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Convenient Radical α-Monoallylations of Carbonyl Compounds

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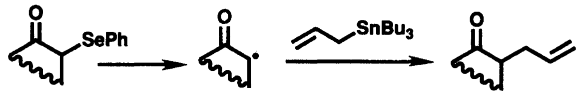
Free radical allylations of α-seleno carbonyl compounds with tributyl-substituted 2,4-pentadienyltin, 2-methyl-2-propenyltin, 2-butenyltin, and 3-methyl-2-butenyltin, are described. Such successful C–C bond formations, in particular with the 2-butenyltin and the 3-methyl-2-butenyltin, are owing to the high reactivity of the α-carbon radical, generated from α-seleno carbonyl compounds, toward allylic tin compounds.

Allylation of alkyl halides by allyltributyltin via a radical process has been reported by several groups.[1] We have found that α-carbon radicals formed from 2-(phenylseleno)-substituted cycloalkanones, lactones, and alkanoates are quite reactive toward allyltributyltin, and used this extremely efficient intermolecular radical alkylation to construction of a prostanoid skeleton.[2] In an investigation which followed, we demonstrated that the radical allylation of alkyl-substituted 2-(phenylseleno)cycloalkanones proceeds with moderate stereoselectivity.[3]

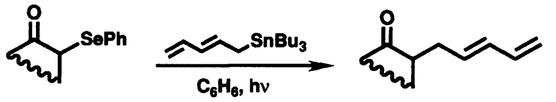


(1)

As a part of the continuing program to establish this α-allylation method, we describe herein α-pentadienylation with tributy(2,4-pentadienyl)tin and α-allylation with 2-butenyltributyltin and tributyl(3-methyl-2-butenyl)tin as well as tributyl(2-methyl-2-propenyl)tin, the 2-butenyl and 3-methyl-2-butenyltin having been reported to give no allylated products in the radical reaction with alkyl halides.[4,5]

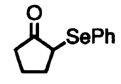
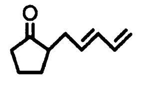
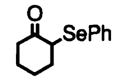
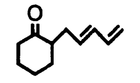
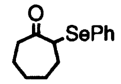
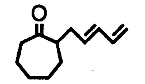
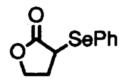
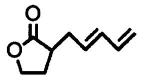
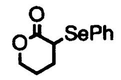
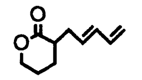
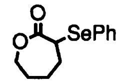
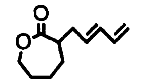
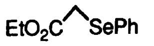
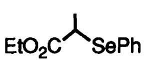
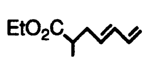
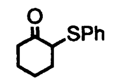
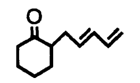
Results and Discussion

A benzene solution of α-phenylseleno carbonyl compounds **1** and a two-fold excess of tributyl(2,4-pentadienyl)tin was irradiated to produce α-pentadienyl carbonyl compounds **2** in high yields via an α-carbon radical intermediate.



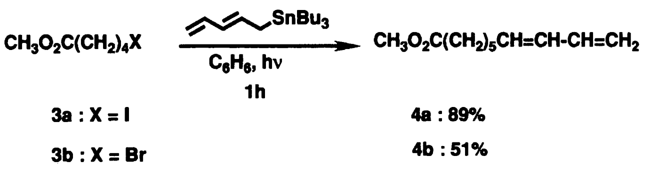
1 **2** (2)

Table 1. Pentadienylation with Tributyl(2,4-pentadienyl)tin

Substrate		Reaction time/h	Product		Yield/%
	**1a**	1.5		**2a**	82
	**1b**	0.8		**2b**[6]	78
	**1c**	0.8		**2c**	78
	1c	0.8		**2c**	48[a]
	**1d**	2		**2d**	72
	**1e**	2		**2e**	87
	**1f**	2		**2f**	57
	**1g**	1.8		**2g**[7]	93
	**1h**	2		**2h**	79
	**1i**	10		**2i**	49

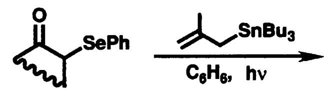
a) Thermally initiated with 10 mol% azobisisobutyronitrile in toluene.

