The oxidation of organocuprates—an offbeat strategy for synthesis

David S. Surry and David R. Spring*

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The creation of carbon–carbon and carbon–heteroatom bonds by the oxidation of organocuprates is useful in a range of challenging contexts including the formation of biaryl bonds within medium rings, diene synthesis and the coupling of tertiary carbon centres. This *tutorial review* introduces these applications and recent developments which have served to improve its functional group tolerance and its utility in organic synthesis.

1 Introduction

The use of transition metals in organic chemistry has revolutionized the way in which syntheses are planned and executed. Particularly noteworthy has been the application of copper in organic synthesis. Although phenylcopper(I) was first made in 1923,[1] the field grew slowly until the first preparation of an organo*cuprate* in 1952 by Gilman.[2] This advance lead to further developments by Corey, House and Whitesides.[3] Today, organocuprates are standard fare; however, their oxidation has been underexploited. This review aims to highlight the recent progress in the oxidation of organocuprates as an unconventional tool in organic synthesis.

The simplest element of organocuprate structure is the $[R–Cu–R]^-$ unit which is approximately linear with carbon–copper bonds of length about 1.9 Å and with a d^{10} electron configuration at the metal centre. With no other salts present lithium organocuprates ("Gilman reagents") tend to exist as dimers; however, if accompanied by metal halides or pseudohalides (*e.g.* cyanide), these may become incorporated into the cuprate structure, depending on the solvent.[4]

Such reagents have proved to be extremely valuable for a range of synthetic transformations including conjugate addition,[5] epoxide opening, halide displacement and carbocupration.[6–8] The success in these processes are characterized by slower addition to carbonyl groups and lower basicity, combined with greater nucleophilicity towards α,β-unsaturated carbonyl compounds and organic halides, compared to other, harder organometallics such as organolithiums and Grignard reagents. The negatively charged organocuprate has a relatively high-lying HOMO composed of a combination of the $3d_{z2}$ and the 3s orbitals of the metal which is well suited to interact with the σ* orbital of a carbon–halogen bond of organic halides (Fig. 1). Furthermore, bending of the C–Cu–C bond to an angle of less than 150° produces a higher energy HOMO comprised of the metal $3d_{xz}$ and the $2p_x$ orbitals of the organic ligands. This new HOMO can interact favourably with the π* orbital of enones and acetylenes in conjugate addition and carbocupration reactions.[9]

The elevated HOMO of organocuprates also means that oxidation of such compounds is a relatively easy process and has been brought about by a range of oxidants including transition metal salts, molecular oxygen, dinitroarenes and quinones. Indeed, it has been adduced that the conjugate addition of organocuprates to doubly activated alkenes[10] and

Department of Chemistry, University of Cambridge, Lensfield Road, Cambridge, UK CB2 1EW. E-mail: drspring@ch.cam.ac.uk; Fax: +44 (0) 1223 336362; Tel: +44 (0) 1223 336498

David S. Surry

David Surry was born in London in 1979 and graduated from the University of Cambridge in 2002. He has just completed his PhD studies on the oxidation of organocuprates with Dr David Spring at the same university. In 2006 he will take up a Research Fellowship from the Royal Commission for the Exhibition of 1851 in the laboratories of Prof. Steve Buchwald at the Massachusetts Institute of Technology.

David R. Spring

David Spring was born in West Bromwich and attended Oxford University for his undergraduate chemistry degree, graduating in 1995. He stayed at Oxford under the supervision of Sir Jack Baldwin and received his DPhil in 1998 for work on the proposed biosynthesis of the manzamine alkaloids. David then spent two and a half years as a Wellcome Trust postdoctoral fellow and Fulbright scholar at Harvard University with Stuart Schreiber. In 2001 he returned to the UK as a BBSRC David Phillips Fellow and Fellow of Queens' College at Cambridge, where he is researching diversity-oriented synthesis and chemical genetics.

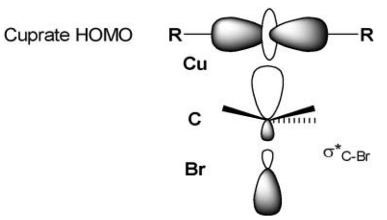
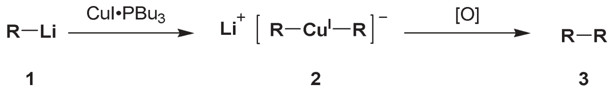


Fig. 1 Interaction of organocuprate HOMO and C–Br bond.

the reaction of organocuprates with alkyl iodides[11] involve initial oxidation of the organometallic species.

2 Early results

The first examination of the oxidation of preformed organocuprates[12] was undertaken by Whitesides.[13] A range of simple organolithium species (**1**) were treated with copper(I) iodide–tri-*n*-butylphosphine complex. The organocuprate (**2**) which resulted from this transmetallation reaction was then oxidized (Scheme 1).

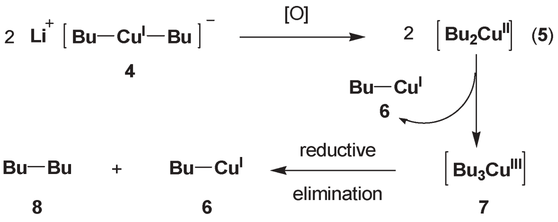


$$\underset{\mathbf{1}}{R{-}Li} \xrightarrow{CuI\bullet PBu_3} \underset{\mathbf{2}}{Li^+\left[R{-}Cu^I{-}R\right]^-} \xrightarrow{[O]} \underset{\mathbf{3}}{R{-}R}$$

Scheme 1 General organocuprate oxidation.

