CHEMCOMM Communication
www.rsc.org/chemcomm

Decarboxylative acylation approach of thiohydroxamate esters

Sunggak Kim,*[a] Chae Jo Lim,[a] Sang-Eun Song[b] and Han-Young Kang[b]

[a] *Center for Molecular Design and Synthesis and Department of Chemistry, School of Molecular Science, Korea Advanced Institute of Science and Technology, Taejon 305-701, Korea. E-mail: skim@mail.kaist.ac.kr*

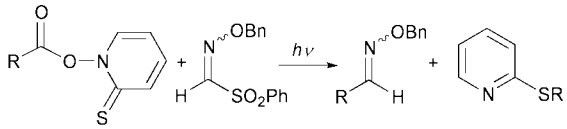
[b] *Department of Chemistry, Chungbuk National University, Cheongju 361-763, Korea*

Received (in Cambridge, UK) 4th May 2001, Accepted 20th June 2001
First published as an Advance Article on the web 12th July 2001

A decarboxylative acylation approach is achieved with thiohydroxamate ester 6, which is less reactive and more stable than Barton's ester 1.

Since *O*-acyl thiohydroxamates were introduced in radical chemistry by Barton,[1] they have attracted a great deal of attention among synthetic chemists as useful radical precursors of alkyl[2] and aminyl radicals.[3] Radical chemistry of *O*-acyl thiohydroxamates **1** were further applied not only to the introduction of synthetically useful functional groups such as a halide[4] and a nitrile[5] but also to the formation of carbon-carbon bonds.[6] However, a highly reactive trapping agent is normally required because the alkyl radical could attack the thiocarbonyl group of **1** concurrently.

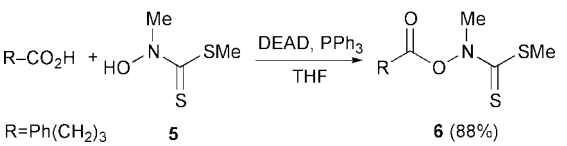
In connection with our recent interest in tin-free radical reactions,[7,8] we have studied the feasibility of decarboxylative acylation approaches of carboxylic acids *via O*-acyl thiohydroxamates **1** using phenylsulfonyl oxime ether **2a** as an acylating trapping agent (eqn. (1)).[9] Irradiation of a solution of **1** and **2a**



(1)

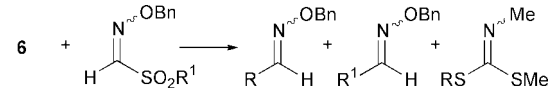
in benzene with a tungsten sun lamp (300 W) for 12 h gave a mixture of oxime ether **3** (32%) and pyridyl sulfide **4** (36%) in a roughly equal ratio, which was anticipated from the previously reported kinetic data.[10] Thus, the key feature for the success of the decarboxylative acylation approach is to reduce the rate of the alkyl radical additions onto the thiocarbonyl group to suppress the formation of **4**.

Our attention was given to somewhat less reactive thiohydroxamate esters that would not undergo aromatization upon radical-mediated fragmentation.[11] In this regard, we expected that a thiohydroxamate ester **6** would be well suited for our purpose. It is noteworthy that a very similar type of the reagent (RCO_2–NMe(C=S)SPh) was previously reported and would have similar properties.[2b] Thiohydroxamate ester **6** was obtained in high yield by treatment of a carboxylic acid with *N*-methylhydroxydithiocarbamate **5**, diethyl azodicarboxylate, and triphenylphosphine in THF and was stable thermally and hydrolytically (eqn. (2)). When **6** was treated with **2b** using 1,1′-



(2)

azobis(cyclohexanecarbonitrile) (V-40) as an initiator in octane at 120 °C for 10 h, a 71 : 16 mixture of oxime ether **3** and **7** was obtained, indicating the addition of the alkyl radical onto **2b** was much faster than the rearrangement to afford **8** (eqn. (3)).

