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Modified Synthesis of Hydantoins under Microwave Irradiation and their Applications

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Abstract: - Hydantoins are very important organic compounds. They have been synthesised by a fast and general procedure under microwave irradiation. The method is very simple and effective. Syntheses have been achieved only in few minutes instead of 2-3 hours. The denial of use of solvent is a beauty of the work. Under solvent free condition, the yield of the products was found satisfactory. The aim of this work is to minimise the cost of the product in synthesis of different hydantoins of medicinal value under microwave irradiation, even in solvent free condition. Disubstituted-1, 2-diketones 1 (a-c) are heated with urea in the presence of 30% aqueous sodium hydroxide, intermediate heterocyclic pinacols, 2(a-c) are obtained under microwave irradication. Now these intermediate heterocyclic pinacols are cooled diluted with water and on acidification with concentrated hydrochloric acid, give hydantoins 3(a-c) as the result of pinacolic rearrangement. With microwaves at 40% (320W) Level of full power, 8000W of the oven used, the reaction was successfully attempted. The traditional heating [14] requires enough time for completion of reaction about 2 – 3 hours. But it takes only 2-3.5 minutes under microwave irradiation .The purity of the compounds is checked by TLC.

KeyWords: - Hydantoins, Microwave irradiation, Solvent free condition.

INTRODUCTION

Worldwide, epilepsy is one of the most common disorders of the central nervous system. There is still an increasing need of research into the newer molecules for treatment of the epileptic seizures. Mainly anticonvulsant drugs are used in the prevention and control of epileptic seizures. The most common choice for the treatment of epileptic seizures are hydantoins.

Microwave irradiation is an efficient and environmentally benign method to activate various organic transformations to afford products in higher yields and in shorter reaction periods. It also results in an increase in the purity of the products and involves very small amount of solvent or no solvent[4-13]. Further, the use of microwave acceleration eliminates the need for heating baths, reaction flasks, and reflux condensers with ground glass joints.

Substituted hydantoins have been prepared by conventional method[14] as well as under microwave irradiation[15]. The aim of the present work is to synthesise the different hydantoins of medicinal value[15] under microwave irradiation, even in solvent free condition to minimise the cost of the product. When disubstituted -1, 2-diketones 1(a-c) are heated with urea in presence of 30% aqueous sodium hydroxide under microwave irradiation, intermediate heterocyclic pinacols, 2(a-c), are obtained. The reaction mixture is cooled to room temperature and diluted with water. The diluted intermediates, on acidification with concentrated hydrochloric acid, give hydantoins 3(a-c) as the result of a pinacolic rearrangement.

EXPERIMENTAL

1a-c (0.025 mol) a compound was mixed with 3.0 g (0.05 mol) of urea and 15ml of 30 percent aqueous sodium hydroxide solution. The reaction mixture was irradiated with microwaves at 40% (320 W) level in a kenstar OM-20 ESP (800 W), unmodified domestic oven operating at 2450 MHz for the time indicated in Table 1. The reaction mixture is cooled to room temperature, diluted with 125 ml of distilled water and then mixed well. The insoluble byproduct is filtered off, after allowing it to stand for 15 minutes. The filtrate is rendered strongly acidic with concentrated hydrochloric acid.Under suction, the precipitated product is filtered. From industrial spirit, the product is recrystallised, finally.

5, 5-Diphenyl - 2, 4-imidazolidinedione (3a) :

IR (Nujol, υ_{max} , cm^{-1}) ; 730 (C-H deformation), 1490-1430 (phenyl ring breathing), 1720 (C=O stretching - C_4), 1780 (C=O stretching - C_2), 3200 (N-H stretching).

