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COUPLING OF FISCHER CARBENE COMPLEXES WITH ALKYNYLSTYRENE OXIDES: SYNTHESIS OF BENZOXEPINONES IN COMPETITION WITH INTERNAL OXYGEN ATOM TRANSFER

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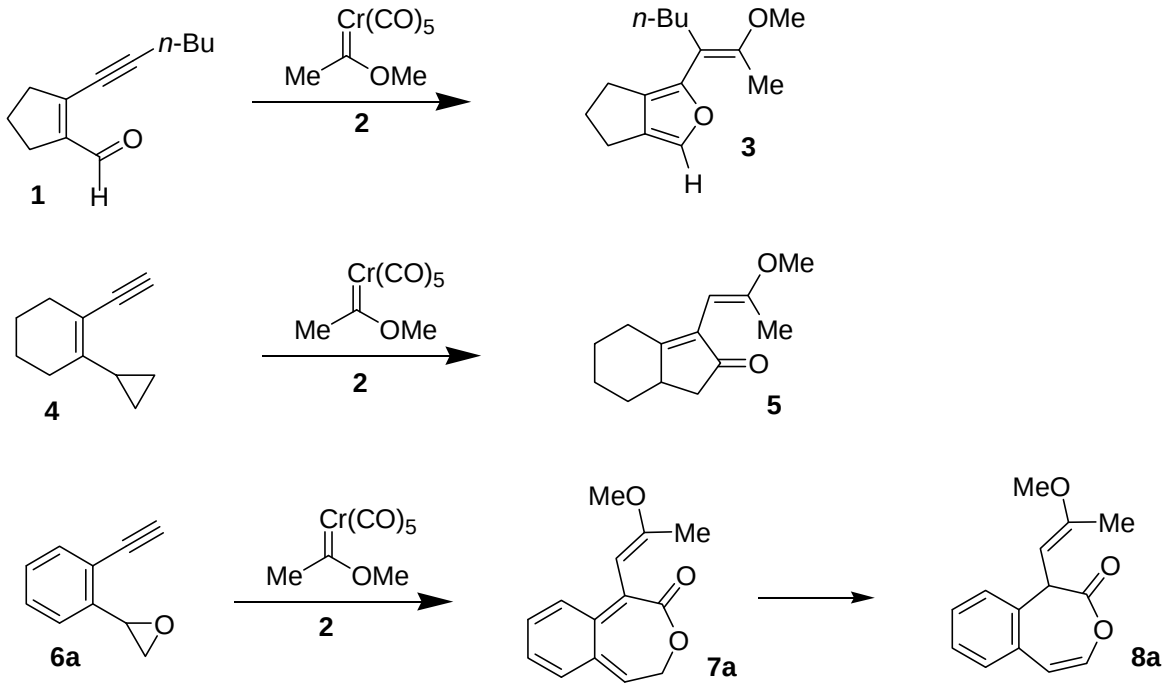
Abstract – The coupling of Fischer carbene complexes with conjugated enyne epoxides has been examined. The reaction proceeds by carbene-alkyne coupling to afford an epoxyvinylcarbene complex, which then undergoes CO insertion and cyclization to afford a benzoxepinone or intramolecular oxygen atom transfer to afford a dienone derivative.

INTRODUCTION

Novel and synthetically useful new ring forming processes have been observed when Fischer carbene complexes (*e.g.* **2**, Scheme 1) couple with conjugated enyne-aldehydes and ketones (e.g., **1**). These

Scheme 1

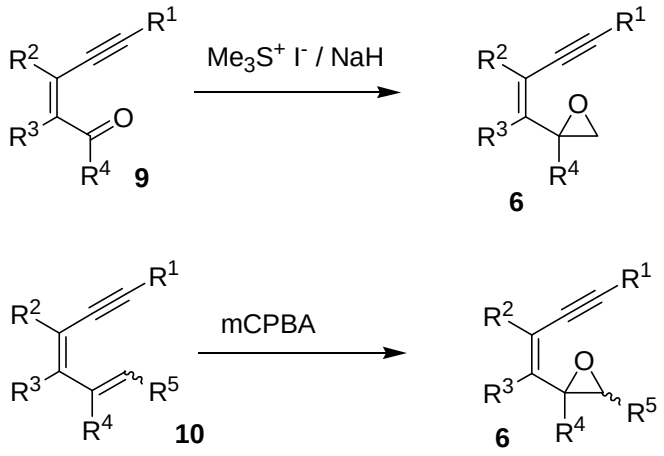


reactions typically provide furan derivatives (*e.g.* **3**)[1] or can lead to the generation of isobenzofuran intermediates.[2] Novel ring-forming processes have also been observed when Fischer carbene complexes couple with cyclopropylvinylacetylenes (*e.g.* **4**).[3] These coupling reactions provide cyclopentenone derivatives (*e.g.* **5**) through a complex mechanistic pathway. This manuscript will focus on the coupling of conjugated enyne epoxides (*e.g.* **6a**) with Fischer carbene complexes, which can be regarded as a "marriage" of the concepts in the reactions producing **3** and **5**. Although this investigation is primarily of an exploratory nature, highly useful new chemistry can result. In the most optimistic scenario, a new synthetic route to 4,5-benzoxepinones (*e.g.* **8a**) from readily available precursors would be realized. Numerous medicinally important compounds possess the 4,5-benzoxepinone ring system.[4]

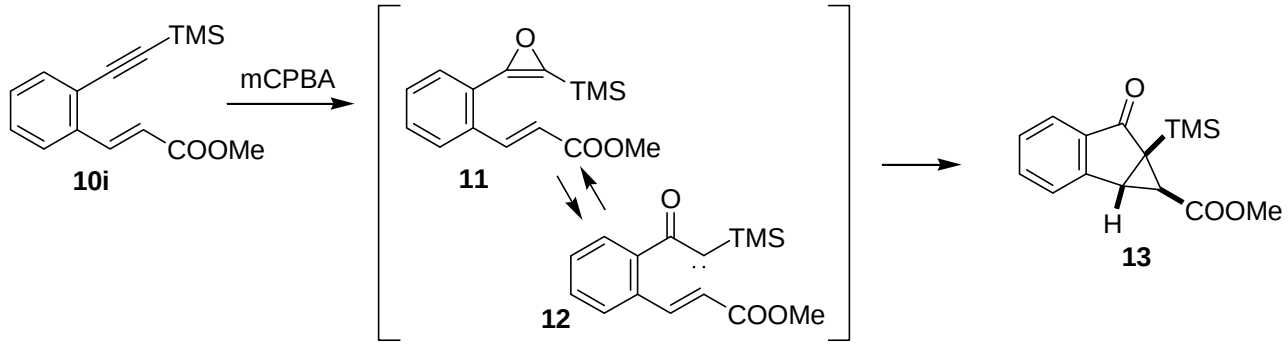
RESULTS AND DISCUSSION

General synthetic routes to alkynylstyrene oxide derivatives (**6**) are depicted in Scheme 2. The two main protocols employed involve either: (1) reaction of alkyne-aldehyde derivatives (**9**) with sulfur ylides, or (2) epoxidation of dienylstyrenes (**10**) with *m*CPBA. In general epoxidation of the alkyne is not a competing process, however this was a problem in one case. Oxidation of alkynylstyrene (**10i**) afforded the cyclopropane derivative (**13**) as the major product. A mechanism involving the formation of the

