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Synthesis of Alkylidenecyclopentenones and Dialkylidenecyclopentenones via the Coupling of Propargylic Alcohol and 2-Alkyne-1,4-diol Derivatives with Cyclopropylcarbene–Chromium Complexes

James W. Herndon,* Jin Zhu and Diego Sampedro

Department of Chemistry and Biochemistry, New Mexico State University, MSC 3C, Las Cruces, NM 88003, USA

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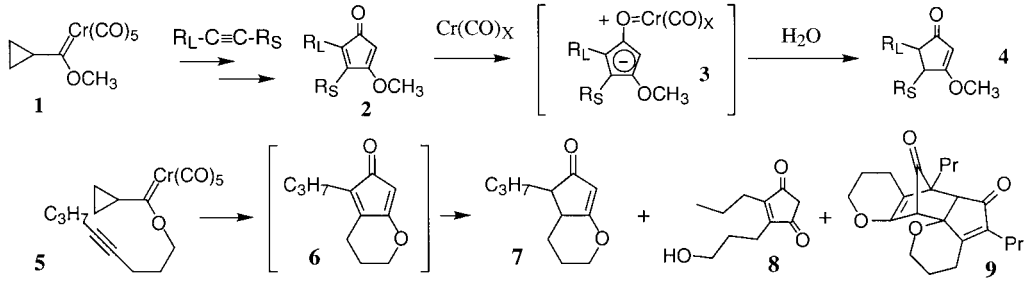
Abstract—The coupling of propargylic alcohols and their derivatives with cyclopropylcarbene–chromium complexes has been investigated. The coupling reaction leads to alkylidenecyclopentenones or alkoxyalkyl-cyclopentenones, depending on the leaving group ability of the propargyl substituent. A mechanism involving formation of a cyclopentadienone, followed by reduction and β-elimination is proposed. Coupling of cyclopropylcarbene complexes with 2-alkyne-1,4-diol derivatives leads to dialkylidenecyclopentenone derivatives via a double elimination process.

Introduction

The synthesis of cyclopentenones (cyclopentannulation) via the coupling of alkynes and cyclopropylcarbene–chromium complex **1** has been demonstrated for a variety of alkyne substrates (Scheme 1).[1] In this reaction, a cyclopentadienone (**2**) is formed through a complex series of steps,[2] which is reduced to the cyclopentenone derivative (**4**)[3] under the reaction conditions. In case of diarylacetylenes, the cyclopentadienone intermediate can be isolated in good yield,[4] and can be subsequently reduced to the corresponding cyclopentenone using chromium(0) sources and water.[5] A mechanism involving a net reduction of the cyclopentadienone to the cyclopentadienone dianion equivalent, followed by the addition of two protons has been proposed. Numerous attempts to capture the cyclopentadienone intermediates by other processes have failed, although alternative cyclopentadienone derived products have been observed in some cases. For example, thermolysis of alkyne–carbene complex **5** at high concentration leads to low yields of the hydrolysis product **8** and the Diels–Alder dimer **9** as well as the anticipated reduction product **7**.[6] This result suggests that reaction pathways other than reduction are possible for the cyclopentadienone intermediates.

In this manuscript, the coupling of cyclopropylcarbene complexes and propargyl alcohol derivatives will be investigated[7] (Scheme 2). Potential synthetic approaches to 4-alkylidene-2-cyclopentenones (**12**), 4,5-dialkylidene-2-cyclopentenones (**15**), and 5-alkylidene-2-cyclopentenones (**18**) can be realized depending on the regiochemistry of the alkyne insertion step and the substitution pattern at the



Scheme 1.

Keywords: alkylidenecyclopentenones; dialkylidenecyclopentenones; coupling reaction; cyclopropylcarbene–chromium complexes.
* Corresponding author. Tel.: +1-505-646-2487; fax: +1-505-646-2649; e-mail: jherndon@nmsu.edu

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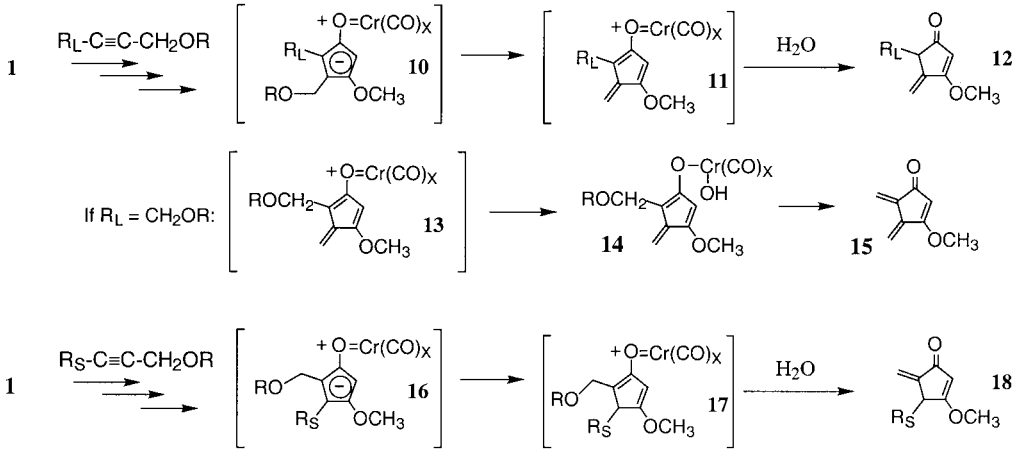


Scheme 2.

