Tandem Isobenzofuran Formation−Diels Alder Reactions in the Coupling of Carbene Complexes with 2-Alkynylbenzaldehyde Derivatives Featuring an Alkyne-Dienophile Tether

Yumei Luo and James W. Herndon*

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

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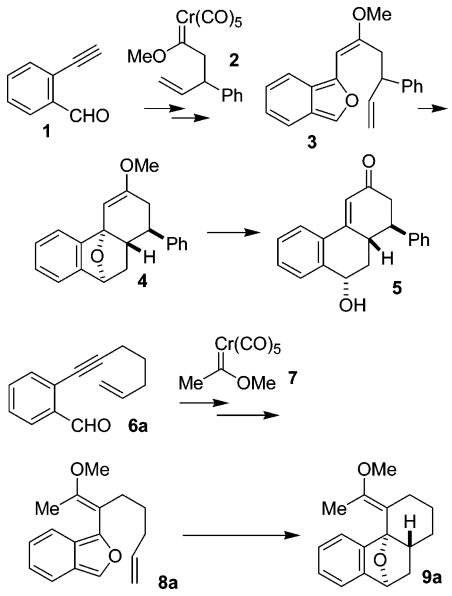
The coupling of carbene complexes and 2-alkynylbenzaldehyde derivatives has been examined for systems where the alkyne is further linked to an alkene. This reaction proceeds via generation of an isobenzofuran followed by a stereoselective intramolecular Diels−Alder reaction, followed by opening of the resulting oxanorbornene ring. A variety of hydrophenanthrene derivatives and heterocyclic analogues have been produced in this reaction. In one case the intramolecular Pauson−Khand reaction is a competing process.

Introduction

In recent papers, the generation of isobenzofuran intermediates (e.g., **3**, Scheme 1) through coupling of Fischer carbene complexes (e.g., **2**) with 2-alkynylbenzaldehyde derivatives (e.g., **1**) has been reported.[1] Isobenzofurans were subsequently trapped either through hydride shifts,[1c] through intramolecular Diels−Alder reaction with unactivated dienophiles,[1a,b] or through intermolecular Diels−Alder reactions with activated dienophiles.[1c] In most of the previous studies of intramolecular Diels−Alder trapping, the dienophile is connected to the future isobenzofuran through the carbene complex (i.e., γ,δ-unsaturated carbene complexes exemplified by **2**). In two cases, connection of the dienophile to the future isobenzofuran through to the carbonyl group of a benzamide derivative was demonstarted.[1d] Coupling of 2-alkynylbenzaldehydes with γ,δ-unsaturated carbene complexes offers an efficient and stereoselective[2] method for synthesis of hydrophenanthrene derivatives (e.g., **5**),[3] including steroids. In this article the focus is on a variant where the dienophile is tethered to the alkyne component, exemplified by the coupling of enyne-aldehyde **6a** with simple carbene complex **7**.

Scheme 1



In general a regioselective alkyne insertion followed by isobenzofuran generation will provide intermediate **8a**, which can undergo intramolecular Diels−Alder reaction to provide oxanorbornene derivative **9a**. This process is likely more challenging than those of ref 1 due to steric interaction of the original carbene substituent and the benzene ring in Diels−Alder adduct **9a**.

Results

The general synthetic route to the requisite enyne-aldehydes (**6**) is depicted in Scheme 2. Sonogashira coupling of enynes of general structure **10** with 2-bromobenzaldehyde (**11**) afforded the desired products in good to excellent yield. A likely side reaction, palladium-catalyzed enyne cycloisomerization of the starting enyne

* To whom correspondence should be addressed. E-mail: jherndon@nmsu.edu.

(1) (a) Ghorai, B. K.; Menon, S.; Johnson, D. L.; Herndon, J. W. *Org. Lett.* **2002**, *4*, 2121−2124. (b) Ghorai, B. K.; Herndon, J. W.; Lam, Y. F. *Org. Lett.* **2001**, *3*, 3535−3538. (c) Jiang, D.; Herndon, J. W. *Org. Lett.* **2000**, *2*, 1267−1269. (d) Ghorai, B. K.; Herndon, J. W. *Organometallics* **2003**, *22*, 3951−3957.

