Transborylation-Enabled Boron Catalysis

Citation for published version:

Digital Object Identifier (DOI):
10.1055/s-0040-1720046

Link:
Link to publication record in Edinburgh Research Explorer

Document Version:
Peer reviewed version

Published In:
Synthesis: Journal of Synthetic Organic Chemistry

General rights
Copyright for the publications made accessible via the Edinburgh Research Explorer is retained by the author(s) and / or other copyright owners and it is a condition of accessing these publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy
The University of Edinburgh has made every reasonable effort to ensure that Edinburgh Research Explorer content complies with UK legislation. If you believe that the public display of this file breaches copyright please contact openaccess@ed.ac.uk providing details, and we will remove access to the work immediately and investigate your claim.
Transborylation-enabled Boron Catalysis

Andrew D. Bage1
Kieran Nicholson1
Thomas A. Hunt2
Thomas Langer3
Stephen P. Thomas4*

1 EaStCHEM School of Chemistry, University of Edinburgh, Edinburgh EH9 3FD, United Kingdom
2 Medicinal Chemistry, Early Oncology, AstraZeneca, Cambridge CB4 0WG, United Kingdom
3 Pharmaceutical Technology & Development, Chemical Development U.K., AstraZeneca, Macclesfield SK10 2NA, United Kingdom
4 Pharmaceutical Technology & Development, Chemical Development U.K., AstraZeneca, Macclesfield SK10 2NA, United Kingdom

stephen.thomas@ed.ac.uk

Click here to insert a dedication.

Abstract This review highlights transborylation (controlled boron-boron exchange) and its applications as a turnover strategy in boron-catalysed methodologies. Catalytic applications of B–C, B–O, B–N, B–F, B–P and B–Se transborylations are discussed in the context of transborylation-enabled catalysis, across a wide range of organic transformations including hydroboration, C–C bond formation, C–H borylation, chemoselective reduction, and asymmetric reduction.

1 Introduction

Stoichiometric redistribution reactions (σ-bond metathesis) between two boron centres are well established, with halide, hydride, alkyl, aryl, thiolate, and alkynyl groups shown to redistribute across two boron centres (Scheme 1a). Similarly, the stoichiometric reactivity of hydridoborane reagents is well known and has been applied broadly throughout organic chemistry. However, stoichiometric organoborane chemistry has been largely superseded by transition metal catalysis. A combination of stoichiometric borane reactivity and stoichiometric redistribution has provided a platform to develop borane-catalysed reactions that use transborylation (the controlled redistribution of substituents by σ-bond metathesis about two boron centres) as a turnover step in catalysis. This short review will provide an overview of the development of transborylation as a turnover strategy and the current state-of-the-art borane-catalysed transformations that exploit transborylation and is organised by the B–X bond undergoing transborylation.

The use of σ-bond metathesis as a means for catalytic turnover has been applied to p-block catalysis using organoborane reagents [e.g. catecholborane (HBcat) and pinacolborane (HBpin)] as the stoichiometric turnover reagents. The gallium-catalysed asymmetric reduction of ketones used Ga–O/B–H σ-bond metathesis with catecholborane (HBcat). Phosphorous-based catalysts have been developed for the hydroboration of pyridines, ketones, and imines, and for the reductive coupling of α,β-unsaturated esters, all using P–X/B–H exchange. Germanium- and tin hydride catalysts have been used in the catalytic reductions of carbonyl species and carbon dioxide, and proceed through M–O/B–H σ-bond metathesis turnover steps. Al–X/B–H σ-bond metathesis has enabled the development of several aluminium-catalysed reactions; the hydroboration of ketones, alkynes, alkenes, aldehydes, carbon dioxide, nitriles, and amides, the borylation of alkynes, and the dehydrocoupling of alcohols.

