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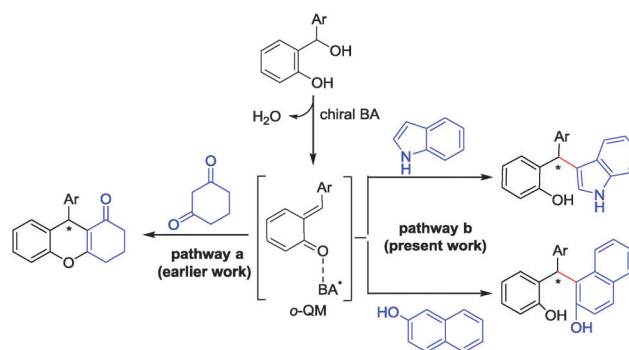
Chiral Brønsted acid-catalyzed Friedel–Crafts alkylation of electron-rich arenes with *in situ*-generated *ortho*-quinone methides: highly enantioselective synthesis of diaryldiarylmethanes and triarylmethanes†

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We disclose herein a highly enantioselective protocol for the Brønsted acid-catalyzed addition of indoles and phenols to *in situ*-generated *ortho*-quinone methides which deliver broadly substituted diaryldiarylmethanes and triarylmethanes, respectively, in a one-pot reaction under very mild conditions. A chiral phosphoric acid catalyst has been developed for this process serving to convert the starting *ortho*-hydroxybenzhydryl alcohols into the reactive *ortho*-quinone methides and to control the enantioselectivity of the carbon–carbon bond-forming event *via* hydrogen-bonding.

Triarylmethanes have gained substantial attention from the synthetic community because of their importance in medicinal chemistry, materials science and as dye precursors.¹ Several of them are known to be potential drug candidates for the treatment of cancer, bacterial infections, and diabetes² and are also core structures in natural products such as for example in cassigarol B.³ Similarly, heteroaryl-substituted analogues of this product class have been shown to be powerful pharmaceuticals and bioactive molecules like letrozole, vorozole, and paraphenyl-substituted diindolymethanes.⁴ Accordingly, novel synthetic methods to access enantiomerically highly enriched triarylmethanes and related compounds continue to be highly desirable.

Although a variety of racemic routes have been developed⁵ only a few enantioselective syntheses are currently available based upon reports from the groups of Jarvo,⁶ Watson,⁷ and Crudden⁸ who employed asymmetric cross-coupling technology to construct the target triarylmethanes in the optically highly enriched form. Apart from that You,⁹ Zhang,¹⁰ and Han¹¹ developed Brønsted acid-catalyzed, enantioselective syntheses of special aryldiindolymethanes starting from both aryl(3-indolyl)-methanols and aryl(2-indolyl)methanols.



Scheme 1 Brønsted acid-catalyzed reaction of *o*-QM with 1,3-diketones (pathway a) and with indoles and 2-naphthols (pathway b).

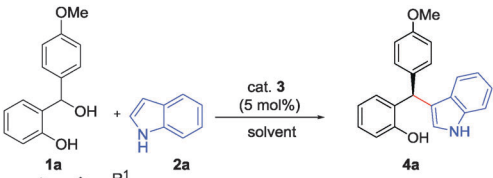
Recently, we have disclosed the phosphoric acid-catalyzed, highly enantioselective conjugate addition of 1,3-dicarbonyl compounds to *in situ* generated *ortho*-quinone methides (*o*-QM).¹² This strategy was applied to a one-pot and straightforward synthesis of optically highly enriched 4-aryl-4*H*-chromenes and related heterocycles through a subsequent cyclodehydration reaction (Scheme 1, pathway a). *o*-QM constitute highly reactive synthetic intermediates participating easily in conjugate additions, hetero Diels–Alder reactions, and 6*π*-electrocyclizations.¹³ It was only recently that a range of catalytic, enantioselective processes have been successfully developed for *o*-QM chemistry including palladium-, cinchona alkaloid-, BINOL- and NHC-catalyzed reactions.¹⁴

In continuation of our interest in enantioselective reactions of hydrogen-bonded *o*-QM we now report that both indoles and naphthols are highly suitable nucleophiles for this purpose and deliver broadly substituted diaryldiarylmethanes and triarylmethanes with excellent yields and enantioselectivities (Scheme 1, pathway b). Bach and coworkers pursued this strategy previously and obtained some addition products with moderate enantioselectivity.¹⁵ Very recently Sun *et al.* have shown that tertiary benzylic alcohols can form triarylmethanes that carry exclusively quaternary chiral centers upon indole addition.¹⁶

