JOC Article

One-Pot Synthetic Routes to Multiply Substituted Indene Derivatives by Hydrolysis of Zirconocene-Mediated Intermolecular Coupling Reactions of Aromatic Ketones and Alkynes

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Two one-pot multicomponent synthetic methods for highly substituted indenes are described. The intermolecular coupling of aromatic ketones with alkynes on low-valent zirconocene species generates oxazirconacyclopentenes, which upon hydrolysis with 20% HCl for 3 h afforded indene derivatives in good to excellent yields. Similarly, the pair-selective coupling of two identical or different alkynes bearing at least one aromatic substituent formed zirconacyclopentadienes. Quenching of the reaction mixture with concentrated H_2SO_4 also results in the formation of highly substituted indenes in high yields.

Introduction

Indene derivatives, in particular multiply substituted ones, have been attractive, and synthetically useful methods for their synthesis have been developed.[1] Among these known procedures, the most frequently used protocol is to use phenyl-substituted alkenes[2−6] or phenyl-substituted allyl alcohols.[7−9] The cycloalkylation process of the phenyl-substituted alkenes results in the formation of indene derivatives, for example, via the photo or thermo rearrangement of 3-arylcyclopropenes[2,3] or via the cyclization of phenylvinyl derivatives.[4−6] *o*-Alkynylstyrenes underwent HI-mediated cyclization to form iodoindene derivatives.[7] When treated with acids, the phenyl-substituted allyl alcohols afford phenyl-substituted allyl cations, which undergo electrocyclic ring closure to form indene derivatives by the elimination of a proton.[8−10]

All these known reactions proceed via the intramolecular reaction pattern. In addition to the limited starting materials, the introduction of different substituents onto the indene rings is difficult. From the point of view of synthetically useful methodologies, the one-pot process of multicomponent reaction systems is highly desirable,[11,12] especially when the highly substituted indene derivatives and their yields are concerned. In this paper, we report two new one-pot synthetic routes to highly substituted indenes from multicomponent reaction processes via (1) the hydrolysis of zirconocene-mediated intermolecular coupling products of aryl ketones with alkynes (Scheme 1) and (2) the hydrolysis of zirconocene-

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(10) (a) Blum-Bergmann, O. *J. Chem. Soc*. **1935**, 1020. (b) Adler, E.; Hagglund, B. *Ark. Kemi* **1945**, *19A*, No. 23. (c) Hausmann, W.; Smith, A. E. W. *J. Chem. Soc*. **1949**, 1030.

(11) The intermolecular formation of indenols by the reaction of ortho-manganated acetophenones with alkynes has been reported. (a) Liebeskind, L. S.; Gasdaska, J. R.; McCallum, J. S.; Tremont, S. J. *J. Org. Chem*. **1989**, *54*, 669. (b) Robinson, N. P.; Main, L.; Nicholson, B. K. *J. Organomet. Chem*. **1989**, *364*, C37. (c) Cambie, R. C.; Metzler, M. R.; Rutledge, P. S.; Woodgate, P. D. *J. Organomet. Chem*. **1992**, *429*, 41.

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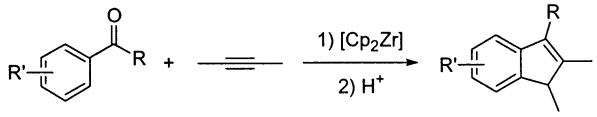
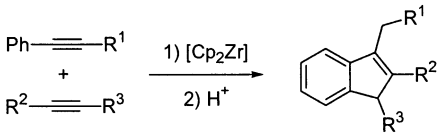
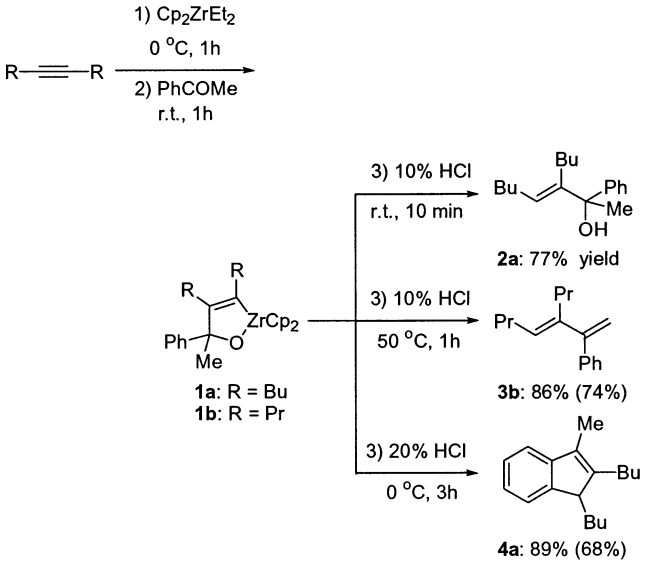
SCHEME 1. One-Pot Formation of Indene Derivatives from Aryl Ketones and Alkynes



SCHEME 2. One-Pot Formation of Indene Derivatives from Two Molecules of Alkynes



SCHEME 3. Hydrolysis of Oxazirconacyclopentenes with 20% HCl Affording Indene Derivatives



