Synthesis of Indanes through Coupling of Ethynylstyrene Derivatives with Carbene Complexes

Lei Zhang and James W. Herndon*

Department of Chemistry and Biochemistry, New Mexico State University, MSC 3C, Las Cruces, New Mexico 88003

Received November 30, 2003

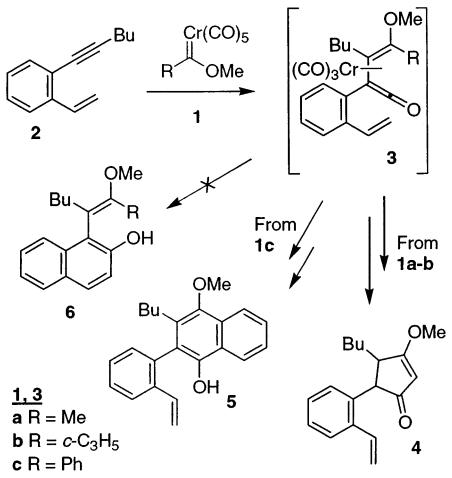
A new synthesis of indane derivatives was developed using the coupling of carbene complexes with 2-alkynylstyrene derivatives as a key step. A mechanism involving attack of a nucleophilic alkene at an electrophilic carbene complex intermediate, followed by formation of an isoindene followed by 1,5-hydride shift, was proposed. This reaction pathway is maximized for highly electrophilic carbene complexes and for styrene derivatives featuring nucleophilic alkenes.

Introduction

In a recent series of papers, the formation of aromatic ring systems through the coupling of Fischer carbene complexes with conjugated dienylacetylene derivatives has been demonstrated.[1] In only one system, the coupling of Fischer carbene complexes with *o*-alkynylstyrene derivatives (e.g., **2**), was a general failure in the annulation process noted.[2] The coupling of alkynylstyrene derivative **2** with carbene complexes results only in products where annulation occurs within the R group and not within the styrene group. Cyclopentannulation processes resulting in cyclopentenone derivative **4** were observed using methylcarbene complex **1a**[3] or cyclopropylcarbene complex **1b**,[4] and benzannulation resulting in naphthol derivative **5** was the exclusive pathway in the coupling of alkyne **2** with phenylcarbene complex **1c**. No compounds resulting from naphthol derivative **6**, the product from annulation onto the styrene group, were obtained. Originally this annulation failure was attributed to the poor complexation ability of an isolated double bond of the aromatic ring relative to a simple alkene and preferred ring closure within the chromium-complexed vinylketene functionality of intermediate **3**.[5]

In this article, the use of terminal alkyne analogues of **2** (e.g., **7**, R^4 = H, Scheme 2) is reported. Annulation within the alkynylstyrene system is observed in these systems, resulting in mixtures of benzannulation (e.g., naphthalene **8**) and cyclopentannulation (e.g., indane **9**) products. Particular emphasis in this article is on delineation of the factors favoring indane formation,

Scheme 1



which is often an "undesired" minor reaction pathway in chromium carbene-based benzannulation reactions.[6−8] The 2-alkylindane ring system is present in numerous medicinally important compounds,[9] and the reaction in Scheme 2 assembles this ring system from readily available precursors.[10]

* Corresponding author. E-mail: jherndon@nmsu.edu.

(1) Herndon, J. W.; Zhang, Y.; Wang, H.; Wang, K. *Tetrahedron Lett.* **2000**, *41*, 8687−8690. (b) Herndon, J. W.; Hayford, A. *Organometallics* **1995**, *14*, 1556−1558. (c) Waters, M. A.; Bos, M. E.; Wulff, W. D. *J. Am. Chem. Soc.* **1999**, *121*, 6403−6413.

(2) Jackson, T. J.; Herndon, J. W. *Tetrahedron* **2001**, *57*, 3859−3868.

(3) Challener, C. A.; Wulff, W. D.; Anderson, B. A.; Chamberlin, S.; Faron, K. L.; Kim, O. K.; Murray, C. K.; Xu, Y. C.; Yang, D. C.; Darling, S. D. *J. Am. Chem. Soc.* **1993**, *115*, 1359−1376.

(4) Tumer, S. U.; Herndon, J. W.; McMullen, L. A. *J. Am. Chem. Soc.* **1992**, *114*, 8394−8404.

(5) This is a critical event in successful benzannulation reactions. Bos, M. E.; Wulff, W. D.; Miller, R. A.; Chamberlin, S.; Brandvold, T. A. *J. Am. Chem. Soc.* **1991**, *113*, 9293−9319.

(6) Herndon, J. W. *Tetrahedron* **2000**, *56*, 1257−1280.

(7) Indenes are the major products from coupling of amino(aryl)-carbene-chromium complexes and alkynes. (a) Yamashita, A. *Tetrahedron Lett.* **1986**, *27*, 5915−5918. (b) Dötz, K. H.; Erben, H. G.; Harms, K. *J. Chem. Soc., Chem. Commun.* **1989**, 692−693.

(8) Indenes have also been prepared from the coupling of carbene complexes in mechanistically unrelated processes. (a) Barluenga, J.; Martínez, S.; Suárez-Sobrino, A. L.; Tomás, M. *J. Am. Chem. Soc.* **2001**, *123*, 11113−11114. (b) Barluenga, J.; Trabanco, A. A.; Florez, J.; Garcia-Granda, S.; LLorca, M. A. *J. Am. Chem. Soc.* **1998**, *120*, 12129−12130.

