Table II. Reaction of the Nitropropane Anion with Aldehydes

aldehyde	no. of equiv of nitronate	yield, % (isolated erythro isomer, %)	erythro:threo ratio[a,b]
a p-$NO_2C_6H_4CHO$	1	50	5.6:1[c]
	2	72 (60)	7:1[c]
b PhCHO	1	41	4.6:1
	2	61	6:1
c p-$MeOC_6H_4CHO$	1	21	1.7:1
	2	47	3.4:1
d o-$NO_2C_6H_4CHO$	1	46	9.4:1[c]
	2	65 (46)	6:1[c]
e o-$CF_3C_6H_4CHO$	1	38	7.3:1
	2	57 (42)	6.7:1[d]
f p-$MeO_2CC_6H_4CHO$	1	45	11.2:1[c]
	2	71 (41)	5.7:1[c]
g β-naphthaldehyde	2	61 (29)	4.9:1[d]
h (E)-cinnamaldehyde	2	43	8:1[d]
i $CH_3(CH_2)_5CHO$	1	13	3.8:1[e]
	2	28	3.8:1[e]
j $CH_3(CH_2)_3CHO$	2	27	2.9:1[e]
k t-BuCHO	2	0	
l MeO_2CCHO	2	36	1:1[e]

[a] Determined from the ^1H NMR spectrum of crude product.[1] [b] All new compounds were fully authenticated by spectroscopic data and microanalyses or high resolution mass spectra. [c] Recrystallization gave a single diastereoisomer. [d] Chromatography gave a single diastereoisomer. The ratio was determined by the ^{13}C NMR spectrum of the crude product.[1] [e] Determined by the ^{13}C NMR spectrum of the isolated β-nitro alcohol fraction.

particularly useful for electron-deficient aromatic aldehydes.[7] In contrast, the method is not efficient with aliphatic aldehydes, probably a consequence of competitive aldol chemistry.[8] There is a bizarre twist to this titanium-mediated Henry reaction. The nitronate **9** (R^1 = $THPOCH_2$) was found to react with isopropoxytitanium trichloride and benzaldehyde at −78 °C for 1 h to produce predominantely (9:1) the threo diastereoisomer **3** (R^1 = $THPOCH_2$, R_2 = Ph), although the conversion was low (~5%). It is reasonable to speculate that both the lower temperature threo-selective and higher temperature (≥−30 °C) erythro-selective processes are both kinetically controlled reactions via different titanium nitronate oligomers.[9] The higher temperature selectivity is not merely the result of threo–erythro equilibration.[10] Variation in quench conditions showed no observable changes in the product selectivity. The nitro alcohols are, however, stable to the reaction conditions.[11] Early results with $(^nBuO)_3ZrCl$, $EtAlCl_2$, and $TiCl_2(OPr^i)_2$ showed similar selectivities.

A typical procedure is as follows: n-BuLi (1.6M in hexane, 6.24 mL) was added dropwise with stirring to a solution of the nitroalkane (10 mmol) in THF (12 mL) at −78 °C. After 15 min a solution of $TiCl_3(OPr^i)$ (5 mmol) in THF (2 mL) and CH_2Cl_2 (3 mL) solution was added. After an additional 15 min, the aldehyde (5 mmol) was added and the mixture allowed to warm up to room temperature (~30 min). Stirring was continued for a further 3.5 h at room temperature and the mixture was quenched with an aqueous slurry of disodium EDTA (1.86 g, 5 mmol) and extracted with Et_2O (3 × 75 mL). The combined Et_2O fractions were washed with dilute hydrochloric acid (2 M, 75 mL), aqueous sodium bicarbonate (75 mL), and water (75 mL), dried, and evaporated in vacuo. Flash column chromatography using Et_2O/hexanes gave the pure nitro alcohols.

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(7) The yields reflect the conversion; remaining starting materials may be recovered by chromatography. Increasing the reaction time leads to better conversions.

