield (%) ^a
1	1.2	0.5	CH ₃ CN	15	46
2	1.2	0.5	CH₃OH	15	38
3	1.2	0.5	EtOH	15	62
4	1.2	0.5	EtOAc	15	25
5	1.2	0.5	THF	15	32
6	1.2	0.5	CH ₂ Cl ₂	15	19
7	1.2	0.5	DMF	15	11
8	1.2	0.5	CF ₃ CH ₂ OH	15	50
9	1.2	0	EtOH	15	0
10	1.2	0.1	EtOH	15	13
11	1.2	0.3	EtOH	15	31
12	1.2	0.8	EtOH	15	77
13	1.2	1.0	EtOH	15	82
14	1.2	1.5	EtOH	15	80
15	1.2	2.0	EtOH	15	81
16	1.2	HI (1.0)	EtOH	15	23
17	1.0	1.0	EtOH	15	63
18	1.5	1.0	EtOH	15	77
19	2.0	1.0	EtOH	15	80
20	1.2	1.0	EtOH	20	78
21	1.2	1.0	EtOH	10	86
22	1.2	1.0	EtOH	6	83
23	1.2	1.0	EtOH	4	67

Table 1. Optimization of the selenation of N,N-dimethylaniline promoted by I₂.

^alsolated yields.

(entry 12). From the results it is obvious that except 3g all obtained arylselanyl anilines are 4-arylselanyl anilines, showing this selenation has a high regioselectivity.

To explore the mechanism, a radical scavenger, 2,6-*di*-tert-butyl-4-methylphenol (BHT), was added to the reaction of **1a** with **2a** and I₂ under the optimized conditions. It was found that BHT was not effective to the selenation, and after 6 h **3a** was obtained in 81% yield, which indicated that the reaction may not undergo a radical pathway. Therefore, a plausible eletrophilic substitution mechanism promoted by I₂ is shown in Scheme 1: thus, I₂ first reacts with diselenide **2** smoothly to form ArSeI.^[18] The *in situ* generated active electrophilic selenium species then reacts with aniline, according 4-aryl-selanyl aniline with high regioselectivity and good yield through an electrophilic aromatic substitution. The by-product HI can also be oxidized by air into I₂.

Conclusions

We have developed a simple iodine-promoted procedure for the synthesis of 4-arylselanyl anilines. This metal-free reaction proceeded smoothly at room temperature and was completed in only 6 h, which provided a series of corresponding compounds with high regioselectivity and in moderate to good yields. Compared with the known methods, this protocol has some advantages such as milder reaction conditions and is suitable for a wide variety of anilines.

4 🕢 Z. ZHOU AND X. HE

Table 2. Preparation of arylselanyl anilines 3.

			R ¹ -N-R ² +	R ³ SeSeR ³ -	I _{2,} EtOH 6h, r.t.	\rightarrow \mathbb{R}^{1-N-}	R ²			
			1	2		3 Seb	< ²			
Entry	Aniline (1)	Diselenide (2)	Product (3)	Yield (%) ^a	Entry	Aniline (1)	Diselenide (2)	Product (3)	Yield (%) ^a	
1	N 1a	PhSeSePh 2a	SePh 3a	83	7	₩H ₂ ↓ 1g	2a	Seph 3g	53	
2	الله الله المعالم المعا المعالم المعالم	2a	SePh 3b	86	8	HN Ih	2a	HN SePh 3h	82	
3	⊂ N L L L L	2a	$\bigcup_{SePh}^{N} \mathbf{3c}$	71	9		2a	HN Ph	51	
4	() N ∎ 1d	2a	O N SePh 3d	78	10	1a	(p-MeC ₆ H ₄ Se) ₂ 2b	SeC ₆ H ₄ Me-p 3 j	81	
5	Phyper Ph	2a	Phyper Physics	21	11	1a	(p-ClC ₆ H₄Se)₂ 2c	SeC ₆ H ₄ Cl- <i>p</i> 3k	78	
6	$\bigcup^{NH_2} \mathbf{1f}$	2a	SePh 3f	69	12	1a	(PhCH ₂ Se) ₂ 2d	SeCH ₂ Ph 3	75	
^a Isolated yields.										

Experimental section

General: Melting points were measured with an XT-4 melting point apparatus and were uncorrected. ¹H NMR and ¹³C NMR spectra were measured on a Bruker-AVANCE III (500 MHz) spectrometer and mass spectra were determined on Waters-GCT Premier. Anilines, diselenides, I_2 , and solvents were commercially available.

General procedure for the preparation of arylselanyl anilines promoted by I_2 : in EtOH (2.0 mL), aniline 1 (0.36 mmol), diselenide 2 (0.15 mmol) and I_2 (0.15 mmol) were added successively. The mixture was vigorously stirred at r. t. for 6 h. Upon completion, aqueous solution of $Na_2S_2O_3$ (sat., 2 mL), aqueous solution of Na_2CO_3 (sat., 5 mL) and H_2O (10 mL) were added to the mixture, respectively. The mixture was extracted with CH_2Cl_2 (3 × 10 mL) and the combined organic phase was dried over



Scheme 1. Proposed mechanism for the selenation of anilines promoted by I₂.

anhydrous Na_2SO_4 , filtered, and concentrated under reduced pressure. The residue was then purified by flash chromatography using petroleum ether as the eluent to furnish arylselanyl anilines **3**.

