

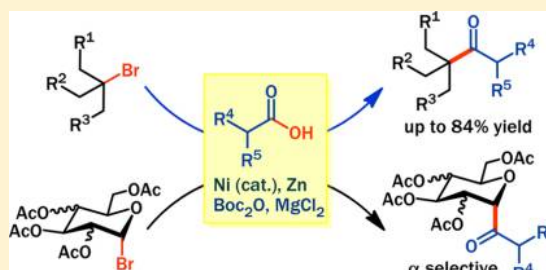
Tertiary α -Acyl C-GlycosidesChenglong Zhao,[†] Xiao Jia,[†] Xuan Wang, and Hegui Gong*

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Supporting Information

ABSTRACT:

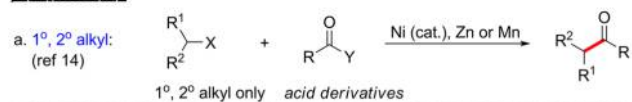
Reaction of tertiary alkyl bromides with α -acyl C-glycosides (1) in the presence of Ni (cat.), Zn, Boc₂O, and MgCl₂ yields α -acyl C-glycosides (2) in up to 84% yield.



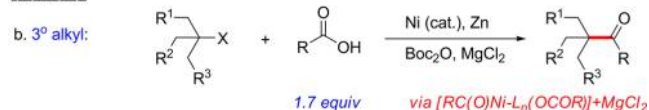
1. INTRODUCTION

The α -acyl C-glycosides (1) are a class of natural products that have attracted much attention in the field of organic chemistry. They are found in various organisms, including plants, animals, and microorganisms. The α -acyl C-glycosides (1) are characterized by the presence of an acyl group at the α -position of the glycoside moiety. They have been found to exhibit a wide range of biological activities, including antibacterial, antifungal, and antiviral activities. The synthesis of α -acyl C-glycosides (1) has been a challenge for many years, but recent advances in organic chemistry have made it possible to synthesize these compounds in a more efficient and selective manner. In this paper, we report a new method for the synthesis of α -acyl C-glycosides (1) using tertiary alkyl bromides and α -acyl C-glycosides (1) in the presence of Ni (cat.), Zn, Boc₂O, and MgCl₂. This method yields α -acyl C-glycosides (2) in up to 84% yield, with α selectivity.

previous work



this work



c. acyl C-glycosides:

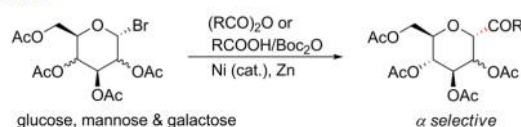
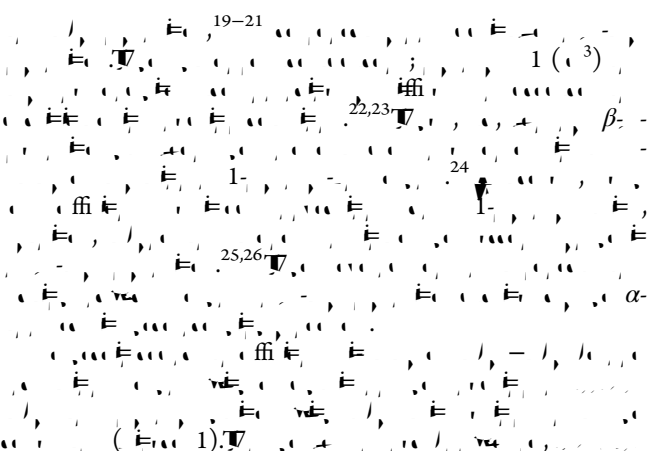


Figure 1.



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27,28

α -alkyl ketones

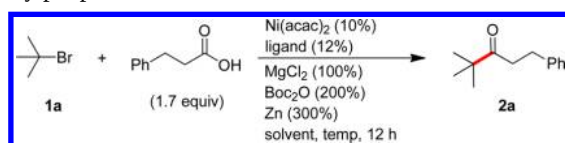
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2. Experimental

2.1. General Procedure for the Reaction of *tert*-Butyl Bromide (1a) with 3-Phenylpropanoic Acid^a

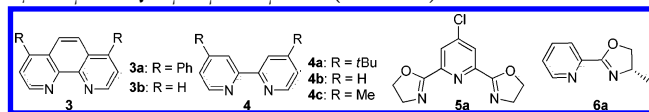
A solution of *tert*-butyl bromide (1a) (1.7 equiv), 3-phenylpropanoic acid (1a) (1.0 equiv), $\text{Ni}(\text{acac})_2$ (10%), ligand (12%), MgCl_2 (100%), Boc_2O (200%), Zn (300%), solvent, temp, 12 h.

