(270 MHz, $CDCl_3$): $\delta = 2.60-3.11$ (br, 30H), 7.00 (br s, 4H, aryl), 7.17 (br s, 8H, aryl); EI-MS (70 eV): *m/z* (%): 630 (100) $[M]^+$; elemental analysis calcd for $C_{45}H_{42}O_3 \cdot 0.5\,H_2O$ (639.83): C 84.52, H 6.57; found: C 84.68, H 6.66.

1: A mixture of **13** (50 mg, $8.0 \cdot 10^{-2}$ mmol), *p*-toluenesulfonic acid (5 mg), and ethylene glycol (31 mg, 0.5 mmol) in a mixture of benzene/nitrobenzene (6 mL, 1/1) were refluxed for 48 h. The reaction mixture was then cooled, and the resulting precipitate was collected and washed carefully with hexane to give **1** (42 mg, 68%); m.p. 345–347 °C; IR (KBr): $\tilde{\nu} = 1103\ cm^{-1}$ (C–O); ^1H NMR (270 MHz, $CDCl_3$): $\delta = 1.91-2.56$ (m, 18H), 2.83–3.31 (m, 8H), 3.93–4.09 (m, 12H, OCH_2), 5.77 (s, 4H, aryl), 6.40–6.62 (m, 8H, aryl); EI-MS (70 eV): *m/z* (%): 762 (17) $[M]^+$; elemental analysis calcd for $C_{51}H_{54}O_6 \times H_2O$ (781.00): C 78.48, H 6.92; found: C 78.46, H 7.02.

Received: February 24, 1998 [Z11512IE]
German version: *Angew. Chem.* **1998**, *110*, 2626–2628

Keywords: cations · cyclic voltammetry · cyclophanes · stacking interactions

[1] T. Benzing, T. Tjivikua, J. Wolfe, J. Rebek, *Science* **1988**, *242*, 266; S. K. Burley, G. A. Petsko, *Science* **1985**, *229*, 23; S. Mataka, J. Ma, T. Thiemann, J. M. Rudziñski, H. Tsuzuki, T. Sawada, M. Tashiro, *Tetrahedron* **1997**, *53*, 885–902; D. A. Evans, K. T. Chapman, D. Tan Hung, A. T. Kawaguchi, *Angew. Chem.* **1987**, *99*, 1197–1199; *Angew. Chem. Int. Ed. Engl.* **1987**, *26*, 1184–1186, and references therein.

[2] A. V. Muehldorf, D. van Engen, J. C. Warner, A. D. Hamilton, *J. Am. Chem. Soc.* **1988**, *110*, 6561–6562; T. Ishi-i, T. Sawada, S. Mataka, M. Tashiro, T. Thiemann, *Chem. Ber.* **1996**, *129*, 289–296.

[3] W. L. Jorgensen, D. L. Severance, *J. Am. Chem. Soc.* **1990**, *112*, 4768–4774, and references therein.

[4] See D. J. Cram, R. H. Bauer, *J. Am. Chem. Soc.* **1959**, *81*, 5971–5977; L. A. Singer, D. J. Cram, *J. Am. Chem. Soc.* **1963**, *85*, 1080–1084.

[5] Review: S. M. Rosenfeld, K. A. Choe in *Cyclophanes* (Eds.: P. M. Keehn, S. M. Rosenfeld), Academic Press, New York, **1983**.

[6] Paracyclophanes show a bathochromic shift in their UV/Vis spectra relative to similarly substituted open-chain arenes. This effect is partly the result of the deformation of the aromatic system. D. Cram has shown that by shortening the ansachain of [*n*]paracyclophanes a bathochromic shift can be observed as a consequence of the deformation of the aromatic ring: D. J. Cram, C. S. Montgomery, G. R. Knox, *J. Am. Chem. Soc.* **1966**, *88*, 515–525.

[7] Nevertheless, the absorption spectra in multilayered [2.2]paracyclophanes show both a bathochromic and a hyperchromic shift with an increasing number of layers. This effect can be quite large relative to that seen in double-layered [2.2]paracyclophanes, and can only result from transannular $\pi-\pi$ electronic interactions: T. Otsubo, S. Mizogami, J. Otsubo, Z. Tozuka, A. Sakagami, Y. Sakata, S. Misumi, *Bull. Chem. Soc. Jpn.* **1973**, *46*, 3519–3530; S. Misumi, *Multilayered Cyclophanes* in reference [5].

