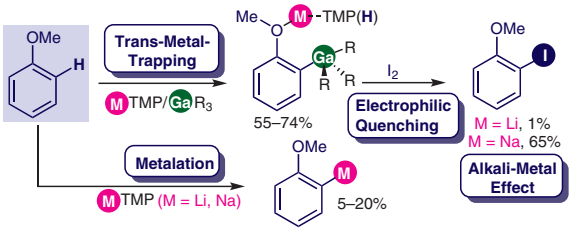
Synthesis R. McLellan et al. THIEME OPEN ACCESS Feature

Alkali Metal Effects in Trans-Metal-Trapping (TMT): Comparing LiTMP with NaTMP in Cooperative MTMP/Ga(CH_2SiMe_3)$_3$ Metalation Reactions

Ross McLellan
Marina Uzelac
Leonie J. Bole
Jose María Gil-Negrete
David R. Armstrong
Alan R. Kennedy
Robert E. Mulvey*
Eva Hevia*

WestCHEM, Department of Pure and Applied Chemistry, University of Strathclyde, Glasgow G1 1XL, UK
r.e.mulvey@strath.ac.uk
eva.hevia@strath.ac.uk

Published as part of the *50 Years SYNTHESIS – Golden Anniversary Issue*



Received: 30.11.2018
Accepted: 05.12.2018
Published online: 15.01.2019
DOI: 10.1055/s-0037-1611646; Art ID: ss-2018-z0802-fa

License terms:

Abstract Stepwise metalation and trapping, so called trans-metal-trapping (TMT), of anisole is studied using LiTMP as base and Ga(CH_2SiMe_3)$_3$ as trap. The isolated 'trapped' intermediate is also assessed in C–C bond forming reactions, highlighting the inherent advantages and remaining challenges of this system. The same base trap mixture is found to metallate N–Me bonds of the diamines TMEDA and PMDETA. Comparative studies replacing LiTMP by NaTMP have found significant alkali metal effects on the extent of both base-trap cocomplexation and onward reactivities of TMT products.

Key words metalation, gallium trans-metal-trapping, carbanions, cooperative effects, lithium, sodium

Deprotonative metalation (C–H to C–M exchange) of aryl and heteroaryl substrates is a widely successful tool, utilised in the construction of important organic molecules, usually producing organometallic intermediates primed for onward reactivity. Longstanding reagents of choice in this context are alkyllithiums and lithium amides.[1] Synthetic drawbacks to these metalation transformations are commonly, poor functional group tolerance (at convenient temperatures) and selectivity, necessitating cryogenic reaction conditions to prevent unwanted side reactions or decomposition of the lithiated species. One solution to these limitations is to employ metal salts such as $MgCl_2$ or $ZnCl_2$·2LiCl as in situ trapping agents during LiTMP metalations of arenes and N-heterocycles in THF, in reactions that have been performed under continuous flow conditions (TMP = 2,2,6,6,-tetramethylpiperidide).[2] A second approach is to use bimetallic systems containing two metals of different polarity within the same molecule. These systems can be shown to behave in concert, resulting in higher selectivity and in many cases using ambient reaction conditions during metalation. Important examples of bimetallic formulations used in deprotonation reactions are the classic Lochmann–Schlosser superbases,[3] Knochel's turbo Hauser reagents,[4] and Uchiyama and Mongin's TMP zincates.[5] This bimetallic approach, combining an alkali metal with a less electropositive metal (e.g., Mg or Zn) into an 'ate' complex has been termed alkali-metal-mediated metalation and, a series of reactivity and structural studies have demonstrated that the high reactivity of the alkali metal can be harnessed by the less polar metal, while retaining the advantages of selectivity that the non-alkali metal provides, thus representing a 'best of both worlds' scenario.[6] Recently we have shown in our Strathclyde research groups that such prodigious metal···metal cooperative effects can, in certain cases work in sequence in a process that has been coined trans-metal-trapping (TMT).[7] A general depiction of TMT is given in Scheme 1, and describes a process reliant upon the stepwise reactivity of the two metal organic reagents with the aromatic substrate. Deprotonation of the substrate with a lithium amide base exists in a pK_a dependent equilibrium that typically lies towards the lithium amide and unreacted aromatic substrate, meaning that when used in isolation, a stoichiometric amount of lithium amide only delivers ca. <10% of product, when intercepted with an electrophile such as iodine.

However, in the presence of the Lewis acidic carbophilic trap, the lithiated intermediate can be readily intercepted, resulting in a so called crossover bimetallic complex that stops short of full transmetalation, where separated lithium

Biographical Sketches

Ross McLellan received his M.Chem. degree in chemistry from Heriot-Watt University in 2007. He obtained his Ph.D. degree from the same institution in 2011 under the supervision of Professor Alan Welch. His first postdoctoral position with Dr Scott Dalgarno focussed on the controlled formation and magnetism of 3d/4f polynuclear metal clusters in collaboration with Professor Euan Brechin. He is currently a postdoctoral research fellow at the University of Strathclyde, where he is interested in developing main group systems and investigating their use in catalysis.

Marina Uzelac obtained her B.Sc. and M.Sci. in chemistry from the University of Zagreb, Croatia. She then moved to the UK, to carry out her Ph.D. studies at the University of Strathclyde under the supervision of Professor Eva Hevia developing new gallium-mediated transformations for C–H functionalisation and small molecule activation processes. She graduated in 2016 and then took up a postdoctoral position working in a collaborative project with Professors Robert Mulvey and Eva Hevia exploiting multicomponent s-block metal reagents in deprotonative metalation and C–C bond forming processes. In 2018 Marina joined the group of Professor Michael J. Ingleson working on the development of new organozinc catalysts with application in bond forming processes.

Leonie J. Bole obtained her undergraduate degree in 2016 from the University of Strathclyde completing her M.Sc. on inverse crown chemistry under the supervision of Dr Charles T. O'Hara. She is currently working towards her Ph.D. in main group organometallic chemistry with Prof. Eva Hevia and Dr Charles T. O'Hara at the University of Strathclyde.

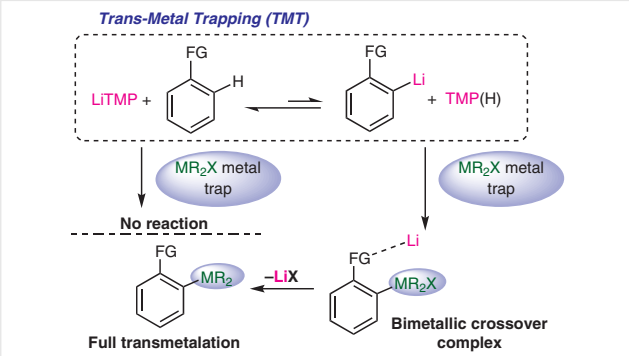
Jose María Gil-Negrete obtained both his B.Sc. and M.Sc. from the University of A Coruña, Spain. Since 2014 he is pursuing a Ph.D. under the direction of Professors Luis Sarandeses and Jose Pérez Sestelo, also at the University of A Coruña. His research is focussed on the development of new applications for indium organometallics in organic synthesis. During the summer of 2017, Jose Maria was a visiting researcher in the University of Strathclyde, Glasgow, within the group of Professor Eva Hevia.

David Armstrong was born in the North-East of England in County Durham and educated at Newcastle University for both his B.Sc. and Ph.D. degrees. The latter was carried out under the supervision of Peter Perkins and was a theoretical investigation of Group III compounds. Appointed at the University of Strathclyde in 1970 as a lecturer and subsequently promoted to a senior lectureship, he currently holds an emeritus position. David has been performing theoretical calculations for about 50 years, publishing over two hundred research papers with his most recent work focussing on different aspects of polar organometallic chemistry.

