Designing Photosystems for Harvesting Photons into Electrons by Sequential Electron-Transfer Processes: Reversing the Reactivity Profiles of α,β-Unsaturated Ketones as Carbon Radical Precursor by One Electron Reductive β-Activation

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Abstract: Two photosystems are developed to harvest visible-light photons into electrons *via* sequential electron transfer processes. Photosystem-A (**PS-A**) consisted of DCA as light harvesting electron acceptor and Ph_3P as sacrificial electron donor, whereas photosystem-B (**PS-B**) employed DCA as usual electron acceptor, DMN as a primary electron donor, and ascorbic acid as a secondary and sacrificial electron donor. α,β-Unsaturated ketones are utilized as secondary electron acceptors. The design of these photosystems is based on the thermodynamic feasibility of electron transfer between each participating components. Electron transfer from $DCA^{\bullet -}$ to α,β-unsaturated ketones leads to their β-activation as carbon centered radicals which cyclizes efficiently to tethered activated olefins. Cyclization with a nonactivated olefin is found to be moderate. The cyclization stereochemistries have been illustrated by studying the PET activation of **5** and **21**. The exclusive *trans*-stereochemistry observed in **8** is explained by considering the thermodynamic equilibration of initially formed *syn*-intermediate **10** from **5**. The isolation of trace amount of **9** in this reaction substantiates the *syn*-intermediacy as primary intermediate which is further confirmed by the isolation of **25** from **21**. Formation of **25** suggests that wherever the *syn*-intermediate is thermodynamically more stable, it invariably undergoes further cyclization to geometrically well-placed enolate double bond. An interesting observation is made by isolating **9** as a major product from the PET activation of **5** using **PS-B**. Stabilization of **10** by ascorbic acid is suggested to be the plausible explanation for this unusual observation. Radicals produced by the reductive β-activation of α,β-unsaturated ketones follow well established radical cyclization rules which is exemplified by studying the reactions of **39** and **40**. Generality of these cyclizations is demonstrated from the PET reactions of **29**−**32**. Synthesis of **49**, an important structural framework of biologically active angularly fused triquinanes, from **48** is included in this study to demonstrate the varied applicability of this strategy.

Introduction

The concept that photoexcitation renders a well defined redox potential difference between an electron rich donor and an electron poor acceptor has been used extensively over the past two decades to initiate primary electron transfer processes[1] and to generate radical ions,[2,3] critical intermediates in the development of recent organic reactivity concept,[4,5] from neutral substrates. Several new and synthetically important organic photoreactions have been discovered[6] employing photosensitized electron transfer (PET) processes, though, the competitive back electron transfer (BET) and the strong influence of the nature of primary intermediates [*viz.* contact ion pair (CIP), solvent separated ion pair (SSIP) and free radical ion pair (FRIP)] on the reactivity profiles of radical ions have raised some restrictions in the designed application of PET reactions in organic synthesis. While partial solutions to retard the impact of BET are suggested,[7] the latter issue which is primarily the function of donor−acceptor redox properties have remained rather unmanipulable except to play with the solvent polarity. We envisaged that this problem could possibly be addressed if PET generated free radical ions, obviously possessing sufficiently large redox potential difference in comparison to other neutral substrates, are directed for initiating secondary dark ET reaction to produce another radical-ionic species, as the kinetics of ET in such cases would be governed differently than primary PET processes. This concept would be analogous to several photosynthetic model systems[8] and to molecular electronic devices,[9] though in this case the donor−acceptor pairs would be free and in diffused state.[10] The success of this attempt could easily be directed to activate substrates in photosensitized manner which otherwise is difficult to achieve by direct PET reactions. An

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(10) In photosynthetic model systems and molecular devices, the donor−acceptor pairs are generally held together in a rigid frame work.

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interesting concept termed "redox-photosensitization" has been made in this context to initiate sequential ET reactions for generating radical cations[11,12] (alkenes) as well as radical anions[11a,13] (aromatic carbonyls and alkenes) however, the reaction in the later case have generally been found to be terminated by the coupling of primary ED and secondary electron acceptors after initial proton reorganizations. Impending development of a suitable photosystem appears to be responsible for the unexplored avenues of radical-anion chemistry.[14,15] Thus, the design of a photosystem where PET generated primary radical anionic species could be utilized as potential one electron donors for promoting one electron reduction reactions would likely add a new dimension in the general area of organic synthetic methodology and PET chemistry in particular.[16] Furthermore, if the primary PET processes are triggered by the visible-light, this approach would stand superior for one electron reduction chemistry from energy as well as from the ecological view point as most of the known one electron reductants are toxic lanthanide salts.[17] We disclose herein the full details[18] of the development of two photosystems consisting of DCA (9,10-dicyanoanthracene) as visible-light harvesting electron acceptor and Ph_3P (triphenylphosphine) as sacrificial electron donor (**photosystem-A; PS-A**) and DMN (1,5-dimethoxynaphthalene) as primary electron donor, ascorbic acid as sacrificial electron donor (**photosystem-B; PS-B**), respectively, to drive one electron reductive β-activation of α,β-unsaturated ketones by secondary dark ET from $DCA^{\bullet-}$. Details of the concept, mechanism, and application for the cyclizations of enolate ketyl radicals to the tethered olefins form the part of this article.

Results and Discussion

Development of the Concept. Toward designing a photosystem for driving sequential ET reaction, our attention at first was drawn to our earlier photosystem, developed for carrying out primary PET oxidative reactions (Figure 1) from select donors.[19] This photosystem has utilized cyanoarenes (ArCN) as light harvesting electron acceptors. The photosensitization concept has relied on the thermodynamic feasibility of ET from $ArCN^{\bullet-}$ to O_2 followed by disproportionation of $O_2^{\bullet-}$ through water as shown in Figure 1. From the above mechanistic paradigm, it was visualized that a photosystem comprising of a sacrificial electron donor (ED) and ArCN, in deoxygenated

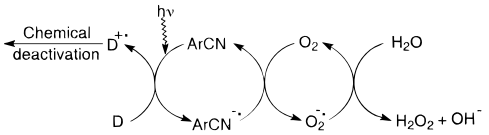

Figure 1.

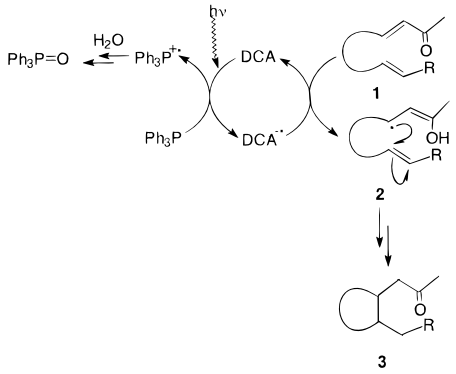

Figure 2.

atmosphere, should be able to drive a secondary ET from $ArCN^{\bullet-}$ to another molecule, provided the redox potentials are matched. For this purpose, we evaluated the utilization of Ph_3P as sacrificial electron donor and DCA as visible-light-harvesting electron acceptor (**PS-A**). The selection of Ph_3P as sacrificial ED was made owing to its established PET phenomena[20] with

$$Ph_3P \xrightarrow[-e]{^1DCA^*} Ph_3P^{\bullet+} \xrightarrow{H_2O} Ph_3P^{\bullet}-OH \xrightarrow{-e} Ph_3P^{+}-OH \xrightarrow{-H^+} Ph_3P{=}O \quad (1)$$

$^1ArCN^*$ and efficient transformation of the resultant $Ph_3P^{\bullet+}$ to chemically as well as photochemically stable $Ph_3P{=}O$ by the reaction of water (eq 1). The efficient transformation of $Ph_3P^{\bullet+}$ to $Ph_3P{=}O$ (*cf.* eq 1) was also perceived as an additional advantage as it would help in controlling the impact of BET, the intrinsic limitation of PET processes.[7] Since the transformation of Ph_3P to $Ph_3P{=}O$ is a sequential two electron process (eq 1), Ph_3P can provide two successive electrons for the reduction. α,β-Unsaturated ketones like **1** were selected as secondary electron acceptors due to their suitability for testing our concept as upon acceptance of an electron this functionality would activate its β-position as carbon centered radical,[21] in contrast to general perception that enones are good free radical acceptors,[22] which would cyclize to tethered olefin to give 1,2-disubstituted cycloalkanoids (Figure 2).

The design of the photosystem for this purpose began by evaluating the feasibility of ET from $DCA^{\bullet-}$ to **1** by estimating the Gibb's free energy change (ΔG_{et}) by utilizing the values of redox potentials of $DCA^{\bullet-}$ (-0.89 eV)[6d] and **1** (-0.4 to -0.76 eV), respectively, in eq 2. The $E_{1/2red}$ of **1** were obtained by cyclic voltammetry experiments [for details see Experimental

$$\Delta G_{et} = E_{1/2(ox)} - E_{1/2(red)} \quad (2)$$

where, $E_{1/2(ox)}$ = oxidation potential of electron donor and $E_{1/2(red)}$ = reduction potential of electron acceptor

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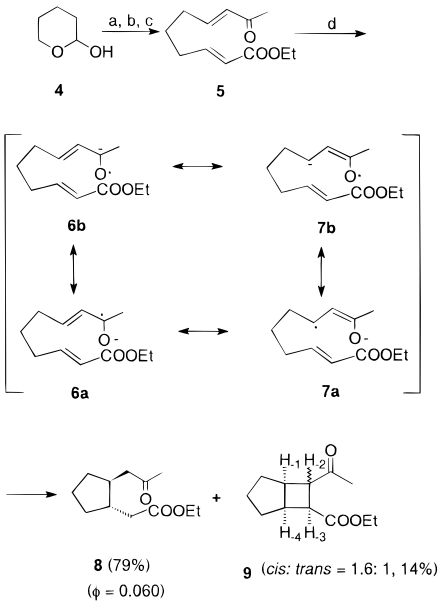
Scheme 1[a]



[a] Reagents: (a) $Ph_3P{=}CHCOOEt$, CH_2Cl_2, room temperature, 2 days, 83%; (b) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, −78 °C, 100%; (c) $Ph_3P{=}CHCOCH_3$, CH_2Cl_2, room temperature, 1 day, 90%; (d) $h\nu$ (λ = 405 nm), DCA, Ph_3P, 18 h.

Section]. Substituting eq 2 with the appropriate values of $E_{1/2ox}$ and $E_{1/2red}$, an endothermic value of −3.0 to −11.29 kcal mol^{-1} were obtained. The exergonic value of −23.29 kcal mol^{-1} for radical-ion generation between Ph_3P and ^{1}DCA* has already been established from our previous[20] study.