The broadest application of σ-bond metathesis in the p-block is in the exchange between two boron atoms. Transborylation, akin to transmetallation, is mechanistically
distinct from ligand exchange and transesterification (Scheme 1b). Transborylation is an isodesmic σ-bond metathesis between two boron-containing species, where the group of interest is exchanged from one boron to another boron. In ligand exchange, the bond between the group of interest and the boron atom in the intermediate remains intact during the σ-bond metathesis step. Instead, the backbone functionalities around each boron atom are exchanged from one boron atom to another. The substituent groups of a boron species can also be changed through transesterification, nor ligand exchange. Reactions that proceed through ligand exchange, including the diol-catalysed 1,4-addition to enones, and the aminoborane-catalysed transesterification with an alcohol, here no transfer of groups, groups of a boron species can also be changed through transesterification, nor ligand exchange. Instead, the backbone functionalities around each boron atom intermediate remains intact during the σ-exchanged from one boron to another boron. In ligand exchange, the bond between the group of interest and the boron atom in the intermediate remains intact during the σ-bond metathesis step. Instead, the backbone functionalities around each boron atom are exchanged from one boron atom to another. The substituent groups of a boron species can also be changed through ligand exchange. Reactions that proceed through ligand exchange, including the diol-catalysed 1,4-addition to enones, and the aminoborane-catalysed transesterification with an alcohol, here no transfer of groups, groups of a boron species can also be changed through transesterification, nor ligand exchange. Instead, the backbone functionalities around each boron atom intermediate remains intact during the σ-bond metathesis step.

2 B–C Transborylation

The first proposed B–C/H transborylation for catalysis was reported for Periasamy for the PhEtN-BH3-catalysed hydroboration of alkenes with HBcat to give alkanyl catechol boronic esters 1_cat (Scheme 2a). It was proposed that PhEtN-BH3 reacted with the alkene to give an alkylboronate which underwent exchange with HBcat (B–C(sp²)/H–B transborylation) to give the alkanyl catechol boronic ester and regenerate the catalyst. Subsequently, Arase and Hoshi used dicyclohexylborane (HBCy₂) or 9-borabicyclo[3.3.1]nonane (H-B-9-BBN) to catalyse the hydroboration of alkenes with HBcat. The reaction was proposed to proceed by the same mechanism as that described by Periasamy. Hoshi expanded this reactivity using HBpin in place of HBcat to give alkanyl pinacol boronic esters 1_pin and B–C(sp²)/H–B transborylation was again proposed as the means for catalytic turnover. Hoshi suggested that the turnover process was more challenging for more hindered, branched alkynylboranes, a similar steric argument to that postulated by Brown for stoichiometric redistribution reactions. Subsequently, Hoshi developed an alternative system for alkene hydroboration using Me₅S·BH₃ and BCy₂H as pre-catalysts to generate Me₅S·BH(C₆F₃)₂ in situ by B–C(sp²)/H–B transborylation. Catalysis was proposed to proceed by hydroboration of the alkene by the in situ-generated Me₅S·BH(C₆F₃)₂ to give an alkanyl(B(C₆F₃)₂ which undergoes B–C(sp²)/H–B transborylation with HBpin to regenerate the catalyst, Me₅S·BH(C₆F₃)₂, and give an alkanyl pinacol boronic ester. An alkanyl(B(C₆F₃)₂ was independently synthesised and used as a pre-catalyst to support the proposal of it being an on-cycle species. Stephan used Pier’s borane, HB(C₆F₃)₂ as a catalyst for the hydroboration of alkenes with HBpin. However, catalysis was proposed to proceed through a mechanism that did not involve transborylation. Vasko, Kamer and Aldridge reported an alkene hydroboration system where HB(C₆F₃)₂ was generated in situ from B–C(sp²)/H–B transborylation between HBpin and a FLP (Frustrated Lewis Pair) pre-catalyst.