Scheme 2



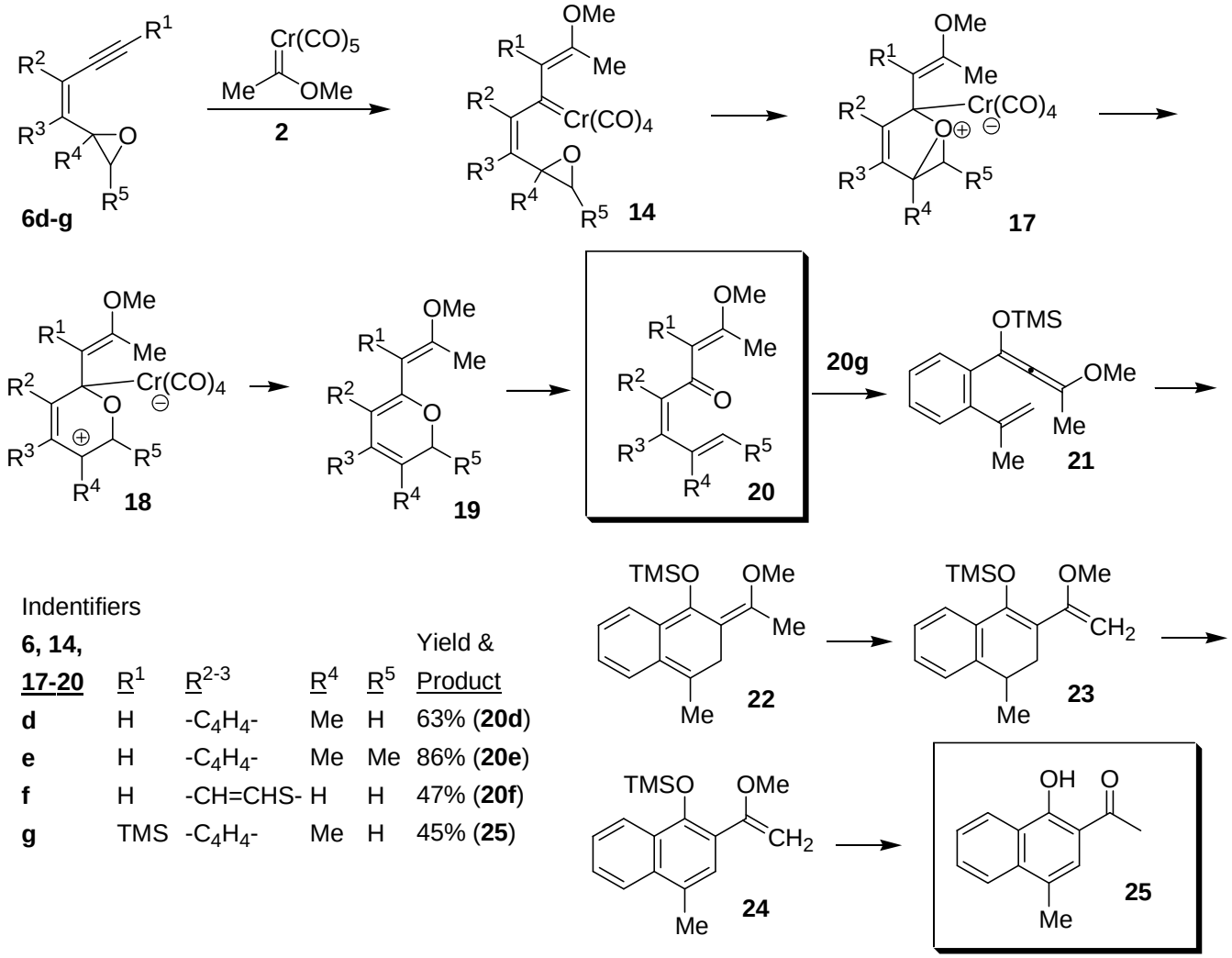
Substituent Identifier **6-10**	R^1	$R^{2,3}$	R^4	R^5
a	H	$-C_4H_4-$	H	H
b	TMS	$-C_4H_4-$	H	H
c	TMS	$-C_4H_4-$	H	Me
d	H	$-C_4H_4-$	Me	H
e	H	$-C_4H_4-$	Me	Me
f	H	-CH=CHS-	H	H
g	TMS	$-C_4H_4-$	Me	H
h	*n*-Bu	$-C_4H_4-$	H	H
i	TMS	$-C_4H_4-$	H	COOMe



oxirene (**11**), followed by rearrangement to the keto-carbene (**12**), followed by intramolecular cyclopropanation[5] can account for formation of this compound. This side reaction is unique to this system due to the reduced nucleophilicity of the alkene. Successful preparation of epoxide (**6i**) was realized through the Darzens condensation reaction of aldehyde (**9i**).

Coupling of methylcarbene complex (**2**) (Scheme 3) with the enyne-epoxide derivative (**6a**) led to benzoxepinone (**8a**) in 46% yield as the only identifiable product. A reasonable mechanism for the formation of this compound is depicted in Scheme 3. Initial formation of vinylcarbene complex (**14**) followed by CO insertion affords vinylketene intermediate (**15**). Nucleophilic attack of the epoxide oxygen at the carbonyl carbon affords **16**, which opens to initially afford *o*-quinoidal species (**7**), which undergoes a 1,5-hydride shift to form the observed product (**8**). This benzoxepinone formation process

Scheme 3



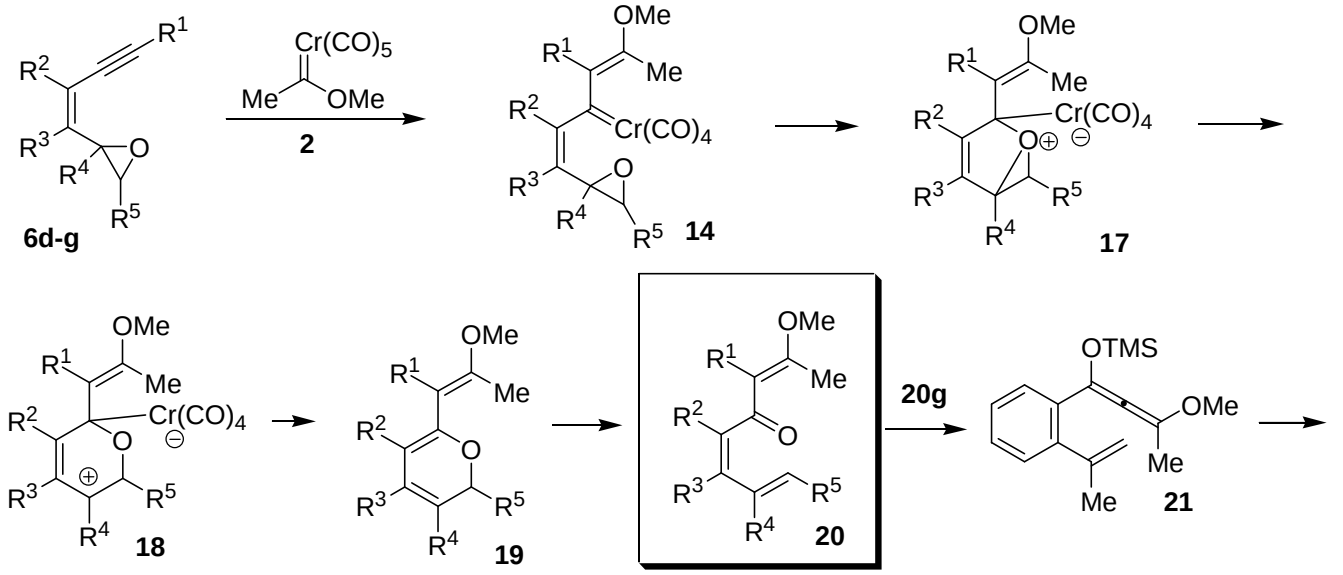
Indentifiers

6, 14, 17-20	R^1	R^{2-3}	R^4	R^5	Yield & Product
d	H	-C_4H_4-	Me	H	63% (**20d**)
e	H	-C_4H_4-	Me	Me	86% (**20e**)
f	H	-CH=CHS-	H	H	47% (**20f**)
g	TMS	-C_4H_4-	Me	H	45% (**25**)

also proceeded in similar yield for silylated alkyne (**6b**) and 1,2-disubstituted epoxides (**6c**). Similar mechanistic steps have been proposed for electronically similar ruthenium vinylidene complex intermediates.[6]

