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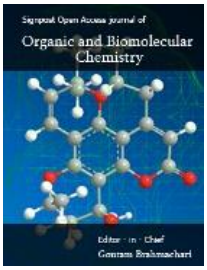

Recent advances in catalysis using transition metals-bounding organic ligands assisted by ultrasound and/or microwave

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Abstract

Usually, in organic and organometallic synthesis an external conventional heat source is applied to carry out a chemical reaction at high temperature. Nonetheless, these conventional heating systems have some disadvantages as the heterogeneous heating causing a low reproducibility of the results and extended reaction times. A promising alternative is the use of microwave (MW) and ultrasound (US) energy. The use of these techniques has led to considerable advantages as better homogeneity in temperature and very short reaction time. By virtue of the effects mentioned above, the MW and US irradiation constitutes a convenient way to accelerate and improve a great number of organic and organometallic reactions. In this paper, we have compiled an overview developed during the last decade in the synthesis of such catalysts and organic transformations assisted by both techniques mentioned above.

Keywords

Organocatalysis, Metal catalysis, Organic Synthesis, Ionic Liquids, Microwave, Ultrasound

Introduction

Organocatalysis is nowadays an area of fast growth in organic chemistry research. The interest in organocatalysis lies on its capability to produce metal-free compounds, to be used for several applications and resolution of stereochemical problems [1-4]. Miao *et al.* [1] have indicated that the ring-opening polymerization of cyclic esters constitutes an especial field of interest on this topic. Aditionally, the organocatalysis is applied for asymmetric synthesis, complementing bio and metal catalysis [5]. Various transformations can be promoted through a unique activation mode by organocatalysis as valuable tools of organic synthesis [6]. Organocatalysts are essentially organic molecules, composed of mainly carbon, hydrogen, nitrogen, oxygen, sulfur, and phosphorus [5]. In 2007, List [7] reported in his review four types of organocatalysts: Lewis bases and acids and Brønsted bases and acids. Chiral organic molecules can be selective and efficient organocatalysts. They offers many advantages i.e. they do not require special reaction vessels, inert atmosphere, air-sensitive reagents, moisture-sensitive Lewis acids, nor toxic metals [2,4].

During the last decade, several authors among which are Xiao [8], Bihelovic *et al.* [9], Yu and co-workers [10] and Zhong and Shi [11] have coincided in pointing out the merged concept of organocatalysis and transition metal catalysis. This synergic combination has emerged as a promising strategy to reveal new reactions currently not viable. Early work on the issue was reported in 2000 by List and co-workers [12] and Ahrendt *et al.* [13]. The first review on this topic appeared in 2009 [14]. The combination of transition-metal catalysts (Pd, Rh, Ru, Cu, Ni, Zn, Fe, Ir, Co, Mn, Ti, Y, In, Nb, Au, Ag, Pt, V) and organocatalysts has attracted much interest as a new approach for valuable reactions and stereocontrol of current chemical transformations [15,16]. One of the main advantages of combining organo- and transition metal catalysis is that potentially unprecedented transformations could now take place [14]. According to Hack et al. [17], the combination is especially attractive because the reaction can be carried out as a one-pot procedure, and purification of the intermediates can be avoided in accordance with the green chemistry principles.

In the last few years, several authors have demonstrated the usefulness of ionic liquids (ILs) as convenient organocatalysts for specific reactions. The interesting properties of ionic liquids (high stability, non-flammability, low volatility), make them promising compounds in catalysis area [18-25]. Lucchini et al. [26] reported a cooperative and independent action as nucleophilic and electrophilic catalysts by anionic and cationic partners of ionic liquids.

In the same direction, Qiao and Headley [27] have proposed immobilized ionic liquid as organocatalysts due to be recyclable catalysts, flexible compounds, effective for numerous reactions, and also environmentally friendly. Wong *et al.* [28] have evaluated the dual role of new ionic liquids as solvents and organocatalysts. These ILs can be recycled and reused continuously without losses in catalytic activity.

A new emerging field in organocatalysis is through the usage of polysaccharide substructures such as chitosan and its derivatives. Chitosan can act as green organocatalyst due to its free primary amino groups which have, among others, the hability of coordinate transition metals [29-32].

Usually, in organic synthesis an external heat source as an oil bath [33] or heating mantles [34] is applied to a chemical reaction, in order to carry out transformations, generally, at higher temperature than room temperature. Nonetheless, this conventional heating system has some disadvantages as the heat transfer itself, since it is relatively slow, inefficient [35] and dependent on thermal conductivity of the materials, specific heat, and density, resulting in higher surficial temperatures, causing heat transfer from the outer surface to the internal core (heterogeneous heating) [35-37]. In addition, according to de la Hoz *et al.* [38] and other authors as Sajjadi et al. [39] the heating proceeds by a conduction-convection mechanism. A promising alternative as a heat source in organic synthesis is the use of microwave (MW) and ultrasound (US).

The use of MW as energy source has often led to considerable advantages as i) very fast heating, ii) better homogeneity in temperature and iii) very short reaction time from days or hours to minutes or seconds [36]. This is due to the interaction of dielectric materials with microwaves. The heating involves primarily two mechanisms: dipolar polarization and ionic conduction.

a) The dipolar polarization is caused by dipole–dipole interactions between the electromagnetic field and polar molecules producing heat generation [38-40].
b) The ionic conduction affects charged particles in a sample, usually ions. This phenomenon is due to the interaction of oscillating electric field with charged species. In this case the microwave irradiation moves the ions back and forth through the sample (colliding with each other) and generates heat. These mechanisms contribute to localize superheating resulting in high temperature gradients. At the same time, the probability of molecular encounters increases by accelerating the molecular/ionic movement which leads to increased reaction rates [41].

The first investigations in microwave-assisted organic synthesis were conducted in 1986 by the research groups of Gedye et al. [42] and Giguère *et al.* [43]. However, effects of high power US, as alternative heating source, have been studied since 1927, as can be seen in the work of Richards and Loomis [44] where they developed the hydrolysis of dimethyl sulfate with iodine as a catalyst.

The use of ultrasound in chemistry is called sonochemistry because it improves or modifies the chemical reactions and in some cases enables reactions that cannot be performed under conventional heating methods. These effects may be due to i) the formation of free radicals that accelerate the reaction, ii) the increase in contact area between the reactants to accelerate dissolution or the surface renewal of a solid reactant or a catalyst [45-47].

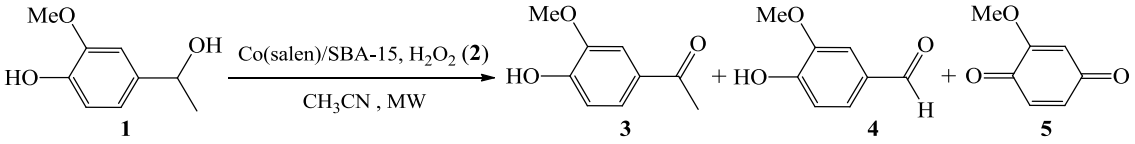
The effects observed in organic reactions are due to cavitation, a physical process to create, expand and implode gaseous and vaporous cavities in an irradiated liquid. Cavitation induces very high local temperatures (4500–5000 K) and pressure (1700 atm) inside the bubbles (cavities) [48-50].

This review covers the years 2004-2015. It provides an overview of the latest works in organocatalysis assisted by microwave and ultrasound, including new trends combining organocatalysis with transition metals and the use of ecological organocatalysts such as chitosan.

2.1 Combining transition metal catalysis and organocatalysis

2.1.1. Cobalt

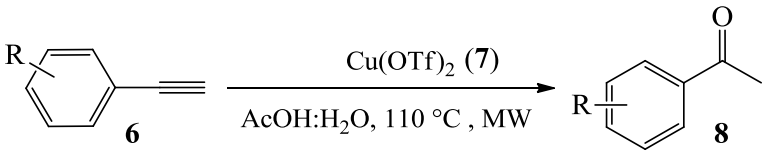
Badamali *et al.* [51] studied the microwave assisted oxidative degradation of a lignin model phenolic monomer, 1-(4-hydroxy-3-methoxyphenoxy)-ethanol (**1**), catalysed by Co(salen)/SBA-15 (**2**) in the presence of hydrogen peroxide as oxidant (**Scheme 1**). The complete degradation of **1** was obtained after 40 min of reaction under microwave irradiation, compared to a poor 57% degradation after 24 h under conventional heating.



Scheme 1. Oxidative degradation of apocynol

2.1.2. Copper

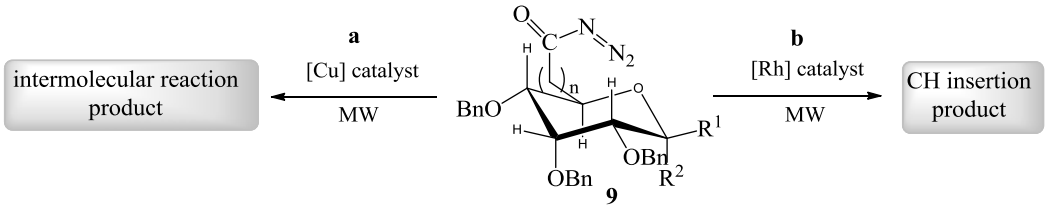
Jha *et al.* [52] reported the first example of microwave-assisted hydration of terminal aryl acetylenes (**6**) in the presence of $Cu(OTf)_2$ (**7**) as catalyst, in aqueous acetic acid (**Scheme 2**). The methodology can be regarded as an efficient, economical, and safer alternative for the catalytic hydration of **6**. Furthermore, the method offers shorter reaction time, wide range of functional group tolerance and low catalyst loading (2.5 mol %). The electron-donor groups facilitated the reaction (60–86%), while the electron-acceptor substituents decreased the reaction yield (38-40%).



R= H, *p*-Me, m-Me, *p*-Et, *p*-^{t}Bu, *p*-OMe, *p*-OPh, *m*-NH_2, *p*-F, *p*-OCOMe, *p*-CHO, 2,4,6-$(Me)_3$, 3,4-$(OMe)_2$, 3,4,5-$(OMe)_3$

Scheme 2. Hydration of aryl acetylenes

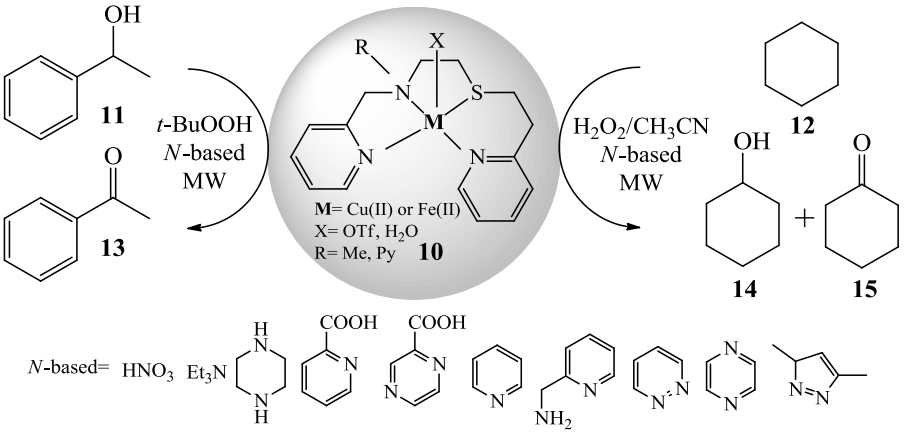
Guan *et al.* [53] have investigated the conversion of diazocarbonyl carbohydrate compounds (**9**) catalyzed by a series of rhodium and copper catalysts, using microwave techniques. Intermolecular reactions rather than intramolecular reactions occurred in the presence of catalysts such as Cu(tfacac)$_2$-CH_3OH (60-66% yield) and Cu(acac)$_2$-CH_3OH (62-76% yield) (**Scheme 3a**). C-H insertion product was obtained in the presence of $Rh_2(OAc)_4$ in 59% yield (**Scheme 3b**). It is noteworthy that the formation of a C–H insertion product provides a novel method for constructing bicyclic ether rings from carbohydrates, and the dimer formation is interesting since it might be applied to connect sugar residues in an oligosaccharide.



