Visible Light Initiated Photosensitized Electron Transfer Cyclizations of Aldehydes and Ketones to Tethered α,β-Unsaturated Esters: Stereoselective Synthesis of Optically Pure *C*-Furanosides†

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Photosensitized one-electron reductive activation of aldehydes/ketones tethered with activated olefins leads to efficient cyclization to give diastereoselective cycloalkanols in high yield. The activation is promoted by secondary and dark electron transfer from visible light (405 nm) initiated photosensitized electron transfer generated 9,10-dicyanoanthracene radical anion ($DCA^{\bullet-}$). The $DCA^{\bullet-}$ is produced by electron transfer using either triphenylphosphine (Ph_3P) as sacrificial electron donor (PS-A) or 1,5-dimethoxynaphthalene (DMN) as primary electron donor and ascorbic acid as sacrificial electron donor (PS-B), to light-absorbing DCA. The cyclization is suggested to involve ketyl radical intermediate. High *trans* diastereoselectivity is observed during the formation of cycloalkanols. This cyclization strategy is further extended for the stereoselective synthesis of optically pure *C*-furanoside (**41**), starting from naturally occuring L-tartaric acid. The stereochemistry of **41** is suggested based on the single-crystal X-ray diffraction data.

Introduction

Reductive coupling of aldehydes and ketones to tethered olefins have emerged as an attractive strategy for the construction of bioactive cyclopentanoids,[1] owing to the retention of some useful functionalities during these cyclizations, in contrast to the conventional radical cyclization protocols. Usually, these reactions have been realized by the reductive activation of a carbonyl moiety to ketyl radicals with low-valent metallic species such as zinc,[2] lanthanide salts,[3] tributyl tin hydride,[4] lithium naphthalemide,[5] etc. Cathodic reductions[6] have also shown promise during the coupling of aldehyde−electron deficient olefins or ketone−normal olefin systems. Photoreductive protocol, reported by Cossy *et al.*[7] using 254 nm light and in the presence of cancer suspect HMPA, is also found to be useful. However, these methodologies are either too difficult to adopt in normal synthetic laboratories[6] or involve toxic reagents[2−5] or conditions.[7] In this present era of increased ecological concern and the requirement of a clean technology in chemical syntheses, it is mandatory on the part of organic chemists to find an alternative strategy to effect this chemistry. In this endeavor, we have developed an attractive strategy to realize diastereoselective cyclizations of aldehydes or ketones to tethered olefins by visible light initiated photosensitized one-electron reductive reactions. We disclose herein the details of the strategy and its application for the construction of *C*-furanoside framework.

Results and Discussion

Recently, our group has developed two photosystems[8] useful for initiating one-electron reductive chemistry. One such application of these photosystems has been in the activation of α,β-unsaturated ketones as carbon-centered radical precursors and their stereoselective cyclizations with proximate olefins.[8] The concept has involved the secondary and dark electron transfer from 9,10-dicyanoanthracene radical anion ($DCA^{\bullet-}$) generated through a primary electron transfer processes employing different sacrificial electron donors. Photosystem A (PS-A, Figure 1) employed DCA as visible light harvesting electron acceptor and triphenylphosphine (Ph_3P) as sacrificial electron donor whereas photosystem B (PS-B, Figure 2) utilized DCA as usual electron acceptor, DMN (1,5-dimethoxynaphthalene) as primary electron donor, and ascorbate ion as secondary and sacrificial electron donor. The design of these photosystems is based on the matching thermodynamic criterion required for electron transfer processes.

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† Dedicated to Professor M. S. Wadia on the occasion of his 60th birthday.

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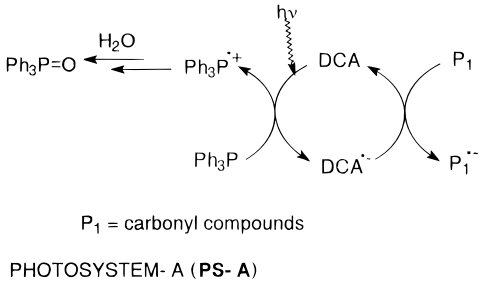


Figure 1.

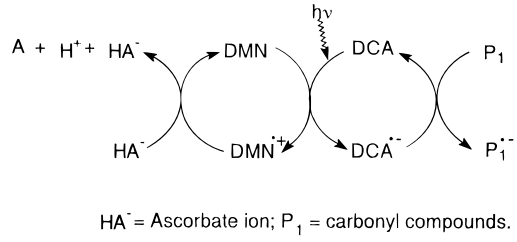
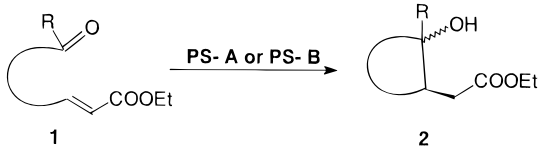
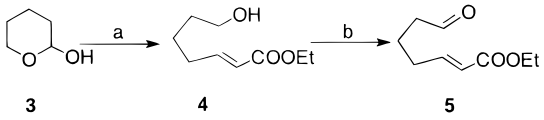


Figure 2.

Scheme 1



Scheme 2[a]

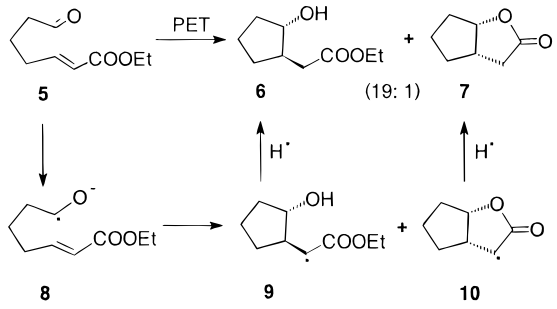


[a] Reagents: (a) $Ph_3P{=}CHCOOEt$, CH_2Cl_2, rt, 2 d, 83%; (b) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, −78 °C, 96%.

The spectacular success of these photosystems in initiating sequential electron transfer processes encouraged[8] us to apply this strategy to realize the reductive cyclization of **1** to produce cyclopentanols of type **2** (Scheme 1). Toward this endeavor, first we evaluated to study the photosensitized electron transfer activation behavior of ethyl 7-oxo-2(*E*)-heptenoate **(5)** employing PS-A as well as PS-B. Compound **5** is easily obtained in 96% yield of Swern oxidation[9] of compound **4**, which in turn is prepared (83%) by the Wittig olefination of 2-hydroxypyran **(3)** with ethyl (triphenylphosphoranylidene)acetate (Scheme 2). The thermodynamic feasibility of electron transfer from $DCA^{\bullet-}$ to **5** is ascertained by estimating negative free energy change ($\Delta G_{et} = -12.45$ kcal/mol) utilizing the equation $\Delta G_{et} = E_{1/2(ox)} - E_{1/2(red)}$. This calculation utilized the literature reported[10] value of −0.89 eV as $E_{1/2(ox)}$ of $DCA^{\bullet-}$ and −0.35 eV as $E_{1/2(red)}$ value of **5**, measured by cyclic voltametry study[11] (for details, see the Experimental Section).

After ascertaining the possibility of electron transfer from $DCA^{\bullet-}$ to **5** through the above photophysical parameter, preparative photosensitized electron transfer activation of **5**, using either PS-A or PS-B, is initiated essentially employing the same reaction conditions as mentioned in our earlier report.[8] Photosensitized electron transfer activation of **5** involved its irradiation in DMF:*i*-PrOH:H_2O (88:10:2) at 405 nm using DCA as light-absorbing electron acceptor and either Ph_3P as sacrificial electron donor (PS-A) or DMN as primary electron donor and ascorbic acid as sacrificial electron donor (PS-B). The irradiation is performed in a specially designed three-chamber photoreactor made of Pyrex glass. The 405 nm light is obtained by using $CuSO_4{\cdot}5H_2O$:NH_3 solution as filter.[12] A 450 W Hanovia medium-pressure lamp is used as light source. Before the irradiation, the reaction mixture is deoxygenated by bubbling argon. After almost quantitative (>98%) conversion (~20 h) of **5** into products, irradiation is discontinued. GC analysis (SP-1000 or methyl silicon capillary column) of the photomixture indicates the formation of two products in the ratio of 19:1. Removal of the solvent followed by column chromatographic (using 100−200 mesh silica gel and petroleum ether:EtOAc as eluent) purification of the photomixture gives **6** in 80% yield. The product **6** is characterized by detailed IR, ^1H NMR, ^{13}C NMR, and mass spectral data which is in agreement with its reported values.[6] The minor product observed in the GC is characterized as **7** by comparing with the authentic sample;[4] however, the same could not be obtained in enough quantity for spectral details. Unchanged DCA and DMN (PS-B) are recovered after the purification. $Ph_3P{=}O$ is formed using PS-A; however, effort is not made to isolate it.