[8] See also: F. Vögtle, *Cyclophane Chemistry—Synthesis, Structures and Reactions*, Wiley, Chichester, **1993**, pp. 57–58,

[9] a) S. J. Cristol, D. C. Lewis, *J. Am. Chem. Soc.* **1967**, *89*, 1467–1487; b) H. Prinzbach, G. Sedelmeier, C. Krüger, R. Goddard, H.-D. Martin, R. Gleiter, *Angew. Chem.* **1978**, *90*, 297–305; *Angew Chem. Int. Ed. Engl.* **1978**, *17*, 271; c) W. Grimme, H. T. Kämmerling, J. Lex, R. Gleiter, J. Heinze, M. Dietrich, *Angew. Chem.* **1991**, *25*, 215–217; *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 205–207; d) S. Mataka, K. Takahashi, T. Hirota, K. Takuma, H. Kobayashi, M. Tashiro, *J. Chem. Soc. Chem. Commun.* **1985**, 973–973.

[10] a) S. Mataka, K. Takahashi, T. Mimura, T. Hirota, K. Takuma, H. Kobayashi, M. Yashiro, K. Imada, M. Kuniyoshi, *J. Org. Chem.* **1987**, *52*, 2653–2656; b) S. Mataka, Y. Mitoma, T. Sawada, M. Tashiro, *Tetrahedron Lett.* **1996**, *37*, 65–68; c) S. Mataka, Y. Mitoma, T. Thiemann, T. Sawada, M. Taniguchi, M. Kobuchi, M. Tashiro, *Tetrahedron* **1997**, *53*, 3015–3026.

[11] Apart from the acetalization of the keto group, a 1,2-addition of a Grignard reagent to the keto group (**14**, X = OH, Y = CH_3, C_6H_5)[10a] and the reduction of the spirocyclopropane substituted compound[12] to a bis-*gem*-dimethyl bridged compound (**14**, X = Y = CH_3) both lead to rigid layered [3.3]orthocyclophanes.

14

[12] S. Mataka, M. Taniguchi, Y. Mitoma, T. Sawada, M. Tashiro, *J. Chem. Res. Synop.* **1997** 48–49; J. Chem. Res. Miniprint **1997**, 437–452.

[13] Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-101215. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

[14] $E^0[Ag\,|\,AgNO_3, (10^{-2}\ M\ in\ CH_3CN)] = +0.53$ V versus normal hydrogen electrode (NHE); see also: C. K. Mann, "Nonaqueous Solvents for Electrochemical Use" in *Electroanalytical Chemistry*, *Vol. 3*, (Ed.: A. J. Bard), Marcel Dekker, New York, **1969**, p. 64.

[15] M. Dietrich, J. Mortensen, J. Heinze, *J. Chem. Soc. Chem. Commun.* **1986**, 1131–1132, and references therein.

Solid-Phase Synthesis of Macrocyclic Systems by a Cyclorelease Strategy: Application of the Stille Coupling to a Synthesis of (*S*)-Zearalenone

K. C. Nicolaou,* Nicolas Winssinger, Joaquin Pastor, Fiona Murphy

In recent years combinatorial chemistry and solid-phase synthesis have emerged as powerful tools for the drug discovery process.[1] Sold-phase synthesis is particularly useful for the construction of combinatorial libraries by virtue of the opportunity to adopt the powerful and elegant encoded split-pool methods[2] as well as convenient purification procedures. Considering the importance of natural products to chemistry, biology, and medicine, we initiated a program directed at the development of solid-phase technologies suitable for the total synthesis of such molecules and of directed libraries of their analogues.[3] Herein, we report a new solid-phase method for the construction of macrocycles by a novel cyclorelease mechanism[4] that employs the Stille coupling,[5] and its application to the total synthesis of (*S*)-zearalenone,[6, 7] a biologically active natural product.[8] Currently, most solid-

[*] Prof. Dr. K. C. Nicolaou, N. Winssinger, Dr. J. Pastor, Dr. F. Murphy
Department of Chemistry and
The Skaggs Institute for Chemical Biology
The Scripps Research Institute
10550 North Torrey Pines Road, La Jolla, California 92037 (USA)
Fax: (+1) 619-784-2469
E-mail: kcn@scripps.edu
and
Department of Chemistry and Biochemistry
University of California, San Diego
9500 Gilman Drive, La Jolla, California 92093 (USA)

[**] We thank Dr. D. H. Huang and Dr. G. Suizdak for assistance with the NMR spectroscopy and mass spectrometry, respectively. This work was supported by The Skaggs Institute for Chemical Biology, the National Institutes of Health USA, a fellowship from the Ministerio de Educación y Ciencia (Spain) (to J.P.), and grants from Merck, DuPont-Merck, and Schering Plough.

  1433-7851/98/3718-2534 $ 17.50+.50/0

phase methods incorporate a heteroatom such as oxygen, sulfur, or nitrogen within a suitably designed protecting device that links the substrate to the polymer support.[9] Release from the polymer is achieved by deprotecting the heteroatom which, however, remains as a vestigial stub in every library member (see Figure 1 A).

