Double Diels–Alder Reaction of *trans*-3-Methylene-1,4-hexadiene and 1-Methyl-3-methylene-4-pentenyl Tosylate

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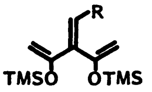
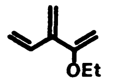
A cross-conjugated triene, *trans*-3-methylene-1,4-hexadiene, is accessible from the Grignard reagent of chloroprene and methyloxirane via 1-methyl-3-methylene-4-pentenyl tosylate. The diene-transmissive Diels–Alder reaction of the triene and the stepwise sequence of double Diels–Alder reaction of the tosylate are investigated. Stereo- and regioselectivity of these reactions in the presence or absence of Lewis acid catalyst are discussed.

The diene-transmissive Diels–Alder reaction of cross-conjugated trienes such as 3-benzylidene- **A**,[1] 3-methoxymethylene-2,4-bis(trimethylsilyloxy)-1,4-pentadiene **B**,[2] and 2-ethoxy-3-methylene-1,4-pentadiene **C**[3] is useful for the synthesis of stereochemically defined and functionalized [6.6] bicyclic systems.[1–7] Stepwise sequence using synthetic equivalents of the cross-conjugated trienes offers a convenient route to cross bis-cycloadducts in which two different dienophiles are incorporated.[3,8,9]

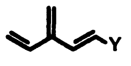


A: R=Ph
B: R=OMe



C

TMS=SiMe$_3$



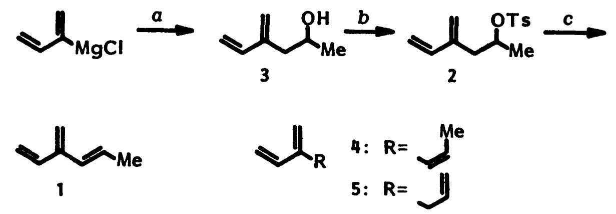
D: Y=OEt
E: Y=SPh

It has been found that triene **C** undergoes the first Diels–Alder reaction exclusively across the 2-monosubstituted diene moiety since the other 2,3-disubstituted diene moiety can hardly occupy an *s-cis* conformation which is essential in the transition state of Diels–Alder cycloaddition.[3] Although cross-conjugated trienes **D** and **E** carrying a diene-activating substituent at the 1-position selectively react with a dienophile across the 1,3-disubstituted triene, they are unfortunately too unstable to be employed as starting materials.[10]

The present article describes the diene-transmissive Diels–Alder reaction of *trans*-3-methylene-1,4-hexadiene (**1**) and the stepwise double cycloaddition of 1-methyl-3-methylene-4-pentenyl tosylate (**2**), a precursor of **1**.

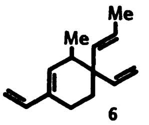
Results and Discussion

In a study of organic synthesis utilizing cross-conjugated trienes, a general and simple preparative method of trienes starting from readily available materials is required. Our synthetic plan of **1** starts from an industrial material, chloroprene, and an epoxide as shown in Scheme 1. 4-Methylene-5-hexen-2-ol (**3**), which is readily accessible by the regioselective reaction of the Grignard reagent of chloroprene with methyloxirane,[11] was tosylated in pyridine at 0 °C to give tosylate **2** in 80% yield. When **2** was heated at 100—110 °C with DBU under reduced pressure, the desired triene **1** was obtained in 64% yield as thermally labile liquid. Although the triene **1** thus obtained was only 90% pure (GLC), its separation from contaminants, the 2:1 mixture of **4** and **5**,[12] by vacuum distillation was unsuccessful. The contaminants could not be removed by distillation under higher vaccum, and under lower vacuum **1** underwent partial dimerization to give a mixture of **6** and **7** in the ratio 74:26 (GLC). Thus, the triene **1** of this purity was used for the following reactions.

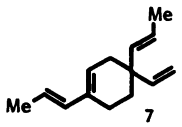


a: 2-methyloxirane, b: TsCl-pyridine, c: DBU

Scheme 1.



6



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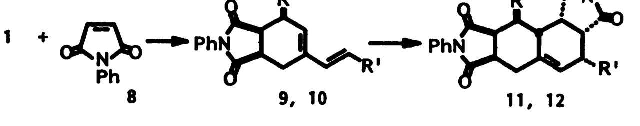
The reaction of **1** with an equivalent amount of *N*-phenylmaleimide (**8**) at room temperature gave a mixture of two isomeric bis-cycloadducts **11** and **12** in 92% yield in the ratio 5:1 (^{1}H NMR) as shown in Scheme 2. Even in a similar reaction below −50 °C, the bis-cycloadducts **11** and **12** (68%, **11**:**12**=4:1 by ^{1}H NMR) were formed together with two isomeric mono-cycloadducts **9** and **10** (24%, **9**:**10**=81:19 by GLC).

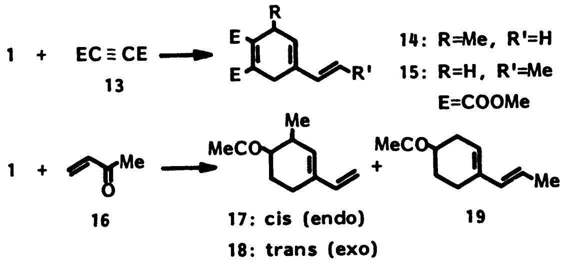


9, 11: R=Me, R'=H
10, 12: R=H, R'=Me

Scheme 2.

As it will be presented later, the minor bis-cycloadduct **12** can be obtained as a single stereoisomer in the reaction of **8** with **10** which is available from the cycloadduct derived from diene tosylate **2** and **8** (Schemes 4, 5, and 6). Accordingly, the major bis-cycloadduct **11** has to be the stereoselective cycloaddition product derived from the other mono-cycloadduct **9**. The structure of **11** was confirmed to be the endo cycloadduct of **8** across 1,3-disubstituted diene moiety of **1** on the basis of spectral data.[13] After all, the Diels–Alder reaction of **1** with **8** has occurred not only across the 1,3-disubstituted diene part but also across the 2-monosubstituted diene, and chemoselectivity between the both dienes does not depend upon the reaction conditions. The selectivity in favor of the methyl-substituted diene in the reaction with **8** was 81—83%.

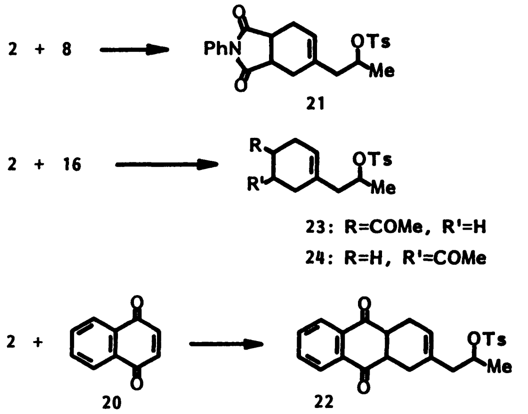
On the other hand, the Diels–Alder reaction of **1** with an equimolar amount of dimethyl acetylenedicarboxylate (DMAD, **13**) at room temperature led to a mixture of two isomeric monocycloadducts **14** and **15** in 77% yield. The chemoselectivity between the 1,3-disubstituted and 2-monosubstituted dienes of **1** was 78:22 (GLC) (Scheme 3). When excess **13** was used and the reaction was carried out in refluxing benzene, a complex mixture containing two mono- and bis-cycloadducts along with their partly or fully aromatized derivatives.



Scheme 3.