No other enyne epoxide led to a benzoxepinone derivative. Reaction of α-methyl epoxide (**6d**) (Scheme 4) with methylcarbene complex (**2**) led to the internal oxygen-transfer product (**20d**). A similar process was observed for the carbene complex containing the extra methyl group (**6e**), and for epoxythiophene derivative (**6f**). A rational mechanism for this oxygen transfer process is depicted in Scheme 4. Attack of the carbonyl oxygen at the carbene carbon in intermediate (**14**) followed by epoxide ring opening would afford intermediate *o*-quinoidal benzopyran derivative (**19**), which should then undergo a rapid electrocyclic ring opening process[7] to provide the observed product (**20**). A secondary cyclization process was observed for the silylalkyne analog (**6g**), resulting in the naphthalene derivative (**25**). A likely route to this compound involves a 1,3-shift of silicon to afford allene (**21**),[8] followed by

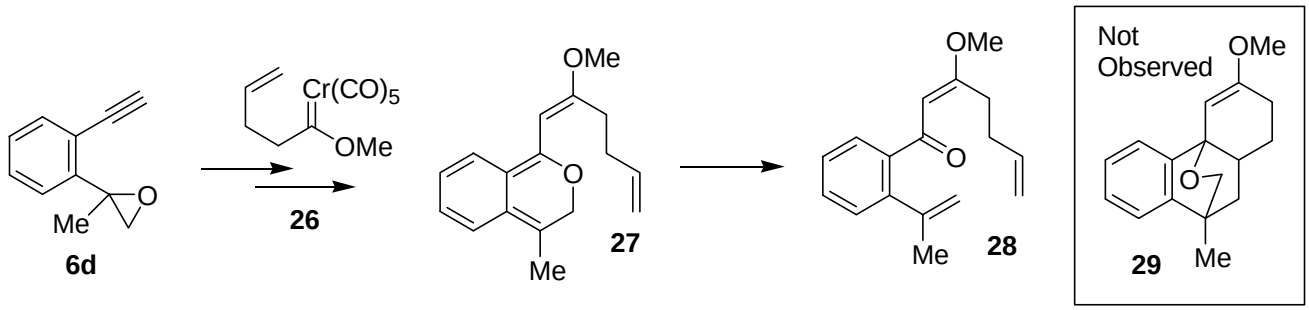
Scheme 4



Indentifiers

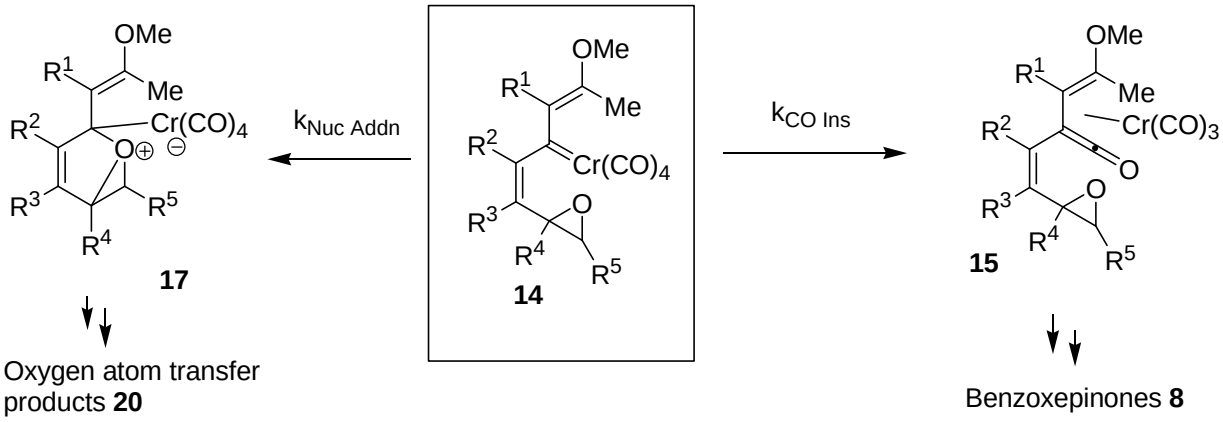
6, 14, 17-20	R^1	R^{2-3}	R^4	R^5	Yield & Product
d	H	-C_4H_4-	Me	H	63% (**19d**)
e	H	-C_4H_4-	Me	Me	86% (**19e**)
f	H	-CH=CHS-	H	H	47% (**19f**)
g	TMS	-C_4H_4-	Me	H	45% (**25**)

Scheme 5



electrocyclic ring closure and aromatization.[9] An attempt to trap the *o*-quinonemethide (**19**) through intramolecular Diels-Alder reaction was unsuccessful (Scheme 5). Coupling of γ,δ-unsaturated carbene complex (**26**) with styrene oxide (**6d**) afforded only the oxygen transfer product (**28**) and none of the Diels-Alder adduct (**29**). The different behavior of the systems where R^4 = H in Scheme 3 compared to system where R^4 = Me in Scheme 4 is intriguing. The difference most likely reflects competition in intermediate (**14**) between CO insertion (forming vinylketene (**15**)) and nucleophilic addition of the epoxide oxygen to the carbene carbon (forming intermediate (**17**)), possibly due to the effect of the methyl group on the conformational equilibria in intermediate (**14**). The conversion of stable a carbene complex to the corresponding carbonyl compound is very well-known,[10] however we are not aware of this conversion for an intermediate vinylcarbene complex obtained through alkyne-carbene complex coupling.