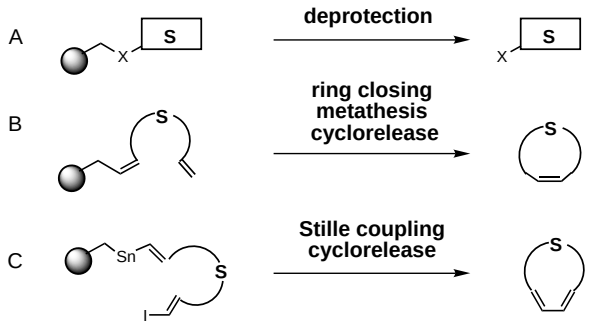
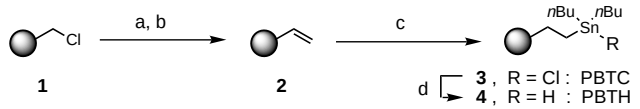


Figure 1. Release of substrate **S** from polymer.

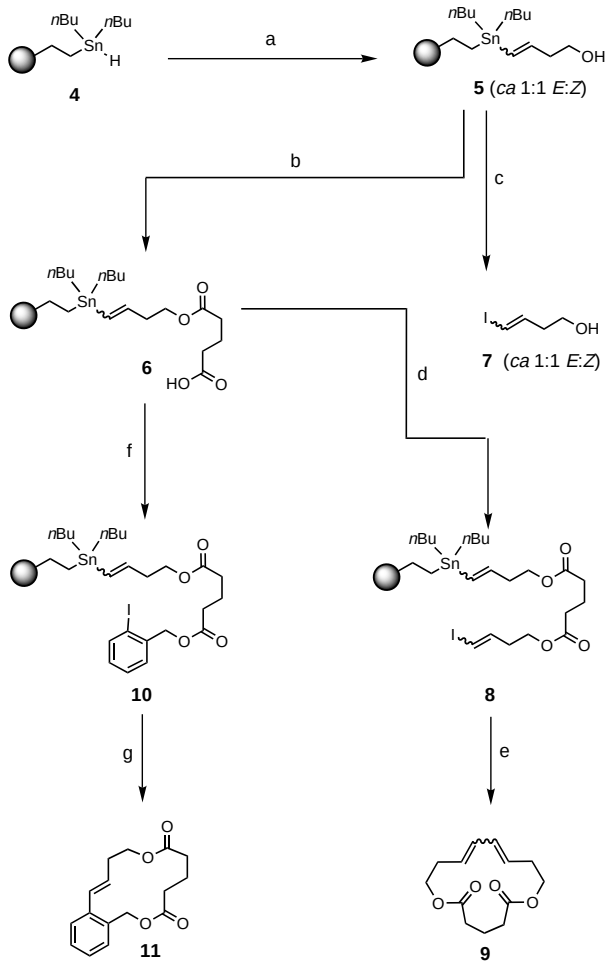
Recently, we applied the ring-closing metathesis in a cyclorelease mode to prepare an epothilone library (Figure 1 B).[10] Applying the Stille coupling to cyclorelease reveals the strategy shown in Figure 1 C for which polymer-supported tin reagents are required. To this end, we prepared[11] resin **3** (polystyrene-di-*n*-butyltin chloride, PBTC) and **4** (polystyrene-di-*n*-butyltin hydride, PBTH) as shown in Scheme 1.



Scheme 1. Synthesis of polymer-supported PBTC (**3**) and PBTH (**4**). Reagents and conditions: a) K_2CO_3 (10.0 equiv), DMSO, 145 °C, 15 h; b) $CH_2{=}PPh_3$ (2.0 equiv), THF, 23 °C, 8 h; c) nBu$_2$SnCl$_2$ (2.0 equiv), nBu$_2$SnH$_2$ (2.0 equiv), AIBN (0.05 equiv), hν, toluene, 0 °C, 4 h (90% from **1**); d) $LiBH_4$ (4.0 equiv), THF, 23 °C, 4 h. AIBN = 2,2′-azobisisobutyronitrile.

Oxidation of Merrifield resin[12] (**1**, Scheme 1) with K_2CO_3 in DMSO at 145 °C, followed by olefination of the resulting aldehyde gave polystyrene vinyl resin **2**, which was allowed to react with nBu$_2$SnHCl[13] (formed in situ from equimolar amounts of nBu$_2$SnH$_2$ and nBu$_2$SnCl$_2$) in the presence of AIBN (toluene, 0 °C) to afford PBTC (**3**) in 90% overall yield.[14] Reduction of **3** with $LiBH_4$ furnished the polymer-supported tin hydride **4** (PBTH).

