CHEMISTRY
A EUROPEAN JOURNAL

DOI: 10.1002/chem.200601880

Highly Efficient Cyclization of *o*-Iodobenzoates with Aldehydes Catalyzed by Cobalt Bidentate Phosphine Complexes: A Novel Entry to Chiral Phthalides

Hong-Tai Chang, Masilamani Jeganmohan, and Chien-Hong Cheng*[a]

Abstract: Methyl 2-iodobenzoates **1a–c** undergo cyclization reactions with various aromatic aldehydes **2a–m** (RC_6H_4CHO: R = H **2a**, 4-CH_3 **2b**, 4-*t*Bu **2c**, 4-OMe **2d**, 3-OMe **2e**, 4-Cl **2f**, 4-CF_3 **2g**, 4-CN **2h**, 4-Ph **2i**; benzo[*d*]-[1,3]dioxole-5-carbaldehyde (**2j**), 1-napthaldehyde (**2k**), benzofuran-2-carbaldehyde (**2l**), and isonicotinaldehyde (**2m**)) in the presence of [CoI_2(dppe)] (dppe = 1,2-bis(diphenylphosphino)-ethane) and Zn powder in dry THF at 75 °C for 24 h to give the corresponding phthalide derivatives **3a–m** and **3q–t** in good to excellent yields. Under similar reaction conditions, less reactive aliphatic aldehydes, heptanal (**2n**), butyraldehyde (**2o**), and 2-phenylacetaldehyde (**2p**) also underwent cyclization reactions with **1a** to provide **3n–p**, respectively, in fair to good yields. The catalytic reaction can be further extended to cinnamyl aldehyde (**2q**) with **1a** to give the corresponding phthalide derivative **3u**. This synthetic method is compatible with a variety of functional groups on the aryl ring of **2**. The high efficiency of the cobalt catalyst containing a dppe (dppe = 1,2-bis(diphenylphosphino)ethane) ligand encouraged us to investigate the asymmetric version of the present catalytic reaction by employing bidentate chiral ligands. Thus, aromatic aldehydes **2a–c**, **2f**, and **2g** undergo cyclization with 2-iodobenzoate (**1a**) smoothly in the presence of [CoI_2\{(*S,S*)-dipamp\}] ((*S,S*)-dipamp = (1*S*,2*S*)-(+)-bis[2-methoxyphenyl]phenylphosphino)ethane) and zinc powder in THF at 75 °C for 24 h, giving the corresponding (*S*)-phthalides **4a–e** in 81–89 % yields with 70–98 % *ee*. A possible mechanism for the present catalytic reaction is proposed.

Keywords: asymmetric synthesis · chiral phthalides · cobalt catalysis · cyclization

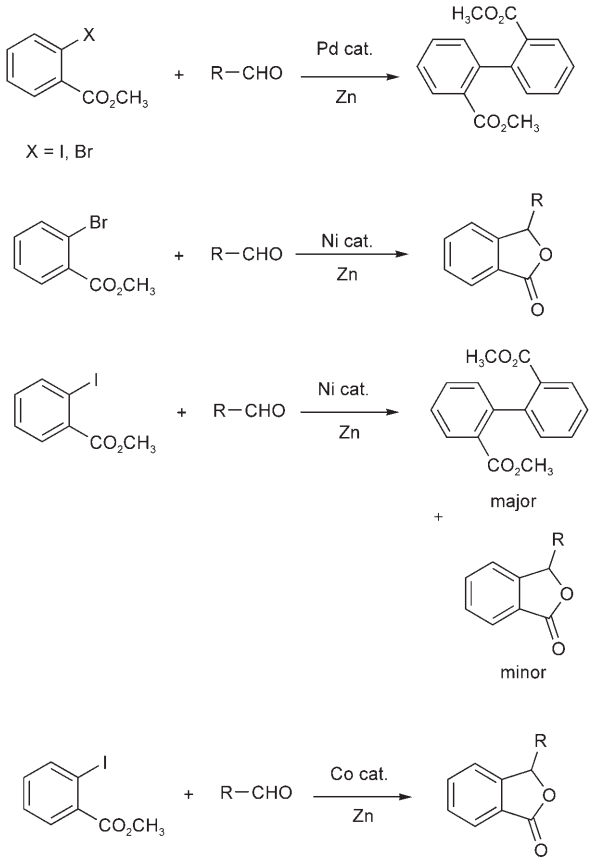
Introduction

Transformation of organic halides into various organic compounds catalyzed by transition metals by means of oxidative addition has been recognized as an important tool in organic synthesis.[1] Palladium and nickel complexes are widely used as the catalysts for this type of reaction due to their facile oxidative addition with aromatic halides.[1] On the other hand, cobalt complexes are well known catalysts for [2+2+2][2] and [2+2] cycloaddition reactions,[3] the Pauson–Khand reaction,[4] en–yne reductive coupling,[5] and hydroformylation.[6] The use of cobalt complexes as catalysts for the activation of aromatic halides by means of oxidative addition is very limited in the literature. In 1998, Cahiez and Knochel reported cobalt-catalyzed cross-coupling reactions of alkenyl halides with organozinc and organomagnesium reagents.[7a–b] Oshima and co-workers described a cobalt-catalyzed Heck-type reaction of alkyl halides with styrenes by a single electron-transfer mechanism.[7c] Gosmini et al. reported the synthesis of aryl zinc reagents from aryl bromides catalyzed by $CoBr_2$ (10–20 mol %) in the presence of $ZnBr_2$ and Zn dust.[8] Later, the same group showed that aryl halides underwent cross-coupling reactions with allylic acetates to give the corresponding allylation products.[9] Recently, we have demonstrated that cobalt phosphine complexes successfully catalyze the carbocyclization reaction of *o*-iodophenyl ketones and aldehydes with carbon–carbon multiple bonds (alkynes, acrylates, and acrylonitrile) under mild reaction conditions to afford indenol and indene derivatives.[10]

Phthalides (isobenzofuranone), five-membered lactones found in plants, are present in a large number of biologically active compounds.[11] The derivatives are also key intermediates for the synthesis of natural products and approaches have been developed for the synthesis of such organic skeletons.[12,13] In this context, very recently, we have demonstrated that nickel complexes efficiently catalyzed the cyclization

