

Communications

Coupling of Fischer Carbene Complexes with Conjugated Enediynes: Generation of Chromium-Complexed Diradicals via the Moore Cyclization and Subsequent Radical Trapping Reactions

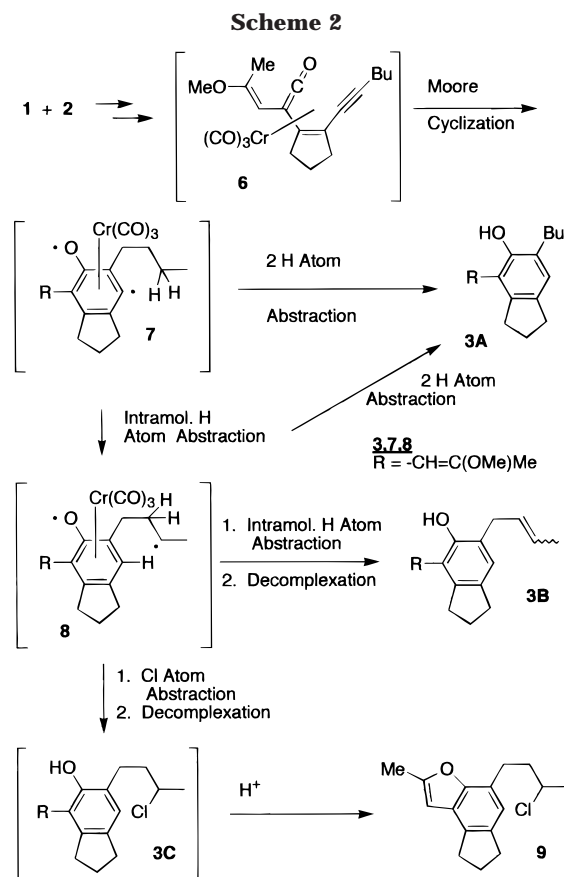
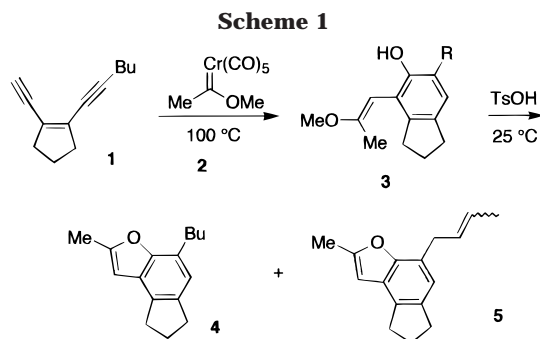
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Received February 20, 1998

Well-established cycloaddition processes involving the coupling of alkynes with either (phenylcarbene)chromium complexes (benzannulation)² or (cyclopropylcarbene)chromium complexes (cyclopentannulation) can be imitated by the coupling of simple chromium carbene complexes with either (*Z*)-phenylvinylacetylenes or (*Z*)-cyclopropylvinylacetylenes, respectively.³ As part of a research program to further examine this alternative annulation method, the reaction of a simple carbene complex with conjugated enediynes⁴ has been undertaken. This coupling should produce benzannulation products by way of diradical intermediates based on the trend established in reference 3 and the intramolecular coupling of alkynes with alkynylcarbene complexes.⁵ Herein, we report the preliminary studies of this novel benzannulation reaction, as well as secondary reactions of the diradical intermediates.

Treatment of enediyne **1** with methylcarbene complex **2** in refluxing dioxane afforded a complex reaction mixture. The crude reaction mixture was greatly simplified by treatment with *p*-toluenesulfonic acid at 25 °C, and three compounds, butylbenzofuran **4** (26%) and an *E*-*Z* mixture of butenylbenzofuran **5** (34%), could be isolated (Scheme 1). All of the products in Scheme 1 feature the benzofuran ring system and can arise via acid-catalyzed cyclization of intermediate phenol–enol ether derivatives **3**; a similar procedure for the simplification of complex mixtures of *o*-enol ether–phenol derivatives was employed in ref 3. The mechanism in Scheme 2 has been proposed to account for formation of these compounds. Selective coupling of the less hindered alkyne⁷ with the carbene complex ultimately affords intermediate enyne–ketene **6**, which undergoes the Moore cyclization⁸ to afford intermediate chromium-complexed diradical **7**.⁵ Formation of butylbenzofuran derivative **4** occurs via hydrogen abstraction from the solvent dioxane



to afford phenol–enol ether **3A**, followed by conversion to the benzofuran **4** upon treatment with acid. Formation of alkene–benzofuran derivatives **5** occurs via sequential intramolecular hydrogen atom transfers⁹ through preferred six-atom transition states (**7** → **8** → **3B**), ultimately affording phenol **3B**, which cyclizes to benzofuran **5** upon acid treatment. Formation of butylbenzofuran **4** could also occur from intermediate diradical **8** via hydrogen atom abstraction processes. When the reaction was conducted in dioxane/deuteriochloroform 49:1, direct formation of benzofuran derivatives **4** (26%) and **5** (29%) and an additional chlori-

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(4) For an additional example of a benzannulation reaction induced through the coupling of enediynes with organometallics, see: Wang, Y.; Finn, M. G. *J. Am. Chem. Soc.* **1995**, *117*, 8045–8046.

