Pergamon

Tetrahedron Vol. 50. No. 19. pp. 5621-5632. 1994

0040-4020/94 $6.00+0.00

0040-4020(94)E0219-J

Synthetic Studies on Dynemicin A. New Quinoline Synthesis for C, D and E Rings.

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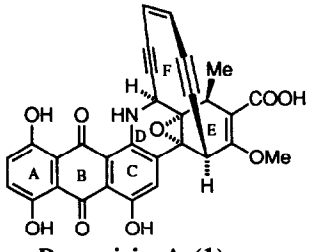
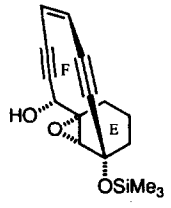
Abstract: The important intermediates for the syntheses of dynemicin A model compounds were prepared by coupling between aryltin compounds and α-bromoenone derivatives in the presence of palladium catalyst. The products were transformed under acidic conditions to substituted quinoline derivatives which contained all the carbon atoms except for the acetylenic group in E ring of dynemicin A.

Dynemicin A (**1**), a cyclic enediyne antibiotic substance isolated from *Micromonospora chersina.*, has strong antimicrobial and antitumor activity which is responsible for double strand DNA cleavage by phenylene diradical *via* Bergman cycloaromatization.[1,2] During a course of our synthetic studies on dynemicin A and its analogs,[3] we have reported the syntheses of two model compounds of dynemicin A (**Figure 1**).[4,5] One model compound **2** having no aniline moiety was inert toward Bergman reaction under acidic conditions,[4] while Bergman reaction of another compound **3** proceeded to result in DNA-cleavage in neutral media.[5] These results prompted us to synthesize potentially stronger bioactive model compounds.

This paper deals with the synthesis of important intermediates **A** and **B** for new variants of our two previously reported models (**Scheme 1**). Compound **A** contains C, D and substituted E rings in dynemicin A. Quinoline derivatives as **A** without substituents on E ring have been reported in the synthesis of enediyne compounds related to dynemicin A by Nicolaou's group.[6,7]



Dynemicin A (1)



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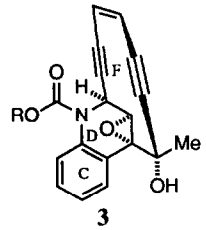

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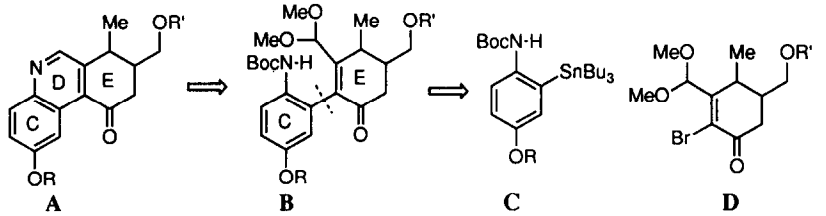
Figure 1

Synthetic plan

Our basic plan for the synthesis of **A** from **B** is outlined in **Scheme 1**. Compound **B** was expected to be produced by palladium catalyzed coupling (so called Migita-Stille coupling)[8] between an α-bromo cyclohexenone derivative **D** (contains E ring) and an aryltin compound **C** (contains C ring). Compound **B** is

a potentially useful intermediate for the aryl substituted model compound **2** according to the previously described plan.[4] Acid treatment of **B** would provided the cyclization product **A**. Compound **A** would be convertible to the compounds as **3** having cyclic enediyne ring according to the previously reported methods.[5] Palladium catalyzed coupling reaction between vinylhalides and aryltin compounds (related to those in **Scheme 1**, for example) has been known more difficult than the coupling with vinyltins.[9] In addition, α-haloenone usually exhibits low reactivity in oxidative addition of Pd(0).[10] We started from the examination of the cross-coupling between simple aryltin and α-bromoenone compounds.



A **B** **C** **D**

Scheme 1

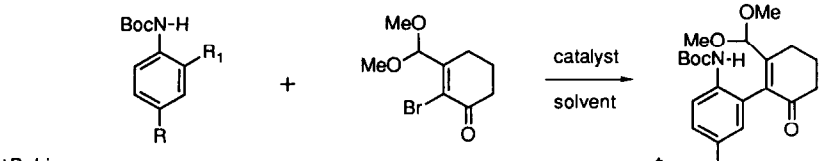
RESULTS AND DISCUSSION

Coupling of C and E rings

Aryltins **5** and **7** as coupling counterparts were prepared from *ortho* lithiation[11] of the N-Boc anilines **4**[12] and **6**[13] followed by stannylation, respectively. On the other hand, simple α-bromocyclohexenone (**8**) was prepared from 1,3-cyclohexanedione according to Horiguchi and Kuwajima's procedure.[14]

Representative results of various experiments using **8** and its coupling partner **5** are listed in **Table 1**. We found that combination of P(*o*-tol)$_3$ as a phosphine ligand and NMP (*N*-methyl-2-pyrrolidone) as a solvent gave good result (entry 4). Combination of Ph_3P and toluene showed poor reproducibility even under higher reaction temperatures (entry 1, 2) to show poor reproducibility. Other attempts such as using TFP (trifurylphosphine)[15] or conditions without ligand[9] failed to improve the yields.

Recently, Johnson and co-workers reported that α-iodoenones and organotin compounds underwent palladium catalyzed coupling with highly toxic triphenylarsine as a ligand to palladium in the presence of CuI.[16] They also described that α-bromoenone is inferior substrate (yields were less than 20 %). On the other hand, our result indicated that α-bromoenone is enough reactive toward this type of palladium catalyzed coupling using non-toxic P(*o*-tol)$_3$ in the absence of CuI. Although the coupling using **7** as a substrate diminished the yield of product **10**, using toluene as a solvent improved the yield (entry 4, 5). The same tendency was observed in the reactions between **7** and other substituted α-bromoenones (*vide infra*).



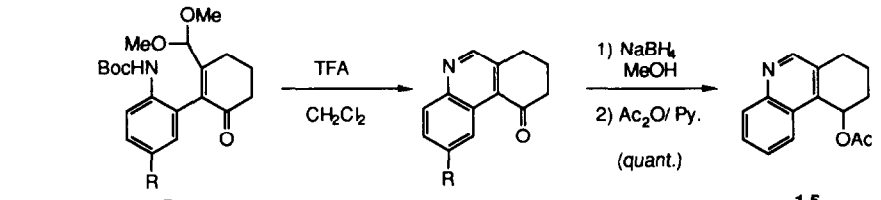
Scheme 2

Table1. Palladium Catalyzed Coupling of α-Bromoenone (8) with Aryltins.

entry	aryl tin	catalyst	solvent	temp, time	product	yield (%)
1	**5**	$Pd[Ph_3P]_4$	toluene	110 °C, 17 h	**9**	45
2	**5**	$PdCl_2[Ph_3P]_2$	toluene	110 °C, 6 h	**9**	46
3	**5**	$Pd(OAc)_2$, P(*o*-tol)$_3$	NMP	60-70 °C, 12 h	**9**	48
4	**5**	$Pd_2[dba]_3$·$CHCl_3$, P(*o*-tol)$_3$	NMP	60-70 °C, 2 h	**9**	78
5	**7**	$Pd_2[dba]_3$·$CHCl_3$, P(*o*-tol)$_3$	NMP	60-70 °C, 2.5 h	**10**	51
6	**7**	$Pd_2[dba]_3$·$CHCl_3$, P(*o*-tol)$_3$	toluene	80 °C, 2 h	**10**	70

Quinoline Ring Formation

The acetal **9** cyclized into the quinoline ring (**12**) by treatment with TFA in CH_2Cl_2 (**Scheme 3**). The ketone **12** was further reduced with $NaBH_4$ and acetylated to the acetate **15** which was identical to the spectroscopic data with one of the Nicolaou's intermediates.[6] On the other hand, the two protected phenols **10** and **11** were also converted into the corresponding quinoline derivatives **13** and **14**, respectively. Methyl ether **11** was prepared from silyl ether **10** in one step (MeI in the presence of TBAF).