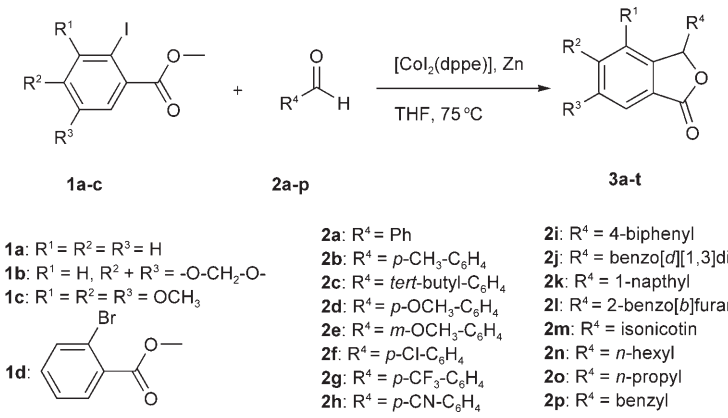
[a] H.-T. Chang, Dr. M. Jeganmohan, Prof. Dr. C.-H. Cheng
Department of Chemistry, National Tsing Hua University
Hsinchu 30013 (Taiwan)
Fax: (+886) 3-572-4698
E-mail: chcheng@mx.nthu.edu.tw

Supporting information for this article is available on the WWW under http://www.chemeurj.org/ or from the author.



Scheme 1. Palladium-, nickel-, and cobalt-catalyzed reactions of *o*-halobenzoates with aldehydes.

reaction of 2-bromophenyl esters with aldehydes to afford phthalide derivatives in good yields (Scheme 1).[14] Our continuous interest in cobalt-catalyzed reactions[2e,3,5] and the recent attention received by the activation of aryl halides by cobalt complexes[10] prompted us to explore the possibility of using cobalt complexes as catalysts for the cyclization reactions of 2-halobenzoates with aldehydes. In this paper, we wish to report that cobalt phosphine complexes effectively catalyze the cyclization of 2-iodobenzoates with aldehydes to afford phthalide derivatives in good to excellent yields. The results of this cobalt-catalyzed reaction are complementary to those from the previously reported nickel-catalyzed reaction. Under similar conditions, nickel and also palladium complexes are not effective for the cyclization of 2-iodobenzoates with aldehydes; the major pathway is the homocoupling of 2-iodobenzoates (Scheme 1). On the other hand, cobalt complexes are not active catalysts for the cyclization of 2-bromobenzoates with aldehydes.



Scheme 2. Cobalt-catalyzed cyclization reaction of *o*-iodobenzoates with aldehydes.

Results and Discussion

Treatment of 2-iodobenzoate (**1a**) with benzaldehyde (**2a**) in the presence of a mixture of $[CoI_2(dppe)]$ (5 mol%) and zinc metal powder (2.75 mmol) in THF at 75°C led to the cocyclization of **1a** with **2a** and the formation of phthalide derivative **3a** in 94% isolated yield (Scheme 2, Table 1, entry 1). Control experiments revealed that in the absence of the cobalt catalyst or Zn powder, no **3a** was obtained.

To understand the nature of this cobalt-catalyzed reaction and to optimize the reaction conditions, various cobalt phosphine complexes were tested for the catalytic activity of the cyclization reaction of **1a** with **2a**. Monodentate phosphine complexes $[CoI_2\{P(PhOMe)_3\}_2]$, $[CoCl_2(PPh_3)_2]$, and $[CoI_2(PPh_3)_2]$ were totally inactive. The use of cobalt complexes with bidentate phosphine ligands, such as $[CoI_2(dppm)]$ (dppm = 1,3-bis(diphenylphosphino)methane) and $[CoI_2(dppp)]$ (dppp = 1,3-bis(diphenylphosphino)propane), gave **3a** in 20 and 15% yields. Among these cobalt complexes tested, $[CoI_2(dppe)]$ appears to be most active, giving **3a** in 96% yield. The results indicate that cobalt bidentate phosphine complexes are more suitable than the monodentate phosphine complexes as the catalysts for the present catalytic reaction. Similar observations have been shown by us in the cobalt and nickel-catalyzed reactions reported previously.[10,14]

In addition to the cobalt complexes, various palladium and nickel complexes were also tested for the catalytic activity of the reaction of **1a** with **2a**. The reaction using $Pd(dba)_2$, $[PdCl_2(PPh_3)_2]$, or $[PdCl_2(dppe)]$ fails to give the phthalide derivative, giving instead the homocoupling product of **1a** $(o\text{-}(C_6H_4)CO_2Me)_2$ (Scheme 1). Whereas the use of nickel complex $[NiBr_2(dppe)]$ gave only 50% of **3a** and

Table 1. Results of cobalt-catalyzed cyclization of *o*-iodobenzoates **1** with aldehydes **2**[a]

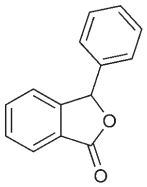
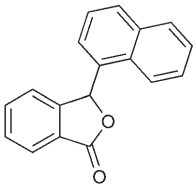
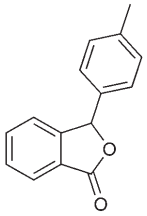
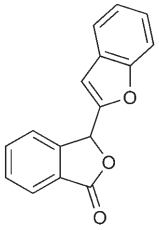
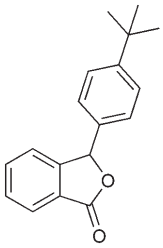
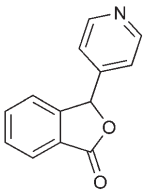
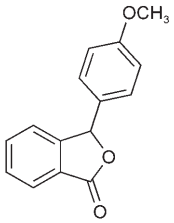
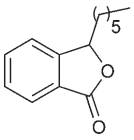
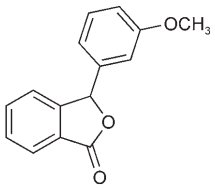
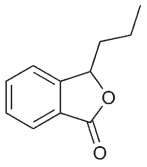
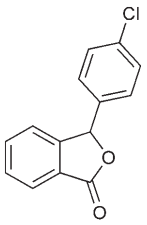
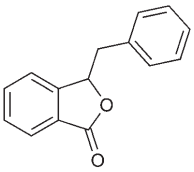
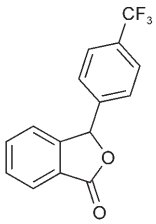
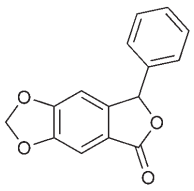
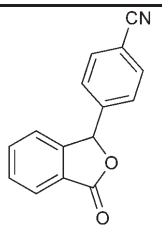
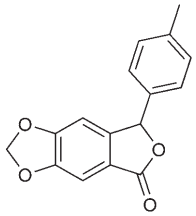
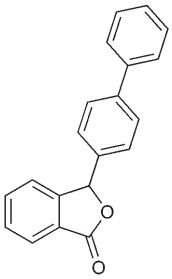
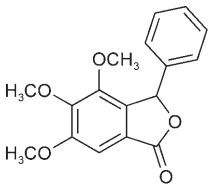
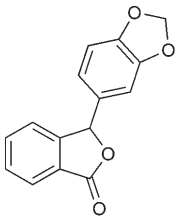
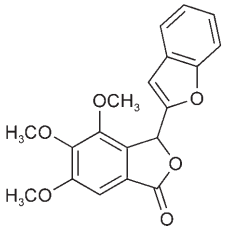
Entry	1	2	Product 3	Yield [%][b]	Entry	1	2	Product 3	Yield [%][b]
1	**1a**	**2a**		94 (96)	11	**1a**	**2k**		38
2	**1a**	**2b**		92	12	**1a**	**2l**		88
3	**1a**	**2c**		93	13	**1a**	**2m**		15
4	**1a**	**2d**		94	14	**1a**	**2n**		54
5	**1a**	**2e**		89	15	**1a**	**2o**		30
6	**1a**	**2f**		86	16	**1a**	**2p**		55
7	**1a**	**2g**		90	17	**1b**	**2a**		71

