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Recent Developments in Cobalt-catalysed C-H Activation Reactions with Alkynes, Allenes and Arene Substrates

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ABSTRACT

Because of its simple availability, low cost, and low toxicity, cobalt (Co) has been the focus of research in the field of C-H functionalisation, replacing noble metals like Pd, Rh, and Ir. The range of transformations using alkynes, allenes, and arene substrates has greatly increased due to recent developments in cobalt-catalysed C–H activation processes. The technique has been used in a number of synthetic processes, including late-stage functionalisation, enantioselective C-H functionalisation, electrooxidative functionalisation, and annulation reactions with allenes. These advancements provide effective methods for building intricate molecular structures. This chapter's focus is on the latest developments in Co-catalysed C-H functionalisation procedures including alkynes, allenes, and arene substrates. A brief overview of various enantioselective transformations is also included.

Keywords: *Alkynes; Allenes; Arene; C-H Activation; Cobalt-Catalysis*

INTRODUCTION

One of the most fundamental areas of scientific study and industrial development, chemical science has many uses, from developing new and enhanced materials with unparalleled capabilities to comprehending the complex mechanistic paths of biological processes. This brief overview essay will look at the most recent advancements and innovative methods in organometallic chemistry, including the use of Co-catalysis to activate carbon chains in quinolone and pyridine-based nitrogen heterocycles using a variety of C-H activation mechanisms. Because it allows a C-H bond to be functionalised directly rather than through the traditional functional group modification method, Co-catalysed C-H activation has drawn a lot of attention in organic chemistry research in recent decades (Baccalini *et al*., 2019). For many naturally occurring, bioactive, and significant compounds, it may be possible to create an atom- and step-efficient synthesis process if a particular carbon-hydrogen bond within the molecule can be targeted and functionalised. When C-H activation chemistry originally emerged, the region was dominated by 4d and 5d transition metals, particularly palladium, rhodium, ruthenium, and iridium. However, new techniques based on easily accessible, low-cost 3D metals like cobalt have recently become more and more popular (Patel *et al*., 2022). In addition to its special electrical properties, this idea is important from an economic and environmental perspective since it permits special patterns of reactivity and selectivity. Research on innovative C-H activation methods based on first-row transition metals is still in its early stages, despite these benefits.

Recent Developments:

i) Alkenylation of 8-Methyl Quinoline with Alkynes:

The authors used 5-decyne as a coupling partner and Cp*Co(Co)I_2 as a catalyst to activate the C(SP^3)-H bond alkenylation of 8-methylquinoline (Figure 1) as a model substrate. To achieve a satisfactory yield, they added $AdCo_2H$ and AgoTf alone with CF_3CH_2OH at 80°C and continued the reaction in argon for 24 hours (Sen *et al*., 2016).

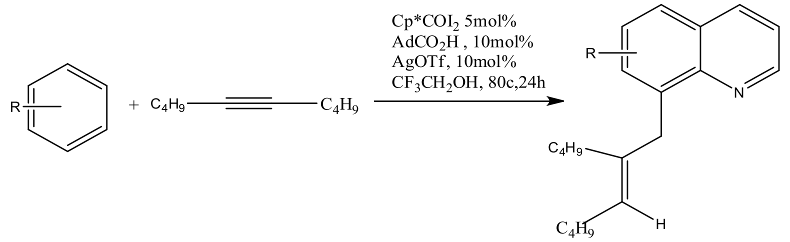

Figure 1: Alkenylation of 8-Methyl Quinoline

The authors' experiments using the aforementioned substrates (Figure 2) generated a range of products with decent yields.

Substrate Scopes:-

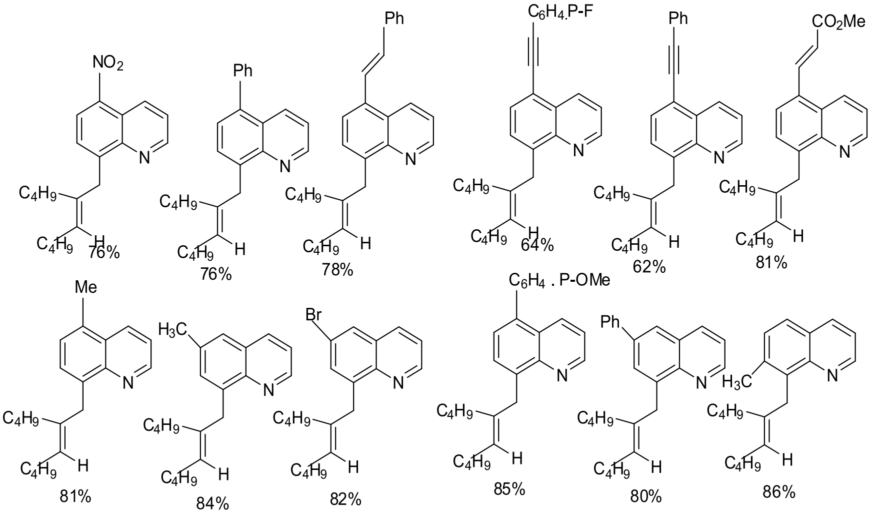

Figure 2 : Substrate scope

ii) Regioselective Intermolecular Annulations: -

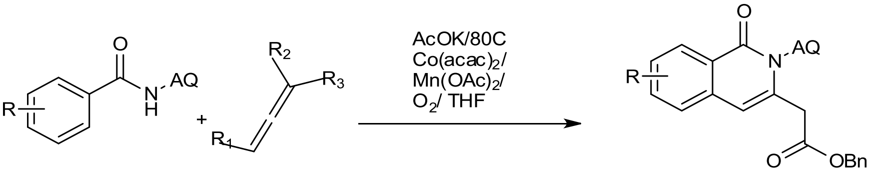

Figure 3: Regioselective Intermolecular Annulations

Under the reaction conditions shown above, the author obtained a good yield by initiating this reaction with the substrate shown in Figure 3. When TFE acts as a solvent, O_2 flows through the capillary after AcOK, $Co(acac)_2$, and $Mn(OAC)_2$ were added to the solution mixer at 80°C (Li *et al.*, 2017).