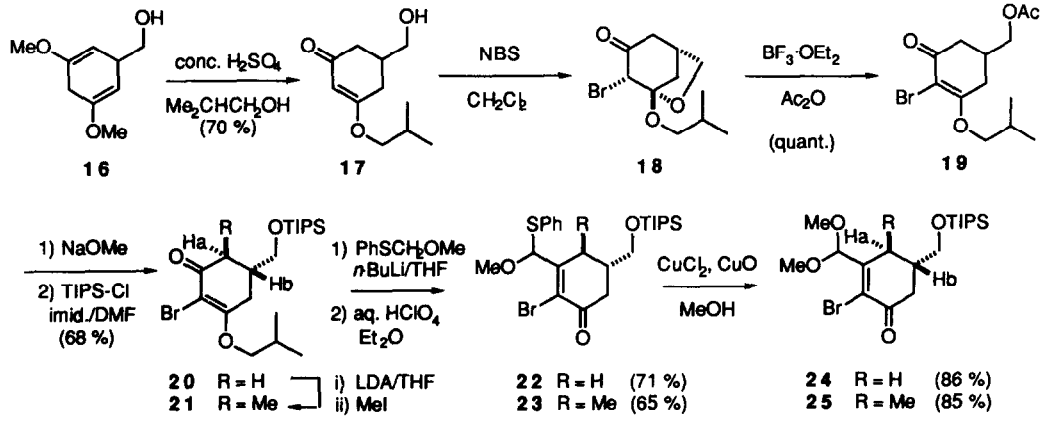
Scheme 3

Two carbon chains are necessary to the synthesis of E ring synthon for compounds **A** and **B**. For this purpose, the functionalized α-bromoenone (**25**) was designed. Its synthesis was started from the vinyl ether (**16**) prepared from gallic acid (3,4,5-trimethoxybenzoic acid) in two steps: (i) Birch reduction, (ii) $LiAlH_4$ reduction.[17] Solvolysis of **16** in isobutanol gave **17**. We initially attempted the next bromination with the TBDMS-ether of **17**, but we found this reaction being too slow to obtain the α-bromoenone such as **20** in a preparative scale. We examined the alternative route which employs direct treatment of **17** with NBS to afford bicyclic acetal **18**, and subsequent acetolysis to the enone acetate **19** with BF_3·OEt_2 in acetic anhydride.[18] The protective group in **18** was converted to TIPS ether (**19**) in two steps.

Methylation of **20** with MeI/LDA at -78 °C (Stork-Danheiser condition)[19] afforded at least 3 products and the thermodynamically stable product (**21**) was obtained by crystallization from hexane. The *trans* stereochemistry of **21** was determined by the coupling constant (*J* a-b = 10 Hz) in its ^1H NMR.

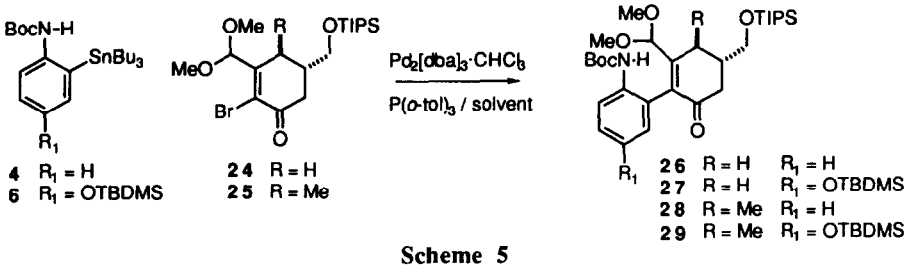
Homologation of **20** with methoxymethyl phenylsulfide[20] was followed by acid treatment to give monothioacetal (**22**). Copper catalyzed methanolysis of **22** under Mukaiyama condition[21] yielded

dimethylacetal (**24**). The homolog (**25**) was synthesized from **21** in the same way . The small coupling constant (*J* a-b = 2 Hz) of the *trans* stereochemistry in **25** will be discussed later.



Scheme 4

The palladium catalyzed coupling reaction between the two aryltin compounds (**4** and **6**) and the two homologous α-bromoenones (**24** and **25**) underwent as described before to afford the corresponding products (**Table 2**). In the case of TBDMS analog (**6**), toluene was superior over NMP as a solvent (entry 2, 3).



Scheme 5

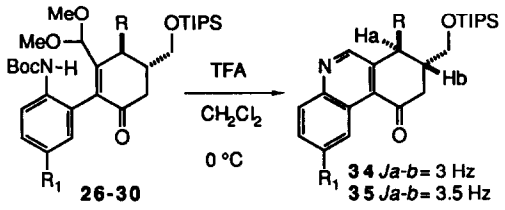
Table 2. Palladium Catalyzed Coupling Reaction Between α-Bromoenones with Aryltins.

entry	aryl tin	bromide	solvent	temp, time	product	yield (%)
1	**4**	**24**	NMP	85 °C, 1 h	**26**	80
2	**6**	**24**	NMP	85 °C, 75 min	**27**	48
3	**6**	**24**	toluene	80 °C, 40 min	**27**	70
4	**4**	**25**	NMP	70 °C, 70 min	**28**	82
5	**6**	**25**	toluene	80 °C, 2 h	**29**	48

The ^{1}H NMR spectra of all products in **Table 2** suggested that these products consist of mixtures of two compounds (ca. 1:1). This was due to the restricted rotational isomers. Acid hydrolysis of the mixture of

isomers (**26-30**) gave the corresponding single cyclization products (**31-35**). The methyl ether (**30**) prepared from **27**, was transformed to **33** in the same manner as for the synthesis of **14**.

Table 3. Quinoline Synthesis.



substrate			product	yield (%)
26	R = H	R_1 = H	**31**	89
27	R = H	R_1 = OTBDMS	**32**	88
30	R = H	R_1 = OMe	**33**	84
28	R = Me	R_1 = H	**34**	92
29	R = Me	R_1 = OTBDMS	**35**	77

In the ^{1}H NMR spectra, *J* a-b of **25** was 2 Hz which was remarkable contrast with 10 Hz for **21**. The difference of the coupling constant between **21** and **25** is rationalized by the conformational change of cyclohexenone ring, that is, methyl and hydroxymethyl substituent occupy di-*equatorial* position in **21**, while steric hindrance between Me group and dimethylacetal group in **25** gave di-*aixial* conformer (**25b**). This assumption was supported by molecular mechanics calculation using MacroModel (MM2 force field).[22,23] Calculated coupling constant (*J* a-b = 1.8 Hz) for more stable conformer (**25b**) is in good agreement with the experimental value (**Figure 2**). The corresponding coupling constants (*J* a-b) of **34** and **35** were also small (3 and 3.5 Hz, respectively) which indicated these two compounds to have a similar conformation to **25** about the cyclohexenone ring. This was also supported by the molecular mechanics calculation (see below).

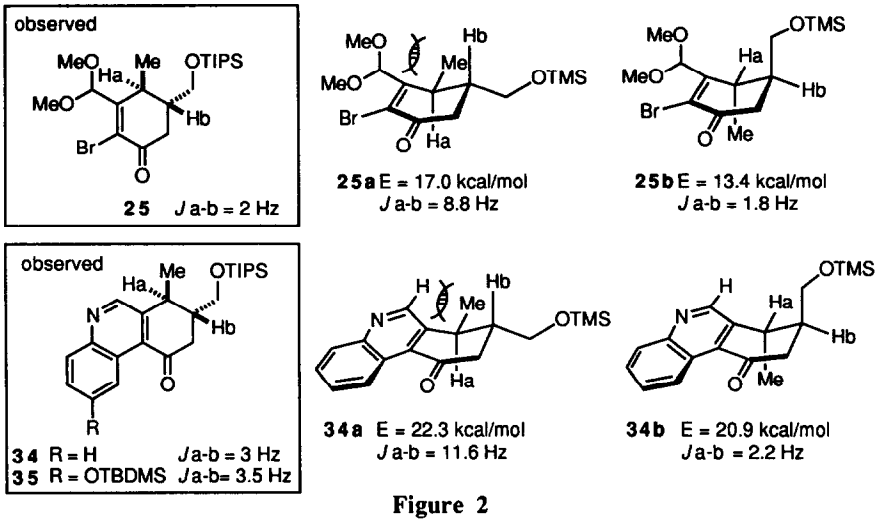


Figure 2

In summary, we have investigated the construction of C, D and E ring of dynemicin A, in particular compound **35** which has a fully functionalized carbon atom on E ring without acetylenic group. This study provided a promising method toward a wide variety of dynemicin A model compounds. Further studies are now in progress.

