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Asymmetric Catalysis

Highly Enantioselective Formation of α-Allyl-α-Arylcyclopentanones via Pd-Catalysed Decarboxylative Asymmetric Allylic Alkylation

Ramulu Akula, Robert Doran, and Patrick J. Guiry*[a]

Abstract: A highly enantioselective Pd-catalysed decarboxylative asymmetric allylic alkylation of cyclopentanone derived α-aryl-β-keto esters employing the (*R*,*R*)-ANDEN-phenyl Trost ligand has been developed. The product (*S*)-α-allyl-α-arylcyclopentanones were obtained in excellent yields and enantioselectivities (up to >99.9% *ee*). This represents one of the most highly enantioselective formations of an all-carbon quaternary stereogenic center reported to date. This reaction was demonstrated on a 4.0 mmol scale without any deterioration of enantioselectivity and was exploited as the key enantioselective transformation in an asymmetric formal synthesis of the natural product (+)-tanikolide.

The catalytic asymmetric generation of quaternary carbon centers continues to be a significant challenge in synthetic organic chemistry. In particular, the enantioselective formation of quaternary centers bearing an aryl group next to a carbonyl has seen particular interest in the past decade. Since the seminal report by Buchwald in 1998,[1] a number of approaches have been developed whereby the aryl group is introduced during the enantiodetermining step, in most cases.[2]

The Pd-catalysed asymmetric decarboxylative allylic alkylation reaction (DAAA) has become a key transformation in the toolkit of modern catalytic asymmetric reactions. In 1980, Tsuji and Saegusa independently reported the first examples of decarboxylative allylation of β-keto allyl esters, using Pd catalysis, to form allylated ketones.[3] Subsequently, Tsuji expanded the precursors for this transformation to allyl enol carbonates,[4] silyl enol ethers[5] and enol acetates.[6] Surprisingly, the first enantioselective example was only reported as recently as 2004, by Stoltz, from allyl enol carbonates and silyl enol ethers.[7] The contributions to this methodology by the groups of Trost and Stoltz have pioneered the field.[8]

Although both the use of allyl enol carbonates and silyl enol ethers have proved successful in the DAAA reaction, there is a considerable problem with the regioselective preparation of these substrates. If poor selectivity is observed for the desired enol ether formation this will be translated into a mixture of allylated products. To circumvent this problem, Stoltz, inspired by the earlier work of Tsuji and Saegusa, looked toward β-keto allyl esters as possible substrates.

Not only is the in situ enolate generation regiospecific but the substrates are relatively simple to prepare and quaternary β-keto esters are bench-stable compounds. These substrates were successfully applied in the DAAA reaction in excellent yields and enantioselectivities.[9]

The substrate scope of the DAAA has been expanded greatly since it was first reported and has been used as a key step in the total synthesis of a number of complex natural products.[8b] Typically, the reaction is carried out on cyclic substrates, with and without a fused aromatic ring, for the synthesis of all-carbon quaternary centers. Variation of the allyl fragment can be achieved with a wide variety of substituents tolerated whilst still giving high levels of enantioselectivity. The final α-substituent of the quaternary center is, in the majority of cases, a methyl or substituted methyl group. To date, the variation of this substituent has been limited and we wished to expand this to a variety of aryl groups, which would generate quaternary α-aryl ketones in an enantioenriched manner.

The application of the DAAA to the synthesis of quaternary α-aryl ketones has been surprisingly limited. The potential reasons for this are twofold; firstly, the difficulty in the preparation of α-aryl-β-keto esters or their enol carbonate equivalents and, secondly, the increased steric bulk of the aryl group, which can have a detrimental effect on reactivity and enantioselectivity. Previously, Taylor reported the DAAA of oxindoles in which phenyl, *ortho*- and *para*-methoxyphenyl and *ortho*-nitrophenyl examples were reported with *ee* values ranging from 78–95%.[10] Stoltz has shown an α-phenyl-α-allyl cyclohexanone example, albeit in 50% *ee*, from allyl enol carbonates using an electron-deficient phosphinooxazoline (PHOX) ligand [Eq. (1), Scheme 1].[11] Trost has had more success with α-phenyl as the substituent using his *P,P* ligand ((*R*,*R*)-ANDEN-Trost) forming α-phenyl-α-allyl cyclohexanone in 90.5% *ee* [Eq. (2), Scheme 1].[8h] Cyclopentanones have also been shown to be challenging substrates to obtain high *ee* in the DAAA until a very recent report by Stoltz for the preparation of α-alkyl/benzyl cyclopentanones in up to 94% *ee* [Eq. (3), Scheme 1].[12]

