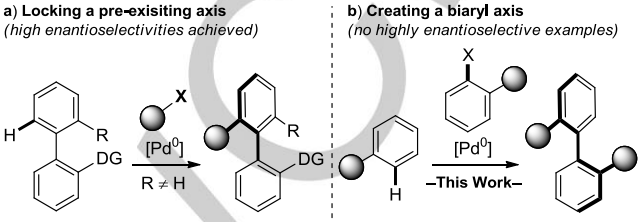
Axially Chiral Dibenzazepinones *via* a Pd(0)–Catalyzed Atropo-enantioselective C–H Arylation

Christopher G. Newton,[a] Elena Braconi,[a],‡ Jennifer Kuziola,[a],‡ Matthew D. Wodrich[b] and Nicolai Cramer[a]*

Abstract: Atropo-enantioselective C–H functionalization reactions are largely limited to the dynamic kinetic resolution of biaryl substrates through the introduction of steric bulk proximal to the axis of chirality. Herein we report a highly atropo-enantioselective palladium(0)-catalyzed methodology that forges the axis of chirality during the C–H functionalization process, enabling the synthesis of axially chiral dibenzazepinones. Computational investigations support experimentally determined racemization barriers, while also indicating C–H functionalization proceeds via an enantio-determining CMD to yield configurationally stable 8-membered palladacycles.

A wide range of natural products[1] and pharmaceuticals[2] exhibit restricted rotation about a biaryl axis, often resulting in differences in biological activity between each stereoisomer. This stereogenic element is also immensely important in the field of asymmetric catalysis, where it commonly serves as the sole source of enantiocontrol.[3] Surprisingly, relatively few atropo-enantioselective approaches towards axially chiral biaryls from achiral precursors have been reported. The most common strategies include biaryl desymmetrization, *de novo* synthesis of an aromatic ring, *in-situ* point-to-axial chirality transfer, or transition-metal catalyzed cross-coupling of functionalized organometallics.[4] Enantioselective C–H functionalization reactions have emerged as a powerful tool for the rapid generation of structural complexity.[5] Within this field, high levels of enantiocontrol have been demonstrated for the synthesis of both point, and planar chiral molecules, across several mechanistically disparate processes.[5e] However, atropo-enantioselective approaches towards axially chiral molecules remain rare, likely as a result of competitive racemization under the typically elevated reaction temperatures. Nevertheless, a small number of examples have been reported, mainly proceeding *via* directed C–H functionalization *ortho* to a preformed biaryl axis (Scheme 1a).[6,7] In contrast, effective control of atropo-enantioselectivity, whilst simultaneously forging the axis of chirality, appears inherently more challenging (Scheme 1b).[8–10] To date, only two substrates have been prepared under Pd catalysis *via* this approach (72 % ee and 27 % yield).[8]



Scheme 1. Palladium-catalyzed atropo-enantioselective C–H functionalization strategies towards axially chiral biaryls.

Our laboratory has a long-standing interest in the development and application of chiral ligand families, particularly for enantioselective C–H functionalization.[11] Recent reports have demonstrated that under Pd(0)/Pd(II) catalysis, TADDOL-derived phosphorus(III) ligands can facilitate C–H functionalization under very mild conditions.[6b,12,13] Given these advancements, coupled with the importance of biaryl atropisomers, we became interested in the development of atropo-enantioselective C–H arylation strategies for the synthesis of configurationally sensitive targets. In particular, axially chiral dibenzazepinones represent an underexplored pharmacophore, especially when considering the prevalence of related benzazepinone and dibenzodiazepine containing drugs.[14] Although both achiral and point chiral dibenzazepinones with potent biological activity are known (Figure 1),[15] enantioselective routes towards derivatives bearing exclusively an axis of chirality have yet to be disclosed.[16] Herein we report the realization of such a strategy via a palladium(0)-catalyzed intramolecular C–H arylation of achiral amides.

