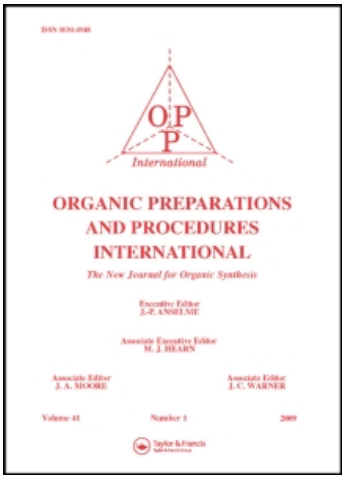


Organic Preparations and Procedures International

Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

Synthesis of Terphenyls

Luis A. Adrio[a]; José M. Antelo Míguez[b]; King Kuok Hii[a]
[a] Department of Chemistry, Imperial College London, South Kensington, London, United Kingdom [b] Departamento de Química Inorgánica, Facultad de Química, Universidad de Santiago de Compostela, Spain

To cite this Article Adrio, Luis A. , Míguez, José M. Antelo and Hii, King Kuok(2009) 'Synthesis of Terphenyls', Organic Preparations and Procedures International, 41: 5, 331 — 358
To link to this Article: DOI: 10.1080/00304940903163632
URL: http://dx.doi.org/10.1080/00304940903163632

Organic Preparations and Procedures International, 41:331–358, 2009

ISSN: 0030-4948 print
DOI: 10.1080/00304940903163632

Synthesis of Terphenyls

Luis A. Adrio,[1] José M. Antelo Míguez,[2]
and King Kuok (Mimi) Hii[1]

[1]Department of Chemistry, Imperial College London, South Kensington, London, United Kingdom
[2]Departamento de Química Inorgánica, Facultad de Química, Universidad de Santiago de Compostela, Spain

Synthesis of Terphenyls

Luis A. Adrio,[1] José M. Antelo Míguez,[2]
and King Kuok (Mimi) Hii[1]

[1]Department of Chemistry, Imperial College London, South Kensington, London, United Kingdom
[2]Departamento de Química Inorgánica, Facultad de Química, Universidad de Santiago de Compostela, Spain

Introduction

A terphenyl molecule consists of a central aromatic ring flanked by two other aryl groups, which may be arranged in 1,2 (*ortho*)-, 1,3 (*meta*)- or 1,4 (*para*)-configurations. Due to their conjugated π-systems, terphenyl derivatives exhibit unique optical[1] and electronic[2] properties that are widely exploited in the fabrication of advanced materials, notably as single- or double-stranded helical polymers,[3] liquid crystals for organic light-emitting diodes (OLEDS),[4–6] polymer-based photovoltaic cells[7] and organic field effect transistors.[8] They also show promise (as dyes) for laser applications[9] and molecular electronic devices.[10] Many terphenyl derivatives are also found in nature, primarily as hydroxylated *m*- and *p*-terphenyls;[11] many of these have potent biological activities, particularly as anti-cancer agents.[12,13] Perhaps unsurprisingly, these structures have been widely examined in medicinal chemistry programs.[14–18]

This review will highlight different synthetic approaches to preparing this interesting and important class of molecules. Generally, synthesis of terphenyls can be classified as one of two methods: (i) aryl-aryl coupling reactions, typically by the reaction of dihalobenzene derivatives with aryl-metal nucleophiles, with or without catalysts; or (ii) using open chain precursor(s) to construct the aromatic rings *via* concerted or stepwise benzannulation reactions. Overall, there are fewer methods for the synthesis of unsymmetrical terphenyls (containing three different aromatic groups), and *ortho*- isomers are much rarer than corresponding *meta*- and *para*-congeners.

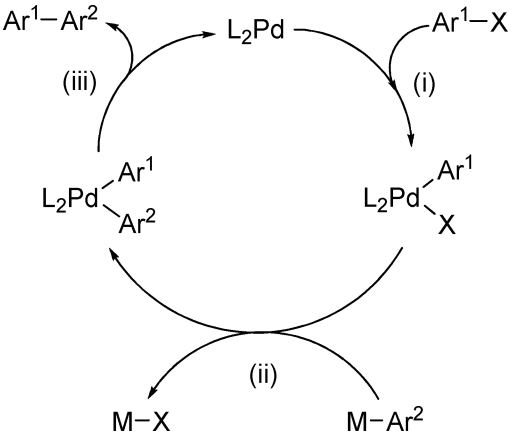
I. Transition Metal-catalyzed Cross-coupling Reactions

Undoubtedly, the development of transition metal-catalyzed cross-coupling reactions has had a major impact on the synthesis of poly-aryls by providing routes for direct C-C

Received April 17, 2009; in final form 19 June, 2009.
Address correspondence to King Kuok (Mimi) Hii, Department of Chemistry, Imperial College London, South Kensington, London SW7 2AZ, United Kingdom. E-mail: mimi.hii@imperial.ac.uk

bond formation between two sp^2 carbons. Discoveries of these reactions began in 1972, when independent reports by the groups of Corriu[19] and Kumada[20] described coupling reactions between alkenyl or aryl halides and Grignard reagents in the presence of nickel catalysts. There ensued a decade of intensive research, during which palladium catalysts gained greater popularity over nickel for these reactions and, more importantly, other organometallic reagents could be used in place of the Grignard reagent. Further stimulus in this area of research was provided in the late 90s; with the discovery of ligands that can induce extremely high catalytic turnover numbers and frequencies under mild reaction conditions (*vide infra*).[21–23]

The general catalytic cycle of cross-coupling reactions can be described by three steps (*Scheme 1*): (i) oxidative addition of an aryl halide (Ar^1-X) to a Pd(0) precursor; (ii) ligand exchange with an organometallic (transmetallating) reagent Ar^2–M (M = Mg, Zn, Sn or B) to generate a diarylpalladium(II) intermediate; and (iii) reductive elimination to furnish the requisite C-C bond. For any given Ar^1-Ar^2 coupling, the relative rates of the first two steps are important. Generally, oxidative addition is dependent on the nature of the nucleofuge (X), found to be I > Br >> Cl for the addition to Pd(0),[24] whereas the transmetallation step is dependent on the nature/reactivity of the electropositive metal.



Scheme 1
General Catalytic Cycle for Pd-catalyzed Cross-coupling Reactions

In earlier reports, *tetrakis*(triphenylphosphine)palladium(0) was often employed as a catalyst. More recent reports tend to employ ligands, such as tri-*tert*-butylphosphine,[23] X-Phos and S-Phos (from a family of dialkylbiarylphosphines known as 'Buchwald' ligands)[22] and *N*-heterocyclic carbenes (NHCs)[21,25] (*Figure 1*), to generate more effective catalysts for 'difficult' reactions, particularly those involving electron-rich aryl bromides and chlorides. For the synthesis of symmetrical terphenyls, sequential bond formations can be simply achieved in 'one-pot' by the reaction of aryl dihalides with two equivalents of the organometallic reagent, or *vice versa*. For unsymmetrical terphenyls, chemoselectivity of the bond forming steps may be achieved using bifunctional aryl precursors containing two sites of different or orthogonal reactivity—this will be presented in the following discussion.

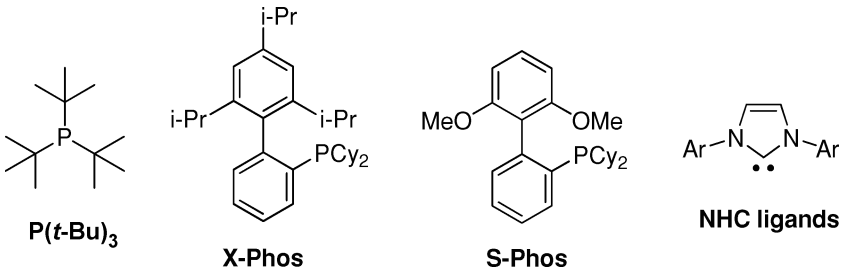


Figure 1
'Modern' More Effective Ligands for Cross-coupling Reactions

In the following sections, cross-coupling reactions are organized according to the type of transmetallating reagent used, in order of their popularity (determined by the number of publications). To keep the discussion succinct, reports containing only a single terphenyl example (particularly if it is symmetrical) will be excluded.

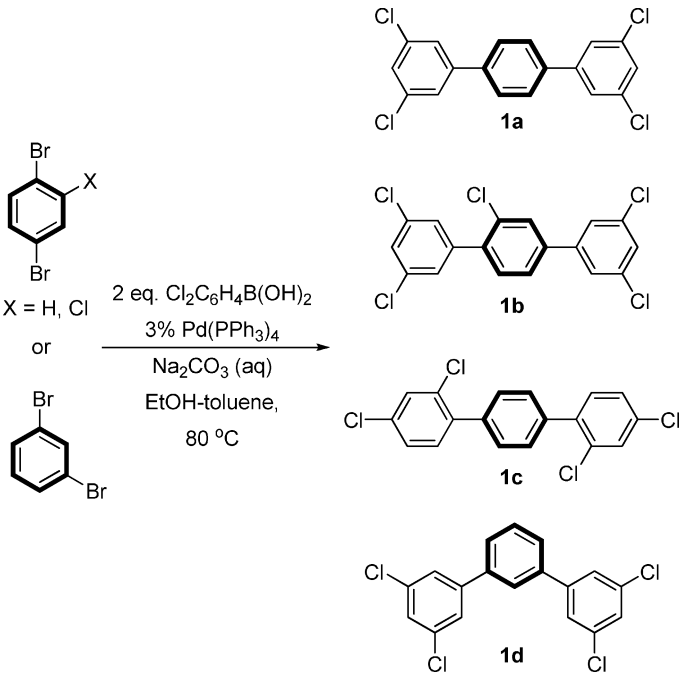
1. Suzuki-Miyaura Cross-coupling

Suzuki-Miyaura (SM) cross-coupling reactions use arylboronic acids as transmetallating reagents. As boron is not much more electropositive than carbon, a nucleophilic base such as OH^- or F^- is needed to promote the aryl transfer, *via* formation of a tetra-coordinated borate species. The SM reaction is often preferred over other cross-coupling methodologies, as arylboronic acids are air- and moisture-stable, as well as being compatible with many functional groups. Thus they have great practicality in organic synthesis.

Key features of a 'classical' SM reaction are demonstrated by the synthesis of polychlorinated *m*- and *p*-terphenyls **1a-d**, which were used as standards for environmental analysis.[26] Using $Pd(PPh_3)_4$ as catalyst, aryl dibromides were coupled with two equivalents of dichlorophenylboronic acid to furnish the requisite terphenyls with yields between 75–85% (*Scheme 2*). Certain important limitations were noted in this study: (i) the reaction is susceptible to steric effects, *i.e*. poor yields were reported for the preparation of *o*-terphenyls from 1,2-dibromoarenes, with the predominant product being the monosubstituted biaryl; and (ii) Ar-Cl bonds are stable under these conditions, *i. e.* dichloroarenes cannot be used as precursors in these reactions.

