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# Manganese Trifluoroacetoxycarbene Complexes Are Convenient Intermediates in the Synthesis of Cyclic Enediynes

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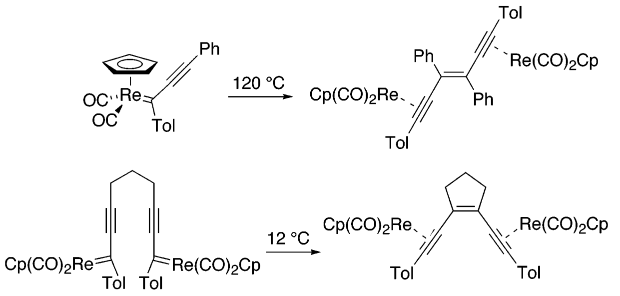
Trifluoroacetoxycarbene complexes generated from reaction of stable manganese acyl complexes with trifluoroacetic anhydride are convenient alternatives to thermally sensitive manganese carbyne complexes in reactions with diynes that lead eventually to free cyclic enediynes. In situ reaction of these trifluoroacetoxycarbene complexes with alkynyl copper intermediates generated from diynes, CuBr, and NEt($i$-Pr)$_2$ led to the isolation of cyclic enediynes via intermediate linked alkynylcarbene complexes and manganese enediyne complexes.

## Introduction

While the utility of heteroatom-substituted alkynylcarbene complexes in organic synthesis is well demonstrated, studies of the use of non-heteroatom-substituted alkynylcarbene complexes have just begun.[1,2] We recently discovered that thermolysis of rhenium alkynylcarbene complexes leads to the formation of dimeric *E*-enediyne complexes by the regioselective “tail-to-tail” coupling[3,4] of the remote alkynyl carbons in a kinetically second-order process (Scheme 1).[5,6] Extension of this chemistry to tethered bis(alkynylcarbene) rhenium complexes has provided an entry into cyclic enediyne complexes below room temperature.[5b] This straightforward route to enediyne complexes under mild conditions has potential value in the synthesis of pharmaceutically interesting enediynes.[7]

### Scheme 1



We recently extended this chemistry to the analogous manganese complexes to circumvent the high cost of stoichiometric rhenium complexes and the difficulty of releasing the enediynes from their highly thermally stable rhenium complexes. Simple manganese alkynylcarbene complexes such as Cp(CO)$_2$Mn═C(Tol)C≡CTol (**1**) were readily prepared from [Cp(CO)$_2$Mn≡CTol]BCl$_4$[8] and lithiotolylacetylene.[9,10] Dimerization to enediyne complexes occurred upon heating to 100 °C, and the free enediynes were obtained upon extended heating at 100 °C (Scheme 2).[9,11] The attempted synthesis of the tethered bis(alkynylcarbene) manganese complex **2** led

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[1] For reviews of heteroatom-substituted alkynylcarbene complexes, see: (a) Aumann, R.; Nienaber, H. *Adv. Organomet. Chem.* **1997**, *41*, 163. (b) Wulff, W. D. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon Press: Oxford, 1995; Vol. 12, Chapter 5.3. (c) Herndon, J. W. *Coord. Chem. Rev.* **1999**, *181*, 177. (d) Sierra, M. A. *Chem. Rev.* **2000**, *100*, 3591. (e) de Meijere, A.; Schirmer, H.; Duetsch, M. *Angew. Chem., Int. Ed.* **2000**, *39*, 3964, and references therein. (f) Herndon, J. W. *Tetrahedron* **2000**, *56*, 1257.

[2] For group 7 Fischer alkynylcarbene complexes, see: (a) Weng, W.; Ramsden, J. A.; Arif, A. M.; Gladysz, J. A. *J. Am. Chem. Soc.* **1993**, *115*, 3824. (b) Weng, W.; Arif, A. M.; Gladysz, J. A. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 891. (c) Terry, M. R.; Kelly, C.; Lugan, N.; Geoffroy, G. L.; Haggerty, B. S.; Rheingold, A. L. *Organometallics* **1993**, *12*, 3607. (d) Weng, W.; Bartik, T.; Gladysz, J. *A. Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2199. (e) Casey, C. P.; Kraft, S.; Powell, D. R.; Kavana, M. *J. Organomet. Chem.* **2001**, *617/618*, 723.

[3] The selective “head-to-head” Pd-catalyzed coupling of (CO)$_5$Cr═C(OEt)C≡CPh to (*E*,*Z*)-PhC≡C(OEt)C═C(OEt)C≡CPh has been reported. Sierra, M. A.; del Amo, J. C.; Mancheño, M. J.; Gómez-Gallego, M. *J. Am. Chem. Soc.* **2001**, *123*, 851.

[4] For earlier work on carbene coupling of metal carbene complexes, see: (a) Casey, C. P.; Anderson, R. L. *J. Chem. Soc., Chem. Commun.* **1975**, 895. (b) Casey, C. P.; Burkhardt, T. J.; Bunnell, C. A.; Calabrese, J. C. *J. Am. Chem. Soc.* **1977**, *99*, 2127. (c) Casey, C. P.; Polichnowski, S. W. *J. Am. Chem. Soc.* **1977**, *99*, 6097. (d) Fischer, H.; Schmid, J. *J. Mol. Catal.* **1988**, *46*, 277. (e) Fischer, H.; Zeuner, S.; Ackermann, K.; Schmid, J. *Chem. Ber.* **1986**, *119*, 1546. (f) Fischer, H.; Zeuner, S.; Ackermann, K. *Chem. Commun.* **1984**, 684. (g) Hohmann, F.; Siemoneit, S.; Nieger, M.; Kotila, S.; Dötz, K. H. *Chem. Eur. J.* **1997**, *3*, 853.