We have previously developed the catalytic asymmetric synthesis of a range of tertiary α-aryl ketones by a Pd-catalysed decarboxylative asymmetric protonation.[13] In these reports we

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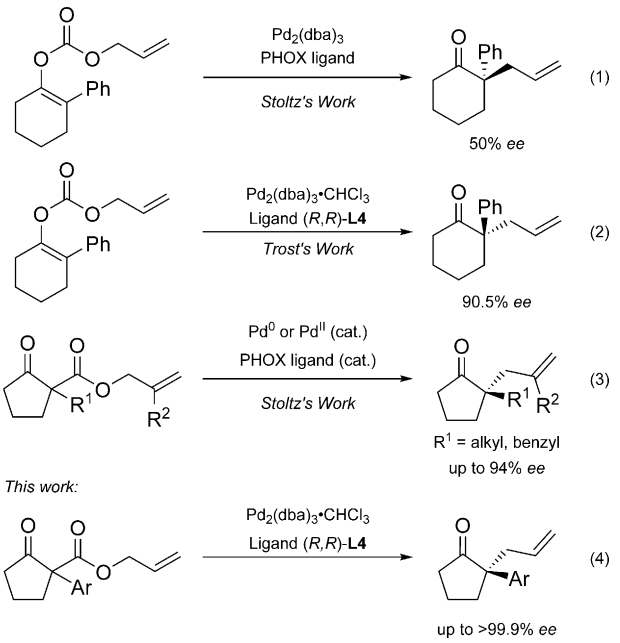


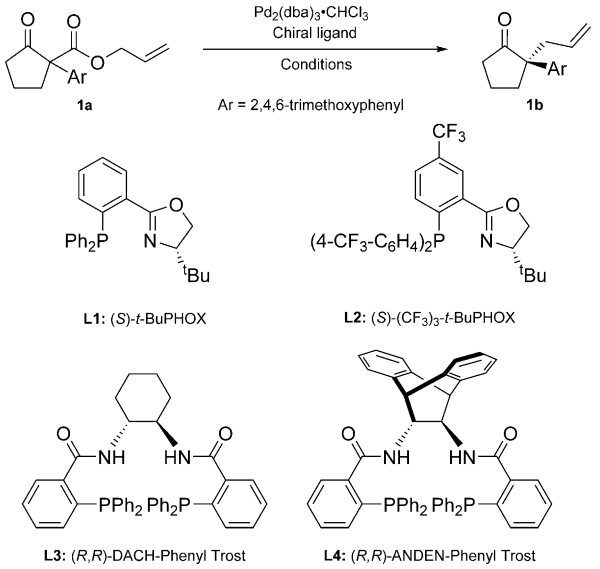
Scheme 1. Transition-metal-catalysed enantioselective decarboxylative allylic alkylation.

overcame the difficulty in the preparation of sterically hindered α-aryl-β-keto esters by the use of aryllead triacetates, which have been shown to be a privileged reagent in the arylation of β-keto esters.[14] Here, we wish to report the catalytic asymmetric synthesis of α-allyl-α-aryl ketones via the DAAA of the corresponding α-aryl-β-keto esters with very high levels of enantioselectivity [Eq. (4), Scheme 1].

