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A Highly Diastereoselective Synthesis of *cis*-4a-Aryloctahydrocyclopenta[*c*]pyridine Derivatives through Tandem Radical Cyclization of α-Amino Radical-Polyene Species

SHINZO KANO,* YOKO YUASA, TSUTOMU YOKOMATSU, KENJI ASAMI, and SHIROSHI SHIBUYA

Tokyo College of Pharmacy, 1432–1 Horinouchi, Hachioji, Tokyo 192–03, Japan

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8a-Aryloxazolo[3,4-*a*]cyclopenta[*d*]pyridines (**9a**—**c**) were prepared *via* a route involving radical cyclization of α-acylamino radical-polyene species generated by treatment of 4-phenylthiooxazolidin-2-ones (**8a**—**c**) with tri-*n*-butyltin hydride in the presence of azobisisobutyronitrile (AIBN). Conversion of **9a** to *cis*-octahydro-2,5-dimethyl-4a-phenylcyclopenta[*c*]pyridine (**19**) was successfully achieved *via* a route involving ring cleavage of the oxazolidinone ring of **9a**, oxidation of hydroxymethyl group, and decarbonylation.

Keywords——radical cyclization; cyclopenta[*c*]pyridine; α-acylamino radical; α-amino radical-polyene; tandem radical cyclization; decarbonylation

Radical cyclization is rapidly becoming an important method for construction of bicyclic systems.[1,2] α-Acylamino radical cyclization at the unsaturated component was used for a synthesis of *N*-heterocycles through carbon–carbon bond formation at the α-position of nitrogen.[3] Although radical-polyene systems were applied to construction of carbopolycyclic compounds through a tandem radical cyclization process,[4] little attention has been paid to a synthesis of aza-polycyclic compounds by using α-acylamino radical-polyene species.[5] In the search for potent and nonaddictive analgesics, many morphine-based structural variants have been prepared in the last decades.[6] The investigation of structural variants of the morphine molecule has been an area of considerable interest. Of special interest to us is a facile synthesis of the 4a-aryloctahydro-1*H*-cyclopenta[*c*]pyridine ring system (**1**), a new analogue of 4a-aryldecahydroisoquinoline that is a simple fragment of morphine. Our synthetic strategy aimed at 4a-aryl-1*H*-cyclopenta[*c*]pyridine is based on tandem radical cyclization of an α-acylamino radical-polyene system (**2**). We wish to disclose that stereocontrolled ring-closure was observed owing to the effect of A-type strain phenomena[7] in the transition state at the mono-cyclization step.

At the first stage, we prepared 4-phenylthiooxazolidin-2-ones (**8a**—**c**), used as precursors for generation of radical species, as outlined in Chart 1 according to the method reported previously.[5,8,9] Deprotonation of the esters (**3a**—**c**) with lithium diisopropylamide (LDA) followed by butenylation by addition of 1-iodo-3-butene afforded the α-(3-butenyl) esters (**4a**—**c**), which were reduced with lithium aluminum hydride to yield the alcohols (**5a**—**c**). Condensation of **5a**, **5b**[8] and **5c**[9] with oxazolidine-2,4-dione by Mitsunobu's method[10] afforded the corresponding *N*-substituted oxazolidine-2,4-diones (**6a**—**c**). Introduction of a phenylthio group at the 4-position was carried out by an application of the modified Walker's method.[11,12] Reduction of **6a**—**c** with sodium borohydride, followed by treatment of the resulting 4-hydroxyoxazolidin-2-ones (**7a**—**c**) with diphenyl disulfide in the presence of tri-*n*-butylphosphine[12] yielded the corresponding 4-phenylthiooxazolidin-2-ones (**8a**—**c**) as a