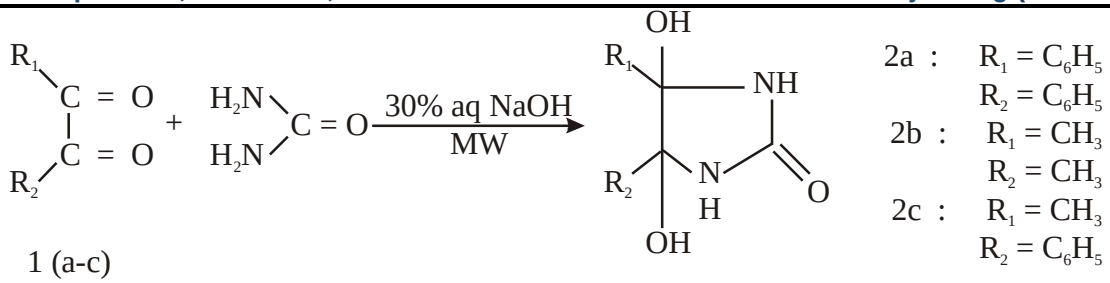
5, 5-Dimethyl -2, 4-imidazolidinedione (3b) :IR (Nujol, υ_{max} cm^{-1}) ; 1150 (C-CH_3 stretching), 1450 (C-H deformation), 1710 (C=O stretching - C_4), 1780 (C=O stretching - C_2), 3030 (C-H stretching), ^{1}H NMR (DMSO - d_6, δ ppm) ; 1.22 (s, 6H), 3.50 (s, 1Ha), 8.00 (s, 1Hb).

5-Methyl-5-phenyl-2, 4-imidazolidinedione (3c) :IR (Nujol, υ_{max} cm^{-1}) ; 1480 (C-C stretching), 1720 (C=O stretching - C_4), 1790 (C=O stretching - C_2) 2980 (C-H stretching), 3300 (N-H stretching). ^{1}H NMR (DMSO - d_6, δ ppm) ; 1.15 (s, 3H), 6.90 (s, 5H), 3.40 (s.1Ha), 8.10 (s, 1Hb).

RESULT AND DISCUSSION

For few minutes, the reaction was attempted first with microwaves at 20% (160 W) level in a Kenstar OM-20 ESP (800 W), whereupon no action was observed. The reaction was successfully attempted with microwaves at 40% (320 W) level of full power, 800W of the oven used. The time taken for completion of reaction was decided by hit and trial method. The time required for completion of reaction by traditional heating[14] is about 2 hours and it is only 2-3.5 minutes by microwave irradiation[15] using solvent like ethanol in large quantity. We have been successful in carrying out the reaction under microwave irradiation according to Scheme1. Ignoring the use of solvent, the cost of the product may be lowered appreciably.

In an open vessel adapted to a microwave oven reactions were carried out under atmospheric pressure. Purity of the compounds were checked by TLC. Melting points were taken in an open glass capillary using Elico melting point apparatus and are uncorrected. The compounds synthesised (3a-c) are all known compounds and have been characterised on the basis of their melting points, IR and NMR.

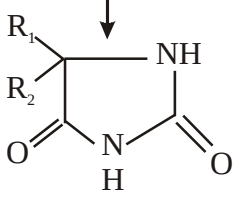


1 (a-c)

1a : $R_1 = C_6H_5$, $R_2 = C_6H_5$
1b : $R_1 = CH_3$, $R_2 = CH_3$
1c : $R_1 = CH_3$, $R_2 = C_6H_5$

2a : $R_1 = C_6H_5$, $R_2 = C_6H_5$
2b : $R_1 = CH_3$, $R_2 = CH_3$
2c : $R_1 = CH_3$, $R_2 = C_6H_5$

2 (a-c)



3 (a-c)

3a : $R_1 = C_6H_5$, $R_2 = C_6H_5$
3b : $R_1 = CH_3$, $R_2 = CH_3$
3c : $R_1 = CH_3$, $R_2 = C_6H_5$

(Scheme-1)**Table - 1**

Results of hydantoins synthesised under microwave irradiation in solvent free condition

Compound	Experimental				Literature[15]	
	Time/ min	Yield%	M.P./^{0}C	Solvent for recrystallisation	Yield%	M.P./ ^{0}C
3a	2.0	90	296-297	Industrial spirit	91.71	297-298
3b	3.0	92	176-177	Industrial spirit	95.23	176-178
3c	3.5	92	146-147	Industrial spirit	94.85	146-148

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