# Palladium catalyzed arylation for the synthesis of polyarenes

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We present the current understanding on the mechanism of palladium-catalyzed arylation, which involves a proton abstraction by the base. In addition, we present selected examples of the application of this reaction for the synthesis of large polyarenes to highlight the variety of catalysts and reaction conditions that are currently used.

## Introduction

Compared with cross-coupling reactions,[1] the direct arylation of arenes catalyzed by palladium is a more direct alternative for the synthesis of biaryls.[2] This reaction has been mostly carried out intramolecularly using substrates of type **1** to form carbo- and heterocycles **2** (Scheme 1).[2–4] Intramolecular arylations

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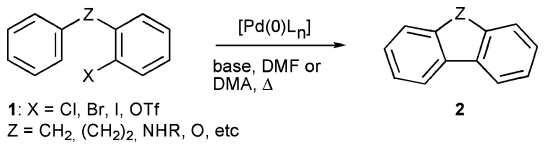



**Scheme 1** General scheme for the palladium-catalyzed arylation.

are also involved in catalytic processes that are mediated by palladacycles.[5–11] Synthetically useful intermolecular palladium-catalyzed arylations have been recently developed.[12–14]

We have been interested in the use of this reaction for the build up of large polyarenes related to the fullerenes.[15,16] In this perspective we review new studies on the mechanism of the palladium-catalyzed arylation as well as recent applications of this process for the construction of non-natural targets to compare the different reaction conditions commonly employed.

## New mechanistic paradigm

The initially formed oxidative addition complex could evolve by different mechanisms through intermediates **3–5** (Fig. 1).

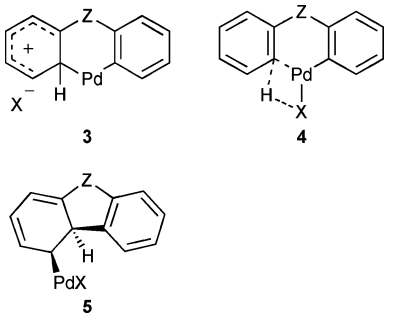
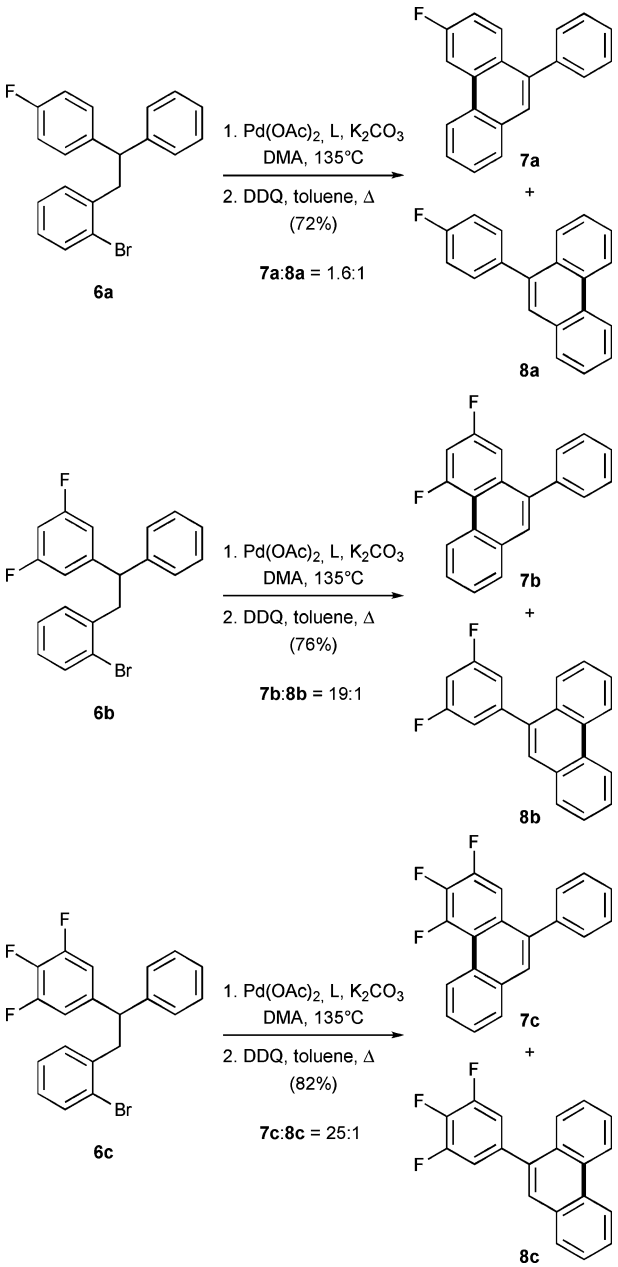



**Fig. 1** Three possible intermediates in the palladium-catalyzed arylation.

Most authors have favored an electrophilic aromatic substitution ($S_EAr$) *via* intermediates **3**.[17] Indeed, substituent effects on the formation of five-membered ring palladacycles by intramolecular palladation has been shown to follow the order X = MeO > H > $NO_2$ for substituents *meta* to the reacting site.[18,19] However, an intramolecular isotope effect $k_H/k_D = 3.5$ has been determined in one case.[4a] A similar intramolecular isotope effect ($k_H/k_D = 4$) was found in the Pd-catalyzed synthesis of oxindoles that proceeds *via* C–H functionalization.[20] In addition, we have reported that the arylation on nitrofluorene[21a] or nitrocarbazole[21b] gives substantial amounts of products by reaction at the positions *ortho* or *para* to a strong electron-withdrawing $NO_2$ group. An interesting mechanistic alternative is a sigma bond metathesis *via* intermediates **4**,[20,22–24] which seems more likely than processes involving C–H oxidative addition. An insertion into the arene to form **5** by a Heck-type process has been proposed. However, recent work indicates that this process is rather unlikely.[25]

Surprisingly, the palladium-catalyzed arylation reaction is facilitated by electron-withdrawing substituents on the aromatic ring, which is clearly inconsistent with an electrophilic aromatic substitution mechanism. This led to the proposal of a proton-abstraction mechanism for this reaction.[26] This mechanistic proposal is in line with recent results on the intra-[4g] and intermolecular palladium arylation[12] that proceeds more easily with arenes or heteroarenes bearing strongly electron-withdrawing substituents. A related mechanism, in which acetate acts as the basic ligand, has been proposed for the cyclometallation of benzylic amines with $Pd(OAc)_2$.[27]