PET Activation of 5. To evaluate the suitability of **PS-A** (Figure 2) for promoting sequential ET reaction, one electron reductive activation of **5** was initiated. It was envisioned that α,β-unsaturated ketone moiety of **5** upon accepting an electron from DCA$^{\bullet-}$ would generate a radical center at its β-position (**7a**) which would immediately add to the tethered olefinic functionality and following the radical termination step by H-abstraction, a cyclic product (**8**) would result. From the general organic chemistry understanding, the coupling between both the β-carbons of α,β-unsaturated ketone and α,β-unsaturated ester of **5** would be considered an uphill task as these carbon atoms possess partial positive (δ+ve) charge. However, upon acceptance of an electron from DCA$^{\bullet-}$ the polarity of the α,β-unsaturated ketone moiety of **5** should get reversed easily and the resultant enolate ketyl radical, owing to its nucleophilic character, would easily, add to activated alkenes. It may be imperative to mention at this stage that cathodic activation of ketones to their corresponding ketyl radicals and their cyclizations with arenes as well as alkenes are reported by Shono *et al.*[23] PET activation of **5** involved irradiation (λ = 405 nm) of a solution of **5** (1.19 mmol) containing Ph_3P (0.724 mmol) and DCA (0.24 mmol) in DMF:*i*-PrOH:H_2O (300 mL, 88:10:2).[24] The *i*-PrOH was used as a hydrogen donor. The 405 nm wavelength light was obtained by utilizing $CuSO_4{\cdot}5H_2O$:NH_3 solution filter[25] from 450-W Hanovia medium pressure mercury lamp. All the light under this experimental setup was absorbed by DCA only. Before irradiation, solution was deoxygenated by bubbling argon for 2 h. After 18 h of irradiation, when **5** was almost consumed (98%, monitored by GC), solvents were removed under vacuo, and the concentrate was purified by silica gel column chromatography using petroleum−ether/EtOAc as eluent, to give the expected cyclized product **8** (79%) and another minor product **9** (14%).[26] DCA was recovered quantitatively (98%) during the purification of the reaction mixture. $Ph_3P{=}O$ was isolated (96%) as a crystalline solid. Product **8** was characterized by detailed ^{1}H NMR and ^{13}C NMR analysis and also by comparing it with authentic sample of **8** prepared by following the Enholm's reaction procedure.[27] The quantum yield for the formation of **8** (ϕ = 0.06) clearly indicates that its formation does not involve radical chain reaction.

The minor product **9** was found to be a mixture of two isomers in the ratio of 1.6:1, determined by capillary GC analysis. The pure diastereomers could be resolved by careful column chromatography. The ^{1}H NMR of the cyclobutane part of *trans*-**9** displayed *H-*$_2$ at δ 3.62 as doublet of doublet (J = 8.7, 8.2 Hz), whereas *H-*$_1$ and *H-*$_3$ were noticed at δ 3.08 as multiplet. *H-*$_4$ appeared at δ 2.88 as doublet of doublet (J = 13.2, 8.2 Hz). These spectral assignments were made by detailed ^{1}H NMR COSY experiment. Similarly, in the ^{13}C NMR, the four methine carbons appeared at δ 47.40, 40.23, 39.99, 38.54 [for detailed spectral data see experimental section]. The ^{1}H NMR of the cyclobutane part of corresponding *cis*-isomer of **9** displayed a multiplet at δ 2.95 integrating to three protons and a doublet of doublet at δ 2.83 (J = 9.8, 4.9 Hz) corresponding to single proton. In the ^{13}C NMR, four methine carbons appeared at δ 50.66, 43.65, 39.05, 38.66. *Cis*-**9** could be isomerized (60%) to thermodynamically stable *trans*-**9** by stirring with DBU in dry THF at room temperature for 20 h.

Stereochemical and Mechanistic Interpretations for the Formation of 8. The observed *anti*-stereochemistry of **8** appeared to be in marked contrast to the general trend of *syn*-stereochemistry expected in 5-hexenyl radical cyclizations. Beckwith's model[28] also suggested that under kinetic control, cyclization of intermediate **7a** should have given cyclized compound with *syn*-appendages (**15**). Thus it may be postulated that the initially produced *syn*-intermediate (**10**) is less stable and it gets transformed to the thermodynamically more stable *anti*-intermediate (**11**) due to resonance stabilization of the enolate ketyl radical as shown in Scheme 2. Thermodynamic control in radical cyclizations is known in literature,[22,29] though, the examples pertaining to this observation have involved formation of six-membered rings only.

The possible formation of **8**, *via* a route involving Michael type addition of resonance structure **7b**, may be ruled out as Russel's group,[21a,c] through the ESR spectra of electrochemically generated radical anions of enones without having acidic hydrogens, have suggested that most of the hyperfine splitting is located on the β-carbon.[21a] This is further supported by the Hückel-spin density calculations which have indicated that at least 50% of the radical density is located on the β- carbon as shown in the resonance contributor **7a**, while the remaining 50% is divided equally between the carbonyl carbon and oxygen as in **6a**.[21a] Thus, it may be argued that the possible contribution of Michael type addition of radical anion (**7b**) to electron deficient olefin during the formation of **8** is very much reduced. Furthermore, if **7b** is to be considered as an alternative valence structure, it is likely to produce reduced product also in

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(24) DMF as solvent was mainly used due to the poor solubility of DCA in other solvents. The reaction can also be performed in CH_3CN, but reaction times are longer due the poor solubility of DCA.

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(26) Product **9** was wrongly assigned as a *cis*-isomer of **8** in our preliminary communication (ref 18). Lapse on our part is highly regretted.

(27) Enholm, E. J.; Kinter, K. S. *J. Org. Chem.* **1995**, *60*, 4850.

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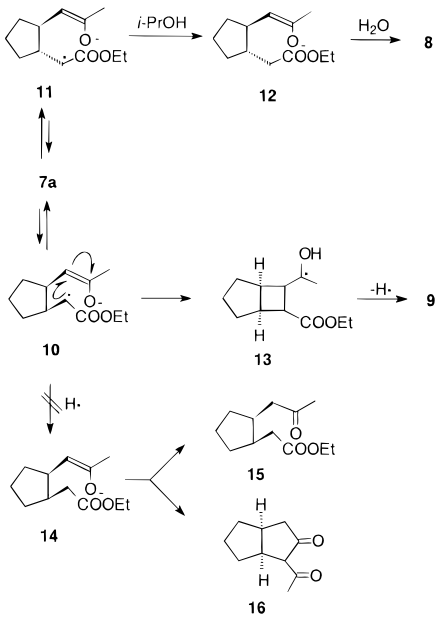
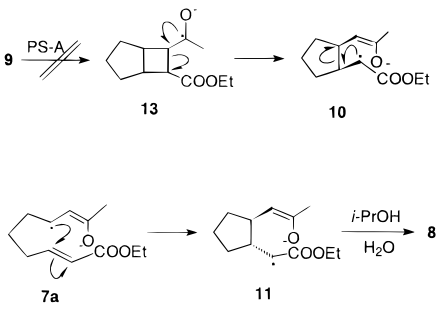
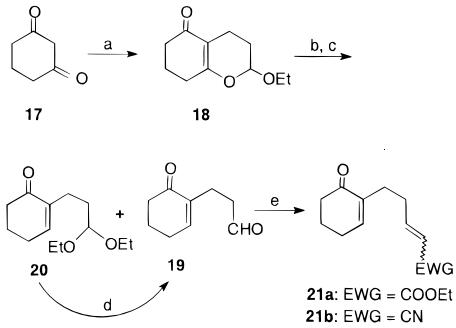
Scheme 2



Scheme 3



Scheme 4[a]



[a] Reagents: (a) (i) CH_2:CHCHO, EtOH, KOH (catalyst), reflux 3 h; (ii) concentrated HCl, room temperature, 2 h, 64%; (b) LAH, Et_2O, 0 °C, 30 min; (c) EtOH, 5% aqueous HCl, room temperature, 1 h; 84%; (d) aqueous HCl, $(CH_3)_2CO$; (e) when EWG = COOEt; Ph_3P═CHCOOEt, CH_2Cl_2, room temperature, 1 day; 85% (*E*-isomer); when EWG = CN; Ph_3P═CHCN,CH_2Cl_2, room temperature, 1 day, 95% (*E*:*Z* = 62:38).

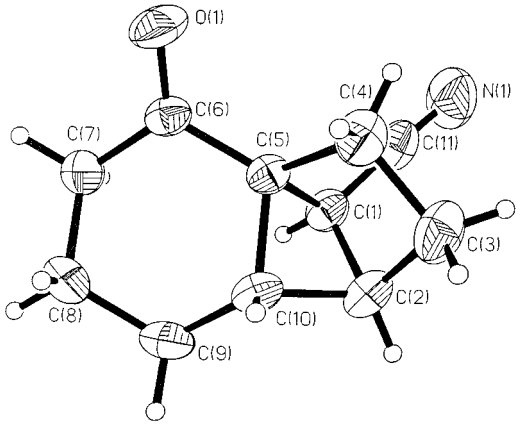


Figure 3. ORTEP diagram of compound **25b**.

competition with cyclization due to the faster rate of protonation of carbanion in aqueous environment. However, our experiments indicate the complete absence of enone reduced product. Therefore, the formation of **8** could be suggested to be arising by involving the radical intermediate **7a**.

In order to provide exclusive evidence to this effect, deuterium labeling experiment by irradiating **5** in a mixture of DMF:*i*-PrOH-d_8:H_2O was also carried out. The ^{1}H NMR of the corresponding product (**8**) indicated deuterium incorporation at α-to ester moiety. The exact deuterium incorporation was estimated to be 72% by GC/MS. Another possibility[30] for the formation of **8** by further PET reaction of **9** (Scheme 3) could also be ruled out from a controlled PET activation experiment of **5** where the ratios of **8** and **9** remained same throughout the entire period of irradiation. Further support to this aspect is obtained by irradiating **9** independently, under identical PET activation conditions as discussed for **5**, showed negligible conversion to **8**.

Mechanism for the Formation of 9. The formation of **9** in this reaction was quite intriguing to us. Its formation by the intramolecular [2 + 2]-cycloaddition reaction of excited enone moiety with the tethered alkene can easily be ruled out as **5** does not absorb light under the present experimental conditions. Therefore, the plausible route for the formation of **9** is likely to be by the efficient cyclization of electrophilic radical of *syn*-intermediate **10** to electron rich enolate double bond[31] due to their geometric proximity. This could be possible only if the rate of termination of radical species in the intermediate **10** by H-abstraction is slower than its further cyclization to enolate double bond.

To provide evidence that the cyclization of **7a** initially produced *syn*-intermediate (**10**) that underwent further cyclization to enolate double bond to produce **9**, in competition with its thermodynamically equilibrated *anti*-intermediate (**11**), the cyclization of **21**(**a** and **b**) were considered. It was envisaged that the corresponding enolate ketyl radicals from **21** would produce only *cis*-cyclized product (**24**), as its reversal to corresponding *anti*-intermediate would be energetically unfavorable. Substrates **21** were prepared by Wittig olefination of **19** in 85−95% yield by following the reaction sequences as depicted in Scheme 4.

Usual PET activation of **21**, produced only tricyclic products **25** (72−84%), presumably formed by further cyclization of the radical moiety to the enolate double bond (**23**). These products were characterized by ^{1}H NMR, ^{13}C NMR, and mass spectral analysis. The tricyclic structure of **25** was unequivocally confirmed by the X-ray crystal structure of **25b** (Figure 3). **25a** was found to be thick liquid which could not be crystallized. This observation suggests that wherever *syn*-cyclized intermediates (e.g., **23**) are thermodynamically more stable, they would invariably undergo further cyclizations to the geometrically favorably placed enolate double bond to produce a double cyclized product before they can get terminated by the intermolecular H-abstraction. Our attempt to arrest the *syn*-monocyclized product (**15** and **24**) from both **5** as well as **21** by using better H-donor (e.g., *t*-BuSH) or increasing the percentage of *i*-PrOH in the reaction mixture, however, failed.