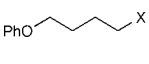
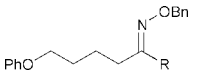
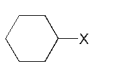
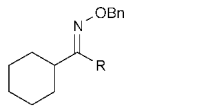
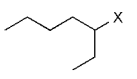
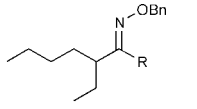
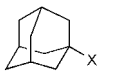
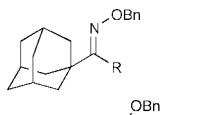
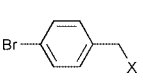
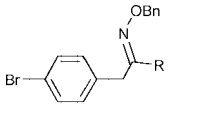
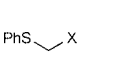
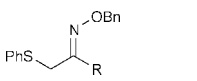


R=Ph(CH$_2$)$_3$	**3**	**7**	**8**
2a: R^1= Ph (100 °C)	78%	0%	0%
= Ph (300 nm)	65%	0%	0%
2b: R^1= Me (120 °C)	71%	16%	0%

(3)

Furthermore, it is evident that a methyl radical, generated from thermal decomposition of a methanesulfonyl radical, attacked **2b** to some extent to yield **7**.[8] Thus, we performed the same reaction with **2a** and it was gratifying to find that thermal reaction of **6** with **2a** and V-40 in refluxing heptane afforded **3** in 78% yield without the formation of **7** and **8**. Furthermore, the decarboxylative acylation approach could be performed under photochemically initiated conditions. Unlike Barton's ester **1**, **6** required irradiation at 300 nm. Irradiation of a benzene solution of **6** with **2a** at 300 nm for 9 h afforded **3** in 65% yield. Thus, the remaining reactions were carried out with **2a** in refluxing heptane (0.25 M) for 12 h. Table 1 summarizes some experimental results and illustrates the efficiency of the decarboxylative acylation approaches. Primary and secondary aliphatic carboxylic acids worked well, yielding the corresponding oxime ethers in high yields. Sterically hindered tertiary

Table 1 Preparation of oxime ethers from thiohydroxamate esters

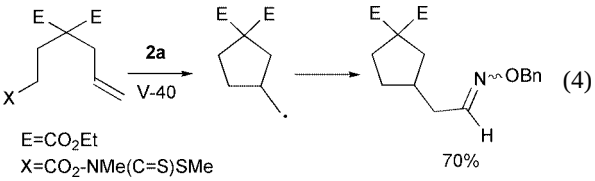
Substrate X = (CO_2–NMe-(C=S)SMe)	Product		Yield[a] (%)
		R = H R = COOMe	76 (64) 62
		R = H R = COOMe	75 (68) 68
		R = H R = COOMe	82 68
		R = H R = COOMe	88 (76) 70
		R = H R = COOMe	87 74
		R = H R = COOMe	84 71

[a] The numbers in parentheses indicate the yields at 300 nm.

 DOI: 10.1039/b104025c

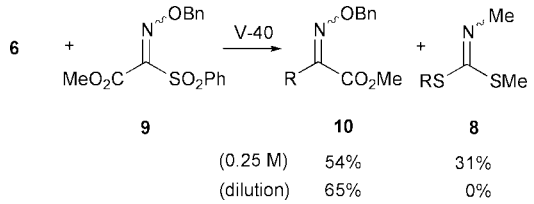
carboxylic acids underwent the decarboxylative acylation cleanly.

Thermal conditions gave somewhat higher yields than photochemical conditions and required 12 h for completion of the reaction. The major advantage of the present method is a sequential cyclization and acylation approach, which was demonstrated successfully in the present study (eqn. (4)).



