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PHENYL SELENIUM TRICHLORIDE IN SYNTHESIS. REACTION WITH KETONES. A NEW VARIATION OF THE SELENOXIDE ELIMINATION REACTION

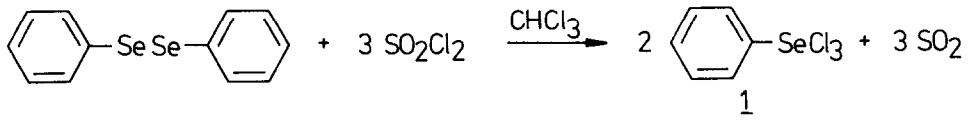
Lars Engman
Department of Organic Chemistry, Royal Institute of Technology
S-100 44 Stockholm, Sweden

Phenyl selenium trichloride was used for the introduction of a $PhSeCl_2$-group into the α-position of ketones. These products were converted to enones (hydrolysis/selenoxide elimination) or α-phenylselenoketones (thiourea-reduction).

A variety of methods are now available for the introduction of selenium into organic molecules. Some highly constructive ways to remove selenium from an organic moiety, once it has served its role as a handle for further functionalization have also been reported.[1] These two characteristics of selenium chemistry have recently focused considerable attention to selenium-mediated transformations in synthetic organic chemistry.[2]

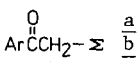
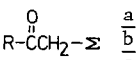
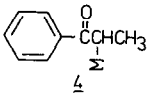
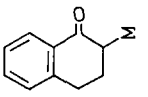
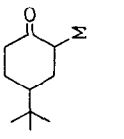
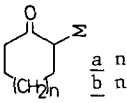
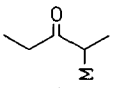
Selenium is commonly introduced in the divalent state into organic molecules, starting from the commercially available benzeneselenenyl halides, elemental selenium, diphenyl diselenide or N-(phenylseleno)phthalimide. We would like to report the introduction of tetravalent selenium by the use of phenyl selenium trichloride, $PhSeCl_3$ (1).

Phenyl selenium trichloride has found very limited use in organic synthesis, probably due to its reputation of being thermally unstable and hygroscopic.[3] We have found that $PhSeCl_3$ can be conveniently prepared on a large scale by treatment of diphenyl diselenide in chloroform with sulfuryl chloride (eq. 1). If the precipitated yellowish material is rapidly filtered, dried and kept in a freezer (-20 °C), it can be stored and used for at least one month without any visible decomposition.

(1) 

Phenyl selenium trichloride readily introduces a $PhSeCl_2$-group into the α-position of a ketonic substrate, as shown below for acetophenone (eq. 2). When the reaction was performed in dry ethyl ether, the insoluble product 2a could be isolated in 73% yield after 13 h. Table 1 summarizes yields, reaction times and temperatures for the reaction of $PhSeCl_3$ with a variety of ketones. The products were often ether-soluble and had to be precipitated (entries 6-19) by the addition of light petroleum. If the compounds (Table 1) were kept at ambient temperature

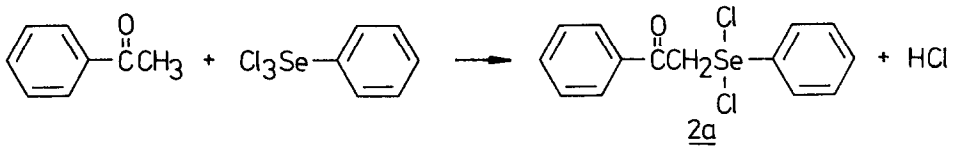
TABLE 1 Reactions of phenyl selenium trichloride with ketones (Σ=$SeCl_2Ph$)

entry	ketone	product		yield(%)	reaction time	temp(°C)
1	acetophenone	 2	a Ar=phenyl	73	13 h	20
2	4-methylacetophenone		b Ar=4-methylphenyl	87	2 h	20
3	4-nitroacetophenone		c Ar=4-nitrophenyl	91	20 h	20
4	2-acetylnaphthalene		d Ar=2-naphthyl	76	16 h	20
5	2-acetylthiophene		e Ar=2-thienyl	97	3 h	20
6	acetone	 3	a R=Me	97	30 min	20
7	ethyl methyl ketone		b R=Et[a]	71	30 min	20
8	methyl propyl ketone		c R=Pr	47	15 min	20
9	pinacolone		d R=t-Bu	83	1 h	20
10	levulinic acid		e R=CH_2CH_2COOH[b]	78	1 h	20
11	propiophenone	 4		62	2 h	20
12	α-tetralone	 5		40	10 min	20
13	4-t-butylcyclohexanone	 6		54	10 min	20
14	cyclopentanone	 7	a n=0	81	20 min	5
15	cyclohexanone		b n=1	65	10 min	5
16	cycloheptanone		c n=2	81	15 min	20[c]
17	cyclooctanone		d n=3	56	15 min	20[c]
18	cyclododecanone		e n=7	60	30 min	20[c]
19	diethyl ketone	 8		58	45 min	20

