

HOMOLYTIC CYCLIZATION OF SELENOL ESTERS. SYNTHESIS OF CHROMANONES

Mario D. Bachi* and Daniella Denenmark

Department of Organic Chemistry, The Weizmann Institute of Science, Rehovot, Israel.

Dedicated to Sir Derek Barton on the occasion of his 70th birthday.

Abstract - Acyl radicals produced by tributyltin hydride-azobisisobutyronitrile induced homolysis of phenylselenol esters undergo highly selective 6-exo-trig addition to double bonds, affording, in a chain reaction, cyclic oxo-compounds in very high yield. Suitably substituted phenylselenosalicylates are thus converted into the corresponding chromanones.

The intramolecular addition of carbon-centered free-radicals to carbon-carbon multiple bonds has recently become an extensively used process for the synthesis of cyclic organic compounds.¹⁻³ A convenient method for the site specific generation of carbon-centered free-radicals involves the chemospecific homolysis of a C-Halogen, C-S or C-Se bond by trialkyltin radicals derived from the corresponding tin hydrides.⁴ The first reports on the application of this method for the synthesis of multifunctional complex organic compounds involved the intramolecular addition of alkyl,⁵ vinyl⁶ and aryl⁷ radicals to carbon-carbon multiple bonds. While these early reports were subsequently followed by scores of others,¹⁻⁴ the analogous cyclization of carbonyl radicals has been rarely employed in synthesis. The first report on the intramolecular addition of acyl radicals to double bonds, dated 1964, is related to the cyclization of α -campholenic aldehyde to camphor induced by diacetyl peroxide.⁸ It was followed by three similar reports on peroxide-induced cyclization of unsaturated aldehydes,^{9,10} and by two contrasting reports on the reductive cyclization of acyl chlorides induced by tributyltin hydride (TBTH) and azobisisobutyronitrile (AIBN).^{11,12} An esr study indicated that at low temperatures, citronelloyl radical does not undergo ring closure.¹³ In 1986, we reported a novel efficient method for the synthesis of α -alkylidene- γ -lactones, which is based on the intramolecular addition of alkoxy carbonyl radicals to triple bonds.¹⁴ The success of this method¹⁵ led us to investigate the suitability of acyl radical annelation for the preparation of chromanones and other 6-membered cyclic ketones.¹⁶ We repeated the reaction of citronelloyl chloride 1a with TBTH/AIBN,¹¹ and compared it to the same reaction

Scheme I

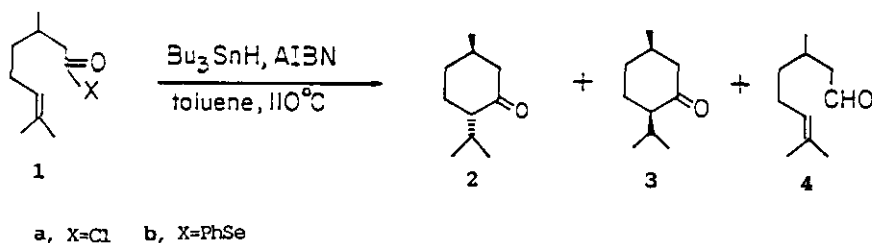


Table I: Reactions of Citronelloyl Chloride **1a** and of Phenylselenenyl Citronelloate **1b** with TBTH (1.15 equiv) and initiator or inhibitor (0.015 equiv) in Toluene at 110°C.

	1 X	Initiator/ Inhibitor	Mode of addition of TBTH/In	Products*			
				Cyclic		Acyclic	
				2+3	2/3	4	1
<u>a</u> **	Cl	AIBN	single	85%	1.5:1	10%	
<u>b</u> ***	Cl	AIBN	90 min	45%	1.5:1	--	
<u>c</u> **	Cl	Galvinoxyl	single	--		8%	
<u>d</u> **	PhSe	AIBN	single	87%	1.6:1	12%	
<u>e</u> ***	PhSe	AIBN	90 min	98%	1.6:1	--	
<u>f</u> **	PhSe	hydroquinone	single	--			100%

*Products determined by GC analysis 20 min after the start of the reaction. **Initial concentration of **1** was 0.02M; standard conditions.¹⁹ ***Individual solutions of TBTH (0.1M) and AIBN (0.01M) were simultaneously added to a solution of **1** (0.033M initial concentration).

