

Novel catalytic method synthesis of calix[4]pyrroles using Preyssler and Wells-Dawson heteropolyacids

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A catalytic synthesis of calix[4]pyrroles and *N*-confused calix[4]pyrroles by reaction of dialkyl or cycloalkyl ketones with pyrrole was performed using Preyssler, sodium30-tungsto pentaphosphate, [NaP₅W₃₀O₁₁₀]¹⁴⁻ and Wells-Dawson heteropolyacids as acidic catalysts. The process occurred under mild, eco-friendly and environmental friendly conditions and as a reusable, green catalyst at room temperature for 6 hours. The results showed that the yield for this synthesis is excellent with the use of Preyssler and Wells-Dawson type tungstophosphoric heteropolyacid, H₆[P₂W₁₈O₆₂], catalysts. The synthesis reaction of calix[4]pyrroles and *N*-confused calix[4]pyrroles was developed using different solvents and the best yields were obtained in chloroform.

Keywords: Calix[4]pyrrole, Heteropolyacid, Preyssler, Wells-Dawson, Catalysis, *N*-confused calix[4]pyrrole.

INTRODUCTION

Heteropolyacids are classified according to their structures. Two classes, the Keggin and the Wells-Dawson structures, have been investigated more extensively than others^{1, 2}. The use of heteropolyacids, HPAs, has recently received considerable attention as nontoxic, eco-friendly and environmentally benign catalysts for various organic transformations to afford the corresponding products in good yield. Due to the numerous advantages associated with these eco-friendly and green catalysts, HPAs and their salts have been explored as powerful, efficient and eco-friendly catalysts in organic reactions³. An important area of supramolecular chemistry is the design and synthesis of the receptors to recognize, sense and bind the anions⁴. Calixarenes, a very important class of macrocyclic compounds which are widely used as ligands in supramolecular chemistry. Modification of the upper rim of calix[4]phenols by means of the S_N^H coupling with electron-deficient triazinones is a new approach to change the molecular cavities of these compounds, which opens new possibilities for the construction of highly selective ligands⁵. The research and development have been made milder methods for the synthesis of porphyrins⁶, N-C isomerization⁷ and higher homologues of porphyrins⁸. The meso-octamethylcalix[4]pyrrole **3a** has been prepared by condensation of pyrrole with acetone in the presence of aqueous hydrochloric acid or methanesulfonic acid in methanol⁹. Calix [4]pyrroles are conformationally flexible macrocycles¹⁰ of significant importance due to their binding under different conditions with anions¹¹, neutral substrates⁹ and metal ions¹². The complexation behavior of calix[4]pyrroles with anions and cations has been widely studied using fluorescent¹³, colorimetric¹⁴ and electrochemical signaling¹⁵ devices. They find interesting applications as raw materials for transformation into novel calix[4]pyridines and calix[4]pyridinopyrroles¹⁶, as new solid supports capable of separating anion mixtures¹⁶, in optical recognition of organic vapors¹⁷ and as biologically active species¹⁵. Porphyrinogens, bearing hydrogen atoms

at meso positions, are key intermediates in biological and chemical synthesis of porphyrins¹⁸.

Synthesis of meso-octamethylcalix[4]pyrrole (**3a**) and the *N*-confused octamethylcalix[4]pyrrole (**4b**) using pyrrole and acetone in the presence of trifluoroacetic acid¹⁹. The reactions of pyrrole with dialkyl ketones in the presence of protic acids (HCl, H₂SO₄), organic acids (CH₃SO₃H) and Lewis acids (BBr₃ and BF₃) have also been used in the synthesis of calix[4]pyrroles²⁰. The reaction of the excess of pyrrole with dialkylketones in the presence of acid gave 5,5-dialkyldipyrromethanes which in a subsequent reaction with dialkylketones in the presence of borontrifluoride-etherate formed strapped calix[4]pyrroles²¹. These acids are considered hazardous and corrosive and their removal from the reaction mixtures is difficult. Recently, condensations in dichloromethane of pyrrole with dialkyl ketones in the presence of the molecular sieve Al-MCM-41 and the zeolite HY afforded dipyrromethane, calix[4]pyrroles and other linear products, but not the *N*-confused calix[4]pyrroles²². Heteropolyacids (HPAs) is an inexpensive and non-hazardous solid acid, useful as a catalyst.

EXPERIMENTAL SECTION

Chemicals and apparatus

All chemical compounds were obtained from commercial sources and used as received.

