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Stereospecific Protodeauration/Transmetalation Generating Configurationally Stable P-Metalated Nucleoside Derivatives

Marcia E. Richard, Rosa M. Ciccarelli, Kevin J. Garcia, Erica J. Miller, Stephanie L. Casino, Robert. D. Pike, and Robert A. Stockland Jr*

Abstract: *Highly efficient transmetalation between gold phosphites and iodopalladium species is presented. In addition to successful transfer of cyclic and acyclic phosphites, studies involving P-chiral substrates revealed that an initial protodeauration as well as the target transmetalation were both stereospecific, and that the overall process occurred with retention of configuration at phosphorus. Building on the mechanistic work, a catalytic approach to the synthesis of chiral P-arylated nucleoside derivatives was developed. This chemistry has the potential to be easily adapted for the preparation of a diverse group of P-chiral species.*

The transfer of organic fragments between metal centers along with the concomitant exchange of a ligand such as a halogen (transmetalation) remains a key step in many catalytic transformations as well as the construction of discrete organometallic species. Main group organometallics such as organoboron reagents[1] along with tin and zinc compounds[2] have been among the most common transmetalating agents used in these reactions. Recently, organogold complexes have received significant attention,[3, 4] and a number of mechanistic and catalytic investigations have been reported demonstrating that gold is an effective transmetalating agent for a number of other metals including Pd,[4] Fe,[5] Ru,[5] Sn,[6] Rh,[7] Ni, and others.[8, 9] A subtle balance of electronic and steric factors controls the direction of transmetalation, and the reverse reaction has been observed[10] with boron[11, 12] and transition metals including Pd,[13] Cu,[14, 15] Rh,[16] Sn,[17] and Zr.[18]

The mechanistic and catalytic studies involving gold-based transmetalating agents have focused on carbon bound fragments and little attention has been given to the transfer of functional groups that were attached to the gold through a heteroatom such as phosphorus. For [M](P(O)(OR)$_2$) species, there are additional complications that must be taken into account when predicting reactivity patterns. Descriptions of the bonding, solution speciation, as well as their reactivity with other metals can be quite complex.[19] Even simple classification of the [P(O)(OR)$_2$]$^-$ group as a X or L type ligand[20a] can be challenging (Figure 1).

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For P-metallated examples, the [P(O)(OR)$_2$]$^-$ group can be described as either an P(III) *O*-anionic phosphito or a P(V) phosphonato ligand (Figure 1).[19] These rigid explanations define the ends of the continuum, and many M[P(O)(OR)$_2$] species are likely to reside between these extremes. Spectroscopic evidence (^{31}P NMR, *vide infra*) as well as a recent computational study suggest that the metal-phosphorus bonding is often more consistent with the former (L-type ligand).[20]

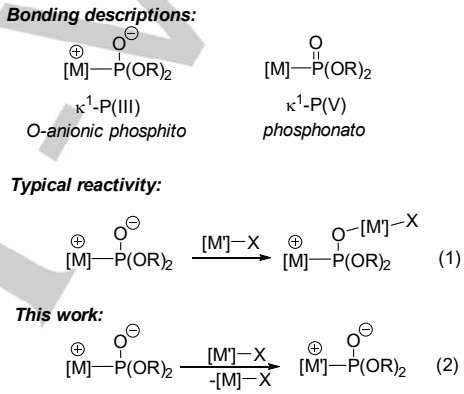


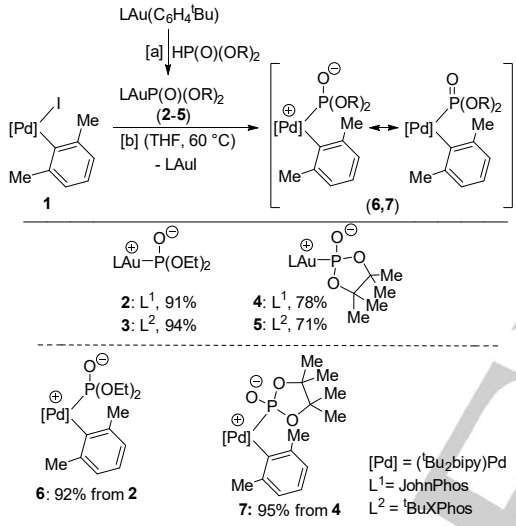
Figure 1. Descriptions for [M](P(O)(OR)$_2$) species and their reactivity.

