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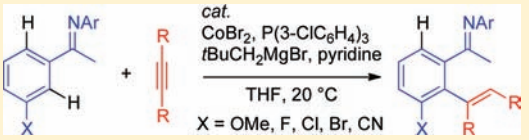
Cobalt-Catalyzed, Room-Temperature Addition of Aromatic Imines to Alkynes via Directed C−H Bond Activation

Pin-Sheng Lee, Takeshi Fujita,† and Naohiko Yoshikai*

Division of Chemistry and Biological Chemistry, School of Physical and Mathematical Sciences, Nanyang Technological University, Singapore 637371, Singapore

Supporting Information

ABSTRACT: A quaternary catalytic system consisting of a cobalt salt, a triarylphosphine ligand, a Grignard reagent, and pyridine has been developed for chelation-assisted C−H bond activation of an aromatic imine, followed by insertion of an unactivated internal alkyne that occurs at ambient temperature. The reaction not only tolerates potentially senstitive functional groups (e.g., Cl, Br, CN, and tertiary amide), but also displays a unique regioselectivity. Thus, the presence of substituents such as methoxy, halogen, and cyano groups at the *meta*-position of the imino group led to selective C−C bond formation at the more sterically hindered ortho positions. Under acidic conditions, the hydroarylation products of dialkyl- and alkylarylacetylenes underwent cyclization to afford benzofulvene derivatives, while those of diarylacetylenes afforded the corresponding ketones in moderate to good yields. A mechanistic investigation into the reaction with the aid of deuterium-labeling experiments and kinetic analysis has indicated that oxidative addition of the ortho C−H bond is the rate-limiting step of the reaction. The kinetic analysis has also shed light on the complexity of the quaternary catalytic system.



INTRODUCTION

Chelation-assisted C−H bond cleavage by a transition metal complex has been established as a versatile strategy for regioselective functionalization of ubiquitous but unreactive C−H bonds since the discovery of ruthenium-catalyzed *ortho*-alkylation of aromatic ketones with olefins by Murai and co-workers.[1,2] Regardless of the mechanism of the C−H bond cleavage, the concept of chelation assistance has proven to be broadly applicable, leading to the development of an extremely wide variety of C−C and C−heteroatom bond-forming reactions through C−H bond functionalization. While second-row transition metals such as ruthenium, rhodium, and palladium have played a major role in this type of transformation, it is desirable to develop cost-effective, alternative processes using naturally abundant first-row transition metals. Furthermore, exploration of catalysis using these metals would offer opportunities to find unique reactivities and selectivities.[3,4]

The potential utility of cobalt, the first-row transition metal of group 9, in chelation-assisted C−H bond functionalization has been known since the mid 1950s, when Murahashi reported that the reaction of an aldimine in the presence of $Co_2(CO)_8$ and high-pressure carbon monoxide (100−200 atm) at high temperatures (>200 °C) led to CO insertion into the *ortho* C−H bond of the aldimine, affording an isoindolinone as the product.[4a] Murahashi also reported the *ortho* C−H functionalization of an azobenzene with carbon monoxide under cobalt catalysis, which afforded an indazolone or a quinazolinedione, depending on the reaction temperature.[4b] However, these seminal findings have only been followed by a few examples of *ortho* C−H functionalization reactions catalyzed by cobalt complexes until very recently.[4c,d] For example, in 1994, Kisch and co-workers reported that the *ortho* C−H bonds of azobenzenes undergo *anti*-addition to diphenylacetylene in the presence of $CoH(N_2)(PPh_3)_3$ or $CoH_3(PPh_3)_3$.[4c] Unfortunately, this reaction has a limited scope, and the mechanism of the *anti*-addition remains ambiguous.

The reactivity of cobalt toward an aromatic C−H bond has also been studied from a stoichiometric point of view.[5,6] In particular, cyclometalation reactions of $Co(CH_3)(PMe_3)_4$ with a series of aromatic substrates such as aryl ketones, imines, phosphines, and thioketones, which have been explored by Klein and co-workers, are noteworthy.[6,7] While these cyclometalation reactions are potential elementary processes for catalytic *ortho* C−H bond functionalization, such a catalytic turnover has yet to be achieved.

Recently, we reported that a ternary catalytic system, consisiting of $CoBr_2$, $PMePh_2$, and MeMgCl, promotes the *syn*-addition reaction of a 2-phenylpyridine derivative to an unactivated internal alkyne to afford a trisubstituted olefin in good yield with a high stereoselectivity (eq 1).[8] This reaction has demonstrated the feasibility of chelation-assisted C−H addition to a C−C multiple bond using a first-row transition metal catalyst[9] and has aroused renewed interest in cobalt-catalyzed C−H bond functionalization.[4a−d,10,11] Nevertheless, the cobalt catalysis required as harsh conditions (100 °C) as those usually required for analogous hydroarylation reactions to alkynes using second- or third-row transition metal catalysts.[12−15]

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Scheme 1. Cobalt-Catalyzed Addition of Aromatic Imines to Alkynes

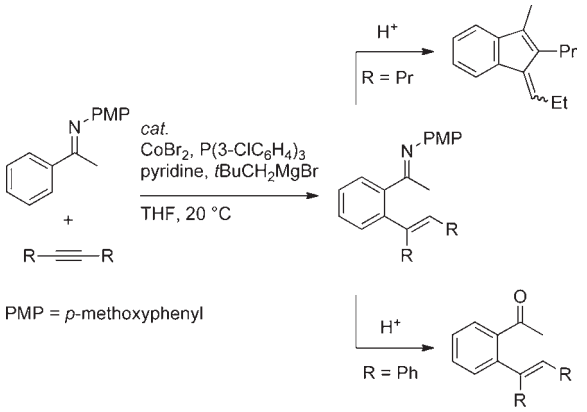
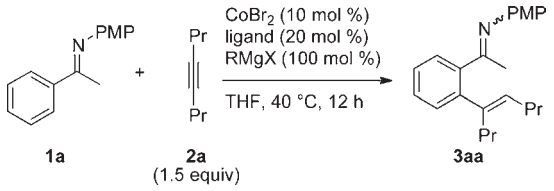
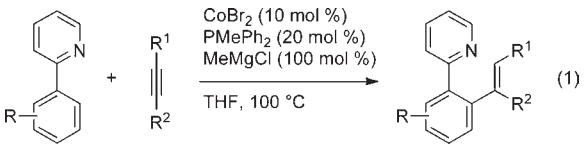


Table 1. Screening of Ligands[a]



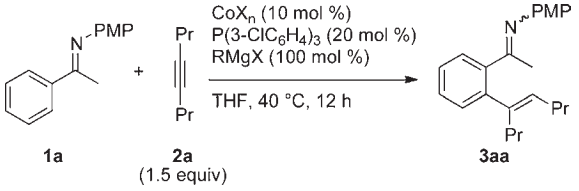
entry	ligand	RMgX	yield (%)[b]
1	$PMePh_2$	MeMgCl	1
2	PPh_3	tBuCH$_2$MgBr	4
3	P(4-MeOC$_6$H$_4$)$_3$	tBuCH$_2$MgBr	2
4	P(4-Me$_2$NC$_6$H$_4$)$_3$	tBuCH$_2$MgBr	8
5	P(3-ClC$_6$H$_4$)$_3$	tBuCH$_2$MgBr	43
6	P(4-ClC$_6$H$_4$)$_3$	tBuCH$_2$MgBr	17
7	P(3-FC$_6$H$_4$)$_3$	tBuCH$_2$MgBr	23
8	P(4-FC$_6$H$_4$)$_3$	tBuCH$_2$MgBr	35
9	P(4-CF$_3$C$_6$H$_4$)$_3$	tBuCH$_2$MgBr	15
10	P(3,5-(CF$_3$)$_2$C$_6$H$_3$)$_3$	tBuCH$_2$MgBr	0
11	P(C$_6$F$_5$)$_3$	tBuCH$_2$MgBr	0
12	P(2-furyl)$_3$	tBuCH$_2$MgBr	2
13	PCy_3	tBuCH$_2$MgBr	0

[a] The reaction was performed on a 0.3 mmol scale. [b] Determined by GC/GC−MS analysis using *n*-tridecane as an internal standard. The imine *E*/*Z* ratio was not determined.



In this Article, we report on a new cobalt-based quaternary catalytic system consisting of $CoBr_2$, P(3-ClC$_6$H$_4$)$_3$, neopentylmagnesium bromide, and pyridine that efficiently promotes an addition reaction of an aromatic imine to an internal alkyne through chelation-assisted C−H bond activation (Scheme 1).[16]

Table 2. Effects of Grignard Reagent and Cobalt Source[a]



entry	CoX_n	RMgX	yield (%)[b]
1	$CoBr_2$	tBuCH$_2$MgBr	43
2	$CoBr_2$	MeMgCl	0
3	$CoBr_2$	nBuMgBr	5
4	$CoBr_2$	iPrMgBr	35
5	$CoBr_2$	tBuMgBr	9
6	$CoBr_2$	Me$_3$SiCH$_2$MgCl	16
7	$CoBr_2$	PhMgBr	5
8	$CoCl_2$	tBuCH$_2$MgBr	30
9	CoI_2	tBuCH$_2$MgBr	1
10	Co(acac)$_3$	tBuCH$_2$MgBr	27
11	Co(acac)$_2$	tBuCH$_2$MgBr	3

[a] The reaction was performed on a 0.3 mmol scale. [b] Determined by GC/GC−MS analysis using *n*-tridecane as an internal standard. The imine *E*/*Z* ratio was not determined.

