Pergamon

Tetrahedron, Vol. 53, No. 27, pp. 9107-9114, 1997

0040-4020/97 $17.00 + 0.00

PII: S0040-4020(97)00610-8

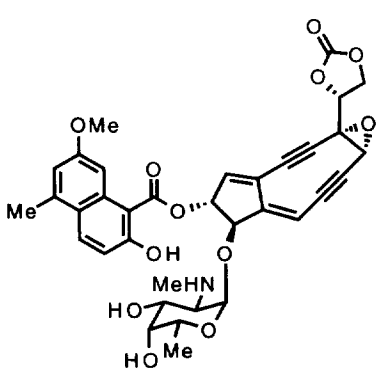
Stereoselective Synthesis of (*Z*)-Ketoeneynes via Pd(0)-Cu(I)-Catalyzed Cross-Coupling of (*Z*)-Ketoenol Triflate with 1-Alkynes†

Wei-Min Dai* and Jinlong Wu§

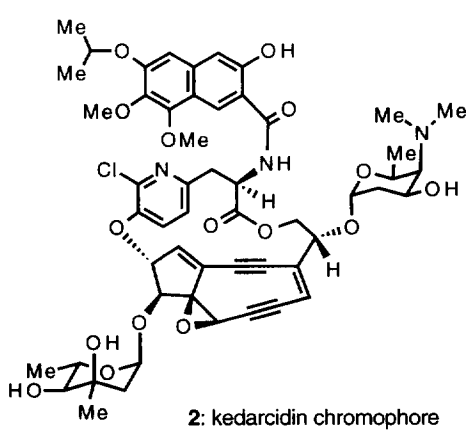
Department of Chemistry, The Hong Kong University of Science and Technology
Clear Water Bay, Kowloon, Hong Kong

Abstract: A general and stereoselective synthesis of (*Z*)-ketoeneynes **9** and **11a-f** was established by using a Pd(0)-Cu(I)-catalyzed cross-coupling of the labile (*Z*)-ketoenol triflate **3** with 1-alkynes under carefully controlled reaction conditions. Isomerization of the coupling products into the more stable (*E*)-ketoeneynes **8** and **12a-f** was observed and could be minimized by carring out the coupling reaction in CH_3CN at low temperature using Et_3N as the base. © 1997 Elsevier Science Ltd.

The palladium-catalyzed cross-coupling reactions of alkenyl/aryl halides or trifluoromethanesulfonates (triflates, TfO) with alkenes (the Heck reaction),[1] 1-alkynes (the Sonogashira reaction, in combination with CuI),[2] organoboron compounds (the Suzuki reaction),[3] and organotin compounds (the Still reaction)[4] are the powerful methods for carbon-carbon bond formation in contemporary organic synthesis.[5] For example, the Sonogashira reaction has enjoyed numerous applications in syntheses of enediyne antitumor antibiotics.[6] Two groups[7,8] constructed a number of monocyclic dienediyne models of neocarzinostatin chromophore (**1**)[9] utilizing the Pd(0)-Cu(I)-catalyzed cross-coupling reactions of monotriflate **4** and bistriflates **5** and **6**.[10] Terashima's group prepared (*E*)-ketoenol triflate **4** and (*E*)-bistriflate **6** from 2-formylcyclopentanone (**10**, in the ketoenol form)[11] and converted **4** and **6** into the (*Z*)-isomers **3** and **5** by a photochemical process.[7b,d] On the other hand, Suffert's group developed a direct stereoselective synthesis of (*Z*)-**3** from **10** and transformed it into (*Z*)-**5** by treating with $LiN(TMS)_2$ and $(Tf)_2O$.[8a,c] Regioselective coupling of bistriflates **5** and **6** with two



