Synthesis of Furano[2,3-*c*]pyran-3-one and Thieno[2,3-*c*]pyran-3-one Derivatives through the Coupling of 3-Alkynyl-2-heteroaromatic Carboxaldehydes with Fischer Carbene Complexes: Total Synthesis of a *Baccharis*-Derived Cadinene Derivative

Yanshi Zhang and James W. Herndon*

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

jherndon@nmsu.edu

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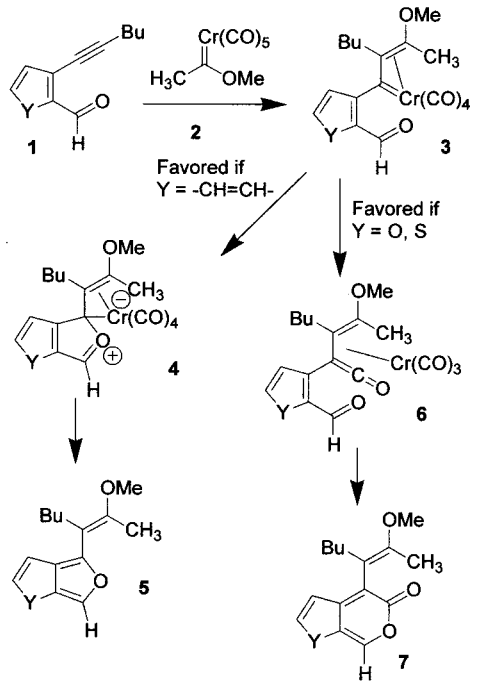
The coupling of Fischer carbene complexes with 3-alkynyl-2-heteroaromatic carboxaldehyde derivatives has been examined. The reaction affords pyrones fused to furans or thiophenes in a single step. The compounds are stable enough for isolation. If the carbene complex features a remote alkene substituent, a subsequent Diels−Alder reaction can occur. This reaction has been used as the key step in the synthesis of a naturally occurring cadinene derivative.

Introduction

In recent publications, the generation of isobenzofuran intermediates (e.g., **5**, Y = −CH=CH−, Scheme 1) through the coupling of Fischer carbene complexes (e.g., **2**) with *o*-alkynylbenzoyl derivatives (**1**) has been demonstrated.[1] In these reactions, coupling of the carbene complex with the alkyne initially provides intermediate alkenylcarbene complex **3** in a regioselective and stereoselective manner, which is then captured to form the carbonyl ylide derivative **4**. Loss of the metal from the carbonyl ylide leads to the isobenzofuran derivative, which is then captured through reaction with an alkene in a Diels−Alder reaction.[2] Similar chemistry resulting in stable furan rings from enyne−aldehyde derivatives had previously been demonstrated.[3] In these examples, capture of the intermediate vinylcarbene complex by the oxygen precedes any CO insertion processes. The hypothetical products of CO insertion, pyrones (e.g., **7**), were not detected in any of these reactions.

In a preliminary report,[4] it was noted that furan and thiophene analogues (e.g., **1**, Y = O or S) do in fact lead to furanopyrones (**7**) and not the furanofurans (**5**). This represents a novel entry into this synthetically useful ring system[5] and is the first example of a chromium carbene-derived ketene undergoing cyclization to a pyrone system.[6,7] In this paper, a full and detailed account of this process will be presented, along with an application of this reaction to the total synthesis of a cadinene natural product isolated from *Baccharis* species.

Scheme 1



Results

Synthesis of Alkyne Aldehydes. The requisite alkyne aldehydes **10A**−**D** were prepared from the corresponding

* To whom correspondence should be addressed. Fax: (505)646-2487.

(1) (a) Jiang, D.; Herndon, J. W. *Org. Lett.* **2000**, *2*, 1267−1269. (b) Ghorai, B. K.; Herndon, J. W.; Lam, Y. F. *Org. Lett.* **2001**, *3*, 3535−3538.

(2) For a review of isobenzofurans, see: Friedrichsen, W. *Adv. Heterocycl. Chem.* **1999**, *73*, 1−96.

(3) Herndon, J. W.; Wang, H. *J. Org. Chem.* **1998**, *63*, 4564−4565.

(4) Zhang, Y.; Herndon, J. W. *Tetrahedron Lett.* **2001**, *42*, 777−779.

(5) This is the first example of this furanopyrone ring system. For previous examples of the thienopyrone ring system, see: (a) Jackson, P. M.; Moody, C. J.; Shah, P. *J. Chem. Soc., Perkin Trans. 1* **1990**, 2909−2918. (b) Jackson, P. M.; Moody, C. J. *J. Chem. Soc., Perkin Trans. 1* **1990**, 681−687.

(6) For an iron-carbene-derived example, see: Semmelhack, M. F.; Tamura, R.; Schnatter, W.; Springer, J. *J. Am. Chem. Soc.* **1986**, *106*, 5363−5364.

(7) Electronically similar compounds have been reported from rearrangement of in situ-generated metal-vinylidene complexes containing a carbonyl substituent. (a) Iwasawa, N.; Shido, M.; Maeyama, K.; Kusama, H. *J. Am. Chem. Soc.* **2000**, *122*, 10226−10227. (b) Iwasawa, N.; Shido, M.; Kusama, H. *J. Am. Chem. Soc.* **2001**, *123*, 5814−5815. (c) Ohe, K.; Miki, K.; Yokoi, T.; Nishino, F.; Uemura, S. *Organometallics* **2000**, *19*, 5525−5528.

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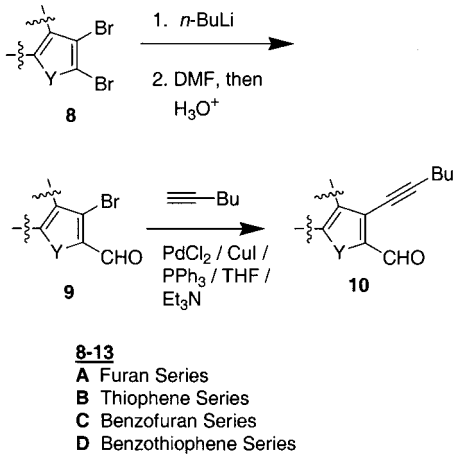
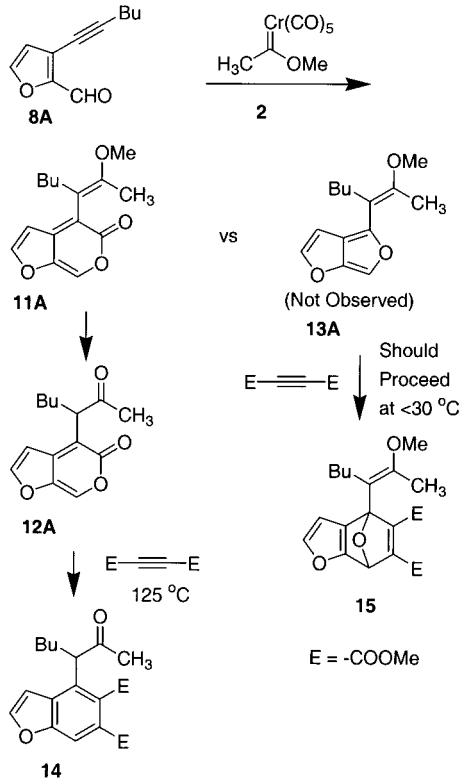
Scheme 2



commercially available (2,3-dibromothiophene) or known[8] dibromo compounds (**8**) according to the sequence of reactions in Scheme 2. Selective halogen−metal exchange followed by treatment with DMF afforded the bromo aldehyde derivatives (**9**),[9] which afforded the requisite alkyne aldehydes after Sonogashira coupling.[9c]

Coupling of Alkyne Aldehydes with Methylcarbene Complex 1. Coupling of carbene complex **1** with furancarboxaldehyde **8A** afforded a moderately stable compound assigned as structure **11A** (Scheme 3). Hydrolysis afforded ketone **12A**, which was more stable and used for characterization purposes. Chemical and spectroscopic properties are consistent only with the furanopyrone structure, and not the furanofuran structure **13A**. The product shows mass, IR, and carbon-13 NMR spectra that confirm the incorporation of a CO ligand and verify the presence of a carbonyl group. As further proof of structure, compound **12A** was unreactive to dimethyl acetylenedicarboxylate (DMAD) at room temperature; furanofuran derivative **13A** should be reactive to DMAD at room temperature based on literature precedent.[9c] The Diels−Alder reaction with DMAD required refluxing chlorobenzene and afforded benzofuran derivative **14**, which presumably arises through Diels−Alder reaction followed by expulsion of CO_2. Although this ring system is unknown,[10] sulfur[5] and nitrogen[11] analogues of **6A** are known and undergo the Diels−Alder reaction with DMAD under comparable conditions, affording the aromatic rings after thermal elimination of carbon dioxide.[12] The optimal conditions for the synthesis of pyrone derivative

Scheme 3



12A are refluxing a 1:1:1 mixture of carbene complex, alkyne, and triphenylphosphine in dioxane, which led to **12A** in 72% yield.

