Microwave Induced an Efficient Synthesis of Alcohols *via* Cross-Cannizzaro Reaction

Julfikar Ali Thakuria, Mukulesh Baruah, and Jagir Singh Sandhu*
Regional Research Laboratory, Jorhat 785006, Assam, India

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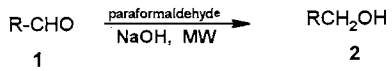
Aromatic aldehydes **1** are converted to alcohols **2** by cross-Cannizzaro reactions under microwave irradiations in dry media within 20-25 sec. in excellent yields.

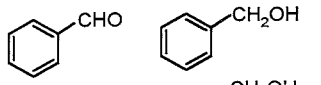
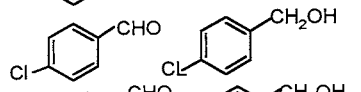
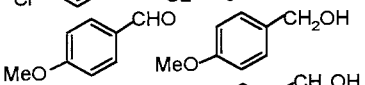
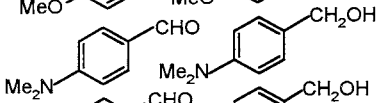
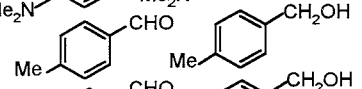
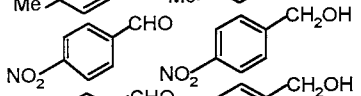
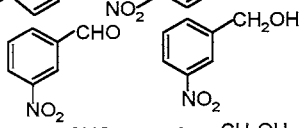
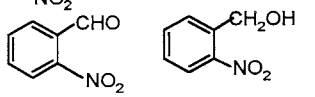
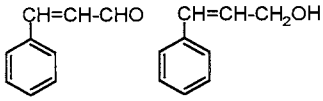
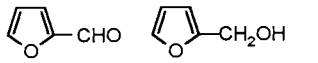
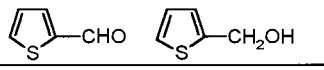
The use of microwave energy in dry media to accelerate organic reactions has been taking a new dimension currently and is a matter of increasing interest and offers several advantages.[1] It has been used for a great variety of organic reactions as esterification, etherification, oxidation, hydrolysis, Diels-Alder (4+2), Reformatsky, Knoevenagel and Bischler Napieralski reactions. Synthesis of molecules which normally require long reflux periods can be achieved conveniently and very rapidly in a microwave oven.[2] Therefore there is merit in developing an efficient method for the production of alcohols using inexpensive reagents under microwave irradiation. In continuation of our studies on synthesis under microwave irradiation[3] we now report a very simple, fast and general method for the cross-Cannizzaro reaction without solvent under microwave activation and using paraformaldehyde. The reaction proceeds efficiently in excellent yields at ambient pressure within seconds time and in the absence of solvent. The cross-Cannizzaro reaction[4] has been reported to be catalysed by aqueous base, but no information in regard to paraformaldehyde[5] on microwave activation has appeared.



1 2

In a typical procedure, a mixture of benzaldehyde (0.53 g, 5 mmol), paraformaldehyde (1 g, 30 mmol) and solid sodium hydroxide (0.16 g, 4 mmol) were taken in an Erlenmeyer flask and placed in a commercial microwave oven operating at 2450 MHz frequency. After irradiation of the mixture for 25 sec (monitored vide TLC), it was cooled to room temperature, extracted with chloroform and dried over anhydrous sodium sulphate. Then the solvent was evaporated to give the corresponding benzylalcohol in 90% yield exclusively without the formation of any side products. Preparative column chromatography with silica gel was used for further purification of the alcohols, eluting with pet.ether (60-80)/$CHCl_3$ (1:1). Further increasing the reaction time had no significant effect on the yield and resulted in minor amount of decomposition. Similar treatment of other aldehydes gave the corresponding alcohols in 85-95% yields and the results are summarised in the table. In the case of cinnamaldehyde the reaction occurred selectively at the aldehydic group and the carbon-carbon double bond in the substrate was not effected. Excellent yields of nitrobenzylalcohols were obtained from nitrobenzaldehydes (entry 6,7, and 8) with o, m or p substituent, the positional relationship of the nitro group in no way influencing the overall reaction and also there was no evidence for the formation of any azobenzenecarboxilic acids as reported by earlier workers.[6] When the same reaction was repeated under thermal condition i.e in refluxing methanol it required longer period (approximately 12 hrs) and gave 50% yield of benzyl alcohol (entry 1). It is also remarkable to note that the reaction rate is enhanced dramatically by microwave activation. The reaction proceeds effectively when formalin solution (40%) and alumina (basic) were used in place of paraformaldehyde and sodium hydroxide under microwave irradiation and the corresponding alcohols were obtained in almost in comparable yields.[7] Interestingly it was also observed that the reaction is not equally effective and slowered the reaction rate when carried out in 30% sodium hydroxide solution under microwave activation and takes about 30-35 min to complete the reaction in 70% yield (entry-1). The reasons for the efficiency of the process on the

Table: Formation of alcohols **2** by cross-Cannizzaro reaction

Entry	Substrate	Alcohols	Time secs	Yield[a] %	Yield[b] %
1			25	90	85
2			20	95	85
3			22	93	80
4			20	90	80
5			22	92	90
6			20	90	86
7			25	90	85
8			20	92	80
9			20	95	83
10			22	90	85
11			25	85	80

[a] All the yields refer to isolated, chromatographically pure compounds
[b] Yields refer to the yield of alcohols when formalin and alumina were used

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solid phase are not yet clear. As shown in the table several structurally varied substrates underwent clean and remarkably fast cross-Cannizzaro reactions with paraformaldehyde and sodium hydroxide under this procedure.

In conclusion, this new method of alcohol formation using paraformaldehyde, without any solvent under microwave irradiation offers significant improvements over the existing procedures and thus help facile entry into a variety of alcohols of potentially high synthetic utility. Also this simple and easily reproducible technique affords various alcohols in shorter reaction time, with excellent yields without involvement of toxic and expensive material and without the formation of any undesirable side products, than the classical homogenous reaction in solvents.

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7 In a typical case, a mixture of benzaldehyde (0.53 g, 5 mmol), formalin solution (40%, 1.5 ml) and basic alumina (ca 4 g) were taken in an Erlenmeyer flask and placed in a commercial microwave oven. After irradiation of the mixture for 30 s (monitored vide TLC) and usual work-up the corresponding benzyl alcohol was obtained in 85% yield exclusively without the formation of any side products. Dark polymeric products were obtained when we further increase the reaction time. Similarly other aldehydes were reacted and their results are summarised in the table. When the same reaction was carried out under thermal condition it required approximately 10 h to complete and gave 60% of the alcohol.