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Synthetic Photochemistry. LXIV.1)
Mild Base-Induced *retro*-Benzilic-Acid Rearrangement of Isolated *proto*-Photocycloadducts of Methyl 2,4-Dioxopentanoate to Terpinolene. Facile Synthesis of α-Chamigrene and α-Chamigren-3-one

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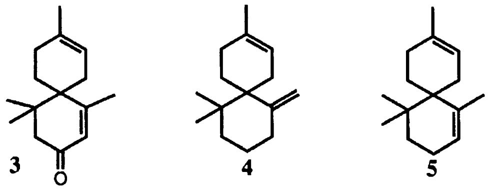
In the photoaddition reaction of terpinolene with methyl 2,4-dioxopentanoate, the products derived from the tetrasubstituted C=C were four *proto*-[2+2] photocycloadducts, together with ene reaction products. When these *proto*-cycloadducts were treated with aqueous sodium carbonate, a facile *retro*-benzilic acid rearrangement to form substituted cyclopentenone derivatives occurred. The product from the other trisubstituted C=C was an ordinary *retro*-aldol product of the [2+2] cycloadduct and an ene reaction product. One of the *proto*-photocycloadducts was transformed into α-chamigren-3-one and further to α-chamigrene.

Photocycloaddition with methyl 2,4-dioxopentanoate (**1**) is useful for regioselectively giving the cycloadducts from di- and trisubstituted alkenes or conjugated olefins.2)

In addition, the recent discovery of the *retro*-benzilic acid rearrangement of the *proto*-photocycloadducts derived from **1** with certain cycloolefins3,4) provides a rare photochemical entry to five-membered carbocycles.

In order to isolate *proto*-photocycloadducts for unambiguous thermal rearrangement, we have carried out studies with **1** and a tetrasubstituted semicyclic olefin, terpinolene (**2**, 1,4(8)-*p*-menthadiene);5) previously, isolation of the *proto*-photocycloadducts derived from **1** with olefins was successful only with certain polysubstituted olefins,3,6,7) while an exclusive *retro*-benzilic acid rearrangement occurred with those from semicyclic olefins.4)

At the same time, those dealdolized photocycloadducts seem to be suitable starting materials for synthesis of chamigrane derivatives. Following the isolations of β-8) and α-chamigrene9) (**4** and **5**), a number of physiologically active halogenated derivatives in this family were isolated from marine organisms,10) and in a view of their biogenetic relationship with thujopsane and related sesquiterpenoids, which easily cause skeletal rearrangements,11,12) a total synthesis of chamigrenes may be of value. Thus, as described herein, we have applied the photocycloaddition reaction with **1** to the synthesis of spirocyclic terpenoids, α-chamigren-3-one (**3**),13) and α-chamigrene (**5**) (Chart 1).



3 α-Chamigren-3-one from *Marchantia polymorpha*

4 β-Chamigrene from *Chamaecyparis taiwanesis*

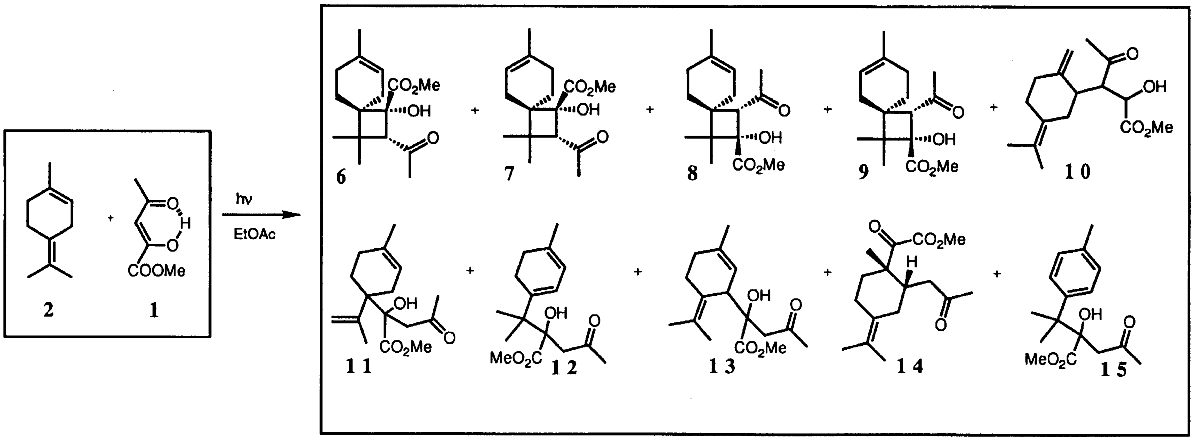
5 α-Chamigrene from *Schizandra chinensis*

Chart 1.

Results and Discussion

Characterization of the Photoproducts. When an ethyl acetate solution of **1** and **2** was internally irradiated by means of a 400-W high-pressure mercury lamp through a Pyrex glass filter for 7 h, a smooth reaction occurred to give four compounds (**6**, 12%, **7**, 8%, **8**, 5%, and **9**, 1%), all colorless oils, which could be immediately identified as the *proto*-[2+2] photocycloadducts from their low-field-shifted singlet signals around $\delta = 3.5$—3.6; the figures are characteristic for methine protons on these types of cyclobutane rings (Scheme 1).14) Additional products isolated after intensive chromatographic fractionation were ene reaction products (**10**, 17%, **11**, 2%, and **12**, 8%), a radical-recombination product (**13**, 4%), a normally-predicted *retro*-aldolized [2+2] cycloadduct (**14**, 7%), and an aromatized derivative (**15**), all colorless oils.

All the *proto*-photocycloadducts were quite stable under work-up conditions, i.e., they survived silica-gel column and high-pressure liquid chromatographic separations, and were isolated, except for the fourth compound (**9**) which was obtained as a 3:1-mixture with **7**. Their ^{1}H NMR spectra showed characteristic signals ascribable to five methyl groups, and the ^{13}C NMR spectra revealed only four sp^2-carbon signals, two of which were acetyl and ester carbonyl carbon signals. Thus, they must be bicyclic. Their regio- and stereoisomerisms were differentiated by nuclear Overhauser effect (NOE) measurements of **6**, **7**, and **8**. Namely, irradiation by the radio frequencies equivalent to the methine proton signals on the conformationally rigid cyclobutane rings of **6**—**8** caused an enhancement of one of the signals ascribable to the *gem*-methyl groups. The irradiation of the *cis*-methyl groups thus identified revealed the stereochemistries of the six-membered ring, as either of the methylene groups adjacent to the spiro carbons revealed an NOE. As a result, the stereochemistries of all of the *proto*-photocycloadducts, in-



Scheme 1.

cluding **9**, were elucidated. The key features of these NOE experiments are shown in Fig. 1.

