An Oxidative Transformation of *N*'-Phenylhydrazide to *t*-Butyl Ester Using a Copper(II) Halide–Lithium *t*-Butoxide System

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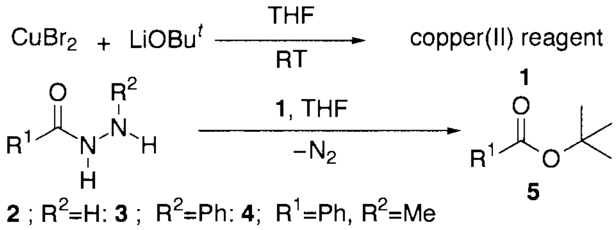
Reactions of hydrazides or *N*'-phenylhydrazides with a copper(II) reagent prepared from copper(II) bromide and lithium *t*-butoxide smoothly proceeded to give the corresponding *t*-butyl ester in high yield.

Previously we reported that a copper(II) reagent (**1**), which was prepared from copper(II) bromide and lithium *t*-butoxide, can be used for oxidative transformation of some functional groups containing a nitrogen atom. In a reaction of primary carboxamide[1] or *N*-substituted urea[2] with **1**, isocyanate is apparently generated as an intermediate. Analogously, it was assumed that treatment of hydrazide with **1** would generate an acyl cation-like species which, in turn, could react with a nucleophile. Now we wish to report that treatment of hydrazides (**2**) or *N*'-phenylhydrazide (**3**) gave the corresponding *t*-butyl esters (**5**) under mild conditions (Scheme 1).



2 ; R^2=H: **3** ; R^2=Ph: **4**; R^1=Ph, R^2=Me
a: R^1=Ph; **b**: R^1=4-MeC_6H_4; **c**: R^1=$PhCH_2$; **d**: R^1=$Ph(CH_2)_3$; **e**: R^1=cinnamyl; **f**: R^1=*c*-C_6H_{11}; **g**: R^1=PhCO-NHCH(CH_2Ph)-; **h**: R^1=Boc-NHCH(CH_2Ph)-; **i**: R^1=Z-NHCH(CH_2Ph)-; **j**: R^1=Z-$NHCMe_2$-.
Boc=*t*-butoxycarbonyl; Z=benzyloxycarbonyl.

Scheme 1.

Among alkyl esters, the *t*-butyl group is an important protecting group of carboxylic acid. Although many methods for the preparation of the *t*-butyl ester are reported,[3] development of new methodology is still required.

Concerning treatment of hydrazide **2** with some oxidants, the first investigation was reported by Curtius who oxidized **2** with iodine to the corresponding diacylhydrazines **6**.[4] Several oxidizing agents, such as chlorine,[5] iodobenzene diacetate,[6] $NaIO_4$,[7] Ag_2O,[7] $K_3[Fe(CN)_6]$,[7] and sodium metaperiodate,[8] are available for the oxidation of hydrazides. However, oxidation of hydrazide bearing some substituents on the nitrogen atom has hardly been reported.

Hydrazides **2** were easily prepared by a reaction of methyl ester with hydrazine hydrate.[9] *N*'-Phenylhydrazides **3** were prepared by treatment of acyl chloride with phenylhydrazine in the presence of triethylamine or by reaction of carboxylic acid with phenylhydrazine with the aid of 1,3-dialkylcarbodiimide as a condensing agent.

The first examination in the present study was treatment of benzhydrazide **2a** with 4.2 molar amounts of **1** at room temperature (Table 1, Run 1). It was found that the reaction proceeded with evolution of nitrogen to give *t*-butyl benzoate **5a** with a small amount of *N*,*N*'-dibenzoylhydrazine **6a**. When the amount of **1** was increased, the yield of **5a** increased (Run 2). A reaction of *N*'-phenylbenzhydrazide **3a** was also performed under similar conditions producing *t*-butyl ester **5** as the main product, and a small amount of *N*',*N*'-diphenylbenzhydrazide was isolated as a by-product, which was confirmed by ^{1}H and ^{13}C NMR, and mass spectra (Run 3).[10] This fact strongly indicated that not only an acyl cation-like species but also a phenyl cation-like species may be generated, followed by a reaction with the starting material **3a** to give a by-product under the reaction conditions. From the above hypothesis, it was expected that the yield of *t*-butyl benzoate **5a** would be increased using *N*'-methyl derivative (**4**) instead of **3a**.[11] However, although there was no formation of *N*',*N*'-dimethylbenzhydrazide, the yield of **5a** was reduced (Run 5).

Table 1. The transformation of benzylhydrazide **2a**, *N*'-phenylbenzhydrazide **3a**, or *N*'-methylbenzhydrazide **4** to *t*-butyl benzoate **5a**[a]

Run	Substrate	**1** /equiv	Time /min	Yield /%
1	**2a**	4.2	20	50[b]
2		6.2	20	88
3	**3a**	4.0	20	70[c]
4		6.0	20	59
5	**4**	4.0	60	28

[a]All reactions were carried out at room temperature. [b]*N*,*N*'-Dibenzoylhydrazine **6a** was detected by IR spectrum. [c]*N*',*N*'-Diphenylbenzhydrazide was obtained in 12% yield.