R^1= H, SPhMe; R^2= H, OMe n= 0,1

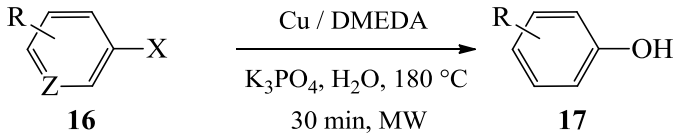
Scheme 3. Conversion of diazocarbonyl carbohydrate compounds

Fernandes *et al.* [54] have been synthesized a series of copper(II) and iron(II) complexes (**10**), bearing bis- and tris-pyridyl amino and imino thioether ligands (**Scheme 4**). In the presence of various, simple and inexpensive, *N*-based additives showed a very good catalytic activity for the solvent- and halogen-free microwave-assisted oxidation of 1-phenylethanol (**11**) by *t*-BuOOH or cyclohexane (**12**) by H_2O_2 in short reaction time. Also, the effects of various factors, such as nature and amount of the additives and metal (Cu or Fe), temperature, time and type of peroxide used, were also investigated. Is remarkable that the reactions require a small catalyst load (0.2-0.05 mol%) and mild temperatures (50-80 °C). For example, Fe(OTf)$_2$(LMe) catalyst in the presence of 2-pyrazinecarboxylic acids as an additive, under solvent-free and MW-assisted oxidation of 1-phenylethanol by t-BuOOH, yields acetophenone in 74%. Moreover, Cu(OTf)(LMe)](OTf) with pyridazine gives acetophenone in 99% yield, for 30 min.



Scheme 4. Bis- and tris-pyridyl amino and imino thioether Cu(II) and Fe(II) complexes

Mehmood and Leadbeater [55] reported a microwave-assisted method for direct preparation of phenols (**17**) from aryl halides (**16**). A simple catalyst system comprising copper and *N*,*N*′-dimethylethylenediamine (DMEDA) ligand is used, together with K_3PO_4 as the base in aqueous medium (**Scheme 5**). Heating at 180 °C for 30 min allows for the conversion of a range of **16** to the corresponding **17**, in 96% yield. It is notable that aryl chlorides are less reactive and thiophene-derived substrates form a catalytically inactive complex with copper and are therefore incompatible with this methodology.

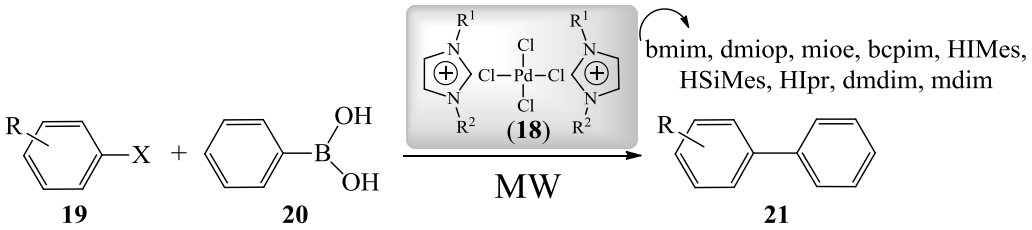


R= *o*-OMe, *p*-OMe, *p*-Me, *p*-COMe, *p*-NO_2, *p*-CN
X= Cl, Br, I
Z= C, N

Scheme 5. Phenols from aryl halides

2.1.3. Palladium

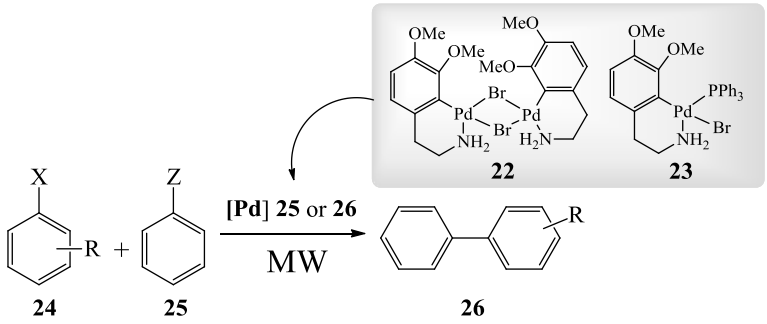
Silarska *et al.* [56] found that Palladium complexes of the type $(IL)_2PdCl_4$ (IL= imidazolium cation) (**18**) were very active catalysts for the Suzuki-Miyaura reaction of aryl halides (**19**) with phenylboronic acid (**20**) in *iso*-propanol or *iso*-propanol:water at 40°C using microwave heating (**Scheme 6**). The obtained results with *iso*-propanol/water mixture, under microwave heating (30 min) increased to 80–90% yields compared to *iso*-propanol only. The formation of Pd(0) nanoparticles, during the catalytic reaction, was evidenced by TEM. Also, mechanistic studies, including Hg(0) tests, showed that Pd(0) nanoparticles acted as a source of catalytically active soluble palladium species.



X= Cl, Br, I
R=H, *o*-Me, *p*-OMe, *o*-Me, *p*-Me, *p*-CHO, *o*-NO_2, *p*-NO_2

Scheme 6. $(IL)_2PdCl_4$ as catalyst for Suzuki-Miyaura reaction

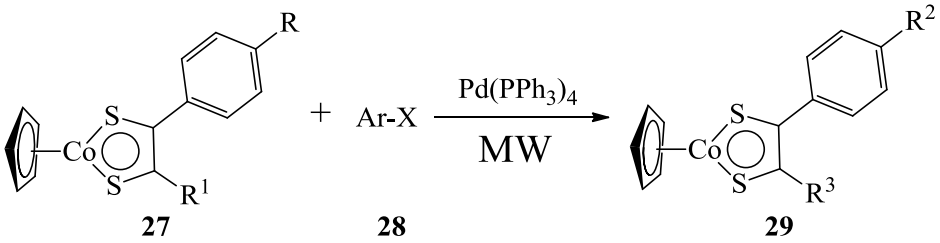
Hajipour and Rafiee [57] have investigated the catalytic activity of dimeric (**22**) and monomeric (**23**) palladium complexes in Stille and Hiyama cross-coupling reactions of various aryl halides (**24**) (**Scheme 7**). The combination of homogenous metal catalyst and microwave irradiation gave high yields of products in short reaction times. By the same operational conditions of solvent (DMF), additive (K_2CO_3), catalyst loading (0.3 mol %), temperature (90 ºC) and power (500 W) using catalyst (**22**) gave lesser yield (88%) than using catalyst (**23**) (97%). Stille reaction of aryl halides using ortho-palladated catalyst (**23**) under microwave irradiation (1-12 min) at 90 ºC and 500 W, gave yields ranging from 66 to 96%. Using KF, NaF, or CsF instead of TBAF as the additive in Hiyama reaction - catalyst (**23**) - under microwave irradiation (600 W, 5 min) variable yields from 40 to 85% were obtained. The best yield (100%) was obtained with DMF as the solvent, $TBAF.3H_2O$ as the promoter, and 0.4 mol % of catalyst loading (**23**).



X= Cl, Br, I
R= H, *p*-NO_2, *m*-NO_2, *p*-OMe, *p*-CN, *p*-CHO, *p*-COMe, *m*-COMe, *o*-COMe, *p*-Cl, *o*-Cl
Z= $Sn(Bu)_3$, $Si(OEt)_3$

Scheme 7. Di and monomeric [Pd] complexes in cross coupling reaction

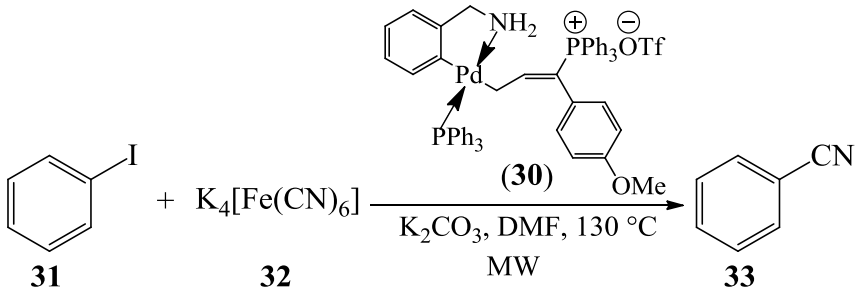
Nomura *et al.* [58] studied the Pd-catalyzed boronations and cross-coupling reactions of the aromatic cobaltadithiolene complexes (**27**) (**Scheme 8**). The microwave-assisted reaction gave better yield with shorter reaction time than that of the conventional heating reaction (e.g. conventional 33%, 18h/MW 62%, 10 min). Furthermore, one possible application of cross-coupling products, for example the complex with a phenyl-pyridyl group, may undergo a cyclometallation toward a luminescent Ir or Pt complex.



R= R^2= H, R^1= Bpin, R^3= Ar Ar= 3-Py, 9-Anth, 1-Np, 2-Th
R^1= R^3= H, R= Bpin, R^2= Ar X= Br, I

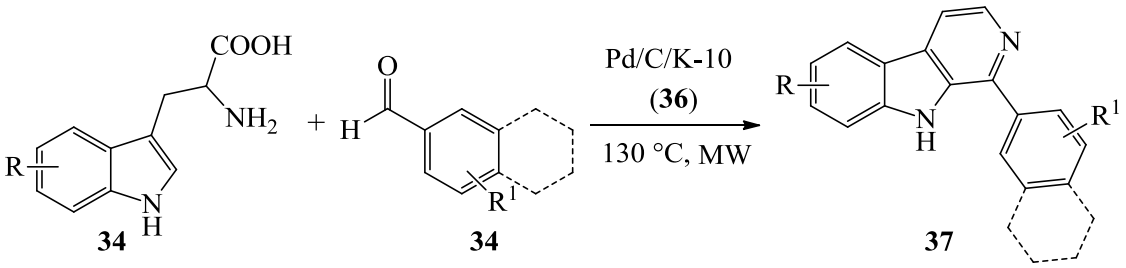
Scheme 8. Suzuki cross-coupling of aromatic cobaltadithiolene complexes

Hajipour *et al.* [59] have synthesized a new palladium-based catalyst (**30**) to be applied in the cyanation reaction of aryl halides (**31**) using $K_4[Fe(CN)_6]$ (**32**) as a source of cyanide. Organic synthesis performed under microwave irradiation in DMF at 130 °C led to a reduction in the reaction time from hours to minutes (**Scheme 9).** The cyanation of iodobenzene was optimized for catalyst concentration (2.5 mol %) in the presence of K_2CO_3 as base, in DMF as solvent and $K_4[Fe(CN)_6]$ as cyanating reagent, under microwave irradiation at 130 ºC. The highest yield was 95%.



Scheme 9. Pd-based catalyst for cyanation reaction

Kulkarni *et al.* [60] have developed a simple and effective three-step one-pot method for the synthesis of β-carbolines (**37**) from tryptamines (**34**) and aromatic aldehydes (**35**) or glyoxals using a bifunctional catalyst (Pd/C/K-10) (**36**) combined with microwave irradiation (**Scheme 10**). From the environmental point of view, the process is very attractive for the benign synthesis of important heterocycles with excellent selectivities and yields (93%) in short reaction time (45min) at 130 ºC.

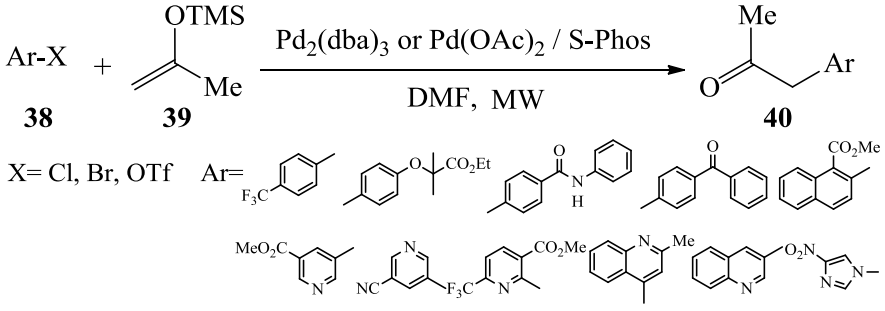


R= H, 5-F, 5-OMe
R^1= H, 4-Me, 4-F

Scheme 10. Synthesis of β-carbolines using Pd/C/K-10

Shore *et al.* [61] have devised a method for the preparation of indole alkaloids by a two-step aryl amination/cross-coupling sequence of bromoalkenes and 2-bromoanilines by microwave-assistance. This process requires both the presence of a metal-lined flow tube and the Pd PEPPSI-IPr (PEPPSI: pyridine, enhanced, precatalyst, preparation, stabilization, and initiation) catalyst. The optimal conditions were flow rate: 15 $Lmin^{-1}$, 75 psi back pressure, 22 W, tempeture: 205 ºC, Pd-coated 1180 mm ID capillary with 81% yield.