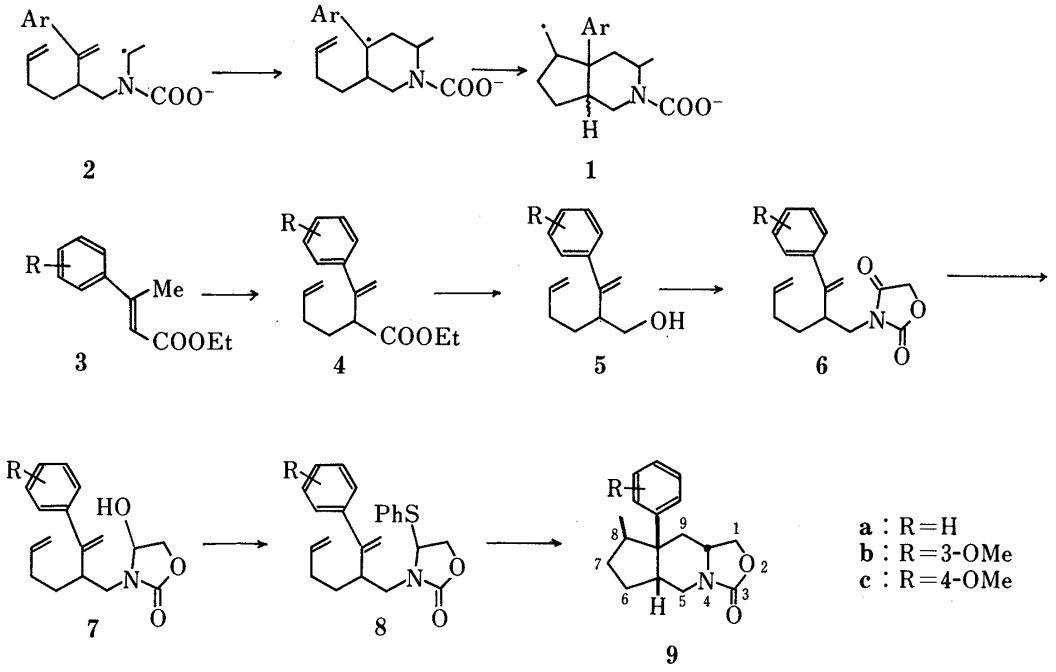
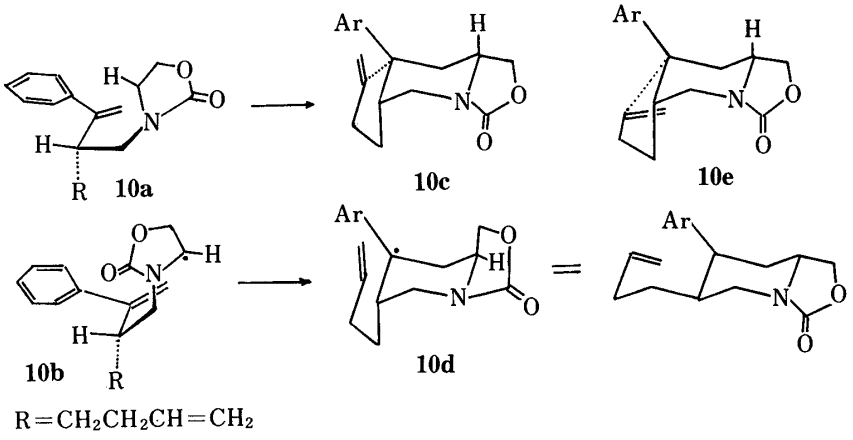


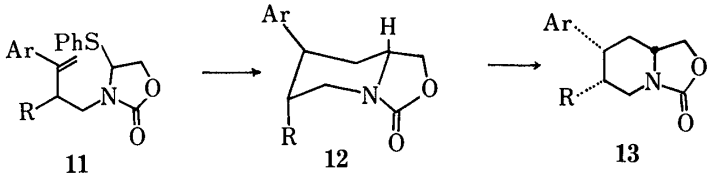
Chart 1

mixture of diastereomers.

A solution of **8a** in benzene was heated in the presence of tri-*n*-butyltin hydride and azobisisobutyronitrile (AIBN) to give the expected 8a-phenyloxazolo[3,4-*a*]cyclopenta[*d*]-pyridine (**9a**) in 57% yield as a single diastereomer. The reaction proceeded with high regio- and stereoselectivities and the formation of the corresponding oxazoloisoquinoline derivative was not observed.

