DOI: 10.1002/chem.200701512

# 1,4-Pentenyne as a Five-Carbon Synthon for Efficient and Selective Syntheses of Natural Products Containing 2,4-Dimethyl-1-penten-1,5-ylidene and Related Moieties by Means of Zr-Catalyzed Carboalumination of Alkynes and Alkenes

**Gangguo Zhu and Ei-ichi Negishi*[a]**

**Abstract:** Two highly efficient protocols for enantioselective synthesis of 2,4-dimethyl-1-penten-1,5-ylidene derivatives involve the combined use of the Zr-catalyzed methylalumination of alkynes (ZMA) and the Zr-catalyzed asymmetric carboalumination of alkenes (ZACA). The ZMA/ZACA protocol has been applied to the synthesis of a nafuredin intermediate **14** and a potential intermediate **18** for milbemycin $\beta_3$, while the ZACA/ZMA protocol has been applied to the synthesis of a (−)-bafilomycin $A_1$ intermediate **25**.

**Keywords:** pentenyne · asymmetric synthesis · catalysis · natural products · zirconium

## Introduction

A large number of natural products and related compounds of biological and medicinal interest contain 2,4-dimethyl-1-penten-1,5-ylidene moieties and derivatives thereof. Nafuredin (**1**),[1] a selective NADH-fumarate reductase inhibitor (NADH = nicotinamide adenine dinucleotide), scyphostatin (**2**),[2] an inhibitor of neutral sphingomyelinase, (+)-ratjadone (**3**),[3] an antifungal metabolite from *Sorangium cellulosum*, milbemycin $\beta_3$ (**4**),[4] a macrolide antibiotic, lacrimin A (**5**),[5] an antihypotensive agent, (−)-bafilomycin $A_1$ (**6**),[6] a potent vacuolar $H^+$-APTase (APTase = adenosine triphosphatase) inhibitor, concanamycin F (**7**),[7] another specific $H^+$-APTase inhibitor, and FK-506 (**8**),[8] an active immunosuppressive agent, are some of the representative examples containing an (*E*)-trisubstituted alkene moiety, whilst discodermolide (**9**),[9] an anticancer marine natural product, for example, contains a (*Z*)-trisubstituted alkene. Others including (−)-callystatin A (**10**),[10] a potential antitumor polyketide, contain a disubstituted (*E*)-alkene, while both di- and trisubstituted alkenes are seen in delactonmycin (**11**).[11]

With the goal of developing widely applicable, efficient, and stereo- and regioselective synthetic protocols, 1,4-pentenyne (**12**) and its silyl derivatives readily preparable by Cu-[12] or Pd-catalyzed[13] reactions of ethynyl- and silyl-protected ethynylmetals containing Li or Zn, respectively, were considered as five-carbon synthons for the two-directional construction of 2,4-dimethyl-1-penten-1,5-ylidene derivatives by means of Zr-catalyzed methylalumination of alkynes (ZMA reaction)[14] and Zr-catalyzed asymmetric carboalumination of alkenes (ZACA reaction).[15] Our recent study has indicated that, whilst conjugated dienes have not so far satisfactorily undergone the ZACA reaction, 1,4-dienes have.[15g] Thus, the 1,4-diene products obtained by means of the ZMA reaction of 1,4-pentenyne (**12**) should undergo the ZACA reaction, as depicted by protocol I (or the ZMA/ZACA protocol; Scheme 1). In contrast, silylated 1,4-pentenynes might selectively undergo the ZACA reaction. If so, the ZMA reaction can be performed at any later stage (protocol II or the ZACA/ZMA protocol). Thus, the main goal of the work described below is to explore the feasibility of both protocols I and II through the preparation of some key intermediates used previously in the synthesis of a few select natural products. For examining the practical synthetic value of protocol I, nafuredin (**1**)[1] and milbemycin $\beta_3$ (**4**)[4] were chosen. In cases for which an early execution of the ZMA reaction must be avoided, the ZACA/ZMA order of execution would be desirable. We encountered this situation

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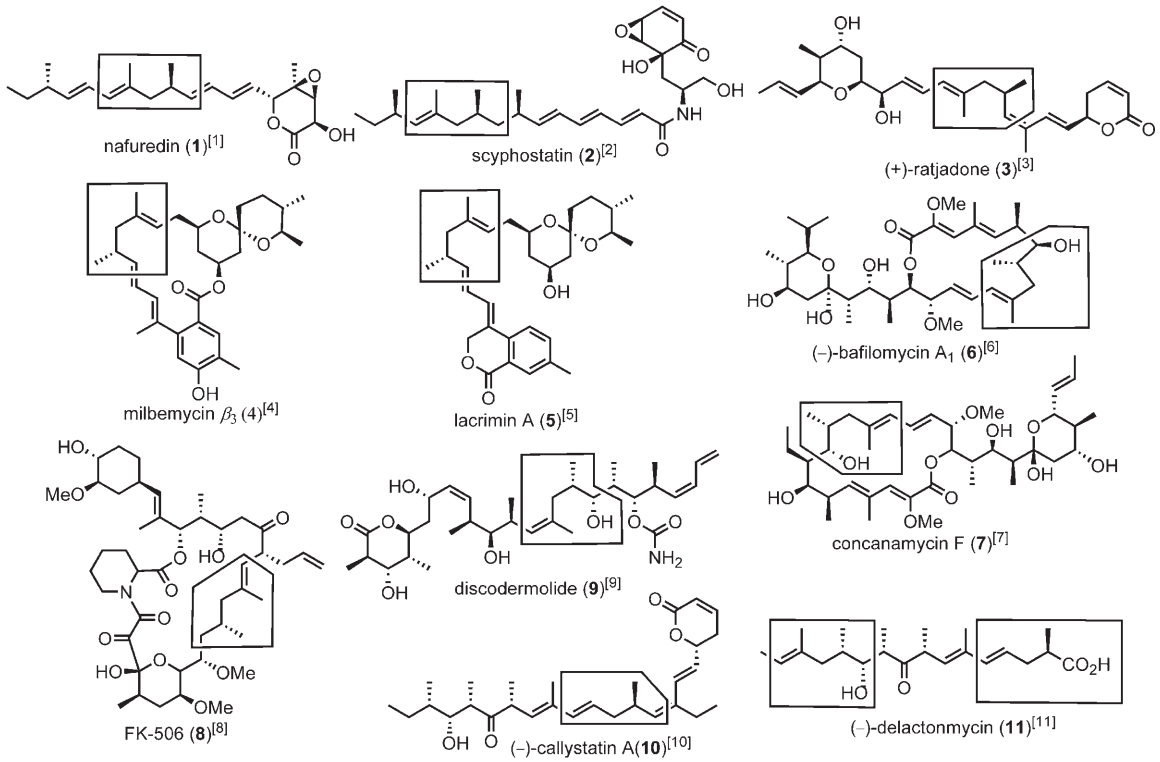
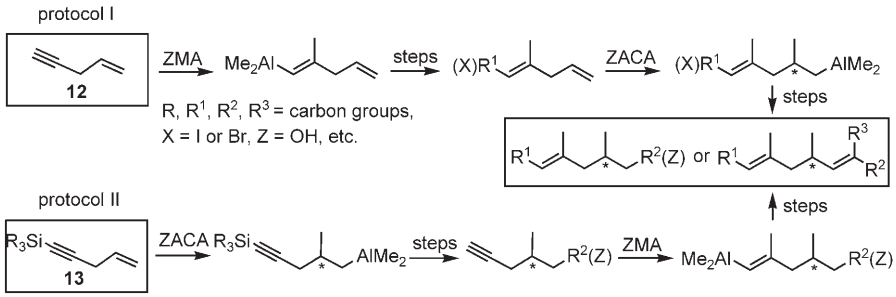