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Table 1 Optimization studies^a


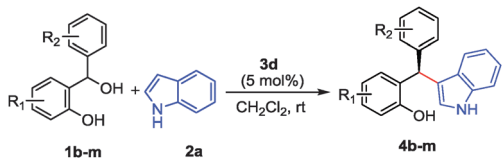
$R^1 = \text{Mes (3a)}$
 $= \text{Me}_5\text{-Ph (3b)}$
 $= \text{TRIP (3c)}$
 $= \text{2,6-Me}_2\text{-4-}^i\text{Bu-Ph (3d)}$
 $= \text{2,6-Me}_2\text{-4-OMe-Ph (3e)}$
 $= \text{2,4,6-Et}_3\text{-Ph (3f)}$

| Entry | Cat. | Solvent | Time (h) | Yield ^b (%) | Er ^c |
|-----------------|------|---------------------------------|----------|------------------------|-----------------|
| 1 | 3a | CH ₂ Cl ₂ | 1.5 | 96 | 80 : 20 |
| 2 | 3b | CH ₂ Cl ₂ | 1.5 | 97 | 89 : 11 |
| 3 | 3c | CH ₂ Cl ₂ | 2 | 94 | 80 : 20 |
| 4 | 3d | CH ₂ Cl ₂ | 1.5 | 94 | 91 : 9 |
| 5 | 3e | CH ₂ Cl ₂ | 1.5 | 94 | 72 : 28 |
| 6 | 3f | CH ₂ Cl ₂ | 1.5 | 96 | 89 : 11 |
| 7 | 3h | CH ₂ Cl ₂ | 1.5 | 97 | 65 : 35 |
| 8 ^d | 3d | CH ₂ Cl ₂ | 4 | 95 | 86 : 14 |
| 9 | 3d | CH ₃ CN | 2.5 | 96 | 79 : 21 |
| 10 | 3d | Toluene | 1.5 | 94 | 81 : 19 |
| 11 ^e | 3d | CH ₂ Cl ₂ | 1.5 | 92 | 92 : 8 |

^a All reactions were carried out with 0.23 mmol (1 equiv.) of **1a**, 0.27 mmol (1.2 equiv.) of **2a** and 5 mol% of catalyst **3a–3f** in 3 mL of CH₂Cl₂ at rt. ^b Isolated yield of the purified product. ^c Er determined through chiral HPLC-analysis (see the ESI). ^d Reaction was carried out at 0 °C. ^e 1.0 equiv. of indole (**2a**) was used as the substrate.

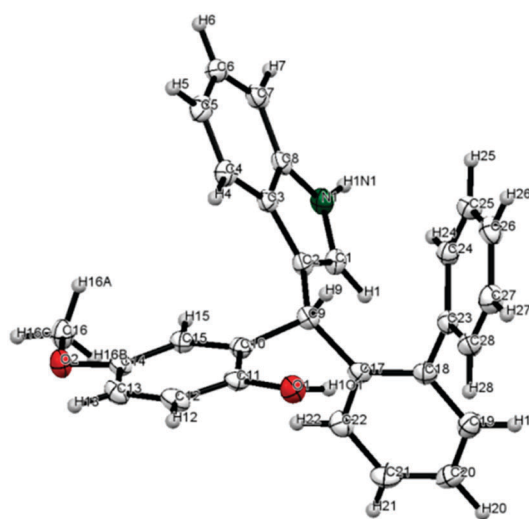
We initiated our studies by investigating the reaction of *ortho*-hydroxybenzhydrol **1a** (1 equiv.) with indole (**2a**) (1.2 equiv.) in CH₂Cl₂ in the presence of various chiral phosphoric acids **3a–g** (5 mol%) (Table 1). The (F–C) adduct **4a** was obtained in good yields in almost all cases within 2.5 h at room temperature. Systematic screening of the catalysts further revealed that sterically demanding 3,3'-aryl substituents in the BINOL-backbone of the Brønsted acid catalyst gave improved enantioselectivities. An optimal selectivity was eventually obtained with phosphoric acid **3d** (Ar = 2,6-Me₂-4-ⁱBuC₆H₂) which delivered the (F–C) addition product **4a** with 94% yield and 91:9 er (Table 1, entry 4). Solvents like toluene and CH₃CN were found to be inferior as compared to CH₂Cl₂, reducing the selectivity to 79:21 er and 81:19 er, respectively, albeit in excellent yields (entries 9 and 10). The amount of indole was further reduced to 1.0 equiv. without compromising the yield or selectivity of the reaction. Under these conditions the (F–C) adduct was isolated in 92% overall yield and with 92:8 er (entry 11). It is important to note that the free NH-moiety within the indole component is crucial for high enantioselectivity presumably *via* additional hydrogen-bonding to the phosphoric acid catalyst.¹⁷

