

## Direct conversion of aldehydes to acyl azides using *tert*-butyl hypochlorite

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**Abstract**—A general method, for the direct conversion of aldehydes to acyl azides using *tert*-butyl hypochlorite and sodium azide is described. The method is simple and occurs under mild conditions.

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Acyl azides are widely utilized in industry and act as a chemical feedstock for a range of useful materials in organic chemistry<sup>1</sup> and especially in pharmaceuticals,<sup>2</sup> dyes<sup>3</sup> and agrochemicals.<sup>4</sup> They are very useful for the preparation of amides and heterocyclic compounds and also undergo facile rearrangement to isocyanates from which amines, urethanes, thiourethanes, ketenimines, carbodiimides and ureas can be obtained.<sup>1c</sup>

Acyl azides are usually prepared from acid derivatives such as acid chlorides and acid hydrazides.<sup>5</sup> There are a few reports on the direct conversion of carboxylic acids to acyl azides using acid activators such as ethyl chloroformate,<sup>6a</sup> DDPA,<sup>6b</sup> NCS-TPP,<sup>6c</sup> triphosgene<sup>6d</sup> and cyanuric chloride.<sup>6e</sup> Aldehydes have also been directly converted into acyl azides. Various reagents and reagent systems have been reported in the literature for this purpose, and include chromic anhydride–trimethyl silylazide,<sup>7</sup>  $\text{PhI}(\text{OAc})_2$ ,<sup>8</sup> triazidochlorosilane–activated  $\text{MnO}_2$ ,<sup>9</sup>  $\text{IN}_3$ <sup>10</sup> and Dess–Martin periodinane.<sup>11a</sup> Modified methods in which carbamoyl azides were formed directly from aldehydes via acyl azides in one-pot<sup>12</sup> have also been reported.

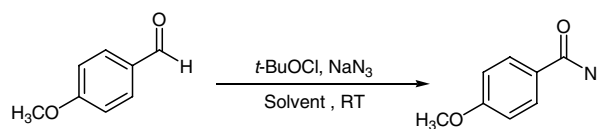
Despite these, additional methods for this conversion are still valuable.

*tert*-Butyl hypochlorite (*t*-BuOCl) is a versatile reagent, is readily available at low cost and is also easy to pre-

pare. It has been used for many oxidative transformations including oxidation of alcohols<sup>13</sup> and sulfides.<sup>14</sup> Recently, we reported a reaction of 1,3-dithiolanes and 1,3-dithianes with *t*-BuOCl to afford dihydro-1,4-dithiins and dihydro-1,4-dithiepins in high yield.<sup>15</sup> As a part of our ongoing programme on the development of new methodologies in organic synthesis, we report a new method for direct conversion of aldehydes to acyl azides. During the course of our studies, we found that treatment of 4-methoxybenzaldehyde with *t*-BuOCl and  $\text{NaN}_3$  gave the corresponding acyl azide in good yield (87%) (Scheme 1).

In a preliminary study, experiments were carried out to optimize the reaction conditions.

To optimize the mole ratio of *t*-BuOCl and  $\text{NaN}_3$  with respect to the aldehyde, experiments were carried out as shown in Table 1. The best result was obtained when the mole ratio of aldehyde: *t*-BuOCl: $\text{NaN}_3$  was 1:2:2 in  $\text{CCl}_4$  as solvent (Table 1, entry 3). These conditions were used for subsequent reactions. In acetonitrile, the reaction was slow and gave only a 32% yield of the acyl azide (Table 1, entry 5). Solvents such as chloroform, dichloromethane and cyclohexane afforded high yields. In *tert*-butanol the reaction was faster, however, 20% of 4-



Scheme 1.

**Keywords:** Aldehyde; Acyl azide; *tert*-Butyl hypochlorite; Sodium azide.

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**Table 1.** Optimization of the reaction conditions for the conversion of 4-methoxybenzaldehyde to the corresponding acyl azide<sup>a</sup>

Entry	<i>t</i> -BuOCl:NaN <sub>3</sub>	Conditions (h)	Yield <sup>b</sup> (%)
1	1:1	CCl <sub>4</sub> , 24	42
2	1.5:1.5	CCl <sub>4</sub> , 24	68
3	2:2	CCl <sub>4</sub> , 24	87
4	2.5:2.5	CCl <sub>4</sub> , 24	85
5	2:2	ACN, 24	32 <sup>c</sup>
6	2:2	CHCl <sub>3</sub> , 24	78
7	2:2	CH <sub>2</sub> Cl <sub>2</sub> , 24	75
8	2:2	<i>tert</i> -Butanol, 6	69 <sup>d</sup>
9	2:2	Cyclohexane, 24	80

<sup>a</sup> Reactions were carried out on 5 mmol scale at room temperature.<sup>b</sup> Isolated yield.<sup>c</sup> 60% starting material was recovered.<sup>d</sup> 4-Methoxybenzoic anhydride was isolated in 20% yield.

methoxybenzoic anhydride was obtained as a side product (Table 1, entry 8).

