Novel calix[4]resorcinarene nanocarriers for enhanced drug solubilisation:

synthesis of octaamino-substituted resorcinarenes

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The problems or challenges

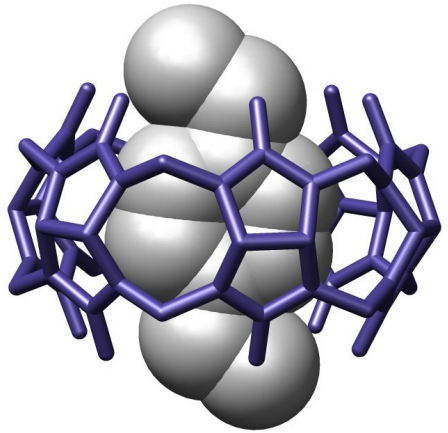
- Increasing percentage of low aqueous soluble drugs (70%) e.g. anticancer therapies *(Khadka, et a., 2014)*
- Poor bioavailability
- Risk of adverse effects in patients
- Low success rate with excipients and other strategies (Khadka, et a., 2014)

Why Resorcinarenes?

Emerging novel formulation technologies found to aid drug solubility and delivery

Have diverse applications in areas of host-guest interactions in supramolecular.

Used as carriers in a number of therapies including anti-cancer drugs.



Calix[4]resorcinarenes

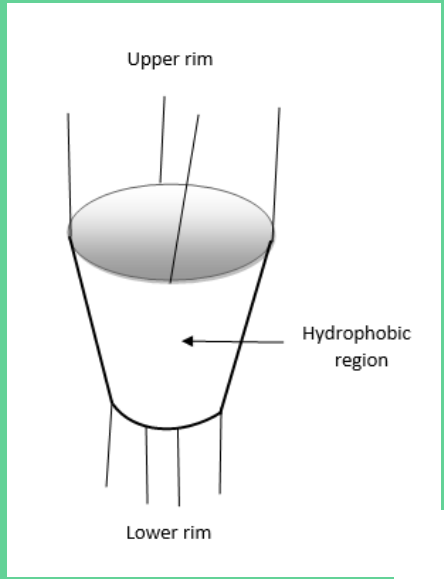
Calix[n]arene related

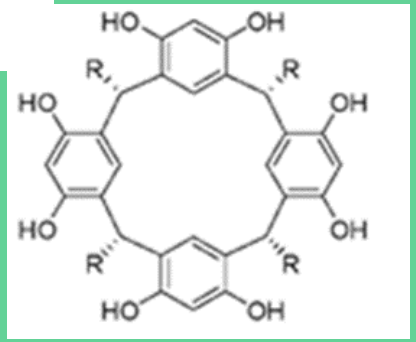
Cyclic oligomers and cone-shaped rigid structure

