Journal of the Korean Chemical Society
1995, *Vol. 39, No. 2*
Printed in the Republic of Korea

항암작용 가능성이 있는 10-Membered Enediyne의 선구물질인 14-Membered Phenylthio Enediyne Lactone의 합성

金 基 棟
상지대학교 자연과학대학 화학과
(1994. 9. 23 접수)

Synthesis of 14-Membered Phenylthio Enediyne Lactone : A Precursor of the Potential Enediyne Antitumor Antibiotics

Kee Dong Kim
Department of Chemistry, Sangji University, Wonju 220-702, Korea
(Received September 23, 1994)

요 약. 본 연구에서는 항암제로서의 가능성이 있는 10-membered enediyne(**6**)의 선구물질로 사용될 수 있는 14-membered phenylthio enediyne lactone을 성공적으로 합성할 수 있었다. 14-membered lactone은 Ireland-Claisen rearrangement에 의해 10-membered enediyne(**11**)으로 변환되며 이 물질(**11**)은 최종물질(**8**)로 전환될 수 있을 것으로 예상된다. 이 14-membered enediyned lactone(**23**)은 DCC/PTSA/Pyridine 하에 enediyne hydroxy acid(**22**)의 락톤화 반응에 의해 합성되었다. Enediyne hydroxy acid는 Pd(0) 촉매하에 methyl pentynoate(**19**)와 enyne alcohol(**17**)을 *cis*-1,2-dichloroethylene과 연속적으로 coupling 반응을 하여 좋은 수득율로 얻을 수 있었다. 그 때 필요한 enyne alcohol(**17**)은 vinyltin(**12**)을 출발물질로 하여 성공적으로 얻을 수 있었다.

ABSTRACT. Phenylthio substituted 14-membered lactone(**23**) which can serve as a precursor of a potential antitumor antibiotics (**6**), was successfully prepared. The synthesis of the lactone was accomplished via lactonization of the corresponding enediyne hydroxy acid (**22**). This hydroxy acid was derived from Pd(0)-catalyzed coupling reaction of methyl pentynoate and *cis*-1,2-dichloroethylene followed by another Pd(0)-catalyzed coupling reaction of the resulting methyl chloroenyne ester (**20**) and enyneol (**17**). The required enyne alcohol was successfully synthesized from vinyltin compound (**12**) in good overall yield.

INTRODUCTION

In 1987 the Lederle[1] and Bristol-Myers[2] groups reported the unprecedented structures of calicheamicinγ1I (**1**), esperamicin A (**2**) (*Fig.* 1). These natural products were isolated from fermentation products of *Micromonospora echinospora* ssp. *calichensis* and cultures of *Actinomadura verrucosospora* BBM 1675 respectively. At present, these compounds are the most potent antitumor antibiotics known, being approximatly 1000 times more active than adriamycin, a clinically useful antitumor antibiotics, when tested in murin tumor models, and represent a new class of natural products based upon the (Z)-enediyne functionality.

The proposed mechanism of these antitumor antibiotics against tumor DNA is shown at *Scheme* 1. The trisulfide is cleaved by nucleophilic attack at the central sulfide atom to give thiol (or thiolate), which can add in a Michael fashion to C-1 to give the dihydrothiophene derivative.[1,2] The resulting hybridization change at C-1 from trigonal (sp^2) to tetrahedral (sp^3) brings about a reduction