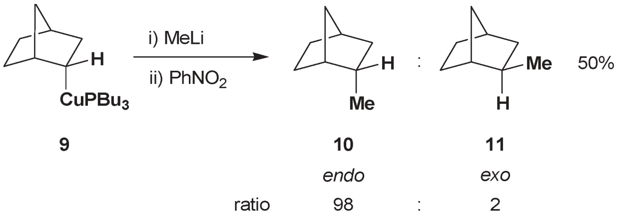
It was found that dimerization of the organic ligands (R groups) occurred in yields of 75–84% for primary alkyl, secondary alkyl-, aryl- and vinyllithium species, but that *tert*-butyllithium gave only 14% recovery of dimer. The nature of the counterion was also important, *n*-butylmagnesium bromide giving a lower yield (67% compared to 84%) of dimer than *n*-butyllithium as the transmetallation partner. The results provided are for the use of molecular oxygen as oxidant, but nitrobenzene and copper(II) chloride–TMEDA complex were reported to be equally effective.

A thorough analysis of the reaction mixture after the oxidation of lithium di-*n*-butylcuprate revealed *n*-octane (84%) and the by-products but-1-ene (14%), *n*-butanol (5%) and a ''moderate yield'' of *n*-butylcopper(I). The presence of but-1-ene and *n*-butanol by-products indicated oxidation of *n*-butylcopper(I) under the reaction conditions. This led to the tentative mechanistic proposal that the lithium di-*n*-butylcuprate (**4**) was initially oxidized to di-*n*-butylcopper(II) (**5**) which rapidly and quantitatively disproportionated to give *n*-octane (**8**) and *n*-butylcopper(I) (**6**), the latter then undergoing further oxidation (Scheme 2). This process may pass through a transient copper(III) species (**7**) which undergoes formal reductive elimination to generate the coupled product (**8**) and *n*-butylcopper(I) (**6**) (Scheme 2). Such copper(III) compounds have been characterized in certain cases[14] and are postulated commonly as intermediates in other copper-mediated reactions.[15] Of course, such a model constitutes a great simplification, because in solution organocuprates are aggregated. Hence, once initial electron transfer from an aggregated species has taken place, intramolecular bond cleavage or redox processes may occur, leading to the products observed.[16]



Scheme 2 Simplistic mechanism of the dimerization of organic ligands upon oxidation of an organocuprate.

Whitesides argued against the possibility of persistent free radicals as intermediates in these reactions based on the following lines of evidence: (i) no rearrangement was witnessed in the oxidation of lithium dineophylcuprate; (ii) double bond geometry was retained in the oxidation of lithium di-*trans*-propenylcuprate; and (iii) a small amount of oxygenated products was produced by the reactions (much more would be expected if free radicals were present in a solution containing a high concentration of molecular oxygen). In addition, the oxidation of organocuprates occurred with retention of stereochemistry; the mixed organocuprate formed by reacting *endo*-2-norbornyl-(tri-*n*-butylphosphine)copper(I) (**9**) with methyllithium was oxidized with nitrobenzene to give 2-methylnorbornane in a 98 : 2 ratio of *endo* (**10**) to *exo* (**11**) isomers (Scheme 3).[17] An *endo*:*exo* isomer ratio closer to 1 : 1 would be expected if the reaction proceeded *via* radical intermediates.

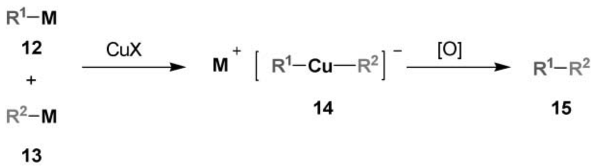


Scheme 3 Retention of stereochemistry in the organocuprate oxidation.

3 Unsymmetrical carbon–carbon bond formation

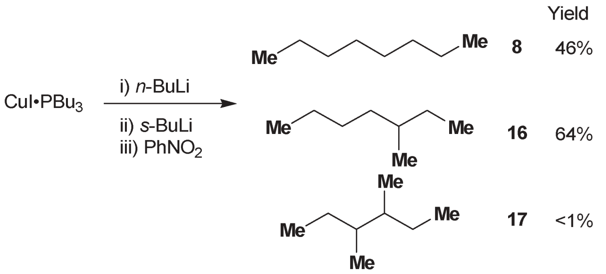
One objective in the study of the organocuprate oxidation has been the development of a cross-coupling procedure, which creates a carbon–carbon bond between two different organometallic components by way of a mixed organocuprate (**14**) (Scheme 4).

Whitesides first looked at this concept by treating a 1 : 1 mixture of phenyllithium and *n*-butyllithium with copper(I)



Scheme 4 Cross-coupling of organic groups by way of a mixed organocuprate.

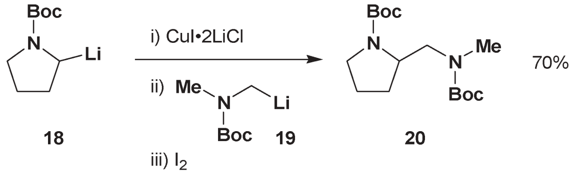
iodide-tri-*n*-butylphosphine complex and oxidizing the resulting organocuprate with molecular oxygen. A mixture of *n*-octane, *n*-butylbenzene and biphenyl was produced in yields of 33%, 33% and 28% respectively. The fact that a simple 1 : 2 : 1 statistical distribution was not observed suggests that not all groups have an equal tendency to couple. This concept was studied later in greater detail[18] and it was demonstrated that the decreased propensity of sterically demanding substrates and (to some extent) phenyl groups to undergo self-coupling allowed reasonable yields of cross-coupled products to be attained (Scheme 5). Alkynyl groups showed little susceptibility to participate in cross-coupling or self-coupling under these conditions, despite the ease of alkyne dimerization by the copper-mediated Glaser reaction.



