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RESEARCH ARTICLE

Synthesis of P-nitrocalix[6]arene Hydroxamic Acids by Microwave Irradiation

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ABSTRACT

P-nitrocalix[6]arene hydroxamic acids has been synthesized by partial reduction of nitro calix[6]arenes with hydrazine hydrate, raney Ni and their coupling with benzoyl chloride under the influence of microwave irradiation with 95% yield.

KEYWORDS

Calixarene, Hydroxamic acid, Microwave

INTRODUCTION

There has been a growing interest in calixarenes in recent years.[1] Calixarenes are a class of cyclooligomers formed via a phenol–formaldehyde condensation[2]. Their rigid conformation enables calixarenes to act as host molecules as a result of their preformed cavities. The synthetic modifications at the upper and lower rim gave a new class of molecular receptors.[3] Calixarenes have been established as cation[4] and anion receptors,[5] organic neutral and charged molecular recognition devices[6], ion selective electrodes[7] and fluorosent devices.[8] In short, calixarene derivatives have been mainly utilized for their active role in host–guest chemistry. Calixarene derivatives, which can be functionalized in various ways, have been noted as useful extractants for the metal ions.[9-15] These novel compounds can recognize a target metal ion by the cavity size of the cyclic molecule together with the chelating effect of their functional groups. Therefore, in recent years functionalized calixarene is one of the most promising extractants for the innovative solvent extraction process and has been tried for the separation of metal ions.[16--19] Hydroxamic acids are versatile extractants and have achieved significant importance as analytical tools for separation and determination of a large number of metal ions.[20-22] The Hydroxamic acids functionalized calixarenes are highly selective reagents for the metal ions. Till now, few reports have appeared on the use of hydroxamic acid functionalized calixarenes for the synthesis and complexation studies.[23-25]

The p-nitrocalix(6)arene was synthesized by the acid-catalyzed condensation reaction of p-nitrophenol and benzaldehyde which was partially reduced with hydrazine hydrate in the presence of Raney Ni(W-4) at 0–10^0 C for 60min. to obtain the corresponding hydroxylamine, which was condensed with benzoyl chloride in the presence of an aqueous suspension of sodium carbonate at 0–10^0 C for 120min. to form bis N-phenyl benzocalix-(6)arenehydroxamic acid(NPCHA). The product is characterized by FT-IR, ^{1}H NMR, ^{13}C NMR spectroscopy and Mass spectroscopy. A rapid and practical procedure for the synthesis of NPCHA under microwave conditions was developed.

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EXPERIMENTAL

Melting points are uncorrected and were obtained using a melting-point apparatus (Electroquip). Microwave synthesis work was carried out using a KENSTAR OM 20 DGQ domestic microwave oven. IR spectra were recorded on JASCO FT/IR 6100 spectrometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on a DRX 300 spectrophotometer operating at 300MHz in $CDCl_3$ with TMS as an internal standard. Column: ACQUITY UPLC™ BEH C18, 1.7 µm, 2.1 × 100 mm, Sample concentration: 0.3 mg/ml, Diluents: - Methanol, Run time: 8 min. Detector:-Tunable U.V Detector, Empower:-2154, Chromatic condition:-Mobile Phase A: 0.05% Tri fluro acetic acid in water, Mobile Phase B: acetonitrile, Flow Rate: 0.4 ml/min. Injection Volume: 1.0 µ L Wave length: 220 nm, Column Temperature: 30°C.

Synthesis of p-nitrocalix(6)arenehydroxamic acid(NPCHA)

Conventional Method

In to a 250 ml round bottom flask, fitted with a reflux condenser, p-nitrophenol (0.035M), 37% benzaldehyde (0.216 M), conc. hydrochloric acid (5 ml) and 50 ml xylene were taken, and heated on a water bath at 80^{o} C for 20 hrs with occasional stirring. The orange solid thus obtained was filtered, washed with hot water and finally with hot alcohol, Yield 70%.

Synthesis of Calix(6)arenehydroxylamine

In to a 100 ml round bottom flask, fitted with a reflux condenser and mechanical stirrer, Nitrocalix(6)arene (0.0073 M) was taken in 50.0 ml chloroform and cooled to $0\text{-}5^{0}$ C with contentious stirring ,Then after Raney-Ni (W-2) (2–2.5 g) in 1,4-dioxane was added followed by the drop wise addition of hydrazine hydrate (0.278 M) to get calix(6)arenehydroxyl amine, which was filtered immediately and used in situ for the preparation of hydroxamic acid derivatives.

