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Radical Carbonylations with Fluorous Allyltin Reagents

Ilhyong Ryu,* Tatsuro Niguma, Satoshi Minakata, Mitsuo Komatsu

Department of Applied Chemistry, Faculty of Engineering, Osaka University, Suita, Osaka 565-0871, Japan

Zhiyong Luo and Dennis P. Curran*

Department of Chemistry, University of Pittsburgh, Pittsburgh, Pennsylvania 15260, USA

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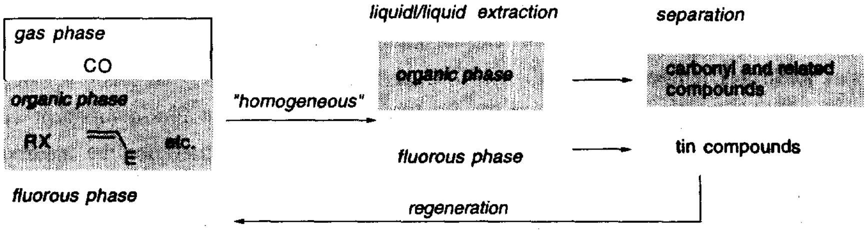
Abstract: "Propylene-spaced" fluorous allyltin reagents **2a** and **2b** were tested as mediators of radical carbonylations and found to be useful for four-component coupling reactions comprising RX **3**, CO, alkenes, and **2** leading to β-functionalized β-allylated ketones **5**. The biphasic workup (acetonitrile/FC-72) was successfully carried out to separate **5** from tin compounds. Competition experiments suggested a modest reactivity of **2a** for the chain propagation involving S_H2' step in comparison with conventional allyltributyltin. © 1999 Elsevier Science Ltd. All rights reserved.

Fluorous methods have emerged as a new powerful technique in modern organic synthesis, which have influenced not only to the way that preparative organic chemistry is carried out but also the way we think about synthetic organic chemistry.[1] This new wave has also been expanding to include free-radical methodologies and the Curran group has recently developed the first fluorous tin hydride reagent **1**,[2,3] which has the potential to be applicable to a wide range of tin hydride based radical reactions. With this new reagent in hand, the tedious procedure of removing organotin byproducts can be circumvented by simple fluorous-organic liquid-liquid extraction or fluorous-solid phase extraction (FSPE)[4] with fluorous reverse phase silica (FRPS).[4,5] We have previously reported that the fluorous techniques with **1** can be applicable to radical carbonylation,[6] in which hydroxymethylation of organic halides was achieved using a catalytic amount of **1** and $NaBH_3CN$.[7] Since allyltributyltin compounds[8] are particularly useful for tandem radical carbonylations

Scheme 1. Radical Carbonylations with Fluorous Tin Mediators



fluorous reagents: $(C_6F_{13}CH_2CH_2)_3SnH$ (**1**)

$(C_6F_{13}CH_2CH_2CH_2)_3SnCH_2CR' = CH_2$ **2a**: R' = H, **2b**: R' = Me (this work)

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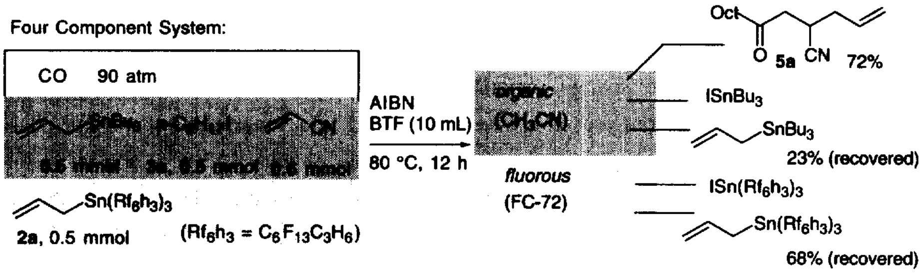
leading to β,γ-unsaturated ketones[9a] and β-functionalized δ,ε-unsaturated ketones,[9b] we jointly set out to evaluate the potential of fluorous allytin reagents **2**,[10] recently developed by the Curran group,[4,11] for these types of free-radical carbonylations (Scheme 1).

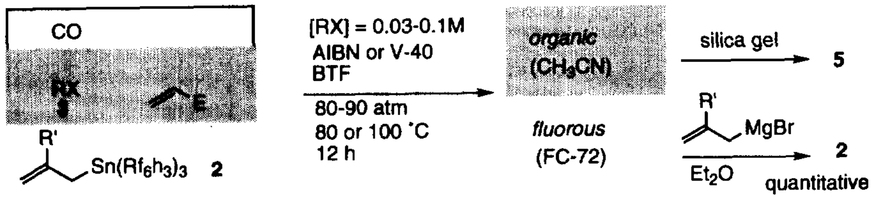
To learn about the chain propagation ability of the fluorous mediator **2a**[12] in comparison with traditional allyltributyltin, we first carried out a competition experiment between **2a** and allyltributyltin for the conversion of octyl iodide (**3a**) to octyl propenyl ketone **4**.[9a] When **3a** was treated with a 1:1 mixture of these tin reagents, 50 mol% of AIBN in BTF (benzotrifluoride)[13] at 80 °C for 12 h under 50 atm of CO, the anticipated enone **4** was formed as the principal product. After the reaction mixture was partitioned into acetonitrile and FC-72[14] layers, GC analysis of both layers showed that 76% of allyltributyltin and 26% of **2a** were consumed, respectively, suggesting that the fluorous allyltin **2a** is less reactive than allyltributyltin for this radical chain reaction involving S_H2' reaction by acyl radicals.[15] Furthermore, the competitive four-component coupling reaction[9b] with acrylonitrile as an additional alkene (Scheme 2) showed the similar reactivity differences in favor of the conventional allyltributyltin, although an α-cyano radical is responsible for the S_H2' step in this case. These results suggested that higher concentrations would be preferable with the use of fluorous allyltin reagent **2a** to compensate for the rather modest chain propagating ability of **2a**. Indeed, at typical substrate concentration of 0.025 M, for which allyltributyltin works well in the four-component process,[9b] a significant amount of **3a** remained unreacted.

