Chemical Science



EDGE ARTICLE

View Article Online



Cite this: Chem. Sci., 2020, 11, 1855

d All publication charges for this article have been paid for by the Royal Society of Chemistry

Received 30th November 2019 Accepted 2nd January 2020

DOI: 10.1039/c9sc06060j

rsc li/chemical-science

Lipshutz-type bis(amido)argentates for directed ortho argentation†

Noriyuki Tezuka, (10 *ab Keiichi Hirano, (10 *ab Andrew J. Peel, (10 c Andrew E. H. Wheatley, och Kazunori Miyamoto and Masanobu Uchiyama ** **abd

Bis(amido)argentate (TMP)₂Ag(CN)Li₂ (3, TMP-Ag-ate; TMP = 2,2,6,6-tetramethylpiperidido) was designed as a tool for chemoselective aromatic functionalization via unprecedented directed ortho argentation (DoAg). X-Ray crystallographic analysis showed that 3 takes a structure analogous to that of the corresponding Lipshutz cuprate. DoAg with this TMP-Ag-ate afforded multifunctional aromatics in high yields in processes that exhibited high chemoselectivity and compatibility with a wide range of functional groups. These included organometallics- and transition metal-susceptible substituents such as methyl ester, aldehyde, vinyl, iodo, (trifluoromethanesulfonyl)oxy and nitro groups. The arylargentates displayed good reactivity with various electrophiles. Chalcogen (S, Se, and Te) installation and azo coupling reactions also proceeded efficiently.

Introduction

Copper and silver are categorized as congeneric elements, being vertically adjacent in the periodic table. They have many similarities, including electronegativity (Cu 1.9 vs. Ag 1.9)1 and coordination geometry. However, whereas organocopper species have opened up many new avenues in organic synthesis,2 the silver analogues are quite poorly characterized,3 partly due to a lack of efficient preparative methods (Fig. 1a). For example, organocopper (R-Cu(1)) compounds are commonly prepared by the oxidative cupration of organic halides with Cu(0).4 Unfortunately, this method cannot be applied to the preparation of organosilver (R-Ag(1)) compounds, because the $Ag(0 \rightarrow I)$ redox potential is 0.8 V (Fig. 1b).^{5,6} Neither hydro (or carbo)-metalation nor halogen-metal exchange, which are also effective methods for the preparation of organocopper compounds, have been effectively applied to organosilver chemistry to date.7 Transmetalation from organometallics to an Ag(I) source is another route offering potential access to the corresponding organosilver species.7b,c,8 However, the high

reactivity (including wrt silver salts) of commonly used organolithiums and organomagnesiums severely restricts the employment of functionalized aromatic compounds as substrates. Directed ortho metalation (DoM) is another synthetic option for the regioselective preparation of aryl metal compounds9,10 and could offer a route to aromatic silver complexes of a type that have recently received attention as potential reaction intermediates.81-n Here we present an unprecedented directed ortho argentation (DoAg) reaction using a newly designed silver ate base, and demonstrate its applicability to the derivatization of a range of functionalized aromatics.

Results and discussion

We initially screened Ag-ate bases prepared by combining a range of silver salts and amido ligands for DoAg using N,Ndiisopropylbenzamide (1a) as a model substrate, followed by

Fig. 1 (a) Preparative strategies for arylargentates, and (b) comparison of electrochemical properties of copper and silver.

3

⁽a) Preparation of Arylargentate (b) Frost Diagram: Aa vs Cu Ago or RAg nE%[V No Report [Ag] AgIX Poor Functional Group Compatibility 3 (TMP)₂Ag(CN)Li₂ 0.15 High Chemoselectivity High Regioselectivity 2

^aGraduate School of Pharmaceutical Sciences, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033, Japan. E-mail: tezuka-noriyuki@g.ecc.u-tokyo.ac.jp; k1hirano@mol.f.u-tokyo.ac.jp; uchiyama@mol.f.u-tokyo.ac.jp

^bCluster of Pioneering Research (CPR), Advanced Elements Chemistry Laboratory, RIKEN, 2-1 Hirosawa, Wako-shi, Saitama 351-0198, Japan

^cDepartment of Chemistry, University of Cambridge, Lensfield Road, Cambridge CB2

¹EW. UK ^dResearch Initiative for Supra-Materials (RISM), Shinshu University, 3-15-1 Tokida, Ueda, Nagano 386-8567, Japan

