For the analysis of aromatic hydrocarbon, the reaction mixture was injected without pretreatment. The eluent was aqueous methanol (CH_3OH/H_2O = 7/3), and the flow rate was 1.5 mL/min.

Spectroscopy. A Hitachi UV-320 spectrometer and a Hitachi MPF-4 spectrofluorometer were used for absorption and fluorescence spectroscopies, respectively. A JNM-PMX 60-MHz ^1H NMR spectrometer (JEOL) and an IR 260-10 infrared spectrometer (Hitachi) were used for structure identification.

Registry No. I, 2222-30-2; II, 104848-69-3; III, 104834-81-3; IV, 104834-82-4; V, 104834-83-5; VI, 104834-84-6; CO_2, 124-38-9; $PhN(Me)_2$, 121-69-7; phenanthrene, 85-01-8; anthracene, 120-12-7; pyrene, 129-00-0.

Catalytic Electrophilic Reactions of Chrysanthemic Acid Derivatives with Unsaturated Organosilanes. An Application to Synthesis of Modified Types of C_{15} and C_{20} Isoprenoids with Non-Head-to-Tail Linkages

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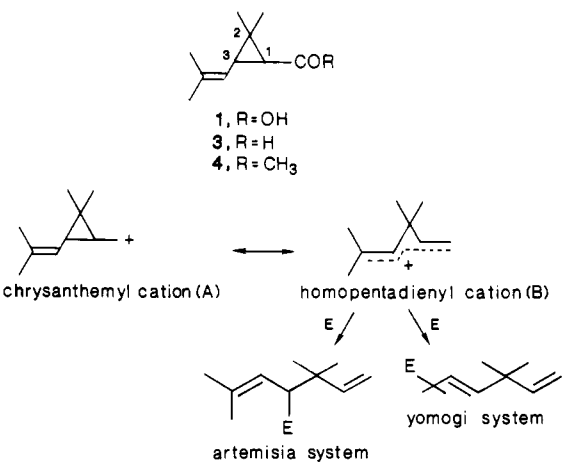
Received July 28, 1986

Chrysanthemyl silyl ether (**2b**) reacted with allylic and enolic silanes in the presence of $TiCl_4$ as a catalyst to give selectively C_1–C_3 ring-opened and ϵ-substituted products (yomogi type product). Chrysanthemaldehyde (**3**) and the corresponding methyl ketone **4** underwent similar electrophilic reactions with these reagents. These results are rationalized by the electrophilic attack of the intermediate homopentadienyl cation formed by the aid of the catalyst on an unsaturated organosilane. As for the reactivity, the trans isomer prevailed over the cis isomer, coinciding with the solvolytic behavior of chrysanthemyl 2,4-dinitrobenzoate (**2c**). The different product pattern from that in the reaction of Ti(IV) enolate with **3** giving a straightforward 1,2 addition product supported that the mechanism for the Mukaiyama reaction involves the initial polarization of a carbonyl group with $TiCl_4$ rather than Ti(IV) enolate formation. This method employing C_5 organosilanes constructed modified C_{15} and C_{20} isoprenoid skeletons with non-head-to-tail linkages by combinations $C_5 + C_{10}$ and $C_5 + C_{10} + C_5$, respectively. Thereby, even the C_{20} compound with all the isoprenoid fusions in middle-to-tail was obtainable. Of particular interest was the reaction of the enone **42** derived from the condensation reaction of the aldehyde **3** and lithium enolate of methyl isopropyl ketone; the reaction occurred at the η-position to the carbonyl center. The unusual elongation of the reactive site may originate from the cyclopropane ring strain relief.

Chrysanthemic acid (1) is a unique terpene possessing a "middle-to-tail" isoprenoid fusion. The cyclopropane ring in **1** and its derivatives is known to be cleaved by catalysis,[1] thermolysis,[2] and photolysis,[3] and thereby, the possible three ways of the ring cleavage give rise to a variety of open-chain and ring-expanded compounds depending on the structure. Specifically, carbonium ion mediated reaction of the chrysanthemyl system results in the formation of the artemisia and/or yomogi systems via a selective C_1–C_3 fission due to the cation-stabilizing ability of the isobutenyl group at C_3[4] (Scheme I).

In this decade unsaturated organosilanes are documented to be reactive with various carbon electrophiles.[5] Among them are resonance-stabilized primary and secondary alkyl cations[6] as well as tertiary alkyl cations,[7]

Scheme I[a]



[a] E = electrophile. Allylic and enolic silanes in this work.

conceptionally S_N1-reactive carbonium ions, as pronounced by Reetz.[8] From our continuous interest in the chemistry of strained organic molecules, it is reasonable to consider a cyclopropylmethyl cation generated in the chrysanthemyl system as an efficient electrophile toward such organosilicon reagents. Thus, we decided to study the Lewis acid

(1) (a) Crombie, L.; Firth, P. A.; Houghton, R. P.; Whiting, D. A.; Woods, D. K. *J. Chem. Soc., Perkin Trans. 1* **1972**, 642. Sasaki, T.; Eguchi, S.; Ohno, M. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 1469. (c) Williams, J. L.; Rettig, M. F. *Tetrahedron Lett.* **1981**, *25*, 1595. (d) Suzukamo, G.; Fukao, M.; Nagase, T. *Chem. Lett.* **1984**, 1799.

(2) (a) Crombie, L.; Harper, S. H.; Thompson, R. A. *J. Sci. Food Agric.* **1951**, *2*, 421. (b) Ohloff, G. *Tetrahedron Lett.* **1965**, 3795. (c) Sasaki, T.; Eguchi, S.; Ohno, M. *J. Am. Chem. Soc.* **1970**, *92*, 3192.

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(4) (a) Bates, R. B.; Feld, D. *Tetrahedron Lett.* **1967**, 4875. (b) Sasaki, T.; Eguchi, S.; Ohno, M.; Umemura, T. *Chem. Lett.* **1972**, 503. (c) *Ibid. J. Org. Chem.* **1971**, *36*, 1968. (d) Poulter, C. D.; Moesinger, S. G.; Epstein, W. W. *Tetrahedron Lett.* **1972**, 67.

(5) (a) Weber, R. P. *Silicon Reagents for Organic Synthesis*; Springer-Verlag: Berlin, 1983. (b) Colvin, E. W. *Silicon in Organic Synthesis*; Butterworths: London, 1981.

(6) Paterson, I. *Tetrahedron Lett.* **1979**, 1519.

(7) (a) Reetz, M. T. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 96. (b) Sasaki, T.; Nakanishi, A.; Ohno, M. *J. Org. Chem.* **1982**, *47*, 3219 and the previous papers.

(8) Reetz, M. T.; Huettenhain, S.; Waltz, P.; Loewe, U. *Tetrahedron Lett.* **1979**, 4971.