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



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

(0.3, 100, %), (170, %), (10, %), (12, %), (200, %), (300, %), (100, %), (1, %).

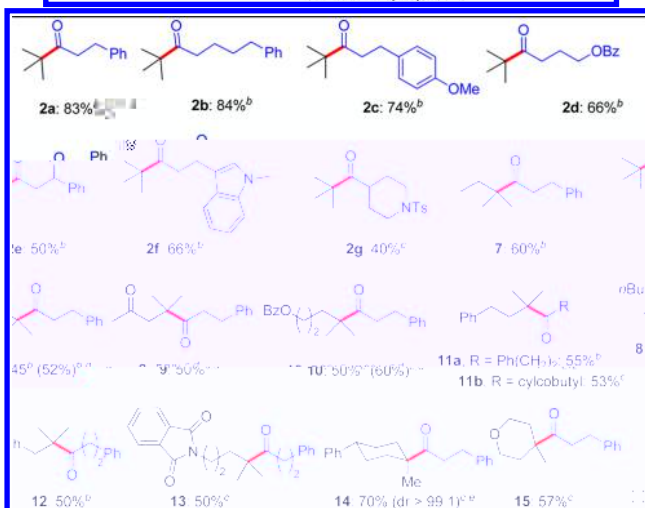
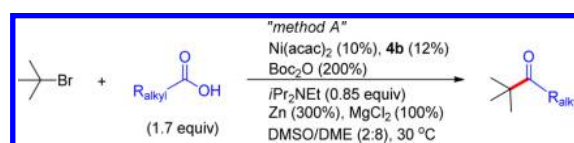


4a (24%), 3a (1-3), 4a (4-5), 8/2 (6-7), 1.5 (8), 4b-c, 5a, 6a (9-12), 1.5 (13), 4a

(8, 13), 4b (14), 1.5 (15), 82% (16), 4a (17).

(1, 16), 2a-f, 2g, 7-15 (2), 14 (4), 29

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



(0.3, 100, %), (170, %), (10, %), (12, %), (200, %), (300, %), (100, %), (1, %).

2.2. General Procedure for the Reaction of *tert*-Butyl Bromide (1a) with 3-Phenylpropanoic Acid^a

10% 1b
 16a (2)
 2.3. C Primary Secondary

CCOC(=O)C1OC(COC(=O)R)OC(COC(=O)C)OC1OC(=O)C **38** ($R = iPr$), 98% ($\alpha:\beta = 2.6:1$)^b

$R =$ CCCCC(=O)c1ccccc1 **40**, 90% ($\alpha:\beta = 2.8:1$)^b

$R =$ CCCCC(=O)c1ccc(OC)cc1 **39**, 99% ($\alpha:\beta = 2.7:1$)^b

CCOC(=O)C1OC(COC(=O)R)OC(COC(=O)C)OC1OC(=O)C **38** ($R = iPr$), 98% ($\alpha:\beta = 2.6:1$)^b

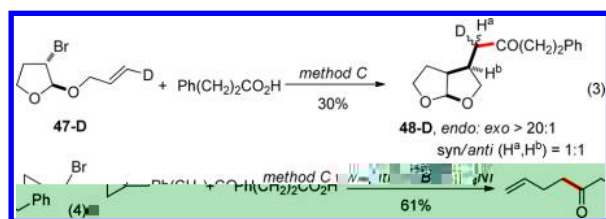
$R =$ CCCCC(=O)c1ccccc1 **40**, 90% ($\alpha:\beta = 2.8:1$)^b

$R =$ CCCCC(=O)c1ccc(OC)cc1 **39**, 99% ($\alpha:\beta = 2.7:1$)^b

The diagram illustrates a catalytic cycle for the carbonylation of alkyl halides using a nickel complex. The cycle is divided into two parts, A and B, showing the conversion of alkyl halides to alkyl carbonyls.

Part A: Shows the initial steps of the cycle. It starts with a nickel complex (I) reacting with an alkyl halide (R-X) to form a nickel complex (II). This intermediate (II) then reacts with a carbonyl compound (R'-C(=O)-R) to form a nickel complex (III). Intermediate (III) further reacts to form a nickel complex (IV), which then reacts with another carbonyl compound (R'-C(=O)-R) to form a nickel complex (V). Finally, intermediate (V) reacts with a carbonyl compound (R'-C(=O)-R) to form a nickel complex (VI).