[†] Electronic supplementary information (ESI) available. CCDC 1919739, 1919740, 1957572 and 1960037. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c9sc06060i

trapping with iodine (Table 1). The use of silver(1) salts with LiCN must play a vital role. Overall, the bond lengths and angles in the solid-state structure of 3(THF) are in good agreement with equimolar TMPLi failed to provide the corresponding iodinated product 2a (entries 1 and 2). We next assessed the reactivity of those obtained by DFT calculation. Meanwhile, preliminary TMP-argentates prepared from several silver sources using attempts to prove the formation of aryl silver species during our a two-fold excess of TMPLi (entries 3-6). (TMP)₂Ag(CN)Li₂ 3, proposed DoAg reactions have been initiated. With this in generated from silver cyanide, uniquely gave the desired mind, equimolar reaction between 1a and 3 has provided product 2a,11 whereas other TMP-argentates were totally evidence for the 1:1 complex of a diarylargentate and bis(TMP) unproductive (entry 6 vs. entries 3-5). Moreover, 3 was capable argentate, presumably the result of a disproportionation of deprotonating two equivalents of substrate 1a (entry 7). From (Fig. 2d). Further evidence that Gilman-type diarylargentates the viewpoint of practical use, it is important to emphasize that can form came from the 2:1 reaction of 1a with 3 (Fig. 2e). AgCN is comparable to CuCN in price.12 Next, we examined Though work is ongoing, the ability of aryl silver species to form amido ligands and solvents. The HMDS-argentate failed to give in these systems is clear. Moreover, Ag-aryl bond lengths in our 2a, presumably due to its low basicity (entry 8). Meanwhile, in initial structures are comparable to those in diarylargentates contrast to the poor yield obtained with (iPr2N)2Ag(CN)Li2,13 2a previously reported by van Koten.8d was obtained quantitatively by using (Cv2N)2Ag(CN)Li2 (entries

meaning that all DoAg operations can be conducted without shading tools (entry 16). Based on these data, all subsequent experiments were conducted without special precautions to exclude light. The structure of the THF-solvate of (TMP)₂Ag(CN)Li₂ 3 was obtained by X-ray crystallography and corroborated by DFT calculations (Fig. 2). Single crystals were obtained from a hexane/toluene solution of 3 prepared from AgCN and TMPLi in a ratio of 1: 2.17 Complex 3(THF) has an almost linear -Aggeometry (176.01(8)°) and the two lithium centers are bridged by cyanide. The resulting lower-order structure mirrors that seen in the corresponding Lipshutz cuprate. 15 However, since the related and yet relatively inert Gilman cuprate18 is also based on linear, lower-order Cu (like the cyanide-free argentate, see ESI Fig. S2†), the geometry of the group 11 element cannot alone explain the high reactivity of 3(THF) in DoAg; the inclusion of

9 vs. 10). This result is practically of great importance in terms

of cost reduction.14 The heteroleptic amidoargentate Me(TMP)

Ag(CN)Li₂ proved unproductive (entry 11).¹⁵ Lastly, THF was

found to be a particularly effective solvent for DoAg (entry 6 vs.

entries 12-15).16 It is worth noting that neither 3 nor the puta-

tive intermediate arylargentate generated was sensitive to light,

With the optimized reaction conditions and an understanding of the nature of the base in hand (Table 1, entry 16 and Fig. 2), we next examined the substrate scope of DoAg (Table 2). We first looked at the choice of DMG. It proved possible to use diethylamide 1b and morpholine amide 1c, both of which are chemically more labile than diisopropylamide 1a. Regioselective argentation of benzonitrile (1d) proceeded smoothly in 95% yield, leaving the cyano group intact. Various esters, including CO₂^tBu, -iPr, and -Et, were compatible with the Agate base (1e-1i). Of considerable importance given that the mechanism of deprotonation in reactions involving the application of 3 is the subject of ongoing study, even methyl ester was tolerated, giving the corresponding iodinated product in high yield (2h).19 Furthermore, traditionally base-susceptible lactones remained intact (2i: 99%). The carbonyl group of a ketone also worked as DMG to give the desired product 2j without any observable side reactions. Benzotrifluoride was also usable; the corresponding iodobenzotrifluoride 2k was obtained in 56% yield with moderate ortho selectivity (78:15:7 for ortho: meta: para).20 PhSF5 was also subjected to the DoAg process and argentation took place with perfect ortho selectivity (21). Though this reaction needs further optimization, it is remarkable that the metalation proceeded, and this strongly