Alan Kennedy was awarded both B.Sc. and Ph.D. (K. Muir and R. Cross) degrees in chemistry by the University of Glasgow (1986–1993). He has worked at the University of Strathclyde since 1994 and is a crystallographer specialising in structure-property relationships in small molecules, notably pharmaceuticals, colourants, and metal complexes. He has published over 550 career papers.

Robert Mulvey was born in Glasgow (Scotland) in 1959 and did his B.Sc. and Ph.D. (R. Snaith) at the University of Strathclyde (1977–1984). Following two years postdoctoral research at the University of Durham (K. Wade), he returned to Strathclyde in 1986 as a Royal Society Research Fellow, and was promoted to Professor in 1995. His research has mainly focused on alkali, alkali-earth, and early p-block metals with emphasis on synergistic effects in bimetallic systems. Prof. Mulvey has received many distinguished prizes including the RSC Meldola Medal, RSC Main Group Element Award, Royal Society Wolfson Research Merit Award, Royal Society Leverhulme Trust Senior Research Fellowship, GDCh Arfvedson Schlenk Prize, and a Humboldt Research Award. A Fellow of both the Royal Society of Edinburgh and Royal Society of Chemistry, he has published approaching 300 papers.

Eva Hevia received her M.Sci. degree in chemistry from the Universidad de Oviedo (Spain) in 1998. She obtained her Ph.D. degree from the same institution in 2002 under the supervision of Professor Victor Riera and Dr Julio Perez. Next she was awarded a Marie Curie Fellowship held at the University of Strathclyde under the direction of Prof. Robert Mulvey. In 2006 she took up a Royal Society University Research Fellowship at the University of Strathclyde where she is currently a Professor of Inorganic Chemistry. Her research interests include s-block metal-mediated transformations with a particular emphasis on green chemistry and catalysis. She has published over 120 peer-reviewed journal articles and her research has been recognised with several awards including the Royal Society of Chemistry (RSC) Harrison-Meldola Prize (2009), SRUK Emerging Investigator Awards (2016), and, most recently, the RSC Corday-Morgan Prize (2017). In 2018 Eva was elected as Fellow of the Royal Society of Edinburgh.



Scheme 1 Description of trans-metal-trapping using LiTMP as base, and comparison with conventional transmetalation

and non-lithium metal products would form. A key aspect of this chemistry proven with lithium is that the base and the trap do not combine to form a bimetallic complex that would be inert towards the substrate. Functioning only on emergence of the deprotonated substrate (carbanion), the trap inserts into the Li–C bond and drives the equilibrium towards the desired metallated substrate.

In this article we present a deeper understanding of key mechanistic insights of trans-metal-trapping (TMT), by combining structural, reactivity, and theoretical studies, using anisole, a classical substrate in directed *ortho*-metalation, as a case study. A key feature of our exploratory studies of TMT is the stepwise reactivity exhibited by the two organometallic constituents. In this respect the bulky tris(trimethylsilylmethyl)gallium has been demonstrated as an excellent trap for diazine and fluoroaromatic anions, that when metallated by conventional bases are prone to rapid decomposition.[8] Therefore this study aims to highlight the benefits of LiTMP/$Ga(CH_2SiMe_3)_3$ in metalation. From a synthetic perspective, liquid $Ga(CH_2SiMe_3)_3$ (hereafter GaR_3) possesses good hydrocarbon solubility (similar to iBu_2AlTMP another successful trapping agent)[7] giving it a decided advantage over salt traps (e.g., $MgCl_2$, $ZnCl_2$),[9] which generally need the use of ethereal solvents (usually THF) and often require low temperatures to avoid competing salt metathesis reactions. More importantly, gallium is characterised by strong carbophilicity and is therefore well equipped to sedate ultra-sensitive anions post metalation with LiTMP. This fact is well illustrated in our comparative studies into the metalation of fluoroarenes, where it was shown that the resultant gallium TMT product had far superior stability against decomposition (via benzyne formation) than the aluminium counterpart.[8b] The poor stability may also be attributed to the fluorophilicity of aluminium meaning that aluminium traps may in general be incompatible with fluorinated substrates. Apart from these intrinsic properties of GaR_3, a key specification of the trapping reagent, as demonstrated with iBu_2AlTMP previously,[7] is its inertness towards co-complexation with LiTMP, and therefore our first step was to establish whether GaR_3 is bulky enough to compromise its ability to form a weakly basic, coordinatively saturated ate complex with LiTMP. Such separation of the organometallic reagents appears a prerequisite for an effective TMT process, and this is underlined by the fact that LiTMP/iBu_2AlTMP mixtures are better TMT agents than LiTMP/iBu_3Al mixtures, which form the aluminate LiAl(TMP)(iBu)$_3$ in a complicated equilibrium mixture of five compounds.[7a] Thus a comparison of the ^{1}H NMR spectra (Figure 1) of an equimolar mixture of LiTMP and GaR_3 and those of the individual components reveals that the two TMT reagents remain separate in benzene-d_6 solution. The lack of co-complexation is best deduced by the informative singlet at δ = 0.13 which corresponds to coincidentally overlapping CH_2 and CH_3 resonances of the CH_2-$SiMe_3$ group on gallium.[10] Furthermore, resonances for both tetrameric and trimeric forms of LiTMP are present and identical to those previously reported.[11]

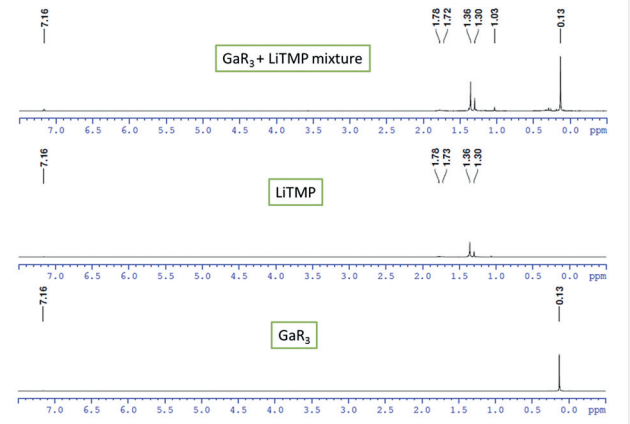
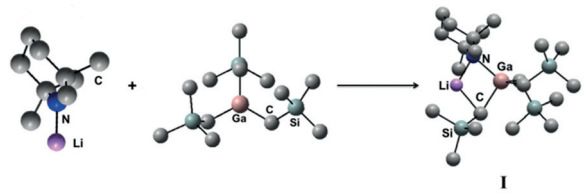


Figure 1 Comparative ^{1}H NMR spectra of free GaR_3 (bottom), free LiTMP (middle), and a mixture of GaR_3 and LiTMP (top) in C_6D_6

To further understand the ability (or lack thereof) to co-complexation we elected to perform some DFT studies, in order to determine energetics of such a process, forming a hypothetical lithium gallate **I**. In the optimised geometry of **I** the metals are connected by a TMP bridge and an alkyl bridge with another two monosilyl groups terminally bonded to the gallium atom. GaR_3 was modelled as a monomer according to its known structure in the solid state,[12] while LiTMP was modelled as a monomer, and a trimer and tetramer which are the two known aggregates of this compound in non-polar solvents.[11] Co-complexation between monomeric LiTMP is energetically favoured (–17.1 kcal mol^{-1}), which is unsurprising given the high energy of monomeric LiTMP (Table 1). Crucially, co-complexation of both trimeric and tetrameric LiTMP with GaR_3 are energetically disfavoured (+9.0 kcal mol^{-1}), and in line with the finding from the solution studies.