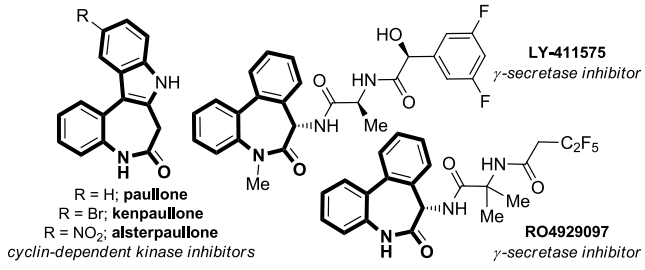


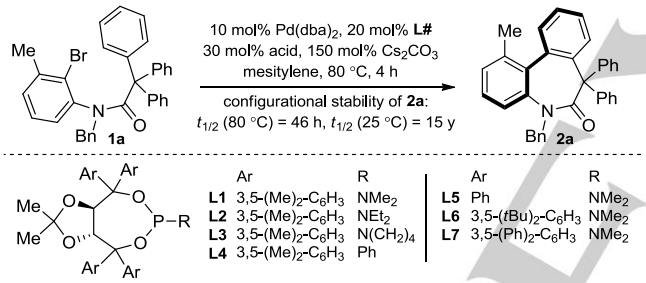
Figure 1. Biologically active dibenzazepinones.

Early scouting experiments in the laboratory were guided by computational prediction of product racemization kinetics. Ultimately, amide **1a** bearing a methyl substituent *ortho* to the aryl-bromide functionality was identified as a promising lead for intramolecular cyclization (Table 1). Despite the sterically crowded nature of the reaction center, dibenzazepinone **2a**

[a] Dr. C. G. Newton, E. Braconi, J. Kuziola, Prof. Dr. N. Cramer
Laboratory of Asymmetric Catalysis and Synthesis
EPFL SB ISIC LCSA, BCH 4305
1015 Lausanne (Switzerland)
E-mail: nicolai.cramer@epfl.ch
Homepage: http://isic.epfl.ch/lcsa
[b] Dr. M. D. Wodrich
Laboratory for Computational Molecular Design
EPFL SB ISIC LCMD, BCH 5121
1015 Lausanne (Switzerland)
[‡] These authors contributed equally to this work.

could be accessed in good yield and enantioenriched form after heating in the presence of a palladium(0) source, and TADDOL-derived phosphoramidite **L1** (er 74:26, entry 1). Given the potential for erosion of enantiopurity over the course of reaction (half-life of **2a** determined to be 46 hours at 80 °C), optimization studies were conducted with incomplete conversion to compare reaction rates. Initial ligand screening focused on phosphorus substitution, confirming the superiority of the *N*Me_2-group over larger phosphoramidite (entries 2–3), and phosphonite (entry 4) derivatives. With respect to aryl-substitution, a similar trend was observed, and phenyl-substituted **L5** outperformed bulkier aryl analogues, providing the target in an improved er of 86:14 (entries 5–7). A brief acid screen highlighted the importance of this cocatalyst for both reactivity and enantioselectivity (entry 8), and a notable improvement in enantiocontrol could be observed with the introduction of aromatics on the acid backbone (entries 9-10). Some chiral carboxylic acids, eg (*R*)- and (*S*)-2-phenylpropanoic acid and protected phenylalanines, were screened but gave inferior results. Reducing the reaction temperature to 60 °C provided a modest increase in er (entry 11), and finally, exchanging Cs_2CO_3 for K_2CO_3 increased the rate of reaction, allowing isolation of **2a** in 91% yield and 94:6 er after 10 hours (entry 12).

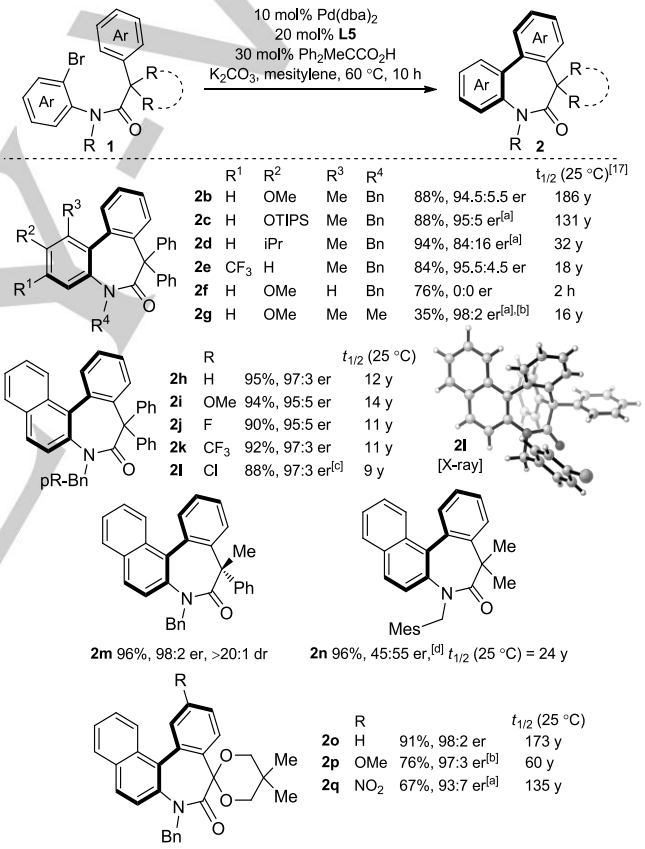
Table 1. Ligand screening and reaction optimization[a]



