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PRELIMINARY RESULTS OF THE REACTION OF CYCLOTRIMERIZATION OF PHENYLACETYLENE [2+2+2] CATALYZED BY [(Cp*)Co(Indene)] COMPLEX

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ABSTRACT

This work describes the catalytic study of [(Cp*)Co(Ind)] (with Cp*= pentamethylcyclopentadienyl, Ind= Indenyl, (C_9H_7)) complex in cyclotrimerization of phenylacetylene. From the cylcotrimerization reaction was possible to obtain products such as substituted pyridines 2-methyl-3,5-diphenylpyridine **(3)**, 2-methyl-4,6-diphenylpyridine **(4)** and the compound 1,2,4-triphenylbenzene **(5)** using acetonitrile as solvent. On the other hand, using toluene as solvent under the same working conditions, the product of reaction was 1,3,5-triphenylbenzene (**1**). Furthermore, by varying the working conditions, the reaction is 90% selective towards the formation of pyridines.

In addition, has been appreciated the formation of another product 1,4-diphenilbuta-1,3-diyne **(2)**, which was isolated and characterized by means NMR and GC-Mass spectrometry.

Keywords: cobalt complex, cyclotrimerization, [2+2+2] cycloadditions.

INTRODUCTION

The transition-metal catalyzed [2+2+2] cycloaddition of alkynes is a very powerful method for the construction of arenes in a single operational step and during the past four decades this reaction has been extensively investigated and the topic reviewed thorough [1-10], and this type of reaction has been extensively studied using several transition metals [11-20].

Cobalt complexes of type [(Cp)Co(L_2)] (L = CO, PR_3, alkenes) have been used extensively for mediating cyclization of alkynes, often with high levels of chemo-, regio-, and stereoselectivity. Although the mechanism of this reaction has been the subject of multiple experimental and computational studies, it is not as yet fully elucidated. After pioneering semiempirical [21,22] and ab initio efforts [23], a more detailed DFT analysis was reported by Albright and co-workers in 1999 [24]. In that work are presented [(Cp)Co(PH_3)$_2$] as a model precatalyst and ethyne as a model reagent. Initially one and then two alkyne moieties displace sequentially two phosphines from the metal to form alkyne complexes. Bisalkyne complex undergoes spontaneous oxidative coupling to give the corresponding coordinatively unsaturated [(Cp)Cobaltacyclopentadiene]. Subsequently, the [(Cp)Cobaltacyclopentadiene] and ethyne transform into the final intermediate [(Cp)Co(η^4-benzene)] for release later a benzene molecule.

On the other hand, Bönnemman in 1978 [25] showed a study in which it is stated that the [(Cp)Co]- unit is responsible for the formation of pyridines by reacting acetylene with acetonitrile. Since that time it is proposed that the mechanism of the reaction both to form an arene as a pyridine passes through an intermediary metallocyclic of 5 members.

In all studies available in literature on cyclotrimerization catalyzed by cobalt complexes of type [(Cp^z)Co(L_2)] (z = H, CH_3; L= CO, PH_3, PR_3) and carried out in organic solvents is accepted for the formation of the products in this type of reaction, in which it is observed that the first step is the discoordination of the ligand of the metal center to generate the catalytically active species [(Cp)Co^I]- which is in charge of forming the metallocycle that give rise to the cyclic compound. However, to the extent of our knowledge, there is little information on examples of half-metallocene complexes without the discoordination of one of its ligands, the sole example of [(Cp)Co(-η^4-cyclooctadiene)] complex [26,27]. On the other hand, to the best of our knowledge, the sole example of cobaltocene species described up to now used as catalyst in cycloaddition reaction copolymerization of 1,11-dodecadiyne with acetonitrile in toluene at 150 °C to afford a poly(pyridine) with a molecular weight up to 18000, which is the first example of an efficient cycloaddition copolymerization of a terminal diyne [28].