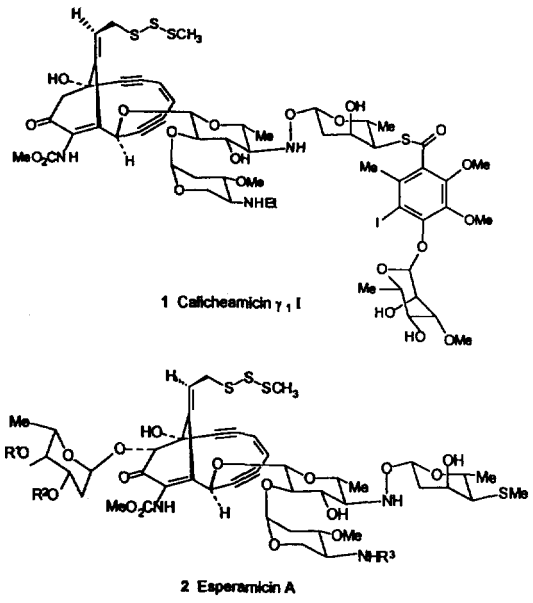
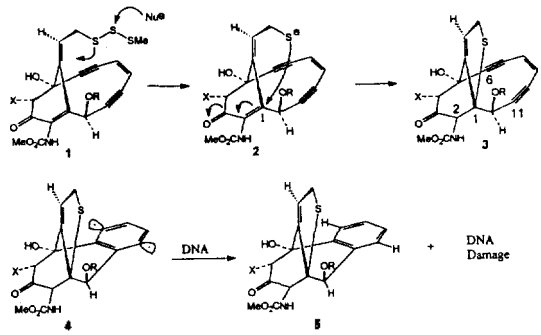


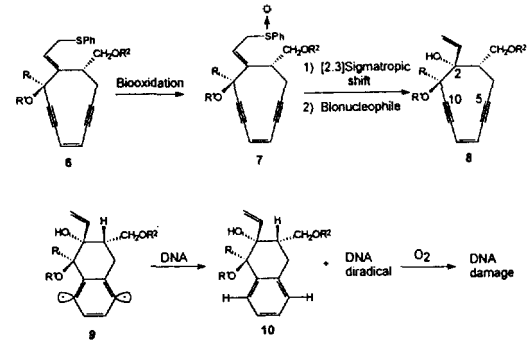
Fig. 1.

of the C-6/C-11 distance from 3.35 to 3.16 Å, thereby causing spontaneous cycloaromatization at ambient temperature to produce 1,4-diyl (**4**), a reaction known ass the Bergman cyclization.[3] Studies on the interaction of **1** with DNA suggested that it binds into the minor groove and the corresponding diyl can abstract a 5'-hydrogen from the sugar phosphate backbond of DNA which ultimatly results in strand scission.

Intrigued by the fascinating mode of action of the enediyne antitumor antibiotics, particulary the role of the enediyne "warhead" as shown in *Scheme* 1, we designed allylic sulfide (**6**) as a simple enediyne structure that could exhibit greater margins of therapeutic value (*Scheme* 2). Specifically, hepatic cytochrome p450-dependent oxidation of **6**[4] to enediyne sulfoxide **7** followed by a [2,3]-allyl sulfoxide-sulfenate ester rearrangement[5] of the latter and bionucleophilic attack at the intermediate sulfenate ester is expected to bring about a change of hybridization at C-2 from sp^2 to sp^3. This geometry change is expected to pull the ends C-5 and C-10 of allylic alcohol **8** closer, thereby trigerring Bergman aromatization to the diyl compound **9** which in turn can abstract hydrogen atoms from DNA to end up DNA cleavage.[6]

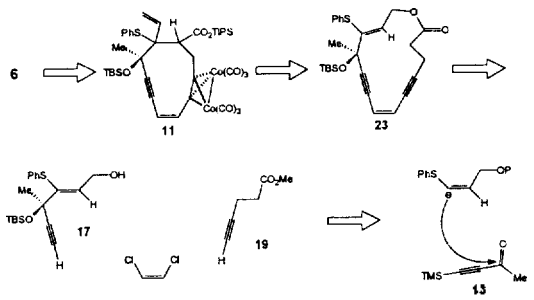


Scheme 1.



Scheme 2.

