Decarboxylative Allylation and Vinylation Approach of Thiohydroxamate Esters†

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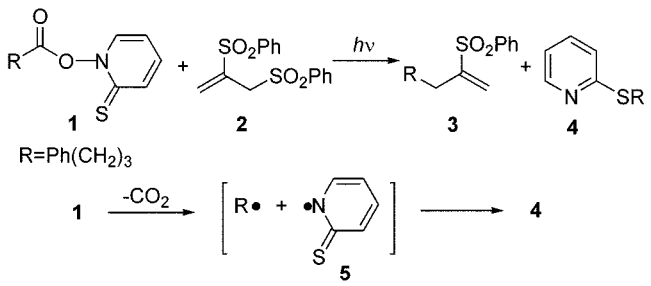
Barton's *O*-acyl thiohydroxamates are very useful to generate alkyl radicals from carboxylic acids *via* *O*-acyl thiohydroxamates[1,2] and have been used to form carbon-carbon bonds by reacting with sulfonyl cyanides[3] and activated olefins.[4] However, Barton esters **1** have some limitations because they are very reactive, thereby yielding a byproduct resulting from attacking the thiocarbonyl group of Barton ester by alkyl radicals. This problem was solved to some extent by using less reactive *O*-acyl thiohydroxamates **6** in radical acylation approach.[5,6]

Decarboxylative allylation was studied with Barton esters and good yields of allylated products were obtained with an allyl sulfide bearing an electron withdrawing group at β-position.[7] To examine the efficiency of *O*-acyl thiohydroxamates **6**, we initially studied radical allylation with Barton ester **1**. Radical reaction of Barton ester **1** with allyl sulfone **2** in benzene for 2 h under photolytic conditions by sun lamp irradiation furnished a 38 : 33 mixture of vinyl sulfone **3** and 2-pyridyl alkyl sulfide **4** (Scheme 1). Since we anticipated that the radical reaction under photolytic conditions might proceed through a radical cage mechanism,[8] the same reactions were carried out under thermal conditions and the experimental results are summarized in Table 1. When Barton ester **1** was treated with **2** in benzene at 80 °C for 2 h, a slightly better result was obtained, yielding a 41 : 29 mixture of **3** and **4**. A similar result was also obtained at 100 °C using V-40 (azobis(cyclohexanecarbonitrile)) as initiator. Furthermore, when the same reaction was carried out in the absence of radical initiator, a similar result was realized, indicating that Barton ester **1** thermally decomposed to generate an alkyl radical along with 2-pyridylthio radical **5**. Addition of **1** into the solution of **2** for 2 h using a syringe pump resulted in a 49 : 35 mixture of **3** and **4**. The byproduct **4** might be formed by direct coupling of an alkyl radical with **5** under thermal and photolytic conditions.



Scheme 1

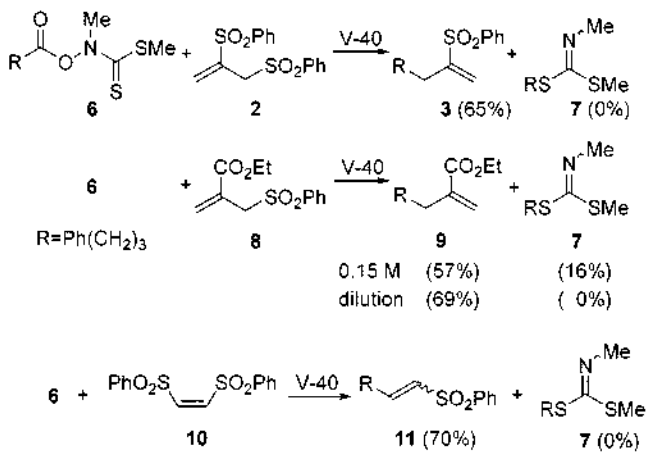
Table 1. Radical Allylation of Barton Ester at Various Condition

	Condition	Time (h)	Solvent	Yield (%) 3	Yield (%) 4
1	25 °C/sun lamp (300W)	2	C_6H_6	38	33
2	80 °C	2	C_6H_6	41	29
3[a]	80 °C/AIBN	4	C_6H_6	49	35
4	110 °C/V-40	2	C_6H_5Cl	45	29

[a]Barton ester and AIBN was slowly added for 2 h.