We began by using cyclopentanone α-aryl-β-keto allyl ester (**1 a**) bearing a 2,4,6-trimethoxyphenyl group as a model substrate to optimise DAAA reaction conditions (Table 1). Previously, a number of *P,N* and *P,P* ligands were successfully utilised in DAAA reactions and are well documented in the literature.[8] We also chose two PHOX ligands (*S*)-**L1**, (*S*)-**L2** and two Trost ligands (*R,R*)-**L3**, (*R,R*)-**L4** to examine the feasibility of the enantioselective transformation. We began by screening each ligand (12.5 mol%) with $Pd_2(dba)_3{\cdot}CHCl_3$ (5.0 mol%) in 1,4-dioxane (0.06 M) as the solvent at 25 °C. All of the reactions went to complete conversion and gave very good isolated yields (86–92%, entries 1–4, Table 1). The level of enantioselectivity obtained when using both of the PHOX ligands was low at 25 and 31% *ee*, respectively (entries 1 and 2, Table 1). The (*R,R*)-DACH-phenyl Trost ligand **L3** provided a much more encouraging result with a good level of enantioselectivity (86% *ee*, entry 3, Table 1). To our delight, the use of (*R,R*)-ANDEN-Trost ligand **L4** gave effectively a single enantiomer of the allylated product (>99.9% *ee*, entry 4, Table 1) in a 92% isolated yield.

We then decided to test the tolerance of the reaction using a variety of different solvents. In general, high levels of of enantioselectivity were obtained (>96% *ee*) using toluene, 2-Me-THF, methyl *tert*-butyl ether (MTBE) and THF (entries 5–7, 9 and 10, Table 1). However, the conversions obtained were significantly lower compared to 1,4-dioxane. For example, toluene and THF gave conversion of 57 and 70%, respectively with THF giving rise to 99.8% *ee* (entries 5 and 9, Table 1). In the case of THF, when the reaction temperature was increased to 40 °C the conversion improved slightly to 76%, maintaining the very high level of enantioselectivity (entry 10, Table 1). We also found that the reaction in 1,4-dioxane at 40 °C gave a comparable result to the reaction at 25 °C, albeit in a reduced reaction time of 5 h (Entry 11, Table 1). Knowing this, we then investigated the effect of lowering the catalyst and ligand loadings. We found that reducing the Pd loading to 2.5 mol% and the ligand to 6.25 mol% led to a significant reduction in conversion to 60% at 40 °C, maintaining the high *ee* (entry 12, Table 1). Lowering the temperature to 25 °C gave a similar result (entry 13, Table 1).

Table 1. Optimisation of decarboxylative asymmetric allylic alkylation using **1 a**.



Entry[a]	Ligand	Solvent	Time [h]	Conv. [%][b]	*ee* [%][c]
1	L1	1,4-dioxane	10	100 (86)	25
2	L2	1,4-dioxane	10	100 (89)	31
3	L3	1,4-dioxane	10	100 (90)	86
4	L4	1,4-dioxane	10	100 (92)	>99.9
5	L4	Toluene	24	57 (50)	96
6	L4	2-Me-THF	24	48 (40)	98
7	L4	MTBE	24	65 (59)	97
8	L4	DME	24	50 (43)	98.6
9	L4	THF	24	70 (63)	99.8
10	L4	THF	24	76 (69)	99.4
11	L4	1,4-dioxane	5	100 (92)	99.8
12	L4	1,4-dioxane	24	60 (54)	99.8
13	L4	1,4-dioxane	24	58 (51)	99.6
14	L4	1,4-dioxane	10	100 (91)	>99.9
15	L4	1,4-dioxane	10	100 (93)	99.8

[a] Entries 1–11 were carried out with $Pd_2(dba)_3{\cdot}CHCl_3$ (5.0 mol%), ligand (12.5 mol%); entries 12 and 13 with $Pd_2(dba)_3{\cdot}CHCl_3$ (2.5 mol%), ligand (6.25 mol%); entries 1–9 and 13–15 at 25 °C; entries 10–12 at 40 °C; entries 1–13 at 0.06 M concentration; entry 14 at 0.03 M; entry 15 at 0.09 M. [b] Determined by ^1H NMR spectroscopy of the crude reaction mixture. Isolated yields in parentheses. [c] Determined by chiral supercritical fluid chromatography (SFC).

