

# Preparation of tertiary amides from carbamoyl chlorides and organocuprates

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## Supporting Information

### General experimental details.

Tetrahydrofuran (THF) was dried and distilled from sodium benzophenone ketyl. Ether was distilled from LiAlH<sub>4</sub> and toluene from sodium. CH<sub>2</sub>Cl<sub>2</sub>, Et<sub>3</sub>N and carbamoyl chlorides were distilled from CaH<sub>2</sub> before use. Organolithium and Grignard reagent solutions were purchased and titrated before use.<sup>1</sup> GC analyses were performed on a 5% Phenyl methylpolysiloxane column BPX5 (0.32 mm Internal Diameter, 30 m Length, 1 µm Film thickness), with 10 psi of nitrogen as gas carrier.

For Table 1: Amides **4a-e**, **8a-e**, **12a-e**, formamides **5**, **9**, **13**, ureas **6**, **10**, **14** and oxalamides **7**, **11**, **15** which were not commercially available, were synthesized by conventional methods using amines and acids or their derivatives. All purified compounds were analysed by GC: 120 °C for 2 min, 120 °C to 250 °C with 20 °C per min, 250 °C for 6 min 30 sec. Calibration curves were established for each product for GC quantification.

GC-MS analyses were performed on a CP-Sil 8CB Low BLEED column (L: 30 m, D: 0.25 mm) and Electronic Impact was the method used on the MS detector.

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<sup>1</sup> For organolithium solutions: Juaristi, E.; Martinez-Richa, A.; Garcia-Rivera, A.; Cruz-Sanchez, J. S. *J. Org. Chem.* **1983**, 48, 2603-2606. For Grignard reagent solutions: Watson, S. C.; Eastham, J. F. *J. Organomet. Chem.* **1967**, 9, 165-168.

**General procedure of reactions using cyano-Gilman lithiocuprates (Table 1).**

Under a nitrogen atmosphere, the organolithium solution (7.2 mmol, 2.4 equiv) was slowly added to a cold ( $-30\text{ }^{\circ}\text{C}$ ) suspension of CuCN (0.32 g, 3.6 mmol, 1.2 equiv) in THF or Et<sub>2</sub>O (30 mL). After 30 min, carbamoyl chloride (3.0 mmol, 1 equiv) was added at  $-30\text{ }^{\circ}\text{C}$ . The reaction was stirred 2 h at cold temperature or rt (see table 1), quenched with a saturated NH<sub>4</sub>Cl solution (2 mL) and dried (MgSO<sub>4</sub>). The volume was completed to 100 mL by addition of CH<sub>2</sub>Cl<sub>2</sub> and a sample was injected to GC (quantification of products). After addition of a 28% NH<sub>4</sub>OH solution (30 mL), stirring was pursued until the color of the solution turned deep blue. The reaction mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub>, the combined organic layers were dried (MgSO<sub>4</sub>) and concentrated to yield crude amides **4**, **8** and **12** which were purified (by flash chromatography or Kugelrohr distillation) when necessary.

**General procedure of reactions using cyano-Gilman magnesiocuprates (Table 2).**

Under a nitrogen atmosphere, the organomagnesium solution (13.66 mmol, 2.1 equiv) was slowly added to a cold ( $-30\text{ }^{\circ}\text{C}$ ) suspension of CuCN (0.61 g, 6.82 mmol, 1.05 equiv) in Et<sub>2</sub>O (60 mL). After 45 min, carbamoyl chloride (6.50 mmol, 1 equiv) was added at  $-30\text{ }^{\circ}\text{C}$ , the reaction mixture was slowly warmed to rt and stirred 15 h. The reaction were quenched with a saturated NH<sub>4</sub>Cl solution (10 mL) and after addition of a 28% NH<sub>4</sub>OH solution (20 mL), stirring was pursued until the color of the solution turned deep blue. The reaction mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub>, the combined organic layers were dried (MgSO<sub>4</sub>) and concentrated to yield crude amides **8** which were purified (by flash chromatography or Kugelrohr distillation) when necessary.