Table 1 Comparison of DFT-Computed Relative Energies of Co-complexation of LiTMP and GaR_3



$\frac{1}{n}$ $(LiTMP)_n + GaR_3 \rightarrow LiGa(TMP)R_3$

n	ΔE Co-complexation (kcal mol^{-1})
1	−17.1
3	+9.0
4	+9.0

Next we determined to ascertain the effect of Lewis donor ligands on the TMT process. In particular PMDETA (*N*,*N*,*N′*,*N″N″*-pentamethyldiethylenetriamine) has been crucial in facilitating the crystallisation of TMT products,[8] which is important since structural data of these complexes provide valuable information on the *modus operandi* of metalation. Reaction between PMDETA, LiTMP, and GaR_3 at room temperature in hexane for one hour lead to the isolation and structural characterization of $[Li\{Me_2NCH_2CH_2N(Me)CH_2CH_2N(Me)CH_2\}(TMP)GaR_2]$ (**1**). The molecular structure of **1** (Figure 2, top) reveals that PMDETA has been metallated at a terminal NCH_3 group. The lithium atom reveals a contacted ion pair arrangement where the two metal centres connect through two anions, namely a TMP bridge and an ambidentate NCH_2 fragment of the metallated PMDETA.

Interestingly, that a TMP anion is retained in the structure might suggest that it is GaR_3 that deprotonated the substrate as the structure incorporates a TMP anion and only two monosilyl groups on gallium. However GaR_3 on its own is not a sufficiently strong base to metallate PMDETA, therefore the α-deprotonation is based on the stepwise cooperation between LiTMP and GaR_3. LiTMP deprotonates the triamine followed by the fast trans-metal-trapping process with GaR_3 yielding a proposed intermediate **A** (Scheme 2) where concomitantly produced TMPH helps to fill the coordination sphere of lithium and is thus in close proximity to GaR_3. The sterically encumbered intermediate and enhanced acidity of coordinated TMPH makes it possible for the otherwise inert gallium alkyl to react affording **1** and Me_4Si.

Although we have no direct evidence for the proposed mechanism, it is supported indirectly by the notion that triorganogallium reagents cannot deprotonate coordinating additives such as PMDETA or TMEDA as C–H bonds adjacent to N centres in tertiary amines are only weakly acidic. In

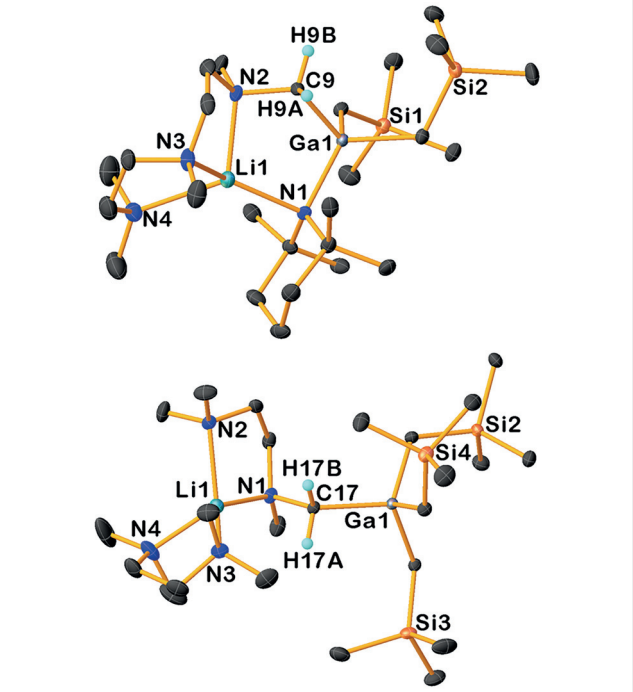
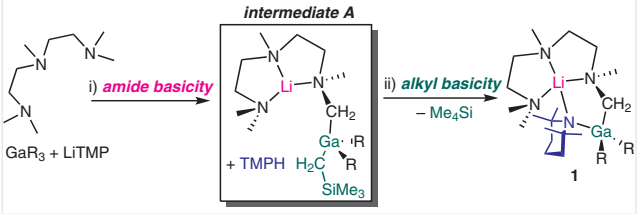


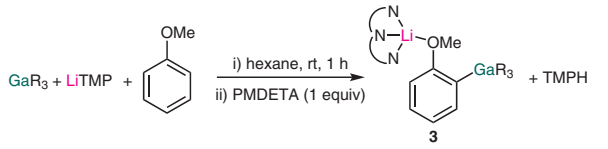
Figure 2 Molecular structure of **1** with 30% probability displacement ellipsoids (top); all hydrogen atoms except those on metallated CH_2 group of PMDETA have been omitted for clarity. Molecular structure of **2** with 30% probability displacement ellipsoids (bottom); all hydrogen atoms except those on metallated CH_2 group of TMEDA have been omitted for clarity.



Scheme 2 Proposed reaction sequence for the surprising formation of **1**

addition, it was found that the bulkiness of a reagent such as GaR_3 precludes chelation and instead, it acts as a bridging ligand as observed in the crystal structure of R_3Ga–TMEDA–GaR_3,[13] Further, to an extent, experimental support for the proposed pathway came from the addition of a similar, but smaller Lewis donor TMEDA to the mixture of LiTMP and GaR_3 from which we were able to isolate crystals of $[(TMEDA)Li\{Me_2NCH_2CH_2N(Me)CH_2\}GaR_3]$ (**2**) (Figure 2, bottom). The molecular structure of **2** has a contacted ion pair structure with three alkyl groups on gallium and no TMP anion incorporation, reminiscent of the proposed intermediate **A**. Here, due to the smaller size of the diamine, N_4-tetracoordinated lithium is capped with two molecules of TMEDA one of which is metallated and the other one is neutral, completing the coordination sphere and avoiding the close

proximity of TMPH and GaR_3, which would induce alkyl basicity. Confident that LiTMP and GaR_3 indeed remain separate in non-coordinating solvent, yet cooperate in metalation reactions we next tested this mixture as a TMT reagent using anisole as a benchmark molecule in directed *ortho*-metalation. Thus, to a hexane suspension of equimolar amounts of GaR_3 and LiTMP at room temperature, a molar equivalent of anisole was added to give a light yellow suspension. After stirring the mixture for one hour, an equivalent of PMDETA was added and the solution placed at –33 °C affording a crop of colourless crystals of [(PMDETA)Li(*o*-C_6H_4OMe)GaR_3] (**3**) in 55% isolated yield (Scheme 3).



Scheme 3 Synthesis of [(PMDETA)Li(*o*-C_6H_4OMe)Ga(CH_2SiMe_3)$_3$] (**3**)

The structure of **3** (Figure 3) revealed the formation of a mixed-metal lithium gallate with the metal centres connected by an ambidentate *ortho*-metallated anisole fragment giving rise to a contacted ion-pair structure. The *ortho* carbon of the metallated anisole fragment bonds to gallium forming a new Ga–C bond (Ga–C13 2.0501(15) Å). The distorted tetrahedral lithium is fully solvated by the tridentate PMDETA as well as from the oxygen atom of anisole. In these studies we have demonstrated that LiTMP and GaR_3 are a highly efficient combination of base and trap, to selectively metallate useful aromatic molecules, illustrated by the potency of LiTMP as a base and of GaR_3 in being able to stabilise the newly formed organic carbanions. Probing the synthetic utility of **3**, I_2 was added as an electrophilic source in an effort to prepare 2-iodoanisole. Interestingly, only a trace amount of ca. 1% of the quenched product was obtained, presumably reflecting the high stability of the metallated C–Ga bond. Thus, this TMT system is excellent in the stabilisation of incipient carbanions albeit the stability likely inhibits the downstream utility in simple electrophilic quenching studies.

