



<http://www.e-journals.net>



ISSN: 0973-4945; CODEN ECJHAO
E-Journal of Chemistry
Vol. 5, No. 1, pp. 39-42, January 2008

Microwave Induced Synthesis and Anti bacterial Activity of Some 6-(2-Hydroxy phenyl)-4-(substituted phenyl) -3-oxo-2, 3, 4, 5- tetrahydro-1H-indazoles

N. S. RAO, B. BAJIA* Y. K. SRIVASTAVA and RAVINDRA KUMAR

Department of Chemistry, M. P. Govt. P.G. College,
Chittorgarh-312001.India

birbal_bajia@yahoo.com

Received 23 March 2007; Accepted 10 May 2007

Abstract: The title compounds were synthesized by condensation of 2-hydroxy chalcones with ethylacetoacetate to get intermediate 3,5-diaryl-6-carbethoxy-2-cyclohexenone which were subsequently treated with hydrazine hydrate to afford the title compounds. All the transformation was carried out under microwave induced conditions. The synthesized compounds were screened for their antibacterial activity *in vitro*.

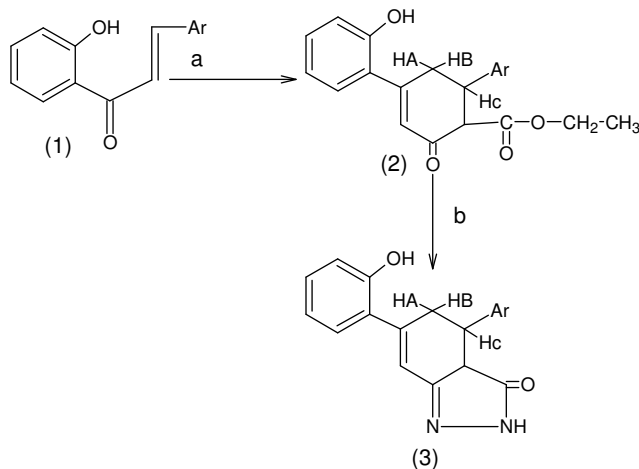
Keywords Carbethoxy, Cyclohexenone, Microwave irradiation, Antibacterial activity

Introduction

Microwave assisted organic reaction enhancement (MORE) is now a days a well established technique for synthesis of various heterocycles. All thermally driven reaction can be accelerated by microwave. The spectacular results *viz.* shorter reaction time, experimental simplicity selectivity of products and easy work up etc were obtained giving clear indication on the potentialities of this technique over conventional heating¹⁻³. The reactions under MWI can be carried out under solvent less solid phase making it a environmentally benign process. Thus microwave induced organic synthesis becomes a part of green chemistry⁴⁻⁵. Now-a-days it is also termed as e-chemistry because it is easy economic, effective and eco-friendly.

Much attention has been paid to the synthesis of heterocycles containing 1,2-diazole systems like indazole mainly due to their broad spectrum of pharmacological properties. Indazole derivatives possess variety of pharmacological activities such as analgesic⁷ elector-seisure⁷, anti inflammatory^{8,9}, antidepressant¹⁰, antitumor¹¹, antihypertensive¹² antiviral¹³ and anticancer¹⁴ activities. Keeping in view of these findings and usefulness of microwave assisted synthesis, we have synthesized some new 6-(2-hydroxyphenyl) -4-aryl-

3-oxo-2, 3, 4, 5 tetrahydro-1H indazoles using microwave assisted method. 2-Hydroxy chalcone (a-f) were subjected to michael addition with ethyl acetoacetate in presence of either anhy. K_2CO_3 /acetone or under solvent free condition using basic alumina¹⁵ to get 6-5 -diaryl-6-carbethoxy-2-cyclohexenones (2a-f). Compounds (2) were condensate with hydrazine hydrate to afford 6-(2- hydroxy phenyl)-4-aryl -3-oxo-2,3,4,5-tetrahyrdo-1H-indazoles (3a-f). (Scheme 1, Table 1 and 2)



Reaction conditions and reagents

- a. $CH_3COCH_2COOC_2H_5$ \ Anhy. K_2CO_3 or
 $CH_3COCH_2COOC_2H_5$ /Basic Alumina ,MWI, 5-7 min.
 b $NH_2NH_2 \cdot H_2O$,MWI,4-8 min

Scheme 1.