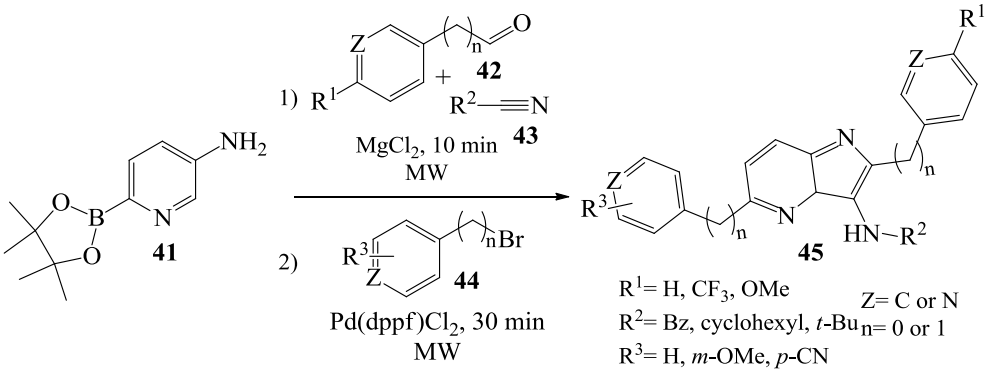
Chobanian *et al.* [62] reported an expedient method for the heteroarylation of acetone (**40**) under tin-free conditions (**Scheme 11**). The cross-coupling was performed using the commercially available 2-trimethylsilyloxypropene (**39**) and a corresponding aryl halide or triflate (**38**) under microwave-assisted conditions, with palladium and 2-(2′,6′-dimethoxybiphenyl) dicyclohexylphosphine (S-Phos) as the catalyst system. It is noteworthy that the microwave irradiation has shortened reaction times from an average of 2-14 h to 15 min. The reaction between 4-bromoisoquinoline and 2-trimethylsilyloxypropene using ZnF_2 as the fluoride source, under microwave assistance at 150 (ºC) 15 min with S-Phos ligand and $Pd_2(dba)_3$ as palladium source in presence of DMF showed an excellent yield (86%).



Scheme 11. Heteroarylation under tin-free condition

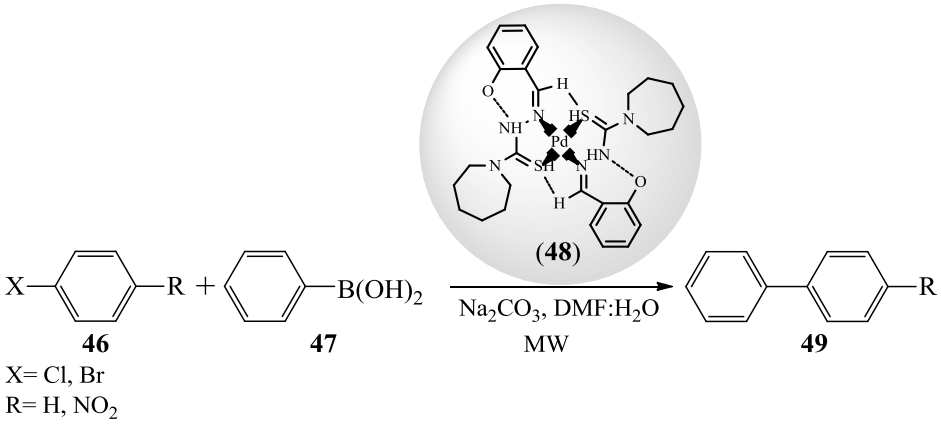
DiMauro and Kennedy [63] have demonstrated a rapid and efficient synthesis of various 2,6-disubstituted-3-amino-imidazopyridines (**45**) from 2-aminopyridine-5-boronic acid pinacol ester (**41**)

using a one-pot cyclization/Suzuki coupling microwave-assisted reaction (**Scheme 12**), in the presence of Pd(dppf)Cl_2 as catalyst in 65% yield. It is important to mention that the boronate functional group is remarkably tolerant to the Lewis acid catalyzed cyclizations, and the subsequent Pd(0) cross-coupling reactions proceeded cleanly in the presence of magnesium salts.



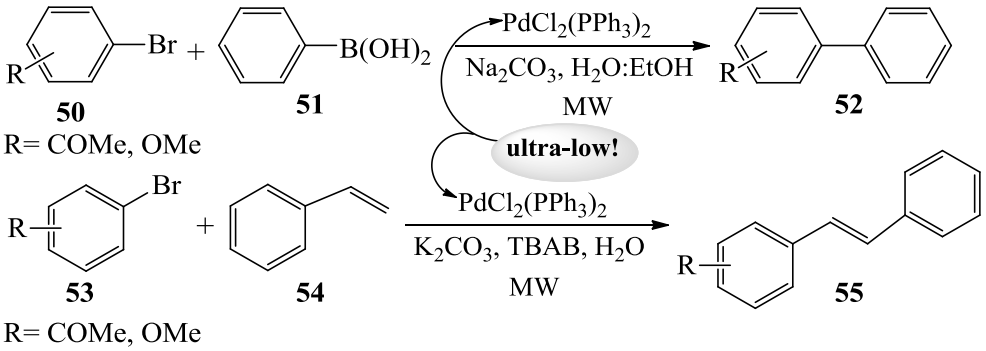
Scheme 12. Synthesis of 2,6-disubstituted-3-amino-imidazopyridines

Kostas *et al.* [64] have synthesized an air- and moisture-stable palladium complex with salicylaldehyde N(4) hexamethyleneiminylthiosemi carbazone (**48**) (**Scheme 13**). In contrast to other palladium complexes with thiosemicarbazones, reported by the same research group [65], this complex was inactive in the Suzuki-Miyaura cross-coupling under aerobic conditions and conventional heating. However, microwave irradiation promoted the effective catalytic activity of the complex for the coupling of aryl halides (**46**) with phenylboronic acid (**47**), under aerobic conditions, with turnover numbers of up to 37,000. Microwave-promoted Suzuki–Miyaura cross-coupling of aryl halides with phenylboronic acid catalyzed by palladium complex (**48**), in air during 60 min gave 85% yield.



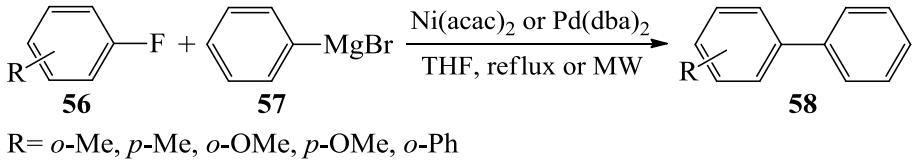
Scheme 13. [Pd] thiosemicarbazones as catalyst in Suzuki-Miyaura coupling

Arvela *et al.* [66] have used an automated batch stop-flow microwave apparatus to study a representative Suzuki and Heck couplings in water using ultra-low catalyst concentrations (250 ppb, 99% yield and 5 ppm, 92% yield , respectively) . (**Scheme 14)**



Scheme 14. Suzuki and Heck couplings using ultra-low [Pd] concentration

By the same time, Arvela [67] showed that the Heck couplings can be performed in water using microwave-assistance and palladium as catalyst in concentrations as low as 500 ppb, giving the desired product in 80% yield. Dankwardt *et al.* [68] have reported the first example of biaryl cross-coupling using unactivated aryl fluorides (**56**) in the presence of palladium (64% yield) or nickel (93% yield) as catalyst under microwave irradiation as heating system (**Scheme 15**).

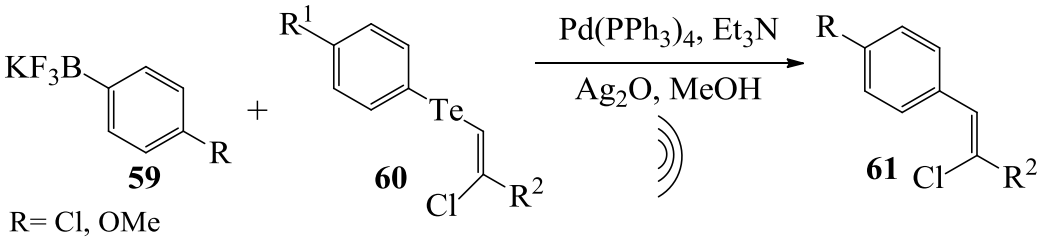


Scheme 15. Biaryl compounds using aryl fluorides

A palladium-catalyzed cross-coupling Suzuki-Miyaura reaction of potassium aryltrifluoroborate salts (**59**) and (*Z*)-butyl(2-chlorovinyl) tellurides (**60**) was also developed with good yields by ultrasound assistance in 2008 by Guadagnin *et al*. [69]. Various palladium catalyst ($PdCl_2$, $Pd(acac)_2$, $Pd_2(dba)_3$, $Pd(AcO)_2$, $PdCl_2(dppf)\cdot CH_2Cl_2$, $Pd(PPh_3)_4$) with diverse combinations of additive, bases, and solvents were tested to come across the best reaction conditions.

The chemoselectivity of the cross-coupling reactions of vinylic chlorides with sterically demanding groups is illustrated by the reaction of **60** containing two electrophilic centers, C-2 connected with a chloro atom and C-1 having aryl/butyltellurium groups (**Scheme 16**). Only tellurium moiety takes part in the cross-coupling reaction and chloro atom remain intact, indicating that tellurium moiety can be a good electrophile different to the usual halides in Suzuki–Miyaura reaction. The reaction product

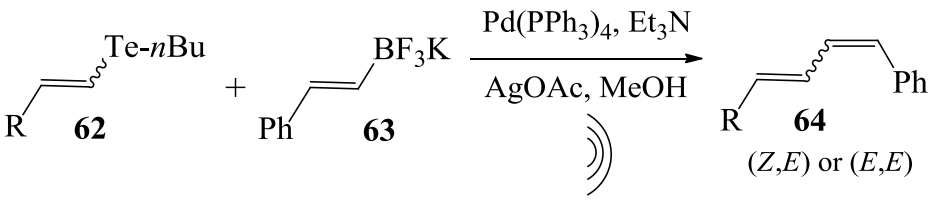
was obtained in 60% isolated yield, for 30 min in ultrasound bath, $Pd(PPh_3)_4$ as catalyst, AgOAc was used as additive, K_2CO_3 as base, and methanol as solvent.