From a retosynthetic point of view, simple enediyne antibiotics **6** can be prepared from a cobalt complex of 10-membered enediyne **11** which can be achieved from 14-membered enediyne lactone **23** via an Ireland-Claisen rearrangement of the corresponding cobalt complexed ketene acetal intermediate (*Scheme* 3).[7] Consequently, developing an efficient way of construction of phenylthio substituted enediyne lactone **23** should be a primary goal of this research. Unfortunately, the only known enediyne lactone synthesis so far is reported by K. C. Nicolaou[8] employing Ramberg-Backlund reaction to make unfunctionalized one. In addition, this methodolgy is not applicable to our case due to its oxidation steps of sulfide to sulfone since the phenylthio group in our lactone should be remained intact. In this article, we report the efficient way of total synthesis of enediyne lactone **23** which will serve as a starting compound of the research described above.

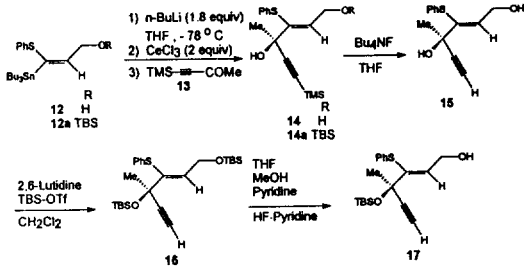


Scheme 3.

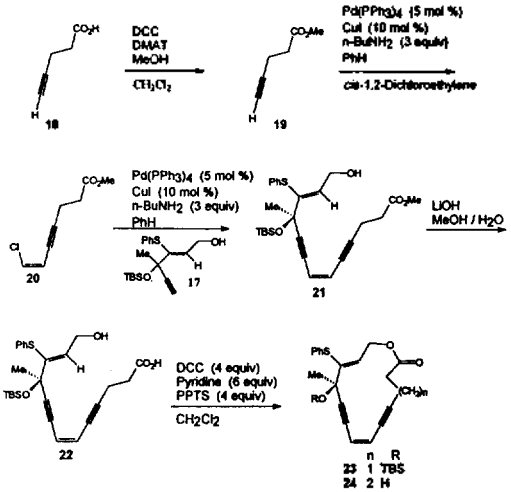
RESULTS AND DISCUSSION

It is clear that disconnection of lactone **23** to three components as shown in *Scheme* 3 provides for a convergent synthesis, since the required *cis*-1,2-dichloroethylene and methyl pentynoate are commercially and readily available respectively. Therefore, the challenging part in the synthesis of lactone **23** remains the construction of enyne alcohol derivative **17** which can in principle be derived by addition of vinyl anion derivative to alkynone **13**.

Preparation of enyne alcohol 17. As shown in *Scheme* 4, enyne alcohol **17**—the key intermediate for the synthesis of phenylthio lactone, can be prepared from vinyltin compound **12**.[9] The treatment of vinyltin compound **12** with *n*-butyllithium (2 equiv) at −78 ℃ in THF to form a dilithium species was followed by transmetallation to the dicerium reagent performed by cannulation to a suspension of pre-dried cerium chloride in THF.[10] Subsequent addition of ketone **13**[11] to the vinylcerium anion produced enyne diol **14** in 61% isolated yield from compound **12**. Most of mass balance (30%) was identified to be a destannylated olefin which was presumably generated by α-hydrogen abstraction from TMS ketone **13**. Use of the more basic dilithium anion increased the yield of the destannylated olefin significantly (80%). Performing this reaction under similar conditions employing the monocerium reagent generated from TBS ether **12a** gave rise to protected enyne alcohol **14a** with no improvement in yield (60%). This result suggested to us that protection of the hydroxyl group of **12** was not necessary. After desilylation



Scheme 4.



Scheme 5.

of **14** with fluoride anion, the resulting dihydroxy enyne **15** was transformed to the corresponding disilyl ether **16** which then was purified by flash chromatography. Selective deprotection of the primary silyl ether with HF·Pyridine in methanol/THF mixture[12] provided the desired alkyne **17** in 83% overall yield from diol **15**.