Experimental Section

General: Melting points were recorded on a Yanaco MP-S3 melting point apparatus and are not corrected. Infrared spectra were recorded on a JASCO FT/IR-8300 spectrophotometer and are reported in wave number (cm^{-1}). Proton nuclear magnetic resonance (^1H NMR) spectra were recorded on JEOL FX-200 (200 MHz) and JEOL EX-270 (270 MHz) spectrometers. Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a JEOL EX-270 (67.9 MHz) spectrometer. Low resolution mass spectra (EI) were recorded on a JEOL JMS-D 100 spectrometer. High resolution mass spectra (HRMS) were recorded on a JEOL DX-705L spectrometer and reported in m/z. Elemental analysis were performed by Analytical Laboratory at Faculty of Agriculture, Nagoya University, to which the authors gratefully acknowledges. Unless otherwise noted, non aqueous reaction were carried out under nitrogen or argon atmosphere. THF was distilled from potassium metal/benzophenone ketyl. Benzene was dried over Na metal and used without distillation. DMF and CH_2Cl_2 were dried over MS 4Å. Pyridine was dried over KOH and used without distillation. All other commercially available reagents were used as received.

Compound 5. To a solution of N-Boc-aniline **4** (8.00 g, 41.4 mmol) in THF (200 mL) cooled to -78 °C was added *t*-BuLi (1.65 M in hexane, 62.7 mL, 103 mmol). After stirring 35 min, the reaction mixture was warmed to -20 °C. After stirring at -20 °C for 2 h 20 min, *n*-Bu_3Sn-Cl (16.8 mL, 62.1 mmol) in THF (30 mL) was added dropwise over 30 min. After stirring at -20 °C for 1 h 15 min, the reaction mixture was poured into aq. $NaHCO_3$ solution and extracted with ether (x3). The combined organic layer was washed with water (x2) and brine (x2), dried over anhydrous Na_2SO_4, then concentrated under reduced pressure. The residue was purified by column chromatography (silica 600 g, ether/hexane = 1:20) to give **5** (8.08 g, 51 %). IR (KBr) ν_{max} 3440, 3339, 2956, 1740, 1510, 1436, 1159 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 0.89 (9H, t, *J* = 7 Hz, ($CH_3CH_2CH_2CH_2)_3Sn$), 1.06-1.14 (6H, m, CH_2 x3), 1.34 (6H, m, CH_2x3), 1.51 (9H, s, *t-Bu)*, 1.45-1.60 (6H, m, CH_2 x3), 6.28 (1H, br s, N*H*), 7.06 (1H, td, *J* = 8, 1.5 Hz, aromatic), 7.24-7.36 (2H, m, aromatic), 7.69 (1H, br d, *J* = 8 Hz, aromatic). Anal. Calcd for $C_{23}H_{41}NO_2Sn$: C, 57.28; H, 8.57; N, 2.90. Found C, 57.28; H, 9.20; N, 2.87.

Compound 6. (1) To a suspension of *p*-aminophenol (5.00 g, 45.8 mmol) in THF (50 mL) was added Boc_2O (10.9 mL, 50.4 mmol). (This reaction was exo-thermic and the starting materials became gradually soluble during the reaction). After stirring at rt for 3 h, the mixture was concentrated under reduced pressure to afford a crude product. This material was sufficiently pure for use in the next reaction. (2) The resulting residue was dissolved in DMF (10 mL) and CH_2Cl_2 (50 mL). To this solution were added TBDMS-Cl (7.59 g, 50.4 mmol) and imidazole (6.85 g, 100 mmol). After stirring at rt for 3 h, the mixture was mixed with water and extracted with ether (x3). The combined organic layer was washed with water (x2) and brine (x2), dried over anhydrous Na_2SO_4, then concentrated under reduced pressure. The residue was purified by column chromatography (silica 350 g, ether/hexane = 1:10) to give **6** (14.4 g, 97 %). Mp 90-90.5 °C. IR (KBr) ν_{max} 3344, 2963, 2860, 1705, 1507, 1256, 1168 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 0.16 (6H, s, $Si(CH_3)_3$), 0.97 (9H, s, $Si(CH_3)_3$), 1.50 (9H, s, $OC(CH_3)_3$), 6.45 (1H, br s, N*H*), 6.76 (2H, br d, *J* = 9 Hz, aromatic), 7.20 (2H, br d, *J* = 9 Hz, aromatic). ^{13}C NMR (67.9 MHz, $CDCl_3$) δ -4.5, 18.1, 25.7, 28.3, 80.1, 120.2, 131.9, 151.3, 153.0. Anal. Calcd for $C_{17}H_{29}NO_3SI$: C, 63.12; H, 9.04; N, 4.33. Found C, 63.24; H, 9.11; N, 4.35.

Compound 7. To a solution of **6** (10.0 g, 30.9 mmol) in THF (250 mL) cooled to -78 °C was added *t*-BuLi (1.65 M in hexane, 46.8 mL, 77.3 mmol) over 15 min. After stirring at -78 °C for 25 min, the mixture was stirred at -20 °C for 3 h. To this solution was added *n*-Bu_3Sn-Cl (12.5 mL, 46.3 mmol) in THF (30 mL) over 25 min. The solution was stirred at -20° C for 2 h 20 min. The mixture was poured into ice-cold aq. $NaHCO_3$ solution and extracted with ether (x3). The combined organic layer was washed with water (x2) and brine (x2), dried over anhydrous Na_2SO_4, then concentrated under reduced pressure. The residue was purified by column chromatography (silica 500 g, ether/hexane = 1:10) to give **7** (13.0 g, 71 %). IR (KBr) ν_{max} 3442, 3344, 2930, 1736, 1585, 1497, 1250, 1156 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 0.18 (6H, s, $Si(CH_3)_3$), 0.90 (9H, t, *J* = 7 Hz, CH_3CH_2 x3), 0.98 (9H, s, $SiC(CH_3)_3$), 1.04-1.12 (6H, m, CH_2 x3), 1.34 (6H, m, CH_2 x3), 1.50 (9H, s, NCO*OtBu*), 1.46-1.60 (6H, m, CH_2 x3), 6.11 (1H, br, N*H*), 6.76 (1H, dd, *J* = 8.5, 3 Hz, aromatic), 6.83 (1H, d, *J* = 3 Hz, aromatic), 7.42 (1H, br d, *J* = 8.5 Hz, aromatic). Anal. Calcd for $C_{29}H_{55}NO_3SiSn$: C, 56.87; H, 9.05; N, 2.29. Found C, 56.64; H, 9.56; N, 2.19.

Compound 9. In a dried flask were placed **8** (200 mg, 0.80 mmol), $Pd_2[dba]_3{\cdot}CHCl_3$(16.5 mg, 0.016 mmol), P(*o*-tol)$_3$ (39.0 mg, 0.128 mmol) and NMP (2 mL), and the whole mixture was degassed, covered with argon, and stirred at rt for 20 min. To this solution was added a solution of aryltin **5** (460 mg, 0.95 mmol) in NMP (3 mL). The mixture was stirred at 70 °C for 2 h. After cooled to rt, the reaction was

quenched with ice-cold $NaHCO_3$ solution, and the mixture was extracted with Et_2O (x3). The combined organic layer was washed with water (x2) and brine (x2), then concentrated under reduced pressure. The residue was purified by column chromatography (silica 25 g, ether/hexane = 1:2 → 1:1) to give **9** (225 mg, 78 %). Mp 106-107.5 °C. IR (KBr) ν_{max} 3333, 2937, 2831, 1727, 1671, 1518, 1448, 1367, 1160. ^1H NMR (270 MHz, $CDCl_3$) δ 1.46 (9H, s, *t-Bu*), 2.11 (2H, m, CH_2), 2.60 (4H, t, *J* = 6.5 Hz, CH_2 x2), 3.22 (3H, s, OCH_3), 3.26 (3H, s, OCH_3), 4.41 (1H, s, $CH(OMe)_2$), 6.26 (1H, br, N*H*), 6.94 (1H, dd, *J* = 7.5, 1.5 Hz, aromatic), 7.10 (1H, td, *J* = 7.5, 1 Hz, aromatic), 7.34 (1H, td, *J* = 8, 1.5 Hz, aromatic), 7.83 (1H, br d, *J* = 8 Hz, aromatic). ^{13}C NMR (50 MHz, $CDCl_3$) δ 22.2, 23.3, 28.3, 38.5, 55.7, 80.2, 104.3, 122.6, 123.7, 126.0, 129.1, 130.6, 135.4, 136.4, 153.2, 157.5, 199.0. MS (EI) m/z 361 (M^+). Anal. Calcd for $C_{20}H_{27}NO_5$: C, 66.46; H, 7.53; N, 3.88. Found C, 66.56; H, 7.37; N, 3.77.