The new mechanism is based on competition experiments carried out with substrates of type **6** using as standard conditions for the palladium-catalyzed arylation those developed by Fagnou *et al.*,[4a] with a bulky phosphine as the ligand for Pd (Scheme 2). Cyclizations were routinely carried out in DMA or DMF at 100–135 °C. The cyclization furnished the corresponding 9,10-dihydrophenanthrenes, which were treated with DDQ to give the corresponding phenanthrenes **7** and **8**. The directing effects exerted by substituents are most clearly seen in the series of substrates

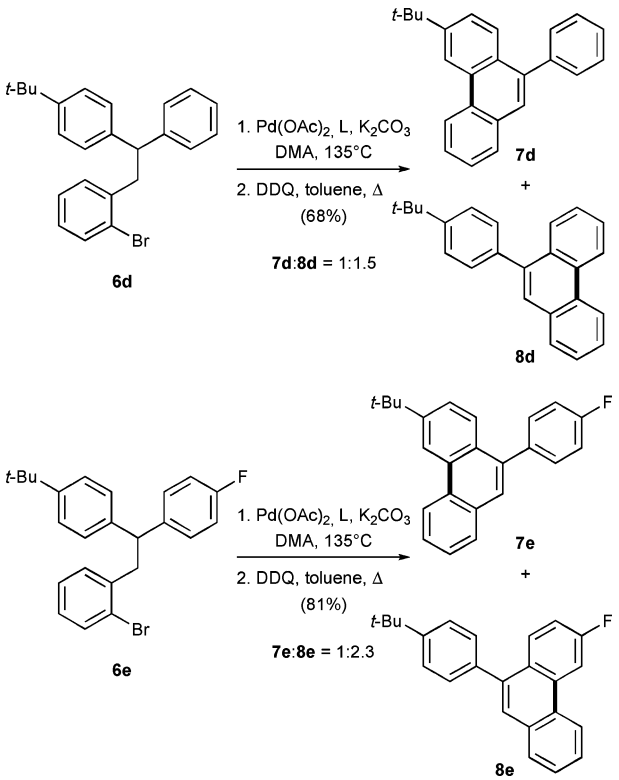



**Scheme 2** Intramolecular arylation reactions of fluorinated substrates **6a–c** with 5 mol% $Pd(OAc)_2$, 10 mol% L = 2-(diphenylphosphino)-2′-(*N*,*N*-dimethylamino)biphenyl, and 3 equiv. $K_2CO_3$ for 16 h (DMA).

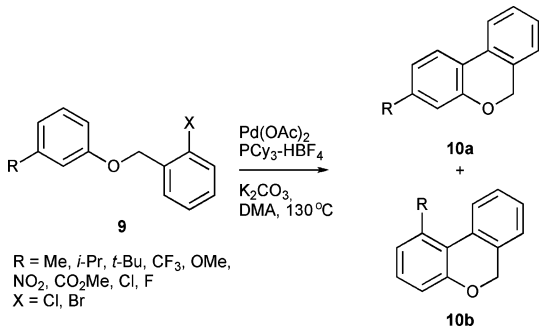
**6a–c** bearing fluorine substituents. A single fluorine substituent in **6a** leads to a moderate control on the regioselectivity leading to a 1.6 : 1 mixture of **7a** and **8a**. Remarkably, substrate **6b**, with fluorine substituents *ortho* to the arylation site, led to **7b** with an excellent regioselectivity (**7b**–**8b** = 19 : 1). Reaction of **6c**, with three fluorine substituents, occurred almost exclusively at the trifluorophenyl ring to give **7c**. Similar regioisomeric ratios (1.1–2.4 : 1), favoring reaction at the substituted aryl ring, were obtained from substrates of type **6** bearing groups that are electron-releasing (OMe) or electron-withdrawing ($CF_3$, Cl) in $S_EAr$ processes.

Interestingly, the arylation of substrates **6** with *t*-Bu and $SiMe_3$ substituents at C-3 (*meta* to the arylation site) took place on the unsubstituted phenyl ring with moderate selectivity. Thus, **6d** gave a 1 : 1.5 ratio of **7d** and **8d** (Scheme 3). The arylation of substrate **6e** gave a 1 : 2.3 ratio of **7e** and **8e**, which is that expected from the approximately additive effects of the fluorine (1.6 : 1) and the *tert*-butyl (1 : 1.5) substituents. Isotope effects are also inconsistent with an electrophilic aromatic substitution. Thus, intramolecular competition experiments between phenyl and pentadeuterophenyl groups led to the determination of intramolecular isotope effects $k_H/k_D$ = 5.0 (135 °C) and = 6.7 (100 °C) for this arylation reaction. Results on the intramolecular arylation on a 5*H*-indeno[1,2-*b*]pyridine derivative, which proceeded selectively at the pyridine ring, are also inconsistent with an electrophilic aromatic substitution mechanism for this reaction.[26]



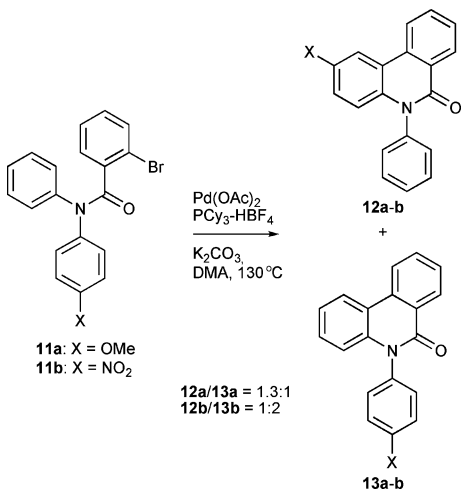

**Scheme 3** Selected examples of intramolecular arylation reactions of substrates **6** with 5 mol% $Pd(OAc)_2$, 10 mol% L = 2-(diphenylphosphino)-2′-(*N,N*-dimethylamino)biphenyl, and 3 equiv. $K_2CO_3$ for 16 h (DMA).

Fagnou *et al.* examined the cyclization of substrates **9** to give regioisomers **10a–b** (Scheme 4).[4g] Regioselectivities ranging between 10 : 1 to >30 : 1 favoring **10a** were obtained with R = Me, i-Pr, *t*-Bu, $CF_3$, OMe, $NO_2$, $CO_2Me$, Cl, F. However, a chloro substituted substrate led to a 3.2 : 1 mixture of **10a** and **10b**, whereas for the fluoro derivative, product **10b** was obtained as the major compound.