(8) Titanium tetrachloride and derived alkoxides have been used in controlling the diastereoselectivities of many carbonyl addition reactions including the aldol reaction. Reetz, M. T. *Organotitanium Reagents in Organic Synthesis*; Springer-Verlag: Berlin, 1986; p 149.

(9) Erythro selectivity was observed at temperatures as low as −30 °C, although conversions are superior at 25 °C.

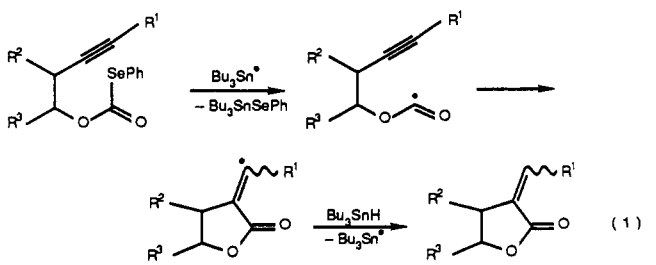
(10) The product ratio is clearly not that observed for isolated nitro alcohols under equilibrating conditions, see ref 1.

(11) Pure *erythro*-2-nitro-1-(2-nitrophenyl)-1-butanol (10 mol %) was recovered unchanged when added to a reacting mixture of 1-nitropropane and 2-(trifluoromethyl)benzaldehyde. In the same way, pure *threo*-2-nitro-1-phenyl-3-(tetrahydro-2-pyranyloxy)-1-propanol (10 mol %) was recovered unchanged when added to a reacting mixture of 2-nitrobenzaldehyde and 1-nitropropane.

Free Radical Cyclization of Thionocarbonic Acid Derivatives of 4-Phenyl-3-butenol. A New Route to Thionolactones

Summary: Treatment of various thionocarbonic acid derivatives of 4-phenyl-3-butenol with tri-n-butyltin hydride and AIBN in boiling benzene provides thionolactones and lactones in good yields via a free radical chain reaction.

Sir: The use of free radical reactions in the synthesis of complex functionalized molecules has recently become widespread.[1] In 1986 we reported a novel method for the preparation of α-alkylidene γ-lactones.[2] This method involves the intramolecular addition of alkoxycarbonyl radicals onto a carbon–carbon triple bond (eq 1). This cyclization reaction is readily extended to the synthesis of other lactones; for example *Se*-phenyl selenocarbonates of alk-3-enols and alk-4-enols yield γ- and δ-lactones, re-



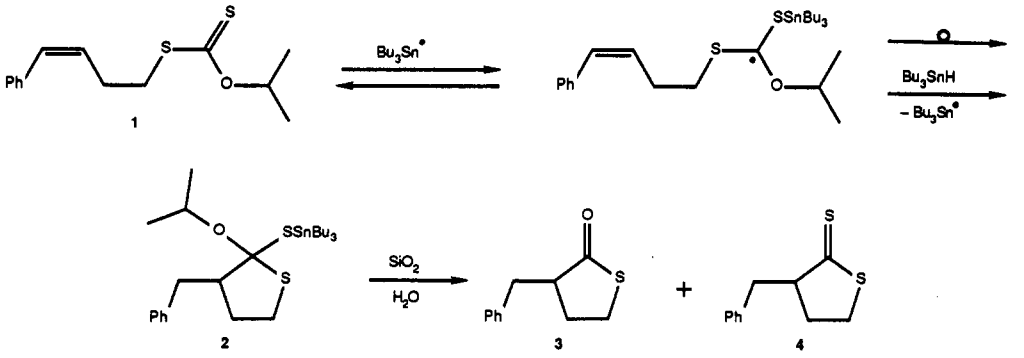
(1)

(1) For reviews, see: (a) Hart, D. J. *Science* **1984**, *223*, 883. (b) Giese, B. *Radicals in Organic Synthesis: Formation of Carbon–Carbon Bonds*; Pergammon Press: Oxford, 1986. (c) Ramaiah, M. *Tetrahedron* **1987**, *43*, 3541. (d) Curran, D. P. *Synthesis* **1988**, 417 and 489.

