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α-PHENYLSELENENYLATION OF ZIRCONIUM OR ALUMINUM ENOLATES

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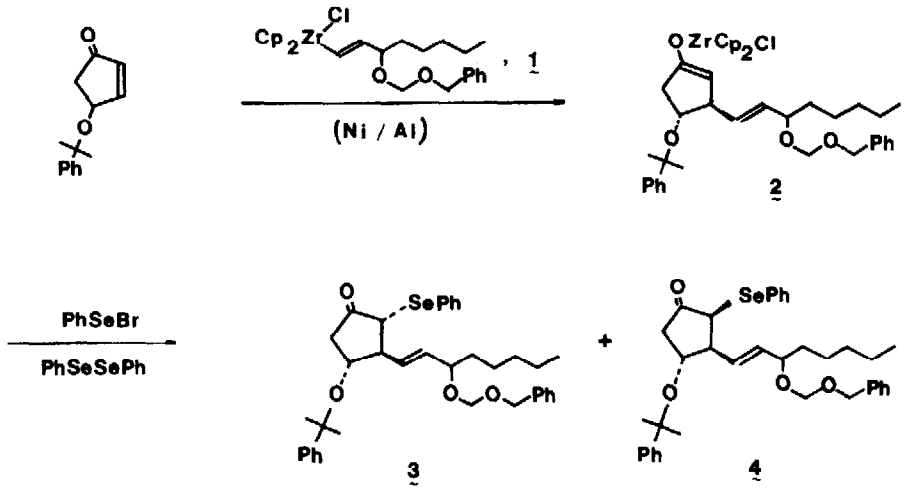
SUMMARY: Zirconium or aluminum O-enolates undergo selenenylation with PhSeBr to give α-(phenylselenenyl) ketones in good to excellent yield.

We recently noted that nickel-catalyzed conjugate addition of alkenylzirconium or alkynyl aluminum complexes to α,β-enones, followed by hydrolysis, could be used to prepare β-alkenyl- or -alkynyl-substituted ketones, respectively, in high yield.[1,2] These reactions proceed through the corresponding metal O-enolates, species of potential utility for the introduction of α-keto substituents, if work-up with reagents other than water is employed.

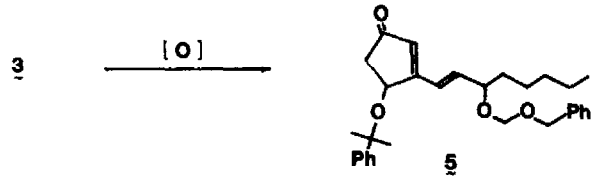
Heretofore, though, we have found that the scope of such alternative work-up procedures is rather circumscribed: Although formaldehyde traps the zirconium O-enolates in high yield[3] (and acetaldehyde reacts with them and with aluminum O-enolates[4] in lower yield), attempts at direct alkylation have been unsuccessful. We have been interested, consequently, in finding cleavage reagents for zirconium or aluminum O-enolates which could be used to introduce non-CH_2O-derived α-chain substituents by indirect means. Since α-phenylselenenylation can be used to direct the regiospecificity of ketone enolate formation,[5] and since such enolates can be readily alkylated, we studied the conversion of zirconium or aluminum O-enolates to the corresponding α-(phenylselenenyl) ketones. Selenenylation procedures which we have developed are described below.

3-(Benzyloxymethoxy)-1-octyne (1.1655 g, 4.731 mmol) was converted to zirconium alkenyl 1 by reaction with $Cp_2Zr(H)Cl$ in toluene at room temperature under argon.[1] Filtration, followed by evaporation of the solvent, afforded 1 as a viscous oil. A solution of the obtained zirconium alkenyl and 4-cumyloxy-2-cyclopentenone (0.6822 g, 3.154 mmol) in THF 50 mL was added to a premixed solution of $Ni(AcAc)_2$ (0.2430 g, 0.946 mmol) and i-Bu_2AlH (2.18 mL of a 0.435 M solution in toluene, 0.946 mmol) in THF 5 mL and the mixture was stirred at 0°C for 3.5 h under Ar. After cooling to -78°C, a solution of PhSeBr and PhSeSePh[6] [from 1.7040 g (5.460 mmol) of PhSeSePh and 188 μℓ (3.639 mmol) of Br_2 in THF 8 mL] was added and the mixture was stirred at the same temperature for 30 min. The resulting cold mixture was poured into saturated aqueous $NaHCO_3$ and the organic layer was extracted with 50% ether-hexane, washed with saturated aqueous NaCl and dried over Na_2SO_4. Evaporation residue was subjected to medium-pressure liquid

chromatography (silica, 20% ethyl acetate-hexane as eluent) to give compounds 3 and 4 in 50% and 31% isolated yield, respectively (based on 4-cumyloxy-2-cyclopentenone). The non-seleno ketone was also obtained (18% yield).[7] The stereochemical assignment of cis and trans isomers



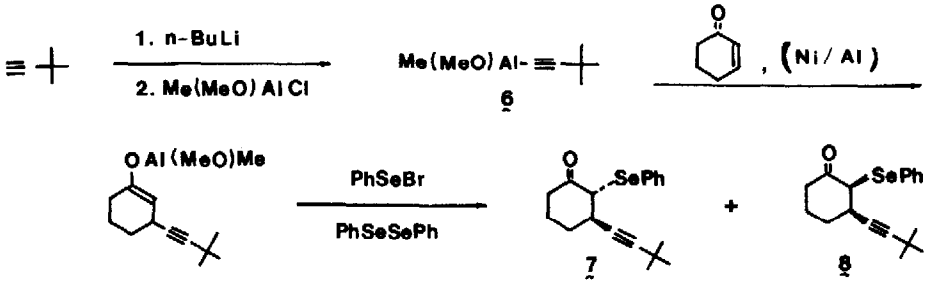
of these two seleno ketones was made by noting results of attempted conversions to oxidized species by selenoxide elimination:[5,8] Compound 3 was oxidized with 30% H_2O_2 in THF containing ammonium chloride/ammonia buffer; the cyclopentenone 5 was obtained in 70% yield (isolated). The other seleno ketone gave rise to a complex mixture of products upon attempted oxidation containing a small amount of 5.



