Available online at www.sciencedirect.com
SCIENCE DIRECT®

Tetrahedron Letters 45 (2004) 1143–1145

Tetrahedron Letters

Cobalt-catalyzed photolytic methoxycarbonylation of bromoalkanes in the presence of a Lewis acid

Daniel Cash,[a] Angela Combs[a] and Veljko Dragojlovic[b,*]

[a]*Department of Math, Science and Technology, Farquhar College of Arts and Sciences, Nova Southeastern University, 3301 College Avenue, Fort Lauderdale, FL 33314, USA*
[b]*Oceanographic Center, Nova Southeastern University, 8000 North Ocean Drive, Dania, FL 33004, USA*

Received 14 November 2003; revised 2 December 2003; accepted 3 December 2003

Abstract—Addition of a water-stable Lewis acid, indium trichloride, improved the rate of photochemical methoxycarbonylation of bromoalkanes. Primary and secondary bromoalkanes were carbonylated in good yields. Carbonylation of tertiary substrates was somewhat more difficult and some of them reacted too slowly for the reaction to be of a preparative value.

It has been reported that photocarbonylation of iodoalkanes proceeds with ease while more readily available and less expensive bromoalkanes are unreactive.[1,2] Photochemical carbonylation reactions are done in the presence of an inexpensive cobalt catalyst at room temperature and at atmospheric pressure of carbon monoxide. However, photochemical carbonylations sometimes suffer from low reaction rates and limited reaction scale. Lewis acids have been shown to increase the rate of thermal carbonylation reactions.[3] Recently, aluminum-based Lewis acids were successfully employed in cobalt-catalyzed thermal carbonylations of epoxides and aziridines.[4,5] We investigated the use of Lewis acids as additives in order to improve the reaction rate and make photocarbonylation of bromoalkanes feasible.

A modified quartz Ace micro-scale photochemical setup equipped with a PenRey 5.5 W low pressure mercury lamp was employed. A relatively weak UV source allowed for the reactions to be done on a small scale and with high reproducibility. For carbonylation to proceed at a reasonable rate, a relatively high catalyst loading (25–50 mol %) had to be employed. Once the reaction conditions were optimized on a micro-scale setup, the procedure was scaled up to a gram-scale reaction by employing a quartz Ace macro-scale apparatus equipped with a 450 W medium pressure mercury lamp and Vycor filter and adjusting the concentrations of the cobalt catalyst (5 mol %), Lewis acid, and bromoalkane. Photocarbonylation reactions of bromoalkanes were done in a mixture of methanol and acetone as solvents. In photocarbonylation of alkenes, it was established that acetone was necessary for the reaction to proceed.[6–8] The authors assumed that acetone was a sensitizer.[7]

Due to different induction periods as well as a change in the reaction rate due to acid (HBr) buildup, it is difficult to compare the relative rates or the catalyst turnover numbers. The best way to compare efficiency of different catalytic systems appears to be comparison of reaction times and yields. Photolytic methoxycarbonylation of bromocyclohexane in the presence of $Co(acac)_2$ as a catalyst source yielded only 3% of methyl cyclohexanecarboxylate after 24 h (Table 1, entry 1). It was proposed that, in thermal carbonylation reactions, Lewis acids increase the reaction rate by coordinating to the carbon monoxide ligand.[3] Addition of commonly used Lewis acids ($BF_3{\cdot}MeOH$, $AlCl_3$, $GaCl_3$) to the reaction mixture failed to improve the yields or increase reaction rates (Table 1, entries 2–4). In fact, the reaction rate of methoxycarbonylation was retarded and the main product was the corresponding aldehyde. Lanthanide chlorides also retarded the reaction rate with formation of the aldehyde as the major reaction products (Table 1, entries 5 and 6). Since protic acids have been shown to suppress photochemical cobalt-catalyzed methoxycarbonylation and to give a mixture of aldehydes and acetals in low yields,[8] we speculated that the Lewis acids reacted

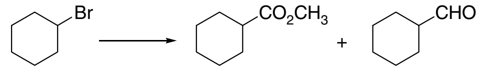
---

Keywords: Bromoalkanes; Cobalt; Photocarbonylation; Lewis acid; Indium trichloride.