Mechanism:-

The oxidation of Co(II) to Co(III), which is aided by $Mn(OAC)_2$, is the first step in the suggested reaction process (Figure 4). The allene can then co-ordinate with Co(III) after Co(III) activates a Sp^2 C-H bond to form an intermediate that undergoes ligand exchange. The allene is then inserted into the cobalt-link to create another intermediate, which, via reductive elimination, yields the cyclic pdt. The type of heterocycle created depends on the additive's base; KOAc produces a thermodynamic endocyclic isoquinone, whilst KOTf produces a kinetic exo-cyclic isoquinolione. The Co-catalyst is renewed by $Mn(OAC)_2$ / O_2. In exo-cyclic isoquinolinone, the arylation of allenes occurs at the electron-rich carbon, with a less sterically hindered face. When compared to Pd/Rh run, the Co-catalyst shows distinct area selectivity, which is influenced by the nature of the allenes. The authors explored the substrate scopes too and obtained good product yields (Figure 5).

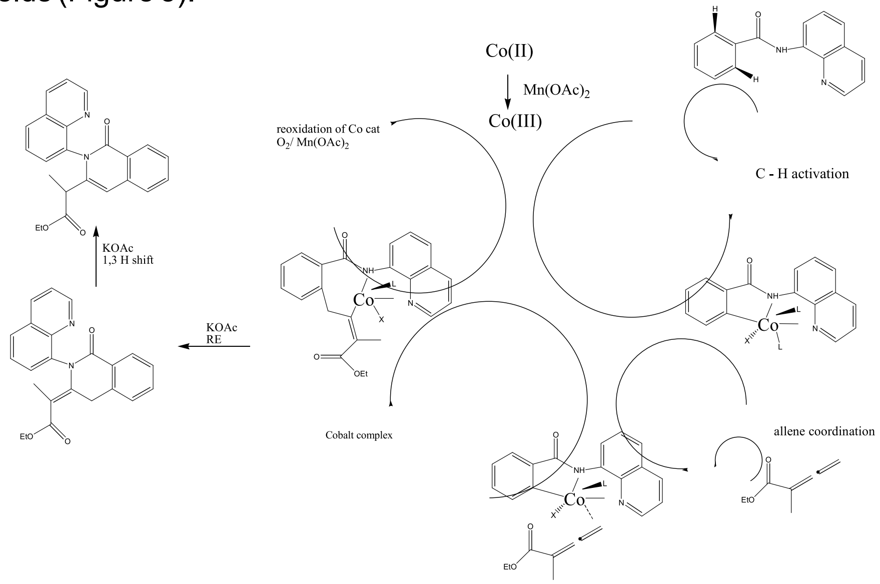

Figure 4: Mechanism of the Reaction

Substrate Scope:

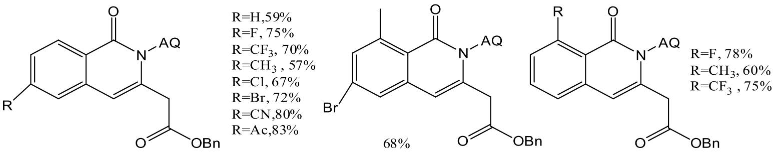

Figure 5: Substrate scope

iii) Regio Selective Intermolecular Annualatin of Sulfonamids with Allenes:-

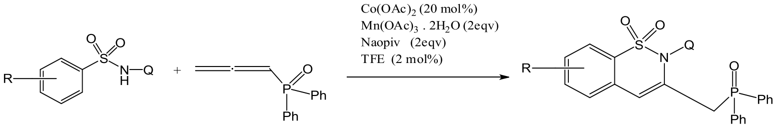

Figure 6: Annualatin of Sulfonamids

In this article, the authors selected tosylsulfonamide and allenyl phosphonate as the coupling substrate to test under conditions for the C-H activation in the first inquiry (Figure 6). Using 20 mol% of $Co(OAC)_2$, $Mn(OAC)_3$, $2H_2O$(eq), and NaOpiv in TFE at 100oC, a 32% yield was obtained (Thrimurtulu, Nallagonda & Volla, 2017).

Mechanism:-

A tenable explanation was put out in light of the aforementioned experiment (Figure 7) and earlier studies on Co-catalysed C-H bond activation. The in situ production of Co(III)- species via the catalytic cycle forms intermediate A by the oxidation of Co(II) precatalyst and the coordination of sulfonamide generated from 8-aminoquinine. When

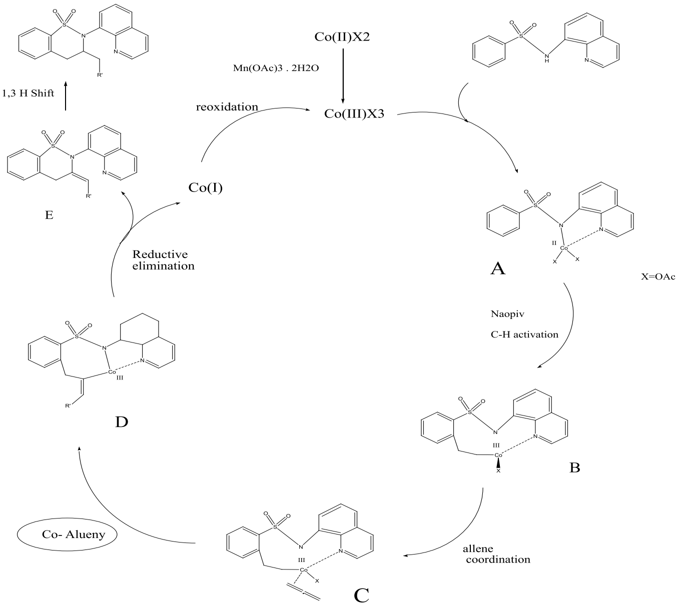

Figure 7: Mechanism of the Reaction

a base is present, C-H activation results in the formation of intermediate B. This intermediate was produced by using aryl sulfonamide to treat stoichiometric quantities of Co(OAC)₂. The seven-membered cobalt cycle intermediate D is produced by the coordinate insertion of the C-Co bond of intermediate C with the less-substituated double bond of allene. After Co(I) is oxidised with an oxidant, reductive elimination from D yields the cyclic product E and regenerates the Co(III) species. The final product was yielded from Intermediate E via a 1,3-hydrogen shift.

The authors experimented with the substrate shown in Figure 8 and obtained a range of products with different yields.