0022-3263/86/1951-4553$01.50/0

Table I. Reaction of 2 with 5

compd	Lewis acid	time	temp	yield,[a] %	product ratio (10/11)[b]
2a (cis)	$ZnCl_2$	3 h	rt	37	18/82
2a (trans)	$ZnCl_2$	12 h	rt	42	25/75
2b (cis/trans = 4/6)	$TiCl_4$	1 min	−78 °C	79	5/95

[a] Isolated. [b] Estimated from relative peak areas on GLC.

catalyzed reactions of chrysanthemic acid derivatives such as chrysanthemyl acetate (**2a**) and silyl ether **2b** and that of chrysanthemaldehyde (**3**) and the corresponding methyl ketone **4** with allylic and enolic silanes.[9] Utilizing an organosilicon reagent as a C_5 component, $C_5 + C_{10}$ and $C_5 + C_{10} + C_5$ combinations may constitute a method for the formation of a variety of nonnatural type of isoprenoids with head-to-middle, middle-to-middle, and middle-to-tail linkages.

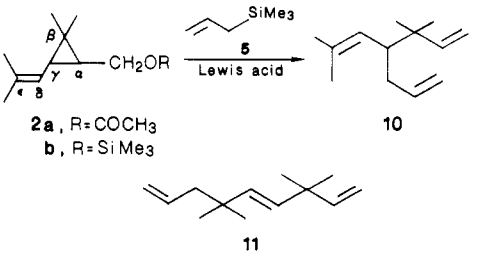
Results and Discussion

Trimethylallylsilane (**5**) is a reagent of choice to examine in detail the electrophilic substitution reaction of the chrysanthemyl cation (A). Thus, *trans*-chrysanthemyl acetate (**2a**) was treated with **5** in CH_2Cl_2 at room temperature catalyzed with $ZnCl_2$. The reaction was completed within 3 h, and the products were purified by silica gel chromatography. The GLC analysis indicated that the products consisted of similar two hydrocarbons in a ratio of 18/82. They seemed to be structural isomers that were finally separated by preparative GLC, and their structures were determined by elemental and spectral analyses. The minor isomer was assigned as 4-allyl-3,3,6-trimethyl-1,5-heptadiene (**10**), a product substituted γ to the primarily generated cationic center (i.e., artemisia-type product); the NMR spectrum showed the presence of vinyl groups (δ 4.7–5.9) and an isobutenyl group (δ 4.78). The major isomer was 3,3,6,6-tetramethyl-1,4,8-nonatriene (**11**) (yomogi-type product), which, in contrast, arised from ϵ substitution; the NMR spectrum showed trans olefinic protons at δ 5.25 (AB q, J = 18 Hz) in addition to vinylic protons. In the same way, cis acetate **2a** was treated with **5** and the products were analyzed as **10**/**11** = 25/75. The reaction time for the *cis*-**2a** was found to be 4 times longer than that for the trans isomer; this difference approximately paralleled the solvolysis rate ratio (1/5.5) for *cis*- and *trans*-chrysanthemyl 2,4-dinitrobenzoates (**2c**, R = 2,4-$(NO_2)_2C_6H_3COO$),[4b] suggesting the chrysanthemyl cation forming step to be rate determining (vide infra).

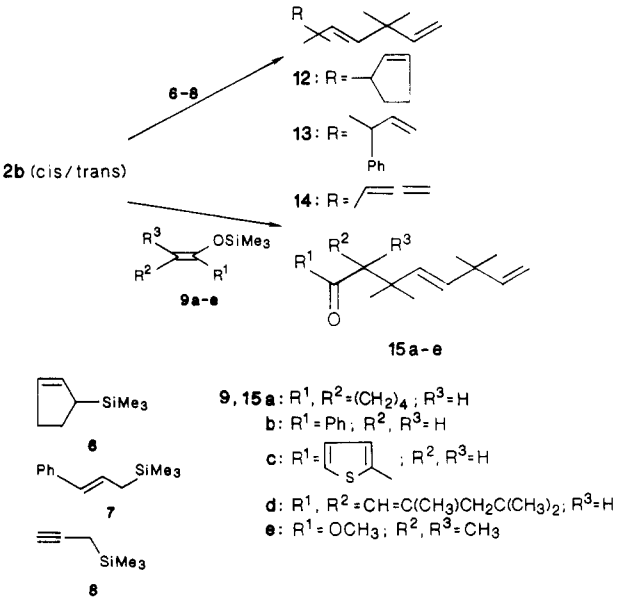
Although the above $ZnCl_2$-catalyzed reaction of the acetate **2a** resulted in only lower yield and selectivity, these disadvantages were improved by using chrysanthemyl silyl ether (**2b**) and $TiCl_4$ as a catalyst at the lower temperature. When a solution of the *trans*-**2b** and **5** was treated with $TiCl_4$ at −78 °C, the reaction was completed in much shorter time (within 1 min). Furthermore, the yield was raised to 79% and the yomogi-type product **11** was obtained in more than 95% selectivity (Table I; Scheme II). When the reaction was conducted in the absence of **5**, **2b** disappeared also within 1 min. These facts intimate that once-generated chrysanthemyl cation (A) reacted spontaneously with **5**. Not unexpectedly, the observed extreme readiness of the reaction never differentiated the cis isomer from *trans*-**2b**, allowing use of a cis and trans mixture bulk, available commercially or supplied from industry.[10]

(9) The 1,7 addition reaction of activated vinylcyclopropanes was reviewed: Danishefsky, S. *Acc. Chem. Res.* **1979**, *12*, 66.

Scheme II



Scheme III



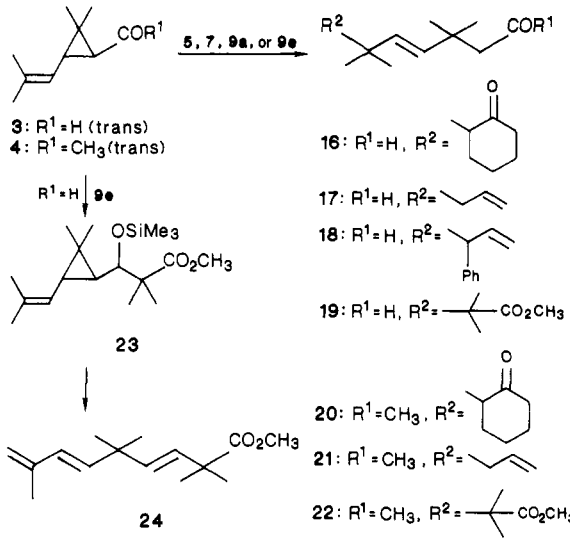
Therefore, the $TiCl_4$-catalyzed reaction was carried out with a 4/6 cis-trans mixture of silyl ether **2b** with other allylsilanes **6**–**8**; both cinnamyl- (**7**) and propargyltrimethylsilanes (**8**) followed the reported γ-substitution pattern.[7b] In like manner, the same reactions with silyl enol ethers **9a**–**e** gave selectively ϵ-substituted products **15a**–**e** (Scheme III). The structural determination for these derivatives was performed by the IR and NMR spectral data; in every case, the NMR spectra showed the characteristic signals due to trans olefinic protons as AB quartets at δ 5.2–5.4 together with the signals required for the added moiety.