(2) Six-membered-ring-forming intramolecular Diels−Alder reactions of isobenzofurans proceed with exo stereochemistry as observed in ref 1. (a) Meegalla, S. K.; Rodrigo, R. *Synthesis* **1989**, 942−944. (b) Yamaguchi, Y.; Yamada, H.; Hayakawa, K.; Kanematsu, K. *J. Org. Chem.* **1987**, *52*, 2040−2046. (c) Tobia, D.; Rickborn, B. *J. Org. Chem.* **1987**, *52*, 2611−2615.

(3) For some recent references to synthesis of hydrophenanthrenes, including morphine alkaloids and abietanes, see: (a) Groth, U.; Richter, N.; Kalogerakis, A. *Eur. J. Org. Chem.* **2003**, 4634−4639. (b) Hanada, K.; Miyazawa, N.; Ogasawara, K. *Org. Lett.* **2002**, *4*, 4515−4517. (c) Nagata, H.; Miyazawa, N.; Ogasawara, K. *Chem. Commun.* **2001**, 1094−1095. (d) Liu, H. J.; Tran, D. D. *Tetrahedron Lett.* **1999**, *40*, 3827−3830. (e) Trauner, D.; Bats, J. W.; Werner, A.; Mulzer, J. *J. Org. Chem.* **1998**, *63*, 5908−5918. (f) Majetich, G.; Liu, S.; Fang, J.; Siesel, D.; Zhang, Y. *J. Org. Chem.* **1997**, *62*, 6928−6951.

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Scheme 2

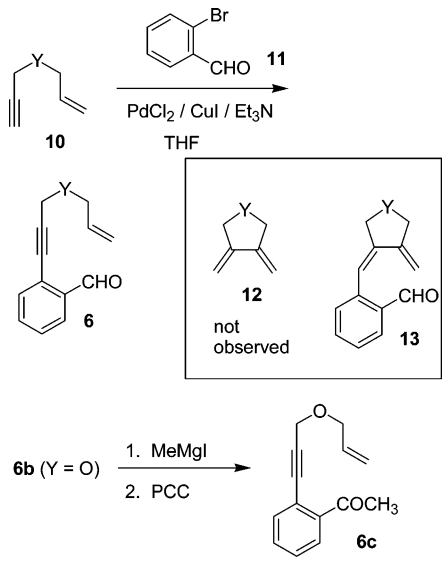
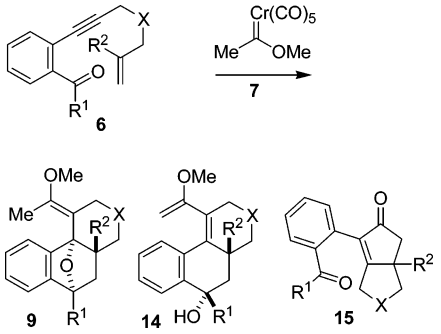


Table 1. Coupling of Enyne-Benzaldehyde Derivatives 6 with Carbene Complex 7



entry[a]	R^1	R^2	X	product(s)
A	H	H	CH_2	**14a** (60%)
B	H	H	O	**14b** (37%)
C	Me	H	O	**14c** (34%)
				15c (13%)
D	H	H	CE_2[b]	**14d** (51%)
E	H	Me	CE_2[b]	**14e** (60%)
F	H	H	NTs	**14f** (56%)

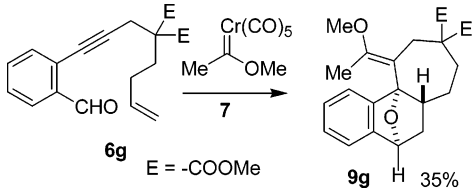
[a] In all discussions of carbene-alkyne adducts and compound **6** there is a correlation between entry letter and substituent letter. [b] E = COOMe.

or the product (resulting in **12** or **13**),[4] does not appear to be a problem. The aldehyde **6b** was easily transformed to the ketone **6c** through Grignard addition followed by oxidation.