Compound 10. NMP as a solvent: In a dried flask were placed bromide **8** (249 mg, 1.00 mmol), $Pd_2[dba]_3{\cdot}CHCl_3$, P(*o*-tol)$_3$ and NMP (4 mL), and the whole mixture was degassed, covered with argon, and stirred at rt for 30 min. To this solution was added aryltin **7** (918 mg, 1.50 mmol) in NMP (2.5 mL). The mixture was stirred at 75 °C for 1.5 h. After cooled to rt, the reaction was quenched with ice-cold $NaHCO_3$ solution, and the mixture was extracted with AcOEt (x3). The combined organic layer was washed with water (x2) and brine (x2), and concentrated under reduced pressure. The residue was purified by column chromatography (silica 60 g, ether/hexane = 1:3 → 1:2) to give **10** (255 mg, 52 %). Mp 103.5-105 °C. IR (KBr) ν_{max} 3409, 2931, 2860, 1723, 1674, 1517, 1164 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 0.17 (3H, s, $SiCH_3$), 0.18 (3H, s, $SiCH_3$), 0.96 (9H, s, $SiC(CH_3)_3$), 1.43 (9H, s, O-*t-Bu*), 2.10 (2H, m, CH_2), 2.58 (4H, m, CH_2x2), 3.21 (3H, s, OCH_3), 3.29 (3H, s, OCH_3), 4.48 (1H, s, $CH(OMe)_2$), 6.08 (1H, br s, N*H*), 6.47 (1H, d, *J* = 3 Hz, aromatic), 6.82 (1H, dd, *J* = 9, 3 Hz, aromatic), 7.54 (1H, br d, *J* = 9 Hz, aromatic). ^{13}C NMR (67.9 MHz, $CDCl_3$) δ -4.5, -4.4, 18.1, 22.1, 23.2, 25.6, 28.2, 38.4, 55.5, 55.6, 79.8, 104.2, 120.2, 121.9, 125.3, 128.7, 129.8, 135.5, 152.1, 153.7, 157.0, 198.8. Anal. Calcd for $C_{26}H_{41}NO_6Si$: C, 63.51; H, 8.40; N, 2.85. Found C, 63.49; H, 8.36; N, 2.66.

Toluene as a solvent: In a dried flask were placed bromide **8** (249 mg, 1.00 mmol), $Pd_2[dba]_3{\cdot}CHCl_3$, P(*o*-tol)$_3$ and toluene (4 mL), and the whole mixture was degassed by two freeze-thaw cycles, covered with argon, and stirred at rt for 2 h 30 min. To this solution was added aryltin **7** (918 mg, 1.50 mmol) in toluene (1.5 + 0.5 mL). The mixture was stirred at 80 °C for 2 h. After cooled to rt, the reaction mixture was concentrated under reduced pressure. The residue was purified by column chromatography (silica 60 g, ether/hexane = 1:5 → 1:3) to give **10** (341 mg, 69 %).

Quinoline 12. The acetal **9** (520 mg, 1.43 mmol) was dissolved in CH_2Cl_2 (20 mL) and cooled to 0 °C. To this solution was added TFA (0.4 mL). After stirring at 0 °C for 1 h, the mixture was diluted with benzene (10 mL), and concentrated under reduced pressure. The residue was purified by column chromatography (silica 30 g, ether/hexane = 1:1 → 3:1) to give quinoline **12** (228 mg, 81 %). IR (KBr) ν_{max} 2958, 1678, 1500, 1307, 1182, 1125 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 2.24 (2H, m, $CH_2CH_2CH_2C{=}O$), 2.79 (2H, dd, *J* = 7, 6 Hz, Ar-CH_2), 3.09 (2H, d, *J* = 6 Hz, CH_2-C=O), 7.60-7.72 (2H, m, aromatic), 8.08 (1H, dd, *J* = 7.5, 2 Hz, aromatic), 8.87 (1H, s, N=C*H*), 9.22 (1H, dd, *J* = 8, 2 Hz, aromatic). ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 22.7, 27.7, 40.6, 123.9, 126.0, 128.8, 129.1, 129.2, 132.0, 137.7, 147.4, 151.8, 200.1. HRMS (EI) for $C_{13}H_{11}NO$ (M^+), calcd 197.0840, found 197.0837.

Acetate 15. The quinoline derivative **12** (26 mg, 0.13 mmol) was dissolved in MeOH (1.0 mL) and the methanolic solution was cooled to 0 °C. To this solution was added $NaBH_4$ (4 mg, 0.13 mmol). After stirring for 5 min, the reaction was quenched with 1 drop of AcOH, and the mixture was evaporated. The residue was dissolved with water, extracted with CH_2Cl_2 (x3), dried over anhydrous Na_2SO_4, then concentrated under reduced pressure. The residue was dissolved in Ac_2O (1 mL)-Py (1 mL) and stirred at rt for 2 h. The mixture was diluted with toluene and evaporated *in vacuo*. The residue was purified by preparative PLC (silica, ether/hexane = 2:1) to give the acetate **15** (31 mg, 100 %). IR (KBr) ν_{max} 2916, 2849, 1729, 1507, 1370, 1229 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 1.89-2.03 (3H, m, CH-CH_2), 2.05 (3H, s, $OCOCH_3$), 2.21-2.32 (1H, m, C*H*), 2.76-2.93 (1H, m, Ar-CH_AH_B), 3.03 (1H, dt, *J* = 17, 3 Hz, Ar-CH_AH_B), 6.57 (1H, m, C*H*-OAc), 7.53 (1H, ddd, *J* = 8, 7, 1 Hz, aromatic), 7.64 (1H, ddd, *J* = 8, 7, 1 Hz, aromatic), 7.76 (1H, dd, *J* = 8, 1 Hz, aromatic), 8.07 (1H, dd, *J* = 8, 1 Hz, aromatic), 8.70 (1H, s, C=N*H*). ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 17.3, 21.2, 26.8, 28.8, 64.5, 122.4, 126.6, 127.3, 128.4, 130.1, 131.2, 136.8, 146.9, 152.5, 170.3. MS (EI) m/z 241 (M^+). HRMS (EI) for $C_{15}H_{15}NO_2$ (M^+), calcd 241.1102, found 241.1117.

Quinoline 13. Prepared in 72 % from **10** in a similar manner to that described for **12**. IR (KBr) ν_{max} 2955, 2856, 1685, 1612, 1500, 1427, 1263, 1238, 941, 858 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 0.33 (6H, s, $Si(CH_3)_2$), 1.03 (9H, s, Si-*t-Bu*), 2.25 (2H, quintet, *J* = 6.5 Hz, CH_2-CH_2-C=O), 2.81 (2H, t, *J* =

6.5 Hz, CH_2), 3.12 (2H, t, J = 6 Hz, CH_2), 7.28 (1H, dd, J = 9, 2.5 Hz, aromatic), 7.97 (1H, d, J = 9 Hz, aromatic), 8.74 (1H, s, N=CH), 8.81 (1H, d, J = 2.5 Hz, aromatic). ^{13}C NMR (67.9 MHz, $CDCl_3$) δ -4.5, 18.2, 22.8, 25.6, 27.8, 40.8, 112.9, 124.4, 125.2, 130.3, 131.0, 138.0, 144.3, 149.4, 156.6, 200.3. MS (EI) m/z 327 (M^+), 270 (M-57). Anal. Calcd for $C_{19}H_{25}NO_2SiCl$: C, 69.68; H, 7.69; N, 4.28. Found C, 69.60; H, 7.61; N, 4.03.