In contrast to these allylic and enolic silanes, less nucleophilic vinylic silanes resulted in no reaction with **2b** under the above conditions, and only decomposition of **2b** was observed.

The present electrophilic substitution reaction can be rationalized mechanistically as follows: The action of a Lewis acid on **2** promoted the generation of a positive center α to the cyclopropyl group [chrysanthemyl cation (A)], and the resonating homopentadienyl cation (B) was trapped by an unsaturated organosilane preferentially at the tertiary ϵ-carbon to give the product (Scheme I). By the $ZnCl_2$ catalysis, the trans isomer was more reactive than the cis one in accordance with the solvolytic behavior, and by the $TiCl_4$ catalysis, regardless of the presence or absence of an organosilicon reagent, **2b** was consumed during the same reaction time. These experimental facts suggest that the key step for this reaction lies in the formation of the chrysanthemyl cation (A), which is influ-

(10) Ethyl chrysanthemate and chrysanthemol (cis/trans) are available from Aldrich Chemical Co. We thank Sumitomo Chemical Co., Ltd. for a gift of **1**.

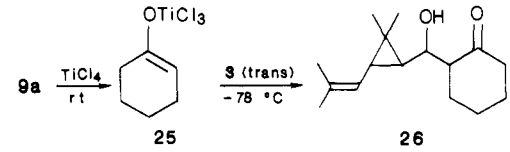
Scheme IV



enced by the different conjugative transmission ability of a cyclopropane ring between the geometrical isomers.[4b]

Aldehydes and ketones are the other class of suitable electrophiles for unsaturated organosilanes,[11] and especially, α,β-unsaturated carbonyl compounds are reported to undergo 1,4 addition reaction.[12] The present chrysanthemyl system seems to be an interesting homologue, and therefore, studies were extended to the similar type of reactions of chrysanthemaldehyde (**3**) and the corresponding methyl ketone **4**. A solution of *trans*-**3** and **9a** was treated with $TiCl_4$ at −78 °C for 30 min, and the purification by silica gel chromatography gave selectively C_1–C_3 ring-opened and ϵ-substituted product, 6-(2-oxocyclohexyl)-3,3,6-trimethyl-4-heptenal (**16**), in 40% yield. By the GLC analysis no positional isomer (e.g., γ-substituted product) was detected. Comparatively, the same reaction for the *cis*-**3** resulted in a low yield (24%) with the longer reaction time (2 h). This fact may again reflect the geometrically different ability of the vinylcyclopropyl system to polarize the carbonyl function with a catalyst. The reaction of the methyl ketone **4** with **9a** proceeded more or less in the same manner (−50 °C, 10 min) as for **3** to give the same type of product **20** in 72% yield. As was seen above, the trans isomer was more advantageous than the cis one for both yield and reaction time, and therefore, the reactions with other organosilicon reagents were carried out by using the pure *trans*-**3** and **4**. All the products **16**–**22** were produced as the result of 1,7 addition; the activation of the carbonyl group with $TiCl_4$ induced the ring opening and the simultaneous attack by an unsaturated organosilane at the ϵ-carbon. This is faithful to the aforementioned substitutive ring-opening mechanism as observed in **2**. Exceptionally, the reaction of **3** with silyl ketene acetal **9e** accompanied the formation of another type of product **24** together with the expected **19** in a ratio of 44/56 (GLC analysis). According to the spectral inspections, **24** had a conjugated diene but no aldehyde and, thus, was assigned as methyl 2,2,5,5,8-pentamethyl-3,6,8-nonatrienoate. This product **24** arised apparently from the initial addition of **9e** to the carbonyl group followed by the eliminative ring opening of the intermediate **23** (Scheme IV).

Scheme V



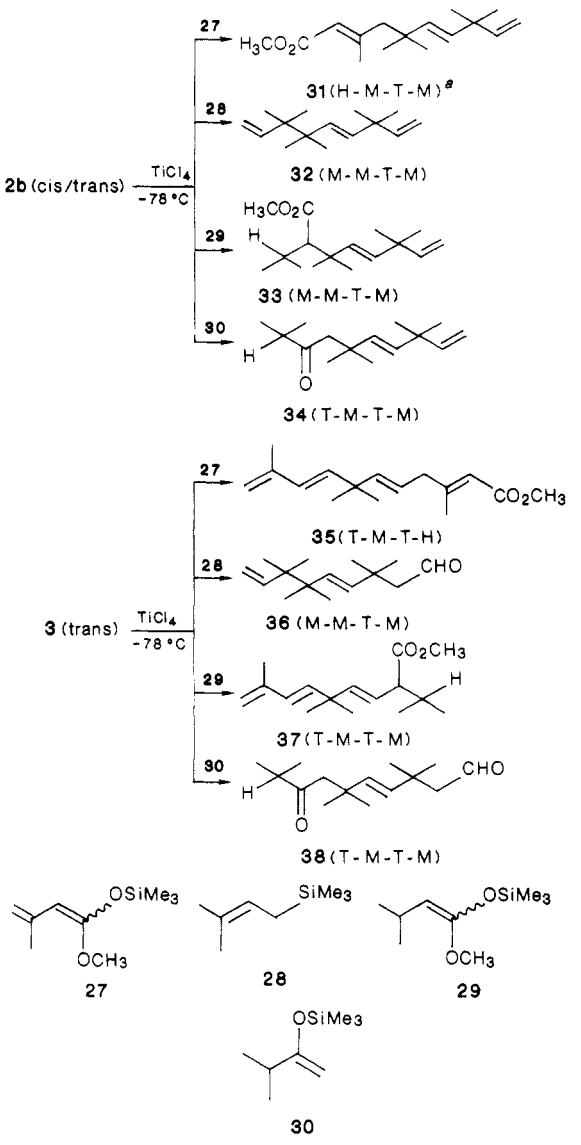
In the above experiments, the reversed addition of the reagents (i.e., addition of an organosilane to a mixture of **3** and $TiCl_4$) was disfavored, because **3** possesses the tendency to acid-catalyzed rearrangement to 4,6-heptadienal;[13] the Lewis acid promoted ring opening must be accompanied by the simultaneous electrophilic substitution with an organosilane. The alternative manner of addition, namely addition of **3** to a mixture of an organosilane and $TiCl_4$, also resulted in the formation of the different product as proved by the reaction of **3** with **9a**. When **3** was treated with the solution that was prepared by mixing $TiCl_4$ and **9a** at room temperature for 2 min (Kuwajima's method for the distinct formation of Ti(IV) enolate **25**[14]), the straightforward 1,2 addition product **26** was obtained rather than **16** (Scheme V). In the same way, only starting **4** was recovered from the reaction of **4** and **25** in contrast to the normal reaction of **4** to **21**.