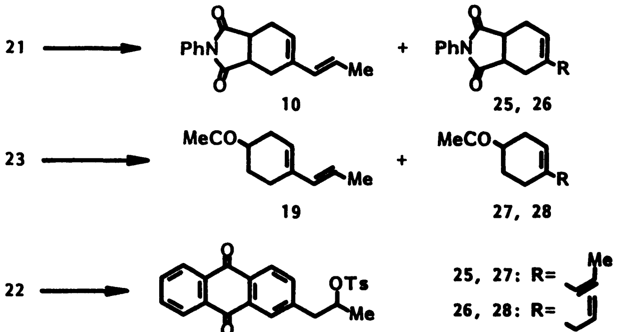
To our surprise, regioselectivity in the first Diels–Alder reaction of **1** was found unexpectedly high. For example, the reaction with methyl vinyl ketone (**16**) as an unsymmetrically substituted dienophile at room temperature gave three regioselective monocycloadducts in 76% yield, two of which are endo **17** and exo cycloadduct **18** across the methyl-substituted diene (**17**:**18**=70:30 by GLC) and the other **19** is the cycloadduct across the 2-monosubstituted diene (**17**+**18**:**19**=69:31 by GLC).[14] When this reaction was carried out in the presence of an equimolar amount of ethylaluminum dichloride as a Lewis acid in toluene at −78 °C for 0.5 h, the *endo*-selectivity increased to 98% (**17**:**18**=98:2). However, the chemoselectivity could not be improved (**17**+**18**:**19**=71:29 by GLC).[15] Since the chemoselectivity between both diene moieties of **1** in the first Diels–Alder reaction was low, we had to give up the route involving diene-transmissive Diels–Alder cycloaddition of triene **1**. Therefore, stepwise sequence of double Diels–Alder reaction using diene tosylate **2** was instead investigated hereafter.

The Diels–Alder reactions of **2** with **8** or 1,4-naphthoquinone (**20**) gave cycloadduct **21** or **22** in 99 or 72% yield, respectively (Scheme 4). Although the regioselectivity found in the reaction of **2** with **16** in refluxing benzene was very low (74%, **23**:**24**=64:36 by GLC),[16,17] a similar reaction in the presence of ethylaluminum dichloride at −50 to −70 °C was exclusively *para*-selective. 67% Yield of **23** was the only isolated product.



Scheme 4.

The elimination of *p*-toluenesulfonic acid from **21** was readily performed by heating with DBU under reflux in toluene to give a mixture of three elimination products in 73% yield (Scheme 5). It was found that purity of the expected trans diene **10** was 91%, and that the contaminants consisted of the corresponding cis isomer **25** and unconjugated diene **26** (9%, **25**:**26**=2:1 by ^{1}H NMR).[18] One-pot procedure for the Diels–Alder reaction of **2** with **8** and the diene formation into **10** was successful: **10** was obtained in 70% yield (**10**:**25**:**26**=91:6:3 by GLC).

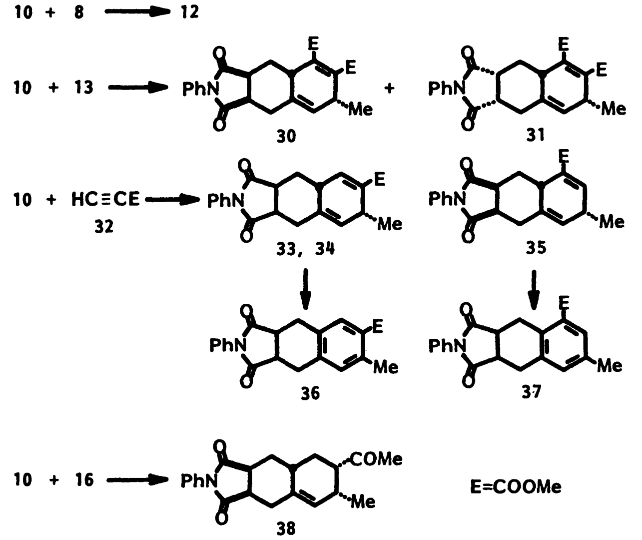


Scheme 5.

The elimination reaction of **23** under similar conditions afforded trans diene **19** as major product, which had been previously obtained as minor product in the reaction of **1** with **16**, together with two isomeric dienes **27** and **28** (76%, **19**:**26**:**27**=87:8:5 by GLC). However, naphthoquinone adduct **22** resulted in the dehydrogenation into **29** instead of the elimination of sulfonic acid.[19]

The second Diels–Alder reaction step of the stepwise sequence was investigated by utilizing diene **10**. Since it was unsuccessful to remove the contaminants **25** and **26**, the diene **10** of 91% purity was used for subsequent reactions. These isomeric dienes **25** and **26** did not affect the second Diels–Alder cycloaddition and were recovered unchanged.

The reaction of **10** with **8** readily took place at room temperature to give bis-cycloadduct **12** as a single stereoisomer in 78% yield, which is identical with the minor bis-cycloadduct formed in the reaction of **1** with **8** (Scheme 6). Therefore, both regioisomeric bis-cycloadducts **11** and **12** are now accessible from the triene **1** and the diene tosylate **2**, respectively, both as either major or single product. This facile and stereoselective cycloaddition may occur because the diene moiety of **10** is not sterically crowded at the side opposite to the fused five-membered ring to allow the endo approach **F** of **8** from this direction (Fig. 1).



Scheme 6.

Compared to high stereoselectivity of the reaction with **8**, the reaction of **10** with DMAD **13** gave two stereoisomers **30** and **31** in 79 and 8% yields, respectively. The major product **30** corresponds to the cycloadduct formed by the attack of **13** from sterically less hindered side of diene **10**.

Regioselectivity of this type of reaction was found very low. For example, three isomers **33**—**35** were formed in 62% yield in the reaction with methyl propynoate (**32**) (**33**:**34**:**35**=2:1:1 by ^{1}H NMR, 25% of **10** was recovered). As **33** and **34** were converted into the same dehydrogenated derivative **36** and **35** was dehydrogenated into its isomer **37**, **33** and **34** are assigned as stereoisomers to each other and **35** is one of their regioisomers.

The stereochemistry of **30**, **31**, and **33**—**35** were determined on the basis of spectral data as well as the stereochemical mode of reactions which are illustrated in Fig. 1. Thus, the major cycloadduct **30** has been formed through the approach **G** of **13** from the side opposite to the fused maleimide ring. The other approach **H** leading to **31** causes some steric repulsion between the ester moiety of **13** and a quasi-axial hydrogen adjacent to the diene moiety or the fused maleimide ring. On the other hand, in the approaches **I** and **J** giving **33** and **34**, one substituent on the dienophile **32** is hydrogen which brings about only negligible steric repulsion at both sides of the diene. Accordingly, the stereoselectivity on the formation of **33** and **34** may have been reduced. It is readily understood that **35** has been formed in a highly stereoselective manner.

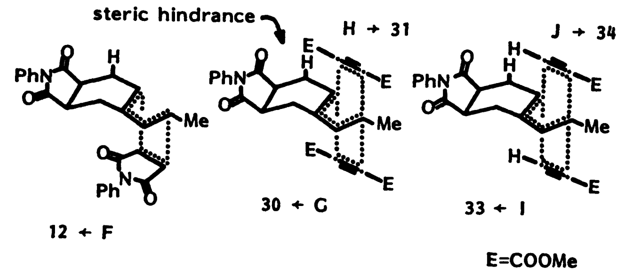


Fig. 1. Stereochemistry of the cycloaddition of **10**.

