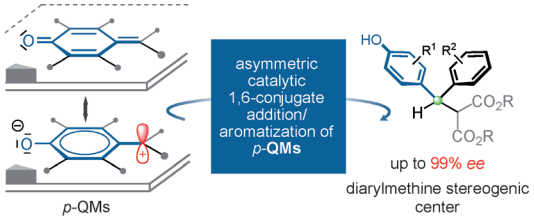
Communications

Asymmetric Catalysis

W.-D. Chu, L.-F. Zhang, X. Bao, X.-H. Zhao, C. Zeng, J.-Y. Du, G.-B. Zhang, F.-X. Wang, X.-Y. Ma, C.-A. Fan* _____ ■■■■–■■■■



Asymmetric Catalytic 1,6-Conjugate Addition/Aromatization of *para*-Quinone Methides: Enantioselective Introduction of Functionalized Diarylmethine Stereogenic Centers

It's just a phase: The title reaction sequence of *para*-quinone methides (*p*-QMs) has been developed with malonates under phase-transfer catalysis. The reaction also offers an alternative route to asymmetric construction of diarylmethine stereocenters in excellent enantioselectivities and high yields.

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DOI: 10.1002/anie.201303928

Asymmetric Catalytic 1,6-Conjugate Addition/Aromatization of *para*-Quinone Methides: Enantioselective Introduction of Functionalized Diarylmethine Stereogenic Centers**

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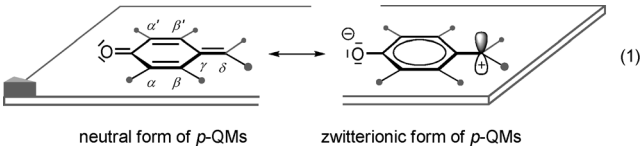
para-Quinone methides [*p*-QMs; Eq. (1)],[1] which are structurally characterized by the unique assembly of carbonyl and olefinic moieties, and chemically defined as neutral and zwitterionic resonance entities, have been already known for



(1)

more than one century in organic chemistry.[2] In nature, *p*-QM units exist in a variety of natural products such as fungal metabolites, terpenes, and plant pigments.[3] As a result of the intrinsic electrophilic reactivity of *p*-QMs, highly reactive transient *p*-QM species generated in situ are implicated in many chemical, medicinal, and biological processes such as lignin biosynthesis, enzyme inhibition, and DNA alkylation and cross-linking.[1,4] Synthetically, *ortho*-quinone methides (*o*-QMs), a structural isomer of *p*-QMs, have been extensively studied for the development of asymmetric methodologies such as 1,4-conjugate addition, [4+2]-cycloaddition, and 6π electrocyclization.[5] But surprisingly, few enantioselective additions of *p*-QMs have been documented, especially in a catalytic asymmetric fashion.[1,6–8] Therefore, the development of an effective catalytic enantioselective addition of *p*-QMs remains an important challenge in modern organic synthesis.

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[**] This research was supported by the 973 Program of MOST (2010CB833200), NSFC (21290180, 21072082), the Fok Ying Tung Education Foundation (121015), NCET (NCET-08-0254), PCSIRT (IRT1138), the Major New-Drug-Development Project of MOST (2012ZX09201101-003), FRFCU (lzujbky-2012-k39 and lzujbky-2013-ct02), and the 111 Project of MOE (111-2-17).
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201303928.

To address this topic, and stimulated by the alternative design for the construction of synthetically important diarylmethine stereogenic centers, which are ubiquitous in many biological natural products and drugs (Figure 1), a novel

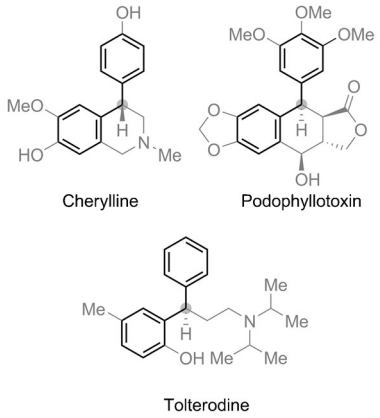
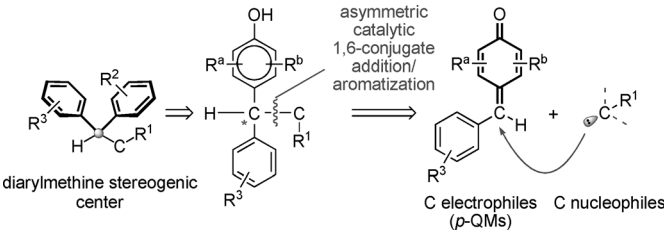


Figure 1. Diarylmethine stereocenters in selected bioactive molecules.

asymmetric catalytic 1,6-conjugate addition[9] of *p*-QMs with C nucleophiles was envisaged (Scheme 1). The additional driving force of aromatization would thermodynamically



Scheme 1. Asymmetric catalytic 1,6-conjugate addition of *p*-QMs.

