Synthesis of bis(indolyl)methane with metal-salen catalysts: [Mn(salen)Cl], [Mn(salcn)Cl] and [Cu(salcn)]

ORK Sovann and NGUYEN Xuan Thanh students at the Faculty of Chemistry, University of Strasbourg
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Introduction:

Bis(indolyl)methanes are made of two indoles groups and are very important (*Figure 1*). They are present in many living terrestrial and marine species especially in their bioactive metabolites[1]. Due to their medical properties many efforts have been made in order to improve their synthesis. Nowadays they are still studied as potential new drugs[2]. Unfortunately their differents synthesis routes are not ideal due the reactions conditions and overall low yields.

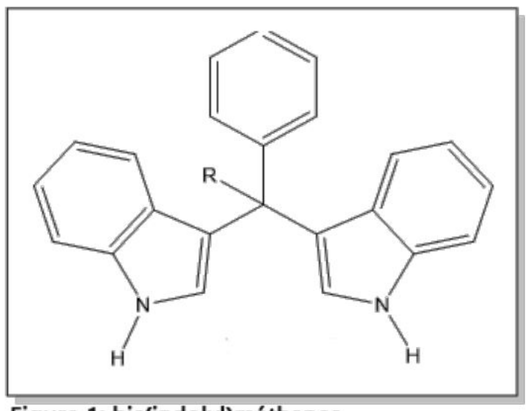


Figure 1: bis(indolyl)méthanes

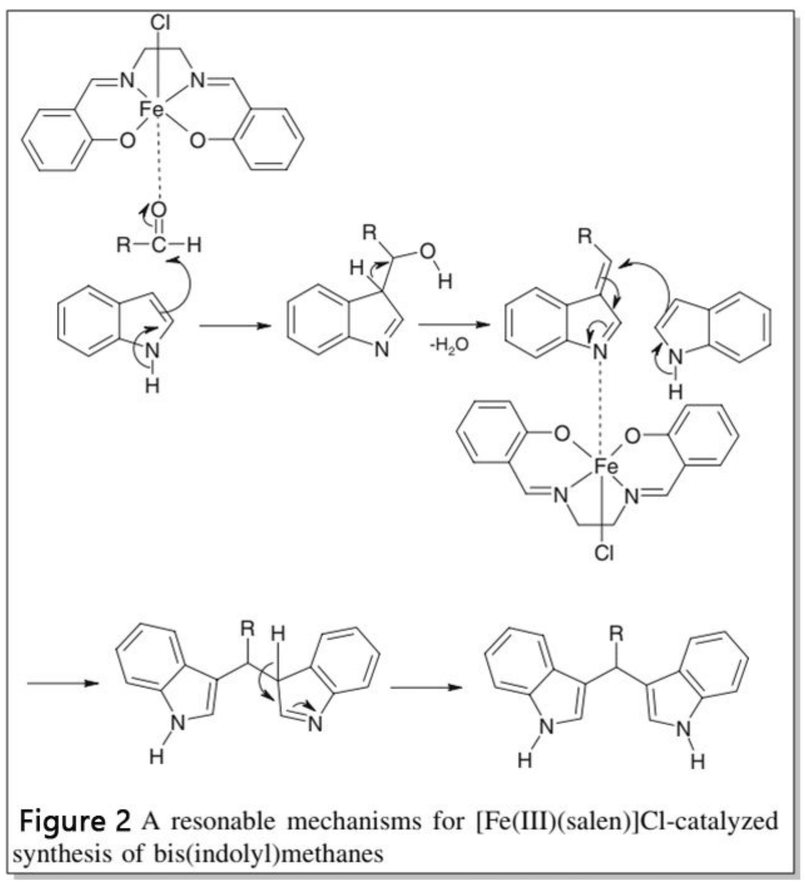


Figure 2 A resonable mechanisms for [Fe(III)(salen)]Cl-catalyzed synthesis of bis(indolyl)methanes

Lately new catalysts (Iron-salen complexes) have been proven efficient for the synthesis in mild and green conditions with a overall good yield[3] (Y=85%) (*Figure 2*). In the continuity of the previous work, we tried differents metal-salen complexes such as [Mn(salen)Cl]•$2H_2O$, [Mn(salcn)Cl]•$2H_2O$ and [Cu(salcn)] (*Figure 3*). As well as the use of a more common solvent such as tetrahydrofuran (THF) compared to the on which was used tetra-n-butylammonium bromide (TBAB).