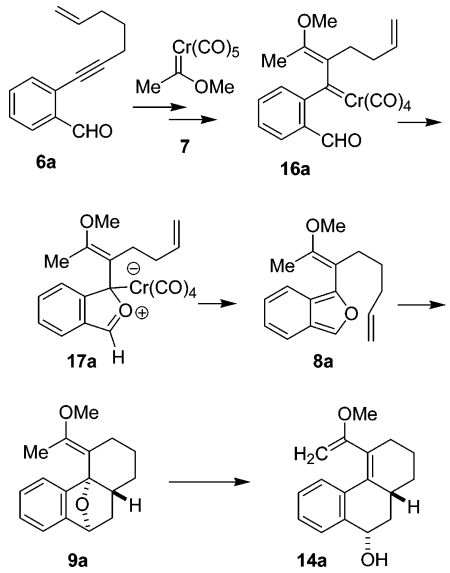
Various enyne-benzaldehyde derivatives of general structure **6** were tested in their reaction with methylcarbene complex **7** (see Table 1). As noted in Table 1, all of the examples tested afforded tricyclic products in moderate to good yield. In all of the cases in Table 1, the major product was an oxanorbornene ring-opening product **14** and not the initial Diels–Alder adduct **9**. Formation of **14** likely occurs via the desired reaction pathway involving isobenzofuran formation followed by intramolecular Diels–Alder reaction, followed by opening of the strained oxanorbornene ring system. The dienol ether derivative **14** was stable provided that the

(4) Trost, B. M.; Tanoury, G. *J. Am. Chem. Soc.* **1987**, *109*, 4753–4755.

Scheme 3



Scheme 4



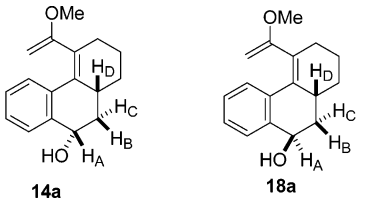
chromatographic purification was conducted in the presence of triethylamine. In one case (entry C), the Pauson–Khand product **15c** was obtained as a significant byproduct. The reaction was less efficient if the tether is increased by one atom (Scheme 3) and led to significant amounts of alkene-containing byproducts. In this example, the intact oxanorbornene product **9g** was obtained.

Discussion

Tricyclic products (**9** or **14**) were produced in the coupling of carbene complex **7** with enyne-benzaldehyde derivatives **6**. The mechanism for formation of the observed products is depicted in Scheme 4 and involves initial alkyne insertion to afford preferentially carbene complex **16**,[5] which undergoes reaction with the carbonyl oxygen to afford carbonyl ylide **17** followed by loss of chromium to afford isobenzofuran derivative **8**.[1c] Intramolecular Diels–Alder reaction from the exo direction[2] affords oxanorbornene **9**, which is unstable and affords the observed enol ether derivatives. The conversion of **9** to **14** is presumably an acid-catalyzed process; however no acid has deliberately been added to the reaction mixture. As in previously studied six-membered-ring-forming intramolecular Diels–Alder reactions of isobenzofurans, the exo Diels–Alder product **9a** is more stable than the corresponding endo product. Ab initio calculations (B3LYP 6-31G*) predict that exo **9a** (de-

(5) (a) Regioselectivity is controlled via steric effects. Wulff, W. D. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 5, pp 1065–1113. (b) High regioselectivity in similar systems has been noted. See the examples in ref 1b and references therein. (c) See also: Anderson, J. C.; Cran, J. W.; King, N. P. *Tetrahedron Lett.* **2002**, *43*, 3849–3852.

Scheme 5



dihedral angles		dihedral angles	
H_A-C-C-H_B	51°	H_A-C-C-H_B	56°
H_A-C-C-H_C	169°	H_A-C-C-H_C	61°
H_B-C-C-H_D	70°	H_B-C-C-H_D	61°
H_C-C-C-H_D	172°	H_C-C-C-H_D	179°