(9) Examples in the 21st century: (a) Lowe, D. B.; Wickens, P. L.; Ma, X.; Zhang, M.; Bullock, W. H.; Coish, P. D. G.; Mugge, I. A.; Stolle, A.; Wang, M.; Wang, Y.; Zhang, C.; Zhang, H. J.; Zhu, L.; Tsutsumi, M.; Livingston, J. N. PCT Int. Appl. 2003, *Chem. Abstr.* **2003**, *138*, 153524. (b) Uchikawa, O.; Fukatsu, K.; Tokunoh, R.; Kawada, M.; Matsumoto, K.; Imai, Y.; Hinuma, S.; Kato, K.; Nishikawa, H.; Hirai, K.; Miyamoto, M.; Ohkawa, S. *J. Med. Chem.* **2002**, *45*, 4222−4239. (c) Fukatsu, K.; Uchikawa, O.; Kawada, M.; Yamano, T.; Yamashita, M.; Kato, K.; Hirai, K.; Hinuma, S.; Miyamoto, M.; Ohkawa, S. *J. Med. Chem.* **2002**, *45*, 4212−4221. (d) Menander, K. B.; Mayle, M. J. PCT Int. Appl. 2000, *Chem. Abstr.* **2000**, *133*, 144943.

(10) For a review of indane syntheses, see: Hong, B. C.; Sarshar, S. *Org. Prep. Proc. Int.* **1999**, *31*, 1−86.

10.1021/om034334j CCC: $27.50
Publication on Web 02/07/2004

Scheme 2

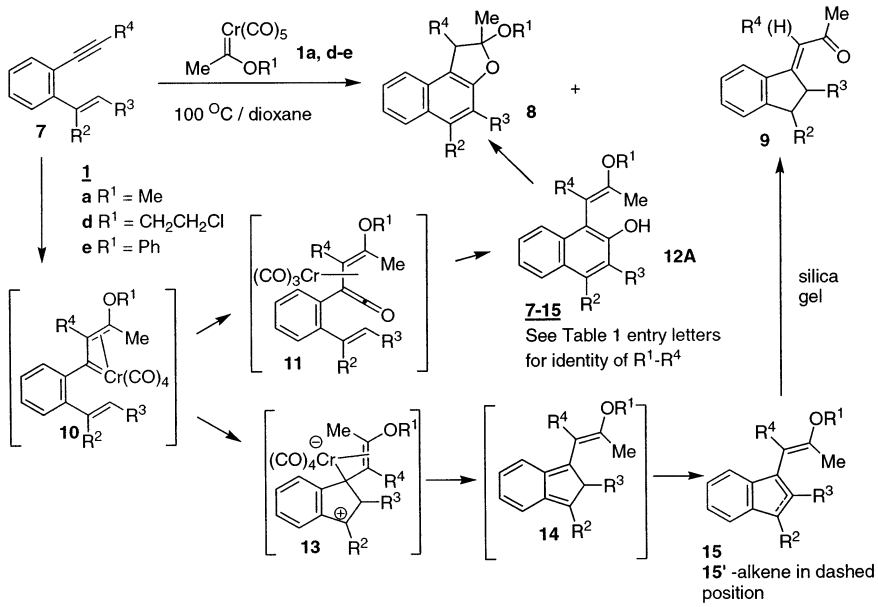
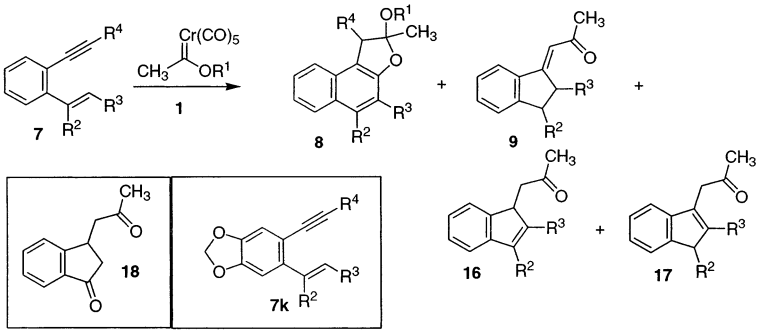


Table 1. Synthesis of Indane Derivatives through Coupling of Fischer Carbene Complexes and *o*-Alkynylstyrene Derivatives



entry[a]	reactants	R^1	R^2	R^3	R^{4b}	yield **8**	yield **9**	yield **16**	yield **17**
A	**1a** + **7a**	Me	H	H	H	28	26	0	0
B	**1d** + **7a**	$-(CH_2)_2Cl$	H	H	H	8	54[c]	0	0
C	**1e** + **7a**	Ph	H	H	H	13	66[c]	0	0
D	**1a** + **7d**	Me	Me	H	H	0	3	73	0
E	**1a** + **7e**	Me	Me	H	TMS (H)	0	5[d]	76[d]	0
F	**1a** + **7f**	Me	Ph	H	H	0	0	89	0
G	**1a** + **7g**	Me	H	Me	H	40	0	0	39
H	**1a** + **7h**	Me	Me	Me	TMS (H)	0	0	40	12
I	**1a** + **7i**	Me	OTMS	H	TMS (H)	0	0	79	0
J	**1a** + **7j**	Me	*c*-C_3H_5	H	TMS[e]	0	8[e]	68[e]	0
K[f]	**1a** + **7k**	Me	H	H	TMS (H)	0	30[f]	35[f]	7[f]

