Recent Developments In The Synthesis And Application Of Indazole Derivatives In Organic Synthesis: A Review

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Abstract

In the past decade, Indazoles are gaining increasing interest because of their unique properties and useful versatile building blocks. The rich chemistry of Indazole derivatives increasing attention both chemists and biologists in recent years. This review has outlined the extensive applications of Indazoles covering the literature the decade from 2014 to 2024 is described in chronological order. This review describes allow further elaboration via a range of facile chemical transformations and an overview of Indazole applications.

Key words: Heterocycle, Indazole derivatives, Synthesis.

Introduction:

Heterocyclic compounds derived from naturally and synthetically due to consistently been at the forefront of interest and have expanded significantly over the last several decades. As per Database of medicinal chemistry (CMC), heterocyclic molecules have gaining interest to make up a vast array of physiologically active and industrially significant molecules[1]. Therefore, the synthesis and application of heterocyclic compounds have always been in the forefront of attention and have rapidly grown in the past few decades.

Among these five member nitrogen containing heterocyclic molecules constitutes important structural motifs and widely found in many natural products. Indazoles has drawn in increasing interest to chemists as well as biologists. Indazoles are Key motif in majority pharmaceutical drugs and medicinal chemistry targets shown in **Fig-1**. Consequently, the Indazoles have made notable contributions in modern organic chemistry and emerged a challenging topic for synthetic community.

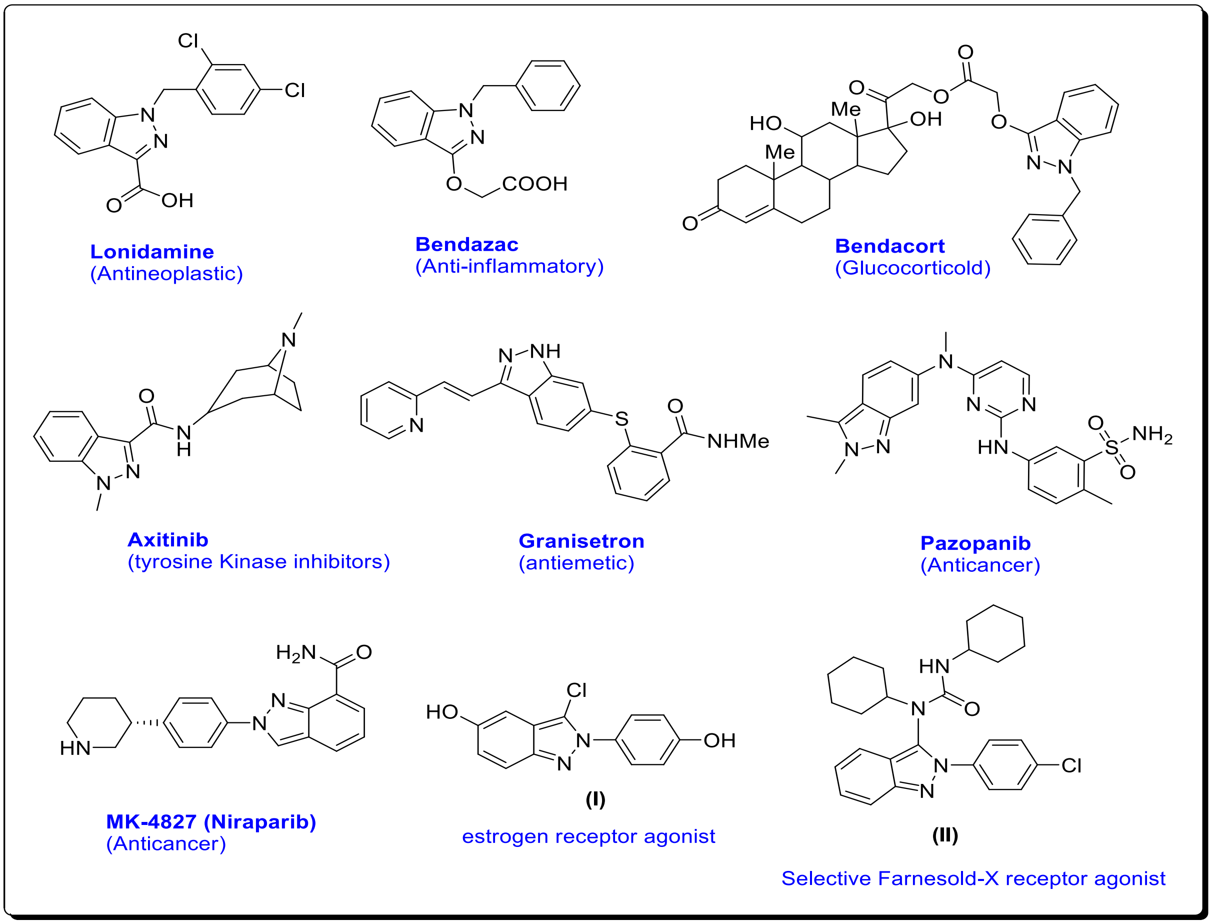


Fig-1: Indazole containing pharmaceutical drugs.

Indazoles are heterocyclic molecule, structurally pyrazole attached to benzene ring. Structurally Indazole has 10 π electrons, two nitrogen atoms presented in five membered rings. Due to π electrons delocalization, it exhibits 3 tautomeric forms (Fig. 2).

1) 1H-Indazole (1a)
2) 2H-Indazoles (1b)
3) 3H-Indaoles (1c)

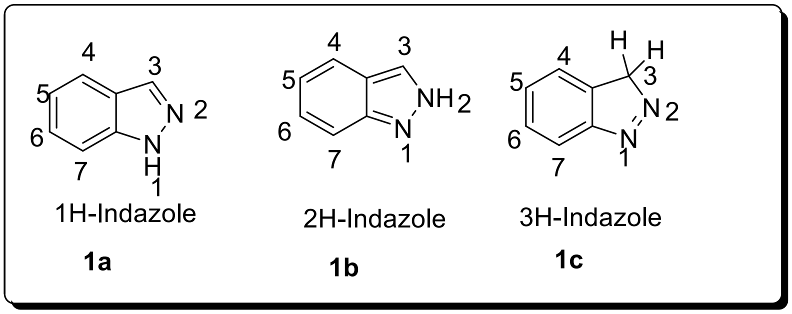


Fig.2: Basic structures of Indazole

The tautomeric form equilibrium between 1H-Indazole, 2H-Indazole in ground state as well as excited state. Because of the difference in energy gap between the tautomers (**Fig.2**), the 1*H*-tautomer (the benzenoid form **1a**) predominates in the gas-phase, solution and solid state is usually more stable 2.3 Kcal mol^{-1} than the corresponding 2*H*-forms (the quinonoid form **1b**)[2-8]. Both tautomeric forms can be identified by using solid state NMR-NQR spectroscopy. Indazole is a weaker base is having p*Ka*=1.31 but stronger acid is having p*Ka*=13.86. Dipole moment of the 2H-Indazole more than the1H-Indazole (**Table-1**).unsubstitutedindazoles and it derivatives are exist as a dimeric form, trimeric form due to the intra molecular hydrogen bonding between N-H…N [9].

Physical technique	1-methyl-1*H*-indazole	2-methyl-2*H*-indazole
Basicity (pKb)	0.42	2.02
Dipole moment (D)	1.50	3.4

Table 1: Basicity and dipole moment comparison of indazole tautomers

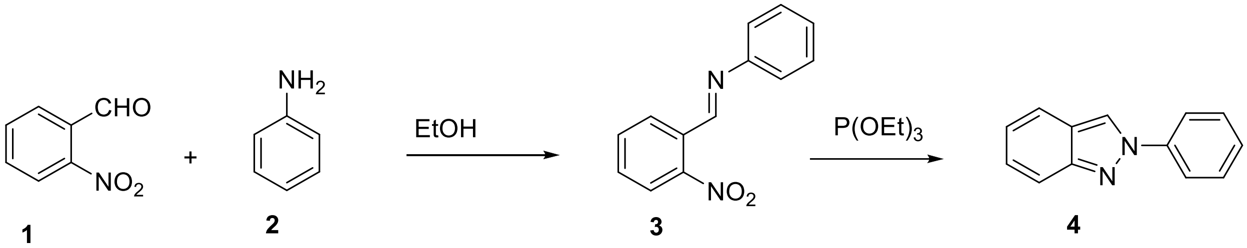
2H-Indazole compounds are having lot of importance due to their broad range spectrum of pharmacological and biological activity. In recent years, 2H-indazole family pharmaceutical drugs is Niraparib, Pazopanib and Axitinib (**Fig-1**). Development the development of asymmetric synthetic strategies for assembling such challenging scaffolds has attracted enormous attention from synthetic chemists. All these advances have driven the curiosity of scientists to constantly search for new applications of 2H-Indazoles, especially the installation of different groups on different positions on aromatic ring. A variety of well-established methods are available in the literature including advancing the development of novel and sustainable methodologies. There are few reviews available on 2H-Indazole[10-11].

These strategies have potential applications in pharmaceuticals, biology, and materials science. The modular nature of these reactions allows for easy variation of the substituents on the 2H-Indazole and other components, thus enabling the synthesis of large libraries of compounds for screening in various biological and material.

This manuscript presents a detailed literature review will deliver the critical insights available on 2-H-Indazoles from 2014 to 2024. We hope this review will provide timely illumination and beneficial guidance for future synthetic efforts for organic chemists who are interested in this area and overall development in the field along with the opportunity for the innovative approaches of further research.

The Chemistry of Indazoles:

2-H-indazoles were synthesized by Cadogan reaction[12]. 2-nitro benzaldehyde (**1**) react with anilines/substituted anilines (**2**) under reflux condition to afford Schiff base (**3**), which was treated with triethyl phosphite to yield 2-Phenyl-2H-indazoles (4) as shown in **scheme-1**.