Table 1. Charactrization data of (2a-f) and (3a-f).

Compd	Ar	Molecular formula (M. Wt.)	M P. °C	Yield %	Reaction Time, min
2a.	Phenyl	$C_{21}H_{20}O_4$ (336)	154	77	5.0
2b.	4-Methoxyphenyl	$C_{22}H_{22}O_5$ (366)	166	79	6.5
2c.	3,4-Dimethoxyphenyl	$C_{23}H_{24}O_6$ (396)	174	80	5.5
2d.	4-Chlorophenyl	$C_{21}H_{19}O_4Cl$ (370.5)	176	80	6.0
2e.	4- Dimethylaminophenyl	$C_{23}H_{25}O_4N$ (379)	152	78	7.0
2f.	2-Furanyl	$C_{19}H_{18}O_5$ (326)	140	75	6.5
3a.	Phenyl	$C_{19}H_{16}O_2N_2$ (304)	242	82	5.0
3b.	4-Methoxyphenyl	$C_{20}H_{18}O_3N_2$ (334)	219	84	6.0
3c.	3,4-Dimethoxyphenyl	$C_{21}H_{20}O_4N_2$ (364)	200	81	5.0
3d.	4-Chlorophenyl	$C_{19}H_{15}O_2 N_2Cl$ (338.5)	237	80	5.0
3e.	4-Dimethylaminophenyl	$C_{21}H_{21}O_2N_3$ (347)	254	80	5.0
3f.	2-Furanyl	$C_{17}H_{14}O_3N_2$ (294)	231	80	6.5

Table 2. Antibacterial activity of synthesized compounds(3a-f)

S.No.	Compound	Zone of inhibition (diameter in mm)				
		<i>E.Coli</i>	<i>P.Valgaris</i>	<i>K. Pneumoniae</i>	<i>S.Aureus</i>	<i>S.Albus</i>
1	3a	10	-	11	13	17
2	3b	09	-	-	15	16
3	3c	12	-	-	13	-
4	3d	12	-	10	14	13
5	3e	11	10	08	10	-
6	3f	10	10	10	11	-
	Amicacin	13	-	20	20	30
	Coffrioxane	23	15	25	21	30

The structure of the synthesized compounds was assigned on the basis of their spectral and elemental analysis. The IR spectra of compound (2) showed a broad absorption band at 3600 cm^{-1} (-OH), $3040\text{-}2800\text{ cm}^{-1}$ (C-H str. for both aliphatic and aromatic C-H) and a sharp band at $1730\text{-}1700\text{ cm}^{-1}$ ($>\text{C}=\text{O}$ of ester). $^1\text{H-NMR}$ spectra of compounds (2) gave signals at δ 2.96-2.98 (dd, 1H, C-H_A), 3.06- 3.08 (dd, 1H, C-H_B) and 3.72-3.75 (dd, 1H, C- H_C), 4.10(q, 2H, CH₂), 1.10(t, 3H,CH₃) and 6.92-8.01 (*m*, aromatic protons)

The IR spectra of compounds (3) gave characteristic bands at $3660\text{-}3500\text{ cm}^{-1}$ (OH), 1650 cm^{-1} ($>\text{C}=\text{O}$), $1595\text{-}1580(\text{C}=\text{N})$ and $3200\text{-}3190(\text{NH})$. $^1\text{H-NMR}$ spectra of compounds (3) gave signals at δ 2.40-2.70 (dd, 1H, C-H_A), 3.1- 3.6 (dd, 1H, C-H_B) and 3.8-4.11 (dd, 1H, C- H_C) confirming presence of cyclohexenone nucleus. Aromatic protons appeared as multiplet at δ 6.67-7.94. The mass spectra of compounds (2) and (3) gave molecular peaks to their molecular masses.

Experimental

Melting points were measured on a Buchi 530 melting point apparatus in open capillaries and are uncorrected. The purity of the compounds was checked by TLC using silica gel-G adsorbent and benzene-ethyl acetate (9:1v/v) as the eluent. IR spectra were recorded on Perkin-Elmer1600 spectrometer using KBr (cm^{-1}). $^1\text{H-NMR}$ spectra were taken on Bruker-DRx-600 Spectrometer using TMS as internal standard and CDCl_3 or DMSO-d_6 as solvent. Mass spectra were obtained on JEOL-SX-DA-600 mass spectrometer (FAB) using *m*-nitro benzyl alcohol as matrix. Matrix peaks appeared at *m/z* 136,137,154,289 and 307. All the transformations were carried out in domestic microwave oven (Samsung 1630N, 600 watt, 2450MHz.)