[a] a mixture of methyl- and methylene-substituted products (57/43) was obtained [b] a mixture of methyl- and methylene-substituted products (66/34) was obtained [c] initially at 0 °C

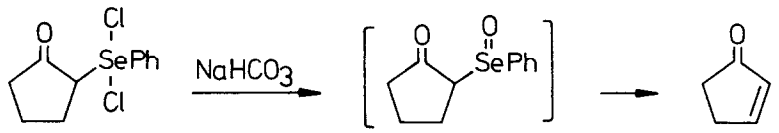
for a prolonged time they slowly decomposed. The white crystals of compound 7b typically turned into a yellowish liquid when exposed to the laboratory atmosphere overnight. In solution this decomposition was even more rapid. However, satisfactory ^1H NMR spectra could be recorded for all compounds.

Methyl propyl ketone cleanly afforded the methyl-substituted product 3c with $PhSeCl_3$. This good regioselectivity was usually not observed with unsymmetrical ketones (Table 1, entries 7 and 10). We also observed that certain ketones failed to give the desired substitution products.[4] Experiments with aldehydes, acids, lactones and esters indicated that these substrates were less reactive than ketones.

(2) 

2a

The selenoxide syn-elimination reaction represents one of the most important reactions for the introduction of unsaturation into organic molecules.[5] The outcome of the process is often critically dependent on the choice of oxidant for the conversion of the selenium(II)-compound to the selenium(IV)-oxide - the active eliminating species. Our products, prepared from $PhSeCl_3$ and ketones already contain tetravalent selenium in the form of a selenium dichloride. If this functional group could be hydrolyzed to a selenoxide, the product would be expected to undergo a rapid elimination reaction, provided β-hydrogens are available. The realization of this protocol is exemplified below for the conversion of compound 7a to 2-cyclopentenone (9a) (eq. 3). Hydrolysis was conveniently effected in a separatory funnel containing aqueous

(3) 

$NaHCO_3/CH_2Cl_2$ and the product was isolated by Kugel-rohr distillation. Table 2 summarizes our attempts to synthesize enones via this new variation of the selenoxide elimination reaction. It should be pointed out that cyclic enones are usually difficult to obtain in good yields by using conventional selenium techniques. Some recent results by Toshimitsu[6] indicate that this may be due to the intrinsicly poor leaving group properties of PhSeOH. For the synthesis of cyclic enones, our new variation of the selenoxide elimination reaction has the definite advantage of avoiding the use of ozone, which is otherwise required. Mechanistically, our reaction sequence bears some resemblance to the benzeneseleninic anhydride-induced conversion of ketones to enones.[7] Both methods introduce selenium(IV) in the crucial step.

Phenyl selenium trichloride may also be useful for the introduction of phenyseleno-groups into organic molecules, provided the $PhSeCl_2$-group can subsequently be reduced to a PhSe-group. This transformation is by no means trivial for the relatively unstable compounds contained in Table 1. However, we have found that thiourea in acetone[8] cleanly reduced many selenium dichlorides, in excellent yields to the corresponding selenides (see Table 3). Our two-step syntheses of α-phenylseleno acetophenone (10a) and α-phenylseleno acetone (11a) are highly advantageous when compared to other published preparations of these compounds.[9] It should be emphasized that the usefulness of α-phenylseleno ketones is not only restricted to the preparation of enones. These materials can also undergo regiospecific alkylation α to selenium.[10] Furthermore, if the carbonyl group is reduced, the resulting β-hydroxyalkyl selenides can be converted to olefines, epoxides or allylic alcohols.[1]

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TABLE 2 Syntheses of enones (selenoxide elimination)

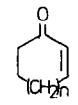
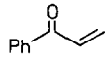
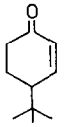
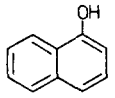
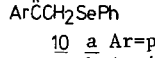
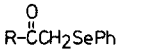
Se(IV)-compound	product		yield(%)
7a		a n=0	64
7b		b n=1	47
7c	9	c n=2	74
7d		d n=3	80
7e		e n=7	79
4			97
6			68
5			52

TABLE 3 Syntheses of α-phenylseleno ketones (thiourea-reduction)

Se(IV)-compound	product		yield(%)
			
2a	10	a Ar=phenyl	98
2b		b Ar=4-methylphenyl	99
2c		c Ar=4-nitrophenyl	71
2d		d Ar=2-naphthyl	93
2e		e Ar=2-thienyl	98
			
3a	11	a R=Me	99
3c		b R=Pr	87
3d		c R=t-Bu	88
3e		d R=CH_2CH_2COOH[a]	99

[a] aqueous $Na_2S_2O_5/CH_2Cl_2$ was used for this reduction

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