

## Basic Resin Mediated Efficient One-Pot Synthesis of Carbazates from the Corresponding Alkyl Halides

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A quick and efficient, one-pot synthesis of carbazates was accomplished in high yields by the reaction of various primary, secondary, and tertiary alkyl halides with a variety of substituted hydrazines using Amberlite IRA 400 basic resin/CO<sub>2</sub> system. The reaction conditions were mild with simpler work-up procedures than the previously reported methods.

**Keywords:** Alkyl halides, Basic resin, Carbon dioxide, Substituted hydrazines, Carbazates

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### INTRODUCTION

Organic carbazates have attracted much attention due to their numerous remarkable medicinal, industrial and synthetic applications [1,2]. They have extensively been used as pharmaceuticals [3], agrochemicals [4], intermediates in organic synthesis [5], protection of amino groups in peptide synthesis [6], linkers in solid phase organic synthesis [7] and as donor ligands in complexation reactions with transition metals [8]. To satisfy the green chemistry demands, the synthesis has been changed from the use of costly and toxic chemicals like phosgene [9] and its derivatives [10] directly or indirectly, to the abundantly available, cheap and safe chemicals like CO<sub>2</sub>. However, their formation using CO<sub>2</sub> employed harsh reaction conditions, such as the use of strong bases, higher reaction temperatures, and longer reaction times [11]. Thus, we were prompted to embark on a research work with the intention of making possible procedural

improvements. Our group [12] has been engaged during the past several years in the development of new methodologies for the preparation of carbamates, dithiocarbamates and related compounds using cheap, abundantly available and safe reagents like CO<sub>2</sub> and CS<sub>2</sub>. Recently [13], we found that Amberlite IRA 400 (basic resin) is the best catalyst for the synthesis of carbamates, dithiocarbamates and dithiocarbonates (xanthates). Furthermore, we have also reported the use of basic resin in the THP-protection of alcohols and phenols [14]. We report herein an efficient, one-pot synthesis of carbazates from a variety of primary, secondary and tertiary alkyl halides and substituted hydrazines using the basic resin/CO<sub>2</sub> system.

### EXPERIMENTAL

Chemicals were procured from Merck, Aldrich, and Fluka Chemical Companies. Reactions were carried out under an atmosphere of Argon. IR spectra 4000-200 cm<sup>-1</sup> were recorded on Bomem MB-104-FTIR spectrophotometer using a neat technique, while NMRs were scanned on AC-300F, NMR

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(300 MHz), instrument using CDCl<sub>3</sub> and some other deuterated solvents and TMS as internal standard. Elemental analysis was conducted by means of a Carlo-Erba EA 1110-CNNO-S analyzer and agreed favorably with the calculated values.

### Typical Experimental Procedure

To a stirred solution (under Ar) of 3 mmol substituted hydrazine in anhydrous DMSO (5 ml) carbon dioxide was slowly and continuously bubbled and basic resin (2 g, in excess) at 60 °C was added. Then the reaction was continued for 0.5 h at which point the required alkyl halide (3 mmol) was added over a period of 5 min. The reaction was further continued till the completion of reaction (*cf* Table 1). The reaction mixture was poured into water (20 ml) and organic layer was extracted with EtOAc (3X10 ml). The organic layer was washed with a solution of HCl (0.1 N, 20 ml), 25 ml of saturated solution of NaHCO<sub>3</sub> and 30 ml of brine and then dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated to get the desired compound.

**N<sup>3</sup>-(4-Methoxyphenyl) hydrazine carboxylic acid butyl ester (1, C<sub>12</sub>H<sub>18</sub>N<sub>2</sub>O<sub>3</sub>).** Yield: 94%; Mp.: oil; IR (neat)  $\tilde{\nu}$  = 1680 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  = 0.96 (t, 3H, *J* = 7.3 Hz), 1.34

(m, 2H), 1.86 (m, 2H), 3.73 (s, 3H), 4.12 (t, 2H), 4.85 (m, NH), 6.74-7.66 (m, 4H), 8.0 (br, NH); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  = 13.7, 19.5, 32.5, 63.5, 112.5, 114.9, 134.5, 152.4, 160.6 (C=O) ppm; MS (EI): *m/z* = 238.

**N<sup>3</sup>-Phenyl hydrazine carboxylic acid 3-phenyl propyl ester (2, C<sub>16</sub>H<sub>18</sub>N<sub>2</sub>O<sub>2</sub>).** Yield: 96%; Mp.: oil; IR (neat)  $\tilde{\nu}$  = 1685 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  = 1.92 (m, 2H), 2.56 (t, 2H, *J* = 7.2 Hz, PhCH<sub>2</sub>), 4.10 (t, 2H), 4.67 (br, NHPh), 6.66-7.12 (m, 10H, Ar-H), 8.0 (br, NH); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  = 32.4, 34.4, 63.5, 112.6, 119.4, 125.7, 128.8, 129.6, 138.7, 161 (C=O) ppm; MS: *m/z* = 270.

