JOC*Note*

Indium(I) Iodide-Promoted Cleavage of Diaryl Diselenides and Disulfides and Subsequent Condensation with Alkyl or Acyl Halides. One-Pot Efficient Synthesis of Diorganyl Selenides, Sulfides, Selenoesters, and Thioesters

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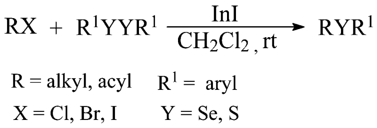
Abstract: Diphenyl diselenides and disulfides undergo facile cleavages by indium(I) iodide and the corresponding generated selenate and thiolate anions condense in situ with alkyl or acyl halides present in the reaction mixture. Thus, a simple, efficient, and general procedure has been developed for the synthesis of unsymmetrical diorganyl selenides, sulfides (thioethers), selenoesters, and thioesters by this one-pot reaction at room temperature.

The importance of indium metal and its salts has been well demonstrated through novel protocols for carbon−carbon bond formation, rearrangements, and a variety of useful reactions over the past decade.[1] Thus, the search for new indium derivatives for more improvement in organic transformations is of much current interest.[2] As a part of our activities in indium-mediated reactions,[1e,3] we are also in this race, and recently we reported the use of indium(I) iodide for the cleavage of diphenyl diselenides followed by in situ condensation of selenate anion with alkyl halides to produce diorganyl selenides in a preliminary communication.[4] We demonstrate here further extension of this work together with application of this indium reagent for the cleavage of diaryl disulfides and subsequent reaction with alkyl or acyl halides to provide diorganyl sulfides and thioesters (Scheme 1).

SCHEME 1. Synthesis of Selenides and Sulfides



$$RX + R^1YYR^1 \xrightarrow[CH_2Cl_2\text{, rt}]{InI} RYR^1$$

R = alkyl, acyl   R^1 = aryl
X = Cl, Br, I   Y = Se, S

The experimental procedure is very simple. A mixture of alkyl (or acyl) halide and diaryl selenide (or sulfide) in methylene chloride was stirred in the presence of indium(I) iodide at room temperature for a certain period of time (TLC). Usual workup and extraction with ether provided the product.

A wide range of structurally diverse alkyl halides underwent reactions with diphenyl diselenides and disulfides by this procedure to produce the corresponding alkyl phenyl selenides and sulfides (thioethers), respectively, in very high yields. The results are presented in Table 1 for selenides and in Table 2 for sulfides. As evident from Tables 1 and 2, primary, secondary, tertiary, benzylic, and allylic chlorides, bromides, and iodides readily participate in this reaction to form the corresponding products. The reaction with relatively sterically congested-bridged halide also proceeds without any difficulty (entry 23 in Table 1). However, the reaction of long-chain alkyl bromides is comparatively slow (entries 11,12, Table 1). In general, formation of sulfides took longer (1−4 h) than those of selenides (<1 h) by this procedure. Several aromatic and nonaromatic acid chlorides also condense with selenate and thiolate anions produced by this cleavage reaction to provide the corresponding selenobenzoates and thiobenzoates in good to high yields. However, aryl halides and vinyl halides remained inactive in this reaction, and on the other hand, nonaromatic diselenides and disulfides failed to undergo any cleavage by this reagent. Several functional groups such as OMe, Cl, NO$_2$, C═O, CO$_2$R, and methylenedioxy remained unaffected under the reaction conditions.

It is speculated[5] that the reactions are going through the intermediacy of bis(phenylseleno/thiophenyl)-iodoindium(III) (**1**), formed readily by the reaction of equimolar quantities of InI (use of less than a stoichiometric amount of InI keeps the reaction incomplete) and diphenyl diselenide/diphenyl disulfide, which then releases selenate/thiolate anion to be alkylated with alkyl/acyl halide (Scheme 2). However, it cannot be ascertained whether it is going exclusively through SN^1 or SN^2 path as, although several primary halides reacted faster, the reactions of two aliphatic bromides (entries 11 and 12 in Table 1) took much longer (300 and 250 min) compared to those with tertiary halides (entries 24−26, 25−31 min). When the tertiary halides are added to the preformed selenide anion, generated by the treatment of indium(I) iodide and diphenyl diselenide, the reactions were found to be slightly faster than the one-pot reactions. Thus, it may be assumed that at least tertiary halides are undertaking an SN^1-type path. However, tertiary halides remained virtually inert when added to the selenide