Scheme 5 Cross-coupling of unfunctionalized alkylithium reagents.

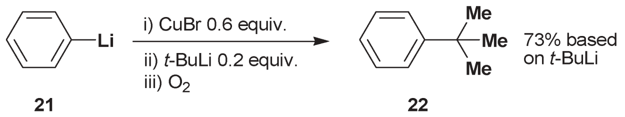
Subsequent investigations by Bertz[19] revealed that the degree of cross-coupling when the coupling partners are similar, both sterically and electronically, could be influenced by the choice of copper(I) salt used for the transmetallation step. These results were taken to imply differences in the structure or intermolecular ligand exchange rate between organocuprates derived from copper(I) iodide and copper(I) cyanide. Interestingly, however, the variation in outcome between the two copper(I) salts was reduced significantly when molecular oxygen replaced *ortho*-dinitrobenzene as oxidant. Better yields for the cross-coupling process can be obtained when both coupling partners have a co-ordinating group (Scheme 6).[20]

The discovery that copper(I) iodide and iodine (oxidant) was the optimal reagent combination is remarkable, as it contrasts strongly with the findings of Bertz for unfunctionalized alkyllithium reagents. Similar yields were achieved for the coupling of primary alkyl groups with *N*-Boc-2-lithiopyrrolidine (**18**); however, the amount of cross-coupled product decreased rapidly along the series *n*-Bu > *s*-Bu > *t*-Bu ≈ Ar. The presence of external ligands such as TMEDA (tetramethylethylenediamine) or tri-*n*-butylphosphine had no effect on the yield of the cross-coupling, but they did serve to reduce the amount of the undesired homo-coupled compound seen. Attempts to perform an enantioselective homo-coupling by oxidation of enantioenriched 2-pyrroldinylcuprate (formed by deprotonation of *N*-Boc-pyrrolidine by *s*-butyllithium and sparteine and transmetallation with a copper(I) salt) gave low enantioselectivity (0–30% ee).



Scheme 6 Cross-coupling of alkylithium reagents possessing a co-ordinating group.

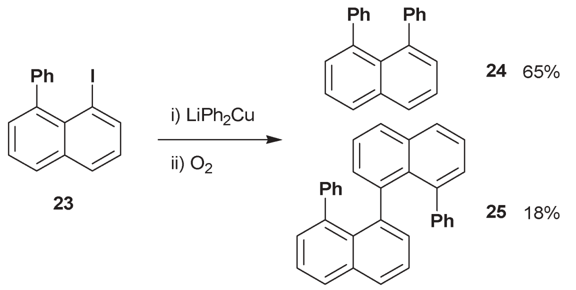
An alternative approach to hetero-coupling is to oxidize a mixed organocuprate in which one of the coupling partners is used in large excess so that the cross-coupled product is made to a reasonable extent. This approach has been shown to be successful even with hindered alkyl groups (Scheme 7).[21]



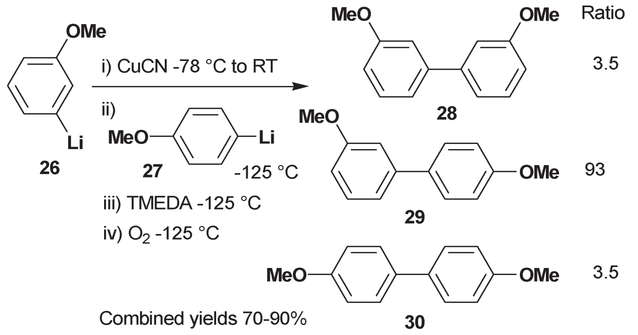
Scheme 7 Cross-coupling of a tertiary alkyl group by making use of excess organometallic.

This outcome may be realised also by treating an aryl iodide with a surplus of a diarylcuprate followed by oxidization. In this reaction halogen–metal exchange processes occurred resulting in a mixed diarylcuprate. Omission of the oxidant led to insignificant return of product. This is in contrast to the reaction between alkyl halides and dialkylcuprates, in which coupling takes place without the need for the addition of oxidant. Although this procedure for biaryl bond formation is inefficient, since a large quantity of one of the coupling partners is wasted, it has seen application in systems where a very hindered biaryl bond is required, *e.g.* napthalene **24** (Scheme 8).[22] When an aryl iodide is treated with a dialkylcuprate, cross-coupling often transpires; however, oxidation of the reaction mixture before hydrolysis can bring about significant increases in yield of the cross-coupled product.[21]

A key development in this field has been the construction of unsymmetrical biaryls by the oxidation of mixed organocuprates under "kinetic" conditions by Lipshutz (Scheme 9).[23] In this protocol copper(I) cyanide (other copper(I) salts were not effective) was exposed to one equivalent of an aryllithium, cooled to -125 °C and then, sequentially, a second aryllithium and TMEDA were added, before oxidation with molecular oxygen. TMEDA was necessary to increase yields; it was suggested that it served to co-ordinate lithium within the



Scheme 8 Generation and oxidation of a mixed organocuprate *in situ* by halogen–metal exchange.

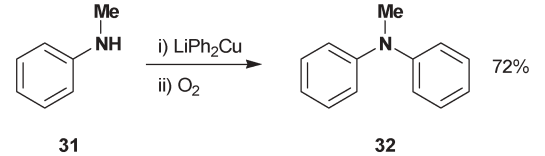


Scheme 9 Cross-coupling by oxidation of "kinetic", mixed organocuprates.