Upon thermolysis, **6** and **7** gave the same thermolysate (**16**), a pale yellow oil, indicating that they are stereoisomers (Scheme 2). Similarly, **8** and **9** formed the other thermolysate (**17**), a pale yellow oil. Methylation of **16** and **17** gave the respective methyl ethers (**18** and **19**).[15] The ^{1}H NMR spectra of **16**, **17**, **18**, and **19** left no ambiguity in their structures as the *retro*-benzilic acid rearrangement products;[3,4] all four showed low-field shifted acetyl methyl signals (δ=2.42 to 2.49) while **18** and **19** also showed enolic methyl signals (δ=4.06 and 4.02). This constitutes the first verification of *retro*-benzilic acid rearrangement with the isolated *proto*-photocycloadducts. Besides this, the rearrangement occurred upon mild treatment with a base; when the *proto*-products were treated with aqueous carbonate at room temperature, yields of **16** and **17** from the *proto*-photocycloadducts were nearly quantitative. Particularly noteworthy is the absence of ordinary *retro*-aldol products among the products, and it is certain that an exclusive occurrence of the *retro*-benzilic acid rearrangement from these *proto*-photocycloadducts should suggest conformations similar to those of methylenecycloalkanes around the oxygen functions.

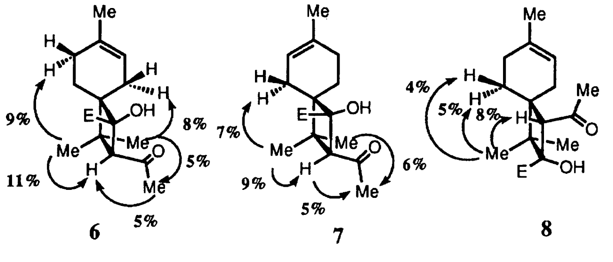
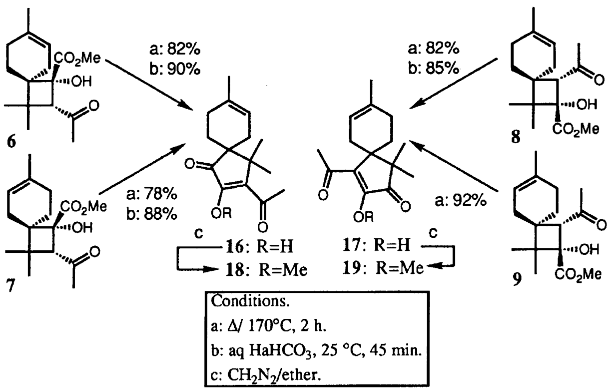


Fig. 1. The NOE measurements and stereochemistries of **6**—**8**.

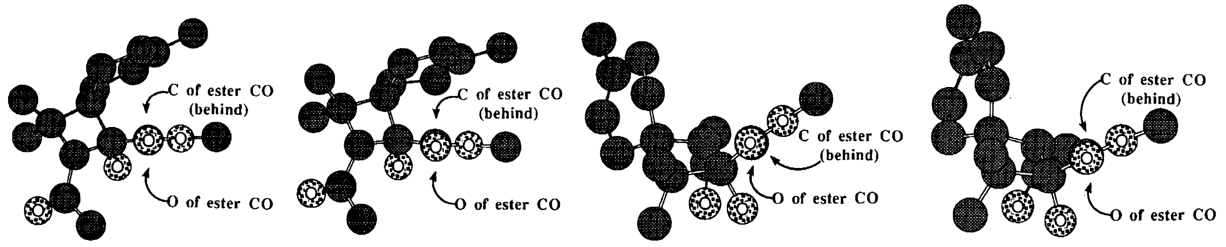


Conditions.
a: Δ/ 170°C, 2 h.
b: aq HaHCO₃, 25 °C, 45 min.
c: CH₂N₂/ether.

Scheme 2.

Since liberation of the bond–angle strain of the four-membered ring should be a driving force of *retro*-benzilic acid rearrangement, either protonation of the ester carbonyl or deprotonation of the tertiary hydroxyl group in the *proto*-cycloadducts should facilitate the rearrangement. However, any acid treatment including Lewis acid treatment has been unsuccessful so far; it always yielded *retro*-aldolized compounds.[16]

As has been mentioned,[3] *retro*-benzilic acid rearrangement is dependent on the conformations of the *proto*-photocycloadducts. According to Chem3D Plus calculations,[17] the most stable conformations of **6** to **9** all revealed disfavored features for normal *retro*-aldol cleavage of the cyclobutanes. The dihedral angles of the ester carbonyls and one of the cyclobutane C–C bonds adjacent to the ester carbons were 88.5° for **6**, 93.3° for **7**, 138.4° for **8**, and 142.3° for **9**; the former two are close to the ideal angle for *retro*-benzilic acid rearrangement, but the latter two show large deviations, 48.5° and 52°, respectively, from the ideal angle, 90°. However, *retro*-benzilic acid rearrangement still occurred exclusively. In **8** and **9**, the dihedral angles of the acetyl carbonyl and the broken C–C bond in the cyclobutane rings, 50.2° (for **9**) and 30.3° (for **8**), were also not appropriate for the *retro*-aldol process. This might suggest a scope for predicting the results from this calculation. Figure 2 provides stereochemical views of the *proto*-photocycloadducts, **6** to **9**, from the direction of the ester carbonyl (oxygen to carbon) axis. One can clearly see that **6** and **7** possess favored geometries for *retro*-benzilic acid rearrangement.



(6) (7) (8) (9)

Fig. 2. Computer-generated stereoviews of photoproducts **6**—**9** (from the direction of ester carbonyls).