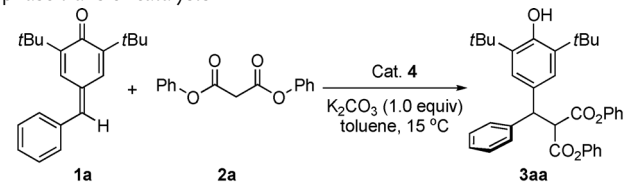
allow such a nucleophilic addition to be more reactive than the addition to the classic conjugated enone system, but it would also be elusive in its stereoselectivity. Regarding the catalytic enantioselective synthesis of diarylmethine stereogenic centers, great effort has been made during the past decades, and mainly includes: 1) conjugate addition of aryl anion equivalents to electron-deficient olefins,[10] 2) Friedel–Crafts alkylation of electron-rich arenes with electron-deficient olefins,[11] 3) hydrogenation of *gem*-diaryl alkenes,[12] 4) allylic arylation of cinnamyl-type phosphates,[13a] 5) hydro-

arylation of styrenes,[13b] and 6) 1,4-conjugate addition of boronates to *ortho*-quinone methides.[13c] Given the appeal for the exploration of new asymmetric methodologies using the *p*-QM chemistry, we report herein an alternative approach for the asymmetric synthesis of functionalized diarylalkanes featuring a novel catalytic enantioselective 1,6-conjugate addition/aromatization of *p*-QMs with malonates under phase-transfer catalysis.[14]

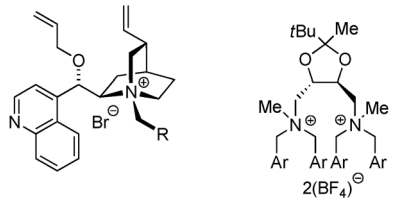
Initially, the asymmetric 1,6-conjugate addition of *p*-QMs was evaluated by the screening of chiral catalysts in the model system (Table 1).[15] Among the examined phase-transfer catalysts, the related N-bridged cinchona ammonium salts **4a** and **4b**[16a,b] (entries 1–2) could promote the given transformation, but with lower efficiencies in both reactivity and enantioselectivity. Surprisingly, the tartrate-derived bis(ammonium tetrafluoroborate) **4c**[16c] was ineffective in the current addition reaction (entry 3). In addition to these center-chiral catalysts, three binaphthyl-modified ammonium halides (**4d–f**) with axial chirality, compounds first discovered by Maruoka and co-workers,[16d–f] were then investigated. Significantly, the homochiral N-spiroquaternary ammonium bromide **4d** gave a higher yield and *ee* value (entry 4). Both the catalyst **4e** (entry 5), with substituent modification at the 3,3′-chiral-binaphthyl moiety, and the catalyst **4f** (entry 6), with simplified substituents at the nitrogen center, had a negative influence on the enantioselectivity. Subsequently, the catalyst and base loadings were also examined (entries 7 and 8), and it should be noted that the catalytic amounts of **4d** can be reduced to 0.01 equivalents in the presence of three equivalents of K_2CO_3 without loss of yield and stereocontrol.

After the above preliminary optimization, we then surveyed the structural influence of nucleophilic active methylene donors on the reactivity and stereoselectivity of asymmetric 1,6-conjugate addition to *p*-QMs (Table 2). A series of malonic esters (**2a–g**) were investigated from a steric

Table 1: Asymmetric 1,6-conjugate addition of *p*-QMs catalyzed by phase-transfer catalysts[a]

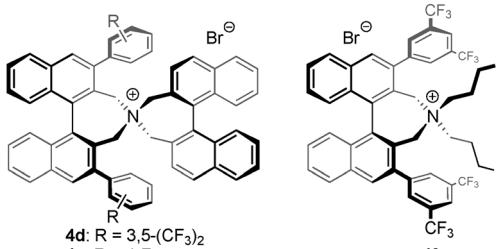


1a **2a** **3aa**



4a: R = Ph
4b: R = 9-anthryl

4c: Ar = 4-MeOC$_6$H$_4$



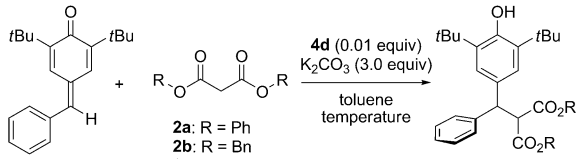
4d: R = 3,5-(CF$_3$)$_2$
4e: R = 4-F

4f

Entry	Cat. (Equiv)	*t* [h]	Yield [%][b]	*ee* [%][c]
1	**4a** (0.1)	44.5	80	8
2	**4b** (0.1)	44.5	65	−32
3	**4c** (0.1)	73.5	trace	–
4	**4d** (0.1)	2.5	96	93
5	**4e** (0.1)	3	96	40
6	**4f** (0.1)	48	81	63
7	**4d** (0.01)	4	96	93
8	**4d** (0.01)	2[d]	96	93

[a] Performed with **1a** (0.05 mmol) and **2a** (0.055 mmol) in the presence of K_2CO_3 (0.05 mmol) and the catalyst **4** (0.005 mmol or 0.0005 mmol) in toluene (0.5 mL). [b] Yield of isolated product. [c] Determined by HPLC analysis using a chiral stationary phase. [d] Three equivalents of K_2CO_3 were used.

