Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Synthesis of a Nine-Membered Ring via the Intramolecular Ni(II)/Cr(II)-Mediated Coupling Reaction. Unusual Effect of Concentration on the Course of the Reaction

Keith R. Buszek [a] & Youngmee Jeong [a]
[a] Department of Chemistry , Kansas State University , Manhattan, KS, 66506
Published online: 16 Feb 2007.

To cite this article: Keith R. Buszek & Youngmee Jeong (1994) Synthesis of a Nine-Membered Ring via the Intramolecular Ni(II)/Cr(II)-Mediated Coupling Reaction. Unusual Effect of Concentration on the Course of the Reaction, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 24:17, 2461-2472, DOI: 10.1080/00397919408010554

To link to this article: http://dx.doi.org/10.1080/00397919408010554

SYNTHETIC COMMUNICATIONS, 24(17), 2461-2472 (1994)

SYNTHESIS OF A NINE-MEMBERED RING VIA THE INTRAMOLECULAR Ni(II)/Cr(II)-MEDIATED COUPLING REACTION. UNUSUAL EFFECT OF CONCENTRATION ON THE COURSE OF THE REACTION

Keith R. Buszek* and Youngmee Jeong

Department of Chemistry, Kansas State University, Manhattan, KS 66506

ABSTRACT: The first synthesis of a nine-membered ring by means of an intramolecular Ni(II)/Cr(II)-mediated coupling reaction between an iodoacetylene and an aldehyde is reported. The yield of the reaction is strongly dependent on the substrate concentration, but is independent of both the $NiCl_2$ and $CrCl_2$ concentration at high dilution. The application of this methodology to the synthesis of neocarzinostatin chromophore and other natural products is discussed.

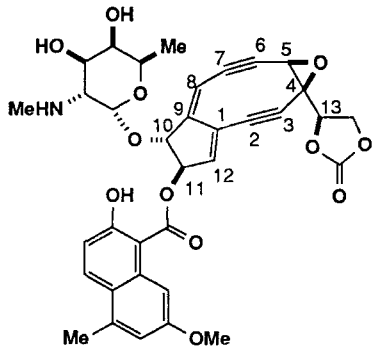
The nickel(II)-catalyzed, chromium(II)-mediated coupling of alkenyl- and alkynyliodides or alkenyltriflates with aldehydes as a mild and stereoselective method of carbon-carbon bond formation has proven its value in natural product synthesis on several occasions.[1] Kishi was the first to employ the intramolecular version of this reaction as an effective strategy for the construction of a strained eight-membered ring in the key step of his elegant total synthesis of ophiobolin C.[2] Since that time, intramolecular Ni(II)/Cr(II)-mediated coupling reactions have been used in the synthesis of macrolides,[3] and more recently, in the synthesis of strained ten-membered ring analogues of the enediyne class of antitumor agents.[4]

---

*To whom correspondence should be addressed.

Despite much research in this area, however, no examples of nine-membered ring formation by this method have been reported to date. In connection with studies directed toward the synthesis of one member of this class, namely, neocarzinostatin