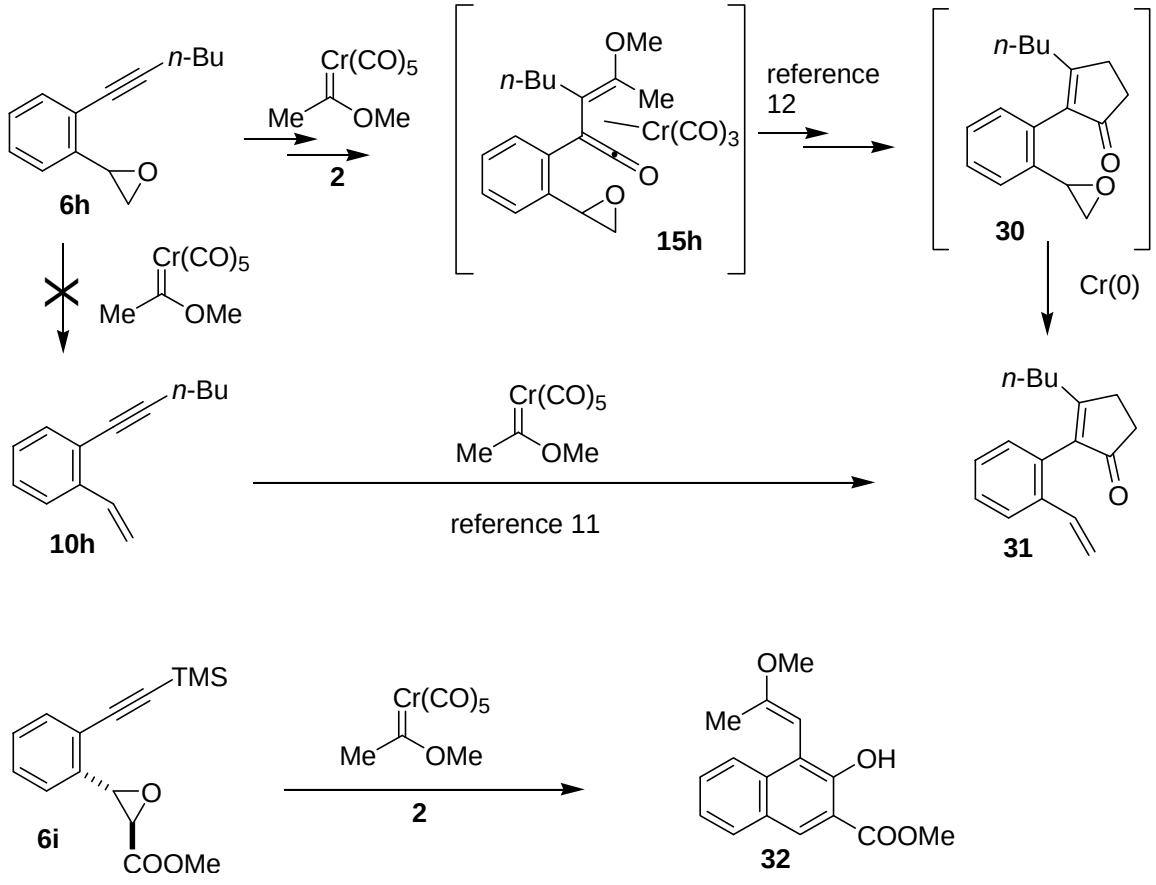
Scheme 6



Reaction of *n*-butylated alkyne-styrene derivative (**6h**) with carbene complex (**2**) afforded only the cyclopentenone (**31**) (Scheme 7). Styrylcyclopentenone (**31**) has previously been reported as one (of many) products from coupling of the carbene complex (**2**) with the alkynylstyrene (**10h**).[11] In a control experiment it was noted that styrene oxide was not reduced by methylcarbene complex (**2**) under the

conditions of this reaction, thus the simple conversion of **6h** to **10h** followed by coupling of **10h** with carbene complex (**2**) can not account for the formation of **31**. Deoxygenation of hypothetical cyclopentannulation product (**30**) by a chromium(0) species generated in the reaction is a more likely pathway. Activation of the allylic C-H bond in chromium-complexed vinylketene functionality of intermediate (**15h**)[12] is preferred over the nucleophilic attack of epoxide oxygen at the vinylketene carbonyl carbon. Reaction of the epoxy-ester complex (**6i**) with Fischer carbene complex (**2**) afforded benzannulation product (**32**) as the only isolable product (less that 10% yield) from a complex reaction mixture.

Scheme 7



CONCLUSION

The reaction of carbene complexes with alkynylstyrene oxides has been demonstrated. In some cases alkyne insertion/CO insertion/epoxide ring opening provided the desired benzoxepinones. In cases where the R^4 substituent was not hydrogen, the more favorable pathway was net oxygen atom transfer, which proceeds through electrocyclic ring opening of a benzopyran derivative. The diverse reactivity patterns exhibited by relatively similar substrates is rather disappointing with regard to our quest to

develop a new synthesis of benzoxepinones, however the simple process of trapping an unstable vinylcarbene complex intermediate through oxidation is without precedent.

EXPERIMENTAL[13]

General Procedure 1. Synthesis of styrene oxides using sulfur ylide chemistry. Sodium hydride (1.92 g, 48 mmol, 60% mineral oil dispersion) was washed with petroleum ether (3×10 mL). The residual petroleum ether was removed under vacuum. Under nitrogen, dry THF (30 mL) and dry DMSO (30 mL) were added and the reaction mixture was cooled to –10°C in an ice/salt bath. A solution of trimethylsulfonium iodide (9.8 g, 48 mmol) in DMSO (40 mL) was added by cannula over 5 min. After the addition was complete, the aldehyde (16 mmol) was added in one portion. The reaction mixture was stirred for 30 min at 0°C and an additional 40 min at rt. The reaction was slowly quenched with 90 mL of ice/water and extracted with dichloromethane (3×100 mL). The combined organic extracts were washed with water (2×100 mL), dried over potassium carbonate, and filtered. The solvent was removed on a rotary evaporator. The crude product was purified by flash column chromatography on silica gel using 20: 1 hexanes/ethyl acetate as the eluent.

General Procedure 2. Synthesis of styrene oxides through *m*CPBA oxidation. To a solution of the alkene (5.0 mmol) in dichloromethane (10 mL), *m*CPBA (6.0 mmol, 1.2 eq.) was added portionwise at 0 °C and the mixture stirred for 24 h at 0 °C. The reaction mixture was allowed to warm to rt and stirred overnight. The resultant milky white mixture was washed 3 times with a saturated sodium bicarbonate solution, and then washed with water and dried over anhydrous sodium sulfate. Removal of the solvent on a rotary evaporator afforded the epoxide as a crude clear yellow liquid. Purification by flash column chromatography on silica gel using 20: 1 hexanes/ethyl acetate as the eluent gave the final product.

Synthesis of styrene oxide (**6a**). General Procedure 1 was followed using 2-ethynylbenzaldehyde (**9a**)[14] to afford epoxide (**6a**) as a light yellow oil in 68% yield. ^{1}H NMR ($CDCl_3$): δ 7.48 (d, 1H, *J* = 7.6), 7.31 (t, 1H, *J* = 7.6), 7.23 (d, 1H, *J* = 7.6), 7.18 (t, 1H, *J* = 7.6), 4.32 (dd, 1H, *J* = 4.2, 2.7), 3.35 (s, 1H), 3.16 (dd, 1H, *J* = 5.8, 4.2), 2.67 (dd, 1H, *J* = 5.8, 2.7); ^{13}C NMR ($CDCl_3$): δ 140.2, 132.6, 129.3, 127.6, 123.7, 121.1, 82.2, 82.1, 51.2, 50.6; IR (neat): 3287 cm^{-1}; LRMS (EI) m/z: 144, 115, 89, 63; HRMS: calcd for $C_{10}H_8O$ 144.0575, found 144.0573.

Synthesis of styrene oxide (**6b**). General Procedure 2 was followed using 1-ethenyl-2-(2-trimethylsilylethynyl)benzene (**10b**)[15] to afford epoxide (**6b**) as a light yellow oil in 72%

yield. ^{1}H NMR ($CDCl_3$): δ 7.44 (d, 1H, *J* = 7.6), 7.28 (t, 1H, *J* = 7.6), 7.20 (t, 1H, *J* = 7.6), 7.14 (d, 1H, *J* = 7.6), 4.33 (dd, 1H, *J* = 4.2, 2.7), 3.18 (dd, 1H, *J* = 5.8, 4.2), 2.65 (dd, 1H, *J* = 5.8, 2.7), 0.22 (s, 9H); ^{13}C NMR ($CDCl_3$): δ 140.0, 132.3, 129.1, 127.6, 123.0, 122.3, 102.3, 99.6, 51.3, 50.8, 0.1; LRMS (CI): 215$(M-H)^+$, 201, 185, 145, 73; HRMS: calcd for $C_{13}H_{15}OSi$ $(M-H)^+$ 215.0892, found 215.0896.