To evaluate the scope of this process various *ortho*-hydroxy benzhydrols **1b–m** were subsequently reacted with indole (**2a**) under the above-optimized reaction conditions and the results are summarized in Table 2. In almost all cases studied, the reaction proceeded smoothly and was typically completed within 2–12 h at rt. The products **4b–m** were obtained in excellent yields and with good to excellent enantioselectivities (entries 1–12). A range of substituents was readily accommodated at various positions

Table 2 Substrate scope^a


| Entry | R ₁ | R ₂ | Product | Yield ^b (%) | Er ^c |
|-------|--------------------|---------------------|-----------|------------------------|-----------------|
| 1 | 4-OMe | 2-Me | 4b | 87 | 96 : 4 |
| 2 | 4-OMe | 2-Ph | 4c | 85 | 98 : 2 |
| 3 | 4-OMe | 2-OMe | 4d | 83 | 95 : 5 |
| 4 | 4-OMe | 2- ⁱ Pr | 4e | 85 | 96 : 4 |
| 5 | 4-OMe | 2,3-Me ₂ | 4f | 91 | 95 : 5 |
| 6 | 4-OMe | 4-Me | 4g | 86 | 92 : 8 |
| 7 | 4-Me | 2-Et | 4h | 92 | 95 : 5 |
| 8 | 4-Me | 2-Me | 4i | 82 | 94 : 6 |
| 9 | 4- ⁱ Bu | 4-Me | 4j | 87 | 92 : 8 |
| 10 | 4- ⁱ Bu | 2-OMe | 4k | 82 | 93 : 7 |
| 11 | 4-Br | 2-Et | 4l | 88 | 97 : 3 |
| 12 | 4-Br | 2-OMe | 4m | 84 | 99 : 1 |

^a All reactions were carried out with 0.42 mmol (1 equiv.) of **1b–m**, 0.42 mmol (1.0 equiv.) of indole (**2a**) and 5 mol% of catalyst **3d** in 4 mL of CH₂Cl₂ at rt for 2–12 h. ^b Isolated yield of the purified product. ^c Er determined through chiral HPLC-analysis (see the ESI).

Fig. 1 X-ray crystal structure of **4c**.

both within the *o*-QM fragment as well as the β -aryl substituent delivering the products with excellent results as well.

A crystal structure of diarylindolymethane **4c** (entry 2) obtained by slow evaporation of CH₂Cl₂ revealed its absolute configuration which was assigned to all other products as well (Fig. 1).¹⁸

In addition, the influence of various functional groups and substituents in the indole component was investigated in this study (Table 3). These results clearly reveal an excellent functional group tolerance of this process and a broad set of heteroaryl-substituted triarylmethanes was obtained in good yields and enantioselectivities irrespective of the electronic properties of the substituents on the indole ring.

Challenging substituents like phenol, formyl, acid, cyano, ester, ether, and halide groups did not interfere with this process and



Table 3 Brønsted acid-catalyzed addition of substituted indoles **2b–j** to *ortho*-hydroxybenzhydryl alcohols **1**^a

