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The First Examples of a *Meta*-Benzannulation from the Reaction of Fischer Carbene Complexes with Alkynes

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The benzannulation reaction of Fischer carbene complexes with alkynes to give *p*-alkoxy phenols was first reported by Dötz[1] and has become one of the most synthetically valuable methods for the synthesis of phenols and quinones.[2] At first glance, it would appear highly improbable that the reaction of a Fischer carbene complex with an alkyne could give rise to a *m*-alkoxy phenol because this would require the breaking of either the carbon−carbon bond of the alkenyl substituent of the carbene complex (to give phenol **4**) or the carbon−carbon bond of the alkyne (to give phenol **5**). Herein, we describe the discovery of a unique pathway that can occur in the reaction of Fischer carbene complexes with alkynes which results in the formation of phenols of the type **4** in a process that involves the breaking of the carbon−carbon bond connecting substituents R^1 and R^2 of the carbene complex (Scheme 1).

In our ongoing studies of the intramolecular reactions of Fischer carbene complexes with alkynes,[3] we had envisioned the possibility of preparing *p*-cyclophanes from the alkenyl carbene complex **6** which had an alkyne tethered to the α-position of the alkenyl substituent. Contrary to expectation, this reaction in fact was found to give the *m*-cyclophane **8** in addition to the bicyclohexenone **9**.[3b] The bicyclohexenone **9b** could be isomerized to the *m*-cyclophane **8b** in the presence of acid, but it was not clear if the *m*-cyclophane **8b** was a secondary product or could be formed by some other mechanism.

Intermolecular reactions of carbene complexes with alkynes are sensitive to the nature of the reaction solvent,[2,4] and thus it should have not been astonishing that the intramolecular reaction would also show the same dependence. Nonetheless, the outcome of the intramolecular reaction of **6b** in benzene was a bona fide surprise. Not only was the originally anticipated *p*-cyclophane **7b** the major product of the reaction, but the reaction also produced the completely unprecedented *meta*-substituted methoxy phenol **10b**. The structure of this aberrant product was confirmed by X-ray analysis of a single crystal to have a *meta*-orientation of the oxygen substituents.

A more extensive investigation of the effect of solvent and tether length on these reactions was undertaken, and the results are presented in Table 1. For tether lengths of six methylenes, only the 6,6-*p*-cyclophane **11a** and corresponding 6,6,6-*p*-cyclophanes (not shown) are observed. Several different solvents were examined for the complex with 10 methylenes, and it was found that coordinating solvents favor the pair of products **8b** and **9b**, whereas noncoordinating solvents favor the product pair **7b** and **10b** (Scheme 2). This solvent dependence persists as the tether length is increased to 13, but it disappears for the complex **6d** with 16 methylenes in the spacer where it was found that THF and benzene give essentially the same product distribution.

Scheme 1

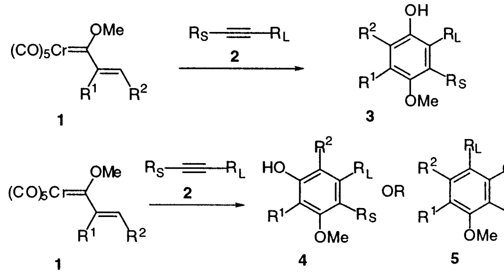
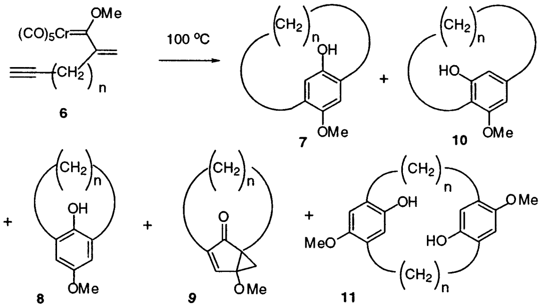


Table 1. Macrocyclizations of Complexes **6**[a]



entry	series	*n*	solvent	yield **7**	yield **10**	yield **8**	yield **9**	yield **11**	total yield
1	a	6	THF					36	49[b]
2	a	6	benzene					28	37[c]
3	b	10	THF	4	Tr	15	42	8	69
4	b	10	CH_3CN	17		24	11	5	57
5	b	10	CH_2Cl_2	22	17	<2		12	51
6	b	10	hexane	22	29			8	59
7	b	10	benzene	40	21	Tr		12	73
8	c	13	THF	5	2	16	38	10	72
9	c	13	benzene	14	18			26	58
10	d	16	THF	56		1	2	10	69
11	d	16	benzene	48	2			9	59

[a] Reaction performed at 0.002 M at 100 °C for 12 h under argon. [b] A 13% yield of trimer was also isolated. [c] A 9% yield of trimer was also isolated.

The mechanism of the reaction of Fischer carbene complexes with alkynes is thought to begin with the formation of an η^1,η^3-vinyl carbene complexed intermediate.[2,5] This species is formed with the regioselective incorporation of the alkyne such that the larger substituent occurs at the end carbon as is the case in intermediate **12** in Scheme 3. A migratory insertion of a carbon monoxide ligand with concomitant coordination of the vinyl substituent of the original carbene complex to the metal center gives the 18 e^- η^6-dienyl ketene complex **13**. The final two steps are the electrocyclic ring closure of the ketene complex to give the cyclohexadienone **16** followed by tautomerization to the phenol **7**.

