

Intramolecular Cyclization of Nerol and the Related Attack of (*Z*)-Allylic Alcohol Moiety on the Terminal Olefin Linkage as Induced by TiCl_4 -PhNHMe Complex. Synthesis of Nezukone

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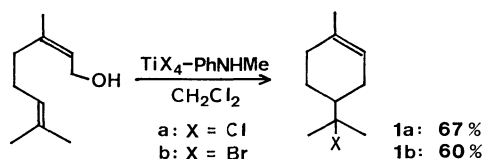
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(Received November 10, 1980)

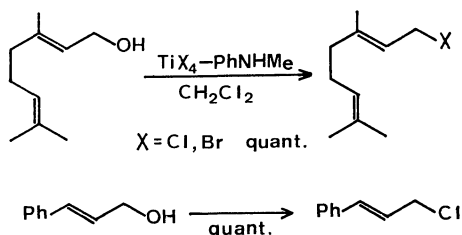
Nerol was cyclized to terpinyl chloride or bromide in the presence of TiX_4 -PhNHMe (1:1) complex (I, X=Cl, Br) in dichloromethane at -23°C , geraniol being converted into geranyl halide by simple halogenation. Terminally modified derivatives $\text{YCH}_2\text{C}(\text{Me})=\text{CHCH}_2\text{CH}_2\text{CMe}=\text{CHCH}_2\text{OH}$ (Y=SiMe₃, SnBu₃) of (2*Z*,6*E*) configuration were cyclized by treatment with I to afford limonene in high yields and 100% selectivity. Cyclization of (2*Z*) isomers of $\text{CH}_2=\text{CR}-\text{CH}_2\text{CH}_2\text{CMe}=\text{CHCH}_2\text{OH}$ (R=H, Me, Cl) produced seven-membered carbocyclic products in fair yields. The novel procedure has been utilized in the synthesis of nezukone from (2*E*)-3-isopropyl-2,6-heptadien-1-ol involving five steps.

The reaction of diethyl neryl phosphate with organoaluminium reagents R_2AlX (X=OR, NHR, etc.) has led to the stereospecific synthesis of limonene and similar cyclic terpenes.¹⁾ The smooth cyclization is ascribed to the combined Lewis acid-base character of the reagents.²⁾ We wish to report on the cyclization technique of this type which is more efficient and much simpler.³⁾

Addition of *N*-methylaniline (1.0 mmol) to a solution of TiX_4 (X=Cl or Br, 1.0 mmol) in dichloromethane at 0°C gave a complex.⁴⁾ Both the chloride and bromide complexes reacted smoothly at -23°C with nerol itself,⁵⁾ providing terpinyl halides **1a** and **1b**, respectively, in fair yields. In contrast to the previous organoaluminium reactions¹⁾ or acid catalyzed solvolytic reactions,⁶⁾ formal carbocation is thus stabilized by halide ion-uptake rather than by proton-loss.⁷⁾

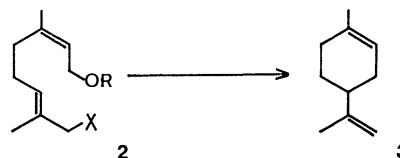


Analogous treatment of geraniol with TiX_4 -PhNHMe complex gave the corresponding geranyl halides in good yields. The drastic alteration in the course of the reaction demonstrates that the steric integrity of the allylic double bond is strictly preserved in a possible intermediate, allylic carbocation.²⁾ The results are similar to those obtained in the reactions of diethyl neryl phosphate or diethyl geranyl phosphate with organoaluminium reagents R_2AlX or R_3Al .^{1a,1b)} The TiX_4 -PhNHMe complex provides an efficient method for the transformation of allylic alcohols into allylic halides as shown below.⁸⁾