[5] (a) Casey, C. P.; Kraft, S.; Powell, D. R. *J. Am. Chem. Soc.* **2000**, *122*, 3771. (b) Casey, C. P.; Kraft, S.; Powell, D. R. *J. Am. Chem. Soc.* **2002**, *124*, 2584.

[6] Casey, C. P.; Kraft, S.; Kavana, M. *Organometallics* **2001**, *20*, 3795.

[7] For reviews of enediynes, see: (a) Nicolaou, K. C.; Smith, A. L. The Enediyne Anitbiotics. In *Modern Acetylene Chemistry*; Stang, P. J., Diederich, F., Eds.; VCH: Weinheim, 1995; p 203. (b) Maier, M. E. *Synlett.* **1995**, 13. (c) Grissom, J. W.; Gunawardena, G. U.; Klingberg, D.; Huang, D. *Tetrahedron* **1996**, *52*, 6453. (d) Smith, A. L.; Nicolaou, K. C. *J. Med. Chem.* **1996**, *39*, 2103. (e) Sander, W. *Acc. Chem. Res.* **1999**, *32*, 669. (f) König, B. *Eur. J. Org. Chem.* **2000**, 381.

[8] Fischer, E. O.; Meineke, E. W.; Kreissl, F. R. *Chem. Ber.* **1977**, *110*, 1140.

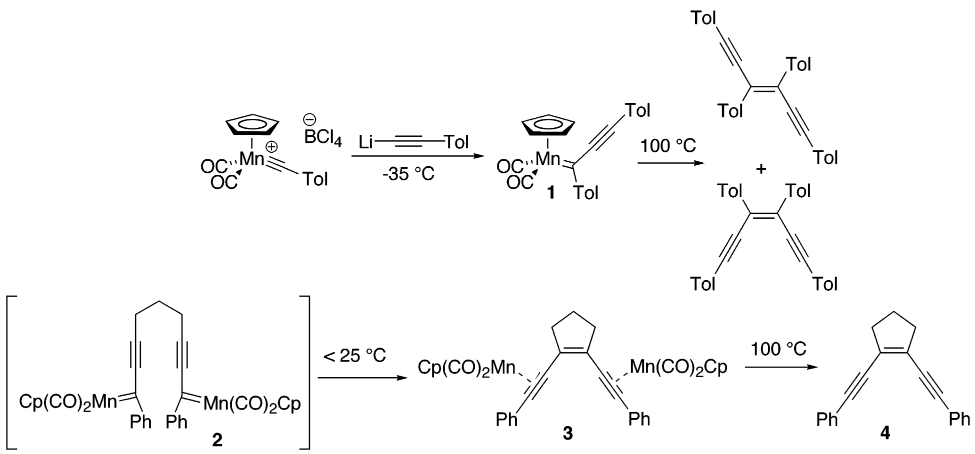
[9] (a) Casey, C. P.; Dzwiniel, T. L.; Kraft, S.; Kozee, M. A.; Powell, D. R. *Inorg. Chim. Acta* **2003**, *345*, 320. (b) Kraft. S. Ph.D. Thesis, University of Wisconsin−Madison, 2001.

[10] Ortin, Y.; Coppel, Y.; Lugan, N.; Mathieu, R.; McGlinchey, M. J. *Chem. Commun.* **2001**, 1690.

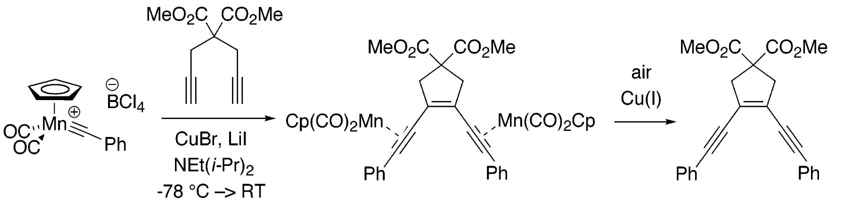
[11] The dimerization of alkynylcarbene manganese complexes catalyzed by substoichiometric amounts of strong reducing agents has been observed and a radical anion pathway has been proposed. Ortin, Y.; Sournia-Saquet, A.; Lugan, N.; Mathieu, R. *Chem. Commun.* **2003**, 1060.

10.1021/om030561+ CCC: $25.00

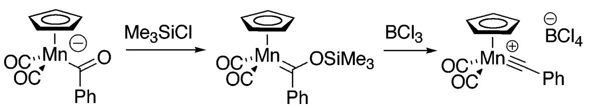
**Scheme 2**



**Scheme 3**



**Scheme 4**



directly to the rearranged cyclic enediyne complex **3**, which released the free enediyne **4** upon heating at 100 °C (Scheme 2).[9]

More recently we reported two major improvements in the synthesis of cyclic enediynes by this manganese alkynylcarbene route (Scheme 3).[12] First, a milder procedure for synthesis of alkynylcarbene complexes from the copper(I)-catalyzed reaction of terminal alkynes with carbyne complexes was developed; this procedure avoids the use of alkynyllithium reagents and allows introduction of ketone, ester, and ether functional groups. Second, three very mild methods for conversion of manganese enediyne complexes to the free enediynes were developed that involve photolysis or Cu-catalyzed air oxidation or stoichiometric Cu(II) oxidation.