Figure 1

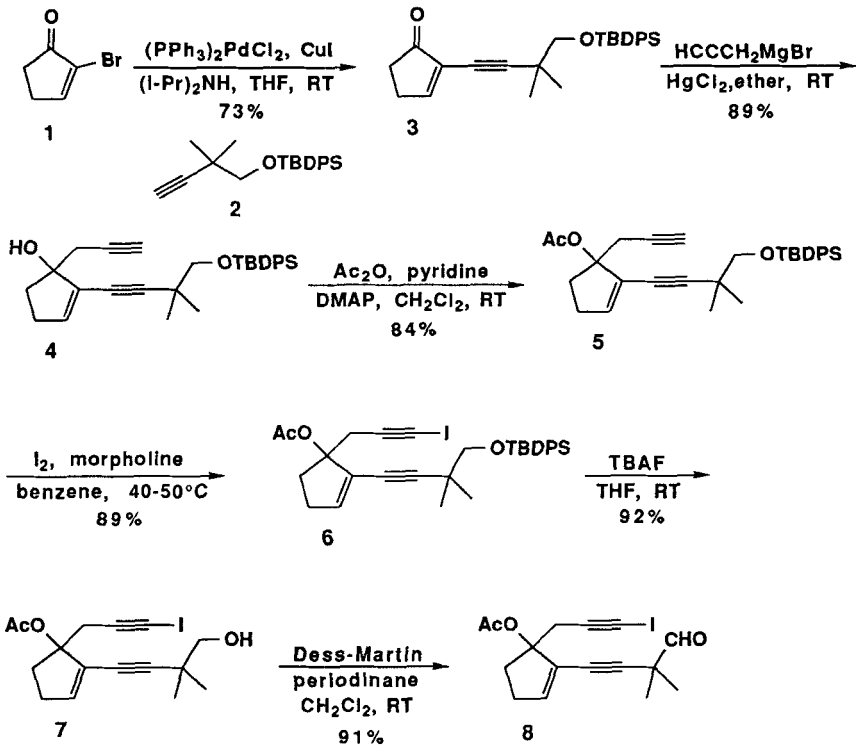


Neocarzinostatin Chromophore

chromophore,[5-7] we attempted the construction of the nine-membered ring of the bicyclo[7.3.0]dodecenediynol **9** by means of an intramolecular Ni(II)/Cr(II)-mediated coupling of an iodoacetylene and an aldehyde.

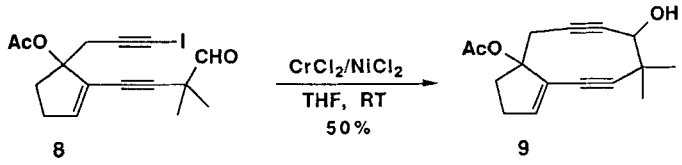
The synthesis is outlined in Scheme 1. Reaction of 2-bromocyclopentenone **1**[8] with the acetylene **2**[9] under modified Stephans-Castro coupling conditions[10] afforded the eneyne **3** in 73% yield. Grignard reaction of **3** with propargylmagnesium bromide gave the alcohol **4** in 89% yield. Sequential acetylation of the alcohol, iodination of the acetylene,[11] and deprotection of the t-butyldiphenylsilyl group with tetrabutylammonium fluoride (TBAF) furnished the alcohol **7** in 69% overall yield. Oxidation with Dess-Martin periodinane[12] gave the aldehyde **8** (91%) which was immediately subjected to Ni(II)/Cr(II)-mediated coupling conditions. The success of this cyclization was highly dependent on the substrate concentration of the reaction. For example, the use of 10 equivalents of

Scheme 1



$CrCl_2$ and catalytic $NiCl_2$ in amounts from 0.001% to 1.0% (as a weight percentage of chromium chloride) in THF (0.01-0.05 M) at room temperature afforded after work-up mainly the corresponding acetylene resulting from reduction. Similar results were obtained using DMF or DMSO as the solvent. Employing substoichiometric quantities of $NiCl_2$ (up to 1.0 equivalent) at the same concentrations resulted in the formation of a mixture of products, the major component of which was again reduction, but also included products presumably derived from homocoupling, and decomposition. To our gratification, decreasing the concentration five- to twenty-fivefold to 0.002 M with 0.6 equivalents of $NiCl_2$ gave the desired product **9** in 35% unoptimized yield with 30% of recovered

Scheme 2



starting material. Further dilution showed a corresponding increase in yield. Thus, treatment of **6** with 10 equivalents of $CrCl_2$ and 1.0 equivalent of $NiCl_2$ in 0.001 M THF afforded **7** in 50% yield (72% based on recovered starting material) as a mixture of diastereomers in a 3:1 ratio as determined by high field ^1H NMR. No change in yield was observed when the amount of $CrCl_2$ was increased. Furthermore, at high dilution the cyclization is apparently insensitive to the amount of $NiCl_2$ used (cf. entries 9 and 10). The results of these experiments are summarized in Table 1. To our knowledge, this represents the first example of nine-membered ring formation by an intramolecular Ni(II)/Cr(II) iodoacetylene-aldehyde coupling reaction.

The intramolecular Ni(II)/Cr(II)-mediated coupling reaction is emerging as a general and powerful method for the construction of strained ring systems. We believe that the yields of previously reported intramolecular coupling reactions might now be significantly improved by adopting the high dilution technique described here. We have also demonstrated that this method represents a potentially flexible, adaptable, and practical approach to the synthesis of neocarzinostatin chromophore and its analogues.

