

Ni-Catalyzed Reductive Coupling of Alkyl Acids with Unactivated *Tertiary* Alkyl and Glycosyl Halides

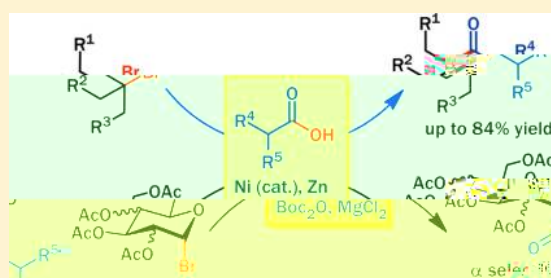
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 Supporting Information

ABSTRACT:

A nickel-catalyzed reductive coupling of alkyl acids with unactivated tertiary alkyl and glycosyl halides is reported. The reaction proceeds in the presence of Ni (cat.), Zn, Boc₂O, and MgCl₂ to give the corresponding tertiary alkyl and glycosyl esters in up to 84% yield. The reaction is highly regioselective and tolerant of various functional groups.



1. INTRODUCTION

The reductive coupling of alkyl acids with unactivated tertiary alkyl and glycosyl halides is a highly regioselective and tolerant of various functional groups. The reaction proceeds in the presence of Ni (cat.), Zn, Boc₂O, and MgCl₂ to give the corresponding tertiary alkyl and glycosyl esters in up to 84% yield. The reaction is highly regioselective and tolerant of various functional groups.

previous work

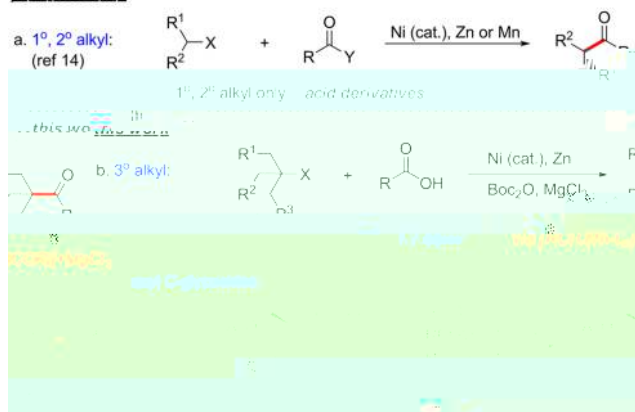


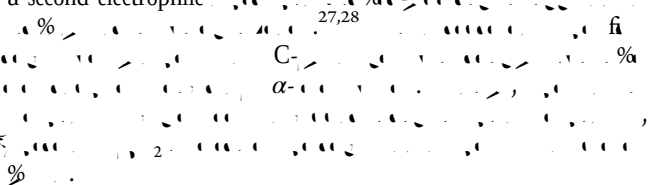
Figure 1.

The reductive coupling of alkyl acids with unactivated tertiary alkyl and glycosyl halides is a highly regioselective and tolerant of various functional groups. The reaction proceeds in the presence of Ni (cat.), Zn, Boc₂O, and MgCl₂ to give the corresponding tertiary alkyl and glycosyl esters in up to 84% yield. The reaction is highly regioselective and tolerant of various functional groups.

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demonstrates the first construction of all carbon quaternary centers via the reductive coupling of unactivated tertiary alkyl halides with a second electrophile.



2. RESULTS AND DISCUSSIONS

2.1. Coupling of *Tertiary* Alkyl Halides with Alkyl Acids.

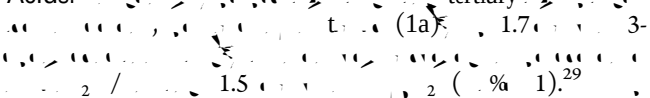


Table 1. Optimization for the Reaction of *t*-BuBr (1a) with 3-Phenylpropanoic Acid^a

