

Microwave Irradiation versus Conventional Heating in the Synthesis of *N*-Methyl-2-pyrrolidone Catalyzed by Highly Active Copper Powder

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ABSTRACT

A convenient one-pot synthesis of *N*-methyl-2-pyrrolidone is achieved either by conventional heating or microwave irradiation. The intermediate *N*-methyl-4-hydroxybutyramide formed from the exothermic reaction of γ -butyrolactone with aqueous methylamine undergoes an intramolecular condensation reaction catalyzed by highly active copper powder to form the pyrrolidone in good yield.

KEYWORDS

Copper catalyst, *N*-methyl-2-pyrrolidone, methylamine, γ -butyrolactone, one-pot synthesis, microwave irradiation.

Introduction

Green Chemistry is associated with reduction or elimination of volatile organic solvents, an initiative which will take time to become fully implemented. While ionic liquids are nonvolatile and may serve as optimal replacements for such volatile industrial solvents, large scale industrial applications of ionic liquids are yet to be realized. In the interim, industry should be encouraged to use less volatile and less toxic organic solvents of which *N*-methyl-2-pyrrolidone (NMP) is an excellent example. It is a dipolar aprotic solvent with a high dielectric constant and completely soluble in water. Its strong and selective solvent nature has established its industrial uses in the recovery of pure hydrocarbons in petrochemical processing, in the desulfurization of acidic gases present in natural or synthesis gases and also finds applications in plastics, surface coatings, plant protection, paint stripping and cleaning in the manufacture of electronic equipment¹. As a versatile industrial solvent it has generated a lot of interest and there are various attempts to manufacture it cheaply in an environmentally friendly way. Synthetic methods, *viz.* hydrogenation of succinonitrile in the presence of ammonia², catalytic hydrogenation of maleic anhydride or succinic acid with methylamine³ and condensation of γ -butyrolactone (GBL) and methylamine (MA)⁴, have all been tried with different degrees of success. The latter has found much favour in industry due largely to the pioneering works of Späth and Lintner⁵ who described the first commercial batch process by reacting two equivalents of gaseous MA and GBL in a sealed pipe reactor at 280 °C for three hours affording NMP in 90 % yield. No mention was made of the reaction pressure. McElvain and Vozza⁶ repeated the reaction and instead of gaseous MA, they used a fourfold equivalent of liquid MA relative to GBL in a steel bomb reactor at 280 °C and obtained 90–93 % yields. Reppe⁷ on the other hand came up with a more general industrial process for NMP in which he introduced suitable diluents and a dehydrating catalyst. However, the low reaction yields of 85–90 % have been ascribed to the ready dimerization of NMP under the given reaction conditions⁸. More recently, Hatada and Ono⁹ described

a continuous flow reactor system with copper exchanged Y-zeolite as catalyst, at 280 °C, and obtained 98 % of NMP. In all these processes, high temperatures and pressures are a common feature.

In light of the above-mentioned synthetic requirements, the relatively low toxicity of NMP, its excellent solvent properties and the fact that it has replaced many a solvent of poorer stability and high vapour pressures, it has given our group the impetus to embark on a comparative study of producing NMP by microwave irradiation and conventional heating.

Results and Discussion

In both the conventional heating and microwave irradiation systems, the reaction between GBL and MA initially generated *N*-methyl-4-hydroxybutyramide, the reaction intermediate which then cyclized with elimination of water to form the anticipated product as depicted in Scheme 1.

Our efforts focused on establishing the best and most cost-effective reaction conditions for both the conventional heating and microwave irradiation systems. Highly active copper powder prepared according to the method of Brewster and Groening¹⁰ proved to be the most effective of all the catalysts tested in both systems. However, it was found that sintering and agglomeration of the catalyst into small copper balls resulted after the conventional heating process and rendered the catalyst inactive. This problem was overcome by using graphite as catalyst support. Results of the conventional heating process are detailed in Table 1.

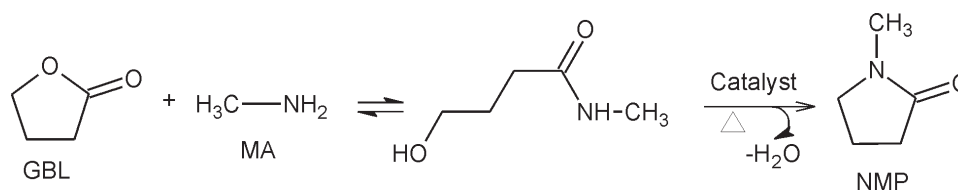
Table 1 Screening of catalysts for the conventional synthesis of NMP.

