Oxidation of Organocopper Compounds

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Contents

I. Introduction 3

II. Formation of C-C Bonds 4

A. Initial Studies 4

B. Cross-coupling 5

C. Biaryl Formation 11

D. Intramolecular Bond Formation 14

E. Dimerisations of Heteroaromatics, Alkenyl and Alkyl Groups and Macrocycle Formation 18

III. Formation of C-N Bonds 21

A. Initial Studies 21

B. Further Developments 22

IV. Conclusion 25

V. References 26

I. Introduction

Although organocopper reagents have been synthesised since the 1800's, it is only with the advent of Gilman cuprates[1] that their synthetic utility has been realised. This trend is also reflected in the oxidation chemistry of organocopper reagents, as wide ranging procedures for the oxidative coupling of mono-organocopper reagents have been in place for over one hundred years[2] (the Glaser alkyne coupling[3] for example) whereas organocuprate oxidations have only begun to be fully exploited in the last couple of decades.[4]

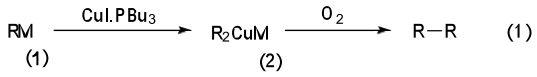
Theoretical studies by Nakamura[5] have shown that the 3d orbitals on copper are around 7 eV higher in dimethyl cuprate than in methylcopper. As these orbitals constitute the HOMO, the oxidation of organocuprates is an attractive reaction as the high lying nature of the orbitals means the oxidation can be performed with relative ease, avoiding the harsher reaction conditions of classical methods. Numerous reagents can be used to effect the oxidation, including dinitroarenes, inorganic salts, oxygen and quinones.

This chemistry is beginning to find its niche in biaryl synthesis, where steric considerations may make other methods difficult, and electrophilic amination[6] where the oxidation of amidocuprates provides a complementary reaction to palladium catalysed methods.

II. Formation of C-C Bonds

A. Initial Studies

The oxidation of organocuprates was first explored systematically by Whitesides, who examined the dimerisation of a number of cuprates formed from readily accessible Grignard reagents and organolithiums.[7] The organocuprate (**2**) was formed by transmetalation of the organometallic (**1**) with copper(I) iodide-tri-*n*-butylphosphine complex and then oxidised. (Equation 1) Nitrobenzene, benzophenone and copper(II) chloride-TMEDA complex were all reported to be effective oxidants, but use of molecular oxygen lead to the best overall yields.

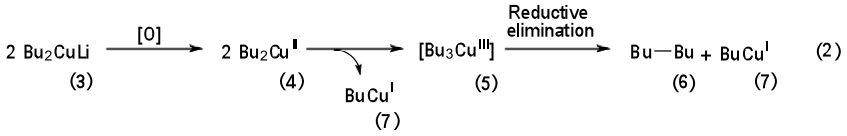


Primary and secondary alkyl, vinyl, alkynyl and aryl centres could be coupled in good yields (67-88%) but tertiary alkyl species proved challenging. The counterion present was also shown to have an effect on the reaction, as in the case of *n*-butyl the lithium reagent gave higher yields of dimer than the Grignard.

Analysis of the product mixture obtained upon oxidation of lithium di-*n*-butylcuprate showed the formation of but-1-ene (14%) and *n*-butanol (5%) as well as the desired *n*-octane (84%) and from this a tentative mechanism was proposed. Butylcopper(I) was

found to be present in incompletely oxidised reaction mixtures and it is oxidation of this species which could explain the formation of both but-1-ene and *n*-butanol.

A radical mechanism was ruled out on the basis that formation of butyl radicals in a solution saturated with oxygen would lead to the formation of much larger amounts of *n*-butanol and thus it was proposed that lithium di-*n*-butylcuprate (**3**) is initially oxidised to di-*n*-butylcopper(II) (**4**) which can disproportionate to octane (**6**) and *n*-butylcopper(I) (**7**). The presence of a short-lived Cu(III) species **5** which can undergo reductive elimination to form the products is also a possibility.[4] (Equation 2)

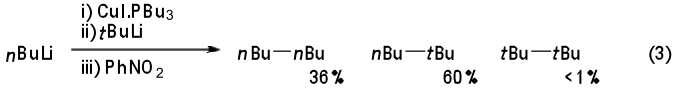


B. Cross-coupling

In order to perform a cross coupling procedure *via* organocuprate oxidation, one must first form a mixed organocuprate (*i.e.* the two ligands on copper are different organic species). Research in this area has concentrated on the formation of the desired cross-coupled product and the avoidance of homo-coupled products, which lead to deleterious yields.

It was Mandeville and Whitesides that first looked at this issue as part of a wider study of selectivity of organic group transfer in mixed organocuprates.[8] They found that upon

oxidation the expected 1:2:1 statistical mixture of homo-coupled and cross-coupled products did not form; instead it was found that some groups had a higher propensity to couple than others. Alkynyl groups were found to be reluctant to participate in any form of coupling, whether it be homo- or cross-, despite the precedent of the Glaser reaction. The sterically hindered *t*-butyl group did not undergo homo-coupling, and so its use as one of the ligands in the mixed cuprate allowed moderate yields of cross-coupled product with less sterically demanding groups. (Equation 3)

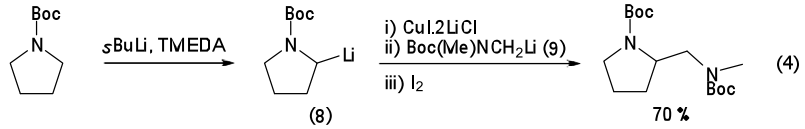


(3)

The copper salt used to form the mixed cuprate was also shown to have an influence on the amount of cross-coupling by Bertz.[9] Electronically and sterically similar alkyl groups were used so the dependence on the copper salt could be investigated. While lower order cuprates prepared from CuI were found to give statistical mixtures of homo- and cross-coupled products on oxidation with *ortho*-dinitrobenzene, the higher order cuprate prepared from CuCN gave a ratio closer to 1:4:1. These contrasting results were taken to imply a difference in the ligand exchange rate (although the oxidation of a mixture of the two preformed higher order homocuprates gave mainly homo-coupling, suggesting ligand exchange does not occur) or differences in the solution structure of the two cuprates.