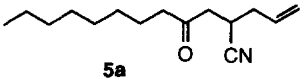
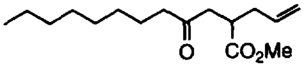
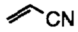
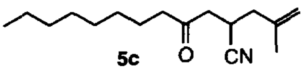
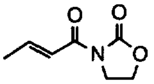
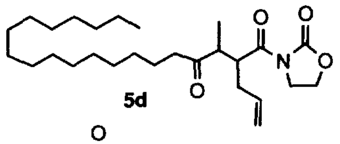
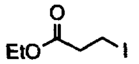
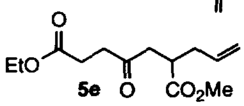
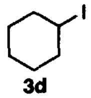
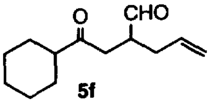
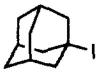
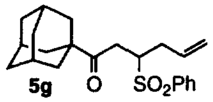
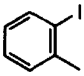
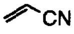
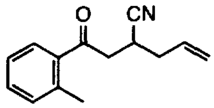
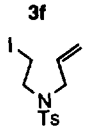
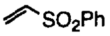
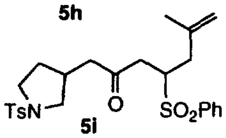
Scheme 2. Competition Experiments between Fluorous Allyltin 2a and Allyltributyltin



The results of the four-component coupling reaction with fluorous allyltin **2a** and methallyltin **2b** are summarized in Table 1. These experiments were carried out using a substrate concentration of 0.03-0.1 M, CO pressures of 80-90 atm, temperatures of 80 or 100 °C, and AIBN or V-40 (1,1'-azobis-(cyclohexane-1-carbonitrile)) as radical initiator. Both **2a** and **2b** work well for the present four-component coupling reaction. The case given in run 9 shows that the initial radical cyclization precedes the intermolecular reactions. Typically octyl iodide (**3a**) was treated with **2a** (2 equiv), acrylonitrile (1.2 equiv), and V-40 (50 mol%) in BTF under 90 atm of CO pressure for 12 h at 100 °C. After the reaction, BTF was removed by vacuum evaporation and the resulting oil was partitioned into acetonitrile (20 mL) and FC-72[14] (20 mL x 2). Evaporation of the acetonitrile layer, followed by short column chromatography on silica gel (hexane/ether = 4) gave pure **5a** in 68% yield. The FC-72-layer contained fluorous tin compounds, from which tin reagent **2a** was regenerated quantitatively by treatment with allylmagnesium bromide in ether.

Table 1. Fluorous Allyltin Mediated Four-Component Coupling Reaction [a]



run	RX	fluorous tin reagent	alkene	product	yield(%)[b]
1	 **3a**	**2a**		 **5a**	68
2		**2a**		 **5b**	60
3		**2b**		 **5c**	61
4[c]	n-$C_{16}H_{33}Br$ **3b**	**2a**		 **5d**	67[d]
5	 **3c**	**2a**		 **5e**	71
6[e]	 **3d**	**2a**		 **5f**	66
7[f]	 **3e**	**2a**		 **5g**	60
8	 **3f**	**2a**		 **5h**	56
9	 **3g**	**2b**		 **5i**	65[g]

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[a] Conditions: **3** (0.5 mmol), **2** (1.0 mmol), alkene (0.55-0.6 mmol), AIBN (0.3 mmol) or V-40 (for runs 1 and 9), BTF (10 mL), CO (80-90 atm), 80 °C (100 °C for runs 1 and 9), 12 h.
[b] Isolated yield by silica gel chromatography.
[c] With substrate concentration of 0.1 M and 1.47 equiv of **3b** and 2 equiv of **2a** to an alkene.
[d] Obtained as a 1 : 1 mixture of diastereomers.
[e] With 6 equiv of **2a**.
[f] With substrate concentration of 0.03 M.
[g] Obtained as a 1 : 1 mixture of diastereomers.

As is evident from the results presented above, fluorous allyltin and methallyltin reagents, **2a** and **2b**, are useful for the free-radical carbonylations of organic halides **3**. The observed modest chain propagating ability of fluorous allyltin reagents in comparison with conventional allyltributyltin reagent required a slight modification of the carbonylation reaction conditions. The simplified liquid/liquid extraction workup to isolate the four-component coupling products will allow for the easy implementation of the parallel synthesis based on these fluorous radical carbonylation reactions.

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