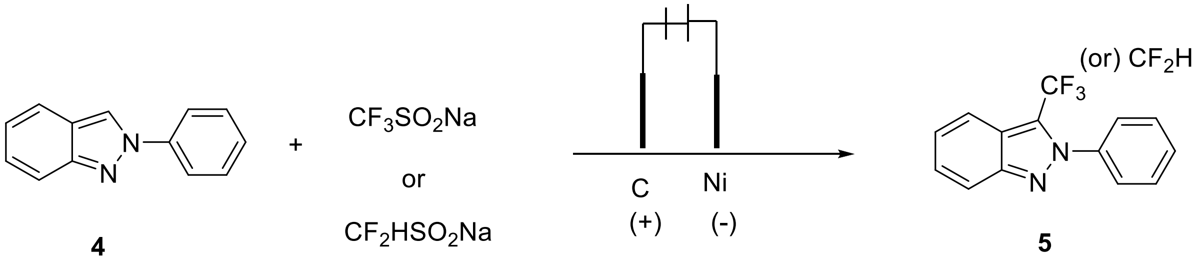


Scheme**-1**: Synthesis of 2H-Indazole

Synthetic application of 3-alkyl indazoles;

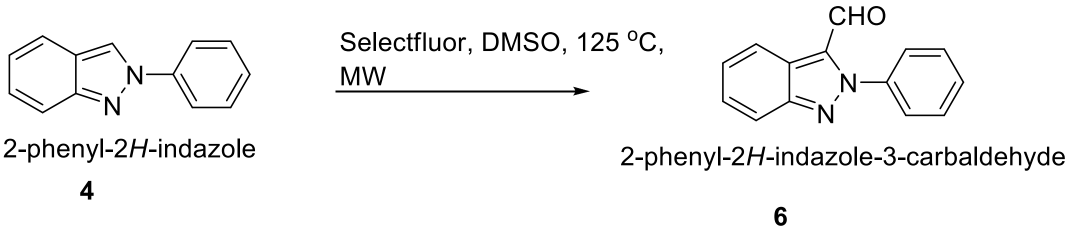
C3 Functionlazation of 2-H-Indazoles:

Regioselective difluro/trifluoro methylation at C-3 position of 2H-Indazole (4) was developed by Ramakrishna[13] et al using C(+)/Ni(-) electrodes by electrochemical method as shown in **Scheme-2**.



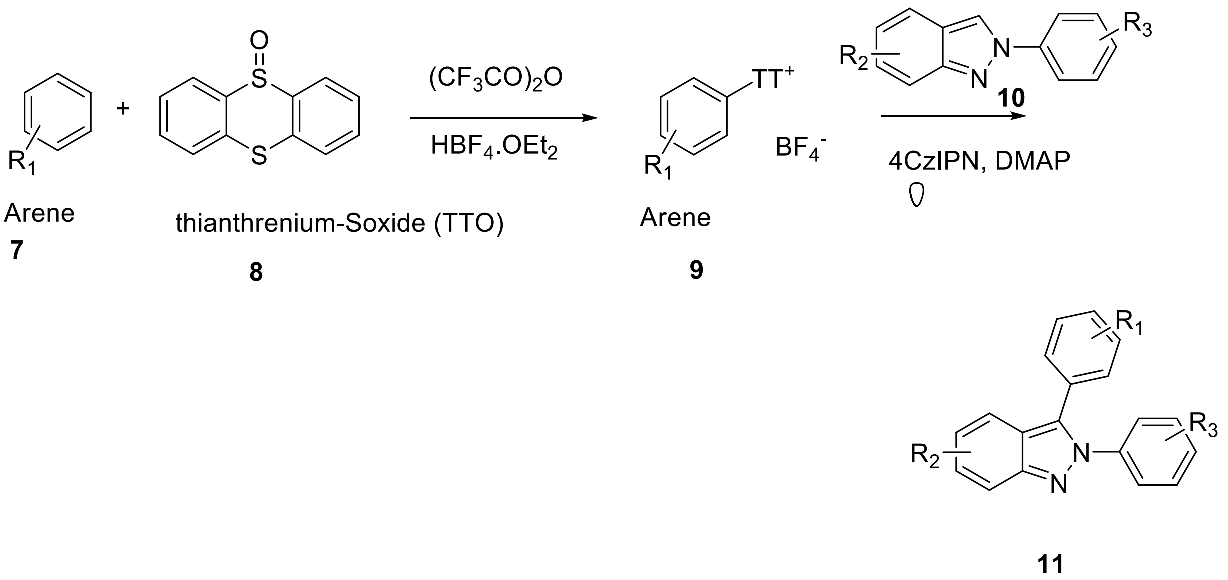
Scheme-2: Synthesis of 3-Fluoromethyl-2H-Indazole

Formylation on 2H-Indazole reported by Manivel pitchai[14]et al at C-3 position by using selectfluor by using microwave condition. 2-Phenyl-2H-Indazole (**4**) converted into 2-phenyl-2H-Indazole-3-carbaldehyde (**6**).



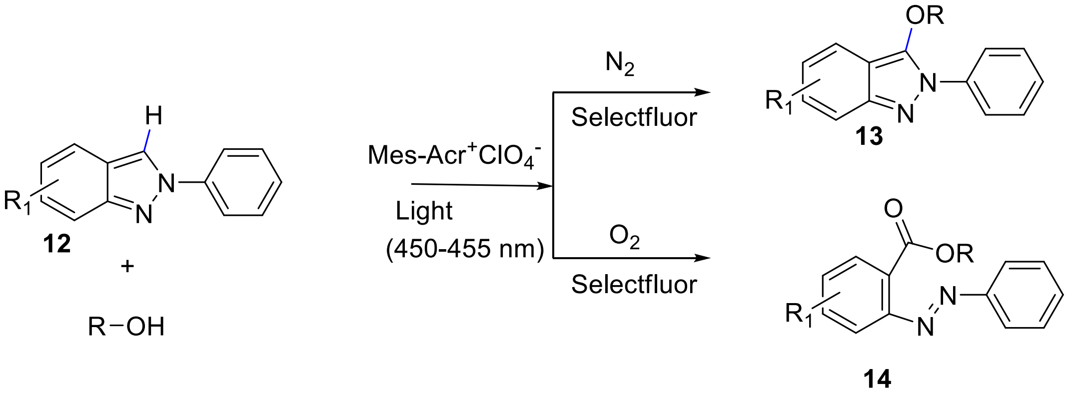
Scheme-3: Synthesis of 3-Formyl-2H-Indazole

Bing Yu[15] et. al. reported the synthesis of 3-aryl-2-aryl indazole under metal free condition. In this approache started with arene (**7**) reacted with thianthrenium-S-oxide (TTO) (**8**) in the presenece of trifluoroacetic anhydride and HBF_4 to afford aryl sulfonium salt (**9**), which react with 2-aryl-2H-indzole (**10**) in the presence of 1,2,3,5-tetrakis(carbazol-9-yl)-4,6-dicyanobenzene (4CzIPN) as an inexpensive photocatalyst and Dimethyl aminopyridine to yield 2-aryl-2H-Indazole (**11**).



Scheme-4: Synthesis of 3-Aryl-2H-Indazole

In 2021, Li[16]et al reported photolytic reaction C3-alkoxylation of 2-H-indazoles (**12**) with alcohols in the presence of Mes-Acr+ClO_4- as a photo sensitizer and selectfulor act as oxidant in the presence of nitrogen atmosphere to yield 3-alkoxy-2-aryl indazole (**13**).

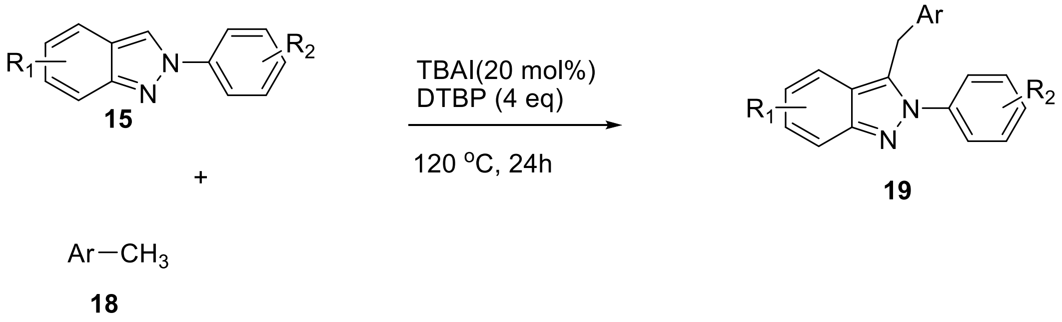


Scheme-5: Synthesis of 3-Alkoxy-2H-Indazole

In 2021, Yu[17] group reported photolytic 3-alkylation reaction of 2-aryl-2H-indazoles (**15**) in the presence of blue LED under mild conditions in the dimethylcarbonate solvent 1,2,3,5-tetrakis(carbazol-9-yl)-4,6-dicyanobenzene (4CzIPN) as an inexpensive photocatalyst, and alkyl *N*-hydroxy phthalimide esters (**16**) to provide 3-alkyl-2-aryl-2H-indazoles (**17**) with good to excellent yield shown in **Scheme-6.**

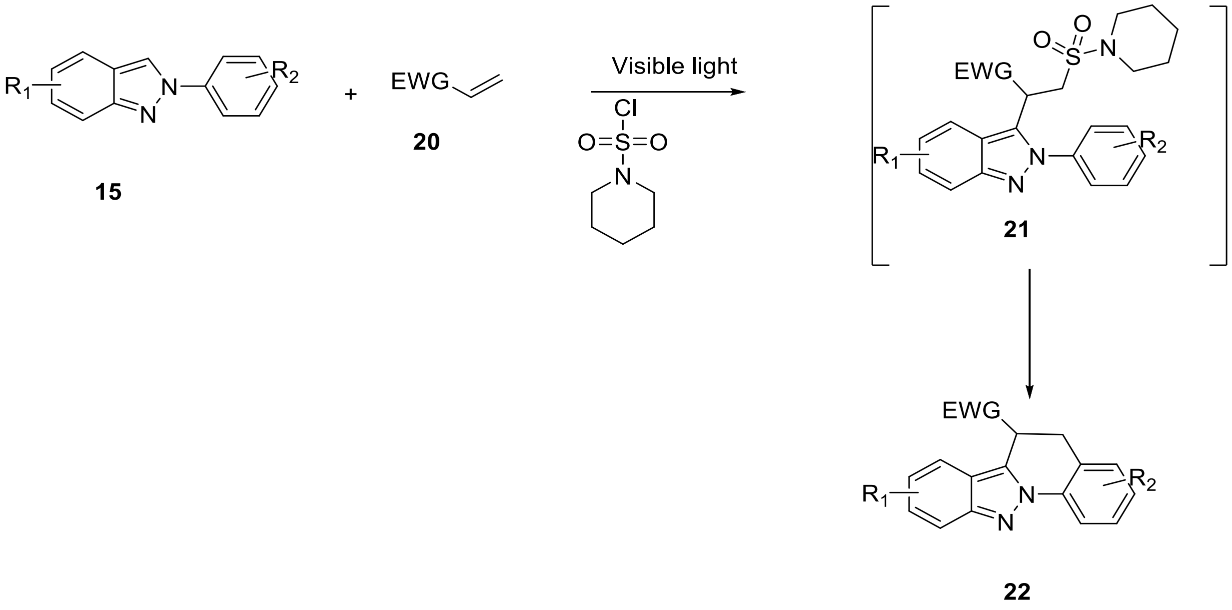
Scheme-6: Synthesis of 3-Alkyl-2aryl-Indazole

In 2020 Chaudhary [18] group reported the synthesis of 3-benzylated-2-aryl-2H– indazoles (**19**) from 2-aryl-2H-indazoles (15) via C(sp2)–H/C(sp3)–H cross dehydrogenative coupling with arene (**18**) at 120 °C in the presence of tetra-n-butylammonium iodide (TBAI) as a catalyst and promoted DTBP (Di-tert-butyl peroxide (DTBP)) to afford the regioselective direct C-3 benzylation product 3-benzylated-2-aryl-2H–indazoles with good to excellent yields. This methodlogy offers broad range of functional group tolerance and wide substrate compatibility as shown in **Scheme 7**.