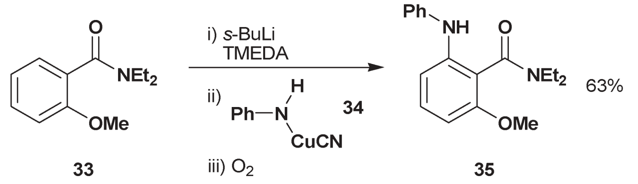
organocuprate cluster and activate it towards oxidative "decomposition". It was proposed that at −125 °C intermolecular exchange of aryl ligands was slow and hence, at this temperature, oxidation of the kinetically formed organocuprate (in which it is supposed two different aryl ligands were bound to each copper centre) occurred.

Attempts were made to substantiate this claim by ^{13}C NMR spectroscopy.[23] The spectrum recorded at −125 °C was different to that if the solution was warmed to −78 °C. This might be taken as evidence that at −78 °C equilibration of the aromatic ligands on the copper centres took place. Curiously, if this solution was then re-cooled to −125 °C the original low temperature spectrum was restored. This result would not be expected if this were the spectrum of a truly kinetic species.

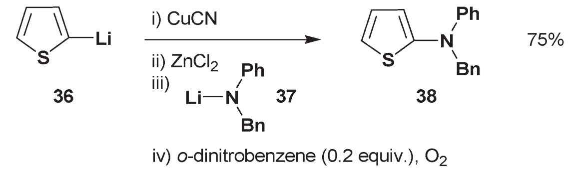
4 Carbon–heteroatom bond formation



Scheme 10 First studies on carbon–nitrogen bond synthesis by organocuprate oxidation.



Scheme 11 The *ortho*-lithiation, organocuprate oxidation route to anthranilamides.



Scheme 12 The application of zinc chloride in the organocuprate oxidation route to carbon–nitrogen bonds.

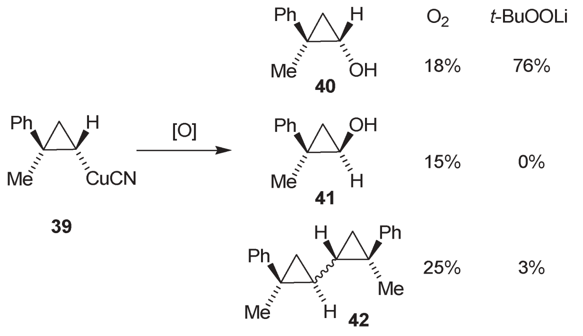
The oxidation of organocuprates may be harnessed also in the formation of carbon–nitrogen bonds. This idea was first used by Yamamoto;[24] when primary and secondary amines and anilines were treated with an excess of an aryl, primary or tertiary alkyl organocuprate and oxidized with molecular oxygen an amine resulted (**32**, Scheme 10). The reported yields were, however, variable (15–94%) and were lowest when tertiary alkyl organocuprates were used. A similar protocol has been developed by Snieckus[25] for the synthesis of anthranilamides by *ortho*-lithiation of a benzamide (**33**), mixing with an excess of a copper anilide (**34**) and molecular oxygen oxidation (Scheme 11). It was subsequently discovered that an excess of the anilide could be avoided under appropriate conditions by using the lithium salt of an amine with a cyanocuprate. Yields remained moderate, but were improved slightly by the addition of stoichiometric zinc chloride to the cyanocuprate before combining with the lithium amide and oxidation (Scheme 12).[26] The authors did not comment on the function of zinc chloride, but it may plausibly act as a Lewis acid activating the organocuprate. It also proved possible to functionalize hydrazines by this method but somewhat lower yields were encountered due to the competitive appearance of azo compounds. The authors proposed that carbon–nitrogen bond formation took place by way of aminyl radicals on the basis of the detection of aminoxyl radicals in the EPR spectra of the reaction mixtures upon oxidation. A salient feature of this work was the first application of *catalytic* copper(II) nitrate or *ortho*-dinitrobenzene in the presence of molecular oxygen as co-oxidant. These conditions were claimed to give faster and higher yielding reactions, but have not yet been applied to making carbon–carbon bonds.

It is interesting to note that no analogous procedures have been reported for the synthesis of ethers using alkoxides instead of amines by this method. Organocuprates can, however, be oxidized to phenols and alcohols. In most of the coupling reactions already discussed in which diarylcuprates are oxidized with molecular oxygen, phenols are a by-product; in some systems these may become dominant.[27] An expedient synthesis of phenols and alcohols may be attained by oxidation of a cyanocuprate with the lithium salt of *tert*-butyl hydroperoxide (Scheme 13).[28] Using this reagent oxidation occurred with retention of configuration. When the oxidation was attempted with molecular oxygen, the stereochemistry was scrambled and accompanied by significant dimerization; this was taken as evidence for radical intermediates under these conditions.

5 Applications in carbon–carbon bond formation

5.1 Hindered biaryl bonds

The formation of biaryl bonds with multiple *ortho* substituents can prove challenging; only the most recent palladium-catalysed reactions are capable of addressing this problem. Organocuprate oxidations, however, have shown themselves to be useful in this context. One notable example has been in Coleman's syntheses of phleichrome and calphostin A (Scheme 14, eqn (1)).[29] In these systems only poor yields of

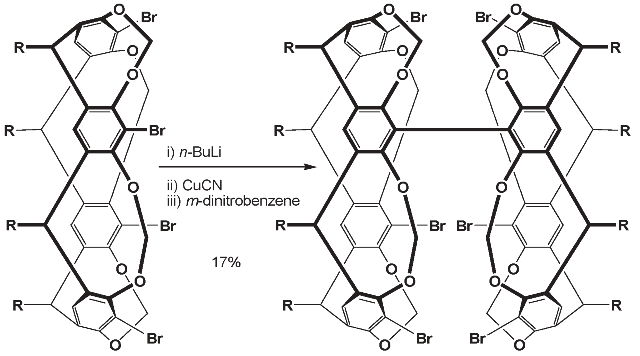


Scheme 13 Studies on the stereochemistry of alcohols resulting from the organocuprate oxidation.