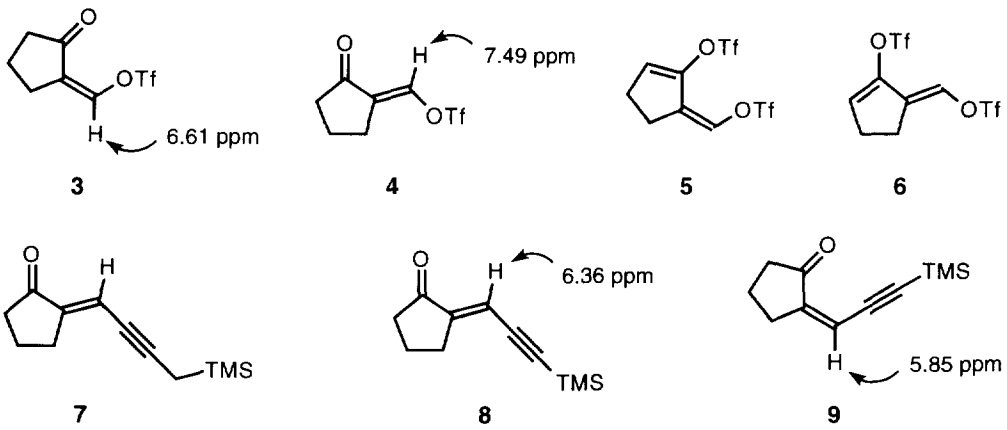
1: neocarzinostatin chromophore



2: kedarcidin chromophore

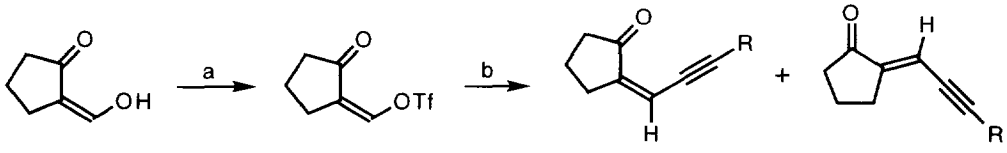
different 1-alkynes was successfully established by Suffert and co-workers.[8]

(*E*)-Ketoeneyne **8** was synthesized by Terashima *et al.* from a ketal derivative of **10**.[7a,c] Irradiation (254 nm) of **8** in acetone gave the (*Z*)-isomer **9** in 36% yield with 55% recovery of **8**.[7a,c] Suffert *et al.* prepared (*E*)-ketoeneyne **7** and other analogs by a Pd(0)-Cu(I)-catalyzed cross-coupling reaction of (*E*)-ketoenol triflate **4** and its nonaflate (NfO = $F_3C(CF_2)_3SO_3$-) in iPr_2NH-THF (1:3) at room temperature.[7d] However, to the best of our knowledge, the Pd(0)-Cu(I)-catalyzed cross-coupling reaction of the labile (*Z*)-ketoenol triflate **3** has not been reported. In connection with our synthetic study on the model compounds of kedarcidin chromophore (**2**),[12] we need to develop a general and efficient synthesis of **9** and the related (*Z*)-ketoeneynes in order to introduce the stereochemically defined epoxy functionality. We report here a stereoselective synthesis of (*Z*)-ketoeneynes **9** and **11a-f** from (*Z*)-ketoenol triflate **3** and 1-alkynes under the Sonogashira reaction conditions.



(*Z*)-Ketoenol triflate **3** was prepared from 2-formylcyclopentanone (**10**)[11] by the reported procedure.[8a,c] The original reaction was carried out at -65 °C in *ca.* 42% yield.[8c] We found that the reaction could be done at -78 °C to give **3** in 44% yield (Scheme 1). Triflate **3** is a very labile compound which can be purified by flash column chromatography over silica gel but decomposes easily when the solution is evaporated to dryness. A sample of **3** turned to dark color after keeping at -20 °C for a few days. For a reliable supply, we freshly prepared triflate **3** from **10**, purified by flash column chromatography, and immediately used for the next coupling reaction after removal of the solvent by rotary evaporator under reduced pressure below 30 °C. *Further*

Scheme 1. Stereoselective cross-coupling of (*Z*)-ketoenol triflate **3** with terminal alknyes.



10 **3** **9**: R = TMS **11a-f** **8**: R = TMS **12a-f**

a) *t*BuLi, THF, -78 °C, 15 min; Tf_2O, 10 min, 44%; b) HC≡C-R, 5 mol% of $Pd(Ph_3)_4$, 15 mol% of CuI, Et_3N-CH_3CN (1:3), 0 °C, see Tables 1 and 2 for details.

drying of 3 under high vacuum should not be attempted in order to avoid substantial decomposition.

In our preliminary experiments, it was found that the Pd(0)-Cu(I)-catalyzed coupling reaction of **3** with (trimethylsilyl)acetylene in iPr$_2$NH-THF (1:3) at room temperature[8d] did not give the product **9**. Isomerization of **9** into the (*E*)-isomer **8** was observed (Scheme 1). For this reason, we replaced iPr$_2$NH by Et$_3$N and conducted the coupling reaction at 0 °C in CH$_3$CN. Table 1 lists some of the results with variations in the catalysts and the reaction time. Decomposition of the coupling product under the reaction conditions may explain the diminished yield of **9** in prolonged reactions. By limiting the reaction time to 10 min at 0 °C (Entry 3, triflate **3** was nearly consumed after 5 min as checked by TLC) (*Z*)-ketoeneyne **9** was isolated in 41% yield together with (*E*)-isomer **8** (6%). Usually alkenyl triflates require high temperature to promote the Pd(0)-Cu(I)-catalyzed cross-coupling reaction,[10] the high reactivity of (*Z*)-ketoenol triflate **3** observed here is rare.