In terms of their reactivity, coordination of the oxygen from the P-O$^-$ fragment to a second metal center dominates the reactivity between organophosphonate and [M](P(O)(OR)$_2$) species with additional metal complexes (eqn 1, Scheme 1).[21-26] Kläui-type metalloligands remain some of the most well studied examples of this class and provide an all oxygen donor environment for a host of metal centers.[27-30] While the metal-phosphorus bond in Kläui ligands and other [M](P(O)(OR)$_2$) species is typically robust, cleavage of these bonds in suitably functionalized substrates can be remarkably facile.[31-33] Interest in this alternate reactivity has been driven by a need to understand and predict the reactivity of key intermediates in metal catalyzed P-C bond forming reactions.[34-37]

The ability to transfer the [P(O)(OR)$_2$]$^-$ group from one metal to another is the subject of this work. Upon successful transfer, the [P(O)(OR)$_2$]$^-$ fragment can attach to the new metal through phosphorus or as a κ^1-*O*-phosphite. To expose the reaction pathways between gold and palladium, the reactivity of discrete gold complexes bearing [P(O)(OR)$_2$]$^-$ groups with representative iodopalladium precursors has been studied.

The initial studies utilized the iodopalladium complex (**1**) and (JohnPhos)Au(P(O)(OEt)$_2$) (**2**) as representative substrates (Scheme 1).[32, 38] Although **2** could be accessed from alkyl[39] or

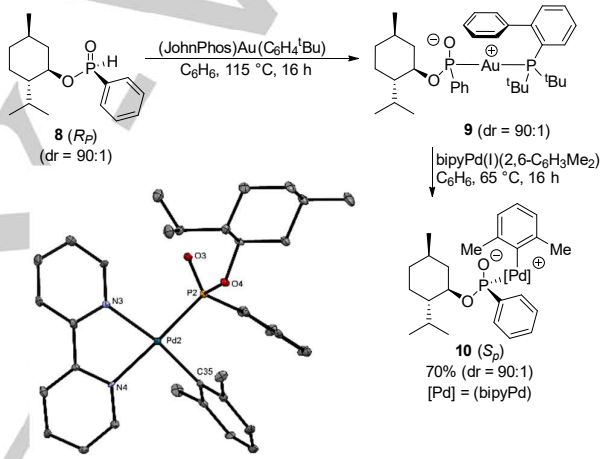
alkynylgold[38] precursors, we found that arylgold species were superior. The bulky dialkylbiaryl phosphine ligand (L^1) was used as the supporting ligand on the gold center to inhibit dynamic processes[40] and generate a single species in solution.[38] In terms of the bonding description for **2**, the ^{31}P chemical shift for the $[P(O)(OEt)_2]^-$ group in **2** (δ = 111.4)[38] is shifted over 100 ppm downfield from $HP(O)(OEt)_2$, and is in the range of simple phosphite gold complexes such as $((MeO)_3P)AuCl$[41] (δ = 121.0) and $((PhO)_3P)AuCl$[42] (δ = 109.7) . Indeed the chemical shift of **2** is further downfield than $((MeO)_2(OH)P)AuCl$[40] (δ = 109.7). This phosphinous acid complex was generated through displacement of dimethylsulfide from Me_2SAuCl by the phosphite tautomer of $HP(O)(OMe)_2$. This suggests that the bonding of the $[P(O)(OEt)_2]^-$ group **2** is consistent with the *O*-anionic P(III) phosphito description (Figure 1).



Scheme 1. Protodeauration/transmetalation.[c] Reaction conditions: [a]$LAuC_6H_4{}^tBu$ (0.22-0.27 M sol. in THF) and $HP(O)(OR)_2$ (1 equiv for R = Et, 1.5 equiv for R = Pin), 60 °C, 16 h. [b] **2-5** (0.13-0.16 M sol. in THF) and **1** (1 equiv), THF, 60 °C, 12-16 h. [c] isolated yields.

