Tetrahedron Letters, Vol.27, No.3, pp 279-282, 1986 0040-4039/86 $3.00 + .00
Printed in Great Britain

THE USE OF MICROWAVE OVENS FOR RAPID ORGANIC SYNTHESIS

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Four different types of organic reactions have been studied and seven different organic compounds have been prepared, under pressure in a microwave oven. Considerable rate increases have been observed.

Microwave ovens have been used in chemical laboratories for moisture analysis[1] and wet ashing procedures of biological and geological materials[2-7] for a number of years. Very recently the rapid heating capability of the microwave oven has been exploited to heat mixtures of ore samples and acid in sealed vessels, leading to considerable savings in dissolution times[8-10]. The applications of microwave technology to the catalytic hydrogenation of alkenes[11], the hydrocracking of bitumen from tar sands[12] and the degradation of polychlorinated hydrocarbons[13] are all currently under intensive investigation. However, there have not yet been any reports concerning the utilisation of microwave ovens in the routine chemical syntheses regularly undertaken in chemical research laboratories.

We report here the results of several experiments in which organic reactions have been carried out in sealed Teflon vessels heated by a microwave oven. The high temperatures and pressures so readily obtained in the reaction vessels have led to remarkable rate enhancements and dramatic savings in reaction times.

Four completely different types of organic reactions were studied: (i) the acid hydrolysis of benzamide to give benzoic acid; (ii) the permanganate oxidation of toluene in basic solution giving benzoic acid; (iii) the esterification of benzoic acid with methanol, propanol and butanol, and (iv) the S_N2 reaction between sodium 4-cyanophenoxide and benzyl chloride, yielding 4-cyanophenyl benzyl ether. Each reaction was carried out both under traditional reflux conditions, and also in a sealed Teflon vessel[14] in a microwave oven. The microwave oven used in these experiments was a domestic Toshiba model ER-8000BTC with nine power settings, starting at 72 watts and increasing by 81 watt increments to 720 watts. Power setting seven was used throughout. The Teflon vessels used for the microwave reactions had a volume of 250ml (approx) and were manufactured by Berghof/America Inc.[14]. The quantities of reactants, and their concentrations, were kept the same under both sets of reaction conditions.

Reaction products were identified by their melting and boiling points and by NMR and IR spectroscopy. The times taken for the reactions and the results of the various experiments are summarised in Table 1.

TABLE 1 - SUMMARY OF RESULTS

Compound Synthesised	Procedure Followed	Reaction Time	Recovery[b] (Product)	Recovery[b] (Reagent)	Rate (microwave) / Rate (classical)
Hydrolysis of benzamide to benzoic acid					
C_6H_5COOH	Classical	1 hr.	90%	5%	
C_6H_5COOH	Microwave	10 min.	99%	2%	6
Oxidation of toluene to benzoic acid					
C_6H_5COOH	Classical	25 min.	40%	-	
C_6H_5COOH[a]	Microwave	5 min.	40%	-	5
Esterification of benzoic acid with methanol					
$C_6H_5COOCH_3$	Classical	8 hr.	74%	19%	
$C_6H_5COOCH_3$	Microwave	5 min.	76%	11%	96
Esterification of benzoic acid with propanol					
$C_6H_5COOC_3H_7$	Classical	7.5 hr.	89%	7%	
$C_6H_5COOC_3H_7$	Microwave	18 min.	86%	11%	25
Esterification of benzoic acid with n-butanol					
$C_6H_5COOC_4H_9$	Classical	1 hr.	82%	12%	
$C_6H_5COOC_4H_9$	Microwave	7.5 min.	79%	17%	8
S_N2 reaction of 4-cyanophenoxide ion with benzyl chloride					
$C_6H_5OCH_2C_6H_5$	Classical	12 hr.	72%	-	
$C_6H_5OCH_2C_6H_5$	Microwave	3 min.	74%	-	240
$C_6H_5OCH_2C_6H_5$	Classical	16 hr.	89%	-	
$C_6H_5OCH_2C_6H_5$	Microwave	4 min.[c]	93%	-	240

[a] very high pressures developed, and the study of this reaction was halted.