The pyrone-forming reaction was tested for various heteroaromatic carboxaldehyde derivatives; the results are presented in Table 1. An efficient pyrone-forming reaction was observed for the examples in Table 1, entries A−C. Hydrolysis of the enol ether product of Table 1, entry D, **11D**, afforded a highly fluorescent compound that was prone to decomposition; the low yield noted is for the relatively unstable enol ether. Only 2-heteroaromatic carboxaldehydes underwent this transformation. No pyrone-containing products were obtained from the reaction of methylcarbene complex **2** with 2-alkynyl-3-furancarboxaldehyde derivative **8E**. A compound tentatively indentified as cyclobutenone **16E** (IR 1768, 1688 cm^{-1})[13] was obtained from this reaction in low yield. Coupling of methylcarbene complex **2** with methyl ketone derivative **8F** afforded an impure compound consistent with furanopyrone structure **11F**; however, all attempts to isolate this compound free of impurities were unsuccessful.

Tandem Pyrone Formation−Diels−Alder Reaction. In the reaction of furan-aldehyde **8B** with butenylcarbene complex **17A**[14] (Scheme 4), the initially formed pyrone derivative **13G** undergoes an intramolecular Diels−Alder reaction to afford lactone derivative **18G** as a single diastereomer,[5] accompanied by a minor amount of alcohol derivative **19G**. Compounds analogous to **19G** were obtained from intramolecular Diels−Alder reactions

(8) (a) 2,3-Dibromofuran: Gronowitz, S.; Michael, U. *Ark. Kemi.* **1970**, *32*, 283−294. (b) 2,3-dibromobenzofuran: Benincori, T.; Brenna, E.; Sannicolo, F.; Trimarco, L.; Antognazza, P.; Cesarotti, E.; Demartin, F.; Pilati, T. *J. Org. Chem.* **1996**, *61*, 6244−6251. (c) 2,3-Dibromobenzothiophene: Chippendale, K. E.; Iddon, B.; Suschitzky, H.; Taylor, D. S. *J. Chem. Soc., Perkin Trans. 1* **1974**, 1168−72.

(9) (a) For 3-bromo-2-furancarboxaldehyde, see: Zaluski,-M. C.; Robba, M.; Bonhomme, M. *Bull. Soc. Chim. Fr.* **1970**, 1838−1846. (b) For 3-bromo-2-thiophenecarboxaldehyde, see: Chadwick, D.; Chambers, J.; Hodgson, P. H. K.; Meakins, G. D.; Snowden, R. L. *J. Chem. Soc., Perkin Trans. 1* **1974**, 1141−1145. (c) For benzo derivatives, see: Eberbach, W.; Laber, N.; Bussenius, J.; Fritz, H.; Rihs, G. *Chem. Ber.* **1993**, *126*, 975−995.

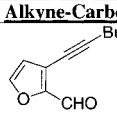
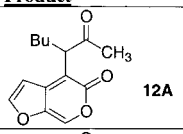
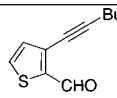
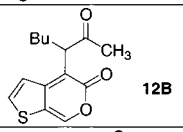
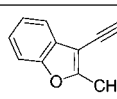
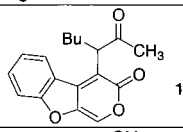
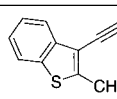
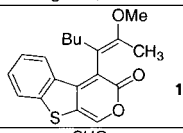
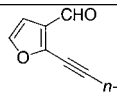
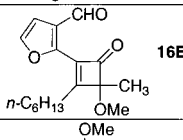
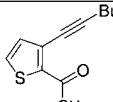
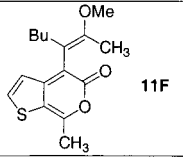
(10) A computer substructure search turned up a single literature citation; however, no compound featuring this ring system is contained in the article. Clavey, E. M.; Page, S. W.; Taylor, L. T. *J. Supercrit. Fluids* **1990**, *3*, 115−120.

(11) (a) Hong, B. C.; Jiang, Y. F.; Kumar, E. S. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 1981−1984. (b) Nag, S.; Saha, K.; Choudhuri, M. A. *J. Plant Growth Reg.* **2001**, *20*, 182−194. (c) Haider, N.; Kaferbock, J.; Matyus, P. *Heterocycles* **1999**, *51*, 2703. (d) Moody, C. J. *Synlett* **1994**, 681−688.

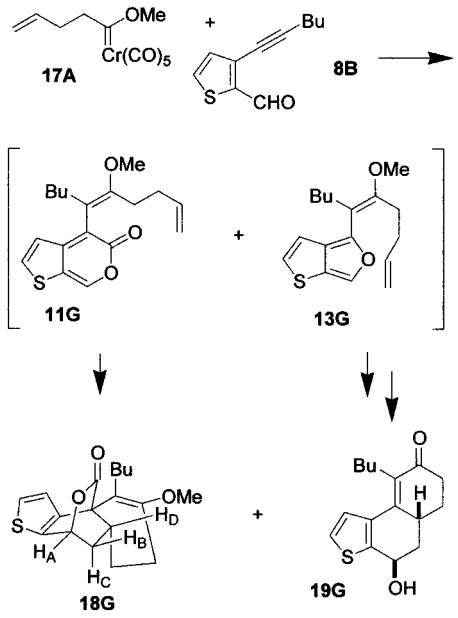
(12) For a review of pyrone Diels−Alder reactions, see: Afarinkia, K. A.; Vinader, V.; Nelson, T. D.; Posner, G. H. *Tetrahedron* **1992**, *42*, 9111−9171.

(13) Cyclobutenones are frequently observed in the coupling of carbene complexes and alkynes. Wulff, W. D. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Paquette, L. A., Eds.; Pergamon: Oxford, 1991; Vol. 5, pp 1065−1113.

Table 1. Scope and Limit for Pyrone Formation with Methylcarbene Complex 2

Entry	Alkyne-Carbonyl Compound	Yield	Product
A	 **8A**	72%	 **12A**
B	 **8B**	75%	 **12B**
C	 **8C**	70%	 **12C**
D	 **8D**	37%	 **11D**
E	 **8E**	6%	 **16E**
F	 **8F**	7%	 **11F**

Scheme 4



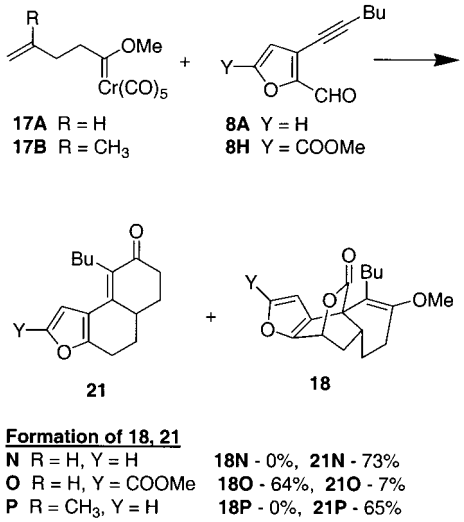
of isobenzofuran intermediates,[1b] and presumably arise from furan **13G**. The stereochemistry has been assigned as the depicted endo isomer since the coupling between H_B and H_D (8.9 Hz) is greater than H_C and H_D (4.8 Hz); similar values have been reported for related compounds.[15] The effect of solvent on the distribution of **18G** and **19G** was briefly examined (Table 2). Optimal yields of **18G** were observed using acetone as the solvent, and this solvent was utilized for subsequent studies. The reaction was tested for similar complexes featuring either a monosubstituted or 1,1-disubstituted alkene appendage; the results are depicted in Table 3. Only in one case (Table 3, entry G) was a compound isolated that failed to undergo the Diels–Alder reaction; however, successful Diels–Alder reaction was observed when the reaction was conducted at 125 °C in refluxing chlorobenzene.