Underscoring the utility of this metal pairing, we next investigated an analogous system using NaTMP in place of LiTMP, rationalising that the larger alkali metal may be better equipped to form a complex with GaR_3, hence limiting the ability of the system to promote TMT. Firstly a control reaction between NaTMP and anisole in hexane at room temperature, followed by a standard iodine quench in THF afforded only ca. 20% of 2-iodoanisole. A second control reaction of the in situ GaR_3/NaTMP mixture with PMDETA reveals metalation of a methyl group of the Lewis donor after structural characterisation. The structure of this product

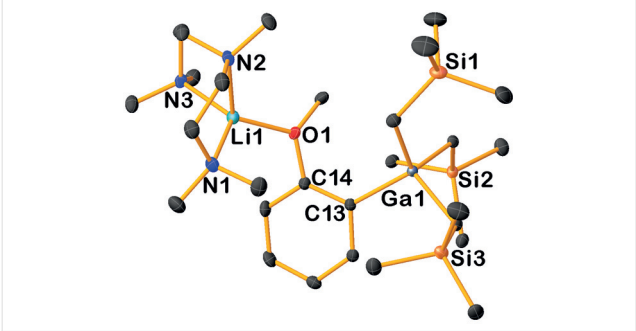


Figure 3 Molecular structure of **3** with 30% probability displacement ellipsoids; all hydrogen atoms have been omitted for clarity

[Na{$Me_2NCH_2CH_2N(Me)CH_2CH_2N(Me)CH_2$}(TMP)$GaR_2$] (**4**) (Figure 4, top) is directly analogous to that of the lithium gallate **1**. Anticipating that since metalation occurs in this instance, then GaR_3 and NaTMP remain as separate entities in solution, GaR_3 was added to NaTMP in a J. Young's NMR tube in C_6D_6, causing dissolution of the normally insoluble NaTMP. The ^1H NMR spectrum after 15 minutes revealed, in contrast to the case with LiTMP, that the characteristic resonance of GaR_3 was absent, indicating the surprising formation of a co-complex, albeit the resonances are broad and indicative of either a mixture of compounds or a system undergoing a degree of exchange. This reaction mixture was probed further by adding anisole directly and reaction monitoring revealed a small amount of metalation alongside the signals of coordinated anisole (Figure 5). Further monitoring by ^1H NMR details that additional metalation does not occur over an 18 hour window at room temperature. Repeating the reaction in a Schlenk flask at room temperature in hexane followed by addition of TMEDA after two hours stirring, and placing at 4 °C, resulted in a crop of crystals that were characterised X-ray diffraction as [(TMEDA)Na(*o*-C_6H_4OMe)GaR_3] (**5**, 17%) (Figure 4, bottom), a sodium analogue of **3**. This result is surprising since reaction of the suggested sodium gallate with anisole would likely possess insufficient basicity to promote metalation, comparable with the LiTMP/*i*$BuAl_3$ mixture that forms a lithium aluminate that lacks the intrinsic basicity to promote C–H bond cleavage.[7a] Thus we attribute the reactivity as the result of unrestricted NaTMP that had not yet formed a complex with GaR_3, in accordance with the busier ^1H NMR spectrum recorded after 15 minutes. Probing the co-complex formation further, an equimolar mixture of NaTMP and GaR_3 in C_6D_6 was monitored by ^1H NMR until the spectra ceased evolving. At this point (3 days) anisole was added and the resulting spectrum detailed that metalation does not occur, giving further evidence to our original hypothesis and emphasizing the importance of the lithium reagent in preventing co-complexation and therefore subdued reactivity (Figure 5).

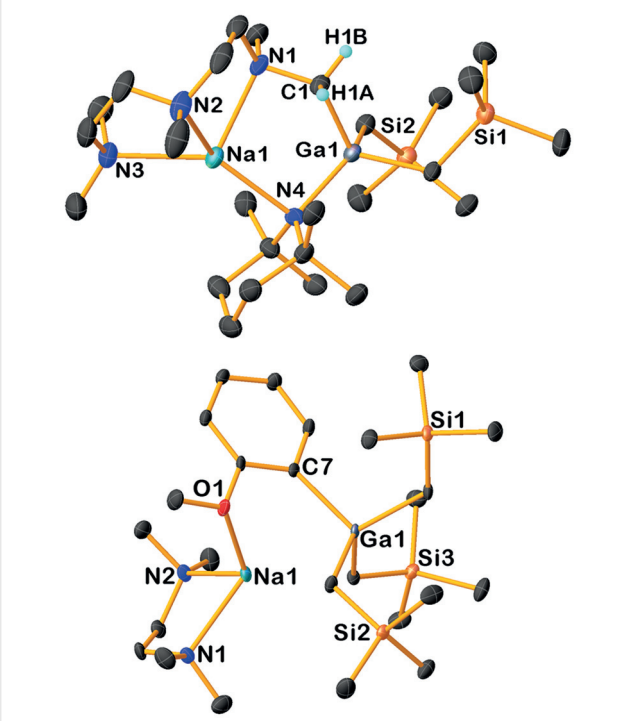


Figure 4 Molecular structure of **4** with 30% probability displacement ellipsoids (top); all hydrogen atoms have been omitted for clarity except for those on the metallated CH_2 group of PMDETA. Molecular structure of **5** with 30% probability displacement ellipsoids (bottom); all hydrogen atoms have been omitted for clarity.

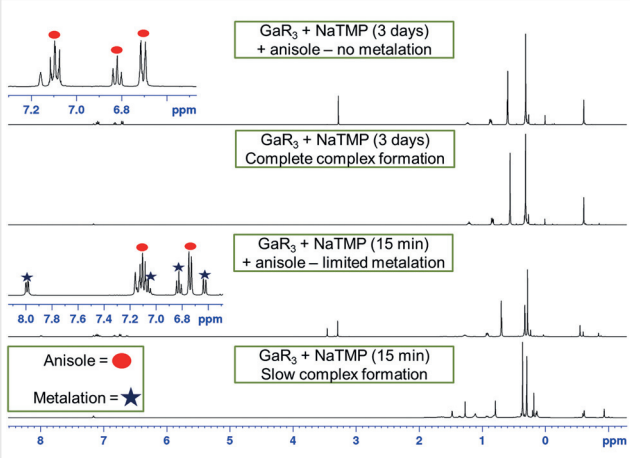
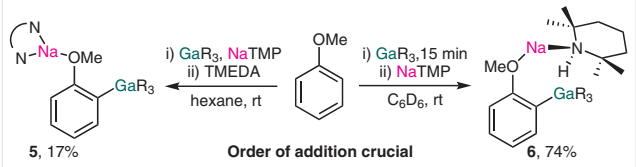


Figure 5 Comparative NMR spectra illustrating that as co-complex formation progresses in time the extent of metalation decreases

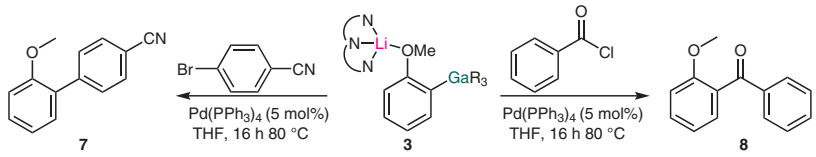
Lastly we sought to investigate whether the order of addition would prejudice the reaction in favour of the metallated (trapped) product, rationalising that pre-complexation of anisole with Lewis acidic GaR_3 would compromise the moderately slow complexation of GaR_3 with NaTMP and hence result in enhanced yields of metallated products. In this case reaction between GaR_3 and anisole in a J. Young's NMR tube in C_6D_6 for 15 minutes was followed by addition of NaTMP. At this point trans-metal-trapped anisole [(TMP(H)Na(*o*-C_6H_4OMe)GaR_3] (**6**) was observed in the ^{1}H NMR spectrum in 74% yield against hexamethylbenzene (C_6Me_6) as internal standard (Scheme 4). Addition of TMEDA to this mixture affords a spectrum reminiscent of **5**.