Compound 11. The TBDMS ether **10** was dissolved in THF (15 mL). To this solution was added MeI (0.17 mL, 2.73 mmol). TBAF (1.0 M in THF, 0.54 mL, 0.54 mmol) was added dropwise. After stirring for 25 min, the reaction was quenched with sat. NH_4Cl solution, and the mixture was extracted with CH_2Cl_2 (x3). The combined organic layer was dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography (silica 20 g, ether/hexane = 1:1 → 3:1) to give methyl ether (**11**) (165 mg, 77 %). IR (KBr) ν_{max} 3347, 2935, 2832, 1716, 1673, 1509, 1164, 1072 cm^{-1}. ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.42 (9H, s, *t-Bu*O), 2.10 (2H, m, C=C-CH$_2$-CH_2) 2.59 (4H, m, C=C-CH_2), 3.21 (3H, s, CH_3O-CH), 3.31 (3H, s, CH_3O-CH), 3.77 (3H, CH_3O-Ar), 4.48 (1H, br s, CH(OMe)$_2$), 6.06 (1H, br s, NH), 6.54 (1H, d, J = 3 Hz, aromatic), 6.90 (1H, dd, J = 9, 3 Hz, aromatic), 7.56 (1H, br d, J = 9 Hz, aromatic). ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 22.1, 23.3, 28.2, 38.4, 55.4, 55.6, 55.7, 79.8, 104.2, 114.5, 115.7, 126.0, 129.3, 135.7, 153.8, 156.4, 157.3, 198.9.

Quinoline 14. Prepared in 74 % from **11** in a similar manner to that described for **12**. IR (KBr) ν_{max} 2964, 1668, 1615, 1504, 1230 cm^{-1}. ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.26 (2H, m, Ar-CH$_2$-CH_2), 2.82 (2H, dd, J = 7, 6 Hz, Ar-CH_2 or CH_2-C=O), 3.12 (2H, t, J = 6 Hz, Ar-CH_2 or CH_2-C=O), 3.98 (3H, s, OCH_3),7.35 (1H, dd, J = 9, 3 Hz, aromatic), 7.98 (1H, d, J = 9 Hz, aromatic), 8.75 (1H, br s, N=CH), 8.77 (1H, d, J = 3 Hz, aromatic). ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 22.9, 28.0, 41.0, 55.6, 104.1, 121.5, 125.6, 130.6, 131.0, 138.2, 144.4, 149.1, 160.4, 200.7. HRMS (EI) for $C_{14}H_{13}NO_2$ (M^+), calcd 227.0946, found 227.0935.

Compound 17. To a solution of **16** (2.04 g, 12 mmol) in 2-methyl-1-pronanol (60 mL) cooled to 0 °C was added conc. H_2SO_4 (1.2 mL) dropwise. After stirring at 0 °C for 20 min, the mixture was poured into ice-cold sat. $NaHCO_3$ (100 mL), and extracted with CH_2Cl_2 (x3). The combined organic layer was washed with water (x2), dried over anhydrous Na_2SO_4, then concentrated under reduced pressure. The residue was purified by column chromatography (silica 80 g, AcOEt) to give **17** (1.67 g, 70 %). IR (KBr) ν_{max} 3424, 2962, 1636, 1601, 1386, 1214 cm^{-1}. ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.97 (6H, d, J = 7 Hz, OCH$_2$C(CH_3)$_2$), 2.03 (1H, m, OCH$_2$CH(CH$_3$)$_2$), 2.11-2.56 (5H, m, CH_2CHCH$_2$), 3.54-3.69 (4H, m, CH_2-OH, OCH_2CH(CH$_3$)$_2$), 5.34 (1H, s, olefinic). MS (EI) m/z 198 (M^+), 167, 143. HRMS (EI) for $C_{11}H_{18}O_3$ (M^+), calcd 198.1255, found 198.1251.

Compound 18. The alcohol **17** (2.69 g, 13.5 mmol) was dissolved in CH_2Cl_2 (50 mL) and the CH_2Cl_2 solution was cooled to 0 °C. To this solution was added NBS (2.53 g, 14.2 mmol) portionwise. After stirring at 0 °C, the mixture was poured into ice-cold sat. $NaHCO_3$, and extracted with CH_2Cl_2 (x3). The combined organic layer was dried over anhydrous Na_2SO_4, then concentrated under reduced pressure. The residue was purified by column chromatography (silica 140 g, ether/hexane = 1:3) to give **18** (3.54 g, 94 %). IR (KBr) ν_{max} 2963, 2877, 1720, 1328, 1134, 1038 cm^{-1}. ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.94 (6H, d, J = 6.5 Hz, OCH$_2$CH(CH_3)$_2$), 1.88 (1H, m, OCH$_2$CH(CH$_3$)$_2$), 2.23 (1H, ddt, J = 12, 4, 2.5 Hz, CH-CH_AH$_B$-C-CBr), 2.47 (1H, br d, J = 17 Hz, O=C-CH_AH$_B$), 2.58-2.69 (2H, m, O=C-CH$_A$$H_B$-C$H$), 2.92 (1H, ddd, J = 16.5, 4, 2 Hz, CH-CH$_A$$H_B$-C-CBr), 3.36 (2H, d, J = 6.5 Hz, O-CH_2CH(CH$_3$)$_2$), 3.76 (1H, dd, J = 8, 1.5 Hz O-CH_AH$_B$-CH), 4.10 (1H, ddd, J = 8, 4, 2 Hz, O-CH$_A$$H_B$-CH), 4.32 (1H, t, J = 1.5 Hz, CH-Br). ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 19.0, 28.2, 33.0, 34.1, 41.9, 51.4, 69.0, 73.6, 108.1, 200.9. MS (EI) m/z 278 (M^+: ^{81}Br), 276 (M^+: ^{79}Br), 222, 220. HRMS (EI) for $C_{11}H_{17}O_3Br$ (M^+), calcd 276.0361, found 276.0348.

Compound 19. The acetal **18** (3.54 g, 12.7 mmol) was dissolved in Ac_2O (53 mL) and the solution was cooled to 0 °C. To this solution was added BF_3·OEt_2 (4.3 mL, 38 mmol). After stirring at 0 °C for 50 min, the mixture was poured into sat. $NaHCO_3$ solution, and extracted with AcOEt (x3). The combined organic layer was washed with brine (x2), dried over anhydrous Na_2SO_4, then concentrated under reduced pressure. The residue was purified by column chromatography (silica 130g, ether/hexane = 5:1) to give acetate **19** (4.08 g, quant.). IR (KBr) ν_{max} 2966, 1739, 1667, 1586, 1245, 1048 cm^{-1}. ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.04 (6H, d, J = 6.5 Hz, O-CH$_2$-CH(CH_3)$_2$), 2.09 (3H, s, OA*c*), 2.30-2.60 (3H, m, CH_2-CH), 2.64-2.90 (2H, m, CH_2), 3.88 (1H, dd, J = 8.5, 6 Hz, O-CH_AH$_B$), 3.95 (1H, dd, J = 8.5, 6, O-CH$_A$$H_B$), 4.09 (2H, m, C$H_2$-OAc). MS (EI) m/z 320 ($M^+$: ^{81}Br), 318 ($M^+$: ^{79}Br), 260, 258. Anal. Calcd for $C_{13}H_{19}NO_4Br$: C, 48.92; H, 6.00. Found C, 48.89; H, 5.82.

Compound 20. (1) The acetate **19** (4.10 g, 13.0 mmol) was dissolved in MeOH (62 mL) and the solution was cooled to 0 °C. To this solution was added NaOMe [2 M in MeOH, 1.3 mL, 2.6 mmol]. After stirring at 0 °C for 40 min, the mixture was poured into sat. NH_4Cl solution, and extracted with $CHCl_3$ (x3). The combined organic layer was dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to give a crude product (3.83 g). (2) The crude product was dissolved in DMF (50 mL). To this solution was added TIPS-Cl (4.2 mL, 19.5 mmol) and imidazole (2.65 g, 39 mmol). After stirring at rt for 2 h, the reaction was quenched with ice-water, and the mixture was extracted with AcOEt (100 mL x3). The combined organic layer was washed with water (200 mL) and brine (150 mL x2), dried over anhydrous Na_2SO_4, then concentrated under reduced pressure. The residue was purified by column chromatography (silica 200 g, ether/hexane = 1:2) to give silyl ether **20** (3.82 g, 68 %). IR (KBr) ν_{max} 2949, 2865, 1667, 1585, 1464, 1235, 1115 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 1.00-1.16 (27H, m, $Si(CH(CH_3)_2)_3$ + $OCH_2CH(CH_3)_2$), 2.07 (1H, m, $OCH_2CH(CH_3)_2$), 2.26-2.48 (2H, m, CH_2), 2.53-2.67 (2H, m, CH_2), 2.79 (1H, dd, J = 17, 4.5 Hz, CHH), 3.70 (2H, m, Si-OCH_2), 3.90 (2H, m, $OCH_2CH(CH_3)_2$). MS (EI) m/z 434, (M^+: ^{81}Br), 432 (M^+: ^{79}Br), 391, 389. Anal. Calcd for $C_{20}H_{37}O_3SiBr$: C, 55.43; H, 8.55. Found C, 55.48; H, 8.54.