Stirring a solution of **1** with **2** (THF, 60 °C) cleanly generated P-palladated **6** in high yield along with (JohnPhos)AuI. Monitoring this reaction by ^{31}P NMR spectroscopy showed gradual loss of the signals for **1** and **2** along with growth of the signals for **6** (^{31}P δ = 71.2) and (JohnPhos)AuI (^{31}P δ = 65.3). No oxygen coordination or bridged species were detected by NMR spectroscopy. The ^{31}P chemical shift of the $[P(O)(OEt)_2]^-$ fragment in **6** is ~40 ppm upfield relative to **2**, suggesting the possibility of increased contribution from the κ^1-P(V) phosphonato form. Thus, the bonding in **6** could lie between the two extremes listed in Scheme 1. Thankfully, transmetalation between **1** and **2** was fast relative to reductive elimination from **6**, and no traces of reductive elimination products were detected. Building on this observation, the chemistry was successfully extended to cyclic secondary phosphites. The transmetalation was sensitive to the steric bulk of the phosphine ligand on the gold phosphite as **2** and **4** reacted with **1** faster than **3** or **5**. Furthermore, the reaction was not reversible under these conditions (*see supporting information*).

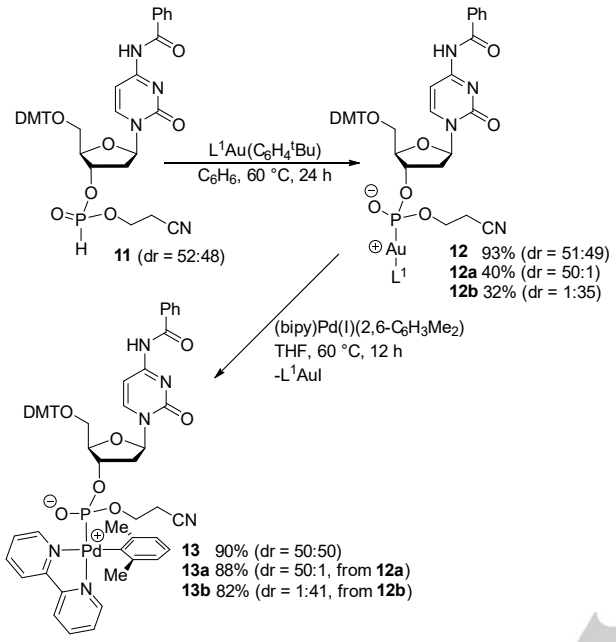
To assess the stereochemical outcome of the process, (R_P)(-) menthyl phenylphosphinate (**8**) was generated and screened (Scheme 2).[43-45] The protodeauration between **8** and $JohnPhosAu(C_6H_4{}^tBu)$ was stereospecific and cleanly generated the gold phosphinate intermediate as a configurationally stable single diastereomer (**9**) (^{31}P δ = 114.3, 67.0, J_{PP} = 396.8 Hz). Similar to **2**, the ^{31}P chemical shift of the $[P(O)R_2]^-$ fragment in **9** is indicative of an *O*-anionic phosphito ligand. The transmetalation between $(bipy)Pd(2,6\text{-}C_6H_3Me_2)I$ and **9** was also stereospecific and generated the palladium complex **10** as a single diastereomer (^{31}P δ = 79.0). The transformation of **8** into **10** could be carried out in steps or as a one-pot process (Scheme 2). X-ray quality crystals of **10** were grown and analysis of the structure revealed an S_P configuration at phosphorus.[46] Thus, the overall protodeauration/transmetalation process was stereospecific and proceeded with a net retention of configuration at phosphorus.



Scheme 2. Stereospecific protodeauration/transmetalation using a P-Chiral menthyl phosphinate. Reaction conditions for step 1: $LAuC_6H_4{}^tBu$ (0.13 M sol. in C_6H_6) and **8** (1 equiv), 115 °C, 16 h. Step 2: $(bipy)Pd(2,6\text{-}C_6H_3Me_2)I$ (1 equiv) was added (65 °C, 16 h). Yields are based upon isolated material, and the diastereomeric ratios were determined using ^1H NMR spectroscopy. Molecular structure of **10** (S_P) with thermal ellipsoids at 50% and hydrogens omitted.