**Scheme 4** Intramolecular arylation reactions of substrates **9**.

Although these results also point towards a proton-abstraction mechanism facilitated by strongly electron-withdrawing substituents, results with substrates **11a–b** were somewhat contradictory (Scheme 5).[4g] In the case of **11a**, a small selectivity was observed with a preference for the reaction occurring at the substituted ring, whereas the opposite was observed for the nitro substituted substrate **11b**. However, interpretation of these results might be complicated by a competing amide rotation, as these systems may be far from Curtin–Hammett conditions. Interestingly, the direct arylation of a simple unsubstituted aryl bromide resulted in a primary kinetic isotopic effect of 4.25. These mechanistic studies revealed a kinetically significant C–H bond cleavage step during arylation, which was rationalized by a mechanism proceeding *via* electrophilic metalation involving either a σ-bond metathesis or an $S_E3$ C–H functionalization step.

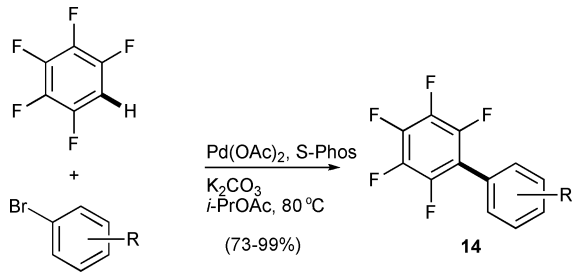



**Scheme 5** Intramolecular arylation reactions of amides **11a–b**.

An interesting finding was the observation that aryl iodides reacted poorly under conditions optimized for aryl bromides,[4g] which was attributed to catalyst poisoning by accumulation of the iodide anion.

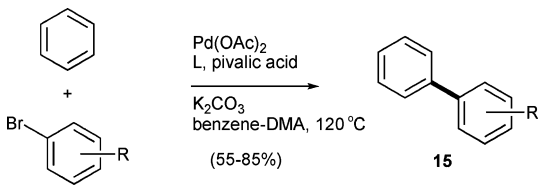
The fact that substrates bearing electron-withdrawing substituents react selectively led to the development of an intermolecular version by Fagnou *et al.* with polyfluoroaromatic

compounds.[12a] The use of the bulky ligand biphenyl(2-(dicyclohexylphosphino)-2′,6′-dimethoxybiphenyl)phosphine (S-Phos), allowed these reactions to be performed in a general way with aryl bromides and chlorides in isopropyl acetate at 80 °C (Scheme 6).[12b]




**Scheme 6** Intermolecular arylation reactions with pentafluorobenzene.

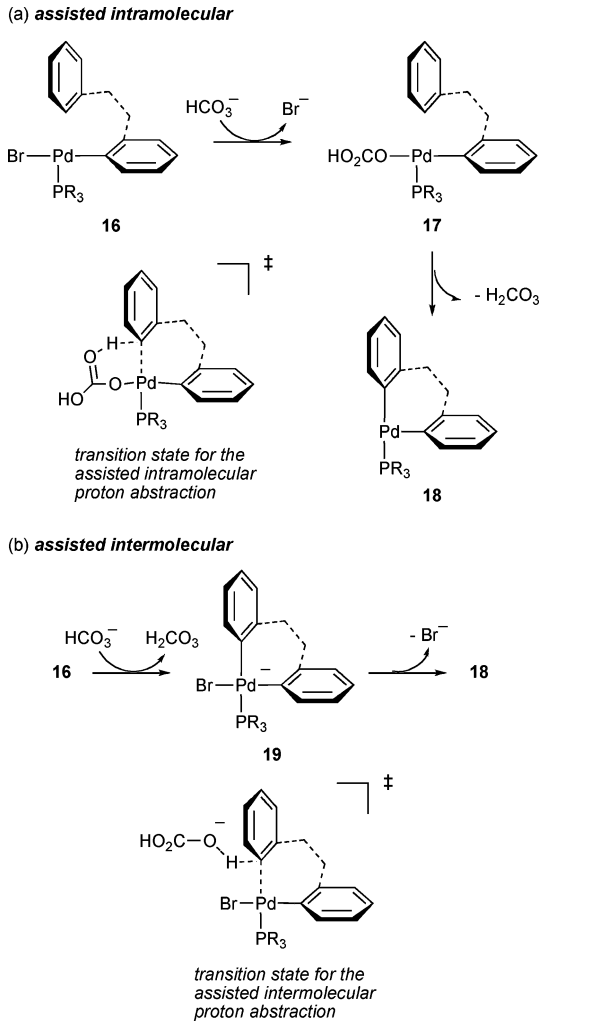
The group of Fagnou has also recently found that by using pivalate as the base the intermolecular reaction can take place with unactivated arenes such as benzene (Scheme 7).[12c] Experimental and theoretical calculations indicate that the pivalate anion is a key component in C–H bond cleaving, lowering the energy barrier of C–H bond cleavage. Other carboxylic acids led to poorer results in this process. Interestingly, a significant intermolecular isotope effect of 5.5 was determined for this arylation.




**Scheme 7** Intermolecular arylation reactions in benzene–DMA. L = Dave-Phos.

All the above results are more consistent with a mechanism proceeding by abstraction of a proton of the arylated ring by the base in a process in which the formation of the metal–carbon bond is concerted with the breaking of the carbon–hydrogen bond. DFT calculations carried out with bicarbonate as a model base for the intramolecular arylation favor two alternatives for the key activation process: a mechanism in which the base coordinates to the Pd(II) center and then acts as an internal base (*assisted intramolecular*) or an intermolecular proton abstraction by an external base (*assisted intermolecular*) (Scheme 8).[26b] Models as **16** and **17** are probably reasonably realistic since phosphines used in these reactions are bulky and bicarbonate experimentally leads to similar results to those obtained with carbonate as a base in these reactions. On the other hand, a mechanism in which bromide ligand acts as an internal base (*nonassisted intramolecular*) appear less likely acoording to the DFT calculations carried out on models shown in Scheme 8.[26b] Independent calculations carried out by Fagnou *et al.* on the intermolecular arylation favor an assisted intramolecular mechanism, although in that case the nonassisted intramolecular process could not be excluded.[12a]

