A new approach to hydrindenones by tautomer-arrested annulations of Fischer carbene complexes

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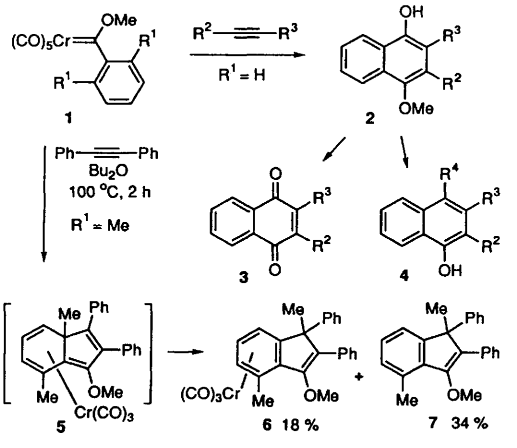
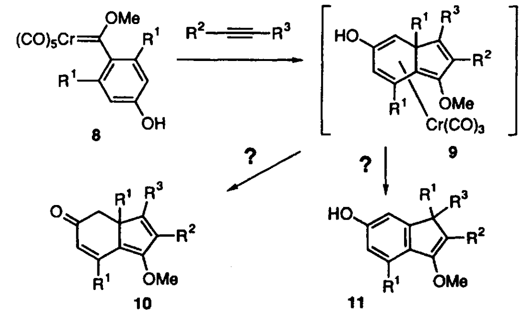
The reactions of 2,6-disubstituted aryl carbene complexes with alkynes give hydrindenone products if a phenol function is present which prevents aromatization to an indene product by a tautomerization of a metal complexed vinyl alcohol intermediate.

The most versatile annulation reaction for the formation of phenols and quinones is the benzannulation reaction of Fischer carbene complexes with alkynes.[1] This process can be utilized for the synthesis of naphthols from aryl carbene complexes, as indicated in Scheme 1, or for the synthesis of phenols from alkenyl carbene complexes (not shown). The predominant primary products of the benzannulation reaction are 4-alkoxyphenols, which can serve as precursors to quinones by oxidation,[2] can be elaborated to aromatics if the phenol function is reduced[3] (**4**, R^4 = H), coupled *via* its triflate in Suzuki and Stille reactions to produce new carbon–carbon bonds,[4a] or coupled *via* a Mitsunobu reaction to make benzopyrans.[4b,c] While the synthetic scope of these reactions is quite broad,[1,5] the reaction is not useful for 2,6-disubstituted aryl carbene complexes (**1**, $R^1 \neq$ H). In this case the reaction path changes dramatically, as shown for the reaction of the dimethylphenyl complex **1a** (R^1 = Me) with diphenylacetylene.[6–9] This reaction gives indene products that are thought to result from cyclization without CO insertion to give intermediate **5**, which undergoes a 1,5-sigmatropic shift of the methyl group to restore the aromaticity of the arene ring. In this work we show that the 1,5-alkyl migration leading to the rearomatization of intermediate **5** can be intercepted by a tautomerization of a vinyl alcohol function to provide a new route to functionalized hydrindenones.



Scheme 1

In considering the outcome of the reaction of complex **8** with alkynes, it is not clear whether tautomerization of intermediate **9** to give hydrindenone **10** would be faster than alkyl migration to give the indene complex **11** (Scheme 2). Although coordination of the chromium to the vinyl alcohol in **9** may stabilize the vinyl alcohol and slow down tautomerization, it is also possible that coordination of the chromium to the aromatic ring in indene **11** may lower the driving force provided by the aromaticity gained by the 1,5-alkyl migration. As the data in Table 1 shows, both processes can occur for the reaction of complex **8a** with various alkynes. The reaction with terminal alkynes appears to be selective for the formation of the hydrindenone product **10f** over the aromatized product **11f**, however, the mass balance is poor even if the alkyne is added slowly. Trimethylsilyl-substituted alkynes give predominately the aromatized product **11**, apparently due to an electronic effect since the selectivity can be reversed by incorporating an enol ether unit in the alkyne as illustrated for the reaction of **17-E** (Scheme 3). In this regard, it is interesting to note that for the reaction of 1-trimethylsilylheptyne, the regioisomer incorporating the trimethylsilyl group at position R^2 gives a 16 : 1 mixture of **11c** and **10c**, whereas the regioisomer incorporating the trimethylsilyl group at position R^3 gives exclusively the hydrindenone **10c**. The reactions with hex-3-yne and 1-phenylpropyne give exclusively hydrindenone products, whereas diphenylacetylene gives a mixture of **10** and **11**. The distribution of **10** and **11** is not



Scheme 2

Table 1 Tautomer arrested annulations of carbene complex **8a** (R^1 = Me)[a]

