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Cross Diene-transmissive Diels-Alder Cycloaddition Reaction of Bis(silyloxy) Cross-conjugated Trienes

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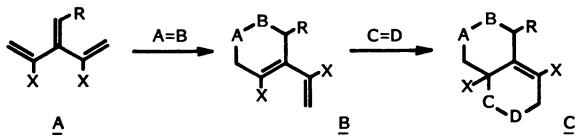
Cross type of diene-transmissive Diels-Alder cycloaddition has been demonstrated by using two bis-silyloxy cross-conjugated trienes. The first cycloaddition stage of cross reaction, which has to be highly selective in the formation of mono-cycloadducts, has been performed by the reactions of an activated triene with cyclic olefins or those of trienes with acyclic olefins. The secod cycloadditions with a variety of dienophiles provide cross types of bis-adducts. The characteristics of these cross reactios are discussed.

The diene-transmissive Diels-Alder reaction is a process that involves two sequential Diels-Alder cycloadditions of cross-conjugated triene.[1] Of great value as a synthetic tool is the cross type of diene-transmissive Diels-Alder reaction in which each different dienophile participates in each stage of cycloadditions leading to the formation of cross bis-cycloadduct (**A**→**B**→**C**). Success of the cross reaction mainly depends upon the chemoselective formation of mono-cycloadduct **B**. This selectivity may be conveniently called "monoselectivity" in the present paper.



A B C

The preceding paper has dealt with the diene-transmissive Diels-Alder reaction of bis (silyloxy) cross-conjugated trienes, 3-(methoxymethylene)- **1** and 3-benzylidene-2,4-bis(trimethylsilyloxy)-1,4-pentadiene **2**.[1] The reaction of **1** with an equivalent of cyclic olefinic dienophiles was highly monoselective, while with two equivalents the bis-cycloadducts were exclusively formed. On the other hand, the reaction of either **1** or **2** with acyclic olefinic dienophiles below 80 °C was also monoselective even if excess of dienophiles was used.

Therefore, the cross type of diene-transmissive Diels-Alder reaction may be achieved through the following two possible approaches: The first method involves the initial formation of the mono-cycloadducts between **1** and cyclic olefinic dienophiles and the followed second cycloaddition with appropriate dienophiles. The second method is initiated by the initial cycloaddition of either **1** or **2** with acyclic olefinic dienophiles and followed by the second cycloaddition with highly reactive dienophiles.

Results and Discussion

The most promising cross process of diene-transmissive Diels-Alder reaction may be achieved by use of the activated triene **1**. When an equivalent of **1** is used, the cycloadduct to cyclic olefinic dienophiles is highly monoselective forming endo mono-cycloadducts. The endo approach of the second molecule of dienophiles from the less hindered side easily occurs giving stereoselective bis-cycloadducts when another equivalent of dienophiles is added.[1]

Each equivalent of **1** and *N*-phenylmaleimide **3a** in benzene was allowed to react at room temperature for 20 h during which time the endo mono-cycloadduct **D** was formed. After the addition of dimethyl acetylenedicarboxylate **4a** (1.5 equivalent) as the second dienophile, the reaction was continued under reflux for an additional 20 h. The usual desilylating work-up with methanol gave a cross bis-adduct **5aa** (Scheme 1 and Table 1). It was assigned that the initially formed ring of **5aa** had trans configuration on the basis of the coupling constant between 3a-H and 4-H (J_{3a-4}=3.0 Hz) This means that the stereochemistry at the 4-position of mono-cycloadduct **D** was inverted. Such inversion, which must have occurred at or later the desilylation stage, has been generally observed in the reactions of **1** with cyclic olefinic dienophiles.[1]

Similar reaction of **1** with *N*-methylmaleimide **3b** and then with **4a** or that of **1** with **3b** and then with dibenzoylacetylene **4b**, under the reaction conditions shown in Table 1, gave the cross bis-adduct **5ba** or **5bb**, respectively.

When maleic anhydride **3c** was used as the first dienophile, the cycloaddition was completed in 2 h at room temperature. The second cycloaddition with **4a** was followed under reflux in benzene for 24 h. Esterification of the reaction mixture with methanol in the presence of *p*-toluenesulfonic acid gave two isomeric cross bis-adducts **6ca** and **7ca**. Their ratio is not so important because **6ca** gradually changes into **7ca** when heated or treated with methanol in the presence of *p*-toluenesulfonic acid. The structures were confirmed on the basis of the coupling constant between 1-H and 2-H (**6ca**: 6.0 Hz; **7ca**: 3.0 Hz).

^{1}H-NMR analysis of the reaction of isolated mono-cycloadduct **D** (X=O) with **4a** showed the formation of aromatized cross bis-adducts **F** and **G** (R=E=COOMe) whose isolation failed. Their ratio was found to change depending upon the reaction temperature and time: Only **F** (after 24 h at room temperature), a mixture of **F** and **G** (4:3, after 24 h under reflux in benzene), and only **G** (after a week at room temperature or after 3 d under reflux in benzene) were formed, indicating that the endo bis-cycloadduct **F** and the exo one **G** are kinetically and thermodynamically controlled products, respectively.

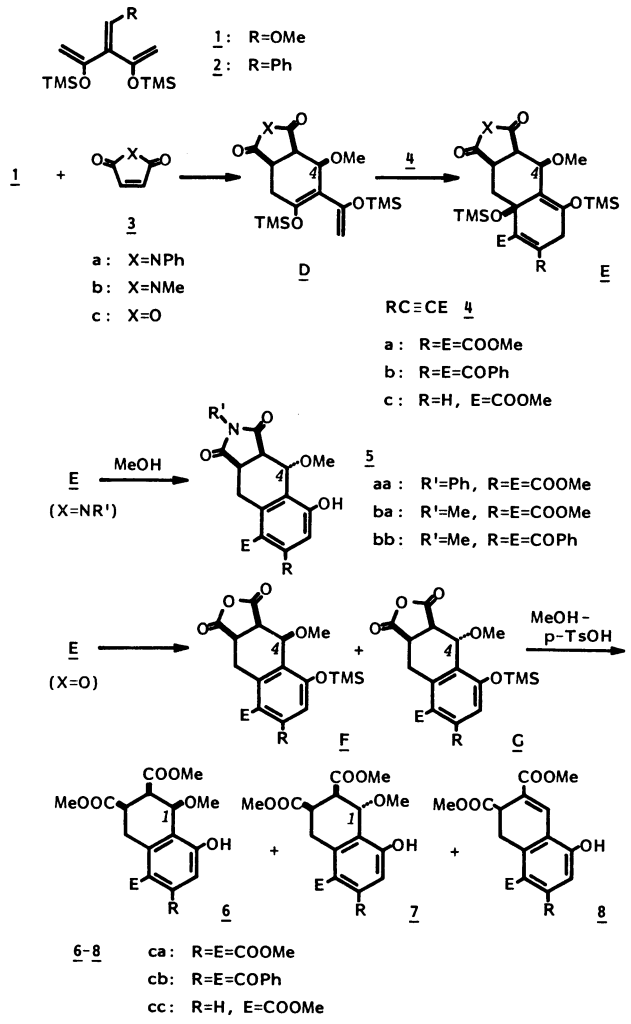
Thus, in the cross cycloadditions of **1** with cyclic

olefinic dienophiles and then with acetylenic ones, the first stage is an endoselective cycloaddition leading to **D**. The acetylenes approach from the less hindered side, opposite to the 4-MeO and fused maleimide ring, forming the stereoselective cross bis-cycloadducts **E** which are immediately aromatized by the elimination of a silanol. The inversion of 4-MeO substituent starts giving more stable isomers probably through an elimination-addition mechanism. In the cases of maleimides, only the inverted bis-adducts **5** were isolated, and in the case of maleic anhydride, a mixture of bis-adducts **6** and **7** was yielded.