The reaction occurs readily at 20 °C, which is a remarkably mild condition as compared to that for related transformations reported thus far.[2,12−15,17−19] Because of the mild reaction conditions, the reaction tolerates a variety of imines and alkynes, including those bearing potentially sensitive functional groups (e.g., Cl, Br, CN, and tertiary amide). Furthermore, the reaction exhibits unique regioselectivity. Thus, in the presence of a substituent such as methoxy, halogen, and cyano groups at the *meta* position, C−H bond cleavage takes place preferentially at the more sterically hindered *ortho* position. Upon hydrolysis, the hydroarylation products are converted to either benzofulvene derivatives[14c,17g,20,21] or ketones, depending on the nature of the alkyne substituents. The present hydroarylation reaction is likely to involve three major elementary steps, that is, chelation-assisted oxidative addition of the *ortho* C−H bond, insertion of the alkyne into the Co−H bond, and reductive elimination of the diorganocobalt species. A mechanistic investigation with the aid of deuterium-labeling experiments and kinetic analysis has indicated that the C−H bond cleavage is the rate-determining step and provided insight into how each of the reactants is involved in the catalytic cycle. The complexity of the quaternary catalytic system was also addressed by the kinetic analysis, which revealed the dependence of the catalytic activity on each of the catalytic components.

RESULTS AND DISCUSSION

Reaction Development. We chose the imine **1a** derived from acetophenone and *p*-anisidine and 4-octyne **2a** as the model substrates and carried out extensive screening of the reaction conditions. Table 1 summarizes the screening data during the early stage. The reaction of **1a** (0.3 mmol) and **2a** (0.45 mmol, 1.5 equiv) was performed at 40 °C by using $CoBr_2$ (10 mol %), a ligand (10−20 mol %), and a Grignard reagent (100 mol %)

in THF (0.2 M) for 12 h. While the catalytic system for the hydroarylation of arylpyridines (i.e., $CoBr_2/PMePh_2/MeMgCl$)[8] gave the hydroarylation product **3aa** in only 1% yield (entry 1), throughout several ensuing experiments we found that a combination of PPh_3 and tBuCH$_2$MgBr afforded a slight increase in the yield of **3aa** (entry 2).

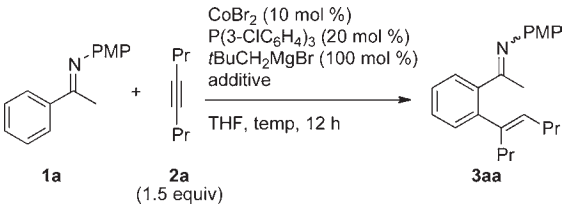
Subsequent screening of triarylphosphine ligands displayed an intriguing trend. While triarylphosphines bearing electron-donating groups at the 4-position did not have a pronounced effect on the catalytic activity (entries 3 and 4), those bearing electron-withdrawing chloro, fluoro, or trifluoromethyl substituents at the 3- or 4-position improved the reaction to give **3aa** in 15−43% yields (entries 5−9). Among these ligands, P(3-ClC$_6$H$_4$)$_3$ emerged as the most promising (entry 5). Other electron-poor ligands, such as P(3,5-(CF$_3$)$_2$C$_6$H$_3$)$_3$ and P(C$_6$F$_5$)$_3$, did not promote the reaction at all (entries 10 and 11), and P(2-furyl)$_3$ exhibited only a poor catalytic activity (entry 12). While PCy_3 was an effective ligand for branched hydroarylation of styrenes,[10b] it did not promote the present alkenylation reaction at all (entry 13). Bidentate phosphines such as dppe, dppp, and Xantphos were entirely ineffective (data not shown).

Having identified the promising triarylphosphine ligand, P(3-ClC$_6$H$_4$)$_3$, we then examined the effects of the Grignard reagent and the cobalt source (Table 2). However, none of our examinations led to an improvement in the catalytic activity. Methyl and primary and tertiary alkyl Grignard reagents afforded much lower yields of **3aa** than did tBuCH$_2$MgBr (entries 2, 3, 5, and 6), except that the use of iPrMgBr resulted in a moderate yield of 35% (entry 4). In addition, PhMgBr poorly promoted the reaction (entry 7). $CoBr_2$ emerged as the best cobalt source, while the use of $CoCl_2$ and Co(acac)$_3$ resulted in moderate activities (entries 8−11).

Further improvement of the reaction was achieved by modifying reaction conditions including the reaction temperature, concentration, and additives (Table 3). Lowering the temperature to 20 °C improved the yield slightly, while increasing the temperature to 50 °C did not lead to any notable change (entries 2 and 3). Increasing the concentration from 0.2 to 0.4 M also improved the yield (entry 4). Furthermore, among several Lewis basic additives examined, pyridine displayed a positive effect on the reaction (entries 5−7). We eventually optimized the reaction by taking the above three observations into consideration. Thus, the reaction of **1a** and **2a** (1.3 equiv) in the presence of 5 mol % $CoBr_2$, 10 mol % P(3-ClC$_6$H$_4$)$_3$, 50 mol % tBuCH$_2$MgBr, and 80 mol % pyridine in THF (0.4 M) at 20 °C afforded the hydroarylation product **3aa** in 87% isolated yield with exclusive *syn*-selectivity and E/Z isomerization of the imine moiety (84:16) (entry 8).[22] The formation of **3aa** was accompanied by a small amount of a dialkenylation product (8%). It is notable that an addition of the Grignard reagent to the imine C═N bond did not take place under the optimized conditions. It should also be noted that only a trace amount of a product due to cyclotrimerization of **2a** was observed.[23] The amount of the Grignard reagent used was critical for the activity of the cobalt catalyst, as in other cases previously reported by our group.[8,10] The use of 40 mol % or less of tBuCH$_2$MgBr led to a significant decrease in the reaction rate, which suggests that the Grignard reagent is not a mere reducing agent for the cobalt precatalyst (vide infra).

Addition of Aryl Imines to Alkylacetylenes. With the quaternary catalytic system in hand, we first performed the hydroarylation reaction of a variety of aromatic imines and alkylacetylenes (Chart 1). Imines derived from substituted acetophenones

Table 3. Effects of Temperature, Concentration, and Additives[a]



entry	temp (°C)	conc (M)	additive (mol %)	yield (%)[b]
1	40	0.2	none	43
2	20	0.2	none	53
3	50	0.2	none	45
4	40	0.4	none	53
5	40	0.2	pyridine (40)	54
6	40	0.2	DMI (40)	37
7	40	0.2	DMPU (40)	43
8[c]	20	0.4	pyridine (80)	87[d]

[a] The reaction was performed on a 0.3 mmol scale. DMI = *N*,*N*-dimethylimidazolidinone. DMPU = 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone. [b] Determined by GC/GC−MS analysis using *n*-tridecane as an internal standard. The imine E/Z ratio was not determined unless otherwise noted. [c] 5 mol % of $CoBr_2$, 10 mol % of P(3-ClC$_6$H$_4$)$_3$, 50 mol % of tBuCH$_2$MgBr, 1.3 equiv of 4-octyne were used. [d] Isolated yield. Imine E/Z ratio was 84/16 as determined by ^{1}H NMR. The dialkenylation product was obtained in 8% yield.

underwent addition to 4-octyne smoothly to afford the corresponding hydroarylation products **3ba**−**3la** in moderate to good yields. While the reaction was generally accompanied by E/Z isomerization of the C═N bond to some extent (80:20−90:10), C−C and C−H bond formation took place with exclusive *syn*-stereoselectivity. Electron-donating (e.g., OMe), neutral, and electron-withdrawing (e.g., CF$_3$) substituents at the *para*- or *meta*-position were tolerated. The presence of potentially sensitive chloro and cyano substituents was also tolerated (see **3ea**, **3ia**, and **3ja**). The catalytic system allowed for a gram-scale reaction. Thus, the reaction of the 3-methylacetophenone imine on a 6 mmol scale (1.44 g) took place as efficiently as the reaction on a 0.3 mmol scale, affording the product **3fa** in 92% yield.