This contribution describes the approach for the preliminary results of the [(Cp*)Co(Ind)] complex in its catalytic behavior in cyclotrimerization [2+2+2] in the presence of acetonitrile and phenylacetylene, in order to gain further knowledge of the working conditions on its selectivity catalytic towards the formation of pyridines.

2. EXPERIMENTAL SECTION

2.1. General Information of the catalyst.

All manipulations were carried out under a pure dinitrogen atmosphere by using a vacuum atmosphere dry box equipped with a Model HE 493 Dri-Train purifier or with the use of a vacuum line by using standard Schlenk techniques.

The solvents were dried and distilled according to standard procedures [29].

The synthesis of the following complex has been reported previously: [(Cp*)Co(Ind)], with Cp*= pentamethylcyclopentadiene, and Ind= Indene, C_9H_7 [30] ^{1}H and ^{13}C NMR spectra were recorded on Bruker AC-400 Spectrometer. Chemical shifts were reported in ppm relative to residual solvents by using deuterated acetone and chloroform.

2.2 General conditions of the catalytic tests

A two-necked flask equipped with a magnetic stirring bar was charged with the catalytic amount of complex [(Cp*)Co(Ind)] and Zn powder. Phenylacetylene was used as substrate and the solvent varied between toluene and acetonitrile depending on the case.

The reactor was evacuated and filled with dinitrogen. The reaction flask was immersed in an 80 ºC thermo-stabilized bath. The progress of the reaction was monitored by GC-MS MAT-95X Thermofinnigan with ionization energy of 70eV. The products obtained were isolated using a silica gel column and eluted with hexane.

3. RESULTS AND DISCUSSION

The simultaneous cyclotrimerization reaction of acetylenes and nitriles makes it possible to prepare various benzene and pyridine derivatives in one step. Cobalt catalysts are generally used as catalysts in these reactions [22-29]. The principles of this reaction process, especially in the case of substituted acetylenes and nitriles, have not been adequately investigated.

Thus, the reaction of 5 mg (0.01 mmol) of [(Cp*)Co(Ind)] with 5 mL (50 mmol) of phenylacetylene at 80 ºC for a period of 3 h, gave the corresponding product depending on the solvent used (toluene or acetonitrile).

3.1 Solvent effect

The reaction carried out in toluene at 80 ºC, it was observed the product formation of cyclotrimerization [2+2+2] 1,3,5-triphenylbenzene **(1)** (scheme 1) analyzed using ^{1}H-NMR and GC-MS (M^+ 306 m/e) (figure 1) and with a reaction time of 12.66 min. Observed 100% selectivity towards the formation of this product.

In the case of the reaction carried out in toluene it is logical that only triphenylbenzene is formed as product of a cycloaddition of phenylacetylene, the noteworthy about this reaction is that only one isomer was formed 1,3,5-triphenylbenzene **(1)**, red color with 100% selectivity, were not observed

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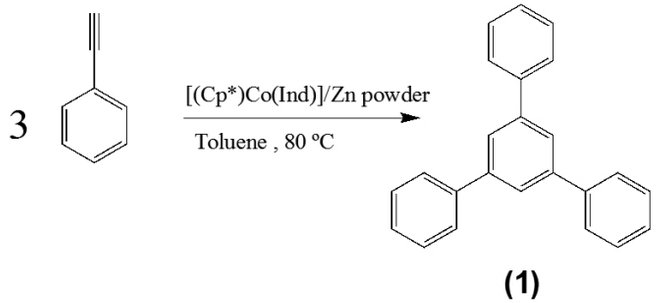
traces by ^{1}H-NMR spectroscopy of isomer 1,2,4-triphenylbenzene **(5)** as it was observed when carrying out the same reaction under the same conditions but using acetonitrile as a solvent. Probably, the difference in the formation of the isomers was primarily due to the nature of the solvent, toluene is a bulkier molecule solvent than the acetonitrile, which could "guide" by steric hindrance to the formation of only one product having phenyls 1,3,5 interleaved positions in respect to benzene.



Scheme 1: Cycloaddition reaction [2+2+2] phenylacetylene catalyzed by [(Cp*)Co(Ind)] in toluene.