Despite these limitations, the catalytic system had been widely used for the synthesis of *m*- and *p*-terphenyls for a number of applications, such as *m*-terphenyl cyclophanes as molecular recognition hosts (*Scheme 3, equation 1*),[27] liquid crystalline *p*-terphenyl[28] polymers that exhibit mesogenic behavior (*Scheme 3, equation 2*),[29] and *p*-terphenyl-based light-emitting diodes (*Scheme 3, equation 3*).[30]

With the advent of more effective catalytic systems for cross-coupling reactions, some reactivity limitations can now be overcome. In a recent study, SM reactions between dihalobenzenes, including 1,2-dibromobenzene, could be performed at room temperature using P(*t*-Bu)$_3$ as a ligand. In most cases, these reactions afforded symmetrical terphenyls as major products, even when the reactants were employed in equimolar quantities.[31]

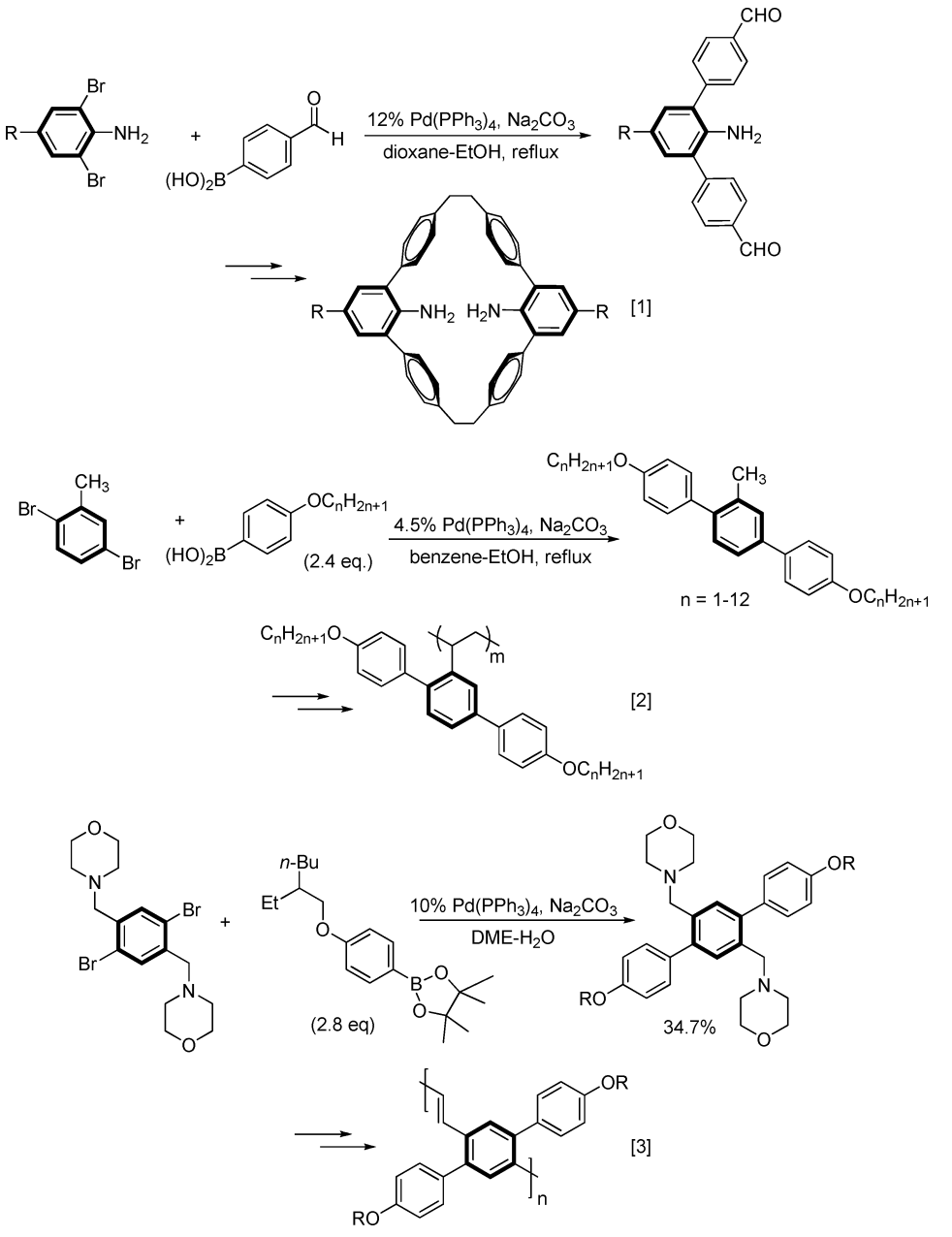


Scheme 2
'One-pot' Synthesis of Polychlorinated Terphenyls from Dibromoarenes (arene rings derived from dibromo precursor are highlighted in bold)

In certain cases, unfavorable steric effects may be overcome by using umpoled reagents. An example is provided in a study by Fritsch *et al.*, where initial attempts to synthesize diamino *p*-terphenyls **4** by SM reactions between dibromoxylene **2** with dinitro- or diaminoarylboronic acids were unsuccessful (*Scheme 4, route 1*). Eventually, the synthesis of five of these compounds was achieved by coupling aryldiboronic acid **3** with bromonitrotoluene. The products were then subjected to catalytic hydrogenation to furnish the required materials in high yields (*Scheme 4, route 2*).[32]

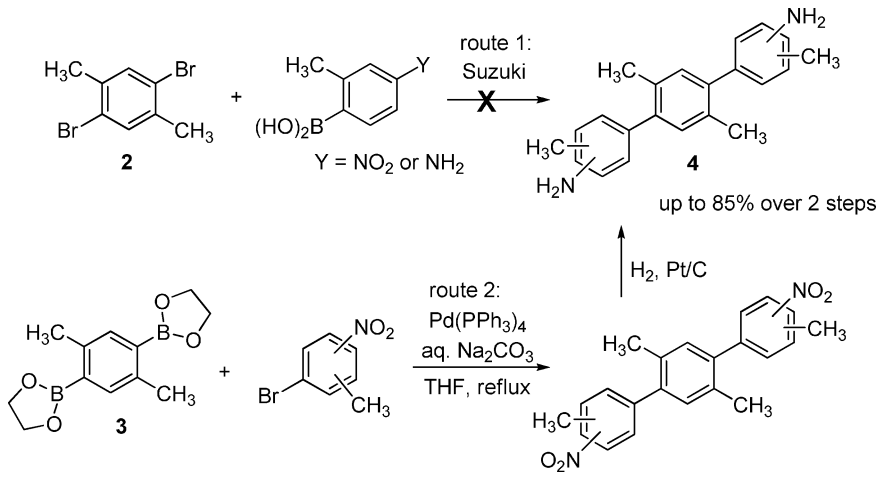
This strategy was also employed in the synthesis of fifteen photo-luminescent alkoxylated *p*-terphenyls containing cyano groups, either on the central or peripheral aromatic rings, with yields between 60–85% (*Scheme 5, equation 1*).[33] Additionally, *p*-terphenyls containing aliphatic side chains were prepared in yields of about 75% (*Scheme 5, equation 2*).[34] The latter were used to produce aromatic polyamides that are able to maintain high dynamic and mechanical properties at temperatures of up to 250°C.

In all of the above cases, arylboronic acids were activated using inorganic bases in aqueous solutions. When the diboronic acid bis-pinacol ester (**5**) was employed instead of a diboronic acid, the use of Ag_2CO_3 was required to effect SM reactions with aryl iodides (*Scheme 6*).[35] Quantitative conversions were often obtained, with the exception of electron-rich (4-iodoanisole) or sterically bulky (2-*tert*-butyl iodobenzene) aryl iodides; in the latter case, only 24% of the mono-substituted product could be isolated from the reaction mixture.

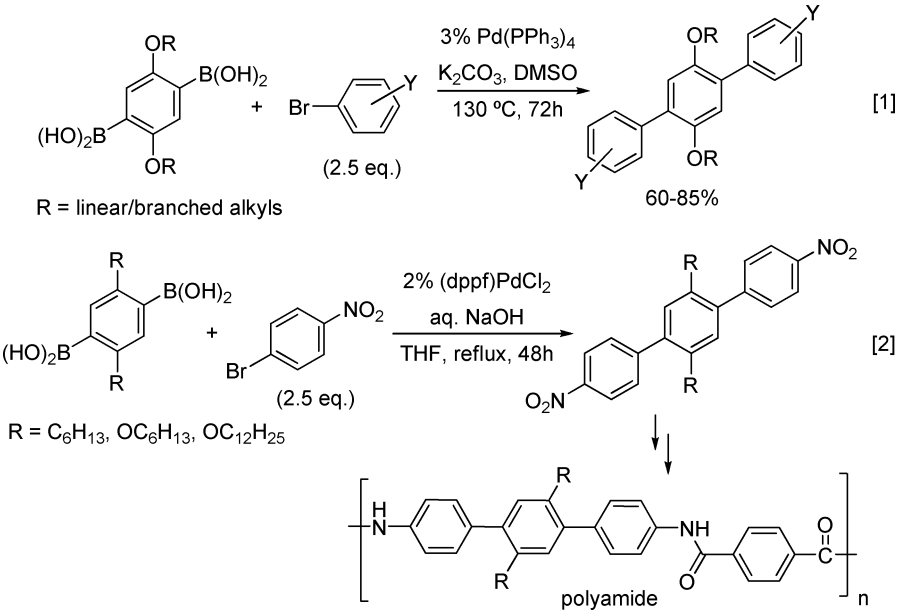


Scheme 3
Synthesis of Advanced Materials by Double Suzuki Reactions of Aryl Dibromides

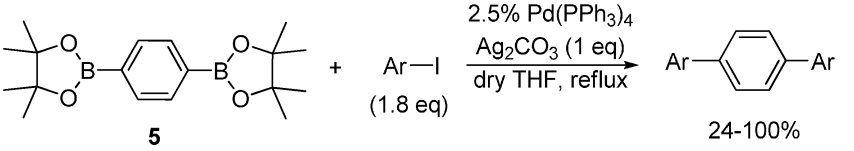
The use of microwave irradiation in cross-coupling processes has been extensively developed in recent years, including the design of flow reactors that can be employed on an industrial scale.[36,37] Instead of refluxing for extended periods, reactions can be accomplished in just 10–15 minutes with microwave irradiation. For the synthesis of terphenyls, 'ligandless' $Pd(OAc)_2$ was employed to catalyze reactions of dibromobenzenes



Scheme 4
Umpoled Reactants in Double Suzuki Reactions



Scheme 5
Synthesis of Advanced Materials by Double Suzuki Reactions of Aryldiboronic Acids



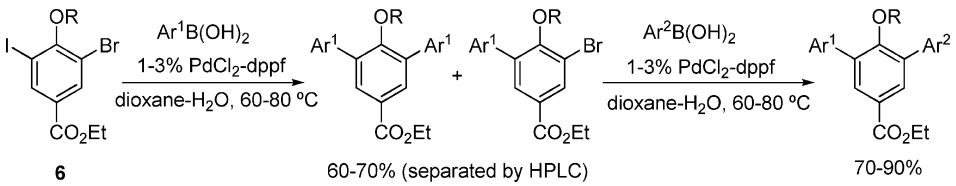
Scheme 6
Double Suzuki Reaction between **5** and Aryl Iodides

with phenylboronic acids over supported KF-Al_2O_3 without using any solvents.[38] Although very good yields of *o*-, *m*- and *p*-terphenyls were reported, no other arylboronic acids were used in this study. In another report, SM reactions between dibromobenzene and phenylboronic acids were conducted using a silica-supported palladium catalyst and K_2CO_3 in an *o*-xylene solution under microwave irradiation, with comparable yields to those using $Pd(OAc)_2$.[39] The penalty for employing a heterogeneous catalyst was longer reaction times (10–20 hours). Nevertheless, the catalyst could be recycled without any loss of activity over 7 runs.

Synthesis of unsymmetrical terphenyls is more challenging. Chemoselectivity is crucial if sequential cross-coupling reactions are to be effective. This may be achieved by using precursors with activating groups of differing reactivity, such as aryl hetero dihalides, or arylboronic halides. In each case, the first bond-forming step has to proceed selectively; the biaryl intermediate can then be subjected to a second coupling with an appropriate counterpart to yield the unsymmetrical terphenyl.