The utilization of PBTH (**4**) in solid-phase synthesis and the proof of concept for the present strategy is demonstrated in Scheme 2. Thus, tin hydride **4** added across the acetylenic bond of 3-butynol (AIBN, 100 °C) to afford a mixture of **5** (*E*:*Z* ca. 1:1),[15] from which vinyl iodide **7** (*E*:*Z* ca. 1:1) was generated by addition of I_2.[16] Coupling of **5** with glutaric anhydride in the presence of 4-DMAP and Et_3N resulted in the formation of **6** to which was attached the vinyl iodide **7** or 2-iodobenzyl alcohol by DCC coupling, furnishing conjugates **8** and **10**, respectively. Finally, cyclorelease was induced by the action of [Pd(PPh$_3$)$_4$] catalyst, leading to macrocyclic systems

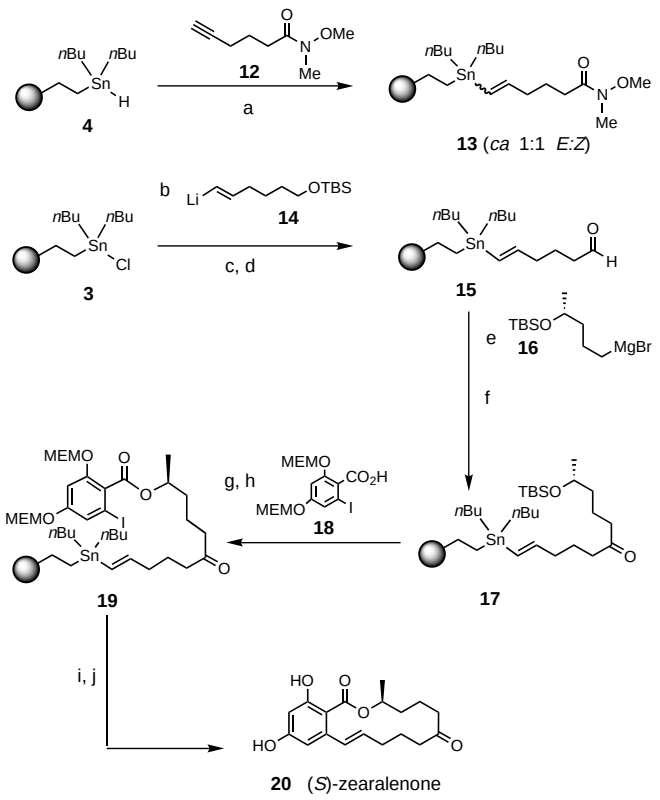


Scheme 2. Solid-phase synthesis of model macrocyclic systems **9** and **11** by a cyclorelease mechanism that employs the Stille coupling strategy. Reagents and conditions: a) 3-butynol (4.0 equiv), AIBN (0.05 equiv), toluene, 100 °C, 8 h, (94% from **3**); b) glutaric anhydride (4.0 equiv), 4-DMAP (0.1 equiv), Et_3N (5.0 equiv), CH_2Cl_2, 23 °C, 15 h (96%). c) I_2 (1.1 equiv), THF, 23 °C, 2 h (quant.); d) **7** (4.0 equiv), DCC (4.0 equiv), 4-DMAP (0.1 equiv), CH_2Cl_2, 23 °C, 18 h (93%); e) Pd(PPh$_3$)$_4$ (0.10 equiv), toluene, 100 °C, 48 h (56% as a 1:1:2 *EE*:*ZZ*:*EZ* mixture); f) 2-iodobenzyl alcohol (4.0 equiv), DCC (4.0 equiv), 4-DMAP (0.1 equiv), CH_2Cl_2, 23 °C, 15 h (95%); g) Pd(PPh$_3$)$_4$ (0.10 equiv), toluene, 100 °C (51% based on loading of *E* isomer). 4-DMAP = 4-dimethylaminopyridine; DCC = 1,3-dicyclohexylcarbodiimide.

9 (56% from **8**) and **11** (51% from **10** based on the loading of the *E* isomer). Notable was the absence of the *Z* isomer of **11** from the cyclorelease of **10**, and the isolation of a dimer (7%) corresponding to **11** possessing one *Z* and one *E* double bond.

The use of the polymer-supported tin reagents **3** and **4** and the demonstration of the power of the method in natural product synthesis is shown in Scheme 3 with the total synthesis of (*S*)-zearalenone (**20**). The adopted strategy (Figure 2) was demonstrated in solution by Stille and Hegedus in 1991.[6] While the addition of PBTH (**4**) to the acetylenic Weinreb amide **12** gave a stoichiometric mixture of *Z*:*E* vinyltin conjugates **13**, the displacement of the chloride from PHTC (**3**) by lithium reagent **14**[17] led, after deprotection and oxidation, exclusively to the *E*-vinyltin polymer **15**. Addition of Grignard reagent **16**[17] to the Weinreb amide **13** or to aldehyde **15** followed by Corey–Kim oxidation gave **17**,