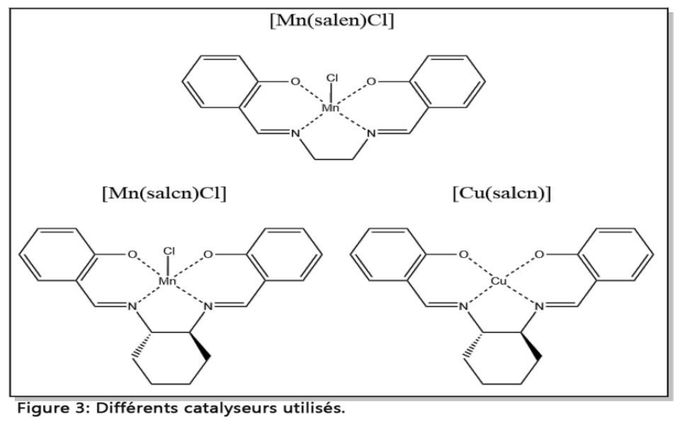


Figure 3: Différents catalyseurs utilisés.

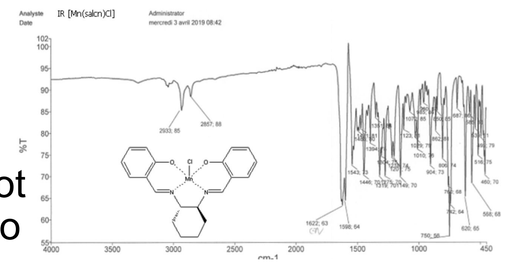
Metal-salen synthesis:

H_2salen and H_2salcn has been synthesized according to the literature[3] from 2-hydroxybenzaldehyde and 1,2-diamine derivative (*Figure 4*).

Metal complexation with salen and salcn ligands has been done in ethanol within 3h at 80°C.

The overall synthesis gave us decent yields:
Yields: [Mn(salen)Cl]•$2H_2O$=58%; [Mn(salcn)Cl]•$2H_2O$=33%; [Cu(salcn)]=69%.

Each compounds have been analysed through ^{1}H NMR, UV spectroscopy and IR spectroscopy (Tables 1-2).



