

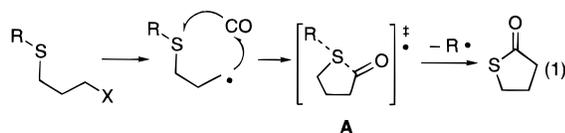
Intramolecular Homolytic Substitution Behavior of Acyl Radicals at Sulfur: New Carbonylative Access to γ -Thiolactones

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Although the inter- and intramolecular addition behavior of acyl radicals has been largely elucidated in the past decade,¹ relatively little is known about homolytic substitution reactions of acyl radicals.^{2,3} In this paper, we focus on the intramolecular S_H2 -type behavior of acyl radicals at sulfur. Carbonylative approaches to the synthesis of γ -thiolactones are still rare, and we are aware of only one such method reported by Alper and co-workers,⁴ who utilized a ring-expansion carbonylation of thiethanes by a Co/Rh mixed-catalyst system. The work reported herein offers a new carbonylative synthesis of γ -thiolactones based on free radical processes (eq 1) and insight into kinetic and mechanistic issues of the first examples of the intramolecular homolytic substitution of acyl radicals at sulfur.



To know how efficient the intramolecular homolytic substitution process is, we prepared acyl selenide **B** having a *tert*-butylthio group and carried out a competitive kinetic study between decarbonylation and S_H2 -type cyclization (Scheme 1). The rate of decarbonylation was obtained from the data reported by Chatgililoglu and

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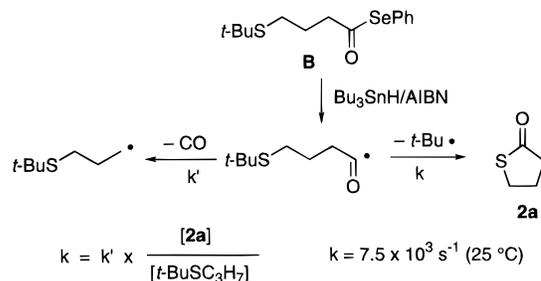
(1) For recent reviews on acyl radicals, see: (a) Brown, C. E.; Neville, A. G.; Rayner, D. M.; Ingold, K. U.; Luszytk, J. *Aust. J. Chem.* **1995**, *48*, 363. (b) Ryu, I.; Sonoda, N. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1050. (c) Crich, D.; Yuan, H. In *Advances in Free Radical Chemistry*; Rawal, V. H., Ed.; JAI Press: Greenwich, CT, 1997; Vol. 2, in press. Also see a review containing C1 radical synthons: (d) Ryu, I.; Sonoda, N.; Curran, D. P. *Chem. Rev. (Washington, D.C.)* **1996**, *96*, 177.

(2) For examples of intermolecular S_H2 -type reactions of acyl radicals at group 16 elements, see: (a) (PhSSPh) Walling, C.; Basedow, O. H.; Savas, E. S. *J. Am. Chem. Soc.* **1960**, *82*, 2181. (b) (PhSeCH₂E) Ryu, I.; Muraoka, H.; Kambe, N.; Komatsu, M.; Sonoda, N. *J. Org. Chem.* **1996**, *61*, 6396. (c) (PhTeTePh, RCOTePh) Crich, D.; Chen, C.; Hwang, J.-T.; Yuan, H.; Papadatos, A.; Walter, R. I. *J. Am. Chem. Soc.* **1994**, *116*, 8937. Also see examples of group 17 element (iodine): (d) Tsunoi, S.; Ryu, I.; Yamasaki, S.; Fukushima, H.; Tanaka, M.; Komatsu, M.; Sonoda, N. *J. Am. Chem. Soc.* **1996**, *118*, 10670. (e) Nagahara, K.; Ryu, I.; Komatsu, M.; Sonoda, N. *J. Am. Chem. Soc.* **1997**, *119*, 5465.

(3) For reviews on inter- and intramolecular S_H2 reactions of alkyl and aryl radicals at group 16 elements, see: (a) Beckwith, A. L. *J. Chem. Soc. Rev.* **1993**, 143. (b) Schiesser, C. H.; Wild, L. M. *Tetrahedron* **1996**, *52*, 13265. (c) Schiesser, C. H. *Main Group Chem. News* **1993**, *1*, 8. (d) Crich, D. In *Organosulfur Chemistry*; Page, P., Ed.; Academic Press: London, 1995; p 49. Also see an early review: (e) Kampmeier, J. A.; Jordan, R. B.; Liu, M. S.; Yamanaka, H.; Bishop, D. J. In *Organic Free Radicals*; Pryor, W. A., Ed.; ACS Symposium Series 69; American Chemical Society: Washington, DC, 1978; p 275. (f) Ingold, K. U.; Roberts, B. P. *Free Radical Substitution Reactions*; Wiley-Interscience: New York, 1971.