Scheme 4 The effect of addition order in TMT using GaR_3/NaTMP system. GaR_3 and NaTMP form complex limiting TMT to give **5** (left). Pre-reaction of GaR_3 with anisole enhances yield of **6** (right).

Repeating this reaction in a Schlenk flask and conducting an electrophilic quench with iodine resulted in formation of 2-iodoanisole in 65% yield. That sodium gallate **5** affords 2-iodoanisole in reasonable yields after an electrophilic quench is itself surprising since the analogous reaction with **3** only affords trace amounts of products. This clear alkali metal effect, with the sodium gallate exhibiting far superior onward reactivity than the lithium counterpart suggests that when paired with the appropriate secondary metal, gallium–carbon bond functionalisation can be facile.

Finally, while we have demonstrated that the GaR_3 trans-metal-trapping system is highly efficient in stabilising emergent carbanions, post metalation with LiTMP, taking this trans-metal-trapping to the next level, that is, using the complexes in further C-element bond formation, remains to be realised as a routine procedure. The challenge is that since the trap must be a strong Lewis acidic carbophilic metal complex, logically that will produce a strong metal–carbon bond that may not be easily broken by an electrophile. Standard electrophilic quenching strategies using either iodine, or *N*-bromosuccinimide proved to be unsuccessful, resulting in essentially hydrolysed material after reaction and aqueous workup. This is rather unsurprising given the robust nature of the Ga–C bonds formed using the LiTMP GaR_3 system. Thus, we turned attention to C–C bond formation via palladium-catalysed cross-coupling protocols. A reaction between **3**, 4-bromobenzonitrile, and $Pd(PPh_3)_4$ in THF at 80 °C for 16 hours was performed. After a standard organic workup, the cross-coupled product 2′-methoxybiphenyl-4-carbonitrile (**7**) was isolated in 73% yield. However the reaction yield was not reproducible (typically yields varied in the range 50–70% on repeated runs), and variable amounts of 4-[(trimethylsilyl)methyl]benzonitrile were obtained, indicating that under these conditions the reaction evidenced poor selectivity. Using a different organic electrophile, benzoyl chloride, under the same conditions resulted in a moderate 62% yield of 2-benzoylanisole (**8**) (Scheme 5).



Scheme 5 Palladium-mediated C–C bond formation from **3**, using 4-bromobenzonitrile or benzoyl chloride, affording 2′-methoxybiphenyl-4-carbonitrile or 2-benzoylanisole, respectively

Rationalising that under the reasonably harsh reaction conditions required to promote cross-coupling, competing reaction of a CH_2SiMe_3 occurs, we decided to perform one more reaction between the homoleptic lithium gallate $LiGaR_4$, and 4-iodoacetophenone. Once more the cross-coupled product was formed in a moderate 62% yield against a ferrocene internal standard. Thus while we demonstrate a rare example of gallium-based cross-coupling,[8b,14] conclusions can be drawn. A major facet of the trans-metal-trapping strategy is the stabilisation of incipient carbanions by forming strong C–Ga bonds. This however, as one would expect, appears to be problematic, from the standpoint of facile onward reactivity. Thus, this case study clearly suggests a way forward for trans-metal-trapping. Finding new pairings of base and trapping agent that do not co-complex in the mild conditions used in reaction is the first goal since the lack of co-complexation promotes higher yielding processes. The choice of trap should also fulfil two requirements: (i) the atom should be able to form strong enough M–C bonds to stabilise the frequently sensitive metalation anions; (ii) the resulting M–C bonds should also be labile enough to promote straightforward reactivity into more complicated and synthetically useful bis-aryl or heteroaryl molecules. Moreover, despite the fact that the LiTMP/GaR_3 system is a superior base/trap pairing, the NaTMP/GaR_3 system is more predisposed to favour onward Ga–C functionalisation. Replacing lithium by sodium as the pre-eminent metallating agent would be attractive from a sustainability viewpoint given their comparative earth abundance. Future work will determine whether this alkali metal effect is due primarily to sodium versus lithium or whether the different coordination spheres involved (e.g., TMEDA versus PMDETA) influences the remarkable difference in iodination efficiency. Current work in our laboratories is focussed on meeting these goals by incorporating the crucial elements into new trans-metal-trapping systems.

All reactions and manipulations were conducted under a protective argon atmosphere using either standard Schlenk techniques or an MBraun glove box fitted with a gas purification and recirculation unit. NMR experiments were conducted in J. Young's tubes oven dried and flushed with argon prior to use. Hexane, toluene, and THF were dried by heating to reflux over sodium benzophenone ketyl and then distilled under N_2 prior to use. All other reagents were purchased commercially from Sigma-Aldrich and dried via distillation (where appropriate) from the appropriate drying agent prior to use. LiTMP[11] and $Ga(CH_2SiMe_3)_3$[15] were prepared as previously described or by slight variations thereof. NMR Spectroscopy: NMR spectra were recorded on a Bruker AV3 or AV 400 MHz spectrometer operating at 400.13 MHz for ^{1}H, 376.46 MHz for ^{7}Li and 100.62 MHz for ^{13}C. All ^{13}C spectra were proton decoupled. ^{1}H and ^{13}C NMR spectra were referenced against the appropriate solvent signal. ^{7}Li NMR spectra were referenced against LiCl in D_2O at δ = 0.00. X-ray Crystallography: Crystallographic data were collected on Oxford Diffraction instruments with Mo Kα radiation (λ = 0.71073 Å) or Cu Kα radiation (λ = 1.54184 Å). Structures were solved using SHELXS[16a] or OLEX2,[16b] while refinement was carried out on F^2 against all independent reflections by the full matrix least-squares method using the SHELXL programs or by the Gauss-Newton algorithm using OLEX2. All non-hydrogen atoms were refined using anisotropic thermal parameters. Selected crystallographic details and refinement details are provided in Table S1. CCDC 1880970–1880974 contains the supplementary crystallographic data for these structures. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/getstructures. DFT computational studies[17] employing the B3LYP method[18,19] and the 6-311G(d,p) basis set.[20]

[(PMDETA)Li(*o*-C_6H_4OMe)Ga(CH_2SiMe_3)$_3$] (3)

To a suspension of LiTMP (0.074 g, 0.5 mmol) and $Ga(CH_2SiMe_3)_3$ (0.165 g, 0.5 mmol) in hexane (10 mL), an equivalent of anisole (0.054 g, 54 µL, 0.5 mmol) was added at r.t. As soon as anisole was added, a yellow fine suspension was formed which persisted during stirring for 1 hour at r.t. PMDETA (0.11 mL, 0.5 mmol) was added, the solvent was exchanged in vacuo for toluene and the yellow solution placed in freezer to obtain **3** (0.17 g, 55%) as colourless crystals suitable for X-ray diffraction analysis.

