J. Indian Chem. Soc.,
Vol. 88, March 2011, pp. 461-463

NOTE

Ultrasonicated synthesis of 1-(2-hydroxyaryl)-3-(pyrrolidin-1-yl)propenones and their antimicrobial screening

Sharad N. Shelke[a]*, Yogesh J. Pawar[a], Sheshrao B. Pawar[a], Somanth S. Gholap[b] and Charnshing H. Gill[c]

[a]P.G. Department of Chemistry, S.S.G.M. College, Kopargaon-423 601, Maharashtra, India

E-mail : snshelke@yahoo.co.in *Fax* : 91-2423-223155

[b]P.G. Department of Chemistry. P. V. P. College, Pravaranagar-413 713, Maharashtra, India

[c]Department of Chemistry, Babasaheb Ambedkar Marathwada University, Aurangabad-431 004, Maharashtra, India

Manuscript received 15 July 2009, revised 16 June 2010, accepted 20 July 2010

Abstract : A facile synthesis of title compounds has been carried out under ultrasound irradiation. The main advantages of the present procedure are shorter reaction time and higher yield. Products have been characterized by IR, PMR, CMR, GC-MS study and screened for their antimicrobial activity.

Keywords : Ultrasonication, 3-formylchromone, enaminoketone, bioactivity.

Introduction

Among the different functionalized chromones, 3-formylchromones occupy a unique position because they can be transformed into various heterocycles by interesting reactions with different nucleophiles[1]. 3-Formylchromone when treated with phenylhydrazine gives 1-phenyl-4-(2-hydroxybenzoyl)pyrazoles[2], whereas substituted 3-formylchromone when treated with pyrrolidine[3] under reflux gives 1-(2-hydroxyaryl)-3-(pyrrolidin-1-yl)-propenone. The enaminoketones[4] constitute an important class of synthon, which can be elaborated to a wide variety of heterocyclic compounds. The titled compound 1-(2-hydroxyaryl)-3-(pyrrolidin-1-yl)propenone was utilized for the synthesis of pyrazoles[3].

Pyrrolidine containing compounds are versatile antidiabetic, antiobesity[5], anticonvulsant[6] and antibacterial agents[7].

The chemical applications of ultrasound, called sonochemistry, have become an exciting new field of research during the last few decades[8]. The use of ultrasound irradiation technique for activating various reactions is well documented in the literature such as synthesis of azoles and diazines[9], Reformatsky reaction[10], oxidation of substrates like hydroquinones[11], conversion of nitro compounds to carbamates[12], Pinacol coupling[13], Ullmann condensation[14], Suzuki cross-coupling[15] and various other transformations in synthetic organic chemistry[16].

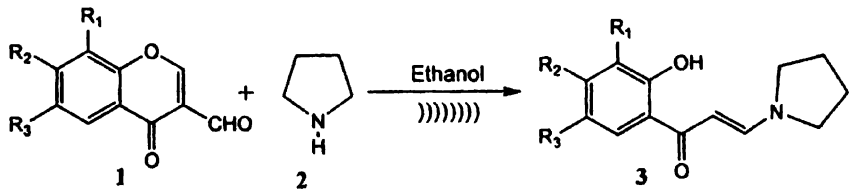
Results and discussion

In view of advantages of ultrasound irradiation in organic synthesis and utility of the titled compound, we aimed the synthesis of 1-(2-hydroxyaryl)-3-(pyrrolidin-1-yl)propenones (**3**) by the reaction of pyrrolidine (**2**) on 3-formylchromones (**1**) under the influence of ultrasound irradiation. In earlier report[13] 2-(hydroxyaryl)-3-(pyrrolidin-1-yl)propenones have been prepared by conventional method. This method was time consuming (requires 5 h for completion) and yield obtained was poor.

In this communication, a number of 3-formylchromones (**1**) are treated with pyrrolidine (**2**) in dry ethanol under influence of ultrasound irradiation. By this method, the time required for completion of the reaction is less and yields are better at room temperature, hence no vigorous heating is required. In general, the reactions using ultrasonication technique is very clean and required shorter time for completion.

Compounds **3c** and **3i** were obtained in good yield within 30–35 min under ultrasonication. Each experiment

using ultrasonication technique was repeated three times to confirm the consistency of the results. Comparative results obtained are tabulated in the Table 1.



Scheme 1

The required 4-oxo-4*H*-1-benzopyron-3-carbaldehydes (**1**) were prepared by Vilsmeir-Haack reaction from variously substituted *o*-hydroxyacetophenones.

Experimental

All experiments under ultrasonication were carried out in bath type ultrasonicator model EN-20U-S manufactured by Enertech Electronica Pvt. Ltd., Mumbai, India having maximum power output of 100 W and 33 KHz operating frequency.

All the recorded melting points were determined in open capillary tubes and are uncorrected. IR spectra were recorded on Perkin-Elmer FTIR spectrophotometer in KBr disc. The ^{1}H NMR and ^{13}C NMR spectra were scanned on Bruker 300 MHz and 400 MHz FT spectrophotometer respectively using DMSO-d_6 or $CDCl_3$ as a solvent and TMS as an internal standard, while mass spectra were recorded on Finnigan mass spectrometer.

General procedure :

1-(2-Hydroxyphenyl)-3-pyrrolidin-1-yl-propenone (**3a**) :

To a 100 mL round bottom flask was added 6-chloro-4-oxo-4*H*-1-benzopyron-3-carbaldehyde (**1a**) (2.08 g, 0.01 mol) and pyrrolidine (**2**) (1.42 g, 0.02 mol) and dry ethanol (10 mL). The reaction vessel was then dipped into a sonication bath and sonicated for 25–40 min till a clear solution was obtained. Progress of the reaction was monitored with the help of TLC. After completion of the reaction the contents were poured into crushed ice and the product obtained was separated by filtration. The product was crystallized from alcohol. This typical experimental procedure was followed to prepare the compounds **3b-i**. The compounds synthesized by above procedures are listed in Table 1 with their characterization data. IR, PMR, CMR and GC-MS data have confirmed their structures and agreement with those obtained for the products synthesized by earlier method[3].