This α-pentadienylation could be generally done with a number of α-seleno carbonyl compounds such as 2-(phenylseleno)-substituted cycloalkanones **1a**—**c**, lactones **1d**—**f**, acetate **1g**, and propionate **1h** and gave the products in high yields (Table 1). When the reaction was done by heating a benzene solution of 2-(phenylseleno)cycloheptanone (**1c**) with 2 mol equiv of tributyl(2,4-pentadienyl)tin under reflux for 18 h in the presence of 10 mol% of azobisisobutyronitrile, 2-(2,4-pentadienyl)cycloheptanone (**2c**) was obtained in 48% yield. We also examined the pentadienylation using other radical precursors. The alkyl radical generated from methyl 5-iodopentanoate (**3a**) could react with the pentadienyltin to afford methyl 7,9-decadienoate[8] (**4**) in 89% yield, but 5-bromopentanoate (**3b**) was less reactive (51% yield).



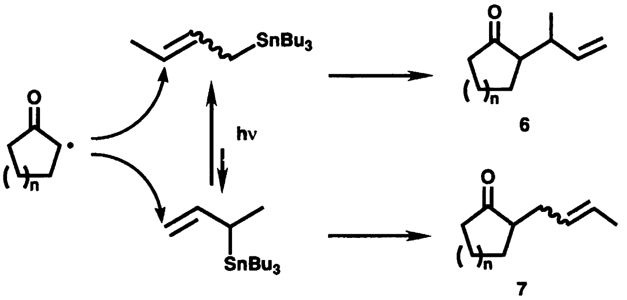
(3)

Irradiation of 2-(phenylthio)cyclohexanone (**1i**) with 2 equiv of the pentadienyltin for 10 h gave the pentadienylated product **2b** in 49% yield. The reaction of α-phenylseleno carbonyl compounds **1** with tributyl(2-methyl-2-propenyl)tin gave 2-methyl-2-propenylated products **5** in high yields. The results are summarized in Table 2.



1 **5** (4)

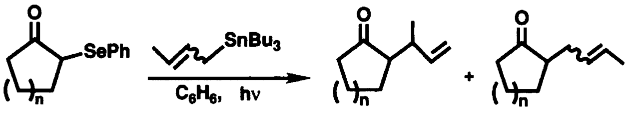
High reactivity of the carbon radical α to a carbonyl was further proved in the reaction with (γ-substituted allyl)tributyltin compounds such as 2-butenyltributyltin and tributyl(3-methyl-2-butenyl)tin. Keck et al. have shown that alkyl radicals generated from alkyl halides give no allylated products in the reaction with 2-butenyltributyltin but abstract a hydrogen at the allylic position of the 2-butenyltin.4) On the other hand, our reaction of the α-carbon radical generated from α-phenylseleno carbonyl compounds **1** with 2-butenyltributyltin quite efficiently gave the allylated products **6** and **7** (Scheme 1).13) Thus, irradiation of a benzene solution of 2-(phenylseleno)cyclopentanone (**1a**) with 2 mol equiv of 2-butenyltributyltin gave the allylated product in 77% yield as a 66 : 34 mixture of 2-(1-methyl-2-propenyl)cyclopentanone (**6a**) and 2-(2-butenyl)cyclopentanone (**7a**).



Scheme 1.

Table 2. Allylation of α-Phenylseleno Carbonyl Compounds with Tributyl(3-methyl-2-butenyl)tin

α-Seleno carbonyl compound	3-Methyl-2-butenyltin/equiv	Reaction time/h	Product	Yield/%
1a	1.5	1.0	**5a**9)	80
1b	1.3	2.5	**5b**10)	93
1c	2.0	1.0	**5c**11)	85
1d	2.0	0.5	**5d**	91
1e	2.0	0.5	**5e**	90
1f	2.0	1.3	**5f**	80
1g	1.3	0.5	**5g**12)	87



1 **6** **7**

(5)