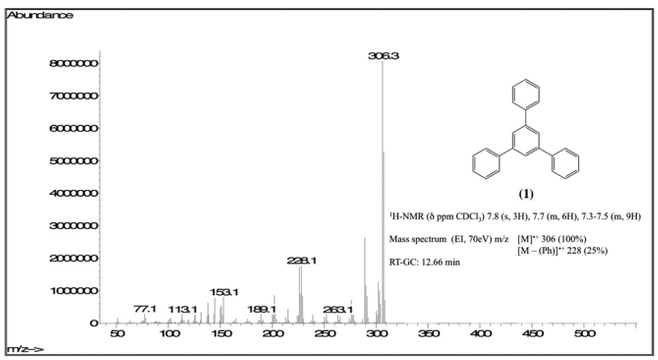
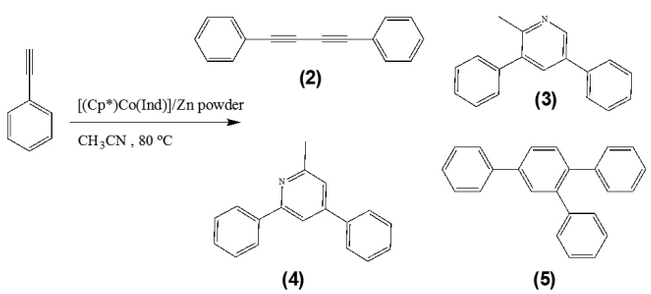


Figure 1: Mass spectrum of 1,3,5-triphenylbenzene (**1**).

On the other hand, when the reaction was carried out in acetonitrile (scheme 2), was observed the formation of four different products. The first of these corresponds to the reaction product of 1,4-diphenylbuta-1,3-diyne **(2)** (M^+ 202 m/e) (figure 2), with a reaction time of de 10.46 min.

The second products correspond to the formation of substituted pyridines. Two structural isomers were observed. The molecular ion corresponds to M^+ 245 m/e with a reaction time of 10.92 min for 2-methyl-3,5-diphenylpyridine **(3)** and reaction time of 11.05 min for 2-methyl-4,6-diphenylpyridine **(4)** (figure 3 and 4 respectively).

The fourth product corresponds to the reaction product of cyclotrimerization 1,2,4-triphenylbenzene **(5)** (M^+ 306 m/e) (figure 5), with a reaction time of 12.61 min.



Scheme 2: Reaction of phenylacetylene catalyzed by [(Cp*)Co(Ind)] in acetonitrile.

The products **(2)** and **(5)** were isolated and characterized by GC-MS independently (see figures 2 and 5). The products **(3)** and **(4)** were observed clearly by GC-MS (figure 3 and 4) but despite many efforts failed to date to separate the two isomers, currently yielding a crystalline solid red intense able to form films.

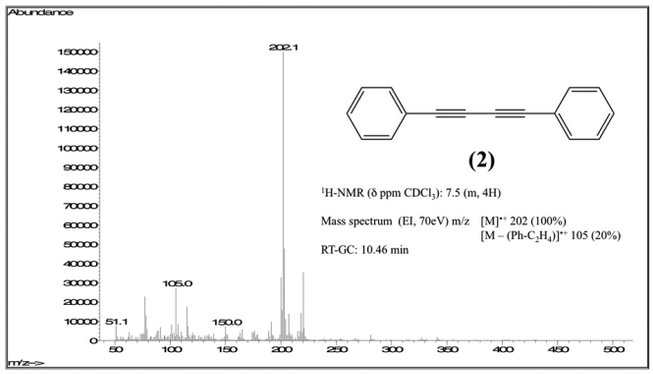


Figure 2: Mass spectrum of 1,4-diphenilbuta-1,3-diyne (**2**)