Part B: Shows the final steps of the cycle. It starts with a nickel complex (VI) reacting with a carbonyl compound (R'-C(=O)-R) to form a nickel complex (VII). This intermediate (VII) then reacts with a carbonyl compound (R'-C(=O)-R) to form a nickel complex (VIII). Intermediate (VIII) further reacts to form a nickel complex (IX), which then reacts with a carbonyl compound (R'-C(=O)-R) to form a nickel complex (X). Finally, intermediate (X) reacts with a carbonyl compound (R'-C(=O)-R) to form a nickel complex (XI).

[illegible][illegible]

2.5.3. Radical Chain versus Double Oxidative Addition Mechanism.

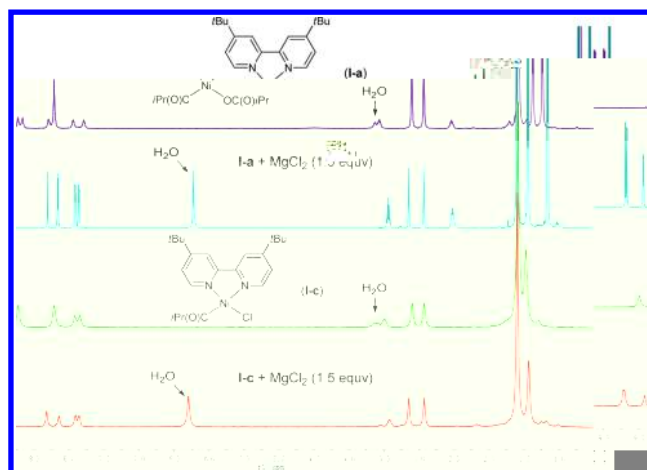
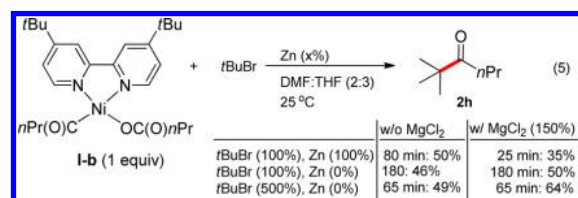
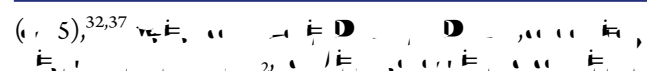
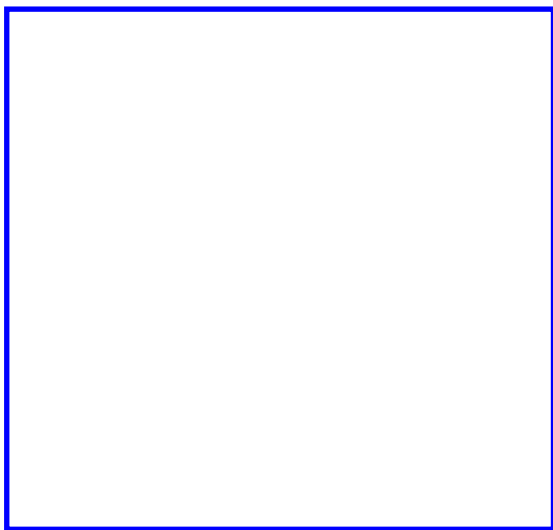


Figure 2. ¹H NMR spectra of (a) 1, (b) 2, (c) 3, and (d) 4. The chemical shifts are given in ppm (TMS) in CDCl₃. The assignments of the peaks are given in the text.



I-b $\frac{D}{D}$ 180 2h 46%,
 (7). 5 2h 50%,
 65 ²⁹
 I-a 16a (4),
 I $\frac{D}{D}$ (1),
 I ³⁵
 I-b $\frac{D}{D}$ (5).
 (1),
 I-b $\frac{D}{D}$ (') ¹⁰
³⁶
 2 I-b $\frac{D}{D}$
 ff (5).
 2 (3-3-)
 (1b) (2)₂ 2 11a
 () ²⁹
 I-a $\frac{D}{D}$ 3 $\frac{D}{D}$ 2) ²⁹
 ~80% ~100% I-a $\frac{D}{D}$ $\frac{D}{D}$ /
 (2:3, /) 1 ()
 3 4) ²⁹ 1
 2 I-a $\frac{D}{D}$
 (2) ^{29,38} / ()
 () - ()

[illegible]

- (5) () β - D -glucopyranosyl, *Chem. Commun.* 2008, 9334.
 (6) () β - D -glucopyranosyl, *Chem. Commun.* 2009, 7532.
 (7) () β - D -glucopyranosyl, *Chem. Commun.* 2010, 125.
 (8) () β - D -glucopyranosyl, *Chem. Commun.* 2011, 1218.
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