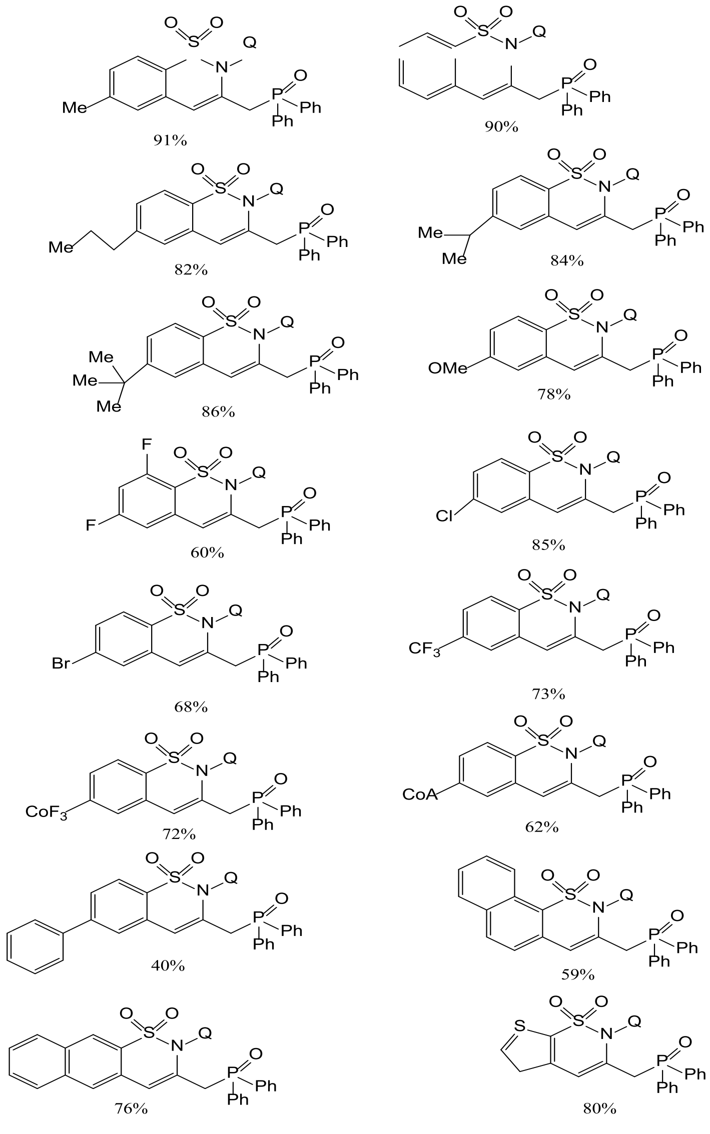

Figure 8: Substrate Scope

iv) Synthesis of Benzofuranones :-

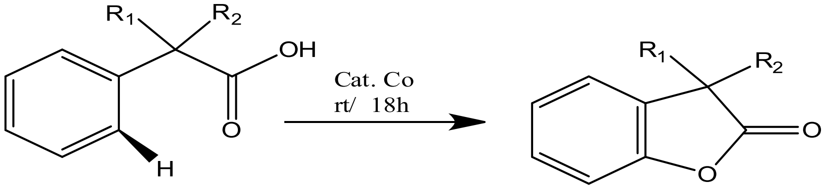

Figure 9: Synthesis of Benzofuranones

Without the use of an external oxidant, the authors of this study reported a Cp-free cobalt-catalysed C-H activation in mild reaction conditions (Figure 9) at room temperature (Hajipour & Khorsandi, 2020).

Mechanism:-

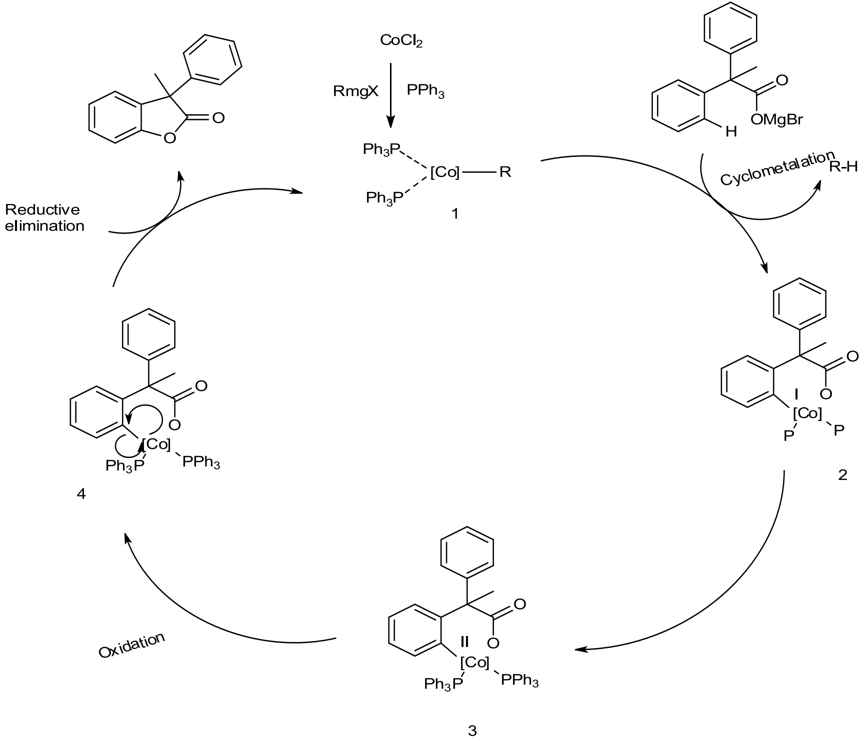

Figure -10: Mechanism of the Reaction

For the synthesis of bezo-furarone at room temperature, the authors presented a simple, effective, environmentally friendly, and cost-effective technique (Figure 10). Using a ternary catalytic system made up of cobalt source, ligand, and grignard reagents, a palladium and external oxidant-free synthesis has been created. The carboxylic group serves as both a guiding and a reactive group in these processes, which included C-H activation and the creation of intermolecular C-O bonds.

