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Approximate Rate Constants for the Addition of Alkyl Radicals to Allylstannanes

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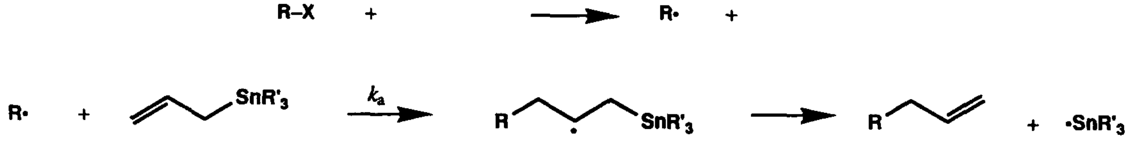
Summary: *Rate constants for the addition of alkyl radicals to allylstannanes lie in the range of* 10^4-10^5 M^{-1} s^{-1} *at 50-80 °C.*

The radical chain allylation of organic halides and related precursors by allylstannane reagents is a powerful and selective method to introduce allyl groups into organic molecules. The overall transformation and the generally assumed mechanism are illustrated in eq 1.[3,4] Beyond simple additions, allylstannanes also show promise as reagents that will permit the planned sequencing of radical reactions.[5] The high yields obtained in these transformations imply that an allylstannane is more reactive than a simple alkene;[6a,7] otherwise the allylated product would compete with the allylstannane for radicals. However, based on FMO theory, there is no reason to believe that allylstannanes should be exceptionally reactive towards nucleophilic radicals. Thus, the rate constant for addition of an alkyl radical to an allylstannane is of fundamental interest, and we briefly describe below experiments indicating that $k_a \approx 10^4$-10^5 M^{-1} s^{-1}. Allylstannanes are therefore at least one order of magnitude more reactive than simple alkenes toward alkyl radicals. This modest activation insures that the starting allylstannane is more reactive than the allylated product and it aids in propagating chains, but it does not compare to the activation provided by powerful electron withdrawing groups.

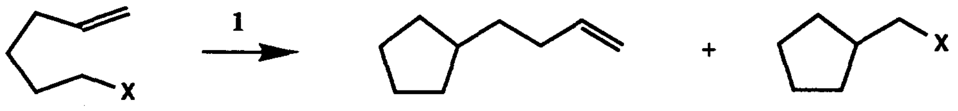
eq 1



1a $R = C_4H_9$
1b $R = CH_3$
1c $R = Ph$

A simple experiment bracketed k_a between 10^2 and 10^5 M^{-1} s^{-1} (eq 2). Heating of allyltributyltin (**1a**) and hexenyl bromide (**2a**) under Keck's conditions[3a] (1.0 M stannane, 0.5 M bromide, 0.1 M AIBN, 80 °C) induced a slow reaction (15 h) to form butenylcyclopentane (**3**) as the only detectable product by GC (80%). During the course of the reaction, neither (bromomethyl)cyclopentane (**4a**) nor 1,8-nonadiene could be detected. Under these conditions, addition of a 1°-alkyl radical to **1a** is slower than hexenyl radical cyclization,[8] but faster than bromine atom transfer between alkyl radicals.[9] However, iodine transfer did compete with allylation. When hexenyl iodide **2b** was heated with **1a** (same conditions as **2a**), the ratio of (iodomethyl)cyclopentane (**4b**) to **3** at early reaction time (10-20% conversion) was about 5/1. From the known rate constant for iodine transfer between 1°-alkyl radicals (k_I),[10] one can calculate k_a by assuming that the product ratio at early conversion represents the $k_I/2k_a$ ratio.[11] According to this analysis, $k_a \approx 4 \times 10^4$ M^{-1} s^{-1} (80 °C).

eq 2



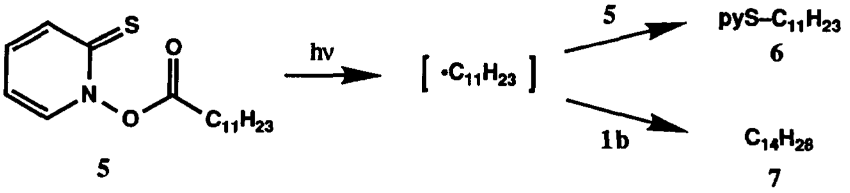
2a X = Br
b X = I

3

4a
b

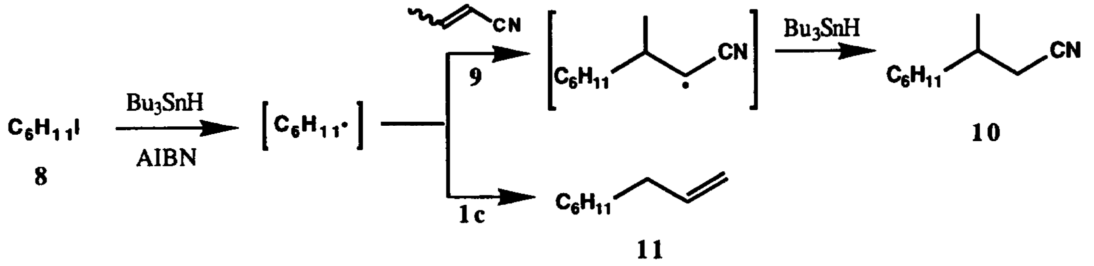
A better estimate can be obtained by Newcomb's kinetic adaptation of the Barton method (eq 3).[12] These experiments were conducted at 50° C. Thiohydroxamate **5** was decomposed in the presence of 20 equivalents of allyltrimethyltin (**1b**), and the ratio of tetraundecene (**7**)/thiopyridylundecane (**6**) was measured by ^1H NMR integration of the crude reaction mixture.[13] From the known rate constant for addition of undecyl radical to its thiohydroxamate precursor, and from the product ratio, a rate constant for the addition of undecyl radical to allyltrimethyltin can be calculated: $k_a \approx 3 \times 10^4$ M^{-1} s^{-1}. Several similar experiments were conducted at different concentrations of **1b**, and calculated rate constants ranged from (3-6) x 10^4 M^{-1} s^{-1} at 50 °C.[14]