Table 1. (Continued)

Entry	1	2	Product 3	Yield [%][b]	Entry	1	2	Product 3	Yield [%][b]
8	**1a**	**2h**		50	18	**1b**	**2b**		68
9	**1a**	**2i**		94	19	**1c**	**2a**		65
10	**1a**	**2j**		60	20	**1c**	**2l**		55

[a] Reactions were carried out by using organic halide (1.20 mmol), aldehyde (1.00 mmol), [CoI_2(dppe)] (0.050 mmol, 5.0 mol%), and Zn (2.75 mmol) in THF (3.0 mL) at 75 °C for 24 h under N_2. [b] Isolated yields were based on the aldehyde used; the yield in parenthesis was determined by ^{1}H NMR spectroscopy by using mesitylene as an internal standard.

50% of homocoupling product of **1a**. Likewise, under the same conditions, **1a** reacted with **2d** to afford exclusively the homocoupling product of **1a**. It is surprising that nickel complexes exhibit excellent catalytic activities with methyl 2-bromobenzoate, but not with methyl 2-iodobenzoate. The cyclization of methyl 2-bromobenzoate with **2a** and with **2d** afforded phthalide derivatives **3a** and **3d** in 86 and 92% yields, respectively.[14]

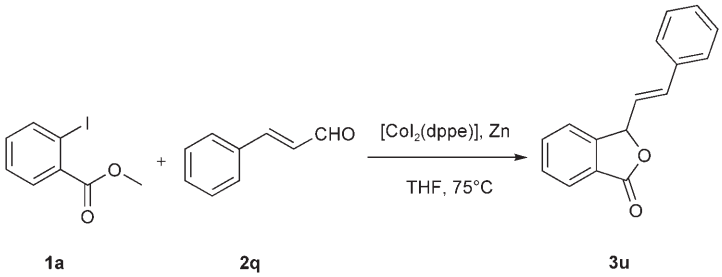
The choice of solvent for the cyclization of **1a** with **2a** to give **3a** by using [CoI_2(dppe)] as the catalyst is also important for the success of the catalytic reactions. Of the solvents examined, THF was most effective giving **3a** in 96% yield. The other solvents, such as CH_3CN, toluene, ethyl acetate, and NMP (NMP = *N*-methyl-2-pyrrolidinone), tested gave **3a** in only 20–10% yields. Based on these optimization studies, we chose [CoI_2(dppe)] as the catalyst and THF as the solvent for the cyclization reactions shown below.

This cobalt-catalyzed cyclization reaction was successfully extended to different aldehydes **2b–p** and substituted methyl 2-iodobenzoates **1b–c**. The results are summarized in Table 1. The reaction of methyl 2-iodobenzoate (**1a**) with 4-methylbenzaldehyde (**2b**) in the presence of [CoI_2(dppe)] and zinc powder affords product **3b** in a 92% yield (entry 2). Similarly, 4-*tert*-butylbenzaldehyde (**2c**), 4-methoxybenzaldehyde (**2d**), and 3-methoxybenzaldehyde (**2e**) react with **1a** to give the corresponding cyclization products, **3c–e**, in 93, 94, and 89% yields, respectively. Under similar conditions, 4-chlorobenzaldehyde (**2f**), 4-(trifluoromethyl)-benzaldehye (**2g**), and 4-cyanobenzaldehyde (**2h**) reacted efficiently with **1a** to afford lactones **3f–h** in 86, 90, and 50% yields. Likewise, the reaction of various bulkier aldehydes, such as 4-phenylbenzaldehyde (**2i**), benzo[*d*]-[1,3]dioxole-5-carbaldehyde (**2j**), and 1-napthaldehyde (**2k**), with **1a** produced **3i–k** in 94, 60, and 38% yields, respectively (entries 9–11). The present catalytic reaction is also applicable to heterocyclic aldehydes **2l** and **2m**. Treatment of benzo[*b*]furan-2-carbaldehyde (**2l**) with **1a** afforded **3l** in 88% yield. However, isonicotinaldehyde (**2m**) reacted with **1a**, providing **3m** in only 15% yield. It is noteworthy that the present catalytic reaction tolerates a variety of functional groups, such as methoxy, chloro, CF_3, cyano, nitrogen, and oxygen on the aryl ring of **2**.

In addition to aromatic aldehydes, the less reactive alkyl aldehydes **2n** and **2o** were also successfully applied as the substrates for the present catalytic reaction. Treatment of heptanal (**2n**) and butyraldehyde (**2o**) with **1a** in the presence of the [CoI_2(dppe)]/Zn system afforded **3n** and **3o** in 54 and 30% yields, respectively (entries 14–15). Likewise, 2-phenylacetaldehyde (**2p**) reacted with **1a** to provide **3p** in 55% yield.