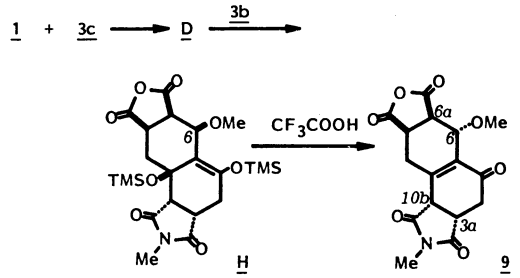
Similar reaction of **1** with **3c** and then with **4b**, under similar reaction conditions (Table 1), gave an exo cross bis-adduct **7cb** together with a methanol-eliminated bis-adduct **8cb**, no trace of endo bis-adduct **6cb** being obtained.

As the diene moiety of mono-cycloadduct **D** carries two silyloxy substituents in a 1,3-relationship, the second cycloaddition to unsymmetrically substituted dienophiles should be regioselective.[2] As expected, the reaction of **1** with **3c** and then with methyl propiolate **4c** gave a regioselective methanol-eliminated cross bis-adduct **8cc**, but in a low yield.

Olefinic dienophiles can be employed as well in the second cycloaddition. Thus, the endo mono-cycloadduct **D** (X=O), which had been formed in the initial cycloaddition of **1** to **3c**, was allowed to react with **3b** and the reaction mixture was treated with trifluoroacetic acid. The only product isolated in 38% yield was a stereoselective cross bis-adduct **9** which was accompanied with the inversion at the 6-position. Although the configuration at the points of fusion (the 3a and 10b positions) was not clear only on the basis of the spectral data, it was tentatively assigned as shown in Scheme 2 according to the most likely approach of **3b**. The second olefinic dienophile **3b** must have approached to **D** in an endo fashion from the opposite side to the 4-MeO and the fused maleimide ring, giving a stereoselective bis-cycloadduct **H**.



Scheme 1.



Scheme 2.

Table 1. Cross cycloadditions of **1** to cyclic olefins **3** and then acetylenes **4**

Olefin (equiv)	Acetylene (equiv)	Reaction Conditions[a] 1st Reaction	2nd Reaction	Product (yield/%)[b]
3a (1.0)	**4a** (1.5)	24 h at r.t.	20 h under Reflux	**5aa** (49)
3b (1.0)	**4a** (1.5)	24 h at r.t.	20 h under Reflux	**5ba** (41)
3b (1.0)	**4b** (1.0)	24 h at r.t.	36 h under Reflux	**5bb** (47)
3c (1.0)	**4a** (1.4)	2 h at r.t.	24 h under Reflux	**6ca** (14), **7ca** (19)
3c (1.0)	**4b** (1.0)	2 h at r.t.	24 h at r.t.	**7cb** (33)[c], **8cb** (6)
3c (1.0)	**4c** (2.0)	2 h at r.t.	48 h under Reflux	**8cc** (15)

a) All the reactions were carried out in dry benzene. The first and second reactions were performed in the same flask. When **3c** was used as the first dienophile, esterification procedure was followed after the second cycloaddition was complete (under reflux in methanol for 24 h in the presence of *p*-toluenesulfonic acid). b) All isolated yields based on **1**. c) A part of **7cb** was isolated as a silylated derivative **G** (R=E=COPh).

As the cross bis-cycloadducts and also their derivatives formed in the cross reactions of **1** with two different cyclic olefinic dienophiles were found all quite labile, the cross reactions with such combinations were not further investigated.

As described in the preceding paper,[1] both trienes **1** and **2** react with acyclic olefinic dienophiles affording only the mixture of endo and exo mono-cycloadducts, even when excess of the dienophiles is used. But, the prolonged reactions at higher temperature produce poor yields of bis-cycloadducts, indicating that the cross type of diene-transmissive Diels-Alder reaction may be achieved by reacting the triene **1** or **2** with acyclic olefins as the first dienophiles and then with highly reactive second dienophiles.

The triene **1** reacted with excess of methyl acrylate **10a** under reflux in benzene for 48 h. It was found from the separate experiment that two isomeric mono-cycloadducts **I** (isomer ratio=1:2)[3] were formed in good yields in this reaction mixture. After the solvent and the excess dienophile **10a** were completely removed, the residue was allowed to react further with the second dienophile **4a** under the conditions shown in Table 2. The work-up with methanol gave two isomeric cross bis-adducts **11aa** and **12aa** (Scheme 3). Again in this case, the isomer ratio is not important because they are interconvertible each other.

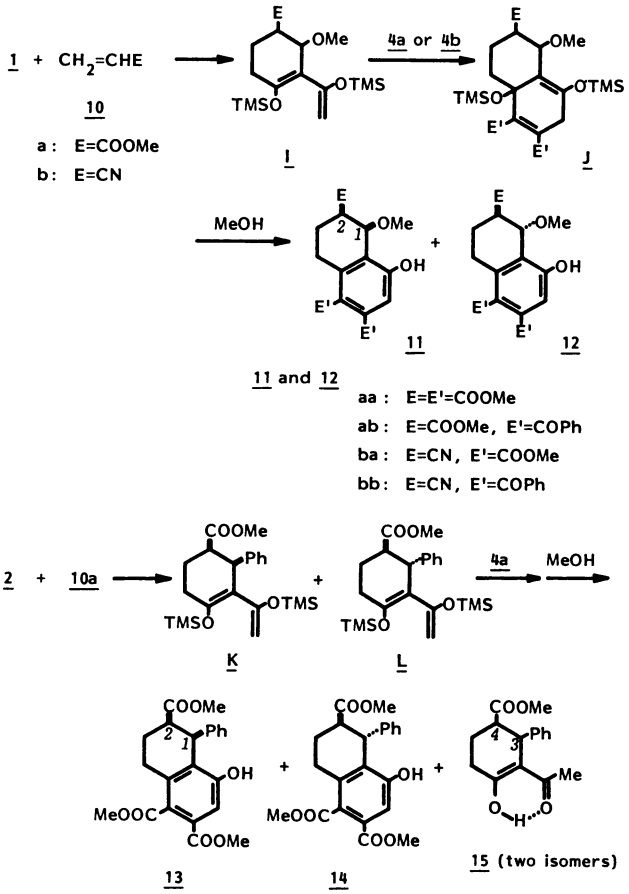
Similar cross reactions were performed by using **10a** or acrylonitrile **10b** as the first dienophile and **4a** or **4b** as the second. Results obtained are listed in Table 2.

In the cross cycloaddition of triene **1**, the use of unsymmetric dienophiles does not make any trouble since the both stage of double Diels-Alder reactions are highly regioselective. Disadvantage is that mono-cycloadducts to acyclic olefins take a half-chair conformation which disturbs the approach of the second dienophiles.[4] This sluggish second cycloaddition is often accompanied with some side reactions. One of them is the Michael reaction. In the reaction of mono-cycloadduct **I** (E=CN) with **4a**, a considerable amount of Michael adduct was obtained.[5]

Heating the triene **2** in large excess of **10a** for a long time (5 d at 80 °C) produces endo- **K** and exo mono-cycloadduct **L** in 22 and 70% yields, respectively.[6] When this mixture was allowed to react with **4a**, two isomeric cross bis-adducts **13** (endo, 10%) and **14** (exo, 36%) were yielded besides the mono-adducts **15** (6%, endo:exo=1:3). This result indicates that the endo mono-cycloadduct **K** cycloadds to **4a** as slowly as the exo one **L** does.

In the cross type of diene-transmissive Diels-Alder reactions using acyclic olefins, the second dienophiles are required to be highly reactive. Although the use of cyclic olefins as the second reagent led to the formation of rather unstable cross bis-adducts such as **9**, their high reactivity is still attracting.