Entry	Catalyst	g (catalyst)	Yield /% ^b
1	Cu ^a	1.5	96
2	Cu/Alumina	4.5	55
3	PPA/CuCl ₂	55/2	45
4	PPA/CuCl	55/2	36
5	PPA	60	28

^a Highly active copper powder, reaction carried out at 220 °C for 5 h.

^b Isolated yield of NMP.

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Scheme 1.

Table 2 Screening of catalysts for the microwave-induced synthesis of NMP.

Entry	Catalyst	g (catalyst)	Temp. /°C	Time /min	Yield /%
1	No catalyst	–	60	4	58
2	Cu powder only	1	100	4	96
3	PPA	10	150	5	30
4	Cu powder/PPA	1/10	100	5	97
5	PPA/CuCl ₂	10/1	100	4.30	69

The pioneering work of Gedye and coworkers¹¹ described utilization and reaction rate enhancement of microwave irradiation in organic reactions. This process has become the cutting edge technology across the pharmaceutical, biotechnological, and fine chemical industries where production volumes are generally much smaller. Application of the full potential of microwave in the bulk manufacturing industry is yet to be realized. Nevertheless, it was of interest to us to establish the feasibility of synthesizing NMP by microwave irradiation which as far as we are aware has not been reported. The results of the test trials are summarized in Table 2.

In both the conventional heating and microwave irradiation processes low-valent copper powder catalyst has emerged to be very effective. This is encouraging given the low cost and simplicity in the preparation of the catalyst. Microwave-induced synthesis of NMP is more attractive than the conventional heating process due to the drastic reduction in reaction times with concomitant enhancement of reaction yields at lower temperatures and pressures. The only real advantage of the conventional heating protocol is in the larger scales of processing materials. However, this may be compensated for by the use of a microwave flow reactor system.

General

Reagents and solvents were obtained from commercial sources and used without further purification. Polyphosphoric acid was purchased from Sigma-Aldrich and *N*-methyl-2-pyrrolidone was provided by Organic Synthesis (Cape Town). All reactions were performed at 300 W in a Milestone START S microwave reactor equipped with an inbuilt IR sensor for temperature control and automatic stirring. GC analysis was performed using Perkin Elmer, Clarus 500 with silica capillary column elite-5 (L-30 m, ID-0.32 mm).

General conventional heating process. A 1 L bomb reactor with thermocouple, stirrer and a gas inlet was charged with γ -butyrolactone (100 g, 1.02 mol) followed by the corresponding catalyst (Table 1) after which 40 % aqueous methylamine (38 g, 1.2 mol) was gradually added during which time the temperature rises to 35 °C. The reactor was sealed and air evacuated with a vacuum pump and then pressurized with argon to 2 MPa. The reactor was then heated to 220 °C and held as such for five hours during which the pressure in the reaction bomb rose to about 4 MPa. The reaction mixture was cooled to room temperature, carefully vented, filtered and the filtrate distilled at 25 mmHg

and at a bath temperature of 98–100 °C to give pure *N*-methyl-2-pyrrolidone identified by GC comparison with an authentic sample.

General microwave irradiation process. γ -Butyrolactone (2.0 g, 0.023 mol) and 40 % aqueous methylamine (2.16 g, 0.07 mol) were mixed together in a 25 mL round bottomed flask. The catalyst (Table 2) was introduced followed by a magnetic stirrer bar and the mixture was heated under reflux in the microwave 300 W for about 4 min at 100 °C. The resulting product was characterized by GC using authentic *N*-methyl-2-pyrrolidone as the reference.

Conclusions

While the importance of solvents as an integral partner in the processing protocols in industry cannot be overemphasized, there is growing environmental concern about their adverse effects on human health and the environment. This has stimulated research initiatives to replace organic solvents as much as possible with more environmentally friendly ones such as ionic liquids. Furthermore, there are ongoing research initiatives into solvent-free industrial reactions. Presently it looks unlikely that organic solvents will be completely replaced and a greater effort needs to be made to produce much less toxic industrial solvents *viz.* NMP.

Acknowledgements

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