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Cobalt-Catalyzed Regioselective Carbocyclization Reaction of *o*-Iodophenyl Ketones and Aldehydes with Alkynes, Acrylates, and Acrylonitrile: A Facile Route to Indenols and Indenes

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Received March 25, 2004

An efficient cobalt-catalyzed carbocylization for the synthesis of indenols and indenes and a new method for reductive decyanation are described. 2-Iodophenyl ketones and aldehydes **1a**−**g** undergo carbocyclization with various disubstituted alkynes **2a**−**k** in the presence of Co(dppe)I_2 and zinc powder in acetonitrile at 80 °C for 3 h to afford the corresponding indenol derivatives **3a**−**s** and **4a**−**m** in good to excellent yields. For some unsymmetrical alkynes, the carbocyclization was remarkably regioselective, affording a single regioisomer. The cobalt-catalyzed carbocyclization reaction was successfully extended to the synthesis of indene derivatives. Thus, the reaction of 2-iodophenyl ketones and aldehydes (**1**) with acrylates $H_2C{=}CHCO_2R$ (**7a**−**d**) and acrylonitrile $H_2C{=}CHCN$ (**7e**) proceeds smoothly in the presence of Co(dppe)Cl_2/dppe and zinc powder in acetonitrile at 80 °C for 24 h to afford the corresponding indenes **8a**−**k** and **9a**−**c** in moderate to good yields. Interestingly, when **7e** was employed for the carbocylization, reductive decyanation also occurred to give an indene derivative without the cyano functionality. A possible mechanism for this cobalt-catalyzed carbocyclization reaction is also proposed.

Introduction

Cobalt complexes are well-established catalysts for [2 + 2 + 2][1,2] cyclotrimerization, [2 + 2][3] cycloaddition reaction, Pauson−Khand reaction,[4] hydroformylation,[5] and en-yne reductive coupling.[6] However, the use of cobalt complexes as catalysts for the activation of aryl and alkyl halides has drawn attention only very recently.[7] Cahiez and Knochel reported cobalt-catalyzed coupling reactions of alkenyl halides with organozinc[7a] and organomagnesium[7b] reagents. Oshima et al. described a cobalt-catalyzed Heck-type reaction of alkyl halides with styrenes via a single electron-transfer mechanism.[7c] Gosmini et al. reported the synthesis of arylzinc compounds from aryl bromides catalyzed by $CoBr_2$ (10−20 mol %) in the presence of $ZnBr_2$ and zinc dust.[7d]

Indenol[8−12] and indene moieties are important and central structural units present in various biologically active compounds. Some indenol derivatives have shown analgesic and myorelaxation activity,[13] and others are used as valuable intermediates for the synthesis of indenyl chrysanthemates that possess insecticidal properties.[14] Palladium complexes were shown to catalyze the carbocyclization of disubstituted alkynes with *o*-bromophenyl ketones to give indenols.[11] We also reported that nickel complexes exhibit similar catalytic properties for the carbocyclization of alkynes with *o*-iodophenyl ketones.[12] Our interest in cobalt-catalyzed reactions[2,3,6] and the recent attention of activation of aryl halides by

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[1] (a) Vollhardt, K. P. C. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 539. (b) Grotjahn, D. B.; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1986**, *108*, 2091. (c) Butenschon, H.; Winkler, M.; Vollhardt, K. P. C. *Chem. Commun.* **1986**, 388. (d) Johnson, E. P.; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1991**, *113*, 381.

[2] Wu, M. S.; Shanmugasundaram, M.; Cheng, C. H. *Chem. Commun.* **2003**, 718.

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

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

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

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

[7] (a) Cahiez, G.; Avedissian, H. *Tetrahedron Lett.* **1998**, *39*, 6159. (b) Avedissian, H. Berillon, L.; Cahiez, G.; Knochel, P. *Tetrahedron Lett.* **1998**, *39*, 6163. (c) Ikeda, Y.; Nakamura, T.; Yorimtsu, H.; Oshima, K. *J. Am. Chem. Soc.* **2002**, *124*, 6514. (d) Fillon, H.; Gosmini, C.; Perichon, J. *J. Am. Chem. Soc.* **2003**, *125*, 3867. (e) Gomes, P.; Gosmini, C.; Perichon, J. *Org. Lett.* **2003**, *5*, 1043.

[8] For other methods of indenol synthesis, see: (a) Liebeskind, L. S.; Gasdaska, J. R.; MaCallum, J. S.; Tremont, S. J. *J. Org. Chem.* **1989**, *54*, 669. (b) Cambie, R. C.; Metzler, M. R.; Rutledge, P. S.; Woodgate, P. D. *J. Organomet. Chem.* **1990**, *381*, C26. (c) Cambie, R. C.; Metzler, M. R.; Rutledge, P. S.; Woodgate, P. D. *J. Organomet. Chem.* **1990**, *398*, C22. (d) Robinson, N. P.; Main, L.; Nicholson, B. K. *J. Organomet. Chem.* **1989**, *364*, C37.

[9] (a) Vicente, J.; Abad J.-A.; Gil-Rubio, J. *J. Organomet. Chem.* **1992**, *436*, C9. (b) Vicente, J.; Abad J. A.; Rubio, J. G. *Organometallics* **1996**, *15*, 3509. (c) Vicente, J.; Abad, J. A.; Lopez-Pelaez, B.; Martinez-Pivente, E. *Organometallics* **2002**, *21*, 58.

[10] Larock, R. C.; Doty, M. J.; Cachi, S. C. *J. Org. Chem.* **1993**, *58*, 4579.

