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PREPARATION OF 1-PHENYLSELENO 2-ALKANONES FROM TERMINAL OLEFINS AND THEIR APPLICATION TO ORGANIC SYNTHESIS

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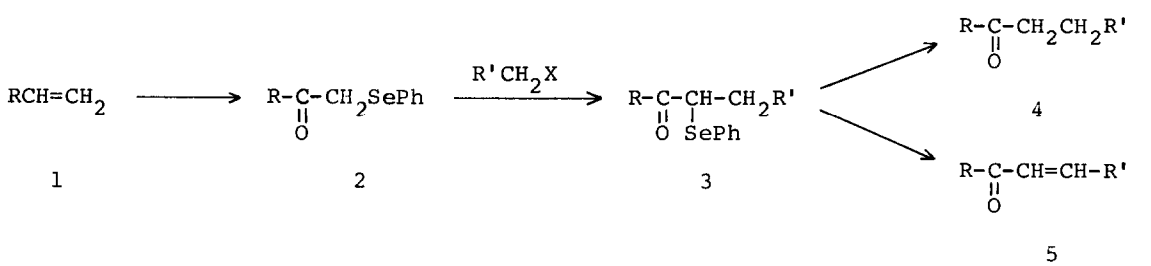
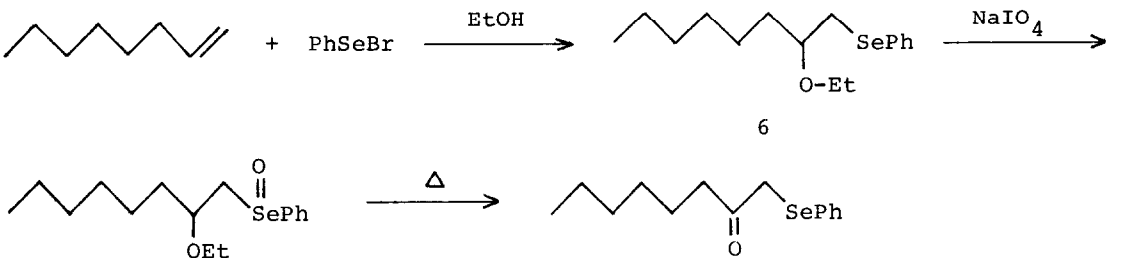
We wish to report a simple preparative method for 1-phenylseleno 2-alkanones 2 from terminal olefins and their use in organic synthesis. The method is based on the addition reaction of phenylselenenyl bromide in ethyl alcohol to terminal olefins, and subsequent oxidation and thermal treatment of the adduct.

Organoselenium compounds are useful reagents on which extensive studies have been carried out.[1-3] Especially facile addition reaction of phenylselenenyl halides to olefins is a well established reaction,[4-9] but so far the reaction is concerned mostly with internal olefins and few detailed studies on the addition reaction of phenylselenenyl halides to terminal olefins have been carried out.[10] α-Phenylseleno ketones are useful intermediate in organic synthesis and they are prepared usually from ketones in order to prepare α,β-unsaturated ketones by elimination. Again no studies have been reported on the synthetic use of 1-phenylseleno derivatives of methyl ketones. 1-Phenylseleno 2-alkanones easily prepared in high yields from terminal olefins by our method are useful compounds because regiospecific generation of an enolate is possible at C_1 position, which can be alkylated to give alkylated ketones 3. The oxidative and reductive removals of the phenylseleno group from the alkylated ketones 3 lead respectively to saturated ketones 4 and unsaturated ketones 5. Thus the following useful overall transformation of terminal olefins to the ketones is possible.



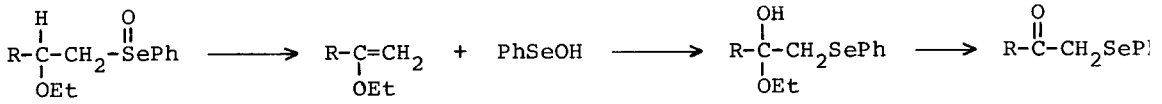
The preparation of phenylseleno ketones 2 was carried out by the following way. To a solution of 1-octene (3 mmol) in dry ethanol (15 ml) was added PhSeBr (3.6 mmol) dissolved in dry ethanol at room temperature, and

1-phenylseleno-2-ethoxyoctane (6) was obtained as an oil in 95% yield. NMR (CCl_4) δ 7.6-7.0 (m, 5H, PhH), 3.7-3.1 (m, 3H, R-CHOCH$_2$CH$_3$), 3.0-2.8 (m, 2H, -CH$_2$-Se-), 2.0-0.6 (m, 16H); IR (neat) 2920, 1580, 1100 cm^{-1}; Rf = 0.64 (2.5% isopropyl alcohol in n-hexane). The adduct 6 was oxidized at room temperature with $NaIO_4$ in aqueous methanol to give thermally labile 1-phenylselenoxy-2-ethoxyoctane (7), Rf = 0.22 (5% isopropyl alcohol in n-hexane), which was heated in toluene at a refluxing temperature for 30 min to give 1-phenylseleno-2-octanone (8) in 85% overall yield from 6. NMR (CCl_4) δ 7.6-7.0 (m, 5H, PhH), 3.40 (s, 2H, -SeCH$_2$-C=O), 2.48 (t, 2H, J = 6.0 Hz, -CH$_2$-CO), 1.8-1.10 (m, 8H), 0.88 (t, 3H, J = 5 Hz, CH$_3$-); IR (neat) 1700 and 1580 cm^{-1}. Similarly, phenylselenoacetophenone was obtained from styrene in 73% overall yield.