Table 2: Effect of malonates in asymmetric addition.[a]



1a

2a: R = Ph
2b: R = Bn
2c: R = Me
2d: R = *t*Bu
2e: R = 4-MeOC$_6$H$_4$
2f: R = 4-BrC$_6$H$_4$
2g: R = 4-ClC$_6$H$_4$

3aa–3ag

Entry	Donor	Product	*T* [°C]	*t* [h]	Yield [%][b]	*ee* [%][c]
1	**2a**	**3aa**	15	2	96	93
2	**2b**	**3ab**	15	2	95	58
3	**2c**	**3ac**	15	2	96	37
4	**2d**	**3ad**	15	48	29	44
5	**2e**	**3ae**	15	2	96	92
6	**2f**	**3af**	15	48	81	10
7	**2g**	**3ag**	15	48	69	9
8	**2a**	**3aa**	0	21	96	96
9	**2a**	**3aa**	−40	33	96	98

[a] Performed with **1a** (0.05 mmol) and **2a–g** (0.055 mmol) in the presence of K_2CO_3 (0.15 mmol) and the catalyst **4d** (0.0005 mmol) in toluene (0.5 mL) at the indicated temperature. [b] Yield of isolated product. [c] Determined by HPLC analysis using a chiral stationary phase.

and electronic standpoint. Compared with the result using diphenyl malonate (**2a**; entry 1), the dialkyl malonates **2b** (entry 2) and **2c** (entry 3) showed the same efficiency in reactivity, but resulted in a considerable decrease in enantioselectivity. The sterically more hindered di-*tert*-butyl malonate (**2d**; entry 4) gave both a low yield and a low *ee* value. Interestingly, the reaction using the electron-donating diaryl ester **2e** (entry 5) proceeded with excellent yield and enantioselectivity. Surprisingly, the 1,6-conjugate addition took place slowly to give a very poor asymmetric induction when the electron-withdrawing diaryl etser **2f** (entry 6) or **2g** (entry 7) was employed, thus revealing an interesting donor electronic effect in the nucleophilic addition. To further improve the enantioselectivity, this reaction was performed at a decreased temperature in the presence of the readily available **2a** (entries 8 and 9), and gratifyingly the optimal

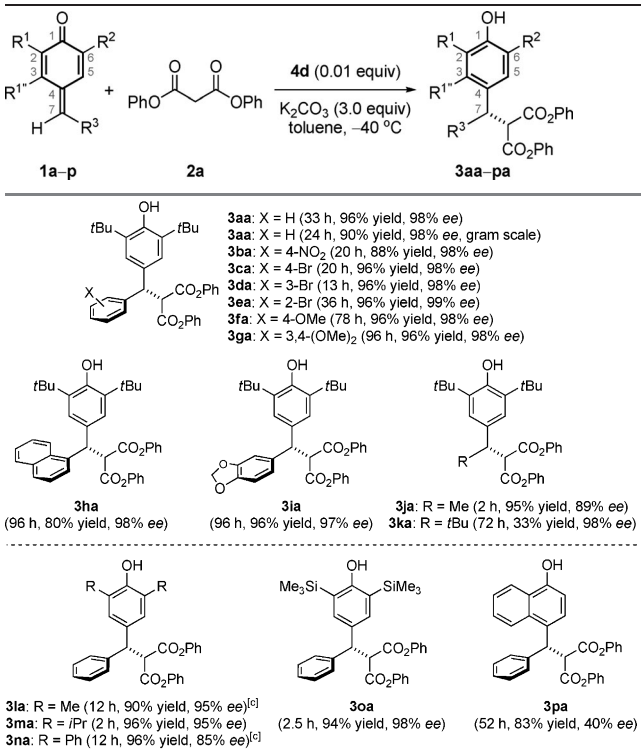
enantioselectivity of 98% *ee* with 96% yield was attainable in the current model, despite a prolonged reaction time.