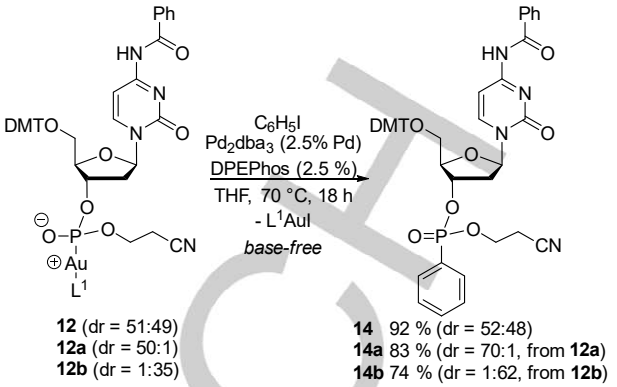
Due to their importance in medicine and chemical biology, significant effort has been devoted to designing and synthesizing new functionalized nucleosides.[47] While metalation of nucleoside purine and pyrimidine bases is common, metalation at phosphorus is remarkably rare.[48] To this end, we surmised that a nucleoside derived secondary phosphite (**11**) would be a convenient entry point for the metalation chemistry. Indeed, protodeauration of $JohnPhosAu(C_6H_4{}^tBu)$ by **11** (dr = 52:48) generated the P-metallated gold complex (**12**, dr = 51:49, Scheme 3). As a consequence of the methodology used for the synthesis of **11**,[49] a mixture of diastereomers was generated due to the presence of the unresolved phosphorus center. Separation of the diastereomers of **11** prior to the protodeauration step was challenging; however, the metalated species (**12**) were separable[50] and found to be configurationally stable in solution. Transmetalation between **12** (dr = 51:49) and $bipyPd(2,6\text{-}C_6H_3$

Me_2)I successfully generated the palladium nucleoside (**13**) (dr = 50:50) as well as JohnPhosAuI. This process was also stereospecific as single diastereomers of **13** (**13a** and **13b**) were generated using **12a** and **12b**.



Scheme 3. Stereospecific protodeauration/transmetalation. Reaction conditions: Preparation of **12**: $LAuC_6H_4{}^tBu$ (0.27 M sol. in THF) and **11** (1 equiv) were heated at 60 °C for 24 h. Preparation of **13**: **12** (0.08 M sol. in THF) and (bipy)Pd(2,6-$C_6H_3Me_2$)I (1.1 equiv) were heated at 60 °C for 12 h. Yields are based upon isolated material, and the diastereomeric ratios were determined using ^{1}H NMR spectroscopy.

Building on the mechanistic work, a base-free stereospecific cross-coupling for the preparation of P-arylated nucleosides was devised (Scheme 4). Historically, these base-assisted P-C bond forming reactions have been challenging to extend to these substrates due to the sensitivity of the cyanoethyl protecting group to the amine or mineral bases typically used in coupling reactions.[51] Furthermore, the acid generated in the cross-coupling reaction cannot simply be ignored due to the acid sensitivity of the trityl protecting group. A recent solution to this problem entailed the use of an epoxide as an HX scavenger.[49, 52] For the chemistry described herein, using **12** as the $[P(O)(OR)_2]^-$ source alleviates the need for additives since the Au/Pd transmetalation generates the requisite palladium phosphite intermediate directly. A ligand screening study was used to identify an effective catalyst system (*see SI*).[31][53] It should be noted that the gold was not sacrificial and could be readily recovered as JohnPhosAuI. The catalytic process was stereospecific and generated single diastereomers of the P-arylated nucleoside derivative when the metalated nucleosides (**12a** and **12b)** were used. This is a valuable method for the stereospecific synthesis of P-C bonds due to its mild conditions and tolerance of sensitive protecting groups.



Scheme 4. Base-free stereospecific P-arylation. Reaction conditions: **12** (0.08 M sol. in THF), iodobenzene (1.1 equiv), Pd_2dba_3 (2.5% Pd), and DPEPhos (2.5%) were heated at 70 °C for 18 h. Yields are based upon isolated material, and the diastereomeric ratios were determined using ^{1}H NMR spectroscopy.

In summary, the transmetalation between P-metalated phosphites and iodopalladium precursors was found to be quite facile. The gold and palladium species presented herein could represent different regions of the $[P(O)(OR)_2]^-$ bonding continuum. Despite these differences, stereochemical studies using P-chiral substrates revealed that the protodeauration and transmetalation reactions were both stereospecific, and the overall process occurred with retention of configuration at phosphorus. Building upon this, the preparation of chiral P-arylated nucleosides was devised. This method has the potential to be easily adapted to the preparation of a diverse group of P-chiral species. A strength of this approach is the tolerance of process to both acid and base sensitive functional groups. Future work will focus on extending the scope of the P-C bond forming reaction and investigating further applications of P-metallated nucleosides.