The structure of the secondary alcohol produced by an ene process, **10**, was deduced from the ^{1}H and ^{13}C NMR spectra. Two methyl signals at $\delta=1.59$ and 1.71 indicated that the original isopropylidene group was still intact, but a newly generated semicyclic methylene group showed signals at $\delta=4.92$ and 4.95. A double doublet signal at $\delta=4.26$ ($J=7.5$ and 2.2 Hz) was ascribable to the signal for the methine proton on the carbon bearing the ester and alcoholic oxygen functions. The introduction of a drop of deuterium oxide changed the splitting pattern to a doublet ($J=2.2$ Hz). All these data are consistent with the depicted formula.

The structures of **11**, **12**, and **13** all showed an α-hydroxy ester function, but their alcoholic function was tertiary; their ^{1}H NMR spectra showed *AB*-type methylene signals with large *gem*-coupling constants, and the ^{13}C NMR spectra all revealed two carbonyl carbon signals, at $\delta=175.0$ and 208.1 (**11**), 175.1 and 208.4 (**12**), and 176.0 and 208.4 (**13**), and signals ascribable to carbons bearing alcoholic oxygen at $\delta=79.9$ (**11**), 80.3 (**12**), and 87.4 (**13**). Since the ^{1}H NMR spectra revealed the intactness of the original trisubstituted double bond as retaining olefinic methyl signals at ca. $\delta=1.7$—1.8, these products were derived from single C–C bond formation at the tetrasubstituted C=C moiety.

Apart from these common features, **11** showed two proton signals due to a terminal olefin group at $\delta=$ 4.83 and 5.18, and generation of an isopropenyl group was also indicated. Compound **12** showed two methyl singles from an sp^{3}-carbon at $\delta=1.15$ and 1.18, and the appearance of one vinyl proton signal ascribable to the trisubstituted C=C led to the solution of the structure. Since **13** showed two methyl signals from the isopropylidene group at $\delta=1.70$ and 1.76, the newly-formed C–C bond is at the doubly allylic C-3 position of **2**.

The *retro*-aldol product (**14**) was shown by the ^{1}H and ^{13}C NMR spectral evidence to be derived from the reaction at the trisubstituted C=C. In particular, the appearance of five methyl proton singlets, at $\delta=1.38$, 1.59, 1.67, 2.11, and 3.87, and three carbonyl carbon signals, at $\delta=160.1$, 201.6, and 207.4, were quite informative. In addition, the ^{1}H NMR spectrum revealed signals ascribable to two methyl groups on the sp^{2}-carbon indicating that the isopropylidene group was still intact. The presence of the methylene group adjacent to the acetyl group, which was indicated by a large *gem*-coupling in the ^{1}H NMR spectrum, left no ambiguity in the depicted structures.

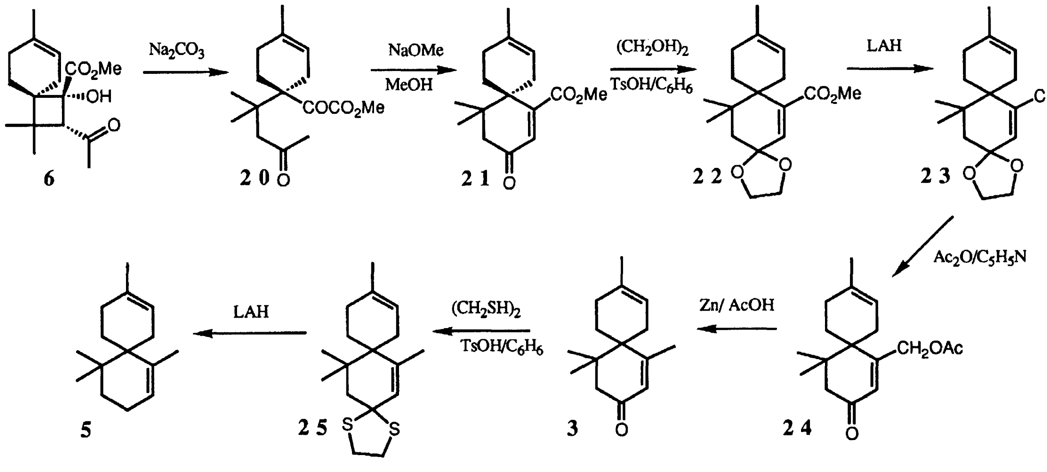
The isolation of an aromatized product (**15**) was attributable to a disproportionation process with the ene reaction product (**12**), as **12** and **15** were detectable from a low stage of conversion, and were not formed during the work-up.

Due to the tetrasubstituted nature of the reaction site, the product distribution was very complicated. However, the material balance was quite good, and despite the sterically hindered substrate, photoadditions of **1** and **2** proceeded smoothly.

Total Synthesis of Chamigrenes. The exclusive formation of either type of compounds from the *proto*-photocycloadducts by a different work-up procedure is remarkable, and a new entry for spirocyclic compounds based on these polysubstituted cyclobutanes prompted us to carry out a synthetic study of chamigrane derivatives. Thus, as target molecules, α-chamigren-3-one (**3**),[13] and α- or β-chamigrenes (**4** or **5**)[8,9] could be derived from the major *proto*-[2+2] photocycloadduct (**6**) or **7**.

Since the above-mentioned experiments demonstrated the easy occurrence of *retro*-benzilic acid rearrangement by a mild acid treatment, **6** was first hydrolyzed with acetic acid to give the expected *retro*-aldol product (**20**); however, its attempted cyclization to a cyclohexenone (**21**) by subsequent treatment with *p*-toluenesulfonic acid in benzene, which has been a preferred method in this type of compounds, was not applicable, since the treatment mainly gave the required **21** in only a 3% yield (Scheme 3). Alternatively, **20** was treated with sodium methoxide in methanol to give **21** in a good yield. Then, **21** was treated with 1,2-ethanediol and *p*-toluenesulfonic acid in benzene to give an acetal (**22**), whose reduction with lithium aluminum hydride (LAH) in ether afforded an unsaturated keto alcohol acetal (**23**). Acid-hydrolysis and acetylation of **23** gave a keto acetate (**24**), whose reduction with zinc in acetic acid quantitatively gave a deoxy derivative, α-chamigren-3-one (**3**).