The reactions of the *meta*-substituted acetophenone imines exhibited intriguing regioselectivities. While the substrates bearing *m*-methyl and *m*-trifluoromethyl groups were selectively alkenylated at the less hindered *ortho* position (see **3fa** and **3ga**, regioselectivity ≥94:6), those bearing *m*-methoxy, *m*-chloro, *m*-cyano, or *m*-fluoro substituents reacted preferentially at the position proximal to these groups to afford **3ha**−**3ka** in 87%, 66%, 58%, and 92% yields, respectively. While the regioisomers of **3ha**, **3ja**, and **3ka** could not be either detected or characterized in our hands, the regioisomer of **3ia** was isolated in 19% yield. While the strong secondary directing effect of the methoxy and fluoro substituents has been reported previously for chelation-assisted C−H functionalization reactions using ruthenium and iridium catalysts,[14c,24] the high regioselectivities observed here for the chloro, cyano, and bromo (vide infra) substituents are unprecedented.[25]

The imine derived from 3,5-difluoroacetophenone was highly reactive and afforded a mixture of mono- and dialkenylated products (ca. 27% and 57% yields, respectively) under the standard

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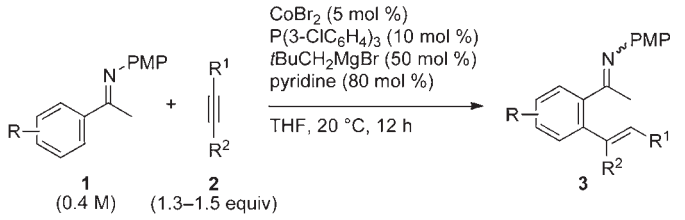
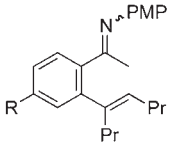
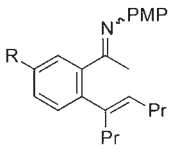
Chart 1. Addition of Aryl Imines to Alkylacetylenes[a]

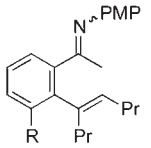




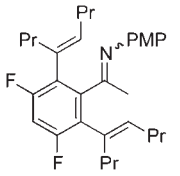
3ba (R = OMe), 80% (83:17)
3ca (R = CF_3), 76% (87:13)
3da (R = Ph), 83% (86:14)[b]
3ea (R = CN), 57% (87:13)



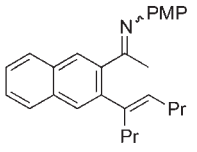
3fa (R = Me), 94% (89:11)[c]
3ga (R = CF_3), 85% (91:9)[b,d]



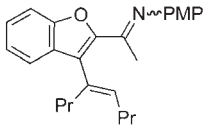
3ha (R = OMe), 87% (89:11)[e,f]
3ia (R = Cl), 85% (88:12)[g]
3ja (R = CN), 58% (88:12)[e]
3ka (R = F), 92% (88:12)[e]



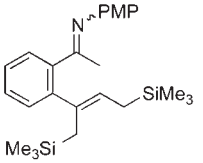
3la, 98% (98:2)[h]



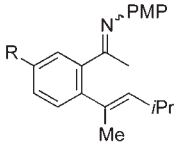
3ma, 91% (93:7)[i]



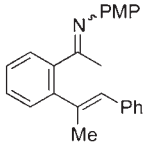
3na, 30% (51:49)[b]



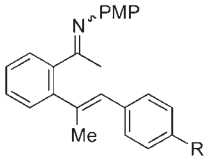
3ab, 57% (88:12)



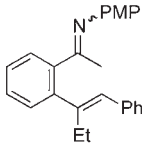
3ac (R = H), 82% (81:19)[j]
3fc (R = Me), 94% (86:14)[j,k]



3ad, 52% (80:20)[b,j]



3ae (R = OMe), 40% (81:19)[l]
3af (R = Cl), 13% (75:25)[j]



3ag, 89% (rr = 3:2)[m]

[a] The reaction was performed on a 0.3 mmol scale. The yields refer to the isolated products. The *E*/*Z* ratio of the imine moiety is shown in parentheses. Unless otherwise noted, the stereochemistry of the olefin moiety was exclusively *E*. [b] The reaction time was 24 h. [c] The regioselectivity was 96:4. [d] The regioselectivity was 94:6. [e] Only the regioisomer shown was isolated, and the presence of the other regioisomer could not be confirmed. [f] *E*/*Z* ratio of the olefin moiety was 89:11. [g] Combined yield of **3ia** (66%) and its regioisomer (19%). [h] 2.6 equiv of 4-octyne was used. [i] The regioselectivity was 57:43. [j] C−C bond formation took place with regioselectivity of >99:1. [k] The regioselectivity of C−H bond cleavage was 89:11. [l] The regioselectivity was 97:3. [m] rr = Regioisomeric ratio as estimated by ^{1}H NMR. See the Supporting Information for the imine *E*/*Z* ratio.

conditions (i.e., 1.5 equiv of 4-octyne). When the amount of 4-octyne was increased to 2.6 equiv, the dialkenylation product **3la** was obtained in near quantitative yield. The high reactivity of this substrate would originate from the strong effect of the *ortho*-fluorine atoms directing C−H bond cleavage.[26] The imine derived from 2-acetonaphthone also participated in the reaction to afford **3ma** in a good yield, while the regioselectivity was only modest (57:43). Heteroarenes such as thiophene and *N*-methylpyrrole bearing the imino group at the 2-position failed to participate in the reaction, while the 3-position of benzofuran could be alkenylated in 30% yield (see **3na**).

Aliphatic alkynes such as 1,4-bis(trimethylsilyl)-2-butyne and 4-methyl-2-pentyne afforded hydroarylation products **3ab**, **3ac**, and **3fc** in moderate to good yields. In the latter two cases, the aryl group was exclusively introduced to the less hindered acetylenic carbon atom. 1-Phenyl-1-propyne and its derivatives also participated in the reaction to afford **3ad**−**3af** in modest yields, where the C−C bond formation took place highly regioselectively (≥97:3) at the acetylenic carbon proximal to the methyl group. In contrast, only modest regioselectivity (ca. 3:2) was observed for the reaction of 1-phenyl-1-butyne (see **3ag**). Note that heteroaryl alkynes such as 1-(2-thienyl)-1-propyne, 1-(2-furyl)-1-propyne, and 1-(2-pyridyl)-1-propyne as well as terminal alkynes such as 1-octyne and phenylacetylene failed to participate in the reaction.

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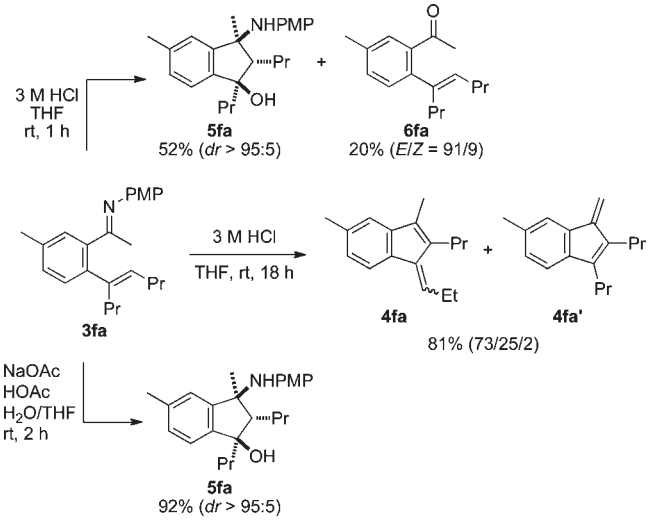
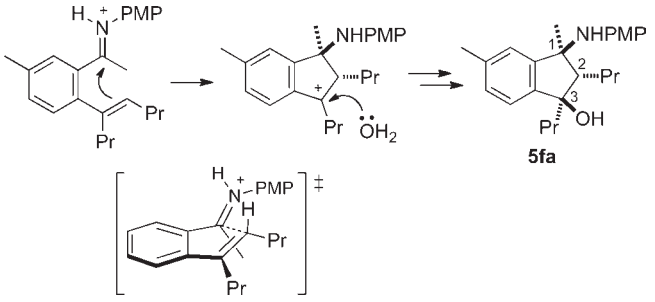
Scheme 2. Transformation of 3fa under Hydrolysis Conditions



Scheme 3



Conversion of Hydroarylation Products to Benzofulvenes. When the hydroarylation product **3fa** was subjected to acidic conditions (3 M HCl, 18 h), a mixture of benzofulvenes **4fa** (a mixture of *E* and *Z* isomers) and **4fa′** was obtained in 81% yield with a ratio of 73:25:2 (Scheme 2).[20,27] The ratio of the isomers was fairly reproducible from run to run, the error being less than 5%. When quenched within a period of 1 h, the reaction afforded an aminoindanol **5fa** (dr > 95:5) and a ketone **6fa** (*E*/*Z* = 91/9) in 52% and 20% yields, respectively.[28] Furthermore, milder hydrolysis conditions (HOAc/NaOAc buffer) effected the conversion of **3fa** to the aminoindanol **5fa** in 92% yield with a high diastereoselectivity (>95:5).[29]

The mechanism of the diastereoselective formation of the aminoindanol **5fa** may be rationalized as illustrated in Scheme 3. Thus, the cyclization process is triggered by protonation of the imine, followed by intramolecular nucleophilic attack of the olefin moiety on the iminium moiety. The relative stereochemistry of the C1 and C2 positions of the final product **5fa** is controlled by the transition structure in this step (see Scheme 3). A water molecule attacks the resulting benzylic cation intermediate selectively from the sterically less hindered side to afford the aminoindanol **5fa**.