When the reaction was done using a larger excess (5 mol equiv) of 2-butenyltributyltin, the reaction was complete within 1 h to give a mixture of **6a** and **7a** in 95% yield, the formation of **6a** being more predominant than in the above reaction. Similar results were obtained in the reaction of 2-(phenylseleno)cyclohexanone (**1b**) with 2-butenyltributyltin. The results are shown in Table 3. The formation of 2-(1-methyl-2-propenyl)cycloalkanones **6** increased compared to the 2-butenyl isomers **7** in both reactions, when a larger excess of 2-butenyltributyltin was used. This suggests that 2-butenyltributyltin undergoes isomerization to tributyl(1-methyl-2-propenyl)tin during irradiation. Indeed, a 1 mol dm^{-3} benzene solution of 2-butenyltributyltin (E : Z = 35 : 65) was irradiated for 5 h to give a 54 : 44 : 2 mixture of the (E)- and (Z)-2-butenyltributyltin (measured by GC) and tributyl(1-methyl-2-propenyl)tin. It is reasonable that the isomerization between the E and Z isomers occurs via the 1,3-shift of the tributylstannyl group or via the allylic radical intermediate.14) Baldwin et al. observed a similar 1,3-shift of the tributylstannyl group in the allyltin system during the thermal reaction with an alkyl halide using α,α-dideuterioallyltriphenyltin.5) It is likely that tributyl(1-methyl-2-propenyl)tin is much more reactive toward the carbon radical than 2-butenyltributyltin because the less steric repulsion at the reaction site is expected in the reaction of tributyl(1-methyl-2-propenyl)tin.15) The concentration of tributyl(1-methyl-2-propenyl)tin may be much lower in the reaction mixture than that of both 2-butenyltin isomers as deduced from the above observation in the isomerization reaction. Thus, tributyl(1-methyl-2-propenyl)tin once formed reacted very rapidly with the α-carbon radical to afford 2-(2-butenyl)cycloalkanones **7** in moderate yield.

We then examined the reaction of 2-(phenylseleno)cycloalkanones **1** with tributyl(3-methyl-2-butenyl)tin, in which the 1,3-shift of the tributylstannyl group on irradiation would also be expected. Irra-

Table 3. Allylation of 2-(Phenylseleno)cycloalkanones with 2-Butenyltin

Selenocycloalkanone	2-Butenyltin/equiv	Reaction time/h	Yield/%	Product distribution[a]
1a	2.0	2.0	77	**6a** : **7a**=66 : 34
1a	5.0	1.0	95	**6a** : **7a**=75 : 25
1b	2.0	3.0	45	**6b** : **7b**=45 : 55
1b	5.0	1.0	61	**6b** : **7b**=53 : 47

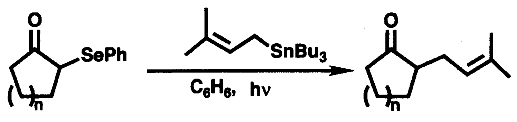
a) Determined by GC. **7** is a mixture of the *E* and *Z* isomers.

Table 4. Spectral Data for Pentadienylated and Methallylated Compounds

Compounds	IR/cm^{-1}	^{1}H NMR, δ, (CCl$_4$)	Exact mass, m/z (M$^+$)	
			obsd	calcd
2a	1735, 1645	1.26—2.85 (9H, m), 4.67—5.39 (2H, m), 3.59—6.60 (3H, m)	150.107	150.105
2c	1710, 1655	1.18—2.66 (13H, m), 4.98 (1H, dd, J=2, 10 Hz), 5.11 (1H, dd, J=2, 17 Hz), 5.64 (1H, dt, J=7.5, 15 Hz), 6.07 (1H, dd, J=10, 15 Hz), 6.30 (1H, ddd, J=10, 10, 17 Hz)[a]	178.137	178.136
2d	1765, 1640	1.56—2.90 (5H, m), 3.85—4.50 (2H, m), 4.50—5.33 (2H, m), 5.33—6.53 (3H, m)	152.086	152.084
2e	1730, 1640	1.47—2.77 (7H, m), 4.03—4.37 (2H, m), 4.37—5.40 (2H, m), 5.40—6.53 (3H, m)	166.102	166.099
2f	1750, 1640	1.40—2.80 (9H, m), 3.93—4.53 (2H, m), 4.53—5.30 (2H, m), 5.30—6.67 (3H, m)	180.116	180.115
2h	1725, 1650	1.25 (3H, d, J=4 Hz), 1.30 (3H, t, J=7 Hz), 2.00-2.97 (3H, m), 4.10 (2H, q, J=7 Hz), 4.83—5.30 (2H, m), 5.30—6.36 (3H, m)	168.115	168.115
6d	1765, 1650	1.77 (3H, s). 1.93—2.87 (5H, m), 4.02—4.37 (2H, m), 4.63—4.87 (2H, m)	140.078	140.083
6e	1720, 1640	1.70—2.90 (7H, m), 1.73 (3H, s), 4.12—4.37 (2H, m), 4.60—4.83 (2H, m)	154.095	154.099
6f	1725, 1640	1.40—2.85 (8H, m), 1.73 (3H, s), 4.03—4.33 (2H, m), 4.57—4.88 (2H, m)	168.116	168.115

a) Obtained as an unseparable (TLC or GC) 9 : 1 mixture of the *E* and *Z* isomers as determined by the integrations of the C′-4 vinyl proton signals at 6.30 and 6.66 ppm for the *E* and *Z* isomers.