Synthesis of styrene oxide (**6c**). General Procedure 2 was followed using 1-(1-propenyl)-2-(2-trimethylsilylethynyl)benzene (**10c**)[15] to afford epoxide (**6c**) as a light yellow oil in 67% yield (*trans: cis* = 3:2). *Trans:* ^{1}H NMR ($CDCl_3$): δ 7.5-7.1 (m, 4H), 4.03 (d, 1H, *J* = 1.9), 2.89 (qd, 1H, *J* = 5.9, 1.9), 1.47 (d, 3H, *J* = 5.9), 0.25 (s, 9H); ^{13}C NMR ($CDCl_3$): δ 144.4, 132.0, 129.0, 127.4, 123.8, 121.9, 102.5, 99.5, 59.1, 58.2, 18.1, 0.1. *Cis:* ^{1}H NMR ($CDCl_3$): δ 7.5-7.1 (m, 4H), 4.26 (d, 1H, *J* = 4.3), 3.39 (qd, 1H, *J* = 5.9, 4.3), 1.04 (d, 3H, *J* = 5.9), 0.25 (s, 9H); ^{13}C NMR ($CDCl_3$): δ 138.3, 131.9, 128.4, 127.3, 126.8, 121.8, 102.5, 99.7, 57.1, 55.1, 12.9, 0.1. LRMS (EI) m/z: 230, 215, 200, 185, 141, 73; HRMS: calcd for $C_{14}H_{18}OSi$ 230.1127, found 230.1130.

Synthesis of styrene oxide (**6d**). General Procedure 2 was followed using 2-(1-ethynyl)-1-(2-methylethenyl)benzene (**10d**)[15] to afford epoxide (**6d**) as a light yellow oil in 61% yield. ^{1}H NMR ($CDCl_3$): δ 7.44 (d, 2H, *J* = 7.7), 7.31 (t, 1H, *J* = 7.7), 7.21 (t, 1H, *J* = 7.7), 3.32 (s, 1H), 2.96 (d, 1H, *J* = 5.2), 2.84 (d, 1H, *J* = 5.2), 1.65 (s, 3H); ^{13}C NMR ($CDCl_3$): δ 144.3, 132.7, 129.1, 127.5, 126.7, 120.2, 82.2, 81.7, 58.4, 55.1, 23.1; IR (neat): 3285 cm^{-1}; LRMS (EI) m/z: 158, 157, 129, 115, 102, 89, 77, 63, 51; HRMS: calcd for $C_{11}H_{10}O$ 158.0731, found 158.0732.

Synthesis of styrene oxide (**6e**). General Procedure 2 was followed using 2-ethynyl-1-(1-methyl-1-propenyl)benzene (**10e**)[15] to afford epoxide (**6e**) as a light yellow oil in 55% yield (*trans: cis* = 3:1). *Trans:* ^{1}H NMR ($CDCl_3$): δ 7.44 (d, 2H, *J* = 7.6), 7.32 (t, 1H, *J* = 7.6), 7.20 (t, 1H, *J* = 7.6), 3.31 (s, 1H), 3.06 (q, 1H, *J* = 5.5), 1.57 (s, 3H), 1.44 (d, 3H, *J* = 5.5); ^{13}C NMR ($CDCl_3$): δ 146.9, 132.6, 129.3, 127.3, 126.3, 119.8, 82.2, 81.7, 62.1, 60.3, 18.5, 14.3. *Cis:* ^{1}H NMR ($CDCl_3$): δ 7.94 (d, 1H, *J* = 7.6), 7.62 (d, 1H, *J* = 7.6), 7.5-7.2 (m, 2H), 3.26 (s, 1H), 3.21 (q, 1H, *J* = 5.5), 1.66 (s, 3H), 1.01 (d, 3H, *J* = 5.5); ^{13}C NMR ($CDCl_3$): δ 135.3, 134.7, 130.4, 130.0, 128.1, 127.7, 82.0, 81.4, 63.3, 61.6, 23.8, 15.0. IR (neat): 3287 cm^{-1}; LRMS (EI) m/z: 172, 128, 102, 77, 43; HRMS: calcd for $C_{12}H_{12}O$ 172.0810, found 172.0806.

Synthesis of vinylthiophene oxide (**6f**). General Procedure 1 was followed using 3-ethynyl-2-thiophenecarboxaldehyde (**9f**)[16] to afford epoxide (**6f**) as a light yellow oil in 65% yield. ^{1}H NMR (C_6D_6): δ 6.75 (d, 1H, *J* = 5.3), 6.52 (d, 1H, *J* = 5.3), 4.12 (dd, 1H, *J* = 4.1, 2.9), 2.90 (s, 1H),

2.58 (dd, 1H, *J* = 5.8, 4.1), 2.47 (dd, 1H, *J* = 5.8, 2.9); ^{13}C NMR (C_6D_6): δ 147.5, 130.7, 124.4, 121.3, 81.6, 77.9, 52.1, 49.1; IR (neat): 3285 cm^{-1}; LRMS (EI) m/z: 150, 121, 77, 63, 45; HRMS: calcd for C_8H_6OS 150.0139, found 150.0143.

Synthesis of styrene oxide (**6g**). General Procedure 2 was followed using 1-(1-methylethenyl)-2-(2-trimethylsilylethynyl)benzene (**10g**)[15] to afford epoxide (**6g**) as a light yellow oil in 61% yield. ^{1}H NMR ($CDCl_3$): δ 7.44 (d, 1H, *J* = 7.2), 7.42 (d, 1H, *J* = 7.2), 7.31 (t, 1H, *J* = 7.2), 7.19 (t, 1H, *J* = 7.2), 2.95 (d, 1H, *J* = 5.2), 2.86 (d, 1H, *J* = 5.2), 1.70 (s, 3H), 0.25 (s, 9H); ^{13}C NMR ($CDCl_3$): δ 144.4, 132.0, 128.9, 127.4, 126.5, 121.2, 103.3, 99.6, 58.6, 55.3, 23.0, 0.0; LRMS (CI) m/z: 229 $(M-H)^+$, 215, 200, 185, 141, 73; HRMS: calcd for $C_{14}H_{17}OSi$ $(M-H)^+$ 229.1049, found 229.1055.

Preparation of styrene oxide (**6h**). General Procedure 1 was followed using 2-(1-hexynyl)benzaldehyde (**9h**)[17] (1.86 g, 10 mmol) to afford epoxide (**6h**) as a light yellow oil in 83% yield (1.66 g). ^{1}H NMR ($CDCl_3$): δ 7.40 (d, 1H, *J* = 7.5), 7.25 (t, 2H, *J* = 7.5), 7.11 (d, 1H, *J* = 7.5), 4.32 (dd, 1H, *J* = 4.2, 2.2), 3.15 (dd, 1H, *J* = 5.7, 4.2), 2.65 (dd, 1H, *J* = 5.7, 2.2), 2.45 (t, 2H, *J* = 7.2), 1.50 (m, 4H), 0.9 (t, 3H, *J* = 7.2); ^{13}C NMR ($CDCl_3$): δ 139.1, 131.8, 127.8, 127.3, 123.3, 123.0, 95.2, 76.8, 51.0, 50.7, 30.7, 21.9, 19.1, 13.5; HRMS: calc. for $C_{14}H_{16}O$ 200.1201, found 200.1203.