picted) is more stable than the endo form by 3.42 kcal/mol.[6] The stereochemical assignment of **14a**−**d** and **14d**−**f** is further supported by the observed coupling constants to the benzylic hydrogen (H_A in compound **14a** in Scheme 5). In all of these cases, this proton appears as a dd at δ 4.5−4.7 with coupling constants of ∼10 and ∼6 Hz. This is consistent with a conformation where the benzylic proton is axial and couples to adjacent axial and equatorial protons, as exists in the energy-minimum conformation of the ring-opening product (**14a**) from **9a**. Dihedral angles from the energy minima of **14a** and the stereoisomer **18a** are listed in Scheme 5. Two small couplings to H_A are predicted for the opposite stereoisomer **18a**. The stereochemistry of **9g** could not be reliably assigned due to overlapping protons. The alkene stereoisomer depicted reflects stereochemical preferences for enol ether formation in chromium carbene−alkyne couplings.[7] The ring stereochemistry arises from an exo Diels−Alder reaction, which is the kinetically preferred pathway in seven-membered-ring-forming intramolecular furan Diels−Alder reactions.[8]

The reactions that employ a gem-diester group or a tosylamide group (entries C−F) in the tether were generally more efficient that the oxygen-tethered examples in entries B and C and can likely be attributed to the gem dialkyl effect.[9] In the case of the seven-membered-ring-forming reaction in Scheme 3, the yield of the reaction was noticeably lower and the oxanorbornene−enol ether linkage appears to be more robust. Unidentified byproducts were obtained that feature monosubstituted alkene functionality. Likely these compounds result from a failed Diels−Alder reaction owing to the inherently more difficult seven-membered-ring forming process.[10]

In entry C, the Pauson−Khand reaction (formation of **15c**) was a competing process. Previous investigators have noted a similar side reaction in Fischer carbene reactions,[11] which they attributed to the metal carbonyl impurity. The origin of this product has not been exhaustively probed in our case.

Conclusion

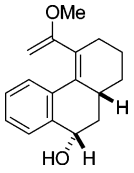
In summary, the coupling of carbene complexes and 2-alkynylbenzaldehyde derivatives has been examined for systems where the alkyne is linked to the dienophile. This reaction proceeds via generation of an isobenzofuran followed by an intramolecular Diels−Alder reaction, followed by opening of the norbornene ring. The reaction affords 6,6-fused ring systems with a high degree of stereoselectivity in yields comparable to that observed in systems where the dienophile is tethered to the carbene complex. A variety of hydrophenanthrene derivatives and heterocyclic analogues have been successfully tested in this reaction. In one case the intramolecular Pauson−Khand reaction was a competing process. The reaction is not ideal for the generation of 6,7-fused analogues due to the lesser efficiency in the intramolecular Diels−Alder step.

Experimental Section[12]

General Procedure for Coupling of Carbene Complexes and Enynes. A solution of methylcarbene complex **7** (0.80 mmol)[13] and enyne **6** (0.60 mmol) in dioxane (50 mL) was heated to 85 °C, and the reaction continued for 18 h. The solvent was removed under reduced pressure, and the residue was purified via flash column chromatography with ethyl acetate/hexane/triethylamine as eluent (1:4:0.1) to give product **9** or **14**.

Entry A of Table 1. The general procedure was followed using alkyne 6a (0.119 g, 0.60 mmol) and carbene complex 7 (0.200 g, 0.80 mmol). After final purification by flash chromatography, compound 14a (0.093 g, 60% yield) was obtained.

Compound 14a. ^{1}H NMR (C_6D_6): δ 7.80 (dd, 1 H, J = 7.3, 1.6 Hz), 7.60 (dd, 1 H, J = 7.3, 1.8 Hz), 7.13 (td, 1 H, J = 7.3, 1.8 Hz), 7.07 (td, 1 H, J = 7.3, 1.8 Hz), 4.72 (dd, 1 H, J = 9.7, 6.0 Hz), 4.16 (d, 1 H, J = 2.0 Hz), 3.99 (d, 1 H, J = 2.0 Hz), 3.18 (s, 3 H), 2.63 (ddd, 1 H, J = 16.4, 4.4, 2.2 Hz), 2.23−2.08 (m, 3 H), 1.86 (br s, 1 H), 1.69−1.06 (m, 5 H). ^{13}C NMR



(C_6D_6): δ 165.1, 141.1, 136.9, 131.8, 129.5, 128.3, 126.8, 84.7, 69.7, 54.8, 42.9, 36.7, 32.7, 32.3, 22.2. IR (KBr, cm^{-1}): 3450 (s, br), 1676 (m). MS (EI): *m/e* 256 (M^+, 10), 238 (89), 195 (14),

(6) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Menucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowki, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, A.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, M.; Callacombe, M.; Gill, P. M. W.; Johnson, B. G.; Chen, W.; Wong, M. W.; Andres, J. L.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian98*; Gaussian, Inc.: Pittsburgh, PA, 1998.