the required biaryl **44** were given by palladium- and nickel-promoted reactions, but oxidation of a suitable organocuprate was more efficacious. The same author used also the Lipshutz protocol for the oxidation of "kinetic" organocuprates to perform a cross-coupling in the synthesis of the eupomatilones (Scheme 14, eqn (2)).[30]

An unusual coupling of this type has been practised by Sherburn in order to make a conjoined cavitand (Scheme 15). Although the yield was low (17%), such substrates are very challenging and the sterically hindered 2,2,2′,2′-*tetra* substituted biaryl bond required could not be made by any other means.[31]

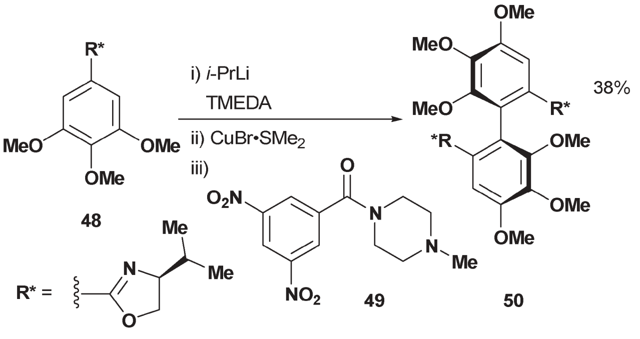
A new development has been the synthesis of the required aryllithium precursors by a directed *ortho*-lithiation rather than a halogen–metal exchange reaction. Ethers, alkoxy ethers, sulfonamides and carboxylates were all suitable directing groups. It was shown that when a chiral oxazoline was used to direct the lithiation, a single atropisomer **50** was observed in the biaryl bond-forming step (Scheme 16).[32] The oxidant **49** was also used, whose separation from the product was facilitated by the presence of a tertiary amine.



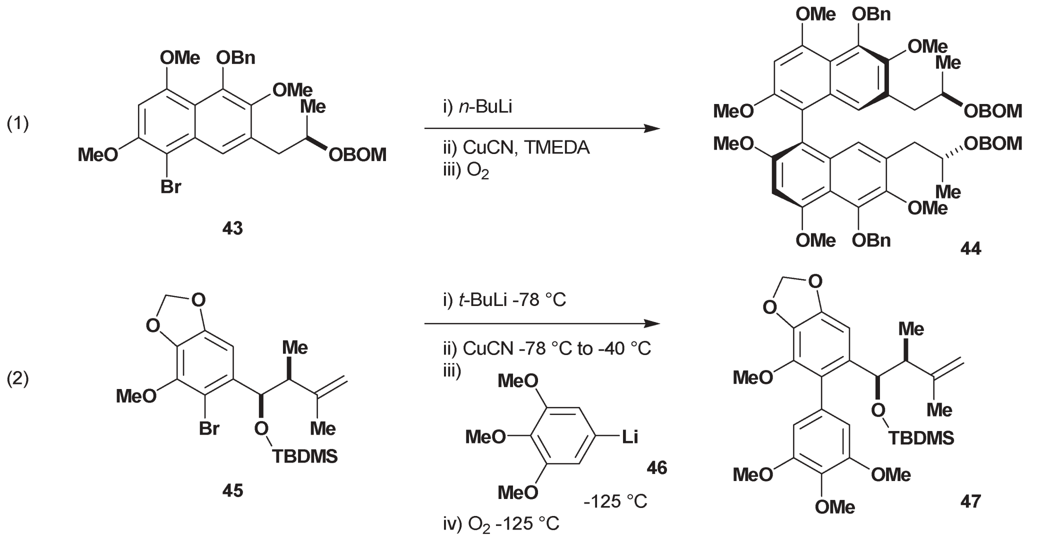
Scheme 15 Sherburn's synthesis of a conjoined cavitand.

5.2 Intramolecular biaryl bonds

The most common application of organocuprate oxidations in organic synthesis has been in the assembly of intramolecular biaryl bonds by way of an intramolecular organocuprate intermediate. Pioneering studies by Lipshutz exploited the process to form non-racemic biaryls by making use of a chiral



Scheme 16 Exploitation of an *ortho*-lithiation, organocuprate oxidation sequence in the generation of atropisomeric biaryls.



Scheme 14 Applications of the organocuprate oxidation in the synthesis of intermolecular biaryl bonds.