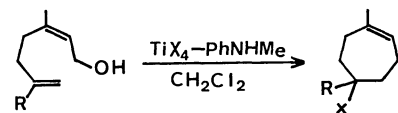
Reaction of nerol with TiCl_4 alone afforded a complex mixture not containing terpinyl chloride. It is apparent that the 1:1 complex behaves differently. The 1:1 molar ratio of TiCl_4 and PhNHMe gave the best result.⁹⁾ Several amines were examined for the reaction of nerol with TiCl_4 -amine complex with reaction conditions and yield of terpinyl chloride as follows: *N*-methylaniline, 20 min at -23°C , 67%; 2,2,6,6-tetramethylpiperidine, 20 min at -23°C , 65%; triethylamine, 1 h at 25°C , 52%; 1,4-diazabicyclo-[2.2.2]octane, 12 h at 25°C , 40%; diethylamine, 20 min at -23°C , 32%; α -methylbenzylamine, 20 min at -23°C , 28%; pyridine, 3 h at 25°C , 0%. Several other metal chlorides similar to TiCl_4 were also examined. A complex VCl_4 -PhNHMe gave **1a** in 50% yield and AlCl_3 -PhNHMe (38%) was found to be marginal. Halides such as ZrCl_4 , WCl_6 , and SnCl_4 gave no sign of cyclized products with or without an amine.

The halides **1a** and **1b** are slowly decomposed on treatment with silica gel in dichloromethane at room temperature to give a complex mixture of hydrocarbons mainly consisting of limonene and terpinolene. Selective synthesis of limonene was achieved in the following way.¹⁰⁾ Treatment of **2a** and **2b** with TiCl_4 -PhNHMe complex resulted in the exclusive formation of limonene ascribed to the expected selective elimination of SiMe₃ or SnBu₃ groups from terpinyl carbocation.¹¹⁾ This method is superior to the previously



	X	R	Reagent	Yield of 3 /%
2a	SiMe ₃	H	TiCl_4 -PhNHMe/ CH_2Cl_2	79
2a'	SiMe ₃	COCH ₃	$\text{MeAl}(\text{OCOCF}_3)_2/\text{hexane}$	29 ^{a)}
2b	SnBu ₃	H	TiCl_4 -PhNHMe/ CH_2Cl_2	73
2b'	SnBu ₃	COCH ₃	$\text{MeAl}(\text{OCOCF}_3)_2/\text{hexane}$	51

a) Polymeric products were obtained.

TABLE 1. SEVEN-MEMBERED RING FORMATION BY MEANS OF TiX_4 -PhNHMe COMPLEXES


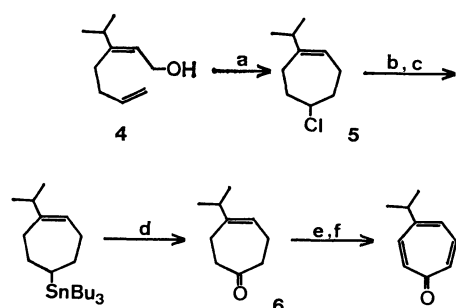
R	X	Y/%
H	Cl	65
H	Br	56
Me	Cl	66
Cl	Cl	18 ^{a)}

a) The corresponding allylic chloride was obtained in a 54% yield.

reported one¹⁰⁾ using organoaluminium reagent $\text{MeAl}(\text{OCOCF}_3)_2$ as far as cyclization yields are concerned.

Treatment of (Z)-allylic alcohols $\text{CH}_2=\text{CR}-\text{CH}_2\text{CH}_2-\text{CMe}=\text{CHCH}_2\text{OH}$ ($\text{R}=\text{H}, \text{Me}, \text{Cl}$) with the complex TiCl_4 -PhNHMe gave seven-membered ring products carrying X on the R-substituted carbon. The novel route to cycloheptenes gives satisfactory yields (Table 1). The (E)-alcohols produce the corresponding allylic halides as in the geraniol case.