Table 1. Stereoselective synthesis of (*Z*)-ketoeneyne **9** from **3**.[a]

Entry	Reaction Conditions	Products (%)[b]
1	1.6 mol % Pd(Ph$_3$)$_4$, 5.1% CuI, 0 °C, 40 min	**9** (29-35)
2	1.6 mol % Pd(Ph$_3$)$_4$, 5.1% CuI, 0 °C, 60 min	**9** (21)
3	5 mol % Pd(Ph$_3$)$_4$, 15% CuI, 0 °C, 10 min	**8** (6), **9** (41)[c]
4	5 mol % Pd(Ph$_3$)$_4$, 15% CuI, 0 °C, 15 min	**9** (30)

[a]Reactions were performed in degassed Et$_3$N-CH$_3$CN (1:3) under nitrogen atomosphere. [b]Isolated yields after flash column chromatography. [c]**8**:**9** = 13:87; **8** was not detected in the reaction mixture by TLC.

Next, we examined the cross-coupling reaction of **3** with a number of 1-alkynes under the above established conditions (Table 2). We checked some of the crude products for the ratios of (*Z*)-**11** to (*E*)-**12**. It was revealed that the cross-coupling reaction of **3** with 1-alkynes gave very high stereoselectivity ranging from

Table 2. Stereoselective synthesis of (*Z*)-ketoeneynes **11a-f** from **3**.[a]

Entry	1-Alkyne (HC≡CR)	time (min)	**11**:**12**[b]	Products (%)[c]
1	R = SiiPr$_3$	15	96:4	**11a** (78)
2	R = Ph	15	91:9	**11b**+**12b** (61, 91:9)
3	R = nBu	35	nd[d]	**11c** (13); **12c** (45)[e]
4	R = (CH$_2$)$_2$OSitBuMe$_2$	45	100:0	**11d** (48)
5	R = (CH$_2$)$_4$OMe	25	100:0	**11e** (54); **12e** (9)
6	R = CH$_2$OCH$_2$C≡CH	30	nd[d]	**11f** (24)

[a]Reactions were performed with 5 mol% of Pd(Ph$_3$)$_4$ and 15 mol% of CuI in degassed Et$_3$N-CH$_3$CN (1:3) under nitrogen atomosphere at 0 °C. [b]Measured by the intergrations of the vinyl protons in the ^{1}H NMR spectrum of the crude product. [c]Isolated yields after flash column chromatography. [d]Not determined by ^{1}H NMR but TLC analysis indicated **11** as the major product. [e]Isomerization occurred during workup; see text for detail.

91:9 to 100:0. However, isomerization of the (*Z*)-isomer **11** could be a serious issue (Entry 3). We realized that filtration of the ethereal extraction of the crude product through a short silica gel plug is essential before removal of the solvent to dryness. This operation may help to remove the trace amount of triflic acid which might promote isomerization of **11** upon condensation. In the case of Entry 3 in Table 2, we did not exercise the filtration and obtained (*E*)-**12c** as the major product (45%) together with (*Z*)-**11c** (13%). Also, (*E*)-**12e** was isolated (Entry 5) which was not detected initially in the crude product. Isomerization of **11e** might take place during the flash column chromatographic purification. We tried the coupling of **3** with a terminal diynes (Entry 6); but the yield was lower (24%). Nevertheless, under the above described cross-coupling conditions we were able to prepare a number of (*Z*)-ketoeneynes **9** and **11a,b,d,e** in 40-78% yield stereoselectively from the unstable triflate **3**. Since the (*Z*)-ketoeneynes **9** and **11a-f** are labile toward isomerization and decomposition, it is suggested to use these compounds for the following reaction as soon as possible.