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(1) (a) Cintas, P. *Synlett* **1995**, 1087. (b) Li, C.-J. *Tetrahedron* **1996**, *52*, 5643. (c) Li, C.-J.; Chan, T. H. *Tetrahedron* **1999**, *55*, 11149. (d) Chauhan, K. K.; Frost, C. G. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3015. (e) Ranu, B. C. *Eur. J. Org. Chem*. **2000**, 2347. (f) Babu, G.; Perumal, P. T. *Aldrichimica Acta* **2000**, *33*, 16. (g) Podelech, J.; Maier, T. C. *Synthesis* **2003**, 633.

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(5) Nobrega, J. A.; Goncalves, S. M. C.; Peppe, C. *Tetrahedron Lett*. **2000**, *41*, 5779; **2001**, *42*, 4745.

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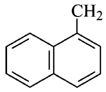
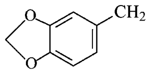
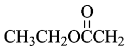
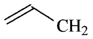
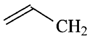
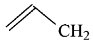
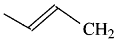
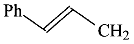
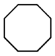
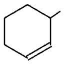
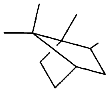
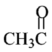
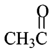
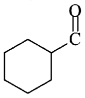
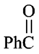
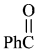
TABLE 1. Synthesis of Alkyl Phenyl Selenides and Alkyl Selenobenzoates

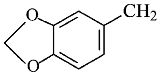
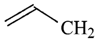
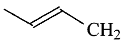
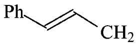
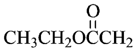
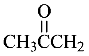
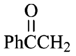
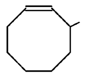
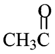
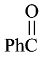
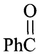
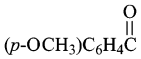
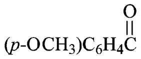
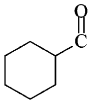
$$R\text{-}X + PhSeSePh \xrightarrow[CH_2Cl_2,\ rt]{InI} R\text{-}SePh$$

entry	R	X	time (min)	yield (%)[a]	Ref
1	$PhCH_2$	Cl	12	91	8c
2	$PhCH_2$	Br	10	94	8c
3	$PhCH_2$	I	5	97	8c
4	$(p\text{-}Cl)C_6H_4CH_2$	Br	10	93	
5	$(p\text{-}OMe)C_6H_4CH_2$	Br	30	89	
6		Br	7	96	
7		Br	12	87	
8	$(p\text{-}NO_2)C_6H_4CH_2$	Br	25	85	
9	$PhCH_2CH_2$	Br	60	89	
10	$PhCH_2CH_2$	I	40	92	
11	$CH_3(CH_2)_{10}CH_2$	Br	300	83	8c
12	$CH_3(CH_2)_3CH_2$	Br	250	80	
13	 $CH_3CH_2O\overset{\overset{O}{\|}}{C}CH_2$	Br	60	87	
14		Cl	25	87	8c
15		Br	17	90	8c
16		I	15	88	8c
17		Br	30	81	8c
18		Br	35	73	
19	$(CH_3)_2CH$	Br	60	80	
20	PhCH(Me)	Br	7	93	
21		I	20	90	
22		Br	10	89	
23		Br	12	83	
24	$(CH_3)_3C$	Cl	31	85	8c
25	$(CH_3)_3C$	Br	30	88	8c
26	$(CH_3)_3C$	I	25	85	8c
27	 $CH_3\overset{\overset{O}{\|}}{C}$	Cl	40	52	
28	 $CH_3\overset{\overset{O}{\|}}{C}$	I	25	64	
29		Cl	30	55	8d
30	 $Ph\overset{\overset{O}{\|}}{C}$	Cl	45	72	8c
31	 $Ph\overset{\overset{O}{\|}}{C}$	I	25	73	8c

[a] Yields refer to those of pure isolated products characterized by IR and ^1H and ^{13}C NMR spectroscopic data and elemental analysis.