As shown in Table 2, various kinds of hydrazides **2** or *N*'-phenyl derivatives **3** were converted to the corresponding *t*-butyl ester **5** under similar conditions. It was found that the reactions of **3** gave better result than that using **2** (Runs 1–7). In all reactions using **3** as a substrate, a small amount of *N*',*N*'-diphenylhydrazide must have been formed. Unfortunately, it was difficult to purify it from the reaction mixture except in Run 3. In the case of *N*'-phenylhydrazide derived from bulky carboxylic acid, the desired product was also obtained in high yield (Run 13).

A typical reaction procedure is as follows: to a THF (3 mL) solution of lithium *t*-butoxide (3.1 mL, THF solution, 1 mol dm^{-3}) was added copper(II) bromide (692 mg, 3.1 mmol) at room temperature under nitrogen, and the mixture was stirred for 15

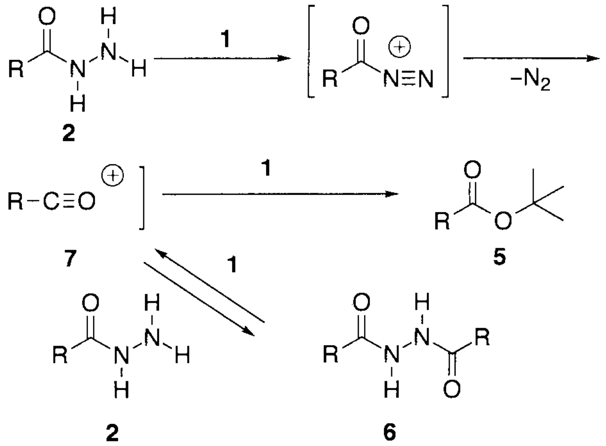
Table 2. The transformation of hydrazides **2** or *N*'-phenylhydrazides **3** to *t*-butyl esters **5**[a]

Run	Substrate	**1** /equiv	Temp.	Time /min	Product	Yield /%
1	**2b**	6.2	RT	20	**5b**	68
2	**3b**	4.0	RT	20		72[b]
3		6.0	50 ℃	10		86[c]
4	**2c**	8.0	RT	20	**5c**	29
5	**3c**	6.2	RT	20		83
6	**2d**	6.2	RT	20	**5d**	49
7	**3d**	4.2	RT	20		84
8	**3e**	4.2	RT	20	**5e**	83
9	**3f**	4.0	50 ℃	20	**5f**	76
10	**3g**	5.0	RT	30	**5g**	56
11	**3h**	4.0	RT	120	**5h**	67
12	**3i**	4.0	RT	90	**5i**	73
13	**3j**	4.0	RT	120	**5j**	78

[a] All reactions were performed by a similar procedure as described in the text, unless otherwise noted. [b] *N*,*N*'-Diphenyl-4-methylbenzhydrazide was obtained in 8% yield. [c] Copper(II) chloride was used instead of copper(II) bromide.

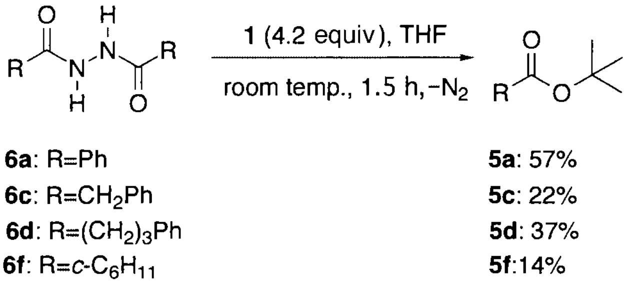
min. Then benzhydrazide **2a** (68 mg, 0.5 mmol) was added to the reaction mixture. After being stirred for 20 min, the reaction was quenched by addition of 7.5% aqueous solution of ammonia. The organic materials were extracted with CH_2Cl_2, and the extract was dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by preparative TLC (*n*-hexane:EtOAc 9:1) and *t*-butyl benzoate **5a** (78 mg) was isolated in 88% yield.

The mechanism of the reaction of **2** or **3** with **1** seems to be complicated. Although the details of the reaction process are uncertain at the present time, a probable mechanism of the formation of *t*-butyl ester **5** is outlined in Scheme 2. Regarding the evolution of nitrogen, an acyldiazonium salt may be generated by the oxidation of **2** with **1**, and decomposed to form an acyl cation-like species (**7**). *t*-Butoxide attacked **7** to give *t*-butyl ester **5**. By competing with *t*-butoxide, **7** may react with starting material **2** to form *N*,*N*'-diacylhydrazine **6**. Reactions using **3** as the starting material generally give better results because the phenyl group could suppress formation of the corresponding diacylhydrazine.



Scheme 2.

From the above proposed pathway, it was expected that **1** had the ability to react with *N*,*N*'-diacylhydrazine **6**, so that treatment of **6** with **1** under similar conditions was examined (Scheme 3). The results, however, showed that all yields of **5** were low.



Scheme 3.

Further investigation using **1** is now in progress.

References and Notes

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10 *N*',*N*'-diphenylbenzhydrazide, ^{1}H NMR (DMSO-d_6, 300 MHz) δ 11.07 (1H, s), 8.07 (2H, d, J = 8.2 Hz), 7.62 (1H, t, J = 8.2 Hz), 7.56 (2H, t, J = 8.2 Hz), 7.33 (4H, t, J = 7.8 Hz), 7.25 (4H, d, J = 7.8 Hz), 7.01 (2H, t, J = 7.8 Hz); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 166.73, 147.02, 133.72, 132.63, 129.67, 129.29, 128.20, 122.86, 119.77.

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