To evaluate the scope and limitations of this asymmetric methodology, various chemically stable *p*-QMs (**1a–p**) in the presence of the matching donor **2a** were subsequently subjected to the above optimized reaction conditions (Table 3). In most cases, this reaction proceeded smoothly with excellent enantioselectivity and in high yield. For example, while using the *p*-QMs **1a–i** ($R^1 = R^2 = t$Bu, $R^{1''}$ = H, R^3 = aryl) with a series of electron-neutral, electron-deficient, or electron-rich aryls at C7, the diarylalkanes **3aa–ia** could be obtained in 97–99% *ee* and 80–96% yield, and the absolute configuration of **3da** was determined unambiguously by X-ray crystallographic analysis.[17] Notably, as exemplified for the formation of **3aa**, the present asymmetric 1,6-conjugate addition/aromatization of *p*-QMs can be carried out on gram scale (90% yield, 98% *ee*). In such examples, the bulky *tert*-butyl group, which is often used as a positional protective group for access to many aromatic compounds in organic synthesis,[18] was preinstalled in the starting *p*-QMs because of the requirement of their chemical stabilization. Notably, a three-step protocol consisting of the transesterification, Krapcho dealkoxycarbonylation, and $AlCl_3$-mediated trans-*tert*-butylation has been illustrated for de-*tert*-butylation[18] of the addition product **3aa** (Scheme 2), thus affording the de-*tert*-butylated phenol **5** in 58% yield over three steps without erosion of optical purity. To expand the generality of this method, the C7-alkyl-substituted *p*-QMs **1j** ($R^1 = R^2 = t$Bu, $R^{1''}$ = H, R^3 = Me) and **1k** ($R^1 = R^2 = R^3 = t$Bu, $R^{1''}$ = H) were also examined (Table 3). Compared with the result for the product **3ja** (2 h, 95% yield and 89% *ee*), the steric bulk of the *tert*-butyl group on C7 of **1k** obviously slowed this 1,6-conjugate addition (72 h, 33% yield) despite the excellent stereocontrol for **3ka** (98% *ee*).

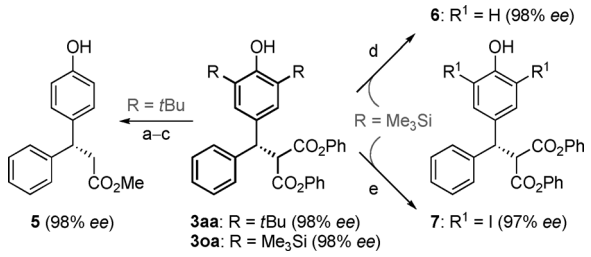
In addition to the above investigation on the influence of the substituents at C7, the *p*-QMs **1l–p** (R^3 = Ph; R^1,R^2 = alkyl, aryl, silyl; Table 3) bearing non-*tert*-butyl substituents at C2 and C6 were also probed for this asymmetric catalytic 1,6-conjugate addition. In comparison with the aforementioned *ee* value and yield of **3aa** obtained from **1a**, the less bulky substituents at C2 and C6 of **1l** ($R^1 = R^2$ = Me, $R^{1''}$ = H, R^3 = Ph) and **1m** ($R^1 = R^2 = i$Pr, $R^{1''}$ = H, R^3 = Ph) may account for an increased reaction rate, thus giving the analogous enantioselectivities and yields for **3la** and **3ma**. When using the *p*-QM **1n** ($R^1 = R^2 = R^3$ = Ph, $R^{1''}$ = H) with the sp^2-hybridized phenyl substituent located at C2 and C6, the reactivity was maintained, but a decrease in enantioselectivity was observed for the formation of **3na** at −60 °C. Importantly, because of the potential application in functionalization and transformation reactions of the C(sp^2)–Si bond in organic synthesis,[19] the bis(silyl)-substituted *p*-QM **1o** ($R^1 = R^2 = Me_3Si$, $R^{1''}$ = H, R^3 = Ph) was designed and examined in this reaction. Interestingly this addition proceeded quickly, and the desired product **3oa** was afforded with 98% *ee* in 94% yield. Further treatment of **3oa** with CF_3CO_2H and ICl gave the *ipso*-protodesilylated phenol **6** and *ipso*-iododesilylated phenol **7**, respectively, in good yields without noticeable loss of the *ee* value (Scheme 2). Moreover, **1p** ($R^1 + R^{1''}$ = 1,3-butadiene-1,4-diyl, R^2 = H, R^3 = Ph) with substituents at C2 and C3 was also considered in this case, but disappointingly a modest enantioselectivity of 40% *ee* for **3pa** was achieved (Table 3).

To further understand the influence of the stereochemistry of exocyclic methylene substituents of *p*-QMs on the

Table 3: Generality of asymmetric 1,6-conjugate addition/aromatization of *p*-QMs.[a,b]

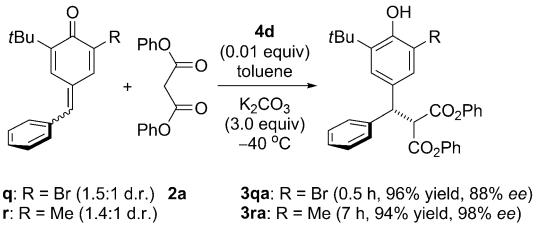


[a] Performed with **1a–p** (0.05 mmol) and **2a** (0.055 mmol) in the presence of K_2CO_3 (0.15 mmol) and the catalyst **4d** (0.0005 mmol) in toluene (0.5 mL) at −40 °C. The yields refer to the isolated products, and the *ee* values were determined by HPLC analysis using a chiral stationary phase. [b] The absolute configuration of **3da** was established by X-ray crystallographic analysis, and accordingly the reaction enantioselectivity in other cases was assigned by analogy. [c] Performed at −60 °C.