References

- Tingoli, M.; Diana, R.; Panunzi, B. N-Phenylselenosaccharin (NPSSac): a New Electrophilic Selenium-Containing Reagent. *Tetrahedron. Lett.* 2006, 47, 7529. DOI: 10.1016/j.tetlet.2006.08.068.
- Gassman, P. G.; Miura, A.; Miura, T. Direct Selenation of Electron-Rich Aromatic Compounds with (Phenylseleno)Dimethylsulfonium Tetrafluoroborate. *J. Org. Chem.* 1982, 47, 951. DOI: 10.1021/jo00345a010.
- [3] Beletskaya, I. P.; Sigeev, A. S.; Peregudov, A. S.; Petrovskii, P. V. New Approaches to the Synthesis of Unsymmetrical Diaryl Selenides. J. Organomet. Chem. 2000, 605, 96. DOI: 10.1016/S0022-328X(00)00265-5.
- Beletskaya, I. P.; Sigeev, A. S.; Peregudov, A. S.; Petrovskii, P. V. Russ. J. Org. Chem. 2001, 37, 1463. DOI: 10.1023/A:1013460213633.
- [5] Thurow, S.; Penteado, F.; Perin, G.; Jacob, R. G.; Alves, D.; Lenardão, E. J. Metal and Base-Free Synthesis of Arylselanyl Anilines Using Glycerol as a Solvent. *Green Chem.* 2014, 16, 3854. DOI: 10.1039/C4GC00874J.
- [6] Ricordi, V. G.; Thurow, S.; Penteado, F.; Schumacher, R.; Perin, G.; Lenardão, E. J.; Alves, D. Copper-Catalyzed Direct Arylselenation of Anilines by C-H Bond Cleavage. Adv. Synth. Catal. 2015, 357, 933. DOI: 10.1002/adsc.201400804.
- [7] Kumar, S.; Engman, L. Microwave-Assisted Copper-Catalyzed Preparation of Diaryl Chalcogenides. J. Org. Chem. 2006, 71, 5400. DOI: 10.1021/j0060690a.
- [8] Saba, S.; Rafique, J.; Braga, A. L. DMSO/Iodine-Catalyzed Oxidative C-Se/C-S Bond Formation: A Regioselective Synthesis of Unsymmetrical Chalcogenides with Nitrogen- or Oxygen-Containing Arenes. *Catal. Sci. Technol.* 2016, 6, 3087. DOI: 10.1039/ C5CY01503K.
- [9] Yu, C.; Shi, H.-W.; Zhu, M.; Yan, J. A Convenient Catalytic Procedure for Direct Synthesis of ArylSelanyl Anilines. *Synlett.* **2015**, *26*, 2139.
- [10] Saba, S.; Rafique, J.; Franco, M. S.; Schneider, A. R.; Espíndola, L.; Silva, D. O.; Braga, A. L. Rose Bengal Catalysed photo-induced selenylation of indoles, imidazoles and arenes: a metal free approach . Org. Biomol. Chem. 2018, 16, 880 DOI: 10.1039/C7OB03177G.
- [11] Uyanik, M.; Okamoto, H.; Yasui, T.; Ishihara, K. Quaternary Ammonium (hypo)iodite catalysis for enantioselective oxidative cycloetherification. *Science*. 2010, 328, 1376 DOI: 10.1126/science.1188217.

6 🔄 Z. ZHOU AND X. HE

- [12] Yang, K.; Ke, M.; Lin, Y.; Song, Q. Sulfonamide Formation from Sodium Sulfinates and Amines or Ammonia under Metal-Free Conditions at Ambient Temperature. *Green Chem.* 2015, 17, 1395. DOI: 10.1039/C4GC02236J.
- [13] Duan, Y.-N.; Zhang, Z.; Zhang, C. Recyclable Hypervalent-Iodine-Mediated Dehydrogenative Cyclopropanation under Metal-Free Conditions. Org. Lett. 2016, 18, 6176 DOI: 10.1021/acs.orglett.6b03209.
- [14] Siddaraju, Y.; Prabhu, K. R. Iodine Promoted Regioselective α-Sulfenylation of Carbonyl Compounds Using Dimethyl Sulfoxide as an Oxidant. Org. Lett. 2016, 18, 6090 DOI: 10.1021/acs.orglett.6b03084.
- [15] Vieira, A. A.; Azeredo, J. B.; Godoi, M.; Santi, C.; da Silva Júnior, E. N.; Braga, A. L. Catalytic Chalcogenylation under Greener Conditions: A solvent-free sulfur- and seleno-functionalization of olefins via I2/DMSO oxidant system. J. Org. Chem. 2015, 80, 2120 DOI: 10.1021/jo502621a.
- [16] Xu, D.-D.; Sun, W.-W.; Xie, Y.-L.; Liu, J.-K.; Liu, B.; Zhou, Y.-B.; Wu, B. Metal-Free Regioselective Hypervalent Iodine-Mediated C-2 and C-3 Difunctionalization of N-Substituted Indoles. J. Org. Chem. 2016, 81, 11081. DOI: 10.1021/acs.joc.6b02078.
- [17] Ambethkar, S.; Vellimalai, M.; Padmini, V.; Bhuvanesh, N. Iodine-Mediated C-N and C-S Bond Formation: regioselective Synthesis of Benzo[4,5]Imidazo[2,1-b]Thiazoles. *New J. Chem.* 2017, 41, 75. DOI: 10.1039/C6NJ02102F.
- [18] Huang, Z.-Z.; Huang, X.; Huang, Y.-Z. Synthesis of Acyl(Phenylselanyl)Methylidene (Triphenyl)-λ 5 -Arsanes and Their Wittig-Type Reactions. J. Chem. Soc. Perkin Trans. I. 1995, 95. DOI: 10.1039/P19950000095.