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Synthesis of Bis(silyloxy) Cross-Conjugated Polyenes and Their Sequential Ring Formations via Electrocyclization

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Presented are the synthesis of several bis(silyloxy) cross-conjugated polyenes and some synthetic utilization of these new types of conjugation systems via thermal or photochemical electrocyclization.

Diene-transmissive Diels-Alder reactions of bis(silyloxy)-substituted cross-conjugated trienes A, as well as equivalent reactions, have found wide synthetic applications as a new strategy to construct carbocycles and heterocycles which consist of two six-membered rings.\textsuperscript{1)} It is especially important that this sequential ring-forming reaction offers a highly regio- and stereoselective synthetic route to fused ring systems with many functional groups.\textsuperscript{2)}

Our long-standing interest in developing the synthetic utilization of bis(silyloxy) cross-conjugated polyenes let us deal in the synthetic work of new types of cross-conjugated polyenes and further investigate a new synthetic method consisting of their sequential cycloaddition or cyclization reactions.

Our new method for sequential cycloaddition reaction of bis(silyloxy) cross-conjugated polyenes B involves i) a moiety of linearly conjugated triene of polyenes B undergoes the initial intramolecular $6\pi$-electrocyclization forming C and ii) the second Diels-Alder cycloaddition reaction across the newly formed bis(silyloxy) diene leading to fused 6/6-ring compounds D as outlined in Scheme 1. Transformation of the cyclization products C into the dehydrogenated compound E, and further into the corresponding chromone derivatives, has been also carried out.

Results and Discussion

Synthesis of Bis(silyloxy) Cross-Conjugated Polyenes. 2,4-Pentanediene underwent ready condensations with aldehydes such as (E)-cinnamaldehyde,\textsuperscript{3)} 2-furanecarbaldehyde,\textsuperscript{4)} and 2-thiophenecarbaldehyde\textsuperscript{4)} to produce the corresponding 3-alkyldene-2,4-pentanediones 1a-c (Scheme 2). These diketones 1a-c were then silylated with chlorotrimethylsilane in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in dichloromethane\textsuperscript{5)} to give 3-cinnamylidene-(2a, 76%), 3-(2-furylmethylene)-(2b, 94%), and 3-(2-thienylmethylene)-2,4-bis(trimethylsilyloxy)-1,4-pen-
tadiene (2c, 97%).

The purity of the polyenes 2a-c thus obtained was about 80%. Although they could be purified by silica gel column chromatography, a significant decomposition of 2 into diketones 1 and dienyl ketones 3 took place on silica gel to result in some critical weight loss of 2. Thus, yields of pure samples of 2 were finally 34% for 2a, 31% for 2b, and 35% for 2c. Attempted separation of pure 2 by vacuum distillation was not successful either, mixtures of 2b and 3b (4:1, 72%) or 2c and 3c (4:1, 68%) being only obtained. Therefore, the polyenes 2a-c obtained pure by silica gel column chromatography were used for the following reactions.

![Scheme 1](image1)

![Scheme 2](image2)

a: R = PhCH=CH(E)
b: R = 2-Furyl
c: R = 2-Thienyl

5a: R = TMS
5b: R = H
On the other hand, when diketone 1a was silylated with chlorotrimethylsilane by use of triethylamine under reflux in dry N,N-dimethylformamide (DMF), a cyclized product 5a was obtained in 30% yield. This unusual reaction probably took place through the steps shown in Scheme 2: i) the initial thermal electrocyclic reaction of polyene 2a forming six-membered ring F with a cross-conjugated triene moiety, ii) a 1,5-proton migration forming another cross-conjugated triene G, and iii) the further 1,5-proton migration leading to aromatic compound 5a. Compound 5a was easily hydrolyzed to 5b in quantitative yield on treatment with MeOH.

This result indicates a possible formation of cross-conjugated trienes, e.g. F, through 6π-electroyclic reaction of cross-conjugated polyenes 2 by a proper choice of reaction conditions. Therefore, an effective utilization of the resulting cross-conjugated trienes in Diels-Alder cycloaddition is expected.

Synthetic Utilization of Bis(silyloxy) Cross-Conjugated Polyenes 2a-c. First of all, a sequence of an electrocyclic reaction and Diels-Alder cycloaddition was investigated by employing polyene 2a. Heating 2a under reflux in dry xylene for 24 h, followed by treating the resulting reaction mixture with an equivalent of dimethyl acetylenedicarboxylate (DMAD) at 90°C for 36 h, afforded a dihydronaphthalene derivative 6 in 25% yield, after work up with methanol (Scheme 3). The structure was confirmed on the basis of the spectral data as well as the elemental analysis.