A major drawback of this synthetic procedure is the need to use very temperature-sensitive ($T_{dec} < -20$ °C) and functional group-intolerant manganese carbyne complexes as starting materials. The synthesis of the previously reported phenyl- and tolyl-substituted carbyne complexes[8] requires reaction of an acyl manganese anion with $Me_3SiCl$, isolation of an intermediate siloxycarbene complex, and subsequent reaction with $BCl_3$ (Scheme 4). The resulting carbyne complexes are air and water sensitive and need to be synthesized and handled below −30 °C. Attempts to synthesize even simple substituted aryl carbyne complexes by similar procedures led to sticky tars despite repeated recrystallization attempts.

Here we report a much more convenient enediyne synthesis that avoids the use of isolated carbyne complexes. The procedure involves the use of thermally stable lithium salts of acyl manganese anions readily prepared by addition of aryllithium reagents to $(C_5H_4CH_3)Mn(CO)_3$. In a one-pot procedure, the acyl manganese compound is treated with trifluoroacetic anhydride, followed by addition of a diyne, CuBr, LiI, and NEt(*i*-Pr)$_2$, and then sun lamp photolysis, which leads to the isolation of cyclic enediynes in good yield.

## Results

Acyloxycarbene complexes are more reactive toward nucleophiles than alkoxycarbene complexes but less reactive than carbyne complexes. In cases where enhanced reactivity of carbene complexes is desired, the use of acyloxycarbene complexes has proven advantageous.[13] For example, Wulff has used acyloxycarbene complexes as entries into alkynyloxycarbene complexes (Scheme 5).[14] Mayr has used the reaction of oxalyl bromide with acylmetal anions as a route to carbyne complexes via an intermediate acyloxycarbene complex.[15]

These precedents encouraged us to seek to substitute acyloxycarbene complexes for carbyne complexes in our enediyne synthesis. Our hypothesis was that a manganeseacyloxycarbene complex might behave as a carbyne precursor or a "carbyne synthon" and show high reactivity toward dialkynyl nucleophiles.

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(13) (a) Connor, J. A.; Jones, E. M. *Chem. Commun.* **1971**, 570. (b) Fischer, E. O.; Selmayr, T.; Kreissl, F. R. *Chem. Ber.* **1977**, *110*, 2947. (c) Semmelhack, M. F.; Bozell, J. J. *Tetrahedron Lett.* **1982**, 2931. (d) Semmelhack, M. F.; Bozell, J. J.; Keller, L.; Sato, T.; Spiess, E. J.; Wulff, W.; Zask, A. *Tetrahedron* **1985**, *41*, 5803. (e) Soderberg, B. C.; Hegedus, L. S.; Sierra, M. A. *J. Am. Chem. Soc.* **1990**, *112*, 4364. (f) Herndon, J. W.; Zora, M.; Patel, P. P.; Chatterjee, G.; Matasi, J. J.; Tumer, S. U. *Tetrahedron* **1993**, *49*, 5507. (g) Yamashita, M.; Ohishi, T. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 1187.

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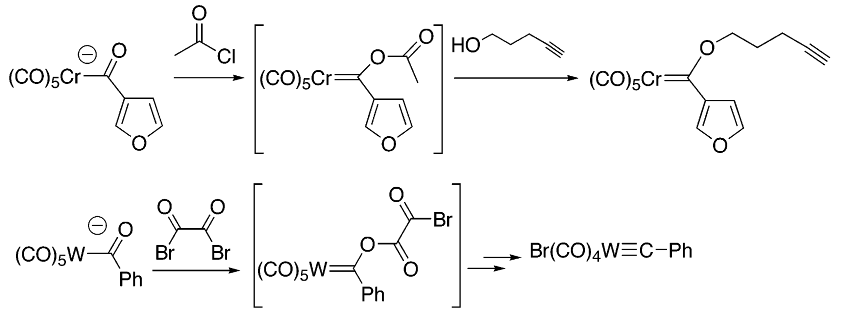
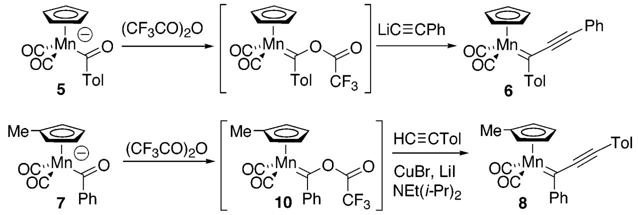
(15) McDermott, G. A.; Dorries, A. M.; Mayr, A. *Organometallics* **1987**, *6*, 925.

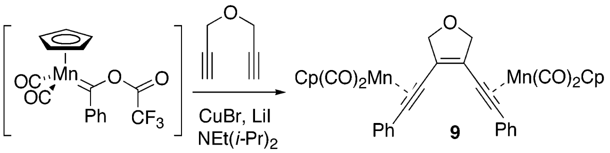
**Scheme 5**



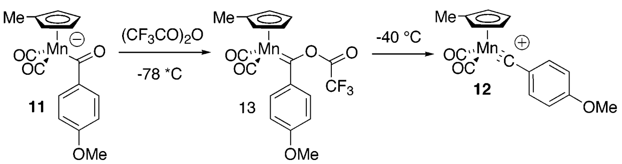
**Scheme 6**



**Scheme 7**



**Scheme 8**



Our initial attempt to use an acetoxycarbene complex in reactions with alkynyllithium reagents failed. Reaction of $[Cp(CO)_2MnC(O)Tol]Li{\cdot}Et_2O$ (**5**) with an equimolar amount of either acetyl chloride or acetic anhydride in $CH_2Cl_2$ at 0 °C caused a slow color change from light orange to brown. However, subsequent reaction with LiC≡CPh failed to give a second color change to the known dark red-black alkynylcarbene, and no tractable material was formed.[16]