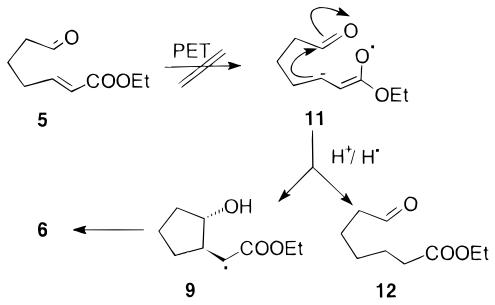
Scheme 3



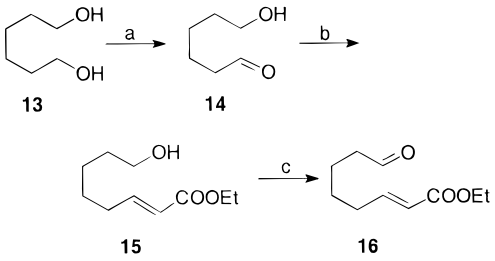
Mechanistically, it is believed that this cyclization involved the activation of **5** to ketyl radical intermediate **(8)** by the transfer of an electron from $DCA^{\bullet-}$. The intermediate **8** upon intramolecular addition to the electron deficient olefin followed by termination of radical intermediates **9** and **10** by H-abstraction, provided by *i*-PrOH (Scheme 3), yields cyclized products **6** and **7**, respectively. The alternate possibility of these cyclizations involving ionic intermediate **11**, by one electron reductive activation of α,β-unsaturated esters, similar to electroreductive cyclizations,[6] could be ruled out since no trace of corresponding olefin reduction product **(12)** is observed as in the case of electroreductions (Scheme 4).[6] Normally, the cyclization stereochemistry of these ketyl radicals have been reported[2−7] to produce mixtures of *trans*- (major) and *cis*- (minor) cyclopentanols in varying ratios. However, in this reaction, high *trans* diastereo-

(9) Mancuso, A. J.; Swern, D. *Synthesis* **1981**, 165.
(10) Mattes, S. L.; Farid, S. *Org. Photochem.* **1983**, *6*, 223.
(11) Since the cyclic voltamogram is irreversible, the reduction potential and ΔG_{et} value are only approximate; however, it agrees generally quite well with experimental result.
(12) Calvert, J. G.; Pitts, J. N. *Photochemistry*; Wiley: New York, 1966; p 736.

Scheme 4

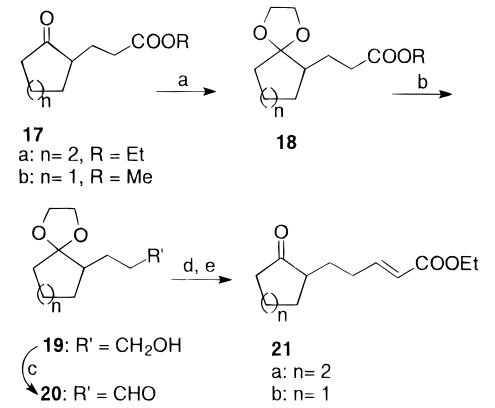


Scheme 5[a]



[a] Reagents: (a) PCC, Celite, CH_2Cl_2, rt, 52%; (b) $Ph_3P{=}CHCOOEt$, CH_2Cl_2, rt, 86%; (c) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, −78 °C, 96%.

Scheme 6[a]



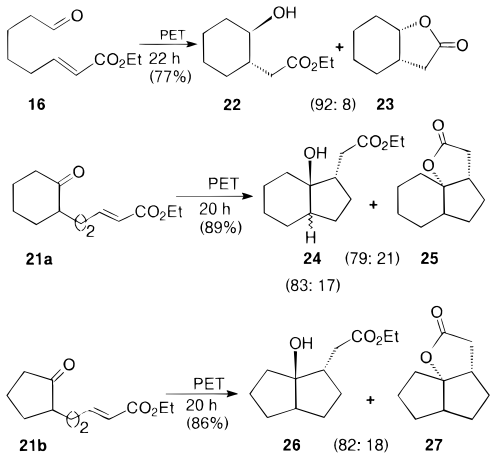
[a] Reagents: (a) $(CH_2OH)_2$, PTSA, C_6H_6, reflux, 82−84%; (b) $LiAlH_4$, THF, reflux, 96%; (c) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, −78 °C, 100%; (d) $Ph_3P{=}CHCOOEt$, CH_2Cl_2, rt, 2 d; (e) PTSA, 5% aqueous MeOH, 80%.

selectivity (>90%) was found to be favored[13] compared to the earlier studies made in organic solvents.[2−7]

To monitor the generality of this cyclization protocol, substrates (**16**, **21a**, and **21b**) are included in our study. Compound **16** is prepared by following the identical reaction sequence as described for compound **5**, starting from 6-hydroxyhexanal **(14)** which is obtained (52%) by partial oxidation of 1,6-hexandiol **(13)** (Scheme 5). Compounds **21a** and **21b** are prepared through the reaction sequences as shown in Scheme 6. Photosensitized electron transfer activation of these compounds, either using PS-A or PB-B (cf. Experimental Section) following identical experimental conditions as mentioned for **5**, produced expected cyclized products (**22**, **24**, and **26**) (Scheme 7) in very good yields (77−89%). The corresponding *cis*-isomers from these substrates are also isolated in their

(13) At this stage we are not sure of the exact mechanistic detail about this observation; however, the effect of aqueous solvent might be pointed out in this regard.

Scheme 7



lactonized forms (**23**, **25**, and **27**). All of the products displayed characteristic spectral data.

The success of photosensitized electron transfer promoted generation of ketyl radicals and their efficient and highly diastereoselective cyclizations with tethered α,β-unsaturated esters encouraged us to extend this methodology for the synthesis of *C*-furanosides. *C*-Furanosides are an important class of compounds as precursor to *C*-nucleosides, possessing antibiotic, anticancer, and antiviral properties,[14] and to many other natural products.[15,16] Generally, these compounds are produced by the intramolecular Michael addition of a hydroxyl group of an intermediate obtained from a carbohydrate precursor to an activated olefins.[17] However, these methods normally produce a mixture of stereoisomers at the "anomeric" carbon center. Similar problems are also encountered in reactions involving radical[18,19] and ionic intermediates.[20] Noyori's[21] and Just's[22] groups have reported the use of non-carbohydrate precursor for the synthesis of optically pure *C*-furanosides, but their strategies involved tedious optical resolution step. In an attempt to overcome these problems, we designed an alternative strategy of constructing *C*-furanoside by the intramolecular addition of photosensitized electron transfer generated ketyl radical derived from **38** to β-alkoxy-

(14) Reviews: (a) Suhadolink, R. J. *Nucleoside Antibiotics*; Wiley-Interscience: New York, 1970; p 354. (b) Daves, G. D., Jr.; Cheng, C. C. *Progr. Med. Chem.* **1976**, *13*, 303. (c) Hanessian, S.; Pernet, A. G. *Adv. Carbohydr. Chem. Biochem.* **1976**, *33*, 111.

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(20) (a) Inuoe, T.; Kuwajima, I. *J. Chem. Soc., Chem. Commun.* **1980**, 251. (b) Stewart, A. O.; Williams, R. M. *J. Am. Chem. Soc.* **1985**, *107*, 4289.

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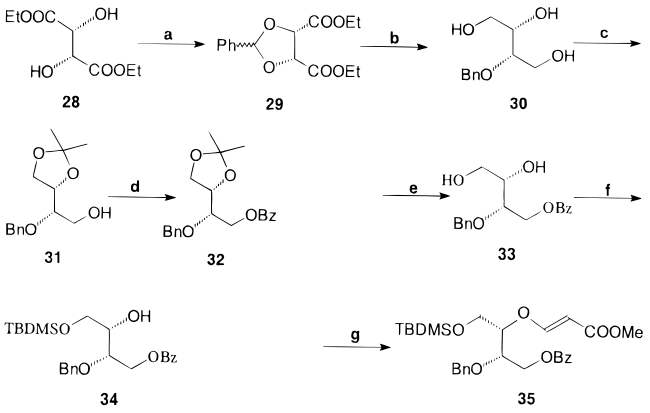
(22) Just, G.; Liak, T. J.; Lim, M.; Potvin, P.; Tsantrizos, Y. S. *Can. J. Chem.* **1980**, *58*, 2024.