The structure of the synthetic sample was independently deduced by NMR spectral analysis including NOE experiments. Irradiation of the frequency of ei-



Scheme 3.

ther one of the *gem*-dimethyl singlet signals caused no enhancement of the signal of the β-methyl signal of the unsaturated keto system. However, irradiation with the β-methyl frequency enhanced two olefinic protons at $\delta=5.50$ (3.1%) and 5.87 (8.7%) together with one of the allylic methylene proton signals at ca. 2.34 (5.4%) which further supported the correctness of the structure of **3**. Recently, **3** was isolated from *Marchantia polymorpha*.[13]

Further transformation of **3** into α-chamigrene (**5**) was achieved via dithioacetal formation to a dithiolane (**25**) and desulfurization. The hydrocarbon thus obtained was identical to ($\pm$)-α-chamigrene (**5**); the ^{1}H NMR spectrum of **5** measured in carbon tetrachloride was identical to the data recorded in the original paper.[9] Although **4** and **5** were initially isolated from conifers, *Schizandra chinesis*[9] and *Chamaecyparis taiwanesis*,[8] their halogenated derivatives, some of which are physiologically active, are continuously isolated from many marine organisms.

Conclusion. Finally, the results unambiguously verified that the *proto*-[2+2]cycloadducts are indeed precursors of *retro*-benzilic acid rearrangement products. The present results also extended the utility of **1** for C_5-homologation of monoterpenes to spirocyclic sequiterpenoids having a rearranged carbon framework.

Experimental

The elemental analyses were carried out by Mrs. R. Hatazoe of the Institute of Advanced Material Study, Kyushu University. The NMR spectra were measured with a JEOL GSX 270H Model spectrometer in $CDCl_3$ unless otherwise specified; the chemical shifts are expressed in δ units. The mass spectra were measured with a JEOL 01SG-2 spectrometer. The IR spectra were taken as liquid films inserted between NaCl plates using a JASCO-IR-A 102 spectrometer. The stationary phase for column chromatography was Wakogel C-300 and the eluent was a mixture of ethyl acetate and hexane.

Photochemical Reaction of 1 and 2. An EtOAc solution (30 cm^3) of **1** (1.5 g) and **2** (15 g) was internally irradiated by means of a 400-W high-pressure Hg-lamp through a Pyrex glass filter at 10—20 °C under N_2 atmosphere for 7 h. The mixture was then distilled in vacuo to remove the volatile material, and the residue thus obtained was chromatographed on a silica-gel column to fractionate roughly three parts; the least polar fraction contained **14**, the next fraction contained *proto*-cycloadducts (**6**—**9**), and the most polar fraction contained ene reaction products (**10**—**13**). Further fractionation to isolate each compound was achieved via high-pressure liquid chromatography.

6: A colorless oil, 350 mg, 12%. Found: C, 68.67; H, 8.70%. Calcd for $C_{16}H_{24}O_4$: C, 68.55; H, 8.63%. ^{1}H NMR δ=1.21 (3H, s), 1.24 (3H, s), 1.58 (3H, br s), 1.68—1.82 (3H, m), 2.0 (1H, m), 2.03 (1H, dm, J=18 Hz), 2.11 (3H, s), 2.33 (1H, br d, J=18 Hz), 3.64 (1H, s), 3.73 (3H, s), 5.2 (1H, s, OH), and 5.37 (1H, m). ^{13}C NMR δ=17.3, 20.3, 22.9, 28.6, 29.6, 30.3, 31.6, 45.2, 45.4, 52.0, 52.3, 79.6, 120.7, 133.4, 172.5, and 213.3. MS m/z 280 (M$^+$), 136 (59), 135 (100), 121 (58), 107 (21), 93 (45), 91 (20), 43 (61), 41 (21), and 28 (19). IR ν 3456, 2956, 1734, 1670, 1437, 1370, 1271, 1044, 817, 781, and 764 cm^{-1}.

7: A colorless oil, 233 mg, 8%. Found: C, 68.14; H, 8.41%. m/z 280.1652 (M$^+$). Calcd for $C_{16}H_{24}O_4$: C, 68.55; H, 8.63%; M, 280.1674. ^{1}H NMR δ=1.19 (3H, s), 1.29 (3H, s), 1.45 (1H, m), 1.57 (3H, s), 1.8—2.1 (2H, m), 2.09 (3H, s), 2.1—2.2 (3H, m), 3.55 (1H, s), 3.64 (3H, s), 5.17 (1H, m), and 5.21 (1H, s, OH). ^{13}C NMR δ=21.0, 23.0 (2C), 25.1, 28.8, 29.7, 30.9, 42.3, 47.8, 52.3, 55.0, 79.6, 117.7, 135.7, 173.2, and 211.7. MS m/z 280 (M$^+$, 4), 136 (61), 135 (100), 121 (55), 93 (32), 83 (17), and 43 (24). IR ν 3466, 2954, 1736, 1685, 1437, 1370, 1268, 1204, 1100, 1080, 818, and 710 cm^{-1}.

8: A colorless oil, 146 mg, 5%. Found: C, 68.53; H, 8.19%. Calcd for $C_{16}H_{24}O_4$: C, 68.55; H, 8.63%. ^{1}H NMR δ=1.00 (3H, s), 1.06 (3H, s), 1.60 (3H, dm, J=1.4 Hz), 1.74 (1H, dt, J=13.2, 6.6 Hz), 1.92 (1H, dt, J=13.2, 6.6 Hz), 2.06 (2H, m), 2.14 (3H, s), 2.21 (1H, br d, J=18 Hz), 2.35 (1H, br d, J=18 Hz), 3.65 (1H, s), 3.74 (3H, s), 5.31 (1H, m), and 6.00 (1H, s, OH). ^{13}C NMR δ=21.2, 23.1, 24.8, 25.4, 26.3, 27.9, 31.1, 42.6, 46.7, 52.4, 54.4, 79.4, 119.1, 133.0, 173.3, and 211.8. MS m/z 280 (M$^+$, 1), 136 (60), 135 (100), 121 (40), 107 (20), 93 (34), and 43 (34). IR ν 3508, 2954, 1723, 1682, 1436, 1268, 1101, 1080, 918, and 701 cm^{-1}.

9: A colorless oil, 47 mg, 1%. ^{1}H NMR δ=0.94 (3H, s), 1.10 (3H, s), 1.60 (3H, br s), 1.7—1.8 (2H, m), 2.17 (3H, s), 2.27 (2H, m), 3.57 (1H, s), 3.73 (3H, s), 5.38 (1H, m), and 6.15 (1H, s, OH). ^{13}C NMR δ=16.8, 20.9, 21.4, 26.9, 28.8, 30.9, 31.8, 34.0, 45.5, 52.0, 53.0, 79.9, 119.2, 134.5, 172.4, and 214.1.

