

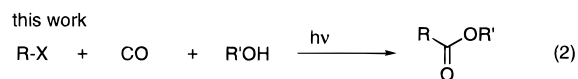
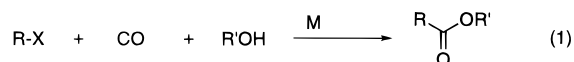
## Radical Carboxylation: Ester Synthesis from Alkyl Iodides, Carbon Monoxide, and Alcohols under Irradiation Conditions

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There is little doubt that transition metal-catalyzed carbonylation of organic halides with CO to give carboxylic acids and their derivatives is a basic and important synthetic process (eq 1).<sup>1,2</sup> It is well-known that the Monsanto Chemical Company produces acetic acid from methanol and CO and that a key step in this process involves the Rh-catalyzed carbonylation of methyl iodide to give acetyl iodide.<sup>3</sup> In this paper, however, we report a conceptually new method for the synthesis of carboxylic acid esters from the combination of alkyl iodides, alcohols, and CO that can be carried out with photoirradiation in the absence of a metal catalyst (eq 2).<sup>4</sup> In our previous paper,



we reported the synthesis of acyl selenides by the photolysis of  $\alpha$ -(phenylseleno)carbonyl compounds in the presence of an alkene and CO.<sup>5</sup> Direct substitution of acyl radical on selenium atom to liberate  $\alpha$ -acyl alkyl radical is the key step in the process. Unlike this case, transfer of iodine atom from alkyl iodide to acyl radical is regarded as inefficient, since the transformation is obviously endothermic. However, we thought that the iodine transfer reaction could be driven by a following ionic reaction of the acyl iodide with alcohol to furnish the ester.<sup>6</sup> We applied successfully this key concept for the present new carbonylation system, which we refer to as catalyst-free radical carboxylation.

When a hexane solution of 2-iodooctane (**1a**) and ethanol (3 equiv) was irradiated with a xenon lamp through a pyrex glass tube under CO pressure (20 atm, 15 h), **1a** was largely recovered unchanged (89%) and no carbonylated product was obtained.

(1) *Carbonylation: Direct Synthesis of Carbonyl Compounds*; Colquhoun, H. M., Thompson, D. J., Twigg, M. V., Eds.; Plenum Press: New York, 1991.

(2) For recent examples of ester synthesis by transition metal-catalyzed carbonylation of alkyl iodides, see: (Pd) (a) Urata, H.; Maekawa, H.; Takahashi, S.; Fuchikami, T. *J. Org. Chem.* **1991**, *56*, 4320 and references cited therein. (Pt) (b) Takeuchi, R.; Tsuji, Y.; Fujita, M.; Kondo, T.; Watanabe, Y. *J. Org. Chem.* **1989**, *54*, 1831. (Pt and  $h\nu$ ) (c) Kondo, T.; Sone, Y.; Tsuji, Y.; Watanabe, Y. *J. Organomet. Chem.* **1994**, *473*, 163. (Pd–Rh) (d) Buchan, C.; Hamel, N.; Woell, J. B.; Alper, H. *J. Chem. Soc., Chem. Commun.* **1986**, 167. (e) Woell, J. B.; Fergusson, S. B.; Alper, H. *J. Org. Chem.* **1985**, *50*, 2134. Also see a pertinent review covering earlier work: (f) Cassar, L.; Chiusoli, G. P.; Guerrieri, F. *Synthesis* **1973**, 509.

(3) It should be noted that for the slow oxidative addition of alkyl iodides and isomerization problem, an extension of Monsanto's acetic acid synthesis to higher alcohols appears less feasible, see: (a) Dekleva, T. W.; Forster, D. *J. Am. Chem. Soc.* **1985**, *107*, 3565. (b) Dekleva, T. W.; Forster, D. *J. Am. Chem. Soc.* **1985**, *107*, 3568.

(4) For cationic carbonylation, see: Bagno, A.; Bukala, J.; Olah, G. A. *J. Org. Chem.* **1990**, *55*, 4284.

(5) Ryu, I.; Muraoka, H.; Kambe, N.; Komatsu, M.; Sonoda, N. *J. Org. Chem.* **1996**, *61*, 6396.

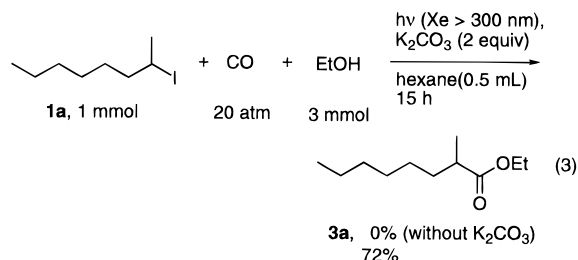
(6) For an example of ionic trap by an internal carbonyl group, see: Tsunoi, S.; Ryu, I.; Yamasaki, S.; Tanaka, M.; Komatsu, M.; Sonoda, N. *J. Am. Chem. Soc.* **1996**, *118*, 10670.