with the selenol ester of citronelloic acid **1b**, as shown in Scheme I and Table I. In experiments performed by mixing all the reagents at the start of the reaction¹⁹ no substantial difference between the reaction patterns of the chloride **1a** and selenol ester **1b** was observed, both compounds (entries a and d) afforded cyclic products (menthone **2** and isomenthone **3**) in good yield, accompanied by non-negligible amount of acyclic reduction product (citronellal **4**). As expected, lowering the TBTH concentration suppressed the formation of acyclic aldehyde **4**. However, while in experiments involving the selenol ester **1b** the yield of ketones increased to a nearly quantitative value (entry e), a pronounced decrease in yield was observed in experiments involving the acyl chloride **1a** (entry b). The superiority of the selenol ester over the

acyl chloride derivative in the TBTH/AIBN induced homolytic cyclization seems to derive mainly from the lower susceptibility of selenol esters to competitive ionic reactions. Noteworthy is the stability of the ester 1b (and 5a-d, which are discussed later) to chromatography. In accord with a previous report on other acyl chlorides,²⁰ the acyl chloride 1a reacts spontaneously with TBTH in the absence of AIBN and in the presence of galvinoxyl²¹ to give citronellal (entry c), while the selenol ester 1b did not react at all under similar conditions (entry f). To study the application of the homolytic cyclization to the synthesis of chromanones the phenylselenosalicylates 5a-d were prepared,^{22,23} and reacted with TBTH/AIBN under standard conditions.¹⁹ In each case, the corresponding chromanone 7, deriving from 6-exo-trig cyclization of intermediate acyl radicals 6, as shown in Scheme II and Table II, was isolated in high yields. In none of these experiments were products derived from hydrogen transfer to an

Scheme II

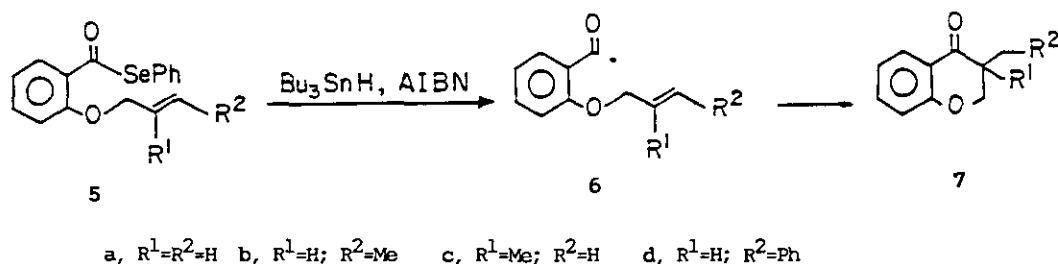
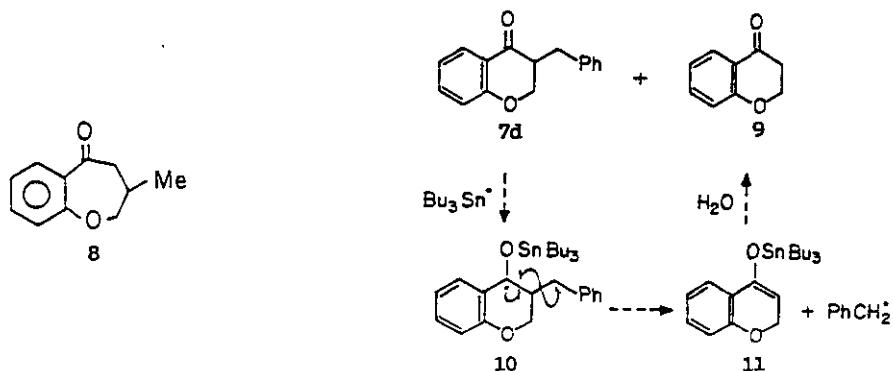


Table II: Reactions of Selenol Esters 5 with TBTH and AIBN.

Selenol Ester	Conditions/ concentration	Products (isolated yield)	
5a	standard ¹⁹ /0.02M	7a (90%)	
5b	standard ¹⁹ /0.02M	7b (87%)	
5c	standard ¹⁹ /0.02M	7c (79%)	8 (8%)
5c	standard ¹⁹ /0.2M	7c (74.5%)	8 (7.5%)
5c	standard ¹⁹ /neat	7c (75%)	8 (7%)
5c	low TBTH conc. ²⁵	7c (77%)	8 (8%)
5d	standard ¹⁹ /0.02M	7d (91%)	9 (3%)
5d	low TBTH conc. ²⁶	7d (70%)	9 (17%)

acyl radical of type 6 identified. Particularly gratifying is the absence of products derived from intramolecular abstraction of allylic hydrogen atoms through a six-membered ring transition state as was observed in an attempted 6-exo-trig cyclization of 6-heptenyl radicals.²⁴

Scheme III



A 7-endo cyclization product was identified in the reaction of the methallyl derivative 5c. Thus, the chromanone 7c was accompanied by the 7-membered ring oxo-compound 8. The observed (Table II) independence of the 7c/8 ratio on the TBTH concentration indicates kinetic partition rather than a thermodynamic process involving ring expansion.^{27,28}

The cyclization of 5d afforded, in addition to the benzylchromanone 7d, the chromanone 9. The formation of this compound is due to attack of tributyltin radical on the primary product 7d, giving the adduct radical 10, which loses benzyl radical through β -cleavage, affording the tin enolate 11 as shown in scheme III.