Preparation of enediyne lactone 23. Our strategy is based on macrolactonization of enediyne hydroxy acid **22**. Pd(0)-catalyzed coupling reaction, discovered by Castro and Stephens,[13] and further developed by Sonogashira,[14] between alkyne ester and commercially available *cis*-1,2-dichloroethylene furnished chloroenyne ester **20** in 93% yield accompanied with only a trace amount of homocoupled dialkyne species (*Scheme* 5). As a general comment, we found these coupling to be sensitive to dioxygen, particularly on a small scale (less than 0.5 mmol). The presence of dioxygen increased the

yield of the side product which was identified to be a homocoupled 1,3-diyne.[16] Two deoxygenation techniques, namely argon purging and several freeze-thaw cycles were considered at the outset. An investigation of their efficiency based on coupling products analysis proved that the freeze-thaw method was more efficient (82~93% yields, 1 mmol scale reaction) than the argon purging method (55~70% yields, 1 mmol scale) regardless of reaction scale. Second coupling reaction of chloroenyne ester **20** with enynol **17** (82% yield, freeze-thaw method was employed) followed by selective hydrolysis of the resulting enediyne methylester **21** with lithium hydroxide[16] furnished hydroxy acid **22**. Macrolactonization of the crude enediyne hydroxy acid according to a modified procedure[17] originally reported by Keck[18] provided 14-membered lactone **23** in good yield. Ultimate proof of macrolactone structure was obtained by X-ray analysis of desilylated 15-membered lactone **24** (72% yield from a corresponding hydroxy ester) which was obtained by macrolactonization of dihydroxy acid. This dihydroxy acid was furnished by coupling reaction between enynediol **15** and chlorooctenynoic ester followed by hydrolysis of methyl ester.

In order to synthesize enediyne lactones, various kind of lactonization strategies—such as Pd (0)-catalyzed intramolecular cyclization, acid catalyzed or DCC/DMAP mediate lactonization and lactonization via thioester formation—are employed. However, all of the methods provided desired lactones in unacceptable yields (<10%) and the only DCC/PPTS/pyridine system afforded the lactones in good yields. Since an interest about enediyne system grows, enediyne lactone should be considered as an important compound itself or an intermediate for the synthesis of various kind of highly functionalized enediyne systems through Ireland-Claisen rearrangements.

EXPERIMENTAL

^1H (270 MHz) and ^{13}C (67.9 MHz) NMR spectra were recorded on JEOL GX-270 NMR spectrometer with $CDCl_3$ as solvent and $CHCl_3$ (^1H δ 7.26) or $CDCl_3$ (^{13}C δ 77.02) as a internal standard. IR spectra were taken on Varian 300 FTIR spectrometer using sodium chloride plates. Data are reported in wavenumbers (cm^{-1}). Elemental analyses were performed by Galbraith Laboratories, Inc. at Knoxville, Tennessee. High-resolution mass spectral analyses were performed by the Mass Spectral Facility at the State University of New York at Stony Brook. Melting points were taken on MEL-TEMP apparatus and are uncorrected. All boiling points are uncorrected.

THF and benzene were distilled from sodium benzophenone ketyl. Methylene chloride was distilled from calcium hydride under argon prior to use. Other reagents were purified by procedure described in the literature.[19] All reagents were purchased from Aldrich Chemical Co. and used directly.