Table 2. Solvent Effects on the Distribution of 18G and 19G[a]

entry	solvent	concn (M)	total yield (%)	**18G/19G**
A	THF	0.03	72	78:22
B	DME	0.03	66	35:65
C[b]	benzene	0.03	not catalyzed	
D	1,2-dichloroethane	0.03	51	63:37
E	acetonitrile	0.03	70	86:14
F	acetone	0.03	77	81:10
G	THF	0.007	88	66:34

[a] All reactions were conducted at the reflux temperature. [b] Only chromium-complexed products were obtained, which could not be efficiently converted to simple organic compounds.

Scheme 5



The tandem pyrone formation–Diels–Alder reactions involving simple furan derivative **8A** and carbene complexes **17A** or **17B** (Scheme 5) proceeded by a different course and provided enone **21N** as the exclusive product. The reaction involving electron-deficient furan **8F** led to the expected Diels–Alder adduct **18O** accompanied by trace amount of compound **21O**.

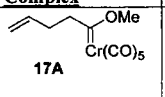
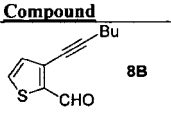
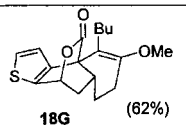
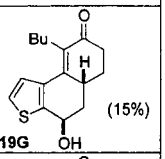
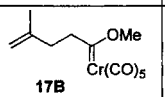
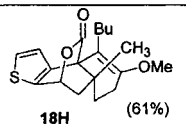
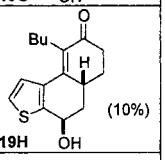
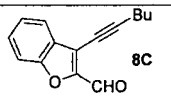
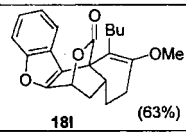
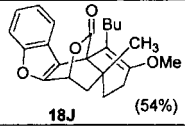
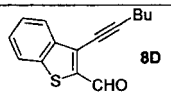
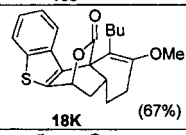
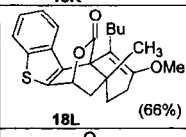
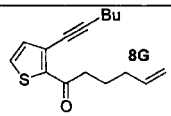
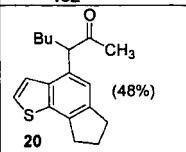
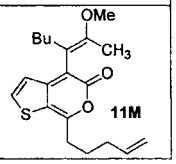
Competitive Benzannulation–Pyrone Formation. Coupling of dialkyne complex **8I** (Scheme 6) with carbene complex **2** led to lactone derivative **25** as the exclusive product of the reaction in 43% yield. In this case, two cyclization modes are possible for intermediate ketene **22**, benzannulation to form phenol aldehyde **23**[16] or cyclization of the aldehyde to form pyrone **24**. Lactone **25** is most likely an oxidation product of phenol aldehyde **23**, thus indicating that pyrone formation is not competitive with the two alkyne benzannulation process.

Discussion

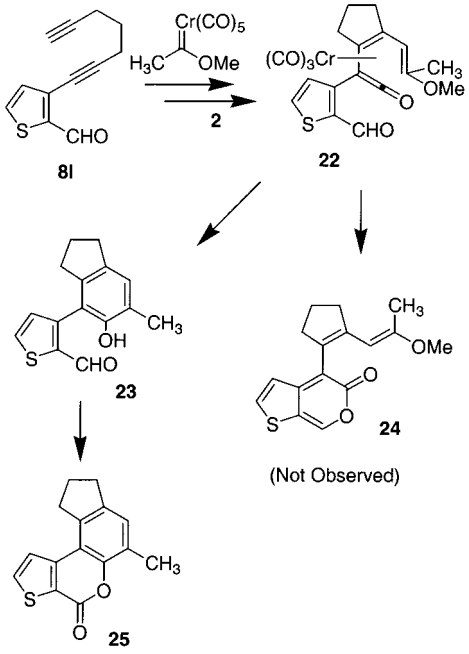
Mechanism of the Pyrone-Forming Reaction. The mechanism for pyrone formation is depicted in Scheme

(14) Hoye, T. R.; Vyvyan, J. R. *J. Org. Chem.* **1995**, *60*, 4184–4195.
(15) Afarinkia, K.; Posner, G. H. *Tetrahedron Lett.* **1992**, *53*, 7839–7842.
(16) Wulff, W. D.; Kaesler, R. W.; Peterson, G. A.; Tang, P. C. *J. Am. Chem. Soc.* **1985**, *107*, 1060–1062.

Table 3

Entry[a]	Carbene Complex	Alkyne-Carbonyl Compound	Major Product	Other Product(s)
A	 **17A**	 **8B**	 **18G** (62%)	 **19G** (15%)
B	 **17B**	**8B**	 **18H** (61%)	 **19H** (10%)
C	**17A**	 **8C**	 **18I** (63%)	
D	**17B**	**8C**	 **18J** (54%)	
E	**17A**	 **8D**	 **18K** (67%)	
F	**17B**	**8D**	 **18L** (66%)	
G[b]	**2**	 **8G**	 **20** (48%)	 **11M**

Scheme 6



7. Formation of pyrone derivatives from these reactions was not expected initially based on previous observations using *o*-alkynylbenzaldehyde derivatives, which lead to isobenzofuran intermediates. Since CO insertion processes are suppressed for electron-rich metal-carbene species,[17] CO insertion should be less likely in the thiophene and furan systems (**8**) than in the less electron rich benzene analogues (**8**, Y = −CH=CH−). The surprising formation of pyrones in these studies might be attributed to the greater ring strain in derivatives such as **13** and the greater distance between the carbonyl oxygen and the carbene carbon in intermediate **26** when fused to a five-membered ring vs a six-membered ring. Thus, the furan ring-closure step in these systems (**26** to **28**) is less favorable than in systems where Y = −CH=CH−,[18] and CO insertion to form ketene **27** is favored over direct ring closure to form **28** and subsequently **13**. Failure of pyrone formation from the 3-thiophenecarboxaldehyde derivative **8E** (Table 1, entry E) might be attributed to the reduced nucleophilicity of the carbonyl oxygen.[19]

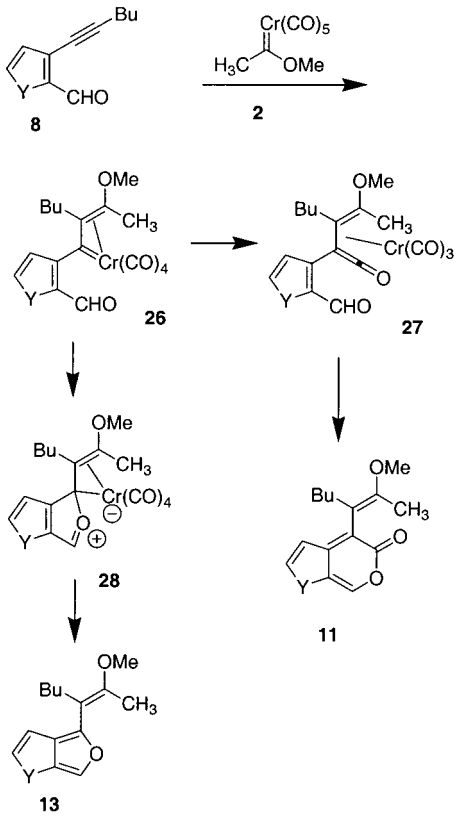
Effect of Alkene Appendages on the Pyrone-Forming Reaction: Formation of the Minor Prod-

(17) (a) Grotjahn, D. B.; Kroll, F. E. K.; Schäfer, T.; Harms, K.; Dötz, K. H. *Organometallics* **1992**, *11*, 298−310. (b) Barluenga, J.; Lopez, L. A.; Martínez, S.; Tomás, M. *J. Org. Chem.* **1998**, *63*, 7588−7589. (c) For a universal discussion of electronic effects in carbene-alkyne couplings, see: Waters, M. A.; Brandvold, T. A.; Isaacs, L.; Wulff, W. D.; Rheingold, A. L. *Organometallics* **1998**, *17*, 4298−4308.