Entry	L#	Acid	*T* [°C]	Yield (Conversion) [%][b]	er
1	**L1**	PivOH	80	70 (85)	74:26
2	**L2**	PivOH	80	71 (80)	70:30
3	**L3**	PivOH	80	60 (68)	51:49
4	**L4**	PivOH	80	7 (29)	–
5	**L5**	PivOH	80	71 (87)	86:14
6	**L6**	PivOH	80	46 (95)	75:25
7	**L7**	PivOH	80	90 (92)	77:23
8	**L5**	–	80	24 (52)	57:43
9	**L5**	$(Ph)_3CCO_2H$	80	48 (72)	87:13
10	**L5**	$(Ph)_2MeCCO_2H$	80	74 (89)	91:9
11[c]	**L5**	$(Ph)_2MeCCO_2H$	60	77 (88)	93:7
12[d]	**L5**	$(Ph)_2MeCCO_2H$	60	91[e] (100)	94:6

[a] 0.05 mmol of **1a**, 10 mol% $Pd(dba)_2$, 20 mol% **L#**, 30 mol% acid, 150 mol% Cs_2CO_3, 0.25 M in mesitylene at 80 °C for 4 h. [b] Determined by ^{1}H NMR. [c] For 15 h. [d] 0.10 mmol scale, with K_2CO_3 for 10 h. [e] Isolated yield.

We next explored the scope of the transformation (Scheme 2). Interestingly, the introduction of electron donating substituents on the aniline-derived moiety, such as in methoxy derivative **2b** and silyl-protected analogue **2c**, greatly enhanced product configurational stability without impacting enantioselectivity. In the latter case, an increased palladium loading was necessary for complete conversion, presumably as a consequence of increased steric bulk near the site of functionalization. This trend also held true for isopropyl-derivative **2d**, however in this case a reduction in enantioselectivity was also observed. Electron poor substrate **2e**, bearing an aryl-trifluoromethyl substituent, reacted smoothly to provide the target in 84% yield and 95.5:4.5 er. As anticipated, the importance of steric bulk adjacent to the biaryl linker was confirmed through preparation of configurationally labile **2f**.



