Stannylformylation of 1,6-Dienes Accompanied by Five-Membered Radical Ring Closure

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Summary: Treatment of 1,6-dienes with tin hydride and AIBN (catalytic) under CO pressure leads to five-membered carbocycles flanked by stannylmethyl and formylmethyl groups at the adjacent carbons by way of a stannyl radical addition—cyclization—carbonylation sequence.

Metal-catalyzed silylformylation of alkynes,[1a–h] aldehydes,[1i–j] and epoxides[1k] has been recently developed as a useful tool for the introduction of both silyl and formyl functionalities into these organic molecules. The reaction of carbon free radicals with CO now constitutes a powerful method for the synthesis of a variety of carbonyl compounds,[2,3] and our continuing interest in this field led us to design silyl- and stannylcarbonylation by free-radical processes. In this paper, we report stannylformylation of 1,6-dienes which occurs with five-membered radical ring closure. As illustrated in eq 1, this new type
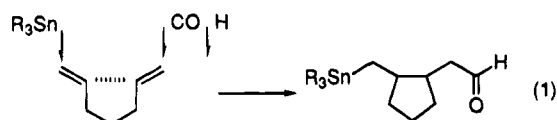
of free-radical carbonylation provides five-membered carbocycles flanked by stannylmethyl and formylmethyl groups at the adjacent carbons.

Encouraged by the recent work of Hanessian and Léger, who reported the successful free-radical addition of trimethyltin hydride to 1,6-dienes to produce stannylmethyl-substituted five-membered carbocycles,[4] we examined the reaction of 1,6-dienes with tributyltin hydride and AIBN (catalytic) under pressurized conditions of CO, in the hope of observing a CO trapping process in this system.[5] The reaction of diallyl ether (1a) (0.05 M) with 1.3 equiv of tributyltin hydride and 0.2 equiv of AIBN in benzene at 80 atm of CO resulted in the formation of the desired stannylformylation product 2a along with an

Table 1. Control Experiments for Stannylformylation of Diallyl Ether (1a)

condns (M, atm)	yield (%) (trans/cis)[a]		
	2a	**3a**	**4a**
0.05, 80	42 (38/62)	39 (38/62)	4
0.03, 80	57 (38/62)	28 (38/62)	4
0.02, 80	59 (39/61)	20 (39/61)	5
0.02, 50	51 (40/60)	31 (40/60)	6
0.02, 20	28 (42/58)	43 (43/57)	10
0.01,[b] 80	53 (41/59)	15 (43/57)	8

[a] Isolated yield. [b] Recovery of 1a: 15%.

almost equal amount of the simple cyclization product 3a (eq 2 and Table 1). The formation of the cyclic aldehyde 2a most likely occurs via (i) stannyl radical addition to the terminal end of 1a, (ii) 5-*exo-trig* cyclization of the resulting radical, (iii) CO-trapping of the cyclized radical 5a, and (iv) the subsequent hydrogen abstraction of the resulting acyl radical from Bu₃SnH to give 2a (Scheme 1). We also isolated a small amount of bicyclic heterocycle 4a, a minor byproduct most likely arising from intramolecular S$_H$2 type cyclization from cis-5a. It is interesting to note that the cis/trans ratios for formylation and reduction are always the same irrespective of the amounts of bicyclic compound 4a. The low concentration ([1a] = 0.02 M) apparently made the effective concentration of CO higher relative to that of tin hydride, but further dilution (0.01 M) did not necessarily improve the yield of 2a because of less effective chain propagation at such a low concentration.

Table 2 lists several examples of stannylformylation of 1,6-dienes. All products were isolated by flash chromatography on silica gel.[6] In general, cis isomers were formed predominantly.[7] With triphenyltin hydride, whose

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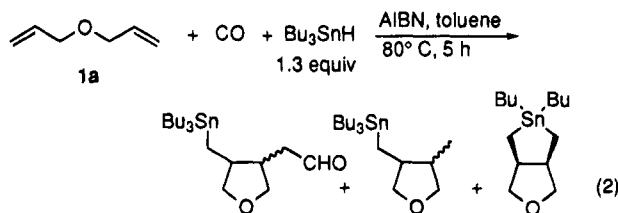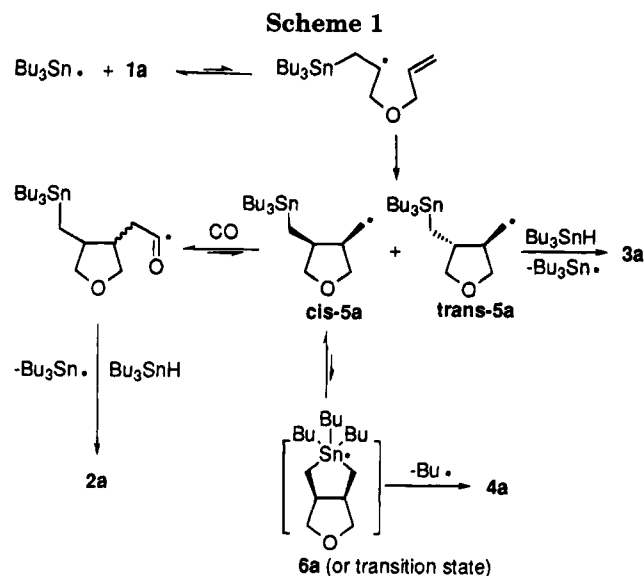
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(6) Typical procedure: benzene (50 mL), diethyl diallylmalonate (1b, 0.244 g, 1.01 mmol), tributyl tin hydride (0.369 g, 1.27 mmol), and AIBN (0.042 g, 0.26 mmol) were placed in a 100-mL stainless steel autoclave containing a glass liner. The autoclave was then pressurized with 80 atm of CO and heated with stirring at 80 °C for 5 h. After excess CO was discharged at rt, the benzene was evaporated. The residue was purified by flash chromatography on silica gel (5%, 10%, 20% ether/hexane eluant). The major fraction eluted from the column afforded 0.248 g of the product, which contained 2b (44%) as a 79:21 mixture of cis and trans isomers. The low polar fraction contained the cyclization—reduction product and the bicyclic tin heterocycle in 16% and 6% yields, respectively.