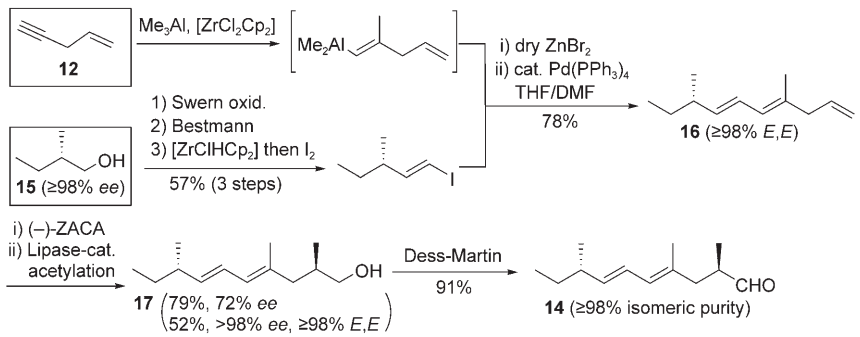

in an attempt to synthesize known key intermediates of (−)-bafilomycin $A_1$ (**6**),[6] which was thus chosen for exploring the feasibility of protocol II.

## Results and Discussion

Nafuredin (**1**) was isolated, identified, and synthesized in 2001.[1] A key intermediate **14** was prepared from commercially available (*S*)-2-methyl-1-butanol (**15**) (TCI, 98% *S*) in 14 steps in 16% overall yield.[1c] This intermediate **14** can be synthesized according to proctocol I in 21% yield in just six steps from **15** (or three steps from **12**), as shown in Scheme 2, featuring the Zr-catalyzed alkyne carboalumination,[14] a controlled and synergistic use of ZACA and lipase-catalyzed acetylation,[16] and the Pd–Zn cocatalyzed alkenyl–alkenyl coupling.[17] Both the Zr-catalyzed methylalumination of alkynes (ZMA) and the alkyne hydrozirconation proceeded




Scheme 1. Two protocols for the conversion of **12** or **13** into 2,4-dimethyl-1-pentene and 2,4-dimethyl-1,5-hexadiene derivatives. ZACA = $Me_3Al$, cat., $[ZrCl_2(nmi)_2]$; ZMA = $Me_3Al$, cat., $[ZrCl_2Cp_2]$.



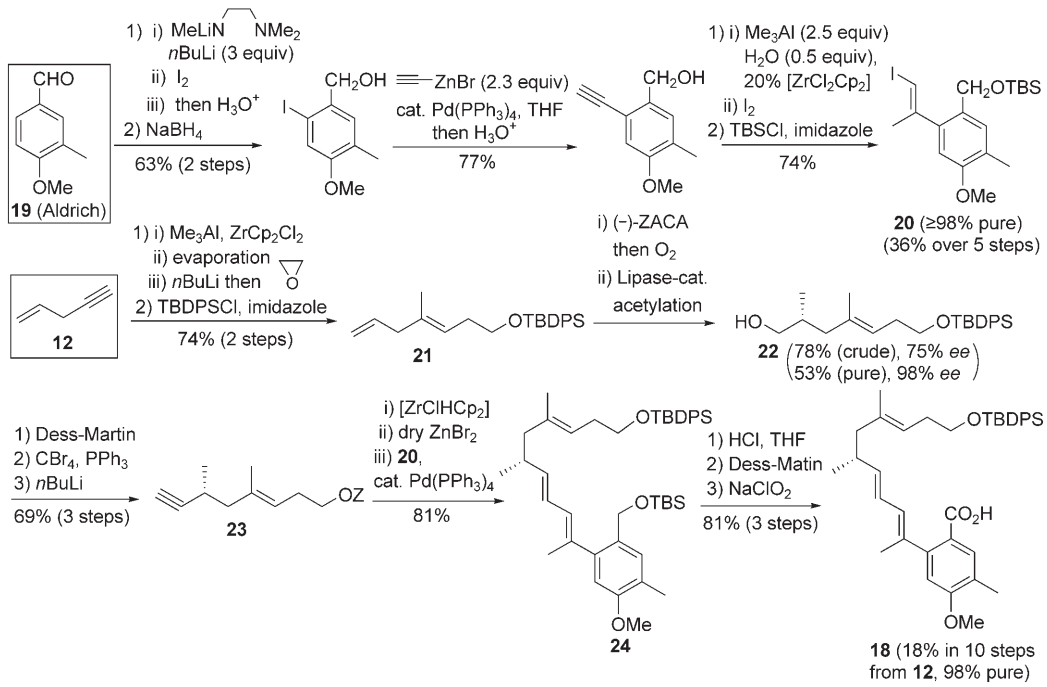

Scheme 2. Synthesis of **14** as a key intermediate of nafuredin (**1**) by means of Zr-catalyzed alkyne carboalumination and ZACA-lipase-catalyzed acetylation. Swern oxidation = $(COCl)_2$ (1.2 equiv), DMSO (2.0 equiv), $Et_3N$ (2.2 equiv); Bestmann = $(MeO)_2POC(N_2)COMe$, $K_2CO_3$, MeOH; (−)-ZACA = $Me_3Al$ (2.5 equiv), 5% $[ZrCl_2\{(-)\text{-}(nmi)_2\}]$, $CH_2Cl_2$, 0 °C; then $O_2$; lipase cat. acetylation = vinyl acetate (5 equiv), Amano PS lipase (30 mg mmol$^{-1}$) $CH_2Cl_2$; Dess–Martin = 1,1,1-tris(acetyloxy)-1,1-dihydro-1,2-benziodoxol-3-(1*H*)one.

with 98% stereoselectivity. The conjugated diene **16** obtained by means of Pd-catalyzed cross-coupling was achieved to give 98% of the *E*,*E* isomer without any stereoisomeric purification. Its ZACA reaction with 5.0 mol% of $[ZrCl_2\{(-)\text{-}(nmi)_2\}]$[18] (nmi = 1-neomenthylindenyl) as a catalyst followed by oxidation with $O_2$ gave **17** with 72% *ee* in 79% yield. Although this compound contains two asymmetric carbon centers with a relatively rigid (*E*,*E*)-diene moiety between them, attempts to purify **17** by column chromatography proved to be difficult. On the other hand, its purification by lipase-catalyzed acetylation by using Amano PS lipase (30 mg mmol$^{-1}$) provided **17** with 98% *ee* in 52% overall yield from **16**. Oxidation of **17** with Dess–Martin periodinane furnished **14** with 98% isomeric purity, as determined by $^{13}C$ and $^{1}H$ NMR spectroscopy, in 91% yield.