| Entry | R ₁ | R ₂ | R ₃ | Yield ^b (%) | Er ^c |
|-------|--------------------|-----------------------|--|------------------------|-----------------|
| 1 | 4-OMe | 2,3-di-Me | 5-Me | 88 (5a) | 94 : 6 |
| 2 | 4-OMe | 2-Et | 5-Me | 86 (5b) | 95 : 5 |
| 3 | 4-OMe | 2-Ph | 5-Me | 85 (5c) | 92 : 8 |
| 4 | 4- ^t Bu | 2-OMe | 5-Br | 84 (6a) | 94 : 6 |
| 5 | 4-OMe | 2-OMe | 5-Br | 90 (6b) | 95 : 5 |
| 6 | 4-OMe | 2-Et | 4-Br | 87 (7a) | 96 : 4 |
| 7 | 4-OMe | 2-Br | 4-Br | 82 (7b) | 92 : 8 |
| 8 | 4-OMe | 2-OMe | 6-Cl | 84 (8a) | 94 : 6 |
| 9 | 4-OMe | 2-Et | 6-Cl | 86 (8b) | 97 : 3 |
| 10 | 4-OMe | 2-Ph | 4-CHO | 82 (9a) | 97 : 3 |
| 11 | 4-OMe | 2-OMe | 4-CHO | 89 (9b) | 93 : 7 |
| 12 | 4-OMe | 2,3-(Me) ₂ | 4,5-(–OC ₂ H ₄ O–) | 90 (10a) | 96 : 4 |
| 13 | 4-Br | 2-Et | 4,5-(–OC ₂ H ₄ O–) | 89 (10b) | 94 : 6 |
| 14 | 4-OMe | 2-Ph | 5-CO ₂ Me | 82 (11a) | 98 : 2 |
| 15 | 4-Br | 2-Et | 5-CO ₂ Me | 81 (11b) | 93 : 7 |
| 16 | 4-Br | 2-Et | 4-OH | 70 (12) | 95 : 5 |
| 17 | 4-OMe | 2-Et | 4-CN | 88 (13a) | 96 : 4 |
| 18 | 4-OMe | 2-Br | 4-CN | 86 (13b) | 96 : 4 |
| 19 | 4-OMe | 2- ⁱ Pr | 5-CO ₂ H | 83 (14) | 86 : 14 |

^a All reactions were carried out with 0.42 mmol (1 equiv.) of **1**, 0.42 mmol (1.0 equiv.) of indoles **2b–j** and 5 mol% of catalyst **3d** in 4 mL of CH₂Cl₂ at rt for 2–12 h. ^b Isolated yield of the purified product. ^c Er determined through chiral HPLC-analysis (see the ESI).

furnished the desired (F–C) addition products in good to excellent enantioselectivities and high yields. The ability to withstand all these functional groups without compromising the yield or selectivity is testimony to the scope of this methodology.

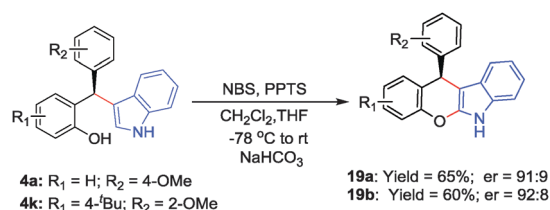
The excellent results obtained for indoles inspired us to pursue this strategy further and extend it to electron-rich naphthols which are also known to be excellent substrates to undergo (F–C) alkylation reactions. A range of Brønsted acid catalysts were screened for the (F–C) alkylation of 2-naphthol (**15a**) with *ortho*-hydroxybenzhydryl **1a** (see the ESI†). It turned out that in the presence of 5 mol% of catalysts **3a**, **3c**, and **3d**, respectively, the unsymmetrically substituted triarylmethanes were obtained in excellent yields in all cases studied. The highest enantioselectivity was obtained again with catalyst **3d** when 4 Å MS was used as an additive in CH₂Cl₂ as the solvent at room temperature.

With these conditions established we examined a range of 2-naphthols in reactions of hydrogen-bonded *o*-QM (Table 4). A series of differently substituted *ortho*-hydroxybenzhydryl alcohols were tested as *o*-QM precursors (entries 1–7). In almost all cases studied the triarylmethanes **17a–g** were isolated in excellent yields and with >96 : 4 er. Further substitution within the 2-naphthol ring with halogen, ester, ether, and aryl substituents was readily tolerated and delivered the products **17h–m** in comparably high yields and enantioselectivities (entries 8–13). Quite interestingly, 1-naphthol (**16**) worked equally well as the substrate and furnished triarylmethane **18** in almost quantitative yield and 93 : 7 er (entry 14).