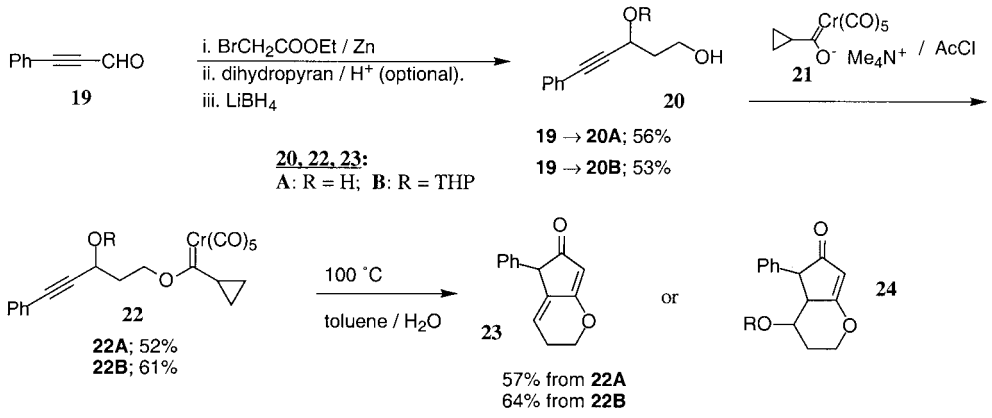
propargyl position. Potential synthesis of 4-alkylidene-2-cyclopentenones can be realized if a propargyl oxygen is on the sterically less hindered side of the alkyne. After construction of the five-membered ring, a β-elimination process can occur at the cyclopentadienide stage (**10**),[8] resulting in a fulvene-enolate intermediate (**11**), which would then afford alkylidenecyclopentenone **12** after protonation. If a 2-alkyne-1,4-diol derivative is employed, a double elimination can occur resulting in 4,5-dialkylidene-2-cyclopentenones (e.g. **15**). The synthesis of 5-alkylidenecyclopentenones (**18**) requires a propargyl oxygen on the more hindered side of the alkyne. As reported in a preliminary communication, this idea is successful for the synthesis of 4-alkylidene-2-cyclopentenones, however numerous side reactions occur in the attempted synthesis of 5-alkylidene-2-cyclopentenones.[7] This manuscript will focus on the preparation of 4-alkylidene-2-cyclopentenones and 4,5-dialkylidenecyclopentenones. The alkylidenecyclopentenone ring system frequently occurs in a variety of medicinally-important compounds, including methylenomycin antibiotics, prostaglandin analogs, kaurene diterpenes, and punaglandin derivatives.[9] One-step cycloaddition reactions have rarely been used to construct this ring system[10] and the reaction in Scheme 1 offers such a process using two readily-available and very simple components, propargyl alcohol derivatives and cyclopropylcarbene–chromium complexes. The dialkylidenecyclopentenone ring system is extremely rare[11] and there is little documentation of the chemical reactivity of these compounds.

Results and Discussion

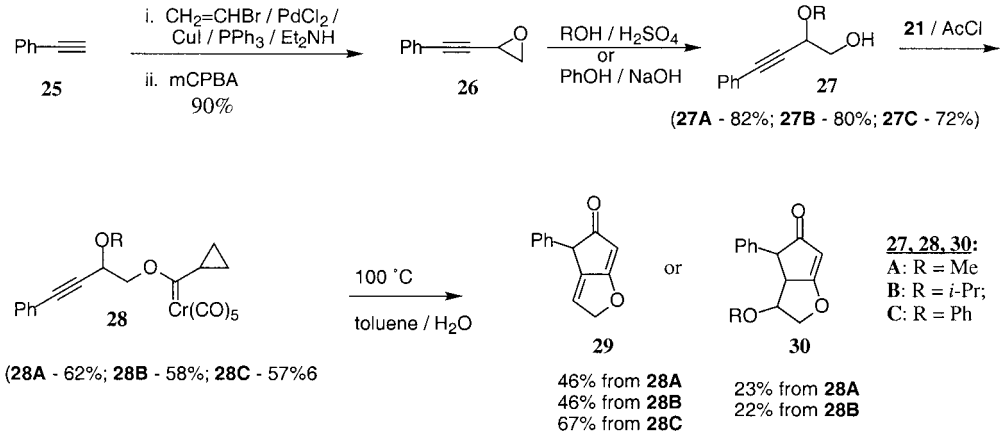
Synthesis of 4-alkylidene-2-cyclopentenones via coupling of propargyl alcohol derivatives with cyclopropylcarbene–chromium complexes

The synthesis of 4-alkylidenecyclopentenones can be achieved in either of two ways: (1) intermolecular coupling involving an internal alkyne where the propargyl oxygen is part of the smaller alkyne substituent (as depicted in Scheme 2, preparation of **12**), or (2) intramolecular alkyne-carbene complex coupling where the propargyl oxygen is within the tether (e.g. as in compound **22** of Scheme 3). Initial evaluation of the reaction was conducted in intramolecular systems, where there is complete control of regioselectivity.

Three-carbon tethered alkyne–carbene complexes (**22A**, **B**) were prepared using the general synthetic protocol in Scheme 3. Use of lithium aluminum hydride instead of lithium borohydride for the preparation of **20** resulted in triple bond reduction products. In the conversion of **20A** to the carbene complex, only the primary alcohol was



Scheme 3.



Scheme 4.

transformed to the carbene complex.[1] Thermolysis of either of the moderately-stable alkyne–carbene complexes **22** resulted in alkylidenecyclopentenone **23** in good yield (57% from **22A**, 64% from **22B**). In both cases, the alkylidenecyclopentenone **23** was the exclusive product; ether derivative **24** was never observed.

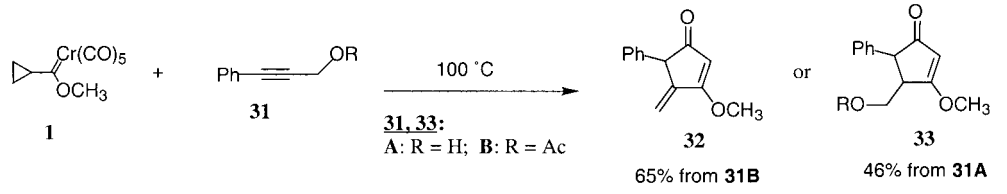
Two carbon-tethered alkyne–carbene complexes (**28A–C**) were prepared according to Scheme 4. The epoxide ring opening step afforded mostly (but not exclusively) the primary alcohol regioisomer depicted by structure **27**, however the carbene complex synthesis was highly selective for the primary alcohol.[1] Thermolysis of the alkyl ether derivatives **28A**,**B** afforded mixtures (~2:1) of the alkylidenecyclopentenone **29** and minor amounts of the compound where the oxygen atom was retained (**30**). The phenoxy derivative afforded exclusively the alkylidene–cyclopentenone in 67% yield.

The intermolecular coupling of phenylpropargyl alcohol (**31A**) and cyclopropylcarbene complex **1** afforded the hydroxymethylcyclopentenone derivative **33A** in 46% yield (Scheme 5); none of alkylidenecyclopentenone **32** was observed in this reaction. When the corresponding propargylic acetate **31B** was used in this coupling, only alkylidenecyclopentenone **32** was obtained in 65% yield.