Table 1 Optimization of conditions^a

$$\begin{array}{c} \text{H} & \text{O} \\ \text{N'Pr}_2 \\ \hline \\ \text{1a} & \text{In the dark} \end{array} \\ \begin{array}{c} \text{Ag-ate base (1.2 equiv)} \\ \text{THF, 0 °C, 2 h} \\ \text{In the dark} \end{array} \\ \begin{array}{c} \text{IA} \\ \text{N'Pr}_2 \\ \hline \\ \text{IA} \\ \text{In the dark} \end{array} \\ \begin{array}{c} \text{IA} \\ \text{II}_2 \text{ (5 equiv)} \\ \text{II}_2 \text{ (5 equiv)} \\ \hline \\ \text{II}_3 \text{ (5 equiv)} \\ \hline \\ \text{II}_4 \text{ (5 equiv)} \\ \hline \\ \text{II}_5 \text{ (5 equiv)} \\ \hline \\ \text{II}_6 \text{ (5 equiv)} \\ \hline \\ \text{II}_7 \text{ (5 equiv)} \\$$

Entry	Ag-ate base	Solvent	Yield (%)	Entry	Ag-ate base	Solvent	Yield (%)
1	(TMP)Ag(NO ₃)Li	THF	ND	9	(ⁱ Pr ₂ N) ₂ Ag(CN)Li ₂	THF	11
2	(TMP)Ag(CN)Li	THF	ND	10	$(Cy_2N)_2Ag(CN)Li_2$	THF	99
3	(TMP) ₂ Ag(NO ₃)Li ₂	THF	ND	11	Me(TMP)Ag(CN)Li ₂	THF	ND
4	$(TMP)_2Ag(1/2 \cdot CO_3)Li_2$	THF	ND	12	$(TMP)_2Ag(CN)Li_2$	Et ₂ O	31
5	(TMP) ₂ Ag(OTf)Li ₂	THF	ND	13 ^c	(TMP) ₂ Ag(CN)Li ₂	Dioxane	ND
6	(TMP) ₂ Ag(CN)Li ₂	THF	99 (92)	14	(TMP) ₂ Ag(CN)Li ₂	Benzene	49
7^b	$(TMP)_2Ag(CN)Li_2$	THF	93	15	$(TMP)_2Ag(CN)Li_2$	Hexane	46
8	(HMDS) ₂ Ag(CN)Li ₂	THF	ND	16^d	(TMP) ₂ Ag(CN)Li ₂	THF	99

^a NMR yields based on mesitylene as an internal standard. Isolated yield in parentheses. ND: not detected. ^b Ag-ate base (0.5 equiv.). ^c Deprotonation conducted at room temperature. ^d Exposed to light. TMP: 2,2,6,6-tetramethylpiperidido. TfO: trifluoromethanesulfonato. Cy: cyclohexyl. HMDS: 1,1,1,3,3,3-hexamethyldisilazido.

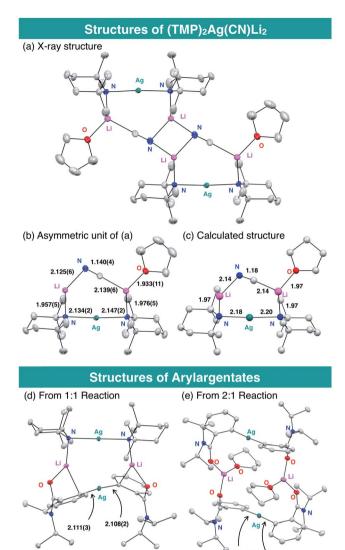


Fig. 2 X-ray and calculated structures of argentates. (a) Crystal structure of the dimer of $(TMP)_2Ag(CN)Li_2(THF)$ [3(THF)]₂; (b) the asymmetric unit (monomer) from (a); (c) the asymmetric unit extracted from the structure of $[3(THF)]_2$ calculated at the M06/6-31+G* θ LanL2DZ(Ag) level; (d) crystal structure of a diarylargentate adduct obtained by 1:1 reaction of 1a and 3 and (e) of a diarylargentate dimer from the 2:1 reaction of 1a and 3. All atomic displacement parameters in crystal structures shown at 30% probability, with H atoms (and THF disorder in (a and b)) omitted. Selected bond lengths in Å.