The regioselective mono-cycloadduct **I** formed in the reaction of **1** with **10a** was allowed to react with an equivalent of **3b** under reflux in benzene for 24 h. The

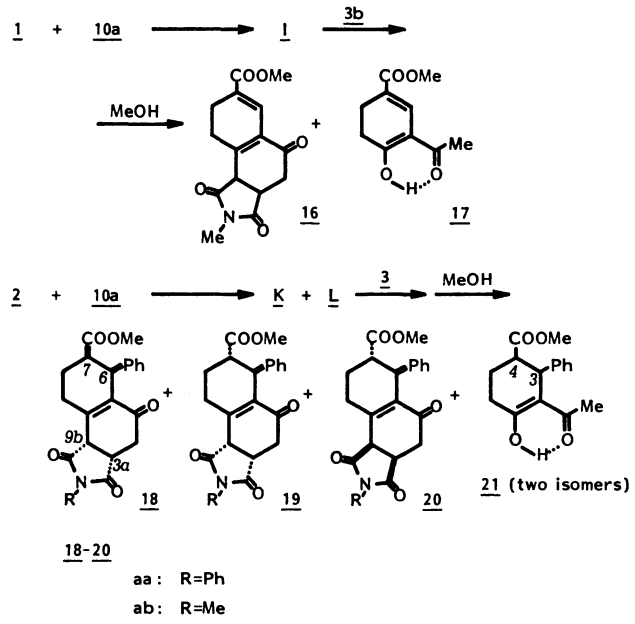


Scheme 3.

Table 2. Cross cycloadditions of **1** and **2** to acyclic olefins **10** and then acetylenes **4**

Triene	Olefin (equiv)	Acetylene (equiv)	Reaction Conditions[a] 1st Reaction	Reaction Conditions[a] 2nd Reaction	Product (yield/%)[b]
1	**10a** (3.0)	**4a** (1.1)	48 h at 80 °C	48 h under Reflux	**11aa** (21), **12aa** (8)
1	**10a** (3.0)	**4b** (1.0)	48 h at 80 °C	48 h under Reflux	**11ab** (15), **12ab** (21)
1	**10b** (5.0)	**4a** (2.0)	48 h at 75 °C	48 h under Reflux	**11ba** (23), **12ba** (12)
1	**10b** (5.0)	**4b** (1.0)	48 h at 75 °C	48 h under Reflux	**11bb** (28), **12bb** (10)
2	**10a** (20.0)	**4a** (1.1)	120 h at 80 °C	48 h under Reflux	**13** (10)[c], **14** (36)[c]

a) After the first cycloadditions in dry benzene was complete, the solvent and excess dienophiles **10** were completely removed off. To the residue were added dry benzene and acetylenes **4**, and the mixture was allowed to react under the shown conditions. b) All isolated yields based on the trienes. c) Separation was unsuccessful. Accompanied with the formation of mono-adduct **15** (endo : exo = 1 : 3, in 6% yield).



Scheme 4.

usual work-up with methanol gave a cross bis-adduct **16** (25%) together with the mono-adduct **17** (28%) which was derived from unreacted **I** (Scheme 4). There are no ambiguities on the stereochemistry of **16** since methanol elimination as well as desilylation has occured. Due to the instability, it failed to purify **16**.

Similar cross reactions were investigated by using triene **2**. When a mixture of **K** (endo) and **L** (exo) (**K**:**L**=22:70) was reacted with an equivalent of **3a** under reflux in benzene for 48 h, three kinds of cross bis-adducts **18aa**, **19aa**, and **20aa** were formed in 49% yield (**18aa**:**19aa**:**20aa**=2:14:3) besides a small amount of isomeric mono-adducts **21** (11%, endo:exo=1:5). Only the major product **19a** was isolated in pure form from a mixture of the other two. The structural assignment was based on the coupling constants between 6-H and 7-H as well as the stereochemical aspect of the reaction paths.[7]

The endo/exo ratio in the mono-cycloadducts (**K**:**L**=22:70) was found quite different from that in the products. The ratio of all the products from **K** to those from **L** was 7:53. This is probably because all of the cross bis-adducts **18aa**—**20aa** are labile. Actually they were partly decomposed when chromatographed over silica gel or heated in methanol. Under the same conditions, the second cycloaddition with **3b** recovered relatively large amount of the mono-cycloadducts **K** and **L** in the forms of **21** (38%, endo:exo=1:3) together with three cross bis-adducts **18ab**, **19ab**, and **20ab** (26%, **18ab**:**19ab**:**20ab**=1:4:2). The isomer ratios of unreacted mono-cycloadducts (endo/exo ratios of **21**) are about the same to the ratio between **K** and **L**, meaning that there is little difference of reactivity between the exo- **K** and endo mono-cycloadduct **L** in the cycloadditions to such cyclic olefins.

Experimental

General and Materials. 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-102 spectrometer. ^{1}H-NMR spectra were recorded on a Hitachi R-40 or a JEOL FX-100 instrument and ^{13}C-NMR spectra were obtained on a JEOL FX-100 spectrometer at 25.05 MHz. Chemical shifts are expressed in parts per million downfield from tetramethylsilane. Mass spectra were measured with a JEOL JMS-01SG-2 spectrometer at 75 eV of ionization energy. Elementary analyses were performed on a Hitachi 026 CHN analyzer. Thin-layer chromatography (TLC) was accomplished on 0.2 mm precoated plates of silica gel 60 F-254 (Merck) or on 0.2 mm precoated plates of aluminum oxide 60 F-254 type E (Merck). Visualization was made with ultraviolet light (254 and 365 nm) or iodine. Wako gel C200 and C300 (Wako) were used for preparative column chromatography. Preparative high performance liquid chromatography (HPLC) was carried out on a Kusano KHLC-201 apparatus with a UV-detector Uvilog-III using a column (22×300 mm) packed with silica gel (Wako gel LC-50H). Micro vacuum distillation was performed with a Sibata GTO-250R Kugelrohr distilling apparatus in a glass tube oven. When this apparatus was used, boiling points were expressed with the oven temperature. Solvents were evaporated with a Tokyo Rikakikai rotary evaporator type V at about 50 °C unless otherwise stated.

Benzene was purified by the distillation from sodium and stored on sodium wire. Both trienes, 3-(methoxymethylene)-**1** and 3-benzylidene-2,4-bis(trimethylsilyloxy)-1,4-pentadiene **2**, were prepared by the silylation of 3-(methoxymethylene)- and 3-benzylidene-2,4-pentanedione with chlorotrimethylsilane, respectively, as shown in the preceding paper.[1] The commercial materials of maleic anhydride **3c**, dimethyl acetylenedicarboxylate **4a**, methyl acrylate **10a**, and acrylonitrile **10b** were purified by distillation. The commercial grades of *N*-phenyl- **3a** and *N*-methylmaleimide **3b** were used without further purification. Dibenzoylacetylene **4b** was synthesized from 1,2-dibenzoylethene.[8] Methyl propiolate **4c** was obtained by the esterification of the commercial propiolic acid in the presence of *p*-toluenesulfonic acid.[9]

Cycloaddition of 1 to 3a and then 4a Leading to 5aa. A solution of freshly distilled **1** (0.773 g, 2.7 mmol) and **3a** (0.425 g, 2.5 mmol) in dry benzene (3 ml) was stirred at room temperature under nitrogen for 24 h. After **4a** (0.523 g, 3.7 mmol) was added, the resulting mixture was heated under reflux for 20 h. All the volatile materials were evaporated *in vacuo* and the residue obtained was stirred in methanol (10 ml) overnight. Evaporation of the methanol *in vacuo* left the residue which was then chromatographed over silica gel using chloroform–ethyl acetate (5:1) to give 0.524 g (49%) of **5aa**. The analytical sample of **5aa** was available through the repeated chromatography since its purification by crystallization was unsuccessful.