Substrate Scopes:-

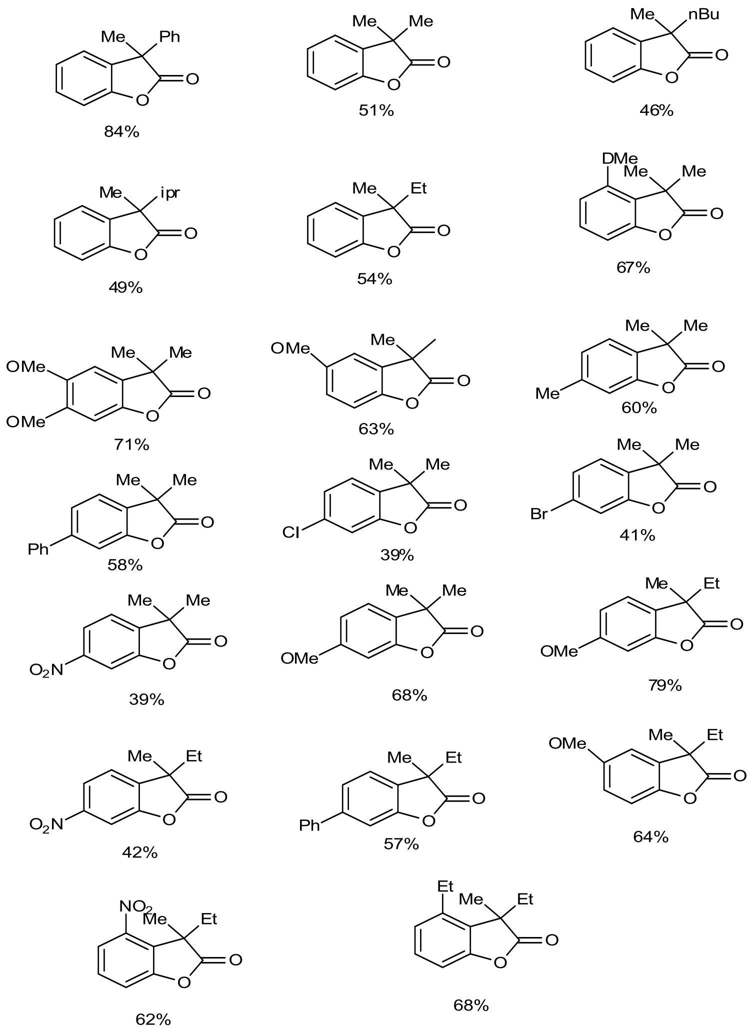

Figure 11: Substrate Scope

This protocol's substrate scope (Figure 11) has also been determined to be good, producing a range of compounds with acceptable yields.

v) Enantio Selective Intermolecular Carboaminations:-

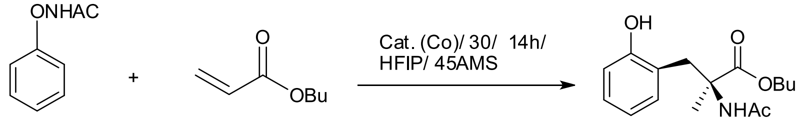

Figure 12: Enantioselective Intermolecular Carboaminations

In this study, phenoxyacetamide and butyl acrylate are used by the authors (Figure 12) to initiate this reaction. Caesium acetate and silver trislate were used as catalyst ingredients in HFIP at 30°C. Co(I) first produced the product in a modest enantiomeric ratio with 41% yield. Co(II) and Co(III) significantly increased yield and achieved outstanding enantiomeric ratios of 99:1 (Ozols *et al.*, 2020).

vi) Lactonization of Benzamides under Acrobic Conditions: -

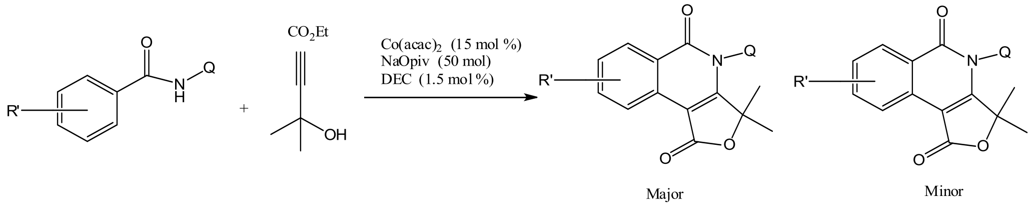

Figure 13: Lactonization of Benzamides

Using a cobalt (II) catalyst, this process explains a unique technique for regioselective alkenylation/annulations followed by lactonization (Figure 13). In contrast to many other methods now in use, this catalysed process reduces metal waste in large-scale synthesis by operating without the need for stoichiometric metal oxidants. The reaction is carried out in an open air setting with mild circumstances, exhibiting operational simplicity. Key variables affecting yield and region selectivity, including temperature, solvent selection, and catalyst type, are identified via optimisation studies. The adaptability of this technology for various applications in inorganic synthesis is highlighted by the fact that different directing groups on the amide moiety influence regioisomer formation (Muniraj, Kumar & Prabhu, 2019).