suggests that DoAg could find a role in the diverse functionalization of pharmaceutically important pentafluorosulfanylarenes. High ancillary functional group (AFG) tolerance is a key feature of the present argentation reaction. Styrene-type substrate **1m** could be employed without observable polymerization as a side reaction. Halogens and *pseudo*-halogens also survived (**2n–2q**). Especially remarkable was the successful retention of the (trifluoromethanesulfonyl)oxy group in **2q**. To our knowledge, this is the first example of this AFG surviving a deprotonative metalation reaction. The highlight of the current development of DoAg is the outstanding

Table 2 Directed ortho argentation^a

chemoselectivity revealed by the first directed ortho metalation of a nitroarene by an amidometal ate base. Deprotonative metalation of nitroarenes has been acknowledged for many years to be especially difficult due to incompatibility between the nitro group and strong bases as well as the instability of generated arylmetals.²³ Thus, until now only specific substrates have enabled this chemistry.24 In contrast, our argentate successfully achieved the conversion of both electron-rich and electron-deficient nitro(hetero)arenes in high yields with perfect regiocontrol next to the nitro group in the presence of other potential DMGs (2r-2t). Our work has also demonstrated that an aldehyde function is tolerant to the use of our Ag-ate (2u).19,24b,c,25 Heteroarenes such as isoquinoline and indoles, with DMGs at the 2- or 3-positions, were also transformed into the desired products in high yields (2v-2x). As expected, (TMP)₂Ag(CN)Li₂ 3 exhibited a stark difference in

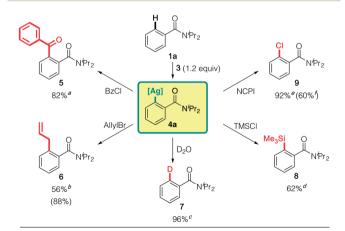
^a Isolated yields. NMR yields in parentheses, based on mesitylene as an internal standard. ^b Argentation at -40 °C. ^c Ortho: meta: para = 78:15:7. ^d Ortho: meta = >29:1. ^e Ortho: meta = 16:1.

chemoselectivity in comparison to its cuprous counterpart, $(TMP)_2Cu(CN)Li_2$.¹⁵ Upon cupration, sterically unshielded methyl and ethyl esters suffered from uncontrollable side reactions (**2g** and **2h**) and the nitroarene gave only trace amounts of the iodined product **2r** due to the redox activity of Cu.

We next investigated the synthetic use of the putative arylargentate $\bf 4a$ in aromatic functionalization (Scheme 1). Reactions with benzoyl chloride (5), allyl bromide (6), D₂O (7), trimethylsilyl chloride (TMSCl: $\bf 8$)²⁶ and *N*-chlorophthalimide (NCPI: $\bf 9$) proceeded well. The reactivity with NCPI was particularly noteworthy, since the alternative use of redox active (TMP)₂Cu(CN)Li₂ led to significantly less of the desired product on account of undesired oxidative biaryl formation ($\bf 9$: 60% and biaryl: 35% NMR yields). Unfortunately, Pd- and Ni-catalyzed cross-coupling reactions^{8l-n} have not yet proved successful.

Interestingly, putative **4a** is reluctant to react with some typical electrophiles, such as methyl iodide and benzyl bromide (see ESI Table S1†). This can be attributed to the high Ag(I \rightarrow III) redox potential, and results in distinctly different reactivity from the S_N2 processes of organocopper reagents, where the positive charge of the Cu center first increases and then decreases as it goes from Cu(I) to Cu(III) and then back to Cu(I).

A study of chalcogen introduction reactions showed that disulfides are excellent substrates for TMP-Ag-ate reaction (Table 3). Unsymmetrically (hetero)arylated sulfides **10a** and **10b** were obtained quantitatively. Excellent chemoselectivity was also observed during reactions with disulfide; benzyl (**10c**), chloro (**10d**), bromo (**10e**), ester (**10f**), and even nitro groups (**10g**) were tolerated, and the corresponding sulfides were obtained in high yields. Taking advantage of the unusual tolerance of the nitro group to our Ag-ate (*vide supra*), the synthesis of diaryl sulfide **10k** with nitro groups on both aryl rings was achieved. In the case of an alkyl substituent, dicyclohexyl disulfide, **10h** was obtained in 54% yield. Diaryl sulfides are