The IR spectra were obtained with a Bruker 500 scientific spectrometer. ¹H NMR spectra were recorded in CDCl₃ with TMS as internal standard on a FT NMR Bruker 100 MHz Aspect 3000 spectrometer. The mass spectra were scanned on a Varian Mat. CH-7 at 70 eV. Melting points were recorded on an Electrothermal type 9100 melting point apparatus.

Preparation of Catalysts

Preyssler catalyst, $H_{14}[NaP_5W_{30}O_{110}]$, ($H_{14}P_5$)

$H_{14}P_5$ was prepared by a passage of a solution of the potassium salt in water through a column (50 cm×1 cm) of Dowex50W×8 in the H^+ form and evaporation of the elute to dryness under vacuum²³.

Wells-Dawson species $H_6[P_2W_{18}O_{62}]$

The Wells-Dawson species $H_6[P_2W_{18}O_{62}]$ was prepared as described elsewhere²⁴, from an aqueous solution of $\alpha/\beta K_6P_2W_{18}O_{62}\cdot 10H_2O$ salt, which was treated with ether and concentrated (37%) HCl solution.

General procedure

Preparation of calix[4]pyrroles (3a-g) and N-confused calix[4]pyrroles (4a-4e):

Synthesis of meso-octamethylcalix[4]pyrrole (**3a**) and *N*-confused octamethyl calix[4]-pyrrole (**4a**):

A mixture of pyrrole (8 mmol), acetone (8 mmol), $CHCl_3$ (10 mL) and heteropolyacids catalyst (0.04 mmol) was added to the bottom flask, this mixture was stirred at room temperature for 6 hours. The reaction progress was monitored by thin layer chromatography (TLC). After the completion of the reaction, the catalyst was removed by filtration and washed thoroughly with $CHCl_3$ to dissolve all the contents. The filtrate was concentrated to give the crude product, which was subjected to column chromatography to afford pure meso-octamethylcalix[4]pyrrole (**3a**). With further elution of the column with petroleum ether-chloroform (2:3, v/v) gave the *N*-confused isomer of octamethylcalix[4]pyrrole (**4a**). The above general method

is used for the synthesis of different calix[4]pyrroles (**3b-3g**) and *N*-confused calix[4]pyrroles (**4b**, **4d** and **4e**).

Reusability of catalyst

The recycled catalyst could be washed with dichloromethane and subjected to a second run of the reaction process with the same substrate. The results of the first experiment and subsequent experiments were almost consistent in yields (83, 82.5 after three runs).

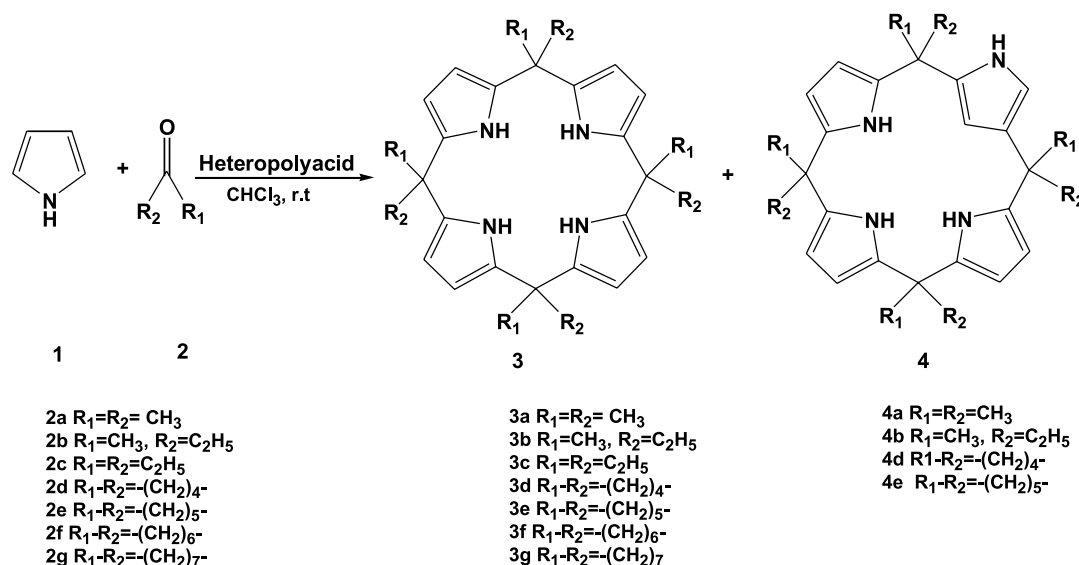
Results and Discussion

We wish to report the synthesis of calix[4]pyrrole (**3a**) and the *N*-confused calix[4]pyrrole (**4a**) use of heteropolyacids as acid catalyst, and we performed this synthesis in chloroform of pyrrole (**1**) with acetone for 6 hrs in the presence of Preyssler catalyst (Scheme 1, Table 1).