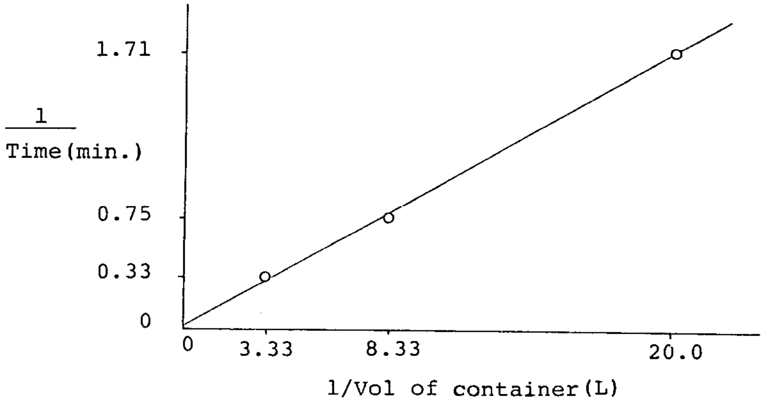
[b] the recovery values are based on isolated yields and represent the average of at least two experiments. The S_N2 reaction was followed by titrating the chloride ion.

[c] value for one run only.

In the microwave oven experiments, very significant rate enhancements were obtained for all the reactions. As would be expected, those occurring in a low-boiling solvent were affected most dramatically. Thus, if we consider the two reactions taking place in methanol, the esterification of benzoic acid proceeds almost one hundred times as fast in the microwave oven as under reflux, while the synthesis of 4-cyanophenyl ether is accomplished with a rate enhancement of about two hundred and forty times. The reaction in propanol, the next lowest-boiling solvent, displays a twenty-fivefold rate increase in the microwave oven. The hydrolysis of benzamide, which is carried out in aqueous solution, proceeds six times faster in the microwave oven. The other reaction in aqueous solution, the oxidation of toluene, shows a fivefold rate enhancement, even though the system is heterogeneous. Unfortunately, when longer reaction times were employed in an attempt to reach completion, dangerously high pressures developed under the microwave oven conditions, resulting in a violent explosion. Further investigation of this system was therefore abandoned. The highest-boiling solvent used, n-butanol, showed an eighfold rate enhancement in the esterification of benzoic acid. This inverse relationship between rate enhancement and the boiling point of the solvent is especially clearly demonstrated in the series of esterifications.

Since the effect of pressure and superheating of solvent appeared to play a significant part in the rate enhancements, the effect of pressure on the preparation of 4-cyanophenyl benzyl ether was studied. Three sizes of Teflon vessels were available, and this reaction was taken to 65% completion under the microwave conditions in each of these vessels separately, a plot (Figure 1) of the reciprocal of the reaction time against the reciprocal of the volume was linear (correlation coefficient 0.996), implying that the reaction rate is directly proportional to the pressure developed in the vessels.

Figure 1-Variation of Reaction Rate with Pressure



In fact, confirmation of this relationship has been observed. In one experiment, a thousand-fold rate enhancement was found when the S_N2 reaction was carried out in a 50ml Teflon bomb in the microwave oven.

Our results convincingly demonstrate that the use of this microwave oven technique can lead to substantial savings in time for many laboratory syntheses, particularly those involving low-boiling solvents or reagents. The method provides rapid and relatively inexpensive access to very high temperatures and pressures. The currently available alternatives require much more elaborate apparatus, longer heating times, and allow virtually no control over energy input. Great care must be exercised when adapting the microwave technique to new reactions, however, since the pressures developed in the vessels can be very great. Our investigations, which are continuing, include a more detailed study of these and other reactions, along with measurements of the temperatures and pressures produced, and the development of more suitable reaction vessels, less prone to deformation, and with bigger volumes enabling a scaling-up of the reactions.

ACKNOWLEDGEMENTS

Financial assistance from NSERC and the SEED project (Govt. of Canada) is gratefully acknowledged

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(Received in USA 2 October 1985)