Scheme 8[a]

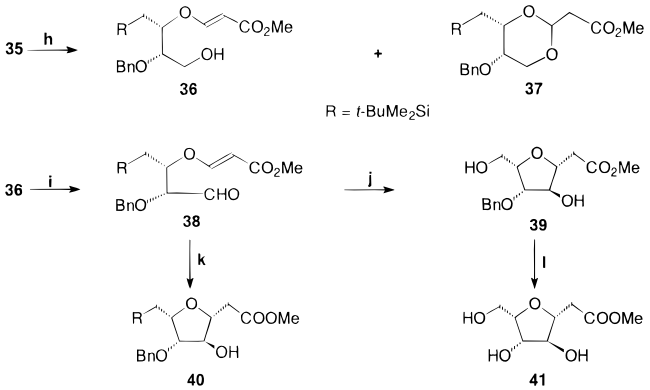


[a] Reagents: (a) PhCHO, PTSA, C_6H_6, reflux (55%); (b) $LiAlH_4$, $AlCl_3$, Et_2O: CH_2Cl_2 (1:1, v/v), reflux (89%); (c) $(MeO)_2CMe_2$, PTSA, CH_2Cl_2, reflux (70%); (d) PhCOCl, Py, CH_2Cl_2 (95%); (e) PTSA, 5% aqueous MeOH (85%); (f) TBDMSCl, ImH, CH_2Cl_2 (95%); (g) HC: CCOOMe, NMM, CH_2Cl_2 (91%).

acrylate moiety, an excellent radical acceptor,[23] obtained from the naturally occurring L-tartaric acid.

Diethyl L-tartarate (**28**) is converted into corresponding benzaldehyde acetal (**29**, 55%) by refluxing with benzaldehyde in C_6H_6 using *p*-toluenesulfonic acid (PTSA) as catalyst (Scheme 8). **29** is reduced by mixed hydride reagent (lithium aluminum hydride−anhydrous aluminum chloride) to afford 2-*O*-benzyl-L-threitol[24] (**30**). An earlier report[24] described the formation of this compound only in 45% yield; however, a little modification during the working up of the reaction mixture (for details, see the Experimental Section) enhanced the yield of **30** to 89%. Heating (7 h) of a mixture of **30** and 2,2-dimethoxypropane in CH_2Cl_2 in the presence of 4A° molecular sieves produced **31** in 70% yield. Benzoyl protection of the hydroxyl group of **31** gave **32** (95%) as a thick liquid. Deprotection of acetonide group from **32**, using PTSA in aqueous MeOH at rt, yielded white fluffy crystals of diol **33** in 86% yield. Selective protection of primary hydroxyl group of **33** as *tert*-butyldimethylsilyl ether (**34**) is obtained (95%) by stirring a mixture of **33** and *tert*-butyldimethylsilyl chloride in CH_2Cl_2 at rt in the presence of imidazole. Compound **34** is converted into **35** in 91% yield by the Michael reaction[25] of **34** with methyl propiolate in the presence of *N*-methylmorpholine in CH_2Cl_2. Our attempt to debenzoylate **35** by stirring with K_2CO_3−MeOH, however, gave an unidentified mixture of products. Milder hydrolysis[26] such as by stirring **35** in Et_3N:MeOH:H_2O (1:5:1) at 0 °C for 42 h gave **36** (52%) as a viscous liquid. A small amount (12%) of **37** is also obtained in this reaction as a colorless oil (Scheme 9). Careful (cf. Experimental Section) Swern oxidation of **36** yielded precursor aldehyde **38**, which is pure enough to proceed to the next step. Photosensitized electron transfer activation of **38**, using either **PS-A** or **PS-B**, led to the cyclized product **39**[27] in 25% yield along with an uncharacterized mixture of products. The low yield of **39** in this reaction is quite surprising to us. To verify

Scheme 9[a]



[a] Reagents: (h) Et_3N:MeOH:H_2O (1:5:1), 0 °C, 42 h (52% for **36** and 12% for **37**); (i) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, −78 °C (100%); (j) PS-A or PS-B (25%); (k) Bu_3SnH, AIBN, C_6H_6, reflux (40%); (l) Pd/C, H_2 (45 psi), MeOH, (95%).

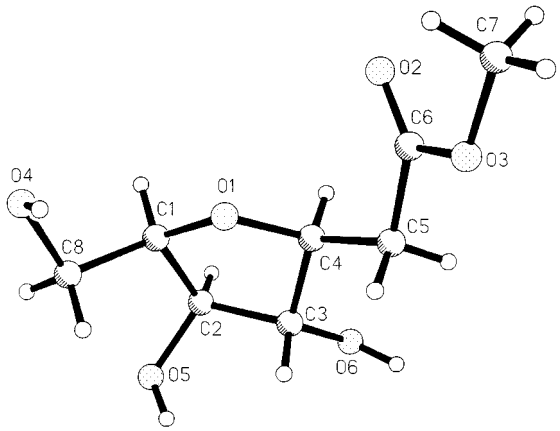


Figure 3. ORTEP diagram of compound **41**.

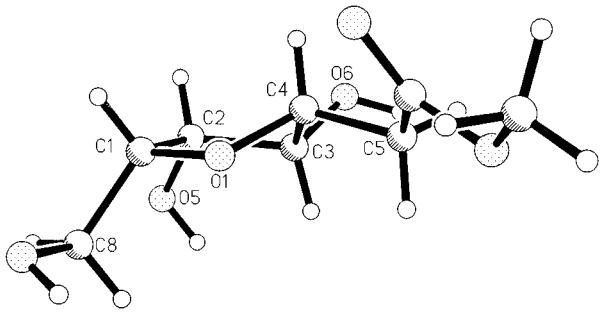


Figure 4. ORTEP diagram of compound **41**.

the cyclization behavior of ketyl radical intermediate obtained from **38**, its alternative generation using Bu_3SnH[23] is also studied. The reaction of **38** with Bu_3SnH in refluxing C_6H_6 did not improve the cyclization yield of **40** to any great extent (~40%). This may be attributed to other possible competing reaction pathways available from the ketyl radical intermediate. Debenzylation of **39** by hydrogenation using Pd/C as catalyst gave **41** (95%). Compound **41** has been characterized by detailed ^1H NMR, ^{13}C NMR, mass, and IR spectroscopy. The stereochemistry of the compound **41** is confirmed by single-crystal X-ray diffraction data (Figures 3 and 4).

In summary, we have reported a novel photosensitized visible light initiated reductive cyclization of aldehydes/ketones with tethered olefins to produce diastereoselective cycloalkanols. The application of this methodology is also successfully demonstrated by the stereoselective

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(27) In our present experimental conditions, we always got cyclized product **40** in desilylated form.

synthesis of optically pure *C*-furanoside, starting with L-tartaric acid.

Experimental Section

Reactions were monitored by thin layer chromatography (TLC) or gas chromatography (GC). All yields reported refer to isolated material. Temperatures above and below ambient temperature refer to bath temperatures unless otherwise stated. Solvents and anhydrous liquid reagents were dried according to established procedures by distillation under argon atmosphere from an appropriate drying agent. Reagents were procured from Aldrich, USA, and SD Fine Chemicals, India.

Analytical TLC was performed using precoated silica gel plates (0.25 mm). Column chromatography was performed using silica gel (100−200 mesh, SD Fine Chemicals, India) by standard chromatographic techniques. Product ratios were determined on a capillary gas chromatography (SP-1000, methylsilicon and phenylsilicon 50 m, 0.25 mm).

All nuclear magnetic resonance spectra were recorded on either Bruker AC 200 FT NMR or Bruker MSL 300 NMR spectrometers. All chemical shifts are reported in parts per million down field from TMS; coupling constants are given in hertz. IR spectra were taken on Perkin-Elmer FTIR 1620 or Unicam ATI Mattison RS-1 or Perkin-Elmer 599B. Mass spectra were obtained at a voltage of 70 eV using Finnigan MAT-1020B instrument. GC/MS was done using Shimadzu GCMS-QP2000A. Melting points (mp) were measured by Yanaco melting point apparatus and were uncorrected.

Cyclic Voltammetry. The reduction potential of compound **5** was measured by a cyclic voltammetry experiment. This experiment was carried out with a three-electrode assembly on a PAR 175 Universal programmer and PAR RE0074 XY recorder. The cell consisted of a Metro E410 hanging mercury drop electrode (HMDE) and Pt wire as auxiliary electrode. Tetraethylammonium perchlorate was used as a supporting electrolyte in DMF solution. Before the experiment, the solution was deoxygenated by bubbling argon for 10 min. The observed cyclic voltamogram was irreversible, and therefore, the reduction potential ($E_{1/2(red)}$) as well as free energy change (ΔG_{et}) value obtained is only approximate; however, it agrees generally quite well with experimental results.

X-ray Crystal and Intensity Data. A colorless crystal of size 0.13 × 0.10 × 0.07 mm of compound **41** was mounted and aligned on a Siemens R3m/v diffractometer. Crystal data: a = 5.566(1) Å, b = 8.220(1) Å, c = 21.551(4) Å, β = 90.0°; space group $P2(1)2(1)2(1)$, V = 986.0(1) Å^3, Z = 4, density (calc) = 1.389 mg/m^3. Intensity data in the 2θ range 3.78−50.08° were collected using ω scan with Mo Kα radiation (λ = 0.710 73 Å). A total of 1070 independent reflections were collected, of which 511 and $I \geq 3\sigma(I)$.

All crystallographic calculations were carried out with the aid of the SHELXTL Plus program package. The positional and anisotropic thermal parameters were refined for all non-hydrogen atoms. A riding model with fixed isotropic U was used for hydrogen atoms. For the observed data final R = 5.1%, R_w = 5.0%, goodness-of-fit = 1.34.

