Pergamon

Tetrahedron Letters 39 (1998) 7317–7320

TETRAHEDRON
LETTERS

# Free Radical-Mediated Carboxylation by Radical Reaction of Alkyl Iodides with Methyl Oxalyl Chloride.

**Sunggak Kim* and Sang Yong Jon**

Department of Chemistry
Korea Advanced Institute of Science and Technology, Taejon 305-701, Korea

Received 10 June 1998; revised 16 July 1998; accepted 23 July 1998

*Abstract: Free radical-mediated carboxylation is achieved by treatment of alkyl iodides with methyl oxalyl chloride and bis(tributyltin) in benzene at 350 nm to afford the corresponding acid chlorides as a major product along with a small amount of the methyl esters.* © 1998 Elsevier Science Ltd. All rights reserved.

Free radical-mediated carboxylation reactions have not been well studied because the additions of alkyl radicals onto C=O bonds are difficult due to their reversibility and the high π-bond strength of the C=O bonds.[1] Since free radical-mediated carboxylation reaction of saturated hydrocarbons with oxalyl chloride was reported by Kharasch in the 1940s (eq 1),[2] much studies have not been done during the last 50 years. An indirect radical carboxylation approach involving carbonylation and iodine atom transfer has recently been developed (eq 2).[3] The direct free radical-mediated carboxylation in supercritical $CO_2$ resulted in limited success and more studies are needed.[4] We also have reported a conceptually new method for radical-mediated carboxylation approach using *S*-phenyl chlorothioformate as a carboxyl equivalent radical acceptor (eq 3),[5] which indicated that the success of radical carboxylation reactions depended very much on the nature of the substituents of phosgene derivatives.[5,6]

In connection with our continuing efforts in free radical-mediated acylation and carboxylation reactions,[7] we have studied the possibility of utilizing oxalyl derivatives (**1**, **2**, **3**, and **4**) as 1,2-dicarbonyl equivalent and/or carboxyl equivalent radical acceptors and have found that treatment of alkyl iodides with methyl oxalyl chloride (**4**) and bis(tributyltin) at 350 nm afforded a mixture of the corresponding acid chlorides and the methyl esters (eq 4).

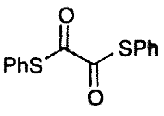
$$\mathrm{RH} + \mathrm{ClCOCOCl} \xrightarrow{h\nu} \mathrm{RCOCl} \qquad (1)$$

$$\mathrm{RI} + \mathrm{CO} + \mathrm{R'OH} \xrightarrow{h\nu} \mathrm{RCOI} \longrightarrow \mathrm{RCO_2R'} \qquad (2)$$

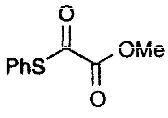
$$\mathrm{RI} + \mathrm{ClCOSPh} \xrightarrow[h\nu]{(\mathrm{Bu_3Sn})_2} \mathrm{RCOCl} \longrightarrow \mathrm{RCOSPh} \qquad (3)$$

$$\mathrm{RI} + \mathrm{ClCOCOOMe} \xrightarrow[h\nu]{(\mathrm{Bu_3Sn})_2} \mathrm{RCOCl} + \mathrm{RCO_2Me} \qquad (4)$$