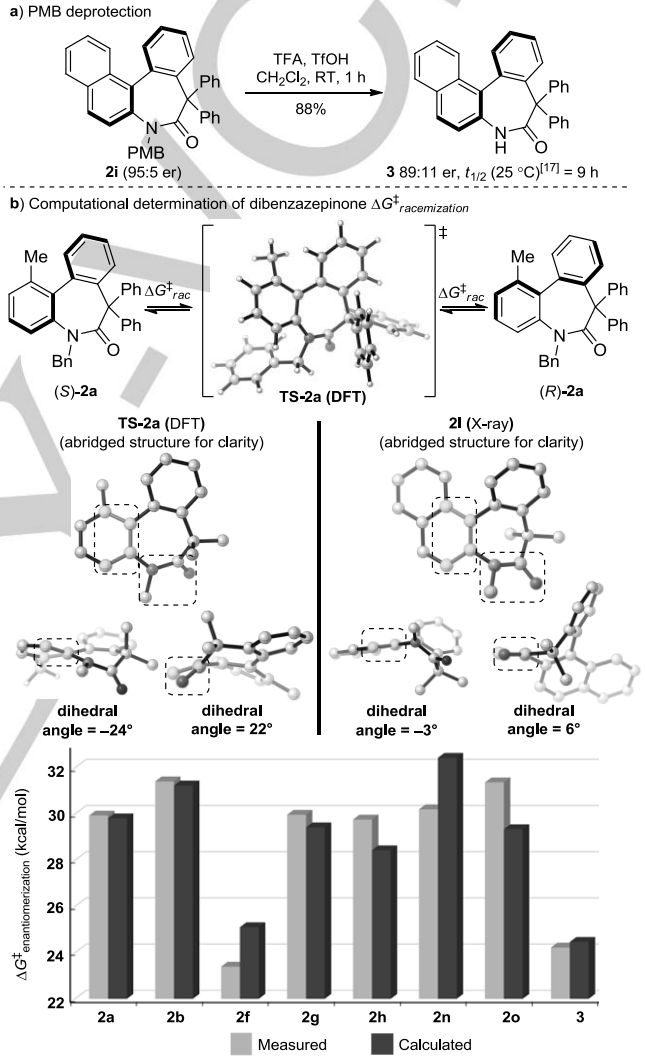
Scheme 2. Scope of atropo-enantioselective C–H arylation: 0.1 mmol **1**, 10 mol% $Pd(dba)_2$, 20 mol % **L5**, 30 mol% Ph_2MeCCO_2H, 150 mol% K_2CO_3, 0.25 M in mesitylene, 60 °C, 10 h; isolated yields. [a] With 20 mol% $Pd(dba)_2$. [b] Determined by ^{1}H NMR. [c] 2.38 mmol **1l**, 5 mol% $Pd(dba)_2$, 10 mol % **L5**, 20 mol% Ph_2MeCCO_2H, 150 mol% K_2CO_3, 0.5 M in mesitylene, 60 °C, 14 h. [d] At 90 °C.

Introduction of a smaller *N*–Me substituent was detrimental for reactivity (**2g**), however enantiocontrol remained markedly high (98:2 er). The functional group tolerance of the reaction was further demonstrated through screening a range of *para*-substituted benzyl derivatives derived from 2-naphthylamine

(**2h**–**2l**). Both electron-rich and electron-poor substrates furnished the corresponding cyclic products in good yields, with little impact on enantioselectivity or product stability. Notably, aryl-chloride **2l** proved to be a competent substrate, and no evidence for competitive oxidative-addition was observed. In this case, the reaction could be conducted on gram-scale, allowing for a reduction in palladium, ligand, and acid loading, while still maintaining a high yield and enantioselectivity (88%, 97:3 er, 1.21 g isolated). Moreover, the absolute configuration of the biaryl axis present in **2l** was confirmed through single crystal X-ray analysis, and found to be *S*.[18] In the interest of accessing more structurally diverse dibenzazepinones, we explored the effect of reducing the number of equivalent phenyl substituents in our cyclization precursors. Dibenzazepinone **2m**, derived from the corresponding diphenyl derivative, was accessed as a single diastereoisomer in 96% yield and 98:2 er. In comparison, the synthesis of dimethyl-derivative **2n** required 90 °C for cyclization, resulting in significant racemization. Ketal derivatives **2p**–**2r** reacted with excellent levels of enantioselectivity (up to 98:2 er), while also demonstrating that altering the electronic nature of the activated phenyl group is well tolerated.