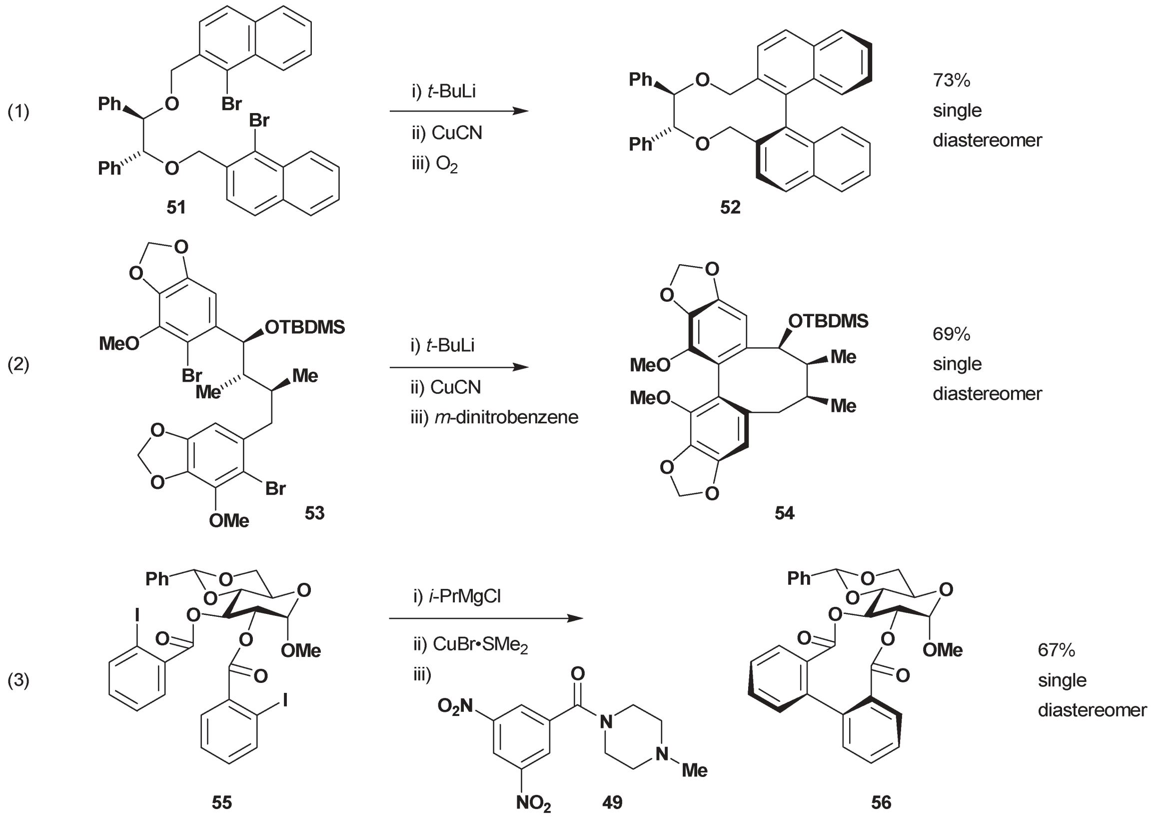
tether; examples of six, eight and ten-membered rings were provided (Scheme 17, eqn (1)).[33] The methodology was soon utilized by others to gain access to chiral biaryls. For example, Coleman has used it as a key step in the synthesis of interiotherin A (Scheme 17, equation 2).[34]

The forging of a biaryl bond within a medium ring (*i.e.* a ring composed of between eight and eleven atoms) is very challenging. Medium rings represent high energy compounds due to a combination of torsional, transannular and large angle strain. The rigidity of the structures also seem to prevent many well precedented biaryl coupling protocols from operating effectively; for example, the ubiquitous palladium-catalysed Stille, Suzuki or Negishi reactions are not useful in this context. A copper-mediated Ullmann reaction can be used, but the somewhat harsh reaction conditions preclude sensitive substrates. Nickel-mediated reactions have also seen some employment but can exhibit vulnerability to steric interactions.[35]

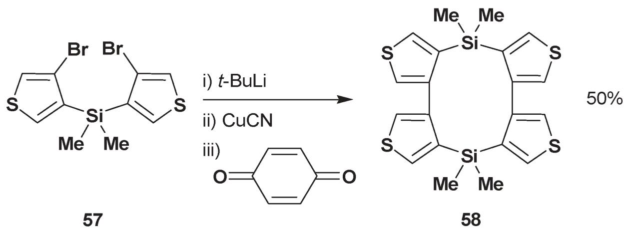
The robustness of medium-ring formation by organocuprate oxidation has been demonstrated by Schreiber in the diversity-orientated synthesis of a library of compounds for chemical genetics.[36] This work produced a number of important results. Firstly, the aptitude of the reaction in the construction of a range of nine-, ten- and eleven-membered rings (which had proved unassailable by more conventional palladium- and nickel-mediated procedures) was illustrated. Secondly, new chiral tethers were introduced which gave good diastereoselectivity. Interestingly, the degree and direction of diastereoselectivity depended strongly upon the choice of oxidant. The atropisomer which resulted upon oxidation with *meta*-dinitrobenzene was not favoured thermodynamically. It was found also that high dilution conditions were not needed in order to ensure that the intramolecular reaction took place (substrate concentrations as high as 0.15 M yielded no oligomers) and that the reaction was successful on an insoluble polystyrene support. Furthermore, the aryl metal species required for organocuprate formation could be generated *via* a halogen–metal exchange of an aryl halide with a magnesium or zinc ate complex (rather than with an alkyllithium).

It has been shown since that Knochel's low temperature iodine–magnesium exchange reaction between an aryl iodide and an alkylmagnesium reagent[37] allowed diarylcuprates to be made, which can be oxidized to give a biaryl. This procedure permitted the presence of a range of electrophilic functional groups which could not be tolerated using organolithium intermediates.[38] The reaction proceeded smoothly in both inter- and intramolecular reactions; the cyclization of **55** (Scheme 17, eqn (3)) holds the promise that the methodology might be applicable to the synthesis of ellagitannin natural products. In addition, it was established that as little as 0.2 equivalents of oxidant **49** could be used without adversely affecting the yield of the reaction as a result of its ability to abstract multiple electrons.

Recently, Iyoda has made use of the oxidation of organocuprates in the synthesis of some structurally compelling ten-membered cyclophanes (**58**) (Scheme 18),[39] while palladium-catalysed coupling gave only an intramolecular reaction.



Scheme 17 Applications of the organocuprate oxidation in the synthesis of intramolecular biaryl bonds.