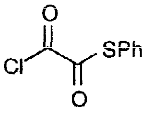
*PII:* S0040-4039(98)01568-8



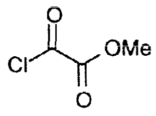
**1**



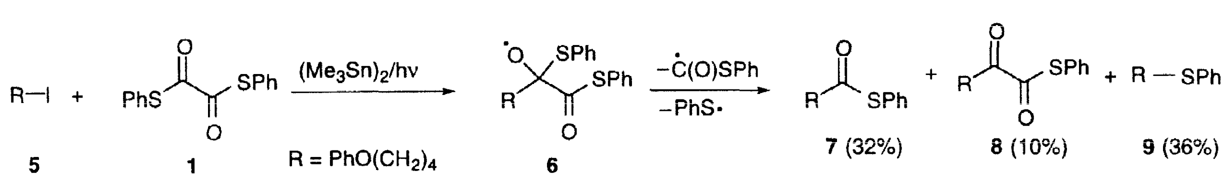
**2**



**3**

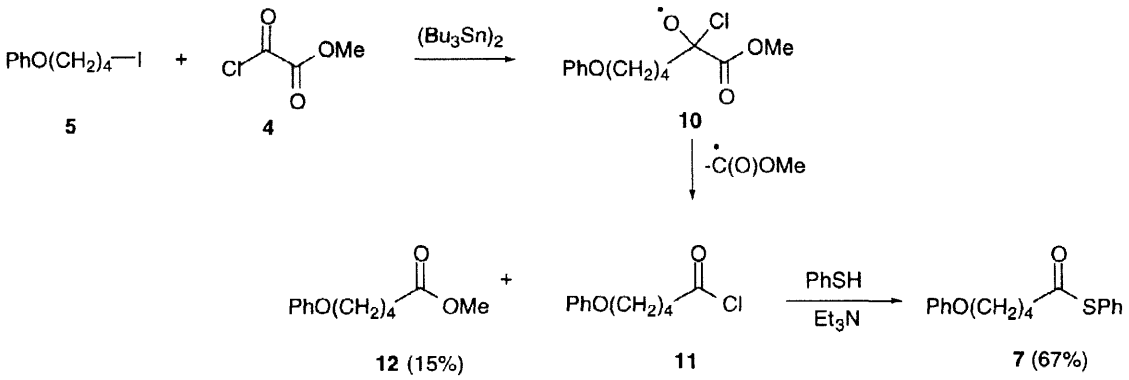


**4**



Scheme 1

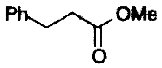
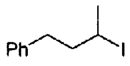
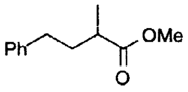
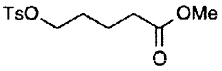
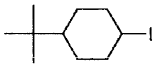
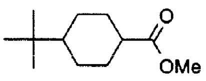
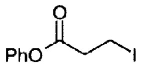
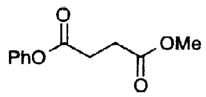
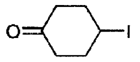
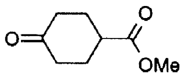
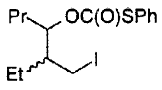
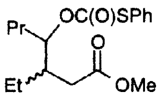
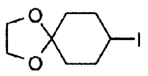
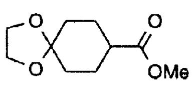
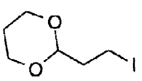
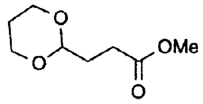
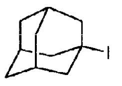
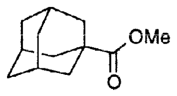
When a solution of 4-phenoxybutyl iodide (**5**) (1.0 equiv), **1** (1.5 equiv) and hexamethylditin (1.2 equiv) in benzene (0.3 M in iodide) was irradiated at 350 nm for 20 h, *S*-phenyl thioate **7** was isolated in 32% yield along with phenyl sulfide **9** (36%) and α-ketothioate **8** (10%). Although we initially anticipated α-ketothioate **8** as a major product as shown in Scheme 1, intermolecular addition of an alkyl radical onto the carbonyl group followed by β-fragmention afforded a mixture of thioate **7** and α-ketothioate **8**. It is noteworthy that β-cleavage of phenylthiocarbonyl radical was favored over that of phenylthio radical. The phenyl sulfide **9** must be obtained through the homolytic substitution of the alkyl radical onto the phenylthio group.[8] Furthermore, the use of **2** and **3** as radical acceptors was unsuccessful. Thus, the reaction of iodide **5** with **2** under the similar conditions afforded a mixture of **7** (10%), **9** (14%) and 4-phenoxybutane (20%), while the use of **3** gave a mixture of **7** (28%) and the corresponding methyl ester (8%) along with the starting material **5** (36%) after treatment with methanol.