[a] Entry letters correlate with substituent letters for compounds **7**, **8**, **9**, **16**, and **17** and intermediates **10**−**15**. [b] The substituent in parentheses refers to the R^4 substituent in the final products, obtained after α-silyl ketone hydrolysis. [c] This is the same product as in entry A and is referred to as **9a**. [d] These are the same products as in entry D and referred to as **9d** and **16d**. [e] The α-silyl ketone precursor was isolated as a 1:1 mixture of diastereomers; deliberate hydrolysis to **9j**/**16j** was accompanied by indene isomerization. [f] 3,4-Methylenedioxybenzene replaces benzene ring in compounds **7k**, **9k**, and **10**−**17k**.

Results and Discussion

Coupling of methylcarbene complex **1a** (Scheme 2 and entry A of Table 1) with the alkynyl-styrene derivative **7a** led to the benzofuran derivative **8a** (28%) and the indane derivative **9a** (26%). Since electronic effects can have a profound effect on the naphthol/indene ratio,[11,12] the reaction of more electron-deficient carbene complexes **1d** (R = CH_2CH_2Cl)[13] and **1e** (R = Ph)[14] with alkyne **7a** was examined. Contrary to expectations based on literature precedent, these more electrophilic

(11) This effect is dramatically illustrated in the following papers: (a) Grotjahn, D. B.; Kroll, F. E. K.; Schaefer, T.; Harms, K.; Dötz, K. H. *Organometallics* **1992**, *11*, 298−310. (b) Hoye, T. R.; Rehberg, G. M. *Organometallics* **1989**, *8*, 2070−2071. (c) Korkowski, P. F.; Hoye, T. R.; Rydberg, D. B. *J. Am. Chem. Soc.* **1988**, *110*, 2676−2678.

(12) Additional factors may influence benzannulation vs cyclopentannulation since the regioselectivity of alkyne insertion is different for the two processes. Waters, M. L.; Bos, M. E.; Wulff, W. D. *J. Am. Chem. Soc.* **1999**, *121*, 6403−6413.

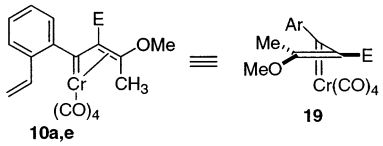
(13) Barluenga, J.; Lopez, S.; Trabanco, A. A.; Florez, J. *Chem. Eur. J.* **2001**, *7*, 4723−4729.

(14) For recent uses of phenoxycarbene complexes see: Waters, M. L.; Brandvold, T. A.; Isaacs, L.; Wulff, W. D.; Rheingold, A. L. *Organometallics* **1998**, *17*, 4298−4308.

complexes led to a dramatic increase in the proportion of indene derivatives. Previous investigators had noted that a decrease in electron density in the vicinity of the carbene complex leads to an increase in the proportion of CO-inserted products.[6,11] To accommodate this unusual observation, the mechanism depicted in Scheme 2 has been proposed to account for the formation of indane derivatives. Initial formation of vinylcarbene complex **10** followed by nucleophilic attack of the alkene at the carbene carbon to afford **13**, followed by loss of the metal, affords isoindene derivative **14**,[15] which undergoes a 1,5-hydride shift to form the observed product after hydrolysis of the enol ether. Enhancement of the proportion of products that do not incorporate CO in the more electron-deficient systems is supportive of the novel mechanism involving nucleophilic attack of the alkene at the carbene carbon since traditional arguments suggest that the more electron-deficient systems should have led to *more* naphthalene (CO-inserted) product. The product **9A** has been tentatively assigned as the *E* alkene since the double bond was formed under thermodynamically controlled conditions, and there is steric interaction between the acetyl group and the phenyl ring in the *Z* alkene.

The proposed mechanism in Scheme 2 implies that formation of the indane derivative could also be accelerated through enhancement of the nucleophilicity of the alkene. A series of alkynylstyrenes that differ in the nucleophilicity of the alkene were prepared and their coupling reactions with Fischer carbene complexes subsequently examined (see Table 1). Coupling of carbene complex **1a** with the 1,1-disubstituted alkene derivative **7d** (entry D) led exclusively to the indane derivative. In this case, the major isomer was **16d**; only a minor amount of the ketone-conjugated derivative **9d** was obtained. An alternate 1,5-hydrogen shift process from intermediate **14d** to afford **15d′** followed by enol ether hydrolysis can account for the formation of **16d**. Coupling of carbene complex **1a** with all of the alkynylstyrenes where $R^2 \neq H$ (entries E, F, and H−J) led to predominantly indane derivatives. Alkynylstyrene **7g** (entry G), where $R^2 = H$, afforded a nearly equal amount of indane and naphthalene products, as in entry A. The indane-forming process was also efficient for silylated alkynes (entries E, H, and I−K), which afford the same products as the terminal alkynes after desilylation using silica gel. The oxygenated alkynylstyrene **7i** also provided only indene derivative **16i**. Surprisingly, silyl enol ether **16i** survived chromatography on silica gel. The proposed structure of **16i** was verified by its conversion to diketone **18** upon acid-catalyzed hydrolysis. Formation of indanes from alkyne **7j** involves a cyclopropylcarbinyl cation intermediate (**13j**); however, no ring-opening product emanating from this intermediate was detected.[16] In the formation of indanes in entry J, the desilylation process was accompanied by isomerization

