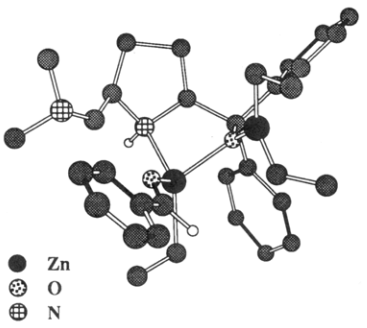

11a

only 83% ee mainly because of competing uncatalyzed reaction of the aldehyde and diethylzinc as demonstrated by a control experiment (*p*-$MeOC_6H_4CHO$, Et_2Zn, toluene, 23 °C, gas chromatographic analysis of rate).[11]

Cinnamaldehyde and diethylzinc in the presence of 10 mol % of **9** react rapidly to form (*S*)-(−)-(*E*)-1-phenylpent-1-en-3-ol, $[\alpha]^{23}_D$ −4.52° (*c* = 1.7, $CHCl_3$) (100% yield, 70% ee). The lower enantioselectivity in this case is partly due to the unusually fast rate of the competing uncatalyzed reaction, but may also be a consequence of nonstereospecific association of this aldehyde with the catalyst at both the oxygen lone pairs (i.e. cis and trans to the formyl hydrogen).

Although it is theoretically possible that the activation of benzaldehyde by catalyst **9** occurs as a consequence of hydrogen bond formation between the ammonium N-H unit of **9** and the aldehyde oxygen, this alternative is not supported by studies of catalyst **14** derived from the reaction of diethylzinc with the bis-tertiary amine alcohol **8**. The ^1H NMR spectrum of **14** resembles closely that of **9** except for the occurrence of an extra N-CH_3 peak and the absence of an N-H proton. Reaction of diethylzinc and benzaldehyde in the presence of 10 mol % of **14** affords (*S*)-(−)-1-phenylpropanol in 90% yield and 92% enantiomeric excess, and the catalyst remains unchanged at the end of the reaction as shown by ^1H NMR analysis. Thus, since the protic catalyst **9** and the aprotic catalyst **14** show virtually identical behavior, catalysis by **9** cannot depend on the presence of an electrophilic proton attached to nitrogen.

The effectiveness of catalysts **9** and **14** depends on their ability to remain monomeric, to coordinate to the aldehyde by internal ligand reorganization, to bind and activate diethylzinc, to bring the activated reactants into proximity, to enforce a three-dimensional preference for the transition-state assembly, and to regenerate themselves by forcing the dissociation of the reaction product. In such behavior there is a striking parallelism between these catalytic molecular robots and the much larger enzymic robots.[12]

Supplementary Material Available: Procedures and physical data for the synthesis of **3** to **9** and the reaction of benzaldehyde and diethylzinc with **7** as catalyst; X-ray data for the structure of **9** including atomic coordinates, anisotropic displacement parameters, idealized H atom coordinates, bond lengths and angles, and packing diagram (19 pages); observed and calculated structure factors for **9** (12 pages). Ordering information is given on any current masthead page.

(11) It is also possible that the lower enantioselectivity with *p*-methoxybenzaldehyde may be partly the result of other competing pathways such as one involving coordination of the aldehyde at the acyclic O-Zn-Et subunit in **9** and adduct formation directly from this structure. The exchange of the dimethylamino ligand for the OZnEt ligand at the central zinc of **10** is another possible source of lower stereoselectivity. Pivaldehyde which also reacts slowly with diethylzinc and 10 mol % of **7** (17% conversion after 60 h at 23 °C) also reacts with lowered enantioselectivity (69% ee).

(12) This research was assisted financially by grants from the National Science Foundation and the National Institutes of Health.

Synthesis of Cyclopentane-Fused Oxygen Heterocycles from the Intramolecular Reaction of Alkynes with Cyclopropylcarbene–Chromium Complexes

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Received October 30, 1989

Summary: The intramolecular reaction between cyclopropylcarbene–chromium complexes and alkynes has been examined. Oxygen heterocycles fused to five-membered rings were obtained from the reaction.

Recently, cyclopropylcarbene–chromium complexes have emerged as valuable reagents for organic synthesis, coupling with alkynes to give cyclopentenone derivatives in good to excellent yields.[1] Excellent regioselectivity was observed in the reaction of terminal alkynes with carbene complex **1**, but mixtures of **2** and **3** were usually obtained using unsymmetrically-substituted internal alkynes (Scheme I). One possible way to control the regioselectivity would be through an intramolecular version of the cycloaddition reaction (Scheme II); this approach has been used in the reaction of alkynes with arylcarbene–chromium complexes.[2] Thermolysis of an alkynylcarbene–chromium complex such as **4** in the presence of water should lead primarily to compound **5** if the chain length is reasonably small. Subsequent ring opening reactions could then provide cyclopentenone derivatives of well-defined regiochemistry. Herein we report preliminary results on the intramolecular version of the reaction in Scheme I.