Acknowledgements

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Keywords: Gold • palladium • phosphonate • stereospecific • protodeauration

[1] A. J. J. Lennox, G. C. Lloyd-Jones, *Angew. Chem. Int. Ed.* **2013**, *52*, 7362-7370.
[2] J. Choi, G. C. Fu, *Science* **2017**, *356,* 152-160.
[3] M. Joost, A. Amgoune, D. Bourissou, *Angew. Chem. Int. Ed.* **2015**, *54*, 15022-15045. M. Joost, A. Amgoune, D. Bourissou, *Angew. Chem.* **2015**, *127*, 15234-15258.
[4] J. J. Hirner, Y. Shi, S. A. Blum, *Acc. Chem. Res.* **2011**, *44*, 603-613.
[5] A. S. K. Hashmi, L. Molinari, *Organometallics* **2011**, *30*, 3457-3460.

[6] Y. Chen, M. Chen, Y. Liu, *Angew. Chem. Int. Ed.* **2012**, *51*, 6181-6186. Y. Chen, M. Chen, Y. Liu, *Angew. Chem.* **2012**, *124,* 6285-6290.
[7] Y. Shi, S. A. Blum, *Organometallics* **2011**, *30*, 1776-1779.
[8] W. M. Khairul, M. A. Fox, N. N. Zaitseva, M. Gaudio, D. S. Yufit, B. W. Skelton, A. H. White, J. A. K. Howard, M. I. Bruce, P. J. Low, *Dalton Trans.* **2009**, 610-620.
[9] M. Contel, M. Stol, M. A. Casado, G. P. M. van Klink, D. D. Ellis, A. L. Spek, G. van Koten, *Organometallics* **2002**, *21*, 4556-4559.
[10] K. Osakada, T. Yamamoto, *Coord. Chem. Rev.* **2000**, *198*, 379-399.
[11] J. J. Hirner, S. A. Blum, *Tetrahedron* **2015**, *71*, 4445-4449.
[12] E. Chong, S. A. Blum, *J. Am. Chem. Soc.* **2015**, *137*, 10144-10147.
[13] A. Toledo, I. Meana, A. C. Albéniz, *Chem. -Eur. J.* **2015**, *21*, 13216-13220.
[14] K. Osakada, R. Sakata, T. Yamamoto, *J. Chem. Soc. Dalton Trans.* **1997**, 1265-1266.
[15] K. Osakada, M. Hamada, T. Yamamoto, *Organometallics* **2000**, *19*, 458-468.
[16] C. Werlé, R. Goddard, A. Fürstner, *Angew. Chem. Int. Ed.* **2015**, *54*, 15452-15456. C. Werlé, R. Goddard, A. Fürstner, *Angew. Chem.* **2015**, *127*, 15672-15676.
[17] E. S. Borren, A. F. Hill, R. Shang, M. Sharma, A. C. Willis, *J. Am. Chem. Soc.* **2013**, *135*, 4942-4945.
[18] T. P. Cornell, Y. Shi, S. A. Blum, *Organometallics* **2012**, *31*, 5990-5993.
[19] P. Sutra, A. Igau, *Coord. Chem. Rev.* **2016**, *308*, 97-116.
[20] a. M. L. H. Green, *J. Organomet. Chem.* **1995**, *500*, 127-148. E. Lebon, R. Sylvain, R. E. Piau, C. Lanthony, J. Pilme, P. Sutra, M. Boggio-Pasqua, J.-L. Heully, F. Alary, A. Juris, A. Igau, *Inorg. Chem.* **2014**, *53*, 1946-1948.
[21] K. J. Gagnon, H. P. Perry, A. Clearfield, *Chem. Rev.* **2012**, *112*, 1034-1054.
[22] G. K. H. Shimizu, R. Vaidhyanathan, J. M. Taylor, *Chem. Soc. Rev.* **2009**, *38*, 1430-1449.
[23] S.-S. Bao, L.-M. Zheng, *Coord. Chem. Rev.* **2016**, *319*, 63-85.
[24] T. Schrader, *J. Inclusion Phenom. Macrocyclic Chem.* **1999**, *34*, 117-129.
[25] T.-Y. Ma, Z.-Y. Yuan, *Chemsuschem.* **2011**, *4*, 1407-1419.
