INTERNATIONAL JOURNAL OF RESEARCH IN PHARMACY AND CHEMISTRY

Available online at www.ijrpc.com

Research Article

MICROWAVE ASSISTED SYNTHESIS OF (3Z)-3-[(Z)-HYRAZYNILIDENE (2-HYDROXY-5-METHYLPHENYL) METHYL]-4-PHENYLBUT-3-EN-2-ONE AS ACTIVE INTERMEDIATES

KJ. Tidke*

Department of Chemistry, Vidyabharti Mahavidyalaya, C. K Naydu Road, Camp, Amravati – 444602, Maharashtra, India.

ABSTRACT

A facile and convenient synthesis of (3Z)-3- [(Z)-hyrazynilidene (2-hydroxy-5-methylphenyl) methyl]-4-phenylbut-3-en-2-one **IVa-f** from 1-(2- hydroxyl -5-methylphenyl)-2-benzylidene-3-methyl-1,3-propanedione under microwave irradiation have been reported in this work as important intermediate in synthesis of various hetrocycles.

Keywords: Knoevengel condensation, M.W.

INTRODUCTION

Hydrazones are of wide interest because of their diverse biological and clinical applications. This created interest in researchers who have synthesized variety of hydrazone derivatives and screened them for their various biological activities. Hydrazones are important compounds for drug design, as possible ligands for metal complexes, organocatalysis and also for the syntheses of heterocyclic compounds. These play an important role in inorganic chemistry, as they easily form stable complexes with most transition metal ions. Hydrazone derivatives have attracted a great deal of interest in synthetic chemistry and considerable research on them in relation to their synthetic utility has been accomplished. Hydrazones are extensively studied as reactants or re- action intermediates since they can readily undergo various ring closure reactions. A number of hydrazone derivatives have been reported to exert notably antimicrobial, antihypertensive, anticonvulsant, analgesic, anti-inflammatory, antituberculosis, antitumoral, antiproliferative and antimalarial activities which have attracted attention of medicinal chemists due to their wide range of pharmacological properties. These compounds are being synthesized as drugs by many researchers in order to combat diseases with minimal toxicity and maximal effects.

Sharma etal[1] synthesis some compounds showed mild to moderate anti-inflammatory and anticonvulsant activity. The coordination chemistry of hydrazones is an intensive area of study and numerous transition metal complexes of these ligands have been investigated. A number of complexes of transition metals with isonicotinoylhydrazone ligands were obtained and characterized. The synthesis and characterization of eight new com- plexes of Cu(II), Co(II), Ni(II) and Zn(II) with isonicotinic acid hydrazide (isoniazid (INH)) and isonicotinic acid (1-naphthylmethylene) hydrazide (INNMH) are reported[2]. Synthesis and properties of hydrazones bearing amide, thioamide and amidine functions are reported[3]. A few biological active hydrazone derivatives reported in the new millennium[4]. Synthesis, Characterization and Antimicrobial Activity of Long-Chain Hydrazones have been carried out by Rauf etal[5]. The synthesis of some new hydrazone derivatives containing the benzothiazole moiety [6] and in vivo anticonvulsant evaluation of 2-chloroquinolinyl hydrazone derivatives [7] are reported. The

exhaustive review study shows that hydrazone having diverse pharmacological[8], antibacterial[9], antimicrobial[10], anticancer[11] and biological activities[12].
So it was thought worthwhile to prepare few potent intermediates of biological importance.

MATERIALS AND METHOD

All the reactions are carried out in microwave irradiation in an LG microwave oven MG604AA at 900w, 2450MHz. IR spectra were recorded on Perkin Elmer R-32 and Varian XL-100A high NMR spectrometer using TMS as refrence in $CDCl_3$ and D_2O, the elemental analysis carried out on "Carbo Erba 1106 analyzer". The purity of sample was checked by TLC on silica gel-G plates. Melting points were determined in open capillaries.

1- (2- hydroxyl-5-methylphenyl)-3-methyl-1,3-propanedione IIa-b:

Synthesis of 1,3-propanediones (IIa-b) as a starting material is carried out by the reaction of 2- hydroxyl- 5-methyl acetophenone (5mg) **Ia** with ethyl acetate (30ml) in the presence of sodium metal was reflux for 1 minute under microwave. On cooling and acidifying this mixture the crude product was filtered and wash with water, which is crystallised in ethanol gives 80% yield of 1- (2- hydroxyl-5-methylphenyl)-3-methyl-1,3-propanedione **IIa**.
Spectral analysis of compound **IIa** : PMR ($CDCl_3$): δ 2.30 (s, 3H, CO-CH_3) , 2.19 (s, 3H, Ar CH_3) , 6.30 (s, 1H, =CH) , 6.8 – 7.5 (m, 3H, Ar-H) , 11.80 (s, 1H, -OH) , 14.95 (s, 1H, =COH), 4.1 (s, 2H, -CH_2) , 11.75 (s, 1H, -OH).
IR (nujol) : 3270 (O-H stretching) , 1660 (C=O) , 1610 (C=C).