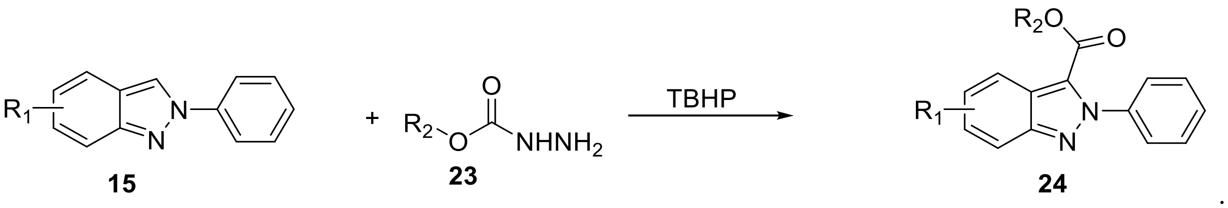
Scheme-7: Synthesis of 3-benzylated-2-aryl-2H– indazoles

Recently Hazra[19] et al reported the synthesis fused 5,6-dihydroindazolo[2,3-*a*]quinolines (**22**). Compound (**21**) formed through the intermediate (**21**), which inturn the reaction between 2-aryl indazole (**15**), electron deficient olefin (**20**) and piperdine-1-sulfonoyl chloride in the presence of visible light mediated oxidation.



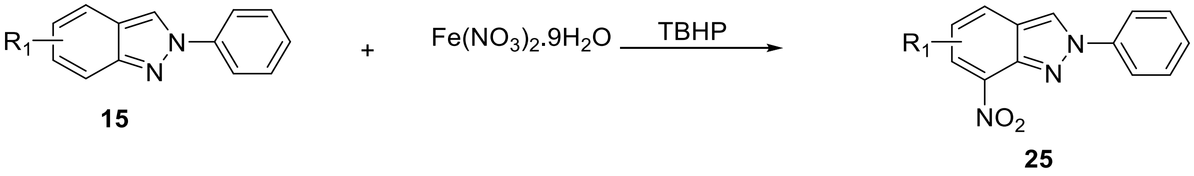
Scheme-8: Synthesis of 5,6-dihydroindazolo[2,3-*a*]quinolines

Hazra[20] reported the metal free condition of Ester group installation at C-3 position of 2-Aryl indazole. 3-carbmoyl-2 aryl-indazole (**24**) prepared from the reaction between 2-aryl indazole (**15**) and alkyl carbazates (**23**) in the presence of tertiary-butylhydrogenperoxide (TBHP).



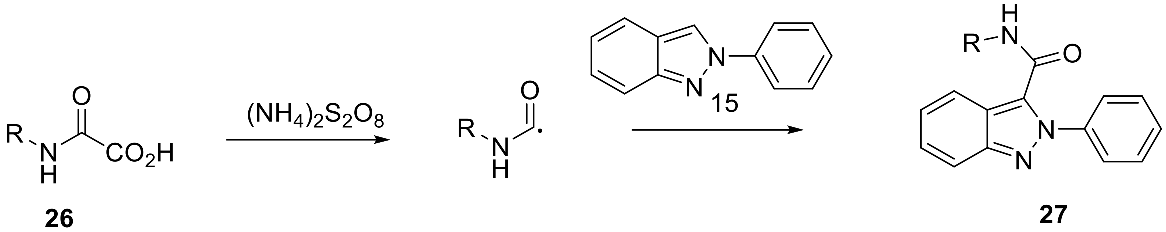
Scheme-9: Synthesis of 3-carbmoyl-2-aryl-indazole

2-Aryl indazole (**15**) react with iron (III) nitrate in the presence of Zn(OTf)$_2$ catalyst to produce selectively nitration at 7th position to produced 7-nitro-2-H-indazole (**25**) was achieved by Hazra[21] et.al.



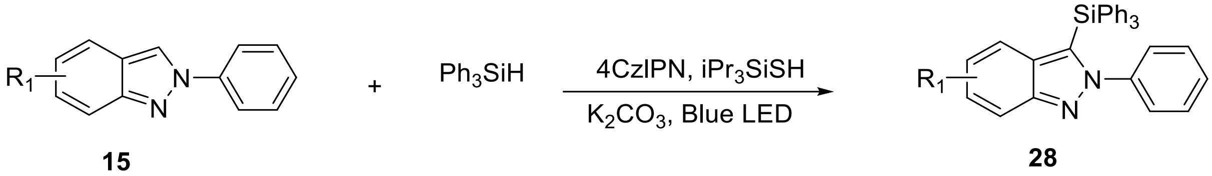
Scheme-10: Synthesis of 7-nitro-2-H-indazole

Carbmoylation installation at C-3 position of 2-Aryl-2H-Indazole was reported by Anna Lee group[22]. Oxamic acid (**26**) reacts with ammonium persulfate to formed corresponding carbmoyl free radical, which was reacted with 2-aryl-2H-indazole to obtained C3-carbmoylated-2H-Indazole (**27**).



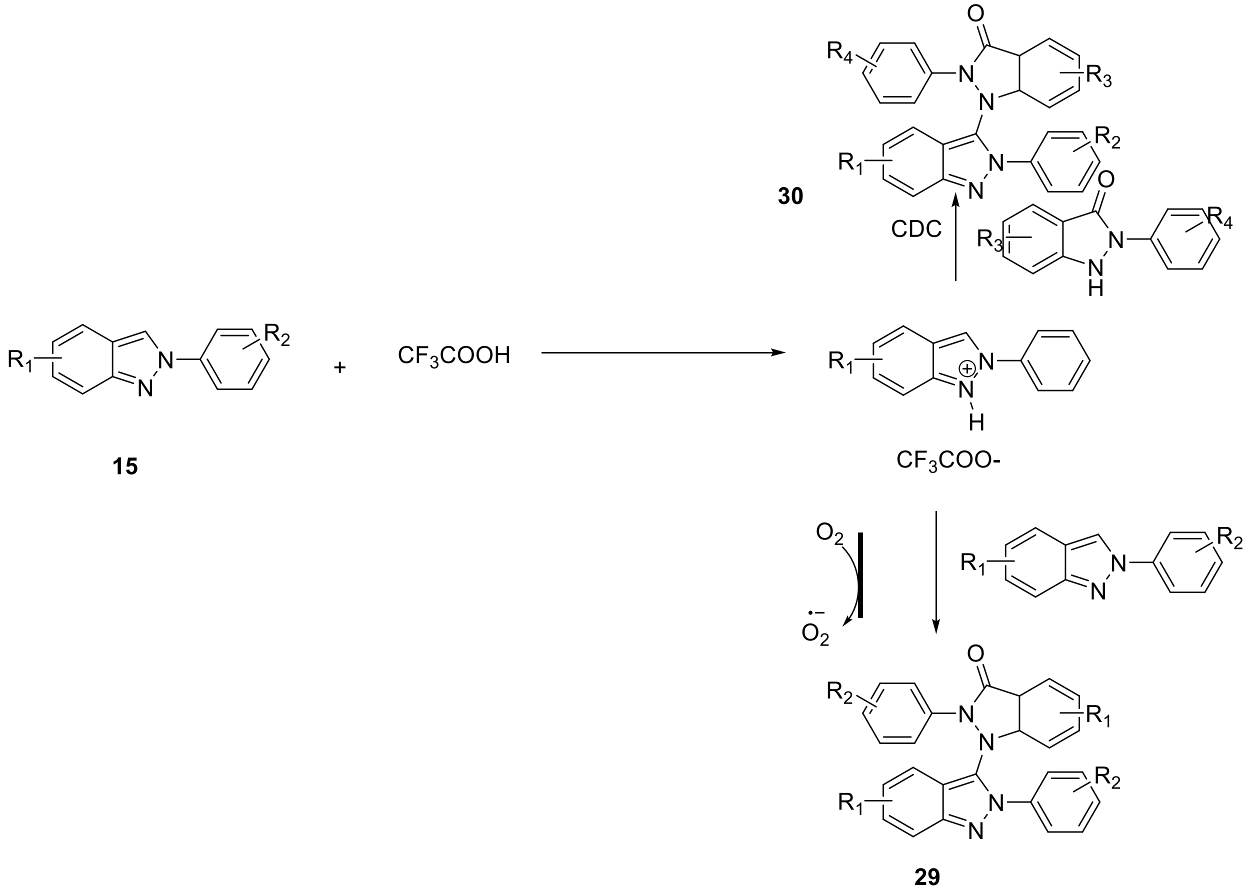
Scheme-11: Synthesis of 7-nitro-2-H-indazole

A metal-free, visible-light-mediated C–H silylation of 2*H*-indazoles (**15**) with triphenylsilane has been developed employing 4CzIPN as a photocatalyst and triisopropylsilanethiol as a hydrogen atom transfer (HAT) reagent under aerobic reaction conditions to afford 3-triphenylsilyl-2-aryl indazole (**28**) was achieved by Hazra[23] group.