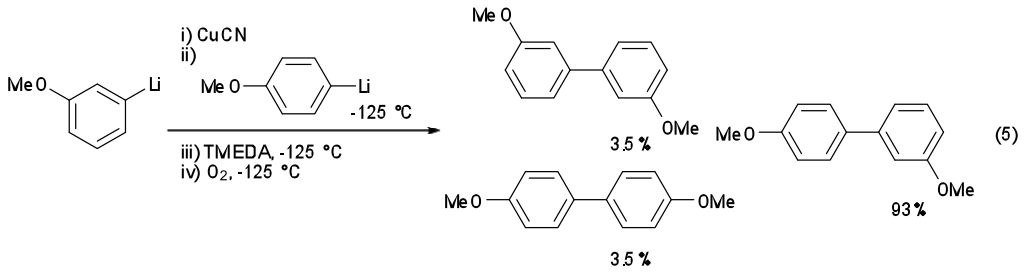
The use of α-functionalised alkyl cuprates allowed higher yields of cross-coupled product to be prepared provided that both ligands contained a heteroatom.[10] The functionalisation of the cuprate also allowed iodine to be used as the oxidant which had previously been

shown to be ineffective for unfunctionalised substrates. *N*-Boc-2-lithiopyrrolidone (**8**) could be coupled with *N*-Boc-*N*-methyl-1-lithiomethylamine (**9**) in 70% yield; similar yields were obtained on coupling with *n*-BuLi. They fell off rapidly with increasing steric hindrance on the alkyl substrate, with *t*-BuLi giving poor yields. (Equation 4) Interestingly, attempted cross-coupling of **8** with ligands containing an α-oxygen rather than nitrogen only took place with a large excess of oxidant.



(4)

High yields of cross-coupled biaryls were achieved by the oxidation of "kinetic" mixed organocuprates by molecular oxygen.[11] These "kinetic" conditions developed by Lipshutz and co-workers involve the formation of a lower order cyanocuprate (solubilised CuI was found to be ineffective) and then addition of the second aryl lithium reagent at -125 ˚C, with the oxidation also carried out at this low temperature. In a comparative study these conditions gave a ratio of 1:26:1 of products as opposed to the statistical mixture of 1:2:1 when the oxidation was carried out at -78 ˚C. (Equation 5)

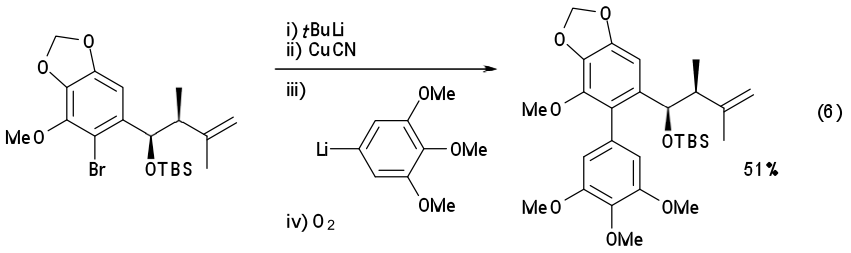


(5)

TMEDA was found to be a necessary additive to achieve high yields, and it was suggested that this activated the cuprate cluster towards decomposition.

If the cuprate was warmed to -78 ˚C and then re-cooled before oxidation, a statistical mixture of products was produced suggesting a kinetic species was formed initially. However when the cuprate was studied spectroscopically, the spectra of the re-cooled cuprate was identical to that of the initial cluster rather than that of the one at -78 ˚C, suggesting that these are not truly kinetic species.

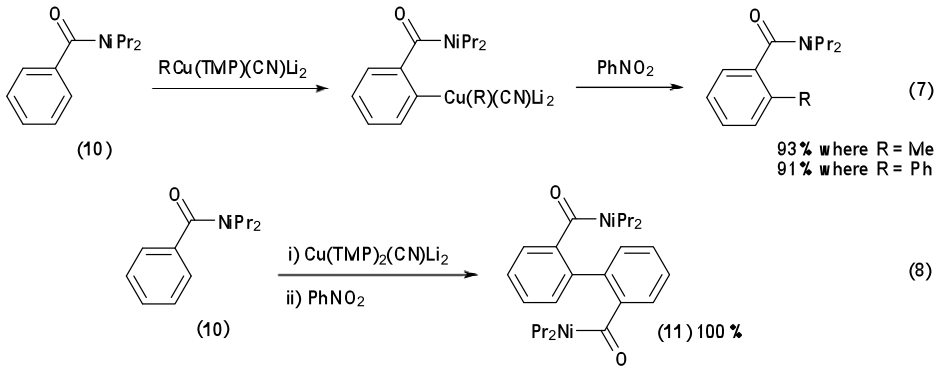
Use of the Lipshutz protocol has been undertaken by Coleman for the formation of biaryls, most recently in the elegant synthesis of eupomatilones 4 and 6.[12] (Equation 6)



(6)

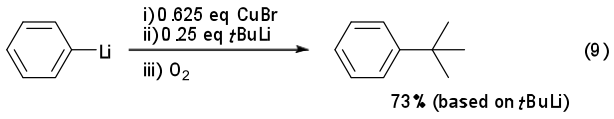
An exciting development in cross-coupling has been the advent of directed *ortho*-cupration methodology.[13] Here, a Lipshutz amidocuprate is used first as a base to effect deprotonation and secondly as a copper source to complete the metalation reaction. It was found in order for the reaction to be high yielding and chemoselective the amine ligand on copper must be 2,2,6,6-tetramethylpiperidine (TMP), however a range of organic groups could be tolerated as the second group on copper.

Oxidations were carried out as part of the studies into the reactivity of the synthesised *ortho*-cuprates, and it was found that the organic ligand of the intermediate cuprate could be coupled to the aryl unit by the action of nitrobenzene. (Equation 7) If both groups on the cuprate used to perform the metalation were TMP, then the homo-coupled biaryl **11** resulted in quantitative yield upon oxidation. (Equation 8)