(7) McCallum, J. S.; Kunng, F. A.; Gilbertson, S. R.; Wulff, W. D. *Organometallics* **1988**, *7*, 2346−2360.

(8) Harwood, L. M.; Jones, G.; Pickard, J.; Thomas, R. M.; Watkin, D. *J. Chem. Soc., Chem. Commun.* **1990**, 605−607. Kinetic preference for the exo isomer was demonstrated using an α,β-unsaturated ketone as dienophile. Since the dienophile of intermediate **8g** is devoid of the ketone group, and since the diene portion is an isobenzofuran, preference for the kinetic (exo) product is expected to be higher.

(9) Jung, M. E.; Gervay, J. *J. Am. Chem. Soc.* **1991**, *113*, 224−232.

(10) Harwood, L. M.; Leeming, S. A.; Isaacs, N. S.; Jones, G.; Pickard, J.; Thomas, R. M.; Watkin, D. *Tetrahedron Lett.* **1988**, *29*, 5017−5020.

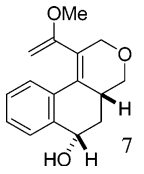
(11) Hoye, T. R.; Suriano, J. A. *Organometallics* **1992**, *11*, 2044−2050.

(12) For a general experimental see: Herndon, J. W.; Zhu, J.; Sampedro, D. *Tetrahedron* **2000**, *56*, 4985−4993.

(13) For a preparation of this compound see: Hegedus, L. S.; McGuire, M. A.; Schultze, L. M. *Org. Synth.* **1987**, *65*, 140−143, or Collective Volume 8, pp 216−219.

179 (58), 165 (46), 115 (12), 77 (9) 43 (100). HRMS: calcd for $C_{17}H_{20}O_2$ 256.146330, found 256.146018.

Entry B of Table 2. The general procedure was followed using alkyne **6b** (0.120 g, 0.60 mmol) and carbene complex **7** (0.210 g, 0.84 mmol). After final purification by flash chromatography, compound **14b** (0.053 g, 37% yield) was obtained.



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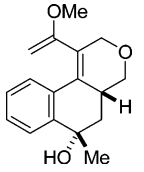
Compound 14b. ^{1}H NMR (C_6D_6): δ 7.78 (dd, 1 H, J = 7.3, 1.6 Hz), 7.62 (d, 1 H, J = 7.3, 1.8 Hz), 7.13 (td, 1 H, J = 7.3, 1.8 Hz), 7. 09 (td, 1 H, J = 7.3, 1.8 Hz), 4.63 (dd, 1 H, J = 16.4, 2.2 Hz), 4.61 (dd, 1 H, J = 10.0, 5.8 Hz), 4.18 (dd, 1 H, J = 16.4, 3.0 Hz), 4.07 (d, 1 H, J = 2.2 Hz), 3.99 (d, 1 H, J = 2.2 Hz), 3.83 (dd, 1 H, J = 11.0, 5.8 Hz), 3.08 (s, 3 H), 3.07 (t, 1 H, J = 11.0 Hz) 2.45 (m, 1 H), 2.14 (br s, 1 H), 1.80 (ddd, 1 H, J = 12.0, 5.8, 4.0 Hz), 1.29 (ddd, 1H, J = 12.0, 12.0, 10.0 Hz). ^{13}C NMR (C_6D_6): δ 160.9, 141.3, 134.9, 134.1, 130.2, 128.1, 127.1, 86.2, 71.0, 70.7, 68.9, 54.8, 36.7, 34.9. IR (KBr, cm^{-1}): 3415 (s, br), 1660 (m), 1615 (m). MS (EI): *m/e* 258 (M^+, 44), 186 (100), 171 (29), 152 (37), 141 (31), 115 (27). HRMS: calcd for $C_{16}H_{18}O_3$ 258.125595, found 258.124687.