The observed results give insight into the mechanistic problem[15] for the $TiCl_4$-mediated condensation of a silyl enol ether with a carbonyl electrophile (Mukaiyama reaction[11]). So far, proposed mechanisms are classified into two routes: (a) attacking of an activated carbonyl group with $TiCl_4$ on an enol double bond; (b) attacking of Ti(IV) enolate formed from $TiCl_4$ and a silyl enol ether on a carbonyl group. Judging from the discrete product pattern and reactivity as observed above, involvement of route a is strongly supported for the Mukaiyama reaction. This is in good agreement with the recent ^{29}Si NMR study by Chan.[15]

The present method can be applied to the synthesis of modified type of sesqui- and diterpenoids that are not routinely found in nature. By employing organosilanes **27**–**30** as a C_5 component, it was possible to obtain the C_{15} (C_{10} + C_5) compounds **31**–**38** containing non-head-to-tail linkages as illustrated in Scheme VI; however, **35** and **37** were produced via the exceptional addition–ring-opening sequence such as **24** from **3**. Also, the C_5 + C_{10} + C_5 combination led to nonnatural diterpenoids **41** and **43** (Scheme VII). The aldehyde **3** was first converted to the secondary alcohol **39** by the addition of prenylmagnesium chloride, and the $TiCl_4$-catalyzed reaction of the silyl ether **40** with **30** gave 2,5,5,8,8,11,11-heptamethyl-6,9,12-tridecatrien-3-one (**41**), in which all the isoprenoid fusions are composed of middle-to-tail. The enone **42** obtained from the condensation reaction of **3** with lithium enolate of methyl isopropyl ketone as a C_5 component underwent markedly extended addition reaction; this enone, **42**, reacted with **30** to give 2,7,7,10,10,13-hexamethyl-5,8-tetradecadiene-3,12-dione (**43**). In this cases, of particular interest is the addition position that is η to the carbonyl group (i.e., 1,9 addition). Since a normal enone reacts in a 1,4 addition manner,[12] this unusual elongation of the reactive site is reasonably attributed to the cyclopropane ring strain relief. All these derivatives were characterized by the elemental and spectral analyses.

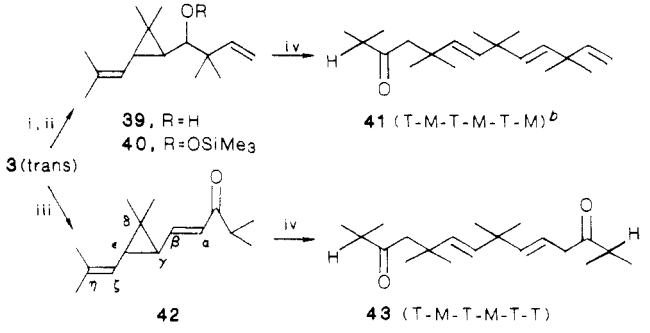
(11) Mukaiyama, T.; Banno, K.; Narasaka, K. *J. Am. Chem. Soc.* **1974**, *96*, 7503. See also ref 5 for other various examples.
(12) (a) Narasaka, K.; Soai, K.; Mukaiyama, T. *Chem. Lett.* **1974**, 1223. (b) Narasaka, K.; Soai, K.; Aikawa, K., Mukaiyama, T. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 779.
(13) Actually, this way of addition reduced the yield to less than half. See ref 1a.
(14) Nakamura, E.; Shimada, J.; Horiguchi, Y.; Kuwajima, I. *Tetrahedron Lett.* **1983**, *24*, 3341.
(15) Chan, T. H.; Brook, M. A. *Tetrahedron Lett.* **1985**, *26*, 2943.

Scheme VI



[a] Mode of isoprenoid fusion: H, head; M, middle; T, tail.

Scheme VII[a]



[a] Reagents: (i) $Me_2C{=}CHCH_2MgCl$; (ii) BTSA; (iii) $CH_2{=}C(OLi)CHMe_2$; (iv) **30**/$TiCl_4$/−78 °C. [b] See Scheme VI for this notation.

Throughout all of these reactions, the best catalyst was $TiCl_4$; the attempted catalytic reactions with $ZnCl_2$, $BF_3{\cdot}Et_2O$, and $SnCl_4$ were found to be less satisfactory.

In conclusion, the reactions of chrysanthemic acid derivatives **2b**, **3**, and **4** with allylic and enolic silanes occur very smoothly at −50 to −78 °C in the presence of $TiCl_4$ to give selectively ϵ-substituted products via ring opening at C_1–C_3. In this way, various modified type of C_{15} and C_{20} terpenoid skeletons could be constructed efficiently.

Experimental Section

Infrared spectra were determined on a Jasco A-100 spectrophotometer, and all the oily products were scanned neat. ^1H NMR spectra were determined at 60 MHz in CCl_4 with a JEOL 60-HL spectrometer, and chemical shifts were recorded in δ with tetramethylsilane as an internal standard. Microanayses were performed with a Perkin-Elmer 240 elemental analyzer. All of the chromatographic separations were carried out on a silica gel column (Fuji-Davison BW-300) with the solvent noted. The chrysanthemic acid derivatives **2a**, **3**, and **4** were prepared by our previous method.[4c,16] Unsaturated organosilanes **5–8**, **9**, and **27–30** were obtained according to the reported procedure.[7b,17–19] Dichloromethane used as a reaction solvent was dried over $CaCl_2$, distilled, and kept over 4-Å molecular sieves.

Reaction of 2a with 5. A mixture of **2a** (208 mg, 1 mmol), **5** (114 mg, 1 mmol), and $ZnCl_2$ (232 mg, 1.7 mmol) in CH_2Cl_2 (3 mL) was stirred at room temperature under atmosphere of nitrogen for 12 h for the cis isomer and 3 h for the trans isomer. The products were extracted with hexane after being poured into water and were dried over Na_2SO_4. Distillation of the solvent left an oil, which was chromatographed with hexane to give a mixture of **10** and **11** in 42% yield from cis and in 37% yield from trans. This mixture was further separated by preparative GLC (Varian aerograph, Model 700, silicon SE-30 at 130 °C) to give pure **10** and **11**.

10: IR 3070, 1670, 1640, 990, 910, 840 cm^{-1}; ^1H NMR δ 5.75 (dd, 1 H, J = 18 and 9 Hz), 5.26–5.90 (m, 1 H), 4.70–5.05 (m, 4 H), 4.78 (br d, 1 H, J = 8 Hz), 1.80–2.44 (m, 3 H), 2.21 (t, 1 H, J = 8 Hz), 2.07 (q, 2 H, J = 8 Hz), 1.72 and 1.57 (br s, each 3 H), 0.94 (s, 6 H). Anal. Calcd for $C_{13}H_{22}$: C, 87.56; H, 12.44. Found: C, 87.31; H, 12.69.

11: IR 3080, 1640, 990, 965, 910 cm^{-1}; ^1H NMR δ 5.75 (dd, 1 H, J = 18 and 10 Hz), 5.35–6.02 (m, 1 H), 5.25 (AB q, 2 H, J = 18 Hz), 4.68–5.08 (m, 4 H), 2.00 (br d, 2 H, J = 7.5 Hz), 1.05 and 0.95 (s, each 6 H). Anal. Calcd for $C_{13}H_{22}$: C, 87.56; H, 12.44. Found: C, 87.59; H, 12.41.