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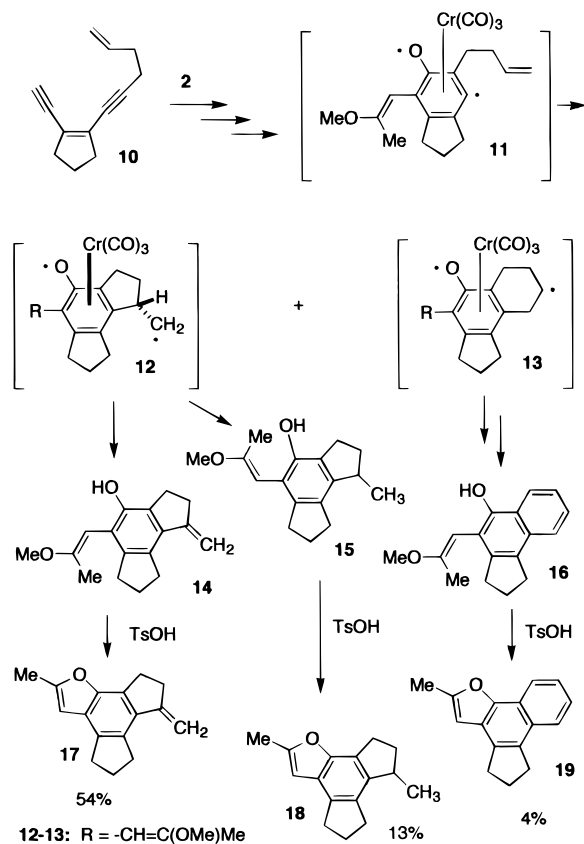
(6) Enediyne **1** was prepared in two steps from 2-(1-hexyn-1-yl)-1-cyclopentene-carboxaldehyde. Wang, K. K.; Liu, B.; Lu, Y. *Tetrahedron Lett.* **1995**, *36*, 3785–3788.

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Scheme 3

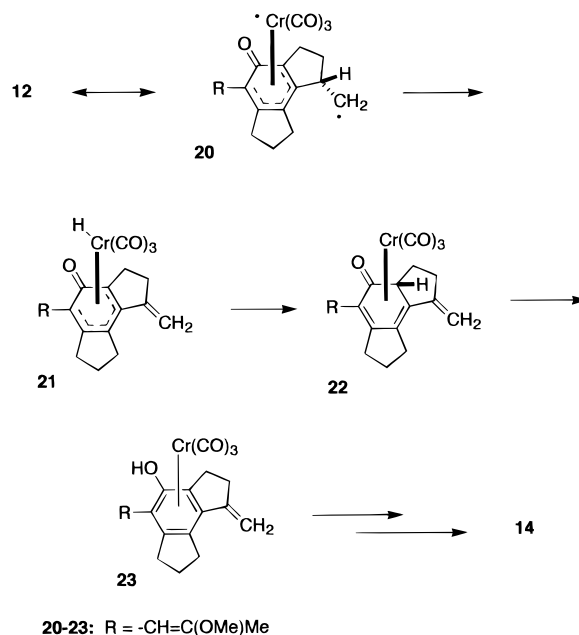


nated compound **9** (7%) was observed. This compound presumably arises via chlorine abstraction by diradical intermediate **8**. The weakly acidic nature of chloroform likely induces cyclization to the benzofuran derivative under the conditions of the coupling.

As further verification of a radical reaction pathway, the reaction of diene-diyne **10** with methylcarbene complex **2** was tested. Coupling of these compounds in refluxing dioxane followed by acid treatment afforded three compounds (Scheme 3). Alkene derivative **17** (54%) was the major product of the reaction. Minor products from the reaction were tentatively identified as the naphthalene derivative **19** (4%) and the methyl derivative **18** (13%). Compounds **17**–**19** arise via radical cyclization of the diradical intermediate (**11**), which is formed similarly to diradical **7** of Scheme 2. The predicted 5-exo ring closure¹⁰ affords diradical **12**,¹¹ and ultimately compounds **17** and **18**, while naphthalene derivative **19** arises via the 6-endo ring closure. Hydrogen abstraction from the solvent ultimately affords **18**, while **19** results from aromatization–dehydrogenation.¹²

Formation of alkene **17** is unanticipated and cannot arise via simple transfer of hydrogen to the oxygen radical; the transition state for this hydrogen atom transfer is very strained. Metal-free diradicals analogous to **12** have previously been generated,^{9a} however, hydrogen abstraction from the solvent was the major reaction pathway, ultimately affording products analogous to **18**. Abstraction of the benzylic hydrogen from intermediate **12** appears to be the

Scheme 4



most favorable reaction pathway since alkene **17** is overwhelmingly the major product of the reaction. A possible rationale for the rapid hydrogen transfer is depicted in Scheme 4. Delocalization of the spin density onto chromium would afford resonance structure **20**.¹³ Since chromium is syn to the abstractable hydrogen, an intramolecular atom transfer affording chromium hydride **21**¹⁴ could occur, which would then afford phenol **14** after reductive elimination to cyclohexadienone complex **22**,¹⁵ enolization, and decomplexation.

In summary, the coupling of carbene complexes with conjugated enediynes provides diradical intermediates, which then undergo free-radical-based processes to provide a variety of products, all containing the benzofuran ring system (after acid treatment). A variety of mechanistically reasonable free radical-based processes, which occur after the benzannulation event, can account the ultimate products of the coupling reaction. These studies also suggest that the chromium-complexed diradicals generated in these studies may feature reactivity patterns that are significantly different from analogous metal-free diradicals. Further study of this reaction process is currently underway, with emphasis on efforts to better control the product distributions in these complex reaction mixtures.

Acknowledgment. We thank the Petroleum Research Fund, administered by the American Chemical Society, for financial support of this research.

Supporting Information Available: Experimental procedures, synthesis of enediynes, and characterization of all products (24 pages).

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