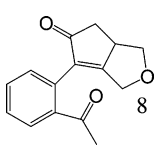
Entry C of Table 2. The general procedure was followed using alkyne **6c** (0.128 g, 0.60 mmol) and carbene complex **7** (0.210 g, 0.84 mmol). After final purification by flash chromatography, compounds **14c** (0.053 g, 34% yield) and **15c** (0.020, 13%) were obtained.

Compound 14c. ^{1}H NMR (C_6D_6): δ 7.76 (dd, 1 H, J = 7.6, 1.8 Hz), 7.63 (dd, 1 H, J = 7.6, 1.8 Hz), 7.13 (td, 1 H, J = 7.6, 1.8 Hz), 7.07 (td, 1 H, J = 7.6, 1.8 Hz), 4.67 (dd, 1 H, J = 16.8, 2.4 Hz), 4.26 (dd, 1 H, J = 16.8, 3.0 Hz), 4.08 (d, 1 H, J = 2.2 Hz), 4.00 (d, 1 H, J = 2.2 Hz), 3.91 (dd, 1 H, J = 11.0, 6.0 Hz), 3.20 (m, 1 H), 3.08 (s, 3 H), 3.07 (d, 1 H, J = 11.0 Hz), 2.62 (m, 1 H), 1.67 (dd, 1 H, J = 11.6, 3.2 Hz) 1.40 (t, 1 H, J = 11.6 Hz), 1.36 (s, 3H). ^{13}C NMR (C_6D_6): δ 160.4, 144.5, 133.9, 129.5,



128.4, 128.3, 128.0, 126.5, 126.3, 85.6, 70.4, 70.34, 70.31, 54.2, 42.6, 34.5, 31.2. IR (KBr, cm^{-1}): 3436 (s, br) 1678 (m). MS (EI): *m/e* 272 (M^+, 35), 254 (19), 209 (41), 186 (96), 179 (29), 165 (144); 155 (37) 128 (30) 43 (100). HRMS: calcd for $C_{17}H_{20}O_3$ 272.141245, found 272.140520.

Compound 15c. ^{1}H NMR (C_6D_6): δ 7.20 (m, 1 H), 7.11 (td, 1 H, J = 7.5, 1.4 Hz), 7.10 (td, 1 H, J = 7.5, 1.4 Hz), 6.8 (dd, 1 H, J = 7.5, 1.4 Hz), 4.38 (d, 1 H, J = 15.6 Hz), 4.19 (d, 1 H, J = 15.6 Hz), 3.83 (dd, 1 H, J = 8.0, 7.8 Hz), 2.94 (dd, 1 H, J = 11.0, 8.0 Hz), 2.59 (m, 1 H), 2.33 (s, 3 H), 2.28 (dd, 1 H, J = 17.2, 6.2 Hz), 1.96 (dd, 1 H, J = 17.2, 4.0 Hz). ^{13}C NMR



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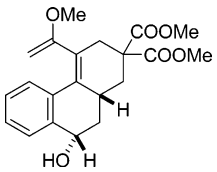
(C_6D_6): δ 205.8, 201.0, 175.6, 140.7, 137.9, 131.4, 130.7, 128.9, 71.8, 65.5, 44.1, 40.5, 28.6. IR (KBr, cm^{-1}): 1714 (s), 1687 (s). MS (EI): *m/e* 242 (M^+, 7), 214 (87), 184 (100), 172 (23), 158 (51), 145 (45), 128 (29), 115 (50). HRMS: calcd for $C_{15}H_{14}O_3$ 242.094294, found 242.095267.

Entry D of Table 2. The general procedure was followed using alkyne **6d** (0.168 g, 0.50 mmol) and carbene complex **7** (0.150 g, 0.60 mmol). After final purification by flash chromatography, compound **14d** (0.094 g, 51% yield) was obtained.