This reaction probably proceeded through the steps shown in Scheme 3. The initial 6π-electrocyclization of 2a forms F that carries a peripheral diene moiety activated by the two trimethylsilyloxy substituents. The intermolecular second cycloaddition with DMAD leads to another intermediate H. A 1,4-elimination of trimethylsilanol from H is followed by hydrolysis into the isolated product 6.

Disappointingly, intermolecular Diels-Alder cycloadditions of the peripheral diene F with olefinic dienophiles were not clean reactions, mixture of complex products being formed. As a
result, dienophiles which can be effectively utilized in the reaction with F would be limited to acetylenic ones such as DMAD.

Since heating 2b under reflux in toluene for 24 h was not sufficient enough to cause a thermal $6\pi$-electrocyclization and 2b was quantitatively recovered, its photochemical cyclization was investigated. Irradiation of the diluted solution of 2b in benzene by using a 400-W mercurry lamp for 6 h gave, after the work up with methanol, a benzofuran derivative 7a in 70% yield (Scheme 4). A similar irradiation procedure of 2c gave a benzothiophene derivative 7b only in 12% yield, which was accompanied by a lot of products insoluble in benzene.

Both 7a and 7b correspond to the products which are derived by a spontaneous dehydrogenation of the photocyclized products I followed by hydrolytic desilylation. This unexpectedly ready dehydrogenation of I forced us to give up their utilization in the further Diels-Alder cycloaddition reaction. 7)

As these transformations are a new process to construct the heterocycle-fused benzene ring bearing both a hydroxy and an adjacent acetyl functional groups, they can be promising synthetic intermediates for the synthesis of heterocycle-fused chromone derivatives. 8)

In this view, the condensation of 7a and 7b with ethyl acetate was carried out to give furochromone 8a (70%) and thiencoerhrome 8b (52%), respectively. Their structures were based upon spectral data. To the best of our knowledge, any process leading to chromones via a photocyclization is unknown. This sequence offers a convenient and short synthesis of heterocycle-fused chromones by starting from readily available 3-(heteroarylmethylene)-2,4-pentadienes (Scheme 4). 9)

![Scheme 4.](image)

Experimental

**General.** Melting points were determined on a Yanagimoto melting point apparatus and are uncorrected. IR spectra were taken with a JASCO A-720 spectrometer. $^1$H NMR spectra
were recorded on a Hitachi R-40 (90 MHz) or a JEOL FX-100 (100 MHz) instrument, and $^{13}$C NMR on a JEOL FX-100 (25.05 MHz) spectrometer. Chemical shifts are expressed in parts per million downfield from tetramethylsilane as an internal standard. Mass spectra as well as high-resolution mass spectra were measured with a JEOL-01SG-2 spectrometer at 70 eV of ionization energy. Elemental analyses were performed on a Hitachi 026 CHN analyzer. For preparative column chromatography Silica gel 60 (Merck) was employed. Micro vacuum distillation was carried out on a Sibata GTO-250R Kugelrohr distilling apparatus. Solvents were evaporated with a Tokyo Rikakikai rotary evaporator type-V at about 50°C unless otherwise stated.

**Material.** 3-Alkylidene-2,4-pentanediones 1a-c were prepared according to the procedure reported in the literatures.3,4

**General Procedure for the Synthesis of Cross-conjugated Polyenes 2.** To a mixture of a 2-alkylidene-2,4-pentanedione derivative 1 and DBU (2 equivalents) in dichloromethane (6-7 ml per 10 mmol of 1) was added chlorotrimethylsilane (2 equivalents) at room temperature. The mixture was heated at 40°C for 24 h under nitrogen and then all the volatile materials were removed in vacuo. The residue was triturated with hexane (20 ml per 10 mmol of 1), the hexane separated from the insoluble DBU · HCl was concentrated in vacuo, and the crude product 2 was purified by column chromatography.