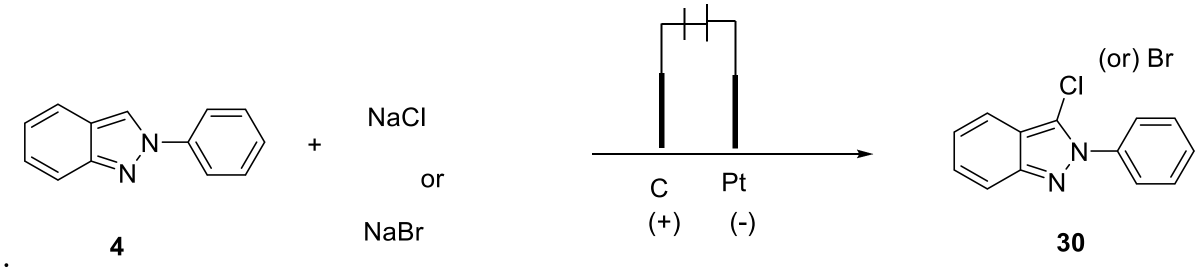
Scheme-12: Synthesis of 3-triphenylsilyl-2-aryl indazole

Hazra[24] group synthesized synthesis of indazolylindazolones (**29**) through oxygen reduction reaction (*e*ORR) induced 1,3-oxo-amination of 2*H*-indazoles, where 2*H*-indazole is used as both aminating agent as well as the precursor of indazolone and unsymmetrical indazolylindazolones (**30**) acheived through direct electrochemical cross-dehydrogenative coupling (CDC).



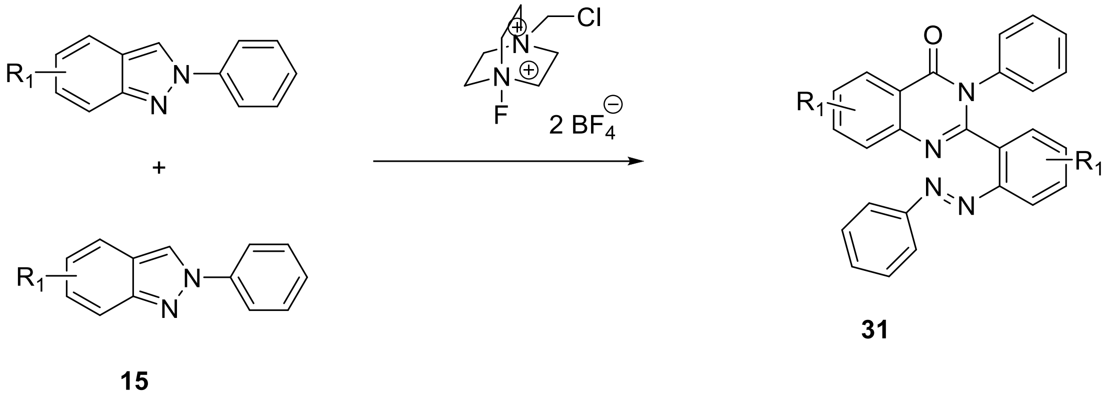
Scheme-13: Synthesis of indazolylindazolones

Zhenlu[25] et al reported efficient electrochemical halogenations on 2-Aryl-2H- indazole with NaCl or NaBr in acetonitrile solvent to produce 3-chloro/bromo-2-aryl indazole (**30**) with moderate to excellent yields.



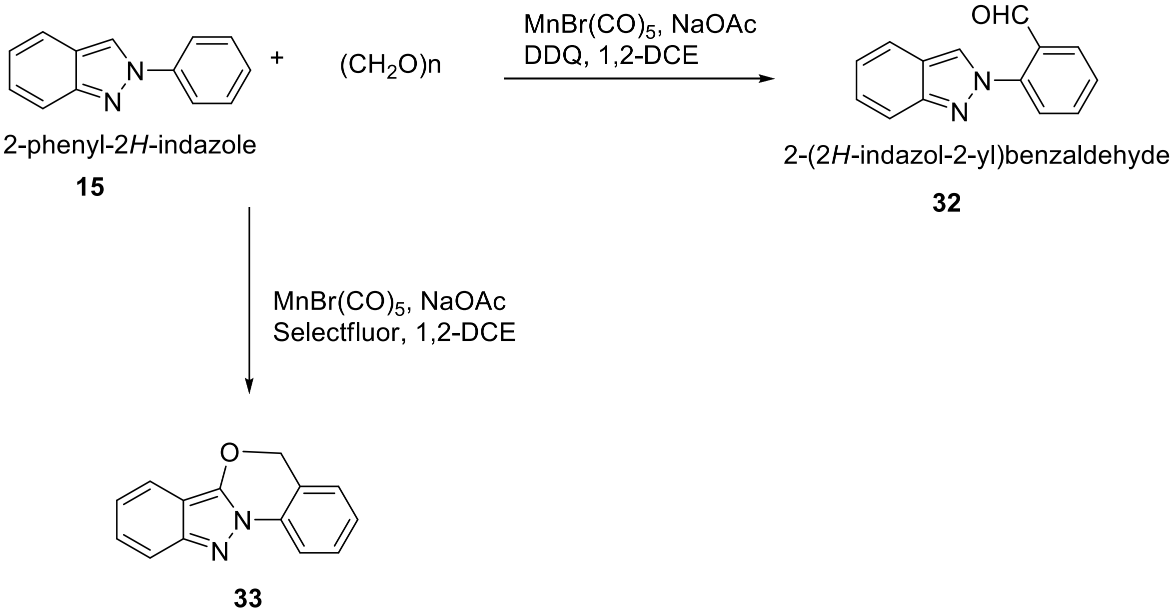
Scheme-14: Synthesis of 3-chloro/bromo-2-aryl indazole

Two molecules of 2-Aryl-2H- indazole in the presence of selectfluorto produce the azo-linked-2,3-disubstituted quinazolin-4-one derivatives (**31**) formed through in-situ generated *N*-centredindazolone radical intermediate were reported by Hazra[26] group.



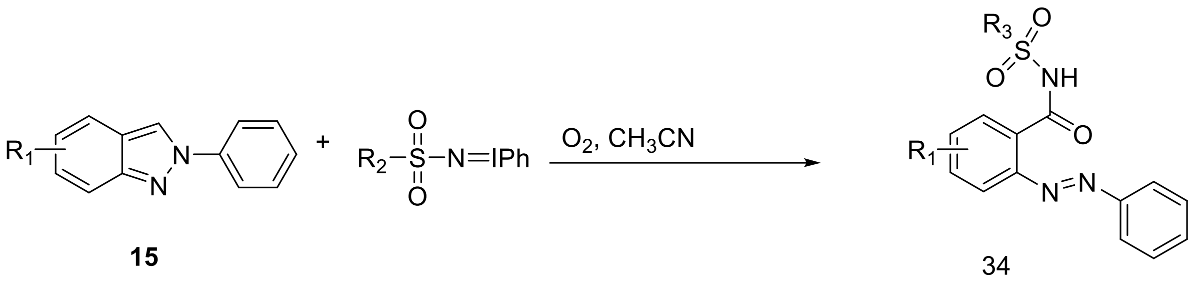
Scheme-15: Synthesis of 2,3-disubstituted quinazolin-4-one derivatives

2-phenyl-2H-indazole react with Paraformaldehyde, MnBr(CO)$_5$, CH$_3$COONa and 1.2 equivalent of DDQ to produce 2-(2H-indazol-2-yl)benzaldehyde (**32**). While same reaction condition with selectfluor to produce the indazolebenzoxazine derivatives (**33**) was achieved by Hazra[27] group.



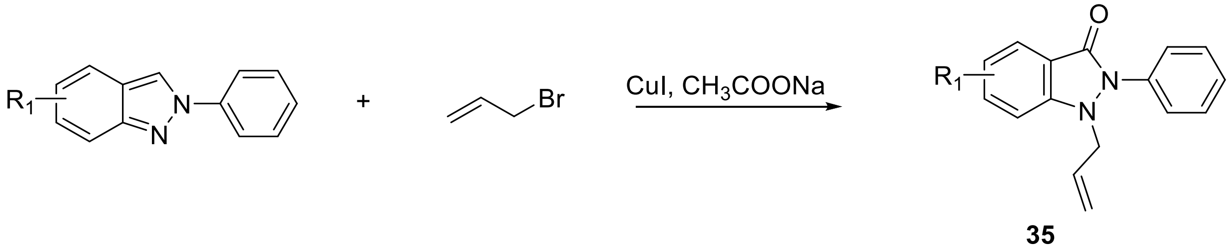
Scheme-16: Synthesis of 2-(2H-indazol-2-yl)benzaldehyde and indazolebenzoxazine derivatives

Hazra[28] et al reported the triggered oxidative iminoiodane ring opening of 2*H*-indazoles via C–N bond cleavage has been developed under metal-free reaction conditions to produce unsymmetrical *ortho*-*N*-acylsulfonamidatedazobenzenes (**34**).