Preparation of 2b. To a solution of chrysanthemol (3.39 g, 22 mmol) and triethylamine (3.33 g, 33 mmol) in dry ether (50 mL) was added trimethylsilyl chloride (4.2 mL, 33 mmol), and the mixture was stirred overnight at room temperature. The precipitates were filtered off through a sintered-glass filter under a nitrogen atmosphere. After evaporation of the solvent and the excess reagents, the residual oil was subjected to trap-to-trap distillation [oven temperature 150 °C (4 mmHg)] to give 4.91 g (98%) of **2b**: IR 1660, 1250, 840 cm^{-1} (cis) and 1670, 1250, 840 cm^{-1} (trans); ^1H NMR δ 4.92 (br d, 1 H, J = 7 Hz), 3.11 (d, 2 H, J = 9 Hz), 1.79 (br s, 6 H), 0.92–1.42 (m, 2 H), 1.23 and 1.09 (s, each 3 H), 0.15 (s, 9 H) (cis) and 4.90 (br d, 1 H, J = 9 Hz), 3.72 and 3.37 (dd, each 1 H, J = 12 and 6 Hz, and 12 and 7 Hz, respectively), 1.69 (s, 6 H), 0.50–1.21 (m, 2 H), 1.12 and 1.05 (s, each 3 H), 0.15 (s, 9 H) (trans). Anal. Calcd for $C_{13}H_{26}OSi$: C, 68.96; H, 11.57. Found: C, 68.84; H, 11.69.

Reaction of 2b with Unsaturated Organosilanes. To a stirred solution of **2b** (225 mg, 1 mmol, cis/trans = 4/6) and an unsaturated organosilane (1 mmol) in CH_2Cl_2 (3 mL) was added $TiCl_4$ (0.11 mL, 1 mmol) at −78 °C under an atmosphere of nitrogen. After 1 min, the reaction mixture was poured into ice water (10 mL)–hexane (20 mL) and shaken vigorously. The organic layer was separated, washed with water, and dried over Na_2SO_4. After evaporation of the solvent, the obtained crude products **11–14** and **15a–e** from **5–8** and **9a–e**, respectively, were purified as follows: **11**, **12**, and **14**, trap-to-trap distillation [oven temperature 150 °C (5 mmHg), 150 °C (3 mmHg), and 110 °C (2 mmHg), respectively]; **13** and **15a–e**, chromatography with hexane and with 2% EtOAc/hexane, respectively.

(16) Sasaki, T.; Eguchi, S.; Ohno, M.; Umemura, T. *J. Org. Chem.* **1973**, *38*, 4095.
(17) (a) House, H. O.; Czuba, L. J.; Gall, M.; Olmstead, H. D. *J. Org. Chem.* **1969**, *34*, 2324. (b) Ainworth, C.; Chen, F.; Kuo, Y.-N. *J. Organomet. Chem.* **1972**, *46*, 59.
(18) Fleming, I.; Goldhill, J.; Paterson, I. *Tetrahedron Lett.* **1979**, 3205.
(19) Pillot, J. P.; Dunogues, J.; Calas, R. *Tetrahedron Lett.* **1976**, 1871.

11 (79% yield): See above for the spectral data.

12 (78% yield): IR 3080, 1645, 990, 965, 910 cm^{-1}; ^1H NMR δ 5.75 (dd, 1 H, J = 18 and 10 Hz), 5.62 (m, 2 H), 5.28 (AB q, 2 H, J = 18 Hz), 4.84 and 4.81 (dd, each 2 H, J = 18 and 1 Hz, and 10 and 1 Hz, respectively), 1.39–2.37 (m, 5 H), 1.05 and 0.92 (s, each 6 H). Anal. Calcd for $C_{15}H_{24}$: C, 88.16; H, 11.84. Found: C, 87.98; H, 12.02.

13 (83% yield): IR 3080, 1645, 1600, 1580, 990, 910 cm^{-1}; ^1H NMR δ 7.10 (s, 5 H), 5.80–6.58 (m, 1 H), 5.75 (dd, 1 H, J = 18 and 10 Hz), 5.26 (AB q, J = 18 Hz), 4.70–5.15 (m, 4 H), 3.00 (d, 1 H, J = 9 Hz), 1.09 (s, 6 H), 1.01 and 0.94 (s, each 3 H). Anal. Calcd for $C_{18}H_{26}$: C, 89.19; H, 10.81. Found: C, 89.43; H, 10.57.

14 (28% yield): IR 3080, 1950, 1645, 990, 965, 910, 850 cm^{-1}; ^1H NMR δ 5.75 (dd, 1 H, J = 18 and 10 Hz), 5.32 (AB q, 2 H, J = 18 Hz), 5.02 (dd, 1 H, J = 8 and 6 Hz), 4.86 and 4.83 (dd, each 2 H, J = 10 and 1 Hz, and 18 and 1 Hz, respectively), 4.65 and 4.64 (d, each 1 H, J = 6 Hz and 8 Hz, respectively), 1.09 and 1.08 (s, each 6 H). Anal. Calcd for $C_{13}H_{20}$; C, 88.56; H, 11.44. Found: C, 88.18; H, 11.82.

15a (53% yield): IR 3080, 1710, 1645, 990, 965, 910 cm^{-1}; ^1H NMR δ 5.75 (dd, 1 H, J = 18 and 5 Hz), 5.34 (AB q, 2 H, J = 18 Hz), 4.87 and 4.82 (dd, each 1 H, J = 18 and 2 Hz, and 10 and 2 Hz, respectively), 1.20–2.40 (m, 9 H), 1.06 (s, 12 H). Anal. Calcd for $C_{16}H_{26}O$: C, 81.19; H, 11.18. Found: C, 81.34; H, 11.03.

15b (70% yield): IR 3080, 1675, 1640, 1600, 1580, 990, 965, 910 cm^{-1}; ^1H NMR δ 7.28–7.95 (m, 5 H), 5.61 (dd, 1 H, J = 18 and 10 Hz), 5.30 (AB q, 2 H, J = 18 Hz), 4.78 and 4.75 (dd, each 1 H, J = 18 and 2 Hz, and 10 and 2 Hz, respectively), 2.82 (s, 2 H), 1.13 and 0.93 (s, each 6 H). Anal. Calcd for $C_{18}H_{24}O$: C, 84.32; H, 9.43. Found: C, 84.45; H, 9.52.

15c (46% yield): IR 3080, 1660, 1520, 1410, 990, 965, 910 cm^{-1}; ^1H NMR δ 6.90–7.60 (m, 3 H), 5.64 (dd, 1 H, J = 18 and 10 Hz), 5.31 (AB q, 2 H, J = 18 Hz), 4.80 and 4.76 (dd, each 1 H, J = 18 and 2 Hz, and 10 and 2 Hz, respectively), 2.73 (s, 2 H), 1.15 and 0.98 (s, each 6 H). Anal. Calcd for $C_{16}H_{24}OS$: C, 72.95; H, 8.80. Found: C, 73.29; H, 8.46.