TABLE 2. Synthesis of Alkyl Aryl Sulfides and Alkyl Thiobenzoates

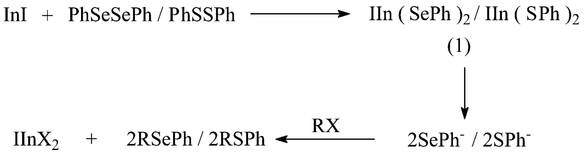
$$R\text{-}X + ArSSAr \xrightarrow[CH_2Cl_2,\ r.t]{InI} R\text{-}SAr$$

entry	R	X	Ar	time (h)	yield (%)[a]	Ref
1	$PhCH_2$	Cl	C_6H_5	3	75	9d
2	$PhCH_2$	Br	C_6H_5	2.5	80	9d
3	$PhCH_2$	I	C_6H_5	2.5	79	9d
4	$PhCH_2$	Br	$(p\text{-}Cl)C_6H_4$	2.5	76	3c
5	$(p\text{-}OCH_3)C_6H_4CH_2$	Br	C_6H_5	2.4	82	3c
6		Br	C_6H_5	2.2	80	3c
7	$CH_3(CH_2)_3CH_2$	Br	C_6H_5	5	70	
8		Br	C_6H_5	3.5	50	9b
9		Br	C_6H_5	4	75	
10		Br	C_6H_5	4	60	
11	 $CH_3CH_2O\overset{\overset{O}{\|}}{C}CH_2$	Br	C_6H_5	3	77	
12	 $CH_3\overset{\overset{O}{\|}}{C}CH_2$	Cl	C_6H_5	2.2	82	
13	 $Ph\overset{\overset{O}{\|}}{C}CH_2$	Br	C_6H_5	2	80	9e
14	$PhCH(CH_3)$	Br	C_6H_5	2.3	81	3c
15	$PhCH(CH_3)$	Br	$(p\text{-}Cl)C_6H_4$	2.5	80	3c
16	PhCH(Ph)	Br	C_6H_5	1	85	
17	$(CH_3)_2CH$	Br	C_6H_5	3	77	9b
18		Br	C_6H_5	3.5	65	
19	$(CH_3)_3C$	Cl	C_6H_5	1.2	80	
20	$(CH_3)_3C$	Br	C_6H_5	1	80	
21	 $CH_3\overset{\overset{O}{\|}}{C}$	Cl	C_6H_5	2	81	8d
22	 $Ph\overset{\overset{O}{\|}}{C}$	Cl	C_6H_5	1.5	86	8d
23	 $Ph\overset{\overset{O}{\|}}{C}$	Cl	$(p\text{-}Cl)C_6H_4$	1.75	82	
24	 $(p\text{-}OCH_3)C_6H_4\overset{\overset{O}{\|}}{C}$	Cl	C_6H_5	1.75	80	9c
25	 $(p\text{-}OCH_3)C_6H_4\overset{\overset{O}{\|}}{C}$	Cl	$(p\text{-}Cl)C_6H_4$	1.5	78	
26		Cl	C_6H_5	1.5	74	8d

[a] Yields refer to those of pure isolated products characterized by IR and ^1H and ^{13}C NMR spectroscopic data and elemental analysis.

anion generated by other reagents such as $NaBH_4$ or lanthanum metal and iodine.[8c] The free radical pathway, although not ruled out, is not favored, as no dimerization was observed during the reactions of benzoyl chloride and iodide, which produced phenyl selenobenzoate (entries 30

SCHEME 2. Possible Reaction Pathway for the Formation of Selenides and Sulfides



and 31, Table 1) or phenyl thiobenzoate (entries 22−25, Table 2) as sole products. The isolation of only the α-addition products from the reactions of crotyl bromide (entry 17 in Table 1 and entry 8 in Table 2) and cinnamyl bromide (entry 18 in Table 1 and entry 10 in Table 2) also does not support the free radical pathway.