Table 4 Brønsted acid-catalyzed addition of naphthols **15a–g** and **16** to *ortho*-hydroxybenzhydryl alcohols **1**^a

| Entry | R ₁ | R ₂ | R ₃ | Yield ^b (%) | Er ^c |
|-----------------|--------------------|--|----------------------|------------------------|-----------------|
| 1 | H | 4-OMe | H | 95 (17a) | 99 : 1 |
| 2 | H | 3,4-(–OC ₂ H ₄ O–) | H | 95 (17b) | 97 : 3 |
| 3 | H | 3,4-di-Me | H | 95 (17c) | 96 : 4 |
| 4 | H | 2,5-di-Me-4-OMe | H | 90 (17d) | 96 : 4 |
| 5 | H | 4-F | H | 90 (17e) | 87 : 13 |
| 6 | 4-Br | 4-OMe | H | 94 (17f) | 96 : 4 |
| 7 | 4- ^t Bu | 4-OMe | H | 94 (17g) | 96 : 4 |
| 8 | H | 4-OMe | 6-Br | 93 (17h) | 97 : 3 |
| 9 | H | 4-OMe | 7-Br | 94 (17i) | 97 : 3 |
| 10 | H | 4-OMe | 7-CO ₂ Me | 90 (17j) | 99 : 1 |
| 11 | H | 4-OMe | 6-Ph | 96 (17k) | 97 : 3 |
| 12 | H | 4-OMe | 7-OMe | 92 (17l) | 95 : 5 |
| 13 | H | 4-OMe | 6-Naphth | 94 (17m) | 97 : 3 |
| 14 ^d | H | 4-OMe | H | 97 (18) | 93 : 7 |

^a All reactions were carried out with 0.2 mmol (1 equiv.) of **1**, 0.24 mmol (1.2 equiv.) of naphthols **15a–g** and **16** using 5 mol% of catalyst **3d** in 2 mL of CH₂Cl₂ at rt for 4–6 h in the presence of a catalytic amount of 4 Å MS. ^b Isolated yield of the purified product. ^c Er determined through chiral HPLC-analysis (see the ESI). ^d 1-Naphthol (**16**) was used as the substrate.

**Scheme 2** Conversion into dihydrochromeno[2,3-*b*]indoles **19a–b**.

To further reveal the synthetic potential of this new process some of the diarylindolylmethanes were subsequently converted into highly versatile dihydrochromeno[2,3-*b*]indoles **19a–b** through a one-pot bromination followed by cyclization and base-catalyzed elimination (Scheme 2).^{14h} The products were obtained in good yields and retained their optical purity almost completely.

On the basis of the crystal structure which we obtained for the (F–C)-product **4c**, we propose a transition structure as shown in Fig. 2, which accommodates double hydrogen-bonding of the catalyst to both the *o*-QM and the nucleophile and intramolecular delivery of the nucleophile to the *re*-face of the *o*-QM because the opposite face is effectively shielded by the neighbouring 3'-Ar-group.¹⁹

In summary, we have developed a highly efficient, Brønsted acid-catalyzed (F–C)-alkylation of electron-rich indoles and



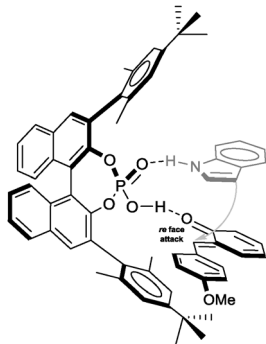


Fig. 2 Plausible transition state structure.

naphthols with *in situ*-generated *o*-QM which furnished a broad range of synthetically useful diarylindolylmethanes and triaryl-methanes with excellent yields and enantioselectivities. The diarylindolylmethanes were subsequently converted into valuable dihydrochromeno[2,3-*b*]indoles through a base-catalyzed addition–elimination reaction with full retention of absolute configuration. This study further underlines the utility and power of phosphoric acid-catalyzed, enantioselective reactions of *o*-QM and significantly extends the scope of this strategy.