In the first phase of this research, the reaction of acetylenic alcohols with the anhydride-like complex **8**[2] (generated in situ from complex **7** and acetyl chloride) was examined, which leads to the desired acetylenic carbene complexes in good yield. The reaction was very sensitive

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(2) Semmelhack, M. F.; Bozell, J. J. *Tetrahedron Lett.* **1982**, *23*, 2931–2934.

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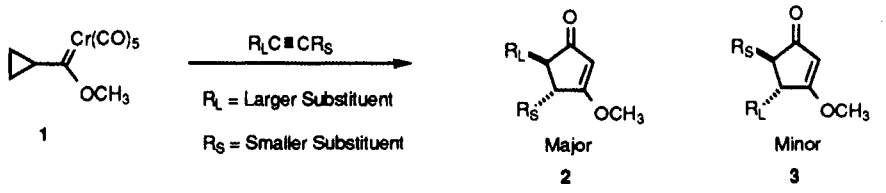
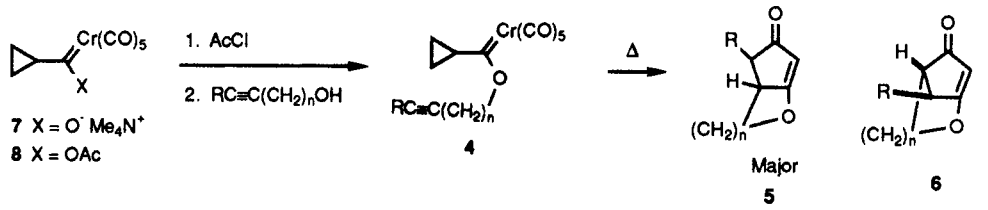
Scheme I



Scheme II



Scheme III

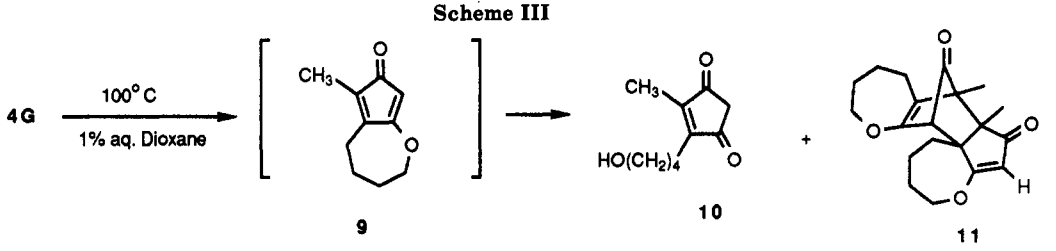


Table Entry Letters Define R and n for Compounds 4 and 5

+ 5G (cis and trans)

to temperature due to decomposition of 8[3] (for a procedure, see ref 4). When an 0.1 M solution of carbene complex **4G** in 1% aqueous dioxane was heated at 80 °C for a period of 2 h, the desired compound **5G** (cis and trans) was obtained only in trace amounts along with the alcohol **10** and possible dimeric structure **11** (Scheme III). Compound **10** is the result of a hydrolysis reaction of the enol ether functionality of cyclopentadienone **9**, which is an intermediate in the reaction.[5] Compound **11** can result from dimerization of the same cyclopentadienone.[6] If the reaction was performed under high dilution conditions as described in ref 7, then compound **5G** (cis and trans) was obtained in higher yield (26%), along with the alcohol **10** (9%) and the cyclopentadienone dimer **11** (20%). In order to assist with the reduction of cyclopentadienone **9**, chromium hexacarbonyl was added to the reaction, giving the expected products **5G** in higher yield (38%), but the dimerization and hydrolysis products were still formed in similar yields. The yields of compound **5G** were considerably higher in toluene (70%), although the reason(s) for this are not presently clear.

Table I. Preparation and Thermolysis of Acetylenic Carbene Complexes

			yield		
entry[a]	*n*	R	4	5[b]	trans:cis 5
A	2	CH_3	66	51	65:35
B	2	H	75	trace	
C	3	C_6H_5	73	74	93:7[c]
D	3	*n*-C_3H_7	82	31	61:49[d]
E	3	2-thienyl	68	51	80:20[c,e]
F	3	H	70	26	
G	4	CH_3	63	38	66:34[c,d]
H	4	H	69	60	
I	5	H	73	30	
J	$PhC{\equiv}C(CH_2)_2CHOHCH_3$		56[f]	61	*g*

[a] Table entry letters define R and *n* for compounds 4 and 5. [b] For a procedure, see ref 7. [c] Chromium hexacarbonyl (1 equiv) was present during the reaction. [d] Cyclopentadienone dimers and cyclopentenediones were also obtained. [e] A 3% yield of the compound having the double bond at the carbon containing R was also obtained. This compound is the natural plant growth regulator chrycorin.[11] [f] An excess of 8 (2 equiv) was used. [g] See text.