General Photoirradiation Procedure. All irradiations were performed in a specially designed photoreactor which consisted of three chambers. The first and outer chamber contained the irradiation solution, and the second one was charged with $CuSO_4 \cdot 5H_2O$:NH_3 filter solution. A 450 W Hanovia medium-pressure mercury lamp was housed into a water-circulated double-jacketed chamber which was immersed into the second one. The whole photoreactor was made of Pyrex glass.

DCA (0.6 mmol) was dissolved in DMF:*i*-PrOH:H_2O (500 mL, 88:10:2) in a round bottom (RB) flask by stirring for about 2 h. Substrate (2.4 mmol) and Ph_3P (1.45 mmol) or DMN (0.4 mmol) and ascorbic acid (6.2 mmol) were introduced to the solution and stirred for an additional 5 min. The resultant mixture was transferred into the outer chamber of the above photoreactor and was deoxygenated by bubbling argon for 0.5 h and properly sealed. Irradiation was performed with the light (405 nm) of a 450 W Hanovia medium-pressure lamp through a $CuSO_4 \cdot 5H_2O$:NH_3 filter solution. The progress of the reaction was monitored by GC. After 18−22 h of irradiation, when substrate was almost consumed (95−98%), the solvents were removed by distillation under reduced pressure. The concentrate was dissolved in Et_2O (50 mL), and the Et_2O layer was washed with H_2O and saturated brine solution and dried over Na_2SO_4. After evaporation of the solvent, the mixture was purified by silica gel column chromatography to give respective cyclized products.

Preparation of Ethyl 7-Hydroxy-2(*E*)-heptenoate (4). To a previously dried 100 mL RB flask was added ethyl (triphenylphosphoranylidene)acetate (11.2 g, 32.1 mmol) and 60 mL of CH_2Cl_2 followed by 2-hydroxypyran (2.4 g, 23.5 mmol) under an argon atmosphere. The reaction mixture was allowed to stir at room temperature (rt) for 2 d. After concentrating, the residue was stirred with 40 mL of Et_2O:petroleum ether (7:3) for 45 min. The resulting suspension was filtered, and the precipitate was washed with 10 mL of the same solvent. The combined filtrate was concentrated in vacuo and the mixture was separated by column chromatography on silica gel to yield 3.36 g (83%) of **4** as a clear liquid: 200 MHz ^{1}H NMR ($CDCl_3$) δ 6.95 (1H, dt, J = 15.6, 7.0 Hz), 5.8 (1H, dt, J = 15.6, 1.4 Hz), 4.17 (2H, q, J = 7.2 Hz), 3.62 (2H, t, J = 6.4 Hz), 2.19 (2H, m), 2.0 (1H, br s, OH), 1.61−1.32 (4H, m), 1.27 (3H, t, J = 7.2 Hz); 50 MHz ^{13}C NMR ($CDCl_3$) δ 166.94, 149.29, 121.50, 62.57, 60.29, 32.49, 32.19, 25.42, 14.32; IR (neat) 3400 (br), 3025, 2940, 2885, 1722, 1655, 1375, 1222, 1045, 988, 765 cm^{-1}.

Ethyl 7-Oxo-2(*E*)-heptenoate (5). In a two-necked 100-mL RB flask a solution of oxalyl chloride (0.95 mL, 11.0 mmol) dissolved in CH_2Cl_2 (30 mL) was cooled to −78 °C under argon atmosphere. DMSO (1.97 mL, 27.8 mmol) in CH_2Cl_2 (8 mL) was introduced dropwise over 5 min into the flask, and the gas evolution was observed. After 5 min of stirring, the alcohol (**4**, 1.2 g, 7 mmol) dissolved in CH_2Cl_2 (10 mL) was added to the reaction mixture over about 5 min. Stirring was continued for additional 1.5 h at −78 °C. Addition of Et_3N (4.85 mL, 34.8 mmol) in CH_2Cl_2 (5 mL) followed afterward. After the reaction mixture was allowed to warm to rt, it was quenched with H_2O (20 mL). The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (1 × 20 mL). The combined organic layers were washed with H_2O (5 × 30 mL) and saturated brine solution, dried over Na_2SO_4, and concentrated in vacuo. Column purification of the concentrate gave **5** (1.15 g, 96%): 200 MHz ^{1}H NMR ($CDCl_3$) δ 9.8 (1H, t, J = 1.4 Hz), 6.94 (1H, dt, J = 15.7, 6.9 Hz), 5.85 (1H, dt, J = 15.7, 1.4 Hz), 4.2 (2H, q, J = 7.2 Hz), 2.51 (2H, td, J = 7.3, 1.4 Hz), 2.27 (2H, m), 1.84 (2H, m), 1.28 (3H, t, J = 7.2 Hz); 75 MHz ^{13}C NMR ($CDCl_3$) δ 201.4, 166.28, 147.37, 122.21, 60.13, 42.85, 31.15, 20.28, 14.13; IR (neat) 2955, 2842, 2727, 1728, 1661, 1441, 1320, 1275, 1200, 1158, 1043, 984 cm^{-1}.

Photoactivation of 5. A solution of compound **5** (0.5 g, 2.94 mmol), Ph_3P (0.54 g, 2.06 mmol), and DCA (0.14 g, 0.60 mmol) in DMF:*i*-PrOH:H_2O (500 mL, 88:10:2) was irradiated in a specially designed photoreactor as mentioned above under an argon atmosphere with light from a 450 W Hanovia medium-pressure lamp filtered by a $CuSO_4 \cdot 5H_2O$:NH_3 solution. The progress of the reaction was monitored by GC. After considerable consumption (98%) of **5** (18 h), the solvent was removed by distillation under reduced pressure. The concentrate was dissolved in Et_2O (50 mL) and washed with H_2O and saturated brine solution. The Et_2O layer was concentrated in vacuo, and the mixture was separated by column on silica gel (100−200 mesh) using petroleum ether:EtOAc as eluent to give compound **6** (0.4 g, 80%): 200 MHz ^{1}H NMR ($CDCl_3$) δ 4.18 (2H, q, J = 7.2 Hz), 3.85 (1H, m), 2.7 (1H, br s, OH), 2.4 (2H, m), 2.27−1.8 (3H, m), 1.61 (3H, m), 1.25 (4H, m); 50 MHz ^{13}C NMR ($CDCl_3$) δ 174.28, 78.978, 60.76, 44.61, 38.67, 34.40, 30.78, 22.00, 14.36; MS m/e 143 (M^+ − electron transfer, 17), 127 (M^+ − OEt, 24), 115, (16), 109 (27), 97 (27), 88 (77), 84 (96), 73 (47), 67 (52), 55 (100); IR (neat) 3420 (br OH), 2960, 2880, 1730, 1378, 1265, 1190, 1145, 1105, 1038 cm^{-1}.

Preparation of Ethyl 8-Hydroxy-2(*E*)-octenoate (15). 1,6-Hexanediol (**13**) (5 g, 42.3 mmol) and 160 mL of CH_2Cl_2 were placed in a 500 mL RB flask equipped with a magnetic

stirring bar and argon gas balloon. A mixture of dry pyridinium chlorochromate (PCC; 7.6 g, 35.2 mmol) and Celite (7.6 g) was slowly added to the solution over 1.5 h by a solid addition funnel at rt. The suspended mixture continued to stir for another 2 h, and 100 mL of Et_2O was added to the reaction mixture. The resulting mixture was passed through a silica gel column and eluted with EtOAc:petroleum ether to give 2.25 g (55%) of a gummy liquid of 6-hydroxyhexanol (**14**). Wittig reaction of **14** with ethyl (triphenylphosphoranylidene)-acetate by following the identical reaction condition as described for **4** gave ethyl 8-hydroxy-2(*E*)-octenoate (**15**, 86%) as an oil: 200 MHz ^{1}H NMR ($CDCl_3$) δ 6.95 (1H, dt, J = 15.8, 6.9 Hz), 5.81 (1H, dt, J = 15.8, 1.4 Hz), 4.17 (2H, q, J = 7.1 Hz), 3.62 (2H, t, J = 6.4 Hz), 2.21 (2H, m), 2.04 (1H, br s), 1.61−1.31 (6H, m), 1.27 (3H, t, J = 7.1 Hz); 50 MHz ^{13}C NMR ($CDCl_3$) δ 166.94, 149.29, 121.50, 62.57, 60.29, 32.49, 32.19, 27.92, 25.42, 14.32; IR (neat) 3400 (br), 3022, 2940, 2877, 1710, 1655, 1375, 1221, 1048, 987, 762 cm^{-1}.