Experimental

General. ^1H NMR spectra were recorded at 400 MHz on a Bruker WM-400 instrument in the indicated solvent. ^{13}C NMR were measured at 100 MHz on a

Table 1. Effect of Concentration on Yield of Ni(II)/Cr(II)-Coupling

Entry	$CrCl_2/NiCl_2$	Solvent	Concentration[a]	Product
1	10 eq/ 0.001% (wt)	THF, DMF, DMSO	0.01-0.05 M	Reduction
2	10 eq/ 0.1% (wt)	THF, DMF, DMSO	0.01-0.05 M	Reduction
3	10 eq/ 1.0% (wt)	THF, DMF, DMSO	0.01-0.05 M	Reduction
4	10 eq/ 0.1 eq	THF	0.01-0.05 M	Reduction
5	10 eq/ 0.3 eq	THF	0.01-0.05 M	Reduction
6	10 eq/ 0.5 eq	THF	0.01-0.05 M	Reduction
7	10 eq/ 1.0 eq	THF	0.01-0.05 M	Reduction
8	10 eq/ 0.6 eq	THF	0.002 M	**7** (35%) + SM (30%)
9	10 eq/ <1% (wt)[b]	THF	0.001 M	**7** (50%)
10	10 eq/ 1.0 eq	THF	0.001 M	**7** (50%) + SM (30%)
11	20 eq/ 1.0 eq	THF	0.001 M	**7** (50%) + SM (30%)

[a]Refers to concentration of the substrate. [b]Approximate Ni content of anhydrous $CrCl_2$ (95% purity) from Fluka Chemical Corp.

Bruker WM-400 instrument. Infrared (IR) spectra were obtained using a Perkin-Elmer Model 1310 infrared spectrophotometer. Chemical ionization (CI) mass spectra were recorded on a Hewlett-Packard 5989A model using a 70 eV electron beam energy source and methane as the ionization agent. Thin layer chromatography (TLC) was performed using E. Merck silica gel (60 F 254) plates of 0.25 mm thickness. Visualization was accomplished using short wavelength ultraviolet light, and anisaldehyde dip reagent. Tetrahydrofuran (THF) and diethyl ether (ether) were distilled from sodium benzophenone ketyl. Hydrocarbon and chlorinated solvents were distilled from calcium hydride. All other solvents and reagents were used as received, except as otherwise noted. All reactions were performed under a positive atmosphere of dry nitrogen or argon.

2-[4-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]-3,3-dimethyl-1-butynyl]-2-cyclopenten-1-one (3). To a solution of 2-bromocyclopentenone **1**[8] (920 mg, 5.71 mmol) in THF (20 mL) was added copper(I) iodide (6.0 mg, 0.032 mmol), bis(triphenylphosphine)palladium(II) chloride (40 mg, 0.057 mmol), and *N*,*N*-diisopropylamine (2.4 mL, 17.1 mmol). The mixture was brought to reflux and the acetylene **2**[9] (1.92 g, 5.71 mmol) added portionwise over 3 h. After cooling to room temperature, the solvents were removed under reduced pressure and the residue subjected to flash chromatography[13] (20% ethyl acetate/hexanes) directly to give 1.73 g (73%) of the coupled compound **3** as an oil: ^{1}H NMR ($CDCl_3$) δ 7.67 (4 H, dd, J = 1.4, 7.8 Hz), 7.62 (1 H, t, J = 3.2 Hz), 7.42-7.33 (6 H, m), 3.55 (2 H, s), 2.65-2.62 (2 H, m), 2.42-2.40 (2 H, m), 1.30 (6 H, s), 1.06 (9 H, s); ^{13}C NMR ($CDCl_3$) δ 205.6, 164.1, 135.6, 133.5, 130.3, 129.5, 127.5, 102.6, 71.5, 71.4, 34.3, 33.8, 26.9, 26.7, 25.4, 19.3; IR (neat) 3060, 2900, 1700, 1100 cm^{-1}; CI ms (*m/e*): calcd for $C_{27}H_{32}O_2Si$: 416; found: 417 (M+1); anal calcd for $C_{27}H_{32}O_2Si$: C, 77.83; H, 7.75. Found: C, 77.48; H, 7.65.

