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Manganese-Catalyzed Carboacylations of Alkenes with Alkyl Iodides

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Abstract

A manganese-catalyzed carboacylation of alkenes with alkyl iodides and carbon monoxide is described. This carbonylative difunctionalization uses both primary and secondary alkyl iodides in reactions with a diverse array of cyclic and acyclic substrates. Examples of successful applications to the synthesis of 5-, 6-, and 7-membered rings are provided. The inexpensive, first-row catalytic system and mild reaction conditions are expected to facilitate applications in complex synthesis.

Graphical abstract

Catalytic reactions of unactivated alkyl halides have led to a diverse set of valuable C–C bond-forming reactions in chemical synthesis.¹ This class of transformations includes alkyl-Mizoroki-Heck-type reactions, constituting fundamental cross-couplings of unactivated alkyl halides with alkenes.² In prior studies, we developed a carbonylative variant of this reaction that yields cyclic enones from alkyl iodides and pendant alkenes (Figure 1).³ We became interested in pursuing an alternative process involving alkene difunctionalization (carboacylation).⁴ Prior to our studies there was limited precedent for this class of alkene difunctionalization; a photochemical palladium-catalyzed carboacylation has been reported, but requires excess alkyl iodide (1.5 equiv) and was limited to ketone synthesis using alkylboranes.⁵

We hypothesized that simple manganese catalysts [e.g., $\text{Mn}_2(\text{CO})_{10}$] could facilitate the desired alkene carboacylation. These complexes have shown promise in both the activation and carbonylation of unactivated alkyl halides—particularly using intense irradiation or electrolysis.⁶ Previous studies involving manganese-catalyzed radical cyclizations required activated α -halocarbonyls as substrates, however.⁷ The use of an inexpensive, first-row metal instead of precious palladium catalysts commonly used in carbonylative processes of

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Supporting Information. Experimental procedures and spectral data for all new compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

complete an iodine atom-transfer cyclization to deliver alkyl iodide 27.⁷ We have observed iodine atom-transfer intermediates in a number of our cyclizations; a representative example is shown in eq 1. Stopping the carboacylation of substrate 1 at partial conversion produces a mixture of both carboacylation product 2 and iodine atom-transfer cyclization product 27 in 19% and 18% yields, respectively (¹H NMR analysis). In a separate experiment, iodide 27 underwent efficient carbonylation under the carboacylation conditions to deliver ester 2 in 81% yield (eq 2). These experiments are consistent with iodine atom-transfer cyclization playing a role in these catalytic transformations, the degree of which is likely dictated by the particular substrate and the energetics of the iodine atom transfer step involved. Ultimately, once acylmanganese 28 is formed, nucleophilic substitution delivers the carboacylation product 2 and regenerates the active catalyst.

In conclusion, we have developed a manganese-catalyzed carboacylation of alkenes using unactivated alkyl iodides and moderate pressures of CO. This reaction exhibits broad scope in carbocycle and heterocycle synthesis, with the potential for good levels of diastereocontrol in the carboacylation process. The common molecular functionality and mild reaction conditions of this alkene difunctionalization are expected to facilitate future applications in complex molecule synthesis.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Figure 1.
Metal-catalyzed, carbonylative alkene additions of alkyl iodides.

Scheme 1.
Plausible Catalytic Cycle

Table 1

Influence of reaction conditions on the Mn-catalyzed carboacylation.

entry	variation from standard conditions above	yield (%) ^a
1	none	84
2	5 mol % $\text{Mn}(\text{CO})_5\text{Br}$ instead of $\text{Mn}_2(\text{CO})_{10}$	14
3	2.5 mol % $\text{Co}_2(\text{CO})_8$ instead of $\text{Mn}_2(\text{CO})_{10}$	0
4	5 mol % $\text{Pd}(\text{PPh}_3)_4$ instead of $\text{Mn}_2(\text{CO})_{10}$	0
5	1 equiv Pr_2EtN instead of 1 equiv KHCO_3	76
6	1 atm CO instead of 10 atm CO	0
7	5 atm CO instead of 10 atm CO	76
8	no ambient light	0
9	no $\text{Mn}_2(\text{CO})_{10}$	0

Reactions were performed with [substrate]₀ = 0.13 M.^aYields determined by ¹H NMR spectroscopy of crude reaction mixture using an internal standard.

Table 2

Manganese-Catalyzed Carboacylations of Acyclic Alkenes.

entry	substrate	product	yield(%) ^a
1	1	2	83 2:1 dr
2	3	4: R = OEt	77 10:1 dr
3		5: R = NEt ₂	67 ^b 8:1 dr
4		6: R = NMePh	73 ^b 10:1 dr
5	7	8	77 ^c 8:1 dr
6	9	10	79 ^c 1:1 dr
7	11	12	64 ^{c,d}
8	13	14	78 ^c 3:1 dr
9	15	16	63 ^{c,d}

See Table 1 for conditions.

^a Isolated yields.^b 2 equiv amine and KHCO₃ used.^c 5 mol % Mn₂(CO)₁₀ used.^d Mixtures of diastereomers produced (see Supporting Information for more details).

Table 3

Manganese-Catalyzed Carboacylations of Cycloalkenyl Substrates.

entry	substrate	product	Yield (%) ^a
1			89 7:1 dr
2			90 ^b 7:1 dr
3			72 9:1 dr
4			73 ^{b,c} 3:1 dr

See Table 1 for conditions.

^a Isolated yields.^b Diastereomeric ratio based on cyclization (see Supporting Information for more details).^c 10 mol % of Mn₂(CO)₁₀ used.