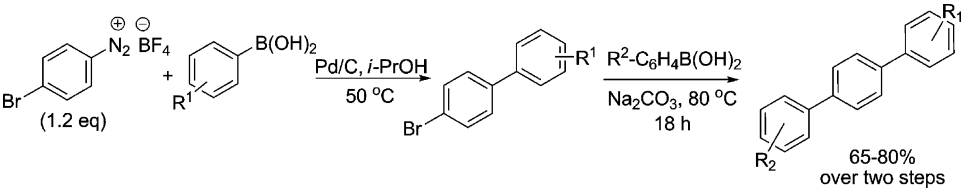
The chemoselectivity of SM reactions between a number of dihalobenzenes and arylboronic acids and esters was examined by Sherburn *et al*. under 'classical' coupling conditions (6% $Pd(PPh_3)_4$, Na_2CO_3, DME, reflux), and best results were obtained with bromoiodobenzenes.[40] In certain cases, sequential reactions can be achieved in 'one-pot' to produce unsymmetrical terphenyls. For example, using 1,3- or 1,4-bromoiodobenzene, sequential addition of different arylboronic acids to the same reaction mixture afforded corresponding *m*- and *p*-terphenyls, respectively, in moderate yields of 55–77%. However, no examples of *o*-terphenyls were provided. [41]

More often, this protocol suffers from poor selectivity in the first step, giving a mixture of mono- and bis-coupled products, which necessitates purification of the intermediate. An example is provided by the coupling between a highly substituted bromoiodoarene **6** with arylboronic acids (*Scheme 7*). The reaction furnished a mixture of mono:bis arylated products in ratios of 2:1 to 4:1, which necessitated separation by HPLC before the second coupling. The final acid-containing terphenyls are useful as insulin receptor modulators.[42] Despite this drawback, these reactions have been employed in many medicinal chemistry programs, including the synthesis of *o*-, *m*- and *p*-terphenyl derivatives with anti-apoptotic activity.[17,18]



Scheme 7
Sequential Suzuki Cross-coupling Reactions for the Synthesis of Unsymmetrical Acid-containing Terphenyls

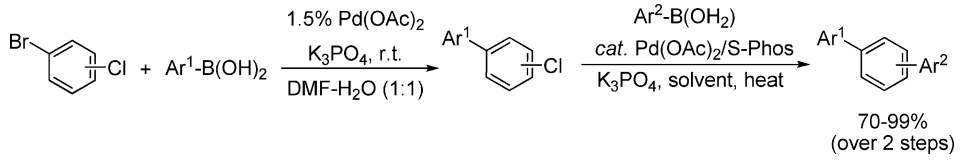
Chemoselectivity of SM reactions can be improved by using nucleofuges other than halides to activate the electrophilic aryl group. Aryldiazonium salts are one such class of compounds, which can undergo cross-coupling with arylboronic acids in the absence of bases.[43] This was exploited by Felpin and Taylor to devise a 'one-pot' route to



Scheme 8
Bromo-Aryldiazonium Salts for the Synthesis of Unsymmetrical p-Terphenyls

unsymmetrical *p*-terphenyls (*Scheme 8*):[44] Starting with a bromophenyl diazonium salt, reaction with a range of arylboronic acids proceeded in the presence of a supported Pd catalyst, with high selectivity for coupling at the diazonium group. The reaction was complete within minutes at 50°C to furnish biaryl bromides in excellent yields. In the subsequent coupling, the reaction was initiated simply by the addition of a base and a second arylboronic acid to the reaction mixture. This one-pot method allows the synthesis of *p*-terphenyls without intermediate purifications, leading to good to excellent overall yields (65–80% over two steps). However, no examples of *o*- or *m*- unsymmetrical terphenyls were provided in this report.

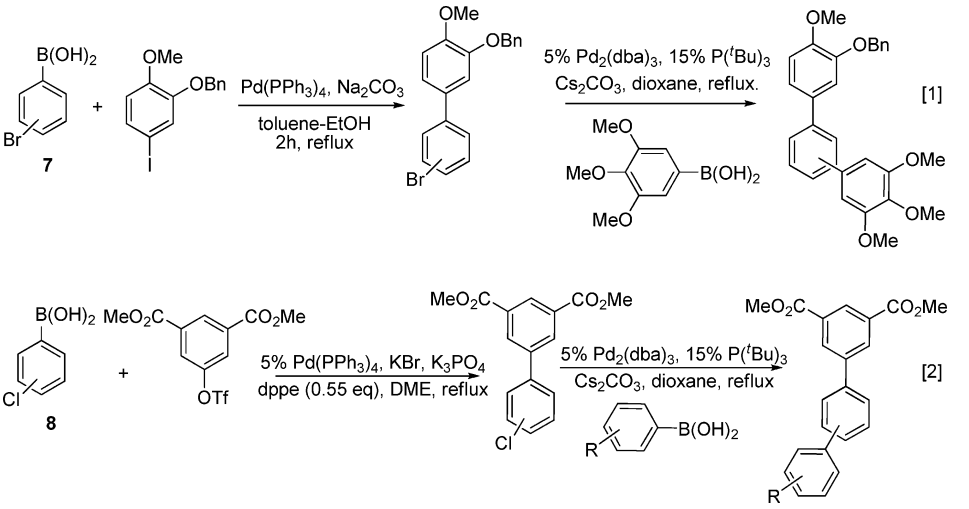
By far, the most general and high-yielding method for the synthesis of unsymmetrical *o*-, *m*- and *p*-terphenyls uses bromochloroarenes in sequential Suzuki-Miyaura cross-coupling reactions (*Scheme 9*).[45] The methodology capitalizes on the fact that SM reactions of aryl bromides can proceed under 'ligandless' conditions at room temperature, combined with recently developed phosphine ligands that enable cross-coupling of aryl chlorides.[46] Thus, from 1,2-, 1,3- or 1,4-bromochlorobenzene, the reaction with arylboronic acids was conducted at room temperature using just $Pd(OAc)_2$ and base. Under these conditions, substitution occurs exclusively at the bromide position with >90% yield. The resultant biaryl chlorides were then subjected to a second SM reaction by employing the S-Phos ligand at 60°C. This allowed the synthesis of *o*-, *m*- and *p*-terphenyls to be accomplished in good to excellent yields (70–99%) over two steps.



Scheme 9
Synthesis of *o*-, *m*- and *p*-Terphenyls from Bromochlorobenzenes

Unsymmetrical terphenyls were also prepared employing precursors with orthogonal reactivities, such as haloarylboronic acids, **7** and **8** (*Scheme 10*). With $Pd(PPh_3)_4$ as catalyst, the synthesis of *o*-, *m*- and *p*- substituted terphenyls could be achieved by subjecting these precursors to a reaction with an aryl halide, before subsequent reaction with an arylboronic acid.

Since Ar-I is easier to activate than Ar-Br, aryl iodides were employed with the bromoarylboronic acid **7** to avoid homocoupling of the bifunctional precursor (*Scheme 10,*



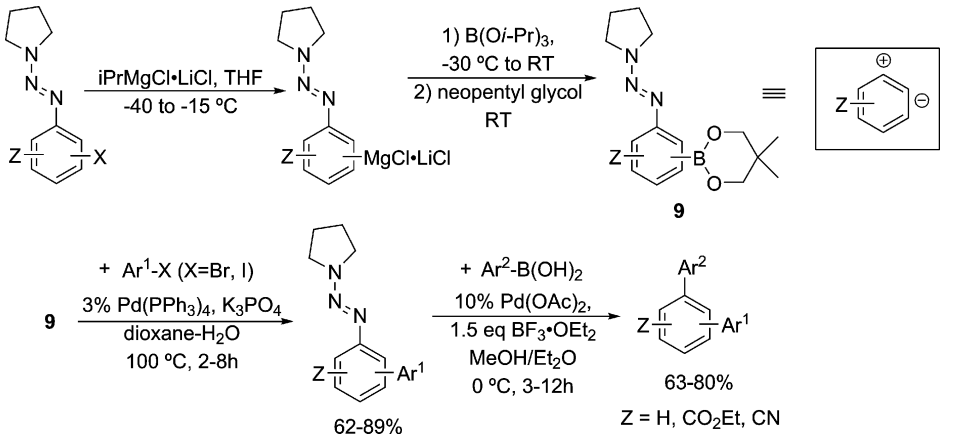
Scheme 10
Synthesis of Terphenyls from Haloarylboronic acid Precursors

equation 1). Good chemoselectivity was reported, but purification of the biaryl bromide intermediate was necessary. The overall yields for two steps were 34/69/47% for the *o*-, *m*- and *p*-isomers, respectively.[16]

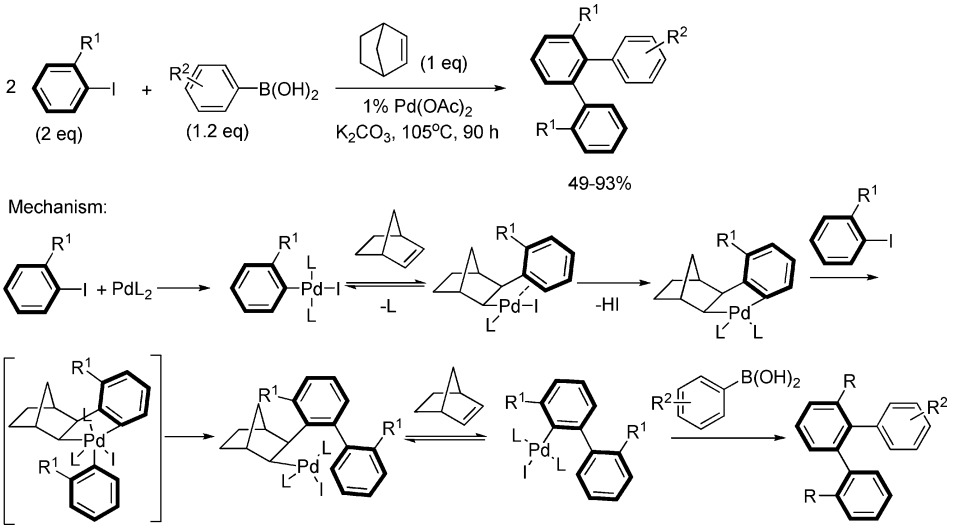
To improve the chemoselectivity, other 'pseudohalides', such as triflates and tosylates, have been explored as electrophilic precursors. These can offer complementary reactivities, as they are generally less reactive towards oxidative addition than their corresponding aryl iodides and bromides, but more reactive than aryl chlorides. This was demonstrated by Clardy *et al.* in the preparation of a class of unsymmetrical terphenyl derivatives as dehydrogenase inhibitors (*Scheme 10, equation 2*). The difference in reactivity between an aryl triflate and an aryl chloride gave rise to very high selectivity in the reaction of the chloroaryl boronic acid **8** and an aryl triflate, using a catalyst generated from $Pd(PPh_3)_4$ and $Ph_2PCH_2CH_2PPh_2$ (dppe). A different phosphine ligand, P(*t*-Bu)$_3$, was used in the second coupling of the less activated chloride. The overall yields using this combination of catalysts ranged between 67–91%.[47]

Using $BF_3{\cdot}OEt_2$ as a Lewis acid, 1-aryltriazenes can be activated towards Suzuki reactions with arylboronic acids.[48] Accordingly, triazene-substituted arylboronic acids (**9**) were prepared and employed as a new class of donor–acceptor substituted coupling reagents.[49] The bifunctional reagent was first subjected to Pd-catalyzed cross-coupling reactions with an aryl halide, followed by a Lewis acid-mediated C-C bond formation with an arylboronic acid (*Scheme 11*). The yields for these two steps were moderate to good.