It may be important to stress that the above mechanistic picture pertains to catalytic systems in which palladium bears a bulky phosphine ligand and a base like carbonate, bicarbonate, or a carboxylate is used. As shown in the next section, many palladium-catalyzed arylation reactions proceed in the presence of excess




**Scheme 8** Base-assisted mechanisms for the palladium-catalyzed arylation.

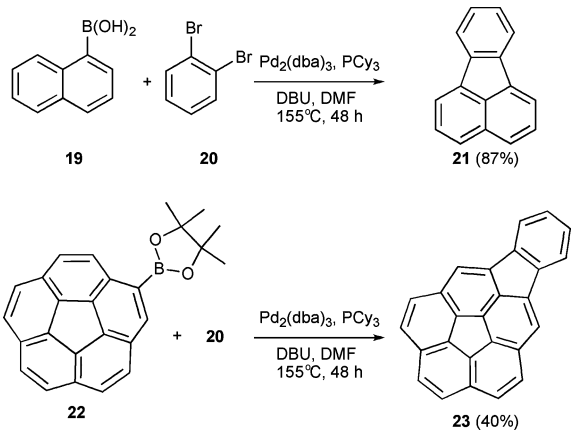
phosphine ligands or under "ligandless" conditions. Regarding the bases, in addition to carbonates, DBU has also been commonly used, although its possible role in a base-assisted mechanism has not been determined.

## Synthesis of large polyarenes

The groups of Scott and de Meijere developed an annulation process based on a domino Suzuki coupling reaction followed by an intramolecular arylation reaction (Scheme 9)[28] as an alternative to flash-vacuum pyrolysis based methods for the synthesis of aromatic molecular bowl compounds.[29,30] The best results for this annulation were obtained with a Pd(0) complex formed *in situ* from $Pd_2(dba)_3$ and $PCy_3$. Other palladium catalysts ($Pd(OAc)_2$, $PdCl_2(PPh_3)_2$, $PdCl_2(MeCN)_2$) and ligands ($PPh_3$, P(*p*-tol)$_3$, P(*n*-Bu)$_3$, dppe) led to less satisfactory results. The optimized reaction conditions were applied in the synthesis of indenocorannulene **23** in moderate yield from pinacol corannuleneboronate **22** and dibromide **20**.

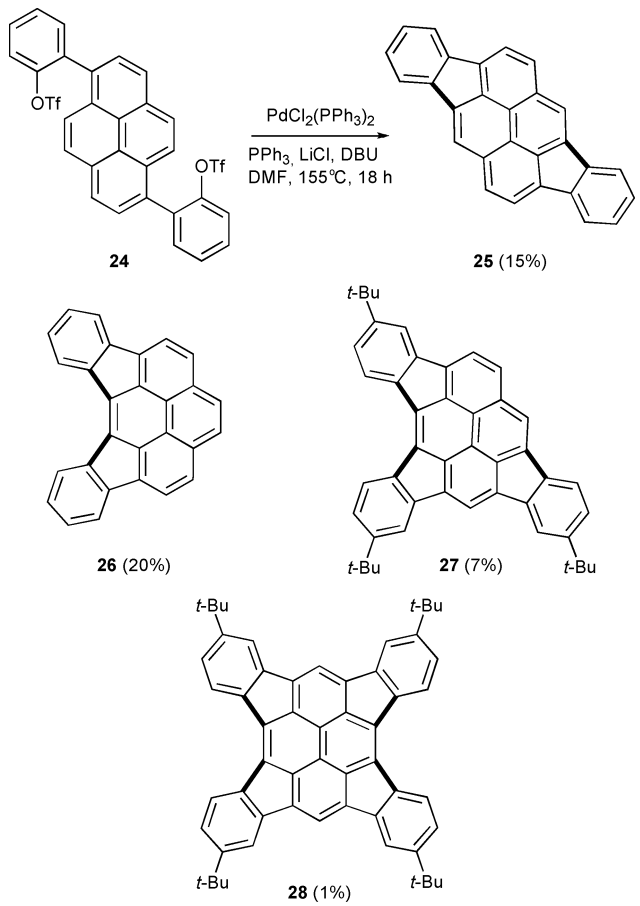
The same groups described the first synthesis of diindenopyrenes **25** and **26**,[31] triindenopyrene **27** and tetraindenopyrene **28**, using conditions previously developed by the group of Scott



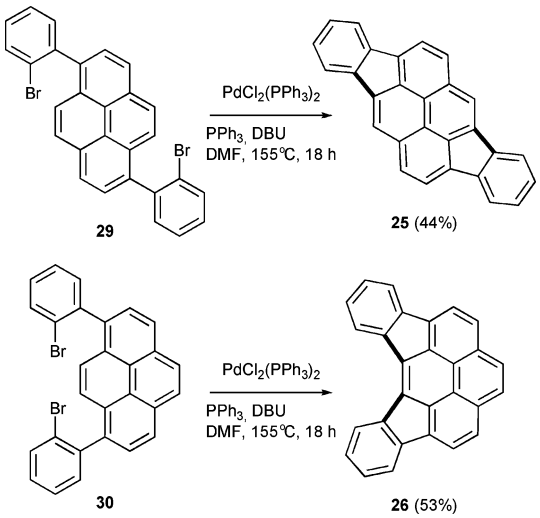

**Scheme 9** Palladium-catalyzed annulation *via* Suzuki coupling–intramolecular arylation.

(Scheme 10).[32,33] These PAHs were obtained from the intramolecular palladium-catalyzed arylation reaction of the corresponding substituted pyrenes, although in low yields. Compounds **25–28** were reported to be stable and have intense red colors. These physical properties could make them useful as long wavelength dyes when high temperature conditions are required.