In contrast, the use of the more reactive trifluoroacetoxycarbene complexes led to the successful synthesis of alkynyl carbene complexes. Reaction of $[Cp(CO)_2MnC(O)Tol]Li{\cdot}Et_2O$ (**5**) with trifluoroacetic anhydride in $CH_2Cl_2$ brought about an immediate color change to deep brown-black. Addition of LiC≡CPh quickly turned the solution a deep red color, characteristic of the alkynyl carbene complexes, and the known $Cp(CO)_2MnC(Tol)C{\equiv}CPh$ (**6**)[9] was isolated in 66% yield after column chromatography. The intermediate trifluoroacetoxycarbene complex was also reactive toward organocopper intermediates generated from terminal alkynes, CuBr, and NEt(*i*-Pr)$_2$. Addition of trifluoroacetic anhydride to $[(C_5H_4Me)(CO)_2MnC(O)Ph]Li{\cdot}Et_2O$ (**7**)[17] followed by addition of TolC≡CH, NEt(*i*-Pr)$_2$, and a catalytic amount of CuBr and LiI led to the isolation of alkynylcarbene complex **8** (Scheme 6).

Activation of acyl manganese anions with trifluoroacetic anhydride was also effective in the conversion of diynes to cyclic enediyne manganese complexes. Addition of trifluoroacetic anhydride to acyl manganese complex $[Cp(CO)_2MnC(O)Ph]Li{\cdot}Et_2O$[18] followed by addition of dipropargyl ether, NEt(*i*-Pr)$_2$, and a catalytic amount of CuBr and LiI led to the isolation of the known manganese enediyne complex **9** (Scheme 7).

**Direct Observation of Trifluoroacetoxycarbene Complexes and of Derived Carbyne Complexes.** Attempted isolation of trifluoroacetoxycarbene complexes at room temperature led only to intractable brown material. Attempted NMR investigation of the reaction of trifluoroacetic anhydride with aroyl manganese complexes was also unsuccessful due to the formation of paramagnetic impurities. Fortunately, IR spectroscopy provided insight into the reaction. Trifluoroacetic anhydride was added to $[(C_5H_4Me)(CO)_2MnC(O)(C_6H_5)]Li{\cdot}Et_2O$ (**7**) in $CH_2Cl_2$ at low temperature, and samples were examined by IR spectroscopy. The IR bands of **7** at 1897 and 1815 cm$^{-1}$ were replaced by new bands at 1960 and 1904 cm$^{-1}$. These new bands are consistent with the formation of a neutral manganese carbene species and are assigned to a trifluoroacetoxy carbene complex, $(C_5H_4Me)(CO)_2Mn{=}C(OCOCF_3)(C_6H_5)$ (**10**). The IR bands of **10** decreased in intensity by about half after 10 min at room temperature, indicating extensive decomposition of **10** at room temperature.

Dramatic differences were seen when the phenyl group of the acyl was replaced by a better electron donor *p*-methoxyphenyl group. Addition of trifluoroacetic anhydride to $[(C_5H_4Me)(CO)_2MnC(O)(C_6H_4\text{-}4\text{-}OMe)]Li{\cdot}Et_2O$ (**11**) in $CH_2Cl_2$ at room temperature led to replacement of the IR bands of the acyl complex at 1899 and 1797 cm$^{-1}$ by very high-frequency bands at 2076 and 2036 cm$^{-1}$ characteristic of a carbyne complex. For example, $[Cp(CO)_2Mn{\equiv}CPh]BCl_4$ has two carbonyl bands at 2088 and 2047 cm$^{-1}$ in $CH_2Cl_2$.[12] Apparently, the strongly electron-donating *p*-methoxy substituent promotes the dissociation of the trifluoroacetate group and stabilizes the resulting electron-deficient carbyne complex $(C_5H_4Me)(CO)_2Mn{\equiv}C(C_6H_4\text{-}4\text{-}OMe)^+$ (**12**) (Scheme 8).

When the addition of trifluoroacetic anhydride to **11** in $CH_2Cl_2$ was monitored by IR spectroscopy at low

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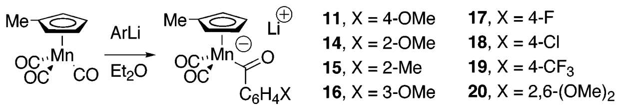
[16] Fischer generated $Cp(CO)_2Mn{=}C(O_2CCH_3)Ph$ at −40 °C and used it to make carbohydroatocarbene complexes. Fischer, H.; Schleu, J. *Chem. Ber.* **1996**, *129*, 385.

[17] For previous use of **7**, see: (a) McGeary, M. J.; Tonker, T. L.; Templeton, J. L. *Organometallics* **1985**, *4*, 2102. (b) Hoye, T. R.; Rehberg, G. M. *Organometallics* **1990**, *9*, 3014. (c) Balzer, B. L.; Cazanoue, M.; Sabat, M.; Finn, M. G. *Organometallics* **1992**, *11*, 1759. (d) Fischer, E. O.; Meineke, E. W.; Kreissl, F. R. *Chem. Ber.* **1977**, *110*, 1140.

[18] Fischer, E. O.; Maasböl, A. *Chem. Ber.* **1967**, *100*, 2445.