The effect of the reaction concentration was then examined. Increasing the concentration to 0.09 M led to a very slight reduction in *ee* (entry 15, Table 1); however, diluting the reaction concentration to 0.03 M had no effect on the *ee* and conversion (entry 14, Table 1). Pre-complex formation prior to substrate addition did not have any effect on the reaction.[15]

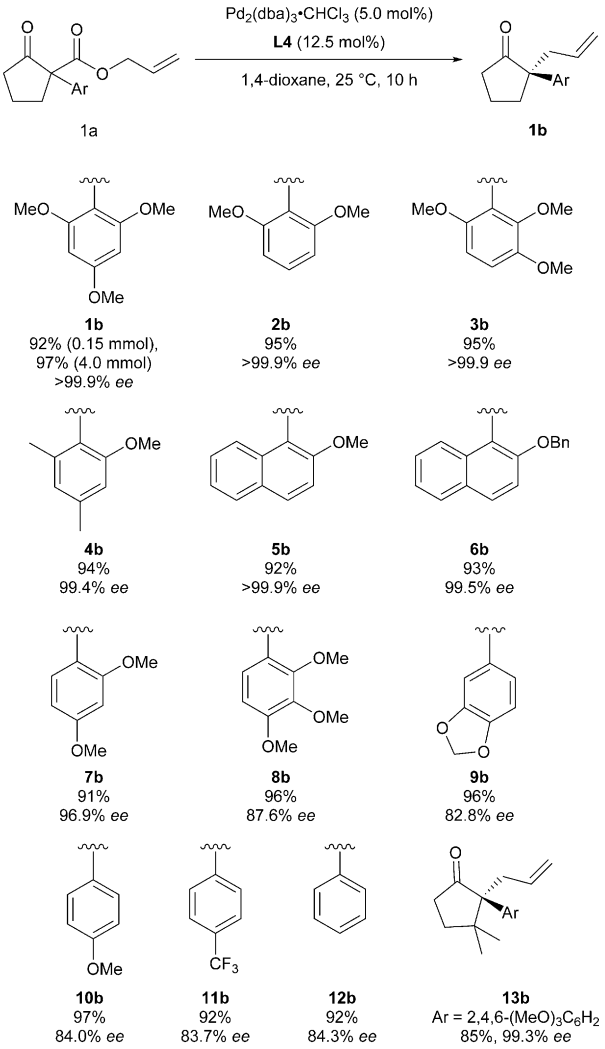
With the optimised reaction conditions in hand (Entry 4, Table 1) we then explored the substrate scope through variation of the α-aryl group (Scheme 2). In general, all of the substrates tested gave excellent yields (85–97%). With di-*ortho* methoxy-substitued aryl groups (**1b**, **2b** and **3b**), excellent levels of enantioselectivity (>99.9% *ee*) were achieved. Other di-substituted aryl groups (**4b**, **5b** and **6b**) also gave excellent enantioselectivity (>99.4% *ee*). Two similar mono-*ortho*-substituted aryl groups gave large differences in enantioselectivity. The 2,4-dimethoxyphenyl example (**7b**) gave a high *ee* of 96.9%, whereas, to our surprise, the 2,3,4-trimethoxyphenyl example (**8b**) gave a much reduced *ee* of 87.6%. Testing substrates possessing other aryl groups lacking an *ortho*-substituent (**9b**–**12b**) led to a reduction in *ee* to 83–84%. It is clear that di-*ortho*-substitution is necessary to obtain excellent levels of enantioselectivity in this transformation.