Plausible Mechanism :-

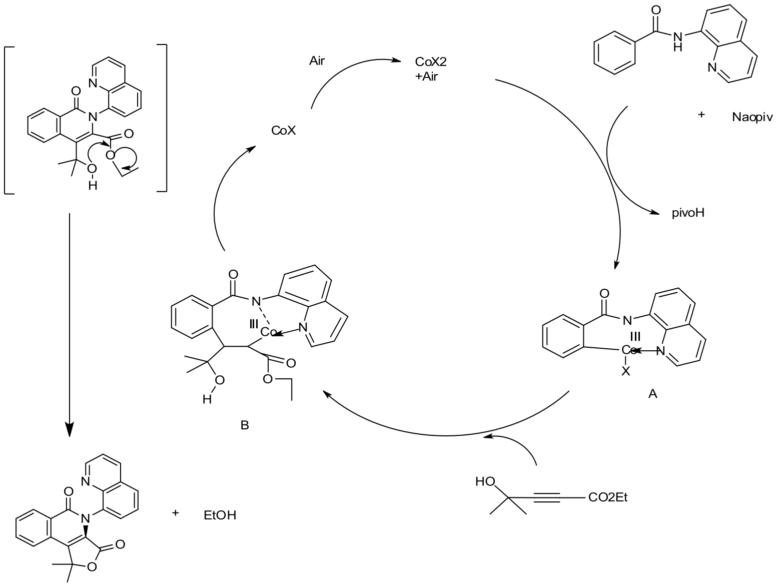

Figure 14: Mechanism of the Reaction

Substrate Scopes :-

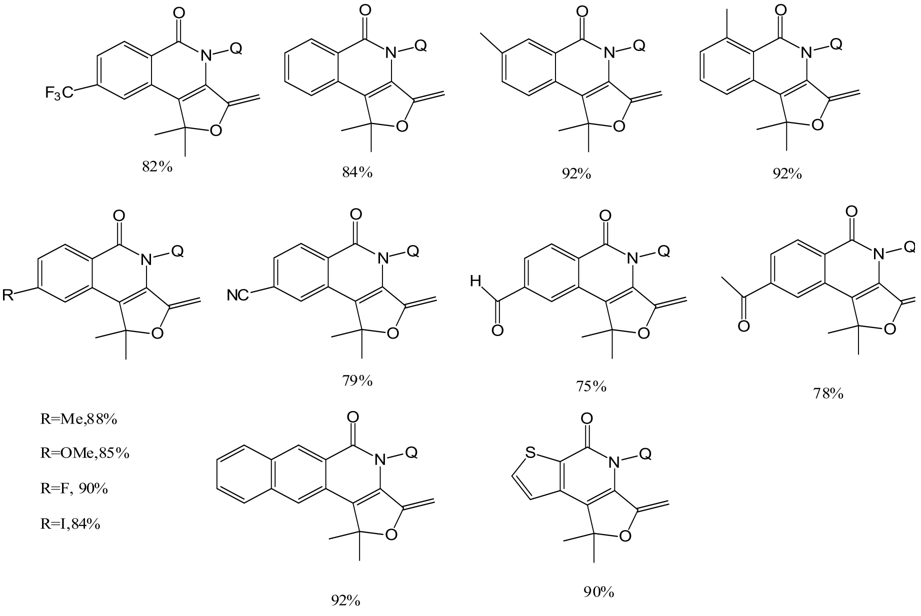

Figure 15: Substrate Scope

According to the suggested mechanism (Figure 14), a catalytic cycle is started by Co(II)–complex binding to the substrate, followed by aerial oxidation to Co(III), and finally, intermediate A is produced by C-H metalation aided by NaOPiv. After the hydroxylalkynoate is inserted, a seven-membered intermediate B is created, which is then subjected to reductive elimination. The cycle is finished when Co(I) is reoxidised to Co(II) via aerial oxidation. Under reaction circumstances, lactone is finally produced by intermediate C. It has also been found that the substrate scope of this technique (Figure 15) is good, yielding a variety of molecules with respectable yields.

vii) Cobalt (II) Catalysed C-H Functionalisation:-

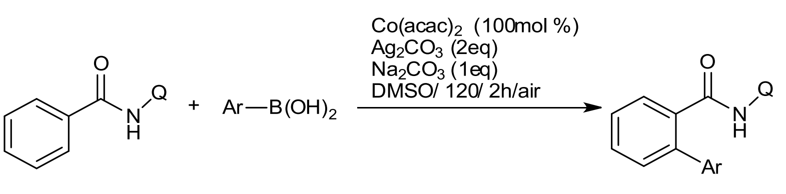

Figure 16: Cobalt (II) Catalysed C-H Functionalisation

The authors of this study used 8-aminoquinoline as the directing agent to investigated Co(II) catalysed arylation (Figure 16) of C-H bonds. The procedure used Na_2CO_3, $Co(acac)_2$, and Ag_2CO_3 as an oxidant in DMSO at 120°C for two hours. A variety of Co(III) salts, including $Co(OAC)_2$, $CoBr_2$ and $CoSO_4$, were tried, however the yields did not increase past high catalyst loading. Significantly, arylboronic acids with electron-donating groups, such as OMe, and electron-neutral substituents produced good yields, but groups that withdrew electrons produced poorer yields (Kommagalla & Chatani, 2017).

Substrate Scopes:-

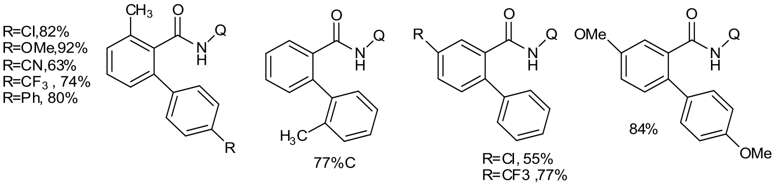

Figure 17: Substrate Scope

Additionally, it has been discovered that this technique's substrate scope (Figure 17) is good, producing a range of compounds with decent yields.

viii) C-H and C-O Coupling of Quinoline N-oxide :-

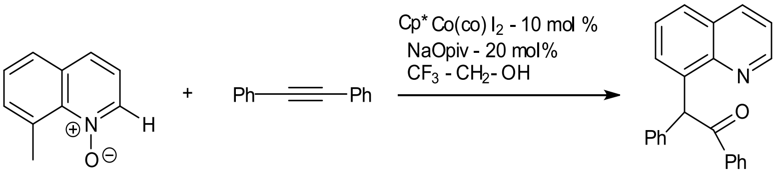

Figure 18: C-H and C-O Coupling of Quinoline N-oxide

The parameters for a reaction involving quinoline oxide and diphenylacetylene were investigated by the researchers (Figure 18). Initial attempts to produce the desired product using Cp*Co(Co)I_2 and NaOAC in dioxane at 80°C failed. They discovered that trifluoroethanor produced the pdt in an 80% yield under ideal circumstances. Yields were further enhanced by substituting Naopiv for other carboxylates. Control tests demonstrated that both the (Co) catalyst and NaOpiv were required for an effective reaction, which failed at lower temperatures. Diluting catalyst loading, temperature, or the use of silver salts did not improve product production. Other sources of Co did not work well for the transition (Barsu *et al.*, 2016).

Mechanism:-

The cyclometallation of a cationic complex is the first step in the suggested process for Co-catalysed functionalisation of quinoline. This is followed by alkyne coordination and migratory insertion to create an alkenyl cobalt acyclic intermediate (Figure 19). Following reductive elimination, a Co(I) intermediate is produced. This intermediate then goes through oxidative addition between nitrogen and oxygen atoms, which leads to a pro-dementalization step. This process produces the C-8 functionalised quinoline molecules and leads to catalyst renewal.