Catellani and co-workers have developed novel methods for aryl-aryl coupling *via* palladacycle intermediates that are mediated by norbornene.[50] In one report, the synthesis of unsymmetrical *o*-terphenyls was achieved by the reaction of two molecules of an *o*-substituted aryl iodide with an arylboronic acid (*Scheme 12*).[51] The reaction follows a precise sequence of steps. After the oxidative addition of the aryl iodide to Pd(0), the insertion of the strained alkene across the Pd-Ar bond occurs with concomitant formation of a palladacycle. Oxidative addition and insertion of a second aryl iodide followed,



Scheme 11
Synthesis of Terphenyls from 1-Aryltriazene Boronic Acids

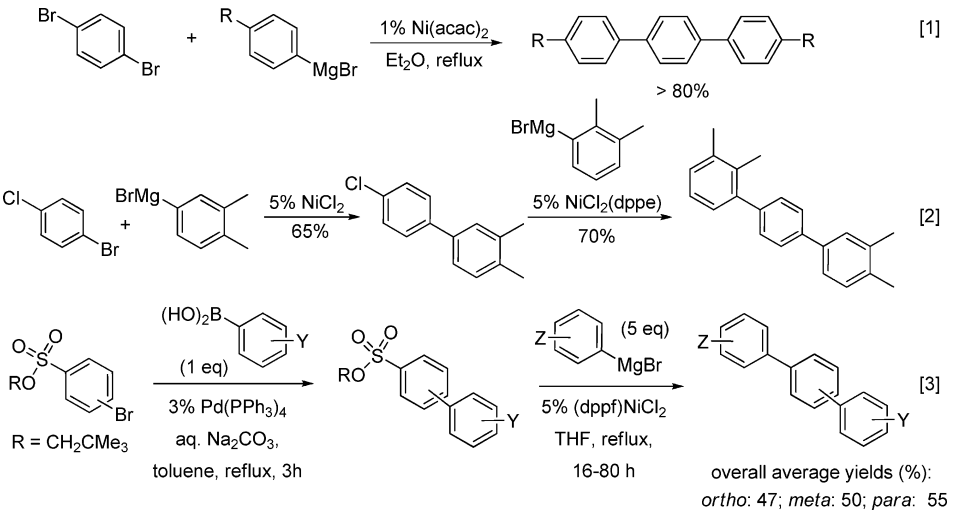


Scheme 12
Terphenyl Synthesis by Coupling Two Aryl Iodides with an Arylboronic acid

terminating with a Suzuki coupling with the arylboronic acid. The reported yields were good to excellent in most cases.

2. Grignard (Corriu-Kumada) Cross-coupling

The synthesis of terphenyls was included in the pioneering report on metal-catalyzed cross-coupling chemistry by Corriu and Masse,[19] where the reaction of 1,4-dibromobenzene and aryl Grignard reagents was effected in the presence of 1 mol% nickel(II) acetylacetonate (*Scheme 13, equation 1*). A later study of the reaction with 1,2-, 1,3- and



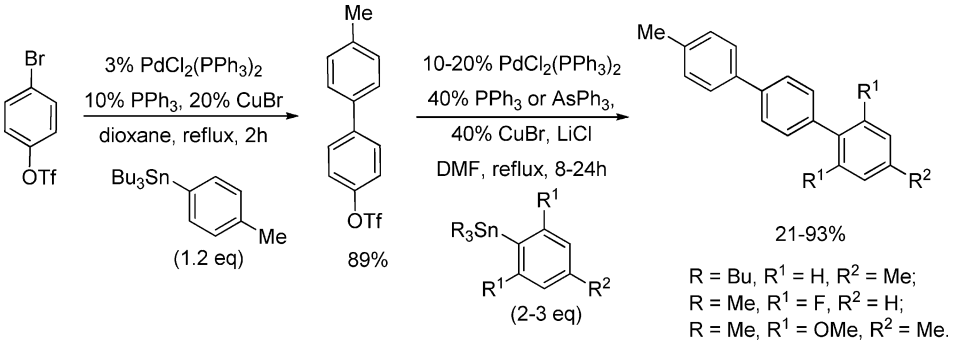
Scheme 13
Synthesis of Terphenyls Using the Corriu-Kumada Cross-coupling Reaction

1,4-bromochlorobenzenes found that coupling occurs preferentially at the bromide with $NiCl_2$ as the catalyst, with moderate to good selectivity. Tandem reactions were subsequently performed to prepare an unsymmetrical *p*-terphenyl in a moderate yield (*Scheme 13, equation 2*), but the generality of the method was not demonstrated.[52]

Using different transmetallating reagents, the Corriu-Kumada reaction was combined with the SM reaction to furnish unsymmetrical *o*-, *m*- and *p*- terphenyls from neopentyl bromobenzenesulfonates (*Scheme 13, equation 3*).[53] The procedure first utilized a Suzuki protocol for the biaryl formation, which occurred selectively at the bromide. This was followed by a nickel-catalyzed coupling with the Grignard reagent. The yields obtained were generally good, but intermediate purifications were necessary. Furthermore, excessively long reaction times and large amounts of Grignard reagents were required for the second step, making the protocol impractical on a large scale.

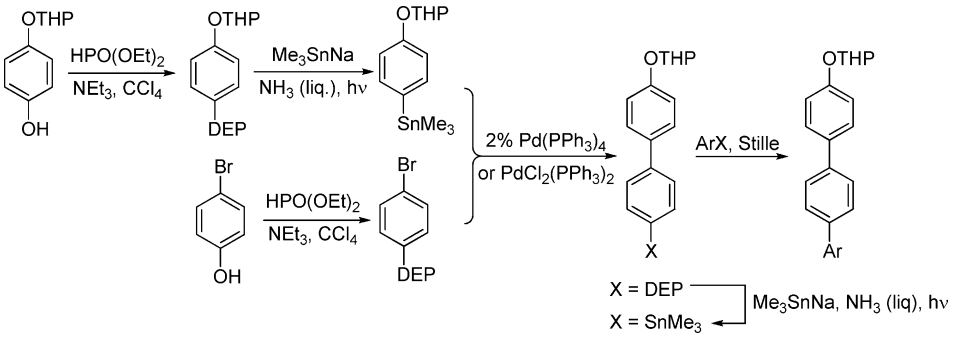
3. Stille Reaction

Palladium-catalyzed coupling reactions using arylstannanes are known as Stille reactions.[54] Despite their good compatibility with air, moisture and other functional groups, application of these reactions is ultimately limited by the toxicity of the organotin reagents and by-products. Given the availability of other effective methodologies, few syntheses of terphenyls are reported using the Stille reaction. Saa and Martorell reported a modified protocol for the synthesis of terphenyls, whereby the successive coupling between 4-bromophenyl triflate and arylstannanes could be achieved using palladium and copper as catalysts under different conditions (*Scheme 14*).[55] The reaction may be conducted in one-pot for symmetrical terphenyls (reaction of phenyl ditriflate was much lower yielding). Overall, the scope of the method was rather limited and the yields reported for some compounds were low, even after extensive reaction optimization, including choice of the palladium catalyst, ligand and the solvent.



Scheme 14
Synthesis of Terphenyls by Successive Stille Reactions

Aryl chlorides and diethylphosphonates (DEP) undergo $S_{RN}1$ reactions with trimethylstannyl ions under photochemical conditions to give arylstannanes in high yields.[56] Using consecutive activation of the DEP group, synthesis of unsymmetrically substituted *para*-terphenyls from commercially available phenols can be achieved in a convergent manner (*Scheme 15*).



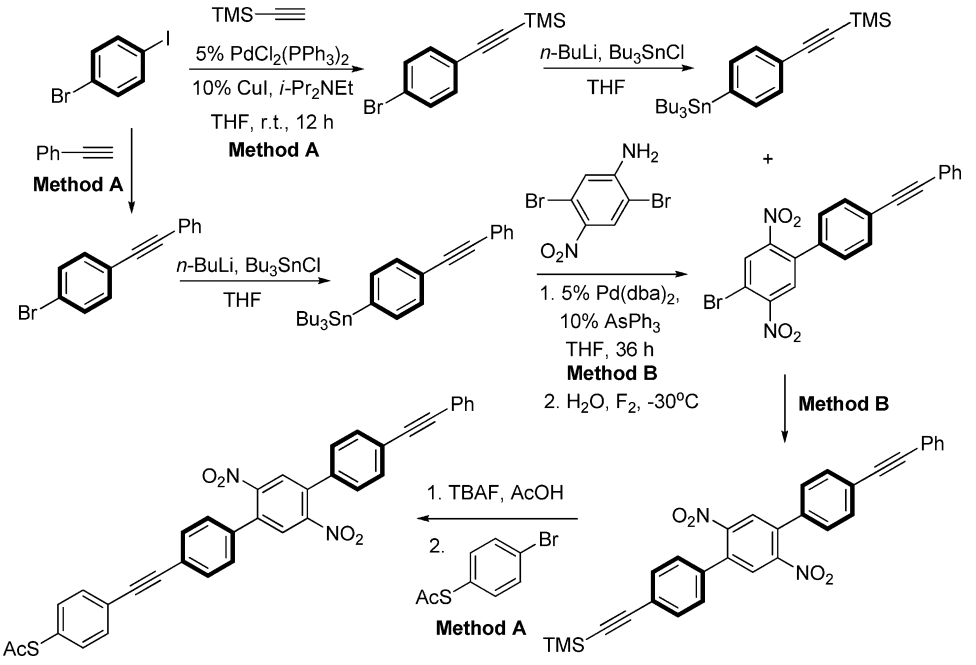
Scheme 15
Use of the DEP Protecting Group in Cross-coupling Chemistry

In a report by Tour *et al.*, the Stille reaction (Method B) was used in combination with a Sonogashira reaction (Method A) to produce a family of *p*-terphenyls as molecular electronic devices (*Scheme 16*).[10]

4. Negishi Cross-coupling

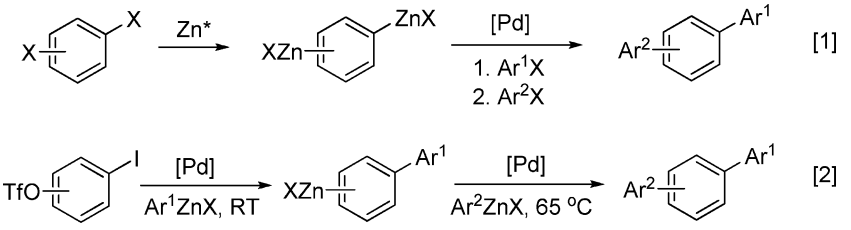
Zn is considerably more electropositive than B or Sn, and thus, organozinc reagents may be expected to be more reactive than organoboron and organostannane compounds.[57,58] Ni- or Pd-catalyzed cross-coupling reactions utilizing arylzinc reagents are known as Negishi reactions.

Phenylenedizinc compounds can be prepared from the reaction of activated zinc with 1,4-dihalobenzene,[59] 1,2-diiodobenzene,[60] 1-iodo-2-trifluoromethylsulfonyloxybenzene,[61] or dibromobenzene, the last instance, in the presence of a cobalt catalyst.[62] These dizinc



Scheme 16
Synthesis of Molecular Electronic Devices using Consecutive Sonogashira-Stille Coupling Reactions (Aromatic Rings Derived from Bromoiodobenzene Highlighted in Bold)

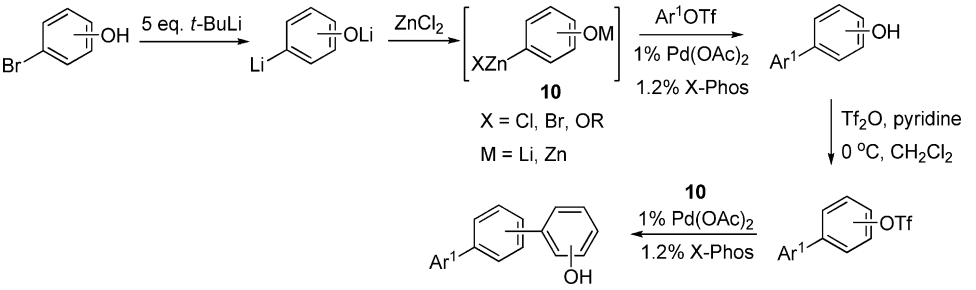
reagents can be subjected to coupling reactions with aryl halides to furnish symmetrical *o*-[60] and *p*-terphenyls.[63] In the latter case, unsymmetrical *p*-terphenyls were prepared in moderate to good yields (55–78%) by successive addition of different aryl halides (*Scheme 17, equation 1*). Arylzinc reagents were found to undergo coupling reaction with aryl iodides at room temperature and with aryl triflates at elevated temperature (65°C). Hence, unsymmetrical terphenyls may be obtained by selective coupling of iodoaryl triflates with arylzinc reagents at different temperatures (*Scheme 17, equation 2*).[64]



Scheme 17
Synthesis of Terphenyls from Successive Negishi Cross-coupling Reactions

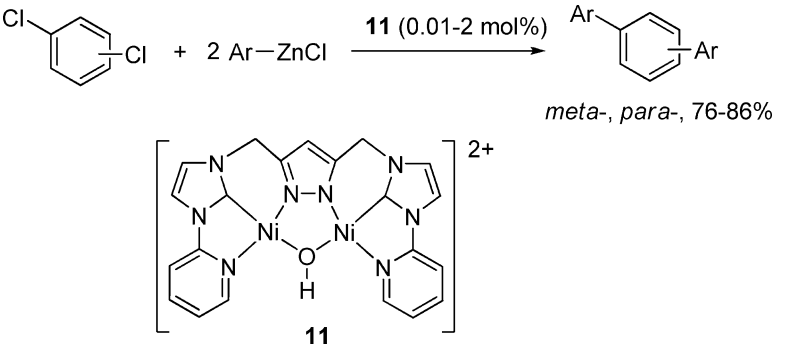
Due to the difficulty in accessing appropriately functionalized arylboronic acids, Shimizu and Manabe transformed bromophenol derivatives into zinciophenoxides **10** (or zinciopyridinoxides from bromohydroxypyridines), which undergo highly efficient cross-coupling reactions with aryl triflates under palladium catalysis in the presence of X-Phos

as a ligand (*Scheme 18*).[65] The protocol allowed the synthesis of unsymmetrical substituted *o*- and *m*-terphenyls under mild reaction conditions with excellent yields. The main disadvantage is the need for purification of intermediates.