  1433-7851/98/3718-2535 $ 17.50+.50/0



Scheme 3. Solid-phase total synthesis of (*S*)-zearalenone (**20**) by a cyclorelease mechanism that employs the Stille coupling strategy. Reagents and conditions: a) **12** (4.0 equiv), AIBN (0.05 equiv), toluene, 100 °C, 4 h (90% from **3**); b) **14** (3.0 equiv), THF, −78→23 °C, 4 h (87%); c) TBAF (10.0 equiv), THF, 23 °C, 5 h (94%); d) NCS (4.0 equiv), Me_2S (5.0 equiv), 0 °C, 15 min; then add resin, 0 °C, 1 h; Et_3N (6.0 equiv) 0→23 °C, 0.5 h; e) **16** (2.0 equiv), THF, 0→23 °C, 4 h (92%, 2 steps); f) NCS (4.0 equiv), Me_2S (5.0 equiv), 0 °C, 15 min; then add resin, −40 °C, 1.5 h; Et_3N (6.0 equiv), −40→23 °C, 0.5 h (97%). g) TBAF (10.0 equiv), THF, 23 °C, 13 h; h) **18** (3.0 equiv), PPh_3 (3.0 equiv), DEAD (4.0 equiv), 0→23 °C, 6 h (76%, two steps); i) $Pd(PPh_3)_4$ (0.10 equiv), toluene, 100 °C, 48 h (54%); j) 2:1 THF/HCl aq. (5%), 23 °C, 5 days (80%). TBAF = tetra-*n*-butylammonium fluoride; NCS = *N*-chlorosuccinimide; DIAD = diisopropyl azodicarboxylate.

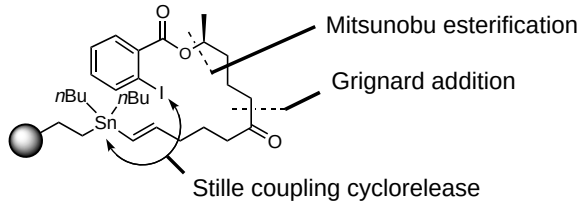


Figure 2. Bond disconections for the solid-phase synthesis of (*S*)-zearalenone (**20**) by a cyclorelease mechanism that employs the Stille coupling strategy.

which was desilylated and coupled to carboxylic acid **18**[17] to afford the desired precursor **19**. As expected, cyclorelease took place smoothly upon exposure of **19** to $[Pd(PPh_3)_4]$ catalyst to afford, after acid-induced deprotection,[6] (*S*)-zearalenone (**20**). Similarly to the previous case (**10**→**11**), the cyclorelease of the *Z* isomer of zearalenone was not observed. Selected physical properties of several of the compounds synthesized here are given in Table 1.

The described solid-phase chemistry extends the utility of the cyclorelease strategy to the synthesis of complex macrocycles, including natural products, by adding the Stille coupling to the repertoire of applicable reactions. This efficient method should facilitate the construction of compound libraries of such systems for biological screening and other uses.

Received: April 14, 1998 [Z11732IE]
German version: *Angew. Chem.* **1998**, *110*, 2677–2680

Keywords: cyclizations · natural products · solid-phase synthesis · Stille coupling · synthetic methods

[1] For reviews, see: a) F. Balkenhohl, C. von dem Bussche-Hünnefeld, A. Lansky, C. Zechel, *Angew. Chem.* **1996**, *108*, 2436–2487; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2288–2337; b) L. A. Thompson, J. A. Ellman, *Chem. Rev.* **1996**, *96*, 555–617; c) M. A. Gallop, R. W. Barret, W. J. Dower, S. P. Foder, E. M. Gorden, *J. Med. Chem.* **1994**, *37*, 1233–1281; d) E. M. Gorden, R. M. Barret, W. J. Dower, S. P. Foder, M. A. Gallop, *ibid*. **1994**, *37*, 1385–1405; e) W. H. Moos, G. D. Green, M. R. Pavia, *Annu. Rep. Med. Chem.* **1993**, *28*, 315–324.

[2] For general references, see: a) J. J. Baldwin, I. Henderson in *Synthesis of Encoded Small Molecule Combinatorial Libraries* (Ed.: J. P. Delvin), Dekker, New York, NY, **1997**; b) A. W. Czarnick, *Curr. Opin. Chem. Biol.* **1997**, *1*, 60–66; c) X. Y. Xiao, C. Zhao, H. Potash, M. P. Nova, *Angew. Chem.* **1997**, *109*, 799–801; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 780–782.

[3] For references relating to non-oligomeric natural product synthesis on solid phase, see: a) K. C. Nicolaou, N. Winssinger, J. Pastor, S. Ninkovic, F. Sarbia, Y. He, D. Vourloumis, Z. Yang, T. Li, P. Giannakakou, E. Hamel, *Nature* **1997**, *387*, 268–272; b) S. Chen, K. D. Janda, *J. Am. Chem. Soc.* **1997**, *119*, 8724–8725.