* Corresponding author. Tel.: +954-262-8332; fax: +954-262-3931; e-mail: veljko@nova.edu

0040-4039/$ - see front matter © 2003 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2003.12.009

Table 1. Effect of Lewis acids on photolytic methoxycarbonylation of bromocyclohexane[a]



1 **2** **3**

Entry	Additive	Time (h)	**2** (%)[b]	**3** (%)[b]
1	None	24	3	<1
2	$BF_3{\cdot}MeOH$	12	0	9
3	$AlCl_3$	12	0	12
4	$GaCl_3$	12	0	11
5	$YbCl_3$	24	4	8
6	$CeCl_3$	24	3	4
7	$InCl_3{\cdot}4H_2O$	24	29	<1
8	$InCl_3$	24	72	4
9	$InCl_3/MgCO_3$	24	85	3
10	$InCl_3/Al_2O_3$	24	40	3
11	$InCl_3/Li_2CO_3$	24	4	0
12	$In(OTf)_3$	24	5	0
13	$Yb(OTf)_3$	24	<1	0
14	LiCl	24	6	0
15	$MgCl_2$	24	10	0

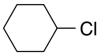
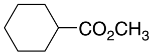
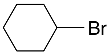
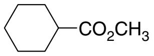
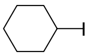
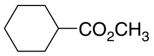
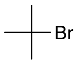
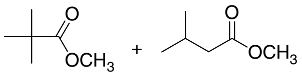
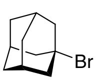
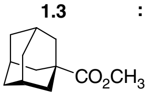
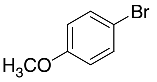
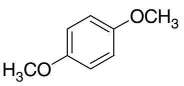
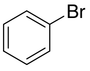
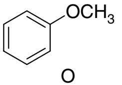
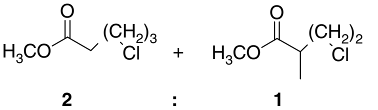
[a] Reaction conditions: $Co(acac)_2$ (0.3 mmol), $InCl_3$ (1.2 mmol), bromoalkane (0.6 mmol), methanol/acetone (3:1, 15 mL), CO (1 atm), 5.5 W PenRey low pressure mercury lamp.

[b] GLC yield.

with methanol to produce the corresponding protic acids. Next, we investigated addition of indium chloride, which is a water-stable Lewis acid.[9] When added in a 0.08–0.10 M concentration, $InCl_3$ provided a considerable increase in the yields of the products and reduction in the reaction times (Table 1, entries 7–10). Addition of an excess of $InCl_3$ resulted in somewhat lower reaction rates. Upon irradiation of the reaction mixture, carbonylation started after an induction period. Length of the induction period depended in the reaction conditions. Addition of $InCl_3$ considerably shortened the induction period. Furthermore, when $InCl_3$ was added a higher concentration of the cobalt catalyst was optimal than without it. A higher concentration of catalyst itself is enough to result in a rate increase. A concentration of the catalyst higher than optimal sharply reduced the reaction rate and further increase in concentration of the catalyst stopped the reaction completely (possibly because of a long induction period, as well as cobalt salt reacting as an internal filter). Addition of water-stable triflate Lewis acids (e.g., $In(OTf)_3$ or $Yb(OTf)_3$) did not result in increased rate of carbonylation. UV–vis analysis showed that there was some chloride exchange between $InCl_3$ and cobalt. Therefore, it appears that chloride anion plays an important role in facilitating the carbonylation reaction.

A byproduct of methoxycarbonylation of bromoalkanes is hydrobromic acid, which accumulates as the reaction progresses. Problems related to accumulation of HBr may be solved by addition of a carbonate salt. Insoluble magnesium carbonate gave the best results. In the presence of $InCl_3$ methyl cyclohexylcarboxylate was

Table 2. Photolytic methoxycarbonylation of haloalkanes[a]

Entry	Haloalkane	Reaction time (h)	Product(s)	Yield (%)
1		24		0
2		28		92[b] 74[c,d,e]
3		4		90[b]
4		18	 **1.3** : **1**	8[b]
5		48		95[b] 88[c]
6		12		94[b]
7		20		<10[b]
8	$BrCH_2(CH_2)_2CH_2Cl$	60	 **2** : **1**	79[b]

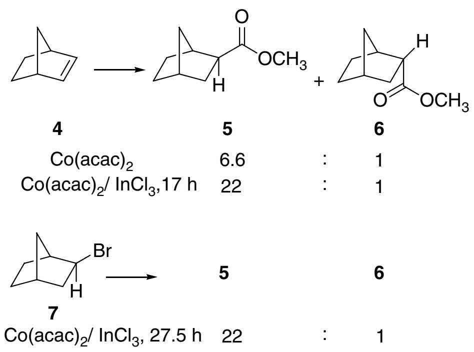
[a] Reaction conditions: $Co(acac)_2$ (0.3 mmol), $InCl_3$ (1.2 mmol), $MgCO_3$ (0.5 g), haloalkane (0.6–1.2 mmol), methanol/acetone (3:1, 15 mL), CO (1 atm), 5.5 W PenRey low pressure mercury lamp.