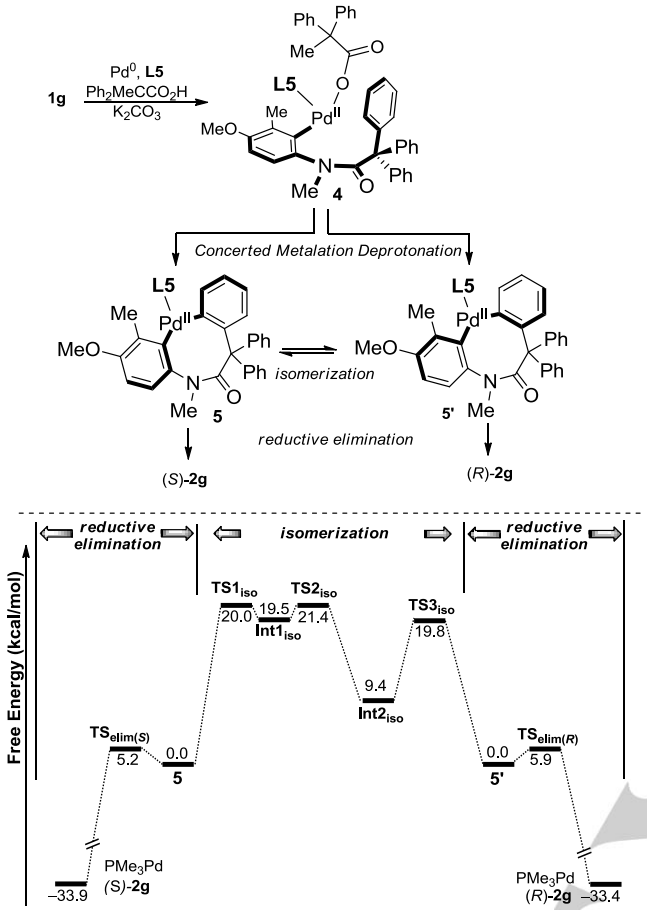
Experimental and computational studies provided further insight into which structural features are responsible for product configurational stability (Scheme 3a). PMB cleavage of **2i** proceeded smoothly, providing secondary lactam **3** in 88 % yield. Although this derivative has a considerably smaller half-life than its substituted precursor, its facile preparation creates opportunity for introduction of functionality not tolerated during C–H functionalization. DFT computations regarding dibenzazepinone enantiomerization were conducted at the PBE0-dDsC/TZ2P//M06/def2-SVP theoretical level, and are summarized in Scheme 3b. For rotation about the biaryl axis to occur, significant puckering of the nitrogen substituted aryl-moiety is necessary, as illustrated by representative example **TS-2a** (cf. X-ray of **2l**). A concomitant decrease in conjugation between the carbonyl and nitrogen atom of the amide functionality is also observed, ultimately resulting in a significant barrier to enantiomerization.[19] Notably, benchmarking of our measured versus calculated configurational stabilities shows good agreement (see SI for detailed data), highlighting the value of this method as a predictive tool for future synthetic studies towards axially chiral dibenzazepinones.

Mechanistically, the selective formation of a chiral axis poses an intriguing problem with broader implications. *Which stage of the catalytic cycle is the enantiodetermining step?* In contrast to the clear identification of this crucial step in the formation of point- and planar chiral molecules, two scenarios can be envisioned (Scheme 4). Scenario I: The interconversion barrier of the two relevant palladacycles **5**→**5'** ($\mathbf{TS_{iso}}$) is lower than the activation energy for the reductive elimination ($\mathbf{TS_{elim(S)}}$ and $\mathbf{TS_{elim(R)}}$). As consequence, the C–H activation step would not be connected to enantioselectivity. Rather, selectivity would be linked to the differences in stability of **5** and **5'** (or $\mathbf{TS_{elim(S)}}$ and $\mathbf{TS_{elim(R)}}$). Scenario II: The barrier of interconversion $\mathbf{TS_{iso}}$ is significantly higher than reductive elimination. In this case, the initial conformation of the palladacycle after the CMD-step would directly translate to the final observed axial chirality. Since the nature of carboxylic acid additive has a bearing on enantioselectivity (Table 1), this provides experimental evidence for the latter proposal.[20] DFT computations further support this scenario. Both isomers **5** and **5'** are roughly isoenergetic and both have a low barrier for the reductive elimination ($\mathbf{TS_{elim(S)}}$=5.2 kcal/mol, $\mathbf{TS_{elim(R)}}$=5.9 kcal/mol). In contrast, the isomerization between the two species **5** and **5'** is largely disfavored, having a substantially higher barrier for $\mathbf{TS_{iso}}$ (21.4 kcal/mol). Consequently, the bound chiral ligand discriminates between enantiotopic faces of the activated phenyl group in **4**, corresponding to an enantiodetermining CMD-step.



Scheme 3. Experimental and computational insight into dibenzazepinone configurational stability.

In summary, we report a palladium-catalyzed atropo-enantioselective C-H functionalization method for the synthesis of axially chiral dibenzazepinones. A simple TADDOL-derived phosphoramidite ligand provides high levels of enantiocontrol. Accompanying computational investigations allow reliable prediction of racemization barriers about the chiral axis. Moreover, calculations suggest an enantiodetermining CMD-step that proceeds via discrimination between enantiotopic faces of a phenyl group to set the chiral axis, followed by a fast reductive elimination.