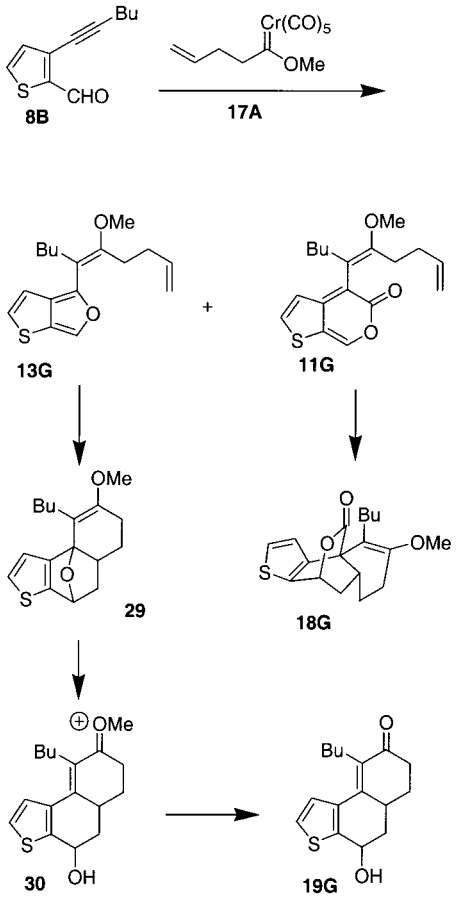
(18) For other examples where a CO insertion process occurs due to ring strain, see: (a) Barluenga, J.; Aznar, F.; Palomero, M. A.; Barluenga, S. *Org. Lett.* **1999**, *1*, 541−543. (b) Wu, H. P.; Aumann, R.; Fröhlich, R.; Wibbeling, B. *Eur. J. Org. Chem.* **2000**, 1183−1192.

(19) Francesco, F.; Gianlorenzo, M.; Taticchi, A. *J. Chem. Soc. B* **1971**, 2302−2303.

Scheme 7



Scheme 8



uct 19. The use of complexes having alkene appendages led to Diels–Alder adducts of general structure **18**; however, a minor product in these processes is the alcohol derivative **19**. A likely mechanism for the formation of alcohol **19** is via formation of furanothiophene derivative **13**, followed by Diels–Alder reaction and ring opening (Scheme 8). Compounds analogous to **19** were formed in the reaction of γ,δ-unsaturated carbene complexes with 2-ethynylbenzaldehyde; this reaction proceeds through isobenzofuran intermediates.[1b] Since none of the furanothiophene compound **13B** was observed in the reaction of thiophenecarboxaldehyde derivative **8B** with methylcarbene complex **2**, this implies that the alkene is to a small extent directing the reaction toward formation of the furanothiophene. A likely role for the alkene group is depicted in Scheme 9, where to some extent intermediate complex **32** is formed by displacement of a carbonyl ligand from intermediate complex **31**. Carbonyl insertion in complex **32** would be less likely than in complex **31** due to the greater electron density at chromium.

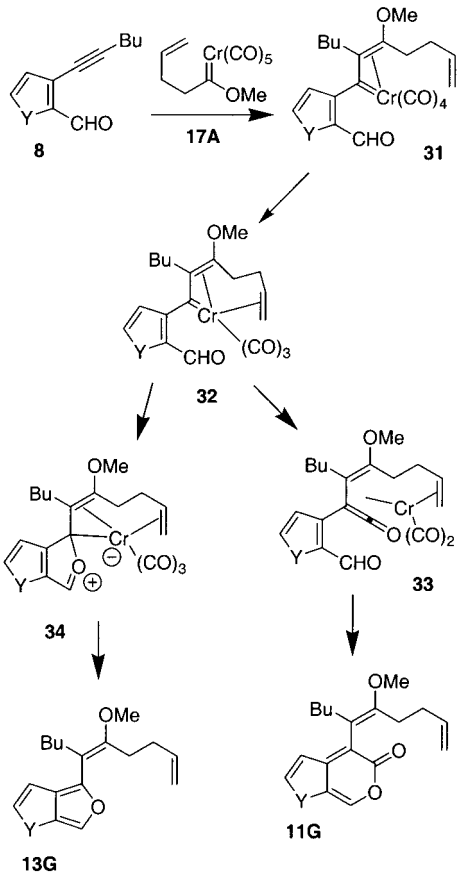
Effect of Solvent of the Distribution of 18G/19G. As noted in Table 2, solvent and concentration play an important role in the distribution of products between Diels–Alder adducts **18G** and **19G**. The amount of **19G** is maximized in DME, a solvent whose ligand properties can best be described as chelating and strongly electron-donating. Similar distributions of **18G** and **19G** were observed in THF, acetonitrile, and acetone, which are all strongly ligating but not chelating. Acetonitrile and acetone also have back-bonding capability. If these species complex to chromium, the electron density at chromium would be less relative to analogous DME or THF complexes, and thus, the CO insertion process would be more favorable. In one case, entry G of Table 3, it was noted that the amount of non CO-inserted product was considerably higher in dilute solution. This is consistent with the allelochemical effect previously described by Wulff and co-workers,[20] in that CO-insertion is suppressed in dilute solution since coordination of a second alkyne ligand is crucial for the CO insertion event.

Formation of Compound 18 from Butenylcarbene Complexes 17. As anticipated, the major products from the coupling of butenylcarbene complex **17** and 3-alkynyl-2-heteroaromaticcarboxaldehydes are adducts of general structure **18**. Surprisingly, the Diels–Alder step is apparently very facile at 56 °C, which is unexpected based on other studies of the intramolecular Diels–Alder reaction in similar system.[5] Although the authors did not report a study of the reaction at different temperatures, they employed a very unconventional solvent system, refluxing bromobenzene (bp 156 °C), to effect the Diels–Alder step. The Diels–Alder step occurs with complete control of stereochemistry, resulting in the endo isomer. The unusually low temperatures coupled with the high degree of stereochemical control might indicate the involvement of chromium in the Diels–Alder step.[21] In two cases, entries E and F of Table 3, efficient formation of Diels–Alder adducts **18K** and **18L** was noted, even though the pyrone synthesis using aldehyde **8D** was inefficient.

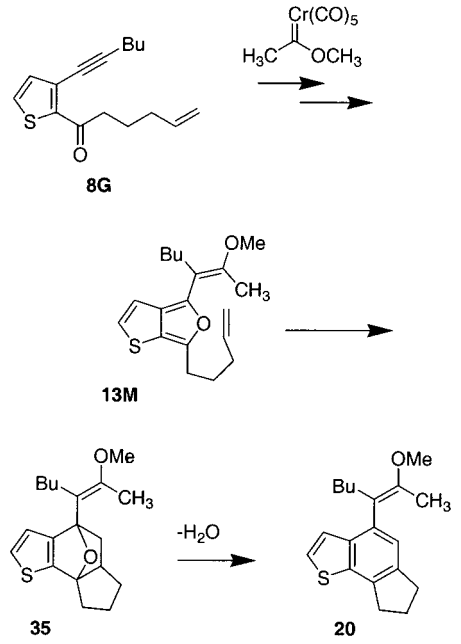
In one of the examples (entry G of Table 3 and Scheme 10) a pyrone derivative, **11M**, which fails to undergo the Diels–Alder reaction, could be isolated in low yield. However, the reaction in refluxing chlorobenzene afforded

(20) Bos, M. E.; Wulff, W. D.; Miller, R. A.; Chamberlin, S.; Brandvold, T. A. *J. Am. Chem. Soc.* **1991**, *113*, 9293–9319.
(21) Rigby, J. H. *Tetrahedron* **1999**, *55*, 4521–4538.

Scheme 9



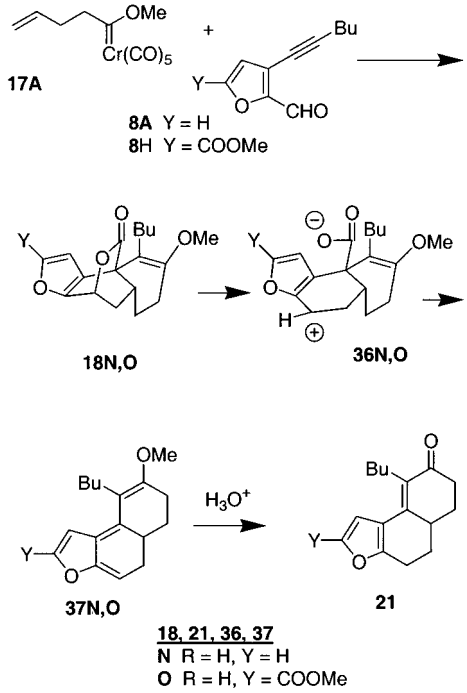
Scheme 10



the benzothiophene derivative **20** as the exclusive product. The origin of benzothiophene **20** is unclear and might result from exclusive formation of furanothiophene **13M** in chlorobenzene, which affords **20** after Diels−Alder reaction and dehydration.