[4] For previous examples of cyclorelease, see: a) X. Beebe, N. E. Schore, M. J. Kurth, *J. Am. Chem. Soc.* **1992**, *114*, 10061–10062; b) S H. Dewitt, J. S. Kiely, C. J. Stankovic, M. C. Schroeder, D. M. R. Cody, M. R. Pavia, *Proc. Natl. Acad. Sci. USA* **1993**, *90*, 6909–6913. For carbon–carbon bond cyclorelease, see: c) J. H. van Maarseveen, J. A. J. den Hartog, V. Engelen, E. Finner, G. Visser, C. G. Kruse, *Tetrahedron Lett.* **1996**, *37*, 8249–8252; d) A. D. Piscopio, J. F. Miller, K. Koch, *ibid*. **1997**, *38*, 7143–7146; reference [3a]; e) M. R. Gowravaram, M. A. Gallop, *ibid*. **1997**, *38*, 6973–6976.

[5] a) J. K. Stille, *Pure Appl. Chem.* **1985**, *57*, 1771–1780; b) J. K. Stille, *Angew. Chem.* **1986**, *98*, 504–520; *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 508–524; c) V. Farina, V. Krishnamurthy, W. Scott, *Org. React. (N.Y.)* **1995**, *50*, 1–676.

[6] K. Kalivretenos, J. K. Stille, L. S. Hegedus, *J. Org. Chem.* **1991**, *56*, 2883–2894.

[7] See the following references and the references therein: a) M. T. Shipchandler, *Heterocycles* **1975**, *3*, 471–476; b) D. Taub, N. N. Girotra, R. D. Hoffsommer, C. H. Kuo, H. L. Slates, N. L. Weber, *Tetrahedron*, **1968**, *24*, 2443–2454; c) E. J. Corey, K. C. Nicolaou, *J. Am. Chem. Soc.* **1974**, *96*, 5614–5616; d) S. Masamune, S. Kamata, W. Schilling, *ibid*. **1975**, *97*, 3515–3516; e) T. Takahashi, K. Kasuga, M. Takahashi, J. Tsuji, *ibid*. **1979**, *101*, 5072–5073.

[8] S. Omura, *Macrolide Antibiotics*, Academic Press, New York, **1984**.

[9] B. J. Backes, J. A. Ellman, *Curr. Opin. Chem. Biol.* **1997**, *1*, 86–93.

[10] K. C. Nicolaou, D. Vourloumis, T. Li, J. Pastor, N. Winssinger, Y. He, S. Ninkovic, F. Sarabia, H. Vallberg, F. Roschangar, N. P. King, R. M. V. Finlay, P. Giannakakou, P. Verdier-Pinard, E. Hamel, *Angew. Chem.* **1997**, *109*, 2181–2187; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2097–2103.

[11] While the preparation of polymer-supported organotin reagents **3** and **4** have been reported on a macroporous resin by Neumann et al., the authors were unsuccessful in their attempts to prepare it on a 2% cross-linked resin: a) M. Peterseim, W. P. Neumann, *React. Polym.* **1993**, *20*, 189–205; b) U. Gerigk, M. Gerlach, W. P. Neumann, R. Vieler, V. Weintritt, *Synthesis* **1990**, 448–452. For some applications of

  1433-7851/98/3718-2536 $ 17.50+.50/0

Table 1. Selected physical properties of compounds **4**, **7**, **9**, **11**, **13**, and **20**.

4: Infrared analysis of the resin revealed an intense Sn–H stretching absorption at 1802 cm^{-1}.

7: $R_f = 0.28$ (silica gel, EtOAc/hexane, 1:3); FT-IR (neat) $\tilde{\nu}_{max} = 3332, 2942, 2878, 1606, 1422, 1216, 1045, 944\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta =$ 6.54 (dt, $J = 14.5, 7.0$ Hz, 1H, C*H*=CHI, *E* isomer), 6.37 (dt, $J = 7.5, 1.0$ Hz, 1H, CH=C*H*I, *Z* isomer), 6.28 (dt, $J = 7.5, 7.0$ Hz, 1H, C*H*=CHI, *Z* isomer), 6.17 (dt, $J = 14.5, 7.0$ Hz, 1H, CH=C*H*I, *E* isomer), 3.75 (t, $J =$ 6.5 Hz, 2H, CH_2O, *Z* isomer), 3.68 (t, $J = 6.5$ Hz, 2H, CH_2O, *E* isomer), 2.44 (dtd, $J = 7.0, 6.5, 1.0$ Hz, 2H, CH_2CH=CHI, *Z* isomer), 2.33 (dtd, $J =$ 7.0, 6.5, 1.0 Hz, 2H, CH_2CH=CHI, *E* isomer); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 142.7, 137.6, 84.8, 77.3, 60.9, 60.8, 39.1, 38.1$.