Furthermore, it has been found that the substrate scope of this approach is good, yielding a variety of compounds with respectable yields (Figure 20).

groups, such as OMe, and electron-neutral substituents produced good yields, but groups that withdrew electrons produced poorer yields (Kommagalla & Chatani, 2017).

Substrate Scopes:-

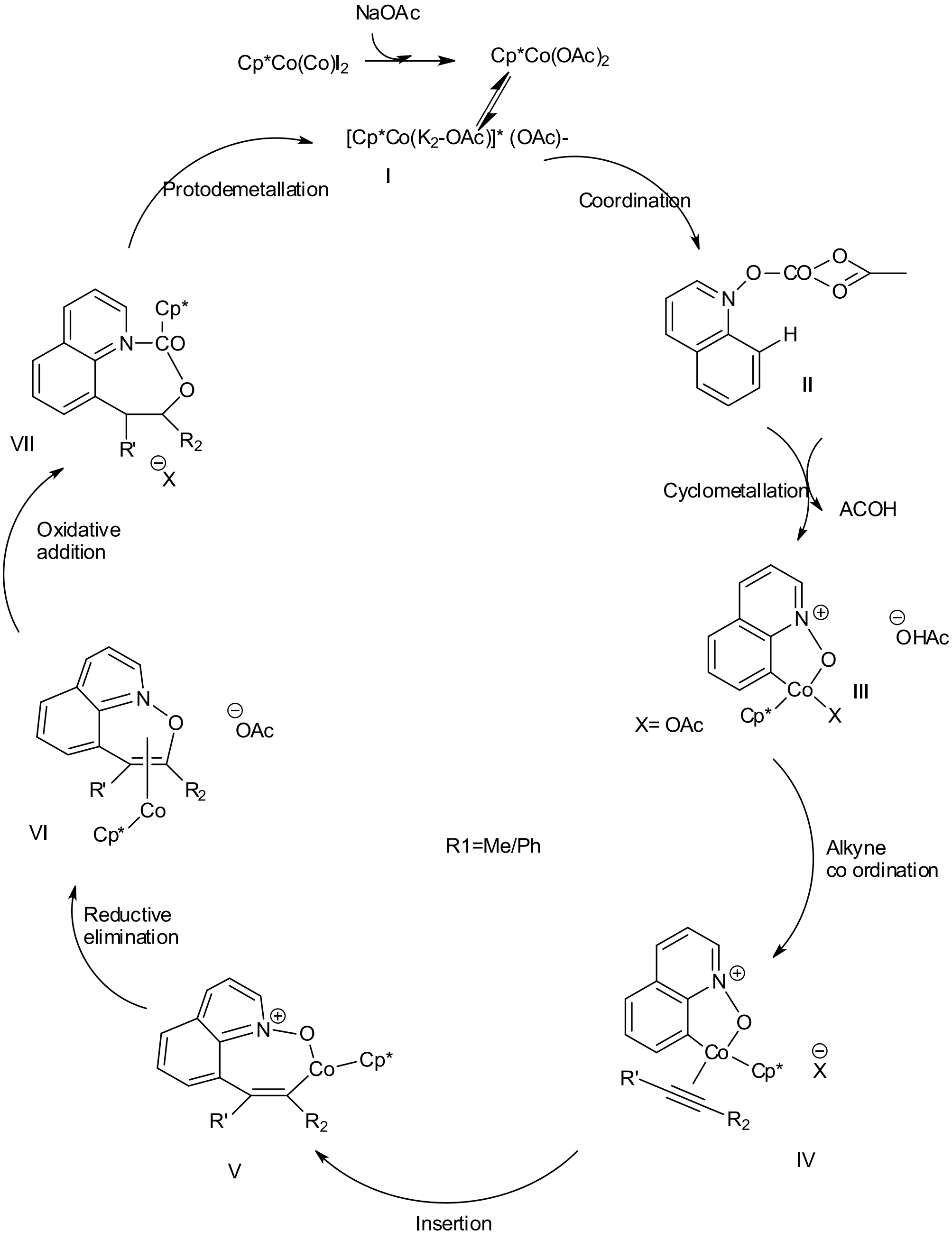

Figure 19: Mechanism of the Reaction

Substrate Scope:-

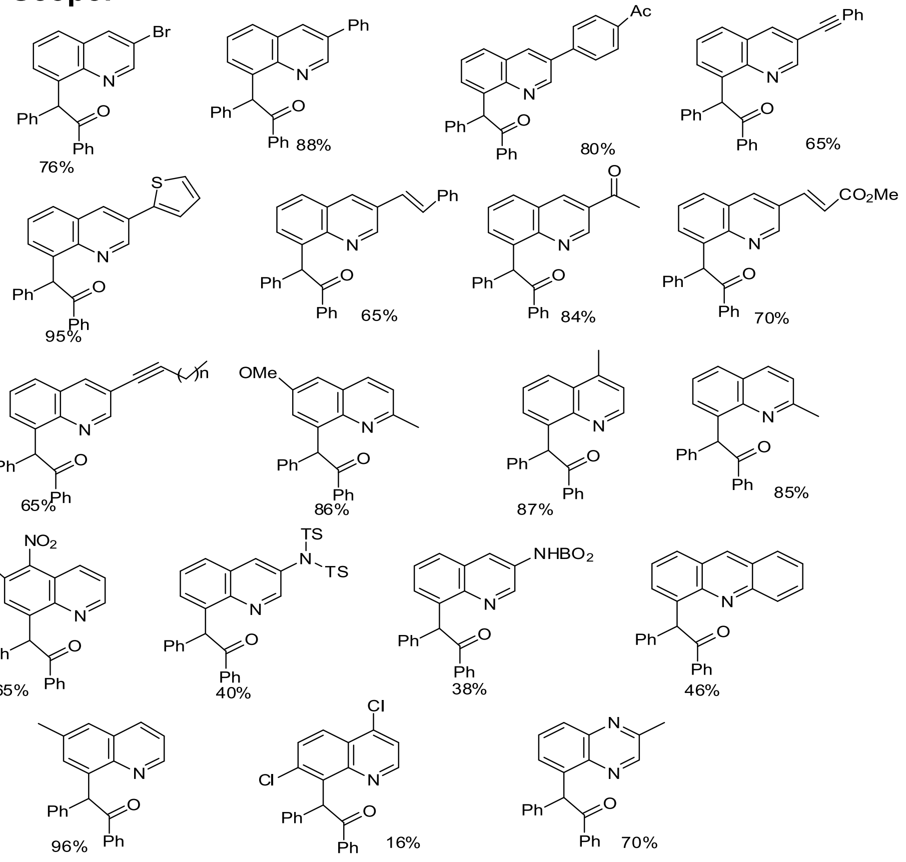

Figure 20: Substrate Scope

ix) Three Component Coupling :-

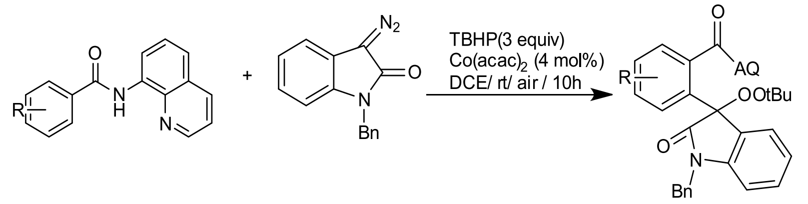

Figure 21: Three Component Coupling Reaction

The coupling reaction (Figure 21) between N-(quinoline-8yl) benzamide, 1-benzyle -3-diazoindolin-2-one and IBHP was investigated by the authors. They initially obtained a 62% yield for the intended product; however, the yield was lowered by solvent modifications, and various additions also showed decreased efficacy. Other cobalt salts also performed poorly; raising the temperature or altering the environment reduced the output. The yield was improved to 70% by further optimising TBHP to 30 eq. In the end, the optimal condition used 4 mol% $Co(acac)_2$ at rt, resulting in a 79% yield control experiment that validated the crucial roles of TBHP and cobalt salt in this reaction (Li *et al.*, 2021).

Plausible Mechanism:-

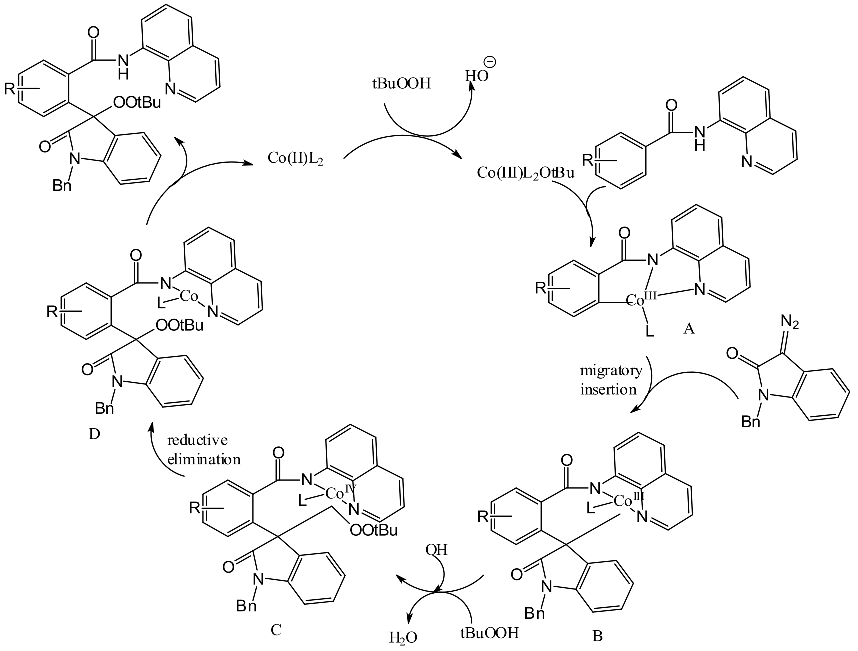

Figure 22: Mechanism of the Reaction

The oxidation of the Co(II) catalyst by TBHP, which yielded Co(III), is the first step in the suggested mechanism (Figure 22). This species forms a five-membered intermediate through a process called concerted metalation deprotonation (CMD). Through migratory