Thomas and Lloyd-Jones investigated the mechanism of the Arase-Hoshi dialkylborane-catalysed hydroboration of alkenes with HBpin (Scheme 2b), using H-B-9-BBN and HB(O₂CMe₂)₂ as catalysts. Kinetic analysis, isotopic-entainment, and isotopic-labelling experiments (H-Bpin and H-B(O₂CMe₂)₂) identified B–C(sp²)/H–B transborylation as the mode of catalytic turnover. When H-Bpin was reacted with the alkenyl(dialkyl)borane 2cat (Scheme 2c), ¹⁰B-alkenyl boronic ester ¹⁰B–1 pin was formed exclusively, supporting the proposal of a transborylation pathway (ligand exchange would have resulted in a mixture of ¹⁰B- and ¹⁰B-alkenyl boronic ester products). The metathesis step was computationally calculated (ΔG = 19.7 kcal mol⁻¹) and was measured experimentally (ΔG = 20.3 kcal mol⁻¹). Catalysis was shown to proceed by hydroboration of the alkene by the dialkylborane catalyst to give an alkenydialkylborane 2. B–C(sp²)/H–B transborylation with HBpin gives the alkynyl pinacol boronic ester ¹⁰B–1 pin concomitantly regenerating the dialkylborane catalyst. Hydroboration of both the alkenydialkylborane 2 and the alkynyl boronic ester ¹⁰B–1 pin by the dialkylborane was shown to be irreversible under reaction conditions, leading to catalyst deactivation and a reduction in alkynyl boronic ester ¹⁰B–1 pin yield.

Oestreich developed the pre-catalyst tris[3,5-bis(trifluoromethyl)phenyl]borane (BAR₃) for the hydroboration of alkenes with HBpin (Scheme 3a). The active
catalysts, HB(Ar)² and H₂BAr, were generated *in situ* through B–C(sp³)/B–H transborylation with HBpin. HBAr² or H₂BAr was proposed to undergo hydroboration of the alkene to give an alkylborane intermediate 3, which reacted with HBpin through B–C(sp³)/B–H transborylation to give the alkyl pinacol boronic ester 4 and regenerate the catalyst (Scheme 3b). Although Stephan reported B(CF₃)₂ as an active catalyst for alkene hydroboration, Oestreich observed only trace product when B(CF₃)₂ was used as a pre-catalyst for alkene hydroboration. Through stoichiometric studies, Oestreich showed that HB(Ar)² and H₂BAr were generated by reaction of HBAr with HBpin, and that Piers’s borane was not generated under the same conditions with B(CF₃)₂. Melen developed a similar system for hydroboration using Lewis acidic borane catalysts. This widely applicable protocol was used for the hydroboration of alkynes, ketones, aldehydes and imines. A mechanism of catalysis was not proposed but may have proceeded through a transborylation mechanism akin to those proposed by Oestreich and Hoshi. However, in a separate report, Melen and Oestreich disclosed the use of boron Lewis acid catalysts for the hydroboration of imines and catalysis was proposed to proceed through Lewis acid catalysis and not transborylation.

Thomas used THF-BH₃ or Me₂S·BH₃ as catalysts for the hydroboration of alkynes and alkynes with HBpin (Scheme 3a). Interestingly HBpin could be reacted with substoichiometric KD/Bu to generate the catalyst, BH₃, in situ. The nucophile-promoted decomposition of boronic esters has been studied in detail for HBcat⁴⁹ and HBpin⁵⁰ and discussed elsewhere.⁵¹ The hydroboration of alkynes and alkynes with HBpin, catalysed by BH₃, and R₂BH₃ₖ species, was proposed to proceed through B–C/B–H transborylation (Scheme 3b).⁵⁰