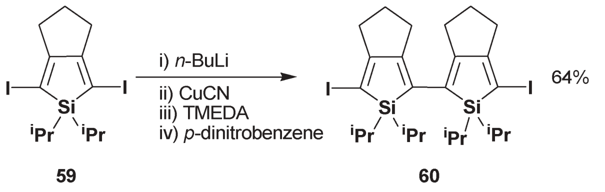


Scheme 18 Synthesis of a cyclophane by organocuprate oxidation.

The facility with which bonds may be installed between aromatic groups, resulting in the closure of a medium ring, is particularly noteworthy. In such systems this capability has been suggested to arise from a templating effect brought about by interactions between copper atoms in an organocopper aggregate and this explanation may apply also in some of the reactions cited above.[40] It has been proposed also that the two aryl groups form a favourable chelate[36] about the copper centre in which interactions that destabilize medium ring compounds are reduced. The long carbon–copper bonds found in the intermediate organocuprate may be significant as they could lessen any unfavourable steric clashes between substituents on the aromatic rings in the intermediate organometallics. This may also go some way to explain the relative success in the formation of intermolecular 2,2,2′2′-*tetra* substituted biaryl bonds.

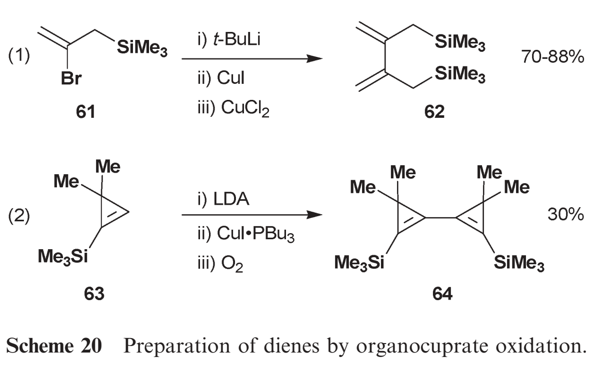
5.3 Miscellaneous dimerizations

The organocuprate oxidation is also useful in the dimerization of heterocycles such as imidazoles (with applications in crystal engineering)[41] and Tamao has utilized it extensively in the synthesis of silole dimers **60** (Scheme 19).[42]



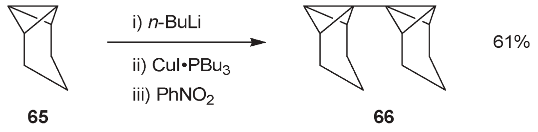
Scheme 19 The construction of a silol dimer by organocuprate oxidation.

The oxidation of divinylcuprates has seen occasional service in the synthesis of dienes. This method enabled Trost to make multi-gram quantities of diene **62** (Scheme 20, eqn (1)),[43] exemplifying the value of the reaction in large scale preparations. A similar dimerization has been performed by metallation and oxidation of the cyclopropene derivative **63**, giving a route to the strained diene **64** (Scheme 20, eqn (2)).[44]



Scheme 20 Preparation of dienes by organocuprate oxidation.

The creation of a bond between two tertiary carbon centres is particularly problematical. This is especially true at bridgehead positions, as nucleophilic substitution chemistry is precluded and other metal-mediated couplings can be difficult. In such demanding situations the organocuprate oxidation has been demonstrated to have some utility. Szeimies, for example, has exploited this facet of reactivity in the dimerization of alkane **65** (Scheme 21).[45] Recently, tetrahedranyl dimers have been synthesized similarly.[46]



Scheme 21 Forging a bond between tertiary carbon centres by organocuprate oxidation.

6 Conclusion

The oxidation of organocuprates has been utilized in a wide range of circumstances over the last forty years. A useful feature of the reaction is that it permits the rather unusual disconnection of a carbon–carbon bond back to two anions. This approach therefore potentially allows for some original synthetic strategies.

Recent advances have served to improve the functional group tolerance and should lead to increasing applications in organic synthesis. Future work will no doubt result in even milder conditions and see further expansion of the substrate scope. A current limitation is the requirement for a stoichiometric copper salt to make the organocuprate. A procedure that is catalytic in the metal would be much more attractive from an environmental and economic standpoint. In many ways the ultimate goal would be the development of a general cross-coupling procedure for aryl halides, as such a reaction would obviate the need for separate synthesis of aryl stannanes, aryl boronic acids, *etc.*, required for palladium-catalysed cross-couplings. The introduction of such a method, however, will have to attend an improved understanding of the mechanism by which bonds are formed between ligands on the copper centre and the role that the oxidant has in determining the detailed course of this process.

References

1 R. Reich, *C. R. Hebd. Seances Acad. Sci.*, 1923, **177**, 322.
2 H. Gilman, R. G. Jones and L. A. Woods, *J. Org. Chem.*, 1952, **17**, 1630.
3 G. H. Posner, *Org. React.*, 1975, **22**, 253 and references therein.
4 G. van Koten, S. L. James and J. T. B. H. Jastrzebski, in *Comprehensive Organometallic Chemistry II*, ed. E. W. Abel, F. G. A. Stone, G. Wilkinson and J. L Wardell, Pergamon, Oxford 1995, vol. **3**, chap. 2, 57 and references therein.
5 S. Woodward, *Chem. Soc. Rev.*, 2000, **29**, 393.

6 *Organocopper Reagents-A Practical Approach*, ed. R. J. K. Taylor, Series ed. L. M. Harwood and C. J. Moody, Oxford University Press, 1994.

7 *Modern Organocopper Chemistry*, ed. N. Krause, Wiley-VCH, Weinheim, 2002.