We next examined the scope and generality of the method. Various aldehydes were studied and the results are summarized in Table 2.<sup>16</sup>

As can be seen from the results in Table 2, a wide variety of substrates including aromatics, heteroaromatics and aliphatic aldehydes (entries 1–12), furnished the desired acyl azides in good yields.<sup>17</sup>

In the case of aliphatic aldehydes, when the reactions were carried out at room temperature, some rearrangement to the corresponding isocyanate was observed.<sup>10</sup> Hence, reactions were carried out at low temperature (Table 2, entries 9–12).

In summary, we have developed a general method for direct conversion of aldehydes to acyl azides using *t*-butyl hypochlorite and sodium azide. The method is simple and occurs under mild conditions. Further applications

**Table 2.** *t*-BuOCl/NaN<sub>3</sub> mediated conversion of aldehydes to acyl azides<sup>a</sup>

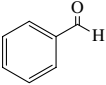
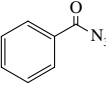
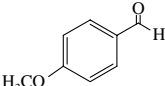
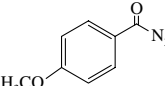
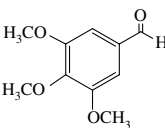
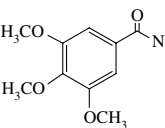
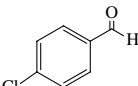
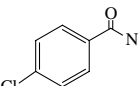
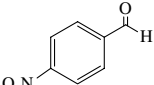
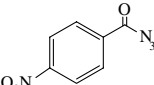
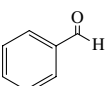
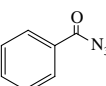
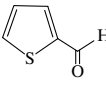
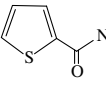
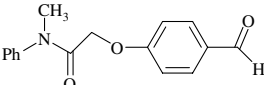
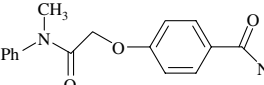
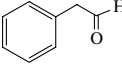
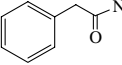
Entry	Substrate	Product <sup>b,c</sup>	Yield <sup>c</sup> (%)	Mp (°C) (lit.)
$\text{RCHO} \xrightarrow[\text{CCl}_4, \text{RT} / 5-10^\circ\text{C}]{t\text{-BuOCl, NaN}_3} \text{RCON}_3$ R = alkyl or aryl				
1			84	25–27 (27) <sup>11b</sup>
2			87	70 (70–71) <sup>11b</sup>
3			72	74–76
4			80	43–44 (43) <sup>11b</sup>
5			83	65–67 (65) <sup>11b</sup>
6			80	68–70 <sup>11b</sup>
7			78	Oil
8			85	105–107
9			80	Oil (—) <sup>d,6c</sup>

Table 2 (continued)

Entry	Substrate	Product <sup>b,c</sup>	Yield <sup>c</sup> (%)	Mp (°C) (lit.)
10			79	Oil (—) <sup>d,10</sup>
11			78	Oil (—) <sup>d,7a</sup>
12			80	Oil (—) <sup>d,6d</sup>

<sup>a</sup> Reactions were carried out on 1–5 mmol scale using 2.0 equiv of *t*-BuOCl and 2.0 equiv of NaN<sub>3</sub> in 20 ml of CCl<sub>4</sub> for 24 h at rt (entries 1–8)<sup>16a</sup> or at 5–10 °C (entries 9–12).<sup>16b</sup>

<sup>b</sup> Structures confirmed by IR, <sup>1</sup>H NMR and <sup>13</sup>C NMR (spectral details are provided).<sup>17</sup>

<sup>c</sup> Isolated yield.

<sup>d</sup> The aliphatic acyl azides decompose upon standing in air at room temperature. Spectra were thus recorded at low temperature (0–5 °C) under nitrogen.<sup>10</sup>

of *tert*-butyl hypochlorite in organic transformations are currently being investigated in our laboratory.