Scheme 3



of the double bond. The desilylation conditions (silica gel at 25 °C in chloroform) should not have caused indene isomerization.[17] The unique isomerization in this system might be attributed to the stability of cyclopropylcarbinyl cation intermediates from protonation of the alkene.[18] The α-silyl ketone precursor to **16j** could be isolated as a 1:1 mixture of diastereomers. The methylenedioxy derivative **7k** (entry K) undergoes the anticipated indane-forming process. Although $R^2 = H$ in this substrate, indane formation is predominant due to stabilization of the carbocation intermediate **13k** by the electron-donating methylenedioxy groups.

Given the results in Scheme 1, it is surprising that alkynes **7** undergo an annulation reaction onto the styrene functionality. The only serious difference between compound **2** of Scheme 1 and compound **7a** of Scheme 2 is that alkyne **7a** is terminal. The differing reaction pathways are likely an electronic effect and not a steric effect since terminal and silylated alkynes give the same result, which is contrary to the results obtained using the *n*-butylated alkyne. The *n*-butyl substituent (*A* value 1.85)[19] is intermediate in steric bulk compared to a hydrogen (*A* value 0) and a trimethylsilyl group (*A* value 3.41).[20] A speculative but plausible reason for successful annulations using terminal and silylated alkynes is stabilization of intermediate vinylcarbene complexes (e.g., **10**) through overlap of the C−E bond with the p-orbital of the C−Cr π-bond (see structure **19** in Scheme 3).[21] The carbene complex intermediate is stabilized when E is electropositive (e.g., H or TMS) relative to when E is an alkyl substituent, and this effect may prevent the undesired processes noted in Scheme 1 and ref 2.

Conclusion

In summary, the coupling of terminal or silylated 2-alkynylstyrene derivatives with Fischer carbene com-

(15) Kamal de Fonseka, K.; Manning, C.; McCullough, J. J.; Yarwood, A. J. *J. Am. Chem. Soc.* **1977**, *99*, 8257−8261.

(16) Formation of ring-opened products from similar carbocation intermediates can proceed with variable degrees of ring opening. (a) For an example where the degree of ring opening is controlled through reaction conditions see: Sarel, S.; Breuer, E.; Ertag, S.; Salamon, R. *Isr. J. Chem.* **1963**, *1*, 451−459. (b) For an example involving only ring opening see: Kanemoto, S.; Shimizu, M.; Yoshioka, H. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 2024−2031. (c) For examples involving no ring opening see: Traas, P. C.; Boelens, H.; Takken, H. J. *Rec. Trav. Chim.* **1976**, *95*, 57−66.

(17) Indene double-bond isomerization can be catalyzed by base or thermolysis. (a) For thermal interconversion, see: Roth, W. R. *Tetrahedron Lett.* **1964**, 1009−1013. (b) For base-catalyzed rearrangement, see: Bergson, J.; Weidler, A. M. *Acta Chim. Scand.* **1964**, *18*, 1487−1497.

(18) (a) An attempt to induce isomerization of indenes by acid failed. Christol, H.; Plenat, M. F.; Huebner, C. F. *Bull. Soc. Chim. Fr.* **1964**, 2640−2643. (b) Acid-catalyzed isomerization of **16j** might have occurred because of the intermediacy of cyclopropylcarbinyl cation intermediates. Richey, H. G., Jr. In *Carbonium Ions*; Olah, G. A., Schleyer, P. von R., Eds.; Wiley-Interscience: New York, 1972; Vol. 3, pp 1201−1294.

(19) Obtained from an MM2 calculation using CHEM 3D.

(20) Oullette, R. J.; Baron, D.; Stolfo, J.; Rosenblum, A.; Weber, P. *Tetrahedron* **1972**, *28*, 2163−2181.

(21) (a) A similar stabilization was suggested to explain the unique regioselectivity exhibited in the coupling of stannylacetylenes and chromium carbene complexes. Although this effect was more strongly noted for tin than for silicon, it is still important for silicon; TMS is much larger than propyl, yet propyl ends up α to OH in the major product of benzannulations using pentynyltrimethylsilane. Chamberlin, S.; Waters, M. L.; Wulff, W. D. *J. Am. Chem. Soc.* **1994**, *116*, 3113−3114. (b) Later studies showed that a similar effect may be operative for alkynylboranes. Davies, M. W.; Johnson, C. N.; Harrity, J. P. A. *J. Org. Chem.* **2001**, *66*, 3525−3532.

plexes has been reported. The reaction appears to be quite general, especially for systems where either (1) the electrophilic character of the carbene complex is enhanced, or (2) carbocation stabilizing groups are present at carbon-1 of the alkene or para to the alkene. Currently efforts are underway to trap the carbocation and isoindene intermediates of the reaction.