[11] (a) Quan, L. G.; Gevorgyan, V.; Yamamoto, Y. *J. Am. Chem. Soc.* **1999**, *121*, 3545. (b) Quan, L. G.; Gevorgyan, V.; Yamamoto, Y. *J. Am. Chem. Soc.* **1999**, *121*, 9485. (c) Quan, L. G.; Gevorgyan, V.; Yamamoto, Y. *Tetrahedron Lett.* **1999**, *40*, 4089.

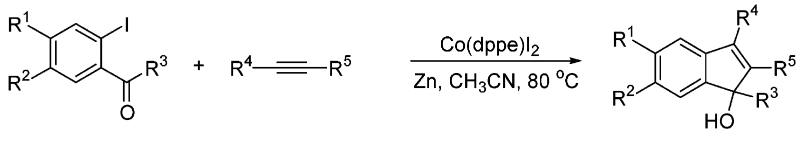
[12] (a) Rayabarapu, D. K.; Cheng, C.-H. *Chem. Commun.* **2002**, 942. (b) Rayabarapu, D. K.; Yang, C.-H.; Cheng, C.-H. *J. Org. Chem.* **2003**, *68*, 6726.

[13] (a) Kurakay Co. Ltd. Jpn. Kokai Tokkyo Koho JP 81,113,740 (C1.C07C69/017), 7 Sept 1981; *Chem. Abstr.* **1982**, *96*, 68724b. (b) Kurakay Co., Ltd. Jpn. Kokai Tokkyo Koho JP 8,204,945 (C1. C07C69/013), 11 Jan 1982; *Chem. Abstr.* **1982**, *96*, 199935u.

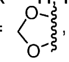
[14] Samula, K.; Cichy, B. *Acta Pol. Pharm.* **1985**, *42*, 256; *Chem. Abstr.* **1986**, *105*, 171931v

10.1021/jo049506g CCC: $27.50

SCHEME 1



1a-g **2a-k** **3a-s, 4a-m**

1a: $R^1 = H, R^2 = H, R^3 = CH_3$
1b: $R^1 = OCH_3, R^2 = H, R^3 = CH_3$
1c: $R^1 = OCH_3, R^2 = H, R^3 = (CH_2)_3CH_3$
1d: $R^1 = OCH_3, R^2 = H, R^3 = Ph$
1e: $R^1 = H, R^2 = H, R^3 = H$
1f: $R^1 = R^2 =$ , $R^3 = H$
1g: $R^1 = C(CH_3)_3, R^2 = H, R^3 = H$

2a: $R^4 = Ph, R^5 = Ph$
2b: $R^4 = CH_2CH_3, R^5 = CH_2CH_3$
2c: $R^4 = CH_2CH_2CH_3, R^5 = CH_2CH_2CH_3$
2d: $R^4 = TMS, R^5 = CH_3$
2e: $R^4 = TMS, R^5 = Ph$
2f: $R^4 = Ph, R^5 = CH_2CH_2CH_2CH_3$
2g: $R^4 = Ph, R^5 = CH_3$
2h: $R^4 = TMS, R^5 = CO_2CH_2CH_3$
2i: $R^4 = (CH_2)_5CH_3, R^5 = CO_2CH_3$
2j: $R^4 = Ph, R^5 = CO_2CH_2CH_3$
2k: $R^4 = Ph, R^5 = p\text{-}C_6H_4CH_3$

complexes of the cobalt family[7] have prompted us to investigate the catalytic activity of cobalt complexes for the carbocyclization[15,16] of *o*-iodobenzaldehydes and *o*-iodophenyl ketones with alkynes. In a preliminary communication, we have shown for the first time that cobalt phosphine complexes successfully catalyze carbocyclization of *o*-iodobenzaldehydes and *o*-iodophenyl ketones with alkynes under mild conditions to afford indenol derivatives in good yields with excellent regioselectivity.[17] Herein, we wish to report the full details of these studies and the extension of the catalytic reaction to the carbocyclization of *o*-iodobenzaldehydes and *o*-iodophenyl ketones with acrylates and acrylonitrile to furnish indene derivatives. The latter provides the construction of an indene core in good yields from easily accessible starting materials under relatively mild reaction conditions. In addition, we observed an interesting reductive decyanation during the carbocyclization with acrylonitrile.

Results and Discussion

Synthesis of Indenols. The reaction of 2-iodoacetophenone (**1a**) with diphenylacetylene (**2a**) in the presence of Co(dppe)I_2 (dppe = bis(diphenylphosphino)ethane) and zinc metal powder in acetonitrile at 80 °C for 3 h proceeded to give indenol **3a** in 93% yield (Scheme 1). The structure of **3a** was established on the basis of its ^{1}H and ^{13}C NMR and mass data. Control experiments indicated that in the absence of either Co(dppe)I_2 or zinc metal, no desired product was observed in the reaction.