Scheme 1 Reaction scope of arylargentate 4a. Isolated yields. DoAg was conducted with $(TMP)_2Ag(CN)Li_2$ (3) (1.2 equiv.), 0 °C, 2 h. ^aBzCl (3.5 equiv.), 80 °C, 16 h. ^bAllylBr (5.0 equiv.), 80 °C, 16 h.; NMR yield in parentheses. ^cD₂O (55 equiv.), rt., 16 h.; D/H = 97/3. ^dTMSCl (5.0 equiv.), 80 °C, 16 h. ^eDoAg for 0.5 h.; NCPI (3.0 equiv.), rt., 1 h. ^fNMR yield when using $(TMP)_2Cu(CN)Li_2$ instead of 3. Bz: benzoyl. TMS: trimethylsilyl. NCPI: *N*-chlorophthalimide.

Table 3 Chalcogen installation^a

^a Isolated yields. ^b 40 °C. ^c 80 °C. ^d Chalcogen source (5.0 equiv.).

important chemical units in medicinal chemistry research.²⁸ Though the reaction of aryllithium or -magnesium reagents with disulfides can be used to access diaryl sulfides, the yields are variable and the AFG compatibility is low, due to the nature of these organometallics.^{29,30} In contrast, our more tolerant argentate-based methodology is a powerful new tool for obtaining diverse diaryl sulfides. Moreover, it allows chalcogen introduction to be extended to the preparation of diaryl selenides and tellurides³¹ (10i and 10j).

We next focused on the synthesis of azo compounds from diazonium salts. Arylmetals generally react with diazoniums in S_NAr or SET fashion (Sandmeyer-type reaction) and electronneutral or electron-deficient arenes do not react with diazonium salts by themselves.32 Minakata's oxidative aniline crosscoupling represents a remarkable advance in this field, albeit with unavoidable formation of the homo-coupled product.³³ We treated 4a with phenyldiazonium tetrafluoroborate, and obtained the corresponding azo compound 11a in 68% yield (Table 4). This approach selectively produced heterocoupling products, and cyano, ester, and even nitro groups remained intact during the reaction, affording the corresponding azo compounds with two electron-deficient arenes in high yields (11b-11d). Aryldiazonium salts without electron-withdrawing groups reacted selectively to give 11e and 11f. As expected, reference experiments showed that the arylcuprate prepared from 1a and (TMP)₂Cu(CN)Li₂ formed biaryl by-products, which strongly suggests that the oxidation of copper competed in this case - something we were able to obviate by using silver.

Table 4 Synthesis of azo compounds^a

Edge Article

^a Azo compounds were isomerized to their *trans* form at 80 °C for 16 h. ^b NMR yields when using (TMP)₂Cu(CN)Li₂ instead of 3.

Conclusions

In summary, we have developed a method for the highly chemoand regioselective deprotonative argentation of a range of (hetero)arenes by designing TMP-Ag-ate base 3, the structure of which is consistent with its deprotonation efficacy. The resultant putative arylargentate 4a exhibited excellent reactivity towards electrophiles, including disulfide, diselenide, and ditelluride, with high ancillary functional group tolerance. Deprotonative argentation was also found to be efficient for preparing unsymmetrically substituted azo compounds in combination with diazonium tetrafluoroborates. Further theoretical and spectroscopic studies to expand the reaction scope and to investigate the physicochemical properties of these unique aromatic silver compounds are underway.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

This work was partly supported by JSPS Grant-in-Aid for Scientific Research on Innovative Areas (No. 17H05430), JSPS KAKENHI (S) (No. 17H06173), NAGASE Science Technology Foundation, Sumitomo Foundation (to M. U.), JSPS Grant-in-Aid for Young Scientists (A) (No. 16H06214), Challenging Research (Exploratory) (No. 18K19390), the Uehara Memorial Foundation, and the Naito Foundation (to K. H.), and Grant-in-Aid for JSPS Fellows (No. 18J12045) and Graduate Program for Leaders in Life Innovation, The University of Tokyo Life Innovation Leading Graduate School from MEXT, Japan (to N. T.). Support also came from the U.K. EPSRC through grants EP/J500380/1 and EP/N509620/1 (to A. J. P.) and also EP/K039520/

 RIKEN Integrated Cluster of Clusters (RICC), HOKUSAI-GreatWave and HOKUSAI-BigWaterfall provided the computer resources for the DFT calculations.