(30) Mattay, J.; Bannioy, A.; Bischof, E. W.; Heidbreder, A.; Runsik, J. *Chem. Ber.* **1992**, *125*, 2119.

(31) Schmittel, M. *Top. Curr. Chem.* **1994**, *169*, 183.

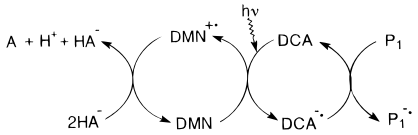
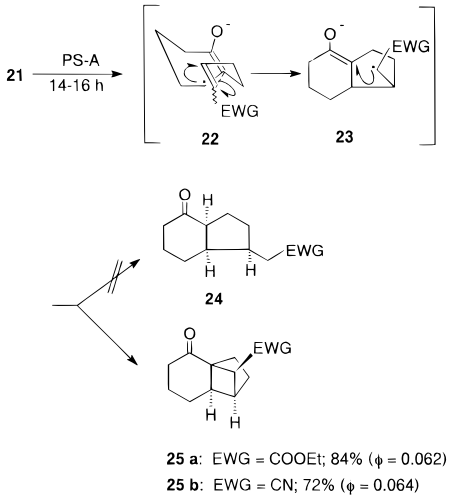
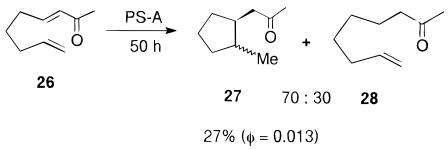


Figure 4. Abbreviations: HA^- = ascorbate ion; P_1 = unsaturated carbonyl compounds.

Scheme 5



Scheme 6



Electronic Behavior of Enolate Ketyl Radicals. To elucidate the electronic nature of the enolate ketyl radicals, generated by the PET activation of α,β-unsaturated ketones, their cyclization behavior with non-activated tethered olefin were also included in our study. In this context, substrate **26** was selected as a model compound which could be obtained (82%) by direct Wittig reaction of 5-hexenal with 1-triphenylphosphoranylidene-2-propanone. PET reductive activation of **26** produced cyclized product **27** (27%) alongwith reduced product **28** (not isolated, characterized by monitoring identical retention time in GC when coinjected with authentic compound[32]). The poor efficiency observed during the cyclization of **26** indicates moderate nucleophilic character of the enolate ketyl radicals. Therefore, it is apparent that for efficient cyclizations such species would require activated olefins.

An Alternative Photosystem. Although, the photosystem-A as shown in Figure 2 represented the success of our basic concept of harvesting photons into electrons and its utilization for triggering one electron reductive β-activation of α,β-unsaturated ketones for radical reactions, we realized that this photosystem may not be considered ideal, owing to the constant build up of $Ph_3P{=}O$. Our zest to design a better photosystem that could have wider acceptability as a synthetic methodology, an alternative photosystem (photosystem-B, **PS-B**) consisting of DCA as visible-light absorbing electron acceptor as usual, DMN as primary electron donor, and ascorbic acid as sacrificial electron donor, was considered. The concept in designing this improved photosystem (Figure 4) was also based on the thermodynamic feasibility of ET between each interacting partners. To establish the PET phenomenon between DMN and ^{1}DCA*, first the fluorescence quenching of DCA (λ_{ex}= 430 nm, λ_{em}= 461 nm) was studied at varying concentrations of DMN which obeyed the Stern−Volmer relation. From the slope of the straight line and singlet lifetime (τ =19.6 ns)[33] of DCA, the quenching rate constant ($K_q = 1.27 \times 10^{10}$ n^{-1} s^{-1}) was calculated and was found to be near diffusion. Excitation and absorption spectra of DCA remained unaffected in the presence of the maximum concentration of DMN. No exciplex emission was noticed in either polar or nonpolar solvents. It was, therefore, reasonable to assume that fluorescence quenching in this case took place *via* a charge transfer (CT) stabilized exciplex. To provide further evidence of PET generation of radical-ion pairs between DMN and ^{1}DCA*, negative free energy change (ΔG_{et}) was also calculated by using Weller[34] equation (eq 3). Substituting eq 3 with appropriate values of

$$\Delta G_{et} = E_{1/2(ox)} - E_{1/2(red)} - E_{0,0} \qquad (3)$$

where $E_{1/2(ox)}$ = oxidation potential of DMN, $E_{1/2(red)}$ = reduction potential of ^{1}DCA*, and $E_{0,0}$ = excitation energy of DCA

oxidation potential of DMN (1.28 eV),[15] reduction potential of ^{1}DCA* (−0.89 eV),[6d] and excitation energy of DCA (2.88 eV),[6d] an exergonic value of −16.37 kcal mol^{-1} was obtained (Table 1). Similarly, ET feasibility from the ascorbic acid to $DMN^{\bullet+}$ was also evaluated by estimating the ΔG_{et} (−4.5 kcal mol^{-1}) employing eq 2. The $E_{1/2(ox)}$ of ascorbic acid (1.084 eV *vs* SCE) was estimated by cyclic voltametry.[14] The oxidative transformation of ascorbate ion to the dehydroascorbic acid and proton as shown in Figure 4 is precedented from the literature report.[35]

In order to test the viability of **PS-B** for triggering sequential ET processes, PET reductive reaction of **5** was once again undertaken. Usual irradiation (405 nm) of a mixture consisting of **5** (1.19 mmol), DCA (0.24 mmol), DMN (0.18 mmol), and ascorbic acid (3.1 mmol) in DMF:*i*-PrOH:H_2O (88:10:2) gave, to our great surprise, **9** (70%) as a major product albeit small amount of **8** (<20%) was also noticed. DCA and DMN both were recovered unchanged from the reaction mixture.

In order to pinpoint either DMN or ascorbic acid responsible for producing **9** in this experiment, a controlled irradiation[36] experiment using a stoichiometric amount of DMN to **5** and without ascorbic acid was performed which indicated the similar ratio (3.2:1) of **8** and **9** as obtained earlier using **PS-A**, though the combined chemical yields were found to be much reduced (40%). During this experiment, fast degradation of DMN to the mixtures of products (not more than 5% each) were observed. Although, none of the products could be isolated in sufficiently pure form, based on the ^{1}H NMR spectra of at least two isolated products, incorporation of isopropoxy as well as 2-hydroxyisopropyl moiety in the DMN may be suggested. The former product could be considered to arise by the nucleophilic addition of *i*-PrOH to $DMN^{\bullet+}$, while the formation of the later could be explained by the coupling of $DMN^{\bullet+}$ with 2-hydroxyisopropyl radical, produced after the $H^{\bullet}$ donation to terminate intermediate **11**. This observation further supports the involvement of radicaloid intermediate of type **7a**, during the PET activation of **5**. This experiment suggests that ascorbic acid is definitely playing a role in the formation of **9**. To rule out the possibility of ascorbic acid changing the UV spectral pattern

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(36) Care was taken so that under this experimental conditions the light was absorbed completely by DCA only.

Table 1. Free Energy Change (ΔG_{et}) for Electron Transfer Processes

donor	acceptor	$E_{1/2ox}$ [eV *vs* SCE]	$E_{1/2red}$ [eV *vs* SCE]	$E_{(0,0)}$ [eV]	ΔG_{et} [kcal mol^{-1}]
Ph_3P	^{1}DCA*	0.98[a]	-0.89[b]	2.88[b]	-23.29[a]
DMN	^{1}DCA*	1.28[c]	−0.89[b]	2.88[b]	−16.37[f]
ascorbic acid	$DMN^{\bullet+}$	1.084[d]	1.28[c]		−4.5[g]
$DCA^{\bullet-}$	**5**	−0.89[b]	−0.40[e]		−11.29[g]
$DCA^{\bullet-}$	**21a**	−0.89[b]	−0.41[e]		−11.07[g]
$DCA^{\bullet-}$	**21b**	−0.89[b]	−0.43[e]		−10.60[g]
$DCA^{\bullet-}$	**26**	−0.89[b]	−0.76[e]		−3.0[g]
$DCA^{\bullet-}$	**29**	−0.89[b]	−0.68[e]		−4.84[g]
$DCA^{\bullet-}$	**30**	−0.89[b]	−0.45[e]		−10.14[g]
$DCA^{\bullet-}$	**31**	−0.89[b]	−0.73[e]		−3.69[g]
$DCA^{\bullet-}$	**32**	−0.89[b]	−0.42[e]		−10.84[g]

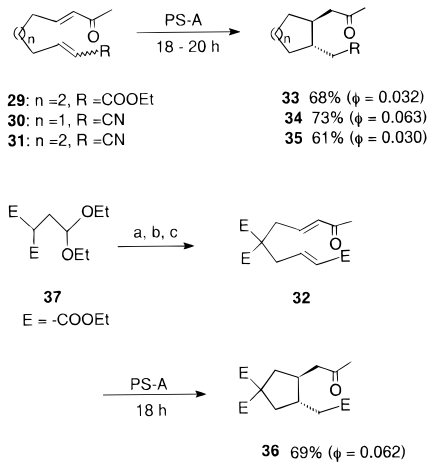
[a−d] Values have been taken from literature.[20,6d,15,14] [e] Measured by cyclic voltametry experiment. Since the observed cyclic voltammograms were irreversible; therefore, the point of inclinations are considered as the reduction potentials[37] [$E_{1/2(red)}$] values which are approximate. The experimentally measured $E_{1/2(red)}$ values were changed[37] to standard calomel electrode (SCE) by adding −0.045 to the values obtained using Ag/AgCl. These free energy change (ΔG_{et}) values are not the absolute; they may be considered approximate. [f] Calculated from Weller equation.[34] [g] Calculated from the equation $\Delta G_{et} = E_{1/2(ox)} - E_{1/2(red)}$.

of the mixtures of DMN-DCA-**5**, detailed spectral analysis of the mixture at varying concentrations of ascorbic acid were also carried out which showed no significant change in UV spectral behavior. Although at this stage we are not sure about the exact mechanistic role of the ascorbic acid for the formation of **9** in the above reaction, it appears that ascorbic acid is somehow stabilizing the *syn*-intermediate (**10**) that retards the equilibration toward the thermodynamically stable *anti*-isomer (**8**). Further studies in this direction are in progress.

Generality: Further Evaluation of PS-A. From the above observations it is clear that the choice of getting monocyclized product from the substrates of type **5** is feasible only by using **PS-A** (Figure 2). To establish the generality of the reaction, substrates **29**−**32** were irradiated in the identical manner as described for **5**, where major cyclized products **33**−**36** (61−73%) were isolated. Although minor products in each case were noticed, enough effort was not made to isolate them for spectral characterizations. It may be important to mention here that the feasibility of ET from $DCA^{\bullet-}$ to all substrates (**5, 21a,b, 26, 29**−**32**) were established by calculating the ΔG_{et} values and are provided in Table 1. Substrates **29**−**31** were obtained by following the identical reaction sequences as of **5** starting with appropriate starting materials. Substrate **32** was, however, prepared starting from ethyl-2-carbethoxy-4,4-diethoxy butanoate (**37**) in three steps (Scheme 7).

