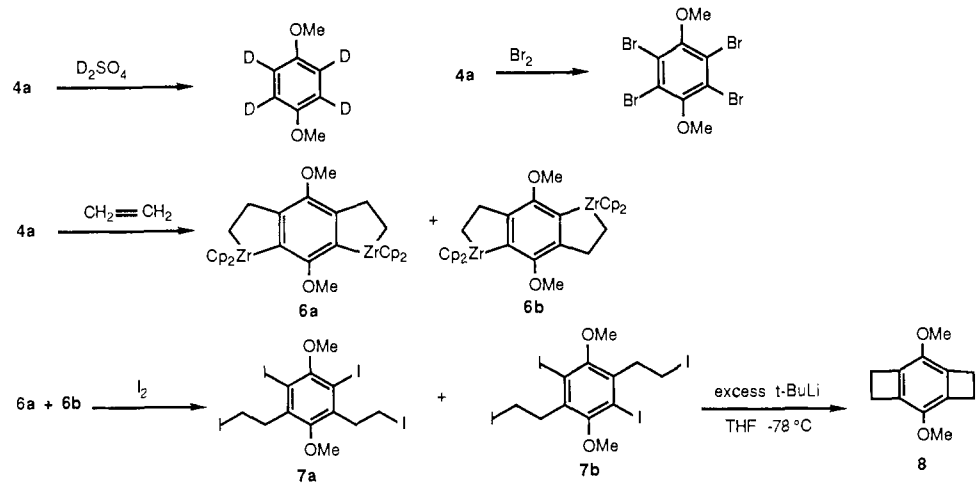
Scheme IV



Zr1-C1	2.194(8)	Å	C1-Zr1-C2	35.2(2)	°
Zr1-C2	2.253(7)		C1-C2-Zr1	74.8(5)	
C1-C2	1.345(11)		C2-C1-Zr1	70.0(4)	
C2-C3	1.398(11)		C1-C2-C3	121.1(6)	
C3-C4	1.401(10)		C2-C3-C4	118.8(7)	
C3-O1	1.412(9)		C6-C1-C2	120.1(6)	
Zr1-P1	2.667(2)				
Zr1-Zr2	6.640				

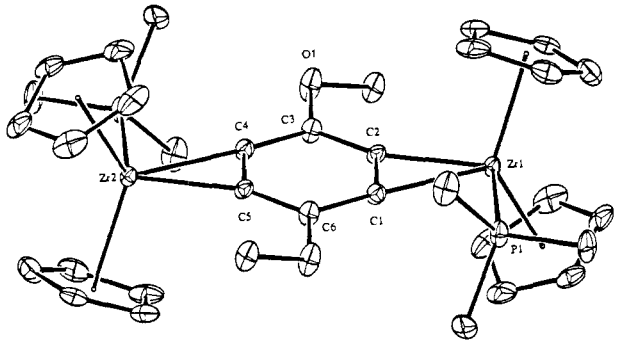


Figure 1.

the plane of the aromatic ring. Although not significantly to within 3σ, the two carbon–carbon "triple" bonds appear shorter than the other carbon–carbon bonds in the aromatic ring. This indicates that there is a great deal of π-back-bonding occurring to reduce the enormous strain which would exist in the free benzdiyne species.

Compound **4** undergoes bis-coupling reactions with unsaturated organic species to form the novel bis-metallacycles, as shown in Scheme III, which were not isolated but were characterized by ^{1}H NMR.

That **4** is in some ways equivalent to an aromatic tetraanion is indicated by its reactions as shown in Scheme IV. Treatment of **4** with excess D_2O/D_2SO_4 in THF provides a 93% yield of 2,3,4,5-tetradeuterio-1,4-dimethoxybenzene. In a similar fashion, **4** yields the known 2,3,4,5-tetrabromo-1,4-dimethoxybenzene[6] in 92% yield upon treatment with bromine. Heating **4** in benzene under 1 atm. of ethylene provides a 5:1 ratio of the bis-metallacycles **6a** and **6b** in quantitative yield. These isomers were not separated and were characterized by ^{1}H and ^{13}C NMR of the mixture. They can be converted to a mixture of regioisomeric tetraiodides **7a** and **7b** in 96% yield upon exposure to excess iodine.[8] Treatment of **7** (as the mixture of regioisomers) with excess *tert*-butyllithium in THF at −78 °C provided a 81% yield of the benzbicyclobutane[9] after flash chromatography.