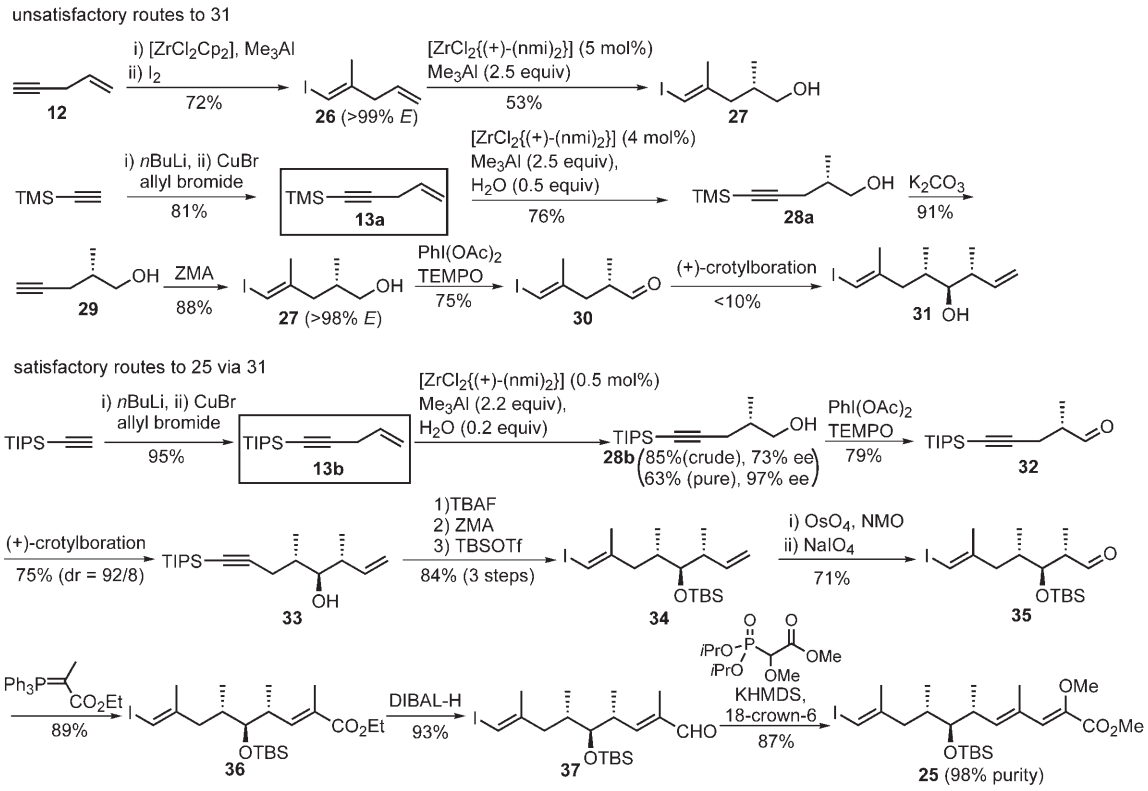
For an efficient and selective synthesis of **18**, a potential key intermediate for the synthesis of milbemycin $\beta_3$ (**4**),[4] a 10-step scheme converting **12** into **18** in 18% overall yield has been developed (Scheme 3). A five-step conversion of commercially available (Aldrich) 3-methyl-4-methoxybenzaldehyde (**19**) into the requisite alkenyl iodide **20** in 36% overall yield is also shown in Scheme 3. Selective iodination of **19** (63% yield after reduction with $NaBH_4$) through the use of 1.05 equivalents of $LiMeN(CH_2)_2NMe_2$,[19] Pd-catalyzed direct ethynylation[20] (77%), Zr-catalyzed alkyne carboalumination–iodinolysis,[14] and protection with *tert*-butyldimethylsilyl chloride (TBSCl) afforded **20** with 98% isomeric purity in 74% yield. In the longer linear sequence starting with **12**, its Zr-catalyzed methylalumination, evaporation of the volatiles, ate complexation of the alane with *n*BuLi (1.3 equiv), and addition of ethylene oxide (3.0 equiv) all in one pot produced **21** in 74% yield, after protection with *tert*-butyldiphenylsilyl chloride (TBDPSCl) and imidazole. The ZACA reaction of **21** with $Me_3Al$ (2.5 equiv) and 1.0% of $[ZrCl_2\{(-)\text{-}(nmi)_2\}]$ gave crude **22** with 75% *ee* in 78% yield, which was purified by treatment with vinyl acetate (5.0 equiv) and Amano PS lipase (30 mg mmol$^{-1}$) to give **22** with 98% *ee* in 53% yield from **21**. After conversion of **22** into **23** in 69% yield over three steps, hydrozirconation–Pd–Zn cocatalyzed alkenyl–alkenyl coupling with **20** permitted the crucial synthesis of **24**, which was converted to 98% isomerically pure **18** in 81% yield over three steps. It should be noted that **23** in Scheme 3 may be expected to serve as a useful intermediate for the synthesis of other related compounds, such as lacrimin A (**5**).[5]

As is widely known, the Zr-catalyzed methylalumination[14] is generally incompatible with various carbonyl compounds and some of those hydroxyl groups protected with commonly used silyl and other protecting groups. Thus, timing of its execution in synthesis is often critically important. It is generally advisable to carry out the Zr-catalyzed alkyne methylalumination before the ZACA reaction (Scheme 1, protocol I) and incorporation of carbonyl groups. In some cases, however, it is desirable to reverse the order of their execution (protocol II). Synthesis of the variously protected preferred intermediate **25**[6e–j] for the synthesis of (−)-bafilomycin $A_1$ is a case in point. Conversion of **12** into **26** proceeded in 72% yield. Disappointing, however, the ZACA reaction of **26** produced, after oxidation with $O_2$, the desired product **27** in only 53% yield. The results point-




Scheme 3. Synthesis of **18** as a potential intermediate for the synthesis of milbemycin $\beta_3$ by means of Zr-catalyzed alkyne carboalumination and ZACA–lipase-catalyzed acetylation. TBS = *t*BuMe$_2$Si, TBDPS = *t*BuPhSi, (−)-ZACA = $Me_3Al$ (2.0 equiv), 1% $[ZrCl_2\{(-)\text{-}(nmi)_2\}]$, IBAO (1.0 equiv), $CH_2Cl_2$, 23 °C.




Scheme 4. Synthesis of a key intermediate **25** for (−)-bafilomycin $A_1$ by means of a ZACA/ZMA protocol. ZMA = i) $[ZrCl_2Cp_2]$ (0.2 equiv), $Me_3Al$ (3.0 equiv), $H_2O$ (0.2 equiv), $CH_2Cl_2$; ii) $I_2$, $CH_2Cl_2$/THF. (+)-crotylboration = *trans*-2-butene, *t*BuOK, *n*BuLi, (+)-$(Ipc)_2BOMe$, $BF_3{\cdot}Et_2O$, ether/THF.

ed to the desirability of deferring the Zr-catalyzed alkyne carboalumination until after execution of the ZACA reaction. And yet, it should nevertheless be performed before incorporation of the carbonyl-containing C1–C5 moiety. With this in mind, the trimethylsilyl- (TMS) and triisopropyl- (TIPS) protected 1,4-pentenynes **13a** and **13b** were prepared by CuBr-catalyzed allylation of lithio derivatives of TMS- and TIPS-protected ethynes with allyl bromide in THF at 50 °C in 81 and 95 % yields, respectively.[12] Their ZACA reaction proceeded cleanly without competition coming from the silyl-protected alkynyl group and produced **28a** and **28b** in 76 and 85 % yields, respectively. Whereas the ZACA reaction of TMS-protected pentenyne **13a** was slower and required 4.0 mol % of $[ZrCl_2\{(+)\text{-}(nmi)_2\}]$ and 0.5 equivalents of water for generation of MAO (methylaluminoxane) as a promoter,[21] the corresponding reaction of TIPS-protected pentenyne **13b** required only 0.5 mol % of $[ZrCl_2\{(+)\text{-}(nmi)_2\}]$ and 0.2 equivalents of $H_2O$ for full consumption of the starting pentenyne **13b** within 5 h at 23 °C. After removal of the TMS or TIPS group by treatment with $K_2CO_3$ or TBAF, **29** was obtained in 91 and 90 % yields, respectively. The Zr-catalyzed methylalumination of **29** with 3.0 molar equivalents of $Me_3Al$, 0.2 equivalents of $[ZrCl_2Cp_2]$ (Cp = cyclopentadienyl), and 0.2 equivalents of $H_2O$ followed by treatment with 2.5 equivalents of $I_2$ cleanly produced **27** (>98 % *E*) in 88 % yield. Oxidation of **27** with tetramethylpiperdinyloxy free radical (TEMPO) and $PhI(OAc)_2$ in $CH_2Cl_2/H_2O$ at 23 °C afforded **30** in 75 % yield. The aldehyde **30** was subjected to the Brown crotylboration[22] by using *trans*-2-butene and (+)-$(Ipc)_2BOMe$, but the crotylboration reaction was not clean, producing an unattractive mixture, which contained the desired compound **31** in <10 % yield, as determined by GC analysis. These unsatisfactory results are summarized in the top part of Scheme 4.