Experimental Section

General Procedure I. Coupling of Carbene Complexes with 2-Alkynylstyrene Derivatives. A solution of carbene complex (0.60 mmol, 1.2 equiv) and 2-alkynylstyrene derivative (0.50 mmol, 1.0 equiv) in dioxane (20 mL) was added dropwise to refluxing dioxane (10 mL) over a 1 h period. When carbene complexes **1d**,**e** were employed, a larger excess of the carbene complex was employed to offset losses due to thermal decomposition. After the addition was complete, the mixture was kept at gentle reflux for a 24 h period. The resulting reaction mixture was allowed to cool to room temperature and then concentrated on a rotary evaporator. The residue was stirred in silica gel/chloroform in the air for another 24 h period and then filtered through a thin layer of Celite. The solvent was removed on a rotary evaporator. Final purification was achieved by flash chromatography on silica gel.

Starting Materials. Compounds **1a**, **1e**,[22] **7a**, **7d**,[23] **7e**,[23] **7g**,[23] and **7h**,[23] were prepared according to literature procedures. Preparation for all other starting compounds is described in the Supporting Information.

Coupling of Carbene Complex 1a with Alkyne 7a (Table, Entry A). General procedure I was followed using carbene complex **1a** (150 mg, 0.6 mmol) and alkyne **7a** (64 mg, 0.5 mmol). Final purification was achieved by flash chromatography on silica gel using 20:1 and 9:1 hexane/ethyl acetate as eluent. Two compounds were isolated and identified as ketal **8a** (30 mg, 28% yield) and indane **9a** (22 mg, 26% yield). **8a**: ^{1}H NMR ($CDCl_3$) δ 7.70 (d, 1 H, J = 7.6), 7.72 (d, 1 H, J = 7.6), 7.58 (d, 1 H, J = 7.6), 7.46 (d, 1 H, J = 7.6), 7.30 (t, 1 H, J = 7.6), 7.14 (t, 1 H, J = 7.6), 3.55 (d, 1 H, J = 16.0), 3.38 (d, 1 H, J = 16.0), 3.32 (s, 3 H), 1.81 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 155.5, 130.2, 129.0, 128.9, 128.5, 126.5, 122.7, 122.5, 117.3, 112.4, 111.5, 49.8, 38.6, 24.9. **9a**: ^{1}H NMR ($CDCl_3$) δ 7.65 (d, 1 H, J = 7.6), 7.40 (d, 1 H, J = 7.6), 7.25 (m, 2 H), 6.75 (t, 1 H, J = 2.5), 3.30 (m, 2 H), 3.05 (m, 2 H), 2.29 (s, 3 H); irradiated at δ 6.75, δ 3.30 (t, J = 7.5), 3.05 (t, J = 7.5); irradiated at δ 2.29, δ 6.75 (s), 3.05 (s); ^{13}C NMR ($CDCl_3$) δ 198.4, 162.1, 150.4, 140.2, 131.3, 127.0, 125.9, 121.7, 115.3, 32.2, 31.8, 30.9; IR (neat) 1610 cm^{-1}; LRMS m/z 172, 157, 129; HRMS calcd for $C_{12}H_{12}O$ 172.0888, found 172.0889.

Coupling of Carbene Complex 1d with Alkyne 7a (Table, Entry B). General procedure I was followed using carbene complex **1d** (299 mg, 1.0 mmol) and alkyne **7a** (64 mg, 0.5 mmol). Final purification was achieved by flash chromatography on silica gel using 20:1 and 9:1 hexane/ethyl acetate as eluent. Two compounds were isolated and identified as ketal **8b** (10 mg, 8% yield) and indane **9a** (46 mg, 54% yield). **8b**: ^{1}H NMR ($CDCl_3$) δ 7.79 (d, 1 H, J = 7.6), 7.72 (d, 1 H, J = 7.6), 7.60 (d, 1 H, J = 7.6), 7.46 (d, 1 H, J = 7.6), 7.30 (t, 1 H, J = 7.6), 7.14 (t, 1 H, J = 7.6), 3.80 (t, 2 H, J = 7.2), 3.61 (t, 2 H, J = 7.2), 3.55(d, 1 H, J = 16.0), 3.40 (d, 1 H, J = 16.0), 1.71 (s, 3 H).

Coupling of Carbene Complex 1e with Alkyne 7a (Table, Entry C). General procedure I was followed using carbene complex **1e** (313 mg, 1.0 mmol) and alkyne **7a** (64 mg, 0.5 mmol). Final purification was achieved by flash chromatography on silica gel using 20:1 and 9:1 hexane/ethyl acetate as eluent. Two compounds were isolated and identified as ketal **8c** (18 mg, 13% yield) and indane **9a** (57 mg, 66% yield). **8c**: ^{1}H NMR ($CDCl_3$) δ 7.9−7.0 (m, 11 H), 3.54 (d, 1 H, J = 16.0), 3.40 (d, 1 H, J = 16.0), 1.70 (s, 3 H).