Finally, the chemical shifts of the vinyl protons for **11a-f** and **12a-c,e** are listed in Table 3. In general, the signals of vinyl protons for *Z*-isomers **11** appear by 0.51-0.54 ppm toward the high field compared to the corresponding *E*-isomers. This finding is consistent with the reported data for (*E*)-**8** and (*Z*)-**9**.[7a,c]

Table 3. Chemical shifts of the vinyl protons for (*Z*)-**11a-f** and (*E*)-**12a-c,e**.[a]

Z-isomer	**11a** (5.88)	**11b** (6.06)	**11c** (5.84)	**11d** (5.83)	**11e** (5.83)	**11f** (5.85)
E-isomer	**12a** (6.39)	**12b** (6.60)	**12c** (6.35)	na[b]	**12e** (6.37)	na[b]
$\delta(E)$-$\delta(Z)$	0.51	0.54	0.51	----	0.54	----

[a]Measured in $CDCl_3$ on a 300 MHz instrument in ppm. [b]Not available.

In summary, we have explored the Pd(0)-Cu(I)-catalyzed cross-coupling reaction of the labile (*Z*)-ketoenol triflate **3** with 1-alkynes and established a stereoselective synthesis of (*Z*)-ketoeneynes **9** and **11a-f** in moderate to good chemical yield. Our method provides a ready access to this class of useful intermediates which was previously obtained from its (*E*)-isomer by a photochemical isomerization.[7a,c] Use of these (*Z*)-ketoeneynes in the synthesis of model compounds for kedarcidin chromophore (**2**) is in progress in our laboratory and the results will be disclosed in due course.[13]

Acknowledgment. Financial support by a Competitive Earmarked Research Grant (HKUST590/95P) from Hong Kong Research Grants Council and by the Department of Chemistry, HKUST is acknowledged. Thanks are also given to Kunming Institute of Botany, The Academy of Sciences of China for the high resolution mass measurements.

Experimental Section

General Techniques. ^1H and ^{13}C NMR spectra were recorded on a Bruker ARX 300 instrument. IR spectra were taken on a Perkin-Elmer FT-IR spectrophotometer. Mass spectra (MS) were measured on a Finnigan TSQ 7000 mass spectrometer. All reactions were carried out under a nitrogen atmosphere and monitored by thin-layer chromatography on 0.25-mm E. Merck silica gel plates (60 F-254) using UV light, or

7% ethanolic phosphomolybdic acid and heating as the visualizing methods. E. Merck silica gel (60, particle size 0.040-0.063 mm) was used for flash column chromatography. Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogeneous materials. 2-Formylcyclopentanone (**10**) was synthesized according to the literature processure.[11] (Trimethylsilyl)acetylene, (triisopropylsilyl)acetylene, phenylacetylene, 1-hexyne, and dipropargyl ether were obtained commercially and used as received. 4-[(*tert*-Butyldimethyl)silyloxy]-1-butyne and 6-methoxy-1-hexyne were derived from 3-butyn-1-ol and 5-hexyn-1-ol, respectively.

(Z)-(2-Oxocyclopentylidene)methyl Trifluoromethanesulfonate (3). To a solution of **10** (1.020 g, 9.10 mmol) in dry THF (60 mL) cooled in a dry ice-acetone bath (-78 °C) was added dropwise *t*BuLi (1.7 M, 5.4 mL, 9.10 mmol) and the mixture was stirred for 15 min. To the resultant yellow solution was added trifluoromethanesulfonic anhydride (1.52 mL, 9.10 mmol) at -78 °C followed by stirring at the same temperature for 10 min. The light yellow reaction mixture was quenched with saturated aqueous $NaHCO_3$ and extracted with ethyl acetate (2 x 80 mL). The combined organic layer was washed with brine, dried over anhydrous $MgSO_4$, and evaporated under reduced pressure. The crude product was quickly purified by flash column chromatography (silica gel, 10% ethyl acetate in hexane) to furnish triflate **3** (0.979 g, 44%).[7d,8c]

3: pale yellow oil; IR (film) 2974, 1736, 1648, 1426, 1248, 1212, 1142, 1026 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.61 (t, *J* = 2.25 Hz, 1 H), 2.70 (td, *J* = 7.17, 2.25 Hz, 2 H), 2.41 (t, *J* = 7.80 Hz, 2 H), 2.02 (quint, *J* =7.47 Hz, 2 H). Literature data of **3**:[8c] brown oil; IR ($CDCl_3$) 2950, 1735, 1650, 1430, 1225, 1215, 1140, 1030 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.62 (t, *J* = 2.4 Hz, 1 H), 2.71 (td, *J* =7.2, 2.3 Hz, 2 H), 2.41 (t, *J* =7.8 Hz, 2 H), 2.03 (tt, *J* = 7.4, 7.4 Hz, 2 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 200.66, 133.52, 126.27, 118.41, 39.44, 27.05, 20.35.