The present method has provided us with a simple route to troponoid derivatives, which has been exemplified by the synthesis of nezukone. The transformation of allylic alcohol **4** into the cycloheptenyl chloride **5** was easily performed in 60% yield by means of TiCl_4 -PhNHMe complex. None of the conceivable $\text{S}_{\text{N}}2$ type reactions worked at all with the C-Cl bond of **5**, which was always recovered intact.¹²⁾ The difficulty was solved by trapping the Grignard reagent derived from **5** with Bu_3SnCl and successive oxidation by Still's method,¹³⁾ which provided cycloheptenone **6** (65%). Nezukone was obtained by simple bromination-debromination procedure (60%).¹⁴⁾



a, TiCl_4 -PhNHMe; b, Mg; c, Bu_3SnCl

d, $\text{CrO}_3 \cdot 2\text{py}$; e, $\left(\begin{array}{c} \text{O} \\ \diagup \quad \diagdown \\ \text{C} \\ \diagdown \quad \diagup \\ \text{NH} \end{array}\right)_3 \text{HBr}_3$

f, $\text{LiCl}-\text{DMF}$

Experimental

Infrared spectra were determined on a Shimadzu IR 27-G spectrometer, mass spectra on a Hitachi RMU 6-L machine, GLPC analyses on a Yanagimoto GCG 550-F, and

NMR spectra on a JEOL C-60H or Varian EM 390H spectrometer. The chemical shifts are given in δ in ppm with TMS as an internal standard. Splitting patterns are denoted by s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Microanalysis was carried out at the Elemental Analyses Center of Kyoto University. All the experiments were carried out under an atmosphere of dry argon. Tetrahydrofuran was dried by distillation from sodium-benzophenone. Thin and thick layer plates were made of E. Merck PF-254, and preparative columns silica gel E. Merck Art. 7734.

Reaction between Nerol and TiCl_4 -PhNHMe Complex. A solution of titanium tetrachloride in dichloromethane (1.0 M, 4.5 ml) was added to a solution of N-methylaniline (0.48 g, 4.5 mmol) in dichloromethane (5 ml) at 0 °C. No evolution of HCl took place. After 20 min, the resulting dark red solution was cooled to -23 °C, treated with nerol (0.46 g, 3.0 mmol), and allowed to stand at -23 °C for 1 h. Water and ether were added and the organic layer was washed with 1 M HCl, saturated aqueous solution of sodium hydrogencarbonate, and brine, dried, and concentrated. Purification by pre-cooled column chromatography on silica gel afforded terpinyl chloride **1a** (0.29 g, 57% yield) as a colorless oil: bp 108–109 °C (15 Torr, 1 Torr = 133.322 Pa); IR (neat) 2930, 1438, 1385, 1368, 1118 cm^{-1} ; NMR (CCl_4) δ 1.50 (s, 3H), 1.55 (s, 3H), 1.63–2.20 (m, 10H), 5.33 (m, 1H); MS m/e (%) 174 (3), 172 (10), 136 (47), 121 (61), 95 (59), 93 (100). Found: C, 69.33; H, 10.14%. Calcd for $\text{C}_{10}\text{H}_{17}\text{Cl}$: C, 69.55; H, 9.92%.

Similarly, the reaction between nerol and TiBr_4 -PhNHMe complex afforded terpinyl bromide **1b** (60% yield): IR (neat) 2950, 1460, 1375, 1358, 1100 cm^{-1} ; NMR (CCl_4) δ 1.50–1.80 (m, 3H), 1.63 (s, 3H), 1.71 (s, 3H), 1.77 (s, 3H), 1.90–2.10 (m, 4H), 5.28 (m, 1H); MS m/e (%) 218 (6), 216 (6), 186 (12), 137 (45), 136 (32), 121 (32), 95 (38), 93 (52), 81 (100).

(2Z)-3-Methyl-2,6-heptadien-1-ol and (2Z)-3,6-Dimethyl-2,6-heptadien-1-ol. These compounds were obtained according to a procedure similar to that for the preparation of (2Z)-6-chloro-3-methyl-2,6-heptadien-1-ol (**7**). Separation of E and Z isomers was performed prior to aluminium hydride reduction.

