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Bhushan M. Khadilkar [a] & Virendra R. Madyar [a]
[a] University Department of Chemical Technology, University of Mumbai, Matunga, Mumbai, 400 019, India
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FRIES REARRANGEMENT AT ATMOSPHERIC PRESSURE USING MICROWAVE IRRADIATION.

Bhushan M. Khadilkar* & Virendra R. Madyar

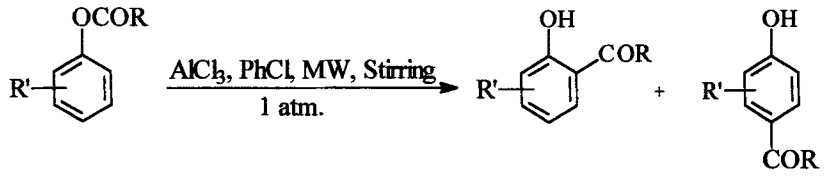
University Department of Chemical Technology, University of Mumbai, Matunga, Mumbai - 400 019, India.

ABSTRACT: A very safe, fast and practical Fries rearrangement with conventional $AlCl_3$ catalyst, carried out in a modified domestic microwave oven at atmospheric pressure is reported.

Microwave heating and its application in organic synthesis is currently under intensive study. Many review articles [1-4] have been published in this field. Earlier reports of Fries rearrangement using microwave heating are those carried out in a sealed tube[5], and dry condition reactions using K-10 montmorillonite[6,7] as a catalyst. The dramatic rate enhancements which result from microwave irradiation of the reactants in a sealed tube are attributed mainly to the superheating of the solvent due to high pressures [8]. The use of sealed tubes or vessels however, can cause hazards due to high pressure built up causing explosion during reactions, and also one has to limit oneself to small quantity of reactants.

* To whom correspondence should be addressed

Scheme:



R = CH_3, CH_2CH_3, Ph.
R' = H, CH_3, NO_2.

We report here for the first time, a very safe, simple, fast Fries rearrangement, at atmospheric pressure, in the presence of $AlCl_3$ in a modified domestic microwave oven. The method avoids the hazards due to high pressures created in the sealed reaction vessels.

Many of the Fries rearranged products that we synthesized such as 4-hydroxyacetophenone, 4-hydroxybenzophenones, 4-hydroxypropiophenones and others are commercially important primary drug intermediates[9] for the preparation of vasodilators, anti-inflammatory, analgesic, antipyretic, gonad-stimulating, cardiac stimulant, local anaesthetic and smooth muscle relaxants.

Experimental Section:

The reaction was carried out in a modified domestic microwave oven (Figure). A 100 ml round bottom flask (corning glass) was placed in it. A condenser was attached as shown in the figure. Opening of the condenser was attached to a

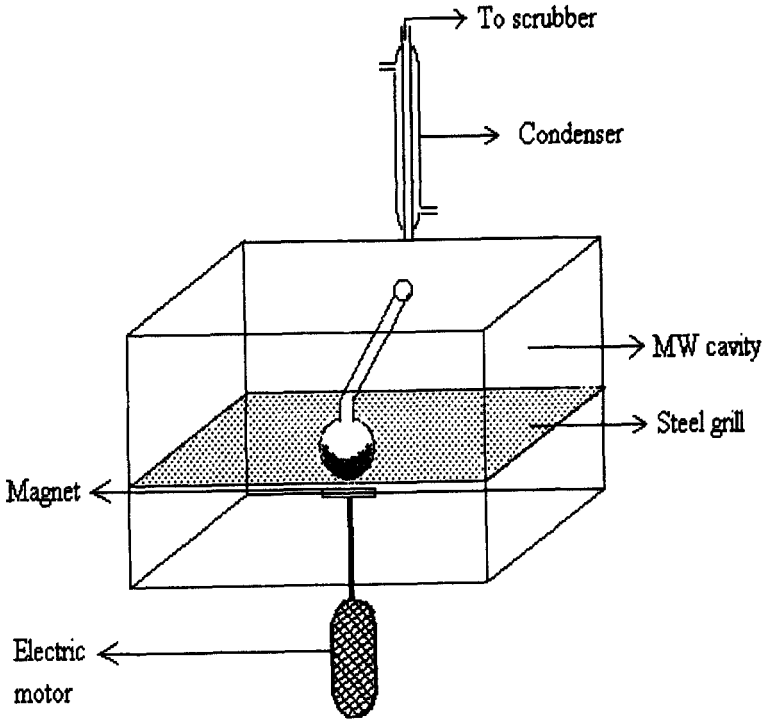


FIG.

Modified Domestic microwave oven

scrubber. The reaction mixture was stirred using a Teflon coated magnetic needle on a magnetic stirrer fitted at the base of the oven.

General procedure:

In a 100 ml round bottom flask the mixture of phenolic ester (10 mmol), dry distilled chlorobenzene (5 ml) and anhydrous $AlCl_3$ (Merck) (15 mmol) was stirred using rotating magnet and irradiated with microwaves for predetermined

Table : Optimized yields of $AlCl_3$ catalyzed MW assisted Fries rearrangement.