**Table 1.** Ester Synthesis via Catalyst-Free Radical Carboxylation of Alkyl Iodides under Irradiation Conditions<sup>a</sup>

entry	alkyl iodide	alcohol/conditions	product	yield <sup>b</sup> (%)
1		<b>2a</b> (1.4 equiv) 30 atm, 12 h		87
2		EtOH <sup>c</sup> 40 atm, 16 h		73
3 <sup>d</sup>		<b>2b</b> (2 equiv) 20 atm, 18 h		(79)
4		<b>2c</b> (2 equiv) 30 atm, 15 h		73
5		<b>2b</b> (2 equiv) 55 atm, 33 h		60
6		<b>2d</b> (1.4 equiv) 20 atm, 24 h		67 <sup>e</sup>
7		EtOH (3 equiv) 50 atm, 17 h		59
8 <sup>f</sup>		EtOH <sup>c</sup> 40 atm, 50 h		(73) <sup>g</sup>
9		<b>2b</b> (1.5 equiv) 40 atm, 18 h		68 <sup>h</sup>

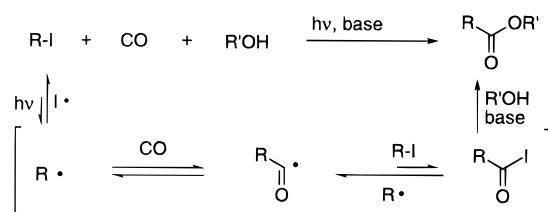
<sup>a</sup> Unless otherwise noted, the following reaction conditions were used: alkyl iodide (1 mmol), hexane (0.5 mL), K<sub>2</sub>CO<sub>3</sub> (2 mmol), alcohol (1.4–3 equiv), CO (20–55 atm), under Xe irradiation (Pyrex) 12–50 h. <sup>b</sup> Isolated yield after flash chromatography on silica gel. Values in parentheses represent the NMR yield. <sup>c</sup> EtOH was used as a solvent. <sup>d</sup> KOH (2 mmol) was used in place of K<sub>2</sub>CO<sub>3</sub>. <sup>e</sup> 91% conversion. <sup>f</sup> Carried out on a 2 mmol scale. <sup>g</sup> 74% conversion. <sup>h</sup> The alcoholysis product was also obtained in 14% yield.

However, the simple addition of a base to this reaction system resulted in a dramatic change. Thus, when the same reaction was carried out in the presence of anhydrous K<sub>2</sub>CO<sub>3</sub> (2 equiv), the desired ethyl ester **3a** was obtained in 72% yield, after isolation by flash chromatography on silica gel (eq 3). Octenes were formed as byproducts in this reaction (1-octene, 10%; 2-octene, 6% (trans/cis = 73:27)).<sup>7</sup> Lower CO pressures (<10 atm) and lower substrate concentrations ([RI] < 1 M) increased these side reaction products.<sup>8</sup> The use of potassium hydroxide and sodium hydroxide was equally effective.

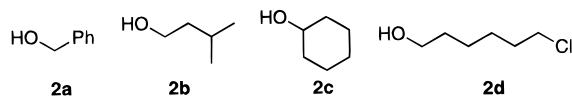


Various alkyl iodides and alcohols were tested and the reaction was found to be general (Table 1). Thus, alkyl iodides

## Scheme 1



**1** were converted into the corresponding esters **3** in good yields. Nearly stoichiometric amounts of alcohols suffice for this ester synthesis. An  $\omega$ -chloro substituent on an alcohol and a  $\gamma$ -phenylthio group on an alkyl iodide can also tolerate this carbonylation (entries 6 and 7). 1-Iodoadamantane (**1g**) also works well for this reaction. In this case to avoid direct  $S_N1$  type alcoholysis of the starting iodide, a nearly equimolar amount of alcohol should be used.



The mechanism of this catalyst-free radical carboxylation is outlined in Scheme 1.<sup>9</sup> In the initiation step, the C–I bond of an alkyl iodide would be cleaved homolytically by irradiation.<sup>10</sup>

(7) For photoirradiation-promoted elimination of HI from alkyl iodides, see: (a) Kropp, P. J. *Acc. Chem. Res.* **1984**, *17*, 131. (b) Kropp, P. J.; Poindexter, G. S.; Pienta, N. J.; Hamilton, D. C. *J. Am. Chem. Soc.* **1976**, *98*, 8135.

(8) Dilution may disfavor the intermolecular atom transfer step.

(9) For reviews of radical carbonylations, see: (a) Ryu, I.; Sonoda, N. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1050. (b) Ryu, I.; Sonoda, N.; Curran, D. P. *Chem. Rev.* **1996**, *96*, 177.

(10) UV irradiation gave inferior results.

Judging from the fact that the irradiation of 5-iodononane (**1b**) in the presence of CO (78 atm) did not give appreciable amounts of acyl iodide, an esterification process by an alcohol and a base to shift the equilibrium may be critical for this reaction to occur. A relatively slow reaction for the case of a primary alkyl iodide (entry 8) may be the result of its slower atom transfer ability, compared with secondary and tertiary iodides.<sup>11</sup>

Ester synthesis from secondary alkyl iodides by transition metal-catalyzed carbonylation often results in the formation of positional isomers associated with  $\beta$ -elimination of the key metal alkyl species,<sup>2a</sup> and for similar reasons, the carbonylation of tertiary iodides is thought to be attainable only with great difficulty. The present ester synthesis, however, takes place selectively at the carbon to which the iodine had been attached, and thus, a wide range of aliphatic iodides including tertiary iodide can be used. The catalyst-free process is clean, simple, and environmentally friendly, since the recovery of neither precious transition metals nor toxic ligands is necessary.

Thus, we have shown that an efficient conversion of aliphatic iodides to the corresponding esters is possible by simply using irradiation in the visible region without the use of a metal catalyst. A free radical mechanism for this reaction is highly likely, but gratifyingly, the process requires neither radical mediator nor photosensitizer. Importantly, the basic principle of photoinduced catalyst-free carboxylation demonstrated here may have promise in terms for a wide range of other carbonyl compounds.

**Supporting Information Available:** Typical experimental procedure and characterization data for products **3** (21 pages). See any current masthead page for ordering and Internet access instructions.

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(11) Newcomb, M.; Sanchez, R. M.; Kaplan, J. *J. Am. Chem. Soc.* **1987**, *109*, 1195.