Scheme 18
Synthesis of Terphenyls Using Successive Negishi Coupling with Zinciophenoxides

Both arylzincs and nickel catalysts continue to be studied and optimized for Negishi reactions. Particularly, much effort has been directed toward the use of less expensive substrates (aryl chlorides instead of aryl bromides or iodides) and also the use of more functionalized aryl derivatives. In this respect, Chen *et al.*[66] reported use of a nickel-NHC complex **11** that catalyzed the Negishi cross-coupling reaction of a number of aryl chlorides, leading to biaryls and *m*- and *p*-terphenyls in good to excellent yields; no *o*-terphenyls were reported using this route (*Scheme 19*).

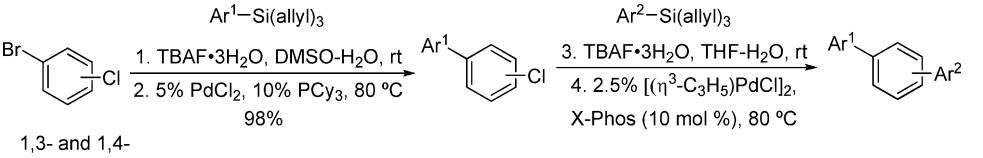


Scheme 19
Nickel-catalyzed Negishi Coupling for the Synthesis of Terphenyls

5. Hiyama Cross-coupling

Organosilicon reagents provide a practical alternative to many organometallic reagents in cross-coupling chemistry.[67] Pioneered by Hiyama and co-workers, organosilanes can be activated towards transmetallation by the formation of hypervalent silicon species, typically by reaction with fluoride.[68] The methodology has been applied to the synthesis of unsymmetrical *m*- and *p*-terphenyls by subjecting 1,3- and 1,4-bromochlorobenzenes to sequential reactions with triallyl(aryl)silanes.[69] Selective coupling at the bromide site was

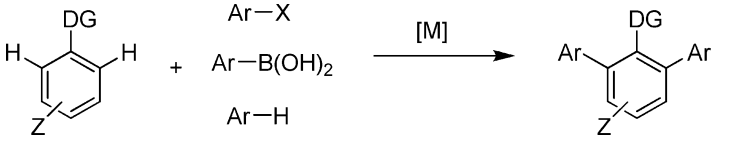
achieved using the PCy_3 as the ligand, whereas X-Phos was used to activate the more inert C-Cl bond (*Scheme 20*). The reactions are high yielding, and the scope of the methodology proved to be fairly wide, and tolerant of many functional groups. The main drawback is the lack of *o*-terphenyl examples.



Scheme 20
Consecutive Hiyama Cross-coupling

6. Aryl-aryl Coupling by C-H Activation

Significant advances have been made in direct activation of C-H bonds, particularly towards cross-coupling reactions, where one or both of the reactants can be replaced by unactivated arenes.[70–73] By eliminating the need for halide and/or organometallic reagents, the atom-economy of the process can be improved greatly. Double *o*-arylation reactions will therefore deliver 2-functionalized *m*-terphenyls (*Scheme 21*). As the area has been extensively reviewed elsewhere,[71,73–83] only a brief summary of the key features is provided here.



Scheme 21
Synthesis of *m*-Terphenyls by Direct *o*-Arylation

(i) The presence of certain directing groups (DG) is necessary for arylation to occur at the *ortho*- position. The DG may be a functional group (*e.g.* carboxylic acids, anilides, benzylamino, nitro, etc.) or a heterocycle (*e.g.* 2-pyridine, azole, benzoxazole, oxazoline, etc);

(ii) The source of the arylating reagent is most commonly an aryl halide or arylmetals (*e.g.* arylboronic acid). In certain cases, an unactivated arene can also be used, but a stoichiometric amount of oxidant (*e.g.* 1,4-benzoquinone) is required;

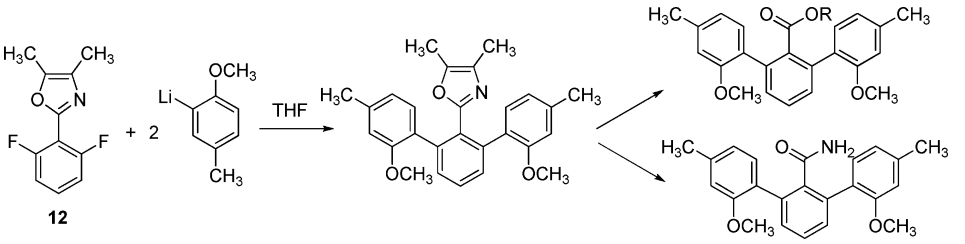
(ii) Several catalytic systems have been developed in recent years, the most common being Rh-, Ru- and Pd- based. Fe was also recently discovered as an active catalyst.[84]

Currently, only *o*-diarylation has been demonstrated in these reactions. However, they are potentially useful for the synthesis of *m*-terphenyls containing a functional group between the two aryl moieties, which may be difficult to achieve using more traditional cross-coupling reactions due to steric hindrance.

II. Non Metal-catalyzed Aryl-aryl Coupling: Nucleophilic Aromatic Substitution

In certain cases, the formation of aryl-aryl bonds by the reaction of aryl halides and organometallic reagents can proceed, without the need for a catalyst, through S_NAr reactions of activated halobenzenes.

With an oxazole acting as the directing group, the synthesis of 1,3-diarylbenzoic acid derivatives was achieved by sequential S_NAr displacement of *o, o′*-difluorides (*e.g.* **12)** with lithiated aryl reagents (*Scheme 22*).[85] The oxazole can later be 'unmasked' to generate various acid derivatives.



Scheme 22
S_NAr reactions of 2,5-difluorophenyloxazoles

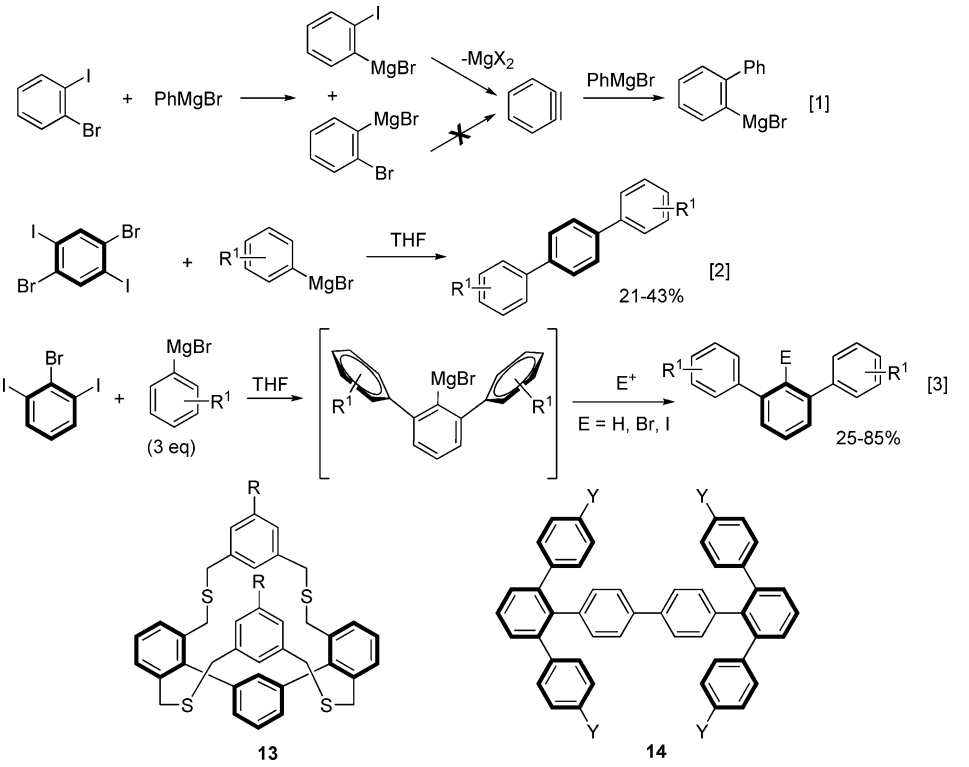
Aryl Grignard reagents undergo metal-halide exchange with aryl iodide/bromide in the absence of catalyst. In a body of work by Hart and co-workers, it was found that if an iodide is present at the *ortho* position, 1,2-elimination can occur to give a benzyne intermediate, which can be trapped by another Grignard reagent to achieve C-C bond formation (*Scheme 23, equation 1*). Using 1,4-dibromo-2,5-diiodobenzene as a precursor, *p*-terphenyls can thus be obtained (*Scheme 23, equation 2*).[86] Similarly, the synthesis of *m*-terphenyls can be obtained from 2,6-dibromoiodobenzene (*Scheme 23, equation 3*).[87] In both cases, symmetrical *m*- and *p*-terphenyls were obtained in moderate to good yields. The method has been used for the synthesis of a series of cappedophanes **13**[88–90] and terphenyl building blocks such as **14**[4] for crystal engineering.

Recently, a synthesis of *m*-terphenyl-2′-carbaldehydes was achieved by using ethyl formate as the electrophilic trapping agent in the reaction of arylmagnesium bromides with 1,3-dichloroiodobenzene.[91] Similarly, Saednya *et al.* described the synthesis of *m*-terphenyls from 1,3-dichlorobenzene in two ways (*Scheme 24*), either by: (i) the reaction with excess aryllithium at room temperature (59–94%); or (ii) lithiation of the dichlorobenzene, followed by the reaction with aryl Grignard reagents (57–93%).[92]

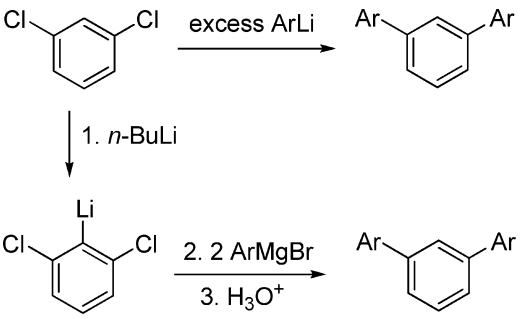
III. Benzannulation Reactions from Acyclic Precursors

1. Concerted [4+2] and [2+2+2] Cycloaddition Reactions

Cycloaddition reactions are among the best strategies for the construction of 6-membered rings. It may be envisaged that the central ring of a terphenyl molecule could be assembled by means of [4+2] or [2+2+2] cycloaddition reactions, followed by aromatization of the resultant cyclohexadiene.