		Yield (%)		Yield (%)		Yield (%)	
Entry	Product	Yield (%)	Yield (%)	Yield (%)	Yield (%)	Yield (%)	Yield (%)
1	3a	0	150	25	16		
2	3b	0	150	25	7		
3	4a	0	150	25	24		
4	4a	0	150	25	25		
5	4a	0	150	25	34		
6	4a	/	= 8:2	0	150	25	44
7	4a	/	= 2:8	0	150	25	36
8	4a	/	= 2:8	150	150	25	47
9	4b	/	= 2:8	150	150	25	19
10	4c	/	= 2:8	150	150	25	46
11	5a	/	= 2:8	150	150	25	<10
12	6a	/	= 2:8	150	150	25	<10
13	4a	/	= 2:8	150	100	25	39
14	4b	/	= 2:8	150	100	25	65
15	4b	/	= 2:8	85	100	25	79
16	4b	DMSO/DME = 2:8	85	100	30	82	
17	4a	/	= 2:8	85	100	30	39

^a Conditions: *t*-BuBr (1a) (0.3 mmol), 3-phenylpropanoic acid (170 μmol), Ni(acac)₃ (10%), ligand (12%), MgCl₂ (100%), Boc₂O (200%), Zn (300%), DMSO/DME (2:8), 30 °C, 12 h.

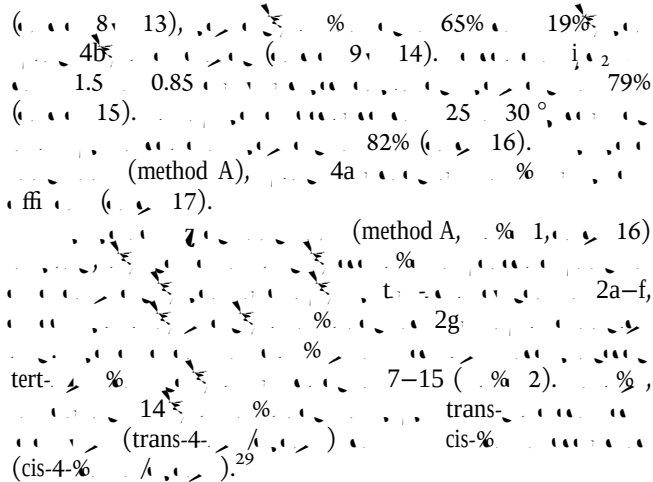
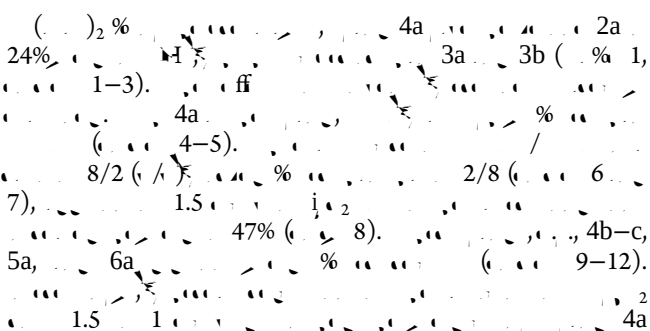
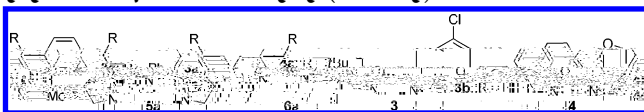
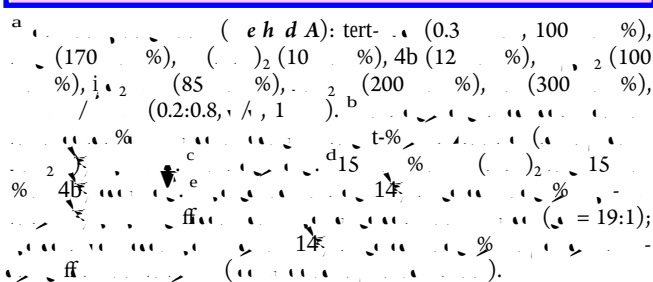
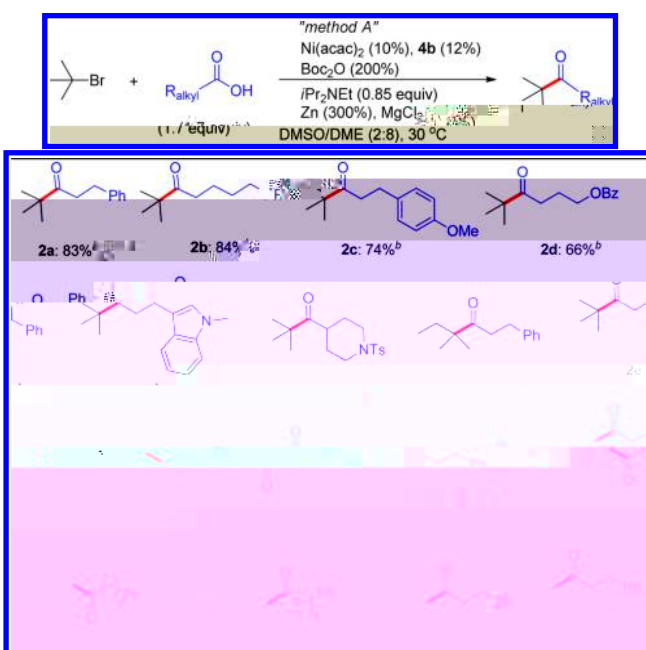
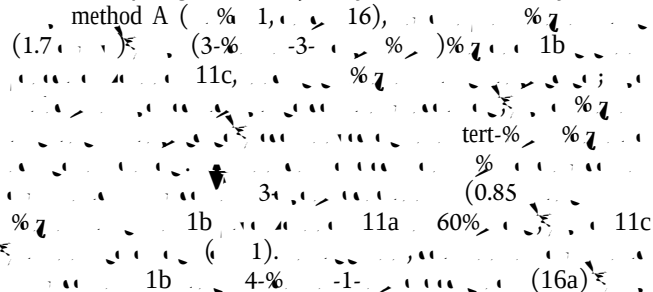