Compound 22. To a solution of methoxymethyl phenylsulfide (0.64 mL, 4.38 mmol) in THF (15 mL) cooled to -78 °C was added *n*-BuLi (1.6 M in hexane, 2.44 mL, 3.91 mmol), and the mixture was stirred at -78 °C for 30 min and at -50 °C for 20 min. After the mixture was cooled to -78 °C again, **20** (1.00 g, 2.25 mmol) in THF (8 mL) was added over 10 min. After stirring at -78 °C for 1 h, the mixture was poured into sat. NH_4Cl solution, and extracted with AcOEt (x3). The combined organic layer was washed with water (x2) and brine (x2), dried over anhydrous Na_2SO_4, then concentrated under reduced pressure. The residue was dissolved in ether (15 mL)-AcOEt (15 mL) and mixed with water (15 mL) and $HClO_4$ (0.15 mL). The whole mixture was stirred at rt for 5 min. The mixture was washed with water (x3), and brine (x2), dried over anhydrous Na_2SO_4, then concentrated under reduced pressure. The residue was purified by column chromatography (silica 50 g, ether/hexane = 1:20) to give **22** (820 mg, 71 %). IR (KBr) ν_{max} 2945, 2866, 1688, 1596, 1466, 1114 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 0.97-1.10 (21H, m, $Si(CH(CH_3)_2)_3$), 1.80-1.96 (1H, m, CH-CH_2O), 2.01 (1H, br d, J = 18.5 Hz, CH_AH_B), 2.23 (1H, dd, J = 18.5, 11 Hz, CH_AH_B), 2.39 (1H, dd, J = 16.5, 13 Hz, CH_CH_D), 2.70 (1H, ddd, J = 16.5, 4, 1.5 Hz, CH_CH_D), 3.40-3.59 (2H, m, CH_2-O-Si), 3.54 (3H, s, OCH_3), 5.67 (1H, s, PhS-CH(OMe)), 7.26-7.38 (3H, m, aromatic), 7.50-7.58 (2H, m, aromatic). ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 11.7, 17.9, 31.0, 36.9, 40.8, 56.5, 65.8, 92.7, 120.6, 128.9, 130.9, 134.5, 135.5, 158.4, 191.3. MS (EI) m/z 436 (M^+: ^{79}Br), 434 (M^+: ^{81}Br), 406, 404. Anal. Calcd for $C_{24}H_{37}O_3SiBrS$: C, 56.13; H, 7.26. Found C, 56.19; H, 7.19.

Dimethyacetal 24. A solution of **22** (820 mg, 1.60 mmol), $CuCl_2$ (430 mg, 3.20 mmol) and CuO (509 mg, 6.40 mmol) in MeOH (20 mL) was heated at reflux for 2 h. After cooling to rt, the mixture was filtered through a pad of Super-Cel®, and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (silica 40 g, ether/hexane = 1:10) to give acetal **24** (599 mg, 86 %). IR (KBr) ν_{max} 2946, 2867, 1693, 1463, 1108, 1070 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 0.98-1.14 (21H, m, $Si(CH(CH_3)_2)_3$), 2.18-2.36 (1H, m, CH_2-CH), 2.39 (1H, dd, J = 17.5, 10 Hz, CH_AH_B), 2.53 (1H, dd, J = 16, 12 Hz, CH_CH_D), 2.69 (1H, ddd, J = 17.5, 4, 1.5 Hz, CH_AH_B), 2.78 (1H, ddd, J = 16, 4, 1.5 Hz, CH_CH_D), 3.46 (3H, s, OCH_3), 3.48 (3H, s, OCH_3), 3.69 (2H, dd, J = 5, 1 Hz, CH_2-OSi), 5.38 (1H, s, $CH(OMe)_2$). MS (EI) m/z 405 (M-30: ^{81}Br), 403 (M-30: ^{79}Br), 393, 391. Anal. Calcd for $C_{19}H_{35}O_4SiBr$: C, 52.40; H, 8.10. Found C, 52.40; H, 8.19.

Compound 21. To a solution of diisopropylamine (0.25 mL, 1.84 mmol) in THF (8 mL) cooled to -78 °C was added *n*-BuLi [1.6 M in hexane, 1.00 mL, 1.61 mmol], and the solution was stirred at -78 °C for 30 min. To this solution was added **20** (500 mg, 1.15 mmol) in THF (4 mL) over 10 min. After stirring at -78 °C for 1 h, MeI (0.14 mL, 2.3 mmol) was added. After stirring at -20°C for 1 h, the mixture was quenched with sat. NH_4Cl solution, and the mixture was extracted with AcOEt (x3). The combined organic layer was washed with water (x2) and brine (x2), dried over anhydrous Na_2SO_4, then concentrated under reduced pressure. The residue was purified by column chromatography (silica 30 g, ether/hexane = 1:4) followed by crystallization (from hexane) to give **21** (409 mg, 80 %). Mp 68-69 °C. IR (KBr) ν_{max} 2941, 2866, 1663, 1594, 1465, 1367, 1245 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 1.00-1.16 (27H, m, $Si(CH(CH_3)_2)_3$, $CH(CH_3)_2$), 1.23 (3H, d, J = 7 Hz, CH_3-CH), 1.93-2.15 (2H, m, OCH_2CHMe_2, CH-CH_2-OSi), 2.45 (1H, dq, J = 10, 7 Hz, CH_3-CH-C=O), 2.74 (1H, dd, J = 17, 7.5 Hz, C=C-CH_AH_B), 2.81 (1H, dd, J = 17, 6 Hz, C=C-CH_AH_B), 3.74 (1H, dd, J = 10, 6 Hz, O-CH_AH_B), 3.79 (1H, dd, J = 10, 4 Hz, O-CH_AH_B), 3.90 (2H, m, OCH_2). ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 11.8, 13.5, 17.9, 18.8, 28.7, 29.2, 41.5, 42.2, 64.0, 75.0, 101.7, 170.8, 193.3. Anal. Calcd for $C_{21}H_{39}O_3SiBr$: C, 56.36; H, 8.78. Found C, 56.31; H, 8.63.

Compound 23. To a solution of methoxymethyl phenylsulfide (0.75 mL, 5.14 mmol) in THF (15 mL) cooled to -78 °C was added *n*-BuLi (1.6 M in hexane, 2.8 mL, 4.6 mmol), and the solution was stirred at -78 °C for 1 h 15 min. To this solution was added **21** (1.15 g, 2.57 mmol) in THF (6 mL) over 5 min. After stirring at -78 °C for 1 h, the mixture was poured into sat. NH_4Cl solution, and extracted with ether-AcOEt (x3). The combined organic layer was washed with water (x2) and brine (x2), dried over anhydrous Na_2SO_4, then concentrated under reduced pressure. The residue was dissolved in ether (10 mL)-AcOEt (10 mL) and mixed with water (10 mL) and $HClO_4$ (0.2 mL). After stirring at rt for 20 min, the organic layer was washed with water (x2) and brine (x2), dried over anhydrous Na_2SO_4, then concentrated under reduced pressure. The residue was purified by column chromatography (silica 85 g, ether/hexane = 1:20) to give **23** (873 mg, 65 %) as a diastereomeric mixture. IR (KBr) ν_{max} 2942, 2865, 1690, 1584, 1464, 1108 cm^{-1}. MS (EI) m/z 485 (M-43: ^{81}Br), 483 (M-43: ^{79}Br), 419, 417.

Dimethylacetal 25. Prepared in 85 % from **23** in a similar manner to that described for **24**. IR (KBr) ν_{max} 2941, 2866, 1694, 1465, 1108, 1073 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 0.98-1.10 (21H, m, $Si(CH(CH_3)_2)_3$), 1.35 (3H, d, J = 7 Hz, CH-CH_3), 2.13 (1H, m, CH-CH_2-OTIPS), 2.71 (1H, br dd, J = 17.5, 3 Hz, CH_AH_B-C=O), 2.88 (1H, dd, J = 17.5, 5 Hz, CH_AH_B-C=O), 3.05 (1H, qd, J = 7, 2 Hz, CH-CH_3), 3.44 (3H, s, CH-OCH_3), 3.53 (3H, s, CH-OCH_3), 3.56-3.63 (2H, m, CH_2-OTIPS), 5.34 (1H, s, $CH(OMe)_2$). ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 11.8, 17.9, 19.8, 32.9, 36.1, 43.0, 55.7, 56.6, 64.8, 106.9, 123.3, 159.0, 190.4. MS (EI) m/z 449 (M^+: ^{81}Br), 447 (M^+: ^{79}Br), 407 (M-43), 405 (M-43). Anal. Calcd for $C_{20}H_{37}O_4BrSi$: C, 53.55; H, 8.32. Found C, 53.56; H, 8.46.