To obviate the problem of the formation of **4**, when the same reaction was carried out with thiohydroxamate **6** using V-40 as initiator in chlorobenzene at 110 °C for 10 h, the allylated product was isolated in 65% yield without giving byproduct **7** (Scheme 2). Apparently, initially generated alkyl radical attacked allyl sulfone **2** preferentially rather than thiohydroxamate **6**.

However, reaction of **6** with allyl sulfone **2** under photolytic condition (UV lamp, 300 nm) furnished a 63 : 7 mixture of **3** and **7**. When the reaction was carried out with cyclohexyl thiohydroxamate under the same conditions, a 46 : 26 mixture of **3** and **7** was obtained. Probably, the slow addition rate of cyclohexyl radical onto **2** might increase the formation of **7**. Thus, the success of the decarboxylative



Scheme 2

†This paper is dedicated to Professor Yong Hae Kim for his outstanding contributions in synthetic organic chemistry.

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Table 2. Decarboxylative Radical Allylation and Vinylation

Substrate R–X X=(CO_2-NMe(C=S)SMe)	Product Yield (%)		
	3	**9**[a]	**11**
PhO–X	66	70	70
Cbz–N(H)–X	60	57	73
X	80	68	73
X	69	63	73
X	79	64	75
Br, X	70	60	66
PhS–X	59	62	71

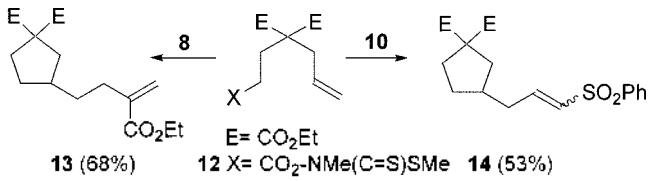
[a]the starting ester and V-40 was slowly added for 5 h by a syringe pump.

allylation approach using **2** under thermal conditions seems to be due to the thermal stability of **6**. Based on the experimental data, remaining reactions were carried out in refluxing chlorobenzene using V-40 as initiator.

Table 2 summarizes some experimental results and illustrates the efficiency of the decarboxylative allylation reactions. Primary and secondary thiohydroxamate esters work well, yielding the corresponding vinyl sulfones in high yields. Sterically hindered tertiary thiohydroxamate ester underwent the decarboxylative allylation cleanly. It is noteworthy that stable radicals such as a benzylic radical and an alkyl radical activated with a phenylsulfanyl group react with allyl sulfone **2** to give the allylated products.

Allylation reactions were also carried out with ethoxycarbonyl substituted allyl sulfone **8** (Scheme 2). When the allylation was repeated under the same conditions described above, the desired product **9** was isolated in 57% yield along with a significant amount of byproduct **7** (16%). Apparently, the addition of the alkyl radical onto **8** was slowed down to some extent, thereby allowing the alkyl radical to attack **6**. The problem of the formation of the byproduct was solved by the addition of **6** into **8** with a syringe pump. Thus, the addition of a 0.05 M chlorobenzene solution of **6** to a 0.3 M chlorobenzene solution of **8** at 110 °C by a syringe pump over 5 h with additional stirring for 2 h afforded the desired **9** in 69% yield without the formation of **7**. Similarly, the formation of several allylated products worked equally well under highly diluted conditions as shown in Table 2.

We have studied radical vinylations using (*Z*)-1,2-bis(phenylsulfonyl)-ethylene (**10**), which are very efficient



Scheme 3

radical acceptors, transferring a vinyl sulfonyl group to an alkyl group. Treatment of **6** with **10** and V-40 in chlorobenzene at 110 °C for 6 h afforded **11** in 70% yield. Various thiohydroxamates worked equally well, yielding (*E*)-1-phenylsulfonyl alkenes in good yields.

The major advantage of the present approach is a sequential carbon-carbon bond formation involving cyclization followed by allylation or vinylation, which has been demonstrated successfully (Scheme 3). Radical reaction of thiohydroxamate ester **12** with **8** afforded **13** in 68% yield, whereas the reaction of **12** with **10** under similar conditions gave **14** in 53% yield.

In conclusion, we have found that a new thiohydroxamate ester, which is much less reactive and more stable than Barton ester, is effective for radical allylation and vinylation under tin-free conditions.[9]

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