Scheme 1

Table 2. Free-Radical Mediated Stannylformylation of 1,6-Dienes[a]

entry	dienes	conditions	products, 2	yields,[b] % (trans/cis[c])
1	1a	[1a] = 0.02 M Bu$_3$SnH 1.3 equiv CO 80 atm	2a	59 (39/61)
2	1a	[1a] = 0.02 M Ph$_3$SnH 1.3 equiv CO 80 atm	2a'	34 (44/56)
3	1b	[1b] =0.02 M Bu$_3$SnH 1.3 equiv CO 80 atm	2b	44 (21/79)
4	1c	[1c] = 0.02 M Bu$_3$SnH 1.3 equiv CO 80 atm	2c	45 (39/61)
5	1d	[1d] = 0.02 M Bu$_3$SnH 1.3 equiv CO 80 atm	2d	50 (41/59)
6	1e	[1e] = 0.05 M[d] Bu$_3$SnH 1.2 equiv CO 80 atm	2e	37[e] (46/54)
7	1f	[1f] = 0.02 M Bu$_3$SnH 1.2 equiv CO 80 atm	2f	41[f] (24/76)

[a] Reactions were conducted on a 1 mmol scale in benzene or toluene (entry 1) at 80 °C for 5 h with AIBN (20–25 mol %) as the radical initiator. For typical procedure, see ref 6. Isolated yields of byproducts via cyclization/reduction: 20% (entry 1), 39% (entry 2), 16% (entry 3), 12% (entry 4), 26% (entry 5), 40% (entry 6), 33% (entry 7). In general bicyclic byproducts were formed in less than 10% yield. [b] Isolated yields by flash chromatography on silica gel. [c] Estimated by GC. [d] At lower concentrations (0.02 M, 0.03 M), considerable amounts of 1e remained intact (30%, 25%). [e] Obtained as a mixture of two stereoisomers (regio isomer was not observed). [f] Product contained ca. 5% of regio isomer.

hydrogen donor ability is higher than that of tributyltin hydride,[8] the yield of formylation product decreased (entry 2).[9] Attempted silylformylation of 1a with tris-(trimethylsilyl)silane (TTMSS)[10] and CO resulted in only trace amounts of the desired δ-silyl aldehyde, the preferred reaction pathway being S$_H$2 type intramolecular cyclization to give the bicyclic heterocycle analogous to 4a.[11] The selectivity of formylation to reduction in the present stannylformylation was somewhat lower than that in free radical formylation of primary alkyl halides.[12]

The reaction of unsymmetrical dienes 1e and 1f exhibited high regioselectivity in Sn radical attack to yield 2e and 2f as the exclusive and predominant (>95%) regioisomer, respectively (entries 6 and 7). Established kinetic studies have shown that rates for the 5-exo mode of 5-hexenyl radical cyclization range from 10^4 to 10^8 s^{-1} at 25 °C depending on substituents,[13] and unsubstituted 5-heptenyl radical falls into the slowest class.[8b] As predicted from this, attempts to convert unsubstituted 1,6-heptadiene to δ-stannyl aldehyde met with little success (<5% under the aforementioned conditions). The slow 5-exo cyclization of the key radical may permit the radical to revert to stannyl radical and the diene.

In summary, we have shown that the free-radical processes described above can effect the stannylformylation of 1,6-dienes accompanied with a five-membered

ring closure.[14] Although modest yields are the rule, the simplicity of this one-step route, coupled with easy availability of 1,6-dienes, may make it attractive for synthetic applications. It may be, thus, worth designing other heteroatom-introduction/carbonylation sequences by free-radical mediated processes.

Supplementary Material Available: Spectral data and copies of ^{1}H NMR spectra for the products 2 (12 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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(12) Octyl bromide can be formylated efficiently with tin hydride/CO,[2a] where the selectivity of formylation to reduction is excellent (4:1 at 0.02 M of [Oct-Br] at 80 atm). The relatively low formylation/reduction ratios observed for the present stannylformylation (at most 2:1) should be further examined.

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