We also investigated the electronic effects of the aryl substituent and found that electron-rich (**9b** and **10b**), neutral (**12b**) and electron-deficient (**11b**) aryl groups had no effect on the enantioselectivity. The reaction was also tolerant of steric hindrance at the β-position as the *gem*-dimethyl-substituted compound (**13b**) was formed with excellent enantioselectivity (99.3%). We also demonstrated that the reaction performed equally well on a larger scale (4.0 mmol) using substrate **1a**.[15]

The absolute sense of stereoinduction was confirmed as (*S*) by obtaining an X-ray crystal structure of product **1b**.[16] Although the traditional 'wall and flap' model can predict the outcome of Pd-catalysed reactions with Trost-type ligands, Lloyd-Jones, Norrby and co-workers conclusively showed that this model does not reflect the true structure of the cationic [allyl-Pd-DACH] complex.[17]

Their NMR and DFT studies indicated a structure in which the allyl unit sits in a fairly open upper-hemisphere above Pd, with the ligand structure (including all four phenyl groups) well away from the allyl, and even further away from the incoming nucleophile for an outer-sphere mechanism.

Using the N–H to guide the enolate carbon above the allyl by hydrogen bonding leads to two possible approaches, pathway A or B (Figure 1). In pathway A, the enolate is oriented such that the aryl group is pointing away from the ligand backbone allowing pro-*S* attack on the allyl group on Pd. In pathway B, the aryl group experiences a large steric clash with the ligand backbone, as the ANDEN framework provides a substantial steric bulk, so this approach is disfavoured. The [allyl-Pd-ANDEN] complex can undergo a conformational inversion, which locates the N–H further away from the allyl group and



Scheme 2. Scope and enantioselectivity of α-allyl-α-arylcyclopentanone synthesis.

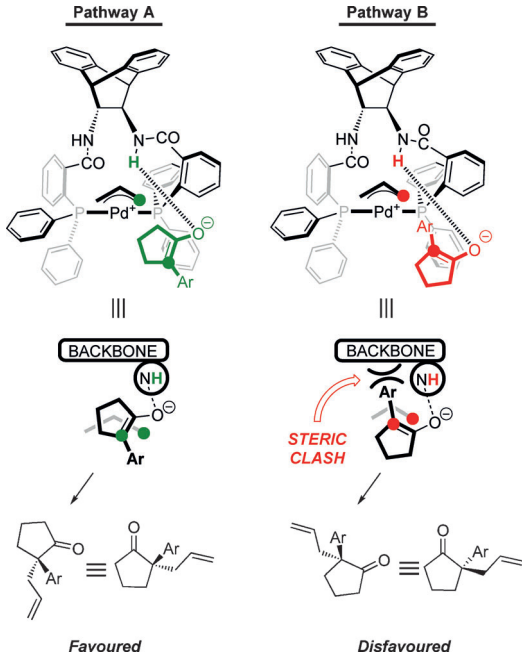
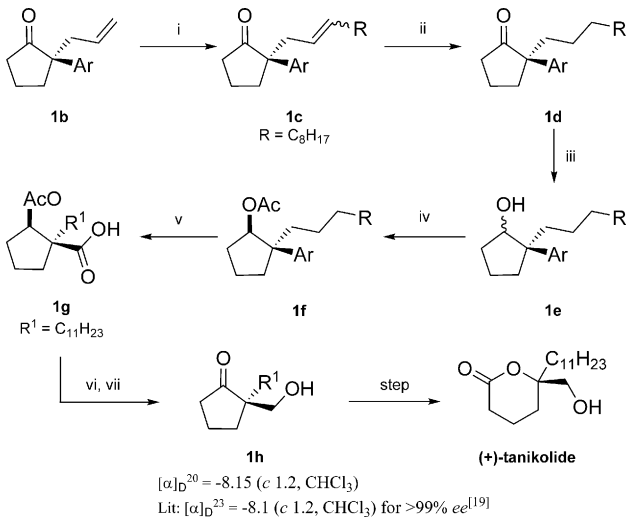


Figure 1. Proposed pathways during enantiodetermining enolate addition.

does not permit an enolate approach free from a steric clash with the ligand backbone (not shown). Rotation of the substrate aryl group becomes degenerate when it is 2,6-disubstituted, leading to very high *ee* values for such substrates.