This cobalt-catalyzed carbocyclization is successfully extended to other alkynes, and the results are demonstrated in Table 1. Thus, **1a** reacts with alkynes **2b**−**e** (**2b**, $CH_3CH_2C{\equiv}CCH_2CH_3$; **2c**, $CH_3(CH_2)_2C{\equiv}C(CH_2)_2CH_3$; **2d**, $TMSC{\equiv}CCH_3$; and **2e**, $PhC{\equiv}CTMS$) in the presence of Co(dppe)I_2 and Zn powder in acetonitrile at 80 °C to provide the corresponding indenols **3b**−**e** in 90%, 99%, 95%, and 89% yields, respectively (Scheme 1, Table 1, entries 2−5). The carbocyclization of **1a** with $TMSC{\equiv}CCH_3$ and $PhC{\equiv}CTMS$ was highly regioselective, and only a single regioisomer was detected in the reaction mixture (entries 4 and 5). The regiochemistry of these products as shown in Table 1 was carefully assigned on the basis of the NOE experiments (Figure 1). Both products **3d** and **3e** have the TMS group away from the hydroxy moiety. In the reaction involving $PhC{\equiv}C(CH_2)_3CH_3$ (**2f**) and $PhC{\equiv}CCH_3$ (**2g**), two regioisomers **3f**/**3f′** and **3g**/**3g′** were obtained in the ratio of 89/11 and 76/24 and in a combined yield 95% and 99%, respectively. The regiochemistry of these isomers was also carefully assigned on the basis of the NOE experiments, and in both cases the major isomer has the phenyl group next to the hydroxy moiety.

For **3g**, selective irradiation of methyl protons at δ 1.47 led to the enhancement of the signals at δ 7.41 aromatic protons by 5.51% and at δ 7.52 by 3.79%, respectively, whereas irradiation of the methyl protons at δ 2.09 attached to the double bond caused enhancement of the aromatic-proton signals at δ 7.31 by 7.5% and at δ 7.52 by 6.27%. No NOE was detected between the two methyl groups at δ 1.47 and δ 2.09. These NOE results strongly support the proposed structure **3g** shown in Figure 2.

Similarly, for **3g′** the selective irradiation of methyl protons at δ 1.57 led to enhancement of the aromatic-proton signal at δ 7.48 by 3.51% and methyl-proton signal at δ 1.99 by 4.92%, respectively, whereas irradiation of the methyl-proton signal attached to the double bond at δ 1.99 resulted in enhancement of the signals at δ 7.45 by 8.71% and at δ 1.57 by 7.12%. The strong NOE effect between the two methyl groups at δ 1.57 and δ 1.99 clearly support the proposed structure **3g′** shown in Figure 2.

The carbocyclization reaction was successfully extended to propiolates also. Thus, the reaction of **1a** with

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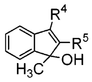
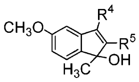
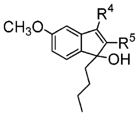
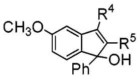
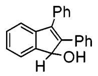
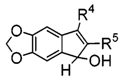
(15) (a) Tsuji, J. *Transition Metal Reagents and Catalysts: Innovations in Organic Synthesis*; Wiley: New York, 2002. (b) Hegedus, L. S. *Transition Metals in the Synthesis of Complex Organic Molecules*, 2 nd. ed.; University Science Books: Sausalito, CA, 1999.

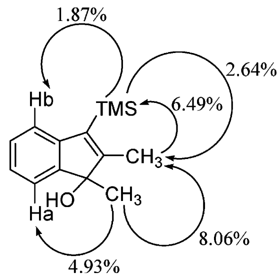
(16) (a) Grotjahn, D. B. In *Comprehensive Organometallic Chemistry II*; Hegedus, L. S., Ed.; Pergamon/Elsevier Science: Kidlington, 1995; Vol. 12, pp 703, 741. (b) Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.* **1996**, *96*, 49. (c) Ojima, I.; Tzamarioudaki, M.; Li, Z.; Donovan, R. J. *Chem. Rev.* **1996**, *96*, 635. (d) Fruhauf, H. W. *Chem. Rev.* **1997**, *97*, 523.

(17) Chang, K.-J.; Rayabarapu, D. K.; Cheng, C.-H. *Org. Lett.* **2003**, *5*, 3963.

TABLE 1. Results of Cobalt-Catalyzed Carbocyclization of 2-Iodophenyl Ketones and Aldehydes (1) with Alkynes (2)[a]

entry	ketone	alkyne	product			yield(%)[b]
					**3**	
			R^4	R^5		
1	**1a**	**2a**	Ph	Ph	**3a**	93
2	**1a**	**2b**	CH_2CH_3	CH_2CH_3	**3b**	90
3	**1a**	**2c**	$CH_2CH_2CH_3$	$CH_2CH_2CH_3$	**3c**	99
4	**1a**	**2d**	TMS	CH_3	**3d**	95
5	**1a**	**2e**	TMS	Ph	**3e**	89
6	**1a**	**2f**	$CH_2(CH_2)_2CH_3$	Ph	**3f**	95 (89:11)
			Ph	$CH_2(CH_2)_2CH_3$	**3f’**	
7	**1a**	**2g**	CH_3	Ph	**3g**	99 (76:24)
			Ph	CH_3	**3g’**	
8	**1a**	**2h**	TMS	CO_2Et	**3h**	95
9	**1a**	**2i**	$CH_2(CH_2)_2CH_3$	CO_2Me	**3i**	97
10	**1a**	**2j**	Ph	CO_2Et	**3j**	88 (75:25)
			CO_2Et	Ph	**3j’**	
						
11	**1b**	**2a**	Ph	Ph	**3k**	99
12	**1b**	**2e**	TMS	Ph	**3l**	83
13	**1b**	**2h**	TMS	CO_2Et	**3m**	70
						
14	**1c**	**2a**	Ph	Ph	**3n**	76
15	**1c**	**2e**	TMS	Ph	**3o**	93
16	**1c**	**2h**	TMS	CO_2Et	**3p**	96
						
17	**1d**	**2a**	Ph	Ph	**3q**	85
18	**1d**	**2e**	TMS	Ph	**3r**	90
19	**1d**	**2h**	TMS	CO_2Et	**3s**	85
						