In general, the reactions are fast, clean, and high-yielding, leading to the synthesis of diorganyl selenides, selenoesters, sulfides (thioethers), and thioesters. Organic selenides are of considerable interest in academia as well as in industry because of their wide involvement as key intermediates in various organic transformations and use as a food supplement.[6] On the other hand, disufides (thioethers) and thioesters are very versatile building blocks for the synthesis of various organo-sulfur compounds, and they also play important roles in biological and chemical processes.[7] Although quite a number of procedures for the synthesis of organoselenium compounds have already been published,[8] most of them usually require the handling of unstable reagents, strongly basic or acidic reaction conditions, and two-step procedures. A recent one-step procedure[8c] using lanthanum metal and iodine, although convenient and efficient for simple substrates, demonstrates virtually no reaction with tertiary alkyl halides and low yield (43% by GC) with benzoyl chloride (no other acid chloride has been addressed). On the other hand, although there are numerous methods available in the literature[9] for the preparation of thioethers and thioesters, the majority of them are carried out under basic conditions with a limited scope and yields are not always satisfactory. However, the present procedure addresses a large number of structurally different substrates, including tertiary alkyl halides and acid chlorides, and involves a new strategy.

Conclusion

It can be concluded that a one-pot procedure for the synthesis of alkyl phenyl selenides, sulfides (thioethers), selenoesters, and thioesters has been developed involving indium(I) iodide-mediated cleavage of diorganyl selenides and sulfides and subsequent reaction with alkyl or acyl halides. The significant advantages offered by this method are operational simplicity, faster reaction, neutral and mild (room temperature) reaction conditions, general applicability (coupling with tertiary alkyl halides and acyl halides), and high isolated yields of products, and thus it provides a better and practical alternative to the existing procedures.[8,9] Moreover, this strategy demonstrates the synthetic potential of indium(I) iodide, and further synthetic applications of this reagent are in progress.

Experimental Section

General Experimental Procedure for the Synthesis of Diorganyl Selenides, Sulfides, Selenoesters, and Thioesters. Representative Procedure for Benzyl Phenyl Sulfide (Thioether). To a stirred solution of benzyl bromide (171 mg, 1 mmol) and diphenyl disulfide (109 mg, 0.5 mmol) in dry methylene chloride (2 mL) was added indium(I) iodide (121 mg, 0.5 mmol) at room temperature under argon. The reaction mixture was stirred for 2.5 h (TLC) and quenched with a few drops of H_2O. The mixture was then extracted with ether (3 × 15 mL), and the combined ether extract was washed with brine, dried (Na_2SO_4), and evaporated to leave the crude product, which was purified by column chromatography over silica gel (hexane/ether 95:5) to furnish the pure benzyl phenyl sulfide (thioether) as a colorless liquid (low melting solid) (160 mg, 80%).[9f] The spectroscopic data (^{1}H and ^{13}C NMR) of this compound are in good agreement with those reported.[10]

This procedure was followed for the synthesis of all products listed in Tables 1 and 2. Although this procedure is described in mmol scale, a few gram scale reactions are also carried out with comparable yields. The known compounds were identified by comparison of their spectral data with those reported (Tables 1 and 2), and the new compounds were properly characterized by their IR, ^{1}H NMR, and ^{13}C NMR spectroscopic data and elemental analysis. One representative example (entry 4, Table 1) is given below, and data for other unknown products are provided in Supporting Information in the order of their entries in Tables 1 and 2.

(4-Chlorophenyl)methyl Phenyl Selenide (Entry 4, Table 1): pale yellow liquid; IR 1475, 1577, 1595 cm^{-1}; ^{1}H NMR δ 4.04 (s, 2H), 7.1 (d, J = 8.4 Hz, 2H), 7.20 (m, 2H), 7.28−7.33 (m, 3H), 7.42−7.45 (m, 2H); ^{13}C NMR δ 31.8, 128.0, 128.9 (2C), 129.4 (2C), 130.2, 130.5 (2C), 132.9, 134.3 (2C), 137.7. Anal. Calcd for $C_{13}H_{11}SeCl$: C, 55.44; H, 3.93. Found: C, 55.49; H, 3.91.

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Supporting Information Available: General experimental requirements and spectroscopic (IR, ^{1}H NMR, and ^{13}C NMR) data and elemental analysis of all new products listed in Tables 1 and 2. This material is available free of charge via the Internet at http://pubs.acs.org.

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