R= Cl, OMe
R^1= *n*-Bu, Ph, *p*-OMePh
R^2= *n*-Pr, *n*-Pentane, *t*-Bu, Ph, CH_2-OMe, vinyl

Scheme 16. Chlorovinyl tellurides for Suzuki–Miyaura reaction

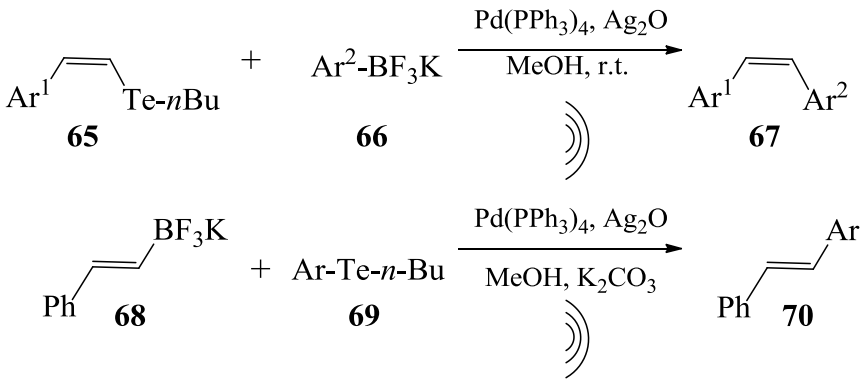
Singh *et al*. [70] carried out a palladium-catalyzed cross-coupling Suzuki-Miyaura reaction of α-styrylbutyltellurides (**62**) and potassium alkynyltrifluoroborate salts (**63**) easily accessible, as an alternative of unstable organoboronic acids. They use ultrasound energy to synthesize functionalized 1,3-enyne scaffolds (**64**), containing aliphatic and aromatic groups, in good to excellent yields (**Scheme 17**). Formerly, a wide variety of stereodefined 1,3-dienes were synthesized by ultrasound assistance *via* Suzuki-Miyaura cross-coupling palladium-catalyzed reactions of vinylic tellurides and potassium β-styryl trifluoroborate salt [71]. The products were obtained in a gentle, rapid, chemoselective procedure and in reasonable yields. The catalyst loadings were evaluated and the best result was with 10 mol% $Pd(PPh_3)_4$ (79% yield).



R= phenyl, naphthyl, alkyl, alkenyl, hydroxy

Scheme 17. Synthesis of stereodefined 1,3-dienes

By 2006, stilbenes and derivative compounds were prepared in good yields by an efficient ultrasound-assisted method. Cella and Stefani [72] reported the synthesis of Z (**67**) and E (**70**) stilbene compounds by the palladium(0)-catalyzed cross-coupling reaction of aryl- (**69**) and vinyl- (**65**) tellurides and potassium aryl- (**66**) and vinyl-trifluoroborate (**68**) salts (**Scheme 18**).

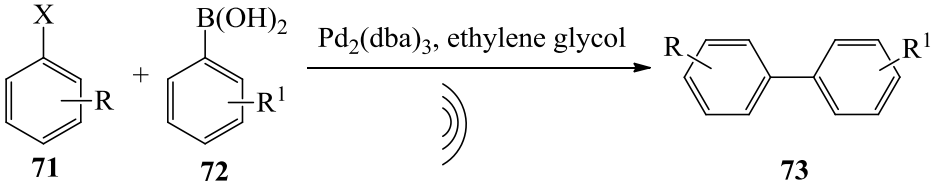


Ar= Ph, Naphthyl, *p*-OMePh, *p*-MePh, *o*-MePh, *p*-OAcPh, *p*-ClPh, *p*-BrPh, *p*-IPh, Py, 2-furanyl
Ar^1= Ph, *p*-MePh, *p*-BrPh
Ar^2= Ph, naphthyl, *p*-OMePh, *o*-OMePh,Py, 2-furanyl

Scheme 18. Synthesis of stilbenes by [Pd] cross-coupling

The best result (82% yield) was attained when 8 mol % of catalyst was employed. At reflux temperature, using magnetic stirring, it was necessary an extended time reaction (18 h). The product *Z*-stilbene was obtained in 63% yield. Many starting materials remained after 24 h if the reaction was developed at room temperature. One characteristic of this method was the tolerance of functional groups in both substrates. The Suzuki–Miyaura cross-coupling reaction was chemoselective. Aryl tellurides were more reactive than aryl halides under these conditions. BuTe>I>Br≥OTf>>Cl was the general reactivity order for Suzuki cross-coupling

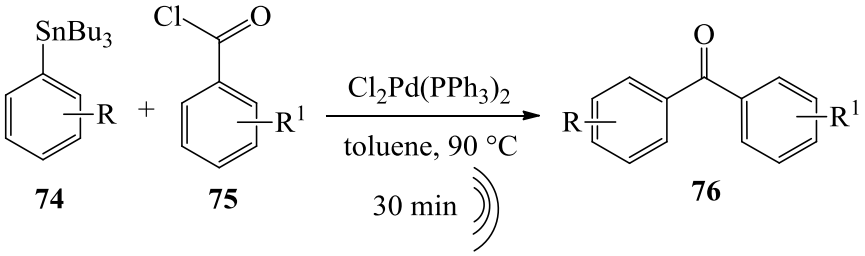
In 2007 Silva *et al*. [73] reported a Suzuki cross-coupling reaction to synthesize biaryls (**73**) (**Scheme 19**). The reaction was carried out in ethylene glycol, an eco-friendly solvent, under phosphine-free conditions with ultrasonic irradiation (thermostated ultrasonic cleaning bath, 47 kHz). The reaction media using $Pd_2(dba)_3$ 2.5% mol as palladium source, tetrabuthylammonium bromide (TBAB 5% mol) as additive and K_2CO_3 gave good to excellent yields (55-100%). The catalyst was cheap and recycled up to three times with good activity in the first and second run.



X= Br, I
R= H, Ac
R^1= H, *p*-F

Scheme 19. Synthesis of biaryls under phosphine-free condition

A series of diaryl ketones (**76**) were synthesized by Luong *et al.* [74] in moderate to excellent yields (30-96%) through the selective cross-coupling reaction of arylstannanes (**74**) with benzoyl chlorides (**75**) using a sonochemical adaptation of the Stille reaction. The scope of the protocol was explored with a variety of arylstannanes and different aroyl chlorides as reaction partners (**Scheme 20**). The ultrasound-promoted cross-coupling reaction was optimized through experimental design.

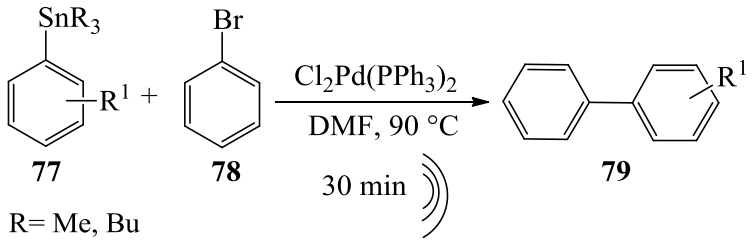


74 **75** **76**

R= *o*-OMe, *m*-OMe, *p*-OMe, *m*-Me, *p*-Me, *m*-Cl, 2,4,6-Me
R^1= *p*-OMe, *p*-Cl, *p*-NO_2

Scheme 20. Synthesis of ketones *via* Stille reaction

Formerly, working in the same research group, Domini *et al.* [75] developed an efficient method for the synthesis of unsymmetrically-substituted biphenyls (**79**) using a sonochemical variation of the Stille coupling, whose results have also been compared with the conventional silent reaction (**Scheme 21**). The possibilities of the reaction were investigated with a selection of arylstannanes (**77**) as precursors. Ultrasound considerably enhanced these organometallic transformations affording the desired products in higher yield (97%) and shorter reaction times than conventional reactions. Remarkably, no by-products resulting from homo-coupling could be detected.



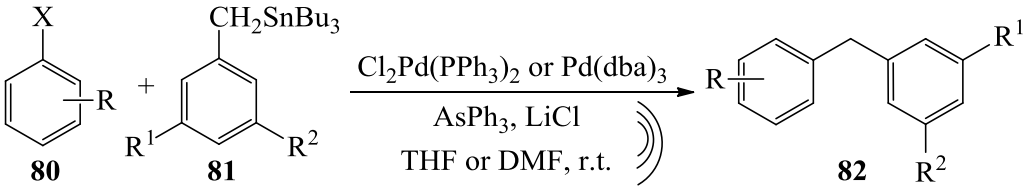
77 **78** **79**

R= Me, Bu
R^1= *o*-OMe, *m*-OMe, *p*-OMe, *m*-Me, *m*-Cl

Scheme 21. Unsymmetrical-biphenyls *via* Stille cross-coupling

Ocampo *et al.* [76] reported the preparation of a variety of diarylmethanes (**82**) obtained *via* ultrasound Stille coupling (**Scheme 22**). The reaction preceded under Pd catalysis between some substituted aryl compounds (**80**) and benzyltributyltin compounds (**81**) generated through sonicated Barbier reaction in a very short time and excellent yield (60-90%). The study compared

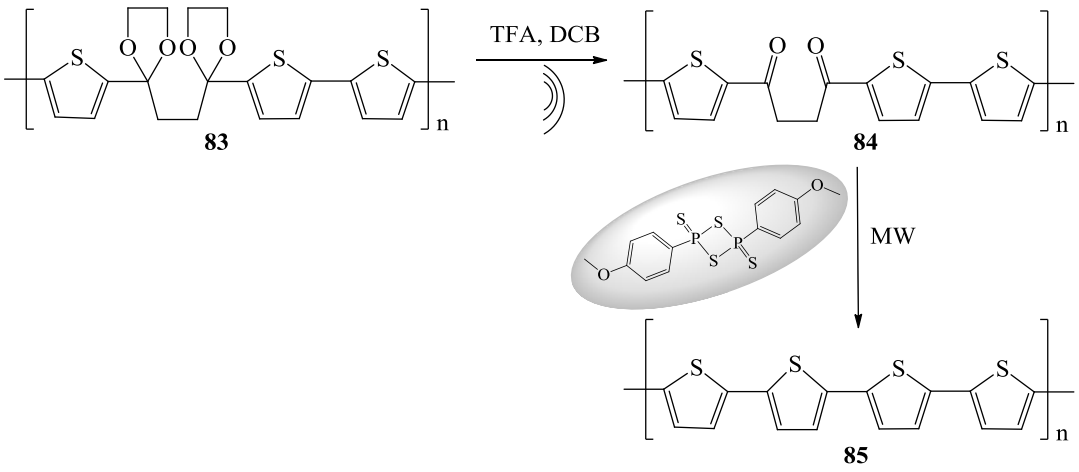
different methods to optimize the synthesis of usually unstable benzyltin derivatives. Substituted carboxylated benzophenones were easily prepared in a very good yield by oxidation of some diarylmethanes.



X= Br, I
R= H, *o*-OMe, *m*-OMe, *p*-OMe, *o*-Me, *m*-Me, *p*-Me
R^1=R^2= H, OMe

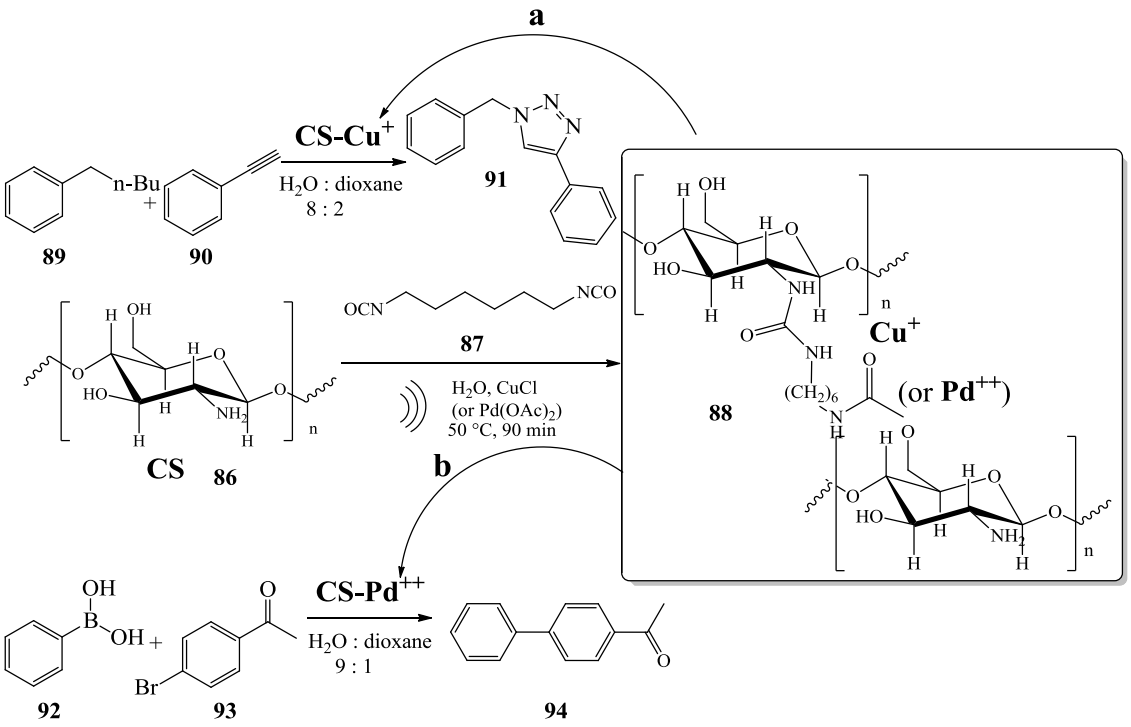
Scheme 22. Synthesis of diarylmethanes *via* Stille coupling

Unsubstituted polythiophene (PT) (**85**) with defined and known high molecular mass (up to ca. 36000 g/mol) and low structural defects (ca. 3.6 mol %) as highly attractive semiconducting material is presented by Chen *et al.* [77] (**Scheme 23**). The new synthetic strategy for this polymer is based on the combination of Stille-type polycondensation reactions, ultrasound-assisted dispersion technique, and microwave-assisted ring-closure reactions. The use of Stille-type polycondensation produces a diketal prepolymer (**84**) with good solubility and prescient and controllable degree of polymerization (DP) for the final insoluble PT. Ultrasonication preserves a high interfacial area, while microwave provides fast and effective heating for the last heterophase ring-closure reaction.