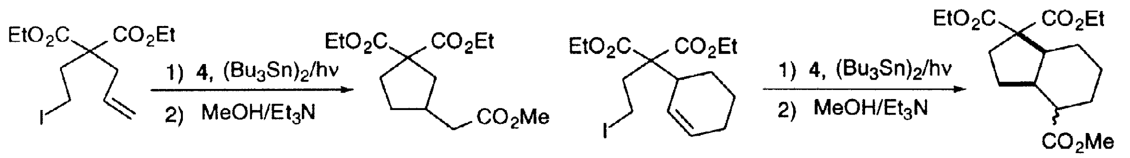
Scheme 2

We next turned our attention to methyl oxalyl chloride (**4**) as a carboxyl equivalent radical acceptor. Treatment of iodide **5** with **4** (3.0 equiv) and bis(tributyltin) (1.2 equiv) in benzene at 350 nm for 20 h followed by addition of thiophenol and triethylamine afforded *S*-phenyl thioate **7** (67%) along with methyl ester **12** in 15% yield.[9] When the reaction was carried out with 1-iodoadamantane under the same conditions, *S*-phenyl 1-adamantanethioate was isolated in 53% yield along with methyl 1-adamantanecarboxylate (17%). Although the exact mechanism awaits further studies, the reaction would proceed via intermediate **10**, from which the β-elimination of the methoxycarbonyl radical would occur to yield acid chloride **11**. Furthermore, methyl ester **12** would be produced by coupling of an alkyl radical with the methoxy carbonyl radical.[10]

**Table 1** Preparation of methyl esters from alkyl iodides with methyl oxalyl chloride

| substrate | product[a] | yield[b], % | substrate | product[a] | yield[b], % |
|---|---|---|---|---|---|
|  |  | 80 |  |  | 74 |
|  |  | 71 |  |  | 75 |
|  |  | 73 |  |  | 67 |
|  |  | 68 |  |  | 66 |
|  |  | 59 |  |  | 76 |

[a] The product was obtained by esterification of the acid chloride with MeOH.
[b] The yield refers to the isolated yield.



13 14 (63%) 15 16 (64%, cis/trans = 1/1.4)

Since the formation of methyl esters in the reaction mixture was inevitable, the remaining reactions were treated with an excess amount of methanol to afford the corresponding methyl esters. Table 1 summarizes the experimental results and illustrates the efficiency and scope of the present method. For most of the cases observed, the reaction required 20 h for completion of the reaction and afforded the methyl esters in good yields. The reaction worked well with primary, secondary alkyl iodides, and sterically hindered 1-iodoadamantane. The present method tolerated acetal, ketone, ester, and even xantate moieties.

In order to extend the utility of the present method, sequential radical reactions involving cyclization and carboxylation were carried out with olefinic iodide **13** and **15**. Radical reaction of **13** with **4** and bis(tributyltin) at 350 nm for 30 h afforded methyl ester **14** in 63% yield after treatment with methanol. A similar result was also obtained with **15**.