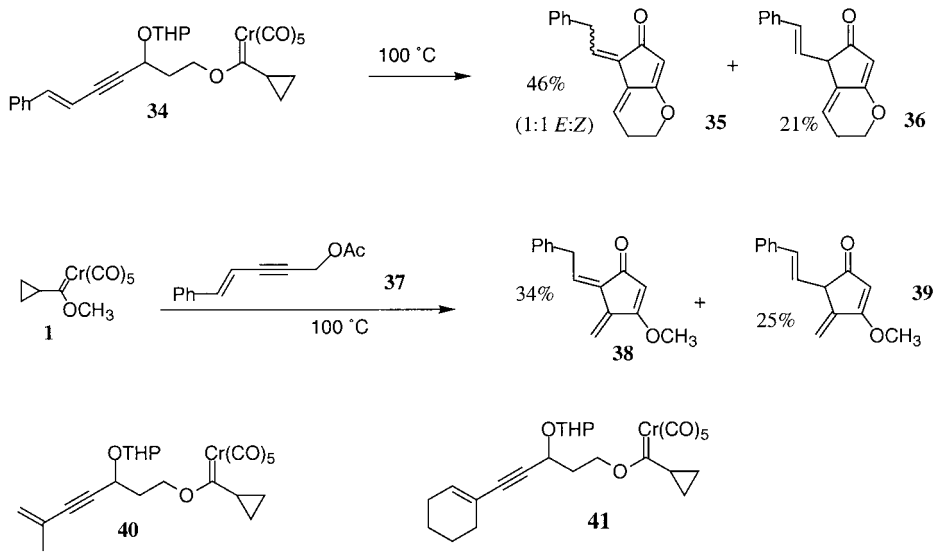
These studies reveal a clear dependence on the leaving group ability for the 4-alkylidenecyclopentenone synthesis. In the formation of the six-membered ring heterocycle (Scheme 3), alkylidenecyclopentenone **23** was the exclusive product of the reaction regardless of the propargyl leaving group. Alkylidenecyclopentenone formation was less favorable in five-membered heterocycle cases (Scheme 4), possibly due to the greater ring strain in the smaller ring cycloalkene, however the alkylidenecyclopentenone was the exclusive product of the reaction when the better leaving group (phenoxy) was present at the propargylic position. Formation of the alkylidene-cyclopentenone derivative appears to be considerably less favorable in the acyclic case (Scheme 5), possibly due to formation of a less substituted alkene. In this case, a hydroxy leaving group led to no detectable quantities of the alkylidenecyclopentenone **32**, however the acetate leaving group was sufficient to drive the reaction completely toward alkylidenecyclopentenone formation.

Synthesis of 4,5-dialkylidene-2-cyclopentenones via coupling of vinylpropargyl alcohol derivatives with cyclopropylcarbene–chromium complexes

Alkenylacetylene analogs of alkynes **22** and **31** also afforded alkylidenecyclopentenone derivatives (Scheme 6). In the cyclic (**34**) and acyclic (**37**) cases, a mixture of the 4,5-dialkylidenecyclopentenone (**35**, **38**) and 5-alkenyl-4-alkylidenecyclopentenone (**36**, **39**) was obtained. The 5-alkyenyl-4-alkylidene-2-cyclopentenones (**36** and **39**) are the anticipated reaction products, which presumably isomerize to the dialkylidenecyclopentenones (**35** and **38**) under the reaction conditions.[12] Monoalkylidenecyclopentenone **36** could never be isolated free of the corresponding dialkylidenecyclopentenone, possibly due to isomerization under the purification conditions. The dialkylidenecyclopentenone ring system is very rare, and in the



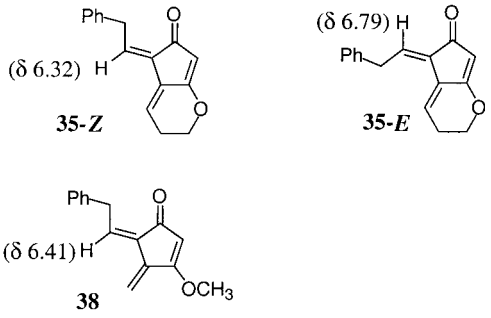
Scheme 5.



Scheme 6.

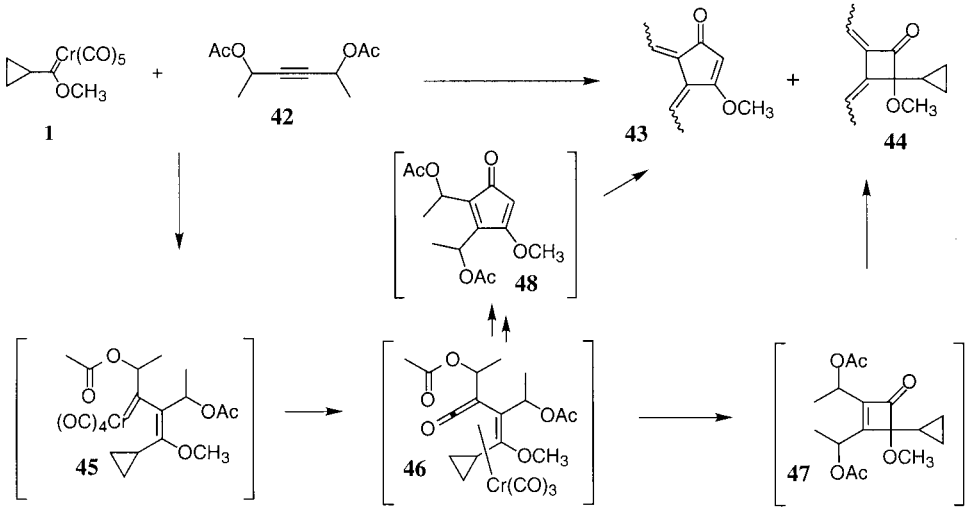
only report of this ring system one of the alkenes is heavily resonance-stabilized.[11] The substitution pattern of the alkene has a profound effect on the five-membered ring-forming reaction. Thermolysis of alkenylacetylene derivatives **40** and **41** led to complex reaction mixtures; the crude NMR showed substantial peaks in the region δ 0.8–0.2, which is indicative of an intact cyclopropane ring.

The stereochemistry of the 5-*exo* double bond in compounds **35** and **38** was assigned by comparison of the chemical shift of the vinylic proton in the 5-alkylidene unit with other alkylidenecyclopentenones in the literature, which feature higher chemical shifts for the vinylic proton of the *E*-isomer, and lower chemical shifts for the exocyclic allylic protons.[13] These protons occur at δ 6.79 and δ 6.32 in the two isomers of **35**; thus the isomer featuring the proton at δ 6.79 was assigned as the *E* 5-alkylidene isomer and the isomer featuring the proton at δ 6.32 was assigned as the *Z* 5-alkylidene isomer. The only isomer of **38** was assigned as the *Z* isomer since the vinylic proton of the 5-alkylidene unit occurs at δ 6.41 and thus more closely resembles the *Z* isomer of **35**.