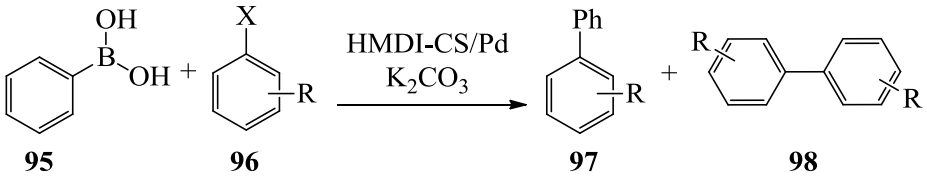
Scheme 23. Synthesis strategy for PT polymer

Martina *et al.* [78] described in 2011 the sonochemical preparation of solid cross-linked chitosan (CS, **86**) derivates CS-Cu(I) and CS-Pd(II) complexes (**88**). The mixture of **86** in HCl at 60 °C with a solution of $Pd(OAc)_2$ or CuCl in 0.1N HCl was stirred and sonicated. Afterwards hexamethylene diisocyanate (**87**) was poured and sonicated during 90 min at 60 W, 50 °C. Also an alternative procedure using hexamethylene 1,6-di(aminocarboxy-sulfonate) was conducted to obtain the polyurethane/urea-bridged CS-Cu and CS-Pd complexes, which are easier to prepare with higher activity and recyclability compared to the adsorbed Cu or Pd/chitosan catalysts. The solid cross-linked CS–Cu(I) or Pd(II) complexes were characterized by FT-IR, XPS, ICP-MS and TGA. The cross-linked CS–Cu(I) catalyst was applied in the Huisgen cycloaddition (Cu-catalyzed azide/alkyne [3+2] cycloaddition, CuAAC) and gave the desired products in yields from 86 to 95% (**Scheme 24 a**), while the cross-linked CS–Pd(II) catalyst was used for Suzuki cross-coupling reactions under thermal conditions (98%, 4h) and microwave irradiation (92%, 1h) (**Scheme 24 b**).



Scheme 24. Chitosan derivatives of Cu(I) and Pd (II)

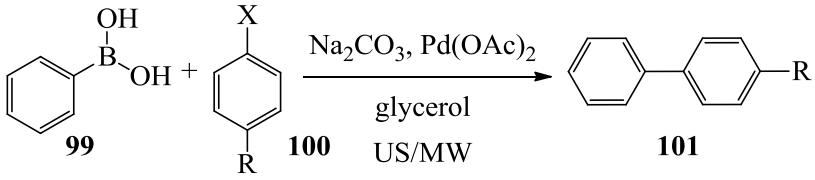
Additionally, Cravotto *et al.* [79] reported a novel protocol for Suzuki cross-couplings using a hexamethylene diisocyanate (HMDI) cross-linked CS/Pd-derivative as recyclable catalyst, prepared in water *via* sonochemical (**Scheme 25**).



X= I, Br, Cl
R= H, *o*-Ac, *m*-Ac, *p*-Ac, *p*-OMe, *m*-OH, *p*-NO_2

Scheme 25. HMDI-CS/Pd in Suzuki reaction

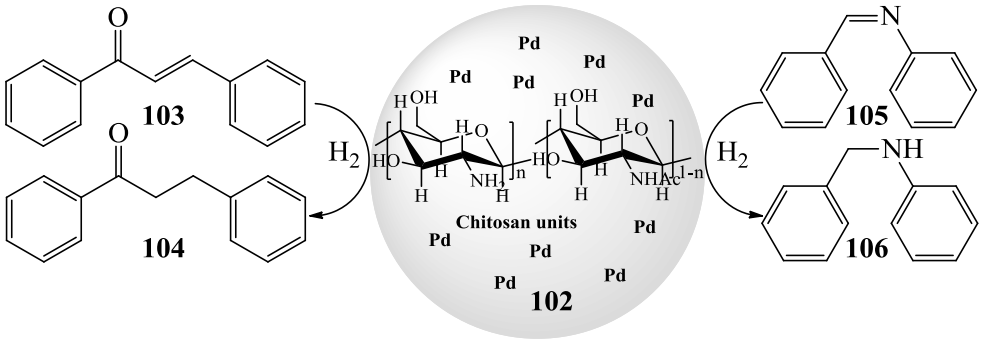
Also, the same research group [80] developed a series of metal-catalyzed C-C coupling reactions in glycerol, using the Suzuki reaction, with yields between 75-98% with a $Pd(OAc)_2$ catalyst. The best results, using US/MW combined were obtained either with 3-bromoanisole or 4-Cl-acetophenone (**Scheme 26**).



X= I, Br, Cl
R=OMe, C(O)Me

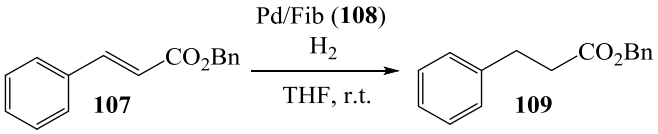
Scheme 26. US/MW combined in Suzuki reaction

A Pd containing catalyst using cross-linked chitosan as the support material (**102**) was successfully prepared by the assistance of ultrasound by Schüßler *et al*. [81]. Chitosan was cross-linked with hexamethylendiisocyanate and loaded with Pd which was subsequently reduced with $NaBH_4$. After the chemical reduction of the Pd(II) ions, the catalyst showed high activity and selectivity in several hydrogenation reactions of α,β-unsaturated carbonyl compounds. Cyclohex-2-enone, benzalacetophenone, 1,2-diphenylacetylene, and N-benzylidenaniline) were hydrogenated successfully in ethanol at mild conditions (50 °C, P H_2~ 6 bar) utilizing a microwave reactor (68% yield) (**Scheme 27**). Reaction parameters like the solvent, temperature and hydrogen pressure were varied. It was shown that the reduction of the catalyst was crucial for catalytic activity. The catalyst was reused ten times for the hydrogenation of cyclohex-2-enone, without showing a dramatic loss in immobilized metal content. Also the polymeric support material did not show any decomposition. HMDI cross-linked chitosan has already been successfully applied as a catalyst support by Cravotto and co-workers [78] for the Suzuki reaction as well as for copper-catalyzed cycloaddition reactions between azides and alkynes. This process incorporated both microwave and ultrasound techniques. These types of catalysts proved to be highly active.



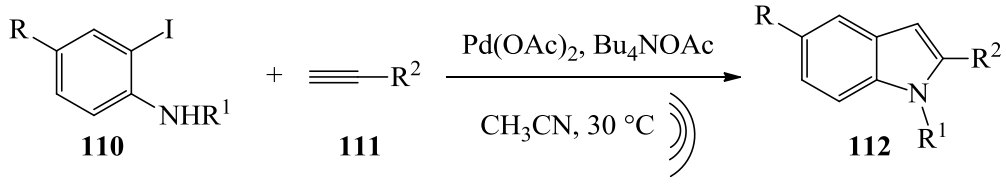
Scheme 27. Chitosan-Pd as catalyst in selective hydrogenation

On the other hand, a practical and efficient preparation method of palladium-fibroin catalyst (Pd/Fib) (**108**), silk-fibroin-supported Pd(0) by means of sonication was developed by Kitamura *et al.* [82]. **108** was prepared starting from commercial silk-fibroin and $Pd(OAc)_2$ in MeOH (**Scheme 28**) at room temperature within 12 h, in contrast with a previous preparation method that required soaking for at least 4 days. The proposed procedure allowed the absorption of Pd(II) on the fibroin surface and the reduction of Pd(II) to Pd(0). The process is applicable to a 100 g– scale preparation of Pd/Fib (2.5%). The resulting dark-gray Pd/Fib selectively catalyzed chemoselective hydrogenation of alkynes, alkenes, and azides without the reduction of coexisting aromatic ketones and halides, benzyl alcohols, esters and N-Cbz protective groups, yields were in the range of 91-100%.



Scheme 28. Pd/Fib as catalyst in selective hydrogenation

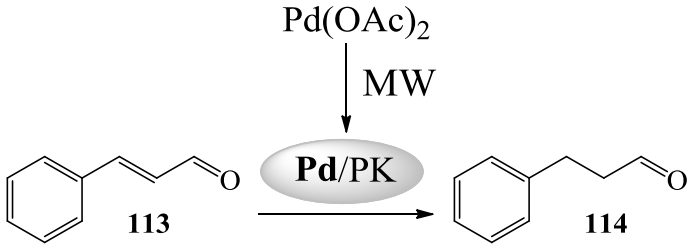
In 2006, Palimkar *et al.* [83] presented a mild, efficient, one-pot synthesis of 2-substituted indoles (**112**) *via* Sonogashira coupling 5-*endo-dig* cyclization in the absence of any ligand, copper, and amine conditions at room temperature using ultrasound irradiation during 5 h (74% yield). The results were compared with the standard stirred conditions (30 h, 71% yield). Significant enhancement of reaction rates was observed with ultrasonic irradiation under 2 mol % of $Pd(OAc)_2$ as the catalyst, Bu_4NOAc as the base, in acetonitrile. Both electron-withdrawing and -donating substituents on the aryl ring of o-iodoanilides were tolerated (**Scheme 29**).



R= H, Me, CO_2Me, COMe
R^1= Ts, Ms
R^2= Ph, *p*-tolyl, 4-OMePh, 3-F-Ph, naphthyl, 1-OH-ethyl

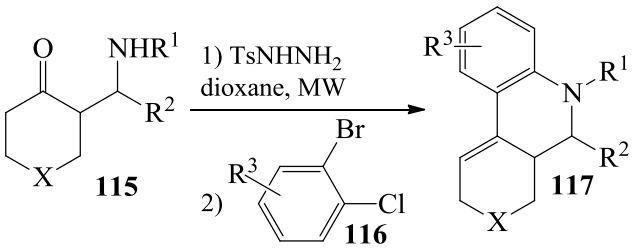
Scheme 29. Synthesis of indoles *via* Sonogashira reaction

Polyketone (poly-3-oxotrimethylene, PK) can be considered a useful candidate as support and stabilizing agent in the preparation of nanoparticles. For the first time, Raspolli Galletti *et al.* [84] have employed this support to stabilize Pd nanoparticles generated by reduction of $Pd(OAc)_2$ in EtOH under microwave irradiation (**Scheme 30**).Then they tested the supported systems in the selective hydrogenation of cinnamaldehyde (**113**) to hydrocinnamaldehyde (**114**) as model reaction. It is noteworthy that this catalyst has high stability and recyclability, ascribed to a stabilizing capacity of this particular polymeric support.