Ethyl 8-Oxo-2(*E*)-octenoate (16). This was obtained by the Swern oxidation of **15** following the identical reaction procedure as described for **5**: 200 MHz ^{1}H NMR ($CDCl_3$) δ 9.75 (1H, t, J = 1.4 Hz), 6.92 (1H, dt, J = 15.8, 6.9 Hz), 5.81 (1H, dt, J = 15.8, 1.4 Hz), 4.16 (2H, q, J = 7.1 Hz), 2.45 (2H, td, J = 7.0, 1.4 Hz), 2.22 (2H, m), 1.69−1.44 (4H, m), 1.27 (3H, t, J = 7.1 Hz); 50 MHz ^{13}C NMR ($CDCl_3$) δ 201.92, 166.35, 148.22, 121.66, 59.99, 43.37, 31.68, 27.36, 21.38, 14.10; IR (neat) 2988, 2942, 2885, 2725, 1720, 1658, 1372, 1315, 1275, 1192, 1162, 1048, 990 cm^{-1}.

Ethyl 2-(2-hydroxycyclohexyl)ethanoate (22): 200 MHz ^{1}H NMR ($CDCl_3$) δ 4.14 (2H, q, J = 7.2 Hz), 3.9 (1H, m), 2.48 (1H, dd, J = 15.2, 7.7 Hz), 2.26 (1H, dd, J = 15.2, 6.7 Hz), 2.03 (1H, m), 1.76−1.35 (8H, m), 1.3 (1H, m), 1.25 (3H, t, J = 7.2 Hz); 50 MHz ^{13}C NMR ($CDCl_3$) δ 173.94, 69.30, 60.57, 38.61, 37.17, 32.76, 27.20, 24.79, 20.70, 14.47; MS m/e 168 ($M^+ - H_2O$, 1), 141 ($M^+ - OEt$, 3), 140 ($M^+ - EtOH$, 6), 122 (4), 111 (10), 97 (21), 96 (29), 94 (9), 83 (14), 81 (100), 79 (27), 68 (63), 67 (75), 55 (64); IR (neat) 3450 (br OH), 2975, 2920, 2852, 1715, 1445, 1372, 1290, 1168, 1110, 1032, 982 cm^{-1}.

Compound 23: 200 MHz ^{1}H NMR ($CDCl_3$) δ 4.52 (1H, m), 2.71 (1H, dd, J = 16.8, 6.0 Hz), 2.38 (1H, m), 2.26 (1H, dd, J = 16, 3.6 Hz), 1.9−1.25 (8H, m); 50 MHz ^{13}C NMR ($CDCl_3$) δ 168.26, 79.36, 37.64, 35.12, 28.03, 27.36, 23.00, 20.12; GC MS m/e 140 (M^+, 32), 112 ($M^+ - CO$, 56), 111 (100), 97 (23), 81 (84), 68 (80), 67 (89), 55 (100), 41 (94); IR (neat) 2928, 2855, 1772, 1178, 1150, 995 cm^{-1}.

Preparation of 18a. Ethyl 3-(2-oxocyclohexyl)propionate[28] (**17a**) (2.25 g, 11.36 mmol), 0.8 g (12.6 mmol) of ethylene glycol, *p*-toluenesulfonic acid (0.05 g), and 40 mL of dry C_6H_6 were charged into a 100 mL RB flask fitted with Dean−Stark apparatus. The whole content was refluxed for 16 h. After cooling, the reaction mixture was washed with 5% $NaHCO_3$ solution, dried over Na_2SO_4, and concentrated in vacuo. Silica gel column purification of the concentrate gave 2.25 g (82%) of **18a**: 200 MHz ^{1}H NMR ($CDCl_3$) δ 4.13 (2H, q, J = 7.2 Hz), 3.94 (4H, m), 2.33 (2H, m), 2.0 (1H, m), 1.85−1.25 (10H, m), 0.25 (3H, t, J = 7.2 Hz); IR (neat) 2938, 2880, 1738, 1458, 1385, 1274, 1190, 1170, 1100, 1060, 962, 949, 872 cm^{-1}.

Preparation of 19a. Lithium aluminum hydride (0.22 g, 5.5 mmol) and 30 mL of THF were placed in a 100 mL of two-necked RB flask equipped with a magnetic stirring bar, reflux condenser, and argon gas balloon. **18a** 2.2 g, (9.1 mmol) dissolved in 5 mL of THF was slowly added to the suspension through a syringe. The whole content was refluxed for 12 h. After cooling, the reaction mixture was quenched with concentrated NaOH solution. The organic layer was separated from the precipitate, and the precipitate was washed with Et_2O (2 × 20 mL). The combined organic layer was dried over Na_2SO_4 and concentrated in vacuo. The concentrate was purified by silica gel column chromatography to yield 1.75 g (96%) of **19a**: 200 MHz ^{1}H NMR ($CDCl_3$) δ 3.95 (4H, m), 3.58 (2H, t, J = 6.5 Hz), 2.24 (1H, br s, OH), 1.88−1.0 (13 H, m); IR (neat) 3380 (br), 2920, 2855, 1640, 1446, 1358, 1340, 1285, 1230, 1163, 1146, 1092, 1060, 1030, 958, 932, 870 cm^{-1}.

(28) Stork, G.; Brizzolara, A.; Landesman, H.; Szmuszkovicz, J.; Terrell, R. *J. Am. Chem. Soc.* **1963**, *85*, 207.

Preparation of 20. Swern oxidation of **19a** by following the identical procedure as described for **5** gave **20a** (100%): 200 MHz ^{1}H NMR ($CDCl_3$) δ 9.77 (1H, t, J = 1.3 Hz), 3.97 (4H, m), 2.50 (2H, m), 2.0 (1H, m), 1.90−1.08 (10H, m); IR (neat) 2938, 2868, 2720, 1737, 1457, 1362, 1350, 1295, 1170, 1110, 1042, 964, 940 cm^{-1}.

Synthesis of 2-(4-Carbethoxy-3-butenyl)cyclohexanone (21a). Wittig olefination of compound **20a** with ethyl (triphenylphosphoranylidene)acetate, as discussed earlier for compound **4** and followed by deprotection of ketal with catalytic PTSA in 5% aqueous MeOH, gave compound **21a** (80%): 200 MHz ^{1}H NMR ($CDCl_3$) δ 6.92 (1H, dt, J = 15.8, 6.8 Hz), 5.8 (1H, dt, J = 15.8, 1.4 Hz), 4.18 (2H, q, J = 7.2 Hz), 2.45−2.15 (5H), 2.15−1.75 (4H, m), 1.65 (2H, m), 1.35 (2H, m), 1.27 (3H, t, J = 7.2 Hz); 50 MHz ^{13}C NMR ($CDCl_3$) δ 212.35, 166.48, 148.65, 121.54, 60.06, 49.68, 42.05, 34.01, 29.63, 27.95, 27.81, 24.97, 14.20; IR (neat) 2930, 2855, 1725, 1708, 1648, 1448, 1372, 1270, 1175, 1042, 990, 865 cm^{-1}.

Compound 24: mixture of two isomers; 200 MHz ^{1}H NMR ($CDCl_3$) δ 4.14 (2H, q, J = 7.1 Hz), 2.73 (1H, br s, OH), 2.54−2.17 (3H, m), 1.98 (2H, m), 1.81−1.1 (14H, m); 50 MHz ^{13}C NMR ($CDCl_3$) δ 174.36, 77.27, 60.40, 46.80, 44.40, 34.15, 28.09, 26.57, 23.87, 23.32, 20.97, 20.17, 14.08; other isomer 173.13, 79.72, 60.23, 45.47, 44.75, 38.48, 33.34, 28.23, 27.57, 25.60, 25.42, 21.14, 14.08; MS m/e 226 (M^+, 21), 208 ($M^+ - H_2O$, 6), 181 ($M^+ - OEt$, 8), 180 ($M^+ - EtOH$, 52), 162 (13), 152 (37), 137 (41), 121 (49), 111 (28), 98 (56), 91 (26), 83 (24), 79 (28), 67 (41), 55 (100); IR (neat) 3480 (br OH), 2935, 2875, 1730, 1455, 1385, 1320, 1275, 1210, 1170, 1040, 1015, 972 cm^{-1}.

Compound 25: 200 MHz ^{1}H NMR ($CDCl_3$) δ 2.87 (1H, dd, J = 17.3, 8.8 Hz), 2.66 (1H, td, J = 9.7, 2.7 Hz), 2.35 (1H, d, J = 17.6 Hz), 2.30−2.02 (2H, m), 1.96 (1H, m), 1.85−1.5 (4H, m), 1.5−1.02 (6H, m); 50 MHz ^{13}C NMR ($CDCl_3$) δ 177.27, 98.10, 44.86, 39.40, 37.40, 32.15, 31.33, 30.09, 28.49, 24.25, 23.52; GC MS m/e 180 (M^+, 2), 152 ($M^+ - CO$, 4), 137 (6), 136 (10), 121 (5), 111 (3), 107 (3), 98 (22), 95 (10), 79 (7), 67 (7), 55 (47), 51 (10), 41 (100), 38 (70); IR (neat) 3022, 2940, 2868, 1768, 1460, 1430, 1225, 1195, 1178, 1153, 1050, 1013, 970 cm^{-1}.