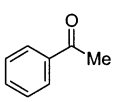
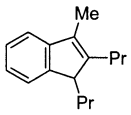
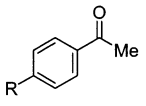
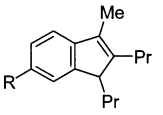
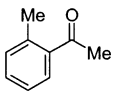
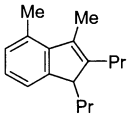
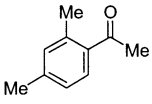
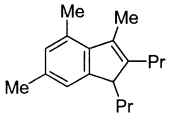
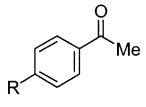
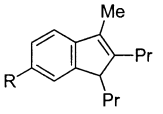
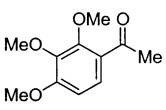
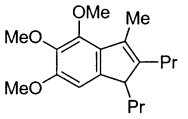
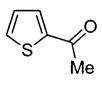
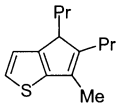
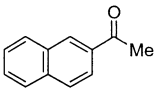
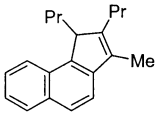
mediated intermolecular coupling products of two molecules of alkynes (Scheme 2).

Results and Discussion

One-Pot Preparation of Indene Derivatives from Aromatic Ketones and Alkynes. We have recently reported a selective intermolecular coupling reaction of alkynes with ketones using zirconocenes. The hydrolysis of the reaction mixture of oxazirconacyclopentenes **1** with 10% HCl affords allylic alcohols **2** in good to excellent yields.[13] During the course of our investigation into further applications of these cross-coupling reactions, we observed that, to our surprise, the quenching of the reaction mixtures with concentrated aqueous acids such as 20% HCl for a longer time afforded the indene derivatives in excellent yields when aromatic ketones were used. As demonstrated in Scheme 3, oxazirconacyclopentene **1a** is generated in situ from the zirconocene-mediated, selective cross-coupling of 5-decyne with acetophenone.[13,14] Allylic alcohol **2a** was obtained in 77% yield as the only product after the hydrolysis of the reaction mixture with 10% HCl for several minutes at room temperature, as previously reported.[13] When quenched at a higher temperature (50 °C) with 10% HCl for 1 h, the reaction mixture of **1b** afforded a dehydration product, 2-phenylbutadiene (**3b**), in 74% isolated yield (86% GC yield). Obviously, dehydration is favored at higher temperatures in an acidic media. However, indene derivative **4a** was formed cleanly in 89% GC yield (68% isolated yield) upon the hydrolysis of the reaction mixture with concentrated aqueous HCl, for example, 20% HCl for 3 h. The same product, **4a**, was also obtained in a similar yield (73% GC yield, 66% isolated yield) when the reaction mixture was quenched with concentrated H_2SO_4.

More examples of indene derivatives prepared by using this one-pot process from alkynes and aromatic ketones are listed in Table 1, with the alkyne in all cases being 4-octyne. A wide variety of aromatic ketones with electron-donating or electron-withdrawing substituents could be used. It is especially noteworthy that the number and

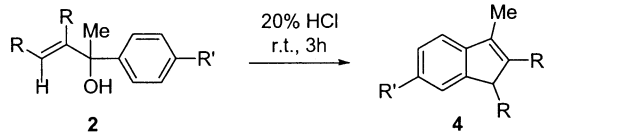
TABLE 1. One-Pot Formation of Indene Derivatives by Hydrolysis of the Zirconocene-Mediated Intermolecular Coupling Products of Aromatic Ketones with Alkynes[a]

Entry	Aromatic ketone	Product **4**	Yield of **4**/%[b]
1		 **4b**	90 (69)
2		 **4c**: R = Me	89 (67)
3		**4d**: R = Ph	70 (58)
4		 **4e**	58 (40)
5		 **4f**	70 (52)
6		 **4g**: R = OMe	90 (67)
7		**4h**: R = Cl	72 (51)
8		**4i**: R = F	52 (33)
9		 **4j**	80 (53)
10		 **4k**	68 (50)
11		 **4l**	88 (63)

[a] Reaction conditions: 1:1 molar ratio of 4-octyne and an aromatic ketone, hydrolyzed with 20% HCl for 3 h at 0 °C. [b] GC yields. Isolated yields are given in parentheses.

(13) Takahashi, T.; Xi, C.; Xi, Z.; Kageyama, M.; Fischer, R.; Nakajima, K.; Negishi, E. *J. Org. Chem.* **1998**, *63*, 6802.