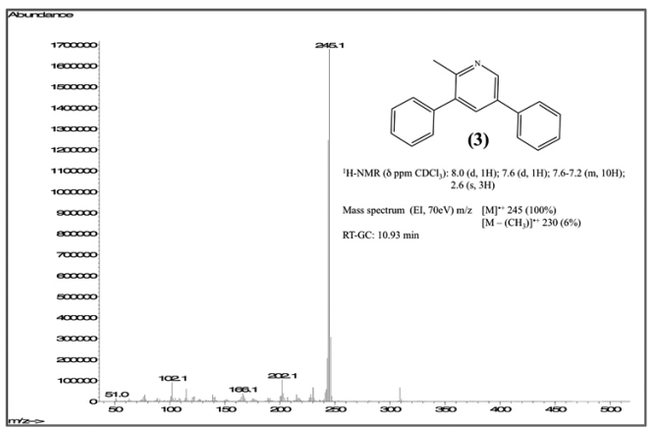


Figure 3: Mass spectrum of 2-methyl-3,5-diphenylpyridine (**3**)

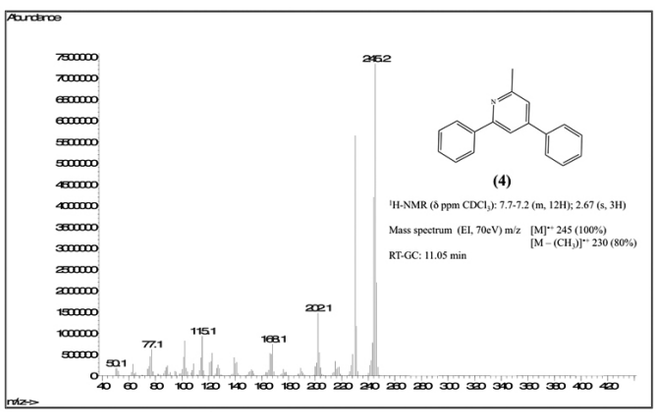


Figure 4 Mass spectrum of 2-methyl-4,6-diphenylpyridine (**4**)

3.2 Study of effect of amount of catalyst on the product distribution.

This study was carried out under the conditions previously described for 3 h of reaction using acetonitrile as solvent and 1.7 mL (1.6 mmol) of phenylacetylene. The range of amount of catalyst [(Cp*)Co(Ind)] was used between 0.003 g ($9.7 \cdot 10^{-3}$ mmol) and 0.500 g (1.6 mmol) maintaining the amount of phenylacetylene. The results obtained are shown in table 1.

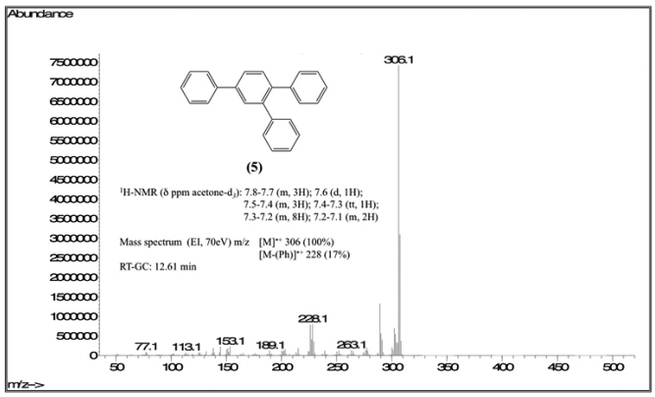


Figure 5: Mass spectrum of 1,2,4-triphenylbenzene (**5**)

Table 1: Distribution of products according to amount of catalyst.

Cat/ phenylacetylene	Catalyst (mol)	Catalyst (g)	Relative proportion (2):(3):(4):(5)
1: 1	1.60 e $^{-3}$	0.500	1 : 9 : 66 : 24
0.5 : 1	8.0 e $^{-4}$	0.250	3 : 12 : 72 : 13
0.25 : 1	4.0 e $^{-4}$	0.124	6 : 11 : 80 : 3
0.01 : 1	1.60 e $^{-5}$	0.005	36 : 5 : 39 : 20
0.005 : 1	9.70 e $^{-6}$	0.003	13 : 0 : 0 : 87

The selectivity shown by the catalyst towards these products was between 60% and 91% depending on the amount of catalyst used. The study of variation of amount of catalyst was obtained that the optimum ratio to achieve high selectivity towards the formation of pyridines is 0.25:1 ratio catalyst/substrate (phenylacetylene), where it is possible see that the sum of **(3)** and **(4)** reaches 91% of products, where the product **(4)** was mostly favored. By drastically reducing the amount of catalyst the products **(3)** and **(4)** were practically not formed, being favored the formation the compounds **(2)** and **(5).** This suggests the importance of the catalyst in the formation of pyridines.