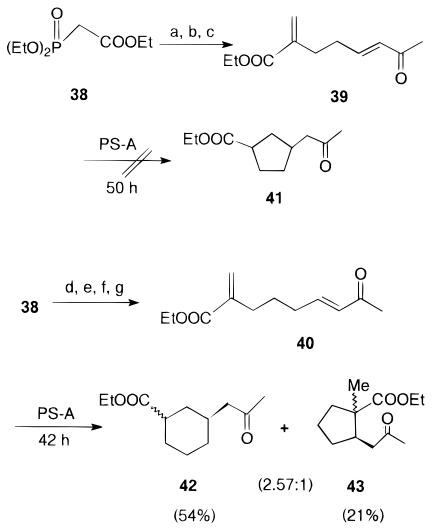
Tests for the Radical Cyclization Rules. From the above examples it is apparent that these cyclizations follow the well established 5- and 6-*exo-trig* radical cyclization rules.[28] However, to examine whether such cyclizations could be forced to undergo 5-*endo-trig* cyclization, substrate **39** was designed as in this substrate the 5-*endo* position is highly activated. The usual PET activation of **39** did not show any evidence for the formation of corresponding cyclized product **41** albeit unidentified mixtures of products were noticed. This observation was not very surprising to us as Baldwin's cyclization rule[38] prohibits such types of cyclizations from occurring. In contrast to the above observation, when compound **40** was activated, cyclization product **42** (nonseparable mixture of two isomers in 3:2 ratio, 54%) along with a minor amount of the 5-*exo-trig* product

Scheme 7[a]



[a] Reagents: (a) NaH/THF, $BrCH_2CH{:}CHCOOEt$, 50 °C, 78%; (b) 5% HCl, CH_3COCH_3, room temperature, 5 min; (c) $Ph_3P{=}CHCOCH_3$, CH_2Cl_2, room temperature, 1 day, 88%.

Scheme 8[a]



[a] Reagents: (a) (i) NaH, $ICH2CH2CH(OCH_2)_2$, C_6H_6, reflux, 8 h; (ii) NaH, $(CH_2O)n$, room temperature, overnight, 55%; (b) 5% HCl, CH_3COCH_3, 5 min; (c) $Ph_3P{=}CHCOCH_3$, CH_2Cl_2, room temperature, 1 day, 85%; (d) (i) NaH, $I(CH_2)_4OTBDMS$, C_6H_6, reflux, 9 h; (ii) NaH, $(CH_2O)n$, room temperature, overnight, 54%; (e) TBAF, THF, 0 °C, 95%; (f) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, −78 °C; (g) $Ph_3P{=}CHCOCH_3$, CH_2Cl_2, room temperature, 1 day, 91%.

43 (21%) were isolated. These experiments indicate that the enolate ketyl radicals, generated from the reductive activation of α,*β*-unsaturated ketones, follow the general rules of radical cyclization reactions.

Application for the Construction of 1-(2--oxopropyl)-2-carbothoxymethyl-bicyclo-[3.3.0]-octane. Now that it was established that the enolate ketyl radical could be effectively generated by sequential PET reactions of α,*β*-unsaturated ketones and that they efficiently undergo intramolecular cyclizations with activated olefins following radical cyclization rules, we directed our attention to extend this methodology for the construction of 1,2-disubstituted bicyclo[3.3.0]octanes framework[39] as these skeletons are present in many biologically active molecules.[40] Toward this endeavor, we designed compound **48** as a precursor which was prepared in five steps starting from **44** (Scheme 9). PET reductive activation of **48**, using **PS-A**,

(37) Bard, A. J.; Faulkner, L. R. *Electrochemical Methods: Fundamentals and Applications;* John Wiley & Sons, Inc.: 1980.
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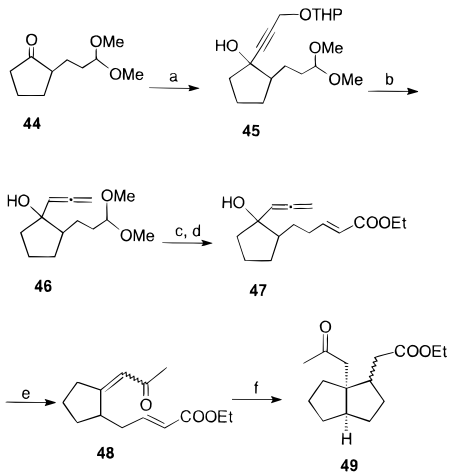
(39) (a) Paquette, L. A.; Meister, P. G.; Friendrich, D.; Sauer, D. R. *J. Am. Chem. Soc.* **1993**, *115*, 49. (b) Rowley, E. G.; Schore, N. E. *J. Org. Chem.* **1992**, *57*, 6853.

Scheme 9[a]



[a] Reagents: (a) $BrMgC{:}CCH_2OTHP$, THF, room temperature, 82%; (b) LAH, Et_2O, room temperature, 90%; (c) 5% HCl, CH_3COCH_3, room temperature, 2 min; (d) $Ph_3P{=}CHCOOEt$, CH_2Cl_2, room temperature, 48%; (e) aqueous 5% H_2SO_4, 50% AcOH, 80 °C, 3 min, 64%; (f) **PS-A**, 16 h, 61%.

gave **49** (61%) as a major product. A minor product could not be isolated in pure form. **49** was characterized on the basis of satisfactory spectral data.

In conclusion, we have developed a conceptually new strategy to drive sequential electron transfer processes, promoted by visible light, to trigger one electron reductive β-activation of α,β-unsaturated ketones to produce carbon centered radical precursor. The cyclization of such radicals to tethered activated olefins are shown to be very efficient and stereoselective. The 1,2-*anti*-stereochemistry observed in the cyclized products are demonstrated to originate from the thermodynamic equilibration of kinetically favored *syn*-intermediates. The application of these photosystems is expected to add a new dimension in generating radical anionic species from a variety of functionalities to study unexplored and interesting chemistry. Moreover, this strategy would be advantageous from an ecological view point.

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 both temperatures unless otherwise stated. Solvents and anhydrous liquid reagents were dried according to established procedures by distillation under argon from an appropriate drying agent. Reagents were procured from Aldrich, U.S.A. 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, methyl silicon and phenyl silicon 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 using $CDCl_3$ as solvent. 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 Mattsion RS-1 or Perkin Elmer 599B. Mass spectra were obtained at a voltage of 70 eV Finnigan MAT-1020B instrument. GC/MS was done using Shimadzu GCMS-QP2000A. HPLC analysis was performed on Perkin Elmer (Model 250 Binary LC Pump along with LC 135C Diode Array Detector) liquid chromatograph using reverse phase C_8 column, eluting with $CH_3CN{:}H_2O$ solvent mixture degassed by thaw cycle procedure. Melting points (mp) were measured by YANACO melting point apparatus and were uncorrected.

Fluorescence spectra were recorded on Spex-Fluorolog 212 spectrofluorimeter. The excitation and emission slit widths were maintained at 0.5 mm. The steady state emission spectral measurements were carried out using a 1 cm × 1 cm quartz cell. A right angle configuration for the cell holder was utilized during the measurement of excitation and emission spectra.

Cyclic Voltammetry. The reduction potential of compounds **5**, **21 (a** and **b)**, **26,** and **29**−**32** were measured by cyclic experiments were carried out with a three electrode assembly on a Bioanalytical systems, Model CV-27. The cell consisted of a Pt inlay working electrode, Ag/AgCl reference electrode, and Pt wire as auxiliary electrode. Tetraethylammonium perchlorate was used as a supporting electrolyte in DMF solution. Before each experiment, the solution was deoxygenated by bubbling argon for 10 min The observed cyclic voltammograms were irreversible, and, therefore, the point of inclinations are considered[37] as the reduction potentials [$E_{1/2(red)}$] values which are approximate. The obtained $E_{1/2(red)}$ values were changed[37] with respect to SCE by adding −0.045.

Fluorescence Quenching of DCA. Quenching of DCA fluorescence was carried out by using DMN as quencher. For the determination of Stern−Volmer constant (K_q), the intensity (I_0) of steady state fluorescence at the maximum emission wavelength (λ_{em}) 461 nm was measured from a DCA solution (3×10^{-4} M) in DMF at 25 °C, keeping the excitation wavelength (λ_{ex}) at 430 nm. Subsequently, the fluorescence quenching intensity (I) was measured as a function of concentration [C] of DMN in the range of 6.04×10^{-4} to 15.1×10^{-3} M. A linear plot obtained on the basis of the following equation from which the slope was determined by least square fit

$$\frac{I}{I_0} = 1 + K_q\tau[C]$$

where I_0 denotes the fluorescence intensity in the absence of the quencher (DMN).

Quantum Yield Measurements. The samples, prepared by pipetting out quantitative volume (4 mL) from the stock solution of respective enones [**5, 21a** and **b, 26, 29**−**32**], Ph_3P (0.6 equiv), and DCA (20 mol % of enones) in DMF:*i*-PrOH:H_2O (88:10:2), were irradiated in Applied Photophysics Quantum Yield reactor (Model QYR-20) using 200 W mercury lamp at 405 nm light. For the isolation of monochromatic 405 nm light, a filter solution[25] of $CuSO_4{\cdot}5H_2O{:}NH_3$ was kept in the middle chamber of light filtration chamber placed between the UV source and the sample cells.

Irradiations were carried out for a short period (2−3 h) to bring about 8−12% of conversion. Quantitative formation of cyclized products were estimated by HPLC (Perkin Elmer 135C, Diode-array detector; C_8-reversed phase column) using $CH_3CN{:}H_2O$ as eluent.

Uranyloxalate actinometer was used to measure the intensity of light.[41] This actinometer was prepared by dissolving uranyl nitrate (1.2782 g, 10 mmol) and oxalic acid (1.6056 g, 5 mmol) in 250 mL of H_2O. Uranyl oxalate solution (4 mL) was irradiated in the above mentioned quantum yield reactor for 1 h. Two milliliters each of the actinometer solution before and after irradiation was titrated by known concentration of $KMnO_4$ (0.0306 M) which was previously standardized by standard sodium oxalate solution (0.0988 N). Intensity of the light (I) was measured by the following equation

$$I = \frac{X_{eq} \times AN}{2 \times \phi_{Ac} \times t}$$

where $X_{eq} = \Delta$ mL (N_{KMnO_4}) (vol_{irr}/vol_{titra}) $\times 10^{-3}$; Δ mL = vol of $KMnO_{4unirrad}$ − vol of $KMnO_{4\ irrad}$ and AN = Avogadro's number.

Substituting the values of Δ mL = 0.4, $N_{KMnO4} = 0.0306$. AN = 6.023×10^{23}, vol-irr = 4 mL, vol-titr = 2 mL, ϕ_{Ac} = quantum yield for disappearance of uranyl oxalate = 0.563 at 405 nm, t = 1 h, the I value was found to be 0.28×10^{16} photons/s.