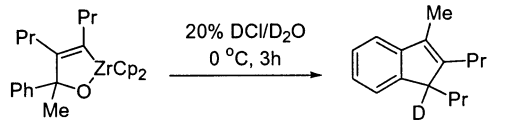
SCHEME 4. Acid-Promoted Transformation of Allylic Alcohols into Indene Derivatives



2: **2a**: R = Bu, R' = H; **2b**: R = Pr, R' = H; **2c**: R = Pr, R' = OMe

4: **4a**: R = Bu, R' = H, > 98%; **4b**: R = Pr, R' = H, > 98%; **4g**: R = Pr, R' = OMe, > 98%

SCHEME 5. Deuteriolysis of the Reaction Mixture



1b

4bD: 90% (69%)
D > 95%

types of substituents on the indene rings can be controlled by choosing the appropriate substituted aromatic ketones. 2-Acetylthiophene (entry 10) could also be applied in this reaction to prepare compound **4k** in 68% yield. When aliphatic ketones such as 3-pentanone were used, alcohols **2** rather than indene derivatives **4** were obtained.[13]

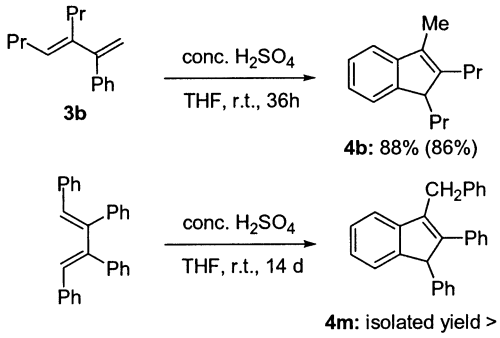
It is interesting that methyl 2-naphthyl ketone afforded **4l** with perfect regioselectivity in 88% yield.

Mechanistic Aspects. It has been known that phenyl-substituted allyl cations, normally formed in situ from phenyl-substituted allyl alcohols in acidic media, readily undergo electrocyclic ring closure to afford indenes by the elimination of a proton.[8−10] The above acid-dependent results strongly suggest that in these reactions indene derivatives **4** are formed from allylic alcohols **2**, via the known process.[8−10] Indeed, as given in Scheme 4, the treatment of **2a**−**c**, which were prepared in high yields by quenching the reaction mixtures of oxazirconacyclopentenes **1** with saturated aqueous $NaHCO_3$,[13] with 20% aqueous HCl at room temperature for 3 h afforded **4a**, **4b**, and **4g** in nearly quantitative yields, respectively. These results demonstrate that indene derivatives **4** are formed via phenyl-substituted allylic alcohols **2** in the above one-pot process.

Deuteriolysis of the reaction mixture with 20% DCl/D_2O instead of hydrolysis afforded **4bD** in 69% isolated yield with a D incorporation of more than 95% (Scheme 5). This result shows that neither proton exchange at the C-1 position nor double-bond migration in the five-membered ring of the formed indene occurs during workup.

One-Pot Preparation of Indene Derivatives from Two Molecules of Alkynes. Two alkynes can easily undergo cyclo-oxidative addition reactions with a low-valent zirconocene species to afford substituted butadienes after the hydrolysis of the in situ generated zirconacyclopentadienes. The selective cross-coupling of two different alkynes can be achieved in excellent yields.[15,16] By using this method, aryl-substituted butadienes can be easily prepared; for example, tetraphenylbutadiene can be obtained in a quantitative yield from two molecules of diphenylacetylenes,[15a] and 1,2-diphenyl-3-propyl-1,3-heptadiene can be formed from diphenylacetylene and 4-octyne by the selective cross-coupling of alkynes.[16a] Phenylalkenes are known to undergo acid-promoted cycloalkylation processes to afford indene derivatives.[2−6] Inspired by the above acid-promoted intermolecular indene formation reactions, we treated **3b** and tetraphenylbutadiene with concentrated H_2SO_4 (Scheme 6), expecting the formation of indene derivatives. Although a long reaction time was required, indene derivatives **4b** and **4m**[3b] were formed in excellent yields as the only products, respectively. No formation of other products such as double-bond positional isomers was observed.

SCHEME 6. Acid-Promoted Formation of Indene Derivatives from Phenyl-Substituted Butadienes

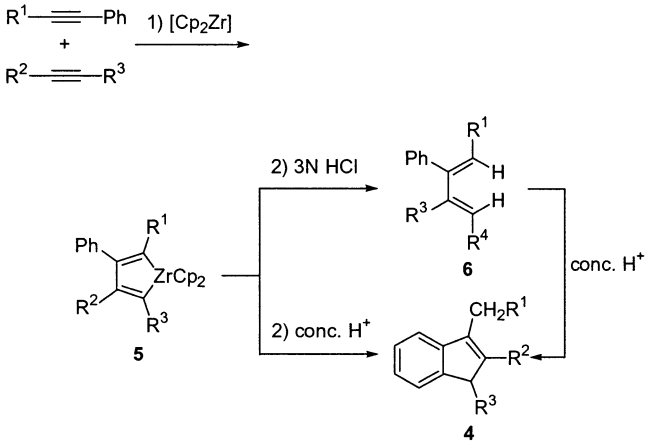


3b

4b: 88% (86%)

4m: isolated yield > 98%

SCHEME 7. Acid-Promoted One-Pot Formation of Indene Derivatives from Two Molecules of Alkynes



5

6

4

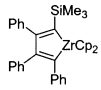
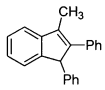
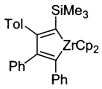
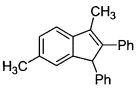
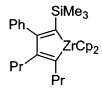
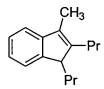
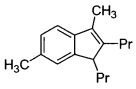
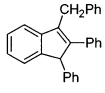
The above results prompted us to quench the zirconocene-mediated intermolecular coupling reactions of two alkynes bearing at least one phenyl group with concentrated acids, aiming at the formation of highly substituted indene derivatives. Thus, a new one-pot procedure for the preparation of indene derivatives directly from two molecules of alkynes could be developed. As shown in Scheme 7, the quenching of the reaction mixture with 10% HCl afforded substituted

(14) (a) Takahashi, T.; Kotora, M.; Hara, R.; Xi, Z. *Bull. Chem. Soc. Jpn.* **1999**, *72*, 2591. (b) Takahashi, T.; Xi, Z.; Kotora, M. *Recent Res. Dev. Pure Appl. Chem.* **1998**, *2*, 170. (c) Kotora, M.; Xi, Z.; Takahashi, T. *J. Synth. Org. Chem., Jpn.* **1997**, *55*, 958.