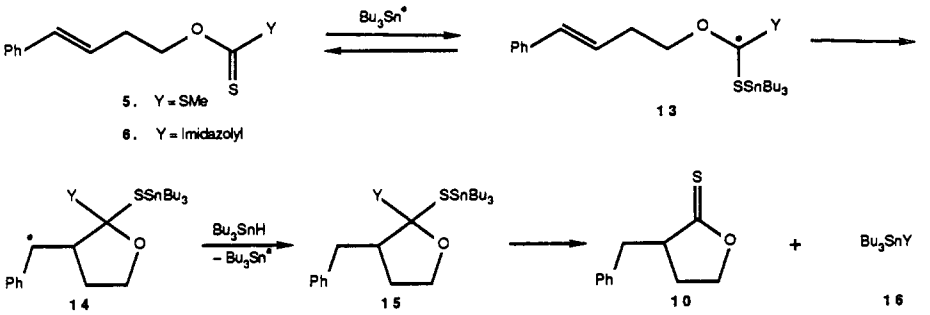
(2) Bachi, M. D.; Bosch, E. *Tetrahedron Lett.* **1986**, *27*, 641.

0022-3263/89/1954-1234$01.50/0

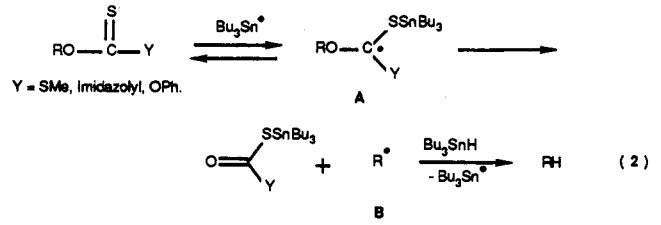
Scheme I



Scheme II



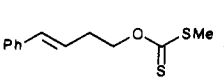
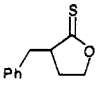
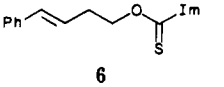
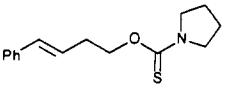
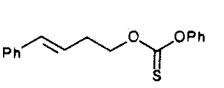
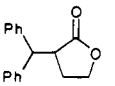
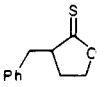
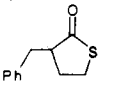
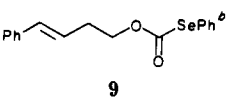
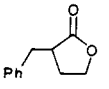
spectively.[3] We envisaged that triheterosubstituted radicals of the type involved in the Barton deoxygenation of alcohols[4,5] (eq 2, radicals A) would be valuable intermediates for the preparation of thionolactones provided that a double bond is suitably positioned in the group R. In-



deed our mechanistic probe of the deoxygenation of secondary alcohols by reduction of their dithiocarbonate derivatives with tri-*n*-butyltin hydride (TBTH) showed that it is possible to trap such radicals via intramolecular addition onto a carbon–carbon double bond (Scheme I).[6] However that particular cyclization was not suitable as a preparative procedure since high yield of product, calculated on TBTH, was only obtained when excess dithiocarbonate was employed. When stoichiometric quantities of reagents were used the yield was drastically reduced; probably due to competing reactions of the product **2** with TBTH. We now report that various thionocarbonic acid derivatives of 4-phenyl-3-butenol are effectively transformed into thionolactones and lactones on treatment with TBTH and AIBN.

The compounds **5**–**8** (Table I) were prepared by conventional methods[7] and then treated with TBTH (1.15 equiv) and AIBN (0.1 equiv) in boiling benzene or toluene.