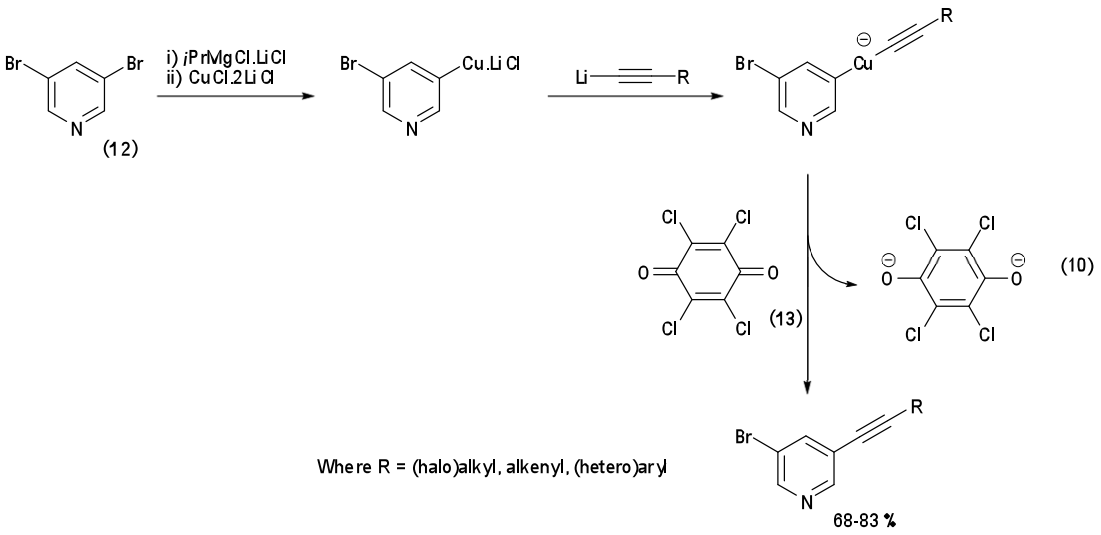
It should be noted that this reaction was only carried out on substrate **10** and so the generality of this reaction is not known, however these results point towards another solution to the cross-coupling problem.

An alterative approach to forming cross-coupled products has been to use one of the coupling partners in a large excess, thus avoiding the production of statistical mixtures. Whitesides showed that this approach could be successfully used with hindered alkyl groups.[14] (Equation 9)

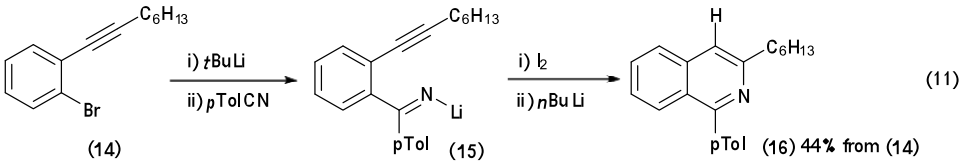


Recently, Knochel and co-workers have developed a procedure for the preparation of polyfunctional alkynes *via* oxidation of an aryl(alkynyl)organocuprate.[15] This uses only 2 equivalents of the lithiated alkyne to form the cuprate and allows the use of sterically hindered arenes and selective mono-coupling of dihaloarenes, the latter of which can be difficult *via* a Sonogashira coupling.

The mixed organocuprate is formed by reacting the lithiated alkyne with an aryl copper species formed by transmetalation from the Grignard reagent. The organocuprate is then oxidised with the quinone chloranil (**13**) to give the cross coupled product. Use of the group's directed magnesiation methodology[16] allowed the coupling of doubly *ortho* substituted arenes in good yields. Also, 3,5-dibromopyridine (**12**) could be selectively mono-coupled with alkynes bearing a range of substituents in 68-83% yield. (Equation 10)



After selective mono-coupling, the remaining halogen of the dihaloarene substrates could be used in further reactions; in this case annulated pyridine formations were undertaken. Lithiation of the bromo alkyne **14** and reaction with *p*-tolylnitrile gave lithiated intermediate **15** which cyclised on addition of iodine to give the iodinated pyridine. Removal of the iodine by *n*-BuLi gave the annulated pyridine **16** in 44% overall yield. (Equation 11)



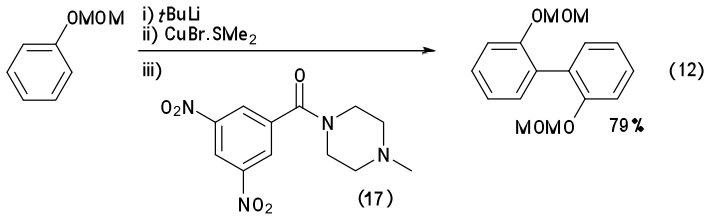
(11)

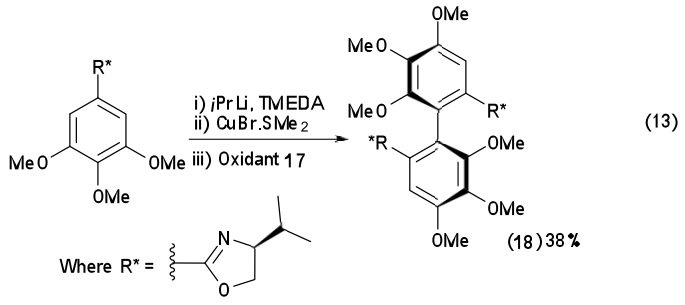
C. Biaryl Formation

The formation of sterically hindered biaryls is one area where organocuprate oxidations have proved useful as palladium and nickel catalysed transformations can struggle in this context. Work by Spring and co-workers has focussed around the development of methodology to forge biaryl bonds in substrates with multiple *ortho* substituents, using transmetalation protocols that are compatible with a wide range of functional groups. This was part of a wider study into medium ring synthesis (*vide infra*).

Starting with transmetalation from aryl lithium reagents, it was recognised that the usual protocol of lithium-halogen exchange requires the presence of a halogen moiety which

can add extra synthetic steps to install. Use was therefore made of an *ortho*-lithiation strategy to form the aryl lithium species prior to transmetalation. Methoxy, alkoxy ether, sulphonamide and carboxylate groups all proved to be effective directing groups and heterocycles were also compatible.[17] (Equation 12) Use of a chiral oxazoline as a directing group allowed the formation of **18** as a single diastereoisomer. (Equation 13)

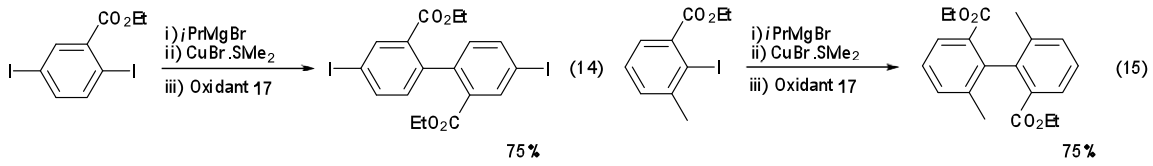




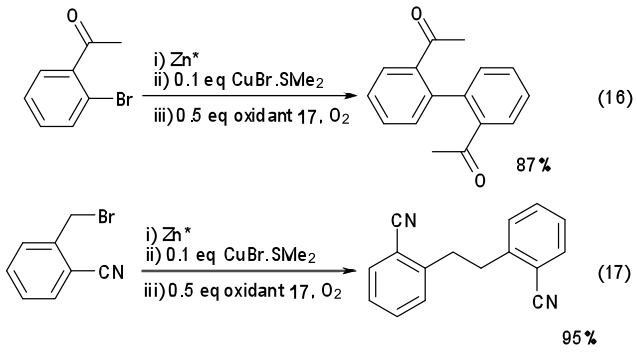
Dinitroarene oxidant **17** was also developed, as it was recognised that dinitrobenzenes were the best oxidants in this context, however the post-oxidation by-products were difficult to remove from the product formed. The inclusion of the piperazine unit allows by-products to be easily removed *via* an acid wash or filtration through silica on work-up.