[b] GLC yield.

[c] Isolated yield.

[d] Reaction conditions: $Co(acac)_2$ (6 mmol), $InCl_3$ (24 mmol), cyclohexyl bromide (120 mmol), methanol/acetone (3:1, 300 mL), CO (1 atm), 450 W Hanovia medium pressure mercury lamp, 40 h.

[e] The product was accompanied by 8% of chlorocyclohexane (GLC), which was not isolated.



Scheme 1.

prepared from bromocyclohexane in a 72% yield after 24 h (Table 1, entry 8). Addition of solid magnesium carbonate to the reaction mixture further increased the yield to 85% after 24 h (Table 1, entry 9) and the reaction was completed in 28 h in a 92% yield (Table 2, entry 2). Soluble carbonates (e.g., Li_2CO_3) retarded the reaction rate (Table 1, entry 11). Basic alumina was also effective in neutralizing hydrogen bromide. However, it reduced the rate of methoxycarbonylation and was, therefore, inferior to magnesium carbonate.

Photocarbonylation of norbornylene **4** gave a mixture of *exo* and *endo* methyl esters in a ratio of 6.6:1. Addition of $InCl_3$ to the reaction mixture increased the *exo*/*endo* ratio to 22:1. Photocarbonylation of *exo*-2-bromonorbornane **7** gave the *exo* and *endo* isomers in an identical ratio (22:1) (Scheme 1).

Among the tertiary bromoalkanes, carbonylation of *tert*-butyl bromide gave a mixture of methyl pivalate and methyl isovalerate in a low yield (Table 2, entry 4). On the other hand, photocarbonylation of 1-adamantyl bromide gave the corresponding methyl ester in an excellent yield (Table 2, entry 5).

Aryl bromides underwent nucleophilic aromatic photosubstitution rather than carbonylation. Activated bromide, 4-bromoanisole, gave the corresponding methoxylation product in a good yield (Table 2, entry 6). Reaction of bromobenzene was slow and gave the corresponding methoxycarbonylation product in a low yield accompanied by several other products (Table 2, entry 7). The same results were obtained when these two substrates were irradiated in a methanol/acetone mixture under a nitrogen atmosphere, in the absence of a cobalt catalyst and carbon monoxide.

Alkyl chlorides were unreactive. Thus, 1-bromo-4-chlorobutane was chemoselectively carbonylated to a mixture of chloroesters albeit with poor regioselectivity (Table 1, entry 8).

The described photocarbonylation is simple and does not involve an advance preparation of the catalyst. All the reagents are inexpensive commercially available compounds.

Acknowledgements

We thank Nova Southeastern University for support in the form of President's Faculty Scholarship Award (Grant no. 338 308) to V.D.

References and notes

1. Kondo, T.; Tsuji, Y.; Watanabe, Y. *Tetrahedron Lett.* **1988**, *29*, 3833–3836.
2. Kondo, T.; Sone, Y.; Tsuji, Y.; Watanabe, Y. *J. Organomet. Chem.* **1994**, *473*, 163–173.
3. Cotton, F. A.; Wilkinson, G.; Murillo, C. A.; Bochmann, M. *Advanced Inorganic Chemistry*. 6th ed.; Wiley: New York, NY, 1999; pp 1212–1213.
4. Getzler, Y. D. Y. L.; Mahadevan, V.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc.* **2002**, *124*, 1174–1175.
5. Mahadevan, V.; Getzler, Y. D. Y. L.; Coates, G. W. *Angew. Chem., Int. Ed.* **2002**, *41*, 2781–2783.
6. Dragojlovic, V.; Gao, D. B.; Chow, Y. L. *J. Mol. Cat. A: Chem.* **2001**, *171*, 43–51.
7. Tao, Y. T.; Chow, T. J.; Lin, J. T.; Lin, C. C.; Chien, M. T.; Chow, Y. L.; Buono-Core, G. E. *J. Chem. Soc., Perkin Trans. 1* **1989**, 2509–2510.
8. Tao, Y. T.; Yeh, W. L.; Tu, C. L.; Chow, Y. L. *J. Mol. Cat.* **1991**, *67*, 105–115.
9. Babu, G.; Perumal, P. T. *Aldrichim. Acta* **2000**, *33*, 16–22.