Thomas investigated the H–B–9–BBN-catalysed dhydroboration of alkynes with HBpin to give gem-diborylalkanes 5 (Scheme 4a). The proposed catalytic pathway proceeded by hydroboration of the alkyne to give an alkenylborane 2, which underwent B–C(sp³)/B–H transborylation with HBpin to give an alkenyl pinacol boronic ester 1₁ₙₖ (Scheme 4b). A second hydroboration of the alkenyl pinacol boronic ester 1₁ₙₖ with H–B–9–BBN gave the mixed gem-diborylalkane intermediate 6 which underwent B–C(sp³)/B–H transborylation to give the gem-diborylalkane product 5. The mixed gem-diborylalkane intermediate 6 was independently synthesised and successfully used as a pre-catalyst. Isotopic labelling experiments (H²⁻Bpin) and kinetic analysis (ΔG° = 36 e.u.) supported the hypothesis of the second turnover step proceeding through B–C(sp³)/B–H transborylation. The large value of ΔG° (28 kcal mol⁻¹) is consistent with transborylation at a sterically congested centre.⁴⁶, ⁴⁷ and the need for a high reaction temperature (120 °C). Ingleson reported a zinc/boron co-catalytic system for the synthesis of 1,1,1-triborylalkanes from alkynes (Scheme 4c). The borylation of the alkyne and the hydroboration of the resulting alkynyl pinacol boronic ester were proposed to be catalysed by the zinc hydride, whereas the hydroboration of the 1,1-diborylalkene was catalysed by BH₃. High reaction temperatures (110 °C) were also required for B–C(sp³)/B–H transborylation to proceed.

---

**Scheme 3**

**A** Proposed Mechanism of Borane-catalysed Alkene Hydroboration

Thomas used THF-BH₃ or Me₂S·BH₃ as catalysts for the hydroboration of alkynes and alkynes with HBpin (Scheme 3a). Interestingly HBpin could be reacted with substoichiometric KD/Bu to generate the catalyst, BH₃, in situ. The nucophile-promoted decomposition of boronic esters has been studied in detail for HBcat⁴⁹ and HBpin⁵⁰ and discussed elsewhere.⁵¹ The hydroboration of alkynes and alkynes with HBpin, catalysed by BH₃, and R₂BH₃ₖ species, was proposed to proceed through B–C/B–H transborylation (Scheme 3b).⁵⁰

Thomas investigated the H–B–9–BBN-catalysed dhydroboration of alkynes with HBpin to give gem-diborylalkanes 5 (Scheme 4a). The proposed catalytic pathway proceeded by hydroboration of the alkyne to give an alkenylborane 2, which underwent B–C(sp³)/B–H transborylation with HBpin to give an alkenyl pinacol boronic ester 1₁ₙₖ (Scheme 4b). A second hydroboration of the alkenyl pinacol boronic ester 1₁ₙₖ with H–B–9–BBN gave the mixed gem-diborylalkane intermediate 6 which underwent B–C(sp³)/B–H transborylation to give the gem-diborylalkane product 5. The mixed gem-diborylalkane intermediate 6 was independently synthesised and successfully used as a pre-catalyst. Isotopic labelling experiments (H²⁻Bpin) and kinetic analysis (ΔG° = 36 e.u.) supported the hypothesis of the second turnover step proceeding through B–C(sp³)/B–H transborylation. The large value of ΔG° (28 kcal mol⁻¹) is consistent with transborylation at a sterically congested centre.⁴⁶, ⁴⁷ and the need for a high reaction temperature (120 °C). Ingleson reported a zinc/boron co-catalytic system for the synthesis of 1,1,1-triborylalkanes from alkynes (Scheme 4c). The borylation of the alkyne and the hydroboration of the resulting alkynyl pinacol boronic ester were proposed to be catalysed by the zinc hydride, whereas the hydroboration of the 1,1-diborylalkene was catalysed by BH₃. High reaction temperatures (110 °C) were also required for B–C(sp³)/B–H transborylation to proceed.

---

**Scheme 4**

**A** Borane-catalysed double hydroboration of alkynes

---

**Diagram**

---
8 (Scheme 5b). Kinetic isotope effect (KIE) studies suggested that the C−H insertion was the rate-limiting step, and a relatively low barrier was calculated by density functional theory (DFT) analysis for $B^{-}\text{C}(\text{sp}^2)/B^{-}\text{H}$ transborylation ($\Delta G^\ddagger = 14.2$ kcal mol$^{-1}$). Fontaine investigated the effect of steric bulk on catalyst activity through several FLP catalyst analogues by modification of the amine functionality. Catalysts with reduced steric bulk were found to undergo more facile C−H activation at the expense of slower dimer dissociation.56 Bernardeau developed air-stable trifluoroborate salt precatalysts for the same transformation,57 showed that the borylation system was effective on both 2 and 50 g scales (Scheme 5c)58, and developed a heterogeneous polymeric version of this catalytic system.59