Preparation of styrene oxide (**6i**). To a solution of methyl chloroacetate (1.1 g, 10.0 mmol) and 2-(2-trimethylsilylethynyl)benzaldehyde (**9b**)[18] (2.02 g, 10.0 mmol) in THF (30 mL) was added sodium hydride (60% mineral oil dispersion, 0.44 g, 11.0 mmol) portion-wise at –5°C. The reaction mixture was allowed to warm to rt slowly and stirred overnight. Ice water (30 mL) was added to quench the reaction. The aqueous layer was extracted with dichloromethane (3 x 50 mL). The organic layers were combined, dried over potassium carbonate, and concentrated under reduced pressure. Purification was achieved by flash chromatography on silica gel using 1: 9 ethyl acetate: hexanes as the eluent. Epoxide (**6i**) was afforded as a colorless oil in 68 % yield (1.86 g). ^{1}H NMR ($CDCl_3$): δ 7.43 (d, 1H, *J* = 7.6), 7.32 (7, 1H, *J* = 7.6), 7.26 (t, 2H, *J* = 7.6), 7.09 (d, 1H, *J* = 7.6), 4.55 (d, 1H, *J* = 2.8), 3.81 (s, 3H), 3.40 (d, 1H, *J* = 2.8), 0.22 (s, 9H); ^{13}C NMR ($CDCl_3$): δ 168.8, 137.6, 132.2, 129.1, 128.4, 124.1, 122.6, 101.7, 100.8, 56.9, 56.4, 52.7; IR (neat): 2157, 1756 cm^{-1}; LRMS (EI) m/z: 274, 259, 170, 142, 73; HRMS: calcd for $C_{15}H_{18}O_3Si$ 274.1025, found 274.1015. The product was assigned as the pure *trans* isomer based of the small coupling constant (2.8 Hz) for the epoxide ring hydrogens.

Attempted preparation of styrene oxide (**6i**) *via m*CPBA oxidation – formation of **13**. To a solution of methyl 3-[2-(2-trimethylsilyl)phenyl]-2-propenoate (**10i**)[19] (1.81 g, 7.0 mmol) in dichloromethane (30

mL) was added *m*CPBA (14.0 mmol, 2 eq.) in one portion at rt, and then saturated sodium bicarbonate solution (30 mL) was added drop-wise. The reaction mixture was refluxed for 48 h. The organic layer was washed with sodium bisulfate (20 mL), dried over magnesium sulfate, and concentrated under reduced pressure. Purification was achieved by flash chromatography on silica gel using 1: 9 ethyl acetate: hexanes as the eluent. Alkene (**10i**) was recovered (2.1 mmol, about 30% of the starting material). Two products were isolated and identified as epoxide (**6i**) (0.28 g, 21% yield based on recovered starting materials) and ketone (**13**) (0.65 g, 48% yield based on recovered starting materials). **13:** ^{1}H NMR ($CDCl_3$): δ 7.59 (d, 1H, *J* = 7.7), 7.47 (m, 2H), 7.30 (m, 1H), 3.70 (s, 3H), 3.28 (d, 1H, *J* = 3.2), 2.14 (d, 1H, *J* = 3.2), 0.20 (s, 9H); ^{13}C NMR ($CDCl_3$): δ 203.2 (C), 168.7 (C), 153.2 (C), 133.9 (C), 133.8 (CH), 127.6 (CH), 125.1 (CH), 124.9 (CH), 52.3 (CH_3), 48.1 (CH), 33.6 (C), 31.0 (CH), -0.8 (CH_3 of TMS); IR (neat): 1735 (s), 1706 (s) cm^{-1}; LRMS m/z: 274, 259, 170, 142, 114, 89, 73, 59, 45; HRMS: calcd for $C_{15}H_{18}O_3Si$ 274.1025, found 274.1031.

General Procedure 3 – coupling of carbene complex with styrene oxide derivatives. A solution of carbene complex (1.2 mmol, 1.2 eq.) and epoxide (1.0 mmol, 1 eq.) in dioxane (20 mL) was added drop-wise to refluxing dioxane (10 mL) over a 1 h period. After the addition was complete, the mixture was kept at gentle reflux for a 24 h period. The resulting reaction mixture was allowed to cool to rt and then concentrated in *vacuo*. The residue was stirred in silica gel/chloroform in the air for another 24 h period and then filtered through a thin layer of Celite. The solvent was removed on a rotary evaporator. Final purification was achieved by flash chromatography on silica gel.

Coupling of carbene complex (**2**) with stryrene oxide (**6a**). General Procedure 3 was followed using methylcarbene complex (**2**)[20] (300 mg, 1.2 mmol) and epoxide (**6a**) (144 mg, 1.0 mmol). Final purification was achieved by flash chromatography on silica gel using 9:1 hexane: ethyl acetate as eluent. One compound was isolated and identified as benzoxepinone (**8a**) (105 mg, 46%). **8a:** ^{1}H NMR ($CDCl_3$): δ 7.5-7.1 (m, 4H), 6.70 (d, 1H, *J* = 7.1), 6.45 (d, 1H, *J* = 7.1), 5.25 (d, 1H, *J* = 7.8), 4.15 (d, 1H, *J* = 7.8), 3.69 (s, 3H), 1.55 (s, 3H); ^{13}C NMR ($CDCl_3$): δ 167.9 (C), 156.8 (C), 138.7 (CH), 134.6 (C), 132.0 (C), 129.3 (CH), 127.7 (CH), 127.6 (CH), 126.7 (CH), 114.4 (CH), 91.1 (CH), 54.8 (CH_3), 46.9 (CH), 16.9 (CH_3); IR (neat) 1762 cm^{-1}; LRMS (EI) m/z 230, 171, 159, 142, 128, 115, 59, 43; HRMS calcd for $C_{14}H_{14}O_3$ 230.0943, found 230.0946.

Coupling of methylcarbene complex (**2**) with styrene oxide (**6b**). General Procedure 3 was followed using methylcarbene complex (**2**)[20] (300 mg, 1.2 mmol) and epoxide (**6b**) (216 mg, 1.0 mmol). Final purification was achieved by flash chromatography on silica gel using 9:1 hexane: ethyl acetate as eluent.

One compound was isolated and identified as benzoxepinone (**8b**) (67 mg, 22%). **8b:** ^{1}H NMR ($CDCl_3$): δ 7.5-7.1 (m, 4H), 6.59 (d, 1H, *J* = 6.6), 6.34 (d, 1H, *J* = 6.6), 5.06 (s, 1H), 3.45 (s, 3H), 2.10 (s, 3H), 0.25 (s, 9H); ^{13}C NMR ($CDCl_3$): δ 171.2, 159.3, 138.5, 135.1, 132.7, 128.5, 128.2, 128.0, 127.1, 115.2, 55.2, 48.4, 17.6, 2.33; IR (neat) 1757 cm^{-1}; LRMS (EI) m/z 302, 185, 153, 141, 73; HRMS calcd for $C_{17}H_{22}O_3Si$ 302.1338, found 302.1341.