The results showed that the yield for this synthesis is excellent with the use of Preyssler and Wells-Dawson type tungstophosphoric heteropolyacid, $H_6[P_2W_{18}O_{62}]$, catalysts. The synthesis reaction (Scheme 1) tested using different solvents and the best yields were obtained in chloroform (Table 2). We also considered the synthesis of calix[4]pyrrole (**3a**) by various heteropolyacids (Table 3).

We continued this synthesis with other ketones (**2b-2g**) and pyrrole in chloroform as a solvent and to use of Preyssler and Wells-Dawson type tungstophosphoric heteropolyacid, $H_6[P_2W_{18}O_{62}]$, catalyst (Table 3).

The reactions of cycloheptanone (**2f**) and cyclooctanone (**2g**) with pyrrole and in the presence of Preyssler catalyst gave the corresponding calix[4]pyrroles (**3f**) and (**3g**) in



Scheme 1. Synthesis of Calix[4]Pyrroles using Preyssler and Wells-Dawson Heteropolyacids

Table 1. The reaction of different ketones (2a–2g) with pyrrole in $CHCl_3$, catalyzed by Preyssler heteropolyacid catalyst

Compound	Time (h)	% Conversion of Pyrrole	^a Yield(%) / mp °C, (3)	(lit. mp °C, [ref.]) (3)	^a Yield(%) / mp °C, (4)	(lit. mp °C, [ref.]) (4)
2a	6	95	84.5/295	(296 [25])	11.5/185	(184–185 [25])
2b	8	88	80/144	(146 [22])	10/121	–
2c	18	71.5	74.5/222	–	–	–
2d	5	93	83/235	(236 [22])	11.5/198	–
2e	5	96	85/273	(271–272 [25])	12/224	(223.2–223.6 [25])
2f	24	37	32/163	–	–	–
2g	48	25.5	21.5/223	–	–	–

^a Isolated yields.

Table 2. Preyssler catalyzed condensation of pyrrole and acetone in different solvents

Entry	Solvent	^a Yield (%) 3a	^a Yield (%) 4a
1	CHCl ₃	84.5 (83, 82.5) ^b	11.5 (11, 10.5) ^b
2	CCl ₄	56	–
3	Benzene	45	–
4	Toluene	44	–
5	DMF	39	–
6	DMSO	36	–
7	Ethanol	71.5	9.5
8	THF	51	–
9	Acetonitril	68	8

^a Isolated yields. ^b Catalyst was reused over three runs.

Table 3. The reaction of different ketones (2a–2g) with pyrrole in CHCl₃, catalyzed by Wells-Dawson and keggin (12-tungstophosphoric acid)

Compound	Reaction time (min)	^a Yield (%) using H ₆ P ₂ W ₁₈ O ₆₂ (3)	^a Yield (%) using H ₃ PW ₁₂ O ₄₀ (3)	^a Yield (%) using H ₆ P ₂ W ₁₈ O ₆₂ (4)	^a Yield (%) using H ₃ PW ₁₂ O ₄₀ (4)
2a	6	81	77	8.5	7
2b	8	76.5	75	8	–
2c	18	70	68	–	–
2d	5	79	74.5	8	–
2e	5	82.5	79	7.5	–
2f	24	26	20	–	–
2g	48	16.5	11.5	–	–

^a Isolated yields.

32% and 21.5% yield at ambient temperature, but the time required for the conversions was considered too long. In the reactions of pyrrole with **2c**, **2f** and **2g**, the corresponding *N*-confused calix[4]pyrroles could not be isolated. This could be attributed to the steric hindrance encountered with these higher acyclic and cyclic ketones. The C-2 and C-5 atoms are more reactive than the C-3 and C-4 positions in pyrrole, hence the electrophilic reaction at C-2 and C-5 position of pyrrole with acetone in

the presence of acid gave calix[4]pyrrole in preference to *N*-confused calix[4]pyrrole²⁵. The recovered catalyst was recycled twice with modest product yield loss being noted (Table 1). The catalytic activity of heteropolyacids catalysts are remarkable and it is environmentally benign. Heteropolyacids catalysts are commercially available. There are spectral data for compounds of (**3a–3g** and **4a**, **4b**, **4d**, **4e**) in Tables 4, 5.