[26] I. Kuzu, I. Krummenacher, J. Meyer, F. Armbruster, F. Breher, *Dalton Trans.*, **2008**, 5836.
[27] W. -H. Leung, Q.-F. Zhang, X.-Y. Yi, *Coord. Chem. Rev.* **2007**, *251*, 2266-2279.
[28] W. Kläui, H. Neukomm, H. Werner, G. Huttner, *Chem. Ber.* **1977**, *110*, 2283-2289.
[29] W. Kläui, *Angew. Chem. Int. Ed.* **1990**, *29,* 627-637. W. Kläui, *Angew. Chem.* **1990**, *102*, 661-670.
[30] V. M. Krishnan, H. D. Arman, Z. J. Tonzetich, *Dalton Trans.* **2017**, *46*, 1186-1193.
[31] M. C. Kohler, T. V. Grimes, X. Wang, T. R. Cundari, R. A. Stockland Jr., *Organometallics* **2009**, *28*, 1193-1201.
[32] M. C. Kohler, R. A. Stockland Jr., N. P. Rath, *Organometallics* **2006**, *25*, 5746-5756.
[33] M. Kalek, J. Stawinski, *Organometallics* **2007**, *26*, 5840-5847.
[34] F. M. J. Tappe, V. T. Trepohl, M. Oestreich, *Synthesis* **2010**, 3037-3062.
[35] I. P. Beletskaya, M. A. Kazankova, *Russ. J. Org. Chem.* **2002**, *38*, 1391-1430.
[36] C. Queffelec, M. Petit, P. Janvier, D. A. Knight, B. Bujoli, *Chem. Rev.* **2012**, *112*, 3777-3807.
[37] C. S. Demmer, N. Krogsgaard-Larsen, L. Bunch, *Chem. Rev.* **2011**, *111*, 7981-8006.
[38] G. F. Manbeck, M. C. Kohler, M. R. Porter, R. A. Stockland Jr., *Dalton Trans.* **2011**, *40*, 12595-12606.
[39] C. Hollatz, A. Schier, H. Schmidbaur, *Chem. Ber.* **1997**, *130*, 1333-1338.
[40] C. Hollatz, A. Schier, H. Schmidbaur, *Inorg. Chim. Acta* **2000**, *300-302*, 191-199.
[41] C. E. Strasser, S. Cronje, H. Schmidbaur, H. G. Raubenheimer, *J. Organomet. Chem.* **2006**, *691*, 4788-4796.
[42] A. Leyva-Perez, J. R. Cabrero-Antonino, A. Cantin, A. Corma, *J. Org. Chem.* **2010**, *75*, 7769.
[43] a) T. L. Emmick, R. L. Letsinger, *J. Am. Chem. Soc.* **1968**, *90*, 3459–3465. b) W. B. Farnham, R. K. Murray, K. Mislow, *J. Am. Chem. Soc.* **1970**, *92*, 5809–5810.
[44] For recent reports on the synthesis of **8** and related compounds see: a) W.-M. Wang, L.-J. Liu, C.-Q. Zhao, L.-B. Han, *Eur. J. Org. Chem.* **2015**, *2015*, 2342-2345. b) R. Bigler, A. Mezzetti, *Org. Process Res. Dev.* **2016**, *20*, 253-261. c) O. Berger and J.-L. Montchamp *Org. Biomol. Chem.* **2016**, *14*, 7552-7562. d) D. Gatineau, L. Giordano, G. Buono *J. Am. Chem. Soc.* **2011**, *133*, 10728-10731. For recent reports on the use of **8** and related compounds in stereospecific functionalizations see: e) Q. Xu, C.-Q. Zhao, L.-B. Han, *J. Am. Chem.Soc.* **2008**, *130*, 12648-12655; f) L.-B. Han, C.-Q. Zhao, *J. Org. Chem.* **2005**, *70*, 10121-10123; g) G. Wang, R. Shen, Q. Xu, M. Goto, Y. Zhao, L.-B. Han, *J. Org. Chem.* **2010**, *75*, 3890-3892; h) Y. Zhou, G. Wang, Y. Saga, R. Shen, M. Goto, Y. Zhao, L.-B. Han, *J. Org. Chem.* **2010**, *75*, 7924-7927. i) O. I. Kolodiazhnyi, A. Kolodiazhna, *Tetrahedron: Asymmetry* **2017**, *28*, 1651-1674. j) O. Berger and J.-L. Montchamp, *Angew. Chem. Int. Ed.* **2013**, *52*, 11377-11380. k) O. Berger and J.-L. Montchamp *Angew. Chem.* **2013**, *125*, 11587-11590. l) L.-J. Liu, W.-M. Wang, L. Yao, F.-J. Meng, Y.-M. Sun, H. Xu, Z.-Y. Xu, Q. Li, C.-Q. Zhao, L.-B. Han, *J. Org. Chem.* **2017**, *82*, 11990-12002.