5aa: Colorless leaflets; mp 230 °C; IR (KBr) 3400 (OH); 1775, 1720, and 1685 cm^{-1} (C=O); ^{1}H-NMR (CDCl$_3$+DMSO-d_6) δ=2.70—3.90 (4H, m, 9-CH$_2$, 3a-, and 9a-H), 3.11 (3H, s, OMe), 3.81, 3.82 (each 3H, s, COOMe), 5.40 (1H, d, J_{4-3a}= 3.0 Hz, 4-H), and 7.10—7.56 (7H, m, ArH, 6-H, and OH); ^{13}C-NMR (CDCl$_3$+DMSO-d_6) δ=23.01, 35.75, 44.09, 50.96, 54.84, 68.10, 113.31, 123.47, 124.49, 125.34, 126.87, 127.40, 128.46, 130.98, 135.27, 154.58, 164.56, 167.03, 173.95, and 177.01; MS *m/z* 439 (M$^+$), 408 (M$^+$−31), and 228 (base peak).

Found: C, 62.78; H, 4.70; N, 3.67%; M$^+$, 439. Calcd for $C_{23}H_{21}NO_8$: C, 62.87; H, 4.82; N, 3.19%; M, 439.

Cycloaddition of 1 to 3b and then 4a Leading to 5ba. A solution of freshly distilled **1** (0.455 g, 1.6 mmol) and **3b** (0.161 g, 1.4 mmol) in dry benzene (2 ml) was stirred at room temperature under nitrogen for 24 h. After **4a** (0.309 g, 2.2 mmol) was added, the mixture was heated under reflux for 20 h. All the volatile materials were evaporated *in vacuo* and the residue was stirred in methanol (10 ml) overnight. Evapo-

ration of the methanol *in vacuo* left viscous oil which was then chromatographed over silica gel using chloroform–ethyl acetate (3:1) to give 0.266 g (41%) of **5ba**. It was purified by repeated chromatography.

5ba: Colorless solid; mp 248 °C; IR (KBr) 3420 (OH), 1785, 1725, and 1670 cm^{-1} (C=C); ^1H NMR (DMSO-d_6) σ=2.60—3.20 (4H, m, 9-CH_2, 3a-, and 9a-H), 2.88 (3H, s, NMe), 3.00 (3H, s, OMe), 3.80 (6H, s, COOMe), 5.23 (1H, d, J_{4-3a}=3.0 Hz, 4-H), 7.28 (1H, s, 6-H), and 8.24 (1H, s, OH); ^{13}C-NMR (DMSO-d_6) δ=24.32, 36.84, 44.98, 52.34, 52.58, 55.85, 68.90 (d, 4-C), 114.32 (d, 6-C), 124.46 (s), 129.72 (s), 136.73 (s), 155.74 (s, 5-C), 165.78, 168.02 (each s, COOMe), 176.01 and 179.18 (each s, 1- and 3-CO); MS *m/z* 377 (M^+), 346 (M^+−31), and 228 (base peak).

Found: C, 57.01; H, 4.92; N, 3.81%; M^+, 377. Calcd for $C_{18}H_{19}NO_8$: C, 57.29; H, 5.07; N, 3.71%; M, 377.

Cycloaddition of 1 to 3b and then 4b Leading to 5bb. A solution of fresh **1** (0.521 g, 1.8 mmol) and **3b** (0.202 g, 1.8 mmol) in dry benzene (3 ml) was stirred at room temperature under nitrogen for 24 h. To this solution was added **4b** (0.426 g, 1.8 mmol) and the mixture was refluxed under nitrogen for 36 h. All the volatile materials were removed off *in vacuo* and the residue was stirred in methanol (10 ml) at room temperature overnight. The methanol was completely evaporated *in vacuo* to afford viscous oil which was chromatographed over silica gel with chloroform–ethyl acetate (4:1). Analytical sample of **5bb** (0.402 g, 47%) was obtained by repeated chromatography.

5bb: Colorless solid; mp 160—162 °C; IR (KBr) 3400 (OH), 1775, and 1705—1650 cm^{-1} (C=O); ^1H-NMR (DMSO-d_6) δ=2.64—3.40 (4H, m, 9-CH_2, 3a-, and 9a-H), 2.84 (3H, s, NMe), 3.10 (3H, s, OMe), 5.34 (1H, d, J_{4-3a}=3.5 Hz, 4-H), 7.00 (1H, s, 6-H), 7.32—7.80 (10H, m, ArH), and 10.58 (1H, s, OH); ^{13}C-NMR (DMSO-d_6) δ=24.31 (q, NMe), 24.83 (t, 9-C), 36.99, 45.09 (each d, 3a- and 9a-C), 55.95 (q, OMe), 69.04 (d, 4-C), 115.43 (d, 6-C), 124.82 (s), 128.16 (d), 128.40 (d), 128.63 (s), 129.57 (s), 130.28 (d), 136.33 (d), 137.27 (s), 137.91(s), 138.79 (s), 155.05 (s, 5-C), 176.01, 179.06 (each s, 1- and 3-CO), 195.27, and 196.56 (each s, COPh); MS *m/z* 469 (M^+), 437 (M^+−32), and 105 (base peak).

Found: C, 71.45; H, 4.89; N, 3.04%; M^+, 469. Calcd for $C_{28}H_{23}NO_6$: C, 71.63; H, 4.94; N, 2.98%; M, 469.

Cycloaddition of 1 to 3c and then 4a Leading to 6ca and 7ca. A solution of freshly distilled **1** (0.579 g, 2.0 mmol) and **3c** (0.18 g, 1.8 mmol) in dry benzene (2 ml) was stirred at room temperature under nitrogen for 2 h. To this solution was added **4a** (0.391 g, 2.8 mmol) and the mixture was heated under reflux for 24 h. After all the volatile materials were evaporated *in vacuo*, the residue was refluxed in methanol (50 ml) in the presence of *p*-toluenesulfonic acid (0.1 g) for 24 h. The residue obtained after evaporation of the methanol *in vacuo* was dissolved in chloroform (30 ml), the chloroform solution was washed with 5% aqueous sodium hydrogen carbonate, dried over magnesium sulfate, and evaporated *in vacuo* to give viscous oil which was found to contain **6ca** and **7ca** in a ratio of 2:3 by ^1H-NMR spectroscopy. The oil was separated into **6ca** (0.1 g, 13%) and **7ca** (0.146 g, 19%) by column chromatography over silica gel using chloroform–ethyl acetate (4:1).

6ca: Colorless solid from chromatography; mp 129—130 °C; IR (KBr) 3280 (OH) and 1720 cm^{-1} (C=O); ^1H-MNR ($CDCl_3$) δ=2.85—3.92 (4H, m, 4-CH_2, 2-, and 3-H), 3.64 (3H, s, OMe), 3.67, 3.72, 3.83, 3.87 (each 3H, s, COOMe), 4.90 (1H, d, J_{1-2}=6.0 Hz, 1-H), 7.23 (1H, s, 7-H), and 8,78 (1H, s, OH); ^{13}C-NMR ($CDCl_3$) δ=25.48, 39.45, 41.68, 51.96, 52.43, 56.95, 79.43, 116.36, 122.76, 126.40, 129.22, 134.33, 157.46, 165.91, 169.43, 169.61, and 172.20; Ms *m/z* 410 (M^+), 378 (M^+−32), and 287 (base peak).

Found: C, 55.33; H, 5.37%; M^+, 410. Calcd for $C_{19}H_{22}O_{10}$: C, 55.61; H, 5.40%; M, 410.

7ca: Colorless leaflets from aqueous methanol; mp 173—174 °C; IR (KBr) 3410 (OH) and 1720 cm-$^{-1}$ C=O)); ^1H-NMR ($CDCl_3$) δ=2.90—3.96 (4H, m, 4-CH_2, 2-, and 3-H), 3.48 (3H, s, OMe), 3.60, 3.74, 3.80, 3.88 (each 3H, s, COOMe), 5.08 (1H, d, J_{1-2}=3.0 Hz, 1-H), 7.19 (1H, s, 7-H), and 7.53 (1H, br. s, OH); ^{13}C-NMR ($CDCl_3$) δ=25.07 (t, 4-C), 36.34, 43.03 (each d, 2- and 3-C), 52.25, 52.60 (each q, COOMe), 72.21 (d, 1-C), 114.49 (d, 7-C), 125.17 (s), 126.99 (s), 129.34 (s), 134.92 (s), 156.41 (s, 8-C), 166.15, 169.43, 170.84, and 173.55 (each s, COOMe); MS *m/z* 410 (M^+), 378 (M^+−32), and 287 (base peak).