^{1}H NMR (400.13 MHz, 298 K, THF-d_8): δ = 7.44 (d, 1 H, Ar-*H*), 6.78 (t, 1 H, Ar-*H*), 6.53 (t, 1 H, *p*-*CH*), 6.40 (d, 1 H, Ar-*H*), 6.40 (d, 1 H, Ar-*H*), 3.59 (s, 3 H, OCH_3), 2.47 (m, 4 H, NCH_2CH_2N), 2.37 (m, 4 H, NCH_2CH_2N), 2.26 (s, 3 H, NCH_3), 2.20 [s, 12 H, $N(CH_3)_2$], –0.19 [s, 27 H, $Si(CH_3)_3$], –0.85 (s, 6 H, CH_2SiMe_3).

^{13}C NMR (100.62 MHz, 298 K, THF-d_8): δ = 166.7 (Ar-*C*), 155.2 (*C*-Ga), 138.8 (Ar-*C*), 125.0 (Ar-*C*), 120.9 (Ar-*C*), 119.4 (Ar-*C*), 107.5 (Ar-*C*), 58.5 (PMDETA), 56.2 (PMDETA), 54.3 (OCH_3), 46.0 (PMDETA), 43.7 (PMDETA), 3.9 [$Si(CH_3)_3$], 0.5 (CH_2SiMe_3).

^{7}Li NMR (376.46 MHz, 298 K, THF-d_8): δ = 0.14.

Anal. Calcd for $C_{28}H_{63}GaLiN_3OSi_3$: C, 54.35; H, 10.26; N, 6.79. Found: C, 54.95; H, 9.94; N, 7.55.

[(TMEDA)Na(*o*-C_6H_4OMe)Ga(CH_2SiMe_3)$_3$] (5)

In a Schlenk flask, $Ga(CH_2SiMe_3)_3$ (0.33 g, 1 mmol) and NaTMP (0.163 g, 1 mmol) were suspended in hexane and stirred at r.t. for 1 h. To this mixture, one equivalent of anisole (0.11 mL, 1 mmol) was added, retaining the white suspension, and stirred at r.t. for a further 2 h. Upon

addition of TMEDA (0.21 mL, 1 mmol), a colourless solution was obtained which, with slow cooling to 4 °C, produced a crop of colourless crystals of **5** (98 mg, 17%).

^{1}H NMR (400.13 MHz, 298 K, C_6D_6): δ = 8.00 (dd, 1 H, Ar-*H*), 7.09 (td, 1 H, Ar-*H*), 7.04 (td, 1 H, Ar-*H*), 6.56 (dd, 1 H, Ar-*H*), 6.40, 3.46 (s, 3 H, OC*H*$_3$), 1.59 [s, 12 H, N(C*H*$_3$)$_2$], 1.54 (s, 4 H, NC*H*$_2$C*H*$_2$N), 0.33 [s, 27 H, Si(C*H*$_3$)$_3$], –0.51 (s, 6 H, C*H*$_2$SiMe$_3$).

^{13}C NMR (100.62 MHz, 298 K, C_6D_6): δ = 165.1 (Ar-*C*), 149.7 (*C*-Ga), 141.4 (Ar-*C*), 127.9 (Ar-*C*), 123.0 (Ar-*C*), 112.2 (Ar-*C*), 56.9 (OC*H*$_3$), 56.5 (TMEDA), 45.1 (TMEDA), 3.6 [Si(*C*H$_3$)$_3$], –0.7 (CH$_2$SiMe$_3$).

2′-Methoxybiphenyl-4-carbonitrile (7)

To a solution of **3** (200 mg, 0.323 mmol) in THF (8 mL) were added 4-bromobenzonitrile (59 mg, 0.323 mmol) and Pd(PPh$_3$)$_4$ (18 mg 5 mol%). The mixture was then stirred at reflux temperature for 16 h. After removal of all volatiles in vacuo, the residue was extracted with Et$_2$O (20 mL), then washed with H$_2$O (2 × 10 mL) and brine (2 × 10 mL). The organic phase was then dried (MgSO$_4$) and concentrated. Column chromatography (silica gel, hexane/EtOAc 95:5–90:10) afforded **7** (49 mg, 0.24 mmol, 73%) as a colourless oil; R_f = 0.45. ^{1}H and ^{13}C NMR spectra are in agreement with those previously published.[21]

2-Benzoylanisole (8)

To a solution of **3** (200 mg, 0.323 mmol) in THF (8 mL) were added Pd(PPh$_3$)$_4$ (18 mg, 5 mol%) followed by benzoyl chloride (0.037 mL, 0.323 mmol) via syringe. The mixture was then stirred at reflux temperature for 16 h. After removal of all volatiles in vacuo, the residue was extracted with Et$_2$O (20 mL), then washed with H$_2$O (2 × 10 mL) and brine (2 × 10 mL). The organic phase was then dried (MgSO$_4$) and concentrated. Column chromatography (silica gel, hexane/EtOAc 95:5–90:10) afforded **8** (43 mg, 0.20 mmol, 62%) as a colourless solid; R_f = 0.35. ^{1}H and ^{13}C NMR spectra are in agreement with those previously published.[22]

NMR Study: Synthesis of [(TMP(H)Na(*o*-C$_6$H$_4$OMe)GaR$_3$] (6)

In a J. Young's NMR tube, Ga(CH$_2$SiMe$_3$)$_3$ (83 mg, 0.25 mmol) and anisole (27 µL, 0.25 mmol) were combined together in C_6D_6 solvent affording a colourless solution. ^{1}H NMR analysis confirmed no reactivity had occurred between these two species. To this mixture, NaTMP (41 mg, 0.25 mmol) was added and upon dissolution gave a colourless solution. Analysis by ^{1}H NMR spectroscopy indicated metalation of anisole had occurred in 74% yield (using C$_6$Me$_6$ as an internal standard) to give **6**. [Note: TMP(H) resonances are lower frequency by ~0.3 ppm than 'free' TMP(H); we propose this is due to coordination of TMP(H) to Na in the absence of any other donor molecules.) Finally, addition of TMEDA (38 µL, 0.25 mmol) resulted in its coordination to the sodium centre and release of TMP(H) (confirmed by ^{1}H NMR).

[(TMP(H)Na(*o*-C$_6$H$_4$OMe)GaR$_3$] (6)

^{1}H NMR (400.13 MHz, 298 K, C_6D_6): δ = 7.97 (dd, 1 H, Ar-*H*), 7.09 (m, 1 H, Ar-*H*), 7.02 (td, 1 H, *p*-C*H*), 6.61 (d, 1 H, Ar-*H*), 3.46 (s, 3 H, OC*H*$_3$), 2.08 (s, C$_6$Me$_6$), 1.28 [m, 2 H, γ-TMP(H)], 0.92 [t, 4 H, β-TMP(H)], 0.70 [s, 12 H, C*H*$_3$ of TMP(H)], 0.26 [s, 28 H, Si(C*H*$_3$)$_3$ + TMP(*H*)], –0.57 (s, 6 H, C*H*$_2$SiMe$_3$).