**Scheme 9**



temperature, evidence for an intermediate trifluoroacetoxycarbene complex was obtained. When the reaction was carried out in a REACTIR instrument at −78 °C, CO bands appeared immediately at 1960 and 1894 $cm^{-1}$, consistent with formation of the neutral carbene complex $(C_5H_4Me)(CO)_2Mn{=}C(OCOCF_3)(C_6H_4\text{-}4\text{-}OMe)$ (**13**). Above −40 °C, these bands disappeared and were replaced by bands at 2070 and 2025 $cm^{-1}$ for carbyne complex **12**.

**Synthesis of Aroyl Manganese Anions.** In contrast to the very temperature-sensitive carbyne complexes, acyl manganese anions are thermally stable and readily isolated. While only a few aroyl manganese anions had been reported, these complexes are conveniently prepared from reaction of the corresponding aryllithium reagents with $(C_5H_4Me)Mn(CO)_3$ or $CpMn(CO)_3$. For example, addition of 4-lithioanisole, formed by lithium−halogen exchange from 4-bromoanisole and *n*-BuLi, to a solution of $(C_5H_4Me)Mn(CO)_3$ in $Et_2O$ gave $[(C_5H_4Me)(CO)_2MnC(O)(C_6H_4\text{-}4\text{-}OMe)]Li\cdot Et_2O$ (**11**) as a light orange powder in 54% yield (Scheme 9). The crystalline aroyl complexes are readily purified by careful washing with $Et_2O$. These aroyl compounds are readily characterized by their low-energy $\nu_{CO}$ IR bands (1899 and 1797 $cm^{-1}$ for **11**) and the high-frequency $^{13}C$ NMR chemical shifts of the acyl carbon and CO groups ($\delta$ 310.2 and 238.5 for **11**). Interestingly, upon extended storage in a glovebox, the solvated ether was lost, causing a color change from orange to a yellow powder. This had no apparent effect on the subsequent reactivity of the compound, although diminished solubility in $CH_2Cl_2$ was observed. When the yellow ether-free acyl complexes were suspended in $CH_2Cl_2$ and ether or THF was added, the acyl complexes dissolved to give orange solutions. A wide range of substituted aroyl manganese complexes was prepared.

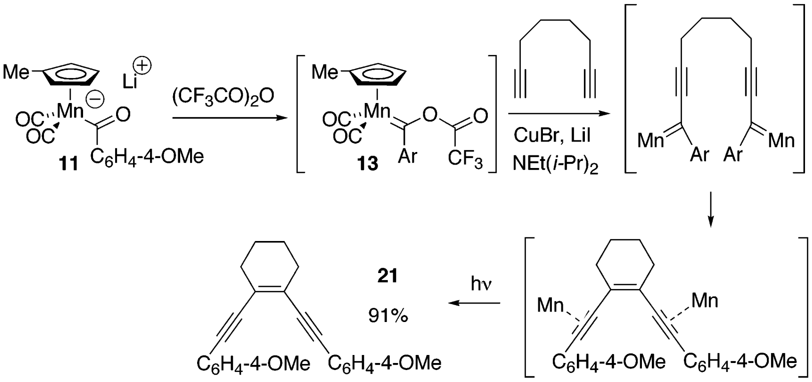
**Trifluoroacetic Anhydride Activation of Aroyl Manganese Complexes in the Synthesis of Symmetric Free Enediynes.** Manganese trifluoroacetoxycarbene complexes were generated from reaction of trifluoroacetic anhydride and aroyl manganese anions in $CH_2Cl_2$ at low temperature. Addition of a diyne and $NEt(i\text{-}Pr)_2$ along with a catalytic amount of CuBr and LiI led to the formation of tethered bis alkynylcarbene complexes, which coupled to give manganese enediyne complexes below room temperature. The solutions of enediyne complexes were poured into methanol and photolyzed with a sun lamp to release the free enediyne. The free enediynes were isolated by chromatography and characterized spectroscopically. For example, reaction of acyl manganese complex **11** with trifluoroacetic anhydride, followed by addition of 1,7-octadiyne, CuBr, LiI, and $NEt(i\text{-}Pr)_2$, and photolysis led to the isolation of cyclic enediyne **21** in 91% yield based on the diyne (Scheme 10). The variety of aromatic substituents, ring sizes, and functional groups accommodated in this cyclic enediyne synthesis are shown in Figure 1.

**Synthesis of Unsymmetric Enediynes.** The reaction of diynes with mixtures of two different acyl manganese complexes resulted in unselective coupling. However, by choosing substituents of significantly different polarity, it was possible to isolate unsymmetric cyclic enediynes in moderate yield. For example, addition of trifluoroacetic anhydride to an equimolar mixture of acyl complexes $[(C_5H_4Me)(CO)_2MnC(O)(C_6H_4\text{-}4\text{-}OMe)]Li\cdot Et_2O$ (**11**) and $[(C_5H_4Me)(CO)_2MnC(O)(C_6H_4\text{-}4\text{-}Cl)]Li\cdot Et_2O$ (**18**), followed by addition of dimethyl dipropargylmalonate, $NEt(i\text{-}Pr)_2$, CuI, and LiI, photolysis, and chromatography, led to the isolation of unsymmetric enediyne **42** (Scheme 11). Further examples are shown in Figure 2.