The reaction of **10** with methyl vinyl ketone (**16**) as an unsymmetrically substituted dienophile was performed in the presence of ethylaluminum dichloride at −70 °C. The regioselective, *endo*-selective, and face-selective cycloadduct **38** was obtained in 78% yield (Scheme 6).

It is concluded that the stepwise sequence of double Diels–Alder reaction of **2** can be performed in a highly selective fashion for the combination of two different olefinic dienophiles, either in the presence or absence of Lewis acid.

Experimental

General. Melting points were determined on a Yanagimoto micro melting point apparatus and uncorrected. IR spectra were taken with a JASCO IRA-1 or a JASCO A-702 spectrometer. ^{1}H NMR spectra were recorded on a Hitachi R-40 (90 MHz) or a JEOL FX-100 instrument (100 MHz) and ^{13}C NMR spectra on a JEOL FX-100 spectrometer at 25.05 MHz. Chemical shifts are expressed in parts per million downfield from tetramethylsilane as internal standard. Mass spectra were measured with a JEOL JMS-O1SG-2 spectrometer at 70 eV of ionization energy. GC–Mass spectra as well as high resolution mass spectra were also obtained on the same instrument. Elementary analyses were performed on a Hitachi 026 CHN micro analyzer. Thin-layer chromatography (TLC) was accomplished on 0.2 mm precoated plates of silica gel 60 F-254 (Merck) or of aluminum oxide 60 F-254 type-E (Merck). Visualization was made with ultraviolet light (254 and 365 nm), iodine, molybdophosphoric acid (5% in ethanol), or *p*-anisaldehyde (5% in ethanol containing 5% of sulfuric acid). For preparative column chromatography, Wakogel C-200, C-300 (Wako) and Silicagel 60 (Merck) were employed. Flash chromatography was carried out on an EYELA EF-10 apparatus using a column (20×180 mm) packed with Silicagel 60 (Merck, size: 0.04—

0.063 mm). Preparative high-performance liquid chromatography (HPLC) was performed on a Kusano KHLC-201 apparatus with a UV-detector Uvilog-III using a column (22×300 mm) packed with silica gel (Wakogel LC-50H). Gas-liquid chromatography (GLC) was accomplished on a Yanaco G-2800 gas chromatograph (Yanagimoto) with an ionization detector using a glass column (SE-30, 3×2000 mm) or a glass capillary column (Sillicone GE, SE-30, 0.25×5000 mm). 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.

Tetrahydrofuran was distilled over sodium wire and then over lithium aluminum hydride prior to its use. Benzene and toluene were also distilled over sodium and stored on sodium wire. The solvents for column chromatography (hexane and ethyl acetate) were used without further purification.

4-Methylene-5-hexen-2-ol (3). Methyloxirane (7 ml, 0.1 mol) in dry THF (25 ml) was slowly added to the 0.1 M solution (1 M=1 mol dm^{-3}) of 1-methylenepropenylmagnesium chloride in THF (100 ml, 0.1 mol) and the mixture was heated at 50—60 °C for 2 h. After cooled to room temperature, the mixture was hydrolyzed with 3N-HCl. The organic layer was separated, and the aqueous layer was extracted with ether (100 ml). The combined organic layer was washed with 5% aqueous sodium hydrogen carbonate, then with brine, and dried over magnesium sulfate. After the solvent was removed by evaporation, the residue was distilled under vacuum (20 mmHg) to give **3** (purity 80% (GLC), 4.66 g, 42%). Repeated vaccum distillation gave pure **3**: Colorless liquid; bp 55—60 °C/2399 Pa (lit,[11] bp 56—60 °C/2660 Pa); ^{1}H NMR (CDCl$_3$) δ=1.20 (3H, d, J=6.5 Hz, Me), 2.29 (1H, ddd, J_{gem}=14.0, J_{2-1}=7.5, J_{long}=1.0 Hz, one of 2-H), 2.34 (1H, s, OH), 2.44 (1H, ddd, J_{gem}=14.0, J_{2-1}=5.0, J_{long}=1.0 Hz, the other of 2-H), 3.93 (1H, m, 1-H), 4.96—5.40 (4H, m, =CH$_2$), and 6.36 (1H, dd, J_{4-5}=11.0 and 17.5 Hz, 4-H).

1-Methyl-3-methylene-4-pentenyl Tosylate (2). A mixture of **3** (0.655 g, 5.84 mmol), *p*-toluenesulfonyl chloride (1.11 g, 5.84 mmol), and pyridine (2 ml) was allowed to stand in a freezer for 36 h. Pyridine hydrochloride precipitated was removed by filteration and the filtrate was chromatographed over silica gel with hexane–ethyl acetate (9:1) to give **2** (1.243 g, 80%): Colorless liquid; IR (neat) 1360, 1190, and 1175 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=1.25 (3H, d, J=6.0 Hz, Me), 2.34 (1H, dd, J_{gem}=14.0 and J_{2-1}=8.0 Hz, one of 2-H), 2.42 (3H, s, *p*-Me), 2.66 (1H, dd, J_{gem}=14.0 and J_{2-1}=6.0 Hz, the other of 2-H), 4.68 (1H, ddq, J_{1-2}=8.0, 6.0 and $J_{1-\mathrm{Me}}$=6.0 Hz, 1-H), 4.84—5.16 (4H, m, =CH$_2$), 6.16 (1H, dd, J_{4-5}=11.0 and 17.5 Hz, 4-H), 7.28, and 7.74 (each 2H, d, J=8.0 Hz, ArH); ^{13}C NMR (CDCl$_3$) δ=20.47, 21.54 (each q, Me), 39.03 (t, 2-C), 78.36 (d, 1-C), 114.03, 119.53 (each t, 3-CH$_2$= and 5-C), 127.77, 129.62 (each d), 137.71 (d, 4-C), 140.93 (s, 3-C), 144.44 (s); MS *m/z* (rel. intensity, %) 266 (M$^+$, 4), 199 (9), 155 (96), 94 (53), 91 (base peak), and 79 (51).

Found: C, 63.06; H, 6.84%. Calcd for C$_{14}$H$_{18}$O$_3$S: C, 63.13; H, 6.81%.

***trans*-3-Methylene-1,4-hexadiene (1).** A mixture of **2** (0.62 g, 2.32 mmol) and DBU (0.709 g, 4.64 mmol) was heated in a micro distilling apparatus, at 110 °C at 2660 Pa for 30 min, to give **1** (0.141 g, 64%, purity 90% (GLC)) which was collected in a receiver cooled in a Dry Ice bath (−78 °C): Colorless liquid; ^{1}H NMR (CDCl$_3$) δ=1.78 (3H, d, J=5.0 Hz, Me), 5.00 (2H, s, 3-CH$_2$=), 5.04 (1H, dd, J_{gem}=1.5 and J_{1-2}=10.5 Hz, one of 1-H), 5.36 (1H, dd, J_{gem}=1.5 and J_{1-2}=17.5 Hz, the other of 1-H), 5.84 (1H, dq, J_{5-4}=16.0 and J_{5-6}=5.0 Hz, 5-H), 6.14 (1H, d, J_{4-5}=16.0 Hz, 4-H), and 6.40 (1H, dd, J_{2-1}=17.5 and 10.5 Hz, 2-H); ^{13}C NMR (CDCl$_3$) δ=18.32 (q, Me), 113.60, 115.13 (each t, 1-C and 3-CH$_2$=), 127.28 (d, 5-C), 129.75 (d, 4-C), 136.68 (d, 2-C), and 144.43 (s, 3-C); GC-MS *m/z* 94 (M$^+$).