General Procedure for Coupling of 3 with 1-Alkynes. (*E*)-2-[3-(Trimethylsilyl)-2-propynylidene]cyclopentanone (8) and (*Z*)-2-[3-(Trimethylsilyl)-2-propynylidene]cyclopentanone (9). To a suspension of $Pd(Ph_3)_4$ (76.5 mg, 6.15 x 10^{-2} mmol) and CuI (35.1 mg, 0.185 mmol) in degassed Et_3N (4 mL) cooled in an ice-water bath (*ca.* 0 °C) was added a solution of **3** (300 mg, 1.23 mmol) in degassed dry CH_3CN (12 mL) and then (trimethylsilyl)acetylene (0.21 mL, 1.48 mmol). The resultant mixture was stirred at 0 °C for 10 min and immediately quenched with saturated aqueous $NaHCO_3$ followed by extraction with ethyl ether (3 x 15 mL). The combined organic layer was washed with brine, dried over anhydrous $MgSO_4$, and condensed to 10 mL under reduced pressure. *This solution containing the crude product must be filtered through a short silica gel plug (5 cm) in order to avoid isomerization of the product after removal of the solvent to dryness.* The filtrate was evaporated under reduced pressure and the residue was purified by flash column chromatography (silica gel, 12% ethyl acetate in hexane) to furnish **8** (14.4 mg, 6%) and **9** (97.4 mg, 41%).

If the above $NaHCO_3$-quenched reaction mixture of **9** was stirred at room temperature for overnight isomerization of **9** occurred and only the more stable (*E*)-isomer **8** was isolated. In another occasion, an NMR sample of pure **9** in $CDCl_3$ was kept at room temparature for 24 h resulting in a 88:12 mixture of **9** and **8**. It is suggested that the base- and acid-labile (*Z*)-ketoeneynes **9** and **11a-f** should be used as soon as possible in order to avoid isomerization and decomposition.

8: pale yellow solid; IR ($CHCl_3$ film) 2960, 2138, 1718, 1616, 1250, 1196, 1094, 990, 846 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.35 (t, *J* = 2.93 Hz, 1 H), 2.79 (td, *J* = 7.29, 2.90 Hz, 2 H), 2.39 (t, *J* = 7.77 Hz, 2 H), 1.97 (quint, *J* = 7.53 Hz, 2 H), 0.20 (s, 9 H). Literature data of **8**:[7c] light yellow plates; mp 51-52.5 °C (fron hexane); IR ($CHCl_3$) 2970, 2140, 1710, 1610, 1095, 990, 845 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.36 (t, *J* = 2.9 Hz, 1 H), 2.79 (dt, *J* = 7.4, 2.9 Hz, 2 H), 2.39 (t, *J* = 7.8 Hz, 2 H), 1.97 (quint, *J* = 7.6 Hz, 2 H), 0.23 (s, 9 H); MS *m/z* (relative intensity) 192 (M^+, 29), 177 (100), 121 (23), 75 (31), 43 (31). Anal. Calcd. for $C_{11}H_{16}OSi$: C, 68.69; H, 8.38. Found: C, 68.62; H, 8.46.

9: pale yellow solid; IR ($CHCl_3$ film) 2960, 2126, 1712, 1608, 1248, 1176, 1056, 860, 840 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.85 (t, *J* = 2.42 Hz, 1 H), 2.72 (td, *J* = 7.21, 2.45 Hz, 2 H), 2.37 (t, *J* = 7.77 Hz, 2 H), 1.92 (quint, *J* = 7.50 Hz, 2 H), 0.24 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.5, 146.5, 112.0, 102.3, 100.3, 39.2, 31.4, 19.9, 0.3; MS (CI^+) *m/z* (relative intensity) 193 (M^++1, 100), 177 (81); HRMS (FAB^+) Calcd. for $C_{11}H_{17}OSi$ (M+1): 193.1049. Found: 193.1042. Literature data of **9**:[7c] yellow plates; mp 99-100.5 °C (fron hexane); IR ($CHCl_3$) 2960, 2120, 1710, 1605, 1050, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.85 (t, *J* = 2.5 Hz, 1 H), 2.73 (The original value is 3.73 perhaps due to a typo error.) (dt, *J* = 7.2, 2.4 Hz, 2 H), 2.37 (t, *J* = 7.8 Hz, 2 H), 1.92 (quint, *J* = 7.5 Hz, 2 H), 0.24 (s, 9 H); MS *m/z* (relative intensity) 192 (M^+, 29), 177 (100), 121 (12), 75 (39). Anal. Calcd. for $C_{11}H_{16}OSi$: C, 68.69; H, 8.38. Found: C, 68.49; H, 8.40.