In short, we have prepared, characterized, and undertaken an initial study of the reactions of the first transition-metal complex of a benzdiyne. We are continuing work in this area to increase regiochemical control of the coupling reactions of these diynes. In addition we have begun work on the synthesis of the 1,3-benzdiyne isomer as well as of the triyne species.

Acknowledgment. We would like to thank the National Institutes of Health (GM-34917), the Camille and Henry Dreyfus Foundation (for a Distinguished New Faculty in Chemistry Grant), and Dr. Alfred Bader and Firmenich SA for their generous financial support of this work. In addition, E.A.L. thanks the National Science Foundation for a graduate fellowship, and we thank the Biomedical Research Support-Shared Instrumentation Grant Program, Division of Research Resources, for funds to purchase X-ray diffraction equipment (NIH Grant S10 RR02243).

Supplementary Material Available: Preparation and spectroscopic characterization of compounds, crystallographic data and procedures, ORTEP diagram of **4**, bond distances and angles, and a table of final positional and thermal parameters (6 pages); table of observed and calculated structure factors for **4** (12 pages). Ordering information is given on any current masthead page.

(6) Kohn, M.; Grün, S. *Monatsh. Chem.* **1924**, *45*, 66.
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Metal Carbonyl Promoted Rearrangement of Cyclopropenes to Naphthols

M. F. Semmelhack,* Suzzy Ho,[1] Michael Steigerwald,[1] and M. C. Lee[2]

Department of Chemistry, Princeton University
Princeton, New Jersey 08544

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The carbene–alkyne cycloaddition with CO incorporation using carbenechromium complexes produces phenol derivatives.[3] Common examples involve arylcarbene ligands (as in **1**, Scheme I) and produce naphthohydroquinones as illustrated with the formation of **2** in Scheme I, path a. The process has been developed as a methodology and applied in specific syntheses.[4-7] There are several general limitations: (a) the starting arylcarbene complexes are available only by reaction of an aryllithium reagent with $Cr(CO)_6$;[8,9] (b) general success has been obtained only with alkoxy-substituted carbene ligands, leading specifically to naphthohydroquinones; and (c) the process is stoichiometric in chromium. Mechanisms have been proposed, involving initial

(1) NIH Postdoctoral Fellowship holder.
(2) Undergraduate research student; results are taken in part from the Senior Thesis of M. C. Lee.
(3) For a recent review and leading reference, see: Dötz, K. H. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 587.
(4) Dötz, K. H.; Popall, M.; Müller, G.; Ackermann, K., *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 911.
(5) (a) Semmelhack, M. F.; Bozell, J. J.; Keller, L.; Sato, T.; Spiess, E.; Wulff, W.; Zask, A. *Tetrahedron* **1985**, *41*, 5803. (b) Semmelhack, M. F.; Bozell, J. J.; Sato, T.; Wulff, W.; Spiess, E.; Zask, A. *J. Am. Chem. Soc.* **1982**, *104*, 5850.