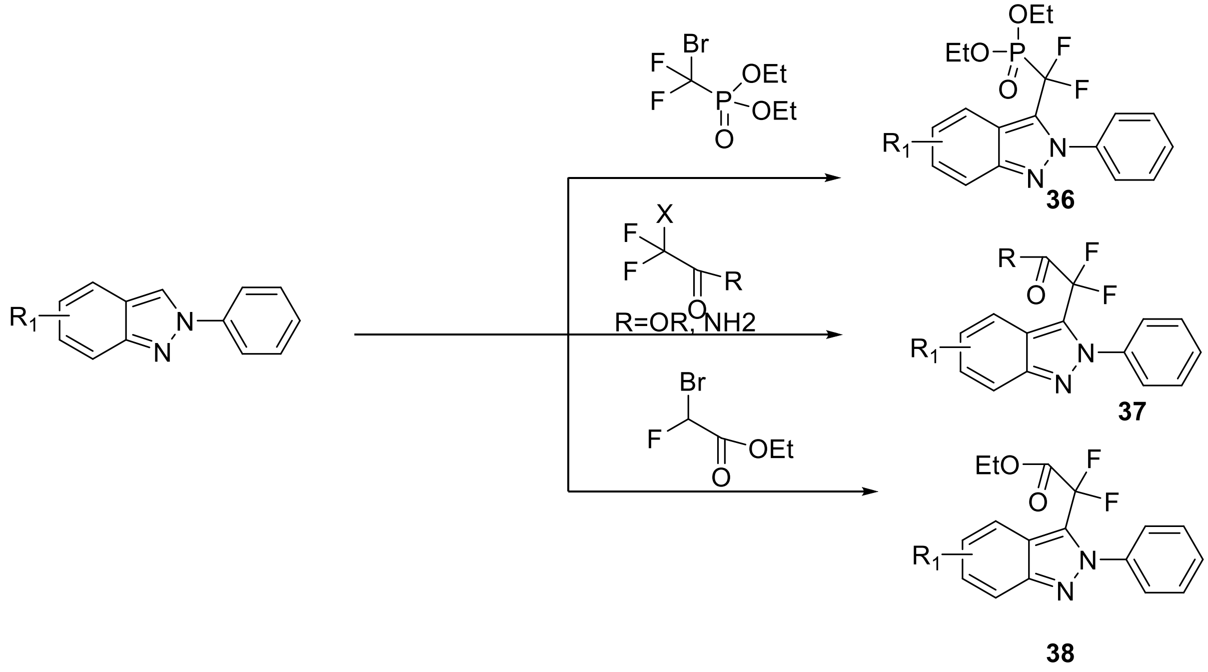
Scheme-17: Synthesis of *ortho*-*N*-acylsulfonamidatedazobenzenes

Hazra[29] group reported the cascade reaction of 2-H-indazole reaction with allyl bromide in the presence of Cu(I)I and sodium acetate to an aerobic oxidation through single electron transfer (SET)constructing *N*-1-alkylated indazolone derivatives (**35**) with good to excellent yields.



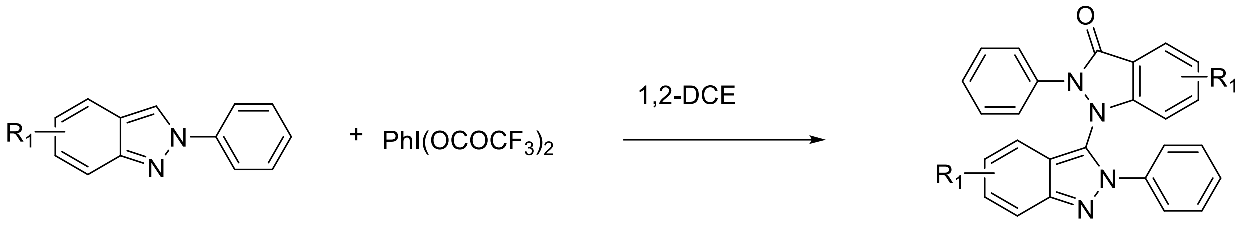
Scheme-18: Synthesis of *N*-1-alkylated indazolone derivatives

Hazra[30] et al reported the visible-light driven fluoroalkylation on 2H-indazole using $Mn_2(CO)_{10}$ catalyst in photolytic to afford good to excellent yields of Difluoro methylenated 2H-Indazole derivatives **36**, **37**, **38**.



Scheme-19: Synthesis of Difluoromethylenated 2H-Indazole

Hazra**[31]** group reported the synthesis of *N*-1 indazolylindazolones (**39**) prepared from the 2H-Indazole. 2H-Indazole react with phenyl iodo trifluoroacetate (PIFA) in 1,2-DCE solvent to afford promptly synthesized in good to excellent yields.



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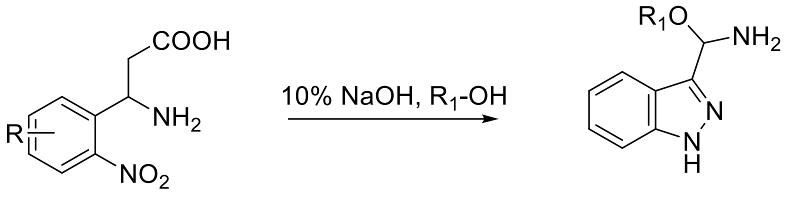
Scheme-20: Synthesis of *N*-1 indazolylindazolones

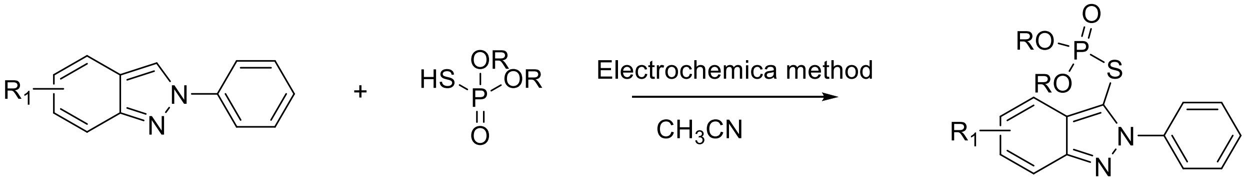
Heating of 3-amino-3-(2-nitroaryl)propanoic acids (**40**) with an appropriate nucleophile/solvent under basic conditions such sodium hydroxide participate in cascade N–N bond forming to yield distinct indazole acetic acid derivatives (**41**) developed by Luke[32] group.



40 **41**

Scheme-21: Synthesis of *N*-1 indazolylindazolones

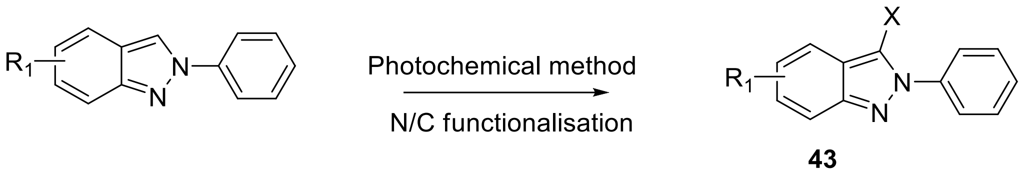
Hazra**[33]** et al claimed a electrochemical method for phosphorothiolation of 2*H*-indazoles using *S*-hydrogen phosphorothioates *via* cross dehydrogenative coupling reaction to 3- phosphoro thioates -2H-indazole (**42**) with good to excellent yields as shown in **scheme-2**1.



15 **42**

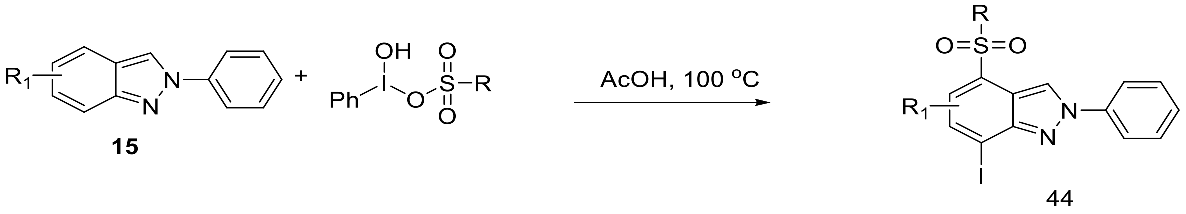
Scheme-22: Synthesis of 3- phosphorothioates -2H-indazole

Hazra group reported the efficient Photocatalysis**[34]** method of 2H-Indazole with N/C coupling partner to yield 3-Substituted -2H-indazole (**43**) as shown in **scheme-22**.



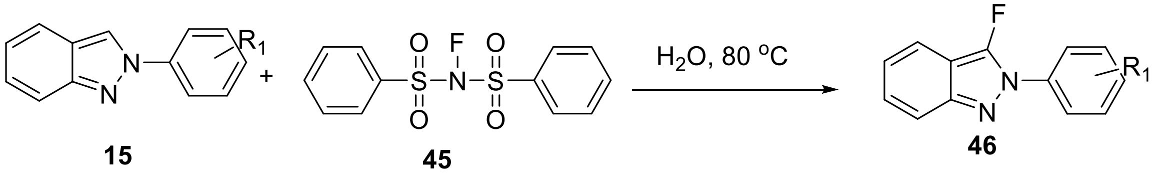
Scheme-23: Synthesis of 3- substituted -2H-indazole

2H-indazole react with Kosers reagent (Hydroxy(4-methylbenzenesulfonato-O)phenyliodine in acetic acid at 100 °C to yield C-4,7-disubstituted-2H-indazole[35] (**44**) with higher selectivity good to excellent yields.



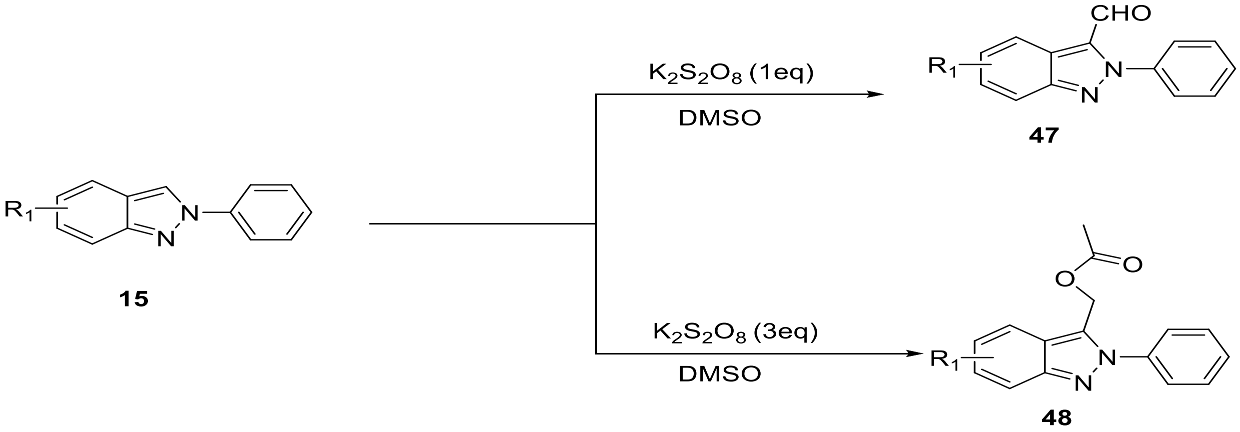
Scheme-24: Synthesis of 4,7-disubstituted-2H-indazole

Metal-free fluorination[36] condition of 2*H*-indazoles with *N*-fluorobenzenesulfonimide (NFSI) (**45**) to afford 3-fluorinated indazole derivatives (**46**) with good to excellent yields. This methodology offers broad functionalities with good to excellent yields.