Scheme 4. Computed free energy profile of the possible stereochemical pathways of the palladacycle.[20]

Acknowledgements

This work is supported by the Swiss National Science Foundation (No. 175507). C. G. N. acknowledges support from the "EPFL Fellows" co-funded by Marie Skłodowska-Curie, Horizon 2020 program (No. 665667). M. D. W. thanks Prof. C. Corminboeuf for financial support and access to computational resources. We thank Dr. R. Scopelliti and Dr. F. Fadaei Tirani for X-ray analysis of compounds **2c**, **2e** and **2l**.

Keywords: Asymmetric Catalysis • C–H Activation • Biaryl Atropisomer • Palladium • Axial Chirality

[1] (a) G. Bringmann, D. Menche, *Acc. Chem. Res*., **2001**, *34*, 615. (b) G. Bringmann, T. Gulder, T. A. M. Gulder, M. Breuning, *Chem. Rev*. **2011**, *111*, 563.

[2] (a) S. R. LaPlante, P. J. Edwards, L. D. Fader, A. Jakalian, O. Hucke, *ChemMedChem* **2011**, *6*, 505. (b) J. Clayden, W. J. Moran, P. J. Edwards, S. R. LaPlante, *Angew. Chem. Int. Ed.* **2009**, *48*, 6398. (c) P. W. Glunz, *Bioorganic Med. Chem. Lett.* **2018**, *28*, 53.

[3] (a) R. Noyori, H. Takaya, *Acc. Chem. Res*. **1990**, *23*, 345. (b) Y. Chen, S. Yekta, A. K. Yudin, *Chem. Rev*. **2003**, *103*, 3155 (c) P. Kočovský, Š. Vyskočil, M. Smrčina, *Chem. Rev*. **2003**, *103*, 3213 (c) (d) T. Akiyama, *Chem. Rev*. **2007**, *107*, 5744.

[4] (a) G. Bringmann, A. J. Price Mortimer, P. A. Keller, M. J. Gresser, J. Garner, M. Breuning, *Angew. Chem. Int. Ed*. **2005**, *44*, 5384. (b) J. Wencel-Delord, A. Panossian, F. R. Leroux, F.Colobert, *Chem. Soc. Rev.* **2015**, *44*, 3418. (c) E. Kumarasamy, R. Raghunathan, M. P. Sibi, J.Sivaguru, *Chem. Rev.* **2015**, *115*, 11239. (d) P. Loxq, E. Manoury, R. Poli, E. Deydier, A. Labande, *Coord. Chem. Rev*. **2016**, *308*, 131. (e) B. Zilate, A. Castrogiovanni, C. Sparr, *ACS Catal.* **2018**, *8*, 2981. (f) D. Lotter, A. Castrogiovanni, M. Neuburger, C. Sparr, *ACS Cent. Sci.* DOI: 10.1021/acscentsci.8b00204.

[5] (a) R. Giri, B.-F. Shi, K. M. Engle, N. Maugel, J.-Q. Yu, *Chem. Soc. Rev.* **2009**, *38*, 3242. (b) J. Wencel-Delord, F. Colobert, *Chem. Eur. J.* **2013**, *19*, 14010. (c) C. Zheng, S.-L. You, *RSC Adv.* **2014**, *4*, 6173. (d) D.-W. Gao, J. Zheng, K.-Y. Ye, C. Zheng, S.-L. You, in *Asymmetric Functionalization of C–H Bonds* (Ed.: S.-L. You), Royal Society of Chemistry: Cambridge, U.K., **2015**, p. 141. (e) C. G. Newton, S.-G. Wang, C. C. Oliveira, N. Cramer, *Chem. Rev.* **2017**, *117*, 8908. (f) T. G. Saint-Denis, R.-Y. Zhu, G. Chen, Q.-F. Wu, J.-Q. Yu, *Science* **2018**, *359*, 759.

[6] Pd-catalyzed: (a) S.-X. Li, Y.-N. Ma, S.-D. Yang, *Org. Lett.* **2017**, *19*, 1842. (b) C. He, M. Hou, Z. Zhu, Z. Gu, *ACS Catal.* **2017**, *7*, 5316. (c) Q.-J. Yao, S. Zhang, B.-B. Zhan, B.-F. Shi, *Angew. Chem. Int. Ed.* **2017**, *56*, 6617. (d) G. Liao, Q. ‐ J. Yao, Z. ‐ Z. Zhang, Y. ‐ J. Wu, D. ‐ Y. Huang, B. ‐ F. Shi, *Angew. Chem. Int. Ed.* **2018**, *57*, 3665.