Coupling of Carbene Complex 1a with Alkyne 7d (Table, Entry D). General procedure I was followed using carbene complex **1a** (150 mg, 0.6 mmol) and alkyne **7d** (71 mg, 0.5 mmol). Final purification was achieved by flash chromatography on silica gel using 9:1 hexane/ethyl acetate as eluent. Two compounds were isolated and identified as indane **9d** (3 mg, 3% yield) and indane **16d** (68 mg, 73% yield). **9d**: ^{1}H NMR ($CDCl_3$) δ 7.61 (d, 1 H, J = 7.6), 7.4−7.2 (m, 3 H), 6.70 (t, 1 H, J = 2.5), 3.62 (ddd, 1 H, J = 19.6, 7.4, 2.5), 3.35 (m, 1 H), 2.82 (dt, 1 H, J = 19.6, 2.5), 2.30 (s, 3 H), 1.31 (d, 3 H, J = 7.2). **16d**: ^{1}H NMR ($CDCl_3$) δ 7.4−7.1 (m, 4 H), 6.10 (s, 1 H), 3.83 (m, 1 H), 2.81 (dd, 1 H, J = 17.5, 6.4), 2.49 (dd, 1 H, J = 17.5, 8.7), 2.15 (s, 3 H), 2.11 (t, 3 H, J = 1.7); irradiated at δ 3.83, δ 2.81 (d, J = 17.5), 2.49 (d, J = 17.5), 2.11 (d, J = 1.7); irradiated at δ 2.11, δ 3.83 (dd, J = 8.7, 6.4); ^{13}C NMR ($CDCl_3$) δ 207.8, 147.6, 145.6, 130.6, 126.9, 125.2, 123.0, 119.3, 45.6, 44.2, 30.5, 13.1; IR (neat) 1714 cm^{-1}; LRMS m/z 186, 143, 128; HRMS calcd for $C_{13}H_{14}O$ 186.1045, found 186.1046.

Coupling of Carbene Complex 1a with Alkyne 7e (Table, Entry E). General procedure I was followed using carbene complex **1a** (150 mg, 0.6 mmol) and alkyne **7e** (64 mg, 0.5 mmol). Final purification was achieved by flash chromatography on silica gel using 9:1 hexane/ethyl acetate as eluent. Two compounds were isolated and identified as indane **9d** (5 mg, 5% yield) and indane **16d** (71 mg, 76% yield).

Coupling of Carbene Complex 1a with Alkyne 7f (Table, Entry F). General procedure I was followed using carbene complex **1a** (150 mg, 0.6 mmol) and alkyne **7f** (102 mg, 0.5 mmol). Final purification was achieved by flash chromatography on silica gel using 9:1 hexane/ethyl acetate as eluent. One compound was isolated and identified as indane **16f** (110 mg, 89% yield). **16f**: ^{1}H NMR ($CDCl_3$) δ 7.61 (t, 3 H, J = 7.1), 7.55−7.20 (m, 6 H), 6.60 (d, 1 H, J = 1.8), 4.12 (ddd, 1 H, J = 8.4, 6.2, 1.8), 3.03 (dd, 1 H, J = 17.8, 6.2), 2.65 (dd, 1 H, J = 17.8, 8.4), 2.19 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 207.5, 148.0, 144.6, 143.4, 135.8, 135.5, 128.8, 127.8, 127.0, 125.5, 123.5, 120.8, 45.4, 44.4, 30.5; IR (neat) 1715 cm^{-1}; HRMS calcd for $C_{18}H_{16}O$ 248.1201, found 248.1194.

Coupling of Carbene Complex 1a with Alkyne 7g (Table, Entry G). General procedure I was followed using carbene complex **1a** (150 mg, 0.6 mmol) and alkyne **7g** (72 mg, 0.5 mmol). Final purification was achieved by flash chromatography on silica gel using 20:1 and 9:1 hexane/ethyl acetate as eluent. Two compounds were isolated and identified as ketal **8g** (45 mg, 40% yield) and indane **17g** (36 mg, 39% yield). **8g**: ^{1}H NMR ($CDCl_3$) δ 7.72 (d, 1 H, J = 7.2), 7.50 (d, 1 H, J = 7.2), 7.45 (s, 1 H), 7.41 (t, 1 H, J = 7.2), 7.25 (t, 1 H, J = 7.2), 3.55 (d, 1 H, J = 17.4), 3.35 (d, 1 H, J = 17.4), 3.30 (s, 3 H), 2.41 (s, 3 H), 1.75 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 155.5, 129.7, 129.3, 128.5, 128.1, 125.8, 123.1, 122.7, 122.3, 116.9, 112.5, 50.0, 39.3, 25.4, 16.2; HRMS calcd for $C_{15}H_{16}O_2$ 228.1150, found 228.1150. **17g**: ^{1}H NMR ($CDCl_3$) δ 7.38 (d, 1 H, J = 7.2), 7.24 (t, 1 H, J = 7.2), 7.18 (d, 1 H, J = 7.2), 7.12 (t, 1 H, J = 7.2), 3.60 (s, 2 H), 3.31 (s, 2 H), 2.12 (s, 3 H), 2.09 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 206.5, 146.0, 142.3, 142.2, 130.4, 126.5, 124.3, 123.5, 118.5, 43.0, 41.5, 29.1, 14.4; IR (neat) 1713 cm^{-1}; HRMS calcd for $C_{13}H_{14}O$ 186.1045, found 186.1048.