The present catalytic reaction can be further extended to substituted 2-iodobenzoates **1b–c**. Under the optimized reaction conditions, the reaction of methyl 6-iodo-1,3-benzodioxole-5-carboxylate (**1b**) with **2a** and **2b** afforded the corresponding phthalide derivatives **3q** and **3r** in 71 and 68% yields, respectively (entries 17 and 18). Similarly, treatment of methyl 2-iodo-3,4,5-trimethoxybenzoate (**1c**) with **2a** and **2l** afforded **3s** and **3t** in 65 and 55% yields, respectively (entries 19 and 20). Under the same reaction conditions, the present catalytic reaction was tested by using 2-bromophenyl ester **1d** with **2a**; nevertheless the catalytic reaction does not proceed.

The generality of the present catalytic reaction can be further demonstrated by the reaction of cinnamyl aldehyde (**2q**) with 2-iodobenzoate (**1a**) in the presence of [CoI_2(dppe)]/Zn to afford **3u** in 65% yield (Scheme 3). As a result, the aldehyde group should compete effectively with the conjugated C=C double bond in **2q** for the insertion into the aryl–cobalt bond in the catalyst intermediate in order to afford product **3u**. This is somewhat surprising in view of the low nucleophilicity of the aryl group in the catalyst intermediate, which generally favors addition to the conjugated C=C double bond.

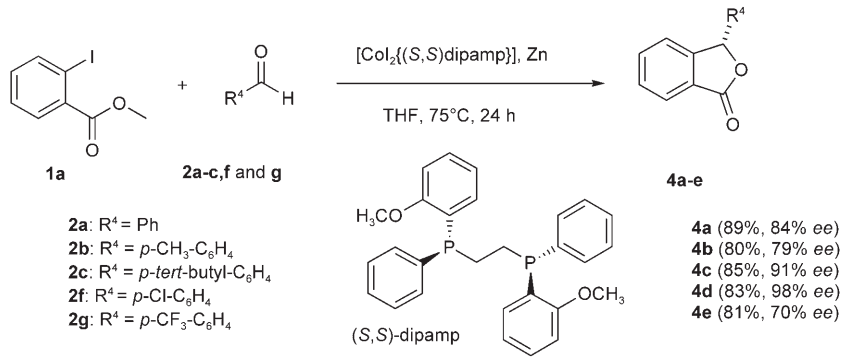


Scheme 3. Cobalt-catalyzed cyclization reaction of 2-iodobenzoate with cinnamyl aldehyde.

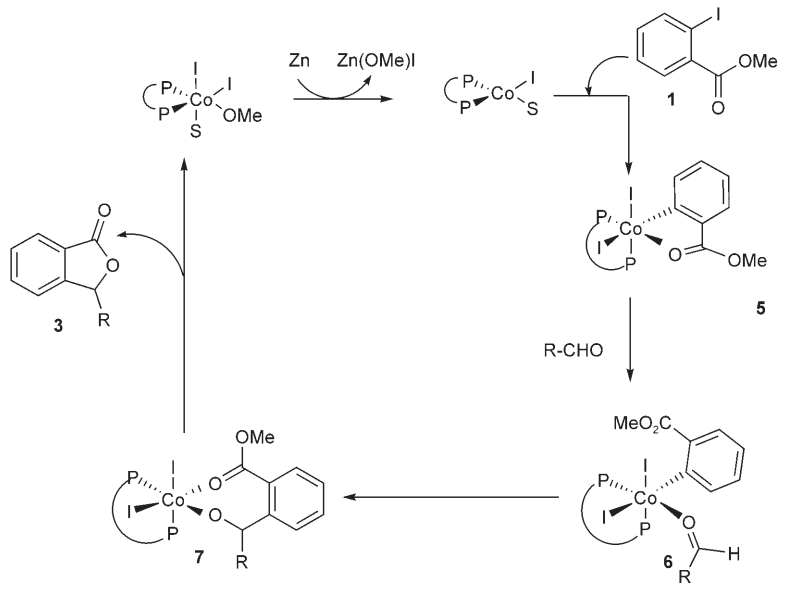
The high efficiency of the cobalt catalyst containing a dppe ligand encouraged us to investigate the asymmetric version of the present catalytic reaction by employing bidentate chiral ligands. Thus, various chiral cobalt bidentate phosphine complexes, such as [CoI_2\{(*R*)-Tol-binap\}] ((R)-Tol-binap = (*R*)-(+)-2,2′-bis(di-*p*-tolyl-phosphino)-1,1′-binapthyl), [CoI_2\{(*R*)-mop\}] ((*R*)-mop = (*R*)-(+)-2-(diphenylphosphino)-2′-methoxy-1-1′-binapthyl), [CoI_2\{(*R*)-prophos\}] ((*R*)-prophos = (*R*)-(+)-1,2-bis(diphenylphosphino)propane), [CoI_2\{(*R*)-quinap\}] ((*R*)-quinap = (*R*)-(+)-1-(2-diphenylphosphino-1-naphthyl)isoquinoline), [CoI_2\{(*S*)-nmdpp\}] (nmdpp = (*S*)-(+)-neomenthyldiphenylphosphine), [CoI_2\{(*S,S*)-chiraphos\}] ((*S,S*)-chiraphos = (2*S*,3*S*)-(−)-bis(diphenylphosphino)butane), [CoI_2\{(*R,R*)-diop\}] ((*R,R*)-diop = (4*R*,5*R*)-(−)-*O*-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane), [CoI_2\{(*S,S*)-bdpp\}] ((*S,S*)-bdpp = (*S,S*)-(−)-2,4-bis(diphenylphosphino)pentane), and [CoI_2\{(*S,S*)-dipamp\}] were examined for the cyclization of 2-iodobenzoate (**1a**) with benzaldehyde (**2a**) in the presence of zinc powder (2.75 mmol) in THF at 75°C for 24 h (Scheme 4). The results showed that [CoI_2\{(*S,S*)-dipamp\}] is most effective, giving (*S*)-3-phenylisobenzofuran-1(3*H*)one (**4a**) in 89% yield with an *ee* of 84%. In addition to [CoI_2\{(*S,S*)-dipamp\}], [CoI_2\{(*S,S*)-bdpp\}] was also effective, affording **4a** in 75% yield with an *ee* of 81%. The other cobalt chiral complexes were less effective, affording **4a** in 40–80% yield with an *ee* of 0–33%.