[7] Rh-catalyzed: (a) F. Kakiuchi, P. Le Gendre, A. Yamada, H. Ohtaki, S. Murai, *Tetrahedron: Asymmetry* **2000**, *11*, 2647. (b) J. Zheng, S.-L. You, *Angew. Chem. Int. Ed.* **2014**, *53*, 13244. (c) J. Zheng, W.-J. Cui, C. Zheng, S.-L. You, *J. Am. Chem. Soc.* **2016**, *138*, 5242.

[8] Pd(II)-catalyzed: (a) K. Yamaguchi, J. Yamaguchi, A. Studer, K. Itami, *Chem. Sci.* **2012**, *3*, 2165. (b) K. Yamaguchi, H. Kondo, J. Yamaguchi, K. Itami, *Chem. Sci.* **2013**, *4*, 3753. (c) Y. Nishimoto, H. Kondo, K. Yamaguchi, D. Yokogawa, J. Yamaguchi, K. Itami, S. Irle, *J. Org. Chem*., **2017**, 82, 4900.

[9] Rh-catalyzed: Z.-J. Jia, C. Merten, R. Gontla, C. G. Daniliuc, A. P. Antonchick, H. Waldmann, *Angew. Chem. Int. Ed.* **2017**, *56*, 2429.

[10] For oxidative coupling of 2-naphthols *via* Cu and V-catalysis, see reference 4d.

[11] (a) B. Ye, N. Cramer, *Acc. Chem. Res.* **2015**, *48*, 1308. (b) C. G. Newton, D. Kossler, N. Cramer, *J. Am. Chem. Soc.* **2016**, *138*, 3935.

[12] (a) J. Pedroni, N. Cramer, *Chem. Commun.* **2015**, *51*, 17647. (b) M. R. Albicker, N. Cramer, *Angew. Chem. Int. Ed.* **2009**, *48*, 9139. (b) T. Saget, N. Cramer, *Angew. Chem. Int. Ed.* **2012**, *51*, 12842. (c) T. Saget, N. Cramer, *Angew. Chem. Int. Ed.* **2013**, *52*, 7865. (d) J. Pedroni, M. Boghi, T. Saget, N. Cramer, *Angew. Chem. Int. Ed.* **2014**, *53*, 9064. (e) L. Liu, A.-A. Zhang, R.-J. Zhao, F. Li, T.-J. Meng, N. Ishida, M. Murakami, W.-X. Zhao, *Org. Lett.* **2014**, *16*, 5336. (f) Z.-Q. Lin, W.-Z. Wang, S.-B. Yan, W.-L. Duan, *Angew. Chem. Int. Ed.* **2015**, *54*, 6265. (g) L. Liu, A.-A. Zhang, Y. Wang, F. Zhang, Z. Zuo, W.-X. Zhao, C.-L. Feng, W. Ma, *Org. Lett.* **2015**, *17*, 2046. (h) J. Pedroni, N. Cramer, *Angew. Chem. Int. Ed.* **2015**, *54*, 11826. (i) J. Pedroni, T. Saget, P. A. Donets, N. Cramer, *Chem. Sci.* **2015**, *6*, 5164. (j) D. Dailler, R. Rocaboy, O. Baudoin, *Angew. Chem. Int. Ed.* **2017**, *56*, 7218.