Zhang developed the benzoic acid-promoted C-2 borylation of indoles (Scheme 6a), providing orthogonal regioselectivity to the C-3 borylation reported by Fontaine.59 Benzoic acid was proposed to promote the decomposition of H8Bpin to give BH3, which reacted with indole to give an arylborane 10 (Scheme 6b). Subsequent $B^{-}\text{C}(\text{sp}^2)/B^{-}\text{H}$ transborylation gave the C-2 indolyl pinacol boronic ester 11 and regenerated the catalyst, BH3.

Fernández reported an (E)-alkenyl boronic ester exchange with diboron species in methanol (Scheme 7a).60 Whilst previous transborylation-mediated reactions have been proposed to proceed by a concerted, redox neutral exchange of boron groups through a σ-bond metathesis pathway, here, the exchange was proposed to proceed by a coordination-migration pathway (Scheme 7b). Methoxide coordination to the diboron reagent 12 gave the diboron ‘ate’ complex 13, which reacted with the alkenyl boronic ester 14 to give a diboron ‘ate’ complex 15. 1,2-Migration of the diboron ‘ate’ complex 15 exchanged the alkenyl group from boron to boron, and subsequent reaction of the new diboron ‘ate’ complex 16 with the boronate ester 17 gave the alkenyl boronic ester 17 and a mixed diboron ‘ate’ species 18. Liberation of methoxide from the mixed diboron ‘ate’ 18 regenerated the catalyst, methoxide. In this instance, the reaction proceeded through a formal $B^{-}\text{C}(\text{sp}^2)/B^{-}\text{B}$ transborylation where the groups are not exchanged in a concerted σ-bond metathesis pathway but by step-wise nucleophilic transfers. Several alkenyl boronic esters were prepared in good yields and with retention of stereochemistry. The reaction was shown to proceed chemoselectively with mixed diboron species, where the more Lewis acidic boron was exchanged, and to gem-diborylalkenes where the trans-boron was selectively exchanged. This method was subsequently used by Fernández to prepare diastereomerically-enriched gem-diborylalkenes for the palladium-catalysed stereoselective cyclopropanation of gem-diborylalkenes (Scheme 7c).61
3 B–O Transborylation

B–O/B–H transborylation is possible for any species containing a B–O bond, including borinic (R₂BOR), boronic (RB(OR)₂), and boronate (B(OR)₃) esters. Investigations into stoichiometric redistribution involving B–O bonds have explored exchange with B–Cl, B–H, and B–C bonds, most notably by Brown in the preparation of allyl catecholboronic esters from trialkylboranes and Bcat (Scheme 8). The redistribution was catalysed by the addition of THF·BH₃ and, whilst a mechanism was not proposed, it may proceed through B–O/B–H and B–C/B–H transborylation steps.