(Z)-2-[3-(Triisopropylsilyl)-2-propynylidene]cyclopentanone (11a). Prepared from **3** and (triisopropylsilyl)acetylene in 78% yield. **11a**: pale yellow oil; IR (film) 2944, 2866, 2122, 1720, 1608, 1464, 1168, 1050, 882 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.88 (t, *J* = 2.42 Hz, 1 H), 2.75 (td, *J* = 7.31, 2.70 Hz, 2 H), 2.36 (t, *J* = 7.68 Hz, 2 H), 1.91 (quint, *J* = 7.46 Hz, 2 H), 1.12 (br s, 21 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.0, 146.9, 111.9, 103.4, 103.0, 39.3, 31.4, 19.9, 18.6, 11.3; MS (CI^+) *m/z* (relative intensity) 277 (M^++1, 100), 233 (100); HRMS (FAB^+) Calcd. for $C_{17}H_{29}OSi$ (M+1): 277.1988. Found: 277.1991.

(Z)-2-(3-Phenyl-2-propynylidene)cyclopentanone (11b). Prepared from **3** and phenylacetylene as a 91:9 inseparable mixture of **11b** and **12b** in 61% yield. **11b**: pale yellow oil; IR (film) 2964, 2186, 1704, 1600, 1584, 1488, 1352, 1190, 1168, 1076, 754 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.59-7.53 (m, 2 H), 7.36-7.32 (m, 3 H), 6.06 (t, *J* = 2.20 Hz, 1 H), 2.79 (td, *J* = 7.23, 2.20 Hz, 2 H), 2.41 (t, *J* = 7.70 Hz, 2 H), 1.96 (quint, *J* = 7.40 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.6, 145.9 132.2, 128.9, 128.3, 123.1, 111.9, 98.9, 87.5, 39.4, 31.5, 20.0; MS (CI^+) *m/z* (relative intensity) 197 (M^++1, 100); HRMS (FAB^+) Calcd. for $C_{14}H_{13}O$ (M+1): 197.0966. Found: 197.0971.

(Z)-2-(2-Heptynylidene)cyclopentanone (11c). Prepared from **3** and 1-hexyne in 13% yield together with **12c** (45% yield, see text for details). **11c**: pale yellow oil; IR (film) 2958, 2206, 1716, 1610, 1348, 1274, 1164, 1066, 750 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.84 (quint, *J* = 2.48 Hz, 1 H), 2.70 (tm, *J* = 7.08 Hz, 2 H), 2.44 (tm, *J* = 6.96 Hz, 2 H), 2.35 (t, *J* = 7.44 Hz, 2 H), 1.90 (quint, *J* = 7.35 Hz, 2 H), 1.60-1.42 (m, 4 H), 0.92 (t, *J* = 7.20 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.7, 144.84, 113.0, 101.9, 78.5, 39.4, 31.3, 30.5, 21.9, 19.9, 19.8, 13.6; MS (CI^+) *m/z* (relative intensity) 177 (M^++1, 100), 121 (16); HRMS (FAB^+) Calcd. for $C_{12}H_{17}O$ (M+1): 177.1279. Found: 177.1251.

(*Z*)-2-[5-((*tert*-Butyldimethyl)silyloxy)-2-pentynylidene]cyclopentanone (11d). Prepared from **3** and 4-[(*tert*-Butyldimethyl)silyloxy]-1-butyne in 48% yield. **11d**: pale yellow oil; IR (film) 2956, 2212, 1720, 1612, 1472, 1256, 1164, 1104, 1066, 836 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.83 (quint, *J* = 2.40 Hz, 1 H), 3.80 (t, *J* = 7.35 Hz, 2 H), 2.74-2.63 (m, 4 H), 2.35 (t, *J* = 6.88 Hz, 2 H), 1.91 (quint, *J* = 7.44 Hz, 2 H), 0.89 (s, 9 H), 0.07 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.6, 145.3, 112.6, 98.1, 79.0, 61.7, 39.4, 31.3, 25.9, 25.8, 24.5, 19.9, -5.3; MS (CI^+) *m/z* (relative intensity) 279 (M^++1, 100), 263 (56), 221 (72), 147 (12); HRMS (FAB^+) Calcd. for $C_{16}H_{27}O_2Si$ (M+1): 279.1780. Found: 279.1735.

