Improved Synthesis of Aromatic Diselenides

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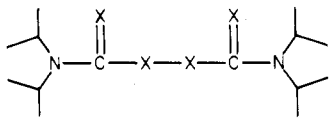
Received July 20, 1982

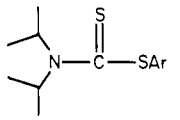
The reaction of aromatic and heterocyclic lithio derivatives with elemental selenium, followed by dimethylthiocarbamyl chloride, gives highly crystalline and readily purified *Se*-aryl *N,N*-dimethylselenothiocarbamates. Alkaline hydrolysis of the latter, followed by ferricyanide oxidation, affords diselenides. Overall yields and purity of the diselenides are superior to those obtained by the standard direct selenation–oxidation method.

In recent years, diaryl diselenides have become increasingly important as basic starting materials for organoselenium-based synthetic methodology.[1] The most direct and simple synthesis of diaryl diselenides involves the reaction of an arylmagnesium halide or an aryllithium with elemental selenium, followed by oxidation of the resulting selenolate or selenol. A survey of the literature (Table I) indicates that this procedure generally affords diselenides in surprisingly modest yields.[2] We surmised that the major problem was one of purification, since diselenides produced in this way should be contaminated with both diaryl triselenides and, especially, the difficulty separable diaryl monoselenides. Indeed, diphenyl selenide has been reported as a byproduct in the reaction of phenylmagnesium bromide with selenium.[3]

Recently, we reported a new synthesis of aromatic thiols in which the key step was the reaction of an aryllithium with tetraisopropylthiuram disulfide (1).[4] In this reaction,



1, X = S
2, X = Se



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nucleophilic attack of the aryllithium takes place exclusively at the disulfide linkage of 1 due to steric shielding of the thiocarbonyls by the bulky isopropyl substituents. The selenium analogue of 1, i.e., 2, would be expected to undergo a similar highly selective attack by an aryllithium at its diselenide bond. Unfortunately, diselenide 2 would not be an inexpensive and readily available reagent, since its synthesis would involve oxidation of a diselenocarbamate derived from diisopropylamine and the very expensive and noxious carbon diselenide.[5]

Since the success of our thiol synthesis was in part dependent on the ease of purification of the intermediary dithiocarbamates 3, we decided to investigate the utility of a diselenide synthesis in which selenation of an aryllithium would be followed by conversion to a selenothiocarbamate, which would then be hydrolyzed and oxidized to a diselenide as shown below. The highly satisfactory

$$ArLi \rightarrow ArSeLi \rightarrow ArSeCSNR_2 \rightarrow ArSeNa \rightarrow ArSeSeAr$$

results obtained by this apparently roundabout procedure are described in the following section.

Table I. Literature Synthesis of Diaryl Diselenides from Organometallics

aryllithium or grignard	yield of diselenides, %	ref
mesitylmagnesium bromide	47	2a
phenylmagnesium bromide	64	2b
xenylmagnesium bromide	31	2c
xenyllithium	45	2c
m-tolylmagnesium bromide		2d
2-thienyllithium		2e

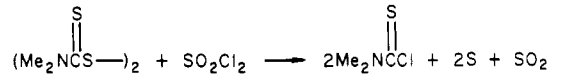
Table II. Synthesis of Selenothiocarbamates and Corresponding Diselenides

starting matl	R	RSeC(S)NMe$_2$ (yield, %)	R$_2$Se$_2$ (yield, %)
phenyllithium	phenyl	6 (89)	16 (99)
p-dibromobenzene	4-bromophenyl	7 (80)	17 (90)
1-bromonaphthalene	1-naphthyl	8 (90)	18 (95)
m-bromotoluene	*m*-tolyl	9 (88)	19 (100)
furan	2-furyl	10 (89)	20 (70)
thiophene	2-thienyl	11 (82)	21 (90)
benzo[*b*]thiophene	2-benzo[*b*]thienyl	12 (86)	22 (94)
bromomesitylene	mesityl	13 (89)	23 (95)
2-bromopyridine	2-pyridyl	14 (75)	(0)[a]
diphenyl ether	*o*-phenoxyphenyl	15 (75)	24 (95)

[a] No diselenide could be isolated in this case.