(2*Z*)-4-Methyl-6-trimethylsilyl-3-phenylthiohexen-5-yne-1,4-diol (14). In a flame dried 50 mL round bottomed flask equipped with a magnetic stirrer and nitorgen inlet were placed 3-phenylthio-3-tributylstannyl-(2*E*)-propenol[9] (**12**, 3 g, 6.6 mmol) and 25 mL of dry THF. The solution was cooled to −20 ℃ and 8 mL of *n*-BuLi (1.5 M in hexane, 12 mmol, 1.8 equiv) was added dropwise with stirring over a 5 min period under nitrogen. After stirring for 1 h at this temperature, the mixture was rapidly cannulated to a suspension of cerium chloride (4.92 g, 13.2 mmol, 2 equiv of $CeCl_3 \cdot 7H_2O$, dried for 3 h at 145 ℃ and 0.1 mmHg) in THF (35 mL). The reaction mixture was stirred for 1 h, treated with 4-trimethylsilyl-3-butyn-2-one[10] (**13**, 1.2 g, 8.6 mol, 1.3 equiv), allowed to stir for 20 min at that temperature, and then warmed to room temperature. After stirring for 1 h, the reaction mixture was quenched with saturated aqueous ammonium chloride (60 mL) and extracted with diethyl ether (2×60 mL). The combined organic extracts were washed with brine (150 mL), dried over anhydrous magnesium sulfate and evaporated under reduced pressure. The dark brown residue was purified by gradient chromatography with diethyl ether/hexane to afford **14** as a dark yellow oil (1.24 g, 61%): R_f (75% diethyl ether/25% hexane) 0.30.

^{1}H NMR ($CDCl_3$): δ 7.17~6.98 (m, 5H), 6.69 (t, J=5.6 Hz, 1 H), 4.13 (d, J=5.3 Hz, 2 H), 1.60 (s, 3H), 0.00 (s, 9H); ^{13}C NMR ($CDCl_3$): δ 136.4, 136.3, 129.0, 128.3, 127.0, 125.6, 107.0, 89.6, 71.4, 61.3, 29.1, −0.28; IR (neat): 3340, 2284 cm^{-1}.

(2*Z*)-4-Methyl-3-phenylthiohexen-5-yne-1,4-diol (15). To 100 mL round bottomed flask were added compound **14** (4 g, 13.1 mmol) and 20 mL of THF. The solution was cooled to 0 ℃ and treated with tetrabutylammonium fluoride (1 M in THF, 19.6 mL, 19.6 mmol, 1.5 equiv). After 15 min, the reaction mixture was poured into water (50 mL) and extracted with diethyl ether (4×40 mL). The combined organic layer was washed with brine (150 mL), dried over anhydrous magnesium sulfate and evaporated under reduced pressure. The crude product was purified by flash chromatography on silica gel with diethyl ether/hexane to furnish **15** (2.5 g, 82%) as a dark brown solid. An analytical sample was obtained by recrystallization from diethyl ether/hexane providing a light brown powder: mp 138~141 ℃, R_f (75% diethyl ether/25% hexane) 0.25.

^{1}H NMR ($CDCl_3$): δ 7.19~7.02 (m, 5H), 6.77 (t, J=5.7 Hz, 1 H), 4.18 (d, J=5.3 Hz, 2 H), 2.64 (s, 1 H), 2.48 (s, 1 H), 2.07 (s, 1 H), 1.63 (s, 1 H); IR (KBr): 3342, 2281 cm^{-1}.

(2*Z*)-4-[*tert*-Butyldimethylsilyl)oxy]-4-methyl-3-phenylthiohexen-5-yn-1-ol (17). A 50 mL round bottomed flask fitted with a magnetic stirrer was charged with enyne diol **15** (1 g, 4.3 mmol), freshly distilled methylene chloride (20 mL) and 2,6-lutidine (2.5 mL, 25.6 mmol, 6 equiv). The mixture was gently stirred at room temperature until the suspension became a light clear brown solution. To this solution was added TBS-OTf (2.5 mL, 10.7 mmol, 2.5 equiv) and the resulting solution was stirred at room temperature for 1 h. The reaction mixture was poured into dilute ice-cold HCl solution (50 mL, 0.5 N) and extracted with diethyl ether (2×40 mL). The combined organic layer was washed successively with saturated aqueous sodium bicarbonate (40 mL), water (40 mL), and brine (80 mL), dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The residue was purified by passing through a short silica gel column with hexane to furnish **16** as a light yellow oil in quantitative yield (1.98 g). The resulting disilyl ether was used for selective desilylation of the primary silyl ether without further purification.