The nature of the ring juncture of the octahydro-1*H*-cyclopenta[*c*]pyridine ring was determined from the magnitude of the J values of the signals due to NCH_2. Of NCH_2, the equatorially oriented proton resonated at δ 3.79 (dd, J=1.48, 13.12 Hz), the axial one resonated at δ 3.01 (dd, J=3.84, 13.12 Hz) and signals with large coupling constants owing to axial–axial interaction was not observed in the proton nuclear magnetic resonance (^{1}H-NMR, 400 MHz) spectrum. The smaller coupling constant, J=1.48 Hz, indicates that the dihedral angle between NCH and angular CH is close to 90°. Thus, the ring juncture was assigned to be *cis* based on correlation of the Dreiding model study and Karplus relation.[13] In the *trans*-fused ring system, a large coupling constant owing to diaxial interaction would be expected. This stereocontrolled ring closure can be accounted for by the effect of A^{1,2} strain[7] in the transition state at the monocyclization step. Of the two possible transition states (**10a**, **b**), **10a** giving **10c** should be preferable to **10b** leading to **10d**, considering the significant steric repulsion of phenyl and oxazolidinone rings. Therefore, it is conceivable that the second C–C bond formation proceeds through **10c**, the butenyl side chain of which takes axial configuration. The relative configuration at 8a-H and 6-H in the mono-cyclized intermediate (**10c**) for this double cyclization is also supported by the radical cyclization product of **11**. Treatment of **11** with tri-*n*-butyltin hydride gives rise to 7-aryl-6-substituted hexahydro-3*H*-oxazolo[3,4-*a*]pyridin-3-one (**13**)[5,14] through **12** in which the substituent at the 6-position is oriented axially and 8a-H and 6-H take a *cis*-relationship. The successive C–H bond formation *via* delivery of a H radical from the less hindered face to **12** gives **13**. The stereochemical feature of the mono-cyclization step in the formation of **9a** from **8a** is consistent with that in the case of **13**. Similar predominant *cis* ring-closure also observed in an *N*-acyliminium ion-polyene cyclization by using **14**, yielding *cis*-fused 4a-aryl-decahydroisoquinolin-6-yl formate (**15**).[8] Although the relative configuration of CH_3 was





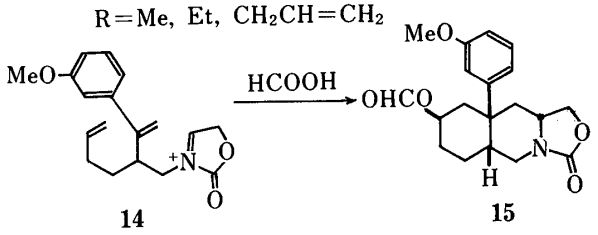


Chart 2

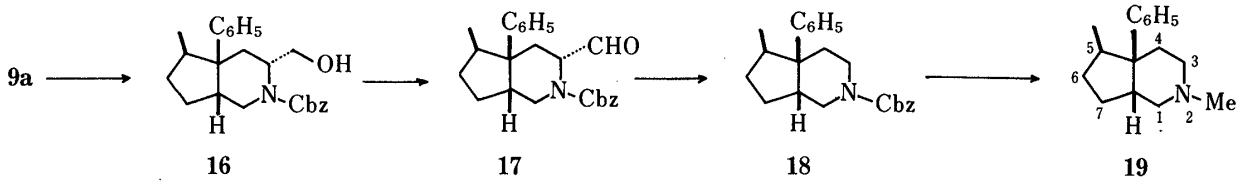


Chart 3

not determined at this stage, upon consideration of the two possible intermediates (**10c**, **e**) for the second cyclization, CH_3 was assumed to take a *cis* relation to the phenyl group. Of **10c**, **e**, **10c** would be more favorable than **10e** because of steric repulsion between the butenyl moiety and oxazolildinone ring in **10e** as shown in Chart 2. The high field signals at δ ($CDCl_3$) 0.77 (d, J=6.64 Hz) due to CH_3 support this assumption.

In a similar way, **8b** and **8c** were also treated with tri-*n*-butyltin hydride to yield the corresponding 8a-aryloxazolo[3,4-*a*]cyclopenta[*d*]pyridine derivatives (**9b**, **c**). The spectral data for **9b**, **c** were similar to those for **9a**.

Conversion of **9a** to the *cis*-fused octahydro-4a-phenyl-2,5-dimethyl-1*H*-cyclopenta[*c*]-pyridine (**19**) was effected by decarbonylation of **17** (easily derived from **9a**). Ring cleavage of **9a** by heating with 10% ethanolic potassium hydroxide, followed by benzyloxycarbonylation, afforded the 3-hydroxymethyl derivative (**16**). Swern oxidation[15] of **16**, followed by treatment of the resulting 3-formyl derivative (**17**) with tris(triphenylphosphine)-rhodium chloride[16] yielded the desired cyclopenta[*c*]pyridine (**18**). Reduction of **18** with

lithium aluminum hydride afforded **19**.

Cyclization of α-acylamino radical-polyene systems should be widely applicable to syntheses of a variety of aza-polycyclic systems.

Experimental

All melting points were determined on a Yanagimoto hot-stage apparatus and are uncorrected. ^{1}H-NMR spectra were recorded on Varian EM-390 (90 MHz) and Bruker AM-400 (400 MHz) spectrometers, and δ values are quoted relative to tetramethylsilane. The following abbreviations are used: br = broad, d = doublet, dd = doublet of doublets, m = multiplet, q = quartet, s = singlet. Only characteristic signals are given for **16**—**18**. Infrared (IR) spectra were taken on a Hitachi 260-30 infrared spectrophotometer. Mass spectra (MS) were measured with a Hitachi RMU-7L spectrometer. Tetrahydrofuran (THF) and ethyl ether were distilled from sodium-benzophenone before use.