[13] Selected examples of asymmetric Pd(0)-catalyzed functionalizations with other ligands: (a) M. Nakanishi, D. Katayev, C. Besnard, E. P. Kündig, *Angew. Chem. Int. Ed.* **2011**, *50*, 7438. (b) S. Anas, A. Cordi, H. B. Kagan, *Chem. Commun.* **2011**, *47*, 11483. (c) D. Katayev, M. Nakanishi, T. Burgi, E. P. Kündig, *Chem. Sci.* **2012**, *3*, 1422. (d) R. Shintani, H. Otomo, K. Ota, T. Hayashi, *J. Am. Chem. Soc.* **2012**, *134*, 7305. (e) T. Saget, S. J. Lemouzy, N. Cramer, *Angew. Chem. Int. Ed.* **2012**, *51*, 2238. (f) N. Martin, C. Pierre, M. Davi, R. Jazzar, O. Baudoin, *Chem. Eur. J.* **2012**, *18*, 4480. (g) R. Deng, Y. Huang, X. Ma, G. Li, R. Zhu, B. Wang, Y.-B. Kang, Z. Gu, *J. Am. Chem. Soc.* **2014**, *136*, 4472. (h) D.-W. Gao, Q. Yin, Q. Gu, S.-L. You, *J. Am. Chem. Soc.* **2014**, *136*, 4841. (i) P. M. Holstein, M. Vogler, P. Larini, G. Pilet, E. Clot, O. Baudoin, *ACS Catal.* **2015**, *5*, 4300. (j) G. Xu, M. Li, S. Wang, W. Tang, *Org. Chem. Frontiers* **2015**, *2*, 1342. (m) L. Yang, R.; Melot, M. Neuburger, O. Baudoin, *Chem. Sci.* **2017**, *8*, 1344. (k) J. Pedroni, N.

Cramer, *J. Am. Chem. Soc.* **2017**, *139*, 12398. (l) D. Grosheva, N. Cramer, *ACS Catal.* **2017**, *7*, 7417. (n) L. Yang, M. Neuburger, O. Baudoin, *Angew. Chem. Int. Ed.* **2018**, *57*, 1394.

[14] Representative examples: (a) F. F. Hou, X. Zhang, G. H. Zhang, D. Xie, P. Y. Chen, W. R. Zhang, J. P. Jiang, M. Liang, G. B. Wang, Z. R. Liu, R. W. Geng, *N. Engl. J. Med*. **2006**; *354*, 131. (b) F. J. B. Junior, L. Scotti, H. Ishiki, S. P. S. Botelho, M. S. Da Silva, M. T. Scotti, *Mini. Rev. Med. Chem.* **2015**, *15*, 630. (c) W. Hunkeler, *Chimia* **1993**, *47*, 141.

[15] (a) M. Leost *et al. Eur. J. Biochem.* **2000**, *267*, 5983. (b) G. T. Wong *et al. J. Biol. Chem.* **2004**, *279*, 12876. (c) J. S. Nair, T. Sheikh, A. L. Ho, G. K. Schwartz, *Anticancer Res.* **2013**, *33*, 1307.

[16] For a resolution by chiral HPLC, see: H. Tabata, H. Suzuki, K. Akiba, H. Takahashi, H. Natsugari, *J. Org. Chem.* **2010**, *75*, 5984.

[17] Half-lives were measured and extrapolated to 25 °C according to the method outlined in the SI.

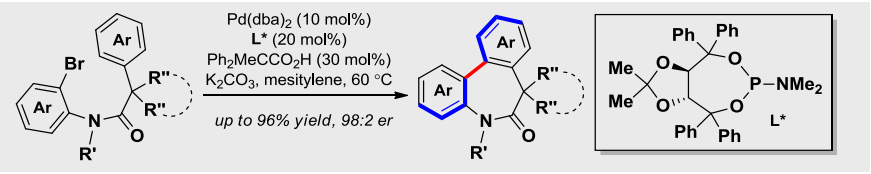
[18] Crystallographic data for **2c**, **2e** and **2l**: CCDC 1843121, 1843122 and 1843124 at: www.ccdc.cam.ac.uk/data_request/cif.

[19] Corresponding amine of **2l** has a calculated $\Delta G^{\ddagger}_{rac}$ of 22.4 kcal/mol.

[20] Computations at the PBE0-dDsC/TZ2P//M06/def2-SVP theoretical level (see SI for full computational details). The very large ligand **L5** has been simplified by PMe_3 for the calculations.

Entry for the Table of Contents

COMMUNICATION



*C. G. Newton, E. Braconi,[‡] J. Kuziola,[‡] M. D. Wodrich, N. Cramer**

Page No. – Page No.

Axially Chiral Dibenzazepinones *via* a Pd(0)–Catalyzed Atropo-enantioselective C–H Arylation

A palladium-catalyzed atropo-enantioselective route towards axially chiral dibenzazepinones has been developed. A TADDOL-derived phosphoramidite ligand provides high levels of enantiocontrol. Computational investigations provide information on racemization barriers and suggest an enantiodetermining C–H functionalization event.