Table I. Cyclization of Carbonic Acid Derivatives of 4-Phenyl-3-butenol with Bu_3SnH/AIBN

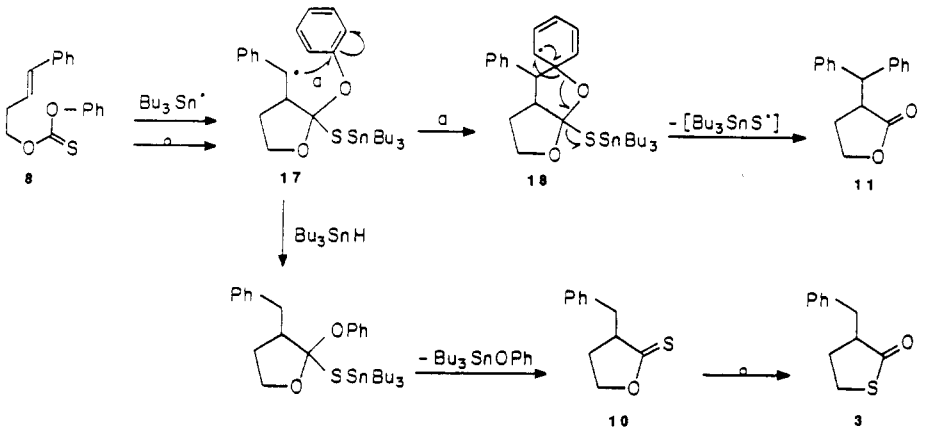
substrate	conditions[a]	products (yield, %)
 **5**	A	 **10** (77)
 **6**	A	**10** (70)
 **7**	A	recovered **7** (76)
 **8**	A	 **11** (47)  **10** (9)  **3** (12)
8	B	**11** (49) **3** (37)
 **9**	A	 **12** (80)

[a] Reactions were carried out with 1 mmol of substrate, Bu_3SnH (1.15 equiv), and AIBN (0.1 equiv) in boiling benzene (A) or toluene (B). [Bu_3SnH] = 0.02 M. [b] See ref 3.

The results of these reactions are compared to the reaction of the corresponding *Se*-phenyl selenocarbonate **9**[3] (Table I). The methyl xanthate **5** and the thiocarbonylimidazolide **6** were both converted to the thionolactone **10** in good yield. We propose that, under the reaction conditions, the expected cyclization product **15** (Y = SMe or Im) is rapidly converted to the thionolactone **10** and the tin compound **16** (Y = SMe or Im, Scheme II). Indeed NMR and UV

(3) Bachi, M. D.; Bosch, E. *Heterocycles*, in press.
(4) (a) Barton, D. H. R.; McCombie, S. W. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1574. (b) Review: Hartwig, W. *Tetrahedron* **1983**, *39*, 2609.
(5) See also: (a) Prisbe, E. J.; Martin, J. C. *Synth. Commun.* **1985**, *15*, 401. (b) Robins, M. J.; Wilson, J. S.; Hansske, F. *J. Am. Chem. Soc.* **1983**, *105*, 4059.
(6) Bachi, M. D.; Bosch, E. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1571.
(7) All compounds gave analytical and spectral data consistent with the assigned structures.

Scheme III



analyses of the crude product of both reactions indicated that the thionolactone was formed during the reaction and not on hydrolytic workup as observed[6] in the cyclization of dithiocarbonate **1** to thiololactone **3** and dithiolactone **4**.

In contrast the thionocarbamate **7** failed to cyclize under the above-mentioned conditions. It seems that due to the stabilization power of the nitrogen atom[8] the triheterosubstituted radical **13** (Y = pyrrolidine) is not sufficiently reactive to maintain a viable chain reaction through addition to the double bond. Barton and McCombie have previously noted that a steroidal thiocarbamate did not undergo the stannane-induced deoxygenation.[4a] Although *O*-phenyl thionocarbonate **8** underwent the expected cyclization the reaction was found to be far more complex, giving a mixture of thiolactones **3** and **10** and lactone **11**.[9] When the reaction was repeated in toluene only **3** and **11** were obtained. This demonstrates that **11** was not formed via attack of the cyclized radical **17** on the solvent benzene. We propose a mechanism involving the intramolecular addition of the radical **17** onto the phenolic ring to give the spirohydroaromatic system **18**. Rearomatization with concommitant elimination of $Bu_3SnS^{\bullet}$ leads to formation of α-diphenylmethyl γ-lactone **11** (Scheme III). A part of the thionolactone **10** resulting from "normal cyclization" (cf. Scheme II) isomerized to the thiololactone **3** in boiling benzene while in boiling toluene this isomerization was complete.