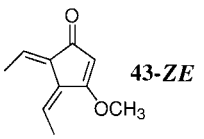
Synthesis of 4,5-dialkylidene-2-cyclopentenones via coupling of 2-alkyne-1,4-diol derivatives with cyclopropylcarbene–chromium complexes

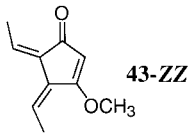
Formation of dialkylidenecyclopentenones via a double elimination process was investigated (Scheme 7). The

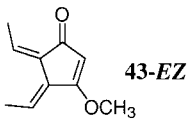


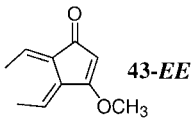
Scheme 7.

Table 1. Assignment of stereochemistry in dialkylidencyclopentenone **43**







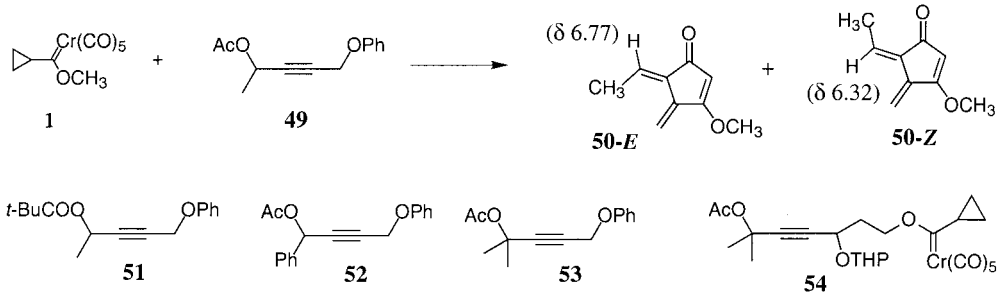


Isomer:	δ Exocyclic alkene H's	Possible structures
A	6.55 and 6.14	*ZE*, *ZZ*, or *EZ*
B	6.66 and 6.32	*EE*
C	6.54 and 6.18	*ZE*, *ZZ*, *EZ*
D	6.23 and 6.01	*ZZ* or *EZ*

reaction of hexyne diacetate (**42**, 1:1 mixture of *meso* and D,L isomers) with carbene complex **1** resulted in a mixture of the desired dialkylidenecyclopentenone **43** (mixture of stereoisomers) and a product tentatively assigned as dialkylidenecyclobutenone **44** (mixture of alkene stereoisomers); the cyclobutenone structure was suggested based on the infrared spectrum (a C=O stretch at 1790 cm^{-1} is present) and NMR spectrum (the cyclopropane ring is intact based on the appearance of peaks in the region δ 0.8–0.2, and numerous quartets were observed in the region δ 7.0–6.0). Based on past success in diversion of the reaction pathway using phosphines,[14] the coupling of complex **1** and hexyne diacetate was examined in the presence of various sterically-hindered phosphine ligands. The most beneficial effect was realized in the presence of one equivalent of tri-*o*-tolyphosphine, where dialkylidenecyclopentenone **43** was obtained in 70% yield accompanied by only a trace amount of the analogous cyclobutenone. No carbene–alkyne coupling was observed when triphenylphosphine or 1,2-bis(diphenylphosphino)ethane were additives. A likely pathway for formation of **44** is decomplexation–ring closure from vinylketene **46** to afford cyclobutenone **47**, followed by reduction to afford diene **44**. The presence of chelating oxygen substituents is known to enhance the production of cyclobutenones from carbene–alkyne couplings,[15] and a likely role of the phosphine ligand is to break the chromium oxygen chelates. The bulky phosphines are effective at shutting down the conversion of **46** to **47** without competing with the alkyne in the initial alkyne complexation step.[16]

Under the optimal conditions (1 equiv. of tri-*o*-tolylphosphine present), dialkylidenecyclopentenone **43** was obtained as a mixture of four out of the four possible alkene stereoisomers; the four isomers, designated as isomers A, B, C and D, were obtained in a 40:17:35:8 ratio, respectively. Coupling in the presence of 1,2-bis(diphenylphosphino)-benzene or 1,1′-bis(diphenylphosphino)ferrocene afforded a 1:1 mixture of stereoisomers C and D in lower (26–40%) yield. A similar result was obtained when tri-*o*-tolylphosphine was used in excess (2 equiv.). The same two isomers were obtained after treatment of the crude mixture of four compounds with diiron nonacarbonyl; the desired diene–iron complex was not obtained under these conditions. Based on these observations, isomers C and D appear to be the thermodynamic products of the reaction.[17] Assignment of stereochemistry to the isomers of dialkylidenecyclopentenone **43** was not definitive however a few generalizations can be made. Since **43-*EE*** suffers from steric interaction between the methyl groups, it is unlikely to be thermodynamic isomers C or D. Since the exocyclic alkene hydrogens of isomer D are most upfield, the 5-alkylidene substituent is most likely of the *Z* configuration.[13] Since the exocyclic alkene hydrogens of isomer B are most downfield, the 5-alkylidene substituent is most likely of the *E* configuration. Isomer B is most likely **43-*EE*** since the 5-alkylidene unit has the *E* configuration and since **43-*EE*** can not be thermodynamic isomers C or D. A summary of the isomer possibilities is depicted in Table 1.

Other examples of this dialkylidenecyclopentenone synthesis were less successful. Coupling of carbene complex **1** with 2-butyne-1,4-diacetate afforded a complex reaction mixture which appears to result from incorporation of multiple carbene units. Coupling of phenoxy derivative **49** with carbene complex **1** led to a compound consistent with the dialkylidenecyclopentenone structure **50** in 19% yield as a 1:1 mixture of stereoisomers (Scheme 8). Compound **50** was very unstable and prone to polymerization reactions, however it could be characterized by ^1H NMR and IR; the chemical shifts of the vinylic proton in the 5-alkylidene unit (δ 6.77 and δ 6.32) were consistent with *Z* and *E* isomers of



Scheme 8.

compounds **35** and **38** noted previously. It is clear that these types of reactions are very sensitive to steric effects. None of the alkynes **51**–**53** coupled with carbene complex **1**, and the analogous intramolecular coupling of complex **54** also failed.

Conclusion

The coupling of propargyl alcohol derivatives with cyclopropylcarbene complexes appears to be a general method for the synthesis of 4-alkylidenecyclopentenones. The leaving groups required for the elimination step of the 4-alkylidenecyclopentenone synthesis vary depending upon the stability of the alkylidene substituent, however propargylic acetates and phenoxides appear to undergo the critical β-elimination event in every system tested. The synthesis of rare 4,5-dialkylidene-2-cyclopentenones can be effected by either coupling of vinylpropargyl alcohol derivatives with cyclopropylcarbene complexes or coupling of 2-alkyne-1,4-diol derivatives with cyclopropylcarbene complexes, however the scope of the latter process appears to be highly limited.