15d (53% yield): IR 3080, 1675, 990, 910 cm^{-1}; ^1H NMR δ 5.60 (dd, 1 H, J = 18 and 10 Hz), 5.75 (m, 1 H), 5.30 (AB q, 2 H, J = 18 Hz), 4.88 and 4.83 (dd, each 1 H, J = 18 and 2 Hz, and 10 and 2 Hz, respectively), 2.10 (br s, 2 H), 1.85 (br s, 3 H), 2.35 (s, 1 H), 1.08 (s, 12 H), 0.98 and 0.92 (s, each 3 H). Anal. Calcd for $C_{19}H_{30}O$: C, 83.15; H, 11.02. Found: C, 82.96; H, 11.21.

15e (67% yield): IR 3080, 1735, 1645, 990, 910 cm^{-1}; ^1H NMR δ 5.75 (dd, 1 H, J = 18 and 10 Hz), 5.31 (AB q, 2 H, J = 18 Hz), 4.88 and 4.85 (dd, each 1 H, J = 18 and 2 Hz, and 10 and 2 Hz, respectively), 3.55 (s, 3 H), 1.06 and 0.99 (s, 18 H). Anal. Calcd for $C_{15}H_{26}O_2$: C, 75.58; H, 10.99. Found: C, 75.54; H, 11.03.

Reaction of 3 with Unsaturated Organosilanes. To a solution of *trans*-**3** (152 mg, 1 mmol) and an unsaturated organosilane (1 mmol) in CH_2Cl_2 (3 mL) was added $TiCl_4$ (0.11 mL, 1 mmol) at −78 °C under an atmosphere of nitrogen, where the brown color appeared instantly. This solution was stirred at this temperature for 30 min and then poured into ice water (10 mL)–ether (20 mL), and the reaction mixture was shaken vigorously. The organic layer was separated, washed with aqueous $NaHCO_3$, and dried over Na_2SO_4. After evaporation of the solvent, the products **16**, **17**, and **18** obtained from **9a**, **5**, and **7**, respectively, were isolated by the chromatography with 2–5% EtOAc–hexane. The mixture of the products **19** and **24** from **9e** were separated also by the chromatography with the same mixed solvent.

16 (40% yield): IR 2720, 1715, 1710, 965 cm^{-1}; ^1H NMR δ 9.58 (t, 1 H, J = 3 Hz), 5.45 (AB q, 2 H, J = 18 Hz), 2.25 (d, 2 H, J = 3 Hz), 1.20–2.40 (m, 9 H), 1.12 (s, 6 H), 1.08 and 1.05 (s, each 3 H). Anal. Calcd for $C_{16}H_{26}O_2$: C, 76.75; H, 10.47. Found: C, 76.88; H, 10.34.

17 (51% yield): IR 3080, 2720, 1725, 1645, 990, 965, 910 cm^{-1}; ^1H NMR δ 9.62 (t, 1 H, J = 3 Hz), 5.42–5.92 (m, 1 H), 5.34 (AB q, 2 H, J = 18 Hz), 4.70–5.10 (m, 2 H), 2.23 (d, 2 H, J = 3 Hz), 2.00 (d, 2 H, J = 7.5 Hz), 1.12 and 0.99 (s, each 6 H). Anal. Calcd for $C_{13}H_{22}O$: C, 80.35; H, 11.41. Found: C, 80.03; H, 11.73.

18 (33% yield): IR 3080, 2720, 1725, 1645, 1600, 1500, 990, 910 cm^{-1}; ^1H NMR δ 9.52 (t, 1 H, J = 3 Hz), 7.10 (s, 5 H), 5.38–6.40 (m, 1 H), 5.30 (AB q, 2 H, J = 18 Hz), 4.70–5.15 (m, 2 H), 3.00 (d, 1 H, J = 6 Hz), 2.19 (d, 2 H, J = 3 Hz), 1.08 (s, 6 H), 0.99 and 0.92 (s, each 3 H). Anal. Calcd for $C_{19}H_{26}O$: 84.39; H, 9.69. Found: C, 84.35; H, 9.73.

19 (12% yield): Obtained as the second fraction in the chromatographic separation; IR 2720, 1720, 975 cm^{-1}; ^1H NMR δ 9.62 (t, 1 H, J = 3 Hz), 5.42 (AB q, 2 H, J = 17 Hz), 3.58 (s, 3 H), 2.25 (d, 2 H, J = 3 Hz), 1.12, 1.07 and 1.00 (s, each 6 H). Anal. Calcd for $C_{15}H_{26}O_3$: C, 70.83; H, 10.30. Found: C, 70.76; H, 10.37.

24 (13% yield): Obtained as the first fraction in the above separation; IR 3060, 1725, 1630, 1600, 965, 880 cm^{-1}; ^1H NMR δ 5.75 and 5.43 (AB q, each 2 H, J = 18 Hz), 4.83 (br s, 2 H), 3.62 (s, 3 H), 1.79 (br s, 3 H), 1.25 and 1.12 (s, each 6 H). Anal. Calcd for $C_{15}H_{24}O_2$: C, 76.23; H, 10.23. Found: C, 76.46; H, 10.01.

Reaction of 4 with Unsaturated Organosilanes. With *trans*-**4**, the products **20**, **21**, and **22** were obtained from **9a**, **5**, and **9e**, respectively, in the same manner as employed for **3** except for stirring at −50 °C for 10 min.

20 (73% yield): IR 1710, 970 cm^{-1}; ^1H NMR δ 5.38 (AB q, 2 H, J = 18 Hz), 2.31 (s, 2 H), 1.98 (s, 3 H), 0.70–2.40 (m, 9 H), 1.05 (s, 12 H). Anal. Calcd for $C_{17}H_{28}O_2$: C, 77.22, H, 10.67. Found: C, 77.15; H, 10.74.

21 (53% yield): IR 3080, 1710, 1645, 990, 965, 910 cm^{-1}; ^1H NMR δ 5.52–6.08 (m, 1 H), 5.38 (AB q, 2 H, J = 18 Hz), 4.70–5.10 (m, 2 H), 1.11 and 1.10 (s, each 6 H). Anal. Calcd for $C_{14}H_{24}O$: C, 80.71; H, 11.61. Found: C, 80.41; H, 11.91.

22 (48% yield): IR 1720, 1710, 1120, 980 cm^{-1}; ^1H NMR δ 5.38 (AB q, 2 H, J = 18 Hz), 3.58 (s, 3 H), 2.33 (s, 2 H), 2.01 (s, 3 H), 1.08 and 0.99 (s, 18 H).