Notes and references

- 1 (a) L. Pauling, J. Am. Chem. Soc., 1932, 54, 3570–3582; (b) Handbook of Chemistry: Pure Chemistry, ed. Chem. Soc. Japan, Maruzen, Tokyo, 1966.
- 2 For a review on organocopper chemistry, see: (a) Modern Organocopper Chemistry, ed. N. Krause, Wiley-VCH Verlag GmbH, Weinheim, 2002. Conjugate addition is a key feature of organocuprates, see: (b) N. Yoshikai and E. Nakamura, Chem. Rev., 2012, 112, 2339–2372; (c) S. Woodward, Chem. Soc. Rev., 2000, 29, 393–401. The reactions between organocoppers and multiple bonds have been investigated in detail, see: (d) H. Yoshida, ACS Catal., 2016, 6, 1799–1811; (e) Y. Shimizu and M. Kanai, Tetrahedron Lett., 2014, 55, 3727–3737.
- 3 The numbers of reports on "Argentate" vs. "Cuprate": 3760 vs. 97269, SciFinder®, Jan 1st 2020.
- 4 R. D. Rieke, D. E. Stack, B. T. Dawson and T.-C. Wu, *J. Org. Chem.*, 1993, **58**, 2483–2491.
- 5 P. Vanýsek, in *CRC Handbook of Chemistry and Physics*, ed. D. W. H. Lide, CRC Press, Boca Raton, 89th edn, 2005, pp. 8-20-8-29.
- 6 A. A. Frost, J. Am. Chem. Soc., 1951, 73, 2680-2682.
- 7 While hydroboration of alkynes *via* borylargentation has been developed by Yoshida and coworkers, this reaction mode is still rare for silver. See: (a) H. Yoshida, I. Kageyuki and K. Takaki, *Org. Lett.*, 2014, **16**, 3512–3515. Tyrra and Naumann revealed fluoroargentation and halogen-metal exchange of extremely electron deficient substrates, see: (b) W. Tyrra and D. Naumann, *J. Fluorine Chem.*, 2004, **125**, 823–830. Seminal work on carboargentation across conjugated triple bonds was reported by Vermeer, see: (c) H. Kleijn, M. Tigchelaar, J. Meijer and P. Vermeer, *Recl. Trav. Chim. Pays-Bas*, 1981, **100**, 337–341 and references therein.
- 8 For the representative reports on the synthesis of organosilvers via transmetalation, see: (a) S. Weske, R. A. Hardin, T. Auth, R. A. J. O'Hair, K. Koszinowski and C. A. Ogle, Chem. Commun., 2018, 54, 5086-5089; (b) D. Joven-Sancho, M. Baya, A. Martín and B. Menjón, Chem.-Eur. J., 2018, 24, 13098-13101; (c) S. Martínez de Salinas, A. L. Mudarra, J. Benet-Buchholz, T. Parella, F. Maseras and M. H. Pérez-Temprano, Chem.-Eur. J., 2018, 11895-11898; (*d*) C. M. P. Kronenburg, J. T. B. H. Jastrzebski, J. Boersma, M. Lutz, A. L. Spek and G. van Koten, J. Am. Chem. Soc., 2002, 124, 11675-11683; (e) C.-S. Hwang and P. P. Power, J. Organomet. Chem., 1999, 589, 234-238; (f) T. Kauffmann, C. Neiteler and S. Robbe, Chem. Ber., 1992, 125, 2409-2418; (g) C. Eaborn, P. B. Hitchcock, J. D. Smith and A. C. Sullivan, J. Chem. Soc., Chem. Commun., 1984, 870-871; (h) J. Blenkers, H. K. Hofstee, J. Boersma and G. J. M. van der Kerk, J. Organomet. Chem., 1979, 168, 251-258; (i) H. K. Hofstee,