eq 3



These measurements confirm the expectation that allylstannanes are more reactive than simple monosubstituted alkenes. The addition reactions of cyclohexyl radicals to crotononitrile (**9**) and allyltriphenyltin (**1c**) also demonstrate the rate increasing effect of a tin substituent at the allyl position (eq 4). The cyclohexyl radical was generated in benzene (3 M) at 80° by treatment of cyclohexyl iodide (0.25 mmol) with tributylstannane (0.25 mmol) and a catalytic amount of AIBN. This radical was trapped with a mixture of crotononitrile (**9**, 1:1 E:Z mixture, 2.5-5.0 mmol) and allyltriphenyltin (**1c**) (2.5-12.5 mmol). The ratio of **10/11** was then determined by GC.

eq 4



Pseudo first order plots[15] show that allyltriphenylstannane (**1c**) reacts with cyclohexyl radicals at 80 °C 3 times faster than with crotononitrile. This means that allyltriphenylstannane (**1c**) is only 10 times slower than methyl acrylate,[16] whereas 1-hexene is 10^2-10^3 less reactive than acrylate.[17] From the known rate for the hydrogen abstraction from tributylstannane[18] and competition experiments between hydrogen abstraction and addition reactions,[16] a rate constant can be calculated for the addition of cyclohexyl radicals to allytriphenyltin: $k_a = 1 \times 10^5\ M^{-1}\ s^{-1}$ at 80 °C. Given that different radicals and allylstannanes are involved, this is in reasonable agreement with the rate constant at 80 °C obtained in eq 2 ($k_a = 4 \times 10^4\ M^{-1}\ s^{-1}$).

Rate constants of 10^4-$10^5\ M^{-1}\ s^{-1}$ (50-80°) are sufficiently high so that unwanted reactions of radicals with the solvent, the product, or other radicals cannot compete[6b] with additions to allylstannanes. Thus, while allylstannanes are powerful synthetic reagents because they propagate tin-radical based chains without using tin hydrides, these chains only succeed because of the modest accelerating effect of the allylic tin substituent on the radical addition reaction.

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References and Notes

1. Dreyfus Teacher-Scholar, 1985-89; National Institutes of Health Research Career Development Awardee, 1987-92.
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8. Hexenyl radical $k_c = 1.5 \times 10^6\ s^{-1}$ (80 °C). Lusztyk, J.; Maillard, B.; Deycard, S.; Lindsay, D. A.; Ingold, K. U. *J. Org. Chem.* **1987**, *52*, 3509.
9. Bromine transfer from butyl bromide to octyl radical $k_{Br} = 6 \times 10^2\ M^{-1}\ s^{-1}$ (50 °C). Newcomb, M. A.; Sanchez, R. M.; Kaplan, J. *J. Am. Chem. Soc.* **1987**, *109*, 1195.
10. Iodine transfer from ethyl iodide to octyl radical $k_I = 2 \times 10^5\ M^{-1}\ s^{-1}$ (50 °C). We estimate that $k_I \approx 4 \times 10^5\ M^{-1}\ s^{-1}$ at 80 °C. See reference 9.
11. At 10-20% conversion, we assume that effective concentrations equal the starting concentrations. The factor of two comes from the twofold excess of allylstannane. Analysis at higher conversions is not meaningful because **4b** is converted to **3**.
12. Rate of addition of octyl radical to its own thiohydroxamate, $k_T = 2.3 \times 10^6\ M^{-1}\ s^{-1}$ (50 °C). Newcomb, M.; Park, S. U. *J. Am. Chem. Soc.* **1986**, *108*, 4132. Newcomb, M.; Kaplan, J. *Tetrahedron Lett.*, **1987**, *28*, 1615.
13. A benzene (or benzene-d_6) solution of **5** (0.046 M) and **1b** (5-20 equiv) was warmed to 47-50°C and irradiated with a sunlamp until 5 was consumed (2-5 min). The ratio of products was determined by ^1H NMR or GC of the crude mixture. Excess **1b** (5-20 equiv) was required to produce significant amounts of 7.
14. The $[5]_{effective}$ was assumed to be half of the starting concentration. Smaller apparent rate constants resulted as the amount of **1b** was increased. The use of NMR ratios (unstandardized) consistently gave higher rate constants (by a factor of about 2) than those obtained by GC yields against an internal standard. In one experiment, the combined yield of expected products was determined to be about 60%. No effort was made to identify other products. Given these potential sources of error, the measured rate constants must be regarded as very approximate.
15. Giese, B.; Kretschmar, G.; Meixner, J. *Chem. Ber.* **1980**, *113*, 2787.
16. Competition experiments at 80 °C for cyclohexyl radicals gave competition constants: $H_2C{=}CHCO_2Me/MeCH{=}CHCN = 30$; $Bu_3SnH/H_2C{=}CHCO_2Me = 3$.
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