Results and Discussion

The key reagent used in this study was *N,N*-dimethylthiocarbamyl chloride (4). The commercially available chloride 4 has been prepared by the action of a limited amount of chlorine on the cheap precursor tetramethylthiuram disulfide (5).[6] We have found that the conversion of 5 into 4 can be carried out even more conveniently by the use of sulfuryl chloride, as shown below.



5 4

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A number of lithium arylselenides, both benzenoid and heterocyclic, were prepared from aryllithiums and selenium and reacted with *N,N*-dimethylthiocarbamyl chloride to give the corresponding *Se*-aryl *N,N*-dimethylselenothiocarbamates as shown in Table II.

The selenothiocarbamates were stable, highly crystalline materials which were obtained in generally excellent yields by passage of the crude reaction mixture through a short silica column. A representative group of selenothiocarbamates were hydrolyzed by ethanolic potassium hydroxide under nitrogen, most of the alkali was then neutralized by acetic acid, and a little over 1 equiv of potassium ferricyanide was added to give the corresponding diselenide in excellent yield and in high purity, as shown in Table II. Yields of diselenides were appreciably reduced when excess ferricyanide and strongly alkaline solutions were employed.

In conclusion, the conversion of an aryllithium to a diaryl diselenide via an *Se*-aryl *N,N*-dimethylselenothiocarbamate is a superior method for the syntheses of a diaryl diselenide, even though the selenothiocarbamate serves only as a readily purified selenolate derivative. By this new procedure, for example, the important reagent diphenyl diselenide can be prepared in 85% overall yield from commercial phenyllithium, as compared with the 65–70% yield for the current literature preparation.[2b] It should be pointed out, however, that the procedure is clearly limited to the use of substrates which can be converted to lithio derivatives in the first step.

Experimental Section

Melting points were determined on a Thomas-Hoover apparatus and are uncorrected. Mass and infrared (KBr) spectra were determined by using Perkin-Elmer 270B and 137 spectrometers, respectively. NMR spectra were recorded on a Bruker 250 FT machine with $CDCl_3$ solutions containing Me_4Si as an internal standard and are reported in δ units (J values are in hertz). Elemental analyses were performed by Galbraith Laboratories. All organic extracts were washed and dried over anhydrous $CaCl_2$ prior to filtration and evaporation. Chromatographic purifications were carried out by using silica, with 7:3 hexane–benzene as the eluant.

***N,N*-Dimethylthiocarbamyl Chloride (4).** To a stirred solution of tetramethylthiuram disulfide (0.05 mol, 12 g) in CCl_4 (40 mL) at room temperature was added slowly a solution of sulfuryl chloride 0.05 mol) in 20 mL of CL_4. The reaction mixture was allowed to stir at room temperature for 10 min and then heated to reflux for 20 min. The precipitated sulfur was filtered, and the solution was concentrated (Büchi) and distilled (Kugelrohr), giving the product: 11.6 g (94%); mp 42.5–43.5 °C.

***Se*-Aryl *N,N*-Dimethylselenothiocarbamates.** A standard procedure for the preparation of *Se*-aryl *N,N*-dimethylselenothiocarbamates from aromatic halides is illustrated below.

***Se*-4-Bromophenyl *N,N*-Dimethylselenothiocarbamate (7).** To a stirred solution of *p*-dibromobenzene (0.05 mol, 11.8 g) in dry THF (150 mL) at −78 °C (N_2) was added slowly 2 equiv of *t*-BuLi. After the mixture was stirred for 2 h, selenium powder (3.95 g, 0.05 mol) was added to the solution. After the selenium was all consumed, the solution was added slowly to *N,N*-dimethylthiocarbamyl chloride (0.05 mol, 6.2 g) in dry THF (100 mL). After the mixture was stirred for 0.5 h, the solution was concentrated (Büchi), and ether (500 mL) was added. The solution was washed twice by 200 mL of H_2O, dried over anhydrous $CaCl_2$, and concentrated to give crude product which was purified by chromatography on column to yield yellow crystals of **7**: 12.9 g (80%); mp 102–104 °C. Anal. Calcd for $C_9H_{10}BrNSSe$: C, 33.46; H, 3.12; Se, 24.44; Found: C, 33.66; H, 3.24; Se, 24.70.