(4) Wang, M.-D.; Calet, S.; Alper, H. *J. Org. Chem.* **1989**, *54*, 20. Also see a review: Khumtaveporn, K.; Alper, H. *Acc. Chem. Res.* **1995**, *28*, 414.

Scheme 1. Rate Constant for Intramolecular S_H2 at Sulfur by an Acyl Radical^a



^a The value of k' was taken from ref 5.

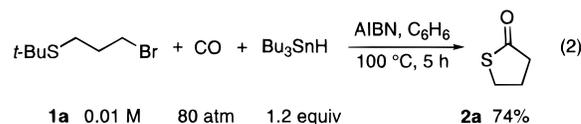
Table 1. Synthesis of γ -Thiolactones by Carbonylation/ S_H2 Reaction Sequence

entry	substrate	product	yield (%)
		R R' R'' R''' X	
1	1a	H H H <i>t</i> -Bu Br	2a 74 ^a
2	1a'	H H H CH ₂ Ph Br	2a 51 ^a
3	1b	H H CH ₃ <i>t</i> -Bu I	2b 75 ^b
4	1c	H Bu H <i>t</i> -Bu I	2c 86 ^c
5	1d	CH ₃ H H <i>t</i> -Bu I	2d 64 ^b
6	1d'	CH ₃ H H CH ₂ Ph I	2d 51 ^c

Conditions: substrate 0.01 M, CO 80 atm, Bu₃SnH 1.2 equiv, AIBN 0.2 equiv, 100 °C, 5 h. a) GC yield. b) NMR yield. c) Isolated yield.

co-workers.⁵ The S_H2 -type reaction, which was accompanied by extrusion of *tert*-butyl radical, was found to be reasonably fast compared with decarbonylation. From the product distribution, the rate of cyclization is approximately $7.5 \times 10^3 \text{ s}^{-1}$ at 25 °C.⁶

Encouraged by these results, we tested the carbonylation/intramolecular S_H2 reaction sequence, which starts with *tert*-butyl 3-bromopropyl thioether (**1a**). When **1a** (0.01 M) was treated with tributyltin hydride (1.2 equiv) and a catalytic amount of AIBN in benzene (100 °C, 5 h, 80 atm of CO), it afforded the desired intramolecular S_H2 -type product, γ -thiobutylolactone (**2a**), in 74% yield (eq 2). Uncyclized 4-(*tert*-butylthio)butanal (5%) and reduced



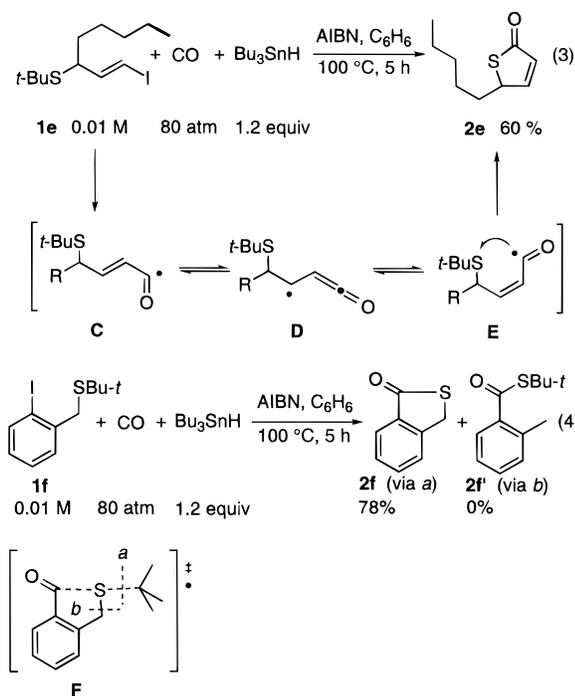
propyl *tert*-butyl thioether (12%) were the only detectable byproducts. Formation of the anticipated γ -thiobutylolactone (**2a**) may involve the addition of *tert*-butylthio-propyl radical to carbon monoxide to give an acyl radical and subsequent intramolecular S_H2 reaction of the acyl radical at the sulfur atom as outlined in eq 1. In this step, *tert*-butyl radical is extruded and is quenched by tributyltin hydride to produce isobutane.