To a 100 mL round bottomed flask equipped with a magnetic stirrer and drying tube were added methanol (20 mL), pyridine (10.3 mg, 10.5 mL, 130 mmol, 60 equiv), THF (10.6 mL, 130 mmol, 60 equiv) and hydrogen fluoride-pyridine (70% HF in pyridine, 1.24 mL, 43.2 mmol, 20 equiv). To the resulting solution was added dropwise disilyl ether **16** (1 g, 2.16 mmol) in 10 mL of methanol and the reaction mixture was stirred 3 h at room temperature. After most of solvent were evaporated under reduced pressure, the residual liquid was poured into dilute ice-cold HCl solution (70 mL, 2 N) and extracted with diethyl ether (3×70 mL). The combined ether layer was washed successively with saturated aqueous sodium bicarbonate (150 mL), water (150 mL), brine (250 mL), and dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure to provide a brown oily residue. This residue was purified by flash chromatography using 20% diethyl ether/80% hexane as the eluting solvent to give **17** as a light yellow oil in 83% yield (1.24 g) from **15**: R_f (50% methylene chloride/7.5% diethyl ether/42.5% hexane) 0.50.

^{1}H NMR ($CDCl_3$): δ 7.22~7.08 (m, 5 H), 6.83 (t, J=5.9 Hz, 1 H), 4.20 (s, 2 H), 2.59 (s, 1 H), 1.70 (s, 3 H), 0.90 (s, 9 H), 0.25 (s, 3 H), 0.21 (s, 3 H); ^{13}C NMR ($CDCl_3$): δ 138.3, 136.9, 136.5, 129.0, 126.8, 125.4, 86.1, 74.7, 72.5, 61.5, 31.1, 25.8, 18.3, −2.8, −3.1; IR (neat): 3306, 2112 cm^{-1}.

Methyl 5-pentynoate (19). In a 50 mL round bottomed flask equipped with a magnetic stirrer and drying tube were dissolved 4-pentynoic acid (980 mg, 10 mmol), a catalytic amount of a dimethylaminopyridine (DMAP, 80 mg, 6.6 mol%) and methanol (6 mL) in methylene chloride (10 mL). To the resulting solution was added a solution of DCC (2.3 g, 11 mmol, 1.1 equiv) dissolved in methylene chloride (10 mL) dropwise and the reaction mixture was stirred for 3 h. The resulting white suspension was poured into dilute HCl solution

(50 mL, 1 N) and extracted with diethyl ether (2×50 mL). The combined organic layer was washed successively with saturated aqueous sodium bicarbonate (100 mL), water (100 mL), brine (100 mL), and dried over anhydrous magnesium sulfate. On removal of the solvent, a yellow oil was obtained which was purified by distillation under reduced pressure to afford methyl 4-pentynoate (**19**) in 72% yield (810 mg) as a colorless liquid (65~68 ℃ at 18 mmHg).

^{1}H NMR ($CDCl_3$): δ 3.69 (s, 3 H), 2.52 (m, 4 H), 1.98 (t, J=2.3 Hz, 1 H); IR (neat): 3297, 2963, 2121, 1734 cm^{-1}.

Methyl (6*Z*)-7-chlorohepten-4-ynoate (20). To a flame dried 10 mL conical flask equipped with a magnetic stirrer and nitrogen inlet (through septum cap) were added alkyne ester **19** (560 mg, 5.0 mmol) and freshly distilled benzene (5 mL).