8 H. Heany and S. Christie, *Science of Synthesis*, 2004, **3**, 305 and references therein.

9 S. Mori, A. Hirai, M. Nakamura and E. Nakamura, *Tetrahedron*, 2000, **56**, 2805.

10 Y. Chounan, H. Horino, T. Ibuka and Y. Yamamoto, *Bull. Chem. Soc. Jpn.*, 1997, **70**, 1953.

11 S. H. Bertz, G. Dabbagh and A. M. Mujsce, *J. Am. Chem. Soc.*, 1991, **113**, 631.

12 For the oxidation of organocopper compounds: T. Kauffmann, *Angew. Chem., Int. Ed. Engl.*, 1974, **13**, 291 and references therein.

13 G. M. Whitesides, J. San Filippo, Jr., C. P. Casey and E. J. Panek, *J. Am. Chem. Soc.*, 1967, **89**, 5302.

14 For example: D. Naumann, T. Roy, K.-F. Tebbe and W. Crump, *Angew. Chem., Int. Ed. Engl.*, 1993, **32**, 1482.

15 For example: W. Nakanishi, M. Yamanaka and E. Nakamura, *J. Am. Chem. Soc.*, 2005, **127**, 1446.

16 For an example of a detailed study of the decomposition of organocopper aggregates see: M. D. Janssen, M. A. Corsten, A. L. Spek, D. M. Grove and G. van Koten, *Organometallics*, 1996, **15**, 2810 and references therein.

17 G. M. Whitesides, J. San Filippo, Jr., E. R. Stedronsky and C. P. Casey, *J. Am. Chem. Soc.*, 1969, **91**, 6542.

18 W. H. Mandeville and G. M. Whitesides, *J. Org. Chem.*, 1974, **39**, 400.

19 S. H. Bertz and C. P. Gibson, *J. Am. Chem. Soc.*, 1986, **108**, 8286.

20 R. K. Dieter, S. Li and N. Chen, *J. Org. Chem.*, 2004, **69**, 2867.

21 G. M. Whitesides, W. F. Fischer, Jr., J. San Filippo, Jr., R. W. Bashe and H. O. House, *J. Am. Chem. Soc.*, 1969, **91**, 4871.

22 H. O. House, D. G. Koepsell and W. J. Campbell, *J. Org. Chem.*, 1972, **37**, 1003.

23 B. H. Lipshutz, K. Siegmann, E. Garcia and F. Kayser, *J. Am. Chem. Soc.*, 1993, **115**, 9276 and references therein.

24 H. Yamamoto and K. Maruoka, *J. Org. Chem.*, 1980, **45**, 2739.

25 M. Iwao, J. N. Reed and V. Snieckus, *J. Am. Chem. Soc.*, 1982, **104**, 5531.

26 F. Canè, D. Brancaleoni, P. Dembech, A. Ricci and G. Seconi, *Synthesis*, 1997, 545 and references therein.

27 G. J. Lambert, R. P. Duffley, H. C. Dalzell and R. K. Razdan, *J. Org. Chem.*, 1982, **47**, 3350.

28 M. Möller, M. Husemann and G. Boche, *J. Organomet. Chem.*, 2001, **624**, 47.

29 R. S. Coleman and E. B. Grant, *J. Am. Chem. Soc.*, 1995, **117**, 10889 and references therein.

30 R. S. Coleman and S. R. Gurrala, *Org. Lett.*, 2004, **6**, 4025.

31 J. L. Irwin, D. J. Sinclair, A. J. Edwards and M. S. Sherburn, *Aust. J. Chem.*, 2004, **57**, 339.

32 D. S. Surry, D. J. Fox, S. J. F. Macdonald and D. R. Spring, *Chem. Commun.*, 2005, 2589.

33 B. H. Lipshutz, F. Kayser and Z.-P. Liu, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 1842.

34 R. S. Coleman and S. R. Gurrala, *Org. Lett.*, 2005, **7**, 1849.

35 T. D. Nelson and R. D. Crouch, *Org. React.*, 2004, **63**, 265.

36 D. R. Spring, S. Krishnan, H. E. Blackwell and S. L. Schreiber, *J. Am. Chem. Soc.*, 2002, **124**, 1354.

37 A. E. Jensen, W. Dohle, I. Sapountzis, D. M. Lindsay, V. A. Vu and P. Knochel, *Synthesis*, 2002, 565 and references therein.

38 D. S. Surry, X. Su, D. J. Fox, V. Franckevicius, S. J. F. Macdonald and D. R. Spring, *Angew. Chem., Int. Ed.*, 2005, **44**, 1870.

39 Y. Miyake, M. Wu, M. J. Rahman and M. Iyoda, *Chem. Commun.*, 2005, 411.

40 G. van Koten and J. G. Noltes, *J. Organomet. Chem.*, 1976, **104**, 127.

41 Y. Morita, T. Murata, S. Yamada, M. Tadokoro, A. Ichimura and K. Nakasuji, *J. Chem. Soc., Perkin Trans. 1*, 2002, 2600.

42 S. Yamaguchi and K. Tamao, *J. Chem. Soc., Dalton Trans.*, 1998, 3693 and references therein.

43 B. M. Trost and M. Shimizu, *J. Am. Chem. Soc.*, 1982, **104**, 4299.

44 F. Grüger and G. Szeimies, *Tetrahedron Lett.*, 1986, **27**, 1563.

45 R. Römer, J. Harnisch, A. Röder, A. Schöffer, G. Szeimies, G. Germain and J. M. Arrieta, *Chem. Ber.*, 1984, **117**, 925.

46 M. Tanaka and A. Sekiguchi, *Angew. Chem., Int. Ed.*, 2005, **44**, 5821.