With a highly enantioselective synthesis of α-allyl- α-aryl cyclopentanones at hand, we carried out a concise asymmetric formal synthesis of (+)-tanikolide from **1b** (Scheme 3). Tanikolide is a brine shrimp toxin and antifungal marine natural product isolated from blue green algae cyanobacterium *Lyngbya*



Scheme 3. Concise formal asymmetric synthesis of (+)-tanikolide. i) Hoveyda–Grubbs II (5.0 mol%), 1-decene (3.0 equiv), CH_2Cl_2, reflux, 24 h, 78%. ii) Pd/C, H_2 (1 atm), EtOAc, RT, 18 h, quant. iii) $LiAlH_4$ (1 M in Et_2O, 1.0 equiv), Et_2O, reflux, 3 h, 88%. iv) Ac_2O (1.2 equiv), Et_3N (1.2 equiv), DMAP (0.2 equiv), CH_2Cl_2, RT, 92%. v) $NaIO_4$ (15 equiv), $RuCl_3$ (0.1 equiv), CCl_4, MeCN and H_2O (1:1:1.5, V V^{-1}), RT, 36 h. vi) $LiAlH_4$ (1 M in Et_2O, 0.5 equiv), Et_2O, reflux, 3 h vii) NaOCl (13 wt%), AcOH, 10 °C, 30 min, 50% over three steps.

majuscula. A number of synthetic approaches have been developed for the asymmetric synthesis of (+)-tanikolide by us and others.[18] Starting with α-allyl- α-arylcyclopentanone (**1b**), Grubbs' cross metathesis with 1-decene furnished disubstituted alkene (**1c**). Reduction of the alkene and carbonyl groups led to alcohol (**1e**, dr = 5:1) was subsequently protected as the acetate (**1f**). Cleavage of the aryl group was accomplished under RuO_4-catalysis forming carboxylic acid (**1g**),[19] demonstrating the power of possessing a functionalisable aryl group, in contrast to previous related work with methyl or benzyl substituents.[8] Finally, reduction afforded the diol (**1h**), an advanced intermediate in a previous synthesis of (+)-tanikolide.[20]

In conclusion, a highly enantioselective Pd-catalysed DAAA of α-aryl-β-keto esters has been developed employing the (*R*,*R*)-ANDEN-phenyl Trost ligand **L4**. Under these conditions, substrates containing di-*ortho*-substituted aryl groups gave excellent enantioselectivities (>99.9% *ee*) of the (*S*)-α-allyl-α-aryl-cyclopentanone products. Mono-*ortho*-substituted aryl groups gave good to very high levels of enantioinduction (88 to 97% *ee*). The absence of an *ortho*-substituent afforded the corresponding products with good enantioselectivities (83 to 84% *ee*). We demonstrated that this reaction was reproducible on a 4.0 mmol scale without any deterioration of enantioselectivity. Finally, we illustrated the application of this asymmetric methodology as the key enantioselective step in the asymmetric formal synthesis of the natural product (+)-tanikolide. We are currently exploiting the DAAA of a range of other α-aryl-containing substrates and the reports of these investigations will be the subject of future reports from these laboratories.

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Keywords: allylic alkylation · asymmetric catalysis · decarboxylation · natural products · palladium