Ethyl 2-(1-Phenylethenyl)-5-hexenoate (4a)——A solution of **3a** (9.5 g, 0.05 mol) in THF (30 ml) was added to a stirred solution of lithium diisopropylamide (prepared from 5.5 g of diisopropylamine and 34 ml of 1.6 M hexane solution of *n*-butyllithium in 50 ml of THF at −78 °C) at −78 °C. Stirring was continued at the same temperature for 0.5 h, then 1-iodo-3-butene (10.9 g, 0.06 mol) was added. After another 2 h's, stirring at room temperature, the mixture was poured into water (100 ml) and extracted with benzene. The extract was washed with brine, dried over Na_2SO_4 and evaporated to give **4a** (9.4 g, 77% yield) as an oil. MS *m/z*: 244 (M^+). Exact MS *m/z*: Calcd for $C_{16}H_{20}O_2$: 244.146. Found: 244.146. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1725 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 1.08 (3H, t, J=7 Hz, CH_3CH_2O–), 1.81—2.08 (4H, m, –CH_2CH_2–), 3.41 (1H, t, J=7 Hz, –CHCOOEt), 4.01 (2H, q, J=7 Hz, CH_3CH_2O–), 4.87—5.20 (2H, m, CH_2=CH–), 5.15, 5.26 (2H, each s, C=CH_2), 5.56—6.07 (1H, m, CH_2=CH–), 7.40 (5H, s, Ar-H).

Ethyl 2-(1-3′-Methoxyphenylethenyl)-5-hexenoate (4b)——This compound was obtained from **3b** (11 g, 50 mmol) under the same conditions as above in 81% yield (11.10 g) as an oil. MS *m/z*: 274 (M^+). Exact MS *m/z*: Calcd for $C_{17}H_{22}O_3$: 274.156. Found: 274.157. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1725 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 1.20 (3H, t, J=7 Hz, CH_3CH_2O–), 1.68—2.28 (4H, m, –CH_2CH_2–), 3.52 (1H, t, J=6 Hz, –CHCOO–), 3.80 (3H, s, O–CH_3), 4.15 (2H, q, J=7 Hz, CH_3CH_2O–), 4.95—5.14 (2H, m, CH_2=CH–), 5.28, 5.40 (2H, each s, –C=CH_2), 5.58—5.98 (1H, m, CH_2=CH–), 6.88 (1H, dd, J=2, 7 Hz, Ar-H), 6.95 (1H, d, J=2 Hz, Ar-H), 7.01 (1H, dd, J=2, 7 Hz, Ar-H), 7.28 (1H, dd, J=7, 7 Hz, Ar-H).

2-(1-Phenylethenyl)-5-hexen-1-ol (5a)——A solution of **4a** (4.88 g, 20 mmol) in ether (50 ml) was added to a stirred solution of $LiAlH_4$ (1.52 g, 40 mmol) in ether (50 ml) under cooling with ice-salt. Stirring was continued for 2 h, then the mixture was decomposed with 10% NaOH and worked up as usual to give **5a** (3.84 g, 95% yield) as an oil. MS *m/z*: no M^+ ion peak was observed in the EI-MS, 184 (M^+ − 18, base peak). ^{1}H-NMR ($CDCl_3$) δ: 1.49—2.22 (4H, m, –CH_2CH_2–), 2.62—2.92 (1H, m, –$CHCH_2$–), 3.50 (2H, d, J=7 Hz, HO–CH_2–), 4.88—5.07 (2H, m, CH_2=CH–), 5.11, 5.36 (2H, each s, –C=CH_2), 5.59—6.03 (1H, m, CH_2=CH–), 7.32 (5H, s, Ar-H).