[45] Han has studied the oxidative addition of **8** and related compounds to low valent metal centers and found that the process occurs with retention of stereochemistry. a) L. -B. Han, C. -Q. Zhao, S. -Y. Onozawa, M. Goto, M. Tanaka, *J. Am. Chem. Soc.* **2002**, *124*, 3842-3843. b) J. Yang, T. Chen, Y. Zhou, S.-F. Yin, L.-B. Han, *Organometallics*, **2015**, *34*, 5095-5098.
[46] CCDC 1823878 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.
[47] a) The compounds presented herein are labelled as nucleosides instead of nucleotides since they do not contain a formal phosphate group. b). D. A. DiRocco, Y. Ji, E. C. Sherer, A. Klapars, M. Reibarkh, J. Dropinski, R. Mathew, P. Maligres, A. M. Hyde, J. Limanto, A. Brunskill, R. T. Ruck, L.-C. Campeau, I. W. Davies, *Science*, **2017**, *356*, 426-430.
[48] a) R. T. Dalla, D. E. Bergstrom, *J. Org. Chem.* **1994**, *59*, 2418-2422. b) O. Pav, M. H. Caruthers, *Tetrahedron Lett.* **2009**, *50*, 5015-5017.
[49] S. Abbas, R. D. Bertram, C. J. Hayes, *Org. Lett.* **2001**, *3*, 3365-3367.
[50] We recently reported the separation of phosphoramidite diastereomers using a similar metalation approach. E. J. Miller, K. J. Garcia, E. C. Holahan, R. M. Ciccarelli, R. A. Bergin, S. L. Casino, T. L. Bogaczyk, M. R. Krout, P. M. Findeis, R. A. Stockland Jr., *Inorg. Chem.* **2014**, *53*, 12680-12682.
[51] For P-arylation reactions involving nucleoside derivatives lacking the cyanoethyl protecting group see: a) M. Kalek, A. Ziadi, J. Stawinski *Org. Lett.* **2008**, *10*, 4637-4640. b) M. Kalek, M. Jezowska, J. Stawinski *Adv. Synth. Cat.* **2009**, *351*, 3207-3216.
[52] S. Abbas, C. J. Hayes, *Tetrahedron Lett.* **2000**, *41*, 4513-4517.
[53] T. Hirao, T. Masunaga, Y. Ohshiro, T. Agawa, *Synthesis* **1981**, 56-57.

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Layout 2:

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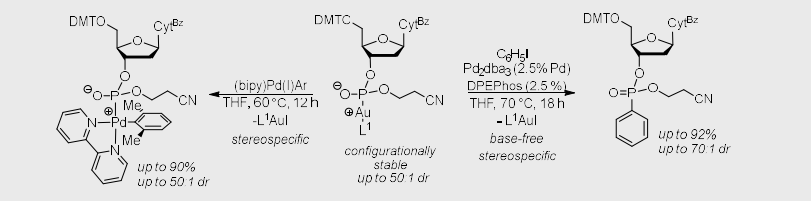

A stereospecific protodeauration/transmetalation sequence facilitated the synthesis of configurationally stable P-metalated species. Mechanistic studies using model systems revealed the overall process to occur with *retention of stereochemistry*. This methodology was adapted for the synthesis of chiral P-arylated nucleoside derivatives.

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