(40) (a) Niu, L.; Dai, J.; Wan, Z.; Liang, D.; Wu, Z.; Zao, Z.; Long, K. *Sci. Sin* **1986**, *29B*, 40. (b) Seto, H.; Yonehara, H. *J. Antibiot.* **1980**, *33*, 92. (c) Bohlmann, F.; Jakupovic, J. *Phytochemistry* **1980**, *19*, 259.

(41) Murov, S. L. *Hand Book Of Photochemistry*; Marcel Dekker: New York, 1973; p 124.

The quantum yields for product formation were obtained by utilizing the following

$$\phi = \frac{C \times P \times V \times \mathrm{AN}}{I \times t}$$

where C = concentration of compound; P = % of formation of cyclized product; V = volume of solution pipetted out for irradiation; AN = Avogadro's number; I = light intensity; and t = time of irradiation.

X-ray Crystal and Intensity Data. A colorless crystal of size 0.15 × 0.15 × 0.15 mm of compound **25b** was mounted and aligned on a Siemens R3m/v diffractometer. Crystal data: a = 6.430 (1) è, b = 16.119 (2) è, c = 9.118 (1) è, β = 93.53 (1)°; space group $P2(1)/n$, V = 943.2 (8) è^3, Z = 4, density (calc) = 1.234 mg/m^3. Intensity data in the 2θ range of 3.0−50.0° were collected using ω scan with MoKα radiation (λ = 0.71073 è). A total of 1904 independent reflections were collected of which 1333 had $I \geq 3\sigma$ (I).

All crystallographic calculations were carried out with the aid of the SHELXTL Plus program package. The positional anisotropic thermal parameters were refined for all non-hydrogen atoms. Riding model with fixed isotropic U was used for hydrogen atoms. For the observed data final R = 5.4%, wR = 6.2%, and goodness-of-fit = 1.3.

HRMS Analysis. Mass spectra were taken on a VG Autospec-M mass spectrometer with Opus V3. IX software. Samples were introduced through a gas chromatograph equipped with HP-5 fused silica capillary column of 30 M length, 0.32 mm id, and 0.25 μm film thickness: injector temperature: 280 °C; transferline temperature: 250 °C; oven temperature; initial 100 °C; initial time 5 min; rate of heating 10 °C/min, final temperature 220 °C. Accurate mass measurement was done at 5000 RP, and PFK was used as the internal reference.

Some of the compounds (**8, 9, 33, 36, 43,** and **49**) did not give intense molecular ion peaks. Hence, mass measurement has been done on the first intense fragmentation from the $M^{\bullet+}$.

General Photoirradiation Procedure. All irradiations were performed in a specially designed photoreactor which consisted of three chambers. The first and outer chamber contained irradiation solution, and the second one was charged with $CuSO_4 \cdot 5H_2O$:NH_3 filter solution.[25] The 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 (20 mol %) was dissolved in DMF:*i*-PrOH:H_2O (88:10:2) in a RB flask by stirring for about 2 h. Enone substrate and Ph_3P (0.6 equiv) or DMN (15 mol %) and ascorbic acid (2.6 equiv) were introduced to the solution and stirred for an additional 5 min The resultant mixture was transferred into the outer chamber of the photoreactor, deoxygenated by bubbling argon for 2 h, and properly sealed. Irradiation was performed with light (405 nm) of 450 W Hanovia medium pressure lamp obtained by using $CuSO_4 \cdot 5H_2O$:NH_3 filter solution.[25] The progress of the reaction was monitored by and GC. After 14−20 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 9-Oxo-7(*E*),2(*E*)-decadienoate (5). Compound (**5**) was synthesized in three steps as described below. (a) *Preparation of Ethyl 7-hydroxy-2(E)-heptenoate.* To a previously dried 100 mL round bottom (RB) flask was added ethyl(triphenylphosphoranylidene) acetate (11.2 g, 32.1 mmol) and 60 mL of CH_2Cl_2 followed by 2-hydroxypyran (**4**, 2.4 g, 23.5 mmol) under argon atmosphere. The reaction mixture was allowed to stir at room temperature for 2 days. 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 mixed solvent. The combined filtrate was concentrated in vacuo, and the mixture was separated by column chromatography on silica gel using petroleum ether:EtOAc (5:1) as eluent to yield 3.36 g (83%) of ethyl-7-hydroxy-2-(*E*)-heptenoate 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}.

(b) Ethyl-7-oxo-2(*E*)-heptenoate. Into a two necked 100-mL RB flask oxalyl chloride (0.95 mL, 11 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 above alcohol (1.2 g, 7 mmol) in CH_2Cl_2 (10 mL) was added over about 5 min. Stirring was continued for an additional 1.5 h at −78 °C. Et_3N (4.85 mL, 34.8 mmol) in CH_2Cl_2 (5 mL) was added dropwise. After allowing the reaction mixture to warm to room temperature, it was quenched with water (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 water (5 × 30 mL) and saturated brine solution, dried over Na_2SO_4, and concentrated in vacuo. The crude aldehyde (1.2 g, 100%) was used as such for Wittig reaction: 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}.

Preparation of Ethyl 9-Oxo-7(*E*),2(*E*)-decadienoate (*5*). 1-Triphenyphosphoranylidene-2-propanone (2.9 g, 9.1 mmol) and 25 mL of CH_2Cl_2 were placed in a 50 mL of a RB flask equipped with a magnetic stirring bar and argon gas balloon. A solution of ethyl-7-oxo-2(*E*)-heptenoate (1.2, 7.0 mmol) in CH_2Cl_2 (5 mL) was introduced to the flask through a syringe, and the reaction mixture was allowed to stir for 30 h at room temperature. The reaction mixture was concentrated in vacuo, and the residue was stirred with 30 mL of Et_2O:petroleum ether (1:1) for 20 min The resulting suspension was filtered and washed with 15 mL of the same mixture of solvents. The combined filtrate was evaporated, and column chromatographic purification over silica gel using petroleum ether:EtOAc (9:1) yielded ethyl-9-oxo-7(*E*),2(*E*)-decadienoate (**5**) as a clear liquid (1.3 g, 90%): 200 MHz ^{1}H NMR ($CDCl_3$) δ 6.95 (1H, dt, J = 16.0, 6.9 Hz), 6.75 (1H, dt, J = 16.0, 6.9 Hz), 6.08 (1H, dt, J = 16.0, 1.5 Hz), 5.8 (1H, dt, J = 16.0, 1.5 Hz), 4.18 (2H, q, J = 7.2 Hz), 2.24 (7H, m), 1.67 (2H, m), 1.28 (3H, t, J =7.2 Hz); 50 MHz ^{13}C NMR ($CDCl_3$) δ 197.97, 166.11, 147.72, 146.88, 131.53, 121.86, 59.92, 31.48, 31.24, 26.65, 26.23, 14.05; IR (neat) 2942, 1724, 1698, 1668, 1632, 1430, 1358, 1252, 1188, 1032, 976 cm^{-1}; MS *m*/*e* (relative intensity) 210 (M^+, 3), 195 (4), 181 (3), 164 (71), 149 (20), 137 (77), 136 (100), 122 (36), 121 (53), 107 (36), 93 (60), 81 (58), 68 (10).

Photoactivation of Ethyl 9-Oxo-7(*E*),2(*E*)-decadienoate (5). A solution of compound **5** (0.25 g, 1.19 mmol), Ph_3P (0.19 g, 0.724 mmol), and DCA (0.055 g, 0.24 mmol) in DMF:*i*-PrOH:H_2O (300 mL, 88:10:2) was irradiated in especially designed photoreactor as mentioned above under an argon atmosphere with light (405 nm) 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 chromatography on silica gel (100−200 mesh) using petroleum ether: EtOAc as eluent to give compound **8** (0.20 g, 79%) and **9** (0.035 g, 14%).

***trans*-Ethyl 2-[2-(2-oxopropyl)cyclopentyl]ethanoate (8):** yield 79%; 200 MHz ^{1}H NMR ($CDCl_3$) δ 4.15 (2H, q, J = 7.2 Hz), 2.68−2.17 (4H, m), 2.12 (3H, s), 1.9 (4H, m), 1.6 (2H, m), 1.25 (5H, m); 50 MHz ^{13}C NMR ($CDCl_3$) δ 208.57, 173.27, 60.32, 49.08, 42.25, 41.02, 39.50, 32.50, 32.23, 30.32, 23.60, 14.4; IR (neat) 2953, 2871, 1729, 1715, 1368, 1183, 1168, 1030 cm^{-1}; MS *m*/*e* (relative intensity) 212 (M^+, 3), 167 (59), 155 (90), 154 (72), 139 (16), 124 (100), 109 (71), 81 (85), 67 (45); HRMS (EI): 167.1067 [($M^{\bullet+}$ − OEt), calcd for $C_{10}H_{15}O_2$ 167.1072].

***cis*-6-Acetyl-7-carboethoxybicyclo[3.2.0]heptane (9):** 200 ^{1}H NMR ($CDCl_3$) δ 4.14 (2H, q, J = 7.3 Hz), 2.95 (3H, m), 2.83 (1H, dd, J =

9.8, 4.9 Hz), 2.1 (3H, s), 1.85 (3H, m), 1.60 (3H, m), 1.25 (3H, t, J = 7.3 Hz); 50 MHz ^{13}C NMR ($CDCl_3$) δ 207.34, 173.50, 60.54, 50.66, 43.65, 39.05, 38.66, 32.35, 32.14, 28.76, 25.09, 14.14; MS (*m*/*e*) (relative intensity) 210 (M^+, 4), 195 ($M^+ - CH_3$, 47), 167 ($M^+ - COCH_3$, 100), 165 ($M^+ -$ OEt, 31), 155 (32), 137 (54), 121 (30), 109 (12), 97 (28), 81 (20), 67 (12), 55 (8).

***trans*-6-Acetyl-7-carboethoxybicyclo[3.2.0]heptane (9):** 200 MHz ^{1}H NMR ($CDCl_3$) δ 4.12 (2H, q, J = 7.2 Hz), 3.62 (1H, dd, J = 8.7, 8.2 Hz), 3.08 (2H, m), 2.88 (1H, dd, J = 13.2, 8.2 Hz), 2.1 (3H, s), 1.70 (3H, m), 1.48 (3H, m), 1.25 (3H, t, J = 7.2 Hz); 50 MHz ^{13}C NMR ($CDCl_3$) δ 205.47, 174.3, 60.29, 47.40, 40.23, 40.0, 38.54, 31.85, 28.12, 27.75, 25.36, 14.08; IR (neat) 2958, 2868, 1732, 1718, 1371, 1195, 1154, 1032 cm^{-1}; MS *m*/*e* (relative intensity) 167 (15), 165 (16), 143 (100), 137 (14), 121 (11), 97 (10), 67 (11) [211 ($M^+ + 1$, 8), 210 (M^+, 12), 195 (22), 165 (100)]; HRMS (EI): 165.0917 [($M^+ -$ OEt), calcd for $C_{10}H_{13}O_2$ 165.0915].