Upon exposure to 3 M HCl, both the isolated aminoindanol **5fa** and the ketone **6fa** afforded a mixture of the benzofulvene derivatives **4fa** and **4fa′** (Scheme 4). However, the constitution of

Scheme 4

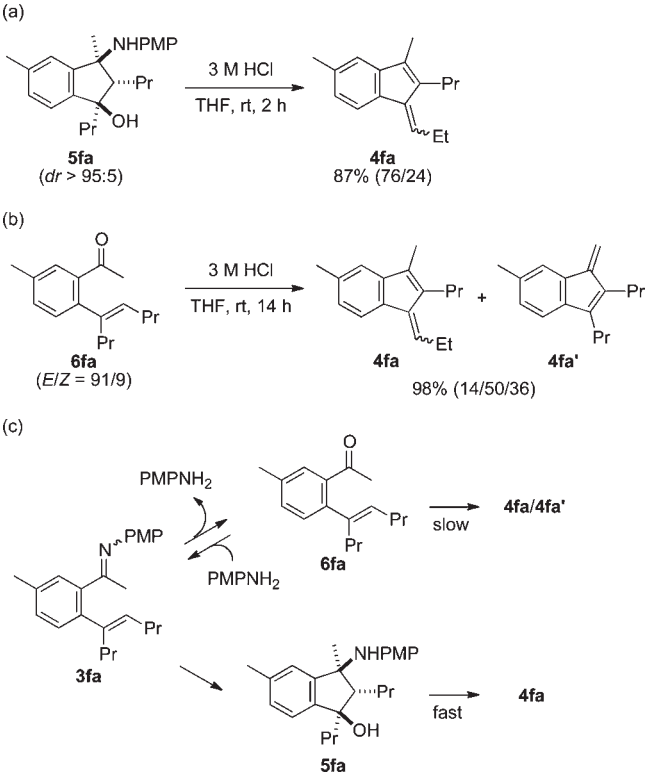
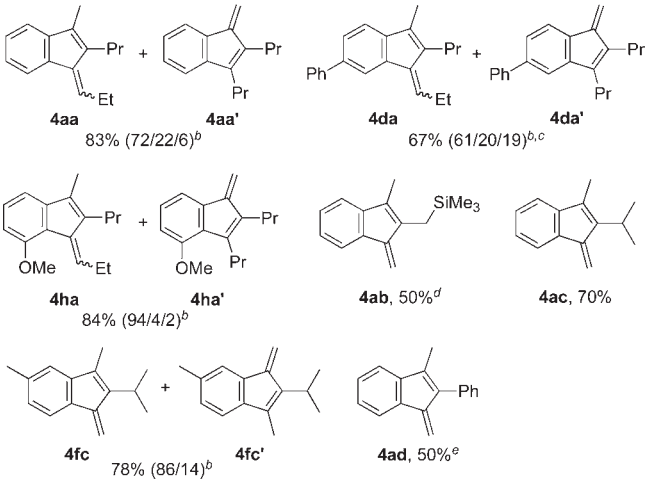


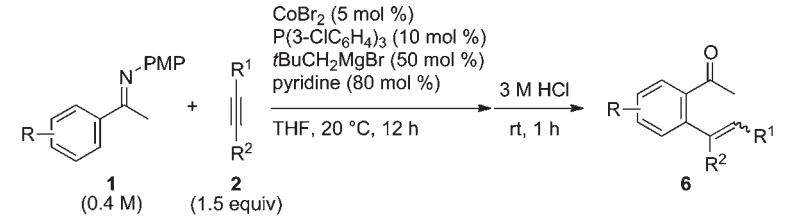
Chart 2. Benzofulvene Derivatives[a]

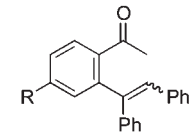


[a] Unless otherwise noted, the reaction was performed at room temperature in 3 M HCl/THF for 18 h. [b] The ratio of the isomers is shown in parentheses. [c] The reaction was performed at 50 °C for 8 h. [d] The reaction time was 72 h. [e] The reaction was performed at 50 °C for 9 h.

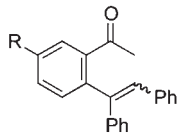
the product mixture was different between the two cases. While **5fa** afforded only the regioisomer **4fa** in 87% yield with a stereoselectivity of 76:24 (Scheme 4a), **6fa** afforded both **4fa** and **4fa′** in 98% yield with a ratio of 14:50:36 (Scheme 4b). Again, the ratios of the benzofulvene isomers obtained by the two reactions were reproducible (error < 5%). Thus, the product composition of the former case was much closer to that observed

Chart 3. Addition of Aryl Imines to Diarylacetylenes[a]

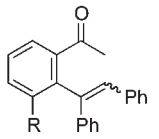




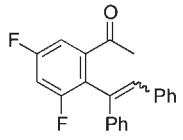
6ah (R = H), 90% (90:10)
6bh (R = OMe), 76% (91:9)
6ch (R = CF_3), 64% (88:12)
6dh (R = Ph), 73% (90:10)
6eh (R = CN), 49% (86:14)
6oh (R = Br), 37% (83:17)
6ph (R = $CONR'_2$), 57% (62:38)[b]



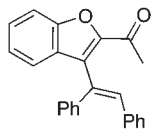
6fh (R = Me), 73% (90:10)[c]
6gh (R = CF_3), 80% (88:12)[c]



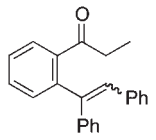
6hh (R = OMe), 70% (92:8)[c]
6ih (R = Cl), 70% (> 99:1)[c]
6jh (R = CN), 76% (58:42)[d]
6kh (R = F), 64% (84:16)[c]
6qh (R = Br), 20% (> 99:1)[c]



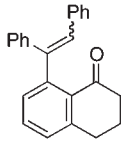
6lh, 54% (96:4)



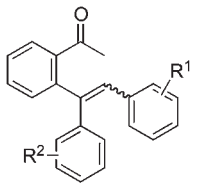
6nh, 30% (> 99:1)



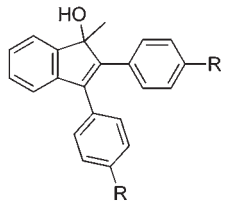
6rh, 76% (88:12)



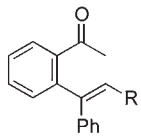
6sh, 78% (85:15)[e]



6ai (R^1, R^2 = 3-Me), 65% (88:12)
6aj (R^1, R^2 = 3-F), 53% (81:19)
6ak (R^1, R^2 = 4-Cl), 36% (92:8)[f]
6al (R^1, R^2 = 3-Br), 34% (51:49)[g]
6am (R^1, R^2 = 4-Br), 17% (90:10)
6an (R^1 = 4-OMe, R^2 = 4-F), 91%[h]



6ao' (R = OMe), 44%[i]
6ap' (R = $SiMe_3$), 42%[j]



6aq (R = $SiMe_3$), 41%
6ar (R = H), 50%[k]

[a] The reaction was performed on a 0.3 mmol scale. The yields refer to isolated products. The *E*/*Z* ratio is shown in parentheses. [b] NR'_2 = morpholino. Combined yield of **6ph** (44%) and its cyclization (i.e., indenol-type) product (13%). [c] The regioselectivity was >99:1 according to ^{1}H NMR analysis of the crude product. [d] Combined yield of **6je** (59%) and its regioisomer (17%). [e] Hydrolysis was performed at 55 °C for 3 h. [f] Concentration was 0.2 M. [g] Catalyst loading was doubled. [h] The major isomer among three is shown. The ratio of the isomers was 63:23:14 as determined by ^{1}H NMR. [i] Combined yield of **6ao'** (37%) and its dehydration (i.e., benzofulvene-type) product (7%). [j] Concentration was 0.3 M. [k] Obtained from the reaction of **6ai** with tetrabutylammonium fluoride (1 M in THF) at 60 °C for 12 h.

in the direct transformation to the benzofulvenes (73:25:2, see Scheme 2). It should also be noted that the conversion of **5fa** to **4fa** required much shorter time (2 h) than the conversion of **6fa** to **4fa**/**4fa'** did (14 h) as monitored by TLC. Therefore, we consider that the direct conversion of the imine **3fa** to **4fa**/**4fa'** in 3 M HCl involves the aminoindanol **5fa** and the ketone **6fa** as the major and minor intermediates, respectively. The conversion of **5fa** to **4fa** would involve acid-mediated sequential deamination and dehydration processes. On the other hand, because of the reversibility of the imine-to-ketone hydrolysis, the conversion of **6fa** to **4fa**/**4fa'** could occur either directly (cf., Scheme 4b) or indirectly via regeneration of **3fa** and its conversion to **5fa** (Scheme 4c). We consider that the latter indirect pathway is more important, because if only the former pathway is operative, the isomer ratios obtained from **3fa** and **5fa** should have been much different.

Some of the other hydroarylation products were also subjected to the acidic conditions to afford the corresponding benzofulvenes (Chart 2).[30] The reaction was found to be sensitive to the electronic property of the substituent. Among the products shown in Chart 1, those bearing electron-donating or neutral substituents at the *ortho*- or *para*-position to the olefin moiety underwent the reaction smoothly to afford the corresponding benzofulvenes in moderate to good yields. In contrast, when an electron-withdrawing substituent was present at the *para*- or *meta*-position (e.g., **3ca**), cyclization of the alkenylated product to the corresponding aminoindanol was observed, while its conversion to the benzofulvene was sluggish. Note that the

cyclization reaction of **3ab** to **4ab** was accompanied by the loss of one of the two Me_3Si groups, which can be ascribed to desilylation occurring during nucleophilic attack of the allylsilane moiety to the iminium moiety.