Under the optimized reaction conditions, various aromatic aldehydes **2b**, **2c**, **2f**, and **2g** underwent cyclization with 2-iodobenzoate (**1a**) smoothly, to give the corresponding chiral phthalides **4b–e** in 87, 80, 83, and 81% yields with 70–98% *ee*. The highest *ee* ratio of 98% was observed with 4-chlorobenzaldehyde (**2f**) and the lowest *ee* ratio of 70% was obtained with 4-(trifluoromethyl)benzaldehyde (**2g**). The absolute configuration at the quaternary carbon atom of these products is shown to be that of an *S* isomer; this is based on the comparison of the reported specific rotation [α] values.[15]

Based on the above observations and the known cobalt and zinc chemistry,[7–10] a conceivable mechanism is proposed in Scheme 5. Reduction of cobalt(II) to (I) by Zn metal likely initiates the catalytic reaction. Oxidative addition of methyl 2-iodobenzoate (**1**) with the cobalt(I) species yields an *o*-metalated methybenzoate complex **5** with both the *o*-carbon atom and the ester oxygen atom bonded to the cobalt(III) center. Coordination of the aldehyde molecule to the cobalt center adjacent to the *o*-metalated methyl benzoate group to give **6**, followed by insertion of the cobalt–carbon bond to the aldehyde affords cobalt–alkoxide intermediate **7**. Intramolecular nucleophilic addition of the coordinated alkoxy group in **7** to the ester group gives the final product **3** and a cobalt(III) species. The latter cobalt(III)



Scheme 4. Cobalt-catalyzed asymmetric cyclization reaction of 2-iodobenzoate with aldehydes.



Scheme 5. Possible mechanism for the cobalt-catalyzed cyclization reaction.

species is reduced by zinc metal to regenerate the active cobalt(I) species.

It is interesting to compare the results of the present cobalt catalytic reactions with those previously reported which use nickel complexes as the catalysts.[14] First, nickel complexes efficiently catalyzed the cyclization reaction of *o*-bromobenzoate with aldehydes to give phthalide derivatives; however, they were not effective for the cocyclization of *o*-iodobenzoates **1** with aldehydes **2** to give the corresponding phthalides. The reaction of *o*-iodobenzoates **1** with aldehydes **2** in the presence of a nickel catalyst gave mainly the homoreductive coupling products of *o*-iodobenzoates and the phthalide derivatives as the minor products. In sharp contrast, the present cobalt complex is effective for the cocyclization of *o*-iodobenzoates with aldehydes to give the corresponding phthalides in excellent yield, and is not active for the reaction of *o*-bromobenzoates with aldehydes. Second, the present cobalt system also catalyzes the reaction of cinnamyl aldehyde (**2q**) with **1a** to afford 1,2-addition product **3u** in good yield (Scheme 3), but nickel complex [$NiBr_2$(dppe)] is not active for this cyclization reaction. Third, the present cobalt complex is highly efficient for electron rich esters, such as **1c**, and heterocyclic aldehydes, that is, **2l** and **2m** (Table 1, entries 12, 13, 19, and 20). However, the nickel complex did not catalyze the reaction of the bromo derivative of **1c** with **2a** and of **1a** with **2m**. Finally, the asymmetric cyclization of *o*-halobenzoate with aldehyde was tested in various chiral nickel and cobalt complexes, but only cobalt complexes gave high enantioselectivity; no asymmetric induction was observed in nickel complexes.

While cobalt and nickel complexes show different catalytic activities with different substrates in the cocyclization of 2-halobenzoates with aldehydes, palladium complexes appear not to be active at all for this cocyclization. The difference in the catalytic behaviors of these metal complexes reflects the nature of these metals. The oxidative addition of 2-iodobenzoates to low-oxidation-state complexes of these metals are all facile, but the nucleophilicity of *o*-metalated benzoate in **6** or the corresponding species towards coordinated aldehydes of cobalt and nickel are expected to be stronger than of palladium. In addition, cobalt and nickel complexes are generally more labile than palladium species due to the weaker metal–ligand bonds. Thus, the coordination of aldehyde to the palladium center and the subsequent insertion of coordinated aldehyde into the aryl–palladium bond are much slower than those for the cobalt and nickel catalysts. This might be the reason for the observation that palladium complexes did not catalyze the cyclization reaction of **1a** with **2a** to give **3a**, but afforded only the homocoupling product.

The observation that 2-bromobenzoates do not undergo cocyclization with aldehydes by using [CoI_2(dppe)]/Zn in THF is probably due to the low reactivity of 2-bromobenzoates relative to 2-iodobenzoates with reduced cobalt species. On the other hand, both 2-iodo- and 2-bromobenzoates were found to react with nickel(0) complexes readily at 75 °C. However, the reaction of 2-iodobenzoates and Ni gave the corresponding homocoupling products (Scheme 1) due to the fast decomposition of the oxidative addition product. This likely explains the reason for the failure of using iodobenzoates as substrates in the nickel-catalyzed synthesis of phthalides. The oxidative addition product of nickel with 2-bromobenzoates is relatively stable for the insertion of aldehyde into the nickel–carbon bond. Other evidence for the stability of the oxidative addition products is that bromoarenes react with [$Ni(PPh_3)_4$] to give isolable products [$Ni(Ar)Br(PPh_3)_2$], but the corresponding nickel complexes from iodoarenes can not be isolated.[16]

Conclusion

We have developed a cobalt-catalyzed cocyclization reaction of 2-iodobenzoates with aldehydes to afford substituted phthalide derivatives in one pot under mild reaction conditions with good to excellent yields. In addition, high enantioselectivity of the cyclization was obtained by employing cobalt complexes with a suitable bidentate chiral ligand. These results revealed that this cobalt-catalyzed cyclization is a good complement to the nickel-catalyzed cyclization reactions. This new cobalt-catalyzed reaction highlights the

potential of using cobalt as an inexpensive and efficient catalyst for coupling of carbon–carbon bonds and for catalytic asymmetric synthesis.

Experimental Section

All reactions were conducted under a nitrogen atmosphere on a dual-manifold Schlenk line by using purified deoxygenated solvents and standard inert atmosphere techniques, unless otherwise stated. Reagents and chemicals were used as purchased without further purification.

General procedure for the cyclization of 2-iodobenzoates 1 with aldehydes 2: A sealed tube containing [CoI_2(dppe)] (0.050 mmol, 5.0 mol%) and zinc powder (2.75 mmol) was evacuated and purged with nitrogen gas three times. Freshly distilled THF (3.0 mL), *o*-iodobenzoate (1.20 mmol), and aldehyde (1.00 mmol) were sequentially added to the system and the reaction mixture was allowed to stir at 75°C for 24 h. The mixture was filtered through a short Celite and silica-gel pad and washed with dichloromethane several times. The filtrate was concentrated and the residue was purified on a silica-gel column by using hexanes/ethyl acetate as the eluent to afford the cyclization product **3**.