20	**1e**	**2a**	Ph	Ph	**4a**	85
21	**1e**	**2c**	$CH_2CH_2CH_3$	$CH_2CH_2CH_3$	**4b**	54
22	**1e**	**2d**	TMS	CH_3	**4c**	60
23	**1e**	**2e**	TMS	Ph	**4d**	58
24	**1e**	**2f**	$CH_2(CH_2)_2CH_3$	Ph	**4e**	80 (88:12)
			Ph	$CH_2(CH_2)_2CH_3$	**4e’**	
25	**1e**	**2g**	CH_3	Ph	**4f**	45 (90:10)
			Ph	CH_3	**4f’**	
26	**1e**	**2k**	*p*-$C_6H_4OCH_3$	Ph	**4g**	86 (50:50)
			Ph	*p*-$C_6H_4OCH_3$	**4g’**	
						
27	**1f**	**2a**	Ph	Ph	**4h**	70
28	**1f**	**2e**	TMS	Ph	**4i**	58
29	**1f**	**2g**	CH_3	Ph	**4j**	53 (84:16)
			Ph	CH_3	**4j’**	
						
30	**1g**	**2a**	Ph	Ph	**4k**	82
31	**1g**	**2e**	TMS	Ph	**4l**	57
32	**1g**	**2g**	CH_3	Ph	**4m**	46 (87:13)
			Ph	CH_3	**4m’**	

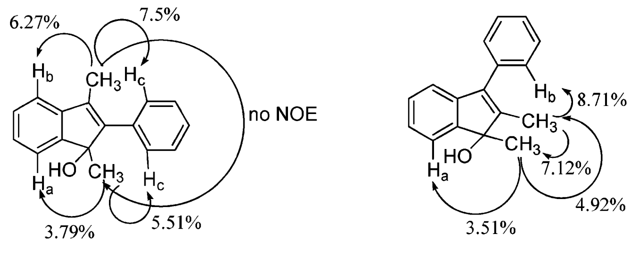
[a] Unless stated otherwise, all reactions were carried out using of *o*-iodophenyl ketone or *o*-iodophenyl aldehyde (1.00 mmol), alkyne (1.50 mmol), Co(dppe)I_2 (0.0500 mmol, 5.0 mol %), and Zn (2.75 mmol) in CH_3CN (3.0 mL) at 80 °C under N_2 for 3 h. [b] Isolated yields with the isomeric ratios of **3**/**3′** or **4**/**4′** are shown in the parentheses.



3d

FIGURE 1. NOE experimental data of compound **3d**.

2h (TMSC≡CCO_2Et) and **2i** ($CH_3(CH_2)_5C$≡CCO_2Et) afforded corresponding indenols in 95% and 97% yields, respectively, and the regioselectivity is excellent, with only single isomer being detected in the crude ^1H NMR.



3g **3g'**

FIGURE 2.

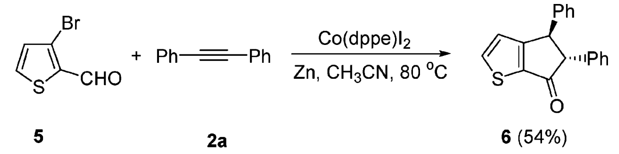
In the case of propiolate **2j** (PhC≡CCO_2Et), two regioisomers **3j**/**3j′** were detected in the ratio of 75/25 and in a combined yield of 88%. The major isomer **3j** has the phenyl group away from the hydroxy group. The regiochemistry of these products suggests that the catalytic cyclization reaction follows a Michael-type addition pattern and is governed by the electronic effect rather than the steric factor of substrate **2**.

Similarly to *o*-iodoacetophenone, various other substituted iodophenyl ketones were tested for this carbocyclization reaction. Treatment of **1b** bearing a methoxy group on the aromatic ring with **2a**, **2e**, and **2h** furnished corresponding indenols **3k**−**m** in 99%, 83%, and 70% yields, respectively. Only a single regioisomer was observed for **3l** and **3m**, and in both cases the TMS group is away from the hydroxy moiety as evidenced in the NOE experiments. The product distribution pattern shows that the regiochemistry is purely governed by electronic factor. 1-(2-Iodo-4-methoxy-phenyl)-pentan-1-one (**1c**) and (2-iodo-4-methoxy-phenyl)-phenyl-methanone (**1d**) reacted with **2a**, **2e**, and **2h** to produce indenols **3n**−**s** in 76−96% yields, and very high regioselectivity was observed for compounds **3o,p** and **3r,s**.