Reaction of 3 with Ti(IV) Enolate 25. $TiCl_4$ (0.11 mL, 1 mmol) was added to a solution of **9a** (170 mg, 1 mmol) in CH_2Cl_2 (2 mL) under an atmosphere of nitrogen, and the resulting brown solution was stirred for 2 min at room temperature and immediately cooled to −78 °C. To this solution was added *trans*-**3** (152 mg, 1 mmol) in CH_2Cl_2 (1 mL), and stirring was continued for 30 min at this temperature. The workup as mentioned above and the chromatographic separation (10% EtOAc–hexane) gave 126 mg (50% yield) of **26** (diastereomeric mixture) as an oil: IR 3500, 1700, 840 cm^{-1}; ^1H NMR δ 4.82 (br d, 1 H, J = 7 Hz), 3.71 (dd, 0.6 H, J = 8.5 and 2 Hz), 3.24 (dd, 0.4 H, J = 9 and 2 Hz), 2.75 (s, 1 H, disappeared with D_2O), 0.9–2.5 (m, 9 H), 1.68 (br s, 6 H), 1.19 and 1.05 (s, each 1.2 H), 1.08 and 0.98 (s, each 1.8 H). Anal. Calcd for $C_{16}H_{26}O_2$: C, 76.75; H, 10.47. Found: C, 76.81; H, 10.41.

Reactions of 2b and 3 with C_5-Unsaturated Organosilanes 27–30. These reactions were carried out by the same procedure as described above for **2b** (cis/trans) and **3** (trans).

Methyl 3,5,5,8,8-pentamethyl-2,6,9-decatrienoate (31) was obtained in 24% yield from **2b** and **27** by the chromatographic separation with 1% EtOAc–hexane: IR 3080, 1715, 1640, 990, 910 cm^{-1}; ^1H NMR δ 5.75 (dd, 1 H, J = 18 and 10 Hz), 5.45 (br s, 1 H), 5,26 (AB q, 2 H, J = 18 Hz), 4.88 and 4.83 (dd, each 1 H, J = 18 and 2 Hz, and 10 and 2 Hz, respectively), 3.58 (s, 3 H), 2.00–2.12 (m, 5 H), 1.06 and 1.02 (s, each 6 H). Anal. Calcd for $C_{16}H_{26}O_2$: C, 76.75; H, 10.47. Found: C, 76.47; H, 10.75.

3,3,6,6,7,7-Hexamethyl-1,4,8-nonatriene (32) was obtained in 48% yield from **2b** and **28** by the trap-to-trap distillation [oven temperature 200 °C (4 mmHg)]: IR 3080, 1645, 990, 910 cm^{-1}; ^1H NMR δ 5.65–5.92 (m, 2 H), 4.70–5.08 (m, 4 H), 5.32 (AB q, 2 H, J = 18 Hz), 1.10 and 0.95 (s, 18 H). Anal. Calcd for $C_{15}H_{26}$: C, 87.30; H, 12.70. Found: C, 87.30; H, 12.70.

Methyl 2-isopropyl-3,3,6,6-tetramethyl-4,7-octadienoate (33) was obtained in 60% yield from **2b** and **29** by the chromatographic separation with 2% EtOAc–hexane: IR 3080, 1735, 1645, 990, 965, 910 cm^{-1}; ^1H NMR δ 5.83 (dd, 1 H, J = 18 and 10 Hz), 5.40 (AB q, 2 H, J = 18 Hz), 4.90 and 4.88 (dd, each 1 H, J = 18 and 2 Hz, and 10 and 2 Hz, respectively), 3.62 (s, 3 H), 2.18 (d, 1 H, J = 8 Hz), 1.58–2.32 (m, 1 H), 1.14 and 1.09 (s, 12 H), 0.99 (d, 3 H, J = 8 Hz). Anal. Calcd for $C_{16}H_{28}O_2$: C, 76.14; H, 11.18. Found: C, 76.14; H, 11.16.

2,5,5,8,8-Pentamethyl-6,9-decadien-3-one (34) was obtained in 49% yield for **2b** and **30** by the chromatographic separation with 2% EtOAc–hexane: IR 3080, 1710, 1645, 990, 965, 910 cm^{-1}; ^1H NMR δ 5.73 (dd, 1 H, J = 18 and 10 Hz), 5.31 (AB q, 2 H, J = 18 Hz), 4.86 and 4.83 (dd, each 1 H, J = 18 and 2 Hz, and 10 and 2 Hz, respectively), 2.45 (septet, 1 H, J = 7 Hz), 2.32 (s, 1 H), 1.08 and 1.06 (s, each 6 H), 0.99 (d, 6 H, J = 7 Hz). Anal. Calcd for $C_{15}H_{26}O$: C, 81.02; H, 11.78. Found: C, 80.86; H, 11.94.

Methyl 3,7,7,10-tetramethyl-2,4,8,10-undecatetraenoate (35) was obtained in 32% yield from **3** and **27** by the chromatographic separation with 2% EtOAc–hexane: IR 3060, 1720, 1645, 1600,

965 cm^{-1}; ^{1}H NMR δ 5.77 (AB q, 2 H, J = 17 Hz), 5.60 (br s, 1 H), 5.58 (AB q, 2 H, J = 15 Hz), 5.13 (dt, 2 H, J = 15 and 5 Hz), 4.85 (br s, 2 H), 3.62 (s, 3 H), 2.81 (br d, 2 H, J = 5 Hz), 2.12 (d, 3 H, J = 1 Hz), 1.81 (br s, 3 H), 1.16 (s, 6 H). Anal. Calcd for $C_{16}H_{24}O_2$: C, 77.38; H, 9.74. Found: C, 77.75; H, 9.77.

3,3,6,6,7,7-Hexamethyl-4,8-nonadienal (36) was obtained in 45% yield from **3** and **28** by the chromatographic separation with 2% EtOAc-hexane: IR 2720, 1725, 990, 965, 910 cm^{-1}; ^{1}H NMR δ 9.61 (t, 1 H, J = 3 Hz), 5.75 (dd, 1 H, J = 16 and 9 Hz), 5.42 (AB q, 2 H, J = 18 Hz), 4.92 and 4.87 (dd, each 1 H, J = 9 and 1.5 Hz, and 18 and 1.5 Hz, respectively), 2.26 (d, 2 H, J = 3 Hz), 1.13, 0.98 and 0.95 (s, each 6 H). Anal. Calcd for $C_{15}H_{26}O$: C, 81.02; H, 11.78. Found: C, 80.79; H, 12.01.

Methyl 2-isopropyl-5,5,8-trimethyl-3,6,8-nonatrienoate (37) was obtained in 30% yield from **3** and **29** by the chromatographic separation with 2% EtOAc-hexane: IR 3060, 1730, 1635, 1600, 965, 880 cm^{-1}; ^{1}H NMR 5.75 (AB q, 2 H, J = 17 Hz), 5.59 (dd, 1 H, J = 17 and 1.5 Hz), 5,28 (dd, 1 H, J = 17 and 6 Hz), 4.84 (br s, 2 H), 3.62 (s, 3 H), 2.58 (td, 1 H, J = 6 and 1.5 Hz), 1.81 (br s, 3 H), 1.40-2.35 (m, 1 H), 1.16 (s, 6 H), 0.90 and 0.88 (d, each 3 H, J = 7 Hz). Anal. Calcd for $C_{16}H_{26}O_2$: C, 76.75; H, 10.47. Found: C, 76.40; H, 10.82.