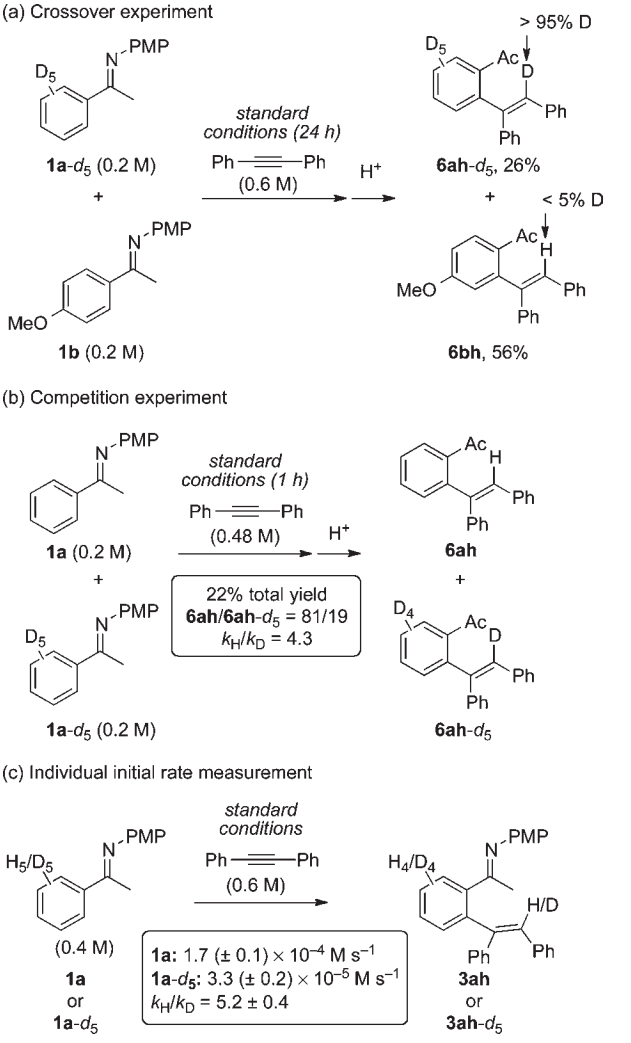
Addition to Diarylacetylenes. The present catalytic system is also applicable to the reaction of aromatic imines with diphenylacetylene **2h** (Chart 3). In contrast to the cases of alkylacetylenes, acidic treatment of the addition product did not cause a cyclization reaction, but cleanly hydrolyzed the imine moiety to afford the corresponding ketone within 1 h, as a mixture of olefinic *E*- and *Z*-isomers (typically 9:1). We confirmed that the minor *Z*-isomer formed during the catalytic reaction but not after quenching, while the mechanism of its formation is not clear at present. The scope of the applicable imines was as wide as that for the reaction with 4-octyne (see Chart 1). Note that the imines derived from propiophenone and tetralone reacted as smoothly as the acetophenone derivatives did (see **6rh** and **6sh**). The reaction tolerated the presence of chloro, bromo, cyano, and tertiary amide substituents (see **6eh**, **6ih**, **6jh**, and **6oh**−**6qh**). The low yields obtained for the bromo-substituted substrates (**6oh** and **6qh**) were because of the sluggishness of the reaction. Thus, unreacted starting material largely remained, and hydrodebromination only took place to a small extent (<10% observed). Note that no alkenylation took place at the ortho position of the amide functional group (see **6ph**).

As we observed in the reactions of 4-octyne, methoxy, halogen (F, Cl, and Br), and cyano groups at the *meta*-position served as secondary directing groups for the cobalt catalyst, leading to selective introduction of the alkenyl group onto the more hindered *ortho* positions (see **6hh**−**6kh** and **6qh**). The reaction of 3,5-difluoroacetophenone imine with diphenylacetylene exclusively afforded the monoalkenylation product **6lh**. This was in stark contrast to the reaction with 4-octyne, which preferentially afforded the dialkenylation product (see **3la** in Chart 1). This difference may be ascribed to the greater steric bulk of the 1,2-diphenylvinyl group than the 4-octenyl group, which should have prevented the second alkenylation.

Symmetric diarylacetylenes bearing 3-methyl, 3-fluoro, 4-chloro, 3-bromo, and 4-bromo substituents reacted with imine **1a** to afford the corresponding hydroarylation products **6ai**−**6am**, respectively, albeit in modest yields.[31] On the other hand, diarylacetylenes having 4-methoxy and 4-trimethylsilyl groups afforded indenol derivatives **6ao′** and **6ap′**, respectively, presumably because these substituents increased the nucleophilicity of the olefinic moieties of the initially formed alkenylation products. An unsymmetrical diarylacetylene substituted with 4-methoxy and 4-fluoro groups underwent C−C bond formation preferentially at the acetylenic carbon promixal to the fluorophenyl group, affording the adduct **6an** as the major isomer, whose regiochemistry was confirmed by 2D-NMR (HMQC and HMBC) analysis. Finally, the reaction of imine **1a** and phenyltrimethylsilylacetylene resulted in exclusive C−C bond formation at the acetylenic carbon atom proximal to the phenyl group, affording the product **6aq** in 41% yield. In addition, deprotection of the silyl group of **6aq** was achieved using tetrabutylammonium fluoride to afford the 1,1-diarylethene **6ar** in a moderate yield.

Deuterium Labeling Experiments and Kinetic Isotope Effects. To probe the reaction mechanism, we initially performed a series of experiments using deuterium-labeled imine **1a**-d_5 (Scheme 5). First, the reaction of an equimolar mixture of **1a**-d_5 and the nondeuterated imine **1b** with diphenylacetylene afforded **6ah**-d_5 and **6bh** in 26% and 56% yields, respectively,

Scheme 5. Deuterium-Labeling Experiments[a]



[a] Standard conditions: $CoBr_2$ (0.02 M), P(3-ClC_6H_4)$_3$ (0.04 M), *t*$BuCH_2MgBr$ (0.2 M), pyridine (0.32 M), THF, 20 °C.

without any noticeable H/D crossover (Scheme 5a). This result clearly demonstrates that the aryl group and the olefinic hydrogen atom in the product molecule come from the same reactant molecule, which excludes a deprotonation mechanism for the *ortho* C−H bond cleavage and conforms to a mechanism involving oxidative addition of the C−H bond. Second, a competitive reaction of an equimolar mixture of **1a** and **1a**-d_5 with diphenylacetylene was quenched at the early stage to yield the hydroarylation products **6ah**/**6ah**-d_5 in 22% total yield with the ratio of 81:19 (Scheme 5b). The kinetic isotope effect (KIE) value of 4.3 determined for the competitive reaction suggests that either aromatic C−H bond cleavage or vinylic C−H bond formation is the first irreversible step of the reaction.[32,33] Third, we measured initial rates of individual reactions of **1a** and **1a**-d_5 with diphenylacetylene under the standard reaction conditions (Scheme 5c, see the Supporting Information for details). The average initial rates of product formation were 1.7 ($\pm$0.1) $\times$ 10^{-4} and 3.3 ($\pm$0.2) $\times$ 10^{-5} M s^{-1} for **1a** and **1a**-d_5, respectively. Thus, a large KIE value of 5.2 $\pm$ 0.4, the magnitude of which was close to the one observed for the competitive reaction (4.3, Scheme 5b), was determined. This suggests that, under the

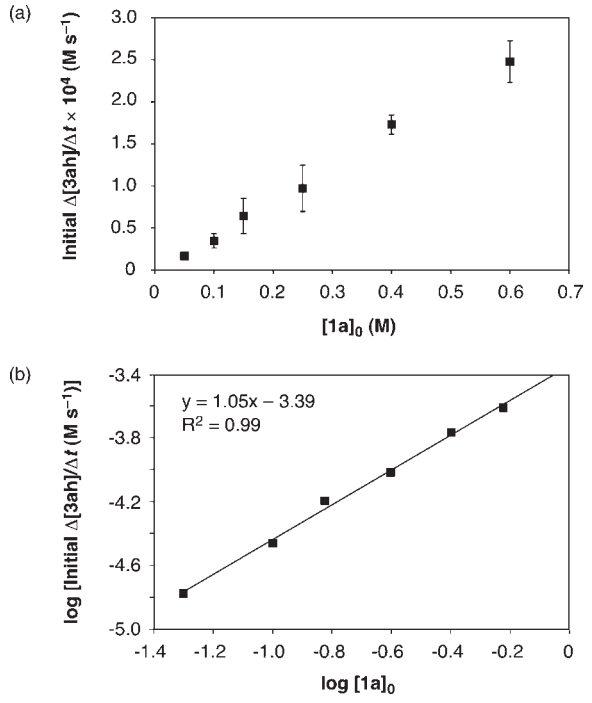


Figure 1. Initial reaction rate against the imine concentration $[\mathbf{1a}]_0$. Reaction conditions: **1a** (0.05−0.6 M), **2h** (0.6 M), $CoBr_2$ (0.02 M), $P(3\text{-}ClC_6H_4)_3$ (0.04 M), tBuCH$_2$MgBr (0.2 M), pyridine (0.32 M), THF, 20 °C, 10−15 min.