The results from a systematic study of the intramolecular cyclization reaction are summarized in Table I. As expected, the reaction was highly regioselective, giving only fused-ring isomers and no bridged-ring isomers. The reaction was general for internal alkynes, with reasonable yields of the expected products **5** formed in most cases. Only in the reactions in entries D and G were significant amounts of dimerization and cyclopentenedione products obtained. The formation of the cyclopenta[*a*]furan ring system (entry A), which is present in prostacyclins[8] and

(3) Connor, J. A.; Jones, E. M. *J. Chem. Soc., Dalton Trans.* **1973**, 2119–2124.

(4) Acetyl chloride (1.0 equiv) was added via syringe to an 0.1 M solution of chromium acylate complex 7[3] in dichloromethane at −20 °C under nitrogen. The solution was allowed to stir 30 min at −20 °C, after which time a solution of the acetylenic alcohol (1.0 equiv) in dichloromethane was added via syringe. The solution was allowed to warm to 0 °C and was stirred at this temperature for a period of 1 h. The solvent was removed on a rotary evaporator; final purification of the carbene complex was achieved by flash chromatography on silica gel.

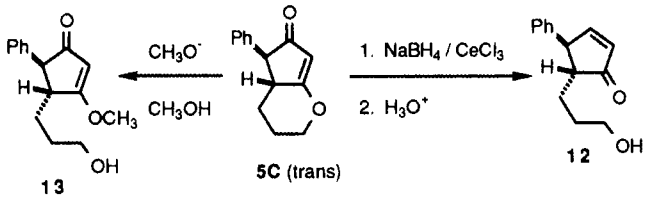
(5) Herndon, J. W.; Tumer, S. U. *Tetrahedron Lett.* **1988**, *30*, 295–296.

(6) Ogliarusso, M. A.; Romanelli, M. G.; Becker, E. I. *Chem. Rev.* **1965**, *65*, 261–367.

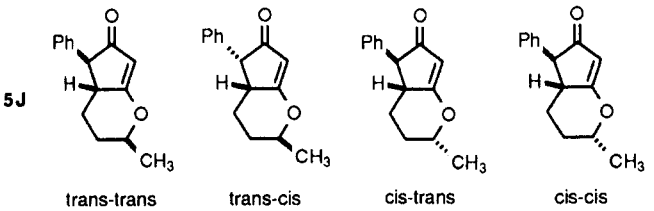
(7) To a refluxing pot of 1% aqueous dioxane under nitrogen was added via syringe an 0.1 M solution of carbene complex 4[4] in dioxane. The addition was accomplished via syringe pump over a period of 1 h. The solution was allowed to stir an additional 1 h at 100 °C. The green solution was allowed to cool to 25 °C and was filtered through silica gel. The solvent was removed from the filtrate on a rotary evaporator. Final purification of the residue after evaporation was achieved by flash chromatography on silica gel.

(8) Johnson, R. A. In *Advances in Prostaglandin, Thromboxane, and Leukotriene Research*; Pike, J. E., Morton, D. R., Eds.; Raven Press: New York, 1985; Vol. 14, pp 131–154.

Scheme IV



in many prostaglandin synthesis intermediates,[9] proceeded in 51% yield. Addition of chromium hexacarbonyl to the reaction in entry C led to an increase in the trans:cis ratio. Thermolysis of complex **4J** in aqueous dioxane led to a 40:35:14:11 mixture of four stereoisomers in 61% yield. The major isomer (trans-trans) differs from the second-most abundant one (trans-cis) only in the configuration of the substituents on the five-membered ring. The methyl group apparently controls the overall stereochemistry of the reaction since the six-membered ring substituents are diequatorial in both of the two major isomers. Reactions involving terminal alkynes (entries B, E, H, I) were less efficient, and highly sensitive to ring size, giving reasonable yields of cycloadducts only in entry H. A similar dependence with regard to length of tether has been observed in the intramolecular reaction of terminal alkynes with arylcarbene-chromium complexes.[2,10]



The vinylogous ester functionality is susceptible to further synthetic manipulation.[12] Reaction of compound **5C** (trans) with sodium borohydride/cerium trichloride,[13] followed by aqueous acid, led to the enone alcohol **12** (trans) in 68% yield (93% based on recovered starting material) (Scheme IV). The corresponding cis isomer underwent the same conversion to give compound **12** as a 3:1 cis:trans mixture. Treatment of compound **5C** (trans) with sodium methoxide/methanol led to the vinylogous ester alcohol **13**; both the cis and the trans isomers of **5C** led to the trans compound **13**.