[1] J. Åhman, J. P. Wolfe, M. V. Troutman, M. Palucki, S. L. Buchwald, *J. Am. Chem. Soc.* **1998**, *120*, 1918–1919.
[2] a) C. C. C. Johansson, T. J. Colacot, *Angew. Chem. Int. Ed.* **2010**, *49*, 676–707; *Angew. Chem.* **2010**, *122*, 686–718; b) T. Hamada, A. Chieffi, J. Ahman, S. L. Buchwald, *J. Am. Chem. Soc.* **2002**, *124*, 1261–1268; c) D. J. Spielvogel, S. L. Buchwald, *J. Am. Chem. Soc.* **2002**, *124*, 3500–3501; d) G. Chen, F. Y. Kwong, H. O. Chan, W.-Y. Yu, A. S. C. Chan, *Chem. Commun.* **2006**, 1413–1415; e) X. Liao, Z. Weng, J. F. Hartwig, *J. Am. Chem. Soc.* **2008**, *130*, 195–200; f) X. Xie, Y. Chen, D. Ma, *J. Am. Chem. Soc.* **2006**, *128*, 16050–16051; g) S. Lee, J. F. Hartwig, *J. Org. Chem.* **2001**, *66*, 3402–3415; h) J. García-Fortanet, S. L. Buchwald, *Angew. Chem. Int. Ed.* **2008**, *47*, 8108–8111; *Angew. Chem.* **2008**, *120*, 8228–8231; i) Y.-X. Jia, J. M. Hillgren, E. L. Watson, S. P. Marsden, E. P. Kundig, *Chem. Commun.* **2008**, 4040–4042; j) J. Guo, S. Dong, Y. Zhang, Y. Kuang, X. Liu, L. Lin, X. Feng, *Angew. Chem. Int. Ed.* **2013**, *52*, 10245–10249; *Angew. Chem.* **2013**, *125*, 10435–10439; k) V. L. Rendina, H. Z. Kaplan, J. S. Kingsbury, *Synthesis* **2012**, 686–693.
[3] a) I. Shimizu, T. Yamada, J. Tsuji, *Tetrahedron Lett.* **1980**, *21*, 3199–3202; b) T. Tsuda, Y. Chujo, S. Nishi, K. Tawara, T. Saegusa, *J. Am. Chem. Soc.* **1980**, *102*, 6381–6384.
[4] J. Tsuji, I. Minami, I. Shimizu, *Tetrahedron Lett.* **1983**, *24*, 1793–1796.
[5] J. Tsuji, I. Minami, I. Shimizu, *Chem. Lett.* **1983**, *12*, 1325–1326.
[6] J. Tsuji, I. Minami, I. Shimizu, *Tetrahedron Lett.* **1983**, *24*, 4713–4714.
[7] D. C. Behenna, B. M. Stoltz, *J. Am. Chem. Soc.* **2004**, *126*, 15044–15045.
[8] a) J. T. Mohr, B. M. Stoltz, *Chem. Asian J.* **2007**, *2*, 1476–1491; b) A. Y. Hong, B. M. Stoltz, *Eur. J. Org. Chem.* **2013**, 2745–2759; c) D. C. Behenna, Y. Liu, T. Yurino, J. Kim, D. E. White, S. C. Virgil, B. M. Stoltz, *Nat. Chem.* **2011**, *4*, 130–133; d) J. A. Keith, D. C. Behenna, N. Sherden, J. T. Mohr, S. Ma, S. C. Marinescu, R. J. Nielsen, J. Oxgaard, B. M. Stoltz, W. A. Goddard, *J. Am. Chem. Soc.* **2012**, *134*, 19050–19060; e) D. C. Behenna, J. T. Mohr, N. H. Sherden, S. C. Marinescu, A. M. Harned, K. Tani, M. Seto, S. Ma, Z. Novák, M. R. Krout, R. M. McFadden, J. L. Roizen, J. A. Enquist, D. E. White, S. R. Levine, K. V. Petrova, A. Iwashita, S. C. Virgil, B. M. Stoltz, *Chem. Eur. J.* **2011**, *17*, 14199–14223; f) B. M. Trost, B. Schäffner, M. Osipov, D. A. A. Wilton, *Angew. Chem. Int. Ed.* **2011**, *50*, 3548–3551; *Angew. Chem.* **2011**, *123*, 3610–3613; g) B. M. Trost, K. Lehr, D. J. Michaelis, J. Xu, A. K. Buckl, *J. Am. Chem. Soc.* **2010**, *132*, 8915–8917;

h) B. M. Trost, J. Xu, T. Schmidt, *J. Am. Chem. Soc.* **2009**, *131*, 18343 – 18357; i) B. M. Trost, R. N. Bream, J. Xu, *Angew. Chem. Int. Ed.* **2006**, *45*, 3109 – 3112; *Angew. Chem.* **2006**, *118*, 3181 – 3184; j) B. M. Trost, J. Xu, *J. Am. Chem. Soc.* **2005**, *127*, 17180 – 17181; k) B. M. Trost, J. Xu, *J. Am. Chem. Soc.* **2005**, *127*, 2846 – 2847.