Preparation of Compound 18. Into a 100 mL RB flask, containing potassium hydroxide (two pellets) in absolute ethanol (40 mL), 1,3-cyclohexadione (**17**, 2.5 g, 22.3 mmol) was added while stirring. Slow addition of acrolein (1.53 mL, 22.9 mmol) followed immediately afterwards. The mixture was allowed to stir at room temperature for 2 h and then refluxed for 3 h. After cooling to 0 °C, it was acidified to pH 2 with concentrated HCl and stirred additionally at room temperature for 2 h. The mixture was diluted with water (20 mL) and extracted with Et_2O (3 × 30 mL). The organic layer was washed with water, $NaHCO_3$ solution (10%), water, and brine and dried over Na_2SO_4. Concentration followed by column chromatographic purification on silica gel using petroleum ether:EtOAc (11:1) as eluent yielded **18** (2.8 g, 64%) as a thick liquid: 200 MHz ^{1}H NMR ($CDCl_3$) δ 5.1 (1H, dd, J = 4.3, 2.8 Hz), 3.85 (1H, m), 3.62 (1H, m), 2.58−2.15 (6H, m), 2.05−1.66 (4H, m), 1.22 (3H, t, J = 7.0 Hz); 50 MHz ^{13}C NMR ($CDCl_3$) δ 197.72, 168.56, 111.74, 98.6, 64.33, 36.44, 28.24, 26.0, 20.68, 14.93, 13.97; IR (neat) 2941, 1655, 1627, 1392, 1346, 1296, 1224, 1182, 1162, 1120, 1066, 1023, 971, 946, 836 cm^{-1}; MS *m*/*e* (relative intensity) 196 (M^+, 2), 167 (30), 151 (23), 150 (28), 139 (78), 122 (30), 107 (68), 97 (70), 94 (68), 72 (100), 66 (30), 55 (46).

2-(3-Oxopropyl)-2-cyclohexen-1-one (19). Into a 100 mL two necked previously dried RB flask equipped with magnetic stirring bar and argon balloon was placed lithium aluminium hydride (0.33 g, 8.7 mmol) and dry Et_2O (40 mL). To this suspension was slowly added at 0 °C a solution of **18** (2.6 g, 13.26 mmol) dissolved in dry Et_2O (10 mL). After stirring for 30 min at 0 °C, the reaction mixture was quenched with saturated NH_4Cl solution and diluted with Et_2O (20 mL). The Et_2O layer was separated, washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was diluted with ethanol (40 mL) containing 5% HCl (10 mL) solution. After stirring for 1 h at room temperature, it was neutralized with 10% of $NaHCO_3$ solution and extracted with Et_2O. The Et_2O layer was washed with saturated brine solution (2 × 50 mL), dried over Na_2SO_4, and concentrated in vacuo. The mixture was separated by usual silica gel column chromatography to give 1.7 g (84%) of **19** and 0.3 g (10%) of compound **20**: 200 MHz ^{1}H NMR of **19** ($CDCl_3$) δ 9.75 (1H, s), 6.8 (1H, t, J = 3.85 Hz), 2.55 (4H, m), 2.32 (4H, m), 1.97 (2H, m); 50 MHz ^{13}C NMR ($CDCl_3$) δ 201.58, 198.77, 146.40, 137.55, 42.35, 38.05, 25.68, 22.68, 22.48; IR (neat) 2930, 2882, 2815, 2727, 1723, 1672, 1658, 1445, 1383, 1224, 1174, 1120, 1084, 1062, 894 cm^{-1}; MS *m*/*e* (relative intensity) 153 ($M^+ + 1$, 3), 152 (M^+, 2.5), 123 (15), 111 (30), 103 (100), 95 (52), 81 (25), 67 (26).

2-(3,3-Diethoxypropyl)-2-cyclohexen-1-one (20): 200 MHz ^{1}H NMR ($CDCl_3$) δ 6.74 (1H, t, J = 4.2 Hz), 4.50 (1H, t, J = 5.8 Hz), 3.72−3.4 (4H, m), 2.50−2.18 (6H, m), 1.98 (2H, m), 1.7 (2H, m), 1.22 (6H, t, J = 7.0 Hz); IR (neat) 2938, 2929, 2876, 1673, 1445, 1374, 1131, 1062 cm^{-1}; MS *m*/*e* (relative intensity) 226 (M^+, 1), 181 (9), 152 (4), 135 (5), 103 (37), 96 (18), 85 (20), 71 (36), 67 (30), 57 (100).

2-(4-Carboethoxy-3-butenyl)cyclohexen-1-one (21a). A 50 mL RB flask equipped with magnetic stirring bar and argon balloon was charged with ethyl triphenylphosphoranylidene acetate (2.4 g, 6.9 mmol) and dry CH_2Cl_2 (25 mL). To this stirring solution, **19** (0.8 g, 5.26 mmol) was added slowly. The stirring was continued for 30 h at room temperature The solvent was removed under vacuum, and Et_2O: petroleum ether (1:1, 20 mL) was added to the residue. After stirring for 15 min, the resulting suspension was filtered, and the precipitate was washed with the same mixed solvent (5 mL). The filtrate was concentrated in vacuo and purified by column chromatography on silica gel using petroleum ether:EtOAc (12:1) as eluent to yield **21a** (1.0 g, 85%): 200 MHz ^{1}H NMR ($CDCl_3$) δ 6.9 (1H, m), 6.72 (1H, t, J = 3.9 Hz), 5.78 (1H, d, J = 15.7 Hz), 4.17 (2H, q, J = 7.2 Hz), 2.6−2.15 (8H, m), 1.94 (2H, m), 1.27 (3H, t, J = 7.2 Hz); 75 MHz ^{13}C NMR ($CDCl_3$) δ 199.02, 166.46, 148.18, 145.96, 138.19, 121.62, 60.02, 38.37, 30.95, 28.31, 25.93, 22.96, 14.16; IR (neat) 2931, 1714, 1668, 1650, 1540, 1455, 1370, 1269, 1173, 1104, 1038 cm^{-1}; MS *m*/*e* (relative intensity) 222 (M^+, 1), 176 (28), 148 (72), 131 (75), 120 (100), 104 (64), 91 (89), 81 (78), 68 (39).

2-(4-Cyano-3-butenyl)-2-cyclohexene-1-one (21b). This was prepared by Wittig olefination reaction following the procedure of compound **21a** except using triphenylphosphoranylidene acetonitrile instead of ethyl triphenylphosphoranylidene acetate: yield 95% (*trans:cis* = 68:32); 200 MHz ^{1}H NMR ($CDCl_3$) δ 6.9−6.4 (2H, m), 5.32 (1H, m), 2.42 (8H, m), 1.98 (2H, m); 50 MHz ^{13}C NMR ($CDCl_3$) δ 198.14, 154.74 (153.63), 146.21, 136.95, 116.83 (115.34), 99.47 (99.36), 37.77, 31.67 (30.40), 27.40 (27.46), 25.42, 22.45; IR (neat) 2931, 2221, 1668, 1622, 1541, 1384, 1173, 1105, 972, 907 cm^{-1}; MS *m*/*e* (relative intensity) 175 (M^+, 32), 147 (17), 135 (14), 119 (23), 109 (40), 91 (18), 81 (100), 67 (16), 53 (27).

Compound (25a): yield 84%; 200 MHz ^{1}H NMR ($CDCl_3$) δ 4.08 (2H, m), 3.38 (1H, m), 2.67 (1H, m), 2.35 (3H, m), 2.09 (1H, m), 1.88 (4H, m), 1.76−1.47 (3H, m), 1.21 (3H, t, J = 7.2 Hz); 50 MHz ^{13}C NMR ($CDCl_3$) δ 208.31, 171.25, 60.55, 58.90, 51.40, 50.52, 43.94, 39.86, 26.77, 25.27, 24.24, 22.99, 14.39; IR (neat) 2963, 1730, 1668, 1537, 1454, 1371, 1224 cm^{-1}; MS *m*/*e* (relative intensity) 223 ($M^+ + 1$, 9), 222 (M^+, 19), 176 (42), 149 (100), 131 (43), 120 (43), 105 (34), 91 (53), 79 (49), 67 (35); HRMS (EI): 222.1257 (calcd for $C_{13}H_{18}O_3$ 222.1255).

Compound (25b): yield 72%; crystalline solid, mp 114 °C; 200 MHz ^{1}H NMR ($CDCl_3$) δ 3.40 (1H, m), 2.78 (1H, m), 2.40 (2H, m), 2.26 (1H, m), 2.08 (3H, m), 1.94−1.53 (5H, m); 50 MHz ^{13}C NMR ($CDCl_3$) δ 206.32, 117.24, 58.59, 51.77, 45.34, 39.54, 36.25, 25.67, 25.30, 24.13, 22.44; IR (neat) 2922, 2231, 1693, 1553, 1454, 1372, 1257, 1102, 939, 848 cm^{-1}; MS *m*/*e* (relative intensity) 176 ($M^+ + 1$, 17), 175 (M^+, 85), 174 ($M^+ - 1$, 30), 146 (82), 135 (59), 119 (100), 91 (74), 81 (92), 79 (99), 67 (48), 65 (49), 53 (85).

3(*E*),8-Dienyl-2-nonanone (26). Wittig reaction of 5-hexenal with 1-triphenylphosphoranylidene-2-propanone, carried out by following identical procedure as discussed for **5,** gave **26** as clear oil: yield 82%; 200 MHz ^{1}H NMR ($CDCl_3$) δ 6.8 (1H, dt, J = 16.0, 6.9 Hz), 6.08 (1H, dt, J = 16.0, 1.4 Hz), 5.8 (1H, m), 5.03 (2H, m), 2.27 (5H, m), 2.1 (2H, m), 1.58 (2H, m); 50 MHz ^{13}C NMR ($CDCl_3$) δ 198.35, 147.91, 137.92, 131.52, 115.18, 33.13, 31.77, 27.29, 26.84; IR (neat) 2900, 2832, 1670, 1645, 1618, 1418, 1352, 1246, 1168, 972, 908 cm^{-1}; MS *m*/*e* (relative intensity) 138 (M^+, 12), 123 (20), 109 (6), 95 (100), 85 (25), 81 (50), 67 (40), 55 (51), 53 (19).

2-(2-Oxopropane)methylcyclopentane (27): yield 27%; 200 MHz ^{1}H NMR ($CDCl_3$) δ 2.67−2.25 (2H, m), 2.14 (3H, s), 1.82 (3H, m), 1.58 (3H, m), 1.35 (1H, m), 1.12 (1H, m), 0.98 (3H, d, J = 6.6 Hz); IR (neat) 2958, 2874, 1720, 1442, 1362, 1256, 1188, 1008 cm^{-1}.