(*Z*)-2-(7-Methoxy-2-heptynylidene)cyclopentanone (11e). Prepared from **3** and 6-methoxy-1-hexyne in 54% yield together with **12e** (9%). **11e**: pale yellow oil; IR (film) 2934, 2864, 2208, 1716, 1610, 1190, 1120, 1066 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.83 (quint, *J* = 2.52 Hz, 1 H), 3.41 (t, *J* = 7.80 Hz, 2 H), 3.31 (s, 3 H), 2.70 (tm, *J* = 7.20 Hz, 2 H), 2.47 (tm, *J* = 6.84 Hz, 2 H), 2.34 (t, *J* = 7.90 Hz, 2 H), 1.90 (quint, *J* = 7.60 Hz, 2 H), 1.75-1.65 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.5, 145.0, 112.8, 101.0, 78.8, 72.2, 58.5, 39.4, 31.3, 28.6, 25.1, 19.93, 19.90; MS (CI^+) *m/z* (relative intensity) 207 (M^++1, 55), 175 (87); HRMS (FAB^+) Calcd. for $C_{13}H_{19}O_2$ (M+1): 207.1385. Found: 207.1394.

(*Z*)-2-(5-Oxa-2,7-octadiynylidene)cyclopentanone (11f). Prepared from **3** and dipropargyl ether in 24% yield. **11f**: pale yellow oil; IR (film) 3282, 2966, 2116, 1716, 1612, 1346, 1160, 1076 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.85 (quint, *J* = 2.30 Hz, 1 H), 4.49-4.46 (m, 2 H), 4.41 (d, *J* = 2.40 Hz, 2 H), 2.73 (tm, *J* = 7.20 Hz, 2 H), 2.44 (t, *J* = 2.31 Hz, 1 H), 2.36 (t, *J* = 7.80 Hz, 2 H), 1.93 (quint, *J* = 7.47 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.5, 146.6, 110.9, 94.0, 84.4, 79.1, 74.8, 57.2, 56.3, 39.2, 31.6, 19.9; MS (CI^+) *m/z* (relative intensity) 189 (M^++1, 7), 133 (100); HRMS (FAB^+) Calcd. for $C_{12}H_{13}O_2$ (M+1): 189.0916. Found: 189.0981.

(*E*)-2-(2-Heptynylidene)cyclopentanone (12c). Prepared from **3** and 1-hexyne in 45% yield together with **11c** (13% yield, see text for details). **12c**: pale yellow oil; IR (film) 2958, 2934, 2210, 1716, 1618, 1224, 1202, 1162 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.35 (quint, *J* = 2.58 Hz, 1 H), 2.73 (td, *J* = 7.20, 2.76 Hz, 2 H), 2.40 (td, *J* = 7.10, 2.25 Hz, 2 H), 2.34 (t, *J* = 7.77 Hz, 2 H), 1.93 (quint, *J* = 7.47 Hz, 2 H), 1.56-1.38 (m, 4 H), 0.91 (t, *J* = 7.23 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.8, 146.4, 113.4, 103.7, 78.6, 38.5, 30.3, 28.8, 21.8, 19.6, 19.3, 13.6; MS (CI^+) *m/z* (relative intensity) 177 (M^++1, 100), 121 (20).

(*E*)-2-(7-Methoxy-2-heptynylidene)cyclopentanone (12e). Prepared from **3** and 6-methoxy-1-hexyne in 9% yield together with **11e** (54%). **12e**: pale yellow oil; IR (film) 2930, 2857, 2210, 1714, 1616, 1224, 1202, 1162, 1120 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.37 (quint, *J* = 2.61 Hz, 1 H), 3.40 (t, *J* = 6.09 Hz, 2 H), 3.33 (s, 3 H), 2.74 (td, *J* = 7.23, 2.85 Hz, 2 H), 2.45 (tm, *J* = 6.75 Hz, 2 H), 2.37 (t, *J* = 7.80 Hz, 2 H), 1.94 (quint, *J* = 7.47 Hz, 2 H), 1.72-1.61 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.5, 146.5, 113.3, 103.3, 79.0, 72.1, 58.6, 38.5, 28.9, 28.7, 25.2, 19.8, 19.3; MS (CI^+) *m/z* (relative intensity) 207 (M^++1, 52), 175 (100).

REFERENCES AND NOTES

†Dedicated to Hangzhou University on the occasion of the 100th anniversary.

§Current address: Department of Chemistry, Hangzhou University, Hangzhou 310028, China.