Preparation of N-benzoylcalix(6)arene Hydroxamic Acid

In 250 ml conical flask fitted with a dropping funnel freshly prepared calix(6)arene hydroxylamine in 50 ml chloroform was taken. An aqueous suspension of 5g sodium bicarbonate in 10 ml of water was added and stirred. After the mixture was cooled to $0\text{-}5^{0}$ C, 3.5 ml benzoyl chloride in 20 ml of anhydrous diethyl ether was added drop wise during period of 30 min. and the stirring was continued for another 15 min. Almost the entire amount of hydroxamic acid formed was precipitated as a pale yellow granular solid. The solid was filtered, washed with water and the ether layer was distilled under vacuum and any solid product thus obtained was combined with the bulk. It was recrystallized from chloroform heptane mixture twice to yield a white compound.

Microwave Method

A mixture of p-nitro phenol (0.035M), 37% benzaldehyde (0.216 M), conc. hydrochloric acid was placed into the Kenstar domestic microwave at 80% power output for 15 min. to obtain an orange solid, which was washed with hot water and with hot alcohol to get p-nitrocalix(6)arene. p-nitrocalix(6)arene (0.0073 M), hydrazine hydrate (0.0278 M) and Raney Ni(W-4) (0.2 g), was placed into Kenstar domestic microwave oven at 0% power output for 5min. to obtain corresponding hydroxylamine. The hydroxylamine was condensed with benzoyl chloride (5 ml) in presence of aqueous suspension of sodium carbonate in oven at 40% power output for 1min. to obtain N-phenylbenzo calix(6)-arenehydroxamic acid(NPCHA).

RESULTS AND DISCUSSION

The methods developed for the synthesis of 37, 38, 39, 40, 41, 42-hexa hydroxy 8, 13, 23, 31-tetra nitro 1,19 [bis N-phenylbenzo]calix(6)-arenehydroxamic acid by conventional and Microwave assisted methodologies are simple and of general applicability.

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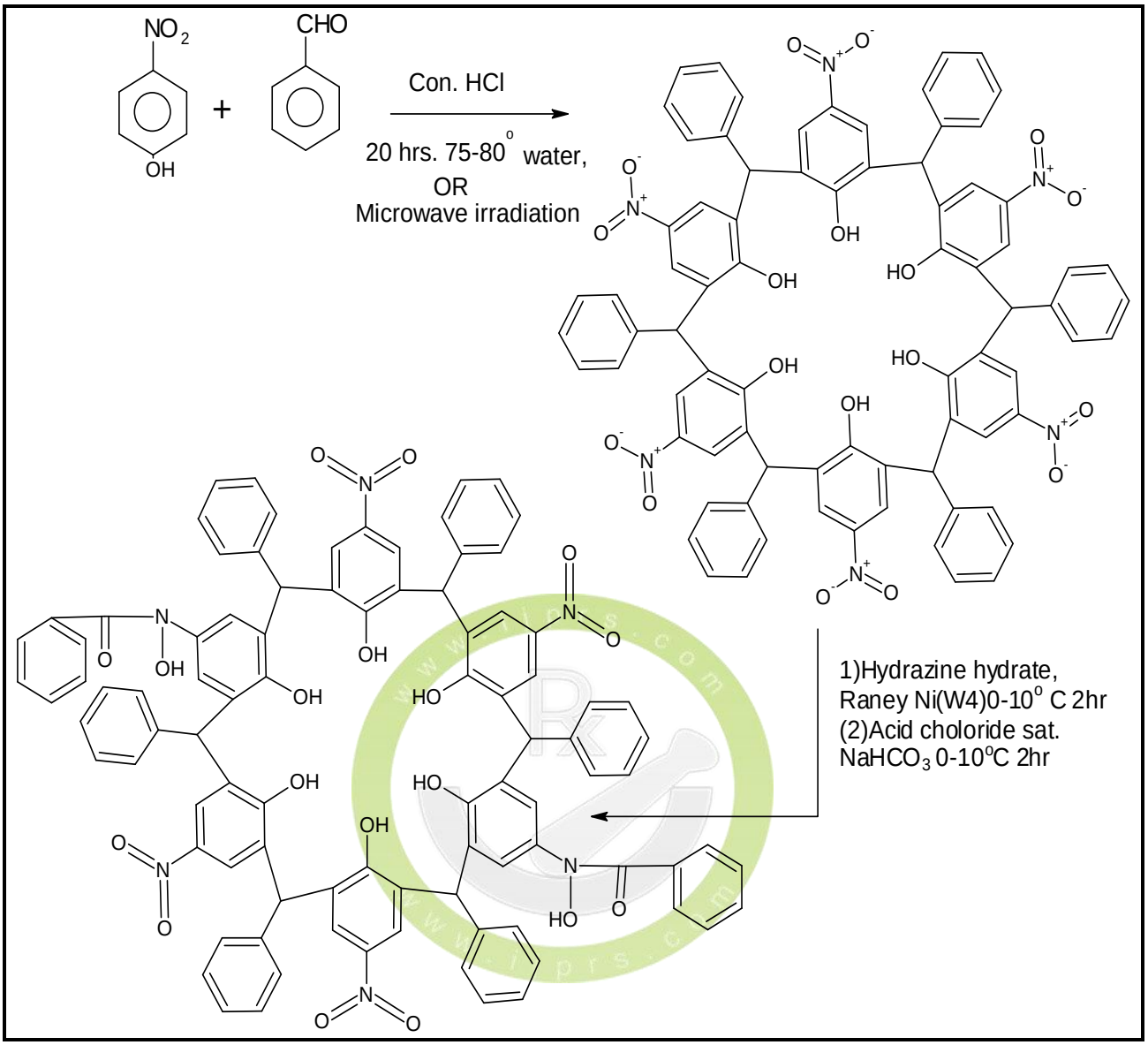