3-Cinnamylidene-2,4-bis(trimethylsilyloxy)-1,4-pentadiene (2a): The reaction between 3-cinnamylidene-2,4-pentanedione (1a, 6.42 g, 30 mmol) and chlorotrimethylsilane (8.5 ml, 67 mmol) in the presence of DBU (9.12 g, 60 mmol) and the followed column chromatography of the crude product (8.2 g, 76%) with hexane-benzene (9:1 v/v) gave 2a (4.0 g, 36%) as a pale yellow oil: IR (neat) 1625, 1595, 1250, and 850 cm⁻¹; $^1$H-NMR (CDCl₃) δ = 0.20, 0.24 (each 9H, s, TMS), 4.30, 4.40, 4.60, 4.76 (each 1H, s, 1- and 5-CH₂), 6.63 (1H, d, J=10.0 Hz, PhCH=CH-CB=C), 6.63 (1H, d, J=16.5 Hz PhCH=), and 7.00-7.50 (6H, m, ArH and PhCH=C); MS m/z 358 (M⁺, base peak).

3-(2-Furylmethylene)-2,4-bis(trimethylsilyloxy)-1,4-pentadiene (2b): The reaction between 3-(2-furylmethylene)-2,4-pentanedione (1b, 3.32 g, 19 mmol) and chlorotrimethylsilane (5.2 ml, 41 mmol) in the presence of DBU (5.67 g, 37 mmol) and the followed column chromatography of the crude product (5.74 g, 94%) with hexane-benzene (1:1 v/v) gave 2b (1.85 g, 31%). The fraction eluted with benzene gave 3b (0.36 g, 8%). Further elution with hexane-ethyl acetate (3:1 v/v) gave 1b (1.71 g, 51%). The attempted purification of the crude 2b (3.45 g) by vacuum distillation (at 120°C at 0.3 mmHg) afforded a 4:1 mixture of 2b and 3b (2.62 g, 72% by $^1$H-NMR). 2b: Pale yellow oil; IR (neat) 1635, 1600, 1250, and 845 cm⁻¹; $^1$H-NMR (CDCl₃) δ = 0.20, 0.28 (each 9H, s, TMS), 4.29, 4.55 (each 1H, d, J=1.0 Hz, 1- and/or 5-CH₂), 4.45, 4.78 (each 1H, br s, 1- and/or 5-CH₂), 6.38 (1H, m, 4-H of furan ring), 6.68 (1H, m, 3-H of furan ring), 6.70 (1H, s, CH=), and 7.34 (1H, m, 5-H of furan ring); $^{13}$C-NMR (CDCl₃) δ = 0.00, 0.20, 95.65, 95.80, 110.98, 111.91, 116.02, 134.32, 142.23, 152.34, 153.32, and 155.22; MS
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\[ \text{m/z (rel intensity) 322 (M^+, base peak), 307 (35), 147 (32), and 73 (over). HRMS Found: m/z 332.1426.} \]

\[ \text{Calcd for C}_{16}\text{H}_{23}\text{O}_{3}\text{Si}_2: M, 322.1421.} \]

3b: Only \(^1\)H-NMR spectrum of this compound is available. \(^1\)H-NMR (CDCl\(_3\)) \(\delta = 0.24 \) (9H, s, TMS), 2.36 (3H, s, COMe), 4.42, 4.65 (each 1H, d, \(J = 1.5 \) Hz, =CH\(_2\)), 6.46 (1H, m, 4–H of furan ring), 6.97 (1H, m, 3–H of furan ring), 7.28 (1H, s, CH=), and 7.49 (1H, m, 5–H of furan ring).

3-(2-Thienylmethylene)-2,4-bis(trimethylsilyloxy)-1,4-pentadiene (2c): The reaction between 3-(2-thienylmethylene)-2,4-pentanedione (1c, 5.83 g, 30 mmol) and chlorotrimethylsilane (8.4 ml, 66 mmol) in the presence of DBU (9.13 g, 60 mmol) and the followed column chromatography of the crude product (9.77 g, 97%) with hexane-benzene (1:1 v/v) gave 2c (3.56 g, 35%) and 3c (1.34 g, 19%). Further elution with hexane-ethyl acetate (3:1 v/v) gave 1c (2.31 g, 40%). An attempted purification of the crude 2c (3.13 g) by vacuum distillation (at 140°C at 0.3 mmHg) gave a 4:1 mixture of 2c and 3c (2.23 g, 68% by \(^1\)H-NMR). 2c: Pale yellow oil; IR (neat) 1630, 1595, 1250, and 845 cm\(^{-1}\); \(^1\)H-NMR (CDCl\(_3\)) \(\delta = 0.20, 0.22\) (each 9H, s, TMS), 4.57, 4.71 (each 1H, d, \(J = 1.0 \) Hz, 1– and/or 5–CH\(_2\)), 4.55, 5.00 (each 1H, br s, 1– and/or 5–CH\(_2\)), 6.67 (1H, dd, \(J = 5.5 \) and 3.5 Hz, 4–H of thiophene ring), 6.87 (1H, dd, \(J = 5.0 \) and 1.5 Hz, 3–H of thiophene ring), 7.06 (1H, dd, \(J = 3.5 \) and 1.5 Hz, 5–H of thiophene ring), and 7.31 (1H, t, \(J = 0.5 \) Hz, CH=); 13C-NMR (CDCl\(_3\)) \(\delta = 0.00, 0.29, 95.48, 97.71, 121.66, 126.77, 127.60, 130.36, 134.83, 140.18, 153.48, \) and 155.78; MS m/z (rel intensity) 338 (M\(^+\), 20) and 73 (base peak).