Spectral data for compounds **3a–c**, **3h–j** and **3s–u** are listed bellow. Spectral data of the remaining compounds **3d–g** and **3k–r** and a copy of the ^{1}H and ^{13}C NMR spectra of all compounds are given in the Supporting Information.

3-Phenyl-3*H*-1-isobenzofuranone (3a): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.40 (s, 1H; CH), 7.39–7.32 (m, 6H; aromatic H), 7.55 (t, ^3J(H,H) = 6.4 Hz, 1H; HC=), 7.65 (t, ^3J(H,H) = 7.6 Hz, 1H; HC=), 7.96 ppm (d, ^3J(H,H) = 7.6 Hz, 1H; HC=); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.48 (C=O), 149.65 (C), 136.40 (C), 134.29 (CH), 129.33 (CH), 129.27 (CH), 128.95 (CH), 128.44 (C), 126.94 (CH), 125.84 (CH), 122.83 (CH), 82.68 ppm (CH); HRMS: *m*/*z*: calcd for $C_{14}H_{10}O_2$: 210.0681; found: 210.0683.

3-(4-Methylphenyl)-3*H*-1-isobenzofuranone (3b): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.35 (s, 3H; CH_3), 6.38 (s, 1H; CH), 7.20–7.14 (m, 4H; aromatic H), 7.31 (d, ^3J(H,H) = 6.8 Hz, 1H; HC=), 7.57 (t, ^3J(H,H) = 7.2 Hz, 1H; HC=), 7.63 (t, ^3J(H,H) = 7.6 Hz, 1H; HC=), 7.96 ppm (d, ^3J(H,H) = 6.4 Hz, 1H; HC=); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.54 (C=O), 149.77 (C), 139.28 (C), 134.23 (CH), 133.36 (C), 129.59 (CH), 129.24 (CH), 127.01 (CH), 125.66 (C), 125.52 (CH), 122.82 (CH), 82.73 (CH), 21.18 ppm (CH_3); HRMS: *m*/*z* calcd for $C_{15}H_{12}O_2$: 224.0837; found: 224.0831.

3-[4-(*tert*-Butyl)phenyl]-1,3-dihydro-1-isobenzofuranone (3c): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.27 (s, 9H; $C(CH_3)_3$), 6.38 (s, 1H; CH), 7.18 (d, ^3J(H,H) = 8.4 Hz, 2H; HC=), 7.35 (d, ^3J(H,H) = 7.6 Hz, 1H; HC=), 7.38 (d, ^3J(H,H) = 7.6 Hz, 2H; HC=), 7.54 (t, ^3J(H,H) = 7.2 Hz, 1H; HC=), 7.62 (t, ^3J(H,H) = 7.6 Hz, 1H; HC=), 7.94 ppm (d, ^3J(H,H) = 8.0 Hz, 1H; HC=); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.51 (C=O), 152.41 (C), 149.67 (C), 134.17 (CH), 133.25 (C), 129.20 (CH), 126.78 (CH), 125.85 (CH), 125.69 (C), 125.51 (CH), 122.91 (CH), 82.63 (CH), 34.61 (C), 31.16 ppm (CH_3); HRMS: *m*/*z*: calcd for $C_{18}H_{18}O_2$: 266.1307; found: 266.1312.

4-(3-Oxo-1,3-dihydro-1-isobenzofuranyl)benzonitrile (3h): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.41 (s, 1H; CH), 7.31 (d, ^3J(H,H) = 7.6 Hz, 1H; HC=), 7.41 (d, ^3J(H,H) = 8.0 Hz, 2H; HC=), 7.56 (t, ^3J(H,H) = 7.2 Hz, 1H; HC=), 7.67–7.63 (m, 3H; aromatic H), 7.94 ppm (d, ^3J(H,H) = 7.6 Hz, 1H; HC=); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.00 (C=O), 148.47 (C), 141.62 (C), 134.67 (CH), 132.79 (CH), 129.86 (CH), 127.31 (CH), 125.98 (CH), 125.08 (C), 122.58 (CH), 118.07 (C), 113.13 (C), 81.18 ppm (CH); HRMS: *m*/*z*: calcd for $C_{15}H_9O_2N$: 235.0633; found: 235.0633.

3-Biphenyl-4-yl-3*H*-isobenzofuran-1-one (3i): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.44 (s, 1H; CH), 7.38–7.32 (m, 4H; aromatic H), 7.42 (t, ^3J(H,H) = 7.6 Hz, 2H; HC=), 7.59–7.54 (m, 5H; aromatic H), 7.65 (t, ^3J(H,H) = 7.2 Hz, 1H; HC=), 7.97 ppm (d, ^3J(H,H) = 7.2 Hz, 1H; HC=); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.70 (C=O), 149.85 (C), 142.56 (C), 140.51 (C), 135.56 (C), 134.59(CH), 129.64 (CH), 129.09 (CH), 127.93 (CH), 127.70 (CH), 127.36 (CH), 125.93 (CH), 123.13 (CH), 114.46 (CH), 82.72 ppm (CH); HRMS: *m*/*z*: calcd for $C_{20}H_{14}O_2$: 286.0994; found: 286.0992.

3-Benzo[1,3]dioxol-5-yl-3*H*-isobenzofuran-1-one (3j): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.59 (s, 2H; CH_2), 6.30 (s, 1H; CH), 6.58 (s, 1H; HC=), 6.82–6.77 (m, 2H; aromatic H), 7.30 (d, ^3J(H,H) = 7.6 Hz, 1H; HC=), 7.54 (t, ^3J(H,H) = 7.2 Hz, 1H; HC=), 7.64 (t, ^3J(H,H) = 7.2 Hz, 1H; HC=), 7.94 ppm (d, ^3J(H,H) = 7.2 Hz, 1H; HC=); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.31 (C=O), 149.51 (C), 148.52 (C), 148.21 (C), 134.27 (CH), 129.98 (C), 129.37 (CH), 125.77(C), 125.57 (CH), 122.87 (CH), 121.48 (CH), 108.39 (CH), 107.25 (CH), 101.40 (CH_2), 82.70 ppm (CH); HRMS: *m*/*z*: calcd for $C_{15}H_{10}O_4$: 254.0579; found 254.0578.