Thomas used B–O/B–H transborylation to transform the stoichiometric Midland reduction into a catalytic reaction using HBpin as the turnover reagent to regenerate H-B-9-BBN through B–O/B–H transborylation, concurrently forming the product as a boronate ester (Scheme 9a). Myrtanyl-9-BBN Regenerated the catalyst, myrtanyl-9-BBN 22 (derived from β-pinene) was used in place of Alpine-Borane, aiding catalyst regeneration and suppressing direct ketone hydroboration. The reaction was proposed to proceed by two interlinked catalytic cycles with B–O/B–H transborylation-enabled catalyst regeneration. This was supported by single-turnover experiments with H²⁶Bpin and Eyring analysis (ΔS° = −21.5 e.u.). Hydroboration of a ketone by myrtanyl-9-BBN 22 gave a borinic ester 23 and liberated β-pinene 24 (Scheme 9b). B–O/B–H transborylation of the borinic ester 23 with HBpin gave the boronate ester product 25 and generated H-B-9-BBN.
Fontaine used B–O/B–H transborylation for the boron-catalysed reduction of esters, lactones, and carbonates to alcohols (Scheme 11a).66 B–O/B–H transborylation between HBpin and B(OH)₃ generated the catalyst, BH₃ (Scheme 11b). The reaction was proposed to proceed through hydroboration of the ester by BH₃, giving a boronic ester, and B–O/B–H transborylation of the boronic ester with HBpin formed a borinic ester and the boronate pinacol ester product. B–O/B–H transborylation between two borinic ester molecules regenerated the catalyst (Scheme 11c). The transition state energies were calculated for each B–O/B–H transborylation with the reaction of the boronic ester with HBpin calculated to have a barrier of ΔG° = 24.5 kcal mol⁻¹. B–O/B–H transborylation between two borinic ester molecules to give BH₃ was calculated to be ΔG° = 14.8 kcal mol⁻¹. The first B–O/B–H transborylation was shown to be the rate-limiting step, possibly due to the decreased Lewis acidity of the boron centre with increasing alkoxide substitution.

\[
\text{[H-9-BBN]_2} + \text{B(OH)₃} \rightarrow \text{BH₃} + \text{pinB} \\
\text{15 examples} \quad \text{Up to 96% yield}
\]

\[
\begin{align*}
\text{B(OH)₃} + \text{H–Bpin} & \rightarrow \text{Bpin} + \text{pinB} \\
\text{15 examples} \quad \text{Up to 96% yield}
\end{align*}
\]

Willcox and Thomas used B–O/B–H transborylation in a boron-catalysed C–F esterification (Scheme 13a).69 Dehydrocoupling of a carboxylic acid with H–B-9-BBN gave the acylob-9-BBN which underwent B–O/B–H transborylation with HBpin to regenerate the catalyst and form the acyloxoboronic ester (Scheme 13b). This reacted with an alkyl fluoride to give the ester 37, and FBpin as a by-product. The reaction was proposed to proceed through B–O/B–H transborylation. The reversibility of B–O/B–H transborylation was shown by the stoichiometric reactions of the acyloxob-9-BBN with HBpin and the acyloxoboronic ester with H–B-9-BBN. The reaction was applied to a broad substrate scope, showing extensive functional group tolerance, and used to generate ester derivatives of numerous biologically-active carboxylic acids.
Nicholson and Thomas demonstrated that H-B-9-BBN catalysed the diastereoselective allylation of ketones with allenes and HBpin (Scheme 14a).70 By using (S)-B-methoxy-phenyl-9-borabicyclo[3.3.2]decane [(S)-Ph-BBD-OMe]71 in place of H-B-9-BBN, an enantioselective variant of this transformation was also developed (Scheme 14b). Single turnover and isotopic-labelling experiments were used to postulate a mechanism (Scheme 14c). HBpin reacted with the pre-catalyst (S)-Ph-BBD-OMe through B-O/B-H transborylation to form the active catalyst, (S)-H-B-phenyl-9-borabicyclo[3.3.2]decane 38. The allene underwent hydroboration by (S)-H-B-phenyl-9-borabicyclo[3.3.2]decane 38 to give the (Z)-allylic borane 39. This underwent a series of 1,3-boratropic shifts, resulting in isomerisation to the (E)-allylic borane 40. The ketone underwent allylation by the (E)-allylic borane 40 to give the anti-homoallylic borinic ester 41. B-O/B-H transborylation between HBpin and anti-homoallylic borinic ester 41 generated the boronate pinacol ester product 42 with concomitant re-formation of the catalyst, (S)-H-B-phenyl-9-borabicyclo[3.3.2]decane 38.

4 B–N Transborylation

Unlike with B–O and B–C bonds, stoichiometric redistribution reactions of B–N containing species have not been widely explored.3 However, numerous stoichiometric reactions of organoboranes result in the formation of a B–N bond, including the reduction of nitriles, amides,12 imines,72 and indoles,73 and the reductive cyanation of enones.74 Therefore, the development of catalytic methods using B–N/B–H transborylation is of synthetic interest.