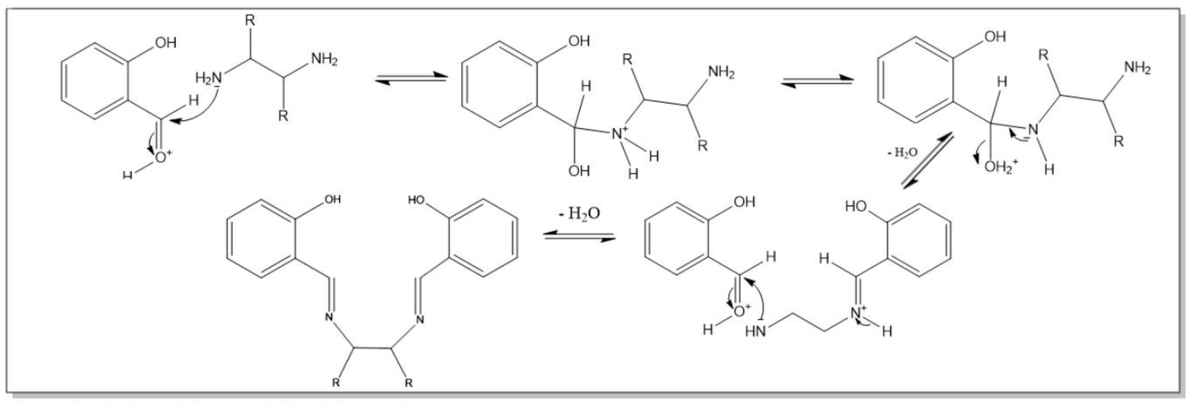


Figure 4: mécanisme de formation de ligand de type salen

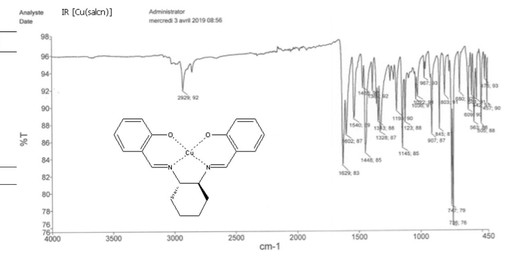
However metal-salen complexes have not been analysed through ^{1}H NMR due to their paramagnetic properties.

Tableau 1 : principales bandes IR du H_2salen et son complexe

ν (cm^{-1})	ν M-N	δ C-H	δ C=C	ν C-O	ν C-N	ν C=C	ν C=N	ν C-H
H_2salen	-	750	855	1150	1280	1500-1575	1610	2900
Mn-salen	575	760	875	1200	1285	1490-1610	1640	2970

Tableau 2 : principales bandes IR du H_2salcn et ses complexes

ν (cm^{-1})	ν M-N	δ C-H	δ C=C	ν C-O	ν C-N	ν C=C	ν C=N	ν C-H
H_2salcn	-	760	845	1150	1280	1500-1580	1625	2920
Mn-salcn	570	750	905	1150	1320	1550-1600	1620	2930
Cu-salcn	560	750	905	1150	1330	1540-1600	1630	2930

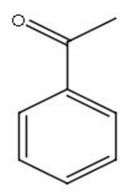
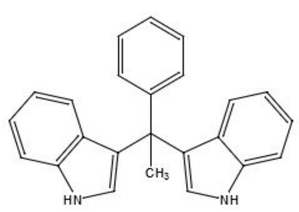
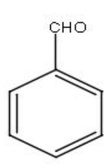
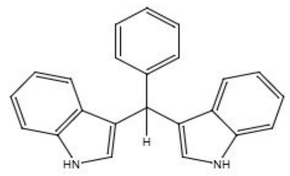


Catalytics studies:

At this stage we tried to synthesized 3,3-bis(indolyl)-4-methylphenylmethane from acetophenone and indole in THF under inert atmosphere with the previous complexes. However no product formation has been observed.

In order to overcome this problem we tried to synthesized bis(indolyl)-4-phénylmethane from distilled benzaldehyde which is easier to synthesized. We have observed a low yields (*Table 3*) compared to the previous work[3].

Tableau 3 : Tableau récapitulatif de la synthèse des bis(indolyl)methanes

Aldéhyde/Cétone	Produit	Catalyseur	Temps (en h)	Rendement
		[Mn(salen)•$2H_2O$]	12	<1
		[Cu(salcn)]	12	<1
		[Mn(salen)•$2H_2O$]	6	7
		[Mn(salcn)•$2H_2O$]	24	8
		[Cu(salcn)]	6	5

Despite our efforts we couldn't optimized the synthesis due to a lack of time.

However it would of been relevant to try the catalyst in more optimal condition with TBAB solvent.

Moreover it would have been pertinent to synthesis the Fer-salen catalyst for comparison.

Conclusion:

-Metal-salen synthesis has been proven efficient with a decent yield.

-Our results suggest that [Mn(salen)Cl]•$2H_2O$, [Mn(salcn)Cl]•$2H_2O$ and [Cu(salcn)] are not catalyst for the synthesis of bis(indolyl)methanes. Nevertheless the use of different solvents or metal-salen could possibly increase the yield of the reaction and thus a lot of optimisation can still be done.

Acknowledge:

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[1]J. K. Porter, C. W. Bacon, J. D. Robins, D. S. Himmelsbach, H. C. Higman; J. Agric. Food Chem. (1977) [2]A. Sarva, J. S. Harinath, S. P. Sthanikam, S. Ethiraj, M. Vaithiyalingam, S. R. Cirandur; Chin. Chem. Lett., (2016)
[3]I. Sheikhshoaie, H. Khabazzadeh, S. Saeid-Nia; Transition Met. Chem. (2009)