Experimental

General considerations

Nuclear Magnetic Resonance (^{1}H and ^{13}C NMR) spectra were recorded on a Bruker AF200 (200 MHz), Bruker AF400 (400 MHz), or Varian AF (200 MHz) spectrometer. Chemical shifts are reported in parts per million (δ) relative to an internal chloroform reference. Coupling constants (J values) are reported in hertz (Hz), and spin multiplicities are indicated by the following symbols: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet). Infrared spectra were recorded on a Nicolet 5DXC FT-IR or Perkin–Elmer model 281 spectrometer. Band positions are reported in reciprocal centimeters (cm^{-1}). Band intensities are reported relative to the most intense band and are listed as: br (broad), vs (very strong), s (strong), m (medium), w (weak); only diagnostic bands (excluding C–H stretches) above 1500 cm^{-1} are reported. Mass spectra (MS) were obtained on a VG 7070E spectrometer using electron impact (El) or chemical ionization (CI) or on a Hewlett–Packard GC–MS 5970B with Mass Selection Detector: *m*/*e* value is reported, followed by the relative intensity in parentheses. Melting points were taken on a Fisher–Johns melting point apparatus (Model 12-144) equipped with a calibrated thermometer. Flash column chromatography was performed using thick-walled glass columns and 'flash grade' silica gel (Bodman 230–400 mesh). Preparative thin layer chromatography was performed using precoated 1000 μm 20×20 silica gel plates purchased from Whatman. Routine thin layer chromatography (TLC) was performed using precoated 0.25 mm silica gel plates purchased from Whatman. Combustion analysis results were obtained from Desert Analytics Laboratory or Galbraith Laboratories.

Tetrahydrofuran (THF), diethyl ether, and 1,4-dioxane were distilled from sodium/benzophenone ketyl. Dichloromethane, *N*,*N*-dimethylformamide (DMF) and toluene were distilled from calcium hydride before use. All reaction solvents were distilled for purity. All other reagents were obtained from commercial suppliers and used without further purification.

Preparation of acylate salt 21. To a solution of cyclopropyl bromide (1.20 g, 10.0 mmol) in diethyl ether (25 mL) at −78°C under nitrogen was added *t*-butyllithium (9.10 mL of a 2.2 M pentane solution, 20.0 mmol) via syringe pump over a period of 10 min. This solution was stirred for 20 min at −78°C and then transferred via cannula to a suspension of chromium hexacarbonyl (2.20 g, 10.0 mmol) in diethyl ether (50 mL) at 0°C. The reaction mixture was warmed to 25°C and allowed to stir for 1 h. The solvent was then removed on a rotary evaporator and the residue was dissolved in a minimum amount of water and filtered through Celite. To the filtrate, 20 mL of saturated aqueous tetramethylammonium bromide solution was added, leading to immediate precipitation of the ammonium salt. The precipitate was collected by suction filtration, then dissolved in dichloromethane and dried over anhydrous sodium sulfate. The solvent was removed on a rotary evaporator to give a yellow solid (1.86 g, 55%) identified as the acylate salt **21**. ^{1}H NMR (acetone-d_6): δ 3.44 (s, 12H), 2.76 (m, 1H),0.65 (m, 2H), 0.27 (m, 2H).

General procedure (I): the synthesis of alkyne-containing carbene complexes

To a solution of acylate salt **21** (0.40 g, 1.20 mmol) in 20 mL of dichloromethane at 0°C under nitrogen was added acetyl chloride (0.08 mL, 1.20 mmol), followed by immediate addition of alkynol (1.20 mmol). The reaction mixture was stirred at 0°C for about 1 h and then warmed to 25°C and stirred for 20 min. The solvent was removed on a rotary evaporator. Flash chromatography of the residue after evaporation using hexane as the eluent gave the pure carbene complex after solvent removal. The resulting alkyne–carbene complexes were used immediately due to mild thermal and oxidative instability. In most cases, these complexes were characterized only through NMR and infrared data.

General procedure (II): intramolecular reaction of carbene complexes with alkynes

To a three-neck round-bottom flask equipped with a reflux condenser and rubber septum, under nitrogen, was added toluene (50 mL) and water (0.5 mL), and the solution was heated to reflux. To this refluxing solution was added a solution of the alkyne-carbene complex in toluene (20 mL) via syringe pump over a period of 4 h. After the addition was complete, the mixture was heated at reflux for an additional 20 h and then cooled to room temperature. The resulting green mixture was filtered through Celite and the solvent was removed on a rotary evaporator. Final purification was achieved by flash chromatography on silica gel using 4:1 hexane–ethyl acetate as eluent unless otherwise noted.

General procedure (III): intermolecular reaction of methoxycarbene–chromium complex 1 with propargyl alcohol derivatives

To a three-neck round-bottom flask equipped with reflux condenser and septum, under nitrogen, was added 99:1 toluene–water (50 mL). This solution was heated to reflux. To this refluxing solution, a solution of carbene complex and propargyl alcohol derivative in toluene (20 mL) was added via syringe pump over a period of 2 h. After the addition was complete, the mixture was heated at reflux for 24 h and then cooled to room temperature. The resulting green mixture was filtered through Celite and the solvent was removed on a rotary evaporator. Final purification was achieved by flash chromatography on silica gel.

Preparation of carbene complex 22A. General procedure I was followed using a solution of propargyl alcohol derivative **20A** (100 mg, 0.57 mmol) in dichloromethane (10 mL), acylate salt **21** (193 mg, 0.57 mmol), and acetyl chloride (0.042 mL, 0.57 mmol) in dichloromethane (20 mL). After chromatographic purification, a yellow oil (130 mg, 52%) identified as carbene complex **22A** was obtained. ^{1}H NMR ($CDCl_3$): δ 7.30 (m, 5H), 5.12 (t, 2H, J=6.2 Hz), 4.80 (dd, 1H, J=5.0, 6.2 Hz), 3.46 (m, 1H), 2.40 (q, 2H, J=6.2 Hz), 1.40 (m, 2H), 1.15 (m, 2H); ^{13}C NMR ($CDCI_3$): δ 223.3, 216.4, 131.4, 128.5, 128.0, 121.6, 87.9, 76.5, 59.5, 41.2, 36.7, 17.7; IR (neat): 2059 (m), 1925 (vs).