10: A colorless oil, 496 mg, 17%. Found: C, 68.18; H, 8.78%; *m/z* 280.1672 (M$^+$). Calcd for $C_{16}H_{24}O_4$: C, 68.55; H, 8.63%; M, 280.1674. ^{1}H NMR δ=1.59 (3H, s), 1.5—1.7 (2H, m), 1.71 (3H, s), 2.07 (1H, dm, J=13.5 Hz), 2.17 (3H, s), 2.25 (1H, m), 2.47 (1H, dt, J=14.3, 2.3 Hz), 2.73 (1H, dm, J=13.5 Hz), 3.01 (1H, d, J=7.5 Hz, OH), 3.12 (2H, m), 3.79 (3H, s), 4.26 (1H, dd, J=7.5, 2.2 Hz), 4.92 (1H, t, J=2.0 Hz), and 4.95 (1H, dd, J=2.0, 1.0 Hz). ^{13}C NMR δ=20.2, 20.5, 30.9, 32.0_8, 32.1_2, 33.5, 43.1, 52.7, 54.7, 70.5, 111.6, 125.9, 126.4, 147.6, 177.5, and 211.0. MS *m/z* 280 (M$^+$, 1), 135 (36), 134 (100), 119 (16), 91 (15), and 43 (16). IR ν 3480, 2966, 1730, 1727, 1438, 1364, 1217, 1118, 914, 819, and 732 cm^{-1}.

11: A colorless oil, 58 mg, 2%. Found: C, 68.35; H, 8.52%. Calcd for $C_{16}H_{24}O_4$: C, 68.55; H, 8.63%. ^{1}H NMR δ=1.58 (3H, d, J=1.5 Hz), 1.76 (3H, d, J=1.6 Hz), 2.0—2.2 (4H, m), 2.14 (3H, s), 2.47 (2H, br d, J=17 Hz), 2.95 (1H, d, J=17.2 Hz), 3.15 (1H, d, J=17.2 Hz), 3.73 (3H, s), 3.75 (1H, s), 4.83 (1H, m), 5.18 (1H, m), and 5.31 (1H, m). ^{13}C NMR δ=22.5, 23.0, 26.5, 28.1, 29.6, 31.0, 47.4, 47.8, 52.4, 79.8, 116.4, 119.5, 134.0, 144.1, 175.0, and 208.1. MS *m/z* 280 (M$^+$, 1), 135 (100), 107 (13), 93 (13), and 43 (17). IR ν 3494, 2956, 1740, 1730, 1437, 1370, 1265, 1219, 1171, 1110, 962, 903, 810, and 792 cm^{-1}.

12: A colorless oil, 234 mg, 8%. Found: C, 68.24; H, 8.63%. Calcd for $C_{16}H_{24}O_4$: C, 68.55; H, 8.63%. ^{1}H NMR δ=1.15 (3H, s), 1.18 (3H, s), 1.79 (3H, s), 2.00 (2H, m), 2.14 (3H, s), 2.23 (2H, m), 2.82 (1H, d, J=17.2 Hz), 3.14 (1H, d, J=17.2 Hz), 3.71 (3H, s), 3.76 (1H, s), 5.66 (1H, dq, J=5.5, 1.5 Hz), and 5.73 (1H, d, J=5.5 Hz). ^{13}C NMR δ=22.7_1, 22.7_6, 22.8_2, 25.4, 29.1, 30.9, 44.7, 47.7, 52.2, 80.3, 119.4, 121.4, 135.6, 139.4, 175.1, and 208.4. MS *m/z* 280 (M$^+$, 2), 133 (100), 105 (19), 84 (12), and 43 (21). IR ν 3492, 2954, 1735, 1729, 1436, 1268, 1019, 908, 809, and 710 cm^{-1}.

13: A colorless oil, 117 mg, 4%. Found: C, 68.35; H, 8.52%. Calcd for $C_{16}H_{24}O_4$: C, 68.55; H, 8.63%. ^{1}H NMR δ=1.70 (3H, br s), 1.74 (3H, d, J=1.8 Hz), 1.77 (3H, d, J=0.7 Hz), 2.0—2.2 (2H, m), 2.13 (3H, s), 2.36 (1H, m), 2.60 (1H, m), 2.88 (1H, d, J=17.0 Hz), 2.93 (1H, d, J=17.0 Hz), 3.42 (1H, s), 3.63 (1H, s, OH), 3.80 (3H, s), and 5.08 (1H, br s). ^{13}C NMR δ=20.2, 21.7, 23.7, 24.6, 31.0, 32.0, 45.4, 49.5, 52.7, 78.4, 118.4, 126.5, 128.0, 140.0, 176.0, and 207.4. MS *m/z* 280 (M$^+$, 5), 160 (13), 146 (29), 135 (100), 93 (71), and 43 (81). IR ν 3448, 2924, 1734, 1718, 1439, 1240, 1169, 1122, 1080, 826, and 808 cm^{-1}.

14: A colorless oil, 205 mg, 7%. Found: C, 68.14; H, 8.35%; *m/z* 280.1660 (M$^+$). Calcd for $C_{16}H_{24}O_4$: C, 68.55; H, 8.63%; M, 280.1674. ^{1}H NMR δ=1.38 (3H, s), 1.59 (3H, s), 1.67 (3H, s), 2.11 (3H, s), 1.48 (1H, dddd, J=13.8, 6.9, 4.3, 0.9 Hz), 1.91 (1H, ddd, J=13.8, 9.9, 4.5 Hz), 2.1—2.35 (5H, m), 2.44 (1H, m), 2.59 (1H, dd, J=17.6, 9.9 Hz), and 3.83 (3H, s). ^{13}C NMR δ=20.0, 21.6, 25.2, 29.7, 30.3, 31.7 (2C), 38.2, 44.2, 49.1, 52.4, 124.2, 127.1, 164.1, 201.6, and 207.4. MS *m/z* 280 (M$^+$, 2), 194 (7), 135 (100), 93 (19), 43 (39), and 41 (14). IR ν 3444, 2956, 1713, 1725, 1732, 1436, 1370, 1280, 1167, 1027, 964, 802, and 780 cm^{-1}.

