2016

Can A Metallated Cyclen Species be used to Prepare New Odorants?

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CAN A METALLATED CYCLEN SPECIES BE USED TO PREPARE NEW ODORANTS?

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Abstract

Scientists in the fragrance industry are constantly searching for new odors to create as well as new, more efficient processes to create them. Scientists mainly look for new ways to synthesize fragrances that will reduce the impact on the environment, produce them at lower costs, produce higher yields, and sometimes to produce a more potent odor [4]. In this research, we investigated the use of metallic macrocycles and/or metal-dioxygen chemistry to prepare new fragrances.

Cyclen (1,4,7,10-tetraazacyclododecane) has significant uses in many pharmaceutical and medicinal research developments such as advances in targeted cancer and Alzheimer's agents. Macrocyclic amines like cyclen are valuable because of their highly selective metal ion chelation. Cyclen was used as a ligand in this research to coordinate a central chromium ion. A similar reagent was employed in the synthesis of a similar intermediate found in the Chemistry and Biodiversity book for the synthesis of (-)-β-Santalol. The (-)-β-Santalol compound was reported to be the "most interesting" component of East Indian Sandalwood Essential Oil . The characteristics of reactivity and odor of the odorant synthesized with the metal-cyclen species were compared to literature with the use of GC and H-NMR data results. We aim to investigate whether the metal-bound cyclen scaffold can be used to influence the stereochemical outcome of a Diels- Alder reaction relevant to the synthesizing of a sandalwood fragrance.

Results

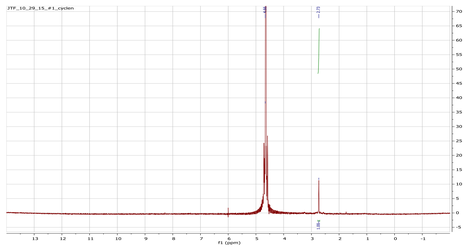
STEP1

HNMR ($CDCl_3$) d 6.7 ppm (2H), 3.7 ppm (4H), 3.2 ppm (8H)

STEP 2

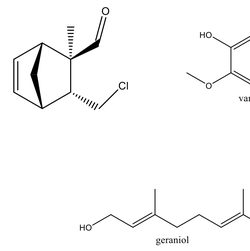
HNMR ($CDCl_3$) d 4.6 ppm (1H), 3.8 ppm (4H), 3.3- 3.5 ppm (6H), 2.5- 3.2 ppm (6H)

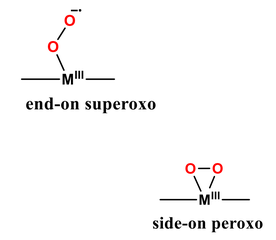
STEP 3



HNMR (D_2O) d 2.73 ppm (cyclen) and 4.66ppm (solvent)

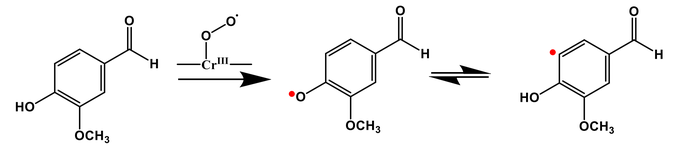
Compared to literatrure HNMR values of d 2.54 ppm in $CDCl_3$





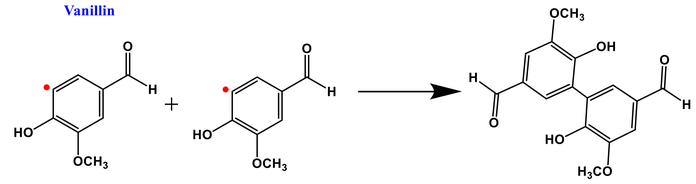
Metal Dioxygen (Cr/O_2) Reactivity

Reacting Vanillin with a chromium-dioxygen adduct should cause a dimer to produce where two Vanillin species are attached to each other



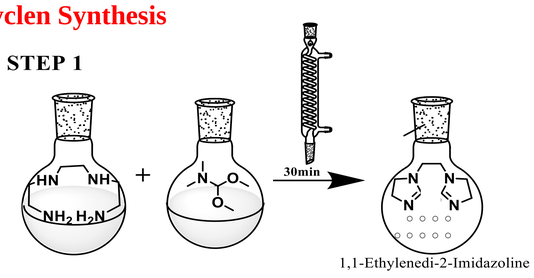
What is the effect?