9: Compound **9** was obtained as a 1:1:2 mixture of *EE*:*ZZ*:*EZ* isomers. (*EE*)-**9**: $R_f = 0.51$ (silica gel, EtOAc/hexane, 1:3); FT-IR (neat) $\tilde{\nu}_{max} = 2991, 2961, 2931, 1736, 1412, 1378, 1210, 1159, 1092, 1022, 1000, 863, 802\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 5.94-5.86$ (m, 2H, CH=C*H*–CH=CH), 5.41–5.29 (m, 2H, C*H*=CH–CH=CH), 4.22 (t, $J = 5.5$ Hz, 4H, CH_2O), 2.37 (t, $J = 6.0$ Hz, 4H, CH_2COO), 2.25 (dt, $J = 6.0, 5.5$ Hz, 4H, CH_2CH=CH), 1.75 (qt, $J = 6.0$ Hz, 2H, CH_2CH_2COO); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta =$ 173.0, 133.5, 128.0, 60.8, 33.9, 31.3, 18.8; HRMS (FAB) calcd for $C_{13}H_{18}O_4$ [MH$^+$]: 239.1283; found: 239.1279.

(*ZZ*)-**9**: $R_f = 0.42$ (silica gel, EtOAc/hexane, 1:3); FT-IR (neat) $\tilde{\nu}_{max} = 2918, 1732, 1697, 1650, 1556, 1536, 1519, 1452, 1241, 1150\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 6.45-6.39$ (m, 2H, CH=C*H*–CH=CH), 5.46–5.40 (m, 2H, C*H*=CH–CH=CH), 4.22 (m, 2H, CH_2O), 4.09 (m, 2H, CH_2O), 2.39–2.31 (m, 8H, CH_2CH=CH, CH_2COO), 1.84 (qt, $J = 6.5$ Hz, 2H, CH_2CH_2COO); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 172.9, 127.8, 126.6, 62.2, 32.0, 31.6, 27.7, 22.6, 14.1$; HRMS (FAB) calcd for $C_{13}H_{18}O_4$ [M+Na$^+$]: 261.1103; found: 261.1110.

(*EZ*)-**9**: $R_f = 0.40$ (silica gel, EtOAc/hexane, 1:3); FT-IR (neat) $\tilde{\nu}_{max} = 2955, 1732, 1454, 1382, 1248, 1150, 1063\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta =$ 6.33 (ddd, $J = 15.0, 10.5, 2.5$ Hz, 1H, CH=C*H*–CH=CH), 6.11 (dd, $J = 10.5,$ 10.5 Hz, 1H, CH=CH–C*H*=CH), 5.62 (dt, $J = 15.0, 7.5$ Hz, 1H, C*H*=CH–CH=CH), 5.34 (dt, $J = 10.5, 7.5$ Hz, 1H, CH=CH–CH=C*H*), 4.20–4.17 (m, 4H, CH_2O), 2.47–2.43 (m, 2H, CH_2CH=CH), 2.42–2.37 (m, 2H, CH_2CH=CH), 2.37 (t, $J = 7.5$ Hz, CH_2COO), 2.34 (t, $J = 7.5$ Hz, CH_2COO), 1.93-1.87 (m, 2H, CH_2CH_2COO); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 172.6, 172.5, 131.7, 130.6, 128.8, 126.0, 62.6, 62.5, 33.5, 33.3, 32.7, 27.5, 20.5, 14.1$; HRMS (FAB) calcd for $C_{13}H_{18}O_4$ [M+Na$^+$]: 261.1103; found: 261.1109.

11: $R_f = 0.30$ (silica gel, EtOAc/hexane, 1:3); FT-IR (neat) $\tilde{\nu}_{max} = 2947, 1731, 1242, 1146, 964, 752\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.42$ (d, $J = 8.0$ Hz, 1H, ArH), 7.33 (ddd, $J = 8.0, 8.0, 2.5$ Hz, 1H, ArH), 7.27–7.21 (m, 2H, ArH), 6.64 (d, $J = 15.5$ Hz, 1H, ArC*H*=CHCH$_2$), 6.05 (dt, $J = 15.5,$ 7.0 Hz, 1H, ArCH=C*H*CH$_2$), 5.13 (s, 2H, PhCH$_2$O), 4.22 (m, 2H, CH$_2$C*H*$_2$O), 2.53 (dt, $J = 7.0, 5.0$ Hz, 2H, CH=CHC*H*$_2$), 2.44 (dd, $J = 6.5,$ 6.0 Hz, 2H, CH$_2$COO), 2.37 (dd, $J = 6.5, 6.0$ Hz, 2H, CH$_2$COO), 2.03–1.96 (m, 2H, COCH$_2$C*H*$_2$); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 173.2, 172.6, 138.6, 132.2, 130.7, 130.1, 129.3, 129.1, 127.2, 127.1, 65.7, 62.9, 32.9, 32.4, 31.4, 20.0$; HRMS (FAB) calcd for $C_{16}H_{18}O_4$ [M+Na$^+$]: 297.1103; found: 297.1109.