Post-TMEDA Addition:

^{1}H NMR (400.13 MHz, 298 K, C_6D_6): δ = 7.90 (dd, 1 H, Ar-*H*), 7.06 (m, 1 H, Ar-*H*), 6.98 (td, 1 H, *p*-C*H*), 6.58 (d, 1 H, Ar-*H*), 3.48 (s, 3 H, OC*H*$_3$), 2.08 (s, C$_6$Me$_6$), 1.65 (m, 16 H, TMEDA), 1.53 [m, 2 H, γ-TMP(H)], 1.24 [t, 4 H, β-TMP(H)], 1.05 [s, 12 H, C*H*$_3$ of TMP(H)], 0.25 [s, 28 H, Si(C*H*$_3$)$_3$ + TMP(*H*)], –0.59 (s, 6 H, C*H*$_2$SiMe$_3$).

NMR Study: Synthesis of [(PMDETA)Li(*o*-C$_6$H$_4$OMe)Ga(CH$_2$SiMe$_3$)$_3$] (3)

In a J. Young's NMR tube, equimolar amounts of Ga(CH$_2$SiMe$_3$)$_3$ (83 mg, 0.25 mmol) and LiTMP (36 mg, 0.25 mmol) were combined in C_6D_6 (0.5 mL) resulting in a white suspension. Addition of anisole (27 µL, 0.25 mmol) was then performed and allowed to react for 1 h at r.t. with a white suspension persisting. Dissolution was achieved by the addition of PMDETA (53 µL, 0.25 mmol) to afford a yellow solution; compound **3** was obtained in 75% yield (^{1}H NMR with C$_6$Me$_6$ as internal standard).

^{1}H NMR (400.13 MHz, 298 K, C_6D_6): δ = 8.19 (d, 1 H, Ar-*H*), 7.06 (t, 1 H, Ar-*H*), 7.02 (dt, 1 H, *p*-C*H*), 6.31 (d, 1 H, Ar-*H*), 3.44 (s, 3 H, OC*H*$_3$), 2.03 (s, 3 H, NC*H*$_3$), 1.83 (m, 4 H, NC*H*$_2$C*H*$_2$N), 1.75 (m, 4 H, NC*H*$_2$C*H*$_2$N), 1.57 [s, 12 H, N(C*H*$_3$)$_2$], 0.32 [s, 27 H, Si(C*H*$_3$)$_3$], –0.34 (s, 6 H, C*H*$_2$SiMe$_3$).

^{13}C NMR (100.62 MHz, 298 K, C_6D_6): δ = 164.6 (Ar-*C*), 142.6 (Ar-*C*), 131.7 (*C*-Ga), 124.3 (Ar-*C*), 125.9 (Ar-*C*), 116.5 (Ar-*C*), 62.7 (OCH$_3$), 57.2 (PMDETA), 53.5 (PMDETA), 45.6 (PMDETA), 44.5 (PMDETA), 4.1 [Si(*C*H$_3$)$_3$], 1.5 (CH$_2$SiMe$_3$).

^{7}Li NMR (376.46 MHz, 298 K, C_6D_6): δ = 0.10.

Metalation of Anisole followed by Electrophilic Quenching Using I$_2$: NaTMP + Anisole

In a Schlenk flask, NaTMP (0.163 g, 1 mmol) was suspended in hexane (10 mL) at r.t. To this, anisole (0.11 mL, 1 mmol) was added affording a white suspension, and the mixture was stirred at r.t. for 2 h. In a separate Schlenk tube, a solution of I$_2$ (6 mmol) was prepared in THF (10 mL). Both Schlenk tubes were then cooled to –78 °C in an acetone/dry ice bath and stirred for 20 min until completely cooled. Then, the I$_2$/THF solution was syphoned into the mixture at –78 °C and allowed to slowly warm up to r.t. over 16 h. Workup of the mixture was achieved by addition of sat. aq Na$_2$S$_2$O$_3$ solution until bleaching occurred (approx. 20 mL), followed by addition of sat. aq NH$_4$Cl (10 mL). The mixture was then extracted with EtOAc (3 × 10 mL) and the combined organic layers were washed with brine (10 mL), dried (MgSO$_4$), and filtered. All organic solvents were then removed under reduced pressure to give a brown solid; 2-iodoanisole was obtained in 20% yield (NMR using C$_6$Me$_6$ a internal standard in CDCl$_3$). Spectroscopic values obtained are in good agreement with those previously reported in the literature.[23]

Metalation of Anisole followed by Electrophilic Quenching Using I$_2$: LiTMP (or NaTMP) + GaR$_3$ + Anisole

In a Schlenk flask, LiTMP (0.146 g, 1 mmol) and Ga(CH$_2$SiMe$_3$)$_3$ (0.33 g, 1 mmol) were suspended in hexane (10 mL) at r.t. To this, anisole (0.11 mL, 1 mmol) was added retaining a white suspension, and the mixture was stirred at r.t. for 2 h [for NaTMP (0.163 g, 1 mmol) reaction, the order of addition was reversed so that NaTMP was added last]. In a separate Schlenk tube, a solution of I$_2$ (6 mmol) was prepared in THF (10 mL). Both flasks were then cooled to –78 °C in an acetone/dry ice bath and stirred for 20 min until completely cooled. Then, the I$_2$/THF solution was syphoned into the mixture at –78 °C and allowed to slowly warm up to r.t. overnight (approx. 16 h in total). Workup of the mixture was achieved by addition of sat. aq Na$_2$S$_2$O$_3$ solution until bleaching occurred (approx. 20 mL), followed by addition of sat. aq NH$_4$Cl (10 mL). The mixture was then extracted with EtOAc (3 × 10 mL) and the combined organic layers were washed with brine (10 mL), dried (MgSO$_4$), and filtered. All organic solvents

were then removed under reduced pressure to give a brown solid. The yield of 2-iodoanisole was 65% (using NaTMP) and 1.5% (LiTMP) (NMR using C_6Me_6 as internal standard in $CDCl_3$). NMR data are in agreement with those previously published for 2-iodoanisole.[23]

Funding Information

We thank the European Research Council (ERC StG, MixMetApps) and the EPSRC (EP/N011384/1) for their generous sponsorship of this research.

Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0037-1611646.

References

(1) (a) Clayden, J. *In Organolithiums: Selectivity for Synthesis* 2002. (b) Snieckus, V. *Chem. Rev.* **1990**, *90*, 879. (c) Mongin, F.; Schlosser, M. *Tetrahedron Lett.* **1996**, *37*, 6551. (d) Schlosser, M. *Angew. Chem. Int. Ed.* **2005**, *44*, 376. (e) Werner, V.; Klatt, T.; Fujii, M.; Markiewicz, J.; Apeloig, Y.; Knochel, P. *Chem. Eur. J.* **2014**, *20*, 8338. (f) Mulvey, R. E.; Robertson, S. D. *Angew. Chem. Int. Ed.* **2013**, *52*, 11470.

(2) Becker, M. R.; Knochel, P. *Angew. Chem. Int. Ed.* **2015**, *54*, 12501.

(3) (a) Schlosser, M. *J. Organomet. Chem.* **1967**, *8*, 9. (b) Lochmann, L.; Pospisil, J.; Lim, D. *Tetrahedron Lett.* **1966**, *7*, 257.

(4) (a) Wunderlich, S. H.; Rohbogner, C. J.; Unsinn, A.; Knochel, P. *Org. Process Res. Dev.* **2010**, *14*, 339. (b) Haag, B.; Mosrin, M.; Ila, H.; Malakhov, V.; Knochel, P. *Angew. Chem. Int. Ed.* **2011**, *50*, 9794.