Found: *m/z* 94.0769. Calcd for C$_7$H$_{10}$: M, 94.0782.

The residue which was left in a distilling flask after the vaccum distillation of **1** was chromatographed over silica gel using hexane–ethyl acetate (19:1) to afford a mixture of **6** and **7** (74:26 checked by GLC). **6**+**7**: Colorless liquid; ^{1}H NMR (CDCl$_3$) δ=0.92 (d, J=7.0 Hz, Me), 1.64, 1.68 (each d, J=5.0 Hz, Me), 1.40—2.40 (m, CH$_2$ and CH), 4.90—6.10 (m, CH$_2$= and CH=), and 6.31 (dd, J=17.5 and 11.0 Hz); ^{13}C NMR (CDCl$_3$) δ=16.66, 18.21, 18.31 (each q, Me), 21.53, 22.17, 30.08, 30.32, 32.08, 35.10 (each t, CH$_2$), 38.38, 38.62 (each d, CH), 41.11, 44.09 (each s), 110.55 (t), 111.96, 112.55, 113.72, 121.63, 122.95, 123.63, 124.61, 124.75, 134.47 (d), 134.71, 137.30, 137.55, 139.84 (each d), 142.67, and 145.26 (each s); GC-MS *m/z* (rel. intensity, %) **6**: 188 (M$^+$, 5), 95 (23), 94 (13), 79 (base peak), and 77 (12); **7**: 188 (M$^+$, 10), 95 (22), 94 (11), 79 (base peak), and 77 (11).

Reaction of 1 with 8 Leading to 11, 12 or 9—12. i) A mixture of **1** (purity 90%, 0.033 g, 0.32 mmol) and **8** (0.060 g, 0.35 mmol) in dry benzene (1 ml) was stirred at room temperature under nitrogen for 20 h. The solvent was evaporated in vacuo and the residue was chromatographed over silica gel with hexane–ethyl acetate (2:1) to provide the 5:1 mixture (^{1}H NMR) of **11** and **12** (0.071 g, 92%) which were separated from each other through HPLC using hexane–ethyl acetate (2:1). ii) To a solution of **1** (purity 90%, 0.104 g, 1 mmol) in dry toluene (2 ml) was added **8** (0.191 g, 1.1 mmol) at −70 °C. The mixture was stirred below −50 °C for 2 h. The solvent was removed by eveporation in vacuo and the residue was chromatographed over silica gel with hexane–ethyl acatate (4:1) to afford a mixture of **9** and **10** (0.7 g, 24%, 81:19 (GLC)) whose separation was unsuccessful. Further elution with hexane–ethyl acetate (2:1) gave the 4:1 mixture (^{1}H NMR) of **11** and **12** (0.163 g, 68% based on **8**). The data for **9**, **11**, and **12** are given below, and **10** was assigned by the comparison of its spectral data with those of the authentic sample prepared from the reaction of **21** with DBU.

9: ^{1}H NMR (CDCl$_3$) δ=1.39 (3H, d, J=7.0 Hz, Me), 2.00—3.40 (5H, m, CH$_2$ and CH), 5.02 (1H, d, J=11.0 Hz, one of =CH$_2$), 5.38 (1H, d, J=17.5 Hz, the other of =CH$_2$), 5.70 (1H, m, 5-H), 6.32 (1H, dd, J=11.0 and 17.5 Hz, 6-$\underline{\mathrm{C}}\underline{\mathrm{H}}$=CH$_2$), and 7.00—7.50 (5H, m, Ph); ^{13}C NMR (CDCl$_3$) δ=16.65 (q, Me), 22.88 (t, 7-C), 31.53 (d, 4-C), 40.30 (d, 7a-C), 44.42 (d, 3a-C), 113.12 (t, =CH$_2$), 126.60 (d, 2×C), 128.60 (d), 129.13 (d, 2×C), 132.13 (s, 6-C), 133.36, 136.72 (each d, 5-C and $\underline{\mathrm{C}}$H=CH$_2$), 137.36 (s), 177.07, and 178.66 (each s, CON); GC-MS *m/z* (rel. intensity, %) 267 (M$^+$, 42), 120 (base peak), and 105 (75).

11: Colorless prisms (ethanol); mp 242—243 °C; IR (KBr) 1765 and 1700 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=1.53 (3H, d, J=6.5 Hz, Me), 1.76—3.44 (10H, m, CH$_2$ and CH), 5.76 (1H, m, 5-H), and 7.00—7.52 (10H, m, Ph); MS *m/z* (rel. intensity, %) 440 (M$^+$, 73), 267 (base peak), and 174 (58).

Found: C, 73.51; H, 5.49; N, 6.45%. Calcd for C$_{27}$H$_{24}$N$_2$O$_4$: C, 73.62; H, 5.49; N, 6.36%.

12: Colorless needles (ethanol); mp 228—229 °C; IR (KBr) 1765 and 1700 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=1.44 (3H, d, J=7.0 Hz, Me), 2.00—3.48 (10H, m, CH$_2$ and CH), 5.60 (1H, br s, 5-H), and 7.00—7.60 (10H, m, Ph); MS *m/z* (rel. intensity, %) 440 (M$^+$, base peak), 267 (21), and 174 (26).

Found: C, 73.88; H, 5.59; N, 6.33%. Calcd for $C_{27}H_{24}N_2O_4$: C, 73.62; H, 5.49; N, 6.36%.

Reaction of 1 with 13 Leading to 14 and 15. A mixture of **1** (purity 90%, 0.028 g, 0.27 mmol) and **13** (0.042 g, 0.3 mmol) in dry benzene (1 ml) was stirred at room temperature under nitrogen for 20 h. The solvent was evaporated in vacuo and the residue was chromatographed over silica gel using hexane–ethyl acetate (4:1) to afford a mixture of **14** and **15** (0.051 g, 77%, 78:22 (GLC)) as colorless liquid, which could not be separated from each other. Their spectral data are given below:

14: ^{1}H NMR (CDCl$_4$) δ=1.17 (3H, d, J=7.0 Hz, Me), 2.90—3.44 (3H, m, CH$_2$ and CH), 3.75, 3.76 (each 3H, s, COOMe), 5.04 (1H, d, J=11.0 Hz, one of =CH$_2$), 5.13 (1H, d, J=17.5 Hz, the other of =CH$_2$), 5.64 (1H, m, 4-H), and 6.36 (1H, dd, J=11.0 and 17.5 Hz, 5-C$\underline{\text{H}}$=CH$_2$); GC-MS *m/z* (rel. intensity, %) 206 (M$^+$−30, 41), 205 (20), and 117 (base peak).

15: ^{1}H NMR (CDCl$_3$) δ=1.76 (dd, J=6.5 and 0.5 Hz, Me). Other signals are hidden in those of **14**; GC-MS *m/z* (rel. intensity, %) 235 (M$^+$−1), 234 (29), and 203 (base peak).