## Summary

The replacement of very temperature-sensitive carbyne complexes by easily synthesized and thermally stable acyl manganese complexes has made the synthesis of cyclic enediynes much more convenient. The acyl manganese complexes are converted to reactive trifluoroacetoxy carbene complexes by treatment with trifluoroacetic anhydride at low temperature. Alkynyl copper intermediates generated from diynes, CuBr, LiI, and $NEt(i\text{-}Pr)_2$ react with the trifluoroacetoxy carbene complexes to give linked alkynyl carbene complexes. The substitution of the trifluoroacetoxy group by an alkynyl copper intermediate probably proceeds by an associative addition−elimination mechanism, but dissociative mechanisms involving carbyne complex intermediates are possible, particularly when electron-donor substituents are present on the aroyl manganese precursor. The tethered alkynylcarbene ligands couple to form enediyne-manganese complexes below room temperature,

**Scheme 10**



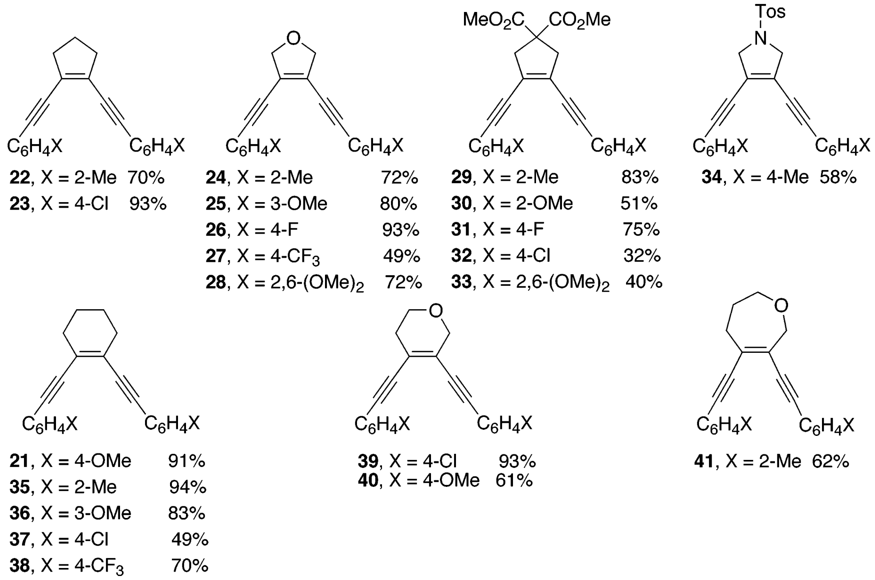


**Figure 1.**

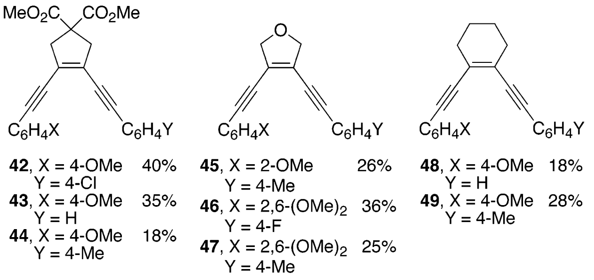
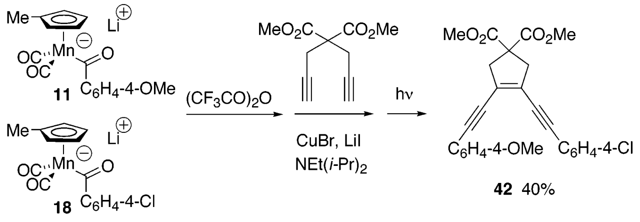


**Figure 2.**

**Scheme 11**



and subsequent photolysis releases the free cyclic enediyne. Overall, we have developed an efficient one-pot conversion of acyl manganese complexes and diynes to cyclic enediynes that works very well for a variety of substituted aroyl manganese complexes. Future work will be directed toward extending the scope of the reaction beyond aryl-substituted cyclic enediynes.

## Experimental Section

**$C_5H_5(CO)_2Mn{=}C(C_6H_4\text{-}4\text{-}CH_3)C{\equiv}CC_6H_5$ (6).** Addition of trifluoroacetic anhydride (82 $\mu$L, 0.580 mmol) to a slurry of $Cp(CO)_2MnC(O)(C_6H_4\text{-}4\text{-}CH_3)Li\cdot Et_2O$ (**5**) (196 mg, 0.52 mmol) in $CH_2Cl_2$ (5 mL) at room temperature resulted in a color change from dark red to brown. Solid $PhC{\equiv}CLi$ (73.7 mg, 0.681 mmol) and THF (5 mL) were added. After 90 min, the solvents were evaporated under vacuum. The residue was extracted with 10% ethyl acetate/hexanes and chromatographed (silica gel, 10% ether/hexanes) to give **6** (131 mg, 66%) as a dark solid, whose IR and NMR spectra matched those reported previously.[9]

**$(C_5H_4Me)(CO)_2Mn{=}C(C_6H_5)C{\equiv}C(C_6H_4\text{-}4\text{-}CH_3)$ (8).** Trifluoroacetic anhydride (172 $\mu$L, 1.22 mmol) was added to a slurry of $(C_5H_4Me)(CO)_2MnC(O)(C_6H_5)Li\cdot Et_2O$ (**7**) (417 mg, 1.11 mmol) in $CH_2Cl_2$ (60 mL) at −78 °C. Then a solution of $TolC{\equiv}CH$ (127 $\mu$L, 1.00 mmol), CuBr (18.3 mg), LiI (18.8 mg), and $NEt(i\text{-}Pr)_2$ (192 $\mu$L) in THF (3 mL) was added. The reaction mixture was slowly warmed to room temperature, and the solvents were evaporated under vacuum. The residue was purified by column chromatography (silica, 10% ether/hexanes) to give **8** (292 mg, 74%) as a dark solid, whose IR and NMR spectra matched those reported previously.[9]