Found: C, 55.82 H, 5.40%; M^+, 410. Calcd for $C_{19}H_{22}O_{10}$: C, 55.61; H, 5.40%; M, 410.

Methanol Elimination of 7ca into 8ca. When **7ca** (0.14 g, 0.34 mmol) was heated under reflux in toluene (10 ml) for 48 h and then cooled to room temperature, colorless solid of **8ca** (0.088 g, 68%) was precipitated. It was washed with ether to give pure sample of **8ca**.

8ca: Colorless solid; mp 222—224 °C; IR (KBr) 3460 (OH) and 1710 cm^{-1} (C=O); ^1H-NMR ($CDCl_3$+DMSO-d_6) δ=2.90 (1H, dd, J_{gem}=16.8 and J_{vic}=8.0 Hz, one of CH_2), 3.28 (1H, dd, J_{gem}=16.8 and J_{vic}=3.5 Hz, the other of CH_2), 3.60—3.90 (1H, m, CHCOOMe), 3.56, 3.79, 3.82 (each 3H, s, COOMe), 7.25 (1H, s, ArH), and 7.90 (1H, s, =CH); ^{13}C-NMR ($CDCl_3$+DMSO-d_6) δ=28.06 (t, CH_6), 37.28 (q, OMe), 51.84, 51.96, 52.13, 52.43 (each q, COOMe), 115.01 (d), 122.12 (s), 124.35 (s), 126.87 (s), 130.46 (s), 130.57 (s), 133.74 (s), 155.74 (s), 165.62, 165.91, 167.97, and 171.73 (each s, COOMe); MS *m/z* 378 (M^+).

Found: C, 57.26; H, 4.82%; M^+, 378. Calcd for $C_{18}H_{18}O_9$: C, 57.14; H, 4.80%; M, 378.

Cycloaddition of 1 to 3c and then 4b Leading to G (R=E=COPh), 7cb, and 8cb. A solution of fresh **1** (0.545 g, 1.9 mmol) and **3c** (0.187 g, 1.9 mmol) in dry benzene (2 ml) was stirred at room temperature under nitrogen for 2 h. After **4b** (0.446 g, 1.9 mmol) was added, the resultant mixture was continued to stir at the same temperature under nitrogen for additional 24 h. All the volatile materials were evaporated *in vacuo* and the residue was treated with methanol (10 ml) to precipitate 0.274 g (27%) of **G** (R=E=COPh). It was collected on a filter and washed with a small amount of methanol (20 ml). To the filtrate was added 80 ml of methanol and this solution was refluxed in the presence of *p*-toluenesulfonic acid (0.1 g) for 24 h. The same work-up as mentioned above gave viscous oil which was chromatographed over silica gel using chloroform–ethyl acetate (4:1) to afford a mixture of **7cb** and **8cb** (0.102 g, 11%, 1:1). Repeated chromatography gave pure **8cb**, but **7cb** was always contaminated with a trace of **8cb**.

G (R=E=COPh): Colorless solid; mp 199—200 °C; IR (KBr) 1860, 1780, 1650 (C=O), 1250, and 845 cm^{-1} (TMS); ^1H-NMR ($CDCl_3$) δ=0.32 (9H, s, TMS), 2.90—3.36 (4H, m, 9-CH_2, 3a-, and 9a-H), 3.20 (3H, s, OMe), 5.38 (1H, d, J_{4-3a}=3.2 Hz, 4-H), 6.93 (1H, s, 6-H), and 7.24—7.72 (10H, m, ArH); MS *m/z* 528 (M^+), 429 (base peak), and 105.

Found: C, 68.24; H, 5.36%; M^+, 528. Calcd for $C_{30}H_{28}O_7Si$: C, 68.16; H, 5.34%; M, 528.

7cb: Colorless solid; IR (KBr) 3200 (OH), 1730, 1710, and 1640 cm^{-1} (C=O); ^1H-NMR ($CDCl_3$+DMSO-d_6) δ=2.60—3.80 (4H, m, 4-CH_2, 2-, and 3-H), 3.56 (6H, s, COOMe), 3.67 (3H, s, OMe), 5.10 (1H, d, J_{1-2}=3.0 Hz, 1-H), 6.96 (1H, s, 7-H), and 9.80 (1H, br. s, OH); MS *m/z* 470 (M^+), 411 (M^+−59, base peak), 105, and 77.

8cb: Colorless solid; mp 142—145 °C; IR (KBr) 3100 (OH), 1705, and 1640 cm^{-1} (C=O); ^1H-NMR ($CDCl_3$+DMSO-d_6) δ=2.82 (1H, dd, J_{gem}=17.0 and J_{vic}=7.5 Hz, one of CH_2), 3.06 (1H, dd, J_{gem}=17.0 and J_{vic}=3.3 Hz, the other of CH_2), 3.67—3.90 (1H, m, CH), 3.41, 3.78 (each 3H,

s, COOMe), 7.00 (1H, s, ArH), 7.20—7.72 (10H, m, ArH), and 7.99 (1H, s, =CH); MS *m/z* 470 (M^+), 411 (M^+−59, base peak), and 105.

Found: C, 70.94; H, 4.79%; M^+, 470. Calcd for $C_{28}H_{22}O_7$: C, 71.48; H, 4.71%; M, 470.

Methanol elimination of **7cb** into **8cb** was achieved as follows: The comound **7cb** (0.125 g, 0.25 mmol) was heated under reflux in toluene for 24 h. Colorless solid which was precipitated on cooling was collected on a filter and washed with ether to give pure **8cb** (0.096 g, 0.204 mmol, 82%).

Cycloaddition of 1 to 3c and then 4c Leading to 8cc. Triene **1** (0.845 g, 2.9 mmol) was treated with **3c** (0.289 g, 2.9 mmol) and then **4c** (0.496 g, 5.8 mmol) in dry benzene (3 ml) under the conditions shown in Table 1. The benzene was removed off *in vacuo*, the residue was refluxed in methanol (50 ml) in the presence of *p*-toluenesulfonic acid (0.1 g), and the methanol was evaporated *in vacuo*. The residue was treated in the usual way as mentioned above and chromatographed over silica gel using chloroform–ethyl acetate (5:1) to give 0.14 g (15%) of **8cc**. It was purified by repeated column chromatography.

8cc: Colorless solid; mp 182—183 °C, IR (KBr) 3340 (OH), 1720, 1700, and 1675 cm^{-1} (C=O); ^{1}H-NMR (DMSO-d_6) δ= 2.92—4.20 (3H, m, CH_2 and CH), 3.50, 3.73, 3.77 (each 3H, s, COOMe), 6.80, 7.70 (each 1H, d, J_{vic}=9.0 Hz, ArH), 7.86 (1H, s, =CH), and 10.92 (1H, s, OH); ^{13}C-NMR (DMSO-d_6) δ=28.06 (t, CH_2), 37.16 (d, CH), 51.67, 51.84, 52.02 (each q, COOMe), 113.60 (d), 119.18 (s), 119.42 (s), 124.64 (s), 131.10 (d), 133.74 (d), 138.67 (s), 158.11 (s), 166.09, 166.32, and 172.49 (each s, COOMe); MS *m/z* 320 (M^+), 261 (M^+−59), and 229 (base peak).

Found: C, 59.85; H, 4.82%; M^+, 320. Calcd for $C_{16}H_{16}O_7$: C, 60.00; H, 5.03; M, 320.

