P75. EFFICIENT AND ENVIRONMENTALLY BENIGN SYNTHESIS OF *BIS*-MANNICH BASES OF 2-NAPHTHOL

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Abstract

An efficient and expeditious microwave assisted-synthesis of *bis*-Mannich bases of 2-naphthols has been devised. With appropriate molar ratios of aromatic aldehydes, piperazine and 2-naphthol, *N,N'*-bis(aryl-2-hydroxynaphthylmethyl)pip erazines were prepared in high yields under solvent-free conditions using a domestic microwave oven.

Introduction

Chiral Mannich bases of 2-naphthol find use in catalyzing asymmetric induction in Zn-mediated alkylation of carbonyl compounds.[1,2] Owing to their ability to chelate strongly to metal ions, they also have the potential to be used as metallo-enzyme inhibitors and/or scavenger of heavy metal poisons.[3,4] One of our research interests is in development of environmentally friendly synthetic methodologies making use of microwave as clean and efficient energy source. As a part of our interest in developing 2-naphthol as versatile building block, we have recently developed a microwave-assisted expeditious synthesis of 2-naphthol Mannich bases involving aromatic aldehydes and cyclic 2° amines.[5,6] As an extension of this project, we herein report an efficient and expeditious synthesis of *N,N'*-bis(aryl-2-hydroxynaphthylme thyl)piperazines (**1-10**).

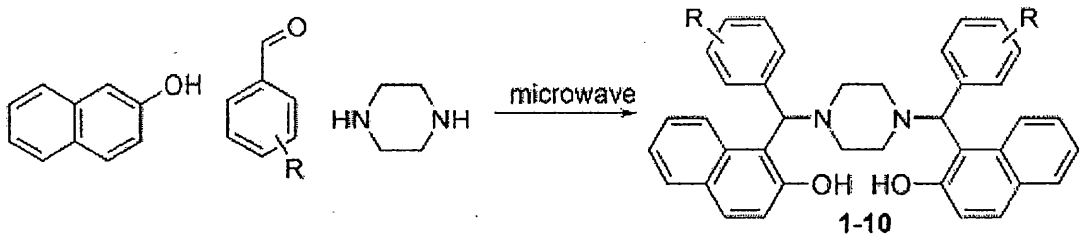
Material and Methods

All chemicals and reagents were obtained from Aldrich Chemical Co. NMR spectra were recorded on Bruker AV300 NMR spectrometer. ESI-MS was recorded at Dalhousie University. IR spectrum was recorded on Nicolet Avatar 330FT-IR spectrophotometer A domestic microwave (Panasonic) was used for irradiation at highest power level (900 W).

2-Naphthol (10 mmol), appropriate aldehyde (10 mmol) and anhydrous piperazine (5 mmol) were mixed in a 100 ml Erlenmeyer flask. The reaction was irradiated with microwave at highest power for 1 minute. The flask was cooled for 2 minutes and then methanol (30 mL) was added. This mixture was then refluxed with vigorous stirring for 1 h. After cooling, the product obtained as fine powder was suction filtered and washed with cold methanol. Melting points and isolated yields are noted in Table 1. Spectroscopic data for a representative compound (**1**) obtained as diastereomeric mixture: ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.20-2.63 (6H, m, 6×NCH), 3.70-3.75 (2H, m, 2×NCH), 5.15/5.17 (2H, s, $Ar_2CHN<$), 7.10-7.29 (10H, m, Ar-H), 7.40 (2H, t, J= 7.2 Hz, Ar-H), 7.55 (4H, d, J= 6.9 Hz, Ar-H), 7.63-7.73 (4H, m, Ar-H), 7.83 (2H, d, J= 8.7 Hz, Ar-H) and 13.20 (2H, s, 2×OH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 51.36/53.95, 71.90, 115.62, 120.12/120.16, 121.42/121.49, 123.05, 127.01, 128.39, 128.62/128.69, 129.20, 129.30, 129.42, 130.17, 132.66, 139.15/139.28 and 155.22/155.28; IR (KBr Disc): 3438, 11621, 384, 950 and 744 cm^{-1}; ESI-MS (% intensity): 551 (75, M+H), 319 (28) and 233 (100).

Results and Discussion

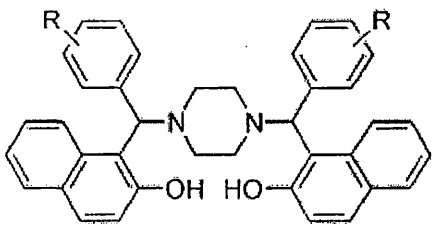
Use of microwave as energy source has emerged as an efficient way of energy transfer and has become extremely popular in synthetic chemistry community finding use in carrying out virtually any reaction requiring heat.[7] With appropriate molar ratios of aromatic aldehydes, piperazine and 2-naphthol, *N,N'*-bis(aryl-2-hydroxynaphthylmethyl)pip erazines were prepared in high yields under solvent-free conditions using a domestic microwave oven (Scheme 1). This procedure yields the products with excellent purity after a simple work-up.



Scheme 1: Synthesis of compounds **1-10**.

The reaction was carried out under solvent-free conditions and unlike several reported procedures of 2-naphthol Mannich base synthesis under microwave conditions,[5,6,8] this procedure did not require use of a solid support or a catalyst. Thus this process can be categorized as a truly green process with excellent atom economy.

Table 1: Structure and physical data of compounds **1-10**.

Structure	Compound	R	m.p. (°C)	Yield (%)
	**1**	H	241-242	62
	2	4-F	243-244	67
	3	4-Cl	238-239	70
	4	4-CH_3	234-235	42
	5	4-OCH_3	248-250	39
	6	4-NO_2	214-215	63
	7	4-$N(CH_3)_2$	225-226	31
	8	3,4-Cl_2	231-232	63
	9	3,4-$(OCH_3)_2$	230	33
	10	3,4-OCH_2O-	240-241	40

In conclusion, we have devised an excellent procedure for the synthesis of *N,N'*-bis(aryl-2-hydroxynaphthylmethyl) piperazines which may find use as catalysts or pharmaceuticals. Detailed study on molecular dynamics and optical resolution of these compounds is in progress and will be reported subsequently.

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