Interestingly, the present cobalt-catalyzed carbocyclization was successfully extended to *o*-iodobenzaldehydes, and the results are demonstrated in Table 1 (entries 20−32). Treatment of 2-iodobenzaldehyde (**1e**) with diphenylacetylene (**2a**) in the presence of Co(dppe)I_2 and zinc metal powder in acetonitrile at 80 °C for 3 h produced indenol **4a** in 85% yield. However, the reaction of 2-bromobenzaldehyde instead of 2-iodobenzaldehyde (**1e**) with diphenylacetylene for 3 h afforded **4a** in only 15% yield. Various alkynes were employed for this catalytic reaction, and thus **1e** reacts with alkynes **2c**−**g** and **2k** (**2c**, $CH_3(CH_2)_2C{\equiv}C(CH_2)_2CH_3$; **2d**, $TMSC{\equiv}CCH_3$ and **2e**, $PhC{\equiv}CTMS$; **2f**, $PhC{\equiv}C(CH_2)_2CH_3$; **2g**, $PhC{\equiv}CCH_3$; and **2k**, $PhC{\equiv}CC_6H_4OMe$) in the presence of Co(dppe)I_2 and Zn powder in acetonitrile at 80 °C to provide the corresponding indenols **4b**−**g** in 54%, 60%, 58%, 80%, 45%, and 86% yields, respectively (Scheme 1, Table 1, entries 21−26). For unsymmetrical alkynes, the regioselectivity is generally excellent except for **2f**,**g**,**k**. Only one regioisomer was detected for $TMSC{\equiv}CCH_3$ (**2d**) and $PhC{\equiv}CTMS$ (**2e**), and the regiochemistry of these products is shown in Table 1. In the reaction of **2f** ($PhC{\equiv}C(CH_2)_3CH_3$) and **2g** ($PhC{\equiv}CCH_3$), two regioisomers **4e**/**4e′ and 4f**/**4f′** were obtained in the ratio of 88/12 and 90/10, respectively, and the regiochemistry of these isomers was carefully assigned on the basis of the NOE experiments. Similarly to the *o*-iodoacetophenone case, both major isomers **4e** and **4f** have the phenyl group next to the hydroxy moiety. For alkyne **2k** ($PhC{\equiv}CC_6H_4OMe$), the regioisomers **4g** and **4g′** were obtained in an almost 1:1 ratio, and no effect of the electron-donating methoxy group on the phenyl ring was observed. Similarly substituted *o*-iodobenzaldehydes **1f** and **1g** react with **2a**, **2e**, and **2g**, giving **4h**−**m** in 46−82% yields. The reaction is highly regioselective for **4i** and **4l**. A small amount of reduction products *o*-iodobenzyl alcohols was observed for these reactions.

A careful examination of the regiochemistry for the carbocyclization using unsymmetrical alkynes **2d**−**g** as substrates shows that in all cases the major products are the regioisomers (**3**, **4**) in which the alkyne carbon bearing a less electron-donating group is connected to the keto or aldehyde group of **1** and the alkyne carbon with a more electron-donating substituent is attached to the ortho carbon of aryl ketone or aldehyde moiety. The electron-donating ability of the substituents in **2d**−**g** are TMS > CH_3 in $TMSC{\equiv}CCH_3$ (**2d**); TMS > Ph in $TMSC{\equiv}CPh$ (**2e**); $CH_3(CH_2)_3$ > Ph in $PhC{\equiv}C(CH_2)_3CH_3)$ (**2f**); and CH_3 > Ph in $PhC{\equiv}CCH_3$ (**2g**). Although these unsymmetrical disubstituted alkynes **2d**−**g** do not have a strong electron-withdrawing group like the ester functionality in propiolates, the Michael-type addition pattern still dominates the product distribution and the trend of regiochemistry is similar to that of propiolate products.

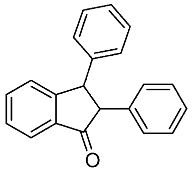
SCHEME 2



Interestingly, the reaction of 3-bromothiophene-2-carbaldehyde (**5**) with diphenylacetylene (**2a**) in the presence of Co(dppe)I_2 and zinc metal powder in acetonitrile at 80 °C proceeded to give highly substituted bicyclic ketone **6** in 54% yield in one pot with a high stereoselectivity (Scheme 2). The structure of **6** with the two phenyl groups trans to each other was established on the basis of ^1H and ^{13}C NMR and high-resolution mass spectraand further confirmed by single crystal X-ray analysis. The present reaction required longer reaction time (30 h) for completion compared to the iodophenyketone reactions (3 h), probably due to the presence of bromo substitution in **5**. The exact reason for the formation ketone product is unclear but it appears that the alcohol formed in the reaction isomerizes during the long reaction period to produce ketone **6**.[11c]

Similarly, the reaction of 2-iodobenzaldehyde (**1e**) with diphenylacetylene (**2a**) in the presence of Co(dppe)I_2 and zinc metal powder in acetonitrile at 80 °C for 20 h furnished indenol product **4a** in 70% yield and indanone **4a′** in 11% yield (Figure 3).

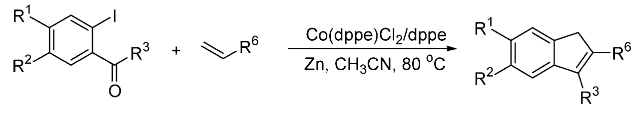
Synthesis of Indenes. The present cobalt-catalyzed reaction was successfully implemented for the synthesis of indene derivatives via cyclization of 2-iodoacetophenones/2-iodobenzaldehydes with acrylates. Treatment of 2-iodoacetophenone (**1a**) (1.0 mmol) with methyl acrylate (**7a**) (2.0 mmol) in the presence of Co(dppe)Cl_2/dppe and zinc metal powder in acetonitrile at 80 °C for 24 h proceeded smoothly to afford methyl 3-methyl-1*H*-2-indene carboxylate (**8a**) in 66% yield (Scheme 3, Table 2, entry 1). The structure of **8** was established on the basis of ^1H and ^{13}C NMR, DEPT, and mass data. Control experiments indicated that in the absence of either Co(dppe)Cl_2 or zinc metal, no desired product was observed in the reaction. The result of this cobalt-catalyzed reaction is intriguing in view of the fact that the catalytic reaction gave the cyclization and dehydration product **8a** instead of the common Heck-type product. There appears no report in the literature of metal-catalyzed carbocy-



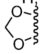
4a'

FIGURE 3.