2-[4-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]-3,3-dimethyl-1-butynyl]-1-(2-propynyl)-2-cyclopenten-1-ol (4). To a stirred suspension of magnesium turnings (510 mg, 21 mmol) in ether (20 mL) in a three neck flask equipped with reflux condenser was added a few crystals of mercury(II) chloride and neat propargyl bromide (0.93 mL, 12.3 mmol). The mixture was stirred vigorously for several minutes to initiate the reaction. Additional propargyl bromide (0.93 mL, 12.3 mmol) and the ketone **3** (1.73 g, 4.2 mmol) were added at a rate to maintain a gentle reflux. After addition, the mixture was stirred at room temperature for an additional 30 min and then cooled to 0°C. Saturated ammonium chloride (2 mL) was added dropwise, and the mixture filtered. The filtrate was concentrated in vacuo and the residue purified by flash column chromatography (10% ethyl

acetate/hexanes) to give 1.7 g (89%) of the alcohol **4** as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.68 (4 H, d, J = 7.4 Hz), 7.43-7.35 (6 H, m), 6.06 (1 H, t, J = 2.4 Hz), 3.53 (2 H, s), 2.66 (1 H, dd, J = 2.4, 16.6 Hz), 2.52-2.25 (4 H, m), 2.10 (1 H, s), 2.03-1.97 (1 H, m), 1.94 (1 H, t, J = 2.4), 1.27 (6 H, s), 1.07 (9 H, s); ^{13}C NMR ($CDCl_3$) δ 138.1, 135.6, 133.5, 129.8, 129.6, 127.6, 99.9, 84.4, 80.5, 74.1, 71.6, 70.0, 36.4, 34.3, 30.1, 29.9, 26.8, 25.6, 19.3; IR (neat) 3425, 3230, 3050, 2910, 1100 cm^{-1}; CI ms (*m/e*): calcd for $C_{30}H_{36}O_2Si$: 456; found: 457 (M + 1).Anal calcd for $C_{30}H_{36}O_2Si$: C, 78.90; H, 7.95. Found: C, 79.15; H, 7.77.

2-[4-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]-3,3-dimethyl-1-butynyl]-1-(2-propynyl)-2-cyclopenten-1-ol Acetate (5). To a solution of the alcohol **4** (1.7 g, 3.7 mmol) in dichloromethane (50 mL) was added pyridine (1.1 mL, 20 mmol) and catalytic amount of 4-dimethylaminopyridine. To this solution was added acetic anhydride (1.13 mL, 12 mmol) and the mixture stirred at room temperature overnight. Water (40 mL) was added and the mixture extracted with dichloromethane (3 x 50 mL). The organic layers were dried, evaporated and subjected to the flash chromatography (10% ethyl acetate/hexanes) to give 1.56 g (84%) of acetate **5** as an oil: ^{1}H NMR ($CDCl_3$) δ 7.67 (4 H, dd, J = 1.3, 6.8 Hz), 7.42-7.34 (6 H, m), 6.17 (1 H, t, J = 1.8 Hz), 3.50 (2 H, s), 3.0 (1 H, dd, J = 2.7, 16.3 Hz), 2.64-2.53 (2 H, m), 2.45-2.33 (3 H, m), 1.93 (3 H, s), 1.87 (1 H, t, J = 2.6 Hz), 1.25 (6 H, s), 1.05 (9 H, s); ^{13}C NMR ($CDCl_3$) δ 169.8, 140.3, 135.7, 133.6, 129.6, 127.6, 126.2, 98.9, 92.6, 79.6, 74.0, 71.6, 69.8, 34.3, 32.9, 31.4, 28.0, 26.8, 25.6, 21.9, 19.4; IR (neat) 3280, 3040, 2950-2850, 1720, 1420, 1355, 1230, 1100 cm^{-1}; CI ms (*m/e*): calcd for $C_{32}H_{38}O_3Si$: 498; found: 499 (M + 1). Anal calcd for $C_{32}H_{38}O_3Si$: C, 77.06; H, 7.68. Found: C, 77.24; H, 7.93.