Scheme 30. Pd/Pk as selective catalyst in hydrogenatin of cinnamaldehyde

By combining organocatalysis and transition-metal catalysis, Barluenga *et al.* [85] have developed a new Pd-catalyzed process for the cross-coupling reaction of the tosylhydrazone of a Mannich adduct with a 1,2-dihalogenated aromatic system (**116**), followed by an intramolecular C-N bond forming reaction to obtain **117** (**Scheme 31**). The interesting contribution about this research is that the combination of organocatalysis and the Pd-catalyzed cross-coupling reaction allows the ready transformation of enantiomerically enriched Mannich adducts. The products were obtained between 30 and 120 min, with microwave assistance, in yields from 30 to 90 % with 92-99 % ee.

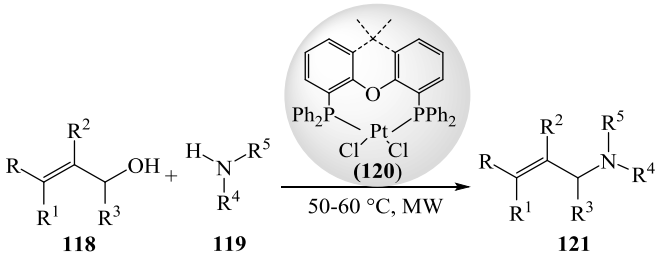


R^1= Ph, *p*-OMePh, *p*-MePh, *p*-Me_2NPh, PMP
R^2= H, Ph, *p*-OMePh, *p*-Me_2NPh
R^3= H, OMe, OBn, CF_3
X= CH_2, $(CH_2)_2$, O, S

Scheme 31. Synthesis of quinoline derivatives

2.1.4. Platinum

Ohshima *et al.* [86] have described the development of a direct catalytic amination of both aryl- and alkyl-substituted allylic alcohols (**118**) with various amines (**119**) using Pt-Xantphos and Pt-DPEphos (**120**) catalyst systems (**Scheme 32**). The selective syntheses of various monoallylamines (**121**) were obtained with good to excellent yield (74-96%) without need for an activator. Furthermore, the microwave-assisted reaction decreased considerably the reaction time compared with conventional heating.

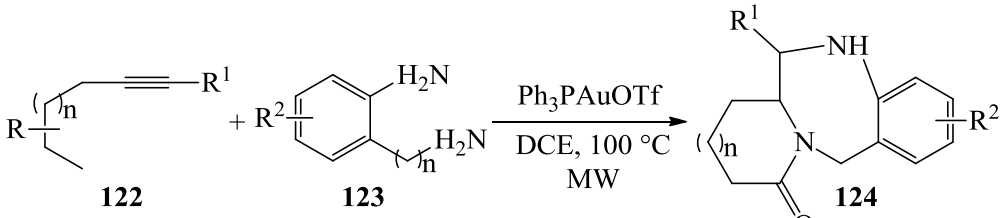


R, R_1, R_2, R_3, R_4, R_5= H, alkyl, aryl

Scheme 32. Direct amination of allylic alcohols

2.1.5. Gold

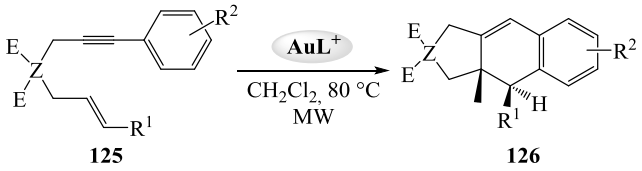
Patil *et al.* [87] have developed a gold(I)-catalyzed cascade raction for the facile synthesis of fused dihydrobenzimidazoles and tetrahydroquinazolines (**124**) under very mild reaction conditions, using microwave techniques, with high yields (96%) and excellent diastereo-/regioselectivities in short reaction time (0.5 h) (**Scheme 33**).



R= H, methyl, *c*-pent, *c*-hex, Ph
R_1= H, Me, Et
R_2= 3-Me, 4-OEt, 4-CF_3, 4-F, 4-Cl, 4-Br
n= 0,1

Scheme 33. Synthesis of fused di and tetrahydroquinazolines

The reactivity of alkenyl- and arylsubstituted 1,6-enynes (**125**) by using cationic gold complexes with tris(2,6-di-*tert*-butylphenyl)phosphite have been studied by Nieto-Oberhuber *et al.* [88] (**Scheme 34**). They have determined that the cationic gold complexes with this ligand were exceptionally reactive as a catalyst for the intramolecular [4+2] cycloadditions (dehydro-Diels-Alder reactions) under microwave heating, in yields from 72 to 90%. This method tolerates a wide variety and positions (*o*-, *m*- and *p*-) of functional groups at the aryl, including electron-releasing (-OMe) and electron-withdrawing (-CN, -NO_2). Computational studies support a stepwise mechanism for the cycloaddition by the initial formation of an anti-cyclopropyl Au(I)-carbene, followed by its opening to form a carbocation stabilized by interaction with the aryl ring, which undergoes a Friedel-Crafts-type reaction.



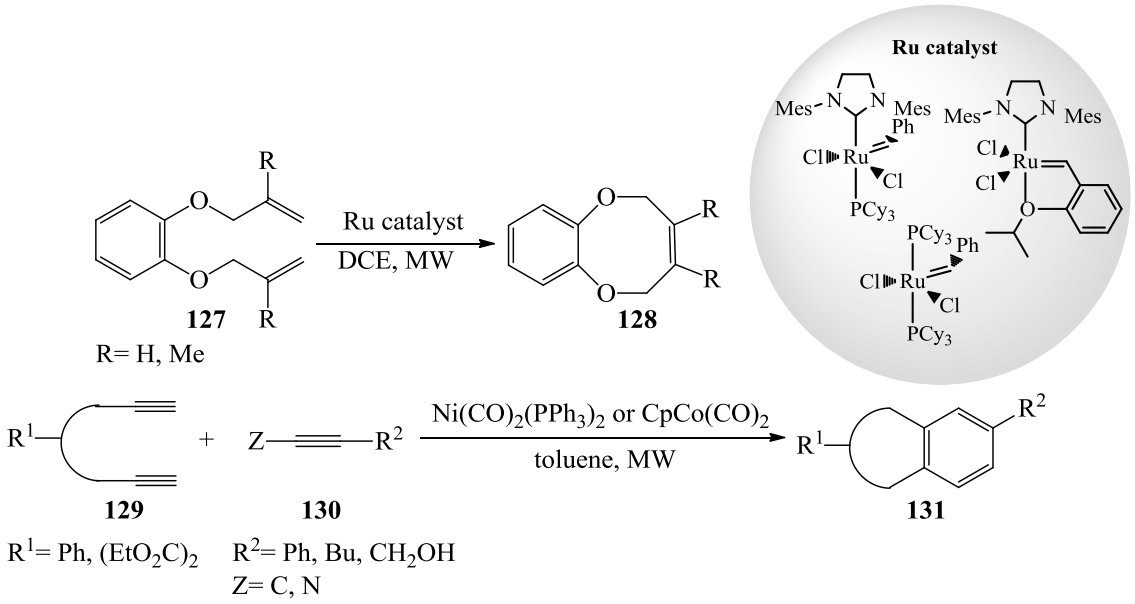
E= CO_2Me, SO_2Ph, OH
Z= CH_2, $(CH_2)_2$, O, Nts
R_1= H, Me, OMe, Ph
R_2= H, *p*-Me, *o*-OMe, *m*-OMe, 3,5$(OMe)_2$, *o*-Ph, *p*-CN, *o*-NO_2, *p*-NO_2

Scheme 34. Intermolecular [4+2] cycloadditions

2.1.6. Ruthenium

Dallinger *et al.* [36] have evaluated the role of wall effects at elevated temperatures applying microwave or conventional thermal heating at the ruthenium-catalyzed ring-closing metathesis transformations leading to eight-membered-ring systems (**128**) (71% yield) and nickel- or cobalt-catalyzed [2+2+2] cyclotrimerizations (**131**) (87% yield) (**Scheme 35**). The reactor setup allowed accurate internal reaction temperature measurements using fiber-optic. In

contrast to previous literature reports, the authors observed no evidence that direct in-core microwave heating can increase catalyst lifetime by minimization or elimination of wall effects. Moreover, no indication for the involvement of non-thermal effects of microwaves in these homogeneous transformations catalyzed by transition metals was observed.



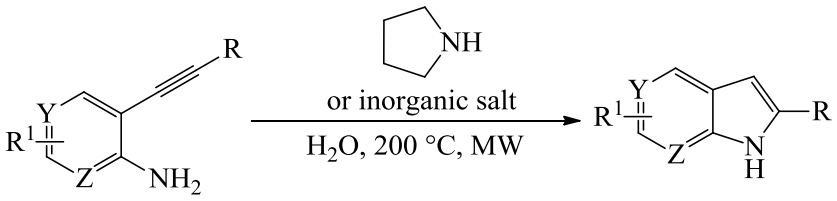
Scheme 35. Eight-memberend-ring and [2+2+2] cyclotrimerizations

Patel *et al.* [89] used a catalyst consisting of polyaniline-anchored metal salts as a Lewis acid to promote the Michael reaction of -unsaturated ketones. The reaction is performed efficiently with imidazole, acetyl acetone, and ethyl acetate as Michael donors and chalcones as the acceptors under ultrasound irradiation. The presence of several nitrogen atoms in solid polyaniline (PANI) provided a perfect handle for the complexation with transition-metal ions, a prerequisite for a suitable catalyst support. These reactions were promoted by ultrasound irradiation to give good conversions (81-95% yield) in short and straightforward reaction conditions

2.2. Organocatalysis

2.2.1. Organic reagents as catalysts

Carpita *et al.* [90] reported a simple and straightforward protocol of differently substituted indoles and azaindoles (**133**) (**Scheme 36**) without any added metal catalyst. This reaction was carried out *via* microwave-assisted cycloisomerization in aquous media under catalytic amounts of inorganic salts such as KCl and $NaHCO_3$ or by the addition of pyrrolidine. Good to very good yields (30-90 %) in the cyclization can be achieved for a variety of 2-amino(hetero)aryl alkynes (**132**).



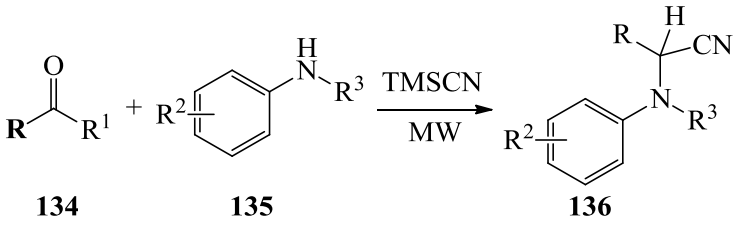
R= H, Ph, 4-OMe-Ph, 4-Cl-Ph
R^1= H, OMe, COMe, CN, Cl
Y,Z= C or N

neutral salt: KCl, KBr, KI, $(n\text{-Bu})_4NBr$, LiCl, LiBr, NaI.
basic or acid salt= NaOH, $NaHCO_3$, NH_4Cl, LiOH, KOH, $KHCO_3$, K_2CO_3, Na_2HPO_4, KF, NaOAc, NH_4Cl.

Scheme 36. Synthesis of indoles and azaindoles

Azeredo *et al.* [91] reported a simple protocol of 3-chalcogenyl-indole synthesis from indoles and diorganyl dichalcogenides, under solvent- and metal-free conditions. This method used DMSO as oxidizing agent and was catalyzed by molecular iodine at 80 C during 5 min at 100 W microwave power. This environmentally friendly procedure allowed the synthesis of several 3-selenyl-compounds with good yields (67-95 %). The protocol was applied to substituted indoles which reacted with diphenyl disulfide. The reaction yields to obtain different 3-sulfenyl-indoles were high (55-98 %).

Nammalwar *et al.* [92] developed a Strecker synthesis from aldehydes or ketones (**134**) with aromatic or aliphatic amines (**135**), in ethanolic media under mild catalyst (3 mol % NH_4Cl), metal-free conditions to obtained α-Aminonitriles (**136**) (**Scheme 37**). This reaction was carried out under microwave irradiation at 400 W, 90 ºC during 240-420 s, in solvent free conditions. This procedure was first proposed for aldehydes (82-96 % yield) and later was applied to ketones (82-92 % yield).