Yet another modification of the synthetic scheme was made here. Thus, the ZACA–lipase-catalyzed acetylation product **28b** was oxidized with $PhI(OAc)_2$ (1.1 equiv) in the presence of 1.0 mol % of TEMPO to afford aldehyde **32** in 79 % yield, which was then subjected to the same Brown crotylboration as above. This reaction proceeded cleanly to give **33** in 75 % yield, and the product consisted of two diastereoisomers (dr 92:8) detectable by $^{13}C$ NMR spectroscopy, while its enantiomeric purity may safely be estimated to be well over 98 %. After deprotection with TBAF, the Zr-catalyzed carboalumination–iodinolysis cleanly produced **31** in 86 % yield over two steps. After protection of the hydroxyl group with TBSOTf (98 % yield), oxidation first with *N*-methylmorpholine-*N*-oxide (NMO) in the presence of 1.0 mol % of $OsO_4$ and then with $NaIO_4$ produced **35** in 71 % yield. The same compound was also used by the Roush[6e,f] and Marshall[6g,h] groups in the synthesis of **25** and eventually of (−)-bafilomycin $A_1$.[6] A similar route to the TES-protected analogue of **25** and (−)-bafilomycin $A_1$ was also reported by Hanessian.[6i] Our conversion of **35** to **25** followed closely the route employed by Roush[6e,f] and Mar-

shall,[6g,h] as shown in Scheme 4. Thus, **25** with 98% isomeric purity was prepared in 11 steps from TIPSC≡CH in 16% overall yield. Besides being efficient, in part by virtue of the use of 1,4-pentenyne and its derivatives permitting the combined use of the ZMA and ZACA reactions, this appears to be the only catalytic and fully enantioselective synthesis of **25** or its analogues with different protective groups.[6e–j]

## Conclusion

The ZMA reaction of 1,4-pentenyne (**12**) followed by the ZACA reaction at an appropriate stage (Scheme 1, protocol I) promises to provide a highly efficient, catalytic, and asymmetric route to a wide range of natural products containing one or more 2,4-dimethyl-1-penten-1,5-ylidene moieties. The ZMA reaction is usually 98% *E* selective. Although the ZACA reaction with $Me_3Al$ has thus far typically provided a 70–80% *ee*, the crude products of either *R* or *S* configuration can be readily and satisfactorily purified by lipase-catalyzed acetylation with vinyl acetate. By using protocol I, the known advanced intermediate **14** for nafturedin (**1**) has been efficiently and selectively synthesized in 21% yield in six steps from **15** or in 37% yield in mere three steps from **12**. Although not an actual intermediate in any of the previous syntheses of milbemycin $\beta_3$,[4] **18**, which appears to be imminently applicable as an advanced intermediate for the synthesis of **4**, was also prepared as a 98% pure compound in 18% yield over 10 steps from **12**. In this synthesis, a five-step procedure for converting commercially available **19** was devised to produce 98% pure **20** in 36% yield over five steps by means of 1) regioselective lithiation–iodinolysis of **19** by using $LiMeN(CH_2)_2NMe_2$, 2) Pd-catalyzed direct ethynylation with HC≡CZnBr, and 3) ZMA reaction followed by iodinolysis.

Difficulties encountered in the ZACA reaction and the crotylboration of iodoalkenyl-containing intermediates in an attempted synthesis of advanced intermediate **25** for the synthesis of (−)-bafilomycin $A_1$ pointed to the need to defer the ZMA reaction followed by iodinolysis until both ZACA and crotylboration reactions have been executed. This was feasible if the TIPS-protected 1,4-pentenyne **13b** was used in place of the parent 1,4-pentenyne (**12**). Crucial to this development was the finding that **13b** would undergo the desired ZACA reaction without a competition coming from the alkynyl group. It was also important to find that little or no cleavage of the TIPS group occurred, whereas partial cleavage of the TMS protecting group was detected in cases in which 1,4-pentenyne was protected with this silyl group. Besides being one of the most efficient synthesis of **25** and related derivatives with different protecting groups, the synthesis herein reported appears to provide the only catalytic and fully enantioselective route to **25**. Even at the current stage of development, this novel, efficient, and catalytic asymmetric method promises to provide alternative routes to a wide range of chiral natural products.

Clearly, it is very desirable to improve the 72–75% *ee* range observed in the ZACA reaction used in this study, which is limiting the yields of pure products. Such efforts are currently in progress in our laboratories.

## Experimental Section

**General methods**: Unless otherwise stated, all starting materials were obtained from commercial suppliers and used without further purification. THF and ether were distilled from sodium and benzophenone. $CH_2Cl_2$ was distilled from $CaH_2$. Flash chromatographic separation was carried out on 230–400 mesh silica gel 60. Gas chromatography was performed on an HP 6890 gas chromatograph by using an HP-5 capillary column (30 m × 0.32 mm, 0.5 μM film) with appropriate hydrocarbons as internal standards. $^1H$ and $^{13}C$ NMR spectra were recorded in $CDCl_3$ on a Varian Inova-300 spectrometer. Optical rotations were measured on an Autopol III automatic polarimeter. $ZnBr_2$ was flame-dried under vacuum prior to use. $[ZrCl_2\{(+)\text{-(nmi)}_2\}]$ and $[ZrCl_2\{(-)\text{-(nmi)}_2\}]$[18] were prepared as reported in the literature. Further intermediates and $^1H$ and $^{13}C$ NMR spectra are given in the Supporting Information.

**5-Triisopropylsilyl-1-penten-4-yne (13b)**: *n*BuLi in hexanes (2.5 M, 21 mL, 52.5 mmol) was added to a solution of triisopropylsilylacetlyne (11.5 mL, 50 mmol) in THF (30 mL) at −78 °C. After stirring for 30 min at −78 °C, CuBr[12] (360 mg, 2.5 mmol) and allyl bromide (4.5 mL, 55 mmol) were added. After stirring for 5 h at 50 °C, the reaction mixture was quenched with saturated aqueous $NH_4Cl$, extracted with ether, washed with brine, dried over $MgSO_4$, and concentrated. Column chromatography (silica gel, hexanes/$Et_2O$ 98:2) afforded **13b** (10.1 g, 95%) as a colorless oil. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta = 1.00$–$1.20$ (m, 21H), 3.05–3.10 (m, 2H), 5.15 (dt, $J = 10.2$, 1.5 Hz, 1H), 5.41 (dd, $J = 17.1$, 1.8 Hz, 1H), 5.75–5.9 ppm (m, 1H); $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta = 11.28$ (3C), 18.61 (6C), 24.11, 83.01, 104.79, 115.97, 132.42 ppm.