Coupling of methylcarbene complex (**2**) with styrene oxide (**6c**). General Procedure 3 was followed using methylcarbene complex (**2**)[20] (300 mg, 1.2 mmol) and epoxide (**6c**) (230 mg, 1.0 mmol). Final purification was achieved by flash chromatography on silica gel using 9:1 hexane: ethyl acetate as eluent. One compound was isolated and identified as benzoxepinone (**8c**) (107 mg, 34%). **8c:** ^{1}H NMR ($CDCl_3$): δ 7.5-7.1 (m, 4H), 6.18 (s, 1H), 5.01 (s, 1H), 3.45 (s, 3H), 2.10 (s, 3H), 2.05 (s, 3H), 0.15 (s, 9H); ^{13}C NMR ($CDCl_3$): δ 170.8, 159.2, 148.2, 134.5, 133.4, 128.6, 127.8, 127.6, 127.2, 111.4, 55.2, 49.1, 21.5, 17.7, 2.3; IR (neat) 1756 cm^{-1}; LRMS m/z 316, 273, 201, 173, 142, 125, 73; HRMS calcd for $C_{18}H_{24}O_3Si$ 316.1495, found 316.1485.

Coupling of methylcarbene complex (**2**) with styrene oxide (**6d**). General Procedure 3 was followed using methylcarbene complex (**2**)[20] (300 mg, 1.2 mmol) and epoxide (**6d**) (158 mg, 1.0 mmol). Final purification was achieved by flash chromatography on silica gel using 9:1 hexane: ethyl acetate as eluent. One compound was isolated and identified as phenone (**20d**) (136 mg, 63%). **20d:** ^{1}H NMR ($CDCl_3$): δ 7.46 (d, 1H, *J* = 7.4), 7.35 (t, 1H, *J* = 7.4), 7.28 (t, 1H, *J* = 7.4), 7.24 (d, 1H, *J* = 7.4), 5.85 (s, 1H), 5.13 (quintet, 1H, *J* = 1.5), 4.98 (dq, 1H, *J* = 1.5, 0.9), 3.64 (s, 3H), 2.38 (s, 3H), 2.06 (dd, 3H, *J* = 1.5, 0.9); ^{13}C NMR ($CDCl_3$): δ 194.9, 173.6, 145.8, 142.2, 141.9, 130.0, 128.8, 127.8, 127.3, 116.0, 100.5, 55.7, 24.5, 20.0; IR (neat) 1667, 1575 cm^{-1}; LRMS (EI) m/z 216, 201, 159, 141, 115, 72, 59, 43; HRMS calcd for $C_{14}H_{16}O_2$ 216.1150, found 216.1150.

Coupling of methylcarbene complex (**2**) with styrene oxide (**6e**). General Procedure 3 was followed using methylcarbene complex (**2**)[20] (300 mg, 1.2 mmol) and epoxide (**6e**) (172 mg, 1.0 mmol). Final purification was achieved by flash chromatography on silica gel using 9:1 hexane: ethyl acetate as eluent. One compound was isolated and identified as phenone (**20e**) (198 mg, 86%). **20e:** ^{1}H NMR ($CDCl_3$): δ 7.46 (d, 1H, *J* = 7.5), 7.34 (t, 1H, *J* = 7.5), 7.26 (t, 1H, *J* = 7.5), 7.20(d, 1H, *J* = 7.5), 5.75 (s, 1H), 5.50 (q, 1H, *J* = 6.8), 3.60 (s, 3H), 2.36 (s, 3H), 1.94 (s, 3H), 1.71 (d, 3H, *J* = 6.8); ^{13}C NMR ($CDCl_3$): δ 195.3, 172.9, 144.1, 142.0, 136.6, 129.9, 128.9, 128.0, 126.7, 125.8, 100.8, 55.5, 19.9, 18.3, 14.4; IR (neat) 1663, 1575 cm^{-1}; LRMS (EI) m/z: 230, 215, 185, 128, 115, 99, 59; HRMS calcd for $C_{15}H_{18}O_2$ 230.1307, found 230.1307.

Coupling of methylcarbene complex (**2**) with vinylthiophene oxide (**6f**). General Procedure 3 was followed using methylcarbene complex (**2**)[20] (300 mg, 1.2 mmol) and epoxide (**6f**) (150 mg, 1.0 mmol). Final purification was achieved by flash chromatography on silica gel using 9:1 hexane: ethyl acetate as eluent. One compound was isolated and identified as thiophenone (**20f**) (98 mg, 47%). **20f:** ^{1}H NMR ($CDCl_3$): δ 7.49 (dd, 1H, *J* = 17.5, 11.4), 7.24 (d, 1H, *J* = 5.7), 7.08 (d, 1H, *J* = 5.7), 5.89 (s, 1H), 5.68 (d, 1H, *J* = 17.5), 5.30 (d, 1H, *J* = 11.4), 3.72 (s, 3H), 2.39 (s, 3H); ^{13}C NMR ($CDCl_3$): δ 187.0, 174.6, 146.8, 140.1, 130.0, 128.6, 122.9, 116.8, 99.7, 55.7, 20.2; IR (neat) 1651, 1574 cm^{-1}; LRMS (EI) m/z 208, 193, 149, 134, 109, 99, 59; HRMS calcd for $C_{11}H_{12}O_2S$ 208.0558, found 208.0556.

Coupling of methylcarbene complex (**2**) with styrene oxide (**6g**). General Procedure 3 was followed using methylcarbene complex (**2**)[20] (300 mg, 1.2 mmol) and epoxide (**6g**) (230 mg, 1.0 mmol). Final purification was achieved by flash chromatography on silica gel using 9:1 hexane: ethyl acetate as eluent. One compound was isolated and identified as naphthalene (**25**) (90 mg, 45%). **25:** ^{1}H NMR ($CDCl_3$): δ 8.52 (d, 1H, *J* = 7.7), 7.90 (d, 1H, *J* = 7.7), 7.71 (t, 1H, *J* = 7.7), 7.57 (t, 1H, *J* = 7.7), 7.46 (s, 1H), 2.72 (s, 3H), 2.60 (s, 3H); ^{13}C NMR ($CDCl_3$): δ 204.4, 161.4, 136.9, 130.2, 125.8, 125.5, 125.1, 124.7, 124.3, 124.2, 112.9, 27.1, 19.2; IR (neat) 3500-2500 (br), 1621 (s) cm^{-1}; LRMS m/z 200, 185, 128; HRMS calcd for $C_{13}H_{12}O_2$ 200.0837, found 200.0830. The OH peak could not be reliably identified in the spectrum. Small amounts of compound consistent with the pre-hydrolysis product (**24**) could also be observed in some experimental runs. ^{1}H NMR ($CDCl_3$): δ 8.13 (dd, 1H, *J* = 7.5, 1.5), 7.90 (d, 1H, *J* = 7.5), 7.48 (m, 2H), 7.31 (s, 1H), 4.57 (d, 1H, *J* = 2.1), 4.45 (d, 1H, *J* = 2.1), 3.77 (s, 3H), 2.60 (s, 3H), 0.21 (s, 9H); ^{13}C NMR ($CDCl_3$): δ 159.9 (C), 147.2 (C), 133.8 (C), 128.8 (C), 127.2 (CH), 126.2 (CH), 125.1 (CH), 124.1 (CH) (likely 2 C's), 123.5 (C), 86.9 (CH_2), 55.1 (CH_3), 18.9 (CH_3), 0.8 (CH_3); IR (neat): 1650 (w), 1616 (m), 1603, (m), 1571 (m) cm^{-1}.