HRMS Found: m/z 338.1186. Calcd for C\(_{16}\)H\(_{26}\)O\(_2\)Si\(_2\): M, 338.1189. 3c: Only \(^1\)H NMR of this compound is available. \(^1\)H-NMR (CD\(_6\)D\(_6\)) \(\delta = 1.50\) (3H, d, \(J = 6.0 \) Hz, Me), 5.00 (1H, q, \(J = 6.0 \) Hz, –CH–O), 6.95 (1H, s, br), and 7.00–7.70 (4H, m).

Sequential Electrocyclization/Diels-Alder Reaction of 1a Leading to 6. A solution of 1a (1.5 g, 4 mmol) in dry xylene (15 ml) was refluxed for 24 h under nitrogen and cooled to room temperature. To the resulting solution was added DMAD (0.5 g, 4 mmol) and the mixture was
heated at 90°C for 36 h under nitrogen. The xylene was evaporated in vacuo and the residue was treated with methanol (20 ml) at room temperature overnight. The methanol was evaporated in vacuo. The viscous oil was chromatographed over silica gel with hexane-ethyl acetate (1:2 v/v) as an eluent to give 6 (0.34 g, 25%): Colorless prisms from diethyl ether-hexane; mp 57.5–58.5°C; IR (KBr) 3400 and 1700 cm⁻¹; ¹H-NMR (CDCl₃) δ=2.80–3.10 (2H, m, 5–CH₂), 3.50–3.70 (1H, m, 6–H), 3.78, 3.83 (each 3H, s, CO₂Me), 6.10 (1H, dd, J=10.0 and 3.2 Hz, 7–H), 6.90 (1H, dd, J=10.0 and 2.5 Hz, 8–H), 7.23 (6H, br s, PhH and 2–H), and 7.20 (1H, s, OH); ¹³C-NMR (CDCl₃) δ=33.64, 40.15, 52.48, 52.66, 115.59, 121.11, 125.22, 126.22, 126.69, 126.81, 127.51, 128.63, 133.56, 134.32, 144.07, 151.88, 166.14, and 170.37; MS m/z (rel intensity) 338 (M+, 59), 307 (50), 306 (base peak), 305 (22), 291 (22), 278 (22), 229 (24), and 91 (25). Found: C, 70.72; H, 5.38%. Calcd for C₂₀H₁₅O₅: C, 70.99; H, 5.36%.

Irradiation of 2b Leading to 7a. A solution of 2b (1.5 g, 4.6 mmol) in dry benzene (360 ml) was irradiated with a 400W mercury lamp for 6h. The solvent was evaporated in vacuo and the residue was treated with methanol overnight. The methanol was evaporated in vacuo and the resulting viscous oil was chromatographed over silica gel with hexane-ethyl acetate (9:1 v/v) as an eluent to give 7a (0.57 g, 70%): Yellow needles from methanol; mp 88.5–89°C; IR (KBr) 1635 (sh), 1620, and 1590 cm⁻¹; ¹H-NMR (CDCl₃) δ=2.64 (3H, s, COMe), 6.66 (1H, m, 3–H), 7.05 (1H, s, 4–H), 7.70 (1H, m, 2–H), 7.80 (1H, s, 7–H), and 12.02 (1H, s, OH); ¹³C-NMR (CDCl₃) δ=26.65, 106.83, 108.13, 112.54, 116.66, 135.42, 148.13, 150.48, 158.37, and 204.19; MS m/z (rel intensity) 176 (M⁺, 51) and 161 (base peak). Found: C, 68.27; H, 4.61%. Calcd for C₁₀H₇O₃S: C, 68.18; H, 4.58%.