The first notable example of B–N/B–H transborylation was reported by Chang as a means of catalytic turnover for the 1,4-reduction of pyridines (Scheme 15a).75 Chang proposed that the nucophile-promoted decomposition of HBpin by KOBu gave borohydride species 43 and BH3 in solution (Scheme 15b). N-coordination by BH3 activated the pyridine to 1,4-reduction by the borohydride species 43 to give a dihydropyridyl borohydride 44, identified as the resting-state by 11B NMR spectroscopy and mass spectrometry. Hydride transfer from the dihydropyridyl borohydride 44 to HBpin regenerated further borohydride species 43 and gave the 1,4-dipyrindylborane 45. B-N/B-H transborylation with HBpin gave the product, N-Bpin-1,4-dihydropyridine 46, and regenerated BH3. This catalytic reduction protocol was also applied to other N-heterocycles including quinolines, isoquinolines, pyrazines, quinoxalines, and imidazoles.

Scheme 13 a) Borane-catalysed C–F esterification b) Proposed catalytic cycle

Scheme 14 a) Borane-catalysed diastereoselective allylation of ketones with allenes b) Asymmetric borane-catalysed allylation of ketones c) Proposed mechanism
Nicholson and Thomas used B-N/B-H transborylation for the borane-catalysed reductive cyanation of enones (Scheme 17a).\textsuperscript{76} Catalysis was proposed to proceed by 1,4-hydroboration of the enone to give the O-B-9-BBN-enolate 26, which reacted with the electrophilic cyanide source, N-cyano-N-phenyl p-toluene sulfonamide 50, to give the amino-9-BBN 51 and form the α-cyano ketone product 52 (Scheme 17b). B-N/B-H transborylation between the amino-9-BBN 51 and HBpin regenerated the catalyst, H-B-9-BBN. The reversibility of the B-N/B-H transborylation was observed by $^1$H NMR spectroscopy. The amino-9-BBN 51 was independently prepared and successfully used as a pre-catalyst, supporting the proposal that this was an on-cycle species.
Me$_2$S-BH$_3$ was used by Thomas to catalyse the hydroboration of nitriles with HBpin (Scheme 18a). A mechanism was proposed based on DFT analysis whereby nitrile hydroboration by Me$_2$S-BH$_3$ gave the N-boryl amine 53. This underwent a second hydroboration to form the $N,N$-bis-boryl amine 54, followed by two sequential $B$-$N$/B-$H$ transborylation reactions to give the $N,N$-bis-Bpin amine 55, and re-form the borane catalyst (Scheme 18b). Alternatively, the $N$-boryl amine 53 underwent $B$-$N$/B-$H$ transborylation to form the $N$-Bpin imine 56, followed by a second hydroboration and $B$-$N$/B-$H$ transborylation to form the $N,N$-bis-Bpin amine 55. DFT analysis suggested that both mechanisms were likely operating.

![Scheme 18](image1)

### 5 B-$F$ Transborylation

The stoichiometric redistribution of boron-halogen bonds received much attention in the 1950s and 1960s, due to the facile access to useful monohalo- and dihaloboranes (Scheme 19a).1,2,4 McCusker proposed that this redistribution proceeded by a $\sigma$-bond metathesis-type pathway.2 These reactions have found limited application beyond stoichiometric redistribution.

![Scheme 19](image2)

The first, and so far only, example of B-halogen transborylation in catalysis was the use of $B$-$F$/B-$H$ transborylation by Willox and Thomas in the borane-catalysed arylation of C-$F$ bonds (Scheme 19b).69 $B$-$F$/B-$H$ transborylation with HBpin converted the stoichiometric C-$F$ arylation reported by Stephan79 into a borane-catalysed process. The reaction was proposed to proceed by a $H$-$B$-$9$-BBN-mediated $S$Ar of the benzylic fluoride with an arene. $B$-$F$/B-$H$ transborylation of the resulting $F$-$B$-$9$-BBN with HBpin regenerated the catalyst (Scheme 19c). The proposed $\sigma$-bond metathesis type pathway for $B$-$F$/B-$H$ transborylation was examined through DFT analysis and the activation barrier was calculated to be 25.8 kcal mol$^{-1}$.