1-(2- hydroxyl -5-methylphenyl)-2-benzylidene-3-methyl-1,3-propanedione IIIa-f:

A solution of 1-(2- hydroxyl-5-methylphenyl)-3-methyl-1,3-propanedione (0.01mol) **IIa** and benzaldehyde (0.015mol) containing few drops of piperidine (0.5ml) was refluxed for 1 minute under microwave. After cooling, crystallised from ethanol to get 1-(2- hydroxyl -5-methylphenyl)-2-benzylidene-3-methyl-1,3-propanedione **IIIa** in 85% yield.
Spectral analysis of compound **IIIa** : PMR ($CDCl_3$) : δ 2.27 (s, 3H, Ar-CH_3), 2.05 (s, 3H, $COCH_3$) , 6.21 (s, 1H, =CH) , 6.65-7.65 (m, 8H, Ar-H) , 16.2 (s, 1H, Ar-OH).
IR (nujol) : 1560 (C=C), 1600-1620 (C=O), 3400 (O-H).

(3Z)-3- [(Z)-hyrazynilidene (2-hydroxy-5-methylphenyl)methyl]-4-phenylbut-3-en-2one IVa-f :

A solution of 1-(2- hydroxyl -5-methylphenyl)-2-benzylidene-3-methyl-1,3-propanedione (0.01mol) **IIIa** and hyrazine hydrate (0.015) was reflux for 1 minute in solvent free condition under M.W. After cooling, crude product was crystallised to get (3Z)-3- [(Z)-hyrazynilidene (2-hydroxy-5-methylphenyl)methyl]-4-phenylbut-3-en-2one **IVa** in 85% yield.
Spectral analysis of compound **IVa** : PMR ($CDCl_3$) : δ 1.84 (s, 3H, -CH_3), 2.24 (s, 3H , -$COCH_3$) , 6.2 (s, 1H, =CH) , 6.8 (d, 1H, Ar-H) , 6.9 (d, 1H, Ar-H) , 7.3-7.4 (m, 5H, Ar-H) , 7.4 (s, 1H, Ar-H) 10.4 (br, 3H, -OH, -NH_2) .
IR (nujol) : 2800-2900 (-CH str sym asym) , 3100 (-CH str aro) , 3651 (-OH) , 3151-3068 (-NH_2) , 1640 (>C=O) ,1955-1811 (sub^{ed} benzene), 1575 (>C=N) , 1300-1400 (bending symmetry –CH) , 700-900 (OOP bending) .

RESULTS AND DISCUSSION

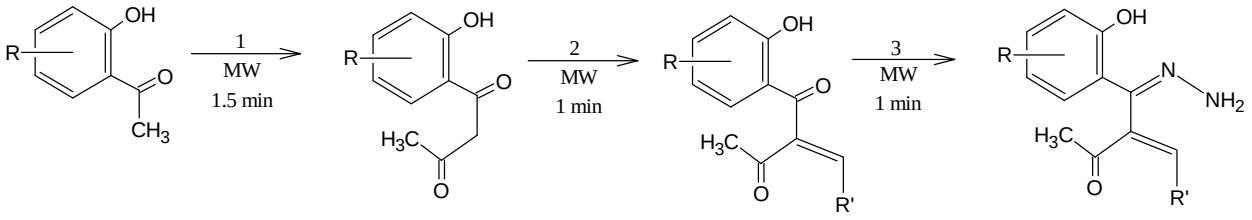
In quest of sustainable approach for synthesis of reactive hydrazones useful in heterocyclic chemistry this work was schematised. Starting compound **Ia-b** have been synthesised by literature method. 1-(2- hydroxyl-5-methylphenyl)-3-methyl-1,3-propanedione **IIa-b** have been synthesised from corresponding acetophenone **Ia-b**, Ethyl acetate and metallic sodium under microwave irradiation for 1.5 minute as describe in literature[21]. Method and structure was confirmed by spectral analysis. It shows signal at δ 2.30 ($COCH_3$), 6.30 (=CH) , 4.1 (s –CH_2) , 14.95 (=C-OH) conforms keto enol tautomerisum in compound **IIa**. This compound **IIa** was treated neat, with benzaldehyde in piperiden (solvent free) under microwave irradiation for a minute. On cooling and crystallisation compound was characterised as 1-(2- hydroxyl -5-methylphenyl)-2-benzylidene-3-methyl-1,3-propanedione **IIIa**. Appearance of signal at 6.21 (=CH) and disappearance of signal at 4.1 (CH_2) and 14.95 (=C-OH) of **IIa** conform the formation of benzylidiene derivative **IIIa**. Compound **IIIa** then treated to hydrazone hydrate in solvent free condition under microwave for 1 minute to get target compound **IVa** instead of cyclised compound. It was conform by appearance of NH_2 and =CH signal at 6.25 in **IVa**. Likewise all six **IVa-f** have been synthesised and characterised by spectral and alimental analysis.