Scheme 2. De-*tert*-butylation and desilylation of diarylalkanes. a) KOH/MeOH (0.1 M), THF, RT, 99% yield; b) NaI, H_2O, DMSO, 160 °C, 70% yield; c) $AlCl_3$, benzene, 60 °C, 85% yield, 98% *ee*; d) CF_3CO_2H, CCl_4, RT, 86% yield, 98% *ee*; e) ICl, CH_2Cl_2, RT, 80% yield, 97% *ee*. DMSO = dimethylsulfoxide, THF = tetrahydrofuran.

asymmetric control of 1,6-conjugate addition/aromatization, a stereoisomeric mixture of either the prochiral *p*-QM **1q** (1.5:1 d.r.) or **1r** (1.4:1 d.r.) was subjected to control experiments (Scheme 3). Remarkably, this reaction proceeded smoothly with an excellent *ee* value and yield, and the absolute configuration of **3qa** was also unambiguously



1q: R = Br (1.5:1 d.r.) **2a**
1r: R = Me (1.4:1 d.r.)

3qa: R = Br (0.5 h, 96% yield, 88% *ee*)
3ra: R = Me (7 h, 94% yield, 98% *ee*)

Scheme 3. Effect of exocyclic stereochemistry of *p*-QMs.

established by X-ray crystallographic analysis.[17] Importantly, the observed unique enantioselectivity implied that the stereodiscrimination to the prochiral *Re* face of either **1q** or **1r** was independent of the configuration of exocyclic methylene substituents of *p*-QMs.

Based on these facts, a rationale for the enantioselectivity under the catalysis of **4d** in the presence of the matching donor **2a** is tentatively proposed (Figure 2). The homochiral N-spirobinaphthyl-derived catalyst **4d**, graphically simplified as the model **A**, provides a unique chiral quaternary ammonium center in a regular tetrahedron (orange yellow). As shown in **I**, the bidentate property of the enolate anion of the malonate **2a**, which is simplified as the model **B**, resulted in a complexation through Coulombic interactions with the chiral ammonium cation from the more accessible C1-C4 edge defined by the intersection of two triangular faces C1-C2-C4 and C1-C3-C4. Alternatively, the same ionic complexation of the enolate anion with the chiral ammonium cation

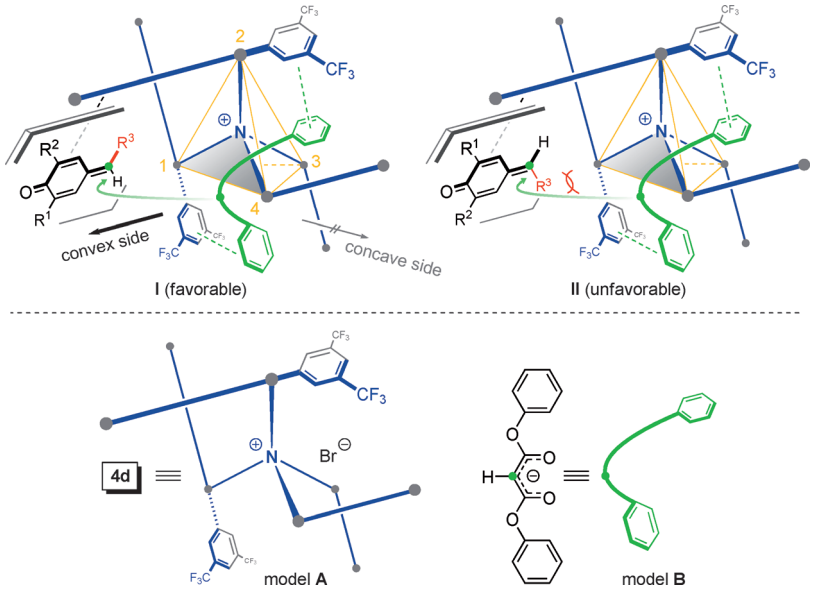


Figure 2. Plausible transition-state models.

could be also accessed in a bidentate fashion from the equally accessible C2-C3 edge defined by the intersection of two faces C1-C2-C3 and C2-C3-C4. According to the aforementioned donor effects (Table 2, entries 1 and 5), the π-stacking interactions between the phenyl group and 3,5-bis(trifluoromethyl)phenyl moiety might be involved in **I**, thus leading to additional strengthening of the noncovalent complexation between the enolate anion and ammonium cation. Compared with the unfavorable orientation of the *p*-QM plane in **II**, the planar prochiral *p*-QMs oriented as depicted in **I** would then approach the enolate anion mainly from the less steric convex side to deliver the observed enantioselectivity, and the additional π-stacking interactions between the electron-deficient *p*-QMs and the naphthyl moiety of catalyst might also be involved.

In summary, a novel catalytic asymmetric 1,6-conjugate addition/aromatization of *p*-QMs with malonates under phase-transfer catalysis was developed for *p*-QM chemistry. A series of synthetically interesting, functionalized diarylalkanes were achieved with good to high yields (up to 96%) and enantioselectivities (up to 99% *ee*) in most of cases, thus providing an alternative approach to the catalytic enantioselective construction of functionalized diarylmethine stereogenic centers. Presently, further synthetic applications as well as the enantiodiscrimination rationale for this reaction are under investigation in our laboratory.