**N<sup>3</sup>-Phenyl-hydrazine carboxylic acid phenethyl ester (3, C<sub>15</sub>H<sub>16</sub>N<sub>2</sub>O<sub>2</sub>).** Yield: 87%; Mp.: oil; IR (neat)  $\tilde{\nu}$  = 1681 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  = 2.83 (2H, t, *J* = 6.7 Hz, PhCH<sub>2</sub>CH<sub>2</sub>O), 4.42 (t, 2H, *J* = 7.2 Hz, PhCH<sub>2</sub>O), 4.77 (br, H, PhNH), 6.69-7.15 (m, 10H, Ar-H), 8.05 (br, NH); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  = 35.5, 65.9, 112.3, 118.6, 128.5, 129.5, 140.3, 142.5, 165.4 (C=O) ppm; MS: *m/z* = 256.

## RESULTS AND DISCUSSION

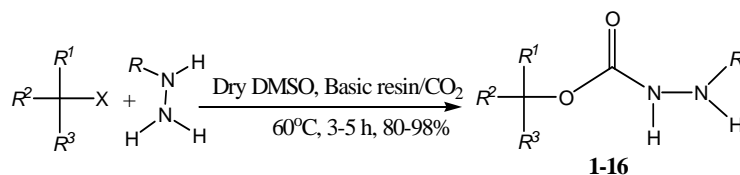
Substituted hydrazine was taken in dry DMSO and purified

**Table 1.** Conversion of Alkyl Halides into Carbazates of Formula 1-16<sup>a</sup>

Entry	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	X	R	Time (h)	Time (h)
1	<i>n</i> -C <sub>3</sub> H <sub>7</sub>	H	H	Br	4-MeOPh	3.0	94
2	PhCH <sub>2</sub> CH <sub>2</sub>	H	H	Br	Ph	3.0	96
3	PhCH <sub>2</sub>	H	H	Cl	Ph	4.0	87
4	Ph	H	H	Cl	Bn	4.5	92
5	C <sub>2</sub> H <sub>5</sub>	Me	H	Br	Bn	4.5	90
6	4-MeOPh	H	H	Cl	3-NO <sub>2</sub> Ph	4.5	85
7	C <sub>3</sub> H <sub>7</sub>	H	H	Br	4-NO <sub>2</sub> Ph	4.5	85
8	C <sub>3</sub> H <sub>7</sub>	H	H	Br	2,4-NO <sub>2</sub> Ph	5.0	80
9	C <sub>3</sub> H <sub>7</sub>	H	H	Br	Naphthyl	4.5	83
10	C <sub>4</sub> H <sub>9</sub>	C <sub>4</sub> H <sub>9</sub>	H	Br	Ph	4.5	89
11	C <sub>4</sub> H <sub>9</sub>	C <sub>4</sub> H <sub>9</sub>	C <sub>4</sub> H <sub>9</sub>	Br	Ph	4.5	88
12	C <sub>5</sub> H <sub>11</sub>	H	H	Cl	<i>n</i> -C <sub>4</sub> H <sub>9</sub>	3.0	96
13	C <sub>7</sub> H <sub>15</sub>	H	H	Cl	Ph	3.0	96
14	C <sub>9</sub> H <sub>19</sub>	H	H	Cl	<i>n</i> -C <sub>4</sub> H <sub>9</sub>	3.0	98
15	C <sub>3</sub> H <sub>7</sub>	C <sub>3</sub> H <sub>7</sub>	H	Br	Ph	4.5	86
16	Ph	CH <sub>3</sub>	H	Br	Ph	5.0	82

<sup>a</sup>All products were characterized by IR, NMR, and Mass spectroscopic data. <sup>b</sup>Isolated yields.

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Scheme 1

CO<sub>2</sub> gas was bubbled in it at 60 °C for 30 min. by constant stirring. Then basic resin (in excess) was slowly added to the mixture. The reaction was continued for another 30 min and then corresponding alkyl halide was added. The reaction was further continued until completion as checked by TLC (see Table 1). It is assumed that the O<sup>-</sup> of the carbazate ion produced would attack the electrophilic carbon of the respective alkyl halide to afford corresponding carbazates. The reaction proved to be successful and the desired product was isolated and the structure was further confirmed by various spectroscopic and analytical techniques. Thus, various substituted hydrazines were reacted with a variety of primary, secondary and tertiary alkyl halides using basic resin/CO<sub>2</sub> system to afford the corresponding carbazates in good to excellent yields (80-98%) as shown in Table 1. The whole reaction conditions are depicted in Scheme 1.

We tried several solvents like *n*-heptane, *n*-hexane, acetonitrile, benzene, toluene, methanol, dichloromethane, chloroform, DMSO, dimethylformamide, hexamethylphosphoric triamide of which dry DMSO proved to be the most suitable.

In conclusion, we have developed a convenient and efficient protocol for the one-pot, three components coupling of various substituted hydrazines with a variety of primary, secondary and tertiary alkyl halides *via* CO<sub>2</sub> bridge using basic resin. This method generates the corresponding carbazates in good to excellent yields. Furthermore, this method exhibits substrate versatility, mild reaction conditions and experimental convenience. This synthesis protocol is believed to offer a more general and applicable method for the formation of carbon-oxygen bonds essential to numerous organic syntheses.

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