insertion, this organometallic Co(II) species combines with a diazo compound to form a six-membered cyclometalated species. One electron is oxidised and Co(IV) is formed as a result of the interaction between hydroxyl radical and TBHP, which generates tBuoo-radical in situ. A Co(II) complex is the result of reductive elimination of this intermediate. Demetalation is the last stage, which regenerates the cobalt catalyst and yields the three-component coupling product.

Substrate Scopes :-

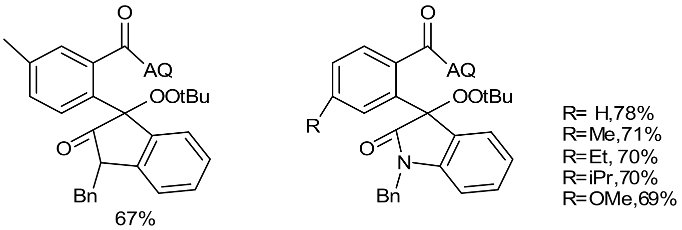

Figure 23: Substrate Scope

The authors discovered that this reaction was a generalised process with respectable product yields when they investigated it using a variety of substrates (Figure 23).

x) Azo-Directed Selective 1,4 – Addition of Ortho C-H Bond to Maleimides:-

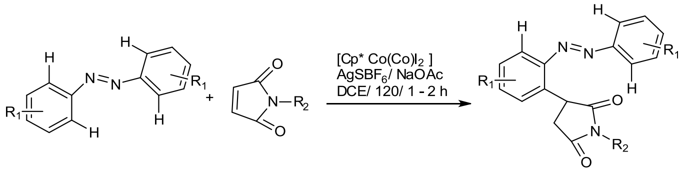

Figure 24: 1,4 – Addition of Ortho C-H Bond to Maleimides

The optimisation investigation of this study (Figure 24) started with the reaction of N-ethylmaleimide and several additives with (E)-1,2-di-p-tolydiozene. Low yields of both mono- and di-activated PDTs were obtained at the initial circumstances. The yield of the product was greatly increased by reducing AgOAc to 20 mol%, which highlights the significance of a catalytic amount of acetate. Additional experiments with various additives, such as CsOAc, NaOAc and KOAc, significantly increased yields; Use of CsOAc and NaOAc pushed the product yield up to 68%. Acidic additions such as AcOH and PivOH also worked well. The yield was further enhanced by adjusting the reactant ratios and it reached a maximum of 75% with two equivalents of the azo-dye substrate (Muniraj & Prabhu, 2017).