(4)

To obtain an oxime ester, a synthetic equivalent of a α-keto ester,[12] when we repeated the reaction with methoxycarbonyl oxime ether **9** in refluxing heptane for 12 h, the desired oxime ester **10** was isolated in 54% yield along with a significant amount of the rearranged product **8** (31%) (eqn. (5)). Apparently,



(5)

the addition of the alkyl radical onto **9** was slowed down to some extent, thereby allowing the alkyl radical to attack **6**. The problem of the formation of the rearranged product was solved by the addition of **6** into **9** with a syringe pump. Thus, the addition of a 0.05 M chlorobenzene solution of **6** to a 0.1 M chlorobenzene solution of **9** at 120 °C by a syringe pump over 8 h with additional stirring for 2 h afforded the desired **10** in 65% yield without the formation of **8**. Similarly, the formation of several oxime esters worked equally well under highly diluted conditions as shown in Table 1.

In conclusion, we have developed a new thiohydroxamate ester, which is much less reactive and more stable than Barton's ester and demonstrated the first examples of decarboxylative acylation approaches under tin-free conditions.

We thank the Center for Molecular Design and Synthesis (CMDS) and BK21 project for financial support.

Notes and references

1 For reviews, see: D. Crich and L. Quintero, *Chem. Rev.*, 1989, **89**, 1413; D. H. R. Barton, *Tetrahedron*, 1992, **48**, 2529; S. Z. Zard, *Angew. Chem., Int. Ed. Engl.*, 1997, **36**, 672.

2 (*a*) D. H. R. Barton, D. Crich and W. B. Motherwell, *Chem. Commun.*, 1983, 939; (*b*) D. H. R. Barton, D. Crich and P. Potier, *Tetrahedron Lett.*, 1985, **26**, 5943.

3 M. Newcomb, S.-U. Park, J. Kaplan and D. J. Marquardt, *Tetrahedron Lett.*, 1985, **26**, 5651; M. Newcomb and T. M. Deeb, *J. Am. Chem. Soc.*, 1987, **109**, 3163; M. Newcomb, T. M. Deeb and D. J. Marquardt, *Tetrahedron*, 1990, **46**, 2317; J. Esker and M. Newcomb, *Tetrahedron Lett.*, 1992, **33**, 5913.

4 D. H. R. Barton, D. Crich and W. B. Motherwell, *Tetrahedron*, 1985, **41**, 3901.

5 D. H. R. Barton, J. S. Jaszberenyi and E. A. Theodorakis, *Tetrahedron*, 1992, **48**, 2613.

6 D. H. R. Barton, H. T. Togo and S. Z. Zard, *Tetrahedron Lett.*, 1985, **26**, 6349; D. H. R. Barton, D. Crich and G. Kretzschmar, *Tetrahedron Lett.*, 1984, **25**, 1055.

7 S. Kim, C. J. Lim, S.-E. Song and H.-Y. Kang, *Synlett*, 2001, 688.

8 S. Kim, H.-J. Song, T.-L. Choi and Y.-J. Yoon, *Angew. Chem., Int. Ed. Engl.*, 2001, **40**, 2524.

9 S. Kim, I. Y. Lee, J.-Y. Yoon and D. H. Oh, *J. Am. Chem. Soc.*, 1996, **118**, 5138.

10 S. Kim and I. Y. Lee, *Tetrahedron Lett.*, 1998, **39**, 1587; M. Newcomb and S. U. Park, *J. Am. Chem. Soc.*, 1986, **108**, 4132; M. Newcomb and J. Kaplan, *Tetrahedron Lett.*, 1987, **28**, 1615; D. P. Curran, A. A. Martin-Esker, S.-B. Ko and M. Newcomb, *J. Org. Chem.*, 1993, **58**, 4691.

11 D. H. R. Barton and G. Kretzschmar, *Tetrahedron Lett.*, 1983, **24**, 5889; D. H. R. Barton, D. Crich and G. Kretzschmar, *J. Chem. Soc., Perkin Trans. 1*, 1986, 39; D. H. R. Barton, P. Blundell and J. C. Jaszberenyi, *Tetrahedron*, 1992, **48**, 7121.

12 S. Kim, J.-Y. Yoon and I. Y. Lee, *Synlett*, 1997, 475.