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Notes and references

- (a) D. F. Duxbury, *Chem. Rev.*, 1993, **93**, 381; (b) R. Muthyala, A. R. Katritzky and X. Lan, *Dyes Pigm.*, 1994, **25**, 303; (c) A. R. Katritzky, V. Gupta, C. Garot, C. V. Stevens and M. F. Gordeev, *Heterocycles*, 1994, **38**, 345; (d) M. S. Shchepinov and V. A. Korshun, *Chem. Soc. Rev.*, 2003, **32**, 170; (e) Y.-Q. Xu, J.-M. Lu, N.-J. Li, F. Yan, X. Xia and Q. Xu, *Eur. Polym. J.*, 2008, **44**, 2404; (f) N. Herron, G. A. Johansson and N. S. Radu, *US Pat.* 2005/0187364, 2005.
- (a) Shagufta, A. K. Srivastava, R. Sharma, R. Mishra, A. K. Balapure, P. S. R. Murthy and G. Panda, *Bioorg. Med. Chem.*, 2006, **14**, 1497; (b) R. Palchaudhuri, V. Nesterenko and P. J. Hergenrother, *J. Am. Chem. Soc.*, 2008, **130**, 10274; (c) M. K. Parai, G. Panda, V. Chaturvedi, Y. K. Manju and S. Sinha, *Bioorg. Med. Chem. Lett.*, 2008, **18**, 289; (d) B. A. Ellsworth, W. R. Ewing and E. Jurica, *US Pat.* 2011/0082165A1, 2011.
- (a) K. Baba, K. Maeda, Y. Tabata, M. Doi and M. Kozawa, *Chem. Pharm. Bull.*, 1988, **36**, 2977; for a recent total synthesis of cassigarol B involving Friedel–Crafts methodology see: (b) S. A. Snyder, S. P. Breazzano, A. G. Ross, Y. Lin and A. L. Zografos, *J. Am. Chem. Soc.*, 2009, **131**, 1753.
- For select examples of letrozole- and vorozole-type triarylmethanes see: (a) H. V. Bossche, G. Willemsens, I. Roels, D. Bellens, H. Moereels, M. C. Coene, L. L. Jeune, W. Lauwers and P. A. Janssen, *Biochem. Pharmacol.*, 1990, **40**, 1707; (b) M. Recanatini, A. Cavalli and P. Valenti, *Med. Res. Rev.*, 2002, **22**, 282; (c) P. M. Wood, L. L. Woo, J. R. Labrosse, M. N. Trusselle, S. Abbate, G. Longhi, E. Castiglioni, F. Lebon, A. Purohit and M. K. Reed, *J. Med. Chem.*, 2008, **51**, 4226; (d) K. Takahashi, G. Yamagishi, T. Hiramatsu, A. Hosoya, K. Onoe, H. Doi, H. Nagata, Y. Wada, H. Onoe, Y. Watanabe and T. Hosoya, *Bioorg. Med. Chem.*, 2011, **19**, 1464; (e) P. M. Wood, L. W. Woo, M. P. Thomas, M. F. Mahon, A. Purohit and B. V. Potter, *ChemMedChem*, 2011, **6**, 1423; for select examples of *para*-phenyl-substituted diindolylmethanes see: (f) S. D. Cho, K. Yoon, S. Chintharlapalli, M. Abdelrahim, P. Lei, S. Hamilton, S. Khan, S. K. Ramaiah and S. Safe, *Cancer Res.*, 2007, **67**, 674; (g) T. Inamoto, S. Papineni, S. Chintharlapalli, S. D. Cho, S. Safe and A. M. Kamat, *Mol. Cancer Ther.*, 2008, **7**, 3825; (h) S. D. Cho, S. O. Lee, S. Chintharlapalli, M. Abdelrahim, S. Khan, K. Yoon, A. M. Kamat and S. Safe, *Mol. Pharmacol.*, 2010, **77**, 396; (i) K. Yoon, S. O. Lee, S. D. Cho, K. Kim, S. Khan and S. Safe, *Carcinogenesis*, 2011, **32**, 836.
- Select recent examples: (a) V. Nair, K. G. Abhilash and N. Vidya, *Org. Lett.*, 2005, **7**, 5857; (b) T. Niwa, H. Yorimitsu and K. Oshima, *Org. Lett.*, 2007, **9**, 2373; (c) J. Y. Yu and R. Kuwano, *Org. Lett.*, 2008, **10**, 973; (d) C. R. Liu, M. B. Li, C. F. Yang and S. K. Tian, *Chem. Commun.*, 2008, 1249; (e) Y. G. I. McGrew, J. Temaimithi, P. J. Carroll and P. J. Walsh, *Angew. Chem., Int. Ed.*, 2010, **49**, 5541; (f) J. Zhang, A. Bellomo, A. D. Creamer, S. D. Dreher and P. J. Walsh, *J. Am. Chem. Soc.*, 2012, **134**, 13765; (g) S. Tabuchi, K. Hirano, T. Satoh and M. Miura, *J. Org. Chem.*, 2014, **79**, 5401; (h) J. Zhang, A. Bellomo, A. D. Creamer, S. D. Dreher and P. J. Walsh, *J. Am. Chem. Soc.*, 2014, **136**, 6276.