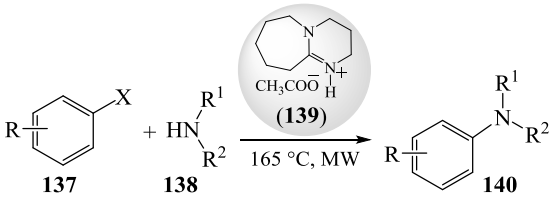
R= Me, Bu, Pent
R^1= Et, Bu, Pent, Ph
R^2= H, *p*-Cl, *p*-CF_3
R^3= H

R= H
R^1= Ph, *o*-Cl-Ph, *m*-OMe-Ph, 2,3,4-$(OMe)_3$-Ph, furanyl
R^2= H, *p*-Cl, *p*-CF_3, *p*-OMe, -$(CH_2)_2O(CH_2)_2$
R^3= H

Scheme 37. Strecker synthesis from aldehydes and ketones

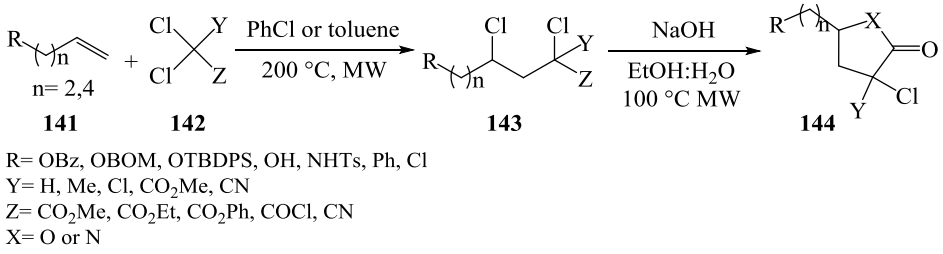
Singh *et al.* [93] proposed the reaction of an aryl halide (**137**) with several amines (**138**) under microwave irradiation to yield different C-N cross-coupling (**Scheme 38**). This reaction was assisted

for Brønsted acid/[DBU][HOAc] (**139**) without adding any metal catalyst with good yields (up to 94%). The reaction was carried out with substrates like ortho-substituted amines/aryl halides chlorobenzene and showed lower yields, while meta/para-substituted analogues, 2,4-dinitrochlorobenzene morpholine, piperidine, cyclohexylamine, and hexylamine indole, pyrrole among others presented good to excellent yield.



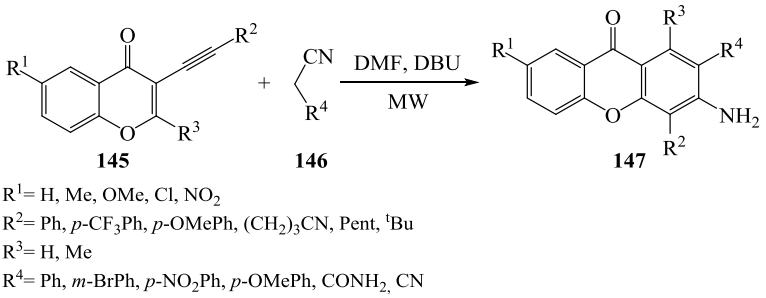
Scheme 38. C-N cross-coupling under metal-free conditions

Kamijo *et al.* [94] synthesized a series of 1,3-dichlorinated adducts (**143**) under microwave irradiation at higher temperature (200 °C) from terminal olefins (**141**) yield from 55 to 98 %. In addition, the reaction was carried out completely and oxygen or a nitrogen unit was introduced to the internal side of the carbon chain *via* nucleophilic cyclization of the **143**. Single-step formation of the five-membered carbocycle was realized through cyclization of the intermediate radical (76-79 % yield) (**Scheme 39**).



Scheme 39. 1,3-dichlorinated compounds as adducts for nucleophilic cyclization

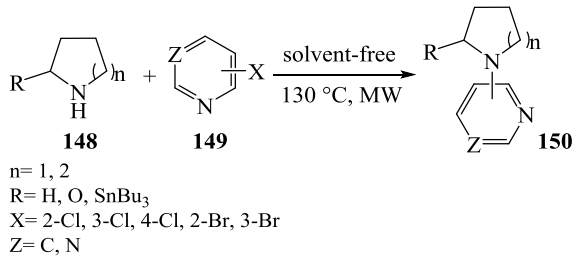
A simple and robust protocol for functionalized amino-substituted xanthones (**147**) has been developed by Liu *et al.* [95] 3-(1-alkynyl)chromones (**145**) effectively reacted with various acetonitriles (**146**) under microwave irradiation (10-15 min, 90-150 °C) and free-catalyst conditions. This reaction involves multiple reactions, such as Michael addition/cyclization/1,2-addition (yield from 55 to 92 %) (**Scheme 40**).



Scheme 40. Synthesis of functionalized xanthones

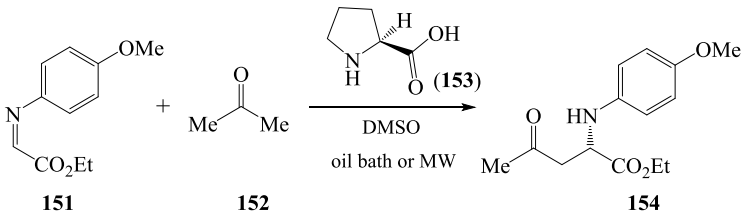
Carpita and Ribecai [96] reported a simple and easy protocol concerning microwave irradiation that accelerated the synthesis of differently substituted indoles, by cycloisomerization of 2-alkynylaniline derivatives in water. The reaction was carried out without any added metal catalyst, acid, or base, and in the presence of Pd salts (ppb) as precursors. This did not appear to increase the yields of the reaction so it was necessary to use microwave.

Narayan *et al.* [97] synthesized the amination of halo-pyridine or -pyrimidine (**149**) under microwave irradiation without transition metal catalyst in the absence of solvent, with good to high yields (**Scheme 41**). They studied the reaction between 2-bromopyridine with pyrrolidine assisted by microwave monitoring of internal probe temperature/pressure. The best performance was obtained by heating at 130° C during 30 min, the microwave power was varied between 50 and 200 W (yield from 55 to 92 %).



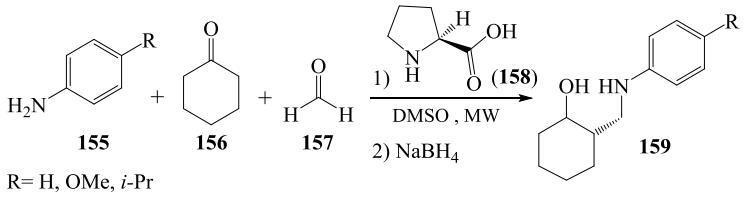
Scheme 41. Amination of halo-pyridines or –pyrimidines

Hosseini *et al.* [5] have studied the microwave effects in organocatalytic processes of five (S)-proline-catalyzed asymmetric Mannich- and aldol-type reactions (**Scheme 42**) with the intention to prove the existence of specific or nonthermal microwave effects compared with conventional thermal heating. Moreover, they applied the concept of simultaneous external cooling while irradiating with microwave power. They have showed that the observed effects (mainly rate enhancements) are a consequence of the increased temperatures attained by microwave dielectric heating and are not related to the microwave field. The most important contribution of their work was the use of fiberoptic to eliminate many of the problems associated with the most commonly employed infrared sensors commercially available microwave reactors. Based upon these results, the authors suggest that using the term "microwave-assisted" may be more appropriate than "microwave-heated". They presented five related examples (90-92 % yield, > 99% ee).



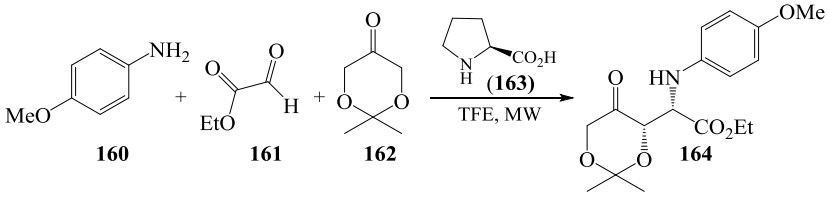
Scheme 42. (*S*)-Proline-catalyzed asymmetric reactions

Rodriguez and Bolm [98] have been studied the proline-catalyzed direct asymmetric Mannich reaction (**Scheme 43**) between various anilines (**155**), cyclohexanone (**156**) and formaldehyde (**157**). Under microwave irradiation and using 0.5 mol % of catalyst (**158**) the Mannich products have been obtained with up to 98% ee after a short period of time. Moreover, the reduction, in situ, of the resulting ketones affords N-aryl amino alcohols (**159**) in up to 86% yield.



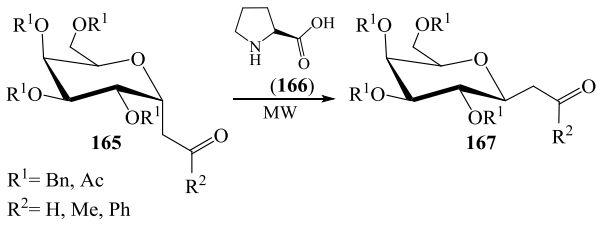
Scheme 43. Direct asymmetric Mannich reaction catalyzed by (S)-proline

Westermann and Neuhaus [99] have reported the synthesis of nitrogen-containing carbohydrate derivatives with very good stereoselectivities from dihydroxyacetone (DHA) derivatives (**162**) and various imines in Mannich reactions. The reaction was improved with 2,2,2-trifluoroethanol (TFE) as a solvent. The application of microwave irradiation shortened the reaction times (10 min, 72 % yield, 94 %ee). **Scheme 44**



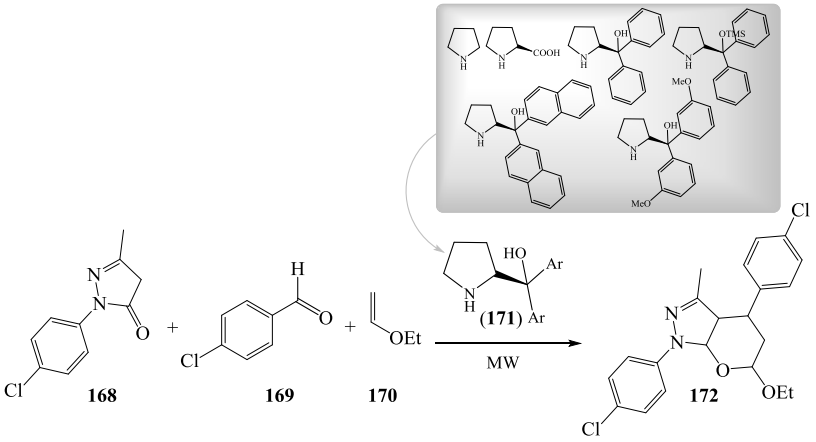
Scheme 44. Dihydroxyacetone in Mannich reactions

Massi *et al.* [100] have studied the microwave-assisted anomerization of α-C-glycosylmethyl aldehydes and ketones (**165**) using L-proline as catalyst (**166**). They postulated an open-chain enamine-based mechanism to promote in a few hours the quantitative anomerization of α-C-glycosylmethyl aldehydes (**165**) into β-isomers (**167**) (**Scheme 45**).