Compound 26. Prepared in 80 % by coupling **4** and **24** in a similar manner to that described for **9**. IR (KBr) ν_{max} 2941, 2866, 1732, 1684, 1518, 1449 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 1.03-1.17 (21H, m, $Si(CH(CH_3)_2)_3$), 1.44 (9/2H, s, $C(CH_3)_3$), 1.46 (9/2 H, s, $C(CH_3)_3$), 2.30-2.80 (5H, m, CH_2-CH-CH_2), 3.21 (3/2H, s, OCH_3), 3.22 (3/2H, s, OCH_3), 3.25 (3/2H, s, OCH_3), 3.26 (3/2H, s, OCH_3), 3.66-3.83 (2H, m, CH_2-OTIPS), 4.42 (1/2H, s, $CH(OMe)_2$), 4.46 (1/2H, s, $CH(OMe)_2$), 6.21 (1/2H, br s, NH), 6.31 (1/2H, br s, NH), 6.91-6.99 (1H, m, aromatic), 7.05-7.15 (1H, m, aromatic), 7.31-7.40 (1H, m, aromatic), 7.79 (1/2H, br d, J = 8 Hz, aromatic), 7.87 (1/2H, J = 8 Hz, aromatic). MS (EI) m/z 547 (M^+). HRMS (EI) for $C_{30}H_{49}NO_6Si$ (M^+), calcd 547.3328, found 547.3313.

Compound 27. Prepared by coupling **6** and **24** in 48 % (using NMP as a solvent) or 70 % (using toluene as a solvent) yield in a similar manner to that described for **10**. IR (KBr) ν_{max} 2941, 2867, 1731, 1680, 1510, 1465, 1169 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 0.16-0.20 (6H, m, $Si(CH_3)_2$), 0.96 (9H, s, $SiC(CH_3)_3$), 1.02-1.12 (21H, m, $Si(CH(CH_3)_2)_3$), 1.42 (9/2H, s, O-$C(CH_3)_3$), 1.43 (9/2H, s, O-$C(CH_3)_3$), 2.26-2.79 (5H, m, CH_2-CH-CH_2), 3.21 (3/2H, s, OCH_3), 3.22 (3/2H, s, OCH_3), 3.29 (3/2H, s, OCH_3), 3.31 (3/2H, s, OCH_3), 3.67-3.83 (2H, m, CH_2-OSi), 4.49 (1/2H, s, $CH(OMe)_2$), 4.56 (1/2H, s, $CH(OMe)_2$), 6.02 (1/2H, br s, NH), 6.13 (1/2H, br s, NH), 6.46 (1/2H, d, J = 3 Hz, aromatic), 6.49 (1/2H, d, J = 3 Hz, aromatic), 6.82 (1H, dd, J = 8.5, 3 Hz, aromatic), 7.48 (1/2H, br d, J = 8.5 Hz, aromatic), 7.59 (1/2H, br d, J = 8.5 Hz, aromatic). HRMS (EI) for $C_{36}H_{63}NO_7Si_2$ (M^+), calcd 677.4142, found 677.4121.

Compound 28. Prepared in 82 % by coupling **4** and **25** in a similar manner to that described for **9**. IR (KBr) ν_{max} 2942, 2866, 1734, 1670, 1507, 1457, 1160, 1070 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 1.00-1.16 (21H, m, $Si(CH(CH_3)_2)_3$), 1.42-1.49 (12H, m, $OC(CH_3)_3$ + CH_3-CH), 2.24 (1H, m, CH-CH_2-OTIPS), 2.41-3.12 (3H, m, CH_2-C=O + CH-CH_3), 3.18 (3/2H, s, OCH_3), 3.21 (3H, br s, OCH_3), 3.22 (3/2H, s, OCH_3), 3.60-3.80 (2H, m, CH_2-OTIPS), 4.36 (1/2H, s, $CH(OMe)_2$), 4.42 (1/2H, s, $CH(OMe)_2$), 6.19 (1/2H, br s, NH), 6.39 (1/2H, br s, NH), 6.85 (1/2H, dd, J = 7.5, 1.5 Hz, aromatic), 6.97 (1/2H, dd, J = 7.5, 1.5 Hz, aromatic), 7.03-7.15 (1H, m, aromatic), 7.28-7.40 (2H, m, aromatic), 7.79 (1/2H, br d, J = 8 Hz, aromatic), 7.86 (1/2H, br d, J = 8 Hz, aromatic). MS (EI) m/z 561(M^+). HRMS (EI) for $C_{31}H_{51}NO_6Si$ (M^+), calcd 561.3485, found 561.3497.

Compound 29. Prepared in 48 % by coupling **6** and **25** in a similar manner (using toluene as solvent) to that described for **10**. IR (KBr) ν_{max} 3330, 2933, 2867, 1728, 1669, 1510, 1162 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 0.15 (3H, s, Si-CH_3), 0.16 (3H, s, Si-CH_3), 0.17 (3H, s, Si-CH_3), 0.18 (3H, s, Si-CH_3), 0.96 (9H, s, $SiC(CH_3)_3$) , 1.01-1.11 (21H, m, Si-$(CH(CH_3)_2)_3$), 1.40-1.48 (12H, m, CH-CH_3, $OC(CH_3)_3$), 3.18 (3/2H, s, OCH_3), 3.20 (3/2H, s, OCH_3), 3.25 (3H, s, OCH_3), 3.61-3.78 (2H, m, CH_2-OTIPS), 4.43 (1/2H, s, $CH(OMe)_2$), 4.48 (1/2H, s, $CH(OMe)_2$), 6.01 (1/2H, br s, NH), 6.22 (1/2H, br s, NH), 6.35 (1/2H, d, J = 3 Hz, aromatic), 6.48 (1/2H, d, J = 3 Hz, aromatic), 6.81 (1H, dd, J = 9, 3 Hz, aromatic), 7.49 (1/2H, br d, J = 8.5 Hz, aromatic), 7.58 (1/2H, br d, J = 8.5 Hz, aromatic). MS (EI) m/z 691 (M^+). HRMS (EI) for $C_{37}H_{65}NO_7Si_2$ (M^+), calcd 691.4299, found 691.4274.

Quinoline 31. Prepared in 89 % from **26** in a similar manner to that described for **12**. IR (KBr) ν_{max} 2941, 2866, 1685, 1460, 1104 cm^{-1}. ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.03-1.15 (21H, m, Si(C*H*(C*H*$_3$)$_2$)$_3$), 2.56 (1H, m, C*H*-CH$_2$-OSi), 2.75 (1H, dd, *J* = 16, 12 Hz, C*H*$_A$H$_B$-C=O), 2.89 (1H, ddd, *J* = 16, 4, 1.5 Hz, CH$_A$*H*$_B$-C=O), 3.11 (1H, dd, *J* = 17, 10 Hz, Ar-C*H*$_A$H$_B$), 3.20 (1H, br dd, *J* = 17, 5 Hz, Ar-CH$_A$*H*$_B$), 3.79 (1H, dd, *J* = 10, 5 Hz, C*H*$_A$H$_B$-OTIPS), 3.85 (1H, dd, *J* = 10, 4.5 Hz, CH$_A$*H*$_B$-OTIPS), 7.62-7.75 (2H, m, aromatic), 8.11 (1H, br d, *J* = 7.5 Hz, aromatic), 8.94 (1H, br s, N=C*H*), 9.29 (1H, br d, *J* = 7.5 Hz, aromatic). ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 11.8, 17.9, 30.6, 38.0, 43.6, 66.3, 123.9, 126.0, 128.7, 129.1, 129.7, 131.7, 137.1, 148.0, 152.4, 200.6. MS (EI) m/z 383 (M$^+$), 340 (M-43), 310. Anal. Calcd for $C_{23}H_{33}NO_2Si$: C, 72.02; H, 8.68; N, 3.65. Found C, 72.01; H, 8.90; N, 3.42.