Use of Knochel's Mg/I exchange methodology[18] to form aryl Grignards allowed the formation of iodinated biaryls and as the exchange could be performed regioselectively

oligomerisation could be avoided. (Equation 14) Biaryls with four *ortho* substituents could also be synthesised by this methodology.[19] (Equation 15)



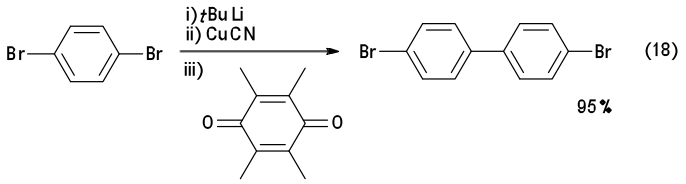
In order to further improve functional group tolerance, transmetalation from zinc was also investigated. This is notable as it is the first example of the oxidation of zinc organocuprates. (Oxidation of zinc amidocuprates is also known – see section III.B) Use of aryl zinc reagents was advantageous as it allowed the use of more readily available aryl bromides and the aryl metals could be synthesised under milder conditions thus allowing functional groups such as ketones to be present.[20] Use of highly active Rieke zinc (Zn*) proved useful in synthesising the required organozinc reagents.



Studies showed that it was possible to perform the coupling using a catalytic amount of copper salt and oxidant **17** in conjunction with molecular oxygen. This proved to be

useful for not only for biaryl formation, as various vinyl and benzyl bromides could also be used as starting materials. (Equations 16 and 17)

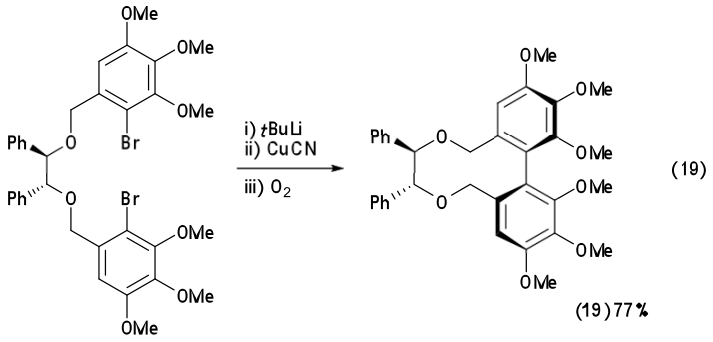
Other recent work in this area includes studies by Iyoda and co-workers into the oxidation of Lipshutz cuprates, utilising quinone oxidants, in order to develop methodology to form macrocyclic cyclophanes.[21] The coupling reactions were in general high yielding, although the use of *t*-BuLi to form the aryl lithium for transmetalation necessarily reduces the functional group compatibility. (Equation 18) Methyl, methoxy and halogen substituted aromatics are given as examples along with thienyl.



(18)

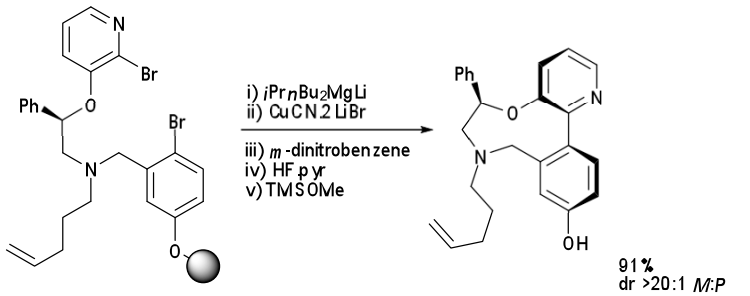
D. Intramolecular Bond Formation

The idea of intramolecular biaryl bond formation using a tether was first introduced by Lipshutz as a way of aiding troublesome heteroaromatic cross-couplings.[22] This was quickly extended to the use of chiral tethers as a means of forming non-racemic biaryls.[23] Compound **19** was used in the synthesis of (+)-*O*-permethyltellimagrandin II on removal of the tether. (Equation 19)



(19)

Intramolecular biaryl formation was developed further by Schreiber and co-workers as a means of accessing medium ring biaryl compounds. The strained structure of a medium ring due to the combination of transannular, torsional and large angle strain means that these compounds can be difficult to access *via* palladium or nickel mediated processes; it was found that the use of copper allowed the formation of the desired biaryl compounds with good atropdiastereoselectivity by utilising a chiral amino alcohol tether.



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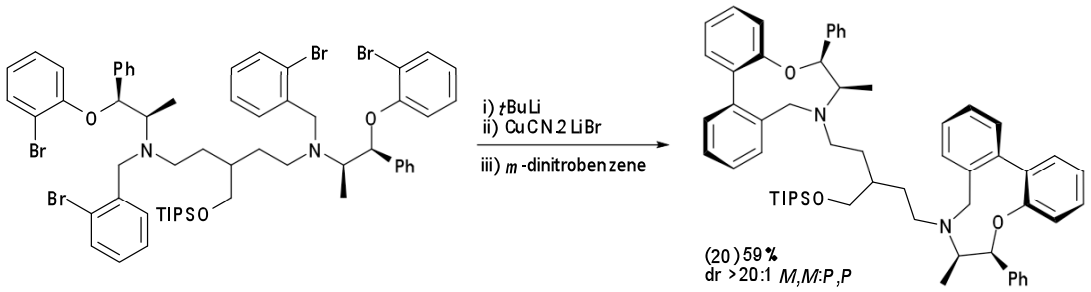
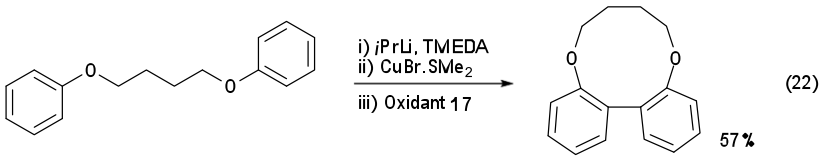


(21)