1-(3-iodo-2-propynyl)-2-[4-[[(1,1-dimethylethyl)diphenylsilyl]-oxy]-3,3-dimethyl-1-butynyl]-2-cyclopenten-1-ol Acetate (6). To a stirred solution of iodine (2.4 g, 9.3 mmol) in benzene (50 mL) under argon was added morpholine (2.2 mL, 24.3 mmol). After disappearance of all iodine and formation of an orange precipitate, a solution of **5** (1.56 g, 3.1 mmol) in benzene (5 mL) was added. The resulting mixture was heated at 40-50°C overnight. The mixture was diluted in ether, washed with saturated sodium thiosulfate, dried, and concentrated under reduced pressure. The mixture was purified by flash column chromatography (10% ethyl acetate/hexanes) to give 1.69 g (89%) of iodoacetylene **6** as an oil: ^{1}H NMR (CD_3COCD_3) δ:7.66 (4 H, dd, J = 1.8, 6.4 Hz), 7.41-7.34 (6 H, m), 6.16 (1 H, t, J = 2.6 Hz), 3.51 (2 H, s), 3.05 (1 H, d, J = 16.4 Hz), 2.75 (1 H, d, J = 16.5 Hz), 2.50-2.42 (1 H, m), 2.38-2.25 (3 H, m), 1.80 (3 H, s), 1.20 (6 H, s), 1.01 (9 H, s); ^{13}C NMR ($CDCl_3$) δ 169.9, 140.0, 135.7, 133.6, 129.6, 127.6, 126.3, 99.0, 92.5, 89.9, 74.0, 71.7, 34.3, 33.3, 31.3, 30.1, 26.8, 25.7, 21.8, 19.4; IR (neat) 3060, 2970, 2215, 1740, 1425, 1360, 1235, 1100 cm^{-1}. CI ms (*m/e*): calcd for $C_{32}H_{37}IO_3Si$: 624; found: 625 (M + 1). Anal calcd for $C_{32}H_{37}IO_3Si$: C, 61.53; H, 5.97. Found: C, 61.24; H, 5.76.

2-(4-hydroxy-3,3-dimethyl-1-butynyl)-1-(3-iodo-2-propynyl)-2-cyclopenten-1-ol Acetate (7). To a stirred solution of **6** (1.69 g, 2.7 mmol) in tetrahydrofuran (50 mL) at 0°C was added tetrabutylammonium fluoride (4.1 mL, 1 M solution in tetrahydrofuran). After 3 h, excess solid ammonium chloride was added and the mixture concentrated under reduced pressure. The residue was extracted with ether several times and subjected to flash chromatography (30% ethyl acetate/hexanes) to give 960 mg (92%) of alcohol **7**: ^{1}H NMR ($CDCl_3$) δ 6.23 (1 H, t, J = 2.5 Hz), 3.40 (2 H, s), 3.21 (1 H, d, J = 19.7 Hz), 2.87 (1 H, d, J = 19.7 Hz), 2.60-2.51 (1 H, m), 2.41-2.28 (3 H, m), 2.15 (1 H, s), 1.96 (3 H, s),

1.19 (6 H, s); ^{13}C NMR ($CDCl_3$) δ: 169.9, 140.9, 126.1, 97.9, 92.5, 89.6, 75.5, 71.7, 34.2, 31.0, 29.7, 25.3, 25.2, 21.8; IR (neat) 3445, 2910, 1700 cm^{-1}; CI ms (*m/e*): calcd for $C_{16}H_{19}IO_3$: 386; found: 387 (M + 1). Anal calcd for $C_{16}H_{19}IO_3$: C, 49.75; H, 4.96. Found: C, 50.05; H, 4.91.

1-(3-iodo-2-propynyl)-2-(3,3-dimethyl-4-oxo-1-butynyl)-2-cyclopenten-1-ol Acetate (8). To a solution of alcohol **7** (100 mg, 0.26 mmol) in dichloromethane (10 mL) at room temperature was added Dess-Martin periodinane (160 mg, 0.39 mmol) in one portion. After 1 h, saturated sodium bicarbonate and 5 eq of sodium thiosulfate were added and stirring continued until the solution changed from a cloudy suspension to clear. The resulting mixture was extracted with dichloromethane (3 x 10 mL), dried, concentrated and chromatographed (20% ethyl acetate/hexanes) to give 90 mg (91%) of aldehyde **8**: ^1H NMR ($CDCl_3$) δ 9.49 (1 H, s), 6.29 (1 H, t, J = 2.7 Hz), 3.13 (1 H, d, J = 16.5 Hz), 2.82 (1 H, d, J = 16.5 Hz), 2.64-2.56 (1 H, m), 2.44-2.32 (3 H, m), 1.99 (3 H, s), 1.34 (6 H, s); ^{13}C NMR ($CDCl_3$) δ 197.8, 170.0, 142.2, 125.5, 92.6, 92.3, 89.5, 78.4, 33.5,31.5, 30.1, 22.9, 21.9; IR (neat) 2940, 2640, 1730 cm^{-1}; CI ms (*m/e*): calcd for $C_{16}H_{17}IO_3$: 384; found: 385 (M + 1). Anal calcd for $C_{16}H_{17}IO_3$: C, 50.02; H, 4.46. Found: C, 50.06; H, 4.65.