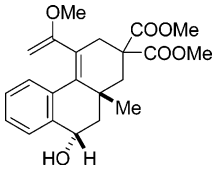
Compound 14d. ^{1}H NMR (C_6D_6): δ 7.80 (dd, 1 H, J = 7.7, 1.6 Hz), 7.59 (d, 1 H, J = 7.3, 1.4 Hz), 7.12 (td, 1 H, J = 7.3, 1.6 Hz), 7. 03 (td, 1 H, J = 7.3, 1.4 Hz), 4.61 (dd, 1 H, J = 9.2, 5.8 Hz), 4.31 (d, 1 H, J = 2.2 Hz), 4.03 (d, 1 H, J = 2.2 Hz) 3.67 (dt, 1 H, J = 18.0, 1.0 Hz), 3.32 (s, 3 H), 3.31 (s, 3 H), 3.17 (s, 3 H), 2.82 (dd, 1 H, J = 18.0, 2.8 Hz), 2.68 (ddd, 1 H, J = 13.0, 6.0, 2.4 Hz); 2.65 (m, 1 H), 2.19 (ddd, 1 H, J = 12.5, 5.8, 3.3 Hz), 1.95 (br s, 1 H), 1.86 (ddd, 1 H, J = 13.0, 12.0 Hz), 1.57 (ddd, 1 H, J = 12.5, 12.0, 9.2 Hz). ^{1}H NMR (COSY



correlations): δ's 7.80 with 7.12, 7.59 with 7.03, 4.61 with 2.19, 4.61 with 1.57, 4.31 with 4.03, 3.67 with 2.82, 2.68/2.65 with 2.19, 2.68/2.65 with 1.86, 2.68/2.65 with 1.57, 2.19 with 1.57. ^{13}C NMR (C_6D_6): δ 172.6, 171.2, 164.0, 141.1, 135.7, 129.5, 128.7, 128.3, 128.2, 126.5, 85.8, 69.4, 54.9, 53.8, 52.7, 52.6, 42.3, 37.9, 34.3, 30.6. IR (KBr, cm^{-1}): 3511 (s, br), 1737 (s), 1653 (m), 1618 (m). MS (EI): *m/e* 372 (M^+, 18), 354 (95), 237 (35), 203 (100), 178 (42), 59 (31). HRMS: calcd for $C_{21}H_{24}O_6$ 372.157289, found 372.157344.

Entry E of Table 2. The general procedure was followed using alkyne **6e** (0.224 g, 0.68 mmol) and carbene complex **7** (0.200 g, 0.80 mmol). After final purification by flash chromatography, compound **14e** (0.150 g, 60% yield) was obtained.

Compound 14e. ^{1}H NMR (C_6D_6): δ 7.74 (dd, 1 H, J = 7.7, 1.4 Hz), 7.59 (dd, 1 H, J = 7.4, 1.4 Hz), 7.12 (td, 1 H, J = 7.2, 1.4 Hz), 7. 04 (td, 1 H, J = 7.2, 1.8 Hz), 4.66 (dd, 1 H, J = 9.0, 5.8 Hz), 4.24 (d, 1 H, J = 2.2 Hz), 3.98 (d, 1 H, J = 2.2 Hz), 3.61 (dd, 1 H, J = 17.6, 1.5 Hz), 3.32 (s, 3 H), 3.29 (s, 3 H), 3.13 (s, 3 H), 2.57 (d, 1 H, J = 17.6 Hz), 2.54 (dd, 1 H J = 14.0, 1.8 Hz) 2.34 (d, 1 H, J = 14.0 Hz), 2.10 (dd, 1 H, J = 13.0, 5.8 Hz), 1.94 (br s, 1 H), 1.73 (dd, 1 H, J = 13.0, 9.0 Hz), 0.80 (s, 3 H). ^{1}H NMR (COSY correlations): δ's 7.74 with 7.04,

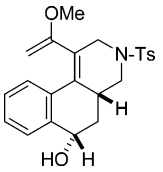


7.59 with 7.12, 4.66 with 2.10, 4.66 with 1.73, 4.24 with 3.98, 3.61 with 2.57, 2.54 with 2.34, 2.10 with 1.73. ^{13}C NMR (C_6D_6): δ 172.6, 171.1, 164.3, 139.7, 138.7, 135.9, 130.0, 129.5, 128.3, 128.1, 127.2, 85.8, 68.0, 54.8, 52.7, 52.4, 52.3, 49.6, 43.6, 37.7, 37.0, 25.1. IR (KBr, cm^{-1}): 3315 (s, br), 1737 (s); 1615 (m). MS (EI): *m/e* 386 (M^+, 61), 342 (57), 293 (100), 223 (31), 202 (34), 178 (23), 43 (25). HRMS: calcd for $C_{22}H_{26}O_6$ 386.172939, found 386.173850.