The formation of the compound **(2)**, *via* dimerization of the phenylacetylene is favored by temperature (80 °C) and the presence of a solvent such as acetonitrile which could shown no steric hindrance as is observed with toluene. In the same way, the formation of the product **(5)** was favored by mentioned above.

3.3 Study of reaction with substrate and catalyst in stoichiometric combination.

3.3.1 Test used as solvent CH_3CN (5 mL) and phenylacetylene stoichiometric amounts of catalyst in a ratio 1:5; 113 mg (0.36 mmoles) of [(Cp*)Co(Ind)] and 0.2 mL (1.83 mmol) of phenylacetylene, in order to observe the effect on the formation of the products **(2), (3)** and **(4)** and consumption of phenylacetylene. Monitoring the reaction, it was performed for 24 h. The results are shown in Table 2.

Table 2: Distribution of products with catalyst and substrate in proportion 1:5.

Entry	Time (h)	Relative proportion (2):(3):(4):(5)
1	0	24 : 14 : 45 : 17
2	8	1 : 30 : 62 : 7
3	24	1 : 29 : 62 : 8

Reaction samples taken every hour checking that the relative ratio remains practically constant during the reaction time, always favoring the concentration of pyridines, especially the product **(4)**. In the figure 6 were plotted some important time of this reaction.

In this case it is possible to appreciate that the selectivity was aimed at the formation of pyridines and by increasing the amount of catalyst was not favored but the relative ratio of the products, being the constant between 8 h and 24 h reaching 92% selectivity.

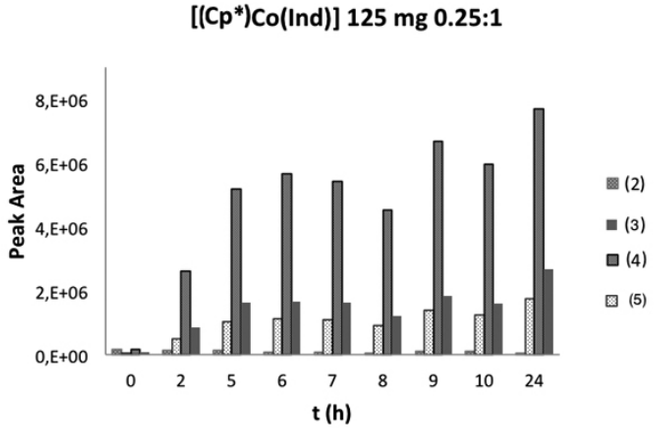


Figure 6: Relative distribution 0.25:1 in Acetonitrile.

3.3.2 Test used as solvent toluene (5mL) and phenylacetylene stoichiometric amounts of catalyst in a ratio 1:3; 187 mg (0.61 mmol) of [(Cp*)Co(Ind)] and 0.2 mL (1.83 mmol) of phenylacetylene in order to observe the effect on product formation **(1)** and phenylacetylene consumption. Monitoring was carried out for 24 h, showing only the formation of 1,3,5-triphenylbenzene (**1**).

3.3.3 Test used as solvent toluene (5 mL) and stoichiometric amounts of catalyst, phenylacetylene and acetonitrile in a ratio 1:5:1; 592 mg (1.92 mmol) of [(Cp*)Co(Ind)] and 1.1 mL (9.59 mmol) of phenylacetylene and 0.1 mL (1.92 mmol) acetonitrile in order to observe the effect on the products **(2) (3)** and **(4)** and consumption of phenylacetylene . The results are shown in Table 3.