4,5,6-Trimethoxy-3-phenylisobenzofuran-1(3*H*)one (3s): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.42 (s, 3H; OCH_3), 3.87 (s, 3H; OCH_3), 3.91 (s, 3H; OCH_3), 6.32 (s, 1H; CH), 7.17 (s, 1H; HC=), 7.25–7.23 (m, 2H; aromatic H), 7.33–7.32 ppm (m, 3H; aromatic H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.40 (C=O), 155.84 (C), 147.82 (C), 147.39 (C), 136.26 (C), 135.61 (C), 129.11 (CH), 128.59 (CH), 127.29 (CH), 120.72 (C), 102.53 (CH), 81.15 (CH), 60.97 (CH_3), 60.24 (CH_3), 56.38 ppm (CH_3); HRMS: *m*/*z*: calcd for $C_{17}H_{16}O_5$: 300.0998; found: 300.0995.

3-(Benzofuran-2-yl)-4,5,6-trimethoxyisobenzofuran-1(3*H*)one (3t): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.63 (s, 3H; OCH_3), 3.93 (s, 3H; OCH_3), 3.96 (s, 3H; OCH_3), 6.50 (s, 1H; CH), 6.83 (s, 1H; HC=), 7.22 (t, ^3J(H,H) = 7.6 Hz, 1H; HC=), 7.23 (s, 1H; HC=), 7.29 (t, ^3J(H,H) = 8.4 Hz, 1H; HC=), 7.40 (d, ^3J(H,H) = 8.4 Hz, 1H; HC=), 7.56 ppm (d, ^3J(H,H) = 7.6 Hz, 1H; HC=); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.66 (C=O), 156.30 (C), 155.17 (C), 150.84 (C), 148.07 (C), 147.25 (C), 131.56 (C), 127.52 (C), 125.26 (CH), 123.10 (CH), 121.52 (CH), 121.44 (C), 111.54 (CH), 107.25 (CH), 102.85 (CH), 73.97 (CH), 61.13 (CH_3), 60.58 (CH_3), 56.48 ppm (CH_3); HRMS: *m*/*z*: calcd for $C_{19}H_{16}O_6$: 340.0947; found: 340.0946.

(*E*)-3-Styrylisobenzofuran-1(3*H*)one (3u): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.00 (d, ^3J(H,H) = 8.0 Hz, 1H; CH), 6.12 (dd, ^3J(H,H) = 15.6 Hz, ^3J(H,H) = 7.6 Hz, 1H; CH=), 6.90 (d, ^3J(H,H) = 15.2 Hz, 1H; HC=), 7.36–7.28 (m, 3H; aromatic H), 7.41–7.38 (m, 2H; aromatic H), 7.45 (d, ^3J(H,H) = 7.6 Hz, 1H; HC=), 7.55 (t, ^3J(H,H) = 7.6 Hz, 1H; HC=), 7.68 (td, ^3J(H,H) = 8.0 Hz, ^4J(H,H) = 1.2 Hz, 1H), 7.93 ppm (d, ^3J(H,H) = 7.6 Hz, 1H; HC=); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.27 (C=O), 148.78 (C), 135.38(C), 135.19 (CH), 134.20 (CH), 129.43(CH), 128.71 (CH), 128.68 (CH), 126.88 (CH), 125.79 (C), 125.76 (CH), 123.85 (CH), 122.66 (CH), 82.05 ppm (CH); HRMS: *m*/*z*: calcd for $C_{16}H_{12}O_2$: 236.0837; found: 236.0838.

General procedure for the asymmetric cyclization of 2-iodobenzoate 1 with aldehydes 2: A sealed tube containing [CoI_2\{(*S*,*S*)-dipamp\}] (0.050 mmol, 5.0 mol%) and zinc powder (2.75 mmol) was evacuated and purged with nitrogen gas three times. Freshly distilled THF (3.0 mL), *o*-iodobenzoate (1.20 mmol), and aldehyde (1.00 mmol) were sequentially added to the system and the reaction mixture was allowed to stir at 75°C for 24 h. The mixture was filtered through a short Celite and silica-gel pad and washed with dichloromethane several times. The filtrate was concentrated and the residue was purified on a silica-gel column by using hexanes/ethyl acetate as the eluent to afford the cyclization product **4**.

Characterization data and chiral HPLC conditions of the obtained optically active phthalides **4a–b** are listed bellow. Spectral data of the remaining compounds **4c–e** and a copy of the ^{1}H NMR spectra for all compounds **4a–e** are given in Supporting Information.

(*S*)-3-Phenylisobenzofuran-1(3*H*)one (4a): $[\alpha]_D^{27} = +40.3$ (c = 1.00 in CH_2Cl_2) for 84% *ee* (lit.[15] $[\alpha]_D^{20} = +49.5$ (c = 2.00 in $CHCl_3$) for 98% *ee* in the *S* isomer; lit.[15] $[\alpha]_D^{20} = -48.6$ (c = 2.1 in $CHCl_3$) for 96% *ee* in the *R* isomer); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.38 (s, 1H; CH), 7.26–7.23 (m, 2H; aromatic H), 7.31 (d, ^3J(H,H) = 7.2 Hz, 1H; HC=), 7.36–7.34 (m, 3H; aromatic H), 7.53 (t, ^3J(H,H) = 7.6 Hz, 1H; HC=), 7.62 (t, ^3J(H,H) = 7.2 Hz, 1H; HC=), 7.94 ppm (d, ^3J(H,H) = 7.2 Hz, 1H; HC=). Compound **4a** was isolated in 89% yield and with 84% *ee*, determined by using HPLC analysis on a chiral OD-H column, detected at 254 nm. Retention times in *n*-hexanes/*i*PrOH 9:1 were 10.5 min (major) and 13.3 min (minor) (1.0 mL min^{-1}).

(*S*)-3-*p*-Tolylisobenzofuran-1(3*H*)one (4b): $[\alpha]_D^{27} = +15.0$ ($c = 1.00$ in CH_2Cl_2) for 79% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 2.33$ (s, 3H; CH_3), 6.36 (s, 1H; CH), 7.13 (d, $^3J(H,H) = 8.4$ Hz, 2H; HC=), 7.16 (d, $^3J(H,H) = 8.4$ Hz, 2H; HC=), 7.53 (t, $^3J(H,H) = 7.6$ Hz, 1H; HC=), 7.62 (t, $^3J(H,H) = 7.6$ Hz, 1H; HC=), 7.94 (d, $^3J(H,H) = 7.6$ Hz, 1H; HC=). Compound **4b** was isolated in 80% yield and with 79% *ee*, determined by using HPLC analysis on a chiral OD-H column, detected at 254 nm. Retention times in *n*-hexane/*i*PrOH 9:1 were 8.9 min (major) and 11.1 min (minor) (1.0 mL min^{-1}).