***Se*-Phenyl *N,N*-dimethylselenothiocarbamate (6),** mp 118–119 °C. Anal. Calcd for $C_9H_{11}NSSe$: C, 44.26; H, 4.54; Se 32.33. Found: C, 44.31; H, 4.57; Se, 32.58.

***Se*-1-Naphthyl *N,N*-dimethylselenothiocarbamate (8),** mp 139–141 °C. Anal. Calcd for $C_{13}H_{13}NSSe$: C, 53.06; H, 4.45; Se, 26.83. Found: C, 52.98; H, 4.50; Se, 27.05.

***Se*-*m*-Tolyl *N,N*-dimethylselenothiocarbamate (9),** mp 56–58 °C. Anal. Calcd for $C_{10}H_{13}NSSe$: C, 46.51; H, 5.07; Se, 30.58. Found: C, 46.43; H, 5.05; Se, 30.72.

***Se*-(2,4,6-Trimethylphenyl) *N,N*-dimethylselenothiocarbamate (13),** mp 66–68 °C. Anal. Calcd for $C_{12}H_{17}NSSe$: C, 50.34; H, 5.98; Se, 27.58. Found: C, 50.34, H, 5.95; Se, 27.81.

***Se*-2-Pyridyl *N,N*-dimethylselenothiocarbamate (14),** mp 94–95 °C. Anal. Calcd for $C_8H_{10}N_2SSe$: C, 39.19; H, 4.11; Se, 32.30. Found: C, 39.29; H, 4.19; Se, 32.39.

A standard procedure for the preparation of *Se*-aryl *N,N*-dimethylselenothiocarbamates from nonhalogenated aromatic precursors is illustrated below.

***Se*-2-Thienyl *N,N*-Dimethylselenothiocarbamate (11).** To a stirred solution of thiophene (0.05 mol, 4.2 g) in dry THF (150 mL) at 0 °C (N_2) was added slowly 1 equiv of *n*-BuLi. After the mixture was stirred for 2 h, selenium powder (3.95 g, 0.05 mol) was added to the solution. After the selenium was all consumed, the solution was added slowly to *N,N*-dimethylthiocarbamyl chloride (0.05 mol, 6.2 g) in dry THF (100 mL). After being stirred for 0.5 h, the solution was concentrated (Büchi) and ether (500 mL) was added. The solution was washed twice by 200 mL of H_2O, dried over anhydrous $CaCl_2$, and concentrated to give crude product which was purified by column chromatography to give yellow crystals of 11: 10 g (82%) mp 91–92 °C. Anal. Calcd for $C_7H_9NS_2Se$: C, 33.60; H, 3.62, Se, 31.55; Found: C, 33.54; H, 3.71; Se, 31.49.

***Se*-2-Furyl *N,N*-dimethylselenothiocarbamate (10),** mp 95–96 °C; Anal. Calcd for C_7H_9NOSSe: C, 35.90; H, 3.87; Se, 33.72. Found: C, 35.82; H, 3.95; Se, 33.85.

***Se*-2-Benzo[*b*]thienyl *N,N*-dimethylselenothiocarbamate (12),** mp 155–157 °C; Anal. Calcd for $C_{11}H_{11}NS_2Se$: C, 44.0; H, 3.69; Se, 26.29. Found: C, 43.77; H 3.74; Se, 26.50.

***Se*-*o*-Phenoxyphenyl *N,N*-dimethylselenothiocarbamate (15),** mp 107–109 °C. Anal. Calcd for $C_{15}H_{15}NOSSe$: C, 53.57; H, 4.50; Se, 23.48. Found: C, 53.35; H, 4.56; Se, 23.50.

Hydrolysis of *Se*-Aryl *N,N*-Dimethylselenothiocarbamates to Diaryl Diselenides. A standard procedure for the preparation of diaryl diselenides from selenothiocarbamates is illustrated below.