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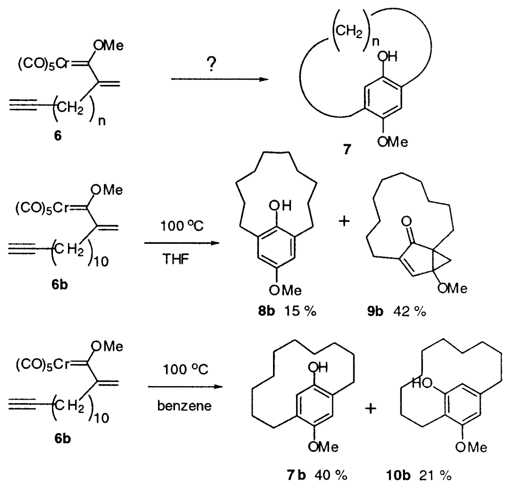
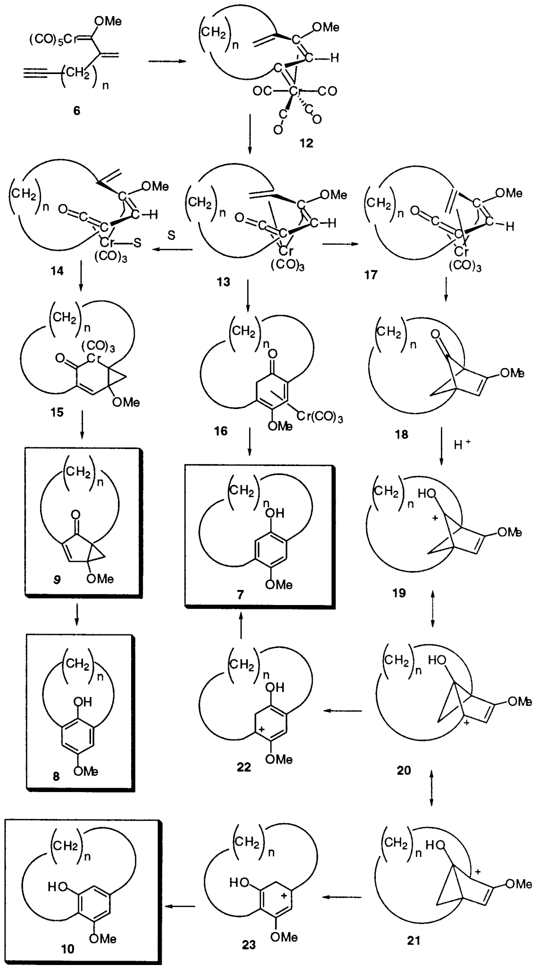
Scheme 2



Scheme 3



We propose that the *p*-cyclophane **10** with the *meta*-orientation of the two oxygen substituents is the result of a crossed [2 + 2] cycloaddition of the ketene function in **17** with the alkenyl group to give the bicyclo[2.1.1]hexenone core of the paddalane intermediate **18** which contains a benzvalenone core. This type of [2 + 2] cycloaddition of a ketene metal complex and an olefin has been observed before in an intramolecular reaction, but not, as is the case here, where the olefin is in conjugation with the vinyl ketene complex.[6] The benzvalenone intermediate **18** should be activated toward ring-opening by protonation or perhaps by a Lewis acidic chromium species.[6b] The resulting cation would be expected to be nonclassical and have significant contributions from the cyclobutyl cation **19** and the cyclopropyl carbinyl cations **20** and **21**. Cleavage of the internal cyclopropane bond in intermediate **21** would give the cyclohexadienyl cation **23** that could lose a proton to give the cyclophane **10**. Cleavage of the internal cyclopropane bond in the intermediate **20** would give intermediate **22** and, upon proton loss, would give an alternative pathway to the *p*-cyclophane **7**.

We had previously proposed that the bicyclo[3.1.0]hexenone product **9** is formed from an *s-trans*-conformation of the vinyl ketene complex via a reductive cyclization leading to the chromahexenone intermediate **15** and then reductive elimination.[3b] The data in Table 1 suggest that the formation of the bicyclohexenone **9** and the cyclophane **8** is enhanced in coordinating solvents, and this could be accounted for as indicated in Scheme 3. The η^1,η^3-vinyl carbene complex **12** is an 18 e^- intermediate, and upon carbon monoxide insertion the resultant vinyl ketene complex is only an 18 e^- complex if, simultaneous with the CO insertion, there is a coordination of the chromium to the vinyl group derived from the original carbene complex. In the presence of coordinating solvents, the alkenyl substituent could be displaced by a molecule of solvent to give the η^4-vinyl ketene complex **14** in which the tethered alkenyl group could adopt an *s-trans*-conformation to relieve strain and thus set up the cyclization to **15**. Apparently, these solvent effects are only revealed for those macrocyclic intermediates that are most sensitive to ring strain ($n = 10, 13$). This is evidenced from the complex with $n = 16$ where the expected *p*-cyclophane **7d** is the major product in either THF or benzene as a solvent.

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Supporting Information Available: Experimental procedures and spectral data for all new compounds and X-ray data for **10b** (PDF and CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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