**(4*E*,8*S*)-4,8-Dimethyl-1,4,6-decatriene (16)**: A solution of **12** (132 mg, 2.0 mmol) in $CH_2Cl_2$ (3 mL) was added to a solution of $[ZrCl_2Cp_2]$ (117 mg, 0.4 mmol) and $Me_3Al$ (0.6 mL, 6.0 mmol) in $CH_2Cl_2$ (2 mL) at 0 °C. After stirring overnight at 0 °C, the solvent and excess $Me_3Al$ were evaporated. The residue was dissolved in THF (2 mL), followed by addition of a solution of $ZnBr_2$ (473 mg, 2.1 mmol) in THF (1 mL) at −78 °C. After stirring for 30 min at 0 °C, (1*E*,3*S*)-1-iodo-3-methyl-1-pentene (650 mg, 3.0 mmol) and $[Pd(PPh_3)_4]$ (115 mg, 0.1 mmol) in THF (2 mL) were added. After stirring overnight at 23 °C, the reaction mixture was quenched with saturated aqueous $NH_4Cl$, extracted with ether, washed with brine, dried over $MgSO_4$, and concentrated. Column chromatography (silica gel, hexanes/$Et_2O$ 95:5) afforded **16** (256 mg, 78%) as a colorless oil. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta = 0.86$ (t, $J = 7.2$ Hz, 3H), 0.99 (d, $J = 6.9$ Hz, 3H), 1.15–1.40 (m, 2H), 1.73 (d, $J = 1.2$ Hz, 3H), 2.0–2.15 (m, 1H), 2.76 (d, $J = 6.9$ Hz, 2H), 5.00–5.10 (m, 2H), 5.46 (dd, $J = 15.0$, 7.8 Hz, 1H), 5.70–5.90 (m, 2H), 6.19 ppm (ddd, $J = 15.0$, 10.5, 0.9 Hz, 1H); $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta = 11.78$, 16.52, 20.26, 29.89, 38.73, 44.21, 115.94, 124.84, 125.77, 134.22, 136.41, 138.86 ppm; MS (70 eV, EI): *m/z* (%): 164 (52) [$M^+$], 135 (26), 93 (100); HRMS (EI): *m/z*: calcd for $C_{12}H_{20}$: 164.1565 [$M^+$]; found: 164.1563.

**(2*R*,4*E*,6*E*,8*S*)-2,4,8-Trimethyl-4,6-decadien-1-ol (17)**

*Representative procedure A*: Compound **16** (164 mg, 1.0 mmol) in $CH_2Cl_2$ (3 mL) was added to a solution of $Me_3Al$ (0.3 mL, 3.0 mmol) and $[ZrCl_2\{(-)\text{-(nmi)}_2\}]$ (33 mg, 0.05 mmol) in $CH_2Cl_2$ (2 mL) at 23 °C. After total consumption of starting material (determined by GC analysis), the reaction mixture was treated with a vigorous stream of oxygen bubbled through it for 1 h at 0 °C, and was then stirred for further 5 h under an oxygen atmosphere at 23 °C. After this time, it was quenched with NaOH (2 N), extracted with $CH_2Cl_2$, washed with saturated aqueous $NH_4Cl$, brine, dried over $MgSO_4$, and concentrated. After passing it through a short path column of silica gel by using EtOAc as an eluent to remove metal-containing impurities, evaporation provided the crude product **17** (155 mg, 79%). The optical purity was determined by Mosher ester anal-

ysis to be 72% *ee*. Amano PS lipase (23 mg, 30 mg mmol$^{-1}$) and vinyl acetate (0.39 mL, 3.9 mmol) were added to a solution of crude **17** (151 mg, 0.77 mmol) in $CH_2Cl_2$ (2.3 mL) at 23°C. After stirring for 5 h (conversion = 30%, as determined by GC analysis), the reaction mixture was filtered, concentrated, and purified by column chromatography (silica gel, hexanes/EtOAc 70:30) to give **17**[1c] (102 mg, 52% from **16**). The optical purity was determined by Mosher ester analysis to be 99% *ee*. $[\alpha]_D^{23} = +41.3$ ($c = 1.2$ in $CHCl_3$); $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 0.87$ (t, $J = 6.9$ Hz, 3H), 0.89 (d, $J = 6.6$ Hz, 3H), 0.99 (d, $J = 7.2$ Hz, 3H), 1.05–1.20 (m, 2H), 1.74 (d, $J = 1.2$ Hz, 3H), 1.80–1.90 (m, 2H), 2.05–2.20 (m, 2H), 3.40–3.55 (m, 2H), 5.46 (dd, $J = 15.3$, 8.1 Hz, 1H), 5.81 (d, $J = 11.1$ Hz, 1H), 6.18 ppm (dd, $J = 15.3$, 11.4 Hz, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta = 11.79$, 16.47, 16.73, 20.18, 29.84, 33.88, 38.62, 44.29, 68.35, 124.61, 126.61, 134.55, 138.73 ppm; MS (70 eV, EI): *m*/*z* (%): 197 (41) [$M^+$+H], 196 (46) [$M^+$], 179 (57), 109 (100).

**(2*R*,4*E*,6*E*,8*S*)-2,4,8-Trimethyl-4,6-decadienal (14)**

*Representative procedure B*: Dess–Martin periodinane (509 mg, 0.6 mmol) was added to a solution of **17** (98 mg, 0.5 mmol) in $CH_2Cl_2$ (3 mL) at 0°C. After stirring for 2 h at 23°C, the reaction mixture was quenched with saturated aqueous $Na_2S_2O_3$, extracted with ether, washed with brine, dried over $MgSO_4$, and concentrated. Column chromatography (silica gel, hexanes/$Et_2O$ 95:5) afforded **14**[1c] (88 mg, 91%) as a colorless oil. $[\alpha]_D^{23} = +28.3$ ($c = 1.0$ in $CHCl_3$); $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 0.86$ (t, $J = 7.2$ Hz, 3H), 0.99 (d, $J = 6.6$ Hz, 3H), 1.06 (d, $J = 6.3$ Hz, 3H), 1.20–1.40 (m, 2H), 1.74 (d, $J = 1.2$ Hz, 3H), 2.00–2.15 (m, 2H), 2.45–2.60 (m, 2H), 5.49 (dd, $J = 15.3$, 7.8 Hz, 1H), 5.82 (d, $J = 10.5$ Hz, 1H), 6.17 (ddd, $J = 15.3$, 10.5, 1.5 Hz, 1H), 9.64 ppm (d, $J = 1.5$ Hz, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta = 11.79$, 13.22, 16.39, 20.12, 29.75, 38.63, 40.87, 44.52, 124.36, 127.62, 131.94, 139.60, 204.99 ppm; HRMS (EI): *m*/*z*: calcd for $C_{13}H_{22}O$: 194.1671 [$M^+$]; found: 194.1675.

**2-Ethynyl-4-methoxy-5-methyl-benzyl alcohol**: A solution of dry $ZnBr_2$ (5.4 g, 24 mmol) in THF (10 mL) was treated with 0.5 M ethynylmagnesium bromide in THF (48 mL, 24 mmol) at 0°C. After stirring for 30 min, a solution of [$Pd(PPh_3)_4$] (462 mg, 0.4 mmol) and 2-iodo-4-methoxy-5-methyl-benzyl alcohol in THF (10 mL) were added. After stirring for 3 h at 23°C, the reaction mixture was quenched with saturated aqueous $NH_4Cl$, extracted with ether, washed with brine, dried over $MgSO_4$, and concentrated. Column chromatography (silica gel, hexanes/EtOAc 70:30) gave the desired product (1.35 g, 77%) as a white solid. $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 2.21$ (s, 3H), 2.20–2.30 (m, 1H), 3.28 (s, 1H), 3.81 (s, 3H), 4.71 (s, 2H), 6.92 (s, 1H), 7.16 ppm (s, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta = 16.19$, 55.38, 63.27, 80.73, 81.66, 113.69, 118.44, 128.52, 130.37, 135.28, 156.70 ppm.