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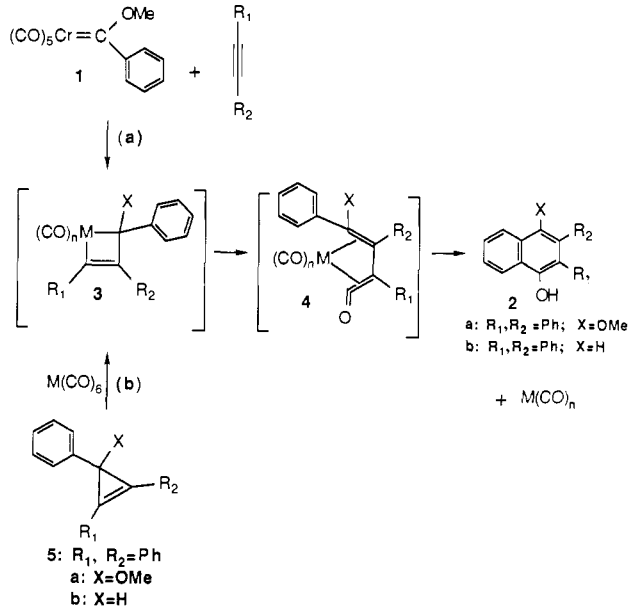
Scheme I. Alternate Pathways to Vinyl Ketene Complexes

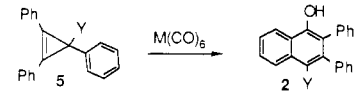


formation of a metallacyclobutene (**3** or equivalent metal-coordinated vinylcarbene) followed by CO insertion to give an arylvinyl ketene complex (**4**). Then, electrocyclic reaction leads to the skeleton of the naphthohydroquinone and proton shift gives the observed product. None of the proposed intermediates has been directly detected, although trapping experiments[10] and isolation of a stable free vinyl ketene from a special substrate[11] are taken as support for the intermediacy of vinyl ketene complexes (**4**). We are interested in devising reactions which will provide alternate entry to the pathway for naphthol synthesis in order to develop catalytic procedures, more general substitution patterns in the aromatic product, and evidence regarding the proposed intermediates.

Vinyl ketene complexes of metals (e.g., **4**) have been formed from reaction of cyclopropenes with metal carbonyls (Scheme I, path b), including many of the first-row carbonyl derivatives, but not with chromium, molybdenum, or tungsten hexacarbonyls.[12,13] None of the known vinyl ketene complexes has been observed to rearrange to a naphthol. Since the starting metal carbonyl is also the expected product (minus one or more CO ligands) after naphthol formation, the cyclopropene rearrangement has the potential of being smoothly catalytic (Scheme I, path b). Here we report the first examples of rearrangement of cyclopropenes into naphthols, including modest catalytic activity.

Our studies began with the readily accessible series of 1,2-diphenyl-3-arylcyclopropenes (**5** and Table I).[14] Entry 1 of Table I involves 1,2,3-triphenyl-3-methoxycyclopropene (**5a**), which should lead to intermediates exactly the same as those proposed for the reaction of diphenylacetylene with $(CO)_5Cr{=}CPh(OMe)$.[3] Reasonable rates were obtained only at elevated temperatures with stoichiometric amounts of $Cr(CO)_6$, and no intermediates were detected. The naphthohydroquinone monomethyl ether (**2a**) was

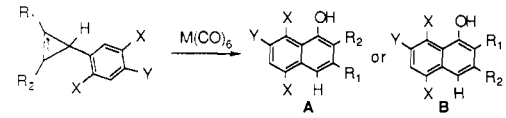
Table I. Rearrangement of 1,2-Diphenyl-3-arylcyclopropenes



entry	Y	M (conditions)[c]	yield,[a] %
1	OMe	Cr (Bu_2O, 3 h)	40
2	H	Cr (Bu_2O, 3–4 h)	45
3	Ph	Cr (Bu_2O, 20 h)	5 (95)[f]
4	Me	Cr (Bu_2O, 20 h)	27 (24)[f]
5	H	Mo (dioxane, 1 h)	78
6	Me	Mo (dioxane, 1 h)	30[b]
7	Me	Mo (dioxane, 2 h, 1.1 atm CO)	27[b]
8	Et	Mo (dioxane, 2 h)	18[b,d]
9	*i*-Pr	Mo (dioxane, 7.5 h)	8[b,e]
10	Ph	Mo (Bu_2O, 2 h)	21[b]
11	H	W (Bu_2O, 22 h)	19[b] (32)[f]

[a] The yields are based on the weight of pure material. [b] Indenes are the major products; see text. [c] The mixture was heated at reflux. [d] A cyclobutenone (4-phenyl-4-ethyl) was isolated in 7% yield. [e] A cyclobutenone (4-phenyl-4-isopropyl) was isolated in 17% yield. [f] The number in parentheses indicates recovered cyclopropene.