(15) (a) Negishi, E.; Cederbaum, F. E.; Takahashi, T. *Tetrahedron Lett.* **1986**, *27*, 2829. (b) Wagenen, B. C. V.; Livinghouse, T. *Tetrahedron Lett.* **1989**, *30*, 3495. (c) Buchwald, S. L.; Nielsen, R. B. *J. Am. Chem. Soc.* **1989**, *111*, 2870.

(16) (a) Xi, Z.; Hara, R.; Takahashi, T. *J. Org. Chem.* **1995**, *60*, 4444. (b) Takahashi, T.; Kageyama, M.; Denisov, V.; Hara, R.; Negishi, E. *Tetrahedron Lett.* **1993**, *34*, 687.

TABLE 2. One-Pot Formation of Indene Derivatives by Hydrolysis of the Zirconocene-Mediated Intermolecular Coupling Products of Two Alkynes[a]

Entry	First alkyne	Second alkyne	Zirconacyclopentadienes	Time	Product **4**		Yield of **4**/%[b]
1	Me_3Si—≡—Ph	Ph—≡—Ph		48h		**4n**	80 (71)[c]
2	Me_3Si—≡—Tol	Ph—≡—Ph		36h		**4o**	85 (73)[c]
3	Me_3Si—≡—Ph	Pr—≡—Pr		60h		**4b**	67 (63)
4	Me_3Si—≡—Tol	Pr—≡—Pr		60h		**4c**	70 (60)[c]
5	Ph—≡—Ph	Ph—≡—Ph		14d		**4m**	(50)[d]

[a] Hydrolyzed with concentrated H_2SO_4 at rt. [b] GC yields. Isolated yields are given in parentheses. [c] $MePPh_2$ was used for selective cross-coupling. [d] 50% of the tetraphenylbutadiene remained unreacted.

butadienes **6**, as is usually observed.[15,16] Much to our satisfaction, when quenched with concentrated H_2SO_4, the reaction mixtures afforded highly substituted indenes in good to excellent yields. The results of the one-pot synthetic process are shown in Table 2. The generated zirconacyclopentadienes need to bear a phenyl group at the β position for the formation of indene derivatives. Silyl-substituted alkynes are known to afford β-silylzirconacyclopentadienes selectively by using the method mentioned above;[16a] therefore, the desired zirconacyclopentadienes can be easily prepared. When $SiMe_3$ was one of the substituents (entries 1−4), the desilylation took place in the concentrated acidic media, affording 3-methylindene derivatives **4n**, **4o**, **4b**, and **4c**. It is interesting that **4b** and **4c** could also be prepared from aromatic ketones and 4-octyne as given in Table 1. Indene **4m** was generated much slower than that by the hydrolysis of the isolated tetraphenylbutadiene; 50% of the tetraphenylbutadiene remained unreacted even after the reaction mixture was stirred at room temperature with concentrated H_2SO_4 for 14 days.

In conclusion, the direct hydrolysis of oxazirconacyclopentenes and zirconacyclopentadienes with concentrated acids resulted in highly substituted indene derivatives. These procedures provide two new synthetic methods in which indene derivatives can be obtained in a one-pot process from aromatic ketones and alkynes or from two molecules of alkynes bearing aromatic substituents. The different types and numbers of substituents on the indene skeleton can be controlled by applying aryl ketones and alkynes bearing the desired types and numbers of substituents.

Experimental Section

General Procedure. Unless otherwise noted, all starting materials were commercially available and were used without further purification. All reactions involving organometallic compounds were run under a slightly positive pressure of dry N_2 with the use of standard Schlenk techniques. Tetrahydrofuran (THF) was refluxed and distilled from sodium benzophenone ketyl under a nitrogen atmosphere.

