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# Fast N-Methylation of Amines Under Microwave Irradiation

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#### FAST N-METHYLATION OF AMINES UNDER MICROWAVE IRRADIATION

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ABSTRACT: Primary and secondary amines are quickly Nmethylated by methanal and formic acid under microwave irradiation.

There are two widely used methods to convert primary or secondary amines into N-methylamines : the Hofmann procedure<sup>1</sup> is the reaction of a primary or secondary amine with an excess of methyl halide in the presence of base, and the Eschweiler-Clarke one<sup>2</sup> is the reaction of the amine with methanal and formic acid.

Whereas the former may lead to a mixture of amines and quaternary ammonium compounds, the later generaly affords good yields of the N-dimethyl and N-methylamines from primary and secondary amines, respectively.

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RR'NH (or R NH<sub>2</sub>) + CH<sub>2</sub>=0  $\xrightarrow{\text{HCO}_2\text{H}}$ RR'NCH<sub>3</sub> (or RN (CH<sub>3</sub>)<sub>2</sub>) + CO<sub>2</sub> + H<sub>2</sub>O

We here report our work to realize the Eschweiler reaction under microwave irradiation. We have first tried to convert hexamethylenimine into its N-methyl derivative without solvent and with paraformaldehyde and formic acid : the best results were obtained with an excess of 150 % of paraform and of formic acid with respect to the amine and under a low power microwave irradiation during four minutes. Similar results were obtained from dibutylamine and benzylamine but cyclohexylamine affords lower yields in these conditions.

Cyclohexylamine and 1,10-diaminodecane were converted in good yields with an excess of 700 % of formic acid and 150 % of a 30% aqueous solution of formaldehyde under reflux during an irradiation of ten minutes. Clarke and al<sup>3</sup> report similar results in the methylation of the diaminodecane by refluxing during 35 hours a mixture of the amine, formaldehyde (14,4 equivalents) and formic acid (19 equivalents). So our procedure allows the fast preparation of good yields tertiary N-methylated or N-dimethylated amines

	N-methylated amine %	
amine	with	with aqueous
	paraformaldehyde	solution of methanal
Hexahydroazepine	67	
Dibutylamine	76	
Benzylamine	57	
Cyclohexylamine	starting compound	43
	partially unreacted	
1,10 diaminodecane	starting compound	51
	partially unreacted	

#### Table - N-methylation of amines under microwave irradiation

#### EXPERIMENTAL

NMR spectra are recorded on a Bruker AC 300 spectrometer in deuterochloroform. Microwave assisted organic reactions are performed in a Whirpool M600 Oven with paraformaldehyde and in a Normatron 112 Oven with aqueous solution of methanal.

### N-methylation of hexahydroazepine (typical procedure with paraformaldehyde )

A mixture of hexahydroazepine (1.12 ml, 10 mmol), formic acid (0.95 ml, 25 mmol) and paraformaldehyde (0.75g, 25 mmol) is introduced in a conical flask fitted with an air condenser and then subjected to microwaves (80 W) during four minutes. The mixture is diluted by 5 ml of water and 10 ml of ether, and acidified by 2 ml of a 6N solution of hydrochloric acid; 2.5 g of potassium hydroxide is added to the aqueous layer which is then extracted twice with 10 ml of ether. These later organic layers are dried over potassium carbonate and distilled.

# N-dimethylation of cyclohexylamine (typical procedure with aqueous solution of methanal )

A mixture of cyclohexylamine (1.16 ml, 10 mmol), formic acid (3 ml, 80 mmol) and formaldehyde (2.5 ml of a 30% aqueous solution of methanal, 25 mmol) is introduced in a flask fitted with an water condenser and then refluxed during ten minutes under microwave irradiation. The mixture is treated as above.

*N-Methyl hexahydroazepine* <sup>4</sup>: bp =  $137^{\circ}$ C / 760 ; <sup>1</sup>H RMN : 1.26-1.46 (m, 8H, H-3, H-4), 2.08 (s, 3H, N-Me), 2.3 (t, 4H, H-2) ; <sup>13</sup>C RMN : 26.4 (C-4), 27.7 (C-3), 47.1 (N-Me), 58.2 (C-2).

*N-Methyldibutylamine* <sup>5</sup>: bp = 162°C / 760 ; <sup>1</sup>H RMN : 0.81-0.91 (t, 6H, H-5), 1.2 -1.45 (m, 8H, H-3, H-4), 2.15 (s, 3H, N-Me), 2.2-2.3 (t, 4H, H2) ; <sup>13</sup>C RMN : 14.0 (C-5), 20.7 (C-4), 29.5 (C-3), 42.3 (N-Me), 57.6 (C-2). *N,N-Dimethylbenzylamine* <sup>6</sup>: bp = 72°C / 20; <sup>1</sup>H RMN : 2.2 (t, 6H, N-Me), 3.6 (s, 2H, CH<sub>2</sub>), 7.3 (m, 5H, aromatic) ; <sup>13</sup>C RMN : 45.4 (N-Me), 64.4 (CH<sub>2</sub>), 127.0 (C-para), 128.2 (C-meta), 129.1 (C-ortho), 138.9 (C-ipso).

*N*,*N*-Dimethylcycloxexylamine <sup>7</sup> : bp =  $84^{\circ}$ C / 10 ; <sup>1</sup>H RMN : 0.8-1.1 (m, 5H, axial H-2, H-3 and H-4), 1.3 - 1.4 (m, 4H, equatorial H-2 and H-3), 1.45-1.75 (m, 1H, equatorial H-4), 1.8-2.0 (m, 1H, H-1), 2.0-2.15 (s, 6H, N-Me) ; <sup>13</sup>C RMN : 25.5 (C-4), 26.0 (C-3), 28.7 (C-2), 41.2 (N-Me), 63.5 (C-1).

*N*,*N*,*N*',*N*'-Tetramethyl-1,10-diaminodecane <sup>3</sup>: bp =  $102^{\circ}$ C / 0.8 ; <sup>1</sup>H RMN : 1.1-1.45 (m, 16H, H-2 to H-9), 2.1 -2.2 (s + t, 16H, H-1, H-10, N-Me) ; <sup>13</sup>C RMN : 27.4 and 27.7 (C-4, C-7 and C-5,C-6), 29.5 and 29.6 (C-2, C-9 and C-3, C-8), 45.5 (N-Me), 59.9 (C-1, C-10).

#### **REFERENCES**

- 1 Hofmann, A. Ann. Chim. Phys.. 1850, 30, 87.
- 2 Eschweiler, W., Chem. Ber. 1905, 38, 880.
- 3 Clarke, H.; Gillepsie, H.; Weisshaus, S. J. Amer. Chem. Soc.. 1933, 55, 4571.
- 4 Lukes, R.; Malek, J. Chem. Listy. 1951, 45, 72.
- 5 Westphal, O.; Jerchel, D. Chem. Ber. 1940, 73B, 1002.
- 6 Pine, S.; Sanchez, B. J. Org. Chem. 1971, 36, 829.
- 7 Heckel, H.; Adams, R. J. Amer. Chem. Soc. 1925, 47, 1712.

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