**Compound 20**

*Representative procedure C*:[14d] $H_2O$ (27 μL, 1.5 mmol) was added to a solution of $Me_3Al$ (1.0 mL, 10 mmol) and [$ZrCl_2Cp_2$] (176 mg, 0.6 mmol) in $CH_2Cl_2$ (5 mL) at −78°C. After stirring for 30 min at −78°C, the reaction mixture was warmed to 23°C over 30 min. To this was added 2-ethynyl-4-methoxy-5-methyl-benzyl alcohol (528 mg, 3.0 mmol) in $CH_2Cl_2$ (5 mL) at −78°C. After stirring for 3 h at 23°C, the reaction mixture was treated with a solution of $I_2$ (1.5 g, 6. 0 mmol) in THF (10 mL) at −78°C. After stirring for 30 min at −78°C, the reaction mixture was stirred for a further 30 min at 0°C, which was followed by addition of saturated aqueous $Na_2S_2O_3$ and extraction with ether. The resulting solution was washed with brine, dried over $MgSO_4$, and concentrated. Column chromatography (silica gel, hexanes/EtOAc 70:30) afforded the desired compound (715 mg, 75%) as a colorless oil. To a solution of the alcohol (636 mg, 2. 0 mmol) obtained above and imidazole (204 mg, 3.0 mmol) in DMF (6 mL) was added TBSCl (320 mg, 2.1 mmol) at 0°C. After stirring for 2 h at 23°C, the reaction mixture was quenched with water, extracted with ether, washed with water, brine, dried over $MgSO_4$, and concentrated. Column chromatography (silica gel, hexanes/EtOAc 97:3) afforded **20** (847 mg, 98%) as a colorless oil. $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 0.10$ (s, 6H), 0.93 (s, 9H), 2.18 (d, $J = 1.2$ Hz, 3H), 2.22 (s, 3H), 3.82 (s, 3H), 4.51 (s, 2H), 6.20 (s, 1H), 6.54 (s, 1H), 7.18 ppm (s, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta = -5.20$ (2C), 15.97, 18.36, 25.99 (3C), 26.61, 55.30, 62.60, 79.81, 109.12, 125.85, 129.13, 131.10, 139.88, 147.35, 156.56 ppm; MS (70 eV, EI): *m*/*z* (%): 432 (2) [$M^+$], 375 (80), 305 (32); 174 (100); HRMS (EI): *m*/*z*: calcd for $C_{18}H_{29}SiIO_2$: 432.0981 [$M^+$]; found: 432.0986.

**(4*E*)-7-(*tert*-Butyldiphenylsilyloxy)-4-methyl-1,4-heptadiene (21)**: A solution of **12** (1.3 g, 20 mmol) in $CH_2Cl_2$ (10 mL) was added to a solution of [$ZrCl_2Cp_2$] (1.2 g, 4.0 mmol) and $Me_3Al$ (4.0 mL, 40 mmol) in $CH_2Cl_2$ (20 mL) at 0°C. After stirring overnight at 0°C, the solvent and excess $Me_3Al$ were evaporated. To the residue thus formed in dry THF (30 mL) was added *n*BuLi in hexanes (2.5 M, 10.4 mL, 26 mmol) at −78°C. After stirring for 30 min at −78°C, ethylene oxide (2.0 mL, 40 mmol) was added, and the reaction mixture was warmed to 23°C overnight. It was quenched with saturated aqueous $NH_4Cl$, extracted with ether, washed with brine, and then dried over $MgSO_4$. Concentration afforded the desired alcohol, which was directly used in the following step. Protection with TBDPSCl according to the procedure used above afforded **21** (5.3 g, 74%, two steps) as a colorless oil. $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 1.14$ (s, 9H), 1.64 (s, 3H), 2.35–2.45 (m, 2H), 2.77 (d, $J = 6.0$ Hz, 2H), 3.70–3.80 (m, 2H), 5.05–5.15 (m, 2H), 5.26 (t, $J = 1.2$ Hz, 1H), 5.80–5.90 (m, 1H), 7.40–7.50 (m, 6H), 7.70–7.80 ppm (m, 4H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta = 16.11$, 19.20, 26.83 (3C), 31.61, 44.15, 63.69, 115.66, 121.50, 127.59 (4C), 129.50 (2C), 134.05 (2C), 135.45, 135.59 (4C), 136.89 ppm.

**(2*R*,4*E*)-7-(*tert*-Butyldiphenylsilyloxy)-2,4-dimethyl-4-hepten-1-ol (22)**: Compound **22** was prepared according to representative procedure A, with the exception that one equivalent of isobutylaluminoxane (IBAO) and 1.0 mol% of [$ZrCl_2$\{(−)-(nmi)$_2$\}] were used to provide **22** in 78% yield. The optical purity was determined by Mosher ester analysis to be 75% *ee*. Lipase-catalyzed acetylation gave **22** (2.1 g, 53%). The optical purity was determined by Mosher ester analysis to be >98% *ee*. $[\alpha]_D^{23} = +22.4$ ($c = 2.0$ in $CHCl_3$); $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 0.87$ (d, $J = 6.6$ Hz, 3H), 1.05–1.1 (m, 10H), 1.57 (s, 3H), 1.75–1.85 (m, 2H), 2.05–2.15 (m, 1H), 2.28 (q, $J = 6.9$ Hz, 2H), 3.40–3.55 (m, 2H), 3.66 (t, $J = 6.9$ Hz, 2H), 5.18 (t, $J = 1.2$ Hz, 1H), 7.15–7.25 (m, 6H), 7.70–7.75 ppm (m, 4H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta = 15.94$, 16.56, 19.11, 26.78 (3C), 31.52, 33.46, 44.15, 63.67, 68.24, 122.25, 127.53 (4C), 129.47 (2C), 133.93 (2C), 134.78, 135.51 ppm (4C); HRMS (EI): *m*/*z*: calcd for $C_{25}H_{37}SiO_2$: 397.2557 [$M^+$+H]; found: 397.2562.

**Compound 24**: To a solution of [$ZrCl_2Cp_2$] (190 mg, 0.65 mmol) in THF (2 mL) was added DIBAL-H (DIBAL-H = diisobutylaluminium hydride) (0.11 mL, 0.65 mmol) at 0°C. After stirring for 30 min at 0°C, a solution of **23** (234 mg, 0.6 mmol) in THF (1 mL) was added. After stirring for 2 h at 23°C, a solution of dry $ZnBr_2$ (146 mg, 0.65 mmol) in THF (1 mL) was added. After stirring for 30 min at 0°C, a solution of [$Pd(PPh_3)_4$] (29 mg, 0.025 mmol) and **20** (216 mg, 0.5 mmol) in THF (2 mL) were added. After stirring for 3 h at 23°C, the reaction mixture was quenched with saturated aqueous $NH_4Cl$, extracted with ether, washed with brine, dried over $MgSO_4$, and concentrated. Column chromatography (silica gel, hexanes/EtOAc 95:5) afforded **24** (282 mg, 81%) as a colorless oil. $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 0.09$ (s, 6H), 0.95 (s, 9H), 1.00 (d, $J = 6.9$ Hz, 3H), 1.08 (s, 9H), 1.58 (s, 3H), 1.93 (dd, $J = 13.2$, 8.7 Hz, 1H), 2.08 (s, 3H), 2.24 (s, 3H), 2.25–2.5 (m, 4H), 3.68 (t, $J = 7.2$ Hz, 2H), 3.82 (s, 3H), 4.59 (s, 2H), 5.17 (t, $J = 7.8$ Hz, 1H), 5.65 (dd, $J = 15.3$, 7.2 Hz, 1H), 5.96 (d, $J = 10.8$ Hz, 1H), 6.34 (dd, $J = 15.0$, 10.5 Hz, 1H), 6.60 (s, 1H), 7.22 (s, 1H), 7.40–7.50 (m, 6H), 7.65–7.75 ppm (m, 4H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta = -5.20$ (2C), 15.97, 16.08, 18.47, 18.89, 19.17, 19.59, 26.05 (3C), 26.83 (3C), 31.63, 34.81, 47.52, 55.36, 62.71, 63.75, 109.65, 122.42, 124.19, 124.81, 127.56 (4C), 129.36, 129.50 (2C), 130.73, 134.07 (2C), 134.69, 135.25, 135.59 (4C), 140.89, 142.78, 156.45 (2C); HRMS (EI): *m*/*z*: calcd for $C_{44}H_{64}Si_2O_3$: 696.4394 [$M^+$]; found: 696.4398.