**Scheme 10** Palladium-catalyzed arylation from aryl triflates with $PdCl_2(PPh_3)_2$–DBU.

Better yields of **25** and **26** were obtained from the dibromides **29** and **30** respectively, under similar reaction conditions used for the aryl triflates (Scheme 11).[31] The same catalytic system has been used for the synthesis of dibezo[*fg,op*]naphthacenes.[34]



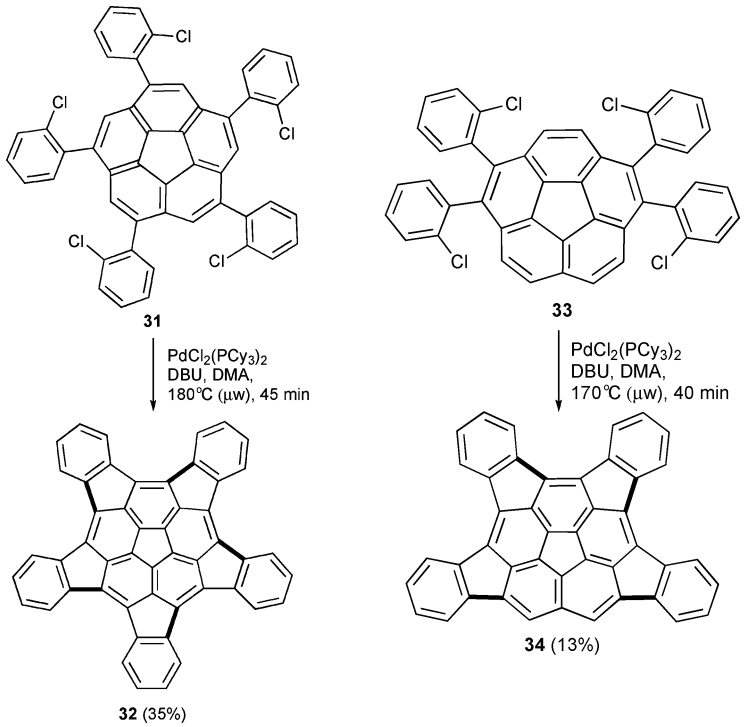

**Scheme 11** Palladium-catalyzed arylation from aryl bromides **29** and **30** with $PdCl_2(PPh_3)_2$–DBU.

More recently, the group of Scott has succeeded in the synthesis of the largest bowl-shape polyarenes ever prepared:[35] pentaindenocorannulene **32** ($C_{50}H_{20}$) and tetraindenocorannulene **34** ($C_{44}H_{18}$) (Scheme 12). Derivative **32** was obtained in 35% isolated yield (81% average yield per C–C bond formation) from 1,3,5,7,9-pentakis(2-chlorophenyl)corannulene **31** through a palladium-catalyzed and microwave induced 5-fold intramolecular arylation reaction. Tetraindenocorannulene **34** was prepared from 1,2,5,6-tetrakis(2-chlorophenyl)corannulene **33** under similar reaction conditions although in only 13% isolated yield. The lower yield in the synthesis of **34** is explained as a result of competitive couplings between the proximal phenyl rings. As the authors pointed out, nowadays rational chemical synthesis of fullerenes, carbon nanotubes and related carbon rich molecules using solution chemical methods has emerged as a competitive alternative to high-temperature gas-phase pyrolysis.

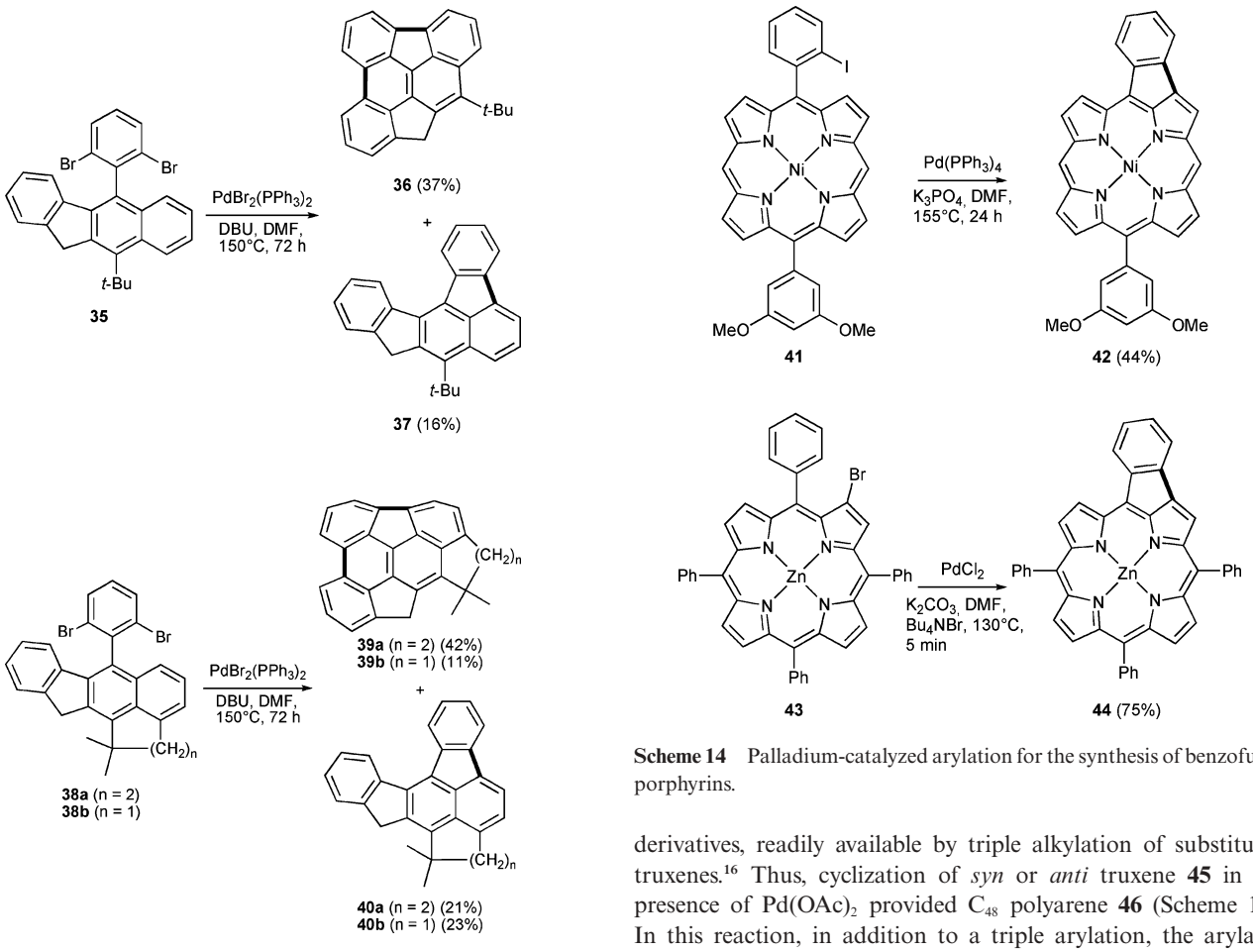
The group of Shevlin have used $PdCl_2(PCy_3)_2$–DBU for the synthesis of bowl-shaped fullerene fragments using aryl chlorides as substrates.[36] Wang and co-workers have prepared the buckybowl **36**[37] using similar reaction conditions. Monocyclized **37** and traces of debrominated starting material were also obtained (Scheme 13). Similarly, polyarenes **39a–b** were synthesized from dibromides **38a–b**. The lower efficiency in the cyclization of **38b** reflects the increased strain due to the presence of an additional five-membered ring.