Reaction of 1 with 16 Leading to 17—19. i) A mixture of **1** (purity 90%, 0.065 g, 0.62 mmol) and **16** (0.097 g, 1.38 mmol) in dry benzene (1 ml) was stirred at room temperature under nitrogen for 20 h. The solvent was evaporated in vacuo and the residue was chromatographed over silica gel with hexane–ethyl acetate (19:1) to give a mixture of the dimers **6** and **7** (0.004 g, 7%, 79:21 (GLC)). Further elution with hexane–ethyl acetate (9:1) afforded a mixture of **17**, **18**, and **19** (0.084 g, purity 93% (GLC), 76%, **17**:**18**:**19**=48:21:31 (GLC)), none of which could be separated in pure form from the other two. ii) To a solution of **16** (0.078 g, 1.12 ml) in dry toluene (1 ml) was added the 1 M solution of ethylaluminum dichloride (in hexane, 1 ml) by use of a syringe at −78 °C. After 0.5 h, **1** (0.105 g, purity 90%, 1 mmol) in dry toluene (1 ml) was introduced and then the mixture was stirred for an additional 0.5 h at the same temperature. Usual hydrolytic work-up with aqueous sodium hydrogencarbonate was followed by the extraction with benzene (10 ml ×2). The benzene was dried over magnesium sulfate and evaporated in vacuo. The residue was chromatographed over silica gel using hexane–ethyl acetate (9:1) to provide a mixture of **17**, **18**, and **19** (0.077 g, 46%, **17**:**18**:**19**=71:2:26 (GLC)). Structural assignment of these products was carried out as follows: The isomer **19** was first identified by the comparison of its spectral data with those of the authentic sample prepared from the reaction of **23** with DBU. The signals of **19** were taken away from the spectrum of the mixture obtained in the Lewis acid-catalyzed reaction. The remaining signals are those of **17**, which make possible to assign the structure of **17**. Finally, the signals for **18** are available in the spectrum of the mixture obtained in the upper reaction. Their spectral data are given below:

17: ^{1}H NMR (CDCl$_3$) δ=0.86 (3H, d, J=7.0 Hz, Me), 1.50—2.92 (6H, m, CH$_2$ and CH), 2.14 (3H, s, COMe), 4.93 (1H, d, J=11.0 Hz, one of =CH$_2$), 5.08 (1H, d, J=18.0, the other of =CH$_2$), 5.56—5.76 (1H, m, 2-H), and 6.32 (1H, dd, J=11.0 and 18.0 Hz, 1-C$\underline{\text{H}}$=CH$_2$); ^{13}C NMR (CDCl$_3$) δ=15.77 (q, Me), 23.59 (t, 2×$\underline{\text{C}}$, 5- and 6-C), 28.59 (q, CO$\underline{\text{Me}}$), 31.41 (d, 3-C), 51.47 (d, 4-C), 111.36 (t, =CH$_2$), 133.77 (d), 135.42 (s, 1-C), 139.54 (d), and 210.90 (s, $\underline{\text{C}}$OMe); GC-MS *m/z* (rel. intensity, %) 164 (M$^+$, 73), 149 (45), 121 (92), 94 (98), 92 (48), and 79 (base peak).

18: ^{1}H NMR (CDCl$_3$) δ=0.96 (3H, d, J=7.0 Hz, Me), 2.15 (3H, s, COMe), 4.93 (1H, d, J=11.0 Hz, one of =CH$_2$), 5.06 (1H, d, J=18.0 Hz, the other of =CH$_2$), 5.56—5.76 (1H, m, 2-H), and 6.32 (1H, dd, J=11.0 and 18.0 Hz, 1-C$\underline{\text{H}}$=CH$_2$); ^{13}C NMR (CDCl$_3$) δ=20.12 (q, Me), 25.53 (t, 2×C, 5- and 6-C), 32.24 (d, 3-C), 55.59 (d, 4-C), 111.07 (t, =CH$_2$), 134.54 (d), and 211.89 (s, $\underline{\text{CO}}$Me). Other signals are overlapping with those of **17**; GC-MS *m/z* (rel. intensity, %) 164 (M$^+$, 71), 149 (54), 121 (base peak), 94 (91), 92 (52), and 79 (76).

Reaction of 2 with 8 Leading to 21. A mixture of **2** (0.346 g, 1.3 mmol) and **8** (0.225 g, 1.3 mmol) in dry benzene (5 ml) was heated under reflux under nitrogen for 15 h. The solvent was removed by evaporation in vacuo and the residue was chromatographed over silica gel with hexane–ethyl acetate (1:1) to afford the 1:1 mixture of two diastereomers of **21** (0.568 g, 99%): Colorless liquid; IR (neat) 1780, 1710, 1380, 1190, and 1175 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=1.12, 1.18 (each 3H, d, J=6.5 Hz, Me), 1.90—2.72 (6H, m), 2.36 (3H, s, *p*-Me), 2.92—3.10 (2H, m), 4.20—4.40 (1H, m, C$\underline{\text{H}}$Me), 5.48—5.72 (1H, m, 6-H), 7.04—7.50 (5H, m, Ph), 7.24, and 7.72 (each 2H, d, J=8.0 Hz, ArH); ^{13}C NMR (CDCl$_3$) δ=20.22, 21.25 (each q, Me), 24.02, 24.12, 27.09, 27.83 (each t), 38.50, 38.59, 39.18 (each d), 44.10, 44.34 (each t), 77.09, 78.55 (each d, $\underline{\text{C}}$HOTs), 123.97, 124.31 (each d, 6-C), 125.97, 127.23, 127.33, 128.06, 128.59, 129.48 (each d), 131.77, 133.81, 133.96, 134.83, 135.03, 144.24, 144.34 (each s), 178.30, and 178.55 (each s, CON); MS *m/z* (rel. intensity, %) 439 (M$^+$, 4), 267 (55), 120 (66), and 91 (base peak).

Found: C, 65.34; H, 5.82; N, 3.41%. Calcd for $C_{24}H_{26}NO_5S$: C, 65.59; H, 5.73; N, 3.19%.

Reaction of 2 with 20 Leading to 22. A mixture of **2** (0.141 g, 0.53 mmol) and **20** (0.084 g, 0.53 mmol) in dry benzene (2 ml) was refluxed under nitrogen for 36 h. The benzene was evaporated in vacuo and the residue was chromatographed over silica gel using hexane–ethyl acetate (3:1) to give the 1:1 mixture of two diastereomers of **22** (0.165 g, 72%): Colorless solid; IR (KBr) 1685, 1590, 1355, and 1170 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=1.04, 1.05 (each 3H, d, J=6.0 Hz, Me), 1.80—2.60 (8H, m), 2.39, 2.43 (each 3H, s, *p*-Me), 3.00—3.20 (2H, m), 4.68 (1H, m, C$\underline{\text{H}}$OTs), 5.40 (1H, m, 3-H), 7.28, 7.30 (each 2H, d, J=8.0 Hz, ArH), and 7.60—8.10 (6H, m, ArH); MS *m/z* (rel. intensity, %) 424 (M$^+$, 5), 252 (51), and 91 (base peak).

Found: C, 68.08; H, 5.74%. Calcd for $C_{24}H_{24}O_5S$: C, 67.91; H, 5.70%.

Reaction of 2 with 16 Leading to 23 and/or 24. i) A mixture of **2** (0.246 g, 0.92 mmol) and **16** (0.3 ml, 3.7 mmol) in dry benzene (2 ml) was refluxed under nitrogen for 48 h. The solvent and excess **16** were evaporated in vacuo and the residue was chromatographed over silica gel with hexane–ethyl acetate (3:1) to give a mixture of **23** and **24** (0.222 g, 74%) whose separation failed. The isomer ratio was determined after their conversion into a mixture of **19** and its regioisomer by the reaction with DBU (**23**:**24** was calculated as 64:36). ii) To a solution of **16** (0.1 ml, 1.23 mmol) in dry toluene (1 ml) was added ethylaluminum dichloride (1 M solution in hexane, 0.6 ml, 0.6 mmol) at −70 °C. After 0.5 h at the same temperature, **2** (0.164 g, 0.62 mmol) in toluene (1 ml) was added and the mixture was allowed to react below −50 °C for 1 h. Usual hydrolytic work-up with aqueous sodium hydrogen carbonate was followed by the extraction with benzene (10 ml×2). The combined extracts were dried over magnesium sulfate and evaporated in vacuo. The residue was chromatographed over silica gel using hexane–ethyl acetate (3:1) to provide **23** (0.139 g, 67%).