Tandem Pyrone Formation-Diels−Alder Reactions Using Simple Furanaldehydes. Coupling of aldehyde **8A**, which contains a simple furan ring, with γ,δ-unsaturated carbene complexes **17** led to compounds

Scheme 11



missing the CO_2 bridge (**21**). The mechanism for formation of this compound is depicted in Scheme 11. Formation of carbocation **36** followed by extrusion of CO_2 leads to conjugated triene **32**, which is subsequently hydrolyzed to the observed enone **21**. Alternatively, direct thermal extrusion of CO_2 from **18** would lead to **37**. The ionic mechanism depicted explains why this reaction pathway is unique to the furan ring system, which is more electron-donating than the other systems employed.[22] Placement of an electron-withdrawing group on the furan ring (**8H**, Y = COOMe) inhibits this reaction pathway due to destabilization of carbocation **36O**, and bridged structure **18O** was the major product from coupling of this substrate with butenylcarbene complex **17A**.

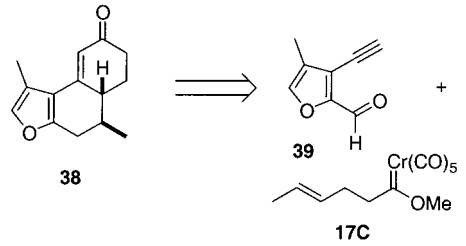
Total Synthesis of *Baccharis*-Derived Cadinene Natural Products. The furanodecalin ring system similar to **21** is found in a number of naturally occurring compounds[23] and has been the target of numerous synthetic efforts.[24] Closely related furanone analogues

(22) (a) Noyce, D. S.; Lipinski, C. A.; Nichols, R. W. *J. Org. Chem.* **1972**, *37*, 2615−2620. (b) Noyce, D. S.; Pavez, H. J. *J. Org. Chem.* **1972**, *37*, 2623−2625. (c) Olah, G. A.; Berrier, A. L.; Prakash, G. K. S. *J. Org. Chem.* **1982**, *47*, 3903−3909.

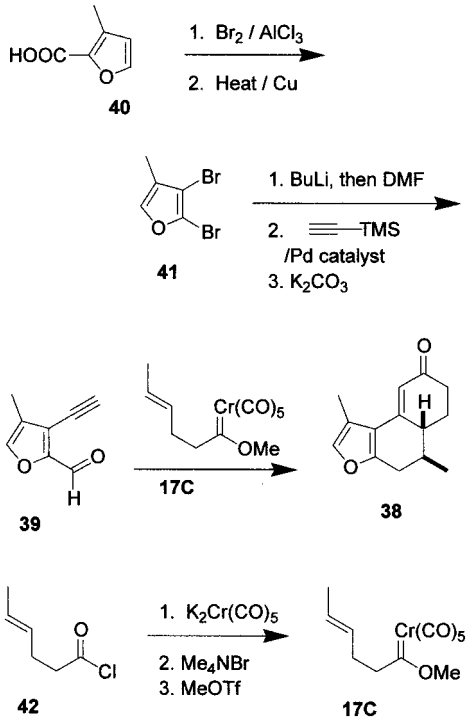
(23) (a) Zdero, C.; Bohlmann, F.; King, R. M.; Robinson, H. *Phytochemistry* **1986**, *25*, 2841−2855. (b) Bohlmann, F.; Singh, P.; Jakupovic, J.; King, R. M.; Robinson, H. *Phytochemistry* **1982**, *21*, 371−374. (c) Bohlmann, F.; Zdero, C.; King, R. M.; Robinson, H. *Phytochemistry* **1979**, *18*, 1177−1179. (d) Loayza, I.; Abujder, D.; Aranda, R.; Jakupovic, J.; Collin, G.; Deslauriers, H.; Jean, F. I. *Phytochemistry* **1995**, *38*, 381−389. (e) Braga de Oliveira, A.; De Oliveira, G. G.; Carazza, F.; Braz Filho, R.; Moreira Bacha, C. T.; Bauer, L.; Silva, G. A. de A. B.; Siqueira, N. C. S. *Tetrahedron Lett.* **1978**, *30*, 2653−2654. (f) Bohlmann, F.; Zdero, C. *Chem. Ber.* **1977**, *110*, 487−490. (g) De Oliveira, A. B.; Carazza, F.; Ramos, L. S.; Maia, J. G. S. *J. Essent. Oil Res.* **1990**, *2*, 49−50. (g) Jakupovic, J.; Schuster, A.; Ganzer, U.; Bohlmann, F.; Boldt, P. E. *Phytochemistry* **1990**, *29*, 2217−2222.

(24) (a) Demir, A. S.; Gercek, Z.; Duygu, N.; Igdir, A. C.; Reis, O. *Can. J. Chem.* **1999**, *77*, 1336−1339. b. Chavan, S. P.; Rao, Y. T. S.; Govande, C. A.; Zubaidha, P. K.; Dhondge, V. D. *Tetrahedron Lett.* **1997**, *38*, 7633−7634. (c) Chavan, S. P.; Dhondge, V. D.; Patil, S. S.; Rao, Y. T. S.; Govande, C. A. *Tetrahedron: Asym.* **1997**, *8*, 2517−2518. (d) Juo, R. R.; Herz, W. *J. Org. Chem.* **1985**, *50*, 700−703. (e) Kano, S.; Ebata, T.; Shibuya, S. *Heterocycles* **1980**, *14*, 43−46.

Scheme 12



Scheme 13



display biological activity as fish toxicants.[25] As a demonstration of the utility of this transformation, total synthesis of compound **38**,[23a] isolated from aerial parts of *Baccharis ulcina*, was undertaken. There is only minimal structural difference between compound **21N** and **38**, and thus the retrosynthetic analysis involves the simple coupling of furan **39** with carbene complex **17C** (Scheme 12). Carbene complex **17C** was synthesized from acid chloride **42**[26] according to the procedure of Hegedus[27] (Scheme 13). Furan **39** was synthesized from commercially available 3-methyl-2-furancarboxylic acid.[28] Coupling of carbene complex **17C** with furan **39** afforded the natural product **38** in 49% yield as a single diastereomer. The spectral data for compound **38** synthesized in this way is identical to that reported for the natural product.[23a]

(25) (a) Miles, D. H.; Lho, D. S.; De la Cruz, A. A.; Gomez, Edgardo D.; Weeks, J. A.; Atwood, J. L. *J. Org. Chem.* **1987**, *52*, 2930−2932. (b) Miles, D. H.; Ly, A. M.; Chittawong, V.; De la Cruz, A. A.; Gomez, E. D. *J. Nat. Prod.* **1989**, *52*, 896−898.

(26) Lin, J. M.; Koch, K.; Fowler, F. W. *J. Org. Chem.* **1986**, *51*, 167−174.

(27) (a) Schwindt, M. A.; Lejon, T.; Hegedus, L. S. *Organometallics* **1990**, *9*, 2814−2819. (b) Semmelhack, M. F.; Lee, G. R. *Organometallics* **1987**, *6*, 1839−1844. (c) For specific use of this reaction for the synthesis of γ,δ-unsaturated carbene complexes, see: Moser, W. H. Hegedus, L. S. *J. Am. Chem. Soc.* **1996**, *118*, 7873−7880.

(28) This compound is quite expensive but easily produced on large scale. Burness, D. M. In *Organic Syntheses*; *Collective*; Rabjohn, N., Ed.; John Wiley and Sons: New York, 1963; Collect. Vol. IV, pp 649−652 and 628−630.

Conclusions

In summary, we have shown a new and general route to the heteroaromatic-fused pyrone ring systems and are further exploring the synthesis and reactivity of these unusual pyrone derivatives. These compounds undergo very facile and highly stereoselective intramolecular Diels−Alder reactions to afford hydronaphthalene rings fused to heteroaromatic rings. If the heterocyclic ring is highly electron rich, the cycloadducts undergo a loss of carbon dioxide to afford simple hydronaphthalene ring systems. The tandem pyrone formation−Diels−Alder−carbon dioxide extrusion process has been utilized as the key step in the one-step synthesis of natural product ketone **38**.

Experimental Section[29]

General Procedure 1. Coupling of Carbene Complex 2 with Alkynyl-Aldehydes. An 0.06 M solution of carbene complex (1 equiv) in dioxane was added dropwise over a period of 15 min to a refluxing 0.06 M solution of alkyne−aldehyde (1 equiv) and PPh_3 (1 equiv) in dioxane. After completion of the addition, the mixture was allowed to reflux for 1.5 h. The resulting red brown solution was dried in vacuo, followed by the hydrolysis using 5 M HCl solution to afford the product as yellow oil. Final purification was achieved by flash chromatography on silica gel using (2:1) hexane/ethyl acetate as eluent. Compounds **12A** and **12B** decomposed during shipment to an external mass spectrometry facility; only the more stable benzo analogue **12C** could be completely characterized.