### 6 B-$S$ Transborylation

Pasto reported the stoichiometric redistribution of BH$_3$ with phenyl mercaptoborane to give borinic and boronic thiosteer products.4 In catalysis, transborylation at $B$-$S$ bonds has been used by Fontaine for the dehydrocoupling of thiols (Scheme 20a).80 This protocol provided an advantage over stoichiometric dehydrocoupling which required high reaction temperatures and extended reaction times.81 A mechanism was proposed based on DFT analysis (Scheme 20b) in which the catalyst 57 underwent dehydrocoupling with the thiol to give an allylthiaborane 58 which reacted with HBpin by $B$-$S$/B-$H$ transborylation to regenerate the catalyst 57 and form the thioborinate 59. Alternatively, the allylthiaborane intermediate 58 underwent a further dehydrocoupling with another equivalent of thiol to give an alkylboronic ester 60, which then underwent $B$-$S$/B-$H$ transborylation with HBpin to give the thioborinate 59 and regenerate the allylthiaborane intermediate 58. $B$-$S$/B-$H$ transborylation was found to be rate determining with a fairly large thermodynamic barrier ($\Delta G^\ddagger$: EtSH = 30.5 kcal mol$^{-1}$, BuSH = 25.9 kcal mol$^{-1}$). This catalytic protocol could be further applied to the dehydrocoupling of selenols with HBpin and is currently the only example of $B$-$Se$/B-$H$ transborylation.
7 Conclusion

This review outlines the developments in the application of transborylation as a turnover strategy for main-group catalysis. Transborylation has emerged as a powerful strategy for developing new boron catalysis by using this redox neutral catalytic turnover process, avoiding the traditional turnover pathways of oxidative addition and reductive elimination, which remain largely inaccessible to boron. Several reactions, which were previously limited to stoichiometric reactivity, are accessible to boron catalysts due to the development of transborylation. More significantly, new reactivity has been developed and enabled by transborylation. This turnover pathway has provided an efficient platform for catalysis across a diverse range of transformations including hydroboration, borylation, asymmetric reduction, and C–C bond forming reactions (Scheme 21). The highly generalisable nature of this catalytic turnover pathway allows it to be applied to turnover at many centres including carbon, oxygen, nitrogen, fluorine, sulfur, and selenium and to terminal reductants including HBpin and HBcat. The use of transborylation in catalysis has provided a highly versatile and simple method of catalysis across a diverse range of transformations including hydroboration, borylation, asymmetric reduction, and C–C bond forming reactions (Scheme 21).

Funding Information

S.P.T. thanks the Royal Society for a University Research Fellowship (URF/R/191015). S.P.T., A.D.B., and K.N. thank AstraZeneca and the EPSRC for PhD studentships.

Conflict of Interest

The authors declare no conflict of interest.

References

60. Dominguez-Molano, P.; Bru, G.; Salvado, O.; Maza, R. J.; Carbó, J. J.; Fernández, E. Chemical Communications 2021.


Biosketches

Stephen Thomas was born in Canada and moved to Somerset (UK) as a teenager. After obtaining his MChem from Cardiff University, working with Prof. Nick Tomkinson, he studied for his PhD at the University of Cambridge with Dr Stuart Warren. Postdoctoral work with Prof. Dr Andreas Pfaltz (University of Basel) was followed by a move to the University of Bristol as Research Officer in the group of Prof. Varinder Aggarwal FRS. Stephen began his independent research career at the University of Edinburgh in 2012 as a Chancellor’s Research Fellow. He was awarded a Royal Society University Research Fellowship in 2014, promoted to Reader in 2016, and to a personal Chair in 2022. The Thomas group is interested in the development and understanding of sustainable catalysis with a focus on Earth-abundant element-based catalysts for organic transformations.