[9] J. T. Mohr, D. C. Behenna, A. M. Harned, B. M. Stoltz, *Angew. Chem. Int. Ed.* **2005**, *44*, 6924 – 6927; *Angew. Chem.* **2005**, *117*, 7084 – 7087.

[10] V. Franckevičius, J. D. Cuthbertson, M. Pickworth, D. S. Pugh, R. J. K. Taylor, *Org. Lett.* **2011**, *13*, 4264 – 4267.

[11] N. T. McDougal, S. C. Virgil, B. M. Stoltz, *Synlett* **2010**, 1712 – 1716.

[12] R. A. Craig, S. A. Loskot, J. T. Mohr, D. C. Behenna, A. M. Harned, B. M. Stoltz, *Org. Lett.* **2015**, *17*, 5160 – 5163.

[13] a) R. Doran, P. J. Guiry, *J. Org. Chem.* **2014**, *79*, 9112 – 9124; b) R. Doran, M. P. Carroll, R. Akula, B. F. Hogan, M. Martins, S. Fanning, P. J. Guiry, *Chem. Eur. J.* **2014**, *20*, 15354 – 15359; c) M. P. Carroll, H. Muller-Bunz, P. J. Guiry, *Chem. Commun.* **2012**, *48*, 11142 – 11144.

[14] J. Pinhey, B. Rowe, *Aust. J. Chem.* **1980**, *33*, 113 – 120.

[15] Complex formed at 40 °C for 30 min and cooled to 25 °C prior to substrate addition.

[16] CCDC 1457351 (**1 b**) contains the supplementary crystallographic data for this paper. These data are provided free of charge by The Cambridge Crystallographic Data Centre.

[17] C. P. Butts, E. Filali, G. C. Lloyd-Jones, P.-O. Norrby, D. A. Sale, Y. Schramm, *J. Am. Chem. Soc.* **2009**, *131*, 9945 – 9957.

[18] R. Doran, L. Duggan, S. Singh, C. D. Duffy, P. J. Guiry, *Eur. J. Org. Chem.* **2011**, 7097 – 7106.

[19] An α-keto ester byproduct was isolated in 30% yield. See the Supporting Information for further information.

[20] F. Wu, R. Hong, J. Khan, X. Liu, L. Deng, *Angew. Chem. Int. Ed.* **2006**, *45*, 4301 – 4305; *Angew. Chem.* **2006**, *118*, 4407 – 4411.

[21] During the manuscript reviewing timeframe an interesting and impressive direct α-allylation of ketones limited to α-arylcyclohexanones has been reported with *ee* values between 91 – 94%, see: G. Pupo, R, Properzi, B, List, *Angew. Chem. Int. Ed.* **2016**, *55*, 6099 – 6102; *Angew. Chem.* **2016**, *128*, 6204 – 6207.

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Asymmetric Catalysis

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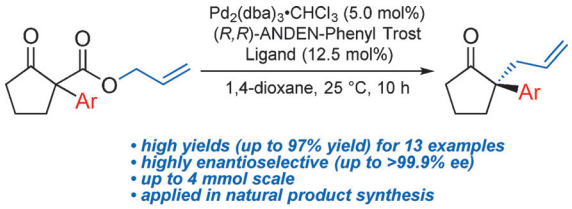
Highly Enantioselective Formation of α-Allyl-α-Arylcyclopentanones via Pd-Catalysed Decarboxylative Asymmetric Allylic Alkylation



Grand Slam! All-Carbon 4° Centres: A highly enantioselective Pd-catalysed decarboxylative asymmetric allylic alkylation of cyclopentanone derived α-aryl-β-keto esters employing the (*R*,*R*)-ANDEN-phenyl Trost ligand has been developed. The product (*S*)-α-allyl-α-arylcyclopentanones were obtained in excellent yields and enantioselectivities (up to $>$99.9% *ee*). This represents one of the most highly enantioselective formations of an all-carbon quaternary stereogenic center reported to date.