In a flame dried 25 mL round bottomed flask equipped with a magnetic stirrer and nitrogen inlet were placed *cis*-1,2-dichloroethylene (2.4 g, 20 mmol, 5 equiv), freshly distilled benzene (5 mL), palladium tetrakistriphenylphosphine (Pd(0) 289 mg, 5 mol%), copper iodide (95 mg, 10 mol%) and *n*-butylamine (1.5 mL, 15 mmol), After degassing by four freeze-thaw cycles, the mixture was gently stirred at room temperature until the suspension became a pale yellowish clear solution. The terminal alkyne solution was also degased by four freeze-thaw cycles and cannulated to the yellowish solution of vinyl chloride and catalysts mixture while stirring was continued over a period of 20 min at room temperature. The resulting reaction mixture was then allowed to stir for 12 h under nitrogen atmosphere. The reaction solution was poured into saturated aqueous ammonium chloride (40 mL) and extracted with diethyl ether (3×40 mL). The combined organic layer was washed with brine, dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The residual blackish residue was purified by gradient chromatography with diethyl ether/hexane to afford chloroenyne ester **20** as a light yellowish oil in 93% yield (801 mg) from alkyne **19**: R_f (25% diethyl ether/75% hexane) 0.15.

^{1}H NMR ($CDCl_3$); δ 6.31 (d, J=7.3 Hz, 1 H), 6.83 (dt, J=7.3, 2.2 Hz, 1 H), 3.67 (s, 3 H), 2.64 (m, 4 H); IR (neat): 3087, 2216, 1736 cm^{-1}.

Methyl(6*Z*,11*Z*)-10-[(*tert*-butyldimethylsilyl)oxy]-13-hydroxy-10-methyl-11-phenylthiotridecadiene-4,8-diynoate (21). To a flame dried 10 mL conical flask equipped with a magnetic stirrer and nitrogen inlet were added terminal alkyne **17** (2.4 g, 7 mmol) and freshly distilled benzene (4 mL).

In a flame dried 25 mL round bottomed flask equipped with a magnetic stirrer and nitrogen inlet were placed chloroenyne ester **20** (941 mg, 8.4 mmol, 1.2 equiv), freshly distilled benzene (4 mL), Pd(0) (404 mg, 5 mol%), copper iodide (133 mg, 10 mmol%) and *n*-butylamine (2.1 mL, 21 mmol, 3 equiv). After degassing by four freeze-thaw cycles, the mixture was gently stirred at room temperature until the suspension became a pale yellowish clear solution. After degassing four freeze-thaw cycles, the terminal alkyne solution was cannualated to the yellowish solution of vinyl chloride and catalysts mixture while stirring was continued over a period of 20 min at room temperature. The resulting reaction mixture was then allowed to stir for 12 h under nitrogen atmosphere. The reaction solution was poured into saturated aqueous ammonium chloride (50 mL) and extracted with diethyl ether (3×50 mL). The combined organic layer was washed with brine, dried under anhydrous magnesium sulfate and concentrated under reduced pressure. The blackish residue was purified by gradient chromatography with diethyl ether/hexane to afford enediyne **21** as a light yellow oil in 82% yield (2.8 g) from alkyne **17**: R_f (50% diethyl ether/50% hexane) 0.20.

^{1}H NMR ($CDCl_3$): δ 7.19~6.96 (m, 5 H), 6.79 (t, J=5.7 Hz, 1 H), 5.70 (dt, J=11.0, 2.0 Hz, 1 H), 5.62 (d, J=11.0 Hz, 1 H), 4.11 (s, 2 H), 3.59 (s, 3 H), 2.6~2.44 (m, 4 H), 1.63 (s, 3 H), 0.79 (s, 9 H), 0.14 (s, 3 H), 0.10 (s, 3 H), ^{13}C NMR ($CDCl_3$): δ 172.4, 138.5, 137.2, 136.8, 128.9, 126.9, 125.3, 120.4, 118.1, 98.4, 96.3, 84.0, 78.8, 73.1, 61.6, 51.9, 33.2, 31.2, 25.9, 18.3, 15.7, −2.9, −3.1; IR (neat): 3426, 2209, 1741 cm^{-1}; Anal. Calcd for $C_{27}H_{36}O_4SSi$: C, 66.91; H, 7.49; S, 6.60. Found: C, 67.18; H, 7.74; S, 6.25.