13: Iodonolysis of resin **13** afforded an inseparable *E*:*Z* (1:1) mixture of the corresponding vinyl iodide. $R_f = 0.22$ (silica gel, EtOAc-hexane, 1:3); FT-IR (neat) $\tilde{\nu}_{max} = 2934, 1666, 1416, 1385, 1178, 996\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 6.45$ (dt, $J = 14.5, 7.0$ Hz, 1H, C*H*=CHI, *E* isomer), 6.21 (m, 1H, CH=C*H*I, *Z* isomer), 6.16 (dt, $J = 7.5, 7.0$ Hz, 1H, C*H*=CHI, *Z* isomer), 6.00 (dt, $J = 14.5, 1.5$ Hz, 1H, CH=C*H*I, *E* isomer), 3.66 (s, 3H, OCH_3), 3.65 (s, 3H, OCH_3), 3.16 (s, 3H, NCH_3), 3.15 (s, 3H, NCH_3), 2.45 (t, $J = 7.0$ Hz, 2H, CH_2CON), 2.40 (m, 2H, CH_2CON), 2.18 (dt, $J = 7.0,$ 7.0 Hz, 2H, CH_2CH=CHI, *Z* isomer), 2.03 (dtd, $J = 7.0, 7.0, 1.5$ Hz, 2H, CH_2CH=CHI, *E* isomer), 1.76 (qt, $J = 7.0$ Hz, 2H, CH$_2$CH_2CH$_2$), 1.72 (qt, $J = 7.0$ Hz, 2H, CH$_2$CH_2CH$_2$); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 145.7, 140.6, 83.1, 75.2, 61.2, 35.4, 34.2, 23.0, 22.8$; HRMS (FAB) calcd for $C_8H_{14}INO_2$ [MH$^+$]: 284.0148; found: 284.0158.

(S)-Zearalenone (20): $R_f = 0.45$ (silica gel, EtOAc/hexane, 1:1); $[\alpha]_D^{23} = -124.2$ ($c = 0.5$, MeOH)[7a] $[\alpha]_D^{24} = -134$ ($c = 1.0$, MeOH); FT-IR (neat) $\tilde{\nu} = 3421, 2938, 1700, 1648, 1611, 1577, 1452, 1355, 1314, 1260, 1201, 1170, 1124, 1018, 970\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 10.10$ (s, 1H, ArOH), 7.00 (dd, $J = 15.5, 1.5$ Hz, 1H, CH=C*H*Ar), 6.41 (d, $J = 2.5$ Hz, 1H, ArH), 6.35 (d, $J = 2.5$ Hz, 1H, ArH), 5.67 (ddd, $J = 15.5, 10.5, 3.5$ Hz, 1H, C*H*=CHAr), 4.98 (m, 1H, CHOCOAr), 2.86 (ddd, $J = 18.5, 12.0, 1.0$ Hz, 1H), 2.60 (m, 1H), 2.36 (m, 1H), 2.21–2.10 (m, 4H), 1.80–1.70 (m, 2H), 1.67–1.61 (m, 2H), 1.49 (m, 1H), 1.36 (d, $J = 6.5$ Hz, 3H, C(CH$_3$)OCOAr); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 211.8, 171.3, 165.4, 160.6, 144.0, 133.2, 132.4, 108.4, 102.4, 73.4, 42.9, 36.7, 34.7, 31.0, 22.3, 21.0, 20.9, 20.8$; HRMS (FAB) calcd for $C_{18}H_{22}O_5$ [MH$^+$]: 319.1545; found: 319.1555. The synthetic zearalenone **20** was identical (^1H, ^{13}C, TLC) to an authentic sample purchased from Aldrich.

polymer supported organotin reagents, see: H. Kuhn, W. P. Neumann, *Synlett* **1994**, 123–124; and M. Gerlach, F. Jordens, H. Kuhn, W. P. Neumann, M. Peterseim, *J. Org. Chem.* **1991**, 56, 5971–5972.

[12] J. M. Frechet, C. Schuerch, *J. Am. Chem. Soc.* **1971**, *93*, 492–496. The reported procedure employed $NaHCO_3$ rather than K_2CO_3.

[13] W. P. Neumann, J. Pedain, *Tetrahedron Lett.* **1964**, 2461–2465.

[14] The yield was calculated based on the mass gain of the polymer. All subsequent yields are based on the amount of compound recovered upon iodonolysis from the resin.

[15] The ratios of polymer bound vinyl tin isomers were extrapolated from the ratio of vinyl iodide isomers obtained upon iodonolysis.

[16] The preparation of spectroscopically homogeneous vinyl iodide **7** was carried out on a 1–10-mmol scale by a) titrating vinyl tin resin **5** with a THF iodine solution slightly beyond the end point (ca. 1.1 equiv) and b) diluting with Et_2O and washing with saturated aqueous $Na_2S_2O_3$.

[17] The spectroscopic characteristics of compounds **14**, **16,** and **18** were identical to those previously reported.[6]

  1433-7851/98/3718-2537 $ 17.50+.50/0