Table II. Formation of Substituted Naphthols from Cyclopropenes



entry	R_1	R_2	X	Y	M	ratio A:B[a]	combined yield,[b] %
1	Et	Et	H	OMe	Cr		44
2	*t*-Bu	Me	H	H	Mo	100:0	40
3	*i*-Pr	Me	H	H	Mo	72:28	35
4	*i*-Pr	Me	H	H	Cr	75:25	40
5	Ph	Me	H	H	Mo	95:5	44
6	Me	H	OMe	H	Mo	100:0	63
7	Et	Me	OMe	H	Mo	60:40	76

[a] Each reaction was run to completion in refluxing dioxane or di-*n*-butyl ether, and the ratios were determined by ^1H NMR integration in the crude product. [b] The yield is based on the sum of the weights of each pure isomer.

obtained in 40–50% yield. Replacement of the methoxy group in the cyclopropene has a strong effect on the rate and product distribution (entries 1–4, Table I). The electron-withdrawing group, CN, completely inhibits reaction; the starting cyclopropene is recovered after 4 h in di-*n*-butyl ether at reflux. Similarly, a phenyl substituent results in ineffective reaction (entry 3). Higher rates are observed when the methoxy group is replaced by H (entry 2) but drop off strongly with introduction of a methyl group (entry 4).

Similar experiments with $Mo(CO)_6$ (Table I) show higher rates and quite efficient processes (e.g., entry 5). However, the effect of alkyl substitution at C-3 is clear and strong (compare entries 5–9). The formation of indenes (e.g., **6**) appears as a significant side process.[18] Triphenylcyclopropene gives the best result in this series (entry 5), a yield of 78% of pure 2,3-diphenyl-1-naphthol,

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(12) The earliest report involved tetramethylcyclopropene and iron pentacarbonyl: King, R. B. *Inorg. Chem.* **1963**, *2*, 642.
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(14) The cyclopropenes were prepared according to general literature methods, by quenching triphenylcyclopropenium cation with lithium aluminum hydride or organomagnesium reagents,[15] by photoinduced rearrangement of the sodium salt of *p*-toluenesulfonylhydrazones derived from α,β-unsaturated ketones,[16] or by lithium carbenoid addition to an alkyne.[17] All new compounds were characterized by NMR, IR, and mass spectral analysis and showed satisfactory elemental analysis or exact mass measurements by mass spectrometry combined with rigorous determination of high purity by chromatographic analysis.
(15) Breslow, R.; Lockhart, J.; Chang, H. W. *J. Am. Chem. Soc.* **1961**, *83*, 2375. (b) Breslow, R.; Dowd, P. *Ibid.* **1963**, *85*, 2729. (c) Breslow, R.; Yuan, C. *Ibid.* **1958**, *80*, 5991.
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(17) For the general procedure, see: Olofson, R. A.; Dougherty, C. M. *J. Am. Chem. Soc.* **1973**, *95*, 581.

with only an 11% yield of indene (**6**). Since the desired naphthol requires CO insertion, the effect of CO pressure was tested. With a small positive pressure of CO (balloon), no significant change in rate or ratio of naphthol to indene was noted. At 4.5 atm of CO, the reaction is strongly inhibited; in addition, no naphthol was detected while indenes formed as usual after extended time.