Received: May 8, 2013
Revised: June 14, 2013
Published online: ■■ ■■, ■■■■

Keywords: arenes · asymmetric catalysis · enantioselectivity · phase-transfer catalysis · quinone methides

[1] For reviews on the chemistry of *p*-QMs, see: a) A. B. Turner, *Q. Rev. Chem. Soc.* **1964**, *18*, 347; b) "Quinone Methides": H.-U. Wagner, R. Gompper in *The Chemistry of the Quinonoid Compounds, Vol. 2* (Ed.: S. Patai), Wiley, New York, **1974**, chap. 18, pp. 1145–1178; c) M. G. Peter, *Angew. Chem.* **1989**, *101*, 572; *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 555; d) T. Itoh, *Prog. Polym. Sci.* **2001**, *26*, 1019; e) *Quinone Methides* (Ed.: S. E. Rokita), Wiley, Hoboken, **2009**; f) M. M. Toteva, J. P. Richard, *Adv. Phys. Org. Chem.* **2011**, *45*, 39.

[2] A. Baeyer, V. Villiger, *Ber. Dtsch. Chem. Ges.* **1903**, *36*, 2792.

[3] For recent selected examples, see: a) K.-i. Takao, T. Sasaki, T. Kozaki, Y. Yanagisawa, K.-i. Tadano, A. Kawashima, H. Shinonaga, *Org. Lett.* **2001**, *3*, 4291; b) B. E. Barragán-Huerta, J. Peralta-Cruz, R. F. González-Laredo, J. Karchesy, *Phytochemistry* **2004**, *65*, 925; c) H. J. Martin, T. Magauer, J. Mulzer, *Angew. Chem.* **2010**, *122*, 5746; *Angew. Chem. Int. Ed.* **2010**, *49*, 5614; d) R. Jansen, K. Gerth, H. Steinmetz, S. Reinecke, W. Kessler, A. Kirschning, R. Müller, *Chem. Eur. J.* **2011**, *17*, 7739.

[4] For selected examples, see: a) A. A. Larsen, *Nature* **1969**, *224*, 25; b) D. Hamels, P. M. Dansette, E. A. Hillard, S. Top, A. Vessières,

P. Herson, G. Jaouen, D. Mansuy, *Angew. Chem.* **2009**, *121*, 9288; *Angew. Chem. Int. Ed.* **2009**, *48*, 9124; c) G. B. Messiano, T. da Silva, I. R. Nascimento, L. M. X. Lopes, *Phytochemistry* **2009**, *70*, 590; d) R. Dehn, Y. Katsuyama, A. Weber, K. Gerth, R. Jansen, H. Steinmetz, G. Höfle, R. Müller, A. Kirschning, *Angew. Chem.* **2011**, *123*, 3968; *Angew. Chem. Int. Ed.* **2011**, *50*, 3882; e) C. Sridar, J. D'Agostino, P. F. Hollenberg, *Drug Metab. Dispos.* **2012**, *40*, 2280.

[5] For selected reviews on the chemistry of *o*-QMs, see Refs. [1a,b,e] and: a) P. Wan, B. Barker, L. Diao, M. Fischer, Y. Shi, C. Yang, *Can. J. Chem.* **1996**, *74*, 465; b) Y. Chiang, A. J. Kresge, Y. Zhu, *Pure Appl. Chem.* **2000**, *72*, 2299; c) R. W. Van De Water, T. R. R. Pettus, *Tetrahedron* **2002**, *58*, 5367; d) H. Amouri, J. Le Bras, *Acc. Chem. Res.* **2002**, *35*, 501; e) S. B. Ferreira, F. de C. da Silva, A. C. Pinto, D. T. G. Gonzaga, V. F. Ferreira, *J. Heterocycl. Chem.* **2009**, *46*, 1080; f) T. P. Pathak, M. S. Sigman, *J. Org. Chem.* **2011**, *76*, 9210; g) N. J. Willis, C. D. Bray, *Chem. Eur. J.* **2012**, *18*, 9160, and references therein.

[6] For non-asymmetric intramolecular cyclizations of *p*-QMs, see: a) D. J. Hart, P. A. Cain, D. A. Evans, *J. Am. Chem. Soc.* **1978**, *100*, 1548; b) S. R. Angle, K. D. Turnbull, *J. Am. Chem. Soc.* **1989**, *111*, 1136; c) S. R. Angle, M. S. Louie, H. L. Mattson, W. Yang, *Tetrahedron Lett.* **1989**, *30*, 1193; d) S. R. Angle, J. D. Rainier, *J. Org. Chem.* **1992**, *57*, 6883; e) S. R. Angle, D. O. Arnaiz, J. P. Boyce, R. P. Frutos, M. S. Louie, H. L. Mattson-Arnaiz, J. D. Rainier, K. D. Turnbull, W. Yang, *J. Org. Chem.* **1994**, *59*, 6322; f) S. R. Angle, T. Wada, *Tetrahedron Lett.* **1997**, *38*, 7955; g) B. C. Raju, P. Neelakantan, U. T. Bhalerao, *Tetrahedron Lett.* **2004**, *45*, 7487.