Cycloaddition of 1 to 3c and then 3b Leading to 9. Triene **1** (0.587 g, 2.0 mmol) and **3c** (0.201 g, 2.0 mmol) were stirred in dry benzene (2 ml) at room temperature under nitrogen for 2 h. To this solution was added **3b** (0.228 g, 2.0 mmol) and the mixture was refluxed for 20 h, cooled to room temperature, treated with a few drops of trifluoroacetic acid, and then triturated with hexane. Colorless precipitate of **9** (0.257 g, 38%) was collected on a filter and washed with ether-hexane.

9: Colorless solid; mp 186—188 °C; IR (KBr) 1885, 1780, and 1720—1640 cm^{-1} (C=O); ^{1}H-NMR ($CDCl_3$+DMSO-d_6) δ=2.70—4.10 (8H, m, 4-, 10-CH_2, 3a-, 6a-, 9a-, and 10b-H), 2.95 (3H, s, NMe), 3.07 (3H, s, OMe), and 4.92 (1H, d, J_{6-6a}=3.7 Hz, 6-H); ^{13}C-NMR (DMSO-d_6) δ=24.19, 32.82, 35.29, 36.17, 42.74, 45.62, 55.95 (OMe), 66.93 (6-C), 131.98 (5a-C), 151.53 (10a-C), 169.67, 172.72, 172.84, 176.01 (COO- and CON-), and 190.51 (5-CO); MS *m/z* 333 (M^+), 301 (M^+−32), and 230 (base peak).

This compound **9** was too unstable to provide an analytically pure sample by chromatography or crystallization. No satisfied analytical data were available.

Cycloaddition of 1 to 10a and then 4a Leading to 11aa and 12aa. A solution of freshly distilled **1** (0.877 g, 3.1 mmol) and **10a** (0.81 ml, 9.2 mmol) in dry benzene (3 ml) was heated at 80 °C under nitrogen for 48 h. The solvent and excess of **10a** were all evaporated completely *in vacuo* and the residue was dissolved in another 3 ml of dry benzene containing **4a** (0.435 g, 3.4 mmol). This solution was refluxed for 48 h. The usual work-up with methanol and column chromatography over silica gel with hexane–ethyl acetate (2:1) gave 0.228 g (21%) of **11aa**. Continued elution with the same solvent afforded 0.086 g (8%) of **12aa**.

11aa: Colorless prisms from benzene–hexane; mp 116—116.5 °C; IR (KBr) 3370 (OH) and 1715 cm^{-1} (C=O) ^{1}H-NMR ($CDCl_3$) δ=1.80—2.30, 2.64—2.88 (each 2H, m, 3- and 4-CH_2), 3.08 (1H, ddd, J_{2-3}=4.0, 10.8, and J_{2-1}=9.0 Hz, 2-H), 3.28 (3H, s, OMe), 3.78, 3.87, 3.89 (each 3H, s, COOMe), 5.36 (1H, d, J_{1-2}=9.0 Hz, 1-H), 7.28 (1H, s, 7-H), and 8.21 (1H, s, OH); ^{13}C-NMR ($CDCl_3$) δ=24.07, 25.60 (each t, 3- and 4-C), 42.33 (d, 2-C), 52.31, 52.55 (each q, COOMe and OMe), 75.80 (d, 1-C), 115.48 (d, 7-C), 124.00 (s), 126.46 (s), 129.45 (s), 136.85, 157.28 (s, 8-C), 166.03, 169.49, and 173.55 (each s, COOMe); MS *m/z* 352 (M^+) and 320 (M^+−32).

Found: C, 58.06; H, 5.81%; M^+, 352. Calcd for $C_{17}H_{20}O_8$: C, 57.95; H, 5.72%; M, 352.

12aa: Colorless needles from aqueous acetone; mp 185—186 °C; IR (KBr) 3260 (OH) and 1710 cm^{-1} (C=O); ^{1}H-NMR ($CDCl_3$) δ=1.92—2.24 (2H, m, 3- or 4-CH_2), 2.40—3.04 (3H, m, 3- or 4-CH_2 and 2-H), 3.42 (3H, s, OMe), 3.74, 3.84, 3.87 (each 3H, s, COOMe), 5.04 (1H, d, J_{1-2}=4.5 Hz, 1-H), 7.24 (1H, s, 7-H), and 7.37 (1H, s, OH); ^{13}C-NMR ($CDCl_3$) δ=17.58, 24.98 (each t, 3- and 4-C), 43.47 (d, 2-C), 51.34, 51.99, 52.46, 58.27 (each q, COOMe and OMe), 70.13 (d, 1-C), 112.75 (d, 7-C), 125.26 (s), 127.25 (s), 128.31 (s), 135.94 (s), 156.43 (s, 8-C), 165.65, 168.46, and 172.58 (each s, COOMe); MS *m/z* 352 (M^+) and 320 (M^+−32).

Found: C, 58.07; H, 5.84%; M^+, 352. Calcd for $C_{17}H_{20}O_8$: C, 57.95; H, 5.72%; M, 352.

Cycloaddition of 1 to 10a and then 4b Leading to 11ab and 12ab. Under the same conditions as shown above (see Table 1), triene **1** (1.249 g, 4.4 mmol) was allowed to react with **10a** (1.2 ml, 13.1 mmol) and then **4b** (1.021 g, 4.4 mmol). The crude product was chromatographed over silica gel using hexane–ethyl acetate (1:1) to give 0.295 g (15%) of **11ab** and then 0.415 g (21%) of **12ab**.

11ab: Colorless prisms from dichloromethane–hexane; mp 133—135 °C; IR (KBr) 3300 (OH), 1725, 1655 (C=O), and 1580 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ=1.80—2.20, 2.50—2.74 (each 2H, m, 3- and 4-CH_2), 3.10 (1H, ddd, J_{2-3}=4.0, 10.8, and J_{2-1}=9.0 Hz, 2-H), 3.34 (3H, s, OMe), 3.76 (3H, s, COOMe), 5.44 (1H, d, J_{1-2}=9.0 Hz, 1-H), 6.97 (1H, s, 7-H), 7.20—7.80 (10H, m, ArH), and 8.32 (1H, s, OH); ^{13}C-NMR ($CDCl_3$) δ= 24.25, 26.18 (each t, 3- and 4-C), 42.45 (d, 2-C), 52.25, 52.96 (each q, COOMe and OMe), 75.91 (d, 1-C), 116.25 (d, 7-C), 123.17, 128.11, 128.98, 129.99, 131.86, 132.86, 133.09, 136.68, 137.67, 137.91, 138.56, 156.67 (s, 8-C), 173.61 (s, COOMe), 195.56, and 198.09 (each s, COPh); MS *m/z* 444 (M^+) and 412 (M^+−32).

Found: C, 72.78; H, 5.42%; M^+, 444. Calcd for $C_{27}H_{24}O_6$: C, 72.96; H, 5.44%; M, 444. **12ab**: Colorless prisms from aqueous acetone; mp 194—195.5 °C; IR (KBr) 3440 (OH), 1715, 1655 (C=O), and 1580 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ=1.80—3.04 (5H, m, 3-, 4-CH_2, and 2-H), 3.50 (3H, s, OMe), 3.72 (3H, s, COOMe), 5.07 (1H, d, J_{1-2}=4.5 Hz, 1-H), 6.90 (1H, s, 7-H), and 7.20—7.80 (11H, m, ArH and OH); ^{13}C-NMR (DMSO-d_6) δ=17.79, 25.71 (each t, 3- and 4-C), 43.62 (d, 2-C), 51.31, 58.53 (each q, COOMe and OMe), 70.57 (d, 1-C), 114.19 (d, 7-C), 126.58, 128.52, 129.57, 130.69, 132.92, 136.56, 137.27, 137.67, 155.70 (s, 8-C), 172.61 (s, COOMe), 195.32, and 197.27 (each s, COPh); MS *m/z* 412 (M^+−32).