Preparation of carbene complex 22B. General procedure I was followed using the solution of propargyl alcohol derivative **20B** (170 mg, 0.65 mmol) in dichloromethane (10 mL), acylate salt **21** (264 mg, 0.78 mmol) and acetyl chloride (0.048 mL, 0.66 mmol) in dichloromethane (20 mL). After chromatographic purification, a yellow oil (204 mg, 61%) identified as carbene complex **22B** was obtained. ^{1}H NMR ($CDCl_3$): δ 7.30 (m, 5H), 5.15 (t, 2H, J=5.8 Hz), 5.10 (br s, 1H), 4.80 (t, H, J=5.8 Hz), 3.65 (m, 2H), 3.45 (m, 2H), 2.46 (q, 1H, J=5.8 Hz), 1.60 (m, 6H), 1.40–1.20 (m, 4H); ^{13}C NMR ($CDCl_3$): δ 352.0, 223.4, 216.7, 131.7, 128.3, 128.2, 122.1, 95.4, 86.2, 76.5, 64.5, 62.1, 61.6, 41.4, 35.7, 30.1, 25.2, 18.9, 17.8; IR: (neat): 1915 (vs).

Preparation of carbene complex 28C. General procedure I was followd using a solution of 2-phenoxy-4-phenyl-3-butyn-1-ol (**27C**) (98 mg, 0.41 mmol) in dichloromethane (10 mL), acylate salt **21** (139 mg, 0.41 mmol), and acetyl chloride (0.030 mL, 0.41 mmol) in dichloromethane (20 mL). After chromatographic purification using pure hexane as eluent, a yellow oil (113 mg, 57%) identified as carbene complex **28C** was obtained. ^{1}H NMR ($CDCl_3$): δ 223.2, 216.4, 156.9, 131.6, 129.5, 128.6, 128.2, 1220.0, 121.3, 115.9, 88.6, 82.6. 79.8, 65.9, 41.9, 18.5; IR (neat): 1916 (vs).

Preparation of carbene complex 34. General procedure I was followed using a solution of the appropriate propargyl alcohol derivative (2° THP ether of 7-phenyl-6-penten-4-yne-1,3-diol, prepared similarly to **20B**)[18] (180 mg, 0.63 mmol) in dichloromethane (10 mL), acylate salt **21** (212 mg, 0.63 mmol), and acetyl chloride (0.045 mL, 0.63 mmol) in dichloromethane (20 mL). After chromatographic purification, a yellow oil (228 mg, 68%) identified as carbene complex **34** was obtained. ^{1}H NMR ($CDCl_3$): δ 7.35 (m, 5H), 6.98 (d, 1H, J=16.2 Hz), 6.14 (dd, 1H, J=16.2, 1.4 Hz), 5.12 (t, 1H, J=6.0 Hz), 5.04 (br s, 1H), 4.79 (t, 1H, J=5.6 Hz), 3.69 (m, 1H), 3.55 (m, 1H), 3.49 (m, 1H), 2.39 (q, 2H, J=6.2 Hz), 1.60 (m, 6H), 1.42 (m, 2H), 1.18 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 223.8, 216.7, 142.2, 136.0, 128.7, 126.6, 126.2, 106.9, 95.4, 88.4, 85.5, 76.9, 62.2, 61.8, 41.4, 35.3, 30.2, 25.2, 18.9, 17.8; IR (neat): 1924 (vs).

Thermolysis of carbene complex 22A. General procedure II was followed using carbene complex **22A** (204 mg, 0.24 mmol). Purification by flash chromatography on silica gel using hexane ethyl acetate (4:1) as the eluent provided **23** as the only product. Further purification was done by preparative thin layer chromatography (hexane–ethyl acetate=3:2) to give 58 mg (57%) of alkylidenecyclopentenone **23**. ^{1}NMR ($CDCl_3$):δ 7.30 (m, 5H), 6.00 (t, 1H, J=4.1 Hz), 5.50 (s, 1H), 4.40 (t, 2H, J=5.4 Hz), 4.05 (s, 1H), 2.52 (td, 2H, J=5.4-t, 4.1-d Hz); ^{13}C NMR($CDCl_3$): δ 205.2, 198.3, 134.1, 129.4, 123.2, 109.4, 108.1, 68.2, 55.6, 23.7; IR (neat): 1684 (s), 1574 (vs); MS (FAB): *m/e* 213 (M+1,18), 212 (100), 184 (30); HRMS: Calcd for $C_{14}H_{12}O_2$: 212.0837; Found: 212.0836. The structure of **23** was further supported by decoupling experiments. Irradiation of the proton at δ 6.00: δ2.52 (t, J=5.4 Hz). Irradiation of the proton at δ 4.40:δ 2.52 (d, J=4.1 Hz). Irradiation of the proton at δ 2.52: δ 6.00 (s, 1H), 4.40 (s).

Thermolysis of carbene complex 22B. General procedure II was followed using carbene complex **22B** (240 mg, 0.48 mmol). Purification by flash chromatography on silica gel using hexane–ethyl acetate: (4:1) as the eluent provided alkylidenecyclopentenone **23** (65 mg, 64%) as the only product. The spectral data were identical to those reported in the previous synthesis of alkylidenecyclopentenone **23** from complex **22A**.

Thermolysis of carbene complex 28C. General procedure II was followed using carbene complex **28C** (116 mg, 0.24 mmol). Purification by flash chromatography on silica gel using hexane ethyl acetate (4:1) as the eluent provided compound **29** as the only product. Further purification was done by preparative thin layer chromatography (hexane–ethyl acetate=3:2) to give 31.7 mg (67%) of compound **29**. ^{1}H NMR ($CDCl_3$: δ 7.23 (m, 5H), 6.22 (br s, 1H), 5.44 (s, 2H), 5.27 (s, 1H), 4.05 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 203.8,191.5, 141.5, 128.7, 127.8, 127.4, 124.0, 111.2, 97.3, 86.1, 51.3; IR (neat): 1694 (m), 1599 (s); MS (El): *m/e* 198 (m, 100), 170 (15), 169 (38), HRMS: Calcd for $C_{13}H_{10}O_2$: 198.0689, Found: 198.0687.