- J. Boersma and G. J. M. van der Kerk, *J. Organomet. Chem.*, 1978, 168, 241–249; (*j*) E. Krause and M. Schmitz, *Ber. Dtsch. Chem. Ges.*, 1919, 52, 2150–2164. Decarboxylative preparation of diphenyl argentate have been reported as well, see: (*k*) M. I. S. Röhr, J. Petersen, C. Brunet, R. Antoine, M. Broyer, P. Dugourd, V. Bonačić-Koutecký, R. A. J. O'Hair and R. Mitrić, *J. Phys. Chem. Lett.*, 2012, 3, 1197–1201. Deprotonative argentation in Pd-catalyzed cross-coupling system is also proposed, see: (*l*) M. D. Lotz, N. M. Camasso, A. J. Canty and M. S. Sanford, *Organometallics*, 2017, 36, 165–171; (*m*) S. Y. Lee and J. F. Hartwig, *J. Am. Chem. Soc.*, 2016, 138, 15278–15284; (*n*) D. Whitaker, J. Burés and I. Larrosa, *J. Am. Chem. Soc.*, 2016, 138, 8384–8387.
- 9 For a comprehensive review on DoM reactions, see: (a) J. Board, J. L. Cosman, T. Rantanen, S. P. Singh and V. Snieckus, *Platinum Met. Rev.*, 2013, 57, 234–258; (b) V. Snieckus and T. Macklin, in *Handbook of C-H Transformations: Applications in Organic Synthesis*, ed. G. Dyker, Wiley-VCH Verlag GmbH, Weinheim, Germany, 2008, vol. 1, pp. 106–115; (c) V. Snieckus, *Chem. Rev.*, 1990, 90, 879–933; (d) P. Beak and V. Snieckus, *Acc. Chem. Res.*, 1982, 15, 306–312. For stereo- and regiocontrolled deprotonative metalation of various types of C–H bonds by utilizing complex-induced proximity effects, see: (e) P. Beak and A. I. Meyers, *Acc. Chem. Res.*, 1986, 19, 356–363.
- 10 For a review on deprotonative metalation using metal amide bases, see: (a) F. Chevallier, F. Mongin, R. Takita and M. Uchiyama, in *Arene Chemistry*, ed. J. Mortier, John Wiley & Sons, Inc, Hoboken, New Jersey, 2015, pp. 777–812; (b) R. E. Mulvey, F. Mongin, M. Uchiyama and Y. Kondo, *Angew. Chem., Int. Ed.*, 2007, 46, 3802–3824.
- 11 Cyanide anion should play an important roll in the deprotonation step rather than the iodination step (Scheme S1†).
- 12 CuCN 0.84 USD per mmol (47.00 USD per 5 g) vs. AgCN 0.85 USD per mmol (63.80 USD per 10 g) at Sigma-Aldrich, Nov. 27th 2019.
- 13 Hydride elimination from ⁱPr₂N anion might account for the low reactivity of the corresponding amidoargentate, see: B.-A. Feit, S. Shapira and A. Herbst, *Tetrahedron*, 1995, 51, 317–328.
- 14 Cy₂NH (0.051 USD per mmol; 27.90 USD per 100 g) is less expensive than TMPH (0.72 USD per mmol; 128.00 USD per 25 g) at Sigma-Aldrich, Nov. 27th 2019. Knochel discussed this issue: (a) M. R. Becker and P. Knochel, *Org. Lett.*, 2016, **18**, 1462–1465; (b) M. R. Becker, M. A. Ganiek and P. Knochel, *Chem. Sci.*, 2015, **6**, 6649–6653.
- 15 (a) S. Usui, Y. Hashimoto, J. V. Morey, A. E. H. Wheatley and M. Uchiyama, J. Am. Chem. Soc., 2007, 129, 15102–15103; (b)
 N. Tezuka, K. Shimojo, K. Hirano, S. Komagawa, K. Yoshida, C. Wang, K. Miyamoto, T. Saito, R. Takita and M. Uchiyama, J. Am. Chem. Soc., 2016, 138, 9166–9171.
- 16 The inability to metalate **1a** in dioxane might be attributed to undesired reaction of the putative argentate with dioxane. For related work, see: J. García-Álvarez, E. Hevia,