(5) (a) Uchiyama, M.; Kameda, M.; Mishima, O.; Yokoyama, N.; Koike, M.; Kondo, Y.; Sakamoto, T. *J. Am. Chem. Soc.* **1998**, *120*, 4934. (b) Kondo, Y.; Shilai, M.; Uchiyama, M.; Sakamoto, T. *J. Am. Chem. Soc.* **1999**, *121*, 3539. (c) Snégaroff, K.; Komagawa, S.; Chevallier, F.; Gros, P. C.; Golhen, S.; Roisnel, T.; Uchiyama, M.; Mongin, F. *Chem. Eur. J.* **2010**, *16*, 8191. (d) Akimoto, G.; Otsuka, M.; Takita, R.; Uchiyama, M.; Hedidi, M.; Bentabed-Ababsa, G.; Lassagne, F.; Erb, W.; Mogin, F. *J. Org. Chem.* **2018**, *83*, 13498.

(6) (a) Mulvey, R. E.; Mongin, F.; Uchiyama, M.; Kondo, Y. *Angew. Chem. Int. Ed.* **2007**, *46*, 3802. (b) Andrikopoulos, P. C.; Armstrong, D. R.; Graham, D. V.; Hevia, E.; Kennedy, A. R.; Mulvey, R. E.; O'Hara, C. T.; Talmard, C. *Angew. Chem. Int. Ed.* **2005**, *44*, 3459. (c) Armstrong, D. R.; Clegg, W.; Dale, S. H.; Graham, D. V.; Hevia, E.; Hogg, L. M.; Honeyman, G. W.; Kennedy, A. R.; Mulvey, R. E. *Chem. Commun.* **2007**, 598. (d) Clegg, W.; Conway, B.; Graham, D. V.; Hevia, E.; Kennedy, A. R.; Mulvey, R. E.; Russo, L.; Wright, D. S. *Chem. Eur. J.* **2009**, *15*, 7074. (e) Armstrong, D. R.; Blair, V. L.; Clegg, W.; Dale, S. H.; Garcia-Alvarez, J.; Honeyman, G. W.; Hevia, E.; Mulvey, R. E.; Russo, L. *J. Am. Chem. Soc.* **2010**, *132*, 9480. (f) Wunderlich, S. H.; Kienle, M.; Knochel, P. *Angew. Chem. Int. Ed.* **2009**, *48*, 7256. (g) Garcia-Álvarez, J.; Kennedy, A. R.; Klett, J.; Mulvey, R. E. *Angew. Chem. Int. Ed.* **2007**, *46*, 1105. (h) Blair, V. L.; Clegg, W.; Conway, B.; Hevia, E.; Kennedy, A. R.; Klett, J.; Mulvey, R. E.; Russo, L. *Chem. Eur. J.* **2008**, *14*, 65. (i) Wunderlich, S. H.; Knochel, P. *Angew. Chem. Int. Ed.* **2009**, *48*, 9717. (j) Alborés, P.; Carrella, L. M.; Clegg, W.; García-Álvarez, P.; Kennedy, A. R.; Klett, J.; Mulvey, R. E.; Rentschler, E.; Russo, L. *Angew. Chem. Int. Ed.* **2009**, *48*, 3317. (k) Nagaradja, E.; Chevallier, F.; Roisnel, T.; Jouikov, V.; Mongin, F. *Tetrahedron* **2012**, *68*, 3063. (l) Bedford, R. B.; Brenner, P. B.; Carter, E.; Cogswell, P. M.; Haddow, M. F.; Harvey, J. N.; Murphy, D. M.; Nunn, J.; Woodall, C. H. *Angew. Chem. Int. Ed.* **2014**, *53*, 1804. (m) Martínez-Martínez, A. J.; Kennedy, A. R.; Mulvey, R. E.; O'Hara, C. T. *Science (Washington, D. C.)* **2014**, *346*, 834.

(7) (a) Armstrong, D. R.; Crosbie, E.; Hevia, E.; Mulvey, R. E.; Ramsay, D. L.; Robertson, S. D. *Chem. Sci.* **2014**, *5*, 3031. (b) Uzelac, M.; Kennedy, A. R.; Hevia, E. *Inorg. Chem.* **2017**, *56*, 8615. (c) Uzelac, M.; Mulvey, R. E. *Chem. Eur. J.* **2018**, *24*, 7786.

(8) (a) Uzelac, M.; Kennedy, A. R.; Hevia, E.; Mulvey, R. E. *Angew. Chem. Int. Ed.* **2016**, *55*, 13147. (b) McLellan, R.; Uzelac, M.; Kennedy, A. R.; Hevia, E.; Mulvey, R. E. *Angew. Chem. Int. Ed.* **2017**, *56*, 9566.

(9) Frischmuth, A.; Fernández, M.; Barl, N. M.; Achrainer, F.; Zipse, H.; Berionni, G.; Mayr, H.; Karaghiosoff, K.; Knochel, P. *Angew. Chem. Int. Ed.* **2014**, *53*, 7928.

(10) Armstrong, D. R.; Brammer, E.; Cadenbach, T.; Hevia, E.; Kennedy, A. R. *Organometallics* **2013**, *32*, 480.

(11) Hevia, E.; Kennedy, A. R.; Mulvey, R. E.; Ramsay, D. L.; Robertson, S. D. *Chem. Eur. J.* **2013**, *19*, 14069.

(12) Kramer, M. U.; Robert, D.; Nakajima, Y.; Englert, U.; Spaniol, T. P.; Okuda, J. *Eur. J. Inorg. Chem.* **2007**, 665.

(13) Hallock, R. B.; Hunter, W. E.; Atwood, J. L.; Beachley, O. T. Jr. *Organometallics* **1985**, *4*, 547.

(14) (a) Han, Y.; Fang, L.; Tao, W.-T.; Huang, Y.-Z. *Tetrahedron Lett.* **1995**, *36*, 1287. (b) Blum, J.; Gelman, D.; Baidossi, W.; Shakh, E.; Rosenfeld, A.; Aizenshtat, Z.; Wassermann, B. C.; Frick, M.; Heymer, B.; Schutte, S.; Wernik, S.; Schumann, H. *J. Org. Chem.* **1997**, *62*, 8681. (c) Gelman, D.; Schumann, H.; Blum, J. *Tetrahedron Lett.* **2000**, *41*, 7555. (d) Mikami, S.; Yorimitsu, H.; Oshima, K. *Synlett* **2002**, 1137.

(15) Dennis, L. M.; Patnode, W. *J. Am. Chem. Soc.* **1932**, *54*, 182.

(16) (a) Sheldrick, G. M. *Acta Crystallogr., Sect. C* **2015**, *71*, 3. (b) Dolomanov, O. V.; Bourhis, L. J.; Gildea, R. J.; Howard, J. A. K.; Puschmann, H. *J. Appl. Crystallogr.* **2009**, *42*, 339.

(17) Kohn, W.; Becke, A. D.; Parr, R. G. *J. Phys Chem.* **1996**, *100*, 12974.

(18) Becke, A. D. *Phys. Rev. A.* **1988**, *38*, 3098.

(19) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B.* **1988**, *37*, 785.

(20) McLean, A. D.; Chandler, G. S. *J. Chem. Phys.* **1980**, *72*, 5639.

(21) Alam, N.; Amatore, C.; Combellas, C.; Pinson, J.; Savéant, J.-M.; Thiébault, A.; Verpeaux, J.-N. *J. Org. Chem.* **1988**, *53*, 1496.

(22) Jafarpour, F.; Rashidi-Ranjbar, P.; Kashani, A. O. *Eur. J. Org. Chem.* **2011**, 2128.

(23) Kulbitski, K.; Nisnevich, G.; Gandelman, M. *Adv. Synth. Catal.* **2011**, *353*, 1438.