Entry F of Table 2. The general procedure was followed using alkyne **6f** (0.188 g, 0.53 mmol) and carbene complex **7** (0.200 g, 0.80 mmol). After final purification by flash chromatography, compound **14f** (0.122 g, 56% yield) was obtained.

Compound 14f. ^{1}H NMR (C_6D_6): δ 7.72 (d, 2 H, J = 8.8 Hz), 7.65 (d, 1 H, J = 7.6 Hz), 7.12 (d, 1 H, J = 7.6 Hz), 7.20–7.05 (m, 2 H), 6.80 (d, 2 H, J = 8.0 Hz), 4.73 (d, 1 H, J = 16.4 Hz), 4.57 (dd, 1 H, J = 9.0, 5.6 Hz), 4.05 (d, 1 H, J = 2.0 Hz), 3.95 (d, 1 H, J = 2.4 Hz), 3.92 (dd, 1 H, J = 11.0, 6.4 Hz), 3.38

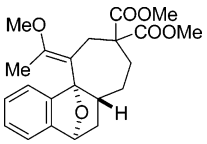
(dd, 1 H, J = 16.4, 2.8 Hz,), 3.08 (s, 3 H), 2.45 (m, 1 H), 2.19 (t, 1 H, J = 10.8 Hz), 1.92 (s, 3 H), 1.82 (dt, 1 H, J = 12.4, 5.6 Hz) 1.28 (ddd, 1 H, J = 12.4, 11.2, 9.0 Hz). ^{13}C NMR (C_6D_6):



δ 160.6, 143.2, 140.5, 134.9, 134.2, 134.1, 128.7, 128.4, 128.1, 128.0, 127.5, 126.6, 126.2, 86.3, 68.3, 54.4, 50.0, 49.7, 37.4, 35.5, 21.0. IR (KBr, cm^{-1}): 3433 (s, br), 1459 (m), 1164 (m), 1108 (m), 1025 (m). MS (EI): *m/e* 411 (M^+, 14), 237 (12), 209 (35), 195 (33), 155 (23), 91 (100). HRMS: calcd for $C_{23}H_{25}NO_4S$ 411.150430, found 411.151083.

Reaction in Scheme 3. The general procedure I was followed using alkyne **6g** (0.197 g, 0.60 mmol) and carbene complex **7** (0.200 g, 0.80 mmol). After final purification by flash chromatography, compound **9g** (0.080 g, 35% yield) was obtained.

Compound 9g. ^{1}H NMR (C_6D_6): δ 7.10−6.91 (m, 4 H), 5.00 (d, 1 H, J = 4.8 Hz), 4.40 (d, 1 H, J = 14.0 Hz), 3.49 (s, 3 H), 3.42 (s, 3 H), 3.10 (s, 3 H), 2.76−2.66 (m, 3 H), 1.87 (s, 3 H), 1.58−1.40 (m, 4 H), 1.34 (m, 1 H). ^{13}C NMR (C_6D_6): δ 173.4,



171.5, 156.1, 149.2, 146.6, 126.6, 126.3, 118.8, 118.3, 109.0, 91.3, 77.7, 57.1, 54.4, 51.9, 51.6, 44.7, 40.0, 36.5, 33.3, 31.5, 14.7. IR (KBr, cm^{-1}): 3456 (s, br), 1729 (s); 1651 (m). MS (EI): *m/e* 386 (M^+, 41), 368 (24), 248 (22), 191 (33), 178 (40), 165 (53), 59 (100). HRMS: calcd for $C_{22}H_{26}O_6$ 386.172939, found 386.172288.

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Supporting Information Available: Procedures for the synthesis of compounds **6a**−**g**, ^{1}H and ^{13}C NMR spectra for compounds **6a**−**g**, **9g**, **14a**−**f**, and **15c**, and COSY spectra for **14d**,**e**. This material is available free of charge via the Internet at http://pubs.acs.org.

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