Diphenyl Diselenide (16). To a stirred solution of 20% ethanolic potassium hydroxide (200 mL) was added phenylselenothiocarbamate (**6**; 0.1 mol, 24.4 g). The reaction mixture was heated to reflux under nitrogen for 3 h and then cooled to room temperature. The solution was almost neutralized by acetic acid, and 1 equiv of potassium ferricyanide in H_2O (200 mL) was added. The precipitate was filtered and washed by water to give very pure diselenide: 15.5 g (yield 99%); mp 61–62 °C (lit.[2b] mp 60–62 °C).

The following were also obtained. **Bis(4-bromophenyl) diselenide (17),** mp 107–108 °C (lit.[7] mp 107–108 °C). **Bis(1-naphthyl) diselenide (18),** mp 85–87 °C (lit.[9] mp 87–88 °C). **Di-*m*-tolyl diselenide (19),** oil (lit.[2d]). **Bis(2-furyl) diselenide (20),** mp 49–51 °C. Anal. Calcd for $C_8H_6O_2Se_2$: C, 32.90; H, 2.07; Se, 54.07. Found: C, 32.88; H, 2.14; Se; 53.86.

Bis(2-thienyl) diselenide (21), mp 57–59 °C (lit.[2e] mp 57–59 °C)

Bis(2-benzo[*b*]thienyl) diselenide (22), mp 145–147 °C (lit.[8] mp 148 °C). **Bis(2,4,6-trimethylphenyl) diselenide (23),** mp 113–114 °C (lit.[2a] mp 113–114.5 °C). **Bis(*o*-phenoxyphenyl) diselenide (24),** mp 95–96 °C. Anal. Calcd for $C_{24}H_{18}O_2Se_2$: C, 58.08; H, 3.66; Se, 31.82. Found: C, 58.19; H, 3.76; Se, 31.99.

Acknowledgment. This work was supported by the National Science Foundation MRL program under Grant DMR 7923647.

Registry No. **4**, 16420-13-6; **5**, 137-26-8; **6**, 85152-76-7; **7**, 85152-77-8; **8**, 85152-78-9; **9**, 85152-79-0; **10**, 85152-80-3; **11**, 85152-81-4; **12**, 85152-82-5; **13**, 85152-83-6; **14**, 85152-84-7; **15**, 85152-85-8; **16**, 1666-13-3; **17**, 20541-48-4; **18**, 1787-80-0; **19**,

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69468-42-4; **20**, 85152-86-9; **21**, 85152-87-0; **22**, 6455-14-7; **23**, 71518-92-8; **24**, 85152-88-1; Se, 7782-49-2; phenyllithium, 591-51-5; *p*-dibromobenzene, 106-37-6; 1-bromonaphthalene, 90-11-9; *m*-bromotoluene, 591-17-3; furan, 110-00-9; thiophene, 110-02-1; benzo[*b*]thiophene, 95-15-8; bromomesitylene, 576-83-0; 2-bromopyridine, 109-04-6; diphenyl ether, 101-84-8.

Supplementary Material Available: Full IR, NMR, and mass spectral data for compounds **4** and **7–24** (5 pages). Ordering information is given on any current masthead page.

Syntheses and Structural Studies in the 4-Phenylbenzo[*g*]indolin-2-one System[1a]

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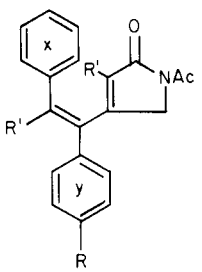
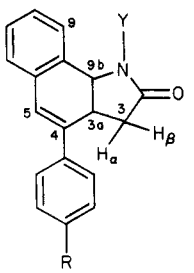
Received September 29, 1982

Acid-catalyzed deacetylation of unsaturated lactam **1** was accompanied by cyclization to yield 4-phenyl-3a,9b-dihydrobenzo[*g*]indolin-2-one (**4**; 71%), which adsorbed 1 mol of hydrogen to form **15**. Compound **15** was also obtained by intramolecular [4 + 2] cycloaddition of 1-[(4-phenyl-3-butynoyl)amino]cyclobutene **21** to give an isomer (**22**; 47%) of **4** and subsequent hydrogenation thereof. Chemical and spectral studies that led to structural elucidation of these compounds and some of their derivatives are presented.