Coupling of Carbene Complex 1a with Alkyne 7h (Table, Entry H). General procedure I was followed using carbene complex **1a** (150 mg, 0.6 mmol) and alkyne **7h** (114 mg, 0.5 mmol). Final purification was achieved by flash chromatography on silica gel using 9:1 hexane/ethyl acetate as eluent. Two compounds were isolated and identified as indane **16h** (40 mg, 40% yield) and indane **17h** (12 mg, 12% yield). **16h**: ^{1}H NMR ($CDCl_3$) δ 7.25 (m, 2 H), 7.20 (d, 1 H, J = 7.0), 7.11 (d, 1 H, J = 7.0), 3.82 (dd, 1 H, J = 8.4, 4.9), 2.85 (dd, 1 H, J = 17.5, 4.9), 2.50 (dd, 1 H, J = 17.5, 8.4), 2.21 (s,

(22) Jiang, W.; Fuertes, M. J.; Wulff, W. D. *Tetrahedron* **2000**, *56*, 2183−2194.

(23) Maeyama, K.; Iwasawa, N. *J. Org. Chem.* **1999**, *64*, 1344−1346.

3 H), 2.00 (s, 3 H), 1.89 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 208.0, 146.3, 140.5, 132.6, 126.7, 124.3, 122.6, 118.3, 47.2, 44.9, 30.8, 12.4, 10.3; IR (neat) 1718 cm^{-1}; LRMS *m/z* 200, 157, 142, 129, 115, 43; HRMS calcd for $C_{14}H_{16}O$ 200.1201, found 200.1202. **17h**: ^{1}H NMR ($CDCl_3$) δ 7.30 (d, 1 H, J = 7.0), 7.25 (d, 1 H, J = 7.0), 7.21 (d, 2 H, J = 7.0), 3.55 (s, 2 H), 3.25 (q, 1 H, J = 7.2), 2.11 (s, 3 H), 2.00 (s, 3 H), 1.25 (d, 3 H, J = 7.2); ^{13}C NMR ($CDCl_3$) δ 206.6, 148.2, 147.3, 144.5, 129.0, 126.7, 124.5, 122.6, 118.5, 47.4, 41.6, 29.0, 15.9, 12.5; IR (neat) 1718 cm^{-1}; LRMS *m/z* 200, 157, 142, 129, 115, 43; HRMS calcd for $C_{14}H_{16}O$ 200.1201, found 200.1209.

Coupling of Carbene Complex 1a with Alkyne 7i (Table, Entry I). General procedure I was followed using carbene complex **1a** (150 mg, 0.6 mmol) and alkyne **7i** (145 mg, 0.5 mmol). Final purification was achieved by flash chromatography on silica gel using 9:1 hexane/ethyl acetate as eluent. One compound was isolated and identified as indane **16i** (103 mg, 79% yield). Indane **16i** was converted to **18** by stirring in dilute $HCl/H_2O/Et_2O$ solution. **16i**: ^{1}H NMR (C_6D_6) δ 7.57 (d, 1 H, J = 7.2), 7.24 (t, 1 H, J = 7.2), 7.21 (d, 1 H, J = 7.2), 7.14 (t, 1 H, J = 7.2), 5.55 (d, 1 H, J = 2.2), 3.91 (ddd, 1 H, J = 8.4, 5.8, 2.2), 2.34 (dd, 1 H, J = 17.5, 5.8), 1.96 (dd, 1 H, J = 17.5, 8.4), 1.62 (s, 3 H), 0.25 (s, 9 H); ^{13}C NMR (C_6D_6) δ 206.0, 154.1, 146.9, 142.2, 127.4, 126.4, 123.7, 119.1, 111.3, 46.2, 41.4, 29.9, 0.22; IR (neat) 1717 cm^{-1}. **18**: ^{1}H NMR ($CDCl_3$) δ 7.71 (d, 1 H, J = 7.4), 7.59 (t, 1 H, J = 7.4), 7.46 (d, 1 H, J = 7.4), 7.37 (t, 1 H, J = 7.4), 3.82 (m, 1 H), 3.03 (dd, 1 H, J = 17.9, 4.9), 3.00 (dd, 1 H, J = 19.2, 7.6), 2.71 (dd, 1 H, J = 17.9, 8.7), 2.25 (dd, 1 H, J = 19.2, 3.5), 2.19 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 206.7(C), 205.6(C), 157.5(C), 136.9(C), 135.0-(CH), 127.9(CH), 125.6(CH), 123.7(CH), 50.0(CH), 43.8(CH_3), 33.4(CH_2), 30.4(CH_2); IR (neat) 1713 cm^{-1}; HRMS calcd for $C_{12}H_{12}O_2$ 188.0837, found 188.0831.