Use of polymer supported synthesis allowed a library of nine, ten and eleven-membered rings with a variety of biaryl substituents to be built up. Since lithium/halogen exchange was not compatible with the polymer beads, the initial aryl metal species was generated *via* exchange with *i*-PrBu$_2$MgLi.[24] A later study[25] generated a further library of nine-membered ring containing compounds *via* solid phase synthesis and also interesting dimeric biaryl **20** in the solution phase. (Equations 20 and 21)

The transmetalation strategies for forming biaryls (*vide supra*) have also been used by Spring and co-workers for the formation of medium rings. *Ortho*-lithiation and Mg/I exchange both allowed the formation of examples of 10 and 11-membered rings after transmetalation to copper.[17, 19] (Equation 22) Cross-coupling of biaryls could be performed using a tethering strategy, and most importantly use of the magnesium organocuprate allowed the formation of **21**, a model for the highly strained core of the natural product sanguiin H-5, with complete diastereoselectivity. (Equation 23)



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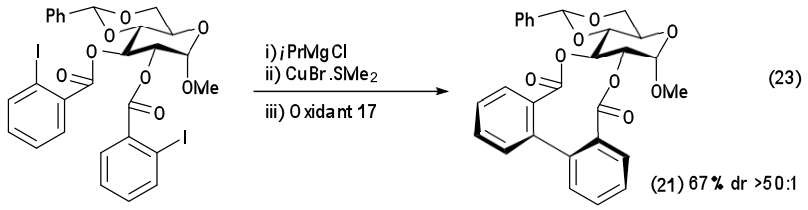
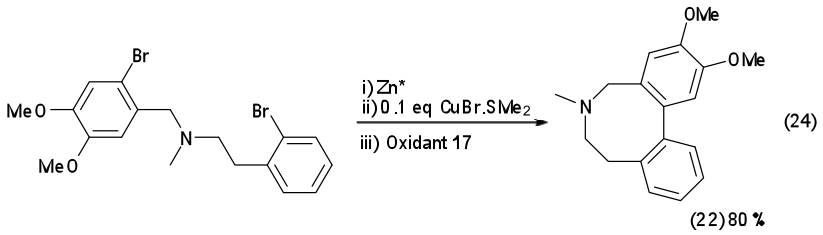


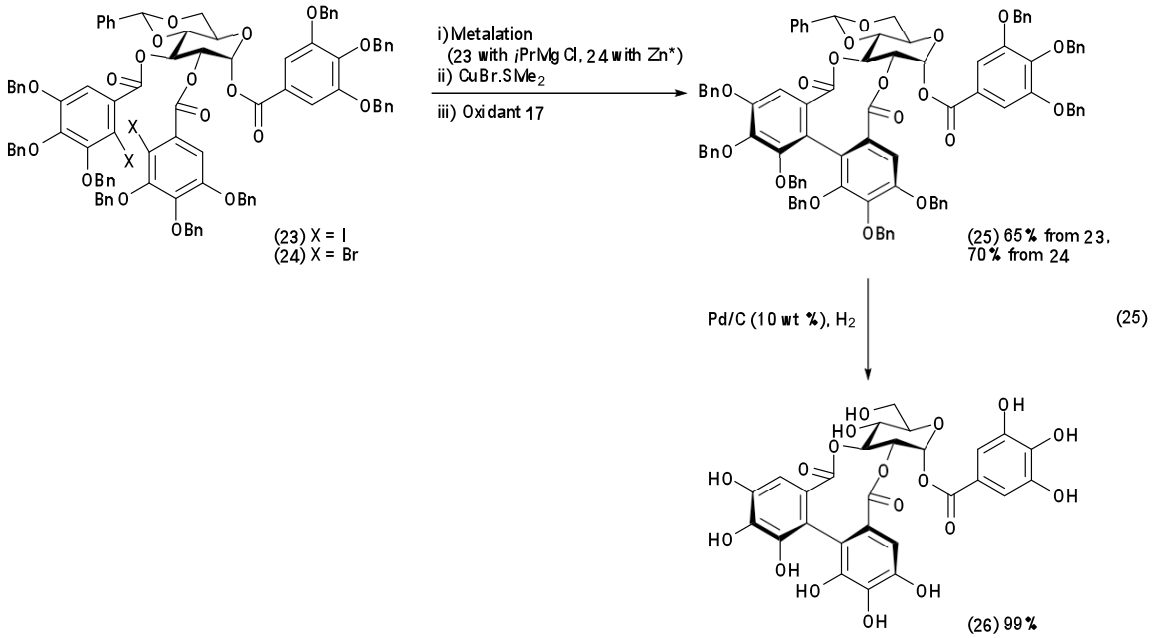
(23)

Insertion of Rieke zinc into aryl bromides allowed zinc organocuprate oxidation methodology to be used in the synthesis of buflavine (**22**).[20] (Equation 24) This represented the first synthesis of the natural product where the medium ring and the biaryl bond are formed simultaneously.



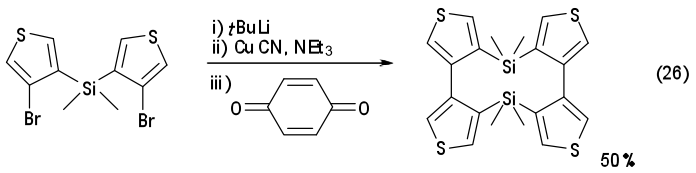
(24)

With proof of the utility of these methods in medium ring formation in hand, attention was turned to completing the synthesis of sanguiin H-5. While the aryl bromide/Zn* route was slightly higher yielding, both this and the use of aryl iodide/Mg exchange provided the key medium ring compound **25** in good yields. Global deprotection *via* hydrogenation provided the natural product (**26**) in quantitative yield.[26] (Equation 25)