In a preceding paper[2] we described the intramolecular cyclizations of *N*-(phenylpropargyl)-*cis*-cinnamamide in refluxing acetic anhydride to form (*Z*)-1-acetyl-4-(1,2-diphenylvinyl)-3-pyrrolin-2-one (**1**; resulting from [2 + 2] cycloaddition–cycloreversion), as well as [4 + 2] cycloaddition products. The bromo derivative **2** and the dideuterio derivative **3** were obtained analogously. Structural elucidations of **1–3** were reported previously.[2,3] The present paper concerns structural changes that **1–3** undergo during acid-catalyzed deacetylation.

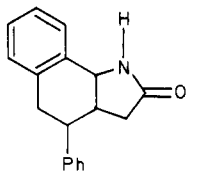




1, R = R' = H
2, R' = H; R = Br
3, R' = D; R = H

4, R = Y = H
5, R = H; Y = Ac
6, R = Br; Y = H
7, R = Br; Y = Ac

Deacetylation–Reacetylation Studies. Refluxing **1** (mp 132 °C) in aqueous hydrochloric and acetic acids effected deacetylation (71%) to yield a colorless compound (mp 214 °C, $C_{18}H_{15}NO$) that showed spectral and polarographic properties inconsistent with the expected **8** but which were indicative of a tricyclic indolinone structure **4** or an isoindolinone structure **14**. Also, reacetylation of the 214 °C compound with Ac_2O failed to regenerate **1**. Instead, it produced a new substance (shown to be **5**, $C_{20}H_{17}NO_2$, mp 143 °C), isomeric with **1** and reconvertible (61%) into the 214 °C compound on deacetylation in the aforementioned manner. Catalytic hydrogenation of the 214 °C compound produced a dihydro derivative (mp 205 °C) that lacked the stilbene chromophore and was presumed to be either **15** or **16**. While neither **4** nor **15** had



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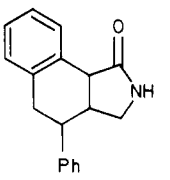

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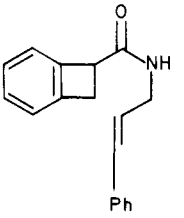

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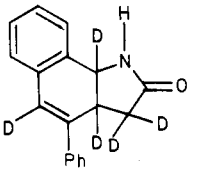
been reported previously, Oppolzer[4] had synthesized all of the four possible racemates of **16** by means of thermal cyclization of **17**. Our 205 °C compound was not identical with any of these racemates so that the isoindolinone structure **14** was eliminated as a possibility for our 214 °C product.

Similarly, deacetylation of bromo compound **2** (to **6**) and subsequent reacetylation formed **7**. The presence of a slightly distorted A_2B_2 multiplet ($J \simeq 8$ Hz) at δ 7.5 in the ^{1}H NMR spectrum of **7** indicated that cyclization had indeed occurred into ring x rather than into ring y.

H–D exchange experiments led to a rationalization for the conversion of **1** into **4**. Thus, when dideuterio **1** (i.e., **3**) was refluxed with HCl–HOAc–H_2O, the product (**4**) contained no deuterium atoms. Also, when **1** (or **3**) was refluxed with DCl–DOAc–D_2O (followed by H_2O workup), the 214 °C product was pentadeuterio **4** (i.e., **18**), wherein



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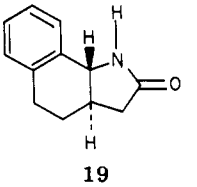

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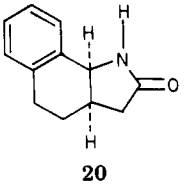

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all protons on aliphatic carbons had been exchanged. As a rationalization of the exchange processes, we invoked the

(1) (a) This investigation was supported in part by research grant GM 12730 from the National Institutes of General Medical Sciences, U.S. Public Health Service. (b) Graduate Teaching and Research Assistant, 1969–1973. (c) Undergraduate Teaching and Research Assistant, 1978–1980.

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(4) We thank Dr. Wolfgang Oppolzer for kindly furnishing copies of ^{1}H NMR spectra from his unpublished studies. For examples of similar intramolecular [4 + 2] cycloadditions, see Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 10; *Synthesis* **1978**, 793.

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