Found: C, 72.96; H, 5.44%. Calcd for $C_{27}H_{24}O_6$: C, 72.90; H, 5.45%.

Cycloaddition of 1 to 10b and then 4a Leading to 11ba and 12ba. Triene **1** (1.306 g, 4.6 mmol) and **10b** (1.5 ml, 22.8 mmol) were heated at 75 °C in dry benzene (3 ml) under nitrogen for 48 h. All the volatile materials were completely evaporated off *in vacuo* and the residue was allowed to react with **4a** (1.296 g, 9.1 mmol) in benzene (3 ml) under reflux for 48 h. After the reaction mixture was subjected to the usual work-up with methanol, it was chromatographed over silica gel with hexane–ethyl acetate (2:1) to give 0.336 g (23%) of **11ba** and 0.175 g (12%) of **12ba**.

11ba: Colorless prisms from benzene–hexane; mp 163—164 °C; IR (KBr) 3400 (OH), 2240 (CN), and 1700 cm^{-1} (C=O); ^{1}H-NMR ($CDCl_3$) δ=1.80—2.40, 2.70-3.00 (each 2H, m, 3-

and 4-CH_2) 3.24 (1H, ddd, J_{2-3}=4.0, 6.5, and J_{2-1}=5.5 Hz, 2-H), 3.46 (3H, s, OMe), 3.85, 3.88 (each 3H, s, COOMe), 4.91 (1H, d, J_{1-2}=5.5 Hz, 1-H), 7.24 (1H, s, 7-H), and 7.50 (1H, s, OH); ^{13}C-NMR (DMSO-d_6) δ=18.32, 22.37 (each t, 3- and 4-C), 27.01 (d, 2-C), 52.19, 52.60, 57.54 (each q, COOMe and OMe), 70.28 (d, 1-C), 113.13 (d, 7-C), 119.71 (s, CN), 124.70 (s), 124.94 (s), 129.22 (s), 134.86 (s), 157.46 (s, 8-C), 165.73, and 168.26 (each s, COOMe); MS *m/z* 319 (M^+) and 287 (M^+−32).

Found: C, 60.09; H, 5.41; N, 4.65%; M^+, 319. Calcd for $C_{16}H_{17}NO_6$: C, 60.18; H, 5.37; N, 4.39%; M, 319.

12ba: Colorless needles from aqueous acetone; mp 158—159 °C; IR (KBr) 3300 (OH), 2250 (CN), and 1720 cm^{-1} (C=O); ^{1}H-NMR ($CDCl_3$) δ=1.80—3.40 (5H, m, 3-, 4-CH_2, and 2-H), 3.68 (3H, s, OMe), 3.84, 3.87 (each 3H, s, COOMe), 4.82 (1H, d, J_{1-2}=4.5 Hz, 1-H), 7.23 (1H, s, 7-H), and 7.87 (1H, s, OH); ^{13}C-NMR ($CDCl_3$) δ=21.61, 24.01 (each t, 3- and 4-C), 30.24 (d, 2-C), 52.66, 58.18 (each q, COOMe and OMe), 73.45 (d, 1-C), 115.43 (d, 7-C), 118.83 (s, CN), 123.94, 129.57, 134.68, 156.70 (s, 8-C), 165.97, and 169.43 (each s, COOMe); MS *m/z* 319 (M^+) and 287 (M^+−32).

Found: C, 59.90; H, 5.34; N, 4.49%; M^+, 319. Calcd for $C_{16}H_{17}NO_6$: C, 60.18; H, 5.37; N, 4.39%; M, 319.

Cycloaddition of ***1*** *to* ***10b*** *and then* ***4b*** *Leading to* ***11bb*** *and* ***12bb***. The same procedure as described above (see Table 1) starting from **1** (1.13 g, 3.9 mmol), **10b** (1.3 ml, 19.7 mmol), and **4b** (0.924 g, 3.9 mmol) gave 0.458 g (28%) of **11bb** and 0.168 g (10%) of **12bb**. The latter was purified by repeated chromatography.

11bb: Colorless needles from ethyl acetate–hexane; mp 220 °C; IR 3300 (OH), 2240 (CN), 1665, 1645 (C=O), and 1585 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ=1.80—2.36, 2.60—2.80 (each 2H, m, 3- and 4-CH_2), 3.22 (1H, ddd, J_{2-3}=3.5, 8.5, and J_{2-1}=6.5 Hz, 2-H), 3.54 (3H, s, OMe), 5.04 (1H, d, J_{1-2}=6.5 Hz, 1-H), 6.96 (1H, s, 7-H), and 7.20—7.76 (11H, m, ArH and OH) ^{13}C-NMR (DMSO-d_6) δ=18.55, 23.01 (each t, 3- and 4-C), 27.12 (d, 2-C), 57.65 (q, OMe), 70.57 (d, 1-C), 114.54 (d, 7-C), 119.89 (s, CN), 124.05 (s), 128.52 (d), 128.69, 129.69, 130.51 (s), 133.09 (d), 135.39 (s), 136.59 (s), 137.73 (s), 137.85 (s), 156.70 (s, 8-C), 195.32, and 197.09 (each s, COPh); MS *m/z* 411 (M^+), 379 (M^+−32), and 105 (base peak).

Found: C, 75.65; H, 5.12; N, 3.65%; M^+, 411. Calcd for $C_{26}H_{21}NO_4$: C, 75.90; H, 5.14; N, 3.40%; M, 411.

12bb: Colorless solid; mp 186—189 °C; IR (KBr) 3280 (OH); 2240 (CN); 1660, 1635 (C=O), and 1580 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ=1.70—3.00 (4H, m, 3- and 4-CH_2), 3.10—3.40 (1H, m, 2-H), 3.69 (3H, s, MeO), 4.86 (1H, d, J_{1-2}=4.5 Hz, 1-H), 6.90 (1H, s, 7-H), 7.10—7.90 (10H, m, ArH), and 8.28 (1H, s, OH); ^{13}C-NMR ($CDCl_3$+DMSO-d_6) δ=20.02, 24.95 (each t, 3- and 4-C), 30.71 (d, 2-C), 59.42 (q, OMe), 69.10 (d, 1-C), 114.19 (d, 7-C), 120.06 (s, CN), 124.41 (s), 127.58, 127.81, 128.22, 129.22, 130.57, 132.22, 132.45, 134.56, 136.27, 137.32, 137.56, 155.63 (s, 8-C), 195.03, and 197.27 (each s, COPh); MS *m/z* 379 (M^+−32) and 105 (base peak).

Found: C, 75.41; H, 5.18; N, 3.52%. Calcd for $C_{26}H_{21}NO_4$: C, 75.90; H, 5.14; N, 3.40%.

Cycloaddition of ***2*** *to* ***10a*** *and then* ***4a*** *Leading to* ***13*** *and* ***14***. A solution of **2** (0.895 g, 2.7 mmol), **10a** (4.9 ml, 54 mmol), and a catalytic amount of 1,4-benzenediol in dry benzene (10 ml) was refluxed under nitrogen for 5 d. All the volatile materials were completely evaporated *in vacuo* and the residue was dissolved in dry benzene (3 ml) containing **4a** (0.421 g, 3.0 mmol). This solution was refluxed under nitrogen for 48 h and the benzene was evaporated *in vacuo*. The residue was treated with methanol (20 ml) at room temperature overnight and the methanol was removed off. The viscous oil obtained was chromatographed over silica gel. The fraction eluted with hexane–ethyl acetate (4:1) afforded 0.045 g (6%) of **15**. The continued elution with hexane–ethyl acetate (2:1) gave a mixture of **13** and **14** (0.496 g, 46%). Both column chromatography over silica gel and high performance liquid chromatography were not effective for the separation of **13** and **14**.