Ethyl 10-oxo-2(*E*),8(*E*)-dodecadienoate (29): yield 95%; 200 MHz ^{1}H NMR ($CDCl_3$) δ 6.95 (1H, dt, J = 15.6, 7.0 Hz), 6.78 (1H, dt, J = 15.6, 7.0 Hz), 6.08 (1H, dt, J = 15.6, 1.4 Hz), 5.8 (1H, dt, J = 15.6, 1.4 Hz), 4.17 (2H, q, J = 7.2 Hz), 2.25 (7H, m), 1.5 (4H, m), 1.27 (3H, t, J = 7.2 Hz); 50 MHz ^{13}C NMR ($CDCl_3$) δ 197.30, 165.66, 147.91, 146.99, 131.01, 121.23, 59.44, 31.58, 31.29, 27.06 (2C), 26.19, 13.76; IR (neat) 2948, 1726, 1695, 1662, 1628, 1446, 1372, 1288, 1240, 1176, 1012, 968 cm^{-1}; MS *m*/*e* (relative intensity) 224 (M^+, 2), 178 (12), 150 (42), 135 (87), 107 (100), 93 (54), 79 (81), 67 (82), 55 (97).

***trans*-Ethyl 2-[2-(2-oxopropyl)cyclohexyl]ethanoate (33):** yield 68%; 200 MHz ^{1}H NMR ($CDCl_3$) δ 4.15 (2H, q, J = 7.0 Hz), 2.64 (1H, dd, J = 16.4, 4.4 Hz), 2.5−2.22 (3H, m), 2.15 (3H, s), 2.08 (1H, m), 1.9−1.45 (6H, m), 1.4−0.95 (6H, m); ^{13}C NMR ($CDCl_3$) δ 208.72, 173.31, 60.38, 48.74, 39.57, 39.40, 37.95, 32.85, 32.64, 30.63, 25.95 (2C), 14.41; IR (neat) 2927, 2855, 1729, 1716, 1447, 1368, 1295, 1245, 1162, 1040 cm^{-1}; MS *m*/*e* (relative intensity): 181 (7), 169 (47), 168

(24), 135 (22), 123 (44), 95 (90), 81 (100), 67 (50), 55 (56), [226 (M^+, 7), 181 (100)]; HRMS (EI) 181.1228 [(M^+ − OEt), calcd for $C_{11}H_{17}O_2$ 181.1228].

9-Oxo-2,7(*E*)-decadienenitrile (30): yield 91%; 200 MHz ^{1}H NMR ($CDCl_3$) δ 6.8−6.4 (2H, m), 6.07 (1H, m), 5.36 (1H, m), 2.6−2.05 (7H, m), 1.67 (2H, m); IR (neat) 2934, 2222, 1696, 1671, 1632, 1364, 1255, 974 cm^{-1}.

***trans*-2-[2-(2-Oxopropyl)cyclopentyl]ethanenitrile (34):** yield 73%; 200 MHz ^{1}H NMR ($CDCl_3$) δ 2.75−2.25 (4H, m), 2.18 (3H, s), 1.99 (3H, m), 1.8 (1H, m), 1.65 (2H, m), 1.48 (1H, m), 1.27 (1H, m); ^{13}C NMR ($CDCl_3$) δ 207.95, 119.26, 48.8, 41.98, 40.41, 32.75, 32.13, 30.28, 23.67, 21.99; IR (neat) 2954, 2874, 2245, 1712, 1424, 1359, 1170 cm^{-1}; MS *m*/*e* (relative intensity) 165 (M^+, 2), 125 (2), 122 (4), 108 (12), 107 (10), 81 (41), 67 (30), 58 (100); HRMS (EI) 165.1153 (calcd for $C_{10}H_{15}NO$ 165.1153).

10-Oxo-2,8(*E*)-dodecadienenitrile (31): yield 90%; 200 MHz ^{1}H ($CDCl_3$) δ 6.9−6.42 (2H, m), 6.1 (1H, dt, J = 16.0, 1.4 Hz), 5.35 (1H, m), 2.55−2.08 (7H, m), 1.52 (4H, m); IR (neat) 2934, 2222, 1694, 1669, 1632, 1436, 1362, 1254, 1184, 1128, 1068, 972 cm^{-1}.

***trans*-2-[2-(2-Oxopropyl)cyclohexyl]ethanenitrile (35):** yield 61%; 200 MHz ^{1}H ($CDCl_3$) δ 2.58 (1H, dd, J = 16.4, 4.4 Hz), 2.48−2.2 (3H, m), 2.14 (3H, s), 2.04 (1H, m), 1.85 (1H, m), 1.72 (2H, m), 1.63−1.36 (3H, m), 1.26 (2H, m), 1.06 (1H, m); 50 MHz ^{13}C NMR ($CDCl_3$) δ 208.02, 118.87, 48.16, 39.02, 37.36, 32.56, 32.39, 30.64, 25.74 (2C), 22.41; IR (neat) 2930, 2857, 2243, 1712, 1454, 1424, 1359, 1288, 1260, 1235, 1163, 1005, 922, 735 cm^{-1}; MS *m*/*e* (relative intensity) 179 (M^+, 2), 136 (2), 122 (4), 121 (11), 95 (14), 81 (27), 58 (100); HRMS (EI) 179.1312 (calcd for $C_{11}H_{17}NO$ 179.1310).

Preparation of Compound 32: Compound (**32**) was prepared as follows. (a) Into a dry 100 mL RB flask fitted with reflux condenser, argon balloon, and a magnetic stirring bar was placed paraffin free NaH (0.35 g, 50%) and 30 mL of dry THF. A solution of **37** (2 g, 7.25 mmol) dissolved in THF (5 mL) was added dropwise to the above stirring mixture at room temperature. The stirring was continued till the solution became clear (∼45 min). Solution of ethyl bromocrotonate (1.4 g, 7.25 mmol) in THF (5 mL) was added slowly to the reaction mixture, and the whole content was heated in an oil bath at 50 °C for overnight. After cooling to room temperature, water (15 mL) was added and diluted with Et_2O (50 mL). The organic layer was separated, and the aqueous layer was further extracted with Et_2O (2 × 20 mL). The combined organic layer was washed with water and a saturated brine solution and dried over Na_2SO_4. After evaporation of the solvent, the residue was purified by silica gel column chromatography using petroleum ether:EtOAc (11:1) as eluent to give 2.2 g (78%) of ethyl 4,4-dicarboethoxy-7-[2-(1,3-dioxolane)]-2-heptenoate: 90 MHz ^{1}H NMR ($CDCl_3$) δ 6.78 (1H, dt, J = 15.6, 7.0 Hz), 5.88 (1H, dt, J = 15.6, 1.4 Hz), 4.55 (1H, t, J = 6.5 Hz), 4.17 (6H, m), 3.7−3.37 (4H, m), 2.94 (2H, m), 2.22 (2H, d, J = 6.5 Hz), 1.27 (15H, m); IR (neat) 2934, 2884, 1722, 1673, 1368, 1254, 1192, 1124, 1056, 984 cm^{-1}.

(b) A solution of ethyl 4,4-dicarboethoxy-7-[2-(1,3-dioxolane)]-2-heptenoate (1.0 g, 2.57 mmol) in 30 mL of acetone containing 5% aqueous HCl (15 mL) was stirred for 5 min at room temperature Saturated brine solution was added, and the reaction mixture was extracted with hexanes (3 × 30 mL). The organic phase was dried over Na_2SO_4 and concentrated in vacuo to yield 0.8 g of crude aldehyde. This aldehyde was used for the Wittig reaction using 1-triphenylphosphoranylidene-2-propanone by following the identical reaction procedure as described for **5** to give 0.8 g (88%) of **32**: 200 MHz ^{1}H NMR ($CDCl_3$) δ 6.7 (2H, m), 6.1 (1H, m), 5.9 (1H, m), 4.2 (6H, m), 2.8 (4H, m), 2.26 (3H, d, J = 6.8 Hz), 1.27 (9H, m); ^{13}C NMR ($CDCl_3$) δ 197.76, 169.82 (2C), 165.79, 141.96, 141.16, 134.84, 125.78, 62.06 (2C), 60.58, 57.08, 36.39, 36.22, 27.16, 14.39, 14.24 (2C); IR (neat) 2930, 1746, 1718, 1696, 1672, 1630, 1432, 1367, 1270, 1254, 1198, 974 cm^{-1}; MS *m*/*e* (relative intensity) 354 (M^+, 4), 308 (17), 281 (10), 235 (17), 195 (100), 191 (20), 189 (21), 165 (31), 161 (50), 147 (47), 119 (47), 95 (33), 91 (49), 68 (84), 55 (66).

***trans*-Ethyl 2-[4,4-dicarboethoxy-2-(2-oxopropyl)cyclopentyl]-ethanoate (36):** yield 69%; 200 MHz ^{1}H NMR ($CDCl_3$) δ 4.17 (6H, m), 2.74−2.18 (6H, m), 2.13 (3H, s), 2.07−1.75 (4H, m), 1.25 (9H, m); 50 MHz ^{13}C NMR ($CDCl_3$) δ 207.21, 172.17, 171.99, 171.85, 61.21 (2C), 60.11, 58.34, 47.4, 40.88, 39.75, 39.61 (2C), 37.94, 29.90, 14.02, 13.80 (2C); IR (neat) 2982, 2916, 1729, 1446, 1368, 1258, 1176, 1152, 1098 cm^{-1}; MS *m*/*e* (relative intensity) 311 (8), 299 (17), 269 (9), 225 (44), 209 (21), 195 (21), 179 (66), 153 (37), 135 (21), 121 (29), 107 (31), 97 (29), 93 (69), 79 (100), 67 (25), 55 (40) [357 (M^+ + 1, 2), 299 (100)]; HRMS (EI): 311.1472 [(M^+ − OEt), calcd for $C_{16}H_{23}O_6$ 311.1494).

Preparation of Ethyl 2-Methylene-7-oxo-5(*E*)-octenoate (39). Compound (**39**) was synthesized in three steps starting from triethylphosphonoacetate (**38**).

(a) Preparation of Ethyl 2-Methylene-5-[2-(1,3-dioxolane)]pentanoate. A previously dried 100 mL two necked RB flask fitted with a reflux condenser was charged with paraffin free NaH (1.07 g, 50%) and dry C_6H_6 (30 mL). Triethylphosphonoacetate (**38**, 5 g, 22.3 mmol) was added to the flask slowly under argon atmosphere at room temperature. The mixture was stirred until it became clear (30 min). 2-(2-Iodoethyl)-1,3-dioxolane (5.1 g, 22.3 mmol) solution in C_6H_6 (5 mL) was added dropwise to the mixture, and the whole content was refluxed for 8 h. After cooling to 0 °C, additional NaH (1.07 g, 50%) was added, and the resulting mixture was allowed to stir for 45 min at room temperature. Solid paraformaldehyde (0.35 g) was introduced portionwise, and the reaction mixture was left stirring overnight at room temperature. The mixture was diluted with 100 mL of Et_2O, suction filtered through small Celite pad, and washed with 25 mL of Et_2O. The filtrates were concentrated in vacuo and silica gel column chromatographic purification of the residue yielded ethyl 2-methylene-5-[2-(1,3-dioxolane)]pentanoate (2.45 g , 55%): 200 MHz ^{1}H NMR ($CDCl_3$) δ 6.15 (1H, s), 5.57 (1H, s), 4.9 (1H, t, J = 4.9 Hz), 4.22 (2H, q, J = 7.2 Hz), 3.95 (2H, m), 3.88 (2H, m), 2.45 (2H, m), 1.8 (2H, m), 1.3 (3H, t, J = 7.2 Hz); IR (neat) 2930, 1721, 1632, 1366, 1272, 1192, 1132, 1084 cm^{-1}.