5-Chloro-1-methylcycloheptene: Bp 90 °C (20 Torr); IR (neat) 2950, 1450, 1235, 820 cm^{-1} ; NMR (CCl_4) δ 1.70–2.50 (m, 11H), 4.17 (m, 1H), 5.50 (m, 1H); MS m/e (%) 146 (10), 144 (27), 109 (33), 95 (33), 93 (100), 91 (27). Found: C, 66.42; H, 9.35%. Calcd for $\text{C}_8\text{H}_{13}\text{Cl}$: C, 66.43; H, 9.06%.

5-Chloro-1,5-dimethylcycloheptene: Bp 96–97 °C (21 Torr); IR (neat) 2940, 1440, 1365, 1190, 1070, 770 cm^{-1} ; NMR (CCl_4) δ 1.60 (s, 3H), 1.70 (s, 3H), 1.65–2.63 (m, 8H), 5.47 (m, 1H); MS m/e (%) 160 (12), 158 (29), 123 (30), 122 (30), 107 (84), 94 (63), 93 (100). Found: m/e 158.0874. Calcd for $\text{C}_9\text{H}_{15}\text{Cl}$: M, 158.0863.

(2Z)-6-Chloro-3-methyl-2,6-heptadien-1-ol (7**).** A solution of methyl acetoacetate (7.5 ml, 70 mmol) in THF (250 ml) was successively treated with sodium hydride (70 mmol) and butyllithium (1.8 M solution in hexane, 40 ml, 72 mmol) at 0 °C.¹⁵⁾ A solution of 2,3-dichloropropene (5.5 ml, 60 mmol) in THF (20 ml) was added to the resulting orange solution at -78 °C. After 3 h at -78 °C and 30 min at 0 °C, the mixture was poured into water and extracted with ethyl acetate. The crude product was dissolved in aqueous sodium hydroxide solution (0.9 M, 200 ml) and heated at reflux for 70 min. Extractive work-up (ether) gave essentially pure 5-chloro-5-hexen-2-one (6.4 g, 49 mmol) in 81% yield. Treatment of the hexenone (2.9 g, 22 mmol) with lithiated ethyl trimethylsilylacetate¹⁶⁾ (20 mmol, pre-

pared *in situ* from lithium dicyclohexylamide and ethyl trimethylsilylacetate) in THF (125 ml) at -78°C for 30 min and at 25°C for 30 min gave an *E* and *Z* mixture of ethyl 6-chloro-3-methyl-2,6-heptadienoate (**8**) in nearly quantitative yield. Pure samples of *E* and *Z* isomer were obtained by preparative TLC (hexane:ether=2:1) and the stereochemistry was assigned by the examination of their NMR spectra in CCl_4 .

E-Isomer: δ 1.25 (t, $J=6.9$ Hz, 3H), 2.14 (s, 3H), 2.43 (bs, 4H), 4.06 (q, $J=6.9$ Hz, 2H), 5.12 (s, 2H), 5.60 (s, 1H).

Z-Isomer: δ 1.25 (t, $J=6.9$ Hz, 3H), 1.91 (s, 3H), 2.56 (m, 2H), 2.83 (m, 2H), 4.06 (q, $J=6.9$ Hz, 2H), 5.12 (s, 2H), 5.60 (s, 1H).

A solution of **8** (4.4 g, 22 mmol, mixture of stereoisomers) in ether (25 ml) was added to a mixture of lithium aluminium hydride (2.1 g, 55 mmol) and aluminium chloride (1.9 g, 14 mmol) in ether (200 ml) at 0°C and the mixture was stirred for 80 min. Purification by silica gel column chromatography (hexane:ether=2:1) gave the title compound **7** (1.7 g, 11 mmol) in 48% yield along with the *E* isomer (0.86 g, 5.4 mmol, 24% yield). The (*Z*) compound (**7**): bp 118°C (bath temp, 21 Torr); IR (neat) 3326, 1660, 1632, 878 cm^{-1} ; NMR (CCl_4) δ 1.74 (s, 3H), 2.36 (bs, 5H), 4.03 (d, $J=6.6$ Hz, 2H), 5.11 (s, 2H), 5.41 (t, $J=6.6$ Hz, 1H); MS m/e (%) 144 (2), 142 (6), 129 (26), 107 (41), 91 (52), 84 (58), 79 (47), 71 (100). Found: C, 59.68; H, 8.10%. Calcd for $\text{C}_8\text{H}_{13}\text{ClO}$: C, 59.81; H, 8.16%.