Table 3: Product distribution and catalyst substrates in a 1:5:1

Entry	Time (h)	Relative proportion (2):(3):(4):(5)
1	0	4 : 41 :43 : 12
2	1	2 : 32 : 56 : 10
3	2	3 : 36 : 53 : 9
4	3	2 : 34 : 55 : 9
5	4	2 : 33 :55 : 10
6	5	2 : 35 : 54 : 9
7	6	3 : 36 : 53: 8
8	7	3 : 36 : 53: 8
9	24	3 : 38 : 51: 8

This test was performed attempting to drive the reaction towards the formation of one of the pyridines, but in this case the formation of the four products was also observed in constant relative ratio over time (table 3). The same phenomenon was observed when performing a test stoichiometric in all participating reactants in the formation of products, ie 1 mol of catalyst : 5 mol of phenylacetylene : 1 mol of acetonitrile in toluene as solvent. Although the relative ratio of the products is constant, in this ratio can be seen that if the amount of product **(3)** obtained compared with that observed in the relationship 0.25:1, this is much more favored decreasing the amount of **(4)** formed (Figure 7). In the figure 7 were plotted some important time of this reaction. If the total selectivity compared toward the formation of both pyridines have this remains in the ranges previously described (≈90%). This reaction was monitored until 24 h where almost total consumption of phenylacetylene used (1.1 mL, 9.59 mmol) was observed.

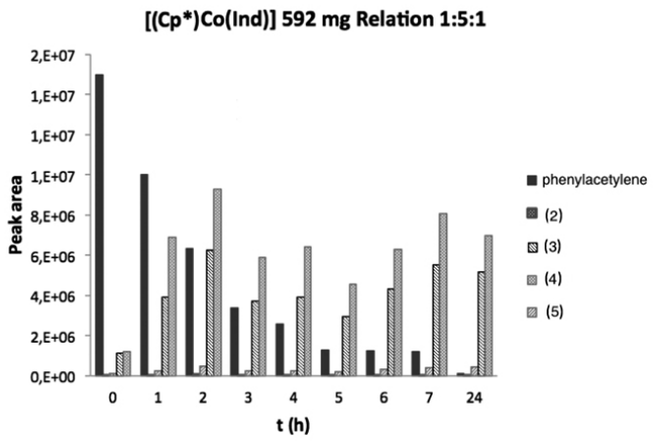


Figure 7: Relative distribution of products in relation cat/phenylacetylene/ acetonitrile 1:5:1 in Toluene.

4. CONCLUSION

Preliminary results have demonstrated that [(Cp*)Co(Ind)] complex is an efficient catalyst in the synthesis of organic compounds *via* cyclotrimerization [2+2+2], especially efficient in the formation of substituted pyridines (**3**) and (**4**) when phenylacetylene cycloaddition reaction performed in the presence of acetonitrile both as solvent and reagent, presenting in both cases 90% selectivity toward the formation of these products, which could be useful in many organic synthesis. The amount of catalyst used in the reaction does not affect the relative proportion of formation of pyridines in all cases maintaining high selectivity. By performing the same reaction in toluene as solvent, the [(Cp*) Co(Ind)] compound, acts as an effective generator 1,3,5-triphenylbenzene (**1**) presenting 100% selectivity towards the formation of this product.

Although the results are promising, it is worth noting that more evidence is needed such as studies of polarity differences of the solvents and the role that plays in the reaction, different substrates and the mechanism of this reaction *via* discoordination of the ligand, presumably as it is reported in much of the literature for such reactions, or perhaps, could occur by changes hapticity of the indenyl ligand. This hypothesis is still under study and a theoretical simulations of this system also could prove the rate-determing step for the catalytic cycle where the highest energy step is the release or changes hapticity of an ancilliary ligand from the cobalt center.

Further studies must be developed to improve the catalytic activity, we also have the intention of performing the synthesis of new heterobimetallic systems in order to get insights on the cooperative effects between metals, catalytic properties and material science applications of these complexes.

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