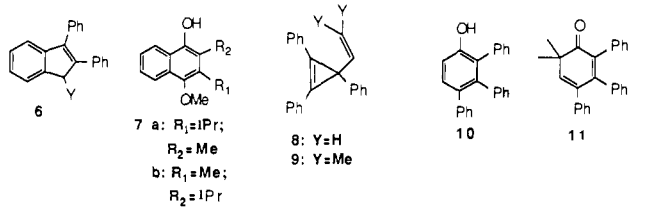
Triphenylcyclopropene was used to demonstrate catalytic activity by $Mo(CO)_6$. In each case, while the same reaction conditions (dioxane, reflux, 1.1 atm of CO) and the same concentration of 1,2,3-triphenylcyclopropene were maintained, the amount of $Mo(CO)_6$ was decreased and the isolated yield of naphthol **2b** was monitored:

$Mo(CO)_6$ (mol equiv)	naphthol **2b** (yield)
1.0 (50 min; no CO)	78%
0.33 (12 h)	73%
0.10 (2.5 h)	63%
0.07 (22 h)	46%

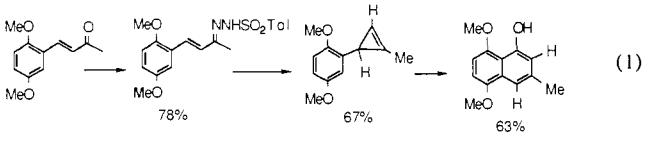
The data demonstrate six or so turnovers of $Mo(CO)_6$ but rather low rates.

A crucial issue in the naphthol synthesis by the alkyne–carbene complex cycloaddition is the regioselectivity in coupling to the alkyne. We have examined this feature of the cyclopropene rearrangements and find a somewhat lower degree of selectivity and *opposite* orientation (Table II, entries 2–7). For example, reaction of isopropylmethylacetylene with carbene complex **1** produces naphthols **7b** and **7a** in the ratio 83:17 (compare Table II, entries 3 and 4).

The special examples **8** and **9** show preferential migration of the vinyl group, leading to monocyclic products **10** (62% yield) and **11** (32% yield), respectively.[20] Substrate **8** is among the most reactive of the cyclopropenes studied, giving complete conversion with $Mo(CO)_6$ after 15 min in 1,2-dimethoxyethane at reflux (83 °C).



The rearrangements reported here provide suggestive evidence for the key intermediates proposed in the alkyne–carbene complex cycloaddition, but no intermediates have been detected. Overall, the metal carbonyl promoted cyclopropene rearrangement has several potential virtues as a preparative method for naphthols: catalytic use of the metal, versatility in the substituents on the naphthol, and several general procedures available to prepare the cyclopropene starting material. In a favorable case illustrated in eq 1, the overall procedure is quite efficient, starting from the aldol product of acetone and 2,5-dimethoxybenzaldehyde.[21]



(1)

(18) Indenes are common products from thermal and Lewis acid promoted rearrangements of phenylcyclopropenes.[19] We have demonstrated that the indene formation reported is catalyzed by the metal carbonyl and is not a direct thermal rearrangement.

(19) (a) Breslow, R. In *Molecular Rearrangements*; de Mayo, P., Ed.; *Interscience*: New York, 1963; Part 1, p 257. (b) McCullough, J. *Can. J. Chem.* **1968**, *46*, 43. (c) Battiste, A.; Halton, B.; Grubbs, R. H. *Chem. Commun.* **1967**, 907. (d) Walker, J. A.; Orchin, M. *Ibid.* **1968**, 1239.

(20) Cho and Liebeskind have investigated rhodium-catalyzed rearrangement of 2-acyl- and 3-vinylcyclopropenes and report phenol formation from the latter. We thank Professor Liebeskind for communicating the results prior to publication.

(21) We wish to acknowledge support from the National Institutes of Health in the form of postdoctoral fellowships to M. Steigerwald and S. Ho and a research grant (CA26727) to M. F. Semmelhack.