Preparation of 18b. This substrate was prepared (78%) by ethylene glycol protection of methyl 3-(2-oxocyclopentyl)-propionate[28] (**17b**) as described for compound **18a**: 200 MHz ^{1}H NMR ($CDCl_3$) δ 3.92 (4H, m), 3.66 (3H, s), 2.3 (2H, m), 2.0−1.15 (9H, m); IR (neat) 2935, 2882, 1736, 1388, 1270, 1190, 1105, 1055, 956, 870 cm^{-1}.

Preparation of 19b. $LiAlH_4$ reduction of **18b** as discussed earlier gave compound **19b** (96%): 200 MHz ^{1}H NMR ($CDCl_3$) δ 3.9 (4H, m), 3.62 (2H, t, J = 6.8 Hz), 1.9 (2H, m), 1.84−1.48 (7H, m), 1.28 (2H, m); IR (neat) 3420 (br), 2990, 2918, 2852, 1430, 1318, 1210, 1145, 1100, 1025, 946, 752 cm^{-1}.

Synthesis of 2-(4-Carboethoxy-3-butenyl)cyclopentanone (21b). This product was obtained by following the reaction sequence as enumerated for compound **21a** starting with **19b** in 78% yield: 200 MHz ^{1}H NMR ($CDCl_3$) δ 6.92 (1H, dt, J = 15.9, 6.8 Hz), 5.84 (1H, dt, J = 15.9, 1.4 Hz), 4.18 (2H, q, J = 7.1 Hz), 2.38−1.65 (9H, m), 1.62−1.33 (2H, m), 1.27 (3H, t, J = 7.1 Hz); 50 MHz ^{13}C NMR ($CDCl_3$) δ 220.44, 166.48, 148.16, 122.0, 60.18, 48.29, 38.04, 30.03, 29.66, 28.15, 20.69, 14.29; IR (neat) 2960, 2880, 1730, 1660, 1455, 1415, 1375, 1320, 1278, 1210, 1190, 1170, 1050 cm^{-1}.

Compound 26: 200 MHz ^{1}H NMR ($CDCl_3$) δ 4.15 (2H, q, J = 7.2 Hz), 3.15 (1H, br s, OH), 2.48 (2H, m), 2.4−2.0 (3H, m), 2.0−1.48 (5H, m), 1.45−1.15 (6H, m), 1.05 (1H, m); 50 MHz ^{13}C NMR ($CDCl_3$) δ 174.66, 91.11, 60.63, 51.35, 46.74, 36.92, 34.92 (2C), 31.19, 29.67, 25.67, 14.15; MS m/e 212 (M^+, 14), 194 ($M^+ - H_2O$, 4), 183 (14), 167 ($M^+ - OEt$, 17), 166 ($M^+ - EtOH$, 96), 148 (15), 138 (56), 137 (88), 124 (22), 107 (43), 97 ( ), 91 (17), 84 (78), 79 (39), 67 (43), 55 (100); IR (neat) 3450 (br OH), 2940, 2860, 1720, 1450, 1378, 1320, 1282, 1215, 1175, 1100, 1020 cm^{-1}.

Compound 27: 200 MHz ^{1}H NMR ($CDCl_3$) δ 2.78 (1H, dd, J = 17.7, 9.1 Hz)), 2.48 (1H, m), 2.35 (1H, m), 2.30 (1H, m), 2.2−1.75 (6H, m), 1.75−1.22 (4H, m); 50 MHz ^{13}C NMR ($CDCl_3$) δ 176.96, 105.22, 49.68, 45.55, 38.25, 34.97, 33.05, 31.89 (2C), 25.49; GC MS m/e 166 (M^+, 2), 138 ($M^+ - CO$, 6), 121 (6), 110 (4), 101 (8), 84 (30), 81 (8), 67 (8), 55 (30), 51 (12),

41 (100), 38 (68), 27 (55); IR (neat) 3028, 2955, 2878, 1770, 1460, 1428, 1227, 1175, 1035, 995, 968 cm^{-1}.

Preparation of (2*R*,3*R*)-Diethyl 2,3-*O*-Benzylidenetartarate (29). (2*R*,3*R*)-Diethyl tartarate (**28**; 56 g, 271 mmol), benzaldehyde (30 g, 283 mmol), *p*-toluenesulfonic acid (0.1 g), and dry C_6H_6 (300 mL) were charged into a 500 mL RB flask. The whole content was heated under reflux with provision for azeotropic removal of water for 22 h. After cooling to rt, the solution was washed with 5% $NaHCO_3$ solution and saturated brine solution and dried over Na_2SO_4. Concentration followed by crystallization from ethanol gave 44.0 g (55%) of **29**, mp 47−49 °C (lit.[29] mp 48−49 °C).

Preparation of 2-*O*-Benzyl-L-threitol (30). Lithium aluminum hydride (5.7 g, 155 mmol) and 1:1 (v/v) Et_2O:CH_2Cl_2 (250 mL) were placed in a 1 L two-necked RB flask equipped with a magnetic stirring bar, reflux condenser, and argon gas Balloon. Compound **29** (14.7 g, 50 mmol) dissolved in Et_2O (60 mL) was slowly added to the above suspension. Anhydrous aluminum chloride (20 g, 150 mmol) in Et_2O (110 mL) was added over 0.5 h. After 1 h of stirring at rt, the reaction mixture was heated under reflux for 4 h. After the mixture was cooled to 0 °C, H_2O (12 mL) was added carefully to destroy excess hydride. An additional 125 mL of H_2O was added to the reaction mixture. The whole content was again heated under reflux for 0.5 h, and organic layer was separated. The aqueous layer was further refluxed with EtOAc (2 × 150 mL) for 0.5 h, and organic layer was separated. The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. The residue was recrystallized from EtOAc:petroleum ether to give 9.5 g (89%) of **30**: mp 77−81 °C (lit.[20] mp 73−76 °C); $[\alpha]^{22}_D = +16.97°$ (c = 1.02, MeOH; lit.[30] +15.7°, c = 1.0, MeOH).

Preparation of 3-*O*-Benzyl-1,2-*O*-isopropylidene-L-threitol (31). Compound **30** (9 g, 42.4 mmol), 2,2-dimethoxypropane (6.6 g, 63.6 mmol), *p*-toluenesulfonic acid (0.15 g), and dry CH_2Cl_2 (200 mL) were placed in a 500 mL RB flask fitted with Soxhlet extractor containing 4 Å molecular sieves. After 3 h of reflux, the sieves were replaced with fresh bath and the heating was continued for additional 4 h. The reaction mixture was cooled to rt, washed with saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated in vacuo. The concentrate was purified by column chromatography using petroleum ether/EtOAc as eluent to yield 7.5 g (70%) of **31**: 200 MHz ^{1}H NMR ($CDCl_3$) δ 7.4 (5H, m), 4.74 (2H, AB q, J = 11.8, 7.1 Hz), 4.33 (1H, dd, J = 12.6, 6.7 Hz), 4.03 (1H, dd, J = 8.4, 6.7 Hz), 3.83 (1H, dd, J = 8.4, 7.0 Hz), 3.74 (1H, m), 3.6 (2H, m), 2.2 (1H, br s), 1.45 (3H, s), 1.4 (3H, s); 50 MHz ^{13}C NMR ($CDCl_3$) δ 138.37, 128.39, 127.87, 127.73, 109.29, 79.59, 76.65, 72.78, 65.61, 61.73, 26.40, 25.37; IR (neat) 3417 (br, OH), 1641, 1070, 744 cm^{-1}.

Preparation of 4-*O*-Benzoyl-3-*O*-benzyl-1,2-*O*-isopropylidene-L-threitol (32). Alcohol **31** (6 g, 23.8 mmol), pyridine (3.85 mL, 47.6 mmol), and dry CH_2Cl (70 mL) were charged into a 250 mL two-necked RB flask equipped with a magnetic stirring bar and argon gas balloon. Freshly distilled benzoyl chloride (3.04 mL, 26.2 mmol) was slowly added at 0 °C, and the reaction mixture was allowed to stir for 12 h at rt. Pyridine was washed off from the reaction mixture with 5% of aqueous $CuSO_4$ solution. The organic layer was washed with H_2O and brine, dried over Na_2SO_4, and concentrated in vacuo. Column chromatographic purification of the concentrate gave 8.1 g (95%) of **32** as a thick liquid: 200 MHz ^{1}H NMR ($CDCl_3$) δ 8.05 (2H, m), 7.58 (1H, m), 7.5−7.25 (7H, m), 4.8 (2H, AB q, J = 12.0, 4.5 Hz), 4.58−4.3 (3H, m), 4.07 (1H, dd, J = 8.4, 6.6 Hz), 3.85 (2H, m), 1.48 (3H, s), 1.40 (3H, s); 50 MHz ^{13}C NMR ($CDCl_3$) δ 166.25, 138.12, 133.06, 129.94, 129.64, 128.38, 128.33, 127.87, 127.70, 109.50, 77.12, 76.12, 73.0, 65.61, 64.17, 26.39, 25.33; MS m/e 356 (M^+, 3), 355 (M^+ − 1, 8), 341 (M^+ − Me, 25), 298 (10), 255 (48), 192 (28), 176 (58), 158 (27), 133 (100), 122 (55), [341 (M^+ − Me, 1), 176 (2), 133 (3), 105 (48), 91 (100), 77 (29), 73 (12), 55 (5)]; IR (neat) 3031, 2984, 2888, 1720, 1602, 1584, 1496, 1453, 1371, 1515, 1274, 1177, 1157, 1109, 1070, 1026, 850, 739, 712 cm^{-1}.