- A. R. Kennedy, J. Klett and R. E. Mulvey, *Chem. Commun.*, 2007, 2402–2404.
- 17 THF was included while the crude 3 was processed in THF prior to recrystallization from hexane/toluene. For details, see ESL†
- 18 A. J. Peel, N. Tezuka, J. M. D'Rozario, M. Uchiyama and A. E. H. Wheatley, *Chem. Sci.*, 2019, **10**, 3385–3400.
- 19 The excellent compatibility of DoAg with nucleophile-sensitive AFGs such as ethyl and methyl esters and aldehyde (Table 2, 2g, 2h and 2u) rules out the formation of arylllithium. For the condensation of *ortho*-lithiated benzoates, see: (a) T. D. Krizan and J. C. Martin, *J. Am. Chem. Soc.*, 1983, 105, 6155–6157; (b) C. J. Upton and P. Beak, *J. Org. Chem.*, 1975, 40, 1094–1098; (c) W. E. Parham and Y. A. Sayed, *J. Org. Chem.*, 1974, 39, 2053–2056.
- 20 J. A. Garden, D. R. Armstrong, W. Clegg, J. García-Alvarez, E. Hevia, A. R. Kennedy, R. E. Mulvey, S. D. Robertson and L. Russo, *Organometallics*, 2013, 32, 5481–5490.
- 21 SF₅ (super trifluoromethyl) is an attractive functional group. Its chemical and physical properties are receiving increasing attention in the pharmaceutical sciences, see: Fluorine in Pharmaceutical and Medicinal Chemistry, Molecular Medicine and Medicinal Chemistry, ed. V. Gouverneur and K. Müller, Imperial College Press, Covent Garden, London, 2012.
- 22 NBO analysis by modeled DFT calculation estimates that the lithium argentate derived from PhSF₅ has a strong interaction between Li and F (10.2 kcal mol^{-1}), while PhCF₃ has a moderate Li–F interaction (6.1 kcal mol^{-1}) (see ESI†).
- 23 (a) G. Bartoli, R. Dalpozzo and M. Nardi, Chem. Soc. Rev., 2014, 43, 4728-4750; (b) M. Makosza, Chem.-Eur. J., 2014, 20, 5536-5545.
- 24 (a) W. C. Black, B. Guay and F. Scheuermeyer, J. Org. Chem.,
 1997, 62, 758–760; (b) S. H. Wunderlich and P. Knochel,
 Angew. Chem., Int. Ed., 2007, 46, 7685–7688; (c) T. Bresser,
 G. Monzon, M. Mosrin and P. Knochel, Org. Process Res.
 Dev., 2010, 14, 1299–1303.
- 25 S. P. Shahi and K. Koide, *Angew. Chem., Int. Ed.*, 2004, **43**, 2525–2527.
- 26 K. Murakami, K. Hirano, H. Yorimitsu and K. Oshima, *Angew. Chem., Int. Ed.*, 2008, 47, 5833–5835.
- 27 W. Nakanishi, M. Yamanaka and E. Nakamura, *J. Am. Chem. Soc.*, 2005, **127**, 1446–1453.
- 28 (a) G. De Martino, G. La Regina, A. Coluccia, M. C. Edler, M. C. Barbera, A. Brancale, E. Wilcox, E. Hamel, M. Artico and R. Silvestri, J. Med. Chem., 2004, 47, 6120-6123; (b) G. Liu, J. R. Huth, E. T. Olejniczak, R. Mendoza, P. DeVries, S. Leitza, E. B. Reilly, G. F. Okasinski, S. W. Fesik and T. W. von Geldern, J. Med. Chem., 2001, 44, 1202-1210; (c) A. Marcincal-Lefebvre, J. C. Gesquiere, C. Lemer and B. Dupuis, J. Med. Chem., 1981, 24, 889-893.
- 29 Several diaryl disulfide syntheses *via* the reaction of diaryl disulfide and either aryl lithium or aryl Grignard reagents have been reported, see: Li: (*a*) G. D. Figuly and J. C. Martin, *J. Org. Chem.*, 1980, 45, 3728–3729; (*b*) J. M. Muchowski and M. C. Venuti, *J. Org. Chem.*, 1980, 45,

Edge Article

4798-4801. Mg: (c) B.-X. Du, Z.-J. Quan, Y.-X. Da, Z. Zhang and X.-C. Wang, Adv. Synth. Catal., 2015, 357, 1270-1276.

- 30 Knochel and co-workers recently reported diaryl sulfide synthesis utilizing aromatic zinc reagents, see; Z.-B. Dong, M. Balkenhohl, E. Tan and P. Knochel, Org. Lett., 2018, 20, 7581-7584.
- 31 H. A. Stefani, J. M. Pena, F. Manarin, R. A. Ando, D. M. Leal and N. Petragnani, Tetrahedron Lett., 2011, 52, 4398-4401.
- 32 Diazo Chemistry I, ed. H. Zollinger, VCH Verlagsgesellschaft mbH, Weinheim, 1994.
- 33 (a) Y. Takeda, S. Okumura and S. Minakata, Synthesis, 2013, 45, 1029-1033; (b) Y. Takeda, S. Okumura and S. Minakata, Angew. Chem., Int. Ed., 2012, 51, 7804-7808.