2-(1-3′-Methoxyphenylethenyl)-5-hexen-1-ol (5b)——This compound was obtained from **4b** (5.48 g, 20 mmol) by reduction with $LiAlH_4$ (1.52 g, 40 mmol) under the same conditions as above in 88% yield (4.08 g) as an oil. MS *m/z*: 232 (M^+). Exact MS *m/z*: Calcd for $C_{15}H_{20}O_2$: 232.149. Found: 232.149, 214 (M^+ − 18, base peak). ^{1}H-NMR ($CDCl_3$) δ: 1.46—1.79 (2H, m, –CH_2CH_2–), 1.96—2.30 (2H, m, –CH_2CH_2–), 2.79 (1H, m, –$CHCH_2$–), 3.62 (2H, dd, J=6, 6 Hz, HO–CH_2–), 3.80 (3H, s, O–CH_3), 4.86—5.18 (2H, m, CH_2=CH–), 5.13, 5.28 (2H, each s, –C=CH_2), 5.59—6.10 (1H, m, CH_2=CH–), 6.87 (2H, dd, J=2, 8 Hz, Ar-H), 6.93 (1H, d, J=2 Hz, Ar-H), 7.16 (1H, dd, J=8, 8 Hz, Ar-H).

***N*-[2-(1-Phenylethenyl)-5-hexenyl]oxazolidine-2,4-dione (6a)**——A solution of diisopropyl azodicarboxylate (4.04 g, 20 mmol) in THF (10 ml) was added to a stirred mixture of **5a** (4.04 g, 20 mmol), triphenylphosphine (5.24 g, 20 mmol), oxazolidine-2,4-dione (4.04 g, 20 mmol) and THF (30 ml) under ice-cooling. Stirring was continued at room temperature for 14 h, the solvent was evaporated off and the remaining residue was chromatographed on silica gel by using hexane–benzene (3 : 1) as an eluant. Removal of the solvent afforded 4.16 g (73% yield) of **6a** as an oil. MS *m/z*: 285 (M^+). Exact MS *m/z*: Calcd for $C_{17}H_{19}NO_3$: 285.136. Found: 285.135. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1808, 1720 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 1.53—1.77 (2H, m, –CH_2CH_2–), 2.00—2.23 (2H, m, –CH_2CH_2–), 3.08—3.33 (1H, m, –$CHCH_2$–), 3.54—3.68 (2H, m, –NCH_2–), 4.30 (2H, s, –$COCH_2O$–), 4.83—5.07 (2H, m, CH_2=CH–), 5.13, 5.34 (2H, each s, –C=CH_2), 5.49—6.00 (1H, m, CH_2=CH–), 7.30 (5H, br s, Ar-H).

***N*-[2-(1-3′-Methoxyphenylethenyl)-5-hexenyl]oxazolidine-2,4-dione (6b)**——This compound (4.41 g, 70% yield) was obtained as an oil by a procedure similar to that described above for the preparation of **6a**, from **5b** (4.64 g, 20 mmol), triphenylphosphine (5.24 g, 20 mmol), oxazolidine-2,4-dione (4.04 g, 20 mmol) and diisopropyl azodicarboxylate (4.04 g, 20 mmol). MS *m/z*: 315 (M^+). Exact MS *m/z*: Calcd for $C_{18}H_{21}NO_4$: 315.147. Found: 315.146. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1810, 1720 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 1.50—1.77 (2H, m, –CH_2CH_2–), 1.97—2.23 (2H, m, –CH_2CH_2–), 3.07—3.33 (1H, m, –$CHCH_2$–), 3.50—3.67 (2H, m, –NCH_2–), 3.77 (3H, s, O–CH_3), 4.30 (2H, s, $COCH_2O$), 4.84—5.07 (2H, m, CH_2=CH–), 5.13, 5.40 (2H, each s, =CH_2), 5.53—5.97 (1H, m, CH_2=CH–), 6.70—6.93 (3H, m, Ar-H), 7.10—7.27 (1H, m, Ar-H).

***N*-[2-(1-4′-Methoxyphenylethenyl)-5-hexenyl]oxazolidine-2,4-dione (6c)**——This compound (4.73 g, 73% yield)

was obtained as an oil by the same procedure as above from **5c**[9] (4.64 g, 20 mmol), triphenylphosphine (5.24 g, 20 mmol), oxazolidine-2,4-dione (2.04 g, 20 mmol) and diisopropyl azodicarboxylate (4.04 g, 20 mmol). MS *m/z*: 315 (M^+). Exact MS *m/z*: Calcd for $C_{18}H_{21}NO_4$: 315.147. Found: 315.147. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1810, 1720 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 1.50—1.77 (2H, m, $-CH_2CH_2-$), 1.97—2.27 (2H, m, $-CH_2CH_2-$), 3.10—3.37 (1H, m, $-CHCH_2-$), 3.57—3.74 (2H, m, $-NCH_2-$), 3.80 (3H, s, $O-CH_3$), 4.37 (2H, s, $COCH_2O$), 4.87—5.13 (2H, m, $CH_2=CH-$), 5.12, 5.38 (2H, each s, $-C=CH_2$), 5.60—6.03 (1H, m, $CH_2=CH-$), 6.90 (2H, d, J=7 Hz, Ar-H), 7.37 (2H, d, J=7 Hz, Ar-H).