Coupling of Carbene Complex 1a with Alkyne 7j (Table, Entry J). General procedure I was followed using carbene complex **1a** (150 mg, 0.6 mmol) and alkyne **7j** (120 mg, 0.5 mmol); the chloroform/silica gel step was omitted. Final purification was achieved by flash chromatography on silica gel using 9:1 hexane/ethyl acetate as eluent. Two compounds were isolated and identified as α-trimethylsilyl ketone precursors to indane **9j** (11 mg, 8% yield) and indane **16j** (97 mg, 68% yield). **16j-**α-Trimethylsilyl ketone (1:1 mixture of α-silyl ketone diastereomers): ^{1}H NMR ($CDCl_3$) δ 7.45 (d, 1 H overlapping of both diastereomers, J = 7.8), 7.33−7.12 (m, 3 H overlapping of both diastereomers), 6.16 (br s, 1 H of one diastereomer), 6.02 (br s, 1 H of one diastereomer), 3.95 (br d, 1 H of one diastereomer, J = 7.5), 3.65 (br d, 1 H of one diastereomer, J = 4.1) 3.08 (d, 1 H of one diastereomer, J = 4.1), 2.61 (d, 1 H of one diastereomer, J = 7.5), 2.19 (s, 3 H of one diastereomer), 1.80 (m, 1 H overlapping for both diastereomers), 1.78 (s, 3 H of one diastereomer), 0.90 (m, 2 H overlapping for both diastereomers), 0.72 (m, 2 H overlapping for both diastereomers), 0.12 (s, 9 H of one diastereomer), 0.00 (s, 9 H of one diastereomer); ^{13}C NMR ($CDCl_3$) δ 210.9, 209.0, 149.0, 147.8, 146.1, 146.0, 145.3, 144.8, 129.6, 129.5, 126.8, 125.3, 125.2, 123.5, 122.8, 119.5, 50.5, 49.3, 48.0, 47.4, 33.2, 31.4, 8.4, 8.3, 6.6, 6.44, 6.36, −0.7, −0.8; IR (neat) 1686 cm^{-1}. The mixture was dissolved in chloroform, and silica gel (5 g) was added. This mixture was stirred at room temperature for 24 h. A 4:2:1 mixture of desilylation products (R^2 = cyclopropyl, $R^{3,4}$ = H) **16j**/**9j**/**17j** was obtained. After flash chromatography on silica gel, **16j** could be isolated in nearly pure form. **9j**: ^{1}H NMR ($CDCl_3$) δ 7.62 (d, 1 H, J = 7.2) 7.4−7.2 (m, 3 H), 6.73 (t, 1 H, J = 2.1), 3.55 (ddd, 1 H, J = 19.7, 7.8, 2.1), 3.05 (ddd, 1 H, J = 19.7, 3.7, 2.1), 2.60 (td, 1 H, J = 7.8, 3.7), 2.30 (s, 3 H), 1.66 (m, 1 H), 0.47 (m, 2 H), 0.30 (m, 2 H). **16j**: ^{1}H NMR ($CDCl_3$) δ 7.47 (d, 1 H, J = 7.2), 7.33 (t, 2 H, J = 7.2), 7.21 (d, 1 H, J = 7.2), 5.98 (s, 1 H), 3.83 (dd, 1 H, J = 8.6, 6.1), 2.85 (dd, 1 H, J = 17.3, 6.1), 2.48 (dd, 1 H, J = 17.3, 8.6), 2.17 (s, 3 H), 1.74 (m, 1 H), 0.87 (m, 2 H), 0.63 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 209.0, 147.8, 145.9, 129.5, 126.8, 125.2, 123.5, 119.5, 49.3, 47.4, 31.4, 8.3, 6.4; IR (neat) 1718 cm^{-1}. Anal. Calcd for $C_{15}H_{16}O$: C, 84.87; H, 7.60. Found: C, 84.81; H, 7.80.

Coupling of Carbene Complex 1a with Alkyne 7k (Entry K). General procedure I was followed using carbene complex **1a** (150 mg, 0.6 mmol) and alkyne **7k** (122 mg, 0.5 mmol). Final purification was achieved by flash chromatography on silica gel using 9:1 hexane/ethyl acetate as eluent. Three compounds were isolated and identified as indane **9k** (32 mg, 30% yield), indane **16k** (38 mg, 35% yield), and indane **17k** (8 mg, 7% yield). **9k**: ^{1}H NMR ($CDCl_3$) δ 6.95 (s, 1 H), 6.75 (s, 1 H), 6.49 (s, 1 H), 6.0 (s, 2 H), 3.25 (t, 2 H, J = 7.2), 2.95 (t, 2 H, J = 7.2), 2.25 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 198.2, 162.4, 151.5, 147.9, 146.4, 134.0, 113.3, 105.5, 101.9, 101.0, 33.1, 30.9, 29.9; IR (neat) 1673 cm^{-1}; LRMS *m/z* 216, 201, 173, 143, 115, 89, 63, 43; HRMS calcd for $C_{13}H_{12}O_3$ 212.0786, found 212.0782. **16k**: ^{1}H NMR ($CDCl_3$) δ 6.85 (s, 1 H), 6.81 (s, 1 H), 6.67 (d, 1 H, J = 5.5), 6.39 (d, 1 H, J = 5.5), 5.95 (s, 2 H), 3.84 (dd, 1 H, J = 7.1, 6.5), 2.76 (dd, 1 H, J = 17.5, 6.5), 2.56 (dd, 1 H, J = 17.5, 7.1), 2.18 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 207.5, 147.0, 146.1, 141.0, 138.0, 137.8, 131.1, 104.9, 102.4, 101.2, 45.3, 30.5; IR (neat) 1715 cm^{-1}; HRMS calcd for $C_{13}H_{12}O_3$ 212.0786, found 212.0782.

Acknowledgment. We thank the SCORE Program of the National Institutes of Health and the National Science Foundation for financial support of this research.

Supporting Information Available: General experimental, synthesis of carbene complex **1b**, and syntheses of alkynes **7f**, **7i**, **7j**, and **7k**. Copies of proton and carbon-13 NMR spectra for all compounds in Table 1 produced in greater than 20% yield. This material is available free of charge via the Internet at http://pubs.acs.org.

OM034334J