E-Isomer of **7**: NMR (CCl_4) δ 1.69 (s, 3H), 2.19–2.57 (m, 4H), 4.03 (q, $J=6.6$ Hz, 2H), 5.17 (s, 2H), 5.45 (t, $J=6.6$ Hz, 1H).

5,5-Dichloro-1-methylcycloheptene. The compound was obtained in 18% yield by treatment of **7** with TiCl_4 -PhNHMe complex: bp 60°C (bath temp, 1 Torr); IR (neat) 2950, 1445, 1190, 1025, 980, 940, 835, 755, 700 cm^{-1} ; NMR (CCl_4) δ 1.70 (s, 3H), 2.10–2.50 (m, 8H), 5.50 (t, $J=6.0$ Hz, 1H); MS m/e (%) 182 (2), 180 (10), 178 (15), 119 (20), 117 (25), 107 (100). Found: C, 53.36; H, 6.97%. Calcd for $\text{C}_8\text{H}_{12}\text{Cl}_2$: C, 53.65; H, 6.75%.

(*2Z*)-1,6-Dichloro-3-methyl-2,6-heptadiene: IR (neat) 1662, 1632, 1254, 883 cm^{-1} ; NMR (CCl_4) δ 1.81 (s, 3H), 2.45 (bs, 4H), 4.03 (d, $J=7.8$ Hz, 2H), 5.19 (s, 2H), 5.53 (t, $J=7.8$ Hz, 1H); MS m/e (%) 182 (0.3), 180 (2), 178 (3), 142 (7), 107 (41), 91 (99), 79 (57), 77 (100).

Reaction between Geraniol and TiCl_4 -PhNHMe Complex. A solution of geraniol (0.31 g, 2.0 mmol) in dichloromethane (2 ml) was added to the TiCl_4 -PhNHMe complex derived from TiCl_4 (2.2 mmol) and PhNHMe (2.2 mmol) in dichloromethane (5 ml) at -23°C . After 1 h, the mixture was diluted with hexane and washed with water and brine. Essentially pure geranyl chloride (NMR analysis) was obtained in quantitative yield after removal of the solvent.

(*2Z*,6*E*)-3,7-Dimethyl-8-trimethylsilyl-2,6-octadien-1-ol (**2a**). Treatment of (*2E*,6*Z*)-8-acetoxyl-1-bromo-2,6-dimethyl-2,6-octadiene **9**¹⁷ (1.3 g, 4.6 mmol) with sodium benzenethiolate (13.5 mmol) in methanol (20 ml) at 65°C for 2 h gave (*2Z*,6*E*)-3,7-dimethyl-8-phenylthio-2,6-octadien-1-ol quantitatively. The sulfide (1.0 g, 4.0 mmol) was dissolved in THF (18 ml) and successively treated with butyllithium (1.7 M solution in hexane, 2.8 ml, 4.8 mmol) and *s*-butyllithium (0.85 M solution in hexane, 5.6 ml, 4.8 mmol) at -78°C . After 15 min, chlorotrimethylsilane (1.5 ml, 12 mmol) was added and the mixture was stirred for 45 min at -78°C and for 15 min at 25°C . Hydrochloric acid (1.0 M, 4.0 ml) was added and the mixture was stirred for an additional 30 min at 25°C . The crude trimethylsilylated sulfide was added to a solution of lithium (0.16 g, 23 mg-atoms) in ethylamine (5 ml) at -70°C . After 40