***N*-[2-(1-Phenylethenyl)-5-hexenyl]-4-phenylthiooxazolidin-2-one (8a)**——$NaBH_4$ (1.5 g, 45.5 mmol) was added in small portions to a stirred solution of **6a** (4.3 g, 15 mmol) in methanol (50 ml) below 0 °C. Stirring was continued at the same temperature for 4 h, the solvent was evaporated off and the resulting residue was diluted with water and extracted with $CHCl_3$. The extract was dried (Na_2SO_4) and evaporated to give 3.76 g (88% yield) of the 4-hydroxyoxazolidin-2-one (**7a**); this was used for the following reaction without purification. A mixture of **7a** (2.87 g, 10 mmol), diphenyl disulfide (2.18 g, 10 mmol), *n*-Bu_3P (2.2 g, 11 mmol) and benzene (30 ml) was stirred at room temperature for 24 h. After evaporation of the solvent, the remaining residue was chromatographed on silica gel (30 g). Elution with hexane–AcOEt (9 : 1) gave **8a** (2.46 g, 63% yield) as an oily mixture of diastereomers. EI-MS did not give an M^+ ion peak, CI-MS *m/z*: 380 (M^++1). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1741 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 1.50—2.17 (2H, m, 3-H_2), 1.93—2.23 (2H, 4-H_2), 2.70—3.17 (1H, m, 2-H), 3.34—4.22 (3H, m, 4-H and NCH_2-), 4.50—5.17 (3H, m, $H_2C=CH-$ and 5-H), 5.36, 5.41 (2H, each s, $PhC=CH_2$), 5.5—6.0 (1H, m, $H_2C=CH-$), 7.33 (10H, br s, Ar-H).

***N*-[2-(1-3′-Methoxyphenylethenyl)-5-hexenyl]-4-phenylthiooxazolidin-2-one (8b)**——This compound (2.66 g, 65% yield) was obtained as an oily mixture of diastereomers by the same procedure as above from **7b** (3.17 g, 10 mmol; obtained by reduction of **6b**), diphenyl disulfide (2.18 g, 10 mmol) and *n*-Bu_3P (2.2 g, 10 mmol). CI-MS *m/z*: 410 (M^++1). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1741 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 1.25—2.27 (4H, m, 3-H_2 and 4-H_2), 2.70—3.20 (1H, m, 2-H), 3.37—3.90 (2H, NCH_2-), 3.82 (3H, s, OCH_3), 4.07—4.30 (2H, 5-H and 4-H), 4.60—5.27 (3H, m, $H_2C=CH-$ and 5-H), 5.43, 5.51 (2H, each s, $PhC=CH_2$), 5.60—6.10 (1H, m, $H_2C=CH-$), 6.77—7.53 (9H, m, Ar-H).

***N*-[2-(1-4′-Methoxyphenylethenyl)-5-hexenyl]-4-phenylthiooxazolidin-2-one (8c)**——This compound (2.74 g, 67% yield) was obtained as an oily mixture of diastereomers by the same procedure as above from **7c** (3.17 g, 10 mmol; obtained from **6c**), diphenyl disulfide (2.18 g, 10 mmol) and *n*-Bu_3P (2.2 g, 10 mmol). CI-MS *m/z*: 409 (M^++1). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1740 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 1.37—2.27 (4H, m, 3-H_2 and 4-H_2), 2.70—3.17 (1H, m, 2-H), 3.47—3.67 (2H, m, $N-CH_2$), 3.80 (3H, s, OCH_3), 4.07—4.37 (2H, m, 5-H and 4-H), 4.63—5.17 (3H, m, $H_2C=CH-$ and 5-H), 5.33 (1H, s, $PhC=CH$), 5.40 (1H, br s, $PhC=CH$), 5.53—6.03 (1H, m, $H_2C=CH-$), 6.87 (2H, d, J=7 Hz, Ar-H), 7.23—7.47 (7H, m, Ar-H).