10a-Acetoxy-4,5,8,9-tetradehydro-1,2,6,7,10,10a-hexahydro-7-cyclopentacyclononenol (9). To a stirred suspension of chromium(II) chloride (320 mg, 2.6 mmol) and nickel(II) chloride (16.9 mg, 0.13 mmol) in tetrahydrofuran (130 mL, Ni(II) concentration: 0.001 M) was added **8** (50 mg, 0.13 mmol) in tetrahydrofuran solution (3 mL). After the mixture was stirred overnight at room temperature, it was diluted with ether and quenched with saturated ammonium chloride (100 mL). The mixture was vigorously stirred until

the organic layer was almost colorless. The layers were separated and the aqueous layer was further extracted with ether (2 x 100 mL). The combined organic extracts were dried over magnesium sulfate and concentrated under reduced pressure. The residue was subjected to the flash chromatography (20% ethyl acetate/hexanes) to give 17 mg of **9** (50%, 72% based on recovered starting material) as a 3:1 mixture of diastereomers and about 15 mg of recovered starting material: Major Diastereomer: ^{1}H NMR ($CDCl_3$) δ 5.99 (1 H, t, J = 2.8 Hz), 3.93 (1 H, s), 3.26 (1 H, dd, J = 2.0, 17.6 Hz), 2.55-2.35 (4 H, m), 2.14-2.04 (1 H, m), 2.01 (3 H, s), 1.24 (6 H, s); ^{13}C NMR ($CDCl_3$) δ 169.9, 135.5, 125.0, 104.8, 93.4, 89.8, 87.8, 83.5,74.7, 44.1, 35.1, 30.5, 29.8, 26.8, 21.8; IR (neat) 3425, 3040, 2920, 2200, 1705, 1415, 1355, 1230, 1035 cm^{-1}; CI ms (*m/e*): calcd for $C_{16}H_{18}O_3$: 258; found 259 (M + 1). Anal calcd for $C_{16}H_{18}O_3$: C, 74.39; H, 7.02. Found: C, 74.58; H, 6.89. Minor Diastereomer: ^{1}H NMR ($CDCl_3$) δ 6.01 (1 H, t, J = 2.8 Hz), 3.99 (1 H, s), 3.36 (1 H, dd, J = 2.0, 17.6 Hz), 2.55-2.35 (4 H, m), 2.14-2.04 (1 H, m), 2.05 (3 H, s), 1.28 (6 H, s); ^{13}C NMR ($CDCl_3$) δ 169.9, 136.0, 127.2, 104.3, 94.8, 90.8, 88.2, 83.3, 74.0, 44.0, 34.9, 30.8, 29.5, 26.3, 21.9.

Acknowledgment. We thank the American Cancer Society (DHP-87), Kansas State University, and the Bureau of General Research, Kansas State University, for generous financial support of this work.

References

1. (a) Jin, H.; Uenishi, J.; Christ, W. J.; Kishi, Y. *J. Am. Chem. Soc.* **1986**, *108*, 5644. (b) Tagashira, M.; Kuroda, T.; Oshima, K.; Utimoto, K.; Nozaki, H. *J. Am. Chem. Soc.* **1986**, *108*, 6048.
2. (a) Rowley, M.; Kishi, Y. *Tetrahedron Lett.* **1988**, *29*, 4909. (b) Rowley, M.; Tsukamoto, M.; Kishi, Y. *J. Am. Chem. Soc.* **1989**, *111*, 2735.

3. (a) Schreiber, S. L.; Meyers, H. V. *J. Am. Chem. Soc.* **1988**, *110*, 5198. (b) Aicher, T. D.; Buszek, K. R.; Fang, F. G.; Forsyth, C. J.; Jung, S. H.; Kishi, Y.; Matelich, M. C.; Scola, P. M.; Spero, D. M.; Yoon, S. K. *J. Am. Chem. Soc.* **1992**, *114*, 3162.