23: Colorless liquid; IR (neat) 1710, 1355, 1190, and 1175 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=1.22, 1.24 (each 3H, d, J=6.2 Hz, Me), 1.30—2.50 (9H, m), 2.12 (3H, s, COMe), 2.42 (3H, s, p-Me), 4.64 (1H, m, C$\underline{\text{H}}$OTs), 5.36 (1H, m, 2-H), 7.24, and 7.72 (each 2H, d, J=8.0 Hz, ArH); ^{13}C NMR (CDCl$_3$) δ=20.82, 21.59 (each q, Me), 24.65, 26.88, 27.94 (each t), 27.94 (q, Me), 44.59, 44.77 (each t), 46.65, 46.77 (each d, 4-C), 78.83 (d, $\underline{\text{C}}$HOTs), 123.83 (d, 2-C), 127.83, 129.95 (each d), 132.54 (s, 1-C), 134.66, 144.77 (each s), and 211.48 (s, $\underline{\text{C}}$OMe); MS m/z (rel. intensity, %) 336 (M$^+$, 4), 164 (29), 121 (59), and 43 (base peak).

Found: C, 64.41; H, 7.23%. Calcd for C$_{18}$H$_{24}$O$_4$S: C, 64.26; H, 7.19%.

24: ^{1}H NMR (CDCl$_3$) δ=1.26 (3H, d, J=6.2 Hz, Me), 1.30—2.50 (9H, m), 2.12 (3H, s, COMe), 2.42 (3H, s, p-Me), 4.64 (1H, m, C$\underline{\text{H}}$OTs), 5.36 (1H, m, 2-H), 7.24, and 7.72 (each 2H, d, J=8.0 Hz, ArH); ^{13}C NMR (CDCl$_3$) δ=44.89, 45.00 (each d, 5-C), 125.07 (d, 2-C), 131.30 (s, 1-C), and 211.19 (s, $\underline{\text{C}}$OMe). Other signals are overlapping with those of **23**.

Reaction of 21 with DBU Leading to 10. A mixtute of **21** (0.233 g, 0.53 mmol) and DBU (0.105 g, 0.69 mmol) in dry toluene (4 ml) was refluxed for 6 h. The toluene was evaporated in vacuo and the residue was subjected to a column chromatography over silica gel using hexane–ethyl acetate (2:1) to give a mixture of **10**, **25**, and **26** (0.104 g, 73%). The isomer ratio **10**+**25**:**26** was determined as 97:3 by GLC. Although **10** and **25** showed the same retention time in the GLC, the mixture of **25** and **26** was recovered unchanged in the reaction of the above mixture with **13** and their ratio was 2:1 (^{1}H NMR). After all, the ratio among them was calculated as **10**:**25**:**26**=91:6:3.

10 (purity 91% (GLC)): Colorless oil; IR (neat) 1780 and 1715 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=1.74 (3H, d, J=6.0 Hz, Me), 2.00—3.40 (6H, m, CH$_2$ and CH), 5.40—5.92 (2H, m, =CH), 6.04 (1H, d, J=16.0 Hz, 5-C$\underline{\text{H}}$=CHMe), and 7.04—7.48 (5H, m, Ph); ^{13}C NMR (CDCl$_3$) δ=18.18 (q, Me), 23.41, 24.59 (each t, 4- and 7-C), 39.41 (d, 2×C, 3a- and 7a-C), 123.36, 124.42, 126.54, 128.54, 129.13 (each d), 131.89 (d), 132.25, 137.83 (each s), and 178.95 (s, 2×C, CON); MS m/z (rel. intensity, %) 267 (M$^+$, 20) and 91 (base peak).

Found: C, 76.38; H, 6.41; N, 5.24%. Calcd for C$_{17}$H$_{17}$NO$_2$: C, 76.45; H, 6.46; N, 5.34%.

25+**26**: ^{1}H NMR (CDCl$_3$) δ=1.74 (d, J=6.0 Hz, Me), 2.00—3.40 (m, CH$_2$ and CH), 5.00 (m, =CH$_2$), 5.32—5.90 (m, =CH), and 7.04—7.48 (m, Ph).

One-Pot Synthesis of 10. A mixture of **2** (0.39 g, 1.46 mmol) and **8** (0.254 g, 1.46 mmol) in dry toluene (6 ml) was heated at 80 °C under nitrogen for 15 h. After DBU (0.29 g, 1.9 mmol) was added, the mixture was refluxed for 6 h. The solvent was evaporated in vacuo and the residue was chromatographed over silica gel using hexane–ethyl acetate (2:1) to give **10** (0.272 g, 70%, purity 91% (GLC), the contaminants are **25** and **26** in the ratio 2:1 (GLC)).

Reaction of 23 with DBU Leading to 19. A mixture of **23** (0.119 g, 0.35 mmol) and DBU (0.07 g, 0.46 mmol) in dry toluene (3 ml) was refluxed under nitrogen for 12 h. The toluene was evaporated in vacuo and the residue was chromatographed over silica gel with hexane–ethyl acetate (9:1) to give a mixture of **19**, **27**, and **28** (0.044 g, 76%, **19**:**27**:**28**=87:8:5) whose separation failed.

19: ^{1}H NMR (CDCl$_3$) δ=1.73 (3H, d, J=6.5 Hz, Me), 1.40—2.70 (7H, m, CH$_2$ and CH), 2.16 (3H, s, COMe), 5.32—5.72 (2H, m, =CH), and 6.02 (1H, d, J=16.0 Hz, 1-C$\underline{\text{H}}$=CHMe); ^{13}C NMR (CDCl$_3$) δ=18.18 (q, Me), 24.24, 24.71, 27.41 (each t, CH$_2$), 28.00 (q, CO$\underline{\text{Me}}$), 47.59 (d, 4-C), 122.36, 124.48, 134.01 (each d), 135.54 (s, 1-C), and 211.66 (s, $\underline{\text{C}}$OMe).

27+**28**: ^{1}H NMR (CDCl$_3$) δ=1.73 (d, J=6.5 Hz, Me), 1.40—2.70 (m, CH$_2$ and CH), 2.17 (s, COMe), 4.98 (m, =CH$_2$), and 5.32—5.72 (m, =CH).

Reaction of 22 with DBU Leading to 29. A mixture of **22** (0.092 g, 0.22 mmol) and DBU (0.043 g, 0.28 mmol) in dry toluene (2 ml) was stirred at room temperature under nitrogen for 2 h. The mixture was chromatographed over silica gel with hexane–ethyl acetate (3:1) to give **29** (0.051 g, 56%): Pale yellow needles (ethanol); mp 122—124 °C; IR (KBr) 1670, 1595, 1185, 1170, 885, 760, and 710 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=1.43 (3H, d, J=6.0 Hz, Me), 2.04 (3H, s, COMe), 2.96 (2H, d, J=6.5 Hz, CH$_2$), 4.78 (1H, tq, J=6.0 and 6.5 Hz, C$\underline{\text{H}}$OTs), 6.96 (2H, d, J=8.0 Hz, ArH), 7.32—7.42, 7.68—7.86 (each 3H, m, ArH), 8.00 (1H, d, J=8.0 Hz, ArH), and 8.10—8.36 (2H, m, ArH); MS m/z (rel. intensity, %) 420 (M$^+$, 5), 248 (38), and 91 (base peak).