SCHEME 3



1a-h **7a-e** **8a-k**

1a: $R^1 = H, R^2 = H, R^3 = CH_3$
1b: $R^1 = OCH_3, R^2 = H, R^3 = CH_3$
1c: $R^1 = OCH_3, R^2 = H, R^3 = (CH_2)_3CH_3$
1d: $R^1 = OCH_3, R^2 = H, R^3 = Ph$
1e: $R^1 = H, R^2 = H, R^3 = H$
1f: $R^1 = R^2 =$ , $R^3 = H$
1h: $R^1 = OCH_3, R^2 = H, R^3 = H$

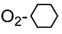
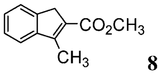
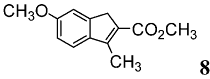
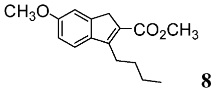
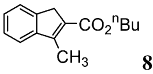
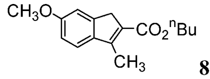
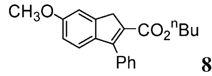
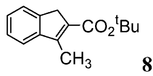
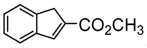
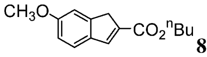
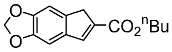
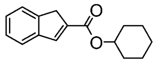
7a: $R^6 = CO_2Me$
7b: $R^6 = CO_2{}^nBu$
7c: $R^6 = CO_2{}^tBu$
7d: $R^6 = CO_2$- 
7e: $R^6 = CN$

TABLE 2. Results of Cobalt-Catalyzed Carbocyclization of 2-Iodophenyl Ketones and Aldehydes (1) with Acrylates (2)[a]

entry	ketone	acrylate	product	yield(%)[b]
33	**1a**	**7a**	 **8a**	66
34	**1b**	**7a**	 **8b**	70
35	**1c**	**7a**	 **8c**	51
36[c]	**1a**	**7b**	 **8d**	75
37[c]	**1b**	**7b**	 **8e**	73
38[c]	**1d**	**7b**	 **8f**	60
39	**1a**	**7c**	 **8g**	41
40[d]	**1e**	**7a**	 **8h**	63
41[c,d]	**1h**	**7b**	 **8i**	65
42[c,d]	**1f**	**7b**	 **8j**	35
43[d]	**1e**	**7d**	 **8k**	62

[a] Unless stated otherwise, all reactions were carried out using *o*-iodophenyl ketones or *o*-iodobenzaldehydes (**1**) (1.00 mmol), acrylates (**7**) (2.00 mmol), $CoCl_2(dppe)$ (0.0500 mmol, 5.0 mol %), dppe (0.0500 mmol, 5.0 mol %) and Zn (2.75 mmol) in CH_3CN (3.0 mL) at 80 °C under N_2 for 24 h. [b] Isolated yields. [c] Reaction time was 48 h for reactions involving *n*-butylacrylate. [d] For the reactions involving *o*-iodobenzaldehydes, 2.00 mmol of alcohol corresponding to acrylate was added.

clization of 2-iodoacetophenones or aldehydes with acrylates or acrylonitrile to give the corresponding indene derivatives. Recently, Gosmini et al. reported a single example of the synthesisbased on of an indene derivative by electrochemical reaction of *o*-bromoacetophenone with methyl vinyl ketone in low yield using Ni as the cathode and Fe as the anode in the presence of $CoBr_2$.[18a]

To understand the nature of this cobalt-catalyzed carbocyclization, the effect of solvent and cobalt complex used on the reaction of **1a** with **7a** were investigated. No desired product was observed when $CoI_2(PPh_3)_2$ or $CoI_2(PPh_3)_2/PPh_3$ and zinc powder was used as the catalysts. The combination of $CoCl_2(dppe)$ and zinc powder as catalyst afforded **8a** in 54% yield, whereas $CoI_2(dppe)/dppe$, $CoI_2(dppp)/dppp$, $CoI_2(dppb)/dppb$, and $CoI_2(dppm)/dppm$ {dppm = bis(diphenylphosphino)methane; dppe = bis(diphenylphosphino)ethane; dppp = bis(diphenylphosphino)propane; dppb = bis(diphenylphosphino)butane} produced **8a** in 52%, 18%, 11%, and 23% yields, respectively. Interestingly, the use of $NiBr_2(dppe)/Zn$ and $PdCl_2(dppe)/Zn$ as catalysts afforded **8a**, only in 49% and 17% yields, respectively. The best result was obtained using $CoCl_2(dppe)$ (5.0 mol %) with an additional 1 equiv of dppe as the catalyst, affording **8a** in 66% isolated yield. The exact reason for the use of additional dppe ligand is yet not clear. One possibility is that excess ligand stabilizes the cobalt complex during the reaction period. In the absence of extra dppe ligand the cobalt complex appears to decompose after a long reaction time. The solvent was also found to be very critical for this cyclization. No reaction was observed in ethyl acetate or dioxane and only a trace of product was observed in THF. Acetonitrile was the solvent of choice in combination with $CoCl_2(dppe)/dppe$ as the catalyst.

Substituted iodophenyl ketones (**1b,c**) underwent carbocyclization with methyl acrylate (**7a**) in the presence of $Co(dppe)Cl_2/dppe$ and zinc powder to give the corresponding indene carboxylates **8b** and **8c** in 70% and 51% yields, respectively (Table 2, entries 34 and 35). Similarly, reaction of iodophenyl ketones **1a,b,d** with *n*-butylacrylate (**7b**) produced corresponding indene derivatives **8d**−**f** in 60−75% yield. Bulky *tert*-butylacrylate **7c** also reacted with 2-iodoacetophenone (**1a**) to afford the indene product **8g** in moderate yield. No desired products were observed for the reaction of **1a** with phenyl vinyl sulfone or methyl vinyl ketone under these reaction conditions. The reason for the failure to observe the expected products for these two substrates is not yet clear.