Substrate	MW irradn. time(min.) /temp(^{0}C)†	MW % yield	Conventional % Yield	mp °C observed. (lit.)
Phenyl acetate	3/106	2-hydroxy 73; 4-hydroxy 23	2-hydroxy 70[10] 4-hydroxy --	212-14 (214)#; 109 (109)
Phenyl propionate	3/106	2-hydroxy 28; 4 -hydroxy 62	2-hydroxy 32[11] 4-hydroxy 45	188 (189)#; 148 (148)
Phenyl benzoate	4/108	4 -hydroxy 70	4-hydroxy - Quantitative[12]	134 - 36 (135-36)
2-Naphthyl benzoate	5/110	1- benzoyl 72	1-benzoyl 66[13]	140 - 42 (141)
3-methyl phenyl benzoate	12/112	4-benzoyl 25*	4-benzoyl 32[14] 6-benzoyl 50	126 - 28 (128)
4-Nitrophenyl benzoate	12/112	2-benzoyl 38	-	124 (124)[15]

mp for 2,4- DNP derivative.

* 57% of the unreacted ester recovered.

† Temperature noted down immediately after the microwave exposure.

time at full power. The temperature of the reaction mixture was noted down using a thermometer immediately after the reaction. The reaction mixture was then cooled down to prevailing room temperature (28 °C) and poured over 5 ml conc. HCl containing a few pieces of crushed ice. The products were separated using usual workup procedures. During optimization of microwave reaction time, progress of the reaction was monitored using thin layer chromatography with toluene as an eluting solvent. All bp/mp for the rearranged products were in accordance with those of the reported compounds. The amount of the ester to catalyst ratio and amount of solvent was kept constant for all the substrates. The

reaction conditions were optimized with respect to microwave time to give maximum yield for each substrate at full power. The microwave oven with an output of 700W at full power was used.

Conclusion:

Rosenmund[10] reported the formation of ortho isomer in a conventional Fries rearrangement for phenyl acetate at 160 ^{0}C in 70% yield, without solvent. We carried out the reaction in chlorobenzene in a preheated oil bath at 120 °C for 5 mins. The yield of ortho isomer was 25% along with 18% para isomer. However when the same reaction was carried out in chlorobenzene as a solvent in microwave oven for 3 min., (end temperature 106 °C) 73% ortho and 23% of para isomer were obtained. When reaction was carried out in microwave oven without solvent charring took place. Above observations point at some specific microwave effects operating in the reaction.

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References:

1. Bose, Ajay, K; Banik, Bimal K; Lavlinskaia, Nina; Jayaraman, Muthuswamy; Manhas, Maghar, S. *Chemtech* **1997,** *27 (9),* 18 - 24.
2. Saskia, A. Galema. *Chemical Soc. Rev*, **1997,** 26, 233 - 238.

3. Christopher. R. Strauss and Robert, W, Trianor, *Aust. J. Chem.* **1995,** *48*, 1665 - 1692.

4. George, Majetich and Rodgers, Hicks. *Radiat. Phys. Chem.* **1995,** *45 (4)*, 567 - 579.

5. Sridar, V. and Sundara Rao V.S. *Indian J. Chem.* **1994,** *33B*, 184 - 185.

6. Kad, G,L; Trehan, I, R; Kaur, J; Nayyar, S; Arora, A; Brar, J. S. *Indian J. Chem.* **1996,** *35B,* 734 -736.

7. Inder, R. Trehan; Jasvinder, S. Brar; Ajay, K. Arora; Goverdhan, L. Kad; *J.Chem. Educ.* **1997,** *74 (3)*, 324.

8. Gedye, R; Westaway, K; Smith. F. *Ceram. Trans.* **1995,** *59*, 525-31 (*ca:* 124: 288858k).

9. Von A. Kleemann and J. Engel. "Pharmazeutische Wirkstoffe. Synthesen, Patents, Anwendungen," 2, neubearbeitete und erweiterte Auflage Georg Thime Verlag. Stuttgart NewYork **1982** pp.71, 120, 123, 230, 297, 386, 484, 725, 726, 810.

10. Rosenmund, K.W. and Schnurr, W. *Ann.* **1928,** *460*, 56-98.

11. Miller, E. and Hartung, W. H. "*Organic Synthesis.*" **1933,** *13*, 90.

12 Rosenmund, K.W. and Schnurr, W. *Ann.* **1928,** *460*, 56-98.

13. Joshi, G.G. and Shah, N.M. *J. Indian Chem Soc.* **1952,** *29*, 225-233.

14. Cox, E.H. *J. Amer. Chem. Soc.*. **1927,** *49*, 1029.

15. Arventiev, B. and Offenberg H. *Chim.***1960,** *11* 305-310. (*ca* 56:11554d).

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