Representative Procedure for the Preparation of Indene Derivatives from Aromatic Ketones and Alkynes. Preparation of 1,2-Dibutyl-3-methylindene (4a). A 50-mL Schlenk tube under dried nitrogen was charged with Cp_2ZrCl_2 (700 mg, 2.4 mmol) and THF (10 mL). To this solution was added ethylmagnesium bromide (1.0 M THF solution, 4.8 mmol, 4.8 mL) at −78 °C. After the mixture was stirred for 1 h, 5-decyne (2 mmol) was added, and the reaction mixture was stirred at 0 °C for 3 h. To this reaction mixture was added acetophenone (2 mmol), and the mixture was stirred at 25 °C for 3 h.[13] The above reaction mixture was quenched with 20% aqueous HCl, stirred at 0 °C for 3 h, and then extracted with ether. The extract was washed with water, a $NaHCO_3$ solution, and brine and dried over $MgSO_4$. The solvent was evaporated in vacuo to give a light brown liquid. Chromatography using petroleum ether as the eluent provided the product **4a** as a light yellow liquid: isolated yield 68% (330 mg), GC yield 89%; ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.80 (t, J = 7.3 Hz, 3H), 0.85−0.90 (m, 1H), 0.93 (t, J = 7.3 Hz, 3H), 0.95−1.08 (m, 1H), 1.14−1.60 (m, 6H), 1.60−1.80 (m, 1H), 1.82−2.13 (m, 4H), 2.15−2.40 (m, 1H), 2.42−2.70 (m, 1H), 3.00−3.66 (br, 1H), 6.91−7.55 (m, 4H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 10.24 (CH_3), 13.98 (CH_3), 14.01 (CH_3), 22.73 (CH_2), 23.13 (CH_2), 26.22 (CH_2), 26.82 (CH_2), 29.63 (CH_2), 31.99 (CH_2), 49.31 (CH), 117.94 (CH), 122.43 (CH), 123.58 (CH), 126.15 (CH), 131.95 (C), 146.17 (C), 146.78 (C), 146.95 (C). HRMS calcd for $C_{18}H_{26}$, 242.2035; found, 242.2038.

1,2-Dipropyl-3-methylindene (4b): light yellow liquid; isolated yield 69% (295 mg), GC yield 90%; ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.80 (t, J = 7.3 Hz, 3H), 0.85−0.99 (m, 4H), 1.02−1.15 (m, 1H), 1.35−1.50 (m, 1H), 1.50−1.68 (m, 2H), 1.88−1.94 (m, 1H), 2.00−2.01 (br, 3H), 2.20−2.26 (m, 1H), 2.41−2.49 (m, 1H), 3.32−3.39 (br, 1H), 7.09 (td, J = 7.2, 1.2 Hz, 1H), 7.17−7.24 (m, 2H), 7.33 (d, J = 7.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 10.23 (CH_3), 14.18 (CH_3), 14.52 (CH_3), 18.10 (CH_2), 23.04 (CH_2), 28.62 (CH_2), 32.32 (CH_2), 49.34 (CH), 118.00 (CH), 122.45 (CH), 123.64 (CH), 126.18 (CH), 132.18 (C), 145.88 (C), 146.78 (C), 146.88 (C). HRMS calcd for $C_{16}H_{22}$, 214.1722; found, 214.1723.

1-Deuterio-1,2-dipropyl-3-methylindene (4bD). To the reaction mixture described above for the preparation of **4b** was added a 20% DCl in D_2O instead of 20% aqueous HCl solution. A light yellow liquid was obtained: isolated yield 69% (298 mg), GC yield 89%; ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.81 (t, J = 7.4 Hz, 3H), 0.90−1.04 (m, 4H), 1.04−1.21 (m, 1H), 1.35−1.50 (m, 1H), 1.56−1.70 (m, 2H), 1.87−1.96 (m, 1H), 1.98−2.10 (br, 3H), 2.15−2.28 (m, 1H), 2.40−2.52 (m, 1H), 7.00−7.38 (m, 4H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 10.22 (CH_3), 14.17 (CH_3), 14.52 (CH_3), 18.08 (CH_2), 23.01 (CH_2), 28.62 (CH_2), 32.24 (CH_2), 48.94 (t, J_{C-D} = 19 Hz, CD), 117.99 (CH), 122.45 (CH), 123.63 (CH), 126.19 (CH), 132.21 (C), 145.88 (C), 146.77 (C), 146.94 (C). HRMS calcd for $C_{16}H_{21}D$, 215.1784; found, 215.1775.

1,2-Dipropyl-3,6-dimethylindene (4c): light yellow liquid; isolated yield 67% (310 mg), GC yield 89%; ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.83 (t, J = 7.2 Hz, 3H), 0.88−1.03 (m, 4H), 1.05−1.20 (m, 1H), 1.30−1.44 (m, 1H), 1.50−1.65 (m, 2H), 1.85−1.95 (m, 1H), 1.98 (s, 3H), 2.18−2.22 (m, 1H), 2.35−2.40 (br, 3H), 3.25−3.40 (br, 1H), 3.43−3.55 (m, 1H), 7.04−7.10 (m, 2H), 7.17 (s, 1H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 10.27 (CH_3), 14.13 (CH_3), 14.52 (CH_3), 18.16 (CH_2), 21.50 (CH_3), 23.00 (CH_2), 28.56 (CH_2), 32.37 (CH_2), 49.13 (CH), 117.63 (CH), 123.50 (CH), 126.76 (CH), 131.91 (C), 133.06 (C), 144.33 (C), 144.87 (C), 147.09 (C). HRMS calcd for $C_{17}H_{24}$, 228.1878; found, 228.1879.