Proposed Mechanism:-

In the procedure shown in Figure 25, [Cp*Co(CO)I₂] reacts with AgSbF6 and NaOAC to produce a cationic Co(III) species (A) following co-dissociation. Following C-H activation, this active catalyst produces cobaltacycle B and releases AcOH. A seven-membered intermediate (C) is created when an alkene is inserted into the cobalocycle; however, because it lacks a syn-peiplanar hydrogen atom, it is unable to remove the hydrogen atom. Ultimately, proto-demetalation produces the required product and regenerates the catalyst (A).

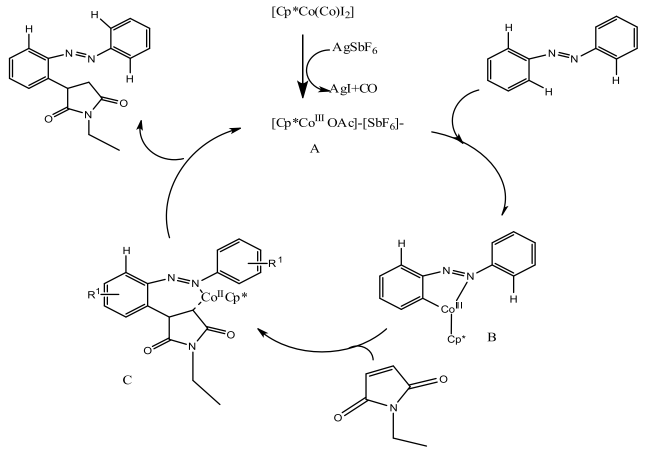

Figure 25: Mechanism of the Reaction

Substrates Scope:-

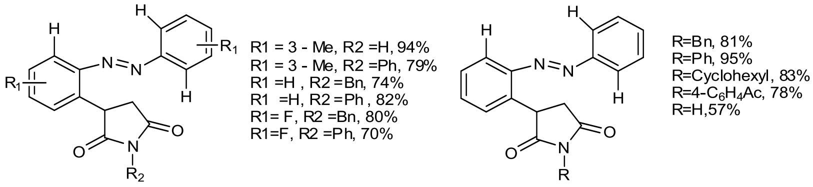

Figure 26: Substrate Scope

When the authors examined this reaction with a range of substrates, they found that it was a generalised process with decent product yields (Figure 26).

xi) Intermolecular Heterocyclizatin with Allenes at Room Temperature: -

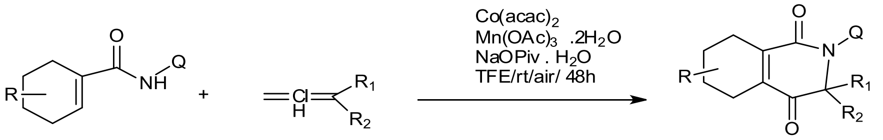

Figure 27: Intermolecular Heterocyclizatin with Allenes

The primary product in the reaction (Figure 27) between benzamide and phenyl allene with Co(acac)₂ at room temperature was quinoline-1(2H)-one, showed a 5:1 ratio of regioisomers formation. Mn(OAC)₃.2H₂O was found to be an essential oxidant, and NaOpiv.H₂O was found to be a crucial base in trifluoroethanol for efficient yielding. In contrast to the Rh(II) catalysed run, which favoured the less hindered side, this reaction exhibits great area selectivity, favouring the more substituted side.

Substrate Scopes:-

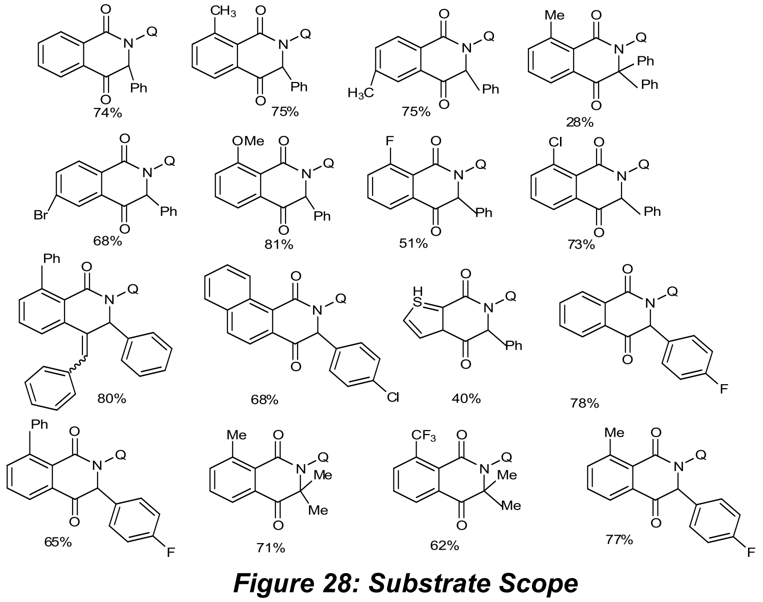

Figure 28: Substrate Scope

This selectivity was attributed to the use of cobalt, which has a smaller ionic radius than Rh. It was shown that a variety of aromatic substrates, both electron-rich and electron-poor, could tolerate functional groups such as methoxyfluoro, chloro, and bromo. Nevertheless, complicated regiosomer combinations with phenyl allene were generated by meta-substituted benzamides (Thrimurtulu *et al.*, 2016).

The authors discovered that this reaction was a generalised method with respectable product yields after analysing it with a variety of substrates (Figure 28).

Conclusion

This book chapter offers a glimpse into the latest developments in organometallic chemistry by highlighting some of the ground-breaking results of co-catalysis and its numerous uses in C-H bond activation methods. These results can undoubtedly be applied to different heterocycle derivatives to encourage more research and collaborative efforts, leading to a deeper understanding of the seemingly endless possibilities in cobalt chemistry. We think that academics from many sub-disciplines will use this article as a starting point to learn about more recent advancements in cobalt-catalysis.

Acknowledgement

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