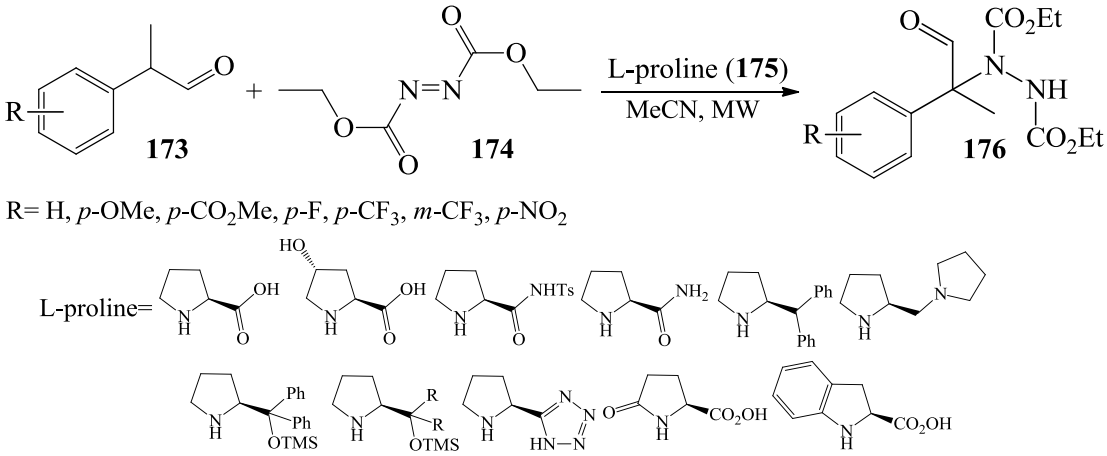
Scheme 45. Anomerization of α-C-glycosylmethyl aldehydes

Radi *et al.* [101] have developed a rapid and efficient multicomponent reaction based on microwave-assisted organocatalytic Knoevenagel/hetero Diels-Alder reaction for the synthesis of 2,3-dihydropyran[2,3-c]pyrazoles (**172**) with potential anti-tuberculosis activity.



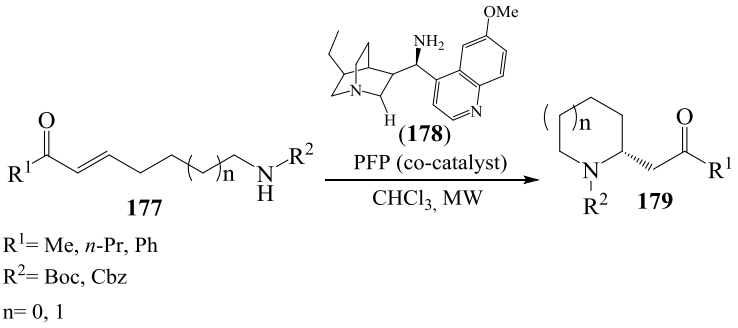
Scheme 46. Knoevenagel/hetero Diels-Alder reaction for the synthesis of 2,3-dihydropyran[2,3-c]pyrazoles

Baumann *et al.* [102] described the fast and efficient synthesis of α,α-disubstituted amino aldehydes (**176**) by the reaction of aldehydes (**173**) and diethylazodicarboxylate (**174**) using L-prolines (**175**) as organocatalyst under microwave conditions (**Scheme 47**). They compared with the previously obtained results at room temperature. Microwave irradiation has reduced considerable the reaction time (days to 30 min) and, both, yield and enantioselectivity have been significantly increased (from 6-85 to 54-97 % yield and from 24-84 to 52-90 % ee).



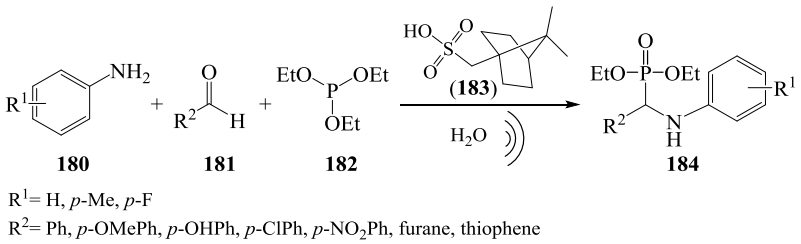
Scheme 47. α-Amination of aldehyde with diethylazodicarboxylate

Fustero *et al.* [103] have developed a protocol for a high organocatalytic enantioselective intramolecular aza-Michael reaction using 9-amino-9-deoxy-epi-hydroquinine (**178**) as the catalyst and pentafluoropropionic acid (PPF) as a co-catalyst (**Scheme 48**). The intramolecular conjugate addition of carbamates to α,β-unsaturated ketones gave a series of piperidines, pyrrolidines, and several benzofused nitrogen heterocycles derivatives (indolines, isoindolines, tetrahydroquinolines, and tetrahydroisoquinolines) in excellent yields and enantioselectivities. Aditionally, the use of microwave irradiation improves the efficiency of the process giving rise to the final products with comparable yields and enantiomeric excesses (from 60 to 95 % and from84 to 98 % ee respectively). Some mechanistic insights were also considered.



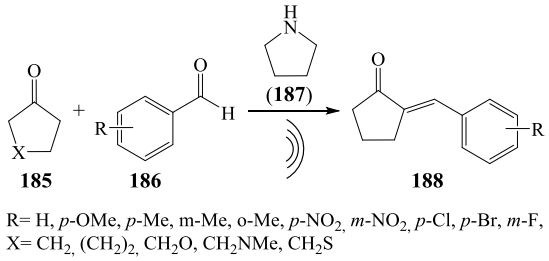
Scheme 48. Enantioselective Intramolecular azaMichael Reaction

Shinde *et al.* [104] reported a facile and rapid synthesis of α-functionalized phosphonates (hydroxy and amino) under solvent-free conditions with the implementation of ultrasound irradiation. The **Scheme 49** shows the general procedure to obtain α-amino phosphonates (**184**) using camphor sulfonic acid (**183**) as organocatalyst. Ultrasound assistance decreased the reaction times, compared to conventional heating, from 30-75 min to 10-20 min giving the desired product in comparable yields (83-93%).



Scheme 49. An organocatalyzed facile and rapid access to α-amino phosphonates

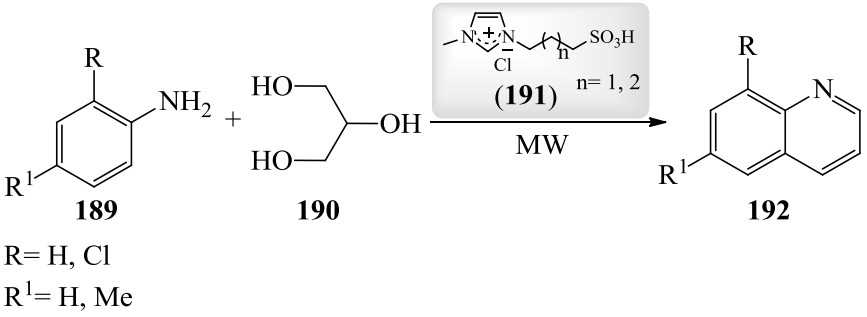
Ultrasonic irradiation was efficiently used by Mojtahedi *et al.* [105] to synthetize monoarylidene derivatives of cyclic systems (**188**) from the reaction of ketone (**185**) with a series of aldehydes (**186**) under solvent-free conditions (**Scheme 50**). The presence pyrrolidine (**187**) as organocatalyst avoid the formation of the undesired by-products. Moreover, the procedure was applicable to both homo- and heterocyclic ketones. The desired products were obtained between 60 and 90% yield at times ranging from 2 to 10 min.



Scheme 50. Synthesis of monoarylidene derivatives

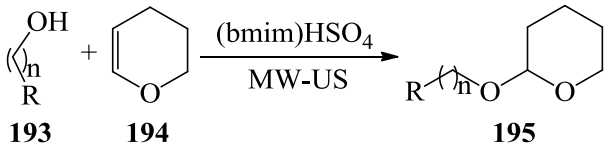
2.2.2 Ionic Liquids (ILs) as catalysts

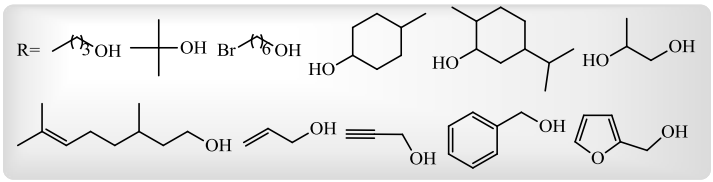
Amarasekara and Hasan [106] studied that 1-(1-alquilsulfonic)-3-methylimidazolium chloride Brønsted acidic ionic liquid (**191**) can be used as catalysts and media reaction to the Skraup quinoline synthesis (**Schemes 51**). This reaction was carried out without using nitrobenzene or another oxidizing agent, or metal catalysts. The higher yield for quinoline Skraup synthesis was 78% using microwave irradiation in a mixture of aniline (**189**), glycerol (**190**), and **191** (1:3:1.5 molar ratios).



Scheme 51. 1-(1-Alquilsulfonic)-3-methylimidazolium chloride as catalyst

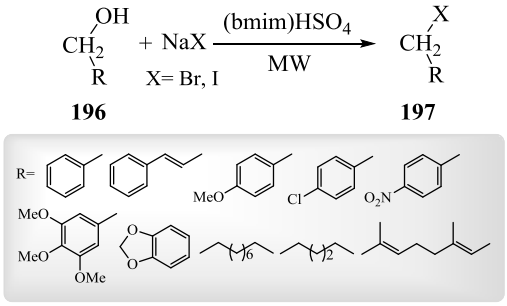
The acid ionic liquid, 1-butyl-3-methylimidazolium acid sulfate, (bmim)HSO_4 was studied as a catalyst in different reactions. Singh and collaborators were working with this acid room temperature ionic liquid (RTILs) since 2005. Conventional agitation at room temperature up to 60 min was also applied. In the first work [107] they used this catalyst for the synthesis of coumarins under microwave irradiation, solvent-free condition. This reaction took place between 2 and 10 minutes with good yields (65-85%). Then, in 2006, this same research group [108] developed the synthesis of monotetrahydropyrany lation of diols (**193**) (**Scheme 52**) working with (bmim)HSO_4 in moderate to excellent yields, using microwave at 160 W during 1.5-2 min and ultrasound for 5 to 7 min as a source of irradiation.





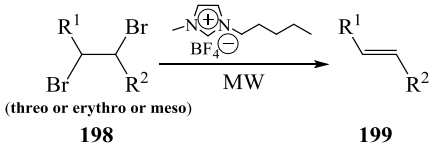
Scheme 52. Monotetrahydropyranylation of diols using (bmim)HSO_4

Subsequently, in the year 2006 [109] this IL was used in the free solvent reaction, for the protection of acetalizacion free/tioacetalizacion of carbonyl compounds, combined with microwave energy and ammonium chloride. The IL was also used for the deprotection of acetals, tioacetales, as well as for transthioacetalization under microwave irradiation. Gupta *et al.* [110] showed that the same IL could be applied to the synthesis of halides (**197**) from alcohols (**196**) using metal halides (NaI, NaBr, CsCl) (**Scheme 53**).This reaction was carried out using radiation of microwave and thermal heating. The microwave radiation shortened the reaction time from 20 h to 10 min while significantly improved the yields (64-90 %).



Scheme 53. Synthesis of halides from alcohols using (bmim)HSO_4

Ranu and Jana [111] developed a very simple and inexpensive procedure for stereoselective debromination of vicinal-dibromides (**198**) to the corresponding (*E*)-alkenes (**199**), as can be observed in **Scheme 54**. Using the ionic liquid 1-methyl-3-pentylimidazolium fluoroborate, (pmim)BF_4, as an efficient catalyst. This reaction presented high yields (65-95%) under microwave irradiation during 2-5 min. These authors demonstrated that this reaction avoided the utilization of any organic solvent and catalysts. In addition the ionic liquid was recycled without any significant loss of its catalytic efficiency.



R^1= OMe, CO_2Et, Ph, *p*-OMePh, OCPh, O(*o*-ClPh), furane, Tiophene
R^2= OMe, CO_2Et, Ph, Me, CO_2Me, NO_2, CN, COPh, O(*o*-ClPh)

Scheme 54. Debromination using (pmin)BF_4

5. CONCLUSIONS

Throughout this review, it is possible to find the most relevant contributions to the synthesis of catalysts or organic transformations, by using microwave or ultrasound irradiation. The advantages of the use of these non-conventional techniques in organic chemistry are well-known for reproducibility and higher yield in the reaction, reduced reaction times, lower costs and mild conditions. Therefore, ultrasound and microwave irradiation both offer important techniques in organometallic synthesis and in the organic chemistry in general receiving attention and use since the last several years.

AUTHOR CONTRIBUTIONS

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

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