1,2-Dipropyl-3-methyl-6-phenylindene (4d): light yellow liquid; isolated yield 58% (338 mg), GC yield 70%; ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.52−0.89 (m, 3H), 0.96−1.50 (m, 6H), 1.58−2.10 (m, 6H), 2.14−2.31 (m, 1H), 2.38−2.60 (m, 1H), 3.32−3.66 (br, 1H), 7.16−7.67 (m, 8H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ

10.30 (CH_3), 14.17 (CH_3), 14.52 (CH_3), 18.25 (CH_2), 22.99 (CH_2), 28.72 (CH_2), 32.37 (CH_2), 49.50 (CH), 118.16 (CH), 121.47 (CH), 125.40 (CH), 126.61 (CH), 127.18 (2CH), 128.67 (2CH), 131.97 (C), 136.86 (C), 142.21 (C), 146.28 (C), 146.74 (C), 147.48 (C). HRMS calcd for $C_{22}H_{26}$, 290.2035; found, 290.2027.

1,2-Dipropyl-3,4-dimethylindene (4e): light yellow liquid; isolated yield 40% (182 mg), GC yield 58%; ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.80 (t, J = 7.2 Hz, 3H), 0.84−0.90 (m, 1H), 0.93 (t, J = 7.2 Hz, 3H), 0.97−1.11 (m, 1H), 1.38−1.67 (m, 3H), 1.84−1.96 (m, 1H), 2.14−2.24 (m, 4H), 2.40−2.51 (m, 1H), 2.58 (s, 3H), 3.20−3.40 (br, 1H), 6.95−7.02 (m, 2H), 7.16−7.24 (m, 1H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 14.26 ($2CH_3$), 14.60 (CH_3), 17.81 (CH_2), 20.44 (CH_3), 23.16 (CH_2), 28.47 (CH_2), 32.53 (CH_2), 49.06 (CH), 120.49 (CH), 123.58 (CH), 129.25 (CH), 129.97 (C), 133.65 (C), 144.31 (C), 146.05 (C), 147.59 (C). HRMS calcd for $C_{17}H_{24}$, 228.1878; found, 228.1871.

1,2-Dipropyl-3,4,6-trimethylindene (4f): light yellow liquid; isolated yield 52% (252 mg), GC yield 70%; ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.29−1.23 (m, 8H), 1.26−2.02 (m, 4H), 2.16−3.12 (m, 11H), 3.22−3.73 (br, 1H), 6.79 (s, 1H), 7.01 (s, 1H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 14.14 ($2CH_3$), 14.54 (CH_3), 17.83 (CH_2), 20.19 (CH_3), 21.15 (CH_3), 23.07 (CH_2), 28.35 (CH_2), 32.55 (CH_2), 48.82 (CH), 121.35 (CH), 129.49 (CH), 129.98 (C), 132.95 (C), 133.33 (C), 141.61 (C), 144.86 (C), 147.90 (C). HRMS calcd for $C_{18}H_{26}$, 242.2035; found, 242.2027.

1,2-Dipropyl-3-methyl-6-methoxyindene (4g): light yellow liquid; isolated yield 67% (327 mg), GC yield 90%; ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.82 (t, J = 7.2 Hz, 3H), 0.96−1.08 (m, 4H), 1.17−1.56 (m, 2H), 1.62−1.96 (m, 3H), 2.03−2.17 (br, 3H), 2.26−2.56 (m, 2H), 3.16−3.55 (br, 1H), 3.88 (s, 3H), 6.79−6.97 (m, 1H), 7.05 (s, 1H), 7.11−7.24 (m, 1H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 10.23 (CH_3), 14.08 (CH_3), 14.43 (CH_3), 17.92 (CH_2), 22.94 (CH_2), 28.55 (CH_2), 32.36 (CH_2), 49.22 (CH), 55.46 (OCH_3), 109.90 (CH), 110.75 (CH), 117.99 (CH), 131.55 (C), 140.13 (C), 143.62 (C), 148.51 (C), 157.26 (C). HRMS calcd for $C_{17}H_{24}O$, 244.1827; found, 244.1826.

1,2-Dipropyl-3-methyl-6-chloroindene (4h): light yellow liquid; isolated yield 51% (252 mg), GC yield 72%; ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.72 (t, J = 7.3 Hz, 3H), 0.88−0.97 (m, 4H), 1.00−1.19 (m, 1H), 1.32−1.84 (m, 4H), 1.94−2.08 (br, 3H), 2.08−2.60 (m, 2H), 3.10−3.60 (br, 1H), 7.06 (dd, J = 7.8, 1.2 Hz, 1H), 7.20 (d, J = 7.8 Hz, 1H), 7.30 (s, 1H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 10.22 (CH_3), 14.16 (CH_3), 14.44 (CH_3), 17.98 (CH_2), 22.92 (CH_2), 28.64 (CH_2), 32.08 (CH_2), 49.41 (CH), 118.72 (CH), 122.91 (CH), 126.24 (CH), 129.67 (C), 131.64 (C), 145.38 (C), 146.54 (C), 148.57 (C). HRMS calcd for $C_{16}H_{21}Cl$, 248.1332; found, 248.1324.