Preparation of 4-*O*-Benzoyl-3-*O*-benzyl-L-threitol (33). A solution of **32** (8 g, 22.4 mmol) and PTSA (0.1 g) in 5% aqueous methanol (120 mL) was stirred at rt overnight. The reaction mixture was concentrated in vacuo, and the concentrate was diluted in Et_2O (70 mL). The Et_2O layer was washed with 5% $NaHCO_3$ solution and saturated brine solution, dried over Na_2SO_4, and evaporated under vacuum. The residue was recrystallized from EtOAc: petroleum ether to give 6.1 g (86%) of **33** as a white fluffy crystals: mp 89−91 °C; $[\alpha]^{22}_D = -19.6°$ (c = 0.6, MeOH); 200 MHz ^{1}H NMR ($CDCl_3$) δ 8.05 (2H, m), 7.58 (1H, m), 7.45 (2H, m), 7.35 (5H, m), 4.85 (1H, d, J = 11.4 Hz), 4.65 (1H, dd, J = 11.8, 5.0 Hz), 4.62 (1H, d, J = 11.4 Hz), 4.5 (1H, dd, J = 11.8, 4.7 Hz), 3.85 (2H, br s), 3.73 (2H, m), 2.8 (1H, br s, OH), 2.35 (1H, br s, OH); 50 MHz ^{13}C NMR ($CDCl_3$) δ 166.59, 137.77, 133.28, 129.94, 129.75, 128.56, 128.21, 128.11, 77.57, 73.28, 71.90, 64.00, 63.58; IR (neat) 2918, 2853, 1709, 1463, 1376, 1293, 1123, 1088, 710 cm^{-1} (intense OH peak is not observed, may be due to the intramolecular H-bonding).

4-*O*-Benzoyl-3-*O*-benzyl-1-[(*tert*-butyldimethylsilyl)-oxy]-L-threitol (34). To a stirring solution of **33** (5.0 g, 15.8 mmol) and imidazole (2.4 g, 35.3 mmol) in CH_2Cl_2 (60 mL) was added *tert*-butyldimethylsilyl chloride (2.5 g, 16.6 mmol) at rt, and stirring was continued for an additional 4 h. The reaction mixture was filtered, and the filtrate was washed with H_2O (2 × 20 mL) and saturated brine solution, dried over Na_2SO_4, and concentrated in vacuo. Silica gel column chromatographic purification of the concentrate afforded 6.46 g (95%) of **34** as a gummy liquid: $[\alpha]^{22}_D = -6.5°$ (c = 0.95, MeOH); 200 MHz ^{1}H NMR ($CDCl_3$) δ 8.05 (2H, m), 7.58 (1H, m), 7.45 (2H, m), 7.33 (5H, m), 4.83 (1H, d, J = 11.6 Hz), 4.66 (1H, d, J = 11.6 Hz), 4.56 (2H, m), 3.95 (1H, m), 3.84 (1H, br s), 3.71 (2H, m), 2.5 (1H, br s, OH), 0.9 (9H, s), 0.08 (6H, s); 50 MHz ^{13}C NMR ($CDCl_3$) δ 166.44, 138.14, 133.12, 129.78, 128.53, 128.14, 128.0, 76.76, 73.45, 71.78, 64.23, 63.70, 26.00, 18.33, −5.24; MS m/e 373 (M^+ − t-Bu, 13), 265 (17), 179 (71), 159 (19), 145 (28), 131 (20), 122 (10), 117 (100), [117 (5), 105 (20), 91 (100), 77 (14), 57 (9)]; IR (neat) 3448 (br, OH), 2928, 1721, 1453, 1274, 1115, 836, 778, 711 cm^{-1}.

Compound 35. Alcohol **34** (6 g, 13.9 mmol), *N*-methylmorpholine (1.55 g, 15.3 mmol), and dry CH_2Cl_2 (100 mL) were placed in a 250 mL two-necked RB flask equipped with a magnetic stirring bar and argon gas balloon. Methyl propiolate (1.3 g, 15.4 mmol) in CH_2Cl_2 (10 mL) was slowly added to the stirring solution, and stirring was continued for 10 h at rt. The reaction mixture was washed with H_2O (3 × 40 mL) and brine solution, dried over Na_2SO_4, and concentrated in vacuo. The concentrate was purified by silica gel column chromatography to give 6.5 g (91%) of **35** as a thick liquid: 200 MHz ^{1}H NMR ($CDCl_3$) δ 8.05 (2H, m), 7.64 (1H, m), 7.57 (1H, d, J = 12.2 Hz), 7.45 (2H, m), 7.35 (5H, m), 5.35 (1H, d, J = 12.2 Hz), 4.73 (2H, AB q, J = 15.2, 11.7 Hz), 4.5 (2H, dd, J = 5.1, 3.1 Hz), 4.15 (1H, m), 3.96 (1H, m), 3.83 (2H, d, J = 5.7 Hz), 3.68 (3H, s), 0.88 (9H, s), 0.05 (6H, s); 50 MHz ^{13}C NMR ($CDCl_3$) δ 168.21, 166.23, 163.60, 137.60, 133.30, 129.84, 128.55, 128.28, 128.11, 97.65, 84.65, 75.80, 73.41, 63.14, 62.51, 51.01, 25.86, 18.26, −5.37; MS m/e 457 (M^+ − t-Bu, 3), 179 (14), 159 (8), 153 (25), 105 (58), 91 (100), 77 (15), 73 (11), 59 (5), [457 (18), 265 (12), 247 (6), 179 (100)]; IR (neat) 2952, 2856, 1722, 1642, 1452, 1272, 1204, 1122, 1026, 837, 780, 752, 712 cm^{-1}.

Compound 36. A solution of **35** (6 g, 11.6 mmol) in Et_3N:MeOH:H_2O (1:5:1, v/v, 100 mL) was stirred in a 250 mL double wall jacketed flask at 0 °C. After 42 h of stirring at 0 °C, the reaction mixture was diluted with 200 mL of H_2O and extracted with Et_2O (3 × 75 mL). The organic layer was washed with H_2O (2 × 50 mL) and saturated brine solution, dried over Na_2SO_4, and concentrated in vacuo. The mixture was separated by silica gel column chromatography to give 2.5 g (52%) of **36** as a viscous liquid and 0.6 g (12%) of **37** as an oil, and 1.5 g (25%) of **35** was recovered: $[\alpha]^{22}_D = +13.71°$

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(31) The author has deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

(c = 0.96, MeOH); 200 MHz ^{1}H NMR ($CDCl_3$) δ 7.57 (1H, d, J = 12.2 Hz), 7.35 (5H, s), 5.37 (1H, d, J = 12.2 Hz), 4.65 (2H, s), 4.1 (1H, m), 3.81 (2H, d, J = 5.6 Hz), 3.7 (3H, m), 3.68 (3H, s), 2.2 (1H, br s, OH), 0.9 (9H, s), 0.07 (6H, s); 50 MHz ^{13}C NMR ($CDCl_3$) δ 168.56, 163.97, 137.91, 128.64, 128.27, 128.16, 97.34, 85.11, 78.86, 73.44, 62.53, 60.96, 51.11, 25.92, 18.32, −5.31; MS m/e [411 ($M^+ + 1$, 2), 378 (M^+ − OMe, 2), 379 (M^+ − MeOH, 3), 353 (M^+ − t-Bu, 7), 321 (5), 251 (14), 245 (9), 231 (8), 221 (11), 189 (32), 175 (36), 161 (100)], 161 (4), 159 (4), 143 (3), 131 (7), 117 (9), 91 (100), 81 (7), 75 (22), 57 (17), 55 (13); IR (neat) 3464 (br), 2928, 2857, 1714, 1640, 1496, 1471, 1437, 1362, 1207, 1138, 835, 778, 743, 699 cm^{-1}.