The carbocyclization of *o*-iodobenzaldehydes with acrylates also proceeds smoothly to furnish the corresponding indene derivatives as shown in Table 2 (entires 40−43). Thus, treatment of 2-iodobenzaldehyde (**1e**) with methyl acrylate (**7a**) (2.0 mmol) in the presence of $Co(dppe)Cl_2/dppe$, zinc metal powder, and methyl alcohol (2.0 mmol) in acetonitrile afforded methyl 1*H*-2-indenecarboxylate (**8h**) in 63% yield. It is noteworthy that the presence of methyl alcohol substantially increases the product yield, likely as a result of inhibition of the hydrolysis of the ester group in product **8h**. Similarly, the reaction of **1h** and **1f** with *n*-butylacrylate (**7b**) gave the corresponding carbocylization products **8i** and **8j**, respectively, in moderate yields. The carbocyclization of **1e** with cyclohexyl acrylate **7d** also worked well, affording indene **8k** in 62%

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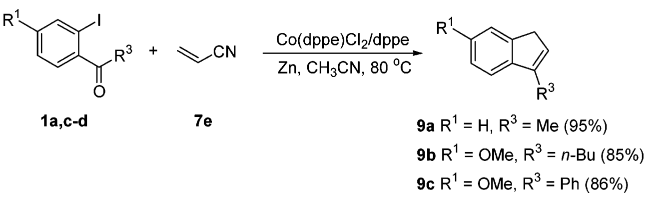
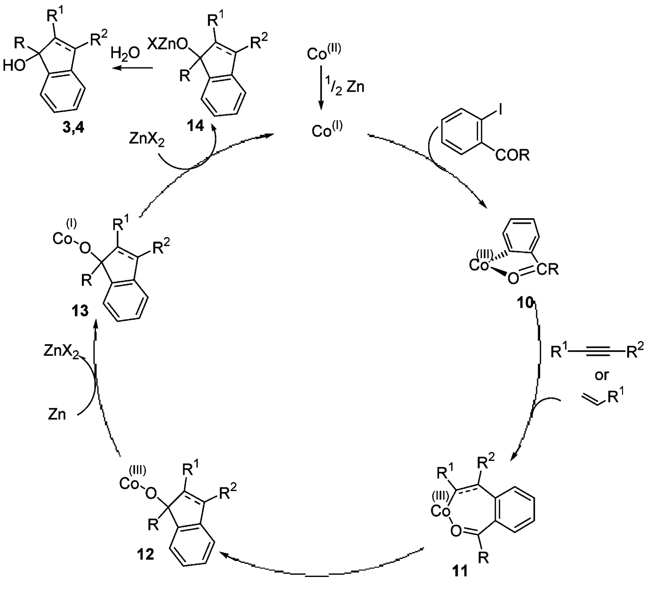
(18) (a) Gomes, P.; Gosmini, C.; Nedelec, J.-Y.; Perichon, J. *Tetrahedron Lett.* **2000**, *41*, 3385. (b) In another electrolysis method using nickel, indene was obtained as byproduct: Condon, S.; Dupre, D.; Falgayrac, G.; Nedelec, J.-Y. *Eur. J. Org. Chem.* **2002**, 105.

SCHEME 4



SCHEME 5. Proposed Mechanism for Cobalt-Catalyzed Carbocyclization

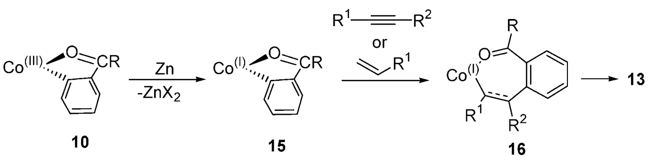


yield (entry 43). In all of these reactions, a small amount of reduction products *o*-iodobenzyl alcohols was also observed.

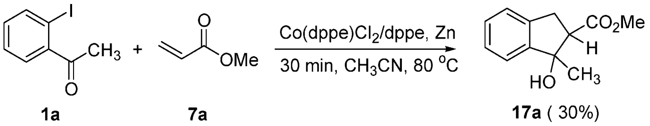
Reductive Decyanation Reaction. The results of carbocyclization reaction of **1** with acrylonitrile (**7e**) is surprising. Treatment of **1a** with **7e** in the presence of cobalt catalyst and zinc powder in acetonitrile at 80 °C for 24 h afforded indene **9a** in 95% yield. Interestingly, no cyano group was present in the product, and it appears that reductive decyanation also occurs during the carbocyclization to give the final product **9a**. Similarly, the reaction of substituted *o*-iodophenyl ketones **1c** and **1d** with acrylonitrile proceeded smoothly to produce reductive decyanation indene products **9b** and **9c** in 85% and 86% yields, respectively (Scheme 4). The reaction provides a mild and practical method for reductive decyanation in high yields. Thus, acrylonitrile acts as a masked "ethylene" in the present carbocylization. The exact reason for this reductive decyanation is still unclear.[19]

Mechanistic Consideration. While the exact mechanism for the present catalytc reaction is not yet clear, on the basis of the known cobalt chemistry and products observed, the following pathway (Scheme 5) is proposed. The catalytic cycle is initiated by the reduction of Co(II) to Co(I) by zinc dust.[7d] Oxidative addition of *o*-iodoacetophenone to Co(I) species affords a five-membered cobalt complex **10** with both the *o*-carbon and the ketone oxygen bonded to the cobalt(III) center.[7d] Intermediate **10** undergoes regioselective insertion with an alkyne/acrylate molecule to generate a seven-membered oxacobaltacycle **11**.[20] Nucleophilic addition of the cobalt−carbon bond in **11** to the coordinated keto group leads to the formation of cobalt alkoxide **12**. Reduction of the cobalt(III) alkoxide by zinc powder affords a Co(I) alkoxide **13**. Transmetalation of **13** with ZnX_2 generates the active Co(I) species and the corresponding zinc alkoxide **14**, which is converted to the final product **3** after hydrolysis. In the case of acrylates further dehydration occurs to give the indene product.

