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The Effect of Propargyl Oxygen Substituents in the Carbene-Chromium/Alkyne Cycloaddition

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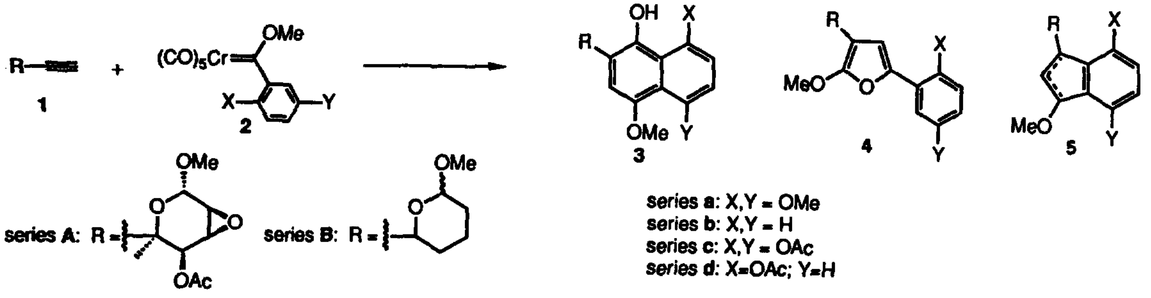
Summary: The usual reaction of alkynes with arylcarbene chromium complexes is deflected by the presence of propargylic alkoxy groups, especially in the case of the 2,5-dimethoxyphenyl carbene ligand; indenes and furans become significant products.

The reaction of alkynes with arylcarbene-chromium complexes to give naphthols has been developed.[1] It involves three carbon-carbon coupling steps: (a) coupling of the carbene ligand with one end of the alkyne, (b) coupling of the other end of the alkyne with a CO ligand, and (c) coupling of the carbon of the same CO ligand with the ortho position of the aryl substituent. The smooth operation of all three stages is general only for chromium complexes with alkoxy-substituted carbene ligands. For example, dialkylamino carbene complexes of chromium react with alkynes to give indenes.[2] With iron and cobalt carbene complexes, stages (a) and (b) occur, but the final ring closure to form the new aromatic ring fails; furans[3,4] and pyrones[5] are the major products after migration of the alkoxy or amino group. Furans are observed as minor products even under optimal conditions for naphthol synthesis.[6]

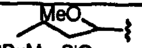
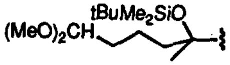
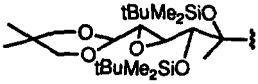
In a specific synthesis problem, we noted that the highly functionalized alkyne **1A** reacted with 2,5-dimethoxyphenylcarbene complex **2a** to produce none of the expected naphthol (**3Aa**), but gave instead the furan **4Aa** and indene **5Aa**.[7] Reaction of a simpler carbene complex (**2b**) with the same alkyne gave the naphthol **3Ab** as the main product (43%) along with furan **4Ab** (34%) and none of the indene (**5Ab**). A simple glycal alkyne (**1B**)[8] with phenyl-carbene complex **2b** produced a 1:1 mixture of naphthol (**3Bb**; 38% isolated) and furan **4Bb** (38%). The methoxy groups in complex **2a** obviously play a role, yet the same complex reacts in a straightforward way with simple alkynes to give naphthols in good yield (Table, entries 1-3). It is primarily with propargylic alkoxy groups on the alkyne that naphthol synthesis begins to be less favorable (Table, entries 4-6). Expecting that the propargylic alkoxy group was coordinating in some way to a chromium intermediate, we added large blocking groups at that oxygen (entries 5,7,8,9). There is an increase in naphthol compared to furan formation (compare entry 4 with 5, and 6 with 7). Substituents such as remote acetals or epoxy groups (entries 8 and 9) deflect the process toward indene formation.

The methoxy groups on the aryl unit in **2a** can be replaced by acetoxy (in **2c**) using an alternative synthesis for the carbene-chromium complex.[9] Then reaction of **2c** with alkyne **1A** leads to diacetoxynaphthol **3Ac** (16%), furan **4Ac** (30%) and the <u>mono</u>acetate **3Ad** (21%). No indene was detected. The monoacetate **3Ad** apparently arises from a reductive cleaveage of one acetoxy group during naphthol formation. The monoacetoxy analog **2d** produced the same naphthol monoacetate **3Ad** in 30-50% yield, along with furan **4Ad**. Clearly, the Doetz process in this series is only moderately efficient, and responds to changes in the peripheral groups on the alkyne and in the aryl group in the carbene ligand; work is in progress to fully define the effects.[10]



series a: X,Y = OMe
series b: X,Y = H
series c: X,Y = OAc
series d: X=OAc; Y=H

Table. Reaction of Monosubstituted Alkynes with (2,5-Dimethoxyaryl)carbene Complex **2a**

entry[a]	alkyne, 1 R =	ratios naphthol	ratios indene[c]	ratios furan[d]	combined yields[b]
1.	$(CH_3)_3$–	90%	0%	10%	91%
2.	$CH_3CH_2(CH_3)CH$–	96%	0%	4%	70%
3.	$MeO_2CCH_2CH_2CH_2$–	93%	7%	0%	70%
4.		17%	64%	19%	64%
5.		52%	48%	0%	58%
6.		60%	0%	40%	40%
7.		100%	0%	0%	46%
8.		27%	73%	0%	55%
9.		0%	100%	0%	40%

(a). A mixture of the alkyne and complex **2a** (equimolar) was heated under argon at 60°in THF for 12 hr. Concentration gave the crude product which was purified by chromatography. (b) The yields are based on the weight of isolated material; new compounds have been fully characterized. (c) The indenes were obtained as 1:1 mixtures of olefin isomers. (d) The furans were purified and oxidized to the corrresponding 2-ene-1,4-diones for characterization.

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7. The indenes (mixture of olefin isomers) were converted to indanones by acid hydrolysis and characterized.
8. Alkyne **1B** was prepared from 1-methylcyclopentene through a reductive ozonolysis, acetalization, lithium acetylide addition, and cyclic acetal formation. The relative configuration has not been established, but it appears to be a single diastereoisomer by carbon NMR. All new compounds were fully characterized by ^{1}H NMR, ^{13}C NMR, IR, low res. MS, and either combustion analysis or high resolution MS. The furans were oxidized to the corresponding 2-ene-1,4-diones for characterization. The indenes were converted to the corresponding indanones by acid hydrolysis for characterization.
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