The intramolecular arylation has also been used in the context of porphyrin chemistry. Thus, nickel porphyrin **41** was transformed into **42** in moderate yield with a Pd(0) catalyst and $K_3PO_4$ as the base (Scheme 14).[38] The arylation can also take place from a haloporphyrine as shown in the reaction of zinc porphyrin **43** to give **44**.[39] The efficiency and the short reaction time required for this transformation using a "ligandless" palladium catalyst are remarkable.

Our group has also worked on the synthesis of fullerene fragments using palladium chemistry. Our synthetic approach is based on the intramolecular arylation reaction of truxene




**Scheme 12** Palladium-catalyzed arylation from aryl chlorides **31** and **33** with $PdCl_2(PCy_3)_2$–DBU.

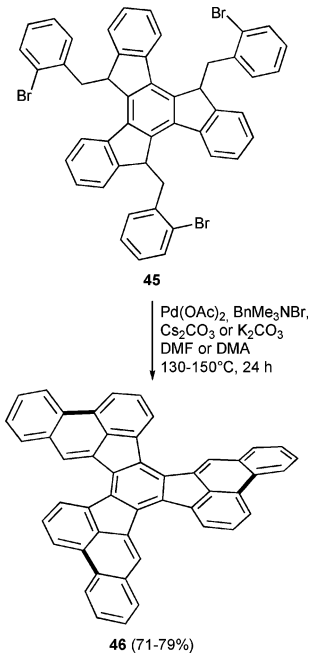



**Scheme 13** Palladium-catalyzed arylation from aryl bromides **35** and **38a–b** with $PdBr_2(PPh_3)_2$–DBU.

**Scheme 14** Palladium-catalyzed arylation for the synthesis of benzofused porphyrins.

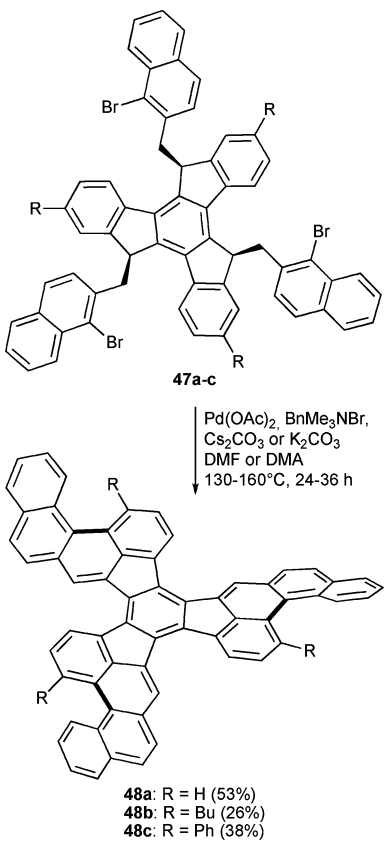
derivatives, readily available by triple alkylation of substituted truxenes.[16] Thus, cyclization of *syn* or *anti* truxene **45** in the presence of $Pd(OAc)_2$ provided $C_{48}$ polyarene **46** (Scheme 15). In this reaction, in addition to a triple arylation, the arylated compound undergoes dehydrogenation to form the fully aromatic compound.



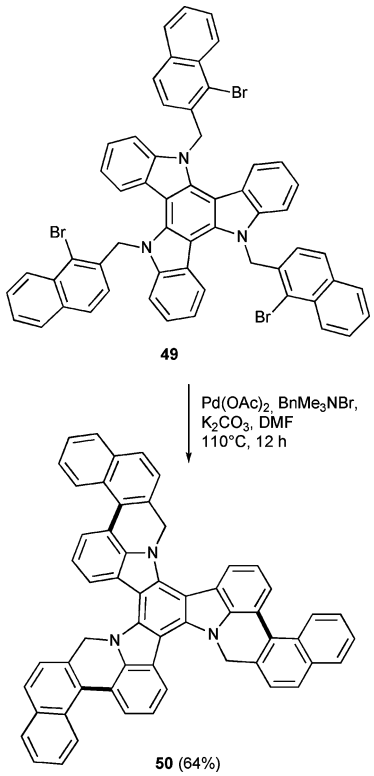

**Scheme 15** Palladium-catalyzed arylation from truxene derivative **45** to give $C_{48}$ polyarene **46**.

Similarly, intramolecular arylation of naphthyl derivatives **49a–c** provided the $C_{60}$ polycyclic aromatic hydrocarbons **48a–c** (Scheme 16).[16,40] Polyarene **48a** was named crushed fullerene as it corresponds to a hypothetical hydrogenolysis product of fullerene $C_{60}$.




**Scheme 16** Palladium-catalyzed arylation from truxene derivatives **47a–c** to give $C_{60}$ polyarenes **48a–c**.

Similarly, we have also applied the palladium-catalyzed arylation for the cyclization of *N*-alkylated triindoles such as **49** to afford **50**, the triaza-analogue of **48** (Scheme 17).[21b] It is noteworthy that formations of **46** (Scheme 15) and **50** proceed with 86–90% yield for each C–C bond forming process.




**Scheme 17** Palladium-catalyzed arylation from triindole derivative **49** to give triazaderivative **50**.

## Conclusions

In this overview we have presented the current understanding of the mechanism of the palladium-catalyzed arylation reaction, whose rate-determining step appears to involve a proton abstraction by the base. However, this mechanism has been proposed for the reaction of bromides with palladium catalysts bearing bulky phosphines. It is not clear if a similar mechanism operates with other substrates (chlorides or triflates) or in the absence of strongly donating ligands (ligandless conditions).