SCHEME 6



SCHEME 7



An alternative pathway (Scheme 6) involving the reduction of Co(III) intermediate **10** by zinc metal powder to **15** cannot be totally ruled out. Regioselective insertion of an alkyne/acrylate molecule into the Co(I)−carbon bond in intermediate **15** gives seven-membered oxacobaltacycle **16**, which then undergoes intramolecular nucleophilic addition to give **13**

It is noteworthy that α-hydroxyindane derivative **17a** from the reaction of 2-iodoacetophenone (**1a**) (1.0 mmol) and methyl acrylate (**7a**) (2.00 mmol) in the presence of $CoCl_2$(dppe)/dppe and zinc metal powder was isolated in ~30% yield (Scheme 7) when the reaction was carried out in acetonitrile at 80 °C for 30 min. This result clearly demonstrates that dehydration of **17a** occurs during the reaction prior to the formation of indene product **8a**.

Conclusion

In conclusion, we have demonstrated that the Co(dppe)I_2/Zn system successfully catalyzed the carbocyclization reaction of *o*-iodobenzaldehydes and *o*-iodophenyl ketones with alkynes to afford indenols in high regioselectivity and excellent yields. The carbocyclization can be extended to the reaction of *o*-iodobenzaldehydes and *o*-iodophenyl ketones with acrylates and acrylonitrile in the presence of the Co(dppe)Cl_2/dppe/Zn system to give indene derivatives in moderate to good yields. It is surprising that for the carbocyclization involving acrylonitrile decyanation occurs. These results clearly demonstrate that cobalt complexes can also catalyze coupling reactions involving aryl iodides as substrates in a similar fashion as palladium and nickel complexes, although a subtle difference in catalytic activity is noticed. Further

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(19) For recent reports on reductive decyanation, please see: (a) Vilsmaier, E.; Milch, G.; Bergstrasser, U. *Tetrahedron* **1998**, *54*, 6403. (b) Liu, H. J.; Yip, J. *Synlett* **2000**, 1119. (c) Walker, J. A.; Zhao, M.; Baker, M. D.; Dormer, P. G.; McNamara, J. *Tetrahedron Lett.* **2002**, *43*, 6747. (d) Guijarro, D.; Yus, M. *Tetrahedron* **1994**, *50*, 3447. (e) Kang, H. Y.; Hong, W. S.; Cho, Y. S.; Koh, H. Y. *Tetrahedron Lett.* **1995**, *36*, 7661. (f) Curran, D. P.; Seong, C. M. *J. Am. Chem. Soc.* **1990**, *112*, 9401. (g) Curran, D. P.; Seong, C. M. *Synlett* **1991**, 107.

(20) For nickel oxametallacycles, see: (a) Kimura, M.; Matsuo, S.; Shibata, K.; Tamaru, Y. *Angew. Chem., Int. Ed.* **1999**, *38*, 3386. (b) Sato, Y.; Takanashi, T.; Mori, M. *Organometallics* **1999**, *18*, 4891.

work in this direction including the asymmetric version is underway.

Experimental Section

All reactions were conducted under nitrogen on a dual-manifold Schlenk line by using standard inert-atmosphere techniques, unless otherwise stated. Reagents and chemical were used as purchased without further purification. Substituted 2-iodophenyl ketones were prepared following literature procedures.[21] The cobalt catalysts $CoCl_2(dppe)$ and $CoI_2(dppe)$ were synthesized according to modified literature procedures.[22]

General Procedure for Cyclization of *o*-Iodoaryl Ketones and *o*-Iodoarylaldehydes 1 with Alkynes 2. A round-bottom sidearm flask (25 mL) containing an *o*-iodobenzaldehydes or *o*-iodophenyl ketones **1** (1.00 mmol), $CoI_2(dppe)$ (0.0500 mmol, 5.0 mol %) and zinc powder (2.75 mmol) was evacuated and purged with nitrogen gas three times. Freshly distilled CH_3CN (3.0 mL) and an alkyne (1.50 mmol) were added to the system, and the reaction mixture was stirred at 80 °C for 3 h. The reaction mixture was cooled, diluted with dichloromethane, and then stirred in the air for 15 min. 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 using hexanes−ethyl acetate as eluent to afford the cyclization products **3**. Compounds **3a**−**s** and **4a**−**m** were synthesized according this procedure.

Acknowledgment. We thank the National Science Council of Republic of China (NSC 92-2113-M-007-044) for the support of this research.

Supporting Information Available: Experimental procedures, spectroscopic data, and ^{1}H NMR spectra for compounds **3a**−**s**, **4a**−**m**, and **8a**−**k**; X-ray crystal structure data for compound **6** in CIF format; NOE experimental data of compounds **3** and **4**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO049506G

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(21) D. Hellwinkel, S. Siegbert, *Chem. Ber.* **1987**, *120*, 1151.

(22) (a) Colquhoun, H. M.; Thompson, D. J.; Twigg, M. V. *Carbonylation*; Plenum Press: New York, 1991. (b) Colquhoun, H. M.; Holton, J.; Thompson, D. J.; Twigg, M. V. *New Pathways for Organic Synthesis-Practical Applications of Transition Metals*; Plenum Press: New York, 1988.