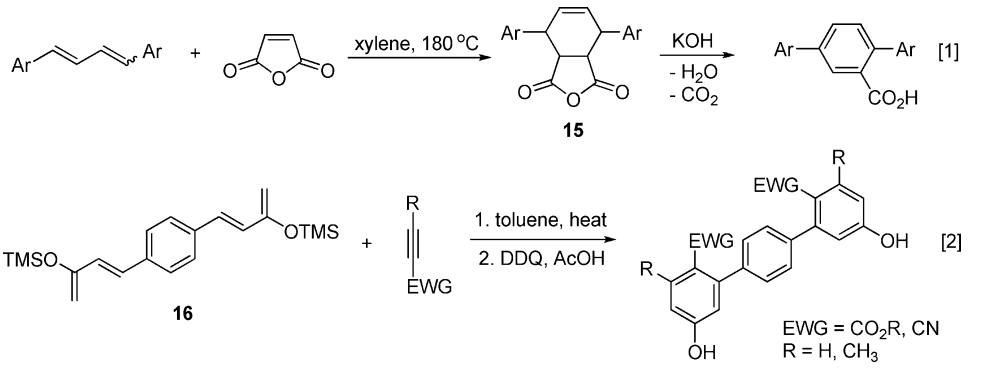
Scheme 23
Synthesis of *m*- and *p*-Terphenyls from Reaction of Mixed Halobenzenes with Aryl Grignard Reagents



Scheme 24
Synthesis of *m*-Terphenyls from 1,3-Dichlorobenzene

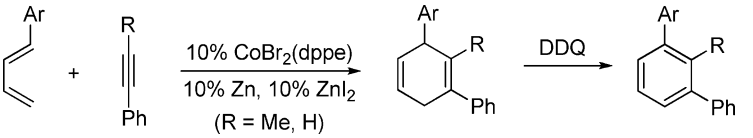
Diels-Alder reactions were employed by Torri for the synthesis of 2,5-diaryl substituted benzoic acids where 1,4-diaryl-substituted butadienes were subjected to cycloaddition reactions with maleic anhydride. Cycloadducts **15** were then subjected to alkaline hydrolysis, followed by dehydrative decarboxylation to give *p*-terphenyl derivatives in good yields (*Scheme 25, equation 1*).[93] Conversely, terminal aromatic rings could be assembled by

treating *bis*-silyoxybuta-1,3-diene **16** with electron-deficient alkynes, to give phenolic *p*-terphenyls after DDQ oxidation (*Scheme 25, equation 2*).[94]



Scheme 25
Synthesis of *m*- and *p*-Terphenyl Derivatives by Diels-Alder Reactions

More recently, a cobalt-catalyzed Diels-Alder-oxidation sequence was reported by Hilt *et al.* for the synthesis of *m*-terphenyls from 1,3-dienes and phenylacetylenes (*Scheme 26*).[95] The regioselectivity reported for the *meta* isomer was very high (at least 98:2) for reactions involving phenylacetylene (R = H). However, internal alkynes (R = Me) gave nearly 1:1 mixtures of *o*- and *m*-terphenyls.

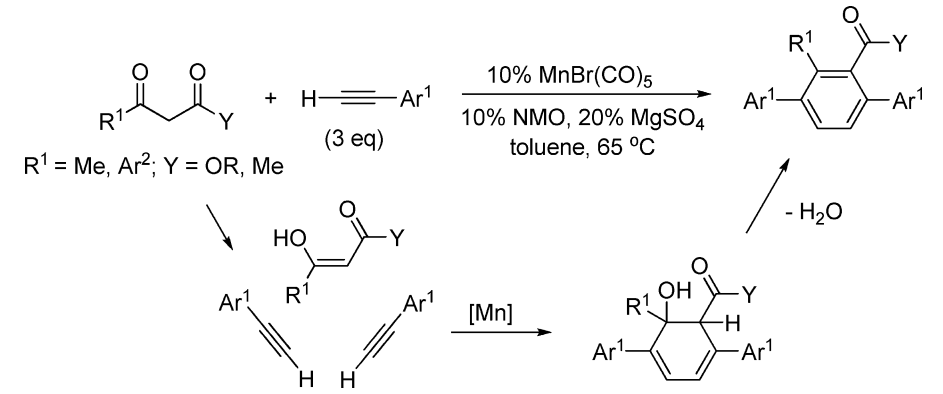


Scheme 26
Synthesis of Terphenyls by Cobalt-catalyzed [4+2] Reactions

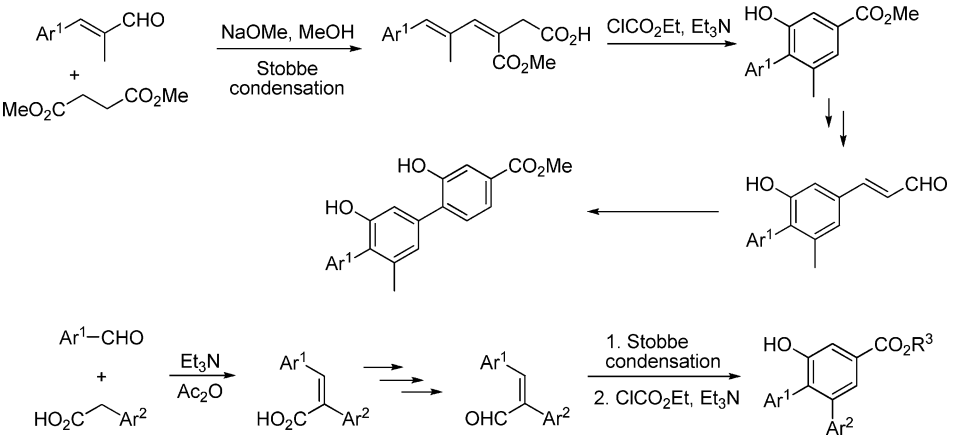
Mn-catalyzed [2+2+2] annulation reactions of 1,3-dicarbonyl compounds with terminal acetylenes furnished *p*-terphenyl compounds with excellent regioselectivity (*Scheme 27*). Reactions occurred under fairly mild conditions in the presence of NMO and a dessicant.[96] Similar reactions were also reported without using any solvents or the *N*-oxide additive.[97]

2. Stepwise Benzannulation Reactions

Condensation reactions are widely used in stepwise benzannulation strategies for terphenyl synthesis. A typical example is a two-step synthesis of diaryl-substituted hydroxybenzoic acids. Starting with a Stobbe condensation of an unsaturated aldehyde with dimethyl succinate, the resultant monoester monoacid was treated with ethyl chloroformate and triethylamine to afford an aromatic ring (*Scheme 28*).[98] The reaction may also be applied in an iterative way to generate a *p*-terphenyl derivative. This strategy was extended to the synthesis of unsymmetrical *o*-terphenyls, where α,β-unsaturated carboxylic acids were prepared *via* Perkin reaction between a benzaldehyde and phenylacetic acid, which was



Scheme 27
Synthesis of *p*-Terphenyls by Mn-catalyzed [2+2+2] Cycloadditions

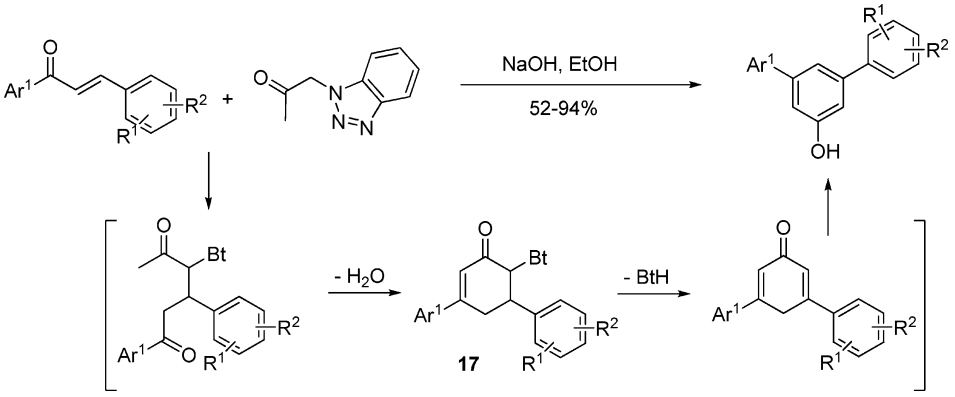


Scheme 28
Benzannulation Reactions by Cyclization of Stobbe Condensation Adducts

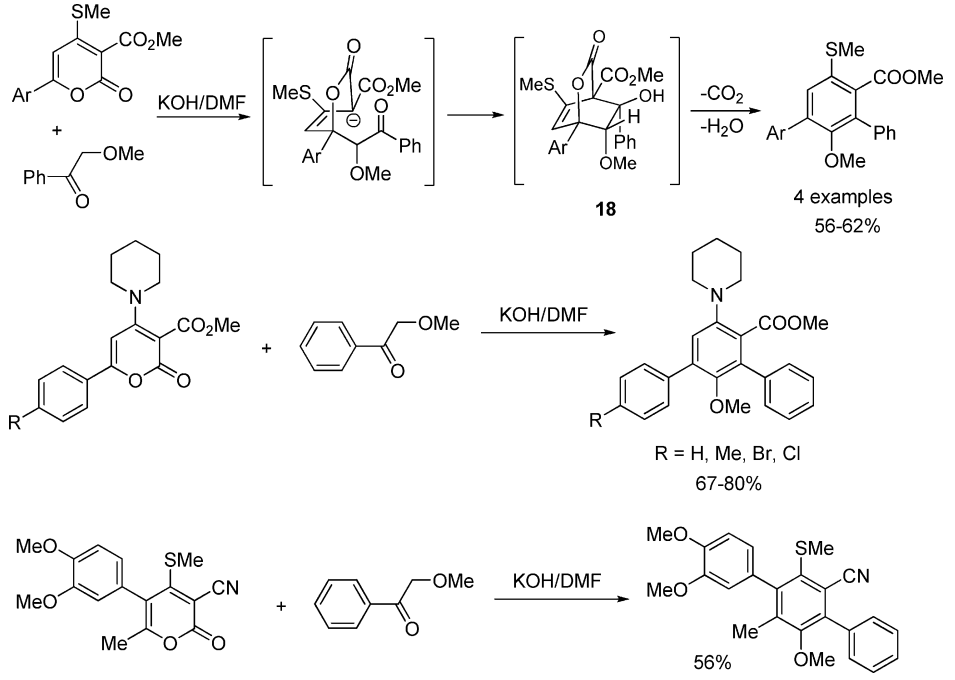
further transformed to the conjugated aldehyde. Subsequent cyclization to the 2,3-diaryl substituted phenol, under previously described conditions, occurred with good to excellent yields of 80–90%.[99]

On the other hand, Katritzky *et al.* reported the synthesis of 3,5-diaryl-substituted phenols by the reaction of 1-(benzotriazol-1-yl)propan-2-one and 1,3-diarylprop-2-enones under basic conditions (*Scheme 29*). The reaction is thought to initiate with a conjugate addition, where the resultant Michael adduct undergoes an intramolecular aldol reaction to generate a cyclohexenone intermediate **17**, which is aromatized by elimination of benzotriazole and dehydration to provide the terphenyl compound.[100]

Similarly, addition of a carbanion generated from 2-methoxyacetophenone to 2*H*-pyra-2-ones was followed by an intramolecular cyclization to furnish a bridged cyclohexene intermediate **18** (*Scheme 30*). Aromatization of the central ring occurs *via* a retro-Diels Alder reaction, driven by elimination of CO_2, to furnish *m*-terphenyls in moderate yields (*Scheme 30*).[101] Better yields were obtained by suppressing formation of side-products through the



Scheme 29
Synthesis of 3,5-Diarylphenols

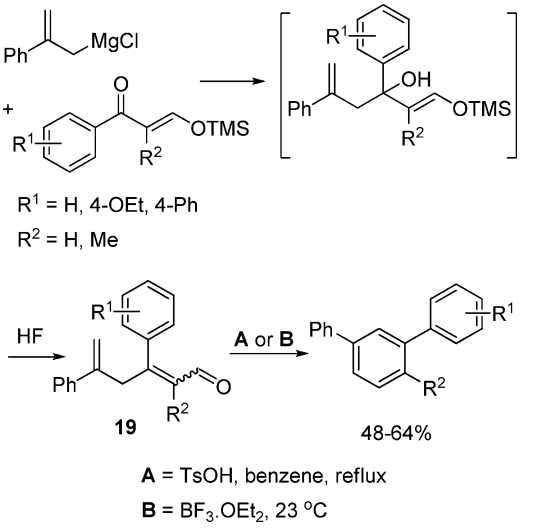


Scheme 30
Synthesis of *m*-Terphenyls from 2*H*-Pyra-2-ones and 2-Methoxyacetophenone

substitution of SMe with a secondary amine. The synthesis of a polysubstituted *p*-terphenyl was also achieved from the reaction of methyl 2-cyano-3,3-di(methylsulfanyl)acrylate and 3,4-dimethoxyphenylacetone in 56% yield.