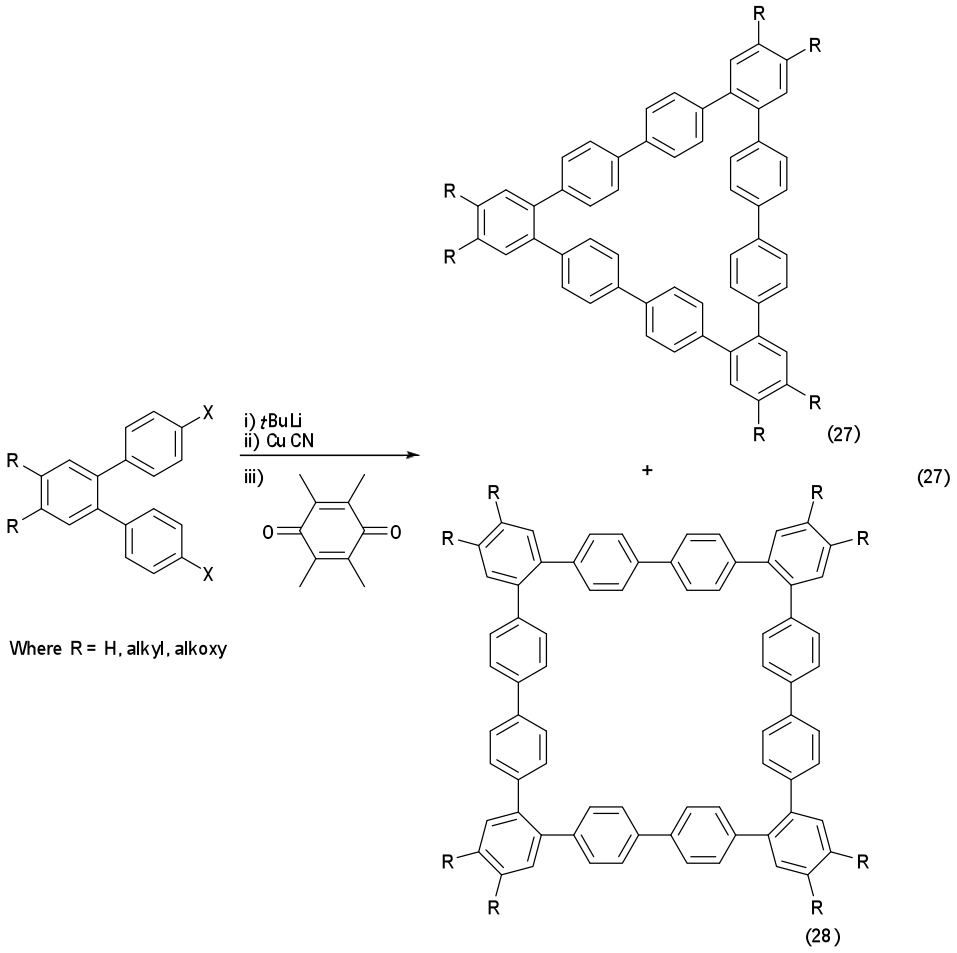


E. Dimerisations of Heteroaromatics, Alkenyl and Alkyl Groups and Macrocycle Formation

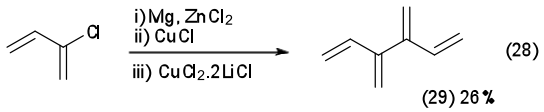
Use of organocuprate oxidation to form C-C bonds has also seen use outside of biaryl couplings and medium ring formation. Iyoda has performed oxidations of Lipshutz cuprates in order to synthesise thiophene-fused cyclophanes and nona- and dodecaphenylenes; the optioelectonic and nanostructural properties of the latter were investigated.[21, 27] The ten-membered cyclophane structure was not accessible *via* palladium couplings and it is suggested that the linear C-Cu-C bond in the organocuprate intermediate favours the intermolecular over intramolecular coupling. (Equation 26)



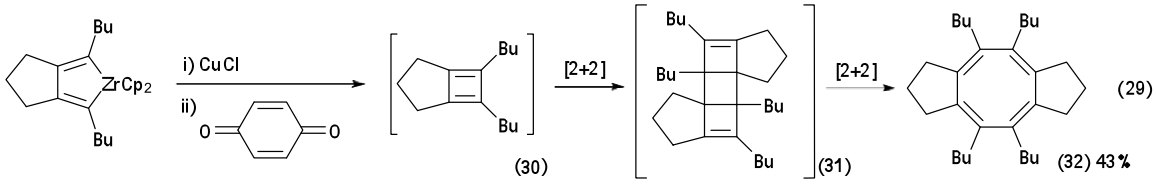
In the second study, the ratio of nona- to dodecaphenylene formed upon oxidation was dependant on the substituents present on the vertex aryl group, although the nona- system **27** could be formed exclusively in 46% yield when this was hydrogen. (Equation 27)



Sherburn's desire to investigate the chemistry of [4]dendralene (**29**) led to the development of a synthesis using oxidation of an alkenyl cuprate. The reaction could be performed on multi-gram scale to provide a usable yield of the desired compound.[28] (Equation 28)

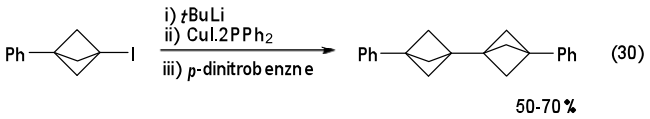


Other recent examples of the coupling of alkenyl copper species include Xi and co-workers' developments in the synthesis of cyclooctatetraene derivatives. Transmetalation from a dilithio or zirconaindene species provides the alkenyl copper intermediate for oxidation with a quinone.[29] This intramolecular coupling forms a cyclobutadiene (**30**), which then dimerises to form the tricycle **31**. A *retro*-[2+2] reaction furnishes the cyclooctatetraene **32**. (Equation 29) This methodology also provides an approach to benzocyclobutadiene derivatives.[30]



Organocuprate oxidation provides a solution to the formation of bonds at bridgehead positions where nucleophilic substitution reactions are impracticable. When Michl attempted to couple bicyclo[1.1.1]pentanes using Pd or Ni mediated processes, products

were formed in low yields (20-40%). However the use of copper chemistry allowed the coupling to take place in reproducibly good yields (50-70%), and the methodology was used to synthesise a variety of staffane derivatives.[31] (Equation 30)



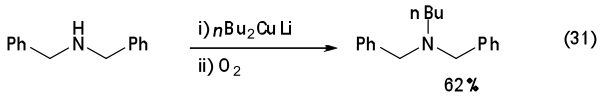
(30)

III. Formation of C-N Bonds

The oxidation of amidocuprates allows the formation of a new carbon-nitrogen bond between the ligands on copper.

A. Initial Studies

The first work in this area was carried out by Yamamoto and Maruoka[32], who used the oxidation reaction to alkylate a variety of primary and secondary amines and anilines. An excess of primary, tertiary or aryl organocuprate was added to the amine and the reaction mixture then oxidised with molecular oxygen. (Equation 31)

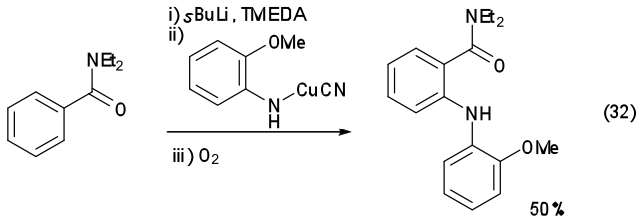


(31)

The resulting yield of amine was variable, with the lowest resulting from the transfer of tertiary alkyl groups. Interestingly, the yields of *N*-methylation products were higher when methyl magnesium chloride rather than methyl lithium was used to form dimethyl

cuprate, showing that the other atoms present in the solution aggregation structure of the cuprate can also affect reactivity in amidocuprates as well as organocuprates.