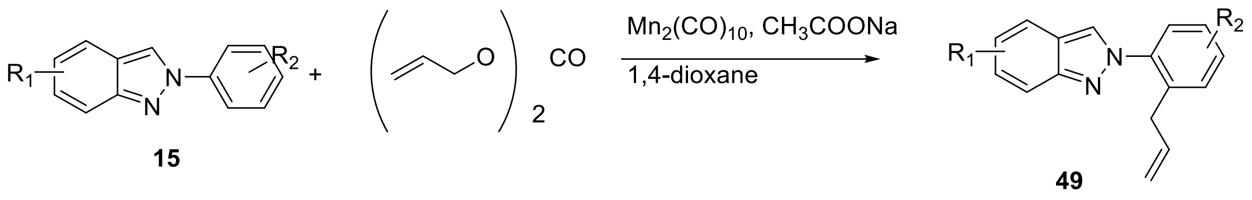
Scheme-25: Synthesis of 3-fluorinated indazole derivatives

2H-indazole react with 1.0 equivalent potassium persulfate ($K_2S_2O_8$) in DMSO to afford 3-Formyl-2H-indazole (**47**), while 3.0 equivalents of potassium persulfate ($K_2S_2O_8$) in DMSO to afford 3-methylacetate-2H-indazole[37] (**48**). This methodlogy offered wide range of substrate scope with good to excellent yield.



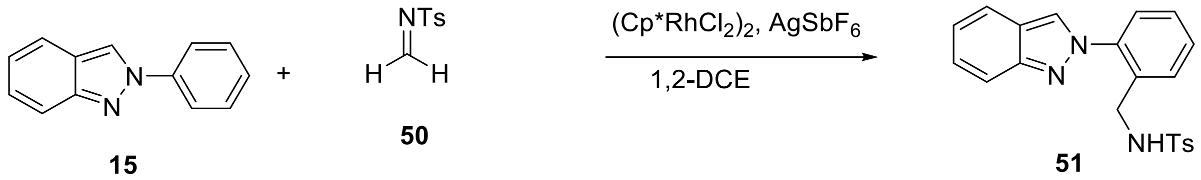
Scheme-26: Synthesis of 3-substituted-2-Aryl indazole derivatives

Allylation on 2H-Indazole in the presence of manganese-catalyst $Mn_2(CO)_{10}$ and sodium acetate in 1,4-dioxane to yield ortho directed C−H allylation of 2-arylindazole[38] (**49**) with good to excellent yield.



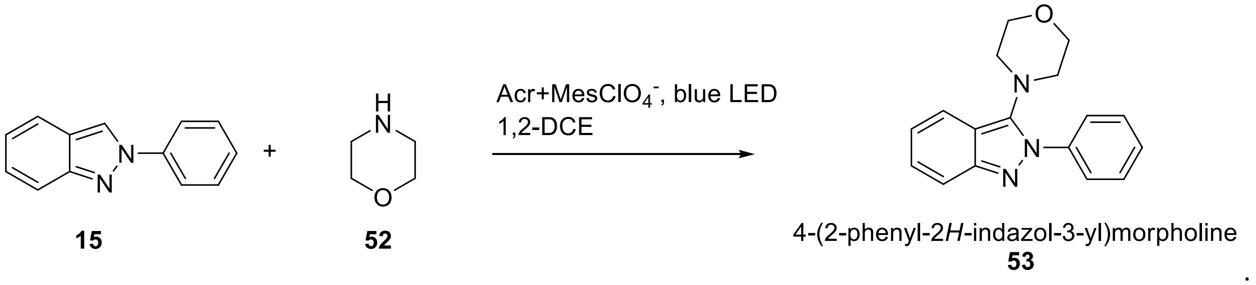
Scheme-27: Synthesis of 2-Aryl indazole derivatives

2-Aryl-2H-indazoe react with N-tosylformaldimine (**50**) react with $[Cp^*RhCl_2]_2$ and AgSbF6 in 1,2-DCE solvent to afford N-(2-(2H-indazol-2-yl)benzyl)-4-methylbenzenesulfonamide[39] (**51**).



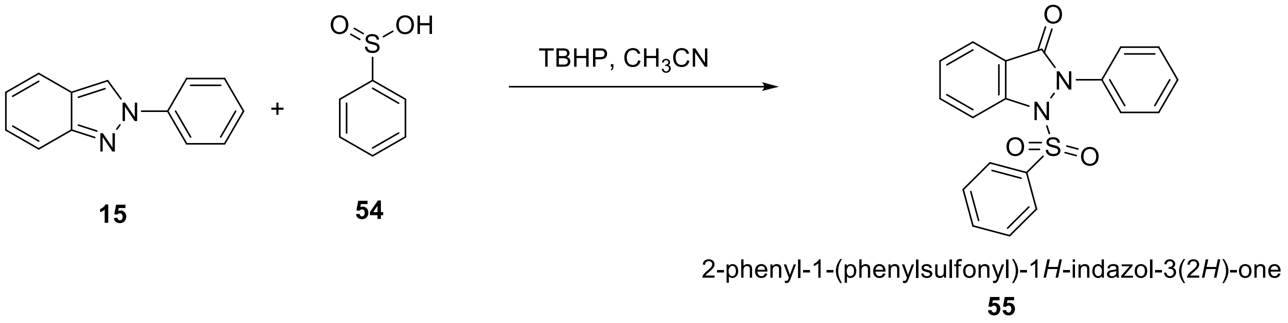
Scheme-28: Synthesis of 2-Aryl indazole derivatives

2-Aryl-Indazole reacts with excess morpholine (**52**) in the presence of catalytic amount of Acr+ -$MesClO_4$ (9-mesityl-10- methylacridinium ion) as photocatalyst in CH_3CN under ue LED irradiation to yield 4-(2-Phenyl-2H-indazol-3-yl) morpholine[40] (**53**) as a final product.



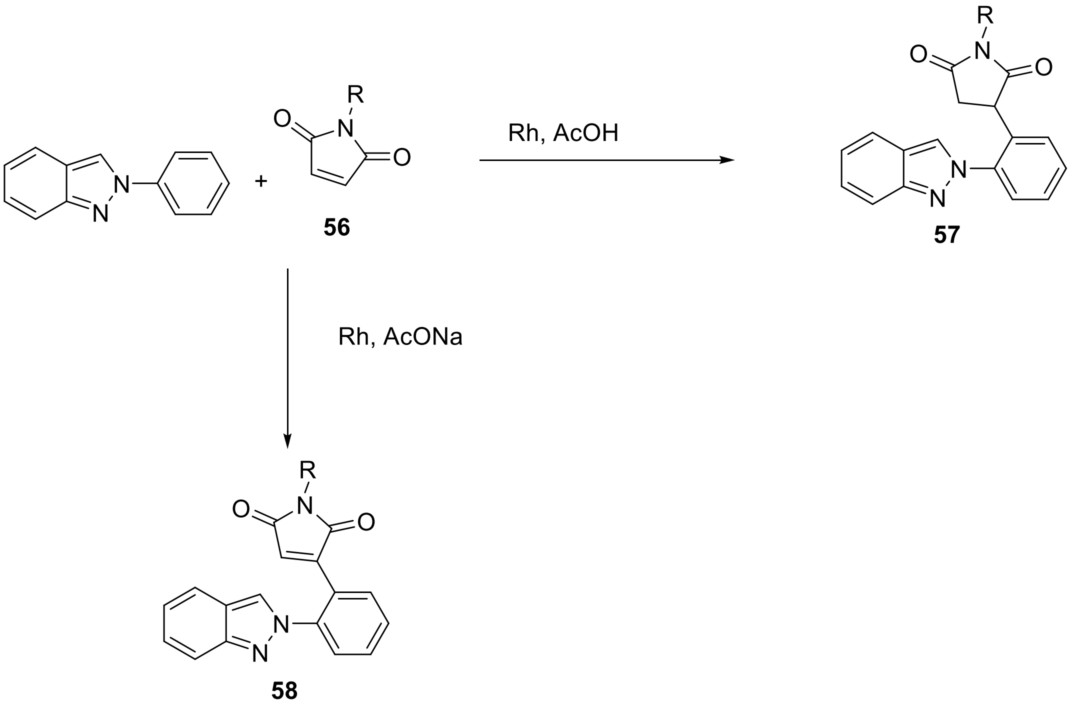
Scheme-29: Synthesis of 4-(2-Aryl indazol-3-yl) derivatives

oxo-sulfonylation protocol reported by Hazra[41] et al for the synthesis of N-sulfonylatedindazolones (**55**) from the reaction between 2H-indazole and sulfinic acid (**54**) in the presence of *tert*-butyl hydroperoxide (TBHP) to yield diverse 1-sulfonylindazol-3(2*H*)-one derivatives were achieved with good to excellent yields.



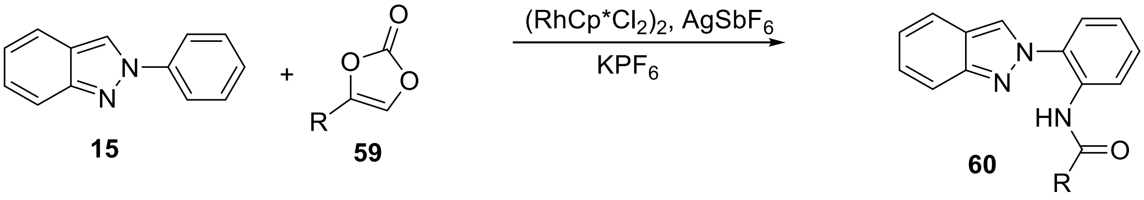
Scheme-30: Synthesis of 4-(2-Aryl indazol-3-yl) derivatives

2-Aryl-2H-Indazole react with maleimides (**56**) in the presence of Rh(III)-catalyst and acetic acid to form highly regioselective 3-(2-(2*H*-indazol-2-yl)phenyl)succinimide (**57**), while sodium acetate replaced with acetic acid to yield 3-(2-(2*H*-indazol-2-yl)phenyl)maleimide derivatives (**58**) with good to excellent yields[**42**].