[7] For non-asymmetric cycloadditions of *p*-QMs, see: a) S. R. Angle, D. O. Arnaiz, *J. Org. Chem.* **1990**, *55*, 3708; b) S. R. Angle, D. O. Arnaiz, *J. Org. Chem.* **1992**, *57*, 5937; c) W. Baik, H. J. Lee, C. H. Yoo, J. W. Jung, B. H. Kim, *J. Chem. Soc. Perkin Trans. 1* **1997**, 587; d) W. Baik, H. J. Lee, S. Koo, B. H. Kim, *Tetrahedron Lett.* **1998**, *39*, 8125; e) S. Kim, Y. Kitano, M. Tada, K. Chiba, *Tetrahedron Lett.* **2000**, *41*, 7079; f) W. Baik, H. J. Lee, J. M. Jang, S. Koo, B. H. Kim, *J. Org. Chem.* **2000**, *65*, 108.

[8] Asymmetric anionic polymerization of prochiral quinone methides by 1,6-conjugate addition has been explored by using chiral initiators (*i*Pr-PhOLi/chiral ligands), but the enantioselectivity was very low (2–6% *ee*) on the initiation step: a) N. Nakagaki, T. Uno, M. Kubo, T. Itoh, *J. Polym. Sci. Part A* **2009**, *47*, 5923; b) S. Lizuka, N. Nakagaki, T. Uno, M. Kubo, T. Itoh, *Macromolecules* **2010**, *43*, 6962; c) R. Nakagawa, T. Uno, M. Kubo, T. Itoh, *Polym. Bull.* **2012**, *68*, 1831; d) T. Nagai, T. Uno, M. Kubo, T. Itoh, *J. Polym. Sci. Part A* **2012**, *50*, 466.

[9] For recent excellent reviews on asymmetric 1,6-conjugate additions, see: a) A. G. Csákÿ, G. de La Herrán, M. C. Murcia, *Chem. Soc. Rev.* **2010**, *39*, 4080; b) A. T. Biju, *ChemCatChem* **2011**, *3*, 1847; c) E. M. P. Silva, A. M. S. Silva, *Synthesis* **2012**, 3109, and references therein.

[10] For recent selected examples, see: a) P. Mauleón, J. C. Carretero, *Org. Lett.* **2004**, *6*, 3195; b) J.-F. Paquin, C. Defieber, C. R. J. Stephenson, E. M. Carreira, *J. Am. Chem. Soc.* **2005**, *127*, 10850; c) J.-F. Paquin, C. R. J. Stephenson, C. Defieber, E. M. Carreira, *Org. Lett.* **2005**, *7*, 3821; d) T. Nishikata, Y. Yamamoto, I. D. Gridnev, N. Miyaura, *Organometallics* **2005**, *24*, 5025; e) N. Tokunaga, T. Hayashi, *Tetrahedron: Asymmetry* **2006**, *17*, 607; f) T. Itoh, T. Mase, T. Nishikata, T. Iyama, H. Tachikawa, Y. Kobayashi, Y. Yamamoto, N. Miyaura, *Tetrahedron* **2006**, *62*, 9610; g) T. Nishikata, Y. Yamamoto, N. Miyaura, *Adv. Synth. Catal.* **2007**, *349*, 1759; h) T. Nishikata, Y. Yamamoto, N. Miyaura, *Tetrahedron Lett.* **2007**, *48*, 4007; i) S. Sörgel, N. Tokunaga, K. Sasaki, K. Okamoto, T. Hayashi, *Org. Lett.* **2008**, *10*, 589; j) Z.-Q. Wang, C.-G. Feng, S.-S. Zhang, M.-H. Xu, G.-Q. Lin, *Angew. Chem.* **2010**, *122*, 5916; *Angew. Chem. Int. Ed.* **2010**, *49*, 5780; k) Y.-X. Liao, C.-H. Xing, M. Israel, Q.-S. Hu, *Org. Lett.* **2011**, *13*, 2058; l) H. M. Turner, J. Patel, N. Niljianskul, J. M. Chong, *Org. Lett.* **2011**, *13*, 5796; m) F. Lang, G. Chen, L. Li, J. Xing, F. Han, L. Cun, J. Liao, *Chem. Eur. J.* **2011**, *17*, 5242; n) T. Nishimura, A. Noishiki, T. Hayashi, *Chem. Commun.* **2012**, *48*, 973; o) F. Xue, D. Wang, X. Li, B. Wan, *J. Org. Chem.* **2012**, *77*, 3071; p) G. Chen, J. Xing, P. Cao, J. Liao, *Tetrahedron* **2012**, *68*, 5908.