min, ether and methanol were added and the mixture was poured into ice-water. Purification by silica gel column chromatography afforded **2a** (0.49 g, 2.2 mmol, 55% yield based on the sulfide) as a colorless oil: bp 122°C (bath temp, 0.5 Torr); IR (neat) 3350, 1665, 1252, 995 cm^{-1} ; NMR (CCl_4) δ 0.00 (s, 9H), 1.41 (s, 2H), 1.54 (s, 3H), 1.66 (s, 3H), 2.00 (m, 4H), 3.95 (d, $J=7.2$ Hz, 2H), 4.91 (m, 1H), 5.35 (t, $J=7.2$ Hz, 1H); MS m/e (%) 147 (4), 143 (3), 141 (4), 134 (3), 121 (5), 105 (3), 75 (27), 73 (100). Found: C, 69.03; H, 11.51%. Calcd for $\text{C}_{13}\text{H}_{26}\text{OSi}$: C, 68.96; H, 11.57%.

(*2Z*,6*E*)-3,7-Dimethyl-8-tributylstannyl-2,6-octadien-1-ol (**2b**). A solution of butyllithium in hexane (1.5 M, 6.0 ml, 9.0 mmol) was added to a solution of hexabutylstannane (5.0 ml, 9.8 mmol) in THF (30 ml) at -23°C .¹⁸ After 15 min, the resulting reddish yellow solution was cooled to -78°C and treated with the bromide **9** (0.63 g, 2.3 mmol) dissolved in THF (2 ml). After 20 min at -78°C and 20 min at 0°C , the mixture was poured into water and extracted with ether. Purification by pre-cooled silica gel column chromatography (hexane:ether=2:1) gave **2b** (0.28 g, 27% yield) as a colorless oil: IR (neat) 3340, 1650, 1364, 1001 cm^{-1} ; NMR (CCl_4) δ 0.77–0.95 (m, 15H), 1.08–1.60 (m, 15H), 1.54 (s, 3H), 1.71 (s, 3H), 2.02 (m, 4H), 3.95 (d, $J=7.2$ Hz, 2H), 4.87 (m, 1H), 5.35 (t, $J=7.2$ Hz, 1H); MS m/e (%) 365 (5), 363 (50), 361 (25), 360 (9), 359 (19), 358 (8), 357 (12), 69 (100).

Reaction between **2a and TiCl_4 -PhNHMe Complex.** A solution of **2a** (0.20 g, 0.88 mmol) in dichloromethane (2 ml) was treated with the TiCl_4 -PhNHMe complex (1.3 mmol) in dichloromethane (5 ml) at -23°C . After 1 h, 1-dodecene (internal standard, 84 mg) was added and the mixture was worked up in the usual way. The yield of limonene (77%) was determined by GLPC analysis (Apiezone L 5% and KOH 1% on Chromosorb WMW dmcs, 2 m, 85°C). Reaction between **2b** and the TiCl_4 -PhNHMe complex was similarly performed (-23°C , 2 h), the yield being determined by GLPC.

Reaction between the Acetate of **2a and Methylaluminum Bis(trifluoroacetate).** A solution of the acetate of **2a** (0.25 g, 0.94 mmol) in hexane (1 ml) was added to methylaluminum bis(trifluoroacetate)¹¹ (1.9 mmol, prepared *in situ*) in hexane (2 ml) and the mixture was stirred at 25°C for 17 h. The yield (28%) was determined by GLPC. The reaction between the acetate of **2b** and the aluminium reagent was similarly performed (25°C , 21 h).

(*2Z*)-3-Isopropyl-2,6-heptadien-1-ol (**4**). Allylation of 3-methyl-2-butanone dimethylhydrazone and subsequent hydrolysis¹⁹ afforded 2-methyl-6-hepten-3-one in 51% yield based on the hydrazone. The allylic alcohol **4** was obtained from this ketone in the usual way.