5,5a,6,7,8,8a,9,9a-Octahydro-8-methyl-8a-phenyl-1*H*,3*H*-oxazolo[3,4-*a*]cyclopenta[*d*]pyridin-3-one (9a)——A solution of tri-*n*-butyltin hydride (1.4 g, 4.8 mmol) in benzene (100 ml) was added to a stirred solution of **8a** (1.14 g, 3 mmol) and azobisisobutyronitrile (15 mg) in benzene (200 ml) under reflux. The mixture was heated under reflux for 4 h. The solvent was evaporated off and the resulting residue was chromatographed on silica gel (30 g). Elution with hexane gave decomposed stannic compounds, which were discarded. Elution with AcOEt–hexane (1 : 5, v/v) gave **9a** (463 mg, 57% yield), mp 130—131 °C[17] (lit.,[5] mp 128—131 °C). MS *m/z*: 271 (M^+). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1738 (C=O). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 0.77 (3H, d, J=6.64 Hz, 8-CH_3), 1.36—1.52 (2H, m, 6-H and 7-H), 1.71—1.81 (1H, m, 6-H), 1.90—2.02 (3H, m, 7-H and 9-H_2), 2.16—2.19 (1H, m, 8-H), 2.70—2.77 (1H, m, 5a-H), 3.01 (1H, dd, J=3.84, 13.12 Hz, 5-H), 3.65 (1H, br signal, 9a-H), 3.63—3.68 (1H, m, 9a-H), 3.79 (1H, dd, J=1.48, 13.12 Hz, 5-H), 3.97 (1H, dd, J=5.60, 8.48 Hz, 1-H), 4.41 (1H, dd, J=8.48, 8.48 Hz, 1-H), 7.33—7.40 (5H, m, Ar-H). *Anal.* Calcd for $C_{17}H_{21}NO_2$: C, 75.24; H, 7.80; N, 5.16. Found: C, 75.63; H, 7.81; N, 5.06.

5,5a,6,7,8,8a,9,9a-Octahydro-8a-(3-methoxyphenyl)-8-methyl-1*H*,3*H*-oxazolo[3,4-*a*]cyclopenta[*d*]pyridin-3-one (9b)——This compound (569 mg, 63% yield) was obtained from 1.23 g (3 mmol) of **8b** by the same procedure as above, mp 123—124 °C. MS *m/z*: 301 (M^+). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1738 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 0.77 (3H, d, J=6.55 Hz, 8-CH_3), 1.35—1.50 (2H, m, 6-H and 7-H), 1.70—1.80 (1H, m, 6-H), 1.84—2.01 (3H, m, 7-H and 9-H_2), 2.62—2.70 (1H, m, 5a-H), 3.01 (1H, dd, J=3.83, 13.64 Hz, 5-H), 3.61—3.68 (1H, m, 9a-H), 3.68 (1H, d, J=13.64 Hz, 5-H), 3.82 (3H, s, $O-CH_3$), 3.96 (1H, dd, J=5.56, 8.49 Hz, 1-H), 4.40 (1H, dd, J=8.49, 8.49 Hz, 1-H), 6.79 (1H, dd, J=2.35, 8.20 Hz, Ar-H), 6.87—6.93 (2H, m, Ar-H), 7.30 (1H, dd, J=8.20, 8.20 Hz, Ar-H). *Anal.* Calcd for $C_{18}H_{23}NO_3$: C, 71.73; H, 7.69; N, 4.65. Found: C, 72.00; H, 7.62; N, 4.65.

5,5a,6,7,8,8a,9,9a-Octahydro-8a-(4-methoxyphenyl)-8-methyl-1*H*,5*H*-oxazolo[3,4-*a*]cyclopenta[*d*]pyridin-3-one (9c)——This compound (587 mg, 65% yield) was obtained from 1.23 g (3 mmol) of **8c** by the same procedure as above, mp 172—174 °C[17] (lit.,[5] mp 160—163 °C). MS *m/z*: 301 (M^+). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1738 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 0.76 (3H, d, J=6.72 Hz, 8-CH_3), 1.36—1.60 (2H, m, 6-H and 7-H), 1.69—1.82 (1H, m, 6-H), 1.89—2.02 (3H, m, 7-H and 9-H_2), 2.72—2.61 (1H, m, 5a-H), 3.01 (1H, dd, J=3.84, 13.60 Hz, 5-H), 3.62—3.69 (1H, m, 9a-H), 3.67 (1H, dd, J=1.32, 13.60 Hz, 5-H), 3.81 (3H, s, $O-CH_3$), 3.96 (1H, dd, J=5.72, 8.40 Hz, 1-H), 4.40 (1H, dd, J=8.40, 8.40 Hz, 1-H), 6.91 (2H, d, J=8 Hz, Ar-H), 7.24 (2H, d, J=8 Hz, Ar-H). *Anal.* Calcd for $C_{17}H_{23}NO_3$: C, 71.73; H, 7.69; N, 4.65. Found: C, 71.76; H, 7.69; N, 4.64.