Geminal Dimethyl Stereochemistry in the Enzymatic Cyclization of Geranyl Pyrophosphate to (+)- and (−)-α-Pinene

Robert M. Coates* and Jon F. Denissen[1]

Department of Chemistry, University of Illinois Urbana, Illinois 61801

Rodney B. Croteau* and Carl J. Wheeler

Institute of Biological Chemistry Washington State University Pullman, Washington 99164

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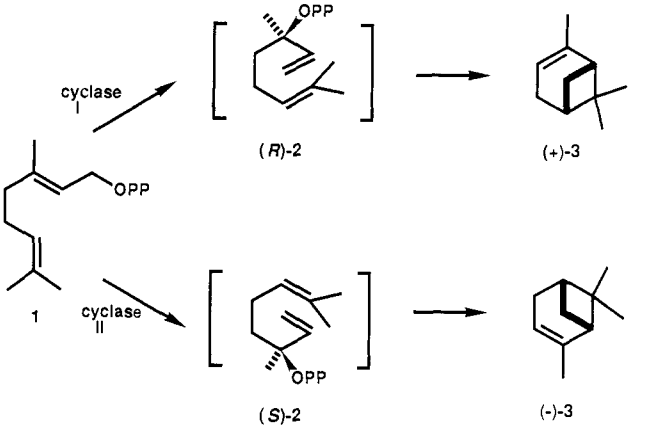
Although a geminal dimethyl bridge is a common structural characteristic among bicyclic monoterpenes, the stereochemistry of the cyclizations which form these prochiral centers is presently unknown. According to current concepts,[2,3] the enantiomeric bridged bicyclic monoterpenes[4,5] are biosynthesized from geranyl pyrophosphate (**1**) via enzyme-catalyzed isomerization[6] to (*R*)- or (*S*)-linalyl pyrophosphate (**2**) followed by anti-S_N' cyclization to C-6 and electrophilic attack of C-7 upon the endocyclic double bond of a transient α-terpinyl carbocation. Previous work[7] has achieved separation of two pinene cyclase activities (I and II) from immature leaves of the common sage plant (*Salvia officinalis*) which catalyze the stereospecific conversion of geranyl pyrophosphate to (+)- and (−)-α-pinene (**3**), respectively. The stereochemistry of (+)-pinene cyclase I and (−)-pinene cyclase II with respect to C-1 of geranyl pyrophosphate (retention) and the configuration of the preferred linalyl pyrophosphate substrate ((*R*)-**2** → (+)-**3**, (*S*)-**2** → (−)-**3**)[2b,8] are consistent with anti-S_N' cyclizations from enantiomeric endo conformations of the presumed tertiary pyrophosphate intermediate.[2,3,9] We wish to report the results of an investigation to elucidate the stereochemical course of these cyclizations at the geminal dimethyl position of the α-pinene enantiomers.



(6*E*)-[8-^{3}H]Geraniol (9.1 mCi, 62 mCi/mmol) was synthesized from (6*E*)-8-hydroxygeranyl benzyl ether[10] in five steps (36%

(1) National Institutes of Health trainee, 1984–1987 (PHS 5 T32 GM 07283).

(2) (a) Croteau, R. In *Biogeneration of Aromas*; Parliment, T. H., Croteau, R., Eds., American Chemical Society: Washington, DC, 1986; pp 134–156. (b) Croteau, R. In *Biochemistry of Plant Lipids: Structure and Function*; Stumpf, P. K., Ed.; Plenum: New York, 1987; pp 11–18.

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(5) (−)-*endo*-Fenchol: Satterwhite, D. M.; Wheeler, C. J.; Croteau, R. *J. Biol. Chem.* **1985**, *260*, 13901–13908.

(6) A suprafacial PP migration is assumed by analogy with cyclonerodiol (a) and linalool (b) biosynthesis: (a) Cane, D. E.; Iyengar, R.; Shiao, M.-S. *J. Am. Chem. Soc.* **1981**, *103*, 914–931. (b) Godtfredsen, S. E., Ph.D. Thesis, ETH Zurich, No. 6243.

(7) Gambliel, H.; Croteau, R. *J. Biol. Chem.* **1984**, *259*, 740–748.

(8) Croteau, R.; Satterwhite, D. M., unpublished results.

(9) Godtfredsen, S.; Obrecht, J. P.; Arigoni, D. *Chimia* **1977**, *31*, 62–63. See also ref 6b.

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