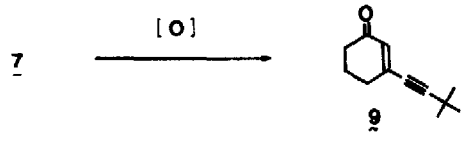
Phenylselenenyl chloride also acts as a selenenylating reagent; however, in much less satisfactory fashion. For example, it reacts with the zirconium enolate to give 3 in only 27% yield; here, no 4 was noted.

Aluminum enolates have been found to be less reactive towards phenylselenenylation than are the zirconium enolates. A typical procedure is noted. A solution of methoxymethylaluminum enolate was prepared[9] as follows: To methoxymethylaluminum chloride [obtained from dimethylaluminum chloride (10.74 mL of a 1.126 M solution in heptane, 12.12 mmol) and methanol (12.12 mmol)] was added previously prepared lithium acetylide and the reaction mixture was stirred

for 2 h at room temperature. To 462.4 mg (1.80 mmol) of $Ni(AcAc)_2$ in 30 mL ether was added at 0^0C 4.14 mL (1.80 mmol) of a 0.435 M i-Bu_2AlH solution in toluene, followed by addition of the above obtained methoxymethylaluminum acetylide 6 and 2-cyclohexenone (8.00 mmol). The reaction mixture was stirred at 0^0C for 4 h and then allowed to warm to room temperature for 12 h. To this mixture was added at -78^0C a solution of PhSeBr and PhSeSePh [from 2.9228 g (9.270 mmol) of PhSeSePh and 318 μl (6.180 mmol) of Br_2 in THF 12 mL] and the mixture was stirred at the same temperature for 4.0 h. The resulting mixture was hydrolyzed with aq KH_2PO_4 and the organic layer was extracted with ether. Products were separated using medium-pressure liquid chromatography (silica gel, 7% ethyl acetate-hexane as eluent). Compounds 7 and 8 were obtained in 33% and 10% yield (based on 2-cyclohexenone), respectively. Non-selenenylated ketone was also obtained (16% yield).[10]



Compound 7 was oxidized with 30% H_2O_2 in THF containing ammonium chloride-ammonia buffer solution to give 9 [11] in 66% isolated yield.



Other types of cleavage processes, which further extend the utility of Zr or Al enolates in organic synthesis, will soon be described.

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REFERENCES AND NOTES

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7. Compound 3 [IR (neat) 1744 cm^{-1}; NMR (CCl_4) δ 0.91 (3 H, t), 1.0-1.8 (8 H, m), 1.52 (6 H, s), 1.9-2.4 (2 H, m), 2.70 (1 H, br s), 3.08 (1 H, m), 3.60 (1 H, m), 4.00 (1 H, m), 4.4-4.8 (4 H, m), 5.3-5.5 (2 H, m), 7.0-7.7 (15 H, m)].

   Compound 4 [IR (neat) 1740 cm^{-1}; NMR (CCl_4) δ 0.90 (3 H, t), 1.0-1.8 (8 H, m), 1.51 (6 H, s), 1.9-2.4 (2 H, m), 2.94 (1 H, br s), 3.80 (1 H, m), 3.6-4.2 (2 H, m), 4.4-4.8 (4 H, m) 5.3-5.6 (2 H, m), 7.0-7.7 (15 H, m)].

8. Compound 5 [IR (CCl_4) 1713, 1644 cm^{-1}; NMR (CCl_4) δ 0.90 (3 H, br t), 1.0-1.8 (8 H, m), 1.62 (6 H, s), 2.0-2.4 (2 H, m), 4.16 (1 H, m), 4.4-4.8 (5 H, m), 5.98 (1 H, s), 6.0-6.4 (2 H, m), 7.0-7.6 (10 H, m)].

9. J. Schwartz, D. B. Carr, R. T. Hansen, and F. M. Dayrit, to be published.

10. Compound 7 [IR (CCl_4) 1705 cm^{-1}; NMR (CCl_4) δ 1.19 (9 H, s), 1.3-2.5 (6 H, m), 3.27 (1 H, br s), 3.66 (1 H, br s), 7.1-7.7 (5 H, m); mass (m/e) 332.334 (M^+)].

    Compound 8 [IR (CCl_4) 1705 cm^{-1}; NMR (CCl_4) δ 1.24 (9 H, s), 1.3-3.1 (7 H, m), 3.91 (1 H, m), 7.1-7.7 (5 H, m); mass (m/e) 332.334 (M^+)].

11. Compound 9 [IR (CCl_4) 2210, 1668 cm^{-1}; NMR (CCl_4) δ 1.29 (9 H, s), 1.7-2.5 (6 H, m), 6.03 (1 H, br s)].

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