2-Benzyloxycarbonyl-2,3,4,4a,5,6,7,7a-octahydro-3-hydroxymethyl-5-methyl-4a-phenyl-*cis*-1*H*-cyclopenta[*c*]-

pyridine (16)——A mixture of **9a** (500 mg, 1.84 mol) and 10% ethanolic sodium hydroxide (10 ml) was heated under reflux for 10 h and the solvent was evaporated off. The resulting residue was diluted with a mixture of water (2 ml) and toluene (15 ml). Benzyl chloroformate (1.15 g of 30% toluene solution (2 mmol) was added to this mixture under ice-cooling and stirring. Stirring was continued at the same temperature for 0.5 h, then the mixture was poured into water (30 ml) and extracted with $CHCl_3$. The extract was washed with water, dried (Na_2SO_4) and evaporated to leave **16** (960 mg, 87% yield) as an oil. CI-MS *m/z*: 380 ($M^+ + 1$). ^{1}H-NMR ($CDCl_3$) δ: 0.87 (3H, d, J=6 Hz, 5-C$\underline{H}_3$), 4.98 (2H, s, PhC$\underline{H}_2$–O).

2-Benzyloxycarbonyl-2,3,4,4a,5,6,7,7a-octahydro-5-methyl-4a-phenyl-*cis*-1*H*-cyclopenta[*c*]pyridine (18)——A solution of dimethyl sulfoxide (0.9 ml of 4.5 M CH_2Cl_2 solution) was added to a stirred solution of oxalyl chloride (4.5 ml of 0.45 M CH_2Cl_2 solution) at −78 °C. After 2 min, a solution of **16** (500 mg, 1.36 mmol) in CH_2Cl_2 (2 ml) was further added. Stirring was continued for 15 min, then Et_3N (1.4 ml) was added. The reaction mixture was stirred at the same temperature for 15 min and then at room temperature for 5 min, saturated citric acid was added, and the whole was extracted with ether. The extract was washed with brine and dried (Na_2SO_4). Removal of the solvent yielded **17** (418 mg, 84% yield) as an oil. ^{1}H-NMR ($CDCl_3$) δ: 0.83 (3H, d, J=7 Hz, 5-C$\underline{H}_3$), 5.00 (2H, s, Ph–C$\underline{H}_2$O–), 9.49 (1H, d, J=2 Hz, 3-C$\underline{H}$O); this was used for the following reaction without purification. A mixture of **17** (377 mg, 1 mmol), tris(triphenylphosphine)rhodium chloride (0.97 g, 1 mmol) and benzene (20 ml) was heated under reflux for 2 h. Ethanol (10 ml) was added and the precipitate was removed by filtration. The filtrate was evaporated and the resulting residue was chromatographed on silica gel (10 g) by using AcOEt–hexane (1 : 9, v/v) as an eluant. Evaporation of the solvent yielded **18** (220 mg, 63% yield) as an oil. MS *m/z*: 349 (M^+). Exact MS *m/z*: Calcd for $C_{23}H_{27}NO_2$: 349.203. Found: 349.204. ^{1}H-NMR ($CDCl_3$) δ: 0.70 (3H, d, J=7 Hz, 5-C$\underline{H}_3$), 5.08 (2H, s, Ph–C$\underline{H}_2$O–).

2,3,4,4a,5,6,7,7a-Octahydro-2,5-dimethyl-4a-phenyl-1*H*-*cis*-cyclopenta[*c*]pyridine (19)——A solution of $LiAlH_4$ (1.2 ml of 1 M THF solution) was added to a solution of **18** (100 mg, 0.29 mmol) under ice-cooling. After being stirred at room temperature for 10 h, the mixture was decomposed with 10% aqueous NaOH and extracted with $CHCl_3$. The extract was dried (Na_2SO_4) and evaporated to leave **19** (56 mg, 85% yield) as an oil. MS *m/z*: 229 (M^+). Exact MS *m/z*: Calcd for $C_{16}H_{23}N$: 229.183. Found: 229.182, 228 ($M^+ - 1$, base peak). ^{1}H-NMR ($CDCl_3$) δ: 0.72 (3H, d, J=6 Hz, 5-C$\underline{H}_3$), 1.44—2.14 (8H, m, 4-$\underline{H}_2$, 5-H, 6-$\underline{H}_2$, 7-$\underline{H}_2$, 7a-$\underline{H}$), 2.08 (3H, s, 2-C$\underline{H}_3$), 2.48—2.78 (4H, m, 1-$\underline{H}_2$, 3-$\underline{H}_2$), 7.29 (5H, br s, Ar-$\underline{H}$).

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