Coupling of butenylcarbene complex (**26**) with styrene oxide (**6a**). General Procedure 3 was followed using carbene complex (**26**)[21] (348 mg, 1.2 mmol) and epoxide (**6a**) (158 mg, 1.0 mmol). Final purification was achieved by flash chromatography on silica gel using 9:1 hexane: ethyl acetate as eluent. One compound was isolated and identified as phenone (**28**) (154 mg, 60%). **28:** ^{1}H NMR ($CDCl_3$): δ 7.46 (d, 1H, *J* = 7.4), 7.36 (t, 1H, *J* = 7.4), 7.31 (t, 1H, *J* = 7.4), 7.26 (d, 1H, *J* = 7.4), 5.85 (ddt, 1H, *J* = 16.9, 10.4, 7.4), 5.81 (s, 1H), 5.13 (quintet, 1H, *J* = 1.5), 5.05 (dd, 1H, *J* = 16.9, 1.5), 5.00 (dq, 1H, *J* = 1.5, 0.9), 4.95 (dd, 1H, *J* = 10.4, 1.5), 3.65 (s, 3H), 2.9 (t, 2H, *J* = 7.4), 2.35 (q, 2H, *J* = 7.4), 2.05 (dd, 3H, *J* = 1.5, 0.9); ^{13}C NMR ($CDCl_3$): δ 194.4, 176.2, 145.8, 142.1, 142.0, 137.9, 130.0, 128.8, 127.8, 127.3, 116.2,

115.1, 100.3, 55.7, 32.3, 31.4, 24.5; IR (neat) 1662, 1574 cm^{-1}; LRMS m/z 256, 241, 227, 213, 155, 141, 129, 115, 97, 55, 41; HRMS calcd for $C_{17}H_{20}O_2$ 256.1463, found 256.1466.

Coupling of methylcarbene complex (**2**) with styrene oxide (**6h**). General Procedure 3 was followed using methylcarbene complex (**2**)[20] (300 mg, 1.2 mmol) and epoxide (**6h**) (200 mg, 1.0 mmol). Final purification was achieved by flash chromatography on silica gel using 5:1 hexane: ethyl acetate as eluent. One compound was isolated and identified as cyclopentenone (**31**) (50 mg, 21%). **31:** ^{1}H NMR ($CDCl_3$): δ 7.65 (d, 1H, *J* = 7.2), 7.34 (m, 2H), 7.10 (d, 1H, *J* = 7.2), 6.55 (dd, 1H, *J* = 16.2, 11.7), 5.75 (d, 1H, *J* = 16.2), 5.25 (d, 1H, *J* = 11.7), 2.75 (t, 2H, *J* = 4.5), 2.55 (t, 2H, *J* = 4.5), 2.05 (t, 2H, *J* = 7.2), 1.35-1.05 (m, 4H), 0.75 (t, 3H, *J* = 7.2); IR (neat) 1700 cm^{-1}. The spectral data are in agreement with that previously reported for this compound.[11]

Coupling of methylcarbene complex (**2**) with alkynylstyrene oxide (**6i**). General Procedure 3 was followed using methylcarbene complex (**2**)[20] (300 mg, 1.2 mmol) and epoxide (**6i**) (274 mg, 1.0 mmol). Final purification was achieved by flash chromatography on silica gel using 9:1 hexane: ethyl acetate as eluent. One compound was isolated and tentatively assigned as naphthol (**32**) (43 mg, 10%). **32:** ^{1}H NMR ($CDCl_3$): δ 7.94 (d, 1H, *J* = 8.2), 7.92 (s, 1H), 7.38 (d, 1H, *J* = 8.2), 7.36 (t, 1H, *J* = 8.2), 7.29 (t, 1H, *J* = 8.2), 5.95 (s, 1H), 3.85 (s, 3H), 3.80 (s, 3H), 2.22 (s, 3H); ^{13}C NMR ($CDCl_3$): δ 164.3 (C), 155.1 (C), 142.5 (C), 138.2 (CH), 134.3 (C), 131.2 (C), 129.8 (CH), 129.7 (CH), 129.6 (CH), 126.2 (CH), 122.2 (C), 109.0 (CH), 98.7 (C), 59.0 (CH_3), 53.5 (CH_3), 13.7 (CH_3); IR (neat): 3420 (br), 1731 (s) cm^{-1}.

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REFERENCES

1. J. W. Herndon and H. Wang, *J. Org. Chem.*, 1998, **63**, 4564.
2. For the latest example, see Y. Luo and J. W. Herndon, *Organometallics*, 2005, **24**, 3099.
3. J. W. Herndon and A. Hayford, *Organometallics*, 1995, **14**, 1556.
4. a. J. G. Marrero, L. S. Andres, and J. G. Luis, *J. Nat. Prod.*, 2002, **65**, 986. b. For leading references, see M. Lautens, J. F. Paquin, and S. Piguel, *J. Org. Chem.*, 2002, **67**, 3972.
5. W. Ruehl, F. Boelsing, E. Hofer, D. Speer, and M. Jansen, *Z. Naturforsch. B*, 1986, **41B**, 772.

6. L. Ming-Yuan, R. J. Madhushaw, and R. S. Liu, *J. Org. Chem.*, 2004, **69**, 7700.
7. This is a well known thermal reaction, for a recent study, see: P. N. Day, Z. Wang, and R. Pachter, *J. Phys. Chem.*, 1995, **99**, 9730. The reaction in the benzopyran compound (**19**) should be far more facile than the well known conversion of pyran to *Z* 2,4-pentadienal.
8. M. Reisser, A. Maier, and G. Maas, *Synlett*, 2002, 1459.
9. Aromatization of dihydroaromatics is a frequent side reaction in chromium carbene alkyne couplings. For an example, see: S. U. Tumer, J. W. Herndon, and L. A. McMullen, *J. Am. Chem. Soc.*, 1992, **114**, 8394.
10. For the latest example, see J. Barluenga, F. Andina, M. A. Fernandez-Rodriguez, P. Garcia-Garcia, I. Merino, and E. Aguilar, *J. Org. Chem.*, 2004, **69**, 7352.
11. T. J. Jackson and J. W. Herndon, *Tetrahedron*, 2001, **57**, 3859.
12. C. A. Challener, W. D. Wulff, B. A. Anderson, S. Chamberlin, K. L. Faron, O. K. Kim, C. K. Murray, Y. C. Xu, D. C. Yang, and S. D. Darling, *J. Am. Chem. Soc.*, 1993, **115**, 1359.
13. For a General Experimental, see: J. W. Herndon, J. Zhu, and D. Sampedro, *Tetrahedron*, 2000, **56**, 4985.
14. R. M. Acheson and G. C. M. Lee, *J. Chem. Soc., Perkin Trans. 1*, 1987, 2321.
15. K. Maeyama and N. Iwasawa, *J. Org. Chem.*, 1999, **64**, 1344.
16. J. Bussenius, N. Laber, T. Muller, and W. Eberbach, *Chem. Ber.*, 1994, **127**, 247.
17. B. Gabriele, G. Salerno, A. Fazio, and R. Pittelli, *Tetrahedron*, 2003, **59**, 6251.
18. T. C. Bedard and J. S. Moore, *J. Am. Chem. Soc.*, 1995, **117**, 10662.
19. Prepared through reaction of 2-(2-trimethylsilylethynyl)benzaldehyde with methyl (triphenylphosphoranylidene)acetate.
20. L. S. Hegedus, M. A. McGuire, and L. M. Schultze, *Org. Synth.*, 1987, **65**, 140, or Coll. Vol. VIII, pp. 216-219.
21. Y. Zhang and J. W. Herndon, *J. Org. Chem.*, 2002, **67**, 4177.