(5) Chatgililoglu, C.; Ferreri, C.; Lucarini, M.; Pedrielli, P.; Pedulli, G. F. *Organometallics* **1995**, *14*, 2672.

(6) For rate constants of the corresponding S_H2 by a primary alkyl radical, see: Franz, J. A.; Roberts, D. H.; Ferris, K. F. *J. Org. Chem.* **1987**, *52*, 2256.

The generality of the carbonylative approach to γ -thiolactones was examined with a variety of substrates. Some of the results are shown in Table 1. In general, the benzyl leaving group is considered to be superior to *tert*-butyl for intramolecular S_{H2} reactions, but in our carbonylation/ S_{H2} system *tert*-butyl is superior. This is due to an undesirable 1,5-H abstraction at the benzylic position that precludes carbonylation (Table 1, entries 2 and 6).⁷

The present reaction need not be restricted only to thio-substituted *alkyl* halides. Equations 3 and 4 illustrate the reactivities of vinyl iodide **1e** and aromatic iodide **1f**, respectively. The carbonylation of **1e** gave α,β -unsatur-



ated γ -thiolactone **2e** in 60% yield after isolation by flash chromatography on silica gel. The rapid isomerization between two isomeric α,β -unsaturated acyl radicals **C**

(7) Indeed, the reaction of **1a'** with Bu₃SnD and AIBN (0.02 M, 80 °C) gave a 1:1 mixture of PhCH₂SCH₂CH₂CH₂D and PhCHDSCH₂CH₂CH₃.

and **E** via ketene α radical **D** satisfactorily accounts for this result.⁸ The reaction of *o*-iodobenzyl *tert*-butyl sulfide (**1f**) gave benzo thiolactone **2f** in good yield. The bond cleavage was selective at *a* in **F**, and no product derived from *b*, which would afford a more stable benzyl radical, was detected. This selectivity strongly suggested the importance of collinear arrangement of both attacking and leaving radicals for the S_{H2} process. This led us to undertake an ab initio MO calculation study. Preliminary calculations at the levels of UMP2/3-21G* and UHF/3-21G* predict that homolytic substitution by an acyl radical at sulfur atom proceeds via a T-shaped transition structure rather than a hypervalent species (for geometries, see the Supporting Information). This transition state is similar to those predicted for intramolecular S_{H2} attack by alkyl radicals.⁹⁻¹¹ However, further work based on higher levels of calculations is needed to clarify this mechanistically intriguing point.

In summary, we have shown that intramolecular homolytic substitution by acyl radicals at sulfur occurs efficiently with extrusion of *tert*-butyl radical. Coupled with this S_{H2} -type reaction, free radical carbonylation methods can be useful alternatives to transition metal methods for γ -thiolactone synthesis with incorporation of carbon monoxide.

Acknowledgment. We are grateful to Dr. Cathleen M. Cruden for useful discussions.

Supporting Information Available: Detailed kinetic data of Scheme 1, geometries of transition state **A** (UHF/3-21G(*) and UMP2/3-21G(*)), and characterization data and a general procedure for compounds **2b-f** (15 pages).

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(8) (a) Hayes, C. J.; Pattenden, G. *Tetrahedron Lett.* **1996**, 37, 271. (b) Herbert, N.; Pattenden, G. *Synlett* **1997**, 69. (c) Balogs, A. Ph.D. Thesis, University of Pittsburgh, Pittsburgh, PA, 1996, pp 128-129.

(9) In general, linear transition structure is important in alkyl radical-induced intramolecular S_{H2} reactions. For recent theoretical studies, see: (a) Smart, B. A.; Schiesser, C. H. *J. Chem. Soc., Perkin Trans. 2* **1994**, 2269. (b) Schiesser, C. H.; Smart, B. A. *Tetrahedron* **1995**, 51, 6051.

(10) For synthesis of γ -thiolactones by an intramolecular S_{H2} process by attacking of alkyl radical to sulfur of thioester, see: (a) Tada, M.; Nakamura, T.; Matsumoto, M. *J. Am. Chem. Soc.* **1988**, 110, 4647. (b) Tada, M.; Matsumoto, M.; Nakamura, T. *Chem. Lett.* **1988**, 199.

(11) (a) Beckwith, A. L. J.; Duggan, S. A. M. *J. Chem. Soc., Perkin Trans. 2* **1994**, 1509. Crich and Yao recently reported an example of intramolecular S_{H2} in which aryl radical attacks at sulfur with extrusion of acyl radicals; see: (b) Crich, D.; Yao, Q. *J. Org. Chem.* **1996**, 61, 3566.