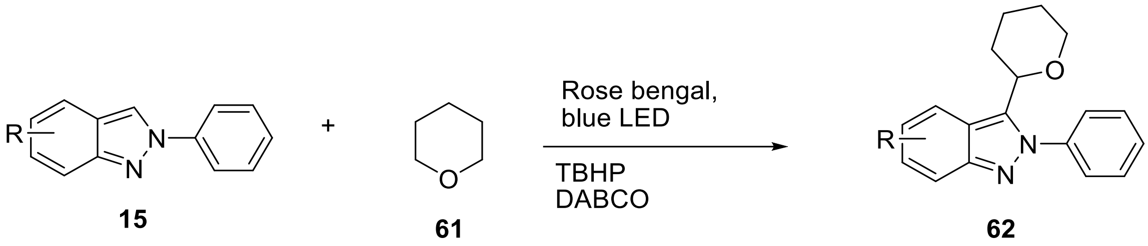


Scheme-31: Synthesis of 2-Aryl indazole-malemide derivatives

Rhodium-catalyzed C–H activation reaction between 2H-indazole and with alkyl, aryl and heteroaryl dioxazolones (**59**) to afford *N*-(2-(2*H*-indazol-2-yl) phenyl)acetamide derivatives (**60**) good to excellent yields[43].

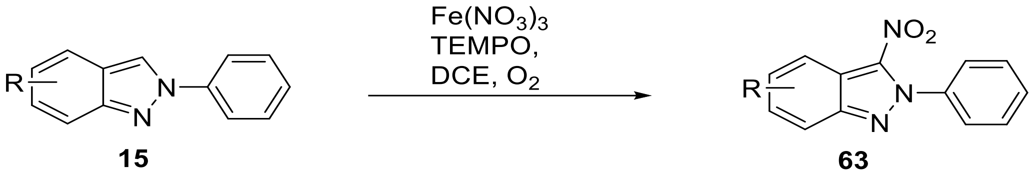


Scheme-32: Synthesis of *N*-(2-(2*H*-indazol-2-yl) phenyl)acetamide derivatives visible-light-promoted regioselective cross-dehydrogenative coupling between 2*H*-indazoles and cyclic ethers (**61**) has been achieved using a catalytic amount of rose bengal as an organophotoredox-catalyst and *tert*-butyl hydroperoxide (TBHP) as an oxidant at ambient temperature under aerobic conditions to obtained variety of C-3 oxyalkylated 2*H*-indazoles[44]have been synthesized (**62**).



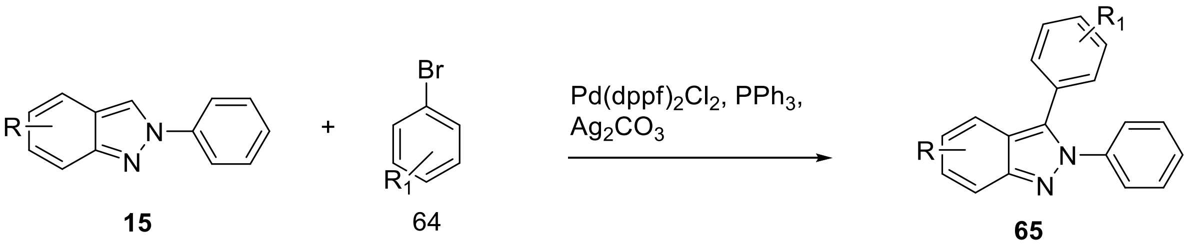
Scheme-33: Synthesis of *N*-(2-(2*H*-indazol-2-yl) phenyl)acetamide derivatives

An efficient C-3 nitration on 2-H-Indazole $Fe(NO_3)_2$ and (2,2,6,6-tetramethylpiperidin-1-yl)oxidanyl (TEMPO) catalyst to provide 3-nitro-2-phenyl-2H-indazole (**63**) with good to excellent yields were reported by Sharada[45] et al in 2018.



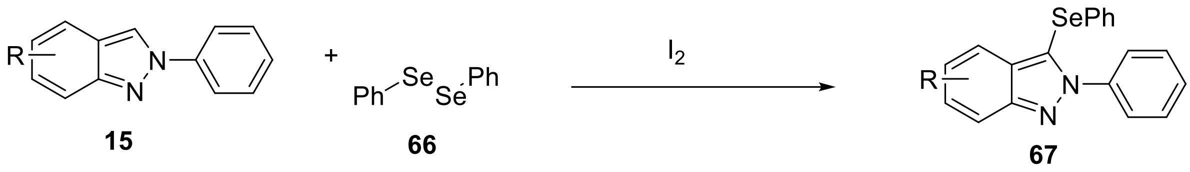
Scheme-34: Synthesis of 3-Nitro-2-aryl indazole derivatives

Perez-Villanueva[46] et al synthesized 3-Aryl-2-H-Indazole (**65**) from 2-H Indazole and aryl halide (**64**) in the presence of palladium catalyst under Heck condition. The newly synthesized compounds were studied for the Anti-microbial and Anti-inflammatory activity. Below compounds were showed significant anti-microbial activity.



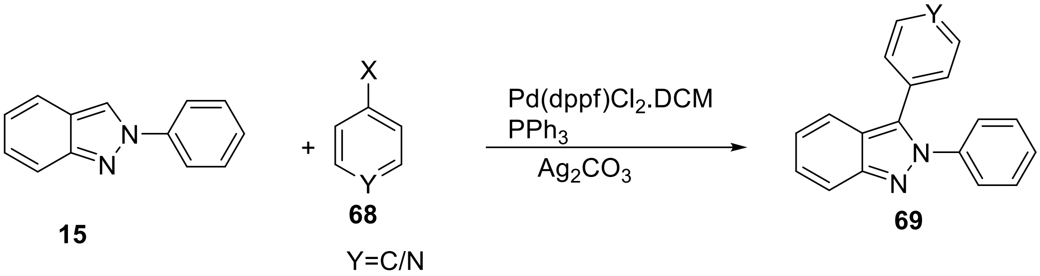
Scheme-35: Synthesis of 2,3-diaryl indazole derivatives

Hazra et al reported selenation at C-3 position of 2-H indazole with diaryldiselnide (**66**) in the presence of catalytic amount of Iodine to provide 3-(phenylselanyl)-2*H*-indazoles[47](**67**). This method offers a wide range of functional groups tolerance with good to excellent yields.



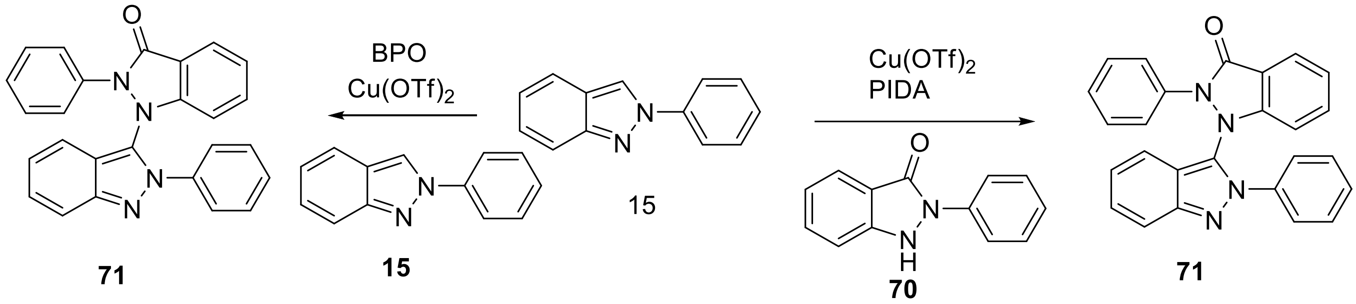
Scheme-36: Synthesis of 3-selenyl-2-aryl indazole derivatives

Greaney[48] et al reported arylation with a variety of aryl halides **(68**) in the presence of Pd(dppf)Cl_2/PPh_3 or Pd(dppb)Cl_2/PPh_3 catalyst and Ag_2CO_3 produced good to excellent yields of 2,3-diarylindazoles (**69**) in water.



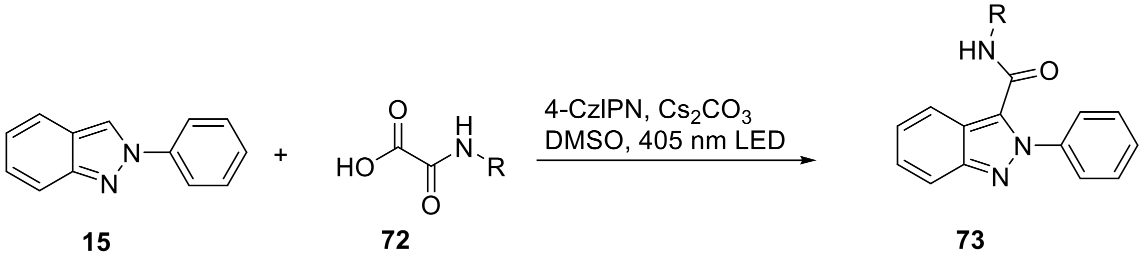
Scheme-37: Synthesis of 3-pyridinyl-2-*aryl* indazole derivatives

A copper-catalyzed C3 amination of 2*H*-indazoles (15) with 2*H*-indazoles and indazol-3(2*H*)-ones (**70**) under mild conditions was developed. A series of indazole-containing indazol-3(2*H*)-one derivatives[49] (**71**) were produced in moderate to excellent yields. The mechanistic studies suggest that the reactions probably proceed through a radical pathway.



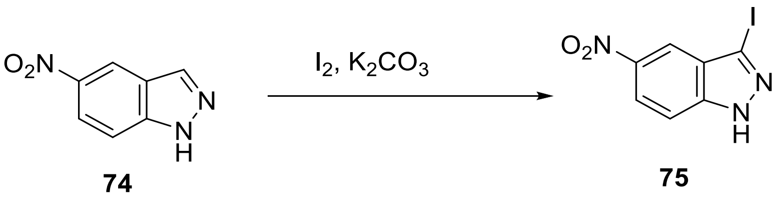
Scheme-38: Synthesis of indazole-containing indazol-3(2*H*)-one derivative

Jiang[50]etal reported the reaction between 2H-Indazole and (2-alkylamino)-2-oxoaceticacid (**72**) in the presence of 4CzlPN as a photocatalyst and 405 nm of blue LED light to afford 3-carbamoylated 2H-Indazole derivative (**73**).