- (a) B. L. H. Taylor, M. R. Harris and E. R. Jarvo, *Angew. Chem., Int. Ed.*, 2012, **51**, 7790; (b) M. R. Harris, L. E. H. M. A. Greene, C. E. Moore and E. R. Jarvo, *J. Am. Chem. Soc.*, 2013, **135**, 3303.
- Zhou, H. D. Srinivas, S. Dasgupta and M. P. Watson, *J. Am. Chem. Soc.*, 2013, **135**, 3307.
- (a) S. C. Matthew, B. W. Glasspoole, P. Eisenberger and C. M. Crudden, *J. Am. Chem. Soc.*, 2014, **136**, 5828; (b) M. Nambo and C. M. Crudden, *Angew. Chem., Int. Ed.*, 2014, **53**, 742.
- F. L. Sun, X. J. Zheng, Q. Gu, Q. L. He and S. L. You, *Eur. J. Org. Chem.*, 2010, 47.
- M. H. Zhuo, Y. J. Jiang, Y. S. Fan, Y. Gao, S. Liu and S. Zhang, *Org. Lett.*, 2014, **16**, 1096.
- S. Qi, C. Y. Liu, J. Y. Ding and F. S. Han, *Chem. Commun.*, 2014, **50**, 8605.
- (a) O. El-Sepelgy, S. Haseloff, S. K. Alamsetti and C. Schneider, *Angew. Chem., Int. Ed.*, 2014, **53**, 7923; (b) After publication of our results another communication appeared: C. C. Hsiao, H. H. Liao and M. Rueping, *Angew. Chem., Int. Ed.*, 2014, **53**, 13258.
- Reviews: (a) R. W. van de Water and T. R. Pettus, *Tetrahedron*, 2002, **58**, 5367; (b) T. P. Pathak and M. S. Sigman, *J. Org. Chem.*, 2011, **76**, 9210; (c) N. J. Willis and C. D. Bray, *Chem. – Eur. J.*, 2012, **18**, 9160.
- (a) Y. Zhang and M. S. Sigman, *J. Am. Chem. Soc.*, 2007, **129**, 3076; (b) A. E. Mattson and K. A. Scheidt, *J. Am. Chem. Soc.*, 2007, **129**, 4508; (c) E. Alden-Danforth, M. T. Scerba and T. Lectka, *Org. Lett.*, 2008, **10**, 4951; (d) K. H. Jensen, T. P. Pathak, Y. Zhang and M. S. Sigman, *J. Am. Chem. Soc.*, 2009, **131**, 17074; (e) T. P. Pathak, K. M. Gligorich, B. E. Welm and M. S. Sigman, *J. Am. Chem. Soc.*, 2010, **132**, 7870; (f) K. H. Jensen, J. D. Webb and M. S. Sigman, *J. Am. Chem. Soc.*, 2010, **132**, 17471; (g) M. Rueping, U. Uria, M. Y. Lin and I. Atodiresei, *J. Am. Chem. Soc.*, 2011, **133**, 3732; (h) R. Jana, T. P. Pathak, K. H. Jensen and M. S. Sigman, *Org. Lett.*, 2012, **14**, 4074; (i) Y. Luan and S. E. Schaus, *J. Am. Chem. Soc.*, 2012, **134**, 19965; (j) H. Lv, W. Q. Jia, L. H. Sun and S. Ye, *Angew. Chem., Int. Ed.*, 2013, **52**, 8607; (k) J. Izquierdo, A. Orue and K. A. Scheidt, *J. Am. Chem. Soc.*, 2013, **135**, 10634; (l) B. S. Zeng, X. Yu, P. W. Siu and K. A. Scheidt, *Chem. Sci.*, 2014, **5**, 2277.
- D. Wilcke, E. Herdtweck and T. Bach, *Synlett*, 2011, 1235.
- W. Zhao, Z. Wang, B. Chu and J. Sun, *Angew. Chem., Int. Ed.*, 2014, **53**, DOI: 10.1002/anie.201405252.
- N*-Boc indole gives rise to the corresponding diarylindolylmethane in 94% yield and with 56:44 er.
- CCDC 1028558 (4c).
- The intermediacy of *ortho*-quinone methides in this transformation is supported by an experiment in which a stable *ortho*-quinone methide prepared separately is treated with indole (2a) and phosphoric acid catalyst 3d under otherwise identical reaction conditions and furnishes the diarylindolylmethane in comparable yield and enantioselectivity.