Acknowledgements

We thank the National Science Council (NSC-95–2113 M-007–005) of Republic of China for the support of this research.

[1] a) J. Tsuji, *Transition Metal Reagents and Catalysts: Innovations in Organic Synthesis*, Wiley, New York, **2002**; b) L. S. Hegedus, *Transition Metals in the Synthesis of Complex Organic Molecules*, 2nd ed., University Science Books: Sausalito, CA, **1999**.

[2] a) K. P. C. Vollhardt, *Angew. Chem.* **1984**, *96*, 525; *Angew. Chem. Int. Ed. Engl.* **1984**, *23*, 539; b) H, Butenschon, M. Winkler, K. P. C. Vollhardt, *Chem. Commun.* **1986**, 388; c) E. P. Johnson, K. P. C. Vollhardt, *J. Am. Chem. Soc.* **1991**, *113*, 381; d) J. A. Varela, C. Saa, *Chem. Rev.* **2003**, *103*, 3787, and references therein; e) H.-T. Chang, M. Jeganmohan, C.-H. Cheng, *Chem. Commun.* **2005**, 4955 and references therein.

[3] K.-C. Chen, D. K. Rayabarapu, C.-C. Wang, C.-H. Cheng, *J. Org. Chem.* **2001**, *66*, 8804.

[4] a) I. U. Khand, G. R. Knox, P. L. Pauson, W. E. Watts, M. I. Foreman, *J. Chem. Soc. Perkin Trans. 1* **1973**, 977; b) P. L. Pauson, *Tetrahedron* **1985**, *41*, 5855; c) I. U. Khand, P. L. Pauson, *J. Chem. Soc. Chem. Commun.* **1974**, 379.

[5] C.-C. Wang, P.-S. Lin, C.-H. Cheng, *J. Am. Chem. Soc.* **2002**, *124*, 9696.

[6] a) T. Zieglar, L. Versluis, *Adv. Chem. Ser.* **1992**, *230*, 75; b) L. H. Slaugh, R. D. Mullineaux, *J. Organomet. Chem.* **1968**, *13*, 469.

[7] a) G. Cahiez, H. Avedissian, *Tetrahedron Lett.* **1998**, *39*, 6159; b) H. Avedissian, L. Berillon, G. Cahiez, P. Knochel, *Tetrahedron Lett.* **1998**, *39*, 6163; c) Y. Ikeda, T. Nakamura, H. yorimtsu, K. Oshima, *J. Am. Chem. Soc.* **2002**, *124*, 6514.

[8] H. Fillon, C. Gosmini, J. Perichon, *J. Am. Chem. Soc.* **2003**, *125*, 3867.

[9] a) P. Gomes, C. Gosmini, J. Perichon, *Org. Lett.* **2003**, *5*, 1043; b) M. Amatore, C. Gosmini, J. Perichon, *Eur. J. Org. Chem.* **2005**, *6*, 989; c) C. Gosmini, M. Amatore, C. Stephanie, J. Perichon, *Synlett* **2005**, 2171; d) I. Kazmierski, C. Gosmini, J. M. Paris, M. Amatore, J. Perichon, *Synlett* **2006**, 881; e) M. Amatore, C. Gosmini, J. Perichon, *J. Org. Chem.* **2006**, *71*, 6130.

[10] a) K.-J. Chang, D. K. Rayabarapu, C.-H. Cheng, *Org. Lett.* **2003**, *5*, 3963; b) K.-J. Chang, D. K. Rayabarapu, C.-H. Cheng, *J. Org. Chem.* **2004**, *69*, 4781.

[11] a) T. K. Devon, A. I. Scott, *Handbook of Naturally Occurring Compounds, Vol. 1*, Academic Press, New York, **1975**, pp. 249–264; b) T. Aoki, T. Furusho, T. Kimura, S. Satake, S. Funayama, Japanese Patent 7324724, **1973**; [Chem. Abstr. **1974**, *80*, 129246]; c) M. Lacova, *Chem. Zvesti.* **1973**, *27*, 525 [M. Lacova, *Chem. Abstr.* **1974**, *80*, 59757]; d) R. C. Elderfield in *Hetrocyclic Compounds, Vol. 2*, Wiley, New York, **1951**, Chapter 2.

[12] a) K. Knepper, R. E. Ziegert, S. T. Brase, *Tetrahedron* **2004**, *60*, 8591 and references therein; b) T. V. Hung, B. A. Mooney, R. H. Prager, J. M. Tippett, *Aust. J. Chem.* **1981**, *34*, 383.

[13] a) A. Cowell, J. K. Stille, *J. Am. Chem. Soc.* **1980**, *102*, 4193; b) R. C. Larock, C. A. Fellows, *J. Am. Chem. Soc.* **1982**, *104*, 1900; c) R. C. Larock, C. A. Fellows, *J. Org. Chem.* **1980**, *45*, 363; d) C. S. Cho, D. Y. Baek, H. Y. Kim, S. C. Shim, D. H. Oh, *Synth. Commun.* **2000**, *30*, 1139, and references therein; e) G. P. Chiusoli, G. Salerno, *Adv. Organomet. Chem.* **1979**, *17*, 291; f) X. Yang, T. Rotter, C. Piazza, P. Knochel, *Org. Lett.* **2003**, *5*, 1229; g) A. Inoue, K. Kitagawa, H. Shinokubo, K. Oshima, *J. Org. Chem.* **2001**, *66*, 4333.

[14] D. K. Rayabarapu, H.-T. Chang, C.-H. Cheng, *Chem. Eur. J.* **2004**, *10*, 2991.

[15] L.-L. Huang, M.-H. Xu, G.-Q. Lin, *J. Am. Chem. Soc.* **2006**, *128*, 5624.

[16] M. Hidai, T. Kashiwagi, T. Ikeuchi, Y. Uchida. *J. Organomet. Chem.* **1971**, *30*, 279.

Received: December 25, 2006
Published online: February 26, 2007