Thermolysis of carbene complex 34. General procedure II was followed using carbene complex **34** (210 mg, 0.39 mmol). Purification by flash chromatography on silica gel using hexane ethyl acetate (4:1) as the eluent provided a mixture of compounds **35-*E***, **35-*Z***, and **36**. The 1:1:1 ratio of these compounds was determined by the NMR integration of the alkene peaks. Further purification was done by preparative thin layer chromatography (hexane–ethyl acetate=3:2) and two fractions were isolated. The compound (22.0 mg, 24%) in the first fraction was identified

as dialkylidenecyclopentenone **35-*Z***. ^{1}H NMR ($CDCl_3$): δ 7.27 (m, 5H), 6.32 (t, 1H, J=7.6 Hz), 6.24 (dt, 1H, J=4.6-t, 1.4-d Hz), 5.55 (br s, 1H), 4.33 (t, 2H, J=6.0 Hz), 4.25 (d, 2H, J=7.6 Hz), 2.54 (td, 2H, J=6.0-t, 4.6-d Hz); ^{13}C NMR ($CDCl_3$): δ 192.8, 174.2, 139.8, 132.4, 131.1, 128.5, 126.2, 116.1, 108.5, 66.6, 33.2, 23.5; IR (neat): 1648 (s), 1572 (s); MS (El): *m/e* 238 (m, 100), 167 (10), 165 (13); HRMS: Calcd for $C_{16}H_{14}O_2$: 238.0994, Found: 238.1014. The stereochemistry of the 5-*exo* double bond was assigned as *Z* by comparing with alkylidenecyclopentenones in literature, which feature higher chemical shifts for the vinylic proton of the *E*-isomer, and lower chemical shifts for the exocyclic allylic protons.[14] The two compounds (40.2 mg, 43%) in the second fraction were presumed to be a mixture of the *E* isomer of dialkylidenecyclopentenone **35** and alkylidenecyclopentenone **36**. A nearly pure sample of the *Z* isomer of **35** was isolated using prep TLC and partial band cutting. ^{1}H NMR ($CDCl_3$): δ 6.79 (t, 1H, J=7.6 Hz), 6.52 (br t, 1H, J=6.0 Hz), 5.56 (br s, 1H), 4.40 (t, 2H, J=6.0 Hz), 3.80 (d, 2H, J=7.6 Hz), 2.65 (q, 2H, J=6.0 Hz). A doublet at δ 6.70 and doublet of doublets at δ 6.10 are suggestive of the styryl group of compound **36**, however a pure sample of this compound was never successfully isolated.

Coupling of cyclopropylcarbene complex 1 with 3-phenylpropargyl alcohol (31A). General procedure III was followed using carbene complex **1**[2] (182 mg, 0.65 mmol) and 3-phenylpropargyl alcohol[19] (**31A**) (86 mg, 0.65 mmol). Toluene was used as the solvent with the addition of 1% water. The purification was done by preparative thin layer chromatography (hexane–ethyl acetate=2:1). A single fraction (65.2 mg, 46%) identified as cyclopentenone **33A** was obtained as a colorless oil. ^{1}H NMR ($CDCl_3$); δ 7.35 (m, 5H), 5.38 (s, 1H), 3.98 (dd, 1H, J=12.0, 3.6 Hz), 3.95 (s, 3H), 3.86 (dd, 1H, J=12.0, 3.0 Hz), 3.62 (d, 1H, J=3.2 Hz), 3.08 (br q, 1H, J=3.3 Hz), 1.80 (br s, 1H); ^{13}C NMR ($CDCl_3$): δ 203.5, 188.7, 138.4, 128.5, 127.9, 126.6, 104.5, 61.2, 59.1, 54.5, 52.1; IR (neat): 3350 (s), 1677 (s), 1588 (vs); MS (El): *m/e* 218 (37), 199 (19) 187 (100); HRMS: Calcd for $C_{13}H_{14}0_3$: 218.0943, Found 218.0935.

Coupling of cyclopropylcarbene complex 1 with 3-phenylpropargyl acetate (31B). General procedure III was followed using carbene complex **1**[2] (136 mg, 0.49 mmol) and 3-phenylpropargyl acetate (**31B**) (85 mg, 0.49 mmol). Toluene was used as the solvent with the addition of 1% water. The purification was done by preparative thin layer chromatography (hexane–ethyl acetate=4:1). A single fraction (63.9 mg, 65%) identified as alkylidenecyclopentenone **32** was obtained as a colorless oil. ^{1}H NMR ($CDCl_3$): δ 7.28 (m, 5H), 5.77 (d, 1H, J=1.6 Hz), 5.57 (d, 1H, J=1.6 Hz), 5.13 (t, 1H, J=1.6 Hz), 4.13 (t, 1H, J=1.6 Hz), 3.96 (s, 3H); ^{13}C NMR ($CDCl_3$): δ 200.9, 181.2, 143.3, 137.4, 128.5, 128.2, 127.0, 111.5, 105.4, 58.4, 55.4; IR (neat): 1695 (s), 1574 (vs); MS (El): *m/e* 200 (m, 100), 199 (31); HRMS: Calcd for $C_{13}H_{12}0_2$: 200.0839, Found 200.0837. Anal. Calcd for $C_{13}H_{12}O_2$: C 78.02%, H 6.04%, Found: C 77.85%, 6.02%.

Coupling of cyclopropylcarbene complex 1 with -5-phenyl--4-penten-2-yn-1-yl acetate (37). General procedure III was followed using carbene complex **1**[2] (182 mg, 0.48 mmol) and 5-phenyl-4-penten-2-yn-1-yl acetate[20] (**37**) (95 mg, 0.48 mmol). Toluene was used as the solvent with the addition of 1% water. The purification was done by preparative thin layer chromatography (hexane–ethyl acetate=5:1). Two fractions were collected. The compound in the first fraction (37.2 mg, 34%) was identified as dialkylidenecyclopentenone **38-*Z***. ^{1}H NMR ($CDCl_3$): δ 7.30 (m, 5H), 6.41 (t, 1H, J=7.6 Hz), 5.59 (s, 1H); 5.47 (s, 1H), 5.41 (s, 1H), 4.26 (d, 2H, J=7.6 Hz), 3.90 (s, 3H), ^{13}C NMR ($CDCl_3$): δ 192.8, 177.5, 139.7, 133.2, 129.8, 128.4, 127.4, 126.0, 106.7 104.2, 57.9, 33.2; IR (neat): 1700 (s), 1601 (vs) cm^{-1}; MS (El): *m/e* 226 (m, 72), 70 (100); HRMS: Calcd for $C_{15}H_{14}0_2$226.0993, Found: 226.0990.The stereochemistry of the 5-*exo* double bond was determined to be *Z* by comparison with *Z*-alkylidenecyclopentenones in literature as before.[14] The product in the second fraction (27.1 mg, 25%) was tentatively identified as alkylidenecyclopentenone **39**. ^{1}H NMR ($CDCl_3$): δ 7.40 (m, 5H), 6.64 (d, 1H, J=16.0 Hz), 6.02 (dd, 1H, J=16.0, 8.0 Hz), 5.73 (s, 1H), 5.50 (s, 1H), 5.27 (s, 1H), 3.74 (d, 1H, J=8.0 Hz), 3.92 (s, 3H); ^{13}C NMR ($CDCl_3$): δ 201.2, 180.2, 138.8, 126.4, 133.8, 128.2, 128.0, 126.2, 124.0, 111.6, 105.8, 58.2, 53.0; IR (neat): 1696 (s), 1571 (vs).