- Intensify /remove odor
- Produce an altered odor



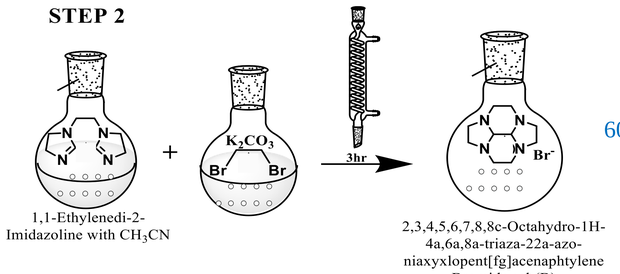
Cyclen Synthesis

STEP 1



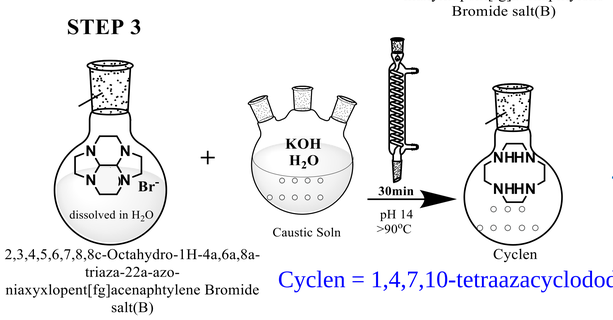
44%

STEP 2



60%

STEP 3



41%

Cyclen = 1,4,7,10-tetraazacyclododecane

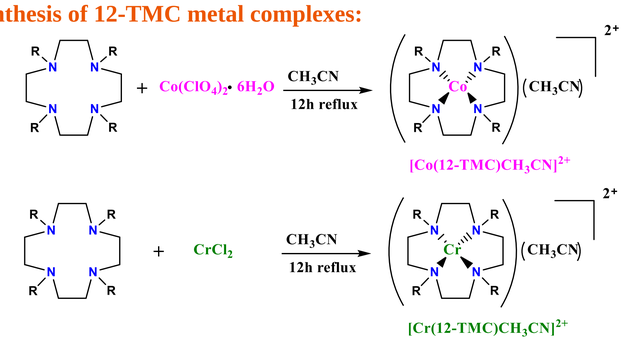
- Overall yield 11% compared to literature 88%

Yield can be improved by doing the following:

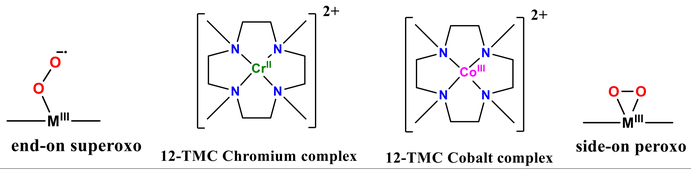
- Reducing the amount of time products stay in solution
- Completing the full synthesis in one day

Metal Coordination and Metal/Dioxygen Chemistry

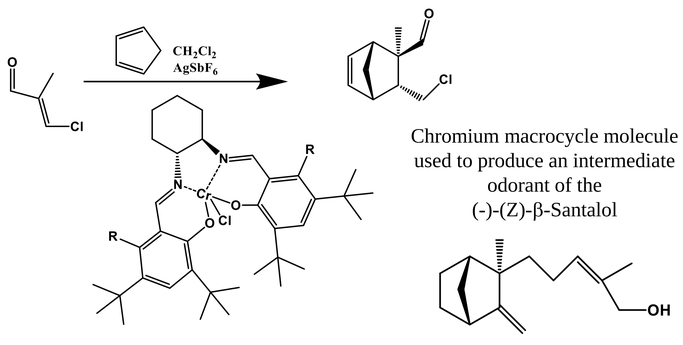
Synthesis of 12-TMC metal complexes:



$Metal/O_2$ studies:

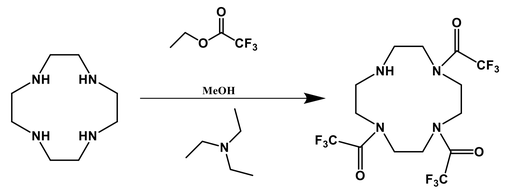


Synthesis of Major Product in Sandalwood Oil



Chromium macrocycle molecule used to produce an intermediate odorant of the (-)-(Z)-β-Santalol

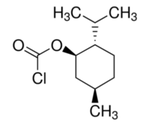
Cyclen Alkylation

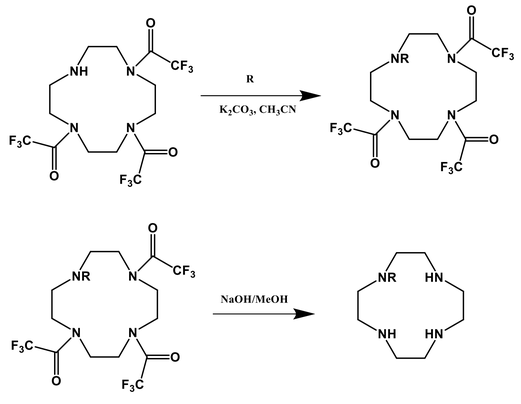


Tri-TFA protection of cyclen

- To be able to successfully attach an R- group onto one Nitrogen atom

R = -H, $-CH_3$,





Cr(II) cyclen with sterochemistry

- Adding one methyl group to a Nitrogen in the cyclen molecule causes cyclen to lose its symmetry and become asymmetric
- Addition of a chiral substituent may enable enantioselective catalysis

Literature Sources

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2. Cho, J.; Woo, J.; Eun Han, J.; Kubo, M.; Ogura, T.; Nam, W. Chromium(v)-oxo and chromium(iii)-superoxo complexes bearing a macrocyclic TMC ligand in hydrogen atom abstraction reactions. *Chemical Science; Chem.Sci.* 2011, *2*, 2057-2062.
3. Cho, J.; Woo, J.; Nam, W. An "end-on" chromium(III)-superoxo complex: crystallographic and spectroscopic characterization and reactivity in C-H bond activation of hydrocarbons. *J. Am. Chem. Soc.* 2010, *132*, 5958.
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