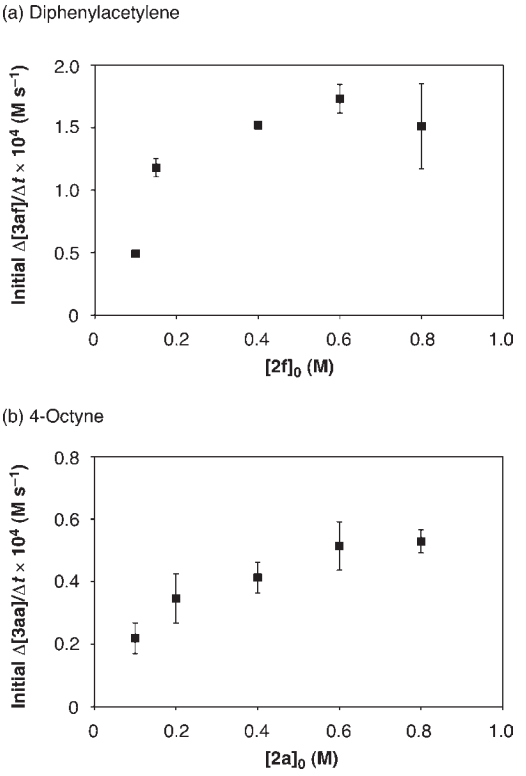


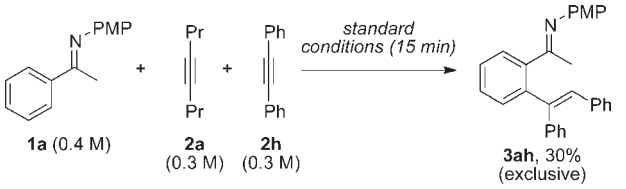
Figure 2. Initial reaction rate against alkyne concentration ((a) diphenylacetylene, $[\mathbf{2h}]_0$; (b) 4-octyne, $[\mathbf{2a}]_0$). Reaction conditions: **1a** (0.4 M), **2h** or **2a** (0.1−0.8 M), $CoBr_2$ (0.02 M), $P(3\text{-}ClC_6H_4)_3$ (0.04 M), tBuCH$_2$MgBr (0.2 M), pyridine (0.32 M), THF, 20 °C, 10−15 min.

standard conditions, the rate-limiting step involves either C−H bond cleavage or C−H bond formation.

Rate Dependence on Imine and Alkyne. We then studied the dependence of the initial reaction rate on each of the reactants (i.e., imine **1a** and alkyne **2h**).[16] First, we measured the initial rate ($\Delta[\mathbf{3ah}]/\Delta t$) against the initial concentration of the imine **1a** ($[\mathbf{1a}]_0$) ranging from 0.05 to 0.6 M and observed a clear positive correlation between $[\mathbf{1a}]_0$ and $\Delta[\mathbf{3ah}]/\Delta t$ (Figure 1a). No obvious saturation kinetics was observed at high concentrations up to 0.6 M. Logarithm plot and linear fitting of these data gave a slope of 1.05, indicating a first-order dependence of the initial rate on the imine concentration (Figure 1b). This, together with the results of the KIE experiments (Scheme 5b,c), suggests that C−H bond cleavage is the rate-limiting step of the reaction at least in the early stage of the reaction under the standard conditions, where a sufficient amount of diphenylacetylene is present (0.6 M).

In contrast to the above first-order relationship, when a similar analysis was performed for diphenylacetylene **2h** (0.1−0.8 M), the initial rate exhibited a saturation behavior at high concentrations (Figure 2a). Thus, the reaction rate showed a positive response to $[\mathbf{2h}]_0$ at low concentrations (0.1−0.15 M) but reached a plateau at the concentration of 0.4 M. Similarly, the initial rate of the reaction of **1a** (0.4 M) and 4-octyne **2a** (0.1−0.8 M) saturated when the concentration of **2a** became as high as 0.6 M (Figure 2b). Furthermore, the initial reaction rates of diphenylacetylene and 4-octyne in the saturation range were significantly different, the former (ca. 1.5×10^{-4} M s^{-1}) being approximately 3 times faster than the latter (ca. 5×10^{-5} M s^{-1}). Notably, the difference of the two alkynes was even more pronounced in a competitive reaction, where **1a** reacted exclusively with diphenylacetylene (Scheme 6).

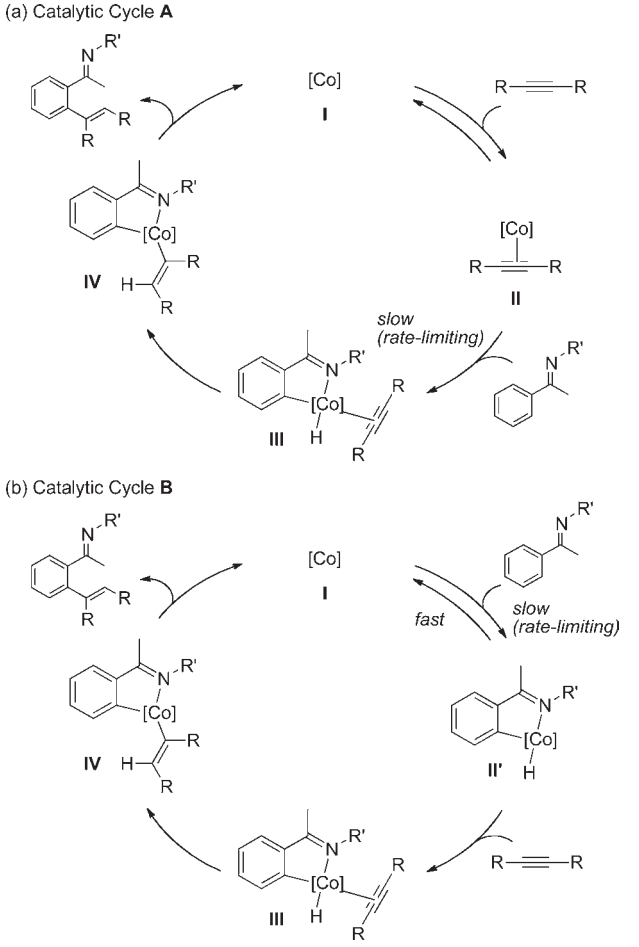
Scheme 6. Alkyne Competition Experiment[a]



[a] Standard conditions: $CoBr_2$ (0.02 M), $P(3\text{-}ClC_6H_4)_3$ (0.04 M), tBuCH$_2$MgBr (0.2 M), pyridine (0.32 M), THF, 20 °C.

Combining the above pieces of information, we suggest two possible catalytic cycles **A** and **B** as illustrated in Scheme 7. The catalytic cycle **A** (Scheme 7a) involves a low-valent cobalt species **I** generated by the reduction of the cobalt(II) precatalyst with the Grignard reagent (vide infra) and its complexation with the alkyne (**II**) prior to the rate-limiting step, that is, chelation-assisted oxidative addition of the *ortho* C−H bond (**II** to **III**).[6,7] The C−H bond cleavage is followed by *syn*-insertion of the coordinated alkyne into the Co−H bond (**III** to **IV**)[5,34−36] and reductive elimination to afford the product and regenerate the cobalt species **I**. The alternative catalytic cycle **B** (Scheme 7b) is initiated by reversible C−H bond activation of the imine with the species **I**, where the forward reaction is slower than the reverse reaction, affording a cobaltacycle **II′** as a transient intermediate. The reaction proceeds in a forward direction via interception of the intermediate **II′** by the alkyne (**II′** to **III**) followed by the alkyne insertion and reductive elimination steps.

Scheme 7. Proposed Catalytic Cycles



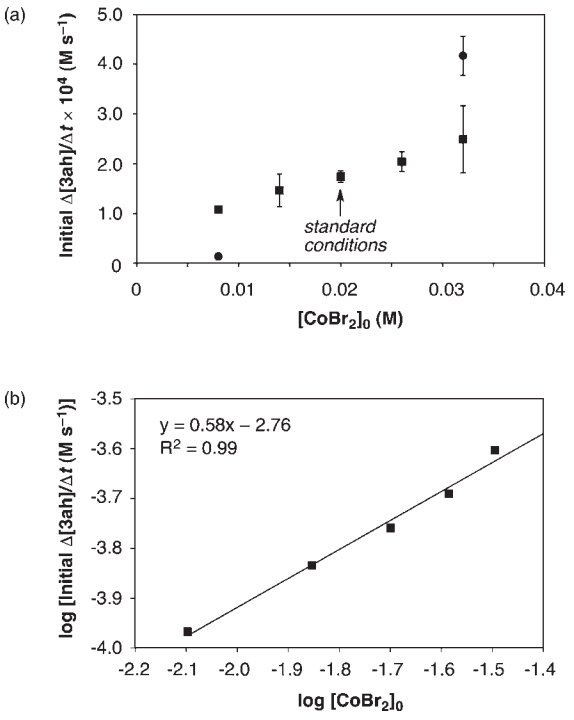


Figure 3. Initial reaction rate against the catalyst concentration. Reaction conditions: **1a** (0.4 M), **2f** (0.6 M), $CoBr_2$ (0.008−0.032 M), THF, 20 °C, 10−15 min. $CoBr_2$:P(3-ClC_6H_4)$_3$:*t*$BuCH_2MgBr$:pyridine = 1:2:10:16 (■); $CoBr_2$:P(3-ClC_6H_4)$_3$:*t*$BuCH_2MgBr$ = 1:2:10, pyridine (0.32 M) (●).