Scheme 1 Synthetic route for the synthesis of N-phenylbenzocalix(6)arenehydroxamic acid(NPCHA).

During the preparation of hydroxyl amines and their further reactions, it is must to maintain the reaction temperature between 0-5^{0}C; otherwise the decomposition of the resulting product may occur. The addition of acid chloride should be very slow and then after the reaction should be stirred at the same temperature for further 60-90 min. in order to complete the reaction.

Conventional method for the synthesis of NPCHA have few disadvantages such as longer time period, low yield and large amount of solvent used in the reaction.

Keeping drawbacks in to consideration, Microwave assisted methodology has been developed for the synthesis of NPCHA. In microwave assisted irradiation, the reaction do not required any solvents and the reaction time significantly reduced with remarkable increase in the yield (Table-1). The purity of NPCHA is found to be 99.12%. This NPCHA were purified and characterized by melting point, elemental analysis, UV, IR, ^{1}H NMR, ^{13}C NMR spectroscopes and Mass spectroscopy. The physico chemical properties and elemental

analysis of the synthesized NPCHA are given in (Table: 2)

Table 1: Comparison of yields and Reaction time of NPCHA under classical and microwave irradiation technique

Comp.	Conventional Method		Microwave Method	
	Time	(%) Yield	Time	(%) Yield
NPCHA	20hr	70	20 min	95

The experimental values are given in parenthesis.

The Fourier transform infrared spectrometer (FT-IR) (KBr) spectrum of NPCHA displayed three sharp bands at 3323, 1657, and 925 cm^{-1}. The band at 3323 cm^{-1} is due to O-H stretching vibration. It is known that O-H stretching vibration bands occur at around 3600 cm^{-1}; hydrogen bonding shifts these bands to lower frequencies. In hydroxamic acids, the -OH group is placed very close to the polar carbonyl C=O group. The band at 1657 cm^{-1} is assigned to the C=O of the hydroxamic acid group. A sharp band at 925 cm^{-1} is attributed to N-O stretching vibrations. NPCHA displayed a sharp band at 1511 cm^{-1} for $-NO_2$ stretching vibrations.

The ^{1}H NMR (DMSO) spectrum of NPCHA displayed singlets at 7.4 ppm for aromatic protons, 7.5 ppm for hydroxyl groups, and 10.27 ppm for hydroxamic acid groups. In addition, NPCHA displayed one doublet at 2.4 ppm for methyl groups at the bridge.

The ^{13}C NMR ($CDCl_3$) spectrum of NPCHA displayed singlets at 120–132 ppm for aromatic carbons and one singlet at 160–180 ppm for ketone groups. In addition, compounds NPCHA displayed one doublet at 38 ppm for bridged methine groups. The results obtained from elemental analysis of NPCHA confirm the presence of hydroxamic acid groups.

Synthesis of 37, 38, 3, 40, 41, 42-hexa hydroxy 8, 13, 23, 31-tetra nitro 1, 19(bis N-phenyl benzo-) calix(6)arene hydroxamic acid Prepared from N-phenyl Hydroxylamine and was obtained in 95% yield as a white solid, mp-220^{o}C; IR(KBr), 3323cm-1 (ν_{OH}), 1657cm-1 ($\nu_{C=O}$); ^{13}C NMR, 140, 138, 135, 129, 128, 120; Mass spectrum [FAB (Xenon 6Kv/10mA] molecular ion peak 1542, base peak 1542; (m/z = 1542, 1402, 1357, 1274, 1262); Anal. Calcd for $C_{92}H_{66}N_6O_{18}$; C: 62.56, H: 3.85, N: 2.43, Found, C: 62.76, H: 3.70, N: 2.28.

CONCLUSION

Synthesis of NPCHA has been developed by conventional and as well as microwave assisted technique. Microwave assisted synthesis method has been discussed and found that it is relatively faster and gives higher yield compare to conventional technique for the synthesis of NPCHA.

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Table 2: Physico-chemical properties of NPCHA

Compound	Molecular Formula	Molecular weight	Color	m.p.	Elemental analysis %		
					C	H	N
NPCHA	$C_{92}H_{66}N_6O_{18}$	1542.44	White	220-225	62.56 (62.76)	3.85 (3.70)	2.43 (2.28)

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