Table 1. Characterization data of synthesized compounds **3a-i**

Compd.	R^1	R^2	R^3	Time (min)	Yield (%)	M.p. (°C)	Lit. Yield[3] (%)
3a	H	H	Cl	25	82	148	79
3b	H	H	F	28	82	170	80
3c	H	H	Me	30	87	174	75
3d	H	Me	Cl	40	80	172	70
3e	H	Me	H	28	79	140	65
3f	Cl	H	Cl	35	81	166	76
3g	Me	H	Me	30	80	158	75
3h	H	H	H	25	82	142	74
3i	H	H	Et	35	84	100	80

Spectral data of representative example **3c** :

Entry **3c** : ^{1}H NMR ($CDCl_3$, 300 MHz) δ : 1.99 (4H, m), 2.30 (3H, s), 3.34 (2H, t), 3.59 (2H, t), 5.70 (1H, d, *J* 18 Hz), 6.82 to 7.47 (3H, m), 8.05 (1H, d, *J* 18 Hz), 13.83 (1H, s); ^{13}C NMR (DMSO, 400 MHz) δ : 189.85, 160.05, 150.21, 134.10, 127.80, 126.14, 119.33, 117.02, 90.03, 52.49, 46.58, 24.59, 24.49, 20.05; IR (KBr) cm^{-1} : 3122, 1623, 1585 and 1544; GC-MS (70 eV) *m/z* : 231 (M^+), 161, 70.

Antimicrobial screening :

Compounds listed in Table 2 were screened (doses of 100 μg) for their antibacterial activity against Gram -ve bacteria *E. coli* and Gram +ve bacteria *S. albus* using filter paper disc method. Plates inoculated with *E. coli* were incubated for 48 h and plates inoculated with *S. albus* for 24 h respectively at RT. Streptomycin sulphate were used as a standard. Inhibition zones were measured in mm and results obtained are shown in Table 2.

All these compounds were also screened (doses of 100 μg) for their antifungal activity against *A. niger* using greseofulvin as a standard. The results are shown in Table 2.

Table 2. Antimicrobial activities of 1-(2-hydroxyphenyl)-3-pyrrolidin-1-yl-propenones **3**

Compd.	Inhibition zone in mm (diameter)		
	E. coli	*S. albus*	*A. niger*
3a	10	12	10
3b	8	6	8
3c	8	6	-
3d	9	10	-
3f	8	10	8
Streptomycin sulphate	18	22	Not tested
Griseofulvin	Not tested	Not tested	12

Acknowledgement

Authors are thankful to the Principal, K. H. Shinde, S.S.G.M. College, Kopargaon, Ahmednagar for providing necessary facilities and constant encouragement.

References

1. (a) C. K. Ghosh, *J. Heterocycl. Chem.*, 1983, **20**, 1437; (b) Sabitha and Gowravaram, *Aldrichimc Acta*, 1996, **29**, 15; (c) C. K. Ghosh and A. Patra, *J. Heterocycl. Chem.*, 2008, **45**, 1529.
2. C. K. Ghosh, *J. Indian Chem. Soc.*, 1978, **55**, 52.
3. (a) S. N. Shelke, N. R. Dalvi, M. S. Shingare, C. H. Gill and B. K. Karale, *Indian J. Heterocycl. Chem.*, 2006, **15**, 403; (b) C. K. Ghosh and S. Khan, *Synthesis*, 1981, **9**, 719.
4. S. A. Mousawi, E. John and N. A. Kandery, *J. Heterocycl. Chem.*, 2004, **41**, 381.
5. T. W. Cheng, S. Chen. P. Devasthale, C. Z. Ding, T. F. Herpin, S. Wu, H. Zhang, W. Wang and X. Ye, PCT Int. Appl. WO 2004004665 A2, 2004, 543.
6. T. Kwon, P. Kwon, S. Song, M. Park and J. Choi, *Bull. Korean. Chem. Soc.*, 2002, **23**, 917.
7. K. Hattori, A. Yamada, S. Kuroda, T. Chiba, M. Murata and K. Sakane, *Bioorg. Med. Chem. Lett.*, 2003, **12**, 383.
8. D. L. Salvatare and H. Yuanjun, *J. Inorg. Chem.*, 2003, **68**, 8261.
9. M. Kidwai, R. Venkataramanan and B. Dave, *J. Heterocycl. Chem.*, 2002, **39**, 1045.
10. V. Singh, V. Sapehiyia and G. L. Kad, *Synthesis*, 2003, **2**, 198.
11. N. A. Ross and R. A. Bartsch, *J. Heterocycl. Chem.*, 2001, **38**, 1255.
12. S. Chandrashekhar, C. Narsihmulu and V. Jagadeshwar, *Synlett.*, 2002, **5**, 771.
13. J.-T. Li, Y.-J. Bian, H.-J. Zang and T.-S. Li, *Synth. Commun.*, 2002, **32**, 542..
14. M. Robin, V. Pique, R. Faure and J. Glay, *J. Heterocycl. Chem.*, 2002, **39**, 1083.
15. R. Rajagopal, D. V. Jarıkote and K. V. Srinivasan, *Chem. Commun.*, 2002, **61**, 616.
16. S. N. Shelke, N. R. Dalvi, S. B. Kale, M. S. More, C. H. Gill and B. K. Karale, *Indian J. Chem., Sect. B*, 2007, **46**, 1174.