The TBTH/AIBN-induced cyclization of selenol esters is clearly a useful method for the preparation of chromanones and other 6-membered ring oxo-compounds under mild non-polar conditions.²⁹

ACKNOWLEDGEMENT

We thank the Minerva Foundation (Munich, Germany) for financial support.

REFERENCES AND NOTES

1. J.-M. Surzur, "Reactive Intermediates", Ed. by A.R. Abramovitch; Plenum Press, New York, 1982, Vol.2, p.121.
2. B. Giese, "Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds", Pergamon Press, Oxford, 1986.

3. (a) D.J. Hart, Science, 1984, 223, 883. (b) M. Ramaiah, Tetrahedron, 1987, 43, 3541. (c) D.P. Curran, Synthesis, 1988, 417.
4. W.P. Neumann, Synthesis, 1987, 665.
5. See for example: (a) G. Büchi and H. Wuest, J. Org. Chem., 1979, 44, 546. (b) M.D. Bachi and C. Hoornaert, Tetrahedron Lett., 1981, 22, 2689; 2693. (c) M.D. Bachi and C. Hoor-naert, Tetrahedron Lett., 1982, 23, 2025. (d) D.J. Hart, Y.-M. Tsai, J. Am. Chem. Soc., 1982, 104, 1430.
6. G. Stork and N.H. Baine, J. Am. Chem. Soc., 1982, 104, 2321.
7. Y. Ueno, K. Chino, and M. Okawara, Tetrahedron Lett., 1982, 23, 2575.
8. R. Dulou, Y. Chretien-Bessiere, and H. Desalbres, C.R. Acad. Sc. Ser. C., 1964, 258, 603.
9. (a) J.-P. Montheard, C.R. Acad. Sc. Ser. C., 1965, 260, 577. (b) M. Chatzopoulos and J.-P. Montheard, C.R. Acad. Sc. Ser. C., 1975, 280, 29.
10. J.A. Kampmeier, S.H. Harris, and D.K. Wedegaertner, J. Org. Chem., 1980, 45, 315.
11. Z. Cekovic, Tetrahedron Lett., 1972, 749
12. E.J. Walsh, Jr., J.M. Messinger, D.A. Grudowski, and C.A. Allchin, Tetrahedron Lett., 1980, 21, 4409.
13. A.G. Davies and R. Sutcliffe, J. Chem. Soc., Chem. Comm., 1979, 473.
14. M.D. Bachi and E. Bosch, Tetrahedron Lett., 1986, 27, 641.
15. See also: M.D. Bachi and E. Bosch, Heterocycles, Preceding paper.
16. While this work was in preparation (ref. no. 29) cyclizations of other selenol esters were reported (ref. no. 17). For other recent ring closures involving carbonyl radicals, see ref. no. 18.
17. (a) D. Crich and S.M. Fortt, Tetrahedron Lett., 1988, 29, 2585. (b) D.L. Boger and K.D. Robarge, J. Org. Chem., 1988, 53, 3377.
18. (a) P. Delduc, C. Tailhan, and S.Z. Zard, J. Chem. Soc., Chem. Comm., 1988, 308. (b) D.J. Coveney, V.F. Patel, and E. Pattenden, Tetrahedron Lett., 1987, 28, 5949.

19. The standard conditions for these reactions are: A solution of phenylselenol ester (or acyl chloride) (1 mmol), AIBN (0.15 mmol), and TBTH (1.15 mmol) in dry deoxygenated toluene (50 ml) was heated at 110°C under argon for 20 min.
20. J. Lusztyk, E. Lusztyk, B. Maillard, and K.U. Ingold, J. Am. Chem. Soc., 1984, 106, 2923
21. The inhibiting ability of galvinoxyl has been questioned, as it reacts with TBTH. Exclusion of AIBN may be sufficient in order to favour the spontaneous over the free-radical reaction.²⁰
22. The phenylselenol esters were prepared by reacting the corresponding acyl chloride with phenylselenol and pyridine.
23. All compounds gave analytical data consistent with the assigned structures.
24. W.R. Leonard and T. Livinghouse, Tetrahedron Lett., 1985, 26, 6431.
25. Individual solutions of TBTH (1.15 mmol) in toluene (10 ml) and AIBN (0.15 mmol) in toluene (10 ml) were added during 90 min to a solution of the selenol ester (1 mmol) in boiling toluene (30 ml).
26. Same procedure as described in note 25, but in boiling benzene.
27. G. Stork and R. Mook, Jr. Tetrahedron Lett., 1986, 27, 4529.
28. A.L.J. Beckwith and D.M. O'Shea, Tetrahedron Lett., 1986, 27, 4525.
29. This work was included in a presentation by M.D. Bachi at the "Nato Workshop on Free-Radicals in Synthesis and Biology", Bardolino, Italy, May 1988.

Received, 24th August, 1988