CONCLUSION

Reactive intermediates play a vital role as synthons in heterocyclic chemistry, on to an environmental bearing method is an earnest need of today's research scenario. Author has successfully attempt this intermediates may help in further research all over.

ACKNOWLEDGEMENT

I am very grateful to the Principal, and management, Vidya Bharti Mahavidyalaya, Amravati, for providing necessary laboratory facilities to perform the research work.



Ia-b IIa-b IIIa-f IVa-f

I and II III and IV R' - a,d - C_6H_5 1 CH_3COOEt / Na

R = a - CH_3 R - a,b,c - CH_3 b,e - $C_6H_4OCH_3$ 2 Piperidine

b - H d,e,f - H c,f - C_4H_3O 3 NH_2 - NH_2

SCHEME

Table 1

Compound	M.P.(^{0}C)	MW (Min)	Yield % MW
IIIb	73	1	90
IIIc	140	1	90
IIId	104	1	90
IIIe	104	1	90
IIIf	160	1	90
IVa	203	1	85
IVb	220	1	90
IVc	205	1	85
IVd	240	1	85
IVe	181	1	90
IVf	185	1	90

REFERENCES

1. Sharma C, Jadon G, Singh H, Ankalgi A and Ranawat M. Int Jr Advance Res In Pharmaceutical and Bio-science. 2012;2(1):28.
2. Kriza A, Ababei L, Cioatera N, Rau I, Stanica N. J Serb Chem Soc. 2010;75(2):229.
3. Belskaya N, Dehaen W and Bakulev V. ARKIVOC. 2010;1:275.
4. Sharma A, Negi J and Ram V. Int Jr Phar Chem. 2012;2(4):100.
5. Rauf A, Banday M and Mattoo R. Acta chim Slov. 2008;55:448.
6. Ozdemir A, Zitouni G, Kaplancikli Z and Altintop M. J Serb Chem Soc. 2012;77(2):141.

7. Kumar S, Bawa S, Drabu S, Kumar R and Machawal L. 2010;67(5):567.
8. Singh M and Raghav N. Int Jr. Pharmacy and Pharmaceutical Sci. 2011;3(4):26.
9. Ozmen U and Olgun G. Spectrochimica Acta. 2008;Part A 70:641.
10. Oniga O, Ndongo J, Moldovan C, Tiperciuc B, Pirnau A, Vlase L and Verite P. Farmacia. 2012;60:6.
11. Patil B, Machakanur S, Hunoor R, Badiger D, Gudasi K and Bligh S. Scholar Research Library. 2011;3(4): 377.
12. Jubie S, Meena S, Ramaseshu K, Jawahar N and Vijayakumar S. Indian Jr Chem. 2010;49(B):1261.
13. Rollas S and Kllcukguzel S. Molecules. 2007;12:1910.
14. Mabkhot Y, Barakat A, Al-majid A, Al-othman Z and Alamary A. Int Jr Mol Sci. 2011;12:7824.
15. Sarikavakli N and Irez G. Turk J Chem. 2005;29:107.
16. Rajput A and Rajput S. Int Jr Pharm Tech Research. 2009;1(4):1605.
17. Monbared H, Pouralimardan O, Janiak C and Naturforsch Z. 2007;62b: 717.
18. Gupta S, Anis M, Gupta S, Kulshrashtha H and Sharma K. Inte Jr Green and Herbal chem. 2012;1(2):140.
19. Hawbecker B, Gladon R, Hitchcock R, Nordeen D, Wyles L and Ohio. Jr Sci. 1972;72(5):276.
20. Hania M. Asian Jr Chem. 2006;18(3): 1701.
21. Solanki P and Wadodkar K. Int Jr Heterocyclic Chemistry. 2003;13:135.