In summary, the intramolecular reaction between cyclopropylcarbene-chromium complexes and alkynes provides cyclopentane-fused oxygen heterocycles in good yield. The products obtained are further susceptible to ring opening reactions. We are actively exploring further the synthetic potential of these processes.

Acknowledgment. We thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the National Institutes of Health (Grant GM-40777) for financial support of this research. We thank the National Science Foundation for funds to purchase a 400-MHz NMR spectrometer. We also thank Dr. Jeff Romine (Bristol-Myers) for a very helpful suggestion.

Supplementary Material Available: Procedures for the above experiments and spectral data for the compounds reported in these studies (57 pages). Ordering information is given on any current masthead page.

(9) Caton, M. P. L.; Hart, T. W. In *Advances in Prostaglandin, Thromboxane, and Leukotriene Research*; Pike, J. E.; Morton, D. R., Eds.; Raven Press: New York, 1985, Vol. 14, pp 73-129.

(10) Wulff, W. D.; McCallum, J. S.; Kunng, F. A. *J. Am. Chem. Soc.* **1988**, *110*, 7419-7434.

(11) Tad, M.; Chiba, K. *Agric. Biol. Chem.* **1984**, *48*, 1367-1369.

(12) Stork, G.; Danheiser, R. L. *J. Org. Chem.* **1973**, *38*, 1775-1776.

(13) Danishefsky, S. J.; Maring, C. J. *J. Am. Chem. Soc.* **1985**, *107*, 1269-1274.

Direct Metalation of *p*-Bromopolystyrene Using Highly Reactive Copper and Preparation and Reaction of Highly Reactive Copper Bound to an Insoluble Polymer

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Received November 30, 1989

Summary: Polymeric organocopper reagents have been prepared involving highly reactive copper with cross-linked *p*-bromopolystyrene and phosphine-containing polymers.

Chemical transformations of insoluble materials such as polymers are normally possible only with soluble reagents present in a solvent system surrounding and permeating the polymer.[1] Accordingly, the direct metalation of a polymer such as the formation of a Grignard reagent from *p*-bromopolystyrene with magnesium metal is not possible even if the magnesium is highly reactive.[2] This problem was recently overcome by the use of the soluble reagent magnesium anthracene.[2] In this paper, we would like to report the first direct copper metalation of halogen-containing polymers using the soluble zero-valent copper reagent recently reported.[3] The resulting copper-derivatized polymers can be reacted with a variety of electrophiles to yield highly functionalized polymers. Also, we would like to report that the soluble zero-valent copper reagent can be prepared attached to a phosphine-containing polymer. This insoluble zero-valent copper will react with alkyl and aryl halides to generate organocopper

(1) For reviews concerning the functionalization of polymers and their uses: Sherrington, D. C., Hodge, P., Eds. *Synthesis and Separations using Functional Polymers*; John Wiley and Sons: New York, 1988; pp 43-122, and references therein.

(2) (a) Itsuno, S.; Darling, G. D.; Stover, H. D. H.; Frêchet, J. M. J. *J. Org. Chem.* **1987**, *52*, 4645 and references therein. (b) Harvey, S.; Raston, C. L. *J. Chem. Soc., Chem. Commun.* **1988**, *10*, 652.

(3) (a) Rieke, R. D.; Burns, T. P.; Wehmeyer, R. M.; Kahn, B. E. *High Energy Processes in Organometallic Chemistry*, ACS Symposium Series No. 333; American Chemical Society: Washington, DC 1987; Chapter 14, p 223. (b) Wu, T. C.; Wehmeyer, R. M.; Rieke, R. D. *J. Org. Chem.* **1987**, *52*, 5057. (c) Wehmeyer, R. M.; Rieke, R. D. *J. Org. Chem.* **1987**, *52*, 5056. (d) Wehmeyer, R. M.; Rieke, R. D. *Tetrahedron Lett.* **1988**, *29*, 4513. (e) Wu, T. C.; Rieke, R. D. *Tetrahedron Lett.* **1988**, *29*, 6753. (f) Rieke, R. D.; Wehmeyer, R. M.; Wu, T. C.; Ebert, G. W. Recent Developments in Organocopper Chemistry; Lipshutz, B. H., Ed.; Tetrahedron Symposia-in-print Number 35; *Tetrahedron* **1989**, *45*, 443.

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