Compound 37: 200 MHz ^{1}H NMR ($CDCl_3$) δ 7.33 (5H, m), 5.08 (1H, t, J = 5.4 Hz), 4.65 (2H, AB q, J = 17.9, 12.2 Hz), 4.23 (1H, dd, J = 12.5, 1.4 Hz), 3.83 (1H, m), 3.79 (2H, m), 3.71 (1H, m), 3.69 (3H, s), 3.38 (1H, d, J = 1.4 Hz), 2.76 (2H, d, J = 5.4 Hz), 0.9 (9H, s), 0.07 (6H, s); 50 MHz ^{13}C NMR ($CDCl_3$) δ 169.77, 138.10, 128.28, 127.86, 127.63, 98.64, 79.59, 71.46, 69.34, 68.12, 61.91, 51.54, 40.23, 25.85, 18.17, −5.35, −5.45; IR (neat) 2928, 2882, 2856, 1744, 1470, 1454, 1410, 1360, 1326, 1254, 1162, 1106, 1042, 1006, 836, 778 cm^{-1}.

Compound 38: In a two-necked 50 mL RB flask oxalyl chloride (0.15 mL, 1.75 mmol) dissolved in CH_2Cl_2 (12 mL) was cooled to −78 °C under argon atmosphere. DMSO (0.36 mL, 4.66 mmol) in CH_2Cl_2 (4 mL) was introduced dropwise over 5 min into the flask, and the gas evolution was observed. After 5 min of stirring the alcohol (**36**; 0.48 g, 1.17 mmol) dissolved in CH_2Cl_2 (4 mL) was added over about 5 min. Stirring was continued for additional 1.5 h at −78 °C. a solution of Et_3N (0.8 mL, 5.75 mmol) in CH_2Cl_2 (3 mL) was added dropwise afterward. After the reaction mixture was allowed to warm to rt, the reaction was quenched with water (10 mL). The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (1 × 15 mL). The combined organic layers were washed with H_2O (5 × 30 mL) and saturated brine solution, dried over Na_2SO_4, and concentrated in vacuo to yield crude aldehyde **38** (0.48 g, 100%): 200 MHz ^{1}H NMR ($CDCl_3$) δ 9.68 (1H, d, J = 1.0 Hz), 7.48 (1H, d, J = 12.3 Hz), 7.35 (5H, s), 5.34 (1H, d, J = 12.3 Hz), 4.7 (2H, AB q, J = 12, 18.5 Hz), 4.25 (1H, m), 4.0 (1H, dd, J = 4.3, 1.0 Hz), 3.8 (2H, d, J = 5.3 Hz), 3.68 (3H, s), 0.9 (9H, s), 0.08 (6H, s); 50 MHz ^{13}C NMR ($CDCl_3$) δ 200.77, 168.01, 162.43, 136.78, 128.80, 128.58, 128.47, 98.47, 83.37, 81.87, 74.00, 61.39, 51.20, 25.89, 18.31, −5.39; IR (neat) 2952, 2857, 1713, 1437, 1408, 1390, 1362, 1328, 1289, 1259, 1205, 1189, 1142, 1120, 1070, 1051, 1027, 1007, 838, 777 cm^{-1}.

Photoreductive Cyclization of 38. A solution of compound **38** (0.48 g, 1.17 mmol) in DMF:*i*-PrOH:H_2O (500 mL, 88:10:2) was irradiated using either PS-A [Ph_3P (0.21 g, 0.82 mmol), DCA (0.06 g, 0.26 mmol)] or PS-B [DCA (0.06 g, 0.25 mmol), DMN (0.025 g, 0.14 mmol) and ascorbic acid (0.54 g, 3.06 mmol)] in a specially designed photoreactor as mentioned above under an argon atmosphere with light from a 450 W Hanovia medium-pressure lamp filtered by a $CuSO_4 \cdot 5H_2O$:NH_3 solution. The progress of the reaction was monitored by GC. After 18 h, the solvent was removed by distillation under reduced pressure. The concentrate was dissolved in EtOAc (50 mL) and washed with H_2O and saturated brine solution. The organic layer was concentrated in vacuo, and the mixture was separated by column chromatography on silica gel (100−200 mesh) using petroleum ether:CH_3COCH_3 as eluent to give compound **39** (0.09 g, 25%): 200 MHz ^{1}H NMR ($CDCl_3$) δ 7.34 (5H, m), 4.77 (1H, d, J = 11.9 Hz), 4.58 (1H, d, J = 11.9 Hz), 4.14 (2H, m), 4.11 (1H, m), 3.98 (1H, m), 3.83 (2H, m), 3.73 (3H, s), 2.96 (1H, dd, J = 16.8, 5.2 Hz), 2.73 (1H, dd, J = 16.8, 8.8 Hz), 1.85 (br s, OH); 75 MHz ^{13}C NMR ($CDCl_3$) δ 172.31, 128.28, 127.67, 127.41, 85.44, 79.88 (3C), 71.77, 61.53, 51.70, 38.09; IR (neat) 3396 (br, OH), 2925, 1728, 1456, 1439, 1398, 1348, 1280, 1215, 1175, 1132, 1111, 1090, 1063, 1041, 837, 737 cm^{-1}.

***n*-Bu$_3$SnH-Mediated Radical Cyclization of Compound 38.** A 50 mL two-necked RB flask and a condenser were flame-dried and allowed to cool under an argon atmosphere. After the flask had cooled, compound **38** (0.22 g, 0.537 mmol) and AIBN (0.022 g, 0.134 mmol) were charged into the flask. Freshly distilled C_6H_6 (20 mL) and *n*-Bu_3SnH (0.2 mL, 0.7 mmol) were syringed into the flask. This solution was carefully degassed for 10 min with argon. The reaction mixture was heated at 85 °C for 8 h. When no starting material was observed on GC/TLC, the reaction mixture was concentrated in vacuo, and the mixture was separated by column chromatography using EtOAc:petroleum as eluent to give compound **40** (0.09 g, 40%) as a colorless liquid: 200 MHz ^{1}H NMR ($CDCl_3$) δ 7.33 (5H, m), 4.63 (2H, AB q, J = 12.0, 11.5 Hz), 4.1 (2H, m), 3.99 (2H, m), 3.82 (2H, m), 3.7 (3H, s), 2.9 (1H, dd, J = 16.7, 5.4 Hz), 2.7 (1H, dd, J = 16.7, 8.9 Hz), 0.88 (9H, s), 0.07 (6H, s); 50 MHz ^{13}C NMR ($CDCl_3$) δ 172.73, 138.49, 128.55, 127.80, 127.74, 85.06, 81.61, 81.11, 80.73, 72.30, 61.78, 51.96, 38.78, 26.17, 18.54, −5.0, −5.1; MS m/e [411 ($M^+ + 1$, 40), 395 (4), 379 (M^+ − OMe, 6), 3.53 (M^+ − t-Bu, 100)], 379 (M^+ − OMe, 2), 353 (M^+ − t-Bu, 32), 321 (6), 261 (6), 243 (20), 231 (20), 169 (21), 129 (25), 117 (26), 91 (100), 75 (42), 73 (42), 65 (18), 57 (28); IR (neat) 3447 (br), 2982, 2930, 2857, 1736, 1439, 1257, 1093, 1061, 1028, 1005, 837 cm^{-1}.

Debenzylation of Compound 39. To a solution of compound **39** (0.07 g, 0.236 mmol) in MeOH (20 mL) was added a catalytic amount of 10% of Pd/C, and it was hydrogenated using Parr apparatus at 45 psi pressure for 7 h. The solution was filtered and concentrated in vacuo. The residue was crystallized from acetone:petroleum ether to yield needle-shaped colorless crystals of **41** (0.046 g, 95%): mp 87−88 °C; $[\alpha]^{22}_D$ = +41.67° (c = 0.32, MeOH); 300 MHz ^{1}H NMR (CD_3COCD_3) δ 4.61 (1H, d, J = 4.05 Hz, OH), 4.54 (1H, d, J = 4.75 Hz, OH), 4.26 (1H, m), 4.20 (1H, m), 4.14 (1H, m), 4.06 (1H, m), 3.90 (2H, m), 3.77 (3H, s), 2.78 (2H, m); 300 MHz ^{1}H NMR (D_2O) δ 4.17 (1H, dd, J = 4.54, 2.66 Hz), 4.08 (2H, m), 3.95 (1H, dd, J = 4.22, 2.66 Hz), 3.78 (1H, dd, J = 12.0, 4.4 Hz), 3.7 (3H, s), 3.68 (1H, dd, J = 12.0, 6.53 Hz), 2.82 (1H, dd, J = 1.6.04, 5.03 Hz), 2.72 (1H, dd, J = 16.04, 8.57 Hz); 75 MHz ^{13}C NMR (CD_3COCD_3) δ 172.91, 82.99, 82.55, 82.49, 79.78, 62.26, 52.24, 39.93; MS m/e 207 ($M^+ + 1$, 2), 175 (M^+ − OMe, 7), 158 (20), 157 (32), 143 (37), 139 (12), 133 (22), 125 (18), 116 (67), 115 (47), 101 (42), 97 (39), 83 (85), 84 (93), 73 (100), 69 (58), 57 (91); IR (Nujol) 3460, 3290, 3182, 2360, 2340, 1716, 1360, 1260, 1214, 1188, 1102, 1076 cm^{-1}.

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Supporting Information Available: ^{1}H NMR, ^{13}C NMR, and mass spectra of compounds (36 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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