15: A colorless oil, 145 mg, 5%. Found: C, 68.67; H, 8.20%. Calcd for $C_{16}H_{22}O_4$: C, 69.04; H, 7.98%. ^{1}H NMR δ=1.43 (3H, s), 1.45 (3H, s), 2.09 (3H, s), 2.32 (3H, s), 2.65 (1H, d, J=17.2 Hz), 3.16 (1H, d, J=17.2 Hz), 3.62 (3H, s), 3.75 (OH), 7.11 (2H, d, J=8 Hz), and 7.29 (2H, d, J=8 Hz). ^{13}C NMR δ=20.9, 24.1, 24.4, 30.8, 43.7, 47.7, 52.2, 79.9, 127.7 (2C), 128.3 (2C), 136.1, 141.4, 174.8, and 208.1. MS *m/z* 278 (M$^+$, 1), 133 (100), 105 (18), 93 (7), 43 (13), and 28 (25). IR ν 3486, 2924, 1725, 1705, 1437, 1364, 1262, 1219, 1168, 1100, 1010, 809, 801, and 710 cm^{-1}.

Thermolysis of 6. Formation of 16. A *p*-cymene solution (6 cm^3) of **6** (30 mg) was refluxed for 2 h. The mixture was then chromatographed on a silica-gel column to give **16** [a pale yellow oil, 18 mg, 65%. Found: C, 72.11; H, 8.12%. Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12%. ^{1}H NMR δ=1.21 (3H, s), 1.28 (3H, s), 1.63—1.85 (2H, m), 1.69 (3H, br s), 1.95 (2H, m), 2.04 (2H, m), 2.49 (3H, s), and 5.42 (1H, m). ^{13}C NMR δ=22.4, 23.2, 26.8, 27.7, 28.3, 28.4, 30.9, 43.5, 53.0, 118.6, 133.7, 135.0, 157.5, 200.5, and 207.3. MS *m/z* 248 (M$^+$, 8), 226 (100), 135 (32), 123 (12), 107 (29), 77 (56), and 59(36). IR ν 3494, 2954, 1723, 1660, 1424, 1365, 1280, 1222, 982, 819, and 718 cm^{-1}].

Thermolysis of 7 to 16. Similarly, a *p*-cymene solution (3 cm^3) of **7** (15 mg) was refluxed for 2 h. The mixture was then chromatographed on a silica-gel column to give **16** (8 mg, 61%).

Methyl Ether of 16. An ether solution of **16** (25.0 mg) was methylated with CH_2N_2 to give **18** [a yellow oil, 21.1 mg, 92%. Found: C, 73.51; H, 8.81%. Calcd for $C_{16}H_{22}O_3$: C, 73.25; H, 8.45%. ^{1}H NMR δ=1.15 (3H, s), 1.19 (3H, s), 1.68 (3H, br s), 1.68—1.85 (2H, m), 1.9—2.02 (4H, m), 2.43 (3H, s), 4.06 (3H, s), and 5.43 (1H, m). ^{13}C NMR δ=21.2, 23.3, 26.0, 27.9, 28.0, 28.5, 32.5, 43.7, 53.4, 58.5, 119.1, 133.1, 144.0, 155.6, 198.5, and 208.3. MS *m/z* 262 (M$^+$, 8), 219 (36), 194 (89), 179 (33), 151 (53) 91 (28), 43 (100), 28 (66). IR ν 2954, 1728, 1668, 1437, 1371, 1266, 1041, 915, 816, and 733 cm^{-1}].

Thermolysis of 8. Formation of 17. A *p*-cymene solution (3 cm^3) of **8** (20 mg) was refluxed for 2 h. The mixture was then chromatographed on a silica-gel column to give **17** [a pale yellow oil, 11 mg, 60%. Found: C, 72.43; H, 8.02%. Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12%. ^{1}H NMR δ=1.13 (3H, s), 1.15 (3H, s), 1.65—1.9 (2H, m), 1.69 (3H, br s), 1.93—2.15 (2H, m), 2.17—2.34 (1H, m), 2.49 (3H, s), 2.58 (1H, dt, J=15.7, 2.6 Hz), 5.38 (1H, m), and 9.41 (1H, OH). ^{13}C NMR δ=20.6, 22.5, 23.4, 28.1 (2C), 31.2, 35.0, 45.4, 51.7, 120.3, 134.0, 138.7, 157.0, 201.2, and 209.7. MS *m/z* 248 (M$^+$, 14), 163 (9), 160 (13), 135 (100), 107 (60), 77 (23), 43 (81), and 26 (11). IR ν 3454, 2924, 1730, 1668, 1372, 1269, 1040, 924, 805, and 733 cm^{-1}].

Methyl Ether of 17. An ether solution of **17** (20.0 mg) was methylated with CH_2N_2 to give **19** [a yellow oil, 17.2 mg, 92%. Found: *m/z* 262.1571 (M$^+$). Calcd for $C_{16}H_{22}O_3$: M, 262.1569. ^{1}H NMR δ=1.06 (3H, s), 1.13 (3H, s), 1.63 (3H, br s), 1.69—1.79 (2H, m), 2.0 (2H, m), 2.09 (1H, br m), 2.42 (3H, s), 2.71 (1H, dm, J=17.7 Hz), 4.02 (3H, s), and 5.33 (1H, m). ^{13}C NMR δ=20.7, 22.3, 23.3, 27.7, 28.0, 32.4, 34.4, 46.0, 52.1, 58.5, 120.3, 133.4, 147.7, 153.5, 200.4, and 209.5. MS *m/z* 262 (M$^+$, 35), 128 (21), 91 (28), 83 (20), 77 (24), 43 (100), and 41 (26). IR ν 2954, 2924, 1728, 1688, 1431, 1372, 1312, 1266, 1208, 1153, 1066, 1042, 915, 808, and 733 cm^{-1}].

Thermolysis and Methylation of a Mixture of 9

and 7. Formation of 19 and 17. A *p*-cymene solution (2 cm^3) of **9** and **7** (3 : 1, 12 mg) was refluxed for 2 h. The mixture was then distilled in vacuo to remove the solvent, and the residue was dissolved in ether and methylated with CH_2N_2. Silica-gel column chromatography of the mixture gave **19** (5.1 mg) and **17** (1.7 mg).

The Base-Treatment of 6. Oily compound **6** (50 mg) was suspended in saturated Na_2CO_3 and kept stirring at room temperature for 45 min. The mixture was then acidified with dil HCl and extracted with EtOAc. The extract was heated in vacuo to remove the solvent. The residue thus obtained was practically pure **16** (40 mg, 90 %).