**$[Cp(CO)_2Mn]_2[\eta^2,\eta^2\text{-}C_6H_5C{\equiv}CC(CH_2OCH_2){=}CC{\equiv}C\text{-}C_6H_5]$ (9).** Trifluoroacetic anhydride (0.207 mL, 1.47 mmol) was added to a slurry of $Cp(CO)_2MnC(O)(C_6H_5)Li\cdot Et_2O$[18] (512 mg, 1.41 mmol) in $CH_2Cl_2$ (70 mL) at room temperature, and then a solution of dipropargyl ether (61 $\mu$L, 0.59 mmol), CuBr (23 mg), LiI (21 mg), and $NEt(i\text{-}Pr_2$ (0.24 mL) in THF (5 mL) was added. The reaction mixture was slowly warmed to room temperature, and the solvents were evaporated under vacuum. The residue was purified by chromatography (silica, 20% ether/hexanes) to give **9** (203 mg, 55%) as a bright red solid, whose IR and NMR spectra matched those reported previously.[12]

**General Procedure for Synthesis of Substituted Aroyl Manganese Complexes.** ArLi (1 equiv) was prepared by the addition of BuLi (1.6 M) in hexanes to a cold (0 °C) solution of ArBr (1 M) in ether. After stirring several hours at 0 °C, $(C_5H_4Me)Mn(CO)_3$ (1 equiv) was added dropwise over 1−2 min. The solution turned orange, and after stirring for several hours at room temperature, a bright orange powder precipitated. The supernatant was removed by cannula transfer. The orange solid was washed with a 1:1 ether/pentane, dried in vacuo, and weighed and handled in a glovebox. Over long-term storage in a glovebox, the orange powder sometimes turned bright yellow as the ether of crystallization was lost.

**$(C_5H_4Me)(CO)_2MnC(O)(C_6H_4\text{-}4\text{-}OCH_3)Li\cdot Et_2O$ (11).** Reaction of $(C_5H_4Me)Mn(CO)_3$ (4.65 mL, 29.4 mmol) with $LiC_6H_4\text{-}4\text{-}OCH_3$ [prepared from 4-bromoanisole (3.68 mL, 29.4 mmol) and BuLi (18.4 mL, 1.6 M, 29.4 mmol)] led to the isolation of **11** (6.41 g, 54%) as an orange solid. $^1H$ NMR (500 MHz, acetone-$d_6$): $\delta$ 7.39 (br s, 2H, $H_{Ar}$), 6.67 (br s, 2H, $H_{Ar}$), 4.26 (br s, 2H, $C_5H_4$), 4.14 (br s, 2H, $C_5H_4$), 3.73 (br s, OMe), 1.794 (br s, Me). $^{13}C$ NMR (125 MHz, acetone-$d_6$): $\delta$ 310.2 (s, *C*OAr), 238.52 (s, CO), 159.55 (s, $C_{Ar}$), 151.52 (s, $C_{Ar}$), 127.24 (d, $^1J_{CH}$ = 156 Hz, $C_{Ar}$), 112.23 (d, $^1J_{CH}$ = 158 Hz, $C_{Ar}$), 100.04 (s, $C_5H_4$-Me), 85.52 (d, $^1J_{CH}$ = 176.5 Hz, $C_5H_4Me$), 84.45 (d, $^1J_{CH}$ = 171 Hz, $C_5H_4Me$), 55.37 (q, $^1J_{CH}$ = 143 Hz, OMe), 14.49 (q, $^1J_{CH}$ = 127 Hz, $C_5H_4Me$). IR ($CH_2Cl_2$): 1899, 1797 $cm^{-1}$.

**General Procedure for Synthesis of Symmetric Cyclic Enediynes from Reactions of Acyl Manganese Com-**

**plexes.** Trifluoroacetic anhydride (1.1 equiv) was added to a cold (≤−35 °C) red-orange solution of [($C_5H_4Me$)$(CO)_2$MnC(O)Ar]Li·$Et_2O$ (1.0−1.5 mmol) in $CH_2Cl_2$ (100 mL). After a minute, a mixture of CuBr (0.1 mmol), LiI (0.1 mmol), NEt(*i*-Pr)$_2$ (1.0 mmol), and a diyne (0.42 mmol) was added to the dark brown solution, and the color changed to a lighter red-brown. The solution was warmed to room temperature, stirred for several hours, and poured into an equal volume of THF. The solution was photolyzed with a 150 W sunlamp for several hours, until the red color had disappeared and a brown precipitate had formed. Solvent was evaporated under vacuum, and the enediyne product was isolated by column chromatography on silica gel. Some enediyne complexes were susceptible to decomposition through polymerization and required rechromatography.