Although, at present, rather harsh reaction conditions (high temperatures and long reactions times) are often required for palladium-catalyzed arylation, the selected results shown for the synthesis of large polyarenes clearly demonstrate that this methodology is practical and proceeds in many cases with high efficiency.

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## Notes and references


1 (*a*) *Metal-Catalyzed Cross-Coupling Reactions*, ed. A. de Meijere and F. Diederich, Wiley, Weinheim, 2004; (*b*) P. Espinet and A. M. Echavarren, *Angew. Chem., Int. Ed.*, 2004, **43**, 4704–4734; (*c*) A. A. C. Braga, N. H. Morgon, G. Ujaque and F. Maseras, *J. Am. Chem. Soc.*, 2005, **127**, 9298–9307.

2 (*a*) J. Hassan, M. Sévignon, C. Gozzi, E. Schulz and M. Lemaire, *Chem. Rev.*, 2002, **102**, 1359–1470; (*b*) G. Bringmann, S. Tasler, R.-M. Pfeifer and M. Breuning, *J. Organomet. Chem.*, 2002, **661**, 49–65; (*c*) L.-C. Campeau and K. Fagnou, *Chem. Commun.*, 2006, 1253–1264; (*d*) T. Satoh and M. Miura, *J. Synth. Org. Chem., Jpn.*, 2006, **64**, 1199–1207; (*e*) D. Alberico, M. E. Scott and M. Lautens, *Chem. Rev.*, 2007, **107**, 174–238.

3 Lead references on applications in natural product synthesis: (*a*) H. Abe, S. Takeda, T. Fujita, K. Nishioka, Y. Takeuchi and T. Harayama, *Tetrahedron Lett.*, 2004, **45**, 2327–2329; (*b*) J. C. Torres, A. C. Pinto and S. J. Garden, *Tetrahedron*, 2004, **60**, 9889–9900; (*c*) T. Harayama, A. Hori, H. Abe and Y. Takeuchi, *Tetrahedron*, 2004, **60**, 1611–1616; (*d*) D. C. Harrowven, T. Woodcock and P. D. Howes, *Angew. Chem., Int. Ed.*, 2005, **44**, 3899–3901; (*e*) K. Ohmori, M. Tamiya, M. Kitamura, H. Kato, M. Oorui and K. Suzuki, *Angew. Chem., Int. Ed.*, 2005, **44**, 3871–3874; (*f*) H. Abe, K. Nishioka, S. Takeda, M. Arai, Y. Takeuchi and T. Harayama, *Tetrahedron Lett.*, 2005, **46**, 3197–3200; (*g*) A. L. Bowie, C. C. Hughes and D. Trauner, *Org. Lett.*, 2005, **7**, 5207–5209; (*h*) D. M. Shen, C. Liu and Q. Y. Chen, *J. Org. Chem.*, 2006, **71**, 6508–6511; (*i*) L. Ackermann and A. Althammer, *Angew. Chem., Int. Ed.*, 2007, **46**, 1627–1629; (*j*) R. B. Bedford and M. Betham, *J. Org. Chem.*, 2007, **71**, 9403–9410.

4 (*a*) L.-C. Campeau, M. Parisien, M. Leblanc and K. Fagnou, *J. Am. Chem. Soc.*, 2004, **126**, 9186–9187; (*b*) M. Lafrance, N. Blaquière and K. Fagnou, *Chem. Commun.*, 2004, 2874–2875; (*c*) M. Parisien, D. Valette and K. Fagnou, *J. Org. Chem.*, 2005, **70**, 7578–7584; (*d*) L.-C. Campeau, P. Thansandote and K. Fagnou, *Org. Lett.*, 2005, **7**, 1857–1860; (*e*) M. Leblanc and K. Fagnou, *Org. Lett.*, 2005, **7**, 2849–2852; (*f*) J.-P. Leclerc, M. Andre and K. Fagnou, *J. Org. Chem.*, 2006, **71**, 1711–1714; (*g*) L.-C. Campeau, M. Parisien, A. Jean and K. Fagnou, *J. Am. Chem. Soc.*, 2006, **128**, 581–590; (*h*) M. Lafrance, N. Blaquiere and K. Fagnou, *Eur. J. Org. Chem.*, 2007, **5**, 811–825.

5 M. Catellani, E. Motti, F. Faccini and R. Ferraccioli, *Pure Appl. Chem.*, 2005, **77**, 1243–1248, and references therein.

6 J. Dupont, C. S. Consorti and J. Spencer, *Chem. Rev.*, 2005, **105**, 2527–2571.

7 (*a*) M. A. Campo and R. C. Larock, *J. Am. Chem. Soc.*, 2002, **124**, 14326–14327; (*b*) J. Zhao, M. Campo and R. C. Larock, *Angew. Chem., Int. Ed.*, 2005, **44**, 1873–1875; (*c*) M. A. Campo, H. Zhang, T. Yao, A. Ibdah, R. D. McCulla, Q. Huang, J. Zhao, W. S. Jenks and R. C. Larock, *J. Am. Chem. Soc.*, 2007, **129**, 6298–6307.

8 (*a*) G. Karig, M.-T. Moon, N. Thasana and T. Gallagher, *Org. Lett.*, 2002, **4**, 3115–3118; (*b*) D. Masselot, J. P. H. Charmant and T. Gallagher, *J. Am. Chem. Soc.*, 2006, **128**, 694–695.

9 A. Singh and P. R. Sharp, *J. Am. Chem. Soc.*, 2006, **128**, 5998–5999.

10 D. J. Cárdenas, B. Martín-Matute and A. M. Echavarren, *J. Am. Chem. Soc.*, 2006, **128**, 5033–5040.

11 T. Furuta, Y. Kitamura, A. Hashimoto, S. Fujii, K. Tanaka and T. Kan, *Org. Lett.*, 2007, **9**, 183–186.

12 (*a*) M. Lafrance, C. N. Rowley, T. K. Woo and K. K. Fagnou, *J. Am. Chem. Soc.*, 2006, **128**, 8754–8756; (*b*) M. Lafrance, D. Shore and K. Fagnou, *Org. Lett.*, 2006, **8**, 5097–5100; (*c*) M. Lafrance and K. Fagnou, *J. Am. Chem. Soc.*, 2006, **128**, 16496–16497.