The Base-Treatment of 7. Oily compound **7** (30 mg) was similarly treated with saturated Na_2CO_3 and kept stirring at room temperature for 45 min. The mixture was then acidified with dil HCl and extracted with EtOAc. The organic extract was distilled in vacuo to furnish practically pure **16** (23.4 mg, 88%).

The Base-Treatment of 8. Oily compound **8** (20 mg) was similarly treated with saturated Na_2CO_3 and kept stirring at room temperature for 45 min. The mixture was then acidified with dil HCl and extracted with EtOAc. The organic extract was then distilled in vacuo to furnish practically pure **17** (15 mg, 85%).

Dealdolization of 6 by Acid Treatment in MeOH. Formation of 20. An MeOH solution (10 cm^3) of **6** (60 mg) and TsOH (5 mg) was stirred at room temperature for 24 h. The mixture was then neutralized with $NaHCO_3$ and extracted with ether. Silica-gel column chromatography of the organic extract gave **20** [a colorless oil, 34 mg, 57%. Found m/z 280.1660 (M^+). Calcd for $C_{16}H_{24}O_4$: M, 280.1674. ^{1}H NMR δ=1.12 (3H, s), 1.14 (3H, s), 1.56 (1H, m), 1.58 (3H, br s), 1.87—2.08 (2H, m), 2.14 (3H, s), 2.16—2.30 (2H, m), 2.54 (1H, d, J=14.7 Hz), 2.56 (1H, d, J=14.7 Hz), 2.70 (1H, dm, J=17.0 Hz), 3.76 (3H, s), and 5.40 (1H, m). ^{13}C NMR δ=22.9 (2C), 23.0, 26.4, 27.5, 28.2, 32.9, 39.2, 49.9, 52.3, 56.1, 120.2, 135.9, 163.9, 201.5, and 208.7. MS m/z 262 (M^+, 3), 181 (53), 135 (100), 122 (24), 121 (79), 93 (25), and 43 (95). IR ν 2964, 1737, 1710, 1517, 1438, 1265, 1151, 1047, and 817 cm^{-1}].

Base-Induced Dehydration of 20. Formation of 21. An MeOH solution (30 cm^3) of **20** (125 mg) was treated with NaOMe (50 mg) at room temperature. After 7 h, the mixture was acidified with dil HCl and heated in vacuo to remove the solvent. The residue thus obtained was chromatographed on a silica-gel column to give **21** [a colorless oil, 89 mg, 76%. Found m/z 262.1571 (M^+). Calcd for $C_{16}H_{22}O_3$: M, 262.1569. ^{1}H NMR δ=1.06, (6H, s), 1.62 (3H, s), 1.85—2.0 (3H, m), 2.15 (1H, d, J=18.3 Hz), 2.1—2.3 (2H, m), 2.46 (1H, dm, J=16.3 Hz), 2.78 (1H, d, J=18.3 Hz), 3.68 (3H, s), 5.29 (1H, m), and 5.97 (1H, s). ^{13}C NMR δ=23.0, 24.0, 24.4, 27.0, 27.9, 40.2, 43.8, 49.0, 52.4, 120.5, 127.9, 134.9, 159.2, 169.9, and 198.6. MS m/z 262 (M^+, 100), 206 (88), 195 (72), 146 (14), 118 (12), 91 (38), and 68 (48). IR ν 2954, 1737, 1691, 1440, 1372, 1277, 1208, and 787 cm^{-1}].

Protection of the Carbonyl Group of 21 by Acetal Formation to 22. An anhydrous benzene solution (30 cm^3) of **21** (40 mg), 1,2-ethanediol (1 cm^3), and TsOH (20 mg) was refluxed for 8 h. The mixture was then washed with aqueous Na_2CO_3 and extracted with ether. The organic extract was chromatographed on an alumina column to give **22** [a colorless oil, 46 mg, 98%. Found m/z 306.1831 (M^+). Calcd for $C_{18}H_{26}O_4$: M, 306.1831. ^{1}H NMR δ=0.94 (3H, s), 1.03 (3H, s), 1.58 (3H, br s), 1.66 (1H, dd, J=11.7, 1.5 Hz), 1.69 (1H, dd, J=11.7, 5.5 Hz), 1.82 (1H, dt, J=4.0, 2.2 Hz), 1.88 (1H, dm, J=4.0 Hz), 2.10 (1H, dm, J=17.0 Hz), 2.29 (1H, d, J=14.7 Hz), 2.38 (1H, dd, J=17.0, 4.4 Hz), 3.60 (3H, s), 3.87—4.01 (4H, m), 5.26 (1H, m), and 5.69 (1H, d, J=1.4 Hz). ^{13}C NMR δ=23.0, 23.8, 27.5, 27.9, 30.4, 37.8, 41.9, 44.6, 51.9, 64.0, 64.6, 104.1, 121.2, 127.6, 134.1, 143.1, and 171.2. MS m/z 306 (M^+, 12), 223 (100), 218 (27), 179 (47), 103 (23), 91 (55), and 79 (24). IR ν 2956, 1725, 1436, 1360, 1238, 1090, 949, 809, and 762 cm^{-1}].

Conversion of 22 to an Unsaturated Keto Acetate (24) via LAH-Reduction and Acid Hydrolysis. To an anhydrous THF solution (5 cm^3) of **23** (45 mg) was added LAH (27 mg) in portions and the mixture was stirred at room temperature for 1 h. The mixture was then treated with EtOAc and washed with aqueous Na_2CO_3 and extracted with ether. The organic extract was chromatographed on an alumina column to give **23** [a yellow oil, 30 mg, 74%. ^{1}H NMR δ=0.94 (3H, s), 0.95 (3H, s), 1.64 (3H, br s), 1.69—1.79 (2H, m), 1.8—2.3 (5H, m), 2.09 (1H, br m), 3.6—4.1 (5H, m), 3.71 (1H, dm, J=17.7 Hz), 5.47 (1H, br s), and 5.70 (1H, m). ^{13}C NMR δ=23.3, 24.0, 25.0, 27.8, 28.4, 29.8, 38.4, 40.8, 45.0, 64.0, 64.5 (2C), 105.0, 121.3, 122.0, 134.2, and 150.3. MS m/z 278 (M^+, 2), 262 (13), 170 (39), 136 (20), 108 (100), and 60 (91). IR ν 3406, 2960, 2350, 1450, 1316, 1046, 949, and 881 cm^{-1}].