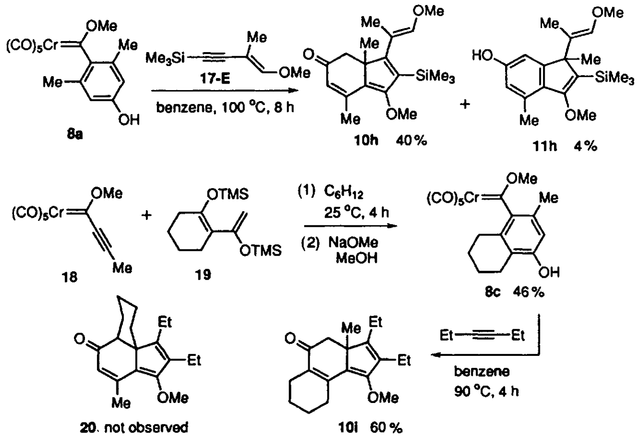
R^2	R^3	Solvent	Additive[b]	Product series	Yield **10** + **11** (%)	**10** : **11**
Et	Et	benzene		**a**	75	100:0
Me	Ph	benzene		**b**	78[c]	100:0
$SiMe_4$	pentyl	benzene	DTBP	**c**	71[d,e]	11:89
Ph	Ph	benzene		**d**	88	49:51
		THF			64	38:62
		MeOH			74	46:54
		benzene	DTBP		76	72:28
		benzene	PHTS		39	92:8
$SiMe_4$	Pr^i	benzene	DTBP	**e**	51[f]	0:100
H	Pr	benzene		**f**	9[g]	100:0

[a] Unless otherwise indicated the reactions were carried out at 110–125 °C at 0.5 to 1.0 M in **8a** with 2 equiv. of alkyne. [b] One equivalent: DTBP = 2,6-di-*tert*-butylpyridine, PHTS = pyridinium tosylate. [c] 3.5 : 1 ratio of regioisomers, R^1 = Ph predominating. [d] **10c** obtained as a 1 : 1 ratio of regioisomers. [e] **11c** isolated as ketone **12c** resulting from hydrolysis of enol ether (R^1 = pentyl) and loss of the silyl group. [f] **11e** isolated as ketone **12e** resulting from hydrolysis of enol ether (R^1 = Pr^i) and loss of the silyl group. [g] Slow addition of alkyne over 1 h.

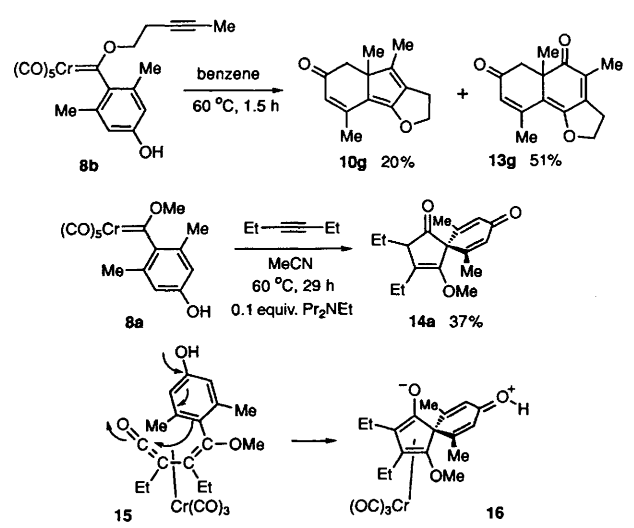
dependent on the solvents listed in Table 1, but can be shifted in favour of the hydrindenone if an acid or base is present.

The intramolecular annulation of complex **8b** gives none of the aromatized product, but gives the decalindione **13g** in addition to the hydrindenone **10g** (Scheme 4). It is not clear why CO insertion occurs for this particular reaction, but it should be noted that this is the first time a cyclohexadienone product has been obtained from the reaction of a 2,6-disubstituted phenyl carbene complex.[10] More of a surprise was the formation of the spirocyclohexadienone **14a**, a completely unprecedented product from the reaction of carbene complexes with alkynes. The reaction of complex **8a** with hex-3-yne gives exclusively the hydrindenone **10c** in benzene, but in acetonitrile the spirocyclohexadienone **14a** was the only observed product. The acetonitrile may stabilize the charge separated intermediate **16**, that would be formed from an ipso attack of the electron-rich aryl ring on the ketene carbon of complex **15**.

The reaction of complex **8a** with alkyne **17-E** gives a 10 : 1 ratio of hydrindenone to aromatized product, revealing that the electronic effect of the silicon can be offset with the vinyl ether group in **17-E** (Table 1, compare with entries 3 and 9), and that hydrindenones can be obtained with functionalized alkynes. The carbene complex **8c** was prepared by the indicated Diels–Alder reaction[12] in an effort to determine whether regiocontrol would be possible in the formation of hydrindenones from an unsymmetrical 2,6-disubstituted carbene complex. The reaction with hex-3-yne occurred with complete regiocontrol, giving the linearly fused tricyclic product **10i** resulting from cyclization onto the aryl carbon bearing the methyl group. The angularly fused tricyclic compound **20** was not observed, indicating that cyclization onto the *ortho*-aryl carbon fused to the cyclohexane ring does not occur.



Scheme 3



Scheme 4

The annulation reactions of alkynes with 2,6-disubstituted aryl carbene complexes bearing a *para*-hydroxy group offer an attractive route to a number of functionalized hydrindenones that promise to serve as important synthetic intermediates. The scope and applications of these reactions will be pursued, as well as the unprecedented formation of spirocyclohexadienones from the reaction of carbene complexes with alkynes.

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