[11] For selected examples, see: a) K. B. Jensen, J. Thorhauge, R. G. Hazell, K. A. Jørgensen, *Angew. Chem.* **2001**, *113*, 164; *Angew. Chem. Int. Ed.* **2001**, *40*, 160; b) N. A. Paras, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2002**, *124*, 7894; c) H. Matsuzawa, Y. Miyake, Y. Nishibayashi, *Angew. Chem.* **2007**, *119*, 6608; *Angew. Chem. Int. Ed.* **2007**, *46*, 6488; d) T.-Y. Liu, H.-L. Cui, Q. Chai, J. Long, B.-J. Li, Y. Wu, L.-S. Ding, Y.-C. Chen, *Chem. Commun.* **2007**, 2228; e) H. Zhang, Y.-H. Liao, W.-C. Yuan, X.-M. Zhang, *Eur. J. Org. Chem.* **2010**, 3215; f) Y. Sohtome, B. Shin, N. Horitsugi, R. Takagi, K. Noguchi, K. Nagasawa, *Angew. Chem.* **2010**, *122*, 7457; *Angew. Chem. Int. Ed.* **2010**, *49*, 7299.

[12] For recent selected examples, see: a) P. Tolstoy, M. Engman, A. Paptchikhine, J. Bergquist, T. L. Church, A. W.-M. Leung, P. G. Andersson, *J. Am. Chem. Soc.* **2009**, *131*, 8855; b) X. Wang, A. Guram, S. Caille, J. Hu, J. P. Preston, M. Ronk, S. Walker, *Org. Lett.* **2011**, *13*, 1881; c) E. Spahn, A. Albright, M. Shevlin, L. Pauli, A. Pfaltz, R. E. Gawley, *J. Org. Chem.* **2013**, *78*, 2731; d) E. N. Bess, M. S. Sigman, *Org. Lett.* **2013**, *15*, 646.

[13] For other examples on the synthesis of diarylalkanes, see: a) R. Shintani, K. Takatsu, M. Takeda, T. Hayashi, *Angew. Chem.* **2011**, *123*, 8815; *Angew. Chem. Int. Ed.* **2011**, *50*, 8656; b) S. M. Podhajsky, Y. Iwai, A. Cook-Sneathen, M. S. Sigman, *Tetrahedron* **2011**, *67*, 4435; c) Y. Luan, S. E. Schaus, *J. Am. Chem. Soc.* **2012**, *134*, 19965.

[14] For recent reviews, see: a) M. J. O'Donnell, *Aldrichimica Acta* **2001**, *34*, 3; b) K. Maruoka, T. Ooi, *Chem. Rev.* **2003**, *103*, 3013; c) M. J. O'Donnell, *Acc. Chem. Res.* **2004**, *37*, 506; d) B. Lygo, B. I. Andrews, *Acc. Chem. Res.* **2004**, *37*, 518; e) J. Vachon, J. Lacour, *Chimia* **2006**, *60*, 266; f) T. Ooi, K. Maruoka, *Angew. Chem.* **2007**, *119*, 4300; *Angew. Chem. Int. Ed.* **2007**, *46*, 4222; g) T. Ooi, K. Maruoka, *Aldrichimica Acta* **2007**, *40*, 77; h) T. Hashimoto, K. Maruoka, *Chem. Rev.* **2007**, *107*, 5656; i) K. Maruoka, *Org. Process Res. Dev.* **2008**, *12*, 679; j) S.-s. Jew, H.-g. Park, *Chem. Commun.* **2009**, 7090; k) K. Maruoka, *Chem. Rec.* **2010**, *10*, 254; l) S. Shirakawa, K. Maruoka, *Angew. Chem.* **2013**, *125*, 4408; *Angew. Chem. Int. Ed.* **2013**, *52*, 4312.

[15] For screening of solvents and bases, see the Supporting Information.

[16] For **4a**, see: a) M. J. O'Donnell, S. Wu, I. Esikova, A. Mi, WO 9506029, **1995**; For **4b**, see: b) M. J. O'Donnell, F. Delgado, C. Hostettler, R. Schwesinger, *Tetrahedron Lett.* **1998**, *39*, 8775; For **4c**, see: c) T. Shibuguchi, Y. Fukuta, Y. Akachi, A. Sekine, T. Ohshima, M. Shibasaki, *Tetrahedron Lett.* **2002**, *43*, 9539; For **4d**, see: d) T. Ooi, M. Taniguchi, M. Kameda, K. Maruoka, *Angew. Chem.* **2002**, *114*, 4724; *Angew. Chem. Int. Ed.* **2002**, *41*, 4542; For **4e**, see: e) T. Ooi, M. Kameda, K. Maruoka, *J. Am. Chem. Soc.* **2003**, *125*, 5139; For **4f**, see: f) K. Maruoka, WO 2005073196, **2005**.

[17] CCDC 931906 (**3da**) and 931907 (**3qa**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[18] S. A. Saleh, H. I. Tashtoush, *Tetrahedron* **1998**, *54*, 14157.

[19] a) E. W. Colvin in *Silicon Reagents in Organic Synthesis* Academic Press, **1988**; b) *The Chemistry of Organic Silicon Compounds* (Eds.: S. Patai, Z. Rappoport), Wiley, New York, **1989**.