Coupling of Alkyne Aldehyde 8A with Carbene Complex 2. General procedure 1 was followed using carbene complex **2** (150 mg, 0.600 mmol), alkyne aldehyde **8A** (106 mg, 0.600 mmol), and triphenylphosphine (157 mg, 0.600 mmol). After final purification, a yellow oil identified as pyrone **12A** was obtained (106 mg, 72% yield): ^{1}H NMR ($CDCl_3$) δ 7.83 (s, 1 H), 7.53 (d, 1 H, J = 2.4 Hz), 6.49 (d, 1 H, J = 2.4 Hz), 4.04 (t, 1 H, J = 6.8 Hz), 2.09 (s, 3 H), 1.97 (m, 1 H), 1.65 (m, 1 H), 1.21 (m, 4 H), 0.78 (t, 3 H, J = 6.9 Hz); ^{13}C NMR ($CDCl_3$) δ 206.8, 162.6, 156.7, 146.4, 143.3, 133.5, 111.3, 104.9, 51.2, 29.5, 29.4, 28.9, 22.4, 13.7; IR (neat) 1696 (s), 1663 (s), 1582 (m) cm^{-1}.

Coupling of Alkyne Aldehyde 8B with Carbene Complex 2. General procedure 1 was followed using carbene complex **2** (150 mg, 0.600 mmol), alkyne aldehyde **8B** (115 mg, 0.600 mmol), and triphenylphosphine (157 mg, 0.600 mmol). After final purification, a yellow oil identified as pyrone **12B** was obtained (119 mg, 75% yield): ^{1}H NMR ($CDCl_3$) δ 7.92 (s, 1 H), 7.57 (d, 1 H, J = 5.6 Hz), 6.83 (d, 1 H, J = 5.6 Hz), 4.00 (dd, 1 H, J = 8.4, 6.1 Hz), 2.03 (s, 3 H), 2.00 (m, 1 H), 1.65 (m, 1 H), 1.15 (m, 4 H), 0.73 (t, 3 H, J = 6.9 Hz); ^{13}C NMR ($CDCl_3$) δ 206.6, 162.3, 153.5, 144.7, 142.5, 122.0, 120.0, 115.1, 51.9, 29.5, 28.8, 28.6, 22.4, 13.6; IR (neat) 1697 (s), 1668 (s) cm^{-1}.

Coupling of Alkyne Aldehyde 8C with Carbene Complex 2. General procedure 1 was followed using carbene complex **2** (125 mg, 0.500 mmol), alkyne aldehyde **8C** (113 mg, 0.500 mmol), and triphenylphosphine (131 mg, 0.500 mmol). After final purification, a yellow oil identified as pyrone **12C** was obtained (104 mg, 70% yield): ^{1}H NMR ($CDCl_3$) δ 7.89 (d, 1 H, J = 8.0 Hz), 7.85 (s, 1 H), 7.59 (t, 1 H, J = 8.0 Hz), 7.34 (d, 1 H, J = 8.0 Hz), 7.27 (t, 1 H, J = 8.0 Hz), 4.17 (dd, 1 H, J = 9.2, 5.0 Hz), 2.27 (m, 1 H), 2.14 (s, 3 H), 1.89 (m, 1 H), 1.23 (m, 4 H), 0.75 (t, 3 H, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 206.0, 162.4, 161.3, 143.2, 142.7, 133.5, 132.1, 126.6, 123.7, 120.2, 117.0, 112.1, 52.5, 29.8, 28.3, 27.3, 22.5, 13.7; IR (neat) 1698 (s), 1670 (s), 1609 (m), 1590 (m) cm^{-1}; MS (FAB) 299 (M + 1, 89), 298 (M, 100), 255 (35), 229 (24), 136 (21); HRMS calcd for $C_{18}H_{19}O_4$ 299.1283, found 299.1255.

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

General Procedure 2. Coupling of Alkyne Aldehydes with Alkenylcarbene Complexes 17A−C. A 0.03 M solution of carbene complex **17** (1 equiv) in acetone was added dropwise to a refluxing 0.036 M solution of alkyne aldehyde (1 equiv) in acetone and kept at reflux for 18 h. The resulting reaction mixture was concentrated in vacuo. The residue was purified by flash chromatography on silica gel using (6:1) hexane/ethyl acetate as the eluent.

Coupling of Alkyne Aldehyde 8B with Carbene Complex 17A. General procedure 2 was followed using carbene complex **17A** (146 mg, 0.500 mmol) and alkyne aldehyde **8B** (96 mg, 0.500 mmol). After final purification, a white solid identified as ester **18G** (99 mg, 62% yield) and a liquid identified as alcohol **19G** (21 mg, 15% yield) were obtained. **18G**: ^{1}H NMR ($CDCl_3$) δ 7.15 (d, 1 H, J = 4.6 Hz), 6.86 (d, 1 H, J = 4.8 Hz), 5.62 (d, 1 H, J = 4.4 Hz), 3.57 (s, 3 H), 2.72 (ddd, 1 H, J = 13.2, 8.9, 4.6 Hz), 2.50−1.10 (m, 9 H), 1.29 (sextet, 2 H, J = 7.0 Hz), 1.12 (dd, 1 H, J = 13.2, 4.8 Hz), 0.88 (t, 3 H, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$) δ 173.1, 152.4, 141.4, 134.5, 125.9, 124.5, 114.7, 72.7, 55.0, 54.6, 35.6, 34.2, 31.0, 29.8, 26.3, 24.9, 23.5, 13.8; IR (neat) 1756 (s), 1666 (m) cm^{-1}; LCMS (EI) 318 (M, 10), 274 (100), 185 (54), 148 (75), 98 (28). Anal. Calcd for $C_{18}H_{22}O_3S$: C, 67.89; H, 6.96; S, 10.07. Found: C, 68.04; H, 7.22; S, 10.02. **19G**: ^{1}H NMR ($CDCl_3$ with D_2O) δ 7.31 (d, 1 H, J = 5.4 Hz), 7.24 (d, 1 H, J = 5.4 Hz), 5.07 (dd, 1 H, J = 10.6, 5.5 Hz), 2.85−2.22 (m, 5 H), 2.08 (m, 1 H), 1.85 (m, 1 H), 1.80 (q, 1 H, J = 10.6 Hz), 1.60−1.15 (m, 5 H), 0.93 (t, 3 H, J = 7.2 Hz); ^{13}C NMR($CDCl_3$) δ 199.4, 149.7, 146.9, 134.9, 133.7, 127.4, 124.8, 67.5, 43.4, 37.9, 36.9, 30.6, 28.4, 26.9, 22.9, 13.8; IR(neat) 3381 (s, br), 1646 (s), 1574 (m) cm^{-1}; MS (EI) 276 (M, 56), 258 (14), 247 (100), 243 (81); HRMS calcd for $C_{16}H_{20}O_2S$ 276.1184, found 276.1192.

Coupling of Alkyne Aldehyde 8B with Carbene Complex 17B. General procedure 2 was followed using carbene complex **17B** (113 mg, 0.37 mmol) and alkyne aldehyde **8B** (72 mg, 0.37 mmol). After final purification, a white solid identified as ester **18H** (75 mg, 71% yield) and a clear liquid tentatively identified as alcohol **19H** (11 mg, 10% yield) were obtained. **18H**: ^{1}H NMR ($CDCl_3$) δ 7.11 (d, 1 H, J = 5.1 Hz), 6.78 (d, 1 H, J = 5.1 Hz), 5.60 (d, 1 H, J = 4.8 Hz), 3.58 (s, 3 H), 2.51 (br t, 1 H, J = 8.8 Hz), 2.35 (dd, 1 H, J = 12.9, 4.8 Hz), 2.22 (m, 1 H), 2.12−1.71 (m, 2 H), 1.70−1.15 (m, 3 H) overlapping with 1.37 (d, 1 H, J = 12.9 Hz) and 1.24 (s, 3 H), 1.05 (td, 1 H, J = 16.9, 6.2 Hz), 0.89 (t, 3 H, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$) δ 171.7, 150.6, 143.6, 134.9, 126.0, 124.2, 115.3, 72.6, 58.4, 55.4, 44.4, 34.9, 32.5, 31.2, 29.2, 24.1, 23.5, 22.0, 13.8; IR ($CDCl_3$) 1758 (s), 1666 (m) cm^{-1}. Anal. Calcd for $C_{19}H_{24}O_3S$: C, 68.74; H, 7.29. Found: C, 68.59; H, 7.41. **19H**: ^{1}H NMR ($CDCl_3$ with D_2O) δ 7.32 (d, 1 H, J = 5.4 Hz), 7.15 (d, 1 H, J = 5.4 Hz), 5.05 (dd, 1 H, J = 10.2, 6.1 Hz), 2.81−2.28 (m, 3 H), 2.17 (dd, 1 H, J = 11.3, 6.1 Hz), 2.05−1.20 (m, 8 H), 1.20 (s, 3 H), 0.92 (t, 3 H, J = 7.2 Hz); IR 3381 (s, br), 1646 (s), 1574 (m) cm^{-1}.