1. Heck, R. F. In *Comprehensive Organic Synthesis*, Trost, B. M.; Fleming, I., Eds., Pergamon Press: New York, 1991, vol. 4, pp. 833-863.
2. (a) Sonogashira, K. In *Comprehensive Organic Synthesis*, Trost, B. M.; Fleming, I., Eds., Pergamon Press: New York, 1991; vol. 3, pp. 521-549. (b) Rossi, R.; Carpita, A.; Bellina, F. *Org. Prep. Proc. Int.* **1995**, 129-160.
3. Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457-2483.
4. Mitchell, T. N. *Synthesis* **1992**, 803-815.
5. Nicolaou, K. C.; Sorensen, E. J. *Classics in Total Synthesis*, VCH: Weinheim, 1996, pp. 566-599.
6. Selected reviews on enediynes: (a) Nicolaou, K. C.; Dai, W.-M. *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 1387-1530. (b) Lhermitte, H.; Grierson, D. S. *Comtemporary Org. Syn.* **1996**, *3*, 41-63 and 93-124. (c) Grissom, J. W.; Gunawardena, G. U.; Klingberg, D.; Huang, D. *Tetrahedron* **1996**, *52*, 6453-6518.
7. (a) Nakatani, K.; Arai, K.; Hirayama, N.; Matsuda, F.; Terashima, S. *Tetrahedron Lett.* **1990**, *31*, 2323-2326. (b) Nakatani, K.; Arai, K.; Yamada, K.; Terashima, S. *Tetrahedron Lett.* **1991**, *32*, 3405-3406. (c) Nakatani, K.; Arai, K.; Hirayama, N.; Matsuda, F.; Terashima, S. *Tetrahedron* **1992**, *48*, 633-650. (d) Nakatani, K.; Arai, K.; Yamada, K.; Terashima, S. *Tetrahedron* **1992**, *48*, 3045-3060. (e) Nakatani, K.; Arai, K.; Terashima, S. *J. Chem. Soc., Chem. Commun.* **1992**, 289-291. (f) Nakatani, K.; Arai, K.; Terashima, S. *Tetrahedron* **1993**, *49*, 1901-1912.
8. (a) Brückner, R.; Scheuplein, S. W.; Suffert, J. *Tetrahedron Lett.* **1991**, *32*, 1449-1452. (b) Suffert, J.; Brückner, R. *Tetrahedron Lett.* **1991**, *32*, 1453-1456. (c) Scheuplein, S. W.; Harms, K.; Brückner, R.; Suffert, J. *Chem. Ber.* **1992**, *125*, 271-278. (d) Suffert, J.; Eggers, A.; Scheuplein, S. W.; Brückner, R. *Tetrahedron Lett.* **1993**, *34*, 4177-4180. (e) Moniatte, M.; Eckhardt, M.; Brickmann, K.; Brückner, R.; Suffert, J. *Tetrahedron Lett.* **1994**, *35*, 1965-1968. (f) Suffert, J.; Brückner, R. *Synlett* **1994**, 51-53. (g) Eckhardt, M.; Brückner, R.; Suffert, J. *Tetrahedron Lett.* **1995**, *36*, 5167-5170.
9. Structure of neocarzinostatin chromophore, see: Edo, K.; Mizuyaki, M.; Koide, Y.; Seto, H.; Furihata, K.; Otake, N.; Ishida, N. *Tetrahedron Lett.* **1985**, *26*, 331-334.
10. Pd(0)-catalyzed coupling reactions of alkenyl or aryl triflates, see: Ritter, K. *Synthesis* **1993**, 735-762.
11. Eaton, P. E.; Jobe, P. G. *Synthesis* **1983**, 796-797.
12. Structure of kedarcidin chromophore, see: Leet, J. E.; Schroeder, D. R.; Hofstead, S. J.; Golik, J.; Colson, K. L.; Huang, S.; Klohr, S. E.; Doyle, T. W.; Matson, J. A. *J. Am. Chem. Soc.* **1992**, *114*, 7946-7947.
13. Synthetic studies on kedarcidin chromophore, see: (a) Iida, K.; Hirama, M. *J. Am. Chem. Soc.* **1995**, *117*, 8875-8876. (b) Takahashi, T.; Tanaka, H.; Yamada, H.; Matsumoto, T.; Sugiura, Y. *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1835-1837. (c) Mikami, K.; Feng, F.; Matsueda, H.; Yoshida, A.; Grierson, D. S. *Synlett* **1996**, 833-836. (d) Magnus, P.; Carter, R.; Davies, M.; Elliott, J.; Pitterna, T. *Tetrahedron* **1996**, *52*, 6283-6306.

(*Received in Japan* 8 *April* 1997; *accepted* 21 *May* 1997)