Both of the proposed catalytic cycles account for the important kinetic features, (1) rate-limiting C−H activation of the imine in the presence of a sufficient amount of the alkyne and (2) saturation of the reaction rate with increase in the alkyne concentration. At present, we cannot distinguish these two possibilities because we have not been able to identify the nature of the reactive species and the resting state of the catalytic reaction (vide infra). We would rather prefer the catalytic cycle **A** because of the large difference in the reaction rates of diphenylacetylene and 4-octyne (cf., Figure 2). Thus, we speculate that the alkyne is intimately involved in the C−H activation step to explicitly influence its activation barrier.[37]

The regioselectivities of the C−H bond cleavage and the C−C bond formation observed in the study of the substrate scope (Charts 1 and 3) warrant discussion in relation to the above mechanistic proposal. The selective C−H bond cleavage at the more hindered *ortho* positions of the *meta*-methoxy, halogen, and cyano-substituted imines (see **3ha**−**3ka** in Chart 1 and **6hf**−**6kf** and **6qf** in Chart 3) may be ascribed to the ability of electron-withdrawing substituents (typically F) to strengthen a metal−carbon bond at the *ortho* position,[26] or to the coordination of lone-pair electrons or π-electrons to the metal center in the C−H oxidative addition process.[24a,25] The selective C−C bond formation at the less hindered acetylenic carbon (see **3ac**−**3af** in Chart 1 and **6aq** in Chart 3) may be rationalized in terms of the preference of the cobalt center to avoid steric repulsion during the alkyne insertion step.[36a] Note that the same sense of regioselectivity has been reported for related hydroarylation and hydroalkenylation reactions of internal alkynes by our group[8,10a] and others,[9,12−14,38] while the difference of the regioselectivities for 1-phenyl-1-propyne and 1-phenyl-1-butyne (see **3ac** and **3ag** in Chart 1) indicates the sensitivity of the cobalt catalyst to subtle steric change. Not only steric but also electronic factors appear to play important roles in the insertion step. Thus, polarization of the putative cobalt hydride intermediate (i.e., Co(δ+)−H(δ−)) may account for the regioselectivity observed in the reaction of 1-fluoro-4-[(4-methoxyphenyl)ethynyl]benzene (see **6an** in Chart 3), where the C−H bond formation took place preferentially on the acetylenic carbon that is proximal to the methoxyphenyl group and is likely to be more electron-poor due to inductive and resonance effects.[39]

Rate Dependence on Catalyst and Catalyst Components. To shed light on the complexity of the quaternary catalytic system, we extended the kinetic analysis to investigate the initial rate dependence on the catalyst loading as well as on each of the catalyst components. First, we measured the initial rate for the reaction of **1a** (0.4 M) and **2h** (0.6 M) against the catalyst concentration ranging from 0.008 to 0.032 M (2−8 mol %, Figure 3). When the analysis was performed with the constant ratio of the catalyst components ($CoBr_2$:P(3-ClC_6H_4)$_3$:*t*$BuCH_2MgBr$:pyridine = 1:2:10:16) as employed for the standard conditions (5 mol % $CoBr_2$, 10 mol % P(3-ClC_6H_4)$_3$, 50 mol % *t*$BuCH_2MgBr$, 80 mol % pyridine), we observed a steady increase of the initial rate with the increase of the catalyst loading (■ in Figure 3a), while logarithm plot and linear fitting of the data indicated a deviation from the first-order dependence (slope = 0.58, Figure 3b). In contrast, a more drastic influence of the

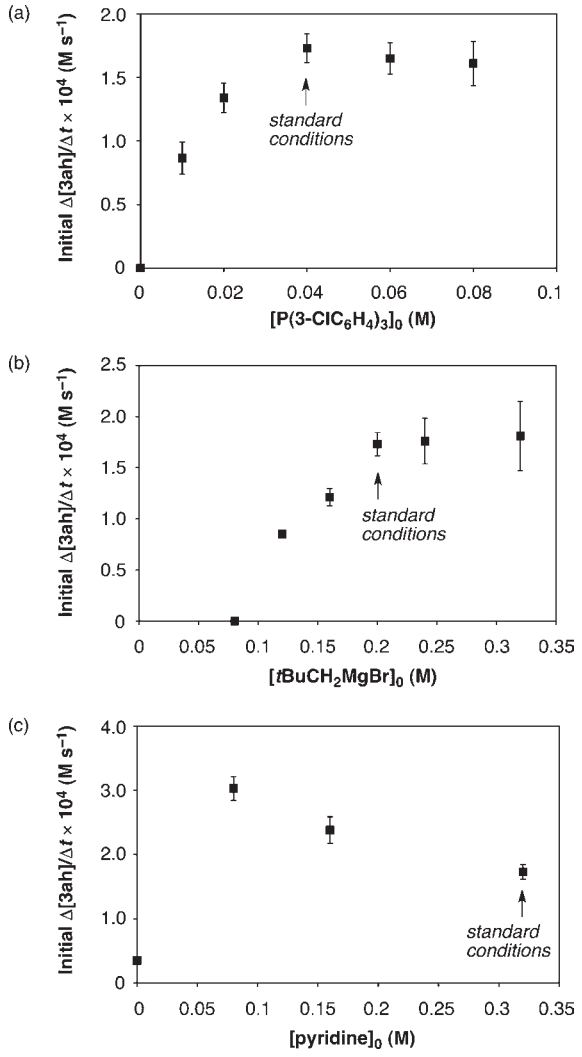
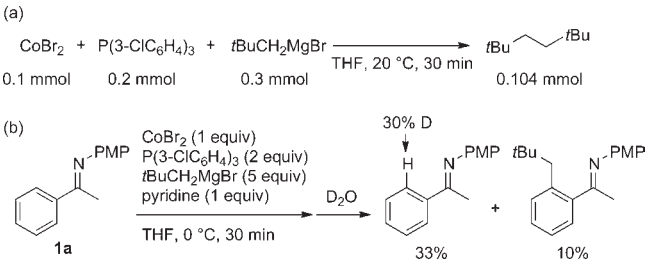


Figure 4. Initial reaction rates against catalyst components ((a) P(3-$ClC_6H_4)_3$, (b) *t*$BuCH_2MgBr$, (c) pyridine). Reaction conditions: **1a** (0.4 M), **2h** (0.6 M), $CoBr_2$ (0.02 M), P(3-$ClC_6H_4)_3$ (0−0.08 M for (a); 0.04 M for (b) and (c)), *t*$BuCH_2MgBr$ (0.08−0.32 M for (b); 0.2 M for (a) and (c)), pyridine (0−0.32 M for (c); 0.32 M for (a) and (b)), THF, 20 °C, 10−15 min.

catalyst loading resulted from the analysis under similar conditions except that a fixed amount of pyridine (80 mol %, 0.32 M) was used (● in Figure 3a). Thus, as compared to the reaction under the standard conditions (5 mol %), the reaction became exceedingly faster (more than twice) with 8 mol % catalyst loading while it almost stopped with 2 mol % loading. These data suggest that an excessive amount of pyridine is detrimental to the reaction (vide infra).

Given the anomalous kinetic behavior observed in the above experiments, we became interested in the influence of each catalyst component on the catalytic activity. Thus, the initial rate was measured for the reaction of **1a** (0.4 M) and **2h** (0.6 M) under the standard conditions (5 mol % $CoBr_2$, 10 mol % P(3-$ClC_6H_4)_3$, 50 mol % *t*$BuCH_2MgBr$, 80 mol % pyridine) except for a change in the amount of either P(3-$ClC_6H_4)_3$ (0−20 mol %), *t*$BuCH_2MgBr$ (20−80 mol %), or pyridine (0−80 mol %) (Figure 4a−c). The phosphine ligand P(3-$ClC_6H_4)_3$ is evidently essential for the reaction, because no reaction took place in its

Scheme 8. Stoichiometric Experiments



absence (Figure 4a). The reaction rate increased with the increase of the phosphine loading from 2.5 to 10 mol % (0.01−0.04 M, 0.5−2 equiv to $CoBr_2$) and reached the maximum with the loading of 10 mol %. Further increase of the phosphine loading to 15−20 mol % (0.06−0.08 M, 3−4 equiv to $CoBr_2$) caused only a slight inhibitory effect on the reaction. For the Grignard reagent, we determined a "threshold" loading of 20 mol % (0.08 M), with which no reaction took place (Figure 4b). Above this threshold, the reaction rate steadily increased with the Grignard loading of 30−50 mol % (0.12−0.20 M), and saturated with 50 mol % and above. Note that the threshold loading (20 mol %) is higher than required to reduce 5 mol % of $CoBr_2$ to Co(0), that is, 10 mol %. Pyridine is not an indispensable catalyst component, because the reaction took place even in its absence (Figure 4c). However, the addition of pyridine (0.08−0.32 M, 20−80 mol %) clearly resulted in rate enhancement. The reaction rate was at its highest (3.0×10^{-4} M s^{-1}) with 20 mol % (0.08 M) of pyridine (ca. 9 times faster than in its absence, 3.5×10^{-5} M s^{-1}). Higher loading of pyridine (40−80 mol %, 0.16−0.32 M) slowed the reaction, which was, however, still much faster than the pyridine-free reaction. The inhibitory effect caused by a large amount of pyridine is consistent with the kinetic behavior observed in Figure 3a, while we did not notice it during the reaction optimization.