Coupling of Alkyne Aldehyde 8C with Carbene Complex 17A. General procedure 2 was followed using carbene complex **17A** (87 mg, 0.300 mmol) and alkyne aldehyde **8C** (68 mg, 0.300 mmol). After final purification, a white solid identified as ester **18I** was obtained (66 mg, 63% yield): ^{1}H NMR ($CDCl_3$) δ 7.48 (m, 2 H), 7.24 (m, 2 H), 5.62 (d, 1 H, J = 4.4 Hz), 3.62 (s, 3 H), 2.81 (ddd, 1 H, J = 13.4, 8.9, 4.5 Hz) 2.50−1.22 (m, 12 H), 0.89 (t, 3 H, J = 7.4 Hz); ^{13}C NMR ($CDCl_3$) δ 172.8, 155.92, 154.91, 152.2, 126.1, 124.0, 123.5, 119.4, 116.8, 113.9, 112.0, 71.0, 55.1, 52.8, 35.7, 34.8, 31.0, 30.3, 26.7, 24.8, 23.6, 13.8; IR (neat) 1760 (s), 1660 (m) cm^{-1}; LCMS (EI) 352 (M, 5), 308 (40), 265 (19), 251 (100). Anal. Calcd for $C_{22}H_{24}O_4$: C, 74.98; H, 6.86. Found: C, 74.94; H, 6.90.

Coupling of Alkyne Aldehyde 8C with Carbene Complex 17B. General procedure 2 was followed using carbene complex **17B** (56 mg, 0.185 mmol) and alkyne aldehyde **8C** (42 mg, 0.185 mmol). After final purification, a white solid identified as ester **18J** was obtained (37 mg, 54% yield): ^{1}H NMR ($CDCl_3$) δ 7.45 (m, 2 H), 7.25 (m, 2 H), 5.59 (dd, 1 H, J = 4.7, 1.0 Hz), 3.63 (s, 3 H), 2.73 (m, 1 H), 2.43 (dd, 1 H, J = 13.2, 4.7 Hz), 2.32 (m, 1 H), 2.0 (m, 2 H), 1.82−1.10 (m, 6 H) overlapping with 1.48 (dd, 1 H, J = 13.2, 1.0 Hz) and 1.29 (s, 3 H), 0.83 (t, 3 H, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$) δ 171.5, 155.9, 155.5, 150.3, 126.2, 124.0, 123.4, 119.4, 118.5, 114.1, 112.0, 71.0, 56.4, 55.3, 44.4, 35.9, 32.7, 31.1, 29.6, 24.0, 23.5, 22.0, 13.9; IR (neat) 1762 (s), 1666 (m) cm^{-1}; MS (FAB) 367 (M + 1, 100), 323 (33), 266 (28); HRMS calcd for $C_{23}H_{27}O_4$ 367.1910, found 367.1898.

Coupling of Alkyne Aldehyde 8D with Carbene Complex 17A. General procedure 2 was followed using carbene complex **17A** (136 mg, 0.47 mmol) and alkyne aldehyde **8D** (114 mg, 0.47 mmol). After final purification, a white solid identified as ester **18K** was obtained (116 mg, 67% yield): ^{1}H NMR ($CDCl_3$) δ 7.81 (m, 2 H), 7.34 (m, 2 H), 5.65 (d, 1 H, J = 4.4 Hz), 3.66 (s, 3 H), 2.77 (ddd, 1 H, J = 13.2, 8.9, 4.4 Hz) 2.55−1.23 (m, 11 H), 1.17 (dd, 1 H, J = 13.2, 4.4 Hz), 0.90 (t, 3 H, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 172.8, 152.2, 140.7, 137.2, 136.7, 134.0, 124.7, 124.2, 123.0, 122.5, 114.3, 72.5, 55.2, 55.0, 35.6, 35.1, 31.5, 31.3, 26.7, 24.9, 23.6, 13.9; IR (neat) 1758 (s), 1662 (s) cm^{-1}; LCMS (EI) 368 (M, 45), 324 (71), 235 (100), 197 (85). Anal. Calcd for $C_{22}H_{24}O_sS$: C, 71.74; H, 6.57. Found: C, 71.34; H, 6.57.

Coupling of Alkyne Aldehyde 8D with Carbene Complex 17B. General procedure 2 was followed using carbene complex **17B** (57 mg, 0.185 mmol) and alkyne aldehyde **8D** (45 mg, 0.185 mmol). After final purification, a white solid identified as ester **18L** was obtained (47 mg, 66% yield): ^{1}H NMR ($CDCl_3$) δ 7.79 (m, 2 H), 7.35 (td, 1 H, J = 7.1, 1.5 Hz), 7.27 (td, 1 H, J = 7.1, 1.4 Hz), 5.58 (dd, 1 H, J = 5.0, 1.1 Hz), 3.65 (s, 3 H), 2.85−2.15 (m, 2 H) overlapping with 2.38 (dd, 1 H, J = 13.0, 5.0 Hz), 2.10−1.80 (m, 2 H), 1.75−0.85 (m, 6 H) overlapping with 1.41 (dd, 1 H, J = 13.0, 1.1 Hz) and 1.29 (s, 3 H) and 0.90 (t, 3 H, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$) δ 171.4, 150.4, 140.6, 137.2, 137.0, 135.5, 124.8, 124.1, 123.0, 122.7, 113.7, 72.4, 59.1, 54.9, 43.9, 35.7, 32.6, 31.2, 30.8, 24.2, 23.5, 21.9, 13.9; IR (neat) 1761 (s), 1662 (m) cm^{-1}; MS (FAB) 383 (M + 1, 61), 339 (24), 307 (23), 282 (28), 235 (38), 211 (64); HRMS calcd for $C_{23}H_{27}O_3S$ 383.1681, found 383.1693.

Diels−Alder Reaction of 12A and Dimethyl Acetylenedicarboxylate. A solution of pyrone ketone **12A** (82 mg, 0.330 mmol) and dimethyl acetylenedicarboxylate (106 mg, 0.745 mmol) in chlorobenzene (5 mL) was heated to reflux for a 24 h period. The solvent was removed on a rotary evaporator, and the residue was purified by flash chromatography on silica gel using (2:3) hexane/ethyl acetate as eluent to afford a white solid identified as diester **14** (82 mg, 72% yield): ^{1}H NMR ($CDCl_3$) δ 8.07 (d, 1 H, J = 0.9 Hz), 7.72 (d, 1 H, J = 2.3 Hz), 6.82 (dd, 1 H, J = 2.3, 0.9 Hz), 3.94 (s, 3 H), 3.88 (s, 3 H), 3.79 (dd,, 1 H, J = 8.3, 6.1 Hz), 2.14 (m, 1 H), 1.98 (s, 3 H), 1.70 (m, 1 H), 1.17 (m, 4 H), 0.74 (t, 3 H, J = 6.7 Hz); ^{13}C NMR ($CDCl_3$) δ 206.8, 169.7, 165.9, 154.1, 148.4, 130.9, 130.0, 129.5, 124.4, 112.8, 106.4, 55.7, 52.5, 52.4, 29.4, 29.3, 29.0, 22.3, 13.6; IR (neat) 1718 (s), 1529 (m) cm^{-1}; LCMS 346 (M, 2), 315 (16), 272 (100), 230 (40), 213 (23); HRMS calcd for $C_{19}H_{22}O_6$ 346.1417, found 346.1414.