**(4-MeO−$C_6H_4$)C≡CC($CH_2CH_2CH_2CH_2$)=CC≡C($C_6H_4$-4-OMe) (21).** Addition of trifluoroacetic anhydride (245 $\mu$L, 1.73 mmol) to ($C_5H_4Me$)$(CO)_2$MnC(O)($C_6H_4$-4-$OCH_3$)Li·$Et_2O$ (**11**) (678 mg, 1.67 mmol) was followed by addition of CuBr (23.4 mg), LiI (24.7 mg), NEt(i-Pr)$_2$ (289 $\mu$L), and 1,7-octadiyne (93 $\mu$L, 0.701 mmol) in $CH_2Cl_2$ (100 mL). The solution was poured into 200 mL of 10% ether/hexanes and photolyzed. Chromatography gave **21** (220 mg, 91% based on diyne) as a slightly yellow oil. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.42 (d, $J$ = 9 Hz, 4H, $H_{Ar}$), 6.85 (d, $J$ = 9 Hz, 4H, $H_{Ar}$), 3.82 (s, OMe), 2.38−2.34 (m, C=C$CH_2$), 1.75−1.65 (m, C=C$CH_2C\mathit{H_2}$). $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 159.42 (s, *C*OMe), 132.86 (d, $^1J_{CH}$ = 168 Hz, $C_{Ar}$), 125.81 (s, C=C), 115.86 (d, $^1J_{CH}$ = 159 Hz, $C_{Ar}$), 113.90 (s, $C_{ipso}$), 93.44 (s, C≡*C*Ar), 89.35 (s, *C*≡CAr), 55.21 (q, $^1J_{CH}$ = 143 Hz, CO*Me*), 30.04 (t, $^1J_{CH}$ = 127 Hz, C=C$\mathit{C}H_2CH_2$), 21.96 (t, $^1J_{CH}$ = 127.8 Hz, C=C$CH_2\mathit{C}H_2$). HRMS(EI): $m/z$ calcd for $C_{24}H_{22}O_2$ ($M^+$) 342.1621; found, 342.1620.

**General Procedure for Synthesis of Unsymmetric Cyclic Enediynes from Reactions of Acyl Manganese Complexes.** Trifluoroacetic anhydride (1.1 equiv) was added to a cold (−78 °C) red-orange solution of two different acyl complexes, [($C_5H_4Me$)$(CO)_2$MnC(O)Ar]Li·$Et_2O$ (0.5 mmol) and [($C_5H_4Me$)$(CO)_2$MnC(O)Ar′]Li·$Et_2O$ (0.5 mmol) in $CH_2Cl_2$ (100 mL) and THF (2 mL). After a minute, a THF solution of CuBr (0.1 mmol), LiI (0.1 mmol), NEt(i-Pr)$_2$ (0.9 mmol), and diyne (0.42 mmol) was added. The mixture was warmed to room temperature over several hours, poured into methanol (80 mL), and photolyzed with a 150 W sun lamp for 6−8 h. The solution was poured into 10% HCl (200 mL) and extracted with $CH_2Cl_2$. The organic layer was washed with water, dried ($MgSO_4$), and evaporated. Column chromatography (silica, ethyl acetate/hexanes) was used to separate three fractions, which showed fluorescent spots on TLC. The middle fraction was the unsymmetric enediyne.

**(4-MeO−$C_6H_4$)C≡CC[$CH_2C(CO_2Me)_2CH_2$]=CC≡C($C_6H_4$-4-Cl) (42).** Addition of trifluoroacetic anhydride (155 $\mu$L, 1.10 mmol) to ($C_5H_4Me$)$(CO)_2$MnC(O)($C_6H_4$-4-$OCH_3$)Li (**11**) (168 mg, 0.51 mmol) and ($C_5H_4Me$)$(CO)_2$MnC(O)($C_6H_4$-4-Cl)Li·$Et_2O$ (**18**) (171 mg, 0.51 mmol) was followed by addition of CuBr (7 mg), LiI (14 mg), NEt(i-Pr)$_2$ (173 $\mu$L), and dimethyl dipropargylmalonate (101 mg, 0.485 mmol) in $CH_2Cl_2$ (90 mL) at −50 °C. The solution was poured into 200 mL of methanol and photolyzed. Chromatography gave **42** (88 mg, 40% based on diyne) as a slightly yellow oil in the middle fraction. The ratio of the three fractions was about 1:2:2. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.42 (d, $J$ = 9 Hz, 2H, $H_{Ar}$), 7.43 (d, $J$ = 8.5 Hz, 2H, $H_{Ar}$), 7.33 (d, $J$ = 8.5 Hz, 2H, $H_{Ar}$), 6.89 (d, $J$ = 8.5 Hz, 2H, $H_{Ar}$), 3.84 (s, OMe), 3.80 (s, $CO_2Me$), 3.35 (s, 4H, $CH_2$). $^{13}$C-{$^1$H} NMR (125 MHz, $CDCl_3$): $\delta$ 171.35 (*C*$O_2$Me), 159.95 (*C*OMe), 134.50 (*C*Cl), 133.16 ($HC_{Ar}$), 132.78 ($HC_{Ar}$), 128.68 ($HC_{Ar}$), 127.47 (C=C), 125.13 (C=C), 121.49 ($C_{ipso}$), 114.86 ($C_{ipso}$), 114.03 ($HC_{Ar}$), 97.49 (s, C≡*C*Ar), 95.41 (s, C≡*C*Ar), 85.99 (s, *C*≡CAr), 83.63 (s, *C*≡CAr), 58.06 (*C*$(CO_2Me)_2$), 55.25 ($CO_2$*Me*), 43.76 ($CH_2$), 43.47 ($CH_2$). HRMS(EI): $m/z$ calcd for $C_{26}H_{21}{}^{35}ClO_5$ ($M^+$) 448.1078; found, 448.1084.

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**Supporting Information Available:** Preparation of compounds and spectroscopic data. This material is available free of charge via the Internet at http://pubs.acs.org.

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