While the above kinetic analysis revealed how each of the catalyst components impacts the catalytic activity, the exact nature of the active cobalt species **I** and other proposed intermediates (Scheme 7) remains elusive. Attempts to gain information from stoichiometric experiments have thus far been met with only limited success (Scheme 8): First, a reaction of $CoBr_2$ (0.1 mmol), P(3-$ClC_6H_4)_3$ (0.2 mmol), and *t*$BuCH_2MgBr$ (0.3 mmol) at 20 °C quantitatively afforded 2,2,5,5-tetramethylhexane (0.104 mmol) as a result of oxidative homocoupling of the Grignard reagent (Scheme 8a), indicating that the cobalt(II) salt was reduced to cobalt(0). Second, a stoichiometric reaction of **1a**, $CoBr_2$ (1 equiv), P(3-$ClC_6H_4)_3$ (2 equiv), *t*$BuCH_2MgBr$ (5 equiv), and pyridine (1 equiv) at 0 °C for 30 min followed by quenching with D_2O afforded a mixture of **1a** with partial *ortho*-deuteration, an *ortho*-neopentylated imine,[11c] and other unidentified products.[40] This may suggest the presence of an intermediate bearing a C(ortho)−Co bond, because a control experiment in the absence of the cobalt salt expectedly resulted in no *ortho*-deuteration.

At this stage, we put forth some speculations on the nature of the catalytically active species and the role of each of the catalyst components: (1) The active species should bear one or two molecules of the phosphine ligand because no reaction took place without the ligand and because the reaction rate reached the maximum with 10 mol % (2 equiv to Co) of the phosphine loading (Figure 4a). (2) The Grignard reagent may not only reduce

cobalt(II) to cobalt(0) but also give rise to an organocobalt(0)ate species as the catalytically active species, because the alkyl group of the Grignard reagent significantly influences the catalytic activity (Table 2) and because an excess amount of the Grignard reagent is necessary to achieve catalytic turnover (Figure 4b). Note that organocobalt(0)ate species have been proposed as reactive species for several cobalt-catalyzed reactions that take place in the presence of excess Grignard reagents.[41] (3) Pyridine appears to serve as a coligand for the cobalt catalyst, while the origin of its rate enhancement remains unclear. The rate inhibition with higher loading of pyridine (Figures 3a and 4c) may be ascribed to competitive binding of pyridine and the imine substrate to the catalyst.

CONCLUSION

We have reported in this Article that a quaternary catalytic system consisting of $CoBr_2$, $P(3\text{-}ClC_6H_4)_3$, tBuCH$_2$MgBr, and pyridine promotes hydroarylation of an internal alkyne with an aromatic imine through chelation-assisted C−H bond cleavage. The reaction takes place smoothly at room temperature to afford the alkenylated imine in moderate to good yield with good regio- and stereoselectivities. The hydroarylation products were, depending on the substituents of the alkynes, transformed to the corresponding benzofulvene or ketone derivatives under acidic conditions. Deuterium-labeling experiments and kinetic analysis suggested plausible mechanistic scenarios that involve oxidative addition of the *ortho* C−H bond of the imine as the rate-limiting step, while the role of the alkyne in the catalytic cycle remains debatable and warrants further investigation. The kinetic analysis also shed some light on the high level of complexity of the quaternary catalytic system. The secondary directing effect of ether, halogen, and cyano groups on the C−H bond cleavage step is also an intriguing subject of further mechanistic studies and may offer unique synthetic approaches to polysubstituted aromatic compounds. On the basis of the present study as well as recent studies of our group and others,[8,10,11] we envision that a wider variety of productive catalytic systems involving cobalt-mediated C−H bond activation could be developed.

ASSOCIATED CONTENT

Supporting Information. Experimental procedures and characterization of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author
nyoshikai@ntu.edu.sg

Present Addresses
[†]Department of Chemistry, Graduate School of Pure and Applied Sciences, University of Tsukuba, Tsukuba, Ibaraki 305-8571, Japan.

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(22) The *E*-stereochemistry of the olefin moiety of the major isomer was confirmed by NOESY experiments. Upon reduction with $NaBH_4$, the major and minor isomers converged into a single product, which confirmed that the formation of the minor isomer was due to *E*/*Z* isomerization of the imine moiety rather than that of the olefin moiety (see the Supporting Information).

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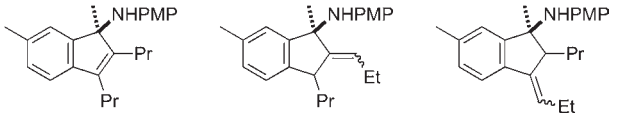
(24) (a) Sonoda, M.; Kakiuchi, F.; Chatani, N.; Murai, S. *Bull. Chem. Soc. Jpn.* **1997**, *70*, 3117–3128. (b) Martinez, R.; Genet, J.-P.; Darses, S. *Chem. Commun.* **2008**, 3855–3857. (c) Martinez, R.; Simon, M.-O.; Chevalier, R.; Pautigny, C.; Genet, J.-P.; Darses, S. *J. Am. Chem. Soc.* **2009**, *131*, 7887–7895. (d) Ackermann, L.; Vicente, R.; Potukuchi, H. K.; Pirovano, V. *Org. Lett.* **2010**, *12*, 5032–5035. (e) Ackermann, L.; Hofmann, N.; Vicente, R. *Org. Lett.* **2011**, *13*, 1875–1877.

(25) A cyano group was reported to serve by itself as a directing group for C−H bond functionalization: Kakiuchi, F.; Sonoda, M.; Tsujimoto, T.; Chatani, N.; Murai, S. *Chem. Lett.* **1999**, 1083–1084.

(26) (a) Clot, E.; Mégret, C.; Eisenstein, O.; Perutz, R. N. *J. Am. Chem. Soc.* **2009**, *131*, 7817–7827. (b) Clot, E.; Eisenstein, O.; Jasim, N.; Macgregor, S. A.; McGrady, J. E.; Perutz, R. N. *Acc. Chem. Res.* **2011**, *44*, 333−348 and references cited therein.

(27) The stereochemistry of the C═C double bond of **4fa** and related benzofulvene derivatives could not be unambiguously determined by NOESY experiments.

(28) The reaction also afforded a mixture of intractable amino compounds. A mixture of aminoindenene derivatives shown below was suggested by GC−MS and ^{1}H NMR analysis.



(29) For an example of biological activities of aminoindanol derivatives, see: Wu, D.; Pontillo, J.; Ching, B.; Hudson, S.; Gao, Y.; Fleck, B. A.; Gogas, K.; Wade, W. S. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 4224–4227.

(30) Upon concentration and standing at ambient temperature, the benzofulvene derivatives underwent polymerization relatively easily (cf., ref 21).

(31) Diheteroaryl alkynes such as bis(2-thienyl)acetylene failed to participate in the reaction.

(32) The observation of the primary H/D KIE for the competitive reaction is consistent with our previous study on the reaction of 2-phenylpyridine (ref 8, KIE = 2.1), but is in stark contrast to the observation of Shi and co-workers on the cobalt-catalyzed direct arylation of benzo[*h*]quinoline (KIE = 1.04, ref 11c).

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(36) (a) Foo, T.; Bergman, R. G. *Organometallics* **1992**, *11*, 1811–1819. (b) Bassetti, M.; Casellato, P.; Gamasa, M. P.; Gimeno, J.; González-Bernardo, C.; Martín-Vaca, B. *Organometallics* **1997**, *16*, 5470–5477. (c) Bassetti, M.; Marini, S.; Díaz, J.; Gamasa, M. P.; Gimeno, J.; Rodríguez-Álvarez, Y.; García-Granda, S. *Organometallics* **2002**, *21*, 4815–4822.

(37) We also feel it reasonable to assume that the alkyne serves as a good π-accepting ligand for the low-valent cobalt species **I** and are tempted to interpret the result of the alkyne competition experiment (Scheme 6) in terms of better π-accepting ability of diphenylacetylene than of 4-octyne.

(38) (a) Colby, D. A.; Bergman, R. G.; Ellman, J. A. *J. Am. Chem. Soc.* **2008**, *130*, 3645–3651. (b) Parthasarathy, K.; Jeganmohan, M.; Cheng, C.-H. *Org. Lett.* **2008**, *10*, 325–328.

(39) NPA charges of the acetylenic carbon atoms of 1-fluoro-4-[(4-methoxyphenyl)ethynyl]benzene were calculated to be +0.012 (proximal to 4-methoxyphenyl) and −0.008 (proximal to 4-fluorophenyl) at the B3LYP/6-31G* level.

(40) A prolonged reaction time (3 h) resulted in deprotonation of the α-position of the imine, as indicated from deuterium incorporation into the α-position.

(41) (a) Ohmiya, H.; Wakabayashi, K.; Yorimitsu, H.; Oshima, K. *Tetrahedron* **2006**, *62*, 2207–2213. (b) Wakabayashi, K.; Yorimitsu, H.; Oshima, K. *J. Am. Chem. Soc.* **2001**, *123*, 5374–5375. (c) Czaplik, W. M.; Mayer, M.; Jacobi von Wangelin, A. *Synlett* **2009**, 2931–2934. (d) Kauffmann, T. *Angew. Chem., Int. Ed.* **1996**, *35*, 386–403.