Posses hydrophobic interiors and upper and lower rims

Hydrophobic and insoluble

Aqueous soluble when functionalised



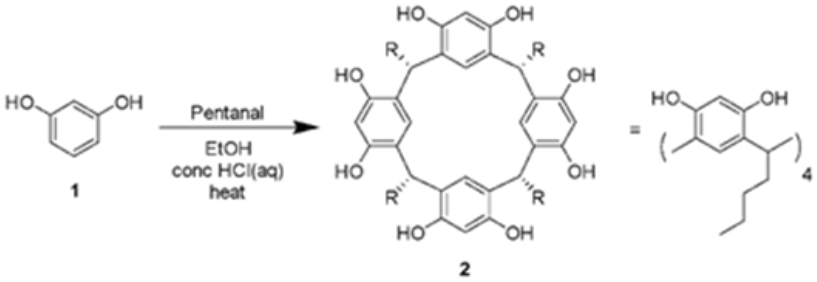


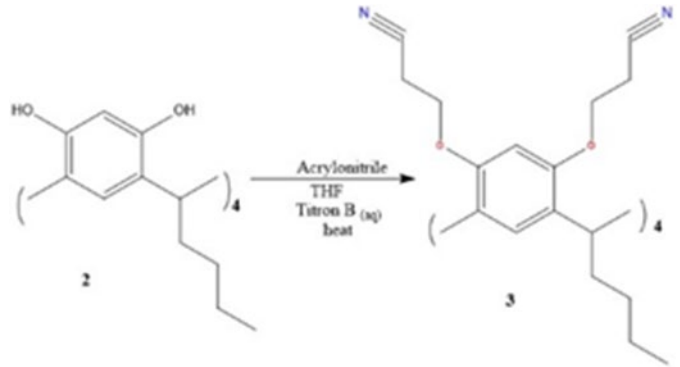
Aim of Research

Synthesise octaamino-substituted resorcinarene using **S_N2 reaction method**

Characterise and evaluate the solubilising potential

Methods and Materials





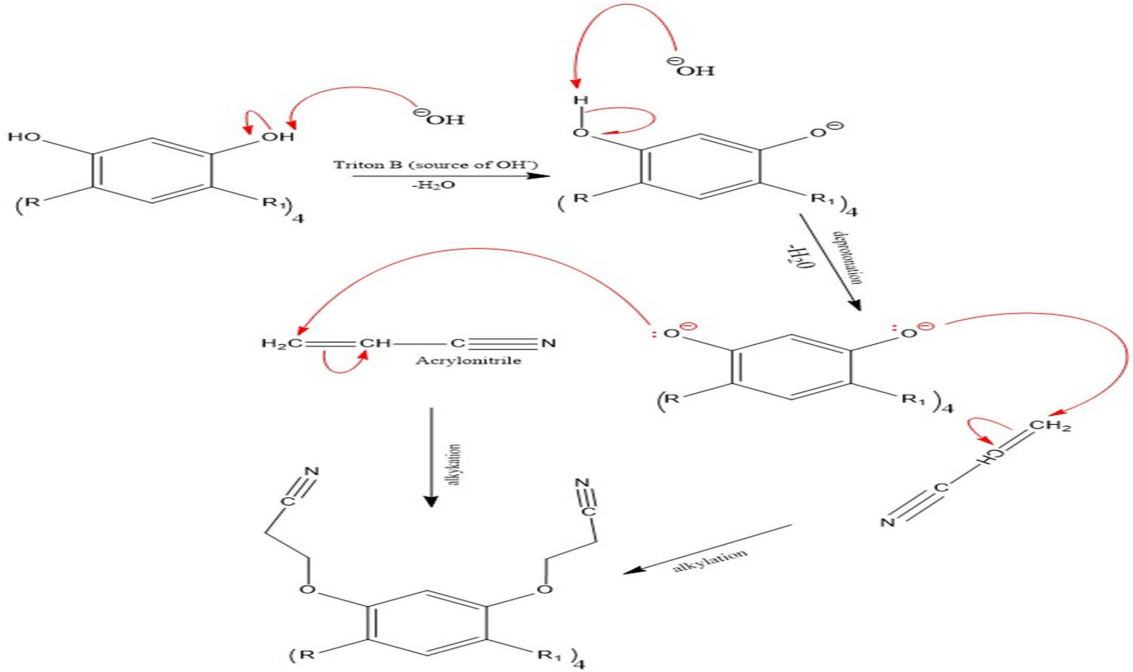
Scheme 1 Synthesis of resorcinarene under acid-catalysed condensation reaction ~ 4 hrs.

High yield (99%)

Scheme 2: Alkylation of the upper and lower rims of resorcinarene under Titron-B catalysed reaction ~ 20 hrs

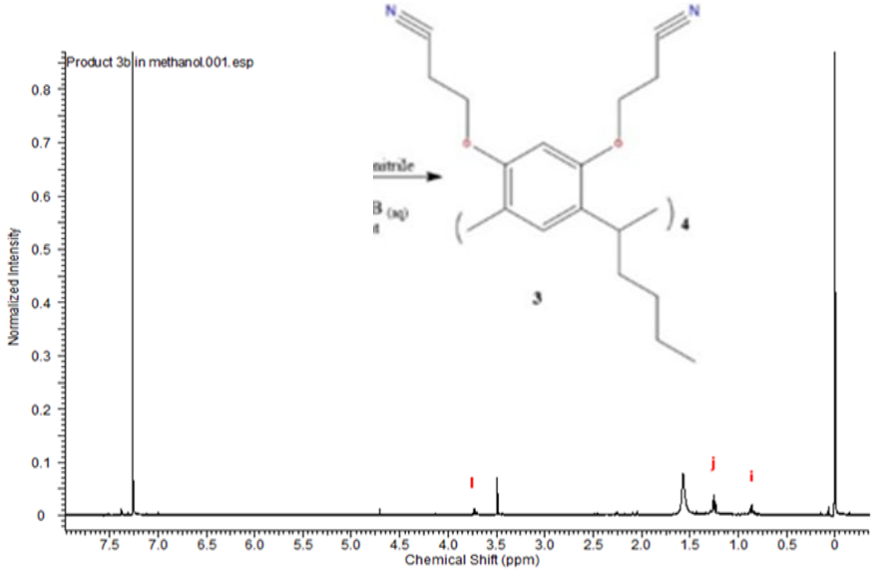
Low yield (19%)