Found: C, 68.64; H, 4.91%. Calcd for C$_{24}$H$_{20}$O$_5$S: C, 68.56; H, 4.79%.

Reaction of 10 with 8 Leading to 12. A mixture of **10** (purity 91%, 0.042 g, 0.14 mmol) and **8** (0.027 g, 0.16 mmol) in dry benzene (1 ml) was stirred at room temperature for 20 h. The solvent was evaporated in vacuo and the residue was chromatographed over silica gel with hexane–ethyl acetate (1:1) to afford **12** (0.049 g, 78%) whose spectral data were shown above.

Reaction of 10 with 13 Leading to 30 and 31. A mixture of **10** (purity 91%, 0.102 g, 0.35 mmol) and **13** (0.108 g, 0.76 mmol) in dry benzene (3 ml) was refluxed under nitrogen for 60 h. The solvent was evaporated in vacuo and the residue was chromatographed over silica gel using hexane–ethyl acetate (2:1) to provide **30** (0.112 g, 79%) and then **31** (0.012 g, 8%).

30: Colorless needles (ethanol); mp 177—178 °C; IR (KBr) 1775, 1735, 1710, 1375, and 795 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=1.22 (3H, d, J=7.0 Hz, Me), 1.32—1.66, 1.92—2.26 (each 1H, m, CH$_2$), 2.64—3.32 (6H, m, CH$_2$ and CH), 3.76 (6H, s, COOMe×2), 5.55 (1H, dd, $J_{5\text{-}6}$=4.0 and $J_{5\text{-}8a}$=1.5 Hz, 5-H), and 7.10—7.56 (5H, m, Ph); ^{13}C NMR (CDCl$_3$) δ=21.83 (q, Me), 30.94 (t, 9-C), 33.41 (d, CH), 35.00 (t, 4-C), 36.53, 40.71, 42.00 (each d, CH), 52.30 (q, 2×C, COO$\underline{\text{Me}}$), 124.06 (d), 126.36 (d, 2×C), 128.53 (d), 129.24 (d, 2×C), 131.66, 132.13, 133.42, 140.18 (each s), 167.31, 168.65 (each s, $\underline{\text{C}}$OOMe), 176.95, and 177.83 (each s, CON); MS m/z (rel. intensity, %) 409 (M$^+$, 2), 377 (22), and 362 (base peak).

Found: C, 67.29; H, 5.61; N, 3.58%. Calcd for C$_{23}$H$_{23}$NO$_6$: C, 67.47; H, 5.66; N, 3.42%.

31: Colorless solid; mp 63—65 °C; IR (KBr) 1775, 1735, and 1710 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=1.14 (3H, d, J=7.0 Hz, Me), 1.10—1.40, 2.26—2.56 (each 1H, m, CH$_2$), 2.68—3.40 (6H, m, CH$_2$ and CH), 3.76 (6H, s, COOMe×2), 5.56 (1H, dd, $J_{5\text{-}6}$=3.5 and $J_{5\text{-}8a}$=1.5 Hz, 5-H), and 7.10—7.56 (5H, m, Ph); MS m/z (rel. intensity, %) 409 (M$^+$, 3), 377 (49), and 362 (base peak).

Found: m/z 409.1517. Calcd for C$_{23}$H$_{23}$NO$_6$: M, 409.1524.

Reaction of 10 with 32 Leading to 33—35. A mixture ot **10** (purity 91%, 0.152 g, 0.52 mmol) and **32** (0.24 g, 2.85 mmol) in dry benzene (3 ml) was refluxed under nitrogen for 40 h. The solvent was evaporated in vacuo and the residue was chromatographed over silica gel using hexane–ethyl acetate (2:1) to give **33** (0.042 g, 23%), the mixture of **33**, **35**, **10**, **25**, and **26** (0.092 g, the isomer ratio was 26:16:40:7:3 (GLC)), and **34** (0.028 g, 15%). The isomer **35** was separated from the mixture through HPLC.

33: Colorless solid; mp 138—139 °C; IR (KBr) 1775, 1700, 1380, and 1250 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=1.16 (3H, d, J=7.0 Hz, Me), 1.45 (1H, dt, J_{gem}=14.5 and J_{9-8a}=J_{9-9a}=6.0 Hz, one of 9-H), 1.90—2.24 (1H, m, the other of 9-H), 2.52—3.32 (6H, m, CH$_2$ and CH), 3.72 (3H, s, COOMe), 5.57 (1H, m, 5-H), 6.77 (1H, d, J_{8-8a}=4.0 Hz, 8-H), and 7.16—7.56 (5H, m, Ph); MS m/z (rel. intensity, %) 351 (M$^+$, 3), 336 (27), 319 (35), and 304 (base peak).

Found: C, 71.95; H, 5.99; N, 4.28%. Calcd for $C_{21}H_{21}NO_4$: C, 71.78; H, 6.02; N, 3.99%.

34: Colorless solid; mp 149—151 °C; IR (KBr) 1775, 1705, 1375, and 1255 cm^{-1}; ^{1}H MMR (CDCl$_3$) δ=1.09 (3H, d, J=7.0 Hz, Me), 1.10—1.48 (1H, m, one of 9-H), 2.20—3.50 (7H, m, CH$_2$ and CH), 3.71 (3H, s, COOMe), 5.57 (1H, m, 5-H), 6.72 (1H, d, J_{8-8a}=4.0 Hz, 8-H), and 7.12—7.56 (5H, m, Ph); MS m/z (rel. intensity, %) 351 (M$^+$, 10), 336 (13), 319 (63), and 304 (base peak).

Found: C, 71.87; H, 6.14; N, 4.21%. Calcd for $C_{21}H_{21}NO_4$: C, 71.78; H, 6.02; N, 3.99%.

35: Colorless needles (ethyl acetate-hexane); mp 227—228 °C; IR (KBr) 1770, 1700, 1370, and 1255 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=1.16 (3H, d, J=7.0 Hz, Me), 1.10—1.54, 2.00—2.32 (each 1H, m, 9-H), 2.48—3.28 (6H, m, CH$_2$ and CH), 3.75 (3H, s, COOMe), 5.49 (1H, br s, 5-H), 6.89 (1H, dd, J_{7-6}=3.0 and J_{7-8a}=1.5 Hz, 7-H), and 7.10—7.56 (5H, m, Ph); MS m/z (rel. intensity, %) 351 (M$^+$, 6), 336 (38), 319 (40), and 304 (base peak).

Found: C, 71.77; H, 6.09; N, 4.16%. Calcd for $C_{21}H_{21}NO_4$: C, 71.78; H, 6.02; N, 3.99%.

Dehydrogenation of 33—35 Leading to 36 and 37. i) A mixture of **33** (0.026 g, 0.097 mmol) and chloranil (0.027 g, 0.11 mmol) in dry toluene (1 ml) was refluxed for 15 h. The toluene was evaporated in vacuo and the residue was chromatographed over silica gel with hexane–ethyl acetate (2:1) to afford **36** (0.025 g, 97%). ii) The isomer **34** was readily dehydrogenated giving **36** when exposed to the air. iii) A mixture of **35** (0.02 g, 0.057 mmol) and chloranil (0.021 g, 0.085 mmol) in dry toluene (1 ml) was refluxed for 15 h. The same procedure as mentioned above gave **37** (0.016 g, 80%).