diation of 2-(phenylseleno)-substituted cyclopentanone (**1a**) or cyclohexanone (**1b**) with 5 mol equiv of tributyl(3-methyl-2-butenyl)tin gave 2-(3-methyl-2-butenyl)cyclohexanone[16] (**8a**) or 2-(3-methyl-2-butenyl)cyclohexanone[17] (**8b**) in 63 and 55% yield, respectively.



1

8a : 63%

8b : 55% (6)

The products are those resulting from the S_H2' reaction between the α-carbon radical and tributyl(1,1-dimethyl-2-propenyl)tin, formed by isomerization of tributyl(3-methyl-2-butenyl)tin. Baldwin et al. observed that thermally initiated reaction of an alkyl halide with tributyl(1,1-dimethyl-2-propenyl)tin gave a significant amount of unreacted but rearranged tributyl(3-methyl-2-butenyl)tin together with a small amount (<5%) of the 3-methyl-2-butenylated product.[5] The successful carbon–carbon bond formation in our reaction with 2-butenyltributyltin as well as tributyl(3-methyl-2-butenyl)tin clearly demonstrates the high reactivity of the electron-deficient α-carbon radical of the carbonyl system toward the electron-rich terminal carbon of olefins.

In summary, this reaction, together with our previous results,[2,3] provides a general method for α-monoallylation of carbonyl compounds. This procedure is based on the high reactivity of the α-carbon radical toward the olefinic carbon of allyltin compounds. Furthermore, the process is notable for its characteristic mode of reaction via a free radical pathway: α-monoallylation with regiospecificity, which can be done under substantially neutral conditions, avoiding the tedious protection of protic groups in a molecule.

Experimental

General. ^{1}H NMR spectra were recorded on either JEOL JNM-PMX60Si (60 MHz) or Varian XL-200 (200 MHz) spectrometers and are reported in δ from tetramethylsilane. IR spectra were reported on a JASCO A-102 spectrometer. Mass spectra were recorded on a Hitachi M-2000 spectrometer. All reactions were monitored by thin-layer chromatography done on 0.25-mm Merck silica gel plates (60F-254), with UV light and 7% phosphomolybdic acid in ethanol/heat as developing agent. Flash column chromatography was done with a Michel Miller column packed with Fuji Davison silica-gel BW-200, equipped with an FMI lab pump RPG 150 and an FMI pulse damper PD-60LF, normally at a pressure of 1—2 $\mathrm{kg\,cm^{-2}}$. Analyses of the products and the reagents were done with a Shimadzu Chromatopac C-R3A instrument attached to Shimadzu GC-9A gas chromatography (column; OV-17, 3 mm×2 m).

Tributyl(2,4-pentadienyl)tin[18)] was prepared from pentadienyllithium and tributyltin chloride by the procedure reported[19)] and used as a *E*/*Z* (76 : 24) mixture, the ratio of which was measured by NMR.[20)] 2-Butenyltributyltin[14,21)] was prepared from tributyltinlithium and 2-butenyl chloride and used as a *E*/*Z* (about 2 : 1) mixture. Tributyl(2-methyl-2-propenyl)tin[18)] and tributyl(3-methyl-2-butenyl)tin[18,22)] were prepared by the procedure reported.

General Procedure for the Photochemical Allylation of α-Phenylseleno Carbonyl Compounds. A Pyrex glass tube containing a degassed benzene solution (1 $\mathrm{mol\,dm^{-3}}$ substrate) of the α-phenylseleno carbonyl compound and an excess of tributylpentadienyltin or the allylic tin compound was externally irradiated under argon at a distance of 15 cm from the mercury lamp (a 400-W high-pressure Toshiba mercury lamp). Irradiation was continued until no starting α-phenylseleno carbonyl compound remained by TLC analysis. The reaction mixture was purified directly by silica-gel column chromatography using petroleum ether/ethyl ether as eluent. Spectral data for all new compounds obtained are listed in Table 4.

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