Coupling of Alkyne Aldehyde 8G with Carbene Complex 2. General procedure 1 was followed using carbene complex **2** (150 mg, 0.60 mmol) and alkyne aldehyde **8G** (104 mg, 0.40 mmol) and using chlorobenzene as solvent; the reaction was conducted at reflux. After final purification, a white solid identified as ketone **20** was obtained (55 mg, 48% yield): ^{1}H NMR ($CDCl_3$) δ 7.45 (d, 1 H, J = 5.5 Hz), 7.38 (d, 1 H, J = 5.5 Hz), 7.09 (s, 1 H), 4.02 (t, 1 H, J = 7.3 Hz), 3.04 (t, 4 H, J = 6.6 Hz), 2.21 (quintet, 2 H, J = 6.6 Hz), 2.15 (m, 1 H), 1.98 (s, 3 H), 1.78 (m, 1 H), 1,24 (m, 4 H), 0.82 (t, 3 H, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$) δ 208.4, 140.7, 137.4, 136.6, 136.2, 132.3, 125.3, 122.1, 120.3, 57.7, 33.1, 32.1, 31.1, 29.9, 28.7, 24.9, 22.6, 13.8; IR (neat) 1713 (s) cm^{-1}; MS (EI) 286 (M, 53), 244 (34), 243 (84), 201 (21), 187 (100); HRMS calcd for $C_{18}H_{22}OS$ 286.1391, found 286.1381.

Coupling of Alkyne Aldehyde 8A with Carbene Complex 17A. General procedure 2 was followed using carbene complex **17A** (139 mg, 0.48 mmol) and alkyne aldehyde **8A** (84 mg, 0.48 mmol) and using THF as solvent; the reaction was conducted at reflux. After final purification, a white solid identified as ketone **21N** was obtained (85 mg, 73% yield): ^{1}H NMR ($CDCl_3$) δ 7.33 (d, 1 H, J = 2.0 Hz), 6.58 (d, 1 H, J = 2.0

Hz), 2.85−2.75 (m, 2 H), 2.70−2.20 (m, 5 H), 2.15−1.90 (m, 2 H), 1.85−1.55 (m, 2 H), 1.55−1.10 (m, 4 H), 0.91 (t, 3 H, J = 6.6 Hz); ^{13}C NMR ($CDCl_3$) δ 198.6, 157.4, 147.1, 141.7, 132.0, 117.4, 109.8, 37.5, 37.3, 31.2, 30.7, 29.2, 25.5, 23.6, 22.9, 13.8; IR (neat) 1660 (s), 1600 (m) cm^{-1}; MS (EI) 244 (M, 66), 229 (19), 215 (92), 201 (100), 188 (11), 174 (31); HRMS calcd for $C_{16}H_{20}O_2$ 244.1463, found 244.1461.

Coupling of Alkyne Aldehyde 8H with Carbene Complex 17A. General procedure 2 was followed using carbene complex **17A** (116 mg, 0.40 mmol) and alkyne-aldehyde **8H** (93 mg, 0.40 mmol) and using THF as the solvent; the reaction was conducted at reflux. After final purification, a white solid identified as ketone **18O** was obtained (92 mg, 64% yield): ^{1}H NMR ($CDCl_3$) δ 7.06 (s, 1 H), 5.55 (d, 1 H, J = 4.6 Hz), 3.87 (s, 3 H), 3.56 (s, 3 H), 2.77 (ddd, 1 H, J = 13.7, 9.0, 4.6 Hz), 2.50−1.95 (m, 5 H), 1.90−1.0.95 (m, 4 H) overlapping with 1.26 (sextet, 2 H, J = 7.0 Hz) and 1.18 (dd, 1 H, J = 13.7, 4.9 Hz), 0.88 (t, 3 H, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$): δ 172.1, 158.8, 156.1, 152.7, 144.6, 123.9, 117.3, 113.5, 70.7, 55,2, 52.5, 51.9, 35.1, 34.6, 31.1, 28.8, 26.4, 24.9, 23.5, 13.7; IR (neat) 1762 (s), 1732 (s), 1662 (m) cm^{-1}; MS (FAB) 361 (M + 1, 18), 316 (31), 245 (10), 189 (21); HRMS calcd for $C_{20}H_{25}O_6$ 361.1651, found 361.1666.

Coupling of Alkyne Aldehyde 8A with Carbene Complex 17B. General procedure 2 was followed using carbene complex **17B** (128 mg, 0.44 mmol) and alkyne aldehyde **8A** (102 mg, 0.44 mmol) and using THF as the solvent; the reaction was conducted at reflux. After final purification, a white solid identified as ketone **21P** was obtained (55 mg, 65% yield): ^{1}H NMR ($CDCl_3$) δ 7.34 (d, 1 H, J = 2.0 Hz), 6.55 (d, 1 H, J = 2.0 Hz), 2.80−2.25 (m, 5 H) overlapping with 2.86 (ddd, 1 H, J = 17.1, 11.4, 5.7 Hz) 2.80 (m, 2 H), 1.88 (td, 1 H, J = 13.5, 5.7 Hz), 1.72 (m, 1 H), 1.60−1.00 (m, 4 H) overlapping with 1.12 (s, 3 H), 0.91 (t, 3 H, J = 6.7 Hz); ^{13}C NMR ($CDCl_3$): δ 198.3, 156.1, 151.0, 141.9, 131.9, 116.8, 110.5, 37.7, 36.4, 35.3, 33.8, 31.1, 25.8, 23.0, 21.0, 20.8, 14.0; IR (neat) 1661 (s), 1601 (m) cm^{-1}; MS (EI): 258 (M, 61), 243 (23), 229 (100), 215 (91), 201 (13), 187 (19); HRMS calcd for $C_{17}H_{22}O_2$ 258.1620, found 258.1625.

Coupling of Dialkyne Aldehyde 8I with Carbene Complex 2. General procedure 1 was followed using carbene complex **2** (150 mg, 0.60 mmol) and dialkyne aldehyde **8I** (101 mg, 0.50 mmol) and using THF as the solvent; the reaction was conducted at reflux. After final purification, a white solid identified as lactone **25** was obtained (55 mg, 43% yield): ^{1}H NMR ($CDCl_3$) δ 7.78 (d, 1 H, J = 5.3 Hz), 7.68 (d, 1 H, J = 5.3 Hz), 7.20 (s, 1 H), 3.27 (t, 2 H, J = 7.4 Hz), 2.97 (t, 2 H, J = 7.4 Hz), 2.45 (s, 3 H), 2.22 (quintet, 2 H, J = 7.4 Hz); ^{13}C NMR ($CDCl_3$) 157.4, 150.0, 145.0, 140.2, 136.9, 135.6, 127.0, 125.1, 124.7, 114.1, 33.8, 32.1, 29.6, 25.0, 16.3; IR 1710 (s) cm^{-1}; MS (EI) 256 (M, 100), 241 (42), 227 (6), 184 (13); HRMS calcd for $C_{15}H_{12}O_2S$ 256.0558, found 261.0564.

Coupling of Alkyne Aldehyde 39 with Carbene Complex 17C. General procedure 2 was followed using carbene complex **17C** (145 mg, 0.48 mmol) and alkyne aldehyde **39** (87 mg, 0.65 mmol) and using THF as the solvent; the reaction was conducted at reflux. After final purification, a white solid identified as ketone **38** was obtained (50 mg, 49% yield): ^{1}H NMR (400 MHz) ($CDCl_3$) δ 7.07 (s, 1 H), 6.26 (d, 1 H, J = 2.0 Hz), 2.81 (dd, 1 H, J = 17.2, 4.9 Hz), 2.65−2.30 (m, 4 H), 2.11 (tdd, 1 H, J = 11.6 (t), 3.6, 2.0 Hz), 2.13 (s, 3 H), 1.85 (m, 1 H), 1.80−1.56 (m, 2 H), 1.15 (d, 3 H, J = 6.5 Hz); ^{13}C NMR ($CDCl_3$) δ 199.2, 158.5, 155.3, 139.3, 119.5, 118.4, 117.0, 42.4, 37.2, 35.6, 32.3, 26.5, 19.4, 10.7. The spectral data were identical to those previously reported for this compound.[23a]

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Supporting Information Available: Experimental procedures for formation of alkynealdehydes, γ,δ-unsatuarted carbene complexes, and the experiments in Table 1, entries D−F. Photocopies of ^{1}H NMR and ^{13}C NMR spectra for compounds **8A**−**C**,**G**−**I**, **11D**, **12A**−**C**, **17C**, **18G**,**J**,**L**,**O**, **19G**, **20**, **21N**,**P**, **25**, and **39**. This material is available free of charge via the Internet at http://pubs.acs.org.

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