13+14: Colorless solid (**13**:**14**=2:7, mp 77—83 °C); IR (KBr) 3400 (OH) and 1720 cm^{-1} (C=O); ^{1}H-NMR ($CDCl_3$) δ=1.80—2.20 (2H, m, CH_2), 2.60—3.00 (3H, m, CH_2 and CH), 3.53, 3,62, 3.76, 3.84, 3.92 (9H, each s, COOMe), 4.75 (1H, br. d, 1-H), 6.40 (1H, s, OH), and 6.80-7.32 (5H, m, ArH); MS *m/z* 398 (M^+).

Cycloaddition of ***1*** *to* ***10a*** *and then* ***3b*** *Leading to* ***16***. Triene **1** (0.94 g, 3.3 mmol) and fresh **10a** (0.89 ml, 9.9 mmol) were heated under reflux in dry benzene (3 ml) under nitrogen for 48 h. All the volatile materials were evaporated off *in vacuo* and the residue was then heated together with **3b** (0.401 g, 3.6 mmol) in dry benzene (3 ml) under reflux for 24 h. The usual work-up of the reaction mixture with methanol gave viscous oil of crude product. It was chromatographed over silica gel using hexane–ethyl acetate (4:1) to afford 0.182 g (28%) of **17**. The continued elution with hexane–ethyl acetate (1:1) gave 0.233 g (25%) of **16** (mp 45—55 °C). During the purification of **16** by column chromatography under the same conditions, only one third of the charged amount was recovered and the purity of **16** was not so improved (mp 55—60 °C). Some spectral data of **16** are given below.

16: ^{1}H-NMR ($CDCl_3$) δ=2.40—3.20 (6H, m, CH_2), 3.00 (3H, s, NMe), 3.40—3.92 (2H, m, CH), 3.76 (3H, s, COOMe), and 7.44 (1H, br. s, 6-H); ^{13}C-NMR ($CDCl_3$) δ=20.49, 25.42, 27.24, 33.70, 37.46, 44.68, 51.90, 127.52, 128.93, 130.98, 150.59, 166.97, 173.72, 176.77, and 190.46; MS *m/z* 289 (M^+) and 274 (M^+−15).

Cycloaddition of ***2*** *to* ***10a*** *and then* ***3a*** *Leading to* ***18aa, 19aa, and 20aa***. A solution of **2** (0.895 g, 2.7 mmol), fresh **10a** (4.8 ml, 54 mmol), and 1,4-benzenediol (trace) in dry benzene (10 ml) was refluxed under nitrogen for 5 d. All the volatile materials were evaporated *in vacuo* and the residue was dissolved in another 3 ml of benzene containing **3a** (0.513 g, 3.0 mmol). The resulting solution was again refluxed for 48 h. The mixture was subjected to the usual work-up with methanol and then the column chromatography over silica gel. The fraction eluted with hexane–ethyl acetate (4:1) afforded **21** (0.082 g, 11%, endo:exo=1:5). The continued elution with hexane–ethyl acetate (1:1) gave 0.156 g (13%, 2:3) of a mixture of **18aa** and **20aa**, and then 0.413 g (36%) of **19aa**. The separation of **18aa** and **20aa** was unsuccessful (^{1}H-NMR ($CDCl_3$) δ=1.60—3.92 (9H, m, CH_2 and CH), 3.52 (3×0.4H, s, COOMe of **18aa**), 3.57 (3×0.6H, s, COOMe of **20aa**), 4.52 (1×0.6H, br. s, 6-H of **20aa**), 4.56 (1×0.4H, d, J_{6-7}=6.0 Hz, 6-H of **18aa**), and 6.80—7.60 (10H, m, ArH)).

19aa: Colorless solid from HPLC; mp 80—83 °C; IR (KBr) 1775, 1720, and 1670 cm^{-1} (C=O); ^{1}H-NMR ($CDCl_3$) δ=1.70—3.84 (9H, m, CH_2 and CH), 3.67 (3H, s, COOMe), 4.45 (1H, br. s, 6-H), and 6.88-7.60 (10H, m, ArH); MS *m/z* 429 (M^+, base peak).

Found: M^+, *m/z* 429.1583. Calcd for $C_{26}H_{23}NO_5$: M, 429.1576.

Cycloaddition of ***2*** *to* ***10a*** *and then* ***3b*** *Leading to* ***18ab, 19ab, and 20ab***. Similar procedures using **2** (0.479 g, 1.4 mmol), **10a** (2.6 ml, 28 mmol), and a trace of 1,4-benzenediol in dry benzene (the first reaction: under reflux for 5 d; the second reaction: under reflux for 48 h) gave viscous oil of crude product. It was chromatographed over silica gel using hexane–ethyl acetate as an eluent to afford 0.15 g (38%) of **21** (endo:exo=1:3). The continued elution with hexane–ethyl acetate (1:1) gave a mixture of **18ab**, **19ab**, and **20ab** (0.138 g, 26%, **18ab**:**19ab**:**20ab**=1:4:2). The separation

of these isomers by column chromatography over silica gel was unsuccessful. Pure **18ab** and **19ab** were obtained through HPLC using dichloromethane–ethyl acetate (2:1) as an eluent.

18ab: Colorless solid from HPLC; mp 225—228 °C; IR (KBr) 1775, 1735, 1700, and 1675 cm^{-1} (C=O); ^{1}H-NMR ($CDCl_3$) δ=1.60—2.04 (2H, m, CH_2), 2.10—3.82 (7H, m, CH_2 and CH), 3.00 (3H, s, NMe), 3.52 (3H, s, COOMe), 4.52 (1H, d, J_{6-7}=5.5 Hz, 6-H), and 6.80—7.36 (5H, m, ArH); MS *m/z* 367 (M^+, base peak).

19ab: Colorless plates from ether–hexane; mp 82—85 °C; IR (KBr) 1775 and 1720—1665 cm^{-1} (C=O); ^{1}H-NMR ($CDCl_3$) δ=1.60—3.60 (9H, m, CH_2 and CH), 3.05 (3H, s, NMe), 3.65 (3H, s, COOMe), 4.41 (1H, br. s, 6-H), and 6.84—7.36 (5H, m, ArH), MS *m/z* 367 (M^+).

Found: M^+, *m/z* 367.1413. Calcd for $C_{21}H_{21}NO_5$: M, 367.1418.

Some characteristic signals of crude **20ab** in the ^{1}H-NMR spectrum in $CDCl_3$ are given as follows: δ=3.00 (3H, s, NMe), 3.60 (3H, s, COOMe), and 4.44 (1H, br. s, 6-H).

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3) After the reaction of **1** with **10a** was complete (reflux in dry benzene for 48 h), all the volatile materials were evaporated *in vacuo* and the residue was subjected to ^{1}H-NMR measurement. The spectrum was very clean and showed that only two isomeric mono-cycloadducts were formed in quantitative yields (isomer ratio was 1:2). the major isomer: δ=0.16, 0.22 (each 9H, s, TMS), 3.36 (3H, s, OMe), and 3.66 (3H, s, COOMe); the minor isomer: δ= 0.18, 0.24 (each 9H, s, TMS), 3.36 (3H, s, OMe), and 3.72 (3H, s, COOMe).

4) According to the molecular model inspection, the approach of the second dienophile across the diene part of mono-cycloadduct is sterically hindered, on both sides, when the cycloadduct has a half-chair conformation. On each side, there are each two repulsive axial substituents in this conformation, disturbing the approach of dienophile.

5) A mixture of two Michael adducts of mono-cycloadduct to **4a** was obtained in 22% yield. The Michael addition of enol silyl ethers is known: K. Yamamoto, S. Suzuki, and J. Tsuji, *Chem. Lett.* , **1978**, 649.

6) When the reaction mixture was treated with methanol at this stage, the endo and exo mono-adducts were isolated in 22 and 70% yields, respectively (see Ref. 1).

7) The configuration of the initially formed six-membered rings was determined on the basis of the coupling constants J_{6-7}. The stereochemistry of fused maleimide rings was based on the stereochemical characteristics of diene-transmissive Diels-Alder cycloaddition.

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