CONCLUSIONS

We reported a catalytic method for synthesis of calix[4]pyrrole using Preyssler and heteropolyacids catalysts as an efficient, reusable and eco-friendly heterogeneous inorganic catalyst. It is noteworthy to mention that the catalyst is reusable. Even after three runs for the calix[4]pyrrole reaction, the catalytic activity of H₁₄[NaP₅W₃₀O₁₁₀] was almost the same as that of the

Table 4. ¹H NMR spectral data for meso-octaalkyl and cycloalkyl calix[4]pyrroles 3a–3g

Compound	¹ H NMR δ (ppm) ^a
3a	7.01 (4H, br s, NH), 5.89 (8H, d, <i>J</i> =2.5 Hz, β-pyrrole), 1.50 (24 H, s)
3b	6.97 (4H, br s, NH), 5.80 (8H, d, <i>J</i> =2.5 Hz, β-pyrrole), 1.79-1.76 (8H, q, -CH ₂), 1.45-1.18 (12H, br s, CH ₃), 0.80-0.63 (12 H, t, CH ₃)
3c	7.05 (4H, br s, NH), 5.89 (8H, d, <i>J</i> =2.3 Hz, β-pyrrole), 1.79-1.57 (16H, q, -CH ₂), 0.71-0.58 (24 H, t, CH ₃)
3d	7.03 (4H, br s, NH), 5.85 (8H, d, <i>J</i> =2.3 Hz, β-pyrrole), 2.21-2.00 (16H, m), 1.68-1.44 (16H, m)
3e	7.25 (4H, br s, NH), 5.89 (8H, d, <i>J</i> =2.5 Hz, β-pyrrole), 1.91-1.90 (16H, m), 1.50-1.41 (24H, m)
3f	6.88 (4H, br s, NH), 5.83 (8H, d, <i>J</i> =2.5 Hz, β-pyrrole), 2.01-1.94 (16H, m), 1.72-1.52 (32H, m)
3g	6.99 (4H, br s, NH), 5.93 (8H, d, <i>J</i> =2.4 Hz, β-pyrrole), 1.97-1.95 (16H, m), 1.52-1.34 (32H, m), 1.23-1.21 (8H, m)

^aAll products are known, characterized by ¹H-NMR and compared with authentic samples [22].

Table 5. ¹H NMR spectral data for meso-octaalkyl and cycloalkyl *N*-confused calix[4]pyrroles 4a, 4b, 4d, 4e

Compound	¹ H NMR δ (ppm)
^a 4a	NH: 7.75 (1H, br), 7.41 (1H, br), 7.26 (2H, br); α-pyrrole: 6.30 (1H, d, <i>J</i> = 2 Hz), β-pyrrole: 6.04 (2H, br), 5.97 (2H, br), 5.93 (2H, m), 5.50 (1H, br); 1.56-1.48 (24H, m)
4b	NH: 7.63 (1H, br), 7.53 (1H, br), 7.35 (2H, br); α-pyrrole: 6.40 (1H, d, <i>J</i> = 2 Hz); β-pyrrole: 6.03 (2H, br), 5.88 (2H, br), 5.78 (2H, m), 5.53 (1H, br); 1.92 (3H, s, CH ₃), 1.83-1.12 (29H, m)
4d	NH: 7.48 (1H, br), 7.29 (1H, br), 7.00 (2H, br); α-pyrrole: 6.42 (1H, d, <i>J</i> =1.97 Hz); β-pyrrole: 6.00 (2H, br), 5.90 (2H, br), 5.88 (2H, m), 5.58 (1H, br); 2.25-1.98 (16H, m), 1.50-1.20 (16H, m)
^a 4e	NH: 7.63 (1H, br), 7.44 (1H, br), 7.10 (2H, br); α-pyrrole: 6.42 (1H, d, <i>J</i> = 1.98 Hz); β-pyrrole: 6.03 (2H, br), 5.97 (2H, br), 5.82 (2H, m), 5.50 (1H, br); 2.70-2.10 (16H, m), 1.60-1.20 (24H, m)

^aProducts *N*-confused calix[4]pyrroles (4a, 4e) are known, characterized by ¹H-NMR and compared with authentic samples [25].

freshly used catalyst. $H_{14}[NaP_5W_{30}O_{110}]$ is non-corrosive and environmentally benign and presents fewer disposal problems.

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