General procedure for synthesis of 3,5-diaryl-6-carbethoxy-2-cyclohexenones(2a-f)

To slurry of 2-hydroxy chalcone (0.01 mole) and ethyl acetoacetate (0.02mole) anhy. K_2CO_3 (0.04 mole) or basic alumina (2.0g) was added and mixed thoroughly. The mixture was air dried and subjected to microwave irradiation for 5-7 minutes. After completion of reaction as indicated by TLC, the reaction mixture was cooled to room temperature and separated solid was extracted with ethanol. The in-organics were filtered off. On standing the filtrate afforded colourless crystals of 2a-f.

6-(2-Hydroxy phenyl)-4-aryl-3-oxo-2, 3, 4, 5-tetra hydro-1H- indazoles (3a-f)

6-Carbethoxy cyclohexenones (2a-f, 0.01 mole) and hydrazine hydrate (0.015 mole) were mixed thoroughly to form intimate mixture. It was then subjected to microwave irradiation for 4-8 minutes. After completion of reaction as indicated by TLC, the mixture was cooled

to room temperature and extracted with ethanol. On standing colourless crystals of indazoles separated out which were filtered.

Antibacterial activity

All the synthesized compounds were screened for their antibacterial activity against gram positive *S.aureus* and *S.albus* and gram negative *E. Coli*, *K. pneumoniae* and *P.vulgaris* invitro using cup plate agar diffusion method¹⁶. Zone of inhibition was measured in mm. Standard drugs used were ampicillin and ciprofloxacin. The screening results are tabulated in Table 2.

Conclusions

In above synthetic scheme we have used microwave irradiation technique, this is a solvent free reaction condition that leads to considerable saving in the reaction time and energetically profitable. The solvent free condition contributes to saving in cost and diminishes the waste disposal problem. Some compounds show potential antibacterial activity

Acknowledgments

The authors are highly thankful to Dr. B. L.Verma Retd. Professor of Chemistry, M.L.Sukhadia University, Udaipur for valuable suggestions and guidance. Thanks are also due to Dr. K. P. Madhusudhan, Director SAIF, CDRI, Lucknow for spectral analysis

References

1. Caddick S, *Tetrahedron*, 1995, **51**, 10403.
2. Verma R S, *Green Chemistry*, 1999, 43.
3. Gelena S A, *Chem. Soc. Rev.*, 1997, **26**, 233.
4. Flanga, Delacruz D and A Delahuzu *Contemp. Org. Synth.*, 1997, 373.
5. Bose A K, Manhas M S, Ghosh M and Shah M, *J.Org. Chem.*, 1991, **56**, 6968.
6. Bose A K, Banik B K, Lavlinskata N, Jayaraman M and Manhas M S *Chemech*, 1997, **27**, 18.
7. Jain A C, Mehta A and Arya P, *Indian J Chem*, 1987, **26B**, 150.
8. Palazzo G, Corsi G and Silnerstrini B, *J Med Chem*, 1996, **9**, 38.
9. Bohem R and Hisschelmars R, *Pharma Zie*, 1980, **35**, 232.
10. Charts E R, Thomas K J and Leo M L, *Eur Pat Appl ER*, 1992. 509,402,
11. Buydin V G, Colbru N L and Givrdeni A B, *J Heterocyclic Chem*, 1998, **28**, 517.
12. Raman B, *Pharmazie*, 1990, **45**, 214.
13. George V D, Zing L and Bacheleree T K, *J Med Chem*, 1998, **41**, 2411.
14. Popat K H, Joshi H S, *Indian J. Chem*, 2003, **42B**, 1497.
15. Jhala Y S, dulawat S S and Verma B L, *Indian J Chem*, 2006, **45(B)**, 466.
16. Barry A L, *Antimicrobial susceptibility test, principle and practices* (Illus lea and fehinger, Philedephia USA) 1976, pp 93-108.