Snieckus further developed the methodology to synthesise anthranilamides as precursors to acridones.[33] Here, an excess of anilidocuprate was added to lithiobenzamides (prepared by a directed *ortho*-lithiation) and the oxidation performed by molecular oxygen. (Equation 32) The use of copper(I) cyanide was reported to give cleaner, higher yielding reactions than that of copper(I) chloride, however stated yields remained moderate despite the use of excess cuprate.

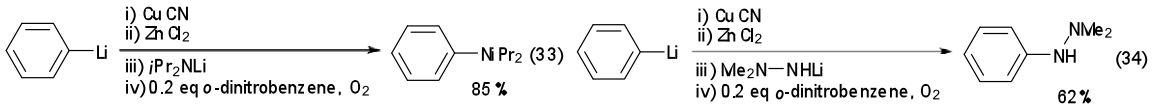


(32)

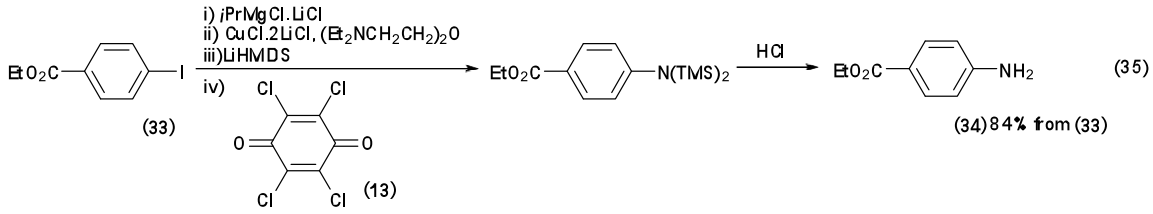
B. Further Developments

While the above two procedures involve adding an excess of cuprate to an organolithium, further work by Dembech, Ricci and co-workers showed that a 1:1 ratio of cuprioamide and organolithium could produce coupled products in useful yields.[34] Molecular oxygen was once again used as the oxidant, as other oxidising agents were found to give lower yields. This study is noteworthy as heteroaromatics were coupled for the first time. The methodology also allows the functionalisation of hydrazines, albeit in low yields due to

the formation of azo compounds as a by-product. Further studies[35] showed that yields of *N*-arylation products and hydrazines could be improved by the addition of zinc chloride to the cyanocuprates before amidocuprate formation coupled with the use of catalytic *ortho*-dinitrobenzene as a co-oxidant alongside molecular oxygen. (Equations 33 and 34)

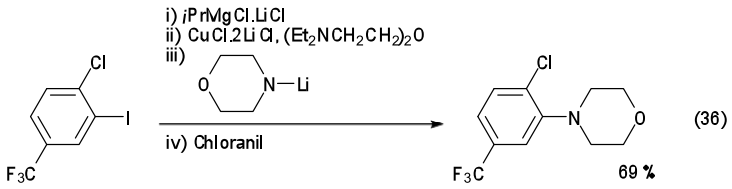


More recently, the Knochel group have used cuprate oxidation methodology to prepare primary, secondary and tertiary aromatic and heteroaromatic amines with the use of the quinone chloranil (**13**) as an oxidant.[36, 37] Here, an organocopper reagent is prepared from a functionalised Grignard reagent formed by an Mg/halogen exchange[18, 38] or a directed magnesiation[16] and combined with a lithiated amine to form the amidocuprate for oxidation. Various electron withdrawing and donating groups on the aromatic moieties can be tolerated, including esters and halogens.



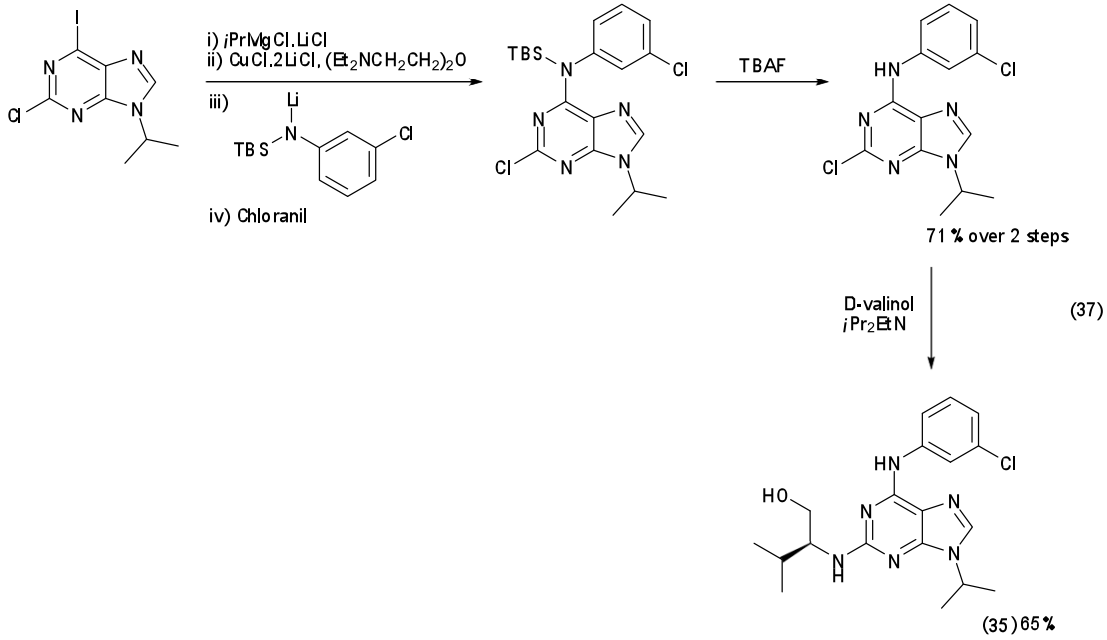
Primary amines are accessed *via* the use of lithium hexamethyldisilazide and subsequent desilylation with TBAF or HCl to reveal the amine. (Equation 35) The methodology also

allows the formation of tertiary aryl and sterically hindered amines, which can be difficult to form by other methods, in yields of 55% and above. (Equation 36)



(36)

This methodology has been further extended to the amination of purine and pyrimidine derivatives.[39] Again, the starting material could be cuprated regioselectively by the appropriate choice of magnesiation method (*vide supra*). This allowed access to uracil, thymine and adenine derivatives in good yields under mild conditions, and the CDK inhibitor purvalanol A (**35**) could be synthesised in 46% overall yield. (Equation 37)



(37)

IV. Conclusion

Organocuprate oxidation has proved itself to be a useful reaction in the forty years since its development. However, it is only recently that the full potential of the reaction has begun to be exploited, with new transmetalation procedures allowing milder reaction conditions and greater functional group tolerance. Hopefully these new advances, such as directed cuprations and the catalytic use of copper, will push forward the development of oxidation methodologies especially in the cross-coupling and C-N bond forming arenas where the reaction remains underexplored.