4. After the present chemistry was in progress, three other accounts of the synthesis of ten-membered rings by intramolecular Ni(II)/Cr(II)-mediated coupling of an iododacetylene and an aldehyde appeared: (a) Crevisy, C.; Beau, J.-M. *Tetrahedron Lett.* **1991**, *32*, 3171. (b) Nicolaou, K. C.; Liu, A.; Zeng, Z.; McComb, S. *J. Am. Chem. Soc.* **1992**, *114*, 9279. (c) Maier, M. E.; Brandstetter, T. *Tetrahedron Lett.* **1992**, *33*, 7511.

5. Isolation: Ishida, N.; Miyazaki, K.; Kumagai, K.; Rikimaru, M. *J. Antibiot.* **1965**, *18*, 68.

6. Structure determination: (a) Edo, K.; Mizugaki, M.; Koide, Y.; Seto, H.; Furihata, K.; Otake, N.; Ishida, N. *Tetrahedron Lett.* **1985**, *26*, 331. (b) Myers, A. G.; Proteau, P. J.; Handel, T. M. *J. Am. Chem. Soc.* **1988**, *110*, 7212.

7. Synthetic studies: (a) Wender, P. A.; Harmata, M.; Jeffrey, D.; Mukai, C.; Suffert, J. *Tetrahedron Lett.* **1988**, *29*, 909. (b) Hirama, M.; Fujiwara, K.; Shigematu, K.; Fukazawa, Y. *J. Am. Chem. Soc.* **1989**, *111*, 4120. (c) Wender, P. A.; McKinney, J. A.; Mukai, C. *J. Am. Chem. Soc.* **1990**, *112*, 5369. (d) Fujiwara, K.; Kurisaki, A.; Hirama, M. *Tetrahedron Lett.* **1990**, *31*, 4329. (e) Nakatani, K.; Arai, K.; Hirayama, N.; Matsuda, F.; Terashima, S. *Tetrahedron Lett.* **1990**, *31*, 2323. (f) Krebs, A.; Welhage, T.; Kramer, C. P. *Tetrahedron Lett.* **1990**, *31*, 3533. (g) Welhage, T.; Krebs, A.; Link, T. *Tetrahedron Lett.* **1990**, *31*, 6625. (h) Suffert, J. *Tetrahedron Lett.* **1990**, *31*, 7437. (i) Myers, A. G.; Harrington, P. M.; Kuo, E. Y. *J. Am. Chem. Soc.* **1991**, *113*, 694. (j) Suffert, J.; Bruckner, R. *Tetrahedron Lett.* **1991**,

32, 1453. (k) Bruckner, R.; Scheulplein, S. W.; Suffert, J. *Tetrahedron Lett.* **1991**, *32*, 1449. (l) Nuss, J. M.; Levine, B. H.; Rennels, R. A.; Heravi, M. M.*Tetrahedron Lett.* **1991**, *32*, 5243. (m) Magnus, P.; Pitterna, T. *J. Chem. Soc., Chem. Commun.* **1991**, 541. (n) Doi, T.; Takahashi, T. *J. Org. Chem.* **1991**, *56*, 3465. (o) Magnus, P.; Davies, M. *J. Chem. Soc., Chem. Commun.* **1991**, 1522. (p) Nakatani, K.; Arai, K.; Yamada, K.; Terashima, S. *Tetrahedron* **1992**, *48*, 3045. (q) Petasis, N. A.; Teets, K. A. *Tetrahedron Lett.* **1993**, *34*, 805, and references contained therein.

8. Smith, A. B.; Branca, S. J.; Guaciaro, M. A.; Wovkulich, P. M.; Korn, A. *Org. Synth.* **1983**, *61*, 65.
9. Prepared in three steps from 2,2-dimethyl-1,3-propanediol by the following sequence: (i) TBDPSCl (1.1 eq), imidazole (2.2 eq), CH_2Cl_2, 0°C to RT, 95%. (ii) $(COCl)_2$ (1.2 eq), DMSO (2.4 eq), Et_3N (5 eq), -78°C, 92%. (iii) $N_2CHP(=O)(OMe)_2$ (1.2 eq), t-BuO^-K^+ (1.3 eq), -78°C, 89%.
10. Stephans, R. D.; Castro, C. E. *J. Org. Chem.* **1963**, *28*, 3313.
11. Southwick, P. L.; Kirchner, J. R. *J. Org. Chem.* **1962**, *27*, 3305.
12. Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4155.
13. Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

(Received in the USA 17 February 1994)