**Compound 18**: 2-Methyl-2-butene (1 mL), followed by $NaH_2PO_4$ (83 mg, 0.6 mmol) and $NaClO_2$ (54 mg, 0.6 mmol) were added to an aldehyde (105 mg, 0.18 mmol), which was deprotected by removal of TBS with HCl (1 N) from **24** and then oxidized by Dess–Martin periodinane, in *t*BuOH (2 mL) and $H_2O$ (1 mL). After stirring overnight at 23°C, the reaction mixture was extracted with ether, washed with brine, dried over $MgSO_4$, and concentrated. Purification by column chromatography (silica gel, hexanes/EtOAc 70:30) gave **18** (96 mg, 89%) as a white solid. $[\alpha]_D^{23} = +2.7$ ($c = 2.0$ in $CHCl_3$); $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 1.03$ (d, $J = 6.6$ Hz, 3H), 1.10 (s, 9H), 1.61 (s, 3H), 1.95 (dd, $J = 13.5$, 8.7 Hz, 1H), 2.14 (s, 3H), 2.26 (s, 3H), 2.30–2.50 (m, 4H), 3.71 (t, $J = 6.6$ Hz, 2H), 3.89

(s, 3H), 5.21 (t, $J$=7.2 Hz, 1H), 5.72 (dd, $J$=15.0, 6.9 Hz, 1H), 6.00 (d, $J$=10.5 Hz, 1H), 6.39 (dd, $J$=15.0, 10.5 Hz, 1H), 6.67 (s, 1H), 7.20–7.30 (m, 6H), 7.70–7.80 (m, 4H), 7.87 ppm (s, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$=15.69, 16.03, 19.00, 19.14, 19.39, 26.83 (3C), 31.61, 34.64, 47.47, 55.47, 63.75, 111.33, 119.14, 122.45, 124.39, 124.95, 127.39, 127.56 (3C), 129.47 (2C), 133.74, 134.02 (2C), 135.22, 135.56 (4C), 137.53, 140.90, 148.39, 160.97, 172.56 ppm; MS (70 eV, EI): $m/z$ (%): 596 (11) [$M^+$], 539 (34), 461 (22), 259 (100); HRMS (EI): $m/z$: calcd for $C_{38}H_{48}Si_2O_4$: 596.3322 [$M^+$]; found: 596.3325.

**(1*E*)-1-Iodo-2-methyl-1,4-pentadiene (26)**: This Compound was prepared according to representative procedure C in absence of $H_2O$ (MAO).[21] Yield: 72%; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$=1.83 (s, 3H), 2.90–2.95 (m, 2H), 5.00–5.10 (m, 2H), 5.70–5.85 (m, 1H), 5.95 ppm (q, $J$=1.2 Hz, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$=23.85, 43.59, 75.91, 117.07, 134.78, 146.04 ppm.

**(2*S*)-2-Methyl-5-triisopropylsilyl-4-pentyn-1-ol (28b)**: The title compound was prepared according to representative procedure A except that 0.5 mol% of [$ZrCl_2$[(+)-(nmi)$_2$]] and 20 mol% of MAO were used. The product was formed in 85% yield with an optical purity, as determined by Mosher ester analysis of the hydrogenated product, of 73% *ee*. Lipase-catalyzed acetylation afforded pure **28b** in 63% yield with an optical purity, as determined by Mosher ester analysis of the hydrogenated product, of 97% *ee*. $[\alpha]_D^{23}$=+7.8 ($c$=1.5 in $CHCl_3$); $^1$H NMR (300 MHz, $CDCl_3$): $\delta$=0.99 (d, $J$=6.9 Hz, 3H), 1.00–1.15 (m, 21H), 1.8–1.95 (m, 1H), 2.25–2.35 (m, 2H), 2.58 (br s, 1H), 3.53 ppm (br s, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$=11.22 (3C), 16.02, 18.52 (6C), 23.69, 35.17, 66.89, 81.66, 106.87 ppm; MS (70 eV, EI): $m/z$ (%): 255 (3) [$M^+$+H], 253 (6), 211 (100), 157 (37); HRMS (EI): $m/z$: calcd for $C_{15}H_{31}SiO$: 255.2139 [$M^+$+H]; found: 255.2143.

**(2*S*)-2-Methyl-4-pentyn-1-ol (29)**: $K_2CO_3$ (62 mg, 0.45 mmol) was added to a solution of **27a** (255 mg, 1.5 mmol) in MeOH (4 mL). After stirring overnight at 23°C, the reaction mixture was quenched with water, extracted with ether, washed with brine, dried over $MgSO_4$, and concentrated. Column chromatography (silica gel, hexanes/$Et_2O$ 70:30) provided **29** (132 mg, 90%) as a colorless oil. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$=1.01 (d, $J$=7.2 Hz, 3H), 1.80–1.95 (m, 1H), 2.00 (t, $J$=3.0 Hz, 1H), 2.20–2.50 (m, 3H), 3.55 ppm (d, $J$=6.3 Hz, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$=15.94, 22.09, 34.75, 66.53, 69.48, 82.59 ppm.

**(2*S*,4*E*)-2,4-Dimethyl-5-iodo-4-peten-1-ol (27)**: This compound was prepared from **29** according to representative procedure C to provide **27** in 88% yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$=0.88 (d, $J$=6.6 Hz, 3H), 1.75–1.90 (m, 1H), 1.83 (s, 3H), 2.02 (dd, $J$=13.5, 8.4 Hz, 1H), 2.36 (dd, $J$=13.5, 6.6 Hz, 1H), 3.40–3.50 (m, 2H), 5.90 ppm (q, $J$=1.2 Hz, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$=16.27, 23.71, 33.70, 43.53, 67.51, 75.60, 146.49 ppm.

**Compound 33**: This compound was prepared according to Brown's crotylboration procedure[22] to give **33** in 75% yield (dr=92:8, as determined by $^{13}$C NMR spectroscopy). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$=1.00–1.15 (m, 27H), 1.75–1.90 (m, 2H), 2.30–2.50 (m, 3H), 3.25–3.35 (m, 1H), 5.05–5.20 (m, 2H), 5.75–5.90 ppm (m, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$=11.28 (3C), 16.53, 17.37, 18.58 (6C), 22.73, 35.73, 40.51, 78.18, 81.60, 107.66, 116.19, 139.24 ppm.