V. References

1. H. Gilman, R. G. Jones and L. A. Woods, *Journal of Organic Chemistry,* **17**, 1630 (1952).
2. T. Kauffman, *Angewandte Chemie, International Edition in English,* **13**, 291 (1974).
3. C. Glaser, *Annalen der Chemie und Pharmacie,* **154**, 137 (1870).
4. D. S. Surry and D. R. Spring, *Chemical Society Reviews,* **35**, 218 (2006).
5. S. Mori, A. Hirai, M. Nakamura and E. Nakamura, *Tetrahedron,* **56**, 2805 (2000).
6. M. Kienle, S. R. Dubbaka, K. Brade and P. Knochel, *European Journal of Organic Chemistry*, 4166 (2007).
7. G. M. Whitesides, J. San Filippo, C. P. Casey and E. J. Panek, *Journal of the American Chemical Society,* **89**, 5302 (1967).
8. W. H. Mandeville and G. M. Whitesides, *Journal of Organic Chemistry,* **39**, 400 (1974).
9. S. H. Bertz and C. P. Gibson, *Journal of the American Chemical Society,* **108**, 8286 (1986).
10. R. K. Dieter, S. J. Li and N. Y. Chen, *Journal of Organic Chemistry,* **69**, 2867 (2004).
11. B. H. Lipshutz, K. Siegmann, E. Garcia and F. Kayser, *Journal of the American Chemical Society,* **115**, 9276 (1993).
12. S. Mitra, S. R. Gurrala and R. S. Coleman, *Journal of Organic Chemistry,* **72**, 8724 (2007).
13. S. Usui, Y. Hashimoto, J. V. Morey, A. E. H. Wheatley and M. Uchiyama, *Journal of the American Chemical Society,* **129**, 15102 (2007).
14. G. M. Whitesides, W. F. Fischer, J. San Filippo, R. W. Bashe and H. O. House, *Journal of the American Chemical Society,* **91**, 4871 (1969).
15. S. R. Dubbaka, M. Kienle, H. Mayr and P. Knochel, *Angewandte Chemie-International Edition,* **46**, 9093 (2007).
16. A. Krasovskiy, V. Krasovskaya and P. Knochel, *Angewandte Chemie-International Edition,* **45**, 2958 (2006).
17. D. S. Surry, D. J. Fox, S. J. F. Macdonald and D. R. Spring, *Chemical Communications*, 2589 (2005).
18. A. E. Jensen, W. Dohle, I. Sapountzis, D. M. Lindsay, V. A. Vu and P. Knochel, *Synthesis-Stuttgart*, 565 (2002).
19. D. S. Surry, X. B. Su, D. J. Fox, V. Franckevicius, S. J. F. Macdonald and D. R. Spring, *Angewandte Chemie, International Edition,* **44**, 1870 (2005).
20. X. B. Su, D. J. Fox, D. T. Blackwell, K. Tanaka and D. R. Spring, *Chemical Communications*, 3883 (2006).
21. Y. Miyake, M. Wu, M. J. Rahman, Y. Kuwatani and M. Iyoda, *Journal of Organic Chemistry,* **71**, 6110 (2006).
22. B. H. Lipshutz, F. Kayser and N. Maullin, *Tetrahedron Letters,* **35**, 815 (1994).
23. B. H. Lipshutz, Z. P. Liu and F. Kayser, *Tetrahedron Letters,* **35**, 5567 (1994).
24. D. R. Spring, S. Krishnan, H. E. Blackwell and S. L. Schreiber, *Journal of the American Chemical Society,* **124**, 1354 (2002).
25. S. Krishnan and S. L. Schreiber, *Organic Letters,* **6**, 4021 (2004).

26. X. B. Su, D. S. Surry, R. J. Spandl and D. R. Spring, *Organic Letters,* **10**, 2593 (2008).
27. M. J. Rahman, J. Yamakawa, A. Matsumoto, H. Enozawa, T. Nishinaga, K. Kamada and M. Iyoda, *Journal of Organic Chemistry,* **73**, 5542 (2008).
28. A. D. Payne, A. C. Willis and M. S. Sherburn, *Journal of the American Chemical Society,* **127**, 12188 (2005).
29. C. Chen, C. J. Xi, C. B. Lai, R. J. Wang and X. Y. Hong, *European Journal of Organic Chemistry*, 647 (2004).
30. C. Chen, C. J. Xi, Y. Y. Liu and X. Y. Hong, *Journal of Organic Chemistry,* **71**, 5373 (2006).
31. C. Mazal, A. J. Paraskos and J. Michl, *Journal of Organic Chemistry,* **63**, 2116 (1998).
32. H. Yamamoto and K. Maruoka, *Journal of Organic Chemistry,* **45**, 2739 (1980).
33. M. Iwao, J. N. Reed and V. Snieckus, *Journal of the American Chemical Society,* **104**, 5531 (1982).
34. A. Alberti, F. Cane, P. Dembech, D. Lazzari, A. Ricci and G. Seconi, *Journal of Organic Chemistry,* **61**, 1677 (1996).
35. F. Cane, D. Brancaleoni, P. Dembech, A. Ricci and G. Seconi, *Synthesis-Stuttgart*, 545 (1997).
36. V. del Amo, S. R. Dubbaka, A. Krasovskiy and P. Knochel, *Angewandte Chemie-International Edition,* **45**, 7838 (2006).
37. M. Kienle, S. R. Dubbaka, V. del Amo and P. Knochel, *Synthesis-Stuttgart*, 1272 (2007).
38. A. Krasovskiy and P. Knochel, *Angewandte Chemie-International Edition,* **43**, 3333 (2004).
39. N. Boudet, S. R. Dubbaka and P. Knochel, *Organic Letters,* **10**, 1715 (2008).