1,2-Dipropyl-3-methyl-6-fluoroindene (4i): colorless liquid; isolated yield 33% (153 mg), GC yield 52%; ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.57−1.00 (m, 7H), 1.06−1.20 (m, 1H), 1.28−1.74 (m, 3H), 1.78−1.92 (m, 1H), 1.98−2.12 (br, 3H), 2.16−2.31 (m, 1H), 2.39−2.55 (m, 1H), 3.14−3.63 (br, 1H), 6.85−6.99 (m, 1H), 7.01−7.15 (m, 2H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 10.30 (CH_3), 14.17 (CH_3), 14.45 (CH_3), 17.93 (CH_2), 22.97 (CH_2), 28.65 (CH_2), 32.18 (CH_2), 49.40 (d, J_{C-F} = 2.5 Hz, CH), 110.33 (d, J_{C-F} = 22.5 Hz, CH), 112.62 (d, J_{C-F} = 22.5 Hz, CH), 118.25 (d, J_{C-F} = 8.3 Hz, CH), 131.50 (C), 142.74 (C), 145.52 (C), 148.85 (d, J_{C-F} = 8.3 Hz, C), 161.03 (d, J_{C-F} = 239.3 Hz, C). HRMS calcd for $C_{16}H_{21}F$, 232.1627; found, 232.1638.

1,2-Dipropyl-3-methyl-4,5,6-trimethoxyindene (4j): yellow liquid; isolated yield 53% (321 mg), GC yield 80%; ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.67−1.17 (m, 7H), 1.20−1.46 (m, 2H), 1.52−1.94 (m, 3H), 2.01−2.28 (m, 4H), 2.33−2.58 (m, 1H), 3.19−3.37 (br, 1H), 3.86 (s, 3H), 3.88 (s, 3H), 3.91 (s, 3H), 6.75 (s, 1H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 12.35 (CH_3), 14.15 (CH_2), 14.49 (CH_2), 17.78 (CH_2), 23.05 (CH_2), 28.23 (CH_2), 32.60 (CH_2), 49.73 (CH), 56.49 (OCH_3), 60.90 (OCH_3), 61.58 (OCH_3), 103.70 (CH), 131.53 (C), 131.76 (C), 141.31 (C), 143.35 (C), 143.69 (C), 147.29 (C), 150.77 (C). HRMS calcd for $C_{19}H_{28}O_3$, 304.2038; found, 304.2038.

Fused compound 4k: dark red liquid; isolated yield 50% (220 mg), GC yield 68%. ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.57−1.14 (m, 6H), 1.20−1.68 (m, 5H), 1.72−1.82 (m, 1H), 1.94−2.10 (br, 3H), 2.24−2.60 (m, 2H), 2.87−3.76 (br, 1H), 6.98 (d, J = 4.8 Hz, 1H), 7.10 (d, J = 4.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 11.84 (CH_3), 14.13 (CH_3), 14.35 (CH_3), 20.01 (CH_2), 23.56 (CH_2), 28.92 (CH_2), 32.30 (CH_2), 47.73 (CH), 122.30 (CH), 122.44 (CH), 128.76 (C), 147.04 (C), 148.09 (C), 148.61 (C). HRMS calcd for $C_{14}H_{20}S$, 220.1286; found, 220.1282.

1,2-Dipropyl-3-methylbenzo[*g*]indene (4l): light yellow liquid; isolated yield 63% (332 mg), GC yield 88%; ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.39−0.59 (m, 1H), 0.66 (t, J = 7.2 Hz, 3H), 0.71−0.86 (m, 1H), 0.88−1.07 (m, 3H), 1.35−1.76 (m, 2H), 1.91−2.10 (m, 4H), 2.24−2.36 (m, 2H), 2.48−2.67 (m, 1H), 3.69−3.96 (br, 1H), 7.23−7.56 (m, 3H), 7.72 (d, J = 7.8 Hz, 1H), 7.86 (d, J = 7.8 Hz, 1H), 8.02 (d, J = 7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 10.43 (CH_3), 14.21 (CH_3), 14.41 (CH_3), 16.39 (CH_2), 23.29 (CH_2), 28.67 (CH_2), 32.90 (CH_2), 49.16 (CH), 118.09 (CH), 123.25 (CH), 123.58 (CH), 125.72 (CH), 127.13 (CH), 129.15 (CH), 129.56 (C), 131.51 (C), 132.60 (C), 141.50 (C), 144.39 (C), 146.36 (C). HRMS calcd for $C_{20}H_{24}$, 264.1878; found, 264.1881.

Representative Procedure for the Preparation of Indene Derivatives from Two Molecules of Alkynes. Preparation of 1,2-Diphenyl-3-methylindene (4n). A 20-mL Schlenk tube under dried nitrogen was charged with Cp_2ZrCl_2 (350 mg, 1.2 mmol) and THF (5 mL). The mixture was cooled to −78 °C (dry ice/acetone bath), and then *n*-BuLi (1.51 mL, 1.59 M, 2.4 mmol) was added dropwise via a syringe. The reaction mixture was stirred at −78 °C for 1 h. After the addition of methyldiphenylphosphine (200 mg, 1.0 mmol), the reaction mixture was stirred at room temperature for 1 h. Phenyltrimethylsilylacetylene (0.197 mL, 1.0 mmol) was then added, and the reaction mixture was stirred for 1 h. After the addition of diphenylacetylene (178 mg, 1.0 mmol), the reaction mixture was gradually warmed to 50 °C and was stirred for 3 h. The reaction mixture was then cooled to 0 °C and quenched with concentrated sulfuric acid (0.7 mL). After it was stirred for 48 h at room temperature, the reaction mixture was extracted with hexane. The extract was washed with brine and dried over $MgSO_4$. The solvent was evaporated in vacuo. Column chromatography on silica gel (100:1 hexane/AcOEt) afforded the product **4n** as a yellow oil:[17] isolated yield 71% (201 mg), GC yield 80%; ^{1}H NMR ($CDCl_3$, Me_4Si) δ 2.33 (d, J = 2.0 Hz, 3H), 4.92−4.96 (m, 1H), 7.01−7.40 (m, 14H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 11.90, 57.79, 119.16, 123.62, 125.44, 126.44, 126.53, 126.84, 128.07, 128.14, 128.46, 128.99, 129.37, 135.57, 136.34, 139.99, 144.97, 145.90, 148.02. HRMS calcd for $C_{22}H_{18}$, 282.1409; found, 282.1418.