(6*Z*,11*Z*)-10-[(*tert*-butyldimethylsilyl)oxy]-10-methyl-11-phenylthiotridecadiene-4,8-diynoate

(23). A 500 mL round bottomed flask equipped with a magnetic stirrer was charged with 45 mL of distilled water and 60 mL of methanol. To the resulting solution was added dropwise *n*-butyllithium (1.45 M in hexane, 12.8 mL, 18.5 mmol. 5 equiv) with stirring. To this LiOH solution was added dropwise hydroxy ester **21** (1.8 g, 3.7 mmol) in methanol (75 mL) at room temperature. The reaction mixture was concentrated to approximatly 50 mL and the residual liquid was quenched with HCl solution (50 mL, 1 N), and extracted with diethyl ether (3×50 mL). The combined ether layer was washed with water (2×50 mL), brine (2×50 mL), dried over anhydrous magnesium sulfate and concentrated in vacuo to furnish hydroxy acid **22** in quantitative yield (1.8 g). The crude hydroxy acid was used for the macrolactonization without further purification.

A flame dried 200 mL round bottomed flask equipped with a magnetic stirrer, nitrogen inlet and syringe pump inlet was charged with ethanol free chloroform (34 mL), DCC (3.1 g, 14.8 mmol, 4 equiv), pyridine (1.8 mL, 22.3 mmol, 6 equiv), and pyridinium *para*-toluenesulfonate (3.9 g, 14.9 mmol, 4 equiv). A solution of hydroxy acid (**22**, 1.7 g, 3.7 mmol) in dry chloroform (50 mL) was infused via a syringe pump over 24 h. After addition was complete, the syringe apparatus was removed and the reaction was allowed to stir for 30 min. Methanol (3 mL) and acetic acid (2 mL) were added to the reaction flask and stirring was continued for 30 min, after which time no DCC was detected by TLC analysis. The mixture was concentrated to about 30 mL, diluted with 30 mL of diethyl ether, filtered and concentrated. The residual oil was purified by gradient chromatography with diethyl ether/hexane to furnish the desired macrolactone **23** in 82% overall yield (1.4 g) from methyl ester **21**: R_f (10% diethyl ether/90% hexane) 0.50.

^{1}H NMR ($CDCl_3$): δ 7.20~6.98 (m, 6H), 5.73 (d, J=11.9 Hz, 1 H), 5.70 (d, J=11.0 Hz, 1 H), 4.59 (dd, J=14.5, 6.4 Hz, 1 H), 4.44 (dd, J=14.5, 3.5 Hz, 1 H), 2.69~2.37 (m, 4 H), 1.64 (s, 3 H), 0.79 (s, 9 H), 0.11 (s, 3 H), 0.07 (s, 3 H); ^{13}C NMR ($CDCl_3$): δ 171.3, 139.5, 136.4, 135.2, 129.0, 127.1, 125.4, 120.9, 117.5, 97.4, 95.7, 85.3, 79.2, 73.1, 62.9, 33.2, 30.6, 25.7, 18.2, 16.9, −3.1, −3.5; IR (neat): 2201, 1744 cm^{-1}; HRMS Calcd for $C_{26}H_{32}O_3SSi$ 452.1841, Found 452.1836.

ACKNOWLEDGEMENT

I wish to thank to all the faculty members of chemistry department of West Virginia University for letting me use their laboratory and facilities to perform this work. Especially I am grateful to Dr. Magriotis in W.V.U. and Dr. Johnson in S.U.N.Y. at Stony Brook for their valuable advices in chemistry and spectroscopy analysis.

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