**(1*E*,4*S*,6*R*)-1-Iodo-5-(*tert*-butyldimethylsilyloxy)-2,4,6-trimethyl-1,7-octadiene (34)**: Lutidine (0.8 mL, 7.0 mmol) and *tert*-butyldimethylsilyl triflate (TBSOTf) (1.4 mL, 6.0 mmol) were added to a solution of **31** (1.23 g, 4.2 mmol) in $CH_2Cl_2$ (8 mL) at 0°C. After stirring for 2 h at 23°C, the reaction mixture was quenched with saturated aqueous $NH_4Cl$, extracted with ether, washed with brine, dried over $MgSO_4$, and concentrated. Column chromatography (silica gel, hexanes/$Et_2O$ 95:5) provided **34** (1.68 g, 98%). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$=0.06 (s, 3H), 0.07 (s, 3H), 0.79 (d, $J$=6.9 Hz, 3H), 0.93 (s, 9H), 1.03 (d, $J$=6.9 Hz, 3H), 1.80 (s, 3H), 1.75–1.85 (m, 1H), 1.95 (dd, $J$=13.5, 10.5 Hz, 1H), 2.35–2.50 (m, 2H), 3.35 (dd, $J$=5.7, 3.3 Hz, 1H), 4.95–5.05 (m, 2H), 5.84 (s, 1H), 5.90 ppm (ddd, $J$=17.4, 10.2, 7.8 Hz, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$=−3.80, −3.63, 16.31, 18.33, 23.57, 26.13 (3C), 35.37, 42.05, 43.00 (2C), 75.09, 79.92, 114.00, 141.43, 147.16 ppm; MS (70 eV, EI): $m/z$ (%): 409 (3), 393 (5), 353 (9), 149 (100); HRMS (EI): $m/z$: calcd for $C_{13}H_{34}SiIO$: 409.1418 [$M^+$+H]; found: 409.1423.

**Compound 35**: NMO (0.8 mL, 3.0 mmol) and $OsO_4$ (80 μL, 0.01 mmol) were added to a solution of **34** (409 mg, 1 mmol) in acetone (8 mL) and $H_2O$ (2 mL). After stirring for 6 h at 23°C, the reaction mixture was quenched with aqueous $Na_2S_2O_3$, extracted with EtOAc, washed with brine, and dried over $MgSO_4$. Concentration gave the crude diol. To a solution of the crude diol obtained above in THF (4 mL) and $H_2O$ (1 mL) was added $NaIO_4$ (320 mg, 1.5 mmol). After stirring for 2 h at 23°C, the reaction was quenched with aqueous $Na_2S_2O_3$, extracted with ether, washed with brine, dried over $MgSO_4$, and concentrated. Column chromatography (silica gel, hexanes/EtOAc 95:5) provided **35** (295 mg, 71%) as a colorless oil. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$=0.065 (s, 3H), 0.071 (s, 3H), 0.82 (d, $J$=6.6 Hz, 3H), 0.89 (s, 9H), 1.11 (d, $J$=6.9 Hz, 3H), 1.80 (d, $J$=1.2 Hz, 3H), 1.85–2.05 (m, 2H), 2.35–2.60 (m, 2H), 3.70–3.75 (m, 1H), 5.88 (s, 1H), 9.77 ppm (d, $J$=2.4 Hz, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$=−4.33, −4.19, 12.04, 15.32, 18.13, 23.58, 25.85 (3C), 36.10, 42.95, 49.54, 75.88, 77.90, 146.15, 204.59 ppm.

**Compound 36**: This compound was prepared by a literature method[6f,h] to give **36** in 89% yield. $[\alpha]_D^{23}$=+27.3 ($c$=1.1 in $CHCl_3$); $^1$H NMR (300 MHz, $CDCl_3$): $\delta$=0.038 (s, 3H), 0.043 (s, 3H), 0.76 (d, $J$=6.6 Hz, 3H), 0.90 (s, 9H), 0.98 (d, $J$=6.9 Hz, 3H), 1.27 (t, $J$=6.9 Hz, 3H), 1.75–1.80 (m, 1H), 1.78 (d, $J$=1.2 Hz, 3H), 1.83 (d, $J$=1.5 Hz, 3H), 1.97 (dd, $J$=13.8, 10.5 Hz, 1H), 2.36 (dd, $J$=13.5, 4.5 Hz, 1H), 2.60–2.70 (m, 1H), 3.44 (t, $J$=4.2 Hz, 1H), 4.10–4.25 (m, 2H), 5.84 (s, 1H), 6.87 ppm (dd, $J$=9.9, 1.5 Hz, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$=−3.94, −3.77, 12.46, 14.17, 15.97, 18.13, 18.27, 23.55, 25.99 (3C), 35.93, 36.46, 42.58, 60.27, 75.37, 79.58, 126.21, 144.91, 146.59, 168.18 ppm.

**Compound 37**: DIBAL-H in hexanes (1.0 M, 1.0 mL, 1.0 mmol) was added to a solution of **36** (248 mg, 0.50 mmol) in dry $CH_2Cl_2$ (3 mL) at −78°C. After stirring for 30 min at −78°C, the reaction mixture was quenched with MeOH (2 mL) at −78°C, which was followed by the addition of saturated aqueous Rochelle salt and extraction with ether. This solution was then washed with brine, dried over $MgSO_4$, and concentrated. Column chromatography (silica gel, hexanes/EtOAc 70:30) afforded **37** (209 mg, 93%) as a colorless oil. $[\alpha]_D^{23}$=+8.7 ($c$=1.0 in $CHCl_3$); $^1$H NMR (300 MHz, $CDCl_3$): $\delta$=0.070 (s, 3H), 0.073 (s, 3H), 0.75 (d, $J$=7.2 Hz, 3H), 0.92 (s, 9H), 1.05 (d, $J$=7.2 Hz, 3H), 1.75 (d, $J$=1.2 Hz, 3H), 1.75–1.80 (m, 1H), 1.79 (s, 3H), 1.97 (dd, $J$=12.9, 9.9 Hz, 1H), 2.36 (dd, $J$=12.9, 4.8 Hz, 1H), 2.85–2.90 (m, 1H), 3.51 (dd, $J$=7.5, 2.7 Hz, 1H), 5.86 (s, 1H), 6.67 (dd, $J$=9.6, 1.2 Hz, 1H), 9.40 ppm (s, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$=−3.88 (2C), 9.32, 15.35, 18.21, 18.38, 23.46, 25.93 (3C), 36.15, 36.52, 43.11, 75.60, 79.16, 137.41, 146.15, 156.84, 195.27 ppm.

**Compound 25**: This compound was prepared by a literature method[6f,h] to give **25** in 87% yield. $[\alpha]_D^{23}$=+43.7 ($c$=1.1 in $CHCl_3$), $^1$H NMR (300 MHz, $CDCl_3$): $\delta$=0.05 (s, 6H), 0.75 (d, $J$=6.9 Hz, 3H), 0.92 (s, 9H), 0.98 (d, $J$=6.6 Hz, 3H), 1.70–1.85 (m, 1H), 1.79 (s, 3H), 1.85–1.95 (m, 1H), 1.97 (d, $J$=1.2 Hz, 3H), 2.35–2.45 (m, 1H), 2.65–2.75 (m, 1H), 3.41 (dd, $J$=4.8, 2.7 Hz, 1H), 3.66 (s, 3H), 3.80 (s, 3H), 5.84 (s, 1H), 5.93 (d, $J$=9.3 Hz, 1H), 6.60 ppm (s, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$=−3.80, −3.74, 14.76, 15.88, 18.36, 18.72, 23.58, 26.10 (3C), 35.96, 36.15, 43.12, 51.96, 60.27, 75.29, 79.78, 129.89, 130.00, 141.91, 142.66, 146.85, 165.49 ppm; HRMS (ESI): $m/z$: calcd for $C_{23}H_{41}SiKO_4$: 575.1450 [$M^+$+K]; found: 575.1453.

## Acknowledgements

We thank the National Institutes of Health (GM 36792), the National Science Foundation (CHE-0309613), and Purdue University for their support of this research. Earlier related studies by Dr. S. Huo are gratefully acknowledged.

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Received: September 24, 2007
Published online: October 30, 2007

  