We conclude that the intramolecular addition of a radical centered on a triheterosubstituted carbon atom (e.g. A, R = alk-3-enyl, Y = SMe or Im) to a suitably positioned double bond is favored over other possible competing processes like β-fission and hydrogen atom abstraction. These triheterosubstituted carbon radicals are synthetic equivalents to alkoxy carbonyl radicals. The former are effective intermediates in the synthesis of thionolactones under mild nonpolar conditions in the same way as the latter are in the synthesis of lactones (cf. eq 1; see ref 3). The rapid cyclization of free radicals of type A having a multiple bond in the side chain R may interfere with planned reactions involving fragmented radicals B.[10] We are currently investigating the scope and limitations of these and related free radical cyclization reactions.

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(8) Padwa, A.; Nimmesgern, H.; Wong, G. S. K. *J. Org. Chem.* **1985**, *50*, 5620.

(9) **11**: NMR (270 MHz, CD_2Cl_2) δ 2.01–2.11 (m, 1 H, C*H*HCH$_2$O), 2.29–2.41 (m, 1 H, C*H*HCH$_2$O), 3.38–3.48 (dt, J = 6.8 Hz, 9.1 Hz, 1 H, CHC=O), 3.93–4.01 (dt, J = 4.0 Hz, 8.7 Hz, 1 H, C*H*HO), 4.08–4.18 (dt, J = 7.2 Hz, 8.7 Hz, 1 H, CH*H*O), 4.46 (d, J = 6.8 Hz, 1 H, Ph_2CH), 7.16–7.44 (m, 10 H); IR (film) 3028, 2912, 1766 vs (C=O), 1601, 1153, 1027 cm^{-1}; mass spectrum, m/e (relative intensity) 252 (M^+, 4), 167 (PhCHPh, 100), 165 (31), 115 (23), 91 (25), 77 (28); exact mass calcd for $C_{17}H_{16}O_2$ m/e 252.1150, found m/e 252.1158. Anal. Calcd for $C_{17}H_{16}O_2$: C, 80.92; H, 6.39. Found: C, 80.97; H, 6.29.

(10) An example has been reported by Clive: Angoh, A. G.; Clive, D. L. J. *J. Chem. Soc., Chem. Commun.* **1985**, 980.

Total Synthesis of (±)-Meloscine and (±)-Epimeloscine[1]

Summary: Total syntheses of the *Melodinus* alkaloids (±)-meloscine and (±)-epimeloscine are reported. These are the first reported total syntheses of members of this structurally unique alkaloid class.

Sir: The *Melodinus* alkaloids, isolated from the New Caledonian plant *Melodinus scandens* Forst., are structurally unique by virtue of incorporating a quinoline moiety within the *Aspidosperma* alkaloid skeleton.[2-4] These alkaloids, e.g. **2–4**, are believed to arise by oxidative rearrangement of 18,19-dehydrotabersonine (**1**), see Scheme I.[2] Although initial efforts to demonstrate this conversion in the laboratory were unsuccessful,[5] significant

(1) Part 20 in the series Synthesis Applications of Cationic Aza-Cope Rearrangements. For part 19, see: Overman, L. E.; Wild, H. *Tetrahedron Lett.*, in press.

(2) Bernauer, K.; Englert, G.; Vetter, W.; Weiss, E. *Helv. Chim. Acta* **1969**, *52*, 1886.

(3) Oberhänsli, W. E. *Helv. Chim. Acta* **1969**, *52*, 1905.

(4) Plat, M.; Hachem-Mehri, M.; Koch, M.; Scheidegger, U.; Potier, P. *Tetrahedron Lett.* **1970**, 3395.

0022-3263/89/1954-1236$01.50/0