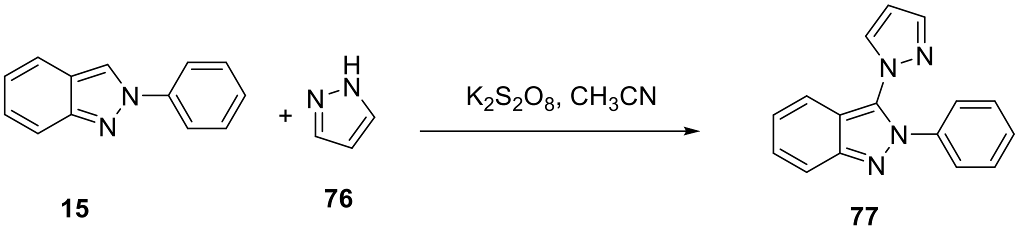
Scheme-39: Synthesis of 3-carbmoyl -2-aryl-indazole derivatives

5-nitro 2H-indazole (74) react with iodine, potassium carbonate in DMF solvent to afford 3-Iodo-5-nitro-2H-indazole (75) reported by the Duan[51] et al in 2020 .



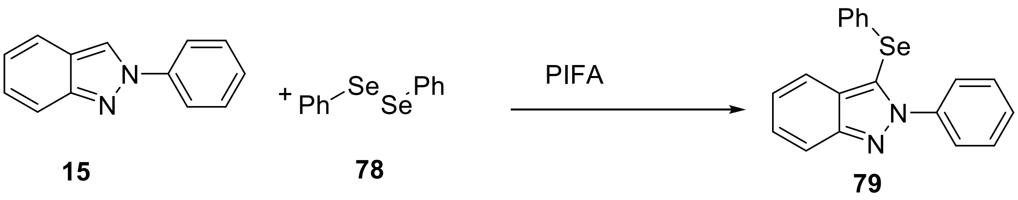
Scheme-40: Synthesis of 3-Iodo-5-nitro-2H-indazole derivatives

C3-Amination of 2-Aryl-2H-Indazole reported by Wang[52] et al 2H-Indazole and pyrazole (**76**) in the presence of potassium persulphate in acetonitrile solvent would provided 3-pyrazole-2H-Indazole (**77**) and Same reaction developed by Sun[53]et al by electrochemically.



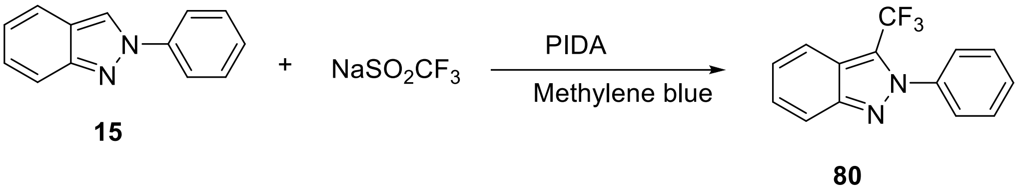
Scheme-41: Synthesis of 3-pyrazole-2H-Indazole derivatives

Song[54] et al reported the synthesis of C3-Selenylation on 2H-Indazole with diphenyldiselenide in the presence of bis(trifluoroacetoxy)iodobenzene (PIFA) in dichloromethane solvent. Same reaction reported by the Saba[55] et al with rosebengal as photo sensitizer and blue LED light.



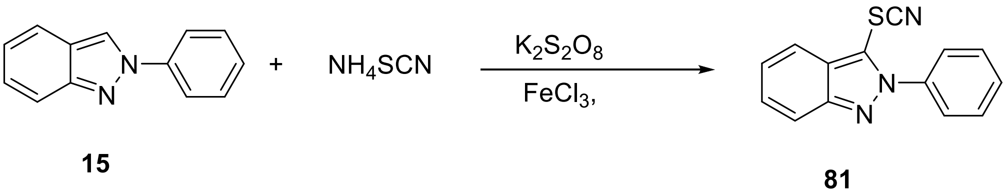
Scheme-42: Synthesis of 3-Selenyl-2H-Indazole derivatives

Sharada[56]et al reported the synthesis of C3-trifluoromethylation on 2H-indazole in the presence of Visible light and phenyliodine(III) diacetate (PIDA) as an oxidant with 2 mol% rosebengal as a photo catalyst to yield a series of C3-trifluoromethylated product.



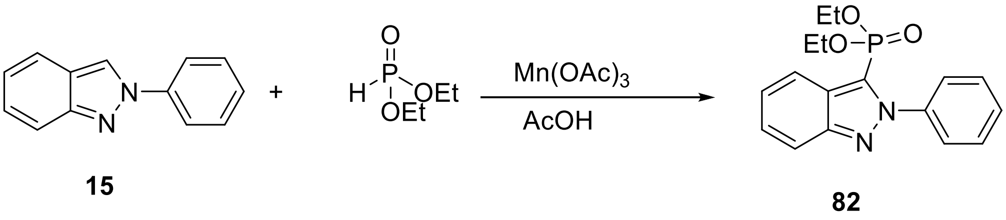
Scheme-43: Synthesis of 3-Trifluoromethyl -2-aryl-indazole derivatives

Thiocyanation on C3-position on 2H-Indazole has been developed by Hazra[57] et al by using potassium persulfate and ammonium thiocyanate in the presence of ferric chloride ($FeCl_3$) catalyst to provide wide range of 2-Aryl-3-thiocyanato-2*H*-indazoles with good to excellent yields.



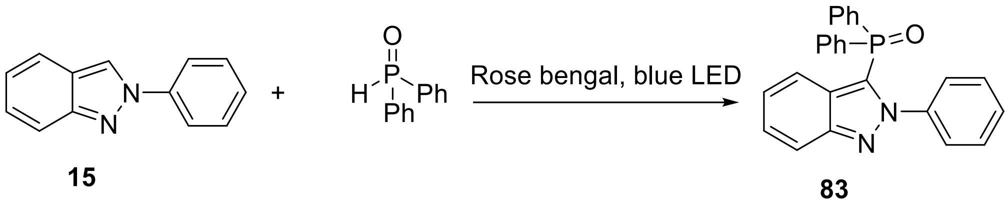
Scheme-44: Synthesis of 3-thiocyano -2-aryl-indazole derivatives

Phosphorylation on C3-position on 2H-indazole has been reported by Hazra[58] et al in the year 2019 the reaction between 2H-Indazole and diethylphosphite in the presence of Manganese (III)acetate $Mn(OAc)_3$ in acetic acid at 80 °C to provide the C3- diethyl (2-phenyl-2*H*-indazol-3-yl) phosphonate. This methodology offers wide range of substrate scope with good to excellent yields.



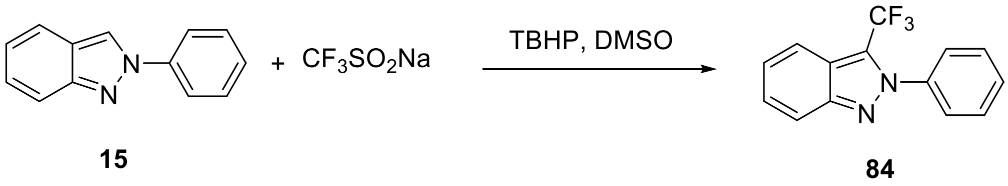
Scheme-45: Synthesis of diethyl (2-phenyl-2*H*-indazol-3-yl)phosphonate

Phosphorylation under photolytic condition on 2H-Indazole has been reported by Hazra[59] et al with diphenylphosphine oxide in the presence of rosebengal photocatalyst in exposure of visible light to yield diphenyl(2-phenyl-2*H*-indazol-3-yl)phosphine oxide with broad functionalities has been synthesized in high yields.



Scheme-46: Synthesis of diphenyl(2-phenyl-2*H*-indazol-3-yl)phosphine oxide

Tert-butyl hydroperoxide-mediated direct trifluoromethylation on 2H- indazoles using sodium trifluoromethanesulfinate has been developed by Hazra**[60]** et al under metal-free conditions to obtain C3-trifluoromethylated products with broad functionalities has been synthesized with moderate to good yields.



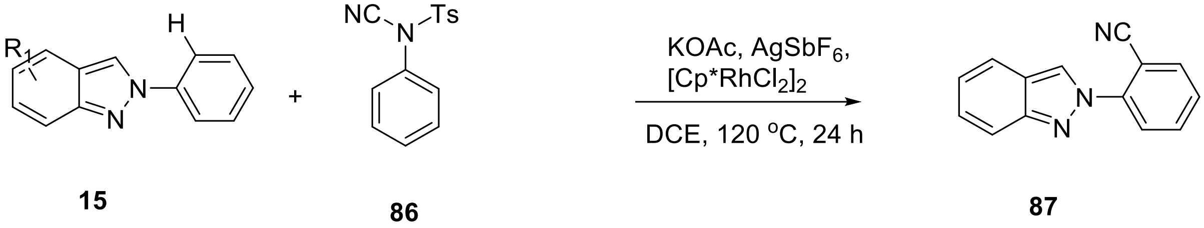
Scheme-47: Synthesis of 3-Trifluoromethyll -2-aryl-indazole derivatives

Johannes[61] et al studied the structure effect of three NH-indazoles (3-methyl, 3-trifluoromethyl and 3-trifluoromethyl-4,5,6,7-tetrafluoroindazoles) have been established by X-ray crystallography.

Lee[62] et al visible light mediated C-3 arylation of 2H-Indazoles from 2H-Indazoles and aryldiazonium salts in the presence of pyridine as shown scheme-48.

Scheme-48: Synthesis of 3-Trifluoromethyll -2-aryl-indazole derivatives

Song [63]et al reported Rh(III) catalyzed direct cyanation 2H-Indazoles rectwith N-Cyano-N-Phenyl –p-toluene sulfonamide via chelation assisted strategy. This methodology offers wide range substrate scope with good to excellent yields.



Scheme-49: Synthesis of 2-(2H-indazol-2-yl)benzonitrile derivatives

Conclusion:

This review highlighted the synthesis of 3-substutied -2-aryl-2H-Indazole derivatives and exploring their activities. Furthermore, it discusses the synthesis and structural modification of 2H-Indazoles and their importance. Moving forward, it advocates future research efforts can be used for the next generation drug discovery will lead to the development of new molecule libraries, which can be screened for their SAR studies will gain much significance in organic chemistry, pharmaceutical chemistry, and material science can only get smoother and more effective in delivering benefits to the society.

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