6 7 8

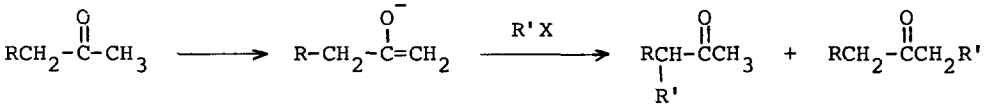
Although more detailed mechanistic studies are necessary, we tentatively explain the formation of 2 by elimination of PhSeOH from 7 and subsequent readdition of PhSeOH to vinyl ether 9 to form hemiacetal 10 which is hydrolyzed to afford ketone 2. As a related reaction, the conversion of 2-(phenylseleno)ethyl ethers to acetaldehyde and alcohols via vinyl ethers has been reported.[11]



7 9 10 2

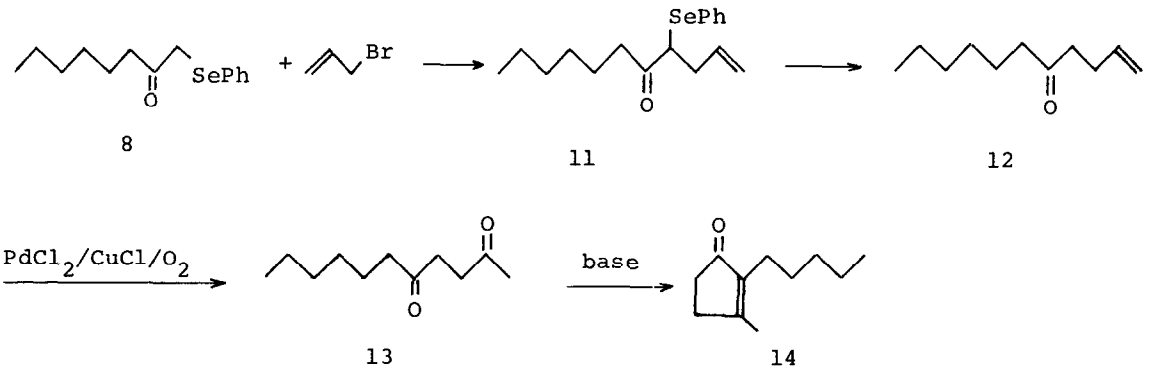
1-Phenylseleno 2-alkanones 2 easily prepared by this method have considerable synthetic utility. Regiospecific reactions of kinetic enolate of methyl ketones are important method in organic synthesis. For example the successful regiospecific aldol condensation of methyl ketones via kinetic enolate at -78° was carried out by Stork.[12] However, the regiospecific

alkylation of the kinetic enolate of methyl ketones is not possible due to rapid equilibration of the anions of methyl ketones during the alkylation.[12,13]



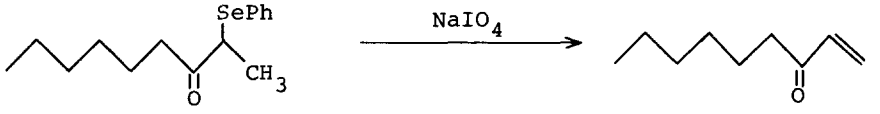
By virtue of the stabilizing effect of the neighbouring phenylseleno group on the carbanion, the regioselective alkylation of 2 can be achieved.

The alkylation of 2 was carried out at 25° in t-butyl alcohol containing one equivalent of t-BuOK with one equivalent of alkyl halide (methyl iodide, n-butyl iodide,[14] and allyl bromide). In a typical example, a solution of t-BuOK (224 mg, 2 mmol) in dry t-butyl alcohol (15 ml) was added dropwise at 25° to a mixture of 1-phenylseleno-2-octanone (8, 283 mg, 1 mmol) and allyl bromide (182 mg, 1.5 mmol) in dry t-butyl alcohol (5 ml) and the mixture was stirred for 30 min. After the usual work-up and column chromatography, 4-phenylseleno-1-undecen-5-one (11, 280 mg, 0.87 mmol 87% yield) was obtained. NMR (CCl_4) δ 7.6-6.8 (m, 5H, PhH), 6.2-4.6 (m, 3H, olefinic) 3.4 (t, 1H, J = 8 Hz, -SeCH-CO-), 2.7-2.2 (m, 4H, $-CH_2-CO-C$, $CH_2=CH-CH_2-$); IR (neat) 1700, 1640, 1580 and 910 cm^{-1}. Similar reaction with methyl iodide afforded the corresponding methylated ketone in 71% yield.



The alkylated phenylseleno ketones are subjected to further modification. For example, reductive removal of the phenylseleno group gives saturated ketones. Thus triethylamine (2 ml) and thiophenol (0.3 ml) were added to the allylated ketone 11 (without isolation) and the mixture was stirred at room temperature for 30 min. By this way, 1-undecen-5-one (12) was obtained in 85% overall yield from 8. We have already reported the conversion of 12 to dihydrojasmone 14 via oxidation catalyzed by $PdCl_2/CuCl/O_2$ system and aldol condensation.[15]

Application of the well established method of oxidative elimination[16,17] of the phenylseleno groups gives the synthetically useful unsaturated ketones. The methylated ketone 15 was oxidized with $NaIO_4$ in methanol-water and 1-nonen-3-one (16) was obtained in 54% overall yield from 8. NMR (CCl_4) δ 6.4-5.5 (m, 3H, olefinic), 2.48 (m, 2H, J = 6.0 Hz, $-CH_2-CO$), 2.0-1.1 (m, 8H), 0.9 (t, 3H, J = 5 Hz, $-CH_3$); IR (neat) 1680 cm^{-1}.



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