Subsequently, to a mixed solution of Ac_2O (1.5 cm^3) and pyridine (4.5 cm^3) was added **23** (30 mg) and the solution was kept at 70 °C for 5 h. The mixture was then evaporated in vacuo, and the residue was washed with aqueous Na_2CO_3 and extracted with ether. The organic extract was chromatographed on a silica-gel column to give **24** [a yellow oil, 26 mg, 87%. Found m/z 276.1723 (M^+). Calcd for $C_{17}H_{24}O_3$: M, 276.1725. ^{1}H NMR δ=0.98 (3H, s), 1.05 (3H, s), 1.69 (3H, br s), 1.76 (2H, m), 2.12 (3H, s), 1.82—2.19 (4H, m), 2.21 (1H, dm, J=17.2 Hz), 2.68 (1H, d, J=17.2 Hz), 4.72 (2H, m), 5.52 (1H, m), and 6.03 (1H, d, J=0.7 Hz). ^{13}C NMR δ=20.9, 23.3, 23.9, 24.7, 27.3, 27.5, 28.1, 40.6, 42.9, 49.0, 64.2, 121.1, 123.5, 134.8, 165.8, 170.2, and 198.4. MS m/z 276 (M^+, 3), 216 (12), 201 (100), 178 (77), 145 (33), 91 (30) and 77 (14). IR ν 2926, 1745, 1671, 1516, 1370, 1107, 1021, 865, and 810 cm^{-1}].

Zn-in-AcOH-Reduction of 24 to α-Chamigren-3-one (3). To an AcOH solution (1 cm^3) of **24** (20 mg) was added Zn powder (60 mg) and the mixture was kept stirring at room temperature for 7.5 h. The mixture was then filtered and the residue was washed with ether. The combined organic solution was fractionated with ether and aq Na_2CO_3, and the organic layer was evaporated in vacuo. The residue was chromatographed on a silica-gel column to give **3** [a yellow oil, 14 mg, 88%. ^{1}H NMR δ=0.95 (3H, s), 1.03 (3H, s), 1.68 (3H, s), 1.74 (1H, d, J=1.1 Hz), 1.75 (1H, d, J=2.2 Hz), 1.88 (1H, dd, J=9.2, 2.2 Hz), 1.95 (1H, d, J=1.5 Hz), 1.98 (3H, d, J=1.5 Hz), 2.02—2.13 (2H, m), 2.23 (1H, dm, J=18.0 Hz), 2.63 (dm, J=18.0 Hz), 5.50 (1H, t, J=1.5 Hz), and 5.87 (1H, s). ^{13}C NMR δ=23.3, 23.9, 24.3, 24.9, 28.0, 28.3, 30.7, 40.5, 43.5, 49.0, 121.6, 127.0, 134.2, 170.5, and 198.8. IR ν 2962, 1660, 1446, 1375, 1169, 977, 944, 912, 870, and 799 cm^{-1}].

Conversion of 3 into a Dithio Acetal (25). An anhydrous benzene solution (50 cm^3) of **3** (150 mg), 1,2-ethanedithiol (37 mg), and BF_3 etherate (4 mg) was refluxed with a Dean–Stark apparatus for azeotropic removal of water for 10 h. The mixture was then treated with aqueous NaOH, and extracted with CH_2Cl_2. Silica-gel column chromatography of the organic extract gave **25** [a yellow oil, 60.0 mg, 99%. Found m/z 294.1475 (M^+). Calcd for $C_{17}H_{26}S_2$: M, 294.1476. ^{1}H NMR δ=0.91 (3H, s), 0.97 (3H, s), 1.6—1.73 (2H, m), 1.64 (3H, d, J=1.5 Hz), 1.69 (3H, d, J=1.1 Hz), 1.88—1.92 (3H, m), 2.10 (1H, dm, J=15.4 Hz), 2.12 (1H, dd, J=115.4, 1.5 Hz), 2.63 (1H, d, J=15.4 Hz), 3.32 (4H, m), 5.45 (1H, dt, J=4.4, 1.5 Hz), and 5.55 (1H, d, J=1.1 Hz). ^{13}C NMR δ=23.4 (2C), 23.9, 25.0, 28.5, 28.7, 30.0, 38.4, 39.0, 40.0, 40.5, 50.6, 63.3, 122.2, 128.2, 134.0, and 140.2. MS m/z 294 (M^+, 47), 233 (100), 198 (21), 165 (26), 133 (25), 91 (38), and 77 (29). IR ν 2922, 1376, 1275, 1024, 849, and 802 cm^{-1}].

Conversion of 25 into 5. An anhydrous $EtNH_2$ solution (5 cm^3) of **25** (40 mg) was reduced with Na (45 mg) at 18 °C for 24 h. After evaporation of $EtNH_2$ and EtOH at room temperature, the residue thus obtained was chromatographed on a silica-gel column to give **5** [a colorless oil, 17.0 mg, 59%. ^{1}H NMR δ=0.83 (3H, s), 0.89 (3H, s), 1.6—1.74 (3H, m), 1.65 (6H, br s), 1.85 (1H, dt, J=18.0, 1.5 Hz), 1.87—2.01 (5H, m), 2.12 (1H, dtd, J=18.0, 4.8, 2.4 Hz), 5.33 (1H, m), and 5.46 (1H, dt, J=4.8, 1.5 Hz). ^{1}H NMR (CCl_4) δ=0.82 (3H, s), 0.89 (3H, s), 1.62 (6H, br s), 1.50—1.78 (3H, m), 1.85—2.05 (6H, m), 2.11 (1H, dm, J=17.6 Hz), 5.26 (1H, m), and 5.39 (1H, m). ^{13}C NMR δ=23.0, 23.3, 23.5 (2C), 25.1, 28.9, 29.1, 30.7, 32.8, 36.0, 40.6, 122.5, 122.8, 133.9, and 140.3. IR ν 2955, 2920, 1659, 856, 831, 811, 764, and 734 cm^{-1}].

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16) It is true that both protic and Lewis acid treatments of the samples which were thought to contain the *proto*-cycloadducts obtained immediately after the low-temperature irradiations facilitated but did not alter the subsequent reactions (unpublished work).

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