Another synthesis of *m*-terphenyls was achieved by the addition of a 2-phenylallyl Grignard reagent to a silyl enol ether generated from 1,3-dicarbonyl compounds. The

product was hydrolyzed immediately with aq. HF to give (*E*)- and (*Z*)-**19**, which cyclized in the presence of Brønsted/Lewis acids to the target compounds (*Scheme 31*).[102]

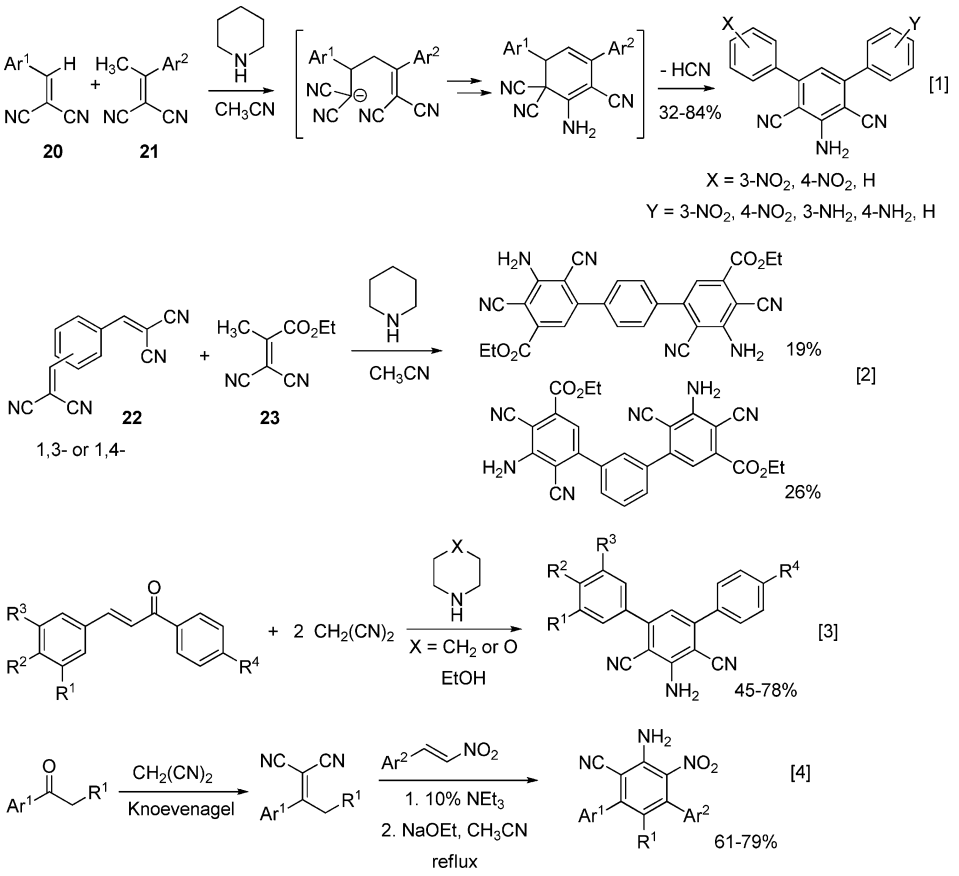


Scheme 31
Preparation of *m*-Terphenyls by the Reaction of an Allyl Grignard Reagent with the Silyl Enolether Generated from a 1,3-Dicarbonyl compound

Based on a variation of the Gewald synthesis,[103] a method for the synthesis of *m*-terphenyls from nitrobenzylidenemalonodinitriles **20** and ethylidenemalonodinitriles **21** was developed (*Scheme 32, equation 1*).[104] The reaction proceeds *via* Michael addition of an anion generated from **21**, to the benzylidenemalonodinitrile **20**. This is followed by the cyclization of the Michael product to furnish a cyclohexadiene system. Finally, the elimination of hydrogen cyanide affords the central ring. The yield of the reaction is dependent on the pattern of substitution on the Michael acceptor. The densely substituted terphenyls products can be further modified, by reduction of the nitro groups or thermal decyanation.

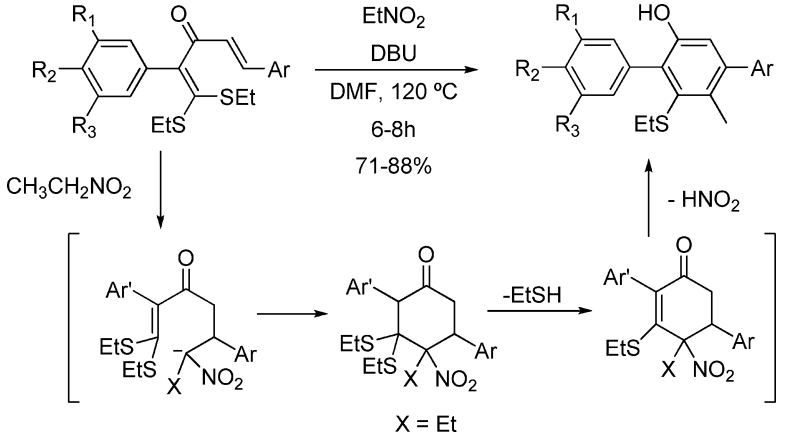
Recently, this strategy was utilized to produce a number of *m*-terphenyl amines as a novel class of cyclooxygenase (COX) inhibitors.[105] The construction of flanking aryl groups may also be achieved by the reaction of arylidenemalonodinitriles **22** and ethyl dicyanomethylenepropanoate **23** (generated from ethyl pyruvate and malononitrile), but in much lower yields (*Scheme 32, equation 2*).[106] A few modifications of this reaction were reported, including the reaction between chalcones and malononitriles (*Scheme 32, equation 3*),[107] or the reaction of vinyl malonodinitriles (obtained by Knoevenagel reactions) with nitroolefins *via* one-pot tandem addition processes (*Scheme 32, equation 4*).[108] Using these reactions, substituted *m*-terphenyls could be obtained in good yields.

A recent report by Liu *et al.* of a further modification led to the synthesis of substituted *p*-terphenyls from α-aryl-α-alkenoyl ketene-(*S*,*S*)-acetals and nitroethane (*Scheme 33*).[109]



Scheme 32

Gewald-type Annulation Reactions of Alkylidenemalodinitriles



Scheme 33

[5+1] Annulation of α-aryl- α-Alkenoyl Ketene-(*S*,*S*)-acetals with Nitroethane

III. Summary

To conclude, the synthesis of terphenyls has been achieved most efficiently using metal-catalyzed cross-coupling reactions. Chemoselectivity issues have been largely resolved by employing aryl precursors containing halides/pseudohalides with complementary activities, such that milder reaction conditions can be employed in the first step, with the (more difficult) second step achieved under different conditions, typically by raising the temperature or by employing certain metal ligands. Sequential Suzuki cross-coupling reactions of bromochlorobenzenes with arylboronic acids proved to be most practical and versatile method for producing numerous symmetrical and unsymmetrical *o*-, *m*- and *p*-terphenyls. When reactivity is a problem, Negishi cross-coupling with arylzincs can offer a viable alternative, although the organometallic reagent has to be prepared and stored under rigorously dry conditions. More recently, the discovery of C-H activation processes offers an atom-economical route to cross-coupling reactions. This has specific utility for the synthesis of symmetrically substituted 1,3-diaryl aromatic rings. However, further developments are necessary before this route can be adopted for the synthesis of unsymmetrical molecules.

On the other hand, non-metal catalyzed methods have also been developed for the synthesis of terphenyl molecules. Although these are rather limited in scope, they are particularly useful specifically for the synthesis of poly-substituted terphenyls, which may be difficult to assemble by cross-coupling due to steric hindrance, or when access to the requisite aromatic precursors is problematic.

Terphenyl molecules are employed in a wide range of important applications, from the discovery of novel scaffolds in medicinal chemistry to the fabrication of advanced materials with novel electrical and optical properties. For these reasons, the quest for atom-efficient, practical and scaleable routes to the synthesis of terphenyls will continue to flourish for the foreseeable future.

Acknowledgements

The authors thank Fundación Caixa Galicia (Becas Postgrado 2008) and Xunta Galicia for an Ángeles Alvariño Fellowship (LAA), and a María Barbeito Fellowship (JAM). We are also grateful to Ministerio de Educación y Ciencia for facilitating the collaboration between Imperial College London and Universidad de Santiago de Compostela (project number CTQ2006-15621-C02-01/BQU).

References

1. M. H. Todd, S. Balasubramanian and C. Abell, *Tetrahedron Lett.*, **38**, 6781 (1997).
2. E. F. Corsico and R. A. Rossi, *Synlett*, 230 (**2000**).
3. E. Yashima, K. Maeda and Y. Furusho, *Acc. Chem. Res.*, **41**, 1166 (2008).
4. B. S. Udayakumar and G. B. Schuster, *J. Org. Chem.*, **57**, 348 (1992).
5. R. S. Wright and T. K. Vinod, *Tetrahedron Lett.*, **44**, 7129 (2003).
6. H.-R. Liao, Y.-J. Lin, Y.-M. Chou, F.-T. Luo and B.-C. Wang, *J. Lumin.*, **128**, 1373 (2008).
7. G. Yu, J. Gao, J. C. Hummelen, F. Wudl and A. J. Heeger, *Science*, **270**, 1789 (1995).

8. F. Garnier, R. Hajlaoui, A. Yassar and P. Srivastava, *Science*, **265**, 1684 (1994).

9. F. Hide, M. A. Diaz-Garcia, B. J. Schwartz and A. J. Heeger, *Acc. Chem. Res.*, **30**, 430 (1997).

10. F. Maya and J. M. Tour, *Tetrahedron*, **60**, 81 (2004).

11. J. K. Liu, *Chem. Rev.*, **106**, 2209 (2006).

12. Y. Sawayama, T. Tsujimoto, K. Sugino, T. Nishikawa, M. Isobe and H. Kawagishi, *Biosci. Biotechnol. Biochem.*, **70**, 2998 (2006).

13. V. Cali, C. Spatafora and C. Tringali, *Stud. Nat. Prod. Chem.*, **29**, 263 (2003).

14. B. P. Orner, J. T. Ernst and A. D. Hamilton, *J. Am. Chem. Soc.*, **123**, 5382 (2001).

15. M. Roberti, D. Pizzirani, M. Recanatini, D. Simoni, S. Grimaudo, A. Di Cristina, V. Abbadessa, N. Gebbia and M. Tolomeo, *J. Med. Chem.*, **49**, 3012 (2006).

16. D. Simoni, G. Giannini, P. G. Baraldi, R. Romagnoli, M. Roberti, R. Rondanin, R. Baruchello, G. Grisolia, M. Rossi, D. Mirizzi, F. P. Invidiata, S. Grimaudo and M. Tolomeo, *Tetrahedron Lett.*, **44**, 3005 (2003).

17. D. Simoni, G. Giannini, M. Roberti, R. Rondanin, R. Baruchello, M. Rossi, G. Grisolia, F. P. Invidiata, S. Aiello, S. Marino, S. Cavallini, A. Siniscalchi, N. Gebbia, L. Crosta, S. Grimaudo, V. Abbadessa, A. Di Cristina and M. Tolomeo, *J. Med. Chem.*, **48**, 4293 (2005).

18. D. Simoni, R. Rondanin, R. Baruchello, M. Rizzi, G. Grisolia, M. Eleopra, S. Grimaudo, A. Di Cristina, M. R. Pipitone, M. R. Bongiorno, M. Arico, F. P. Invidiata and M. Tolomeo, *J. Med. Chem.*, **51**, 4796 (2008).