Coupling of cyclopropylcarbne complex 1 with 3-hexyne-2,4-diacetate (42) in the presence of tri-o-tolylphosphine. General procedure III was followed using carbene complex 1[2] (134 mg, 0.48 mmol), 3-hexyne-2,4-diacetate[21] (**42**) (95 mg, 0.48 mmol), and tris-*o*-tolylphosphine (169 mg, 0.48 mmol). Dioxane was used as the solvent without the addition of any proton source. The purification was done by preparative thin layer chromatography (hexane–ethyl acetate=4:1). Three fractions were collected. The compound in the first fraction (4.4 mg, 5%) was cyclobutenone **44**. Isomers of dialkylidenecyclopentenone **43** were obtained in the second (14.2 mg, 18%) and third (29.1, 37%) fractions. One isomer from the third fraction (Isomer C) could be successfully isolated free of the other isomers. ^{1}H NMR ($CDCl_3$): δ 6.54 (q, 1H, J=7.4 Hz), 6.18 (q, 1H, J=7.6 Hz), 5.37 (s, 1H), 3.88 (s, 3H), 2.33 (d, 3H, J=7.4 Hz), 2.00 (d, 3H, J=7.6 Hz); ^{13}C NMR ($CDCl_3$): δ 194.0, 178.4, 134.5, 132.7, 131.0, 120.7, 103.7, 57.7, 14.2; IR (neat): 1694 (s), 1599 (s) cm^{-1}; MS (*m/e*): 164 (M, 63), 150 (100), HRMS: Calcd for $C_{10}H_{12}O_2$: 164.0837, Found: 164.0832. The 3:2 mixture of compounds in the second fraction (major isomer is isomer A, minor isomer is isomer B) display the following ^{1}H NMR spectrum: δ 6.66 (q, 1H, J=7.7 Hz, *minor isomer*), 6.55 (q, 1H, J=7.7 Hz, *major isomer*) 6.32 (q, 1H, J=7.7 Hz, *minor isomer*), 6.14 (q, 1H, J=7.7 Hz, *major isomer*), 5.48 (s, 1H, *minor isomer*), 5.32 (s, 1H, *major isomer*), 3.88 (s, 3H, *overlapping for both isomers*), 2.13 (d, 3H, J=7.7 Hz, *minor isomer*), 2.00(d, 3H, J=7.7 Hz, *minor isomer*), 1.99 (d, 3H, J=7.7 Hz, *major isomer*), 1.98 (d, 3H, J=7.7 Hz, *major isomer*). The remaining isomer in the third fraction (isomer D) displays the following ^{1}H NMR spectrum. 6.23 (q, 1H, J=7.6 Hz), 6.01 (q, 1H, J=7.6 Hz), 5.54 (s, 1H), 3.85 (s, 3H), 2.26 (d, 3H, J=7.6 Hz), 2.08 (d, 3H, J=7.6 Hz). The crude ^{1}H NMR spectrum shows the four isomers were formed in a 35:22:30:13 A:B:C:D ratio. Since the crude ^{1}H NMR spectrum and the ^{1}H NMR spectra for isolated compounds suggest different isomer ratios, isomerization during purification is likely.

Coupling of cyclopropylcarbene complex 1 with 3-hexyne-2,4-diacetate (42) in the presence of 1,1′-bis(diphenylphosphino)ferrocene. General procedure III was followed using carbene complex **1**[2] (134 mg, 0.48 mmol), 3-hexyne-2,4-diacetate[21] (**42**) (95 mg, 0.48 mmol), and 1,1' bis(diphenylphosphino) ferrocene (266 mg, 0.48 mmol). Dioxane was used as the solvent without the addition of any proton source. The purification was done by preparative thin layer chromatography (hexane–ethyl acetate=4:1). A single fraction (26 mg, 40%) was collected and identified as a 3:2 mixture of isomers C and D of **43**. This fraction corresponds to a 3:2 mixture of the two isomers (isomers C and D) in the third fraction from the previous experiment.

Coupling of cyclopropylcarbene complex 1 with 4-phenoxy-2-pentyn-1-yl acetate (49). General procedure III was followed using carbene complex **1** (134 mg, 0.48 mmol), 4-phenoxy-2-pentyn-1-yl acetate[22] (**49**) (104 mg, 0.43 mmol), and tris-*o*-tolylphosphine (146 mg, 0.48 mmol). Dioxane was used as the solvent without the addition of any proton source. The purification was done by preparative thin layer chromatography (hexane–ethyl acetate=4:1). A single fraction containing an inseparable 1:1 mixture of dialkylidenecyclopentenones **50** (13.1 mg, 19%) was obtained. This compound was unstable and totally decomposed when stored for one week in the refrigerator at −23°C. ^{1}H NMR ($CDCl_3$) *reported for both isomers*: δ 6.77 (q, 1H, J=7.4 Hz), 6.32 (q, 1H, J=7.4 Hz), 6.15 (s, 1H), 5.82 (s, 1H), 5.80 (s, 1H), 5.62 (s, 1H), 5.48 (s, 1H), 5.46 (s, 1H), 3.90 (s, 3H), 3.89 (s, 3H), 2.05 (d, 3H, J=7.4 Hz), 2.04 (d, 3H, J=7.4 Hz), IR (neat): 1694 (s), 1599 (s) cm^{-1}.

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18. This compound was prepared according to the following sequence: (1) Sonogashira coupling of β-bromostyrene and propargyl alcohol, (2) Swern oxidation, and (3) the resulting aldehyde was transformed to the diol derivative according to the sequence used for the coupling of **19**–**20B**.
19. This compound was prepared via Sonogashira coupling of propargyl alcohol and iodobenzene.
20. This compound was prepared according to the following sequence: (1) Sonogashira coupling of β-bromostyrene and propargyl alcohol followed by (2) acetylation using acetyl chloride and pyridine.
21. This compound was prepared by acetylation (acetyl chloride/pyridine) of commercially available 3-hexyne-2,4-diol, which is a mixture of *meso* and D, L isomers.
22. This compound was prepared via the following sequence: (1) deprotonation of phenyl propargyl ether (commercially available from GFS chemicals) with *n*-butyllithium followed by addition of acetaldehyde, and (2) acetylation with acetyl chloride/pyridine.