1,2-Diphenyl-3,6-dimethylindene (4o). The procedure was the same as that for the preparation of **4n**. Column chromatography on silica gel (100:1 hexane/AcOEt) afforded **4o** as white crystals: isolated yield 73% (220 mg), GC yield 85%; mp 168.2−170.3 °C; ^{1}H NMR ($CDCl_3$, Me_4Si) δ 2.45−2.48 (m, 3H), 2.68 (s, 3H), 4.84−4.90 (m, 1H), 6.95−7.28 (m, 13H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 15.65, 20.44, 57.97, 121.82, 125.26, 126.34, 126.48, 127.96, 128.20, 128.37, 129.26, 129.83, 131.19, 136.64, 136.91, 140.19, 143.15, 145.92, 148.83. Anal. Calcd for $C_{23}H_{20}$: C, 93.20%; H, 6.80%. Found: C, 93.08%; H, 6.85%. HRMS calcd for $C_{23}H_{20}$, 296.1560; found, 296.1565.

1,2-Dipropyl-3,6-dimethylindene (4c). 4c was obtained in a similar way. Column chromatography on silica gel (hexane) afforded **4c** as pale yellow liquid: isolated yield 60% (151 mg), GC yield 70%.

1,2-Dipropyl-3-methylindene (4b). A 20-mL Schlenk tube under dried nitrogen was charged with Cp_2ZrCl_2 (350 mg, 1.2 mmol) and THF (5 mL). The mixture was cooled to −78 °C (dry ice/acetone bath), and then *n*-BuLi (1.51 mL, 1.59 M, 2.4 mmol) was added dropwise via a syringe. The reaction mixture was stirred at −78 °C for 1 h. After the addition of phenyltrimethylsilylacetylene (0.197 mL, 1.0 mmol), the reaction mixture was warmed to room temperature and stirred for 3

(17) Pettit, W. A.; Wilson, J. W. *J. Am. Chem. Soc.* **1977**, *99*, 6372.

h. Then, 4-octyne (0.148 mL, 1 mmol) was added, and the reaction mixture was warmed to 50 °C and was stirred for 3 h. The reaction mixture was then cooled to 0 °C and was quenched with concentrated sulfuric acid (0.7 mL) for 60 h at room temperature. The reaction mixture was extracted with hexane. The extract was washed with brine and dried over $MgSO_4$. The solvent was evaporated in vacuo. Column chromatography on silica gel (hexane) afforded **4b** as yellow liquid: isolated yield 63% (134 mg), GC yield 67%.

1,2-Diphenyl-3-benzylindene (4m). A 20-mL Schlenk tube under dried nitrogen was charged with Cp_2ZrCl_2 (350 mg, 1.2 mmol) and THF (5 mL). The mixture was cooled to −78 °C (dry ice/acetone bath), and *n*-BuLi (1.51 mL, 1.59 M, 2.4 mmol) was added dropwise via a syringe. The reaction mixture was stirred at −78 °C for 1 h. After the addition of diphenylacetylene (356 mg, 2.0 mmol), the reaction mixture was stirred at room temperature for 3 h.[15a] The reaction mixture was then cooled to 0 °C and quenched with concentrated sulfuric acid (1.2 mL). After it was stirred for 14 days at room temperature, the reaction mixture was extracted with hexane. The extract was washed with brine and dried over $MgSO_4$. The solvent was evaporated in vacuo. Column chromatography on silica gel (hexane) afforded the product **4m** as a white powder:[3b] isolated yield 50% (178 mg); mp 118.1−119.4 °C; ^{1}H NMR ($CDCl_3$, Me_4Si) δ 4.09−4.20 (m, 2H), 5.07 (m, 1H), 7.09−7.33 (m, 19H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 32.25, 58.15, 120.33, 123.73, 125.42, 126.13, 126.57, 126.84, 126.99, 128.22, 128.25, 128.57, 128.64, 128.68, 135.89, 137.37, 139.52, 139.72, 144.91, 147.44, 148.15. HRMS calcd for $C_{28}H_{22}$, 358.1721; found, 358.1725.

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Supporting Information Available: Copies of ^{1}H and ^{13}C NMR spectra of **4a**−**o** and the structure of **4o**. This material is available free of charge via the Internet at http://pubs.acs.org.

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