13 (*a*) L.-C. Campeau, S. Rousseaux and K. Fagnou, *J. Am. Chem. Soc.*, 2005, **127**, 18020–18021; (*b*) J.-P. Leclerc and K. Fagnou, *Angew. Chem., Int. Ed.*, 2006, **45**, 7781–7786.

14 Lead references on intermolecular arylations of heterocycles: (*a*) K. Kobayashi, A. Sugie, M. Takahashi, K. Masui and A. Mori, *Org. Lett.*, 2005, **7**, 5083–5085; (*b*) J. Koubachi, S. El Kazzouli, S. Berteina-Raboin, A. Mouaddib and G. Guillaumet, *Synlett*, 2006, 3237–3242; (*c*) I. Cerna, R. Pohl, B. Klepetarova and M. Hocek, *Org. Lett.*, 2006, **8**, 5389–5392; (*d*) H. A. Chiong and O. Daugulis, *Org. Lett.*, 2007, **9**, 1449–1451.

15 A. M. Echavarren, B. Gómez-Lor, J. J. González and Ó. de Frutos, *Synlett*, 2003, 585–597.

16 (*a*) Ó. de Frutos, B. Gómez-Lor, T. Granier, M. Á. Monge, E. Gutiérrez-Puebla and A. M. Echavarren, *Angew. Chem., Int. Ed.*, 1999, **38**, 204–207; (*b*) B. Gómez-Lor, E. González-Cantalapiedra, M. Ruiz, Ó. de Frutos, D. J. Cárdenas, A. Santos and A. M. Echavarren, *Chem.–Eur. J.*, 2004, **10**, 2601–2608.

17 (*a*) B. S. Lane and D. Sames, *Org. Lett.*, 2004, **6**, 2897–2900; (*b*) B. S. Lane, M. A. Brown and D. Sames, *J. Am. Chem. Soc.*, 2005, **127**, 8050–8057; (*c*) C.-H. Park, V. Ryabova, I. V. Seregin, A. W. Sromek and V. Gevorgyan, *Org. Lett.*, 2004, **6**, 1159–1162.

18 B. Martín-Matute, C. Mateo, D. J. Cárdenas and A. M. Echavarren, *Chem.–Eur. J.*, 2001, **7**, 2341–2348.

19 M. Catellani and G. P. Chiusoli, *J. Organomet. Chem.*, 1992, **425**, 151–154.

20 E. J. Hennessy and S. L. Buchwald, *J. Am. Chem. Soc.*, 2003, **125**, 12084–12085.

21 (*a*) J. J. González, N. García, B. Gómez-Lor and A. M. Echavarren, *J. Org. Chem.*, 1997, **62**, 1286–1291; (*b*) B. Gómez-Lor and A. M. Echavarren, *Org. Lett.*, 2004, **6**, 2993–2996.

22 A. J. Mota, A. Dedieu, C. Bour and J. Suffert, *J. Am. Chem. Soc.*, 2005, **127**, 7171–7182.

23 B. Biswas, M. Sugimoto and S. Sakaki, *Organometallics*, 2000, **19**, 3895–3908.

24 A. Pinto, L. Neuville, P. Retailleau and J. Zhu, *Org. Lett.*, 2006, **8**, 4927–4930.

25 C. C. Hughes and D. Trauner, *Angew. Chem., Int. Ed.*, 2002, **41**, 1569–1572.

26 (*a*) D. García-Cuadrado, A. A. C. Braga, F. Maseras and A. M. Echavarren, *J. Am. Chem. Soc.*, 2006, **128**, 1066–1067; (*b*) D. García-Cuadrado, P. de Mendoza, A. A. C. Braga, F. Maseras and A. M. Echavarren, *J. Am. Chem. Soc.*, 2007, **129**, 6880–6886.

27 D. L. Davies, S. M. A. Donald and S. A. Macgregor, *J. Am. Chem. Soc.*, 2005, **127**, 13754–13755.

28 H. A. Wegner, L. T. Scott and A. de Meijere, *J. Org. Chem.*, 2003, **68**, 883–887.

29 V. M. Tsefrikas and L. T. Scott, *Chem. Rev.*, 2006, **106**, 4868–4884.

30 Y.-T. Wu and J. S. Siegel, *Chem. Rev.*, 2006, **106**, 4843–4867.

31 H. A. Wegner, H. Reisch, K. Rauch, A. Demeter, K. A. Zachariasse, A. de Meijere and L. T. Scott, *J. Org. Chem.*, 2006, **71**, 9080–9087.

32 H. A. Reisch, M. S. Bratcher and L. T. Scott, *Org. Lett.*, 2000, **2**, 1427–1430.

33 Earlier work on the arylation of aryl triflates: (*a*) J. E. Rice and Z. W. Cai, *Tetrahedron Lett.*, 1992, **33**, 1675–1678; (*b*) J. E. Rice and Z. W. Cai, *J. Org. Chem.*, 1993, **58**, 1415–1424; E. Rice, Z. W. Cai, Z.-M. He and E. J. LaVoie, *J. Org. Chem.*, 1995, **60**, 8101–8104.

34 X. H. Cheng, S. Höger and D. Fenske, *Org. Lett.*, 2003, **5**, 2587–2589.

35 E. A. Jackson, B. D. Steinberg, M. Bancu, A. Wakamiya and L. T. Scott, *J. Am. Chem. Soc.*, 2007, **129**, 484–485.

36 (*a*) L. Wang and P. B. Shevlin, *Tetrahedron Lett.*, 2000, **41**, 285–288; (*b*) L. Wang and P. B. Shevlin, *Org. Lett.*, 2000, **2**, 3703–3705 (erratum 2000, **2**, 4115).

37 D. Kim, J. L. Petersen and K. K. Wang, *Org. Lett.*, 2006, **8**, 2313–2316.

38 S. Fox and R. W. Boyle, *Chem. Commun.*, 2004, 1322–1323.

39 D.-M. Shen, C. Liu and Q.-Y. Chen, *J. Org. Chem.*, 2006, **71**, 6508–6511.

40 (*a*) B. Gómez-Lor, Ó. de Frutos and A. M. Echavarren, *Chem. Commun.*, 1999, 2431–2432; (*b*) B. Gómez-Lor, C. Koper, R. H. Fokkens, E. J. Vlietstra, T. J. Cleij, L. W. Jenneskens, N. M. M. Nibbering and A. M. Echavarren, *Chem. Commun.*, 2002, 370–371.


 