36: Colorless prisms (ethanol); mp 170—171 °C; IR (KBr) 1770, 1700, 1390, and 1265 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=2.53 (3H, s, Me), 2.70—3.50 (6H, m, CH$_2$ and CH), 3.84 (3H, s, COOMe), 6.76—6.92 (2H, m, Ph), 7.04 (1H, s, 8-H), 7.20—7.40 (3H, m, Ph), and 7.72 (1H, s, 5-H); MS m/z (rel. intensity, %) 349 (M$^+$, 5), 318 (39), and 317 (base peak).

Found: C, 72.14; H, 5.47; N, 4.11%. Calcd for $C_{21}H_{19}NO_4$: C, 72.19; H, 5.48; N, 4.01%.

37: Colorless solid; mp 58—60 °C; IR (KBr) 1770 and 1700 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=2.30 (3H, s, Me), 2.80—3.48 (5H, m, CH$_2$ and CH), 3.86 (3H, s, COOMe), 4.06 (1H, dd, J_{gem}=15.0 and J_{4-3a}=3.0 Hz, one of 4-H), 6.70—6.96 (2H, m, Ph), 7.11 (1H, br s, 8-H), 7.20—7.40 (3H, m, Ph), and 7.56 (1H, br s, 6-H); MS m/z (rel. intensity, %) 349 (M$^+$, 18), 318 (31), and 317 (base peak).

Found: m/z 349.1306. Calcd for $C_{21}H_{19}NO_4$: M, 349.1313.

Reaction of 10 with 16 Leading to 38. To a solution of **16** (0.074 ml, 0.9 ml) in dry toluene (1 ml) was added ethylaluminum dichloride (1 M solution in hexane, 0.9 ml, 0.9 mmol) at −70 °C. After 0.5 h, **10** (purity 91 %, 0.237 g, 0.81 mmol) in toluene (1 ml) was added and the mixture was stirred at the same temperature for 2 h. Usual work-up with aqueous sodium hydrogen carbonate was followed by the extraction with benzene (10 ml×2). The benzene was dried over magnesium sulfate and evaporated in vacuo. The residue was chromatographed over silica gel with hexane–ethyl acetate (2:1) to give **38** (0.211 g, 78%): Colorless solid; mp 111—112 °C; IR (KBr) 1770 and 1700 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=0.78 (3H, d, J=7.0 Hz, Me), 1.10—3.28 (11H, m, CH$_2$ and CH), 2.10 (3H, s, COMe), 5.48 (1H, dd, J_{5-6}=4.0 and J_{5-8a}=2.0 Hz, 5-H), and 7.10—7.52 (5H, m, Ph); ^{13}C NMR (CDCl$_3$) δ=16.47 (q, Me), 25.65 (t), 28.35 (q, CO$\underline{\text{Me}}$), 29.01, 29.77 (each t), 31.00, 33.36, 39.41, 39.71 (each d), 51.36 (d, 7-C), 126.42 (d, 2×C), 127.95, 128.48 (each d), 129.13 (d, 2×C), 132.25, 134.18 (each s), 178.89 (s, 2×C, $\underline{\text{C}}$OOMe), and 210.31 (s, $\underline{\text{CO}}$Me); MS m/z (rel. intensity, %) 337 (M$^+$, base peak), 319 (42), 295 (65), 294 (99), 91 (54), and 77 (30).

Found: C, 74.88; H, 6.94; N, 4.40%. Calcd for $C_{21}H_{23}NO_3$: C, 74.75; H, 6.87; N, 4.15%.

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References

1) O. Tsuge, E. Wada, and S. Kanemasa, *Chem. Lett.*, **1983**, 239.

2) O. Tsuge, S. Kanemasa, H. Sakoh, and E. Wada, *Chem. Lett.*, **1984**, 273.

3) S. Kanemasa, H. Sakoh, E. Wada, and O. Tsuge, *Bull. Chem. Soc. Jpn.*, **58**, 3312 (1985).

4) O. Tsuge, E. Wada, and S. Kanemasa, *Chem. Lett.*, **1983**, 1525.

5) O. Tsuge, S. Kanemasa, H. Sakoh, and E. Wada, *Chem. Lett.*, **1984**, 277.

6) O. Tsuge, E. Wada, S. Kanemasa, and H. Sakoh, *Bull. Chem. Soc. Jpn.*, **57**, 3221 (1984).

7) O. Tsuge, S. Kanemasa, H. Sakoh, and E. Wada, *Bull. Chem. Soc. Jpn.*, **57**, 3234 (1984).

8) O. Tsuge, E. Wada, S. Kanemasa, and H. Sakoh, *Chem. Lett.*, **1984**, 469.

9) O. Tsuge, E. Wada, S. Kanemasa, and H. Sakoh, *Chem. Lett.*, **1984**, 709.

10) The trienes **D** and **E** can be synthesized by the reaction of the Grignard reagent of chloroprene with 2-bromovinyl ethyl ether and 2-bromovinyl phenyl sulfide in the presence of Ni(dppp)Cl$_2$ at −78 °C to room temperature, respectively. They can be only isolated as solution in THF because of the ready polymerization. They react with *N*-methylmaleimide to give the corresponding bis-cycloadducts as single isomers (Our unpublished results).

11) S. Nunomoto and Y. Yamashita, *J. Org. Chem.*, **44**, 4788 (1979).

12) GLC analysis of this mixture showed only two peaks in the ratio 90:10. However, cycloaddition of this mixture with *N*-phenylmaleimide (**8**) produced bis-cycloadducts **11** and **12** as major products and two monocycloadducts of **4** and **5** (GLC and ^{1}H NMR).

13) Stereostructures of **9**, **11**, and **12** can not be determined only on the basis of the spectral data. Endo structure of **9** and that of the second six-membered ring of **12** are based on

a rule that cyclic dienophiles undergo highly *endo*-selective cycloaddition (J. Sauer, *Angew. Chem. internat. Edit.*, **6**, 16 (1967)). As **11** and **12** are the only stereoisomers formed, the second molecule of **8** is most likely to have attacked **9** and **10** from the less hindered side of diene, opposite to the preexistent fused maleimide ring. Similar stereoselectivity has been previously reported (Ref. 6).

14) Endo and exo structures of **17** and **18** were confirmed on the basis of chemical shifts of the ring methyl and also of the fact that **17** was mainly obtained in the Lewis acid-catalyzed cycloaddition (T. Inukai and T. Kojima, *J. Org. Chem.*, **31**, 2032 (1966)).

15) An example of Lewis acid-catalyzed Diels–Alder reaction: T. Inukai and T. Kojima, *J. Org. Chem.*, **32**, 869 (1967).

16) The ratio between **23** and **24** was determined by GLC analysis after their conversion into the corresponding dienes. The para:meta ration in the Diels–Alder reaction of 2-methyl-1,3-butadiene with **16** was reported as 71:29 (E. F. Lutz and G. M. Bailey, *J. Am. Chem. Soc.*, **86**, 3899 (1964)).

17) Regiochemistry of **23** and **24** was determined by the fact that **23** is the only regioisomer formed in the Lewis acid-catalyzed Diels–Alder reaction of **2** and **16**.

18) When **10** containing 9% of **25** and **26** is subjected to a Diels–Alder cycloaddition, **25** and **26** as contaminants can be recovered unchanged. It is known that cis 1-substituted 1,3-diene is much less reactive than the trans isomer (See the reference in Ref. 13).

19) Such dehydrogenation which presumably took place via an enol intermediate can be seen in a literature (K. Hayakawa, K. Ueyama, and K. Kanematsu, *J. Org. Chem.*, **50**, 1963 (1985)).