3,3,6,6,9-Pentamethyl-8-oxo-4-decenal (38) was obtained in 55% yield from **3** and **30** by the chromatographic separation with 5% EtOAc-hexane: IR 2720, 1735, 1700, 965 cm^{-1}; ^{1}H NMR δ 9.61 (t, 1 H, J = 3 Hz), 5.42 (AB q, 2 H, J = 16 Hz), 2.46 (septet, 1 H, J = 7 Hz), 2.37 (s, 2 H), 2.25 (d, 2 H, J = 3 Hz), 1.13 and 1.10 (s, each 6 H), 1.01 (d, 6 H, J = 7 Hz). Anal. Calcd for $C_{15}H_{26}O_2$: C, 75.58; H, 10.99. Found: C, 75.73; H, 10.84.

Preparation of 40. To a suspension of prenylmagnesium chloride in ether (10 mL) prepared from prenyl chloride (523 mg, 5 mmol) and Mg powder (365 mg, 15 matom) was added a solution of *trans*-**3** (304 mg, 2 mmol) in ether (2 mL) at 0 °C under an atmosphere of nitrogen, and the mixture was stirred overnight at room temperature. The products were extracted with ether after being poured into cold aqueous NH_4Cl and were dried over Na_2SO_4. Evaporation of the solvent left an oil, which was chromatographed with 5% EtOAc-hexane to give 350 mg (79% yield) of **39**, which had absorptions at 3450, 3080, 1670, 1640, 970, 905, and 860 cm^{-1} in the IR spectrum. This alcohol was silylated by stirring with bis(trimethylsilyl)acetamide (0.75 mL, 3 mmol) at room temperature for 12 h, and the product was purified by the chromatography with hexane to give 380 mg (82%) of **40** as an oil: IR 3080, 1640, 1250, 1080, 1000, 915, 850 cm^{-1}; ^{1}H NMR δ 6.83 (dd, 1 H, J = 18 and 10 Hz), 4.85 and 4.80 (dd, each 1 H, J = 10 and 2 Hz, and 18 and 2 Hz, respectively), 4.66 (br d, 1 H, J = 8 Hz), 3.06 (d, 1 H, J = 9 Hz), 1.70 and 1.62 (br s, each 3 H), 1.14 and 1.00 (s, each 3 H), 1.00 (dd, 1 H, J = 8 and 6 Hz, superimposed with the methyl group), 0.96 (s, 6 H), 0.58 (dd, 1 H, J = 9 and 6 Hz), 0.10 (s, 9 H). Anal. Calcd for $C_{18}H_{34}OSi$: C, 73.40; H, 11.63. Found: C, 73.43; H, 11.60.

2,5,5,8,8,11,11-Heptamethyl-6,9,12-tridecatrien-3-one (41) was obtained in 53% yield from **40** and **30** by the same procedure as employed for the reaction of **5b**: IR 3070, 1710, 1640, 980, 910 cm^{-1}; ^{1}H NMR δ 5.81 (dd, 1 H, J = 18 and 10 Hz), 5.30 (AB q, 2 H, J = 16 Hz), 5.26 (AB q, 2 H, J = 18 Hz), 4.84 and 4.81 (dd, each 1 H, J = 10 and 2 Hz, and 18 and 2 Hz, respectively), 2.34 (septet, 1 H, J = 7.5 Hz), 2.33 (s, 2 H), 1.08 (s, 12 H) 1.05 (s, 6 H), 1.00 (d, 6 H, J = 7.5 Hz). Anal. Calcd for $C_{20}H_{34}O$: C, 82.69; H, 11.80. Found: C, 82.62; H, 11.87.

Preparation of 42. To a solution of lithium diisopropylamide in THF (6 mL) prepared from *n*-butyllithium (1.9 mL of 15% hexane solution, 3 mmol) and diisopropylamine (0.42 mL, 3 mmol) was added methyl isopropyl ketone (250 mg, 2.9 mmol) at -78 °C under an atmosphere of nitrogen, and the solution was stirred for 1 h. Then, to this solution was added **3** (456 mg, 3 mmol) at this temperature, and the mixture was stirred at room temperature for 3 h. The products were extracted with ether after being poured into brine and were dried over Na_2SO_4. Evaporation of the solvent left an oil, which was chromatographed with 5% EtOAc-hexane to give 462 mg (70% yield) of **42** as an oil: IR 1690, 1660, 1610, cm^{-1}; ^{1}H NMR δ 6.50 (dd, 1 H, J = 15 and 9 Hz), 6.12 (d, 1 H, J = 15 Hz), 4.87 (br d, 1 H, J = 8 Hz), 2.62 (septet, 1 H, J = 7 Hz), 1.68 (br s, 6 H), 0.90-1.58 (m, 2 H), 1.22 and 1.12 (s, each 3 H), 1.07 (d, 6 H, J = 7 Hz). Anal. Calcd for $C_{15}H_{24}O$: C, 81.76; H, 10.98. Found: C, 81.80; H, 10.94.

2,7,7,10,10,13-Hexamethyl-5,8-tetradecadiene-3,12-dione (43) was obtained in 40% yield from **42** and **30** by the same procedure as employed for the reaction of **4**: IR 1710, 1670 cm^{-1}; ^{1}H NMR δ 5.52 (dt, 1 H, J = 16 and 4 Hz), 5.32 (AB q, 2 H, J = 16 Hz), 5.25 (dd, 1 H, J = 16 and 1 Hz), 3.07 (dd, 2 H, J = 4 and 1 Hz), 2.60 (septet, 2 H, J = 7 Hz), 2.35 (s, 2 H), 1.06 and 0.98 (d, each 6 H, J = 7 Hz), 1.08 (s, 12 H). Anal. Calcd for $C_{20}H_{34}O_2$: C, 78.38; H, 11.18. Found: C, 78.52; H, 11.04.

Chiral Synthons for the Total Synthesis of Fluoro Amino Acids and Fluoro Analogues of Antibiotic Sugars

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Received May 21, 1986

Configurationally different 3-azido-2,3-dideoxy-2-fluoro and 2-azido-2,3-dideoxy-3-fluoro sugars, synthetic precursors of biologically important fluoro amino acids, were synthesized. Axial alcohols involved in vicinal diaxial systems undergo fluorodehydroxylation with configurational retention in the presence of (diethylamino)sulfur trifluoride.

Appropriate synthetic schemes for the preparation of optically active β-fluorinated α amino acids are of considerable importance in view of the potential for a variety of these compounds to act as enzyme-activated irreversible inhibitors[1] or suicide substrates with interesting biological properties. During recent years, several methods involving fluorodehydroxylation,[2] photofluoration,[3] or aziridine ring

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0022-3263/86/1951-4558$01.50/0