**Table 1.** Qualitative and quantitative results of the reaction between carbamoyl chlorides and cyano-Gilman reagents

<div>R<sup>3</sup></div> <div>a <i>n</i>-Bu</div> <div>b <i>s</i>-Bu</div> <div>c <i>t</i>-Bu</div> <div>d Ph</div> <div>e Me</div>	<div></div>	<div><math>\xrightarrow[\text{THF or Et}_2\text{O}]{(\text{R}^3)_2\text{CuLi} \cdot \text{LiCN}}</math></div>	<div></div>	<div></div>	<div></div>	<div></div>										
	<b>1</b> X = NEt <sub>2</sub>		<b>4a-e</b>	<b>5</b>	<b>6</b>	<b>7</b>										
	<b>2</b> X =		<b>8a-e</b>	<b>9</b>	<b>10</b>	<b>11</b>										
	<b>3</b> X =		<b>12a-e</b>	<b>13</b>	<b>14</b>	<b>15</b>										
entry	sm <sup>a</sup>	cuprate <sup>b</sup>	T (°C)		amide (%) <sup>c</sup>		formamide (%) <sup>c</sup>		urea (%) <sup>c</sup>		oxalamide (%) <sup>c</sup>					
		R <sup>3</sup>	THF	Et <sub>2</sub> O	THF	Et <sub>2</sub>	THF	Et <sub>2</sub>	THF	Et <sub>2</sub>	THF	Et <sub>2</sub>				
						O		O		O		O				
1	<b>1</b>	<i>n</i> -Bu	-30 to 0	-30 to rt	<b>4a</b>	85	70	<b>5</b>	0	2	<b>6</b>	5	0	<b>7</b>	0	0
2	<b>1</b>	<i>s</i> -Bu	-30 to 0	-30 to 0	<b>4b</b>	90	62	<b>5</b>	0	11	<b>6</b>	0	0	<b>7</b>	0	0
3	<b>1</b>	<i>t</i> -Bu	-30 to 0	-30 to 0	<b>4c</b>	37 <sup>f</sup>	33 <sup>f</sup>	<b>5</b>	0	8	<b>6</b>	4	13	<b>7</b>	0	3
4	<b>1</b>	Ph	-30 to rt	-30 to rt	<b>4d</b>	50	70	<b>5</b>	0	0	<b>6</b>	2	16	<b>7</b>	0	0
5	<b>1</b>	Me	-30 to rt	-30 to 0	<b>4e</b>	90	80	<b>5</b>	0	0	<b>6</b>	0	0	<b>7</b>	0	0
6	<b>2</b>	<i>n</i> -Bu	-30	-30 to 0	<b>8a</b>	83 <sup>e</sup>	38	<b>9</b>	0	2	<b>10</b>	9	25	<b>11</b>	4	0
7	<b>2</b>	<i>s</i> -Bu	-30 to rt	-30 to rt	<b>8b</b>	50 <sup>e</sup>	33 <sup>d</sup>	<b>9</b>	2	8	<b>10</b>	8	4	<b>11</b>	14	4
8	<b>2</b>	<i>t</i> -Bu	-30	-30 to rt	<b>8c</b>	62 <sup>e</sup>	43 <sup>d</sup>	<b>9</b>	2	5	<b>10</b>	9	6	<b>11</b>	1	4
9	<b>2</b>	Ph	-30	-30 to 0	<b>8d</b>	64	70	<b>9</b>	0	0	<b>10</b>	4	4	<b>11</b>	4	3
10	<b>2</b>	Me	-30	-30 to rt	<b>8e</b>	30	20	<b>9</b>	0	0	<b>10</b>	2	16	<b>11</b>	8	4
11	<b>3</b>	<i>n</i> -Bu	-30	-30 to 0	<b>12a</b>	75	70	<b>13</b>	0	4	<b>14</b>	6	5	<b>15</b>	0	0
12	<b>3</b>	<i>s</i> -Bu	-30 to rt	-30 to rt	<b>12b</b>	75	70	<b>13</b>	0	10	<b>14</b>	1	1	<b>15</b>	1	0
13	<b>3</b>	<i>t</i> -Bu	-30 to 0	-30 to 0	<b>12c</b>	85 <sup>e</sup>	55 <sup>f</sup>	<b>13</b>	0	1	<b>14</b>	0	1	<b>15</b>	0	0
14	<b>3</b>	Ph	-30 to 0	-30 to 0	<b>12d</b>	84	83	<b>13</b>	0	0	<b>14</b>	5	5	<b>15</b>	1	0
15	<b>3</b>	Me	-30	-30	<b>12e</b>	70	68	<b>13</b>	0	0	<b>14</b>	1	0	<b>15</b>	0	0

<sup>a</sup> Starting material. <sup>b</sup> Cyanocuprate reagents were prepared at -30 °C. Reaction time: 2 h. <sup>c</sup> GC yields.

<sup>d</sup> 5-10% unreacted carbamoyl chloride. <sup>e</sup> 10-20% unreacted carbamoyl chloride. <sup>f</sup> 20-40% unreacted carbamoyl chloride.