Quinoline 32. Prepared in 88 % from **27** in a similar manner to that described for **12**. IR (KBr) ν_{max} 2943, 2864, 1685, 1611, 1499, 1264, 1237 cm^{-1}. ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.33 (6H, s, Si(C*H*$_3$)$_2$), 1.03 (9H, s, SiC(C*H*$_3$)$_3$), 1.01-1.12 (21H, m, Si(C*H*(C*H*$_3$)$_2$)$_3$), 2.54 (1H, m, C*H*-CH2-OTIPS), 2.72 (1H, dd, *J* = 16, 12 Hz, C*H*$_A$H$_B$-C=O), 2.87 (1H, dd, *J* = 16, 4, 1.5 Hz, CH$_A$*H*$_B$-C=O), 3.07 (1H, dd, *J* = 17, 9.5 Hz, Ar-C*H*$_A$H$_B$), 3.16 (1H, br dd, *J* = 17, 5 Hz, Ar-CH$_A$*H*$_B$), 3.78 (1H, dd, *J* = 10, 5 Hz, C*H*$_A$H$_B$-OTIPS), 3.84 (1H, dd, *J* = 10, 4.5 Hz, CH$_A$*H*$_B$-OTIPS), 7.28 (1H, dd, *J* = 9, 3 Hz, aromatic), 7.97 (1H, d, *J* = 9 Hz, aromatic), 8.76 (1H, s, N=C*H*), 8.82 (1H, d, *J* = 3 Hz, aromatic). MS (EI) m/z 513 (M$^+$), 470 (M-43). HRMS (EI) for $C_{29}H_{47}NO_3Si_2$ (M$^+$), calcd 513.3094, found 513.3081.

Compound 30. Prepared in 70 % from **27** in a similar manner to that described for **12**. IR (KBr) ν_{max} 2946, 2866, 1724, 1683, 1508, 1457, 1163 cm^{-1}. ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.03-1.17 (21H, m, Si(C*H*(C*H*$_3$)$_2$)$_3$), 1.42 (9/2H, s, C(C*H*$_3$)$_3$), 1.43 (9/2H, s, C(C*H*$_3$)$_3$), 2.22-2.80 (5H, m, C*H*$_2$-C*H*-C*H*$_2$), 3.21 (3/2H, s, CH-OC*H*$_3$), 3.22 (3/2H, s, CH-OC*H*$_3$), 3.31 (3/2H, s, CH-OC*H*$_3$), 3.33 (3/2H, s, CH-OC*H*$_3$), 3.68-3.80 (2H, m, C*H*$_2$OTIPS), 3.77 (3H, s, Ar-OC*H*$_3$), 4.49 (1/2H, s, C*H*(OMe)$_2$), 4.53 (1/2H, s, C*H*(OMe)$_2$), 6.00 (1/2H, br s, N*H*), 6.10 (1/2H, br s, N*H*), 6.53 (1/2H, d, *J* = 3 Hz, aromatic), 6.56 (1/2H, d, *J* = 3 Hz, aromatic), 6.86-6.94 (1H, m, aromatic), 7.50 (1/2H, br d, *J* = 8.5 Hz, aromatic), 7.60 (1/2H, br d, *J* = 8.5 Hz, aromatic). MS (EI) m/z 577 (M$^+$). HRMS (EI) for $C_{31}H_{51}NO_7Si$ (M$^+$), calcd 577.3434, found 577.3452.

Quinoline 33. Prepared in 84 % from **30** in a similar manner to that described for **12**. IR (KBr) ν_{max} 2942, 2865, 1676, 1617, 1506, 1227 cm^{-1}. ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.02-1.18 (21H, m, Si(C*H*(C*H*$_3$)$_3$), 2.46-2.62 (1H, m, C*H*-CH$_2$-OTIPS), 2.74 (1H, dd, *J* = 16, 12 Hz, C*H*$_A$H$_B$-C=O), 2.88 (1H, ddd, *J* = 16, 4.5, 1.5 Hz, CH$_A$*H*$_B$-C=O), 3.02-3.23 (2H, m, C*H*$_2$-Ar), 3.81 (2H, m, C*H*$_2$-OTIPS), 3.98 (3H, s, Ar-OC*H*$_3$), 7.34 (1H, dd, *J* = 9, 3 Hz, aromatic), 7.98 (1H, d, *J* = 9 Hz, aromatic), 8.76 (1H, s, N=C*H*), 8.78 (1H, d, *J* = 3 Hz, aromatic). ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 11.8, 17.9, 30.7, 38.0, 43.8, 55.6, 66.4, 103.9, 121.4, 125.4, 130.2, 131.0, 137.5, 144.4, 149.4, 160.3, 201.0. MS (EI) m/z 413 (M$^+$), 370 (M-43), 340. HRMS (EI) for $C_{24}H_{35}NO_3Si$ (M$^+$), calcd 413.2386, found 413.2373.

Quinoline 34. Prepared in 92 % from **28** in a similar manner to that described for **12**. IR (KBr) ν_{max} 2944, 2866, 1689, 1499, 1462, 1112 cm^{-1}. ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.90-1.06 (21H, m, Si(C*H*(C*H*$_3$)$_2$)$_3$), 1.55 (3H, d, *J* = 7 Hz, CH-C*H*$_3$), 2.35 (1H, m, C*H*-CH$_2$-OTIPS), 2.80 (1H, dd, *J* = 17, 5.5 Hz, C*H*$_A$H$_B$-C=O), 3.05 (1H, dd, *J* = 17, 5 Hz, CH$_A$*H*$_B$-C=O), 3.44 (1H, qd, *J* = 7, 3.5 Hz, C*H*-CH$_3$), 3.70 (1H, dd, *J* = 10, 6.5 Hz, C*H*$_A$H$_B$-OTIPS), 3.82 (1H, dd, *J* = 10, 5.5 Hz, CH$_A$*H*$_B$-OTIPS), 7.60-7.76 (2H, m, aromatic), 8.10 (1H, br d, *J* = 7.5 Hz, aromatic), 8.96 (1H, s, N=C*H*), 9.22 (1H, br d, *J* = 7.5 Hz, aromatic). MS (EI) m/z 354 (M-43). HRMS (EI) for $C_{21}H_{28}NO_2Si$ (M-C_3H_7), calcd 354.1889, found 354.1868.

Quinoline 35. Prepared in 77 % from **29** in a similar manner to that described for **12**. IR (KBr) ν_{max} 2946, 2866, 1683, 1612, 1500, 1264, 1239, 1105 cm^{-1}. ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.33 (6H, s, Si(C*H*$_3$)$_2$), 0.91-1.02 (21H, m, Si(C*H*(C*H*$_3$)$_3$), 1.03 (9H, s, Si(C*H*$_3$)$_3$), 1.53 (3H, d, *J* = 7 Hz, CH-C*H*$_3$), 2.32 (1H, m, C*H*-CH$_2$-OTIPS), 2.77 (1H, dd, *J* = 17, 5 Hz, C*H*$_A$H$_B$-C=O), 3.03 (1H, dd, *J* = 17, 5.5 Hz, CH$_A$*H*$_B$-C=O), 3.39 (1H, qd, *J* = 7, 3.5 Hz, C*H*-CH$_3$), 3.69 (1H, dd, *J* = 10, 6.5 Hz, C*H*$_A$H$_B$-OTIPS), 3.80 (1H, dd, *J* = 10, 5 Hz, CH$_A$*H*$_B$-OTIPS), 7.28 (1H, dd, *J* = 9, 2.5 Hz, aromatic), 7.96 (1H, d, *J* = 9 Hz, aromatic), 8.76 (1H, d, *J* = 2.5 Hz, aromatic), 8.78 (1H, s, N=C*H*). ^{13}C NMR (67.9 MHz, $CDCl_3$) δ -4.4, 11.8, 17.9, 21.9, 25.7, 33.0, 39.8, 42.9, 65.4, 113.0, 124.6, 124.9, 129.7, 130.9, 141.1, 144.0, 149.7, 156.7, 200.0. MS (EI) m/z 527 (M$^+$), 484 (M-43). HRMS (EI) for $C_{30}H_{49}NO_3Si_2$ (M$^+$), calcd 527.3250, found 527.3267.

Acknowledgment. This work was financially supported by Grant-in-aid for Scientific Research from Ministry of Education, Science and Culture of Japan.

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(*Received in Japan* 7 *February* 1994; *accepted* 25 *February* 1994)