19. J. P. Corriu and J. P. Masse, *J. Chem. Soc., Chem. Commun.*, 144 (**1972**).

20. K. Tamao, K. Sumitani and M. Kumada, *J. Am. Chem. Soc.*, **94**, 4374 (1972).

21. N. Marion and S. P. Nolan, *Acc. Chem. Res.*, **41**, 1440 (2008).

22. R. Martin and S. L. Buchwald, *Acc. Chem. Res.*, **41**, 1461 (2008).

23. G. C. Fu, *Acc. Chem. Res.*, **41**, 1555 (2008).

24. C. Amatore, A. Jutand and A. Suarez, *J. Am. Chem. Soc.*, **115**, 9531 (1993).

25. S. Wurtz and F. Glorius, *Acc. Chem. Res.*, **41**, 1523 (2008).

26. M. Bahadir, A. Pieper, R. Vogt, H. Wichmann, J. Grunenberg and H. Hopf, *Chemosphere*, **50**, 1151 (2003).

27. D. H. Camacho, E. V. Salo and Z. B. Guan, *Org. Lett.*, **6**, 865 (2004).

28. Z. N. Yu, H. L. Tu, X. H. Wan, X. F. Chen and Q. F. Zhou, *Mol. Cryst. Liq. Cryst.*, **391**, 41 (2003).

29. Z. G. Zhu, J. G. Zhi, A. H. Liu, J. X. Cui, H. Tang, W. Q. Qiao, X. H. Wan and Q. F. Zhou, *J. Polym. Sci., Part A: Polym. Chem.*, **45**, 830 (2007).

30. Y. Jin, J. Kim, S. H. Park, H. Kim, K. Lee and H. Suh, *Bull. Korean Chem. Soc.*, **26**, 1807 (2005); *Chem. Abstr.*, **145**, 293396 (2005).

31. C.-G. Dong and Q.-S. Hu, *J. Am. Chem. Soc.*, **127**, 10006 (2005).

32. M. Al-Masri, H. R. Kricheldorf and D. Fritsch, *Macromolecules*, **32**, 7853 (1999).

33. C. J. J. Wu, C. H. Xue, Y. M. Kuo and F. T. Luo, *Tetrahedron*, **61**, 4735 (2005).

34. F. Kakali, V. Andrikopoulos, K. Gravalos and J. K. Kallitsis, *Polymer*, **39**, 1493 (1998).

35. H. Chaumeil, C. Le Drian and A. Defoin, *Synthesis*, 757 (**2002**).

36. B. K. Singh, N. Kaval, S. Tomar, E. van der Eycken and V. S. Parmar, *Org. Process Res. Dev.*, **12**, 468 (2008).

37. X. W. Zhao and Y. C. Cui, *Prog. Chem.*, **18**, 1652 (2006).

38. B. Basu, P. Das, M. M. H. Bhuiyan and S. Jha, *Tetrahedron Lett.*, **44**, 3817 (2003).

39. S. Paul and J. H. Clark, *Green Chem.*, **5**, 635 (2003).

40. D. J. Sinclair and M. S. Sherburn, *J. Org. Chem.*, **70**, 3730 (2005).

41. C. M. Unrau, M. G. Campbell and V. Snieckus, *Tetrahedron Lett.*, **33**, 2773 (1992).

42. A. A. Greenfield, J. A. Butera and C. E. Caufield, *Tetrahedron Lett.*, **44**, 2729 (2003).

43. S. Darses, T. Jeffery, J. P. Genet, J. L. Brayer and J. P. Demoute, *Tetrahedron Lett.*, **37**, 3857 (1996).

44. R. H. Taylor and F. X. Felpin, *Org. Lett.*, **9**, 2911 (2007).

45. J. M. A. Miguez, L. A. Adrio, A. Sousa-Pedrares, J. M. Vila and K. K. Hii, *J. Org. Chem.*, **72**, 7771 (2007).

46. T. E. Barder, S. D. Walker, J. R. Martinelli and S. L. Buchwald, *J. Am. Chem. Soc.*, **127**, 4685 (2005).

47. A. E. Sutton and J. Clardy, *Tetrahedron Lett.*, **42**, 547 (2001).

48. T. Saeki, E. C. Son and K. Tamao, *Org. Lett.*, **6**, 617 (2004).

49. C. Y. Liu, A. Gavryushin and P. Knochel, *Chem. Asian J.*, **2**, 1020 (2007); *Chem. Abstr.*, **148**, 331362 (2007).

50. M. Catellani, E. Motti and N. Della Ca, *Acc. Chem. Res.*, **41**, 1512 (2008).

51. E. Motti, A. Mignozzi and M. Catellani, *J. Mol. Cat. A: Chem.*, **204**, 115 (2003).

52. Y. Ikoma, K. Ando, Y. Naoi, T. Akiyama and A. Sugimori, *Synth. Commun.*, **21**, 481 (1991).

53. C. H. Cho, I. S. Kim and K. Y. Park, *Tetrahedron*, **60**, 4589 (2004).

54. J. K. Stille, *Pure Appl. Chem.*, **57**, 1771 (1985).

55. J. M. Saa and G. Martorell, *J. Org. Chem.*, **58**, 1963 (1993).

56. A. B. Chopa, G. F. Silbestri and M. T. Lockhart, *J. Organomet. Chem.*, **690**, 3865 (2005).

57. E. Negishi, A. O. King and N. Okukado, *J. Org. Chem.*, **42**, 1821 (1977).

58. E. I. Negishi, *Acc. Chem. Res.*, **15**, 340 (1982).

59. L. Zhu, R. M. Wehmeyer and R. D. Rieke, *J. Org. Chem.*, **56**, 1445 (1991).

60. K. Takagi, Y. Shimoishi and K. Sasaki, *Chem. Lett.*, 2055 (**1994**).

61. M. Amano, A. Saiga, R. Ikegami, T. Ogata and K. Takagi, *Tetrahedron Lett.*, **39**, 8667 (1998).

62. H. Fillon, C. Gosmini and J. Perichon, *J. Am. Chem. Soc.*, **125**, 3867 (2003).

63. T. Kawamoto, S. Ejiri, K. Kobayashi, S. Odo, Y. Nishihara and K. Takagi, *J. Org. Chem.*, **73**, 1601 (2008).

64. M. Rottaelander, N. Palmer and P. Knochel, *Synlett*, 573 (**1996**).

65. H. Shimizu and K. Manabe, *Tetrahedron Lett.*, **47**, 5927 (2006).
66. Z. X. Xi, Y. B. Zhou and W. Z. Chen, *J. Org. Chem.*, **73**, 8497 (2008).
67. S. E. Denmark and C. S. Regen, *Acc. Chem. Res.*, **41**, 1486 (2008).
68. T. Hiyama, *Chem. Rec.*, **8**, 337 (2008).
69. A. K. Sahoo, T. Oda, Y. Nakao and T. Hiyama, *Adv. Synth. Catal.*, **346**, 1715 (2004).
70. D. Alberico, M. E. Scott and M. Lautens, *Chem. Rev.*, **107**, 174 (2007).
71. L. C. Campeau and K. Fagnou, *Chem. Commun.*, 1253 (**2006**).
72. F. Kakiuchi and N. Chatani, *Adv. Synth. Catal.*, **345**, 1077 (2003).
73. B. J. Li, S. D. Yang and Z. J. Shi, *Synlett*, 949 (**2008**).
74. X. D. Zhao and Z. K. Yu, *J. Am. Chem. Soc.*, **130**, 8136 (2008).
75. K. Cheng, Y. H. Zhang, J. L. Zhao and C. S. Xie, *Synlett*, 1325 (**2008**).
76. S. Oi, R. Funayama, T. Hattori and Y. Inoue, *Tetrahedron*, **64**, 6051 (2008).
77. S. Oi, Y. Ogino, S. Fukita and Y. Inoue, *Org. Lett.*, **4**, 1783 (2002).
78. S. Oi, H. Sato, S. Sugawara and Y. Inoue, *Org. Lett.*, **10**, 1823 (2008).
79. F. Yang, Y. J. Wu, Z. W. Zhu, J. L. Zhang and Y. N. Li, *Tetrahedron*, **64**, 6782 (2008).
80. L. Caron, L. C. Campeau and K. Fagnou, *Org. Lett.*, **10**, 4533 (2008).
81. H. A. Chiong, Q. N. Pham and O. Daugulis, *J. Am. Chem. Soc.*, **129**, 9879 (2007).
82. A. Lazareva and O. Daugulis, *Org. Lett.*, **8**, 5211 (2006).
83. D. Shabashov and O. Daugulis, *Org. Lett.*, **8**, 4947 (2006).
84. J. Norinder, A. Matsumoto, N. Yoshikai and E. Nakamura, *J. Am. Chem. Soc.*, **130**, 5858 (2008).
85. D. J. Cram, J. A. Bryant and K. M. Doxsee, *Chem. Lett.*, 19 (**1987**).
86. H. Hart, K. Harada and C. J. F. Du, *J. Org. Chem.*, **50**, 3104 (1985).
87. C. J. F. Du, H. Hart and K. K. D. Ng, *J. Org. Chem.*, **51**, 3162 (1986).
88. T. K. Vinod and H. Hart, *J. Org. Chem.*, **55**, 881 (1990).
89. T. K. Vinod and H. Hart, *Cyclophanes*, **172**, 119 (1994).
90. T. K. Vinod and H. Hart, *J. Org. Chem.*, **56**, 5630 (1991).
91. B. Rashidzadeh, F. Jafarpour and A. Saednya, *ARKIVOC*, 167 (**2008**).
92. A. Saednya and H. Hart, *Synthesis*, 1455 (**1996**).
93. H. Tanaka, A. Kosaka, S. Yamashita, K. Morisaki and S. Torii, *Tetrahedron Lett.*, **30**, 1261 (1989).
94. Y. Yamamoto, K. Nunokawa, M. Ohno and S. Eguchi, *Synthesis*, 949 (**1996**).
95. G. Hilt and M. Danz, *Synthesis*, 2257 (**2008**).
96. H. Tsuji, K. I. Yamagata, T. Fujimoto and E. Nakamura, *J. Am. Chem. Soc.*, **130**, 7792 (2008).
97. Y. Kuninobu, M. Nishi, S. S. Yudha and K. Takai, *Org. Lett.*, **10**, 3009 (2008).
98. E. Brenna, C. Fuganti, V. Perozzo and S. Serra, *Tetrahedron*, **53**, 15029 (1997).

99. E. Brenna, C. Fuganti and S. Serra, *J. Chem. Soc., Perkin Trans. 1*, 901 (**1998**).

100. A. R. Katritzky, S. A. Belyakov, S. A. Henderson and P. J. Steel, *J. Org. Chem.*, **62**, 8215 (1997).

101. A. Goel, D. Verma and F. V. Singh, *Tetrahedron Lett.*, **46**, 8487 (2005).

102. M. A. Tius and S. Savariar, *Synthesis*, 467 (**1983**).

103. K. Gewald and W. Schill, *J. prak. Chem.*, **313**, 678 (1971).

104. P. Milart, J. Wilamowski and J. J. Sepiol, *Tetrahedron*, **54**, 15643 (1998).

105. J. D. Bauer, M. S. Foster, J. D. Hugdahl, K. L. Burns, S. W. May, S. H. Pollock, H. G. Cutler and S. J. Cutler, *Med. Chem. Res.*, **16**, 119 (2007).

106. P. Milart and J. Sepiol, *Tetrahedron Lett.*, **31**, 2735 (1990).

107. V. Raghukumar, P. Murugan and V. T. Ramakrishnan, *Synth. Commun.*, **31**, 3497 (2001).

108. D. Xue, J. Li, Z. T. Zhang and J. G. Deng, *J. Org. Chem.*, **72**, 5443 (2007).

109. L. Zhang, F. S. Liang, X. Cheng and Q. Liu, *J. Org. Chem.*, **74**, 899 (2009).