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### Supplementary data

Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.tetlet.2007.06.020](https://doi.org/10.1016/j.tetlet.2007.06.020).

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- (a) *General experimental procedure (entries 1–8)*: To a stirred suspension of *t*-BuOCl (1.1 g, 10 mmol) and NaN<sub>3</sub> (0.65 g, 10 mmol) in CCl<sub>4</sub> (20 ml), aldehyde (5 mmol) was added at room temperature. The reaction mixture was stirred at the same temperature until complete consumption of starting material as indicated by TLC. The reaction mixture was diluted with dichloromethane and the organic layer was washed successively with 5% sodium thiosulfate solution (2 × 15 ml), 5% sodium bicarbonate solution (2 × 15 ml), water (2 × 15 ml) and brine (15 ml). The organic layer was dried over sodium sulfate and concentrated in vacuo. Purification by silica gel column chromatography (5% EtOAc/*n*-hexane) afforded the pure acyl azide; (b) *General experimental procedure (entries 9–12)*: To a stirred and cooled (5–10 °C) suspension of *t*-BuOCl (1.1 g, 10 mmol) and NaN<sub>3</sub> (0.65 g, 10 mmol) in CCl<sub>4</sub> (20 ml), aldehyde (5 mmol) was added. The reaction mixture was stirred at the same temperature until complete consumption of starting material as indicated by TLC. The reaction mixture was diluted with cold dichloromethane and worked-up using cold solutions. The organic layer

was washed successively with 5% sodium thiosulphate solution ( $2 \times 15$  ml), 5% sodium bicarbonate solution ( $2 \times 15$  ml), water ( $2 \times 15$  ml) and brine (15 ml). The organic layer was dried over sodium sulfate and concentrated in vacuo without heating. Purification by silica gel column chromatography (*n*-hexane) afforded the pure acyl azide. **Caution!** *tert*-Butyl hypochlorite decomposes exothermically when exposed to UV light to give acetone and chloromethane. Glass containers have burst because of pressure build up after exposure to fluorescent lighting or daylight. It reacts violently with rubber and should not be heated to its boiling point. **Caution!** During reactions and isolations, we have not observed any explosive hazards but it is known that azido compounds may represent an explosion hazard when being concentrated under vacuum or stored neat. A safety shield and appropriate handling procedures are recommended.

17. Spectral data for novel acyl azides (Table 2): Entry 3: 3,4,5-Trimethoxybenzoyl azide IR (KBr)  $\nu_{\max} = 2137$ ,  $1679$   $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 60 MHz):  $\delta$  3.83–3.88 (m,

9H), 7.17 (m, 2H) ppm;  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  55.28, 61.01, 106.66, 125.52, 143.53, 153.06, 171.82 ( $-\text{CON}_3$ ) ppm. Elemental analysis: Calculated for  $\text{C}_{10}\text{H}_{11}\text{N}_3\text{O}_4$ : C, 50.63; H, 4.64; N, 17.72. Found: C, 50.60; H, 4.66; N, 17.69. Entry 7: Thiophene-2-carbonyl azide IR (neat)  $\nu_{\max} = 2155$ ,  $1680$   $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 60 MHz):  $\delta$  7.02–7.80 (m, 3H) ppm;  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  128.47, 134.49, 134.85, 153.06, 166.61 ( $-\text{CON}_3$ ) ppm. Elemental analysis: Calculated for  $\text{C}_5\text{H}_3\text{N}_3\text{OS}$ : C, 39.21; H, 1.96; N, 27.45. Found: C, 39.19; H, 1.99; N, 27.42. Entry 8: 4-[2-(*N*-Methyl-*N*-phenyl)amino-2-oxo-ethoxy]benzoyl azide IR (KBr)  $\nu_{\max} = 2127$ ,  $1684$   $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 60 MHz):  $\delta$  3.26 (s, 3H), 4.43 (s, 2H), 6.71 (d, 2H,  $J = 8.82$  Hz), 7.33 (m, 5H), 7.81–7.94 (d, 2H,  $J = 8.82$  Hz) ppm;  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  37.62, 66.07, 114.52, 123.78, 126.92, 128.72, 130.24, 131.64, 162.97, 166.72, 171.59 ( $-\text{CON}_3$ ) ppm. Elemental analysis: Calculated for  $\text{C}_{16}\text{H}_{14}\text{N}_4\text{O}_3$ : C, 61.93; H, 4.51; N, 18.06. Found: C, 61.95; H, 4.49; N, 18.09.