5-Chloro-1-isopropylcycloheptene (5**).** A solution of **4** (0.80 g, 5.3 mmol) in dichloromethane (3.5 ml) was added to the TiCl_4 -PhNHMe complex (8.0 mmol) in dichloromethane (15 ml) at 0°C . After 15 min at 0°C and 10 min at 25°C , the mixture was worked up. The crude product was subjected to silica gel column chromatography to give **5** (0.55 g, 3.2 mmol) in 60% yield as a colorless oil: bp 120°C (bath temp, 10 Torr); IR (neat) 1650, 1245, 830, 790, 735 cm^{-1} ; NMR (CCl_4) δ 0.93 (d, $J=7.0$ Hz, 6H), 1.5–2.6 (m, 9H), 4.10 (m, 1H), 5.53 (t, $J=6.3$ Hz, 1H). Found: C, 69.77; H, 9.70%. Calcd for $\text{C}_{10}\text{H}_{17}\text{Cl}$: C, 69.55; H, 9.92%.

4-Isopropyl-4-cycloheptenone (6**).** A mixture of the chloride **5** (1.0 g, 6.0 mmol), granular magnesium (0.43 g, 18 mg-atoms), and ether (8.5 ml) was refluxed for 20 min, a solution of tributylstannyl chloride (3.3 g, 10 mmol) in

ether (3 ml) being added. After 20 min at reflux, the mixture was poured into saturated aqueous ammonium chloride and extracted with ether. The crude product was dissolved in dichloromethane (25 ml) and added to a mixture of pyridine (19 ml, 0.24 mol) and chromium(VI) oxide (12 g, 0.12 mol) in dichloromethane (300 ml). After 12 h at 25 °C, the mixture was filtered through a pad of Celite 545, the filtrate being washed with 5% sodium hydroxide solution (three times), 1 M HCl (three times), and brine. Purification by silica gel column chromatography gave **6** (0.60 g, 3.9 mmol, 65% yield based on the chloride **5**): bp 80 °C (bath temp, 3 Torr); IR (neat) 1705, 1660, 1460, 1260 cm^{-1} ; NMR (CCl_4) δ 1.00 (d, $J=7.0$ Hz, 6H), 2.0–2.6 (m, 9H), 5.57 (t, $J=5.7$ Hz, 1H); MS m/e (%) 152 (M^+ , 94), 137 (34), 124 (28), 119 (27), 110 (36), 109 (76), 95 (100). Found: m/e 152.1189. Calcd for $\text{C}_{10}\text{H}_{16}\text{O}$: M , 152.1200.

Nezukeone. Pyrrolidone hydrotribromide (0.20 g, 0.40 mmol) was added to a solution of the cycloheptenone **6** (20 mg, 0.13 mmol) in THF (5 ml) and the mixture was stirred in the dark at 25 °C for 24 h. The solvent was removed under reduced pressure and the residue was diluted with water (25 ml) and chloroform (10 ml). The aqueous layer was extracted with chloroform (10 ml, four times). The crude product was dissolved in DMF (5 ml) and the solution heated at 150 °C for 1 h in the presence of anhydrous lithium chloride (0.10 g). Water was added and the product was extracted with chloroform. Purification by preparative TLC (benzene: ether=2:1) gave nezukeone (12 mg, 0.08 mmol) in 62% yield whose spectral characteristics (IR, NMR, MS) were identical with those reported.²⁰⁾

Financial support by the Ministry of Education, Science and Culture, Japanese Government, (Grant-in-Aid No. 403022 and No. 375472) is acknowledged.

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- 9) In an attempt to find the suitable molar ratio between TiCl_4 and PhNHMe, we studied the reaction of nerol with a variety of complexes derived from different molar ratios. The yields of terpinyl chloride were 67% (TiCl_4 : PhNHMe=1:1), 20% (1:2), and 0% (1:3 and 1:4).
- 10) Another solution of this problem on the termination of the cationic cyclization was provided by the use of bulky O-base in the R_2AlOAr system. See Ref. 1d.
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- 12) The failure of all the $\text{S}_{\text{N}}2$ type reactions attempted is ascribed to the opposed π bond. See S. J. Rhoads, J. M. Watson, and J. G. Kambouris, *J. Am. Chem. Soc.*, **100**, 5151 (1978).
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