Scheme of Reaction: Scheme 2



ORANGE – BROWN – CLOUDY PURPLE – CLEAR SUSPENSION – CLOUDY WHITE - BROWN

Results and Discussion



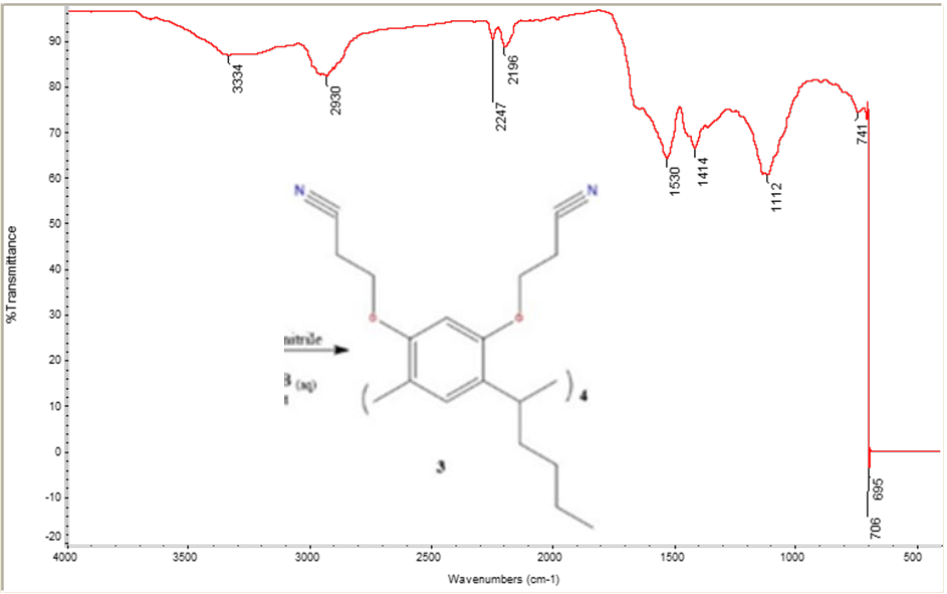
The ^{1}H-NMR spectrum of purified octaamino-substituted resorcinarene

Purification using column chromatography

Shows the evidence of typical structure of calix[4]resorcinarene

Missing peaks

Results and Discussion



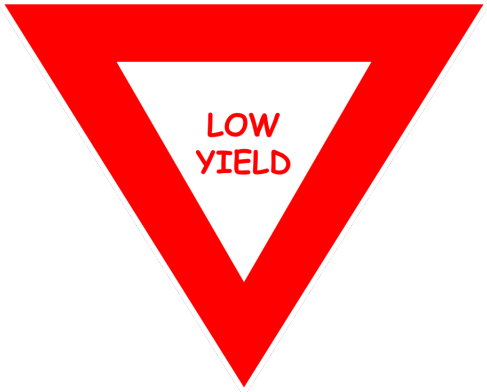
FT-IR spectrum of purified product

Presence of nitrile functional group (peak at 2247 cm-1)

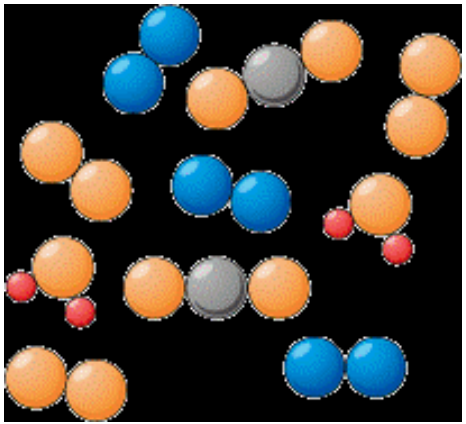
Evidence of alkylation OH– group

Not all OH – groups were alkylated due to presence of peak at 3334 cm-1

Discoveries and Limitations



1. Low yield suggested to be affected by the longer reaction time, the catalyst and solvent used
2. Material not enough for ^{13}C NMR analysis (1.1% natural abundance)
3. Presence of impurities
4. Short research timeline



Conclusion

S_N2 reaction method using **acrylonitrile** and **Titron B catalyst** in **THF solvent** shows a **promising route** of **synthesis** of octaamino-substituted resorcinarene

Future Studies

Optimisation of the reaction condition (i.e. reagents, solvents, catalyst)

Solubility potential of synthesised product

Toxicology studies to validate safety clinical relevance of this system.

References

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Yousaf, A., Hamid, S. A., Bunnori, N. M. and Ishola, A. A., 2015. Applications of calixarenes in cancer chemotherapy: facts and perspectives. *Drug Des Devel Ther*, 9, p. 2831.

THANK YOU!

ANY QUESTIONS????