Table 2. Coupling of Unactivated *ε*-Alkyl Bromides with Acids^a



2.2. Coupling of *Tertiary* Alkyl Halides with Aryl Acids.



10%
 16a 1b
 (2).
 ffi
 tertiary
 secondary %
 tertiary %

2.3. Coupling of *Primary* and *Secondary*

... % ... % ...
 ... I, ...
 ... (... 1, ...)³⁵ ... %
 ... % ... (III') ...
 ... (IV') ... III' ...
 ... % ... I ...
 ... 1 () - 4 .0/ 9 , 8 428(117 15726 269.4614 .015414 0) ... 0328 9986. (...)-9()10 ,

$$(I-C) = \frac{29,39}{C} \frac{2+}{1+I} \frac{2}{n} \frac{I-}{I-a/2} (0)$$

- (5) () . Angew. Chem., Int. Ed. 2008, 47, 9334.
- (%) . J. Am. Chem. Soc. 2009, 131, 7532.
- () . Nat. Chem. 2010,

- Chem. 1981, 21, 451. (%)
- J. Organomet. Chem. 1993, 447, 131.
- (33) ()
- (15).
- (34)
- % : ()
- Angew. Chem., Int. Ed. 2007, 46, 8790. (%)
- J. Am. Chem. Soc. 2006, 128, 13175.
- (35) ()
- J. Am. Chem. Soc. 2013, 135, 12004. (%)
- J. Am. Chem. Soc. 2013, 135, 16192. ()
- J. Am. Chem. Soc. 2014, 136, 48. ()
- Science 2014, 345, 433. ()
- Science 2014, 345, 437. ()
- J. Am. Chem. Soc. 2014, 136, 16588–16593.
- (36) ()
- J. Am. Chem. Soc. 2006, 128, 5360. (%)
- J. Am. Chem. Soc. 2005, 127, 510. ()
- Org. Lett. 2011, 13, 2138. ()
- Chem. Sci. 2013, 4, 4022. ()
- Science 2012, 338, 647.
- (37)
- I-a (I-a] % ¹H, ¹³C
- ()
- (38)
- J. Am. Chem. Soc. 2009, 131, 16656.
- (39)
- ()
- %
- Organometallics 2014, 33, 5874.
- (40)
- Angew. Chem., Int. Ed. 2014, 53, 4386.