**Acknowledgement:** We thank The Korea Research Foundation for financial support.

## References

1. (a) Beckwith, A. L. J.; Hay, B. P. *J. Am. Chem. Soc.* **1989**, *111*, 230, 2674. (b) Walton, R.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1991**, *113*, 5791.
2. (a) Kharasch, M. S.; Brown, H. C. *J. Am. Chem. Soc.* **1942**, *64*, 329. (b) Kharasch, M. S.; Kane, S. S.; Brown, H. C. *J. Am. Chem. Soc.* **1942**, *64*, 333. (c) Kharasch, M. S.; Kane, S. S.; Brown, H. C. *J. Am. Chem. Soc.* **1942**, *64*, 1621. (d) Hedaya, E.; Kyle, L. M. *J. Org. Chem.* **1967**, *32*, 197. (e) Tabushi, I.; Hamuro, J.; Oda, R. *J. Org. Chem.* **1968**, *33*, 2108.
3. Ryu, I.; Nagahara, K.; Komatsu, M.; Sonoda, N. *J. Am. Chem. Soc.* **1997**, *119*, 5465.
4. Hadida, S.; Michael, S. S.; Beckman, E. J.; Curran, D. P. *J. Am. Chem. Soc.* **1997**, *119*, 7406.
5. Kim, S.; Jon, S. Y. *J. Chem. Soc., Chem. Commun.* **1998**, 815.
6. (a) Kim, S.; Lee, I. Y.; Yoon, J. Y.; Oh, D. H. *J. Am. Chem. Soc.* **1996**, *118*, 5138. (b) Kim, S.; Yoon, J. Y. *J. Am. Chem. Soc.* **1997**, *119*, 5982. (c) Kim, S.; Yoon, J. Y.; Lee, I. Y. *Synlett* **1997**, 475.
7. (a) Kim, S.; Jon, S. Y. *J. Chem. Soc., Chem. Commun.* **1996**, 1335. (b) Kim, S.; Yoon, J. Y. *J. Am. Chem. Soc.* **1997**, *119*, 5982.
8. (a) Tada, M.; Nakagiri, H. *Tetrahedron Lett.* **1992**, *33*, 6657. (b) Tada, M.; Kaneko, K. *Chem. Lett.* **1995**, 843. (c) Schiesser, C. H.; Wild, L. M. *Tetrahedron* **1996**, *52*, 13265.
9. A typical procedure for the radical reaction of methyl oxalyl chloride with an alkyl iodide is as follows. A benzene solution (0.65 ml, 0.3 M in the iodide) of 4-phenoxybutyl iodide (56 mg, 0.2 mmol), methyl oxalyl chloride (74 mg, 0.6 mmol) and bis(tributyltin) (140 mg, 0.24 mmol) in a pyrex tube was degassed for 10 min and irradiated (4 x 350 nm lamps) in a Rayonet photochemical reactor for 20 h. After methylene chloride (1 ml) was added to the reaction mixture, MeOH (80 ul) and triethylamine (140 ul) were successively added to the reaction mixture at 0°C. After being stirred at room temperature for 30 min, the reaction mixture was concentrated under reduced pressure. Ethyl acetate (5 ml), water (2-3 drops), and potassium fluoride (120 mg, 2 mmol) were then added and the mixture was stirred at room temperature for 30 min. After the reaction mixture was filtered through a short column of silica gel, the filterate was concentrated under reduced pressure. The crude product was purified by flash silica gel column chromatography to give methyl 5-phenoxypentanoate (34 mg, 81 %) as a colorless oil : $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.65-1.72 (m, 4H), 2.38 (t, J=7.0 Hz, 2H), 3.65 (s, 3H), 3.95 (t, J=5.9 Hz, 2H), 6.85-6.93 (m, 3H), 7.22-7.28 (m, 2H); $^{13}$C NMR (50 MHz, $CDCl_3$) $\delta$ 21.6, 28.6, 33.6, 51.4, 62.0, 114.2, 120.3, 129.1, 158.6, 173.5; IR (NaCl) 2925, 1728, 1215, 930 cm$^{-1}$.
10. Radical-radical coupling may be difficult due to relatively low concentration of an alkyl radical and the methoxy carbonyl radical. Thus, the direct attak of an alkyl radical onto the methoxycarbonyl group followed by elimination of chlorocarbonyl radical would be also possible. We thank the referees for helpful suggestions.