Irradiation of 2c Leading to 7b. A solution of 2c (2.136 g, 6.12 mmol) in dry benzene (400 ml) was irradiated with a 400W mercury lamp for 20h. Work up of the reaction mixture was similar to that described above. The resultant viscous oil was column-chromatographed over silica gel by using a mixture of hexane-ethyl acetate (9:1 v/v) as an eluent to give 7b (0.14 g, 12%): Yellow needles from methanol; mp 119–120°C; IR (KBr) 1630 and 1560 cm⁻¹; ¹H-NMR (CDCl₃) δ=2.67 (3H, s, COMe), 7.16 (1H, d, J=5.5 Hz, 3–H), 7.28 (1H, s, 4–H), 7.62 (1H, d, J=5.5 Hz, 2–H), 8.20 (1H, s, 7–H), and 11.91 (1H, s, OH); ¹³C-NMR (CDCl₃) δ=26.65, 110.83, 118.36, 123.48, 125.66, 130.30, 133.71, 146.13, 158.89, and 204.25; MS m/z (rel intensity) 192 (M⁺, 63), 177 (base peak), 121 (29), and 42 (21). Found: C, 62.34; H, 4.16%. Calcd for C₁₀H₃O₅S: C, 62.48; H, 4.19%.

Transformation of 7a into Furochromone 8a. To a solution of 7a (1.0 g, 5.7 mmol) in dry ethyl acetate (10 ml) was added sodium hydride (60% in mineral oil, 1.0 g, 25 mmol). The mixture was stirred at room temperature for 24 h under nitrogen and then poured into ice-cold 0.1M hydrochloric acid (6 ml). The resultant precipitates were collected by filtration to give 8a (0.8 g, 70%): Colorless needles from methanol; mp 173–174°C; IR (KBr) 1650, 1460, 1430, and 855 cm⁻¹; ¹H-NMR (CDCl₃) δ=2.39 (3H, s, Me), 6.11 (1H, s, 7–H), 6.81 (1H, d, J=3.3 Hz, 3–H), 7.56 (1H, s, 4–H), 7.75 (1H, d, J=3.3 Hz, 2–H), and 8.43 (1H, s, 9–H); ¹³C-NMR
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(CDCls) $\delta$=20.66, 29.70, 106.55, 106.85, 108.84, 109.02, 127.78, 149.65, 151.90, 152.60, 166.09, and 178.64; MS m/z (rel intensity) 200 (M+, base peak), 172 (28), 160 (48), and 132 (25). Found: C, 72.13; H, 4.35%. Calcd for C12H8O3: C, 72.00; H, 4.03%.

Transformation of 7b into Thiochromone 8b. To a solution of 7b (0.077 g, 0.40 mmol) in dry ethyl acetate (2 ml) was added sodium hydride (60% in mineral oil, 0.08 g, 2.0 mmol). The mixture was stirred at room temperature overnight under nitrogen, poured into ice-cold 0.1M hydrochloric acid, and extracted with dichloromethane (30 ml). The extracts were dried over anhydrous magnesium sulfate and evaporated in vacuo. To the residue was added acetic acid (3 ml) and a few drops of conc. hydrochloric acid. The mixture was stirred at room temperature and then concentrated in vacuo. The resultant viscous oil was chromatographed over silica gel by using hexane-ethyl acetate (9:1 v/v) as an eluent to give 7b (0.018 g, 23%). Further elution with hexane-ethyl acetate (3:1 v/v) afforded 8b (0.045 g, 52%): Colorless needles from methanol; mp 144–146°C; IR (KBr) 1640 and 1600 cm$^{-1}$; $^1$H-NMR (CDCl3) $\delta$=2.40 (3H, s, Me), 6.18 (1H, s, 7–H), 7.35 (1H, d, J=5.5 Hz, 3–H), 7.70 (1H, d, J=5.5 Hz, 2–H), 7.80 (1H, s, 4–H), and 8.67 (1H, s, 9–H); MS m/z (rel intensity) 216 (M+, base peak), 176 (39), and 57 (27). Found: C, 66.41; H, 3.91%. Calcd for C12H8O2S: C, 66.65; H, 3.73%.

References

7) It is a rare case that an aromatic double bond serves as a part of reactive 1,3-diene system in Diels-Alder reactions. M. C. Klotzel, Org. Reactions, 4, 1 (1948).