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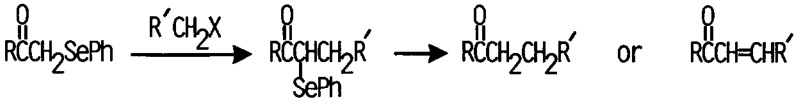
HOMOLOGATION OF SELENOESTERS TO (PHENYLSELENO)- OR (METHYLSELENO)METHYL KETONES WITH DIAZOMETHANE

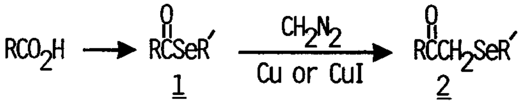
Thomas G. Back* and Russell G. Kerr
Department of Chemistry, University of Calgary
Calgary, Alberta, Canada, T2N 1N4

Abstract: The copper or cuprous iodide-catalyzed insertion of diazomethane into the acylselenium linkage of selenoesters 1a- 1f and selenocarbonate 1g afforded the corresponding ketones 2a- 2f and the ester 2g, respectively, as the chief products.

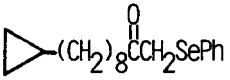
The synthetic utility of α-phenylseleno ketones has been previously described and stems from their ability to undergo regiospecific alkylation via their enolates. The alkylated products may be further converted to either saturated or α, β-unsaturated ketones by the reductive or oxidative removal of the selenium-containing residue[1].



The selenenylation of ketone enolates has been a common source of α-phenylseleno ketones, despite potential difficulties in achieving regiochemical control[1]. More recently, (phenylseleno)methyl ketones have also been prepared from terminal olefins[2] or acetylenes[3], as well as from Grignard reagents and phenylselenoacetaldehyde[4]. We now report an alternative approach to these compounds based on the novel homologation of selenoesters 1 with diazomethane in the presence of copper powder or cuprous iodide to provide the desired ketones 2 as the principal products[5]. Since selenoesters are themselves readily available from a variety of carboxylic acid derivatives[6], the present technique provides a versatile complement to existing methodology.



The experimental procedure is simple to perform. Typically, the selenoester (ca. 150 mg) and the catalyst (ca. 100 mg) were stirred in excess ethereal, alcohol-free diazomethane behind a safety shield until tlc or gc indicated consumption of the starting material (4-12 h). Additional portions of the diazomethane solution were added during the reaction to maintain the reagent in excess at all times. Workup was effected by filtration of the catalyst and preparative tlc of the crude reaction mixture on silica gel. The results are summarized in the accompanying Table. Aryl, alkyl and heterocyclic selenoesters 1a- 1e were thus converted to the corresponding (phenylseleno)methyl ketones 2a- 2e in yields of 42%- 65%. The method is compatible with unsaturated substrates and the formation of 2e was accompanied by only a trace (5 %) of the cyclopropane derivative 3. Cyclopropanation[7] is apparently less facile than the desired insertion reaction of the selenoester moiety. The homologation process was also successfully applied to the Se-methyl selenoester 1f and the selenocarbonate 1g , providing the ketone 2f and the ester 2g in yields of 46% and 48% respectively. We also observed that thioester 4 failed to react significantly with diazomethane in the presence of copper powder. Similarly, selenoester 1a did not undergo insertion when treated with ethyl diazoacetate. Evidently, selenoesters are considerably more reactive than their sulfur analogues in this process, and diazo compounds are inactivated by the presence of the delocalizing ester group.



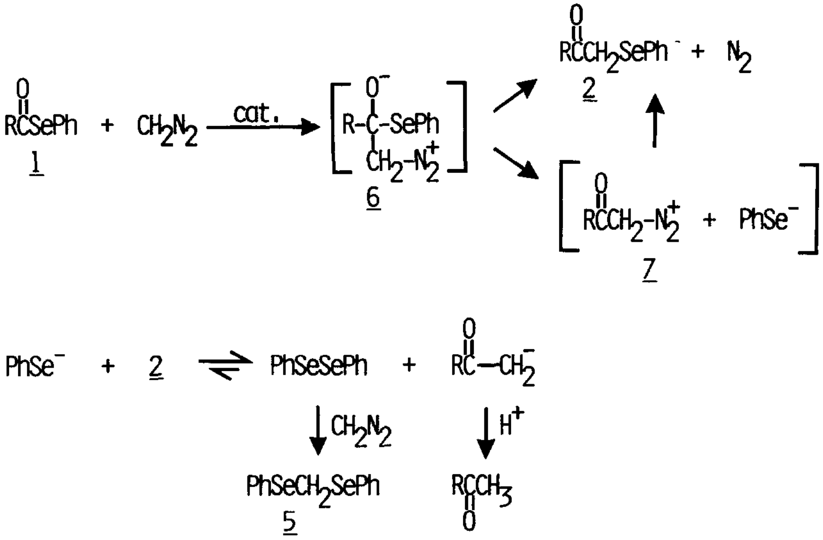
3

$PhC(=O)SPh$

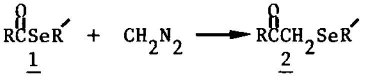
4

Diphenyl diselenide and bis(phenylseleno)methane(5) were isolated in substantial amounts during the preparation of compounds 2a- 2e and 2g. Acetophenone was also detected by gc-mass spectral analysis as a major byproduct of 2a. These byproducts would be difficult to rationalize if the reaction proceeded by a simple carbene or carbenoid insertion of methylene into the acyl-selenium bond. A more satisfactory explanation invokes the initial formation of the tetrahedral intermediate 6, followed by rearrangement[8] to the (phenylseleno)methyl ketones 2 or by collapse of 6 to species 7 and selenolate anion ($PhSe^-$). In the latter instance, nucleophilic displacement of nitrogen from 7 by the anion would again provide 2. The selenolate is also known to equilibrate with α-phenylseleno ketones to generate diphenyl diselenide and the corresponding enolate[9]. Protonation of the enolate accounts for the observed formation of acetophenone from 1a, while further reaction of the diselenide with diazomethane provides the remaining product 5[10]. These processes are depicted in the Scheme. The lower reactivity of ethyl diazoacetate compared to diazomethane is also consistent with this mechanism as intermediate 6 should form more readily from the more nucleophilic diazo compound. The role of the catalyst is as yet unclear, but it is possible that it serves to activate the selenoester towards nucleophilic attack in the initial step[11]. The reactions of other organoselenium compounds with diazo species may also prove of synthetic value and are under continued investigation.

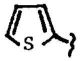
Scheme



Table



$RC(O)SeR' + CH_2N_2 \longrightarrow RC(O)CH_2SeR'$

Product[a]	R	R′	Catalyst	Isolated Yield (%)
2a	Ph	Ph	Cu	53
2b	Me	Ph	Cu CuI	65 63
2c	$PhCH_2$	Ph	Cu	56
2d		Ph	Cu	42
2e	 $(CH_2)_8$	Ph	CuI	55
2f	Ph	Me	CuI	46
2g[b]	MeO	Ph	CuI	48

a) All products were identified by their ir, nmr and mass spectra. New compounds 2d, 2e and 2f gave satisfactory combustion analyses. All products were oils except 2d, mp 45-46° C, and 2e, mp 37-39° C.

b) A longer than normal reaction time of 2 days was required.

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