(b) Preparation of Ethyl 2-Methylene-7-oxo-5(E)-octenoate (39). It was synthesized by following the similar reaction procedure as of **32** starting from compound ethyl 2-methylene-5-[2-(1,3-dioxolane)]-pentanoate; yield 85%; 200 MHz ^{1}H NMR ($CDCl_3$) δ 6.8 (1H, dt, J = 16.0, 6.5 Hz), 6.25 (1H, d, J = 0.90 Hz), 6.15 (1H, dt, J = 16.0, 1.3 Hz), 5.58 (1H, d, J = 0.90 Hz), 4.24 (2H, q, J = 7.2 Hz), 2.48 (4H, m), 2.24 (3H, s), 1.34 (3H, t, J = 7.2 Hz); 50 MHz ^{13}C NMR ($CDCl_3$) δ 198.01, 166.51, 146.56, 139.29, 131.60, 125.25, 60.54, 31.14, 30.35, 26.66, 14.02; IR (neat) 2954, 1720, 1678, 1626, 1434, 1362, 1252, 1184, 1126, 998 cm^{-1}.

Preparation of Ethyl 2-Methylene-8-oxo-6(*E*)-nonenoate (40). This compound was prepared in four steps following the similar reaction sequence as of compound (**39**).

(a) Preparation of 5-[(*tert*-Butyldimethylsilyl)oxy]-2-methylene-hexanoate. The title compound was synthesized by following the procedure of ethyl 2-methylene-5-[2-(1,3-dioxolane)]pentanoate using 4-[(*tert*-butyldimethylsilyl)oxy]iodobutane as alkylating reagent instead of 2-(2-iodoethyl)-1,3-dioxolane: yield 54%; 200 MHz ^{1}H NMR ($CDCl_3$) δ 6.15 (1H, s), 5.54 (1H, m), 4.22 (2H, q, J = 7.2 Hz), 3.67 (2H, m), 2.35 (2H, m), 1.52 (4H, m), 1.35 (3H, t, J = 7.2 Hz). 0.9 (9H, s), 0.05 (6H, s); IR (neat) 2836, 2832, 1714, 1649, 1466, 1378, 1365, 1272, 1193, 1075, 1043, 982 cm^{-1}.

(b) Preparation of Ethyl 5-Hydroxy-2-methylenehexanoate. To a stirring solution of 5-[(*tert*-butyldimethylsilyl)oxy]-2-methylenehexanoate (1.5 g, 5.24 mmol) in CH_3CN (20 mL) was added aqueous solution of 48% HF (0.5 mL, 10.5 mmol) at 0 °C, and the progress of the reaction was monitored by TLC. After 30 min, 10% $NaHCO_3$ solution (5 mL) was added, and the mixture was extracted with Et_2O (3 × 25 mL). The combined organic layer was washed with water saturated brine solution and dried over Na_2SO_4. Concentration in vacuo followed by column chromatographic purification of the residue on silica gel using petroleum ether:EtOAC (5:1) as eluent gave ethyl-5-hydroxy-2-methylenehexanoate (0.85 g, 94%): 200 MHz ^{1}H NMR ($CDCl_3$) δ 6.15 (1H, d, J = 1.35 Hz), 5.5 (1H, m), 4.22 (2H, q, J = 7.1 Hz), 3.68 (2H, t, J = 6.0 Hz), 2.35 (2H, t, J = 6.5 Hz), 1.75 (1H, br s, OH), 1.6 (4H, m), 1.32 (3H, t, J = 7.1 Hz); 50 MHz ^{13}C NMR ($CDCl_3$) δ 167.54, 140.84, 124.68, 62.35, 60.75, 32.18, 31.62, 24.74, 14.24; IR (neat) 3428 (br., OH), 2936, 1716, 1648, 1372, 1274, 1188, 1042, 982 cm^{-1}; MS *m*/*e* (relative intensity) 173 (M^+ + 1, 7), 155 (4), 142 (12), 126 (99), 111 (57), 98 (95), 81 (100), 67 (58), 55 (56).

(c) Preparation of Ethyl 2-Methylene-8-oxo-6(*E*)-nonenoate (40). This compound (**40**) was prepared by the Wittig reaction of the aldehyde, obtained by Swern oxidation of ethyl 5-hydroxy-2-methylene

hexanoate by following the procedure of ethyl-7-oxo-2(*E*)-heptenoate: yield 91%; 200 MHz ^{1}H NMR ($CDCl_3$) δ 6.78 (1H, dt, J = 16, 6.8 Hz), 6.15 (1H, d, J =1.15 Hz), 6.08 (1H, dt, J = 16, 1.4 Hz), 5.54 (1H, m), 4.2 (2H, q, J = 7 Hz), 2.5−2.1 (7H, m), 1.67 (2H, m), 1.28 (3H, t, J = 7 Hz); 50 MHz ^{13}C NMR ($CDCl_3$) δ 197.6, 166.36, 147.10, 139.97, 131.22, 124.39, 60.14, 31.43, 31.03, 26.54, 26.33, 13.79; IR (neat) 2951, 1718, 1676, 1629, 1472, 1365, 1254, 1181, 995 cm^{-1}; MS *m*/*e* (relative intensity) 164 (2), 137 (5), 121 (10), 97 (100), 93 (28), 81 (26), 69 (8), 57 (7).

Ethyl 3-(2-oxopropyl)cyclohexanecarboxylate (42): nonseparable mixture of two isomers (ratio 3:2); yield 54%; 200 MHz ^{1}H NMR ($CDCl_3$) δ 4.13 (2H, m), 2.6 (1H, m), 2.35 (2H, d, J = 6.5 Hz), 2.15 (3H, s), 2.0−1.45 (7H, m), 1.42−0.95 (5H, m); 75 MHz ^{13}C NMR (major isomer, $CDCl_3$) δ 208.03, 174.93, 59.97, 49.57, 38.91, 33.24, 31.42, 29.88, 29.58, 27.47, 21.67, 14.05; (minor isomer) δ 207.79, 175.43, 59.97, 50.80, 43.02, 34.97, 32.74, 32.07, 30.33, 28.55, 25.06, 14.05; IR (neat) 2942, 2863, 1732, 1719, 1435, 1362, 1260, 1192, 1178 cm^{-1}; GC/MS (major isomer) *m*/*e* (relative intensity) 213 (M^+ + 1, 11), 212 (M^+, 24), 166 (8), 155 (12), 109 (10), 95 (24), 81 (55), 43 (100); GC/MS (minor isomer) *m*/*e* (relative intensity) 213 (M^+ + 1, 17), 155 (47), 109 (35), 81 (83), 43 (100); HRMS (EI) 212.1398 (calcd for $C_{12}H_{20}O_3$ 212.1412).

Ethyl-1-methyl-2-(2-oxopropyl)cyclopentanecarboxylate (43): yield 21%; 200 MHz ^{1}H NMR ($CDCl_3$) δ 4.12 (2H, q, J = 7.0 Hz), 2.6 (1H, dd, J = 16.2, 4.1 Hz), 2.4−2.1 (5H, m), 2.0 (1H, m), 1.8 (3H, m), 1.65−1.30 (2H, m), 1.25 (3H, t, J = 7.0 Hz), 1.2 (3H, s); 75 MHz ^{13}C NMR ($CDCl_3$) δ 208.04, 176.67, 60.13, 51.93, 46.05, 45.09, 37.26, 31.44, 30.34, 23.86, 22.62, 14.24; IR (neat) 2964, 2874, 1721, 1465, 1365, 1158 cm^{-1}; MS *m*/*e* (relative intensity) 213 (M^+ + 1, 4), 212 (M^+, 3), 211 (M^+ − 1, 2), 169 (24), 167 (25), 155 (62), 140 (37), 109 (19), 95 (77), 81 (100), 67 (20); HRMS (EI): 169.1229 [(M^+ − $COCH_3$), calcd for $C_{10}H_{17}O_2$ 169.1228].

1-[3-(Tetrahydro-2-pyranyloxy)-1-propynyl]-2-(3,3-dimethoxypropyl)cyclopentanol (45). To a 100 mL two necked RBF containing the Grignard reagent, prepared in THF (40 mL) from magnesium (0.36 g, 14.8 mmol) and ethyl bromide (1.6 g, 14.7 mmol), was added dropwise a solution of 3-(tetrahydro-2-pyranyloxy)propyne (1.98 g, 14.1 mmol) in THF (10 mL) at 10−15 °C. The mixture was stirred for 20 min at room temperature. 2-(3,3-Dimethoxypropyl)-cyclopentanone (**44**; 2.5 g, 13.4 mmol) dissolved in THF (5 mL) was slowly added, and stirring was continued for another 4 h at room temperature. Afterwards, the mixture was poured onto an ice-cold saturated NH_4Cl solution and extracted with Et_2O (2 × 100 mL). The organic layer was washed with water and a saturated brine solution, dried over Na_2SO_4, and concentrated in vacuo. The concentrate was purified by silica gel column chromatography using petroleum ether: EtOAc (6:1) as eluent to yield a clear oil (3.6 g, 82%): 200 MHz ^{1}H NMR ($CDCl_3$) 4.82 (1H, m), 4.48 (1H, m), 4.32 (2H, m), 3.85 (1H, m), 3.55 (1H, m), 3.34 (6H, s), 2.22−1.17 (18H, m); IR (neat) 3434 (br), 2946, 2862, 1452, 1392, 1360, 1200, 1125, 1064, 1025, 946, 898, 856 cm^{-1}.

1-Propadienyl-2-(3,3-dimethoxypropyl)cyclopentanol (46). To a refluxing suspension of lithium aluminium hydride (0.52 g, 13.7 mmol) in Et_2O (50 mL) was slowly introduced a solution of **45** (3.2 g, 9.8 mmol) in Et_2O (10 mL) with constant stirring at such a rate that gentle reflux was maintained. The contents were refluxed for an additional 30 min After cooling, the mixture was cautiously poured onto a mixture of ice and NH_4Cl. The Et_2O layer was separated, and an aqueous phase was extracted with Et_2O (2 × 25 mL). The combined organic layer was washed with water and a saturated brine solution, dried over Na_2SO_4, and concentrated in vacuo. The concentrate was purified by column chromatography on silica gel using petroleum ether: EtOAc (8:1) as eluent to give a clear viscous liquid (2 g, 90%): 200 MHz ^{1}H NMR ($CDCl_3$) δ 5.3 (1H, m), 4.9 (2H, m), 4.35 (1H, t, J = 5.4), 3.32 (6H, s), 2.1−1.37 (10H, m), 1.2 (2H, m); 50 MHz ^{13}C NMR ($CDCl_3$) [mixture of two isomers (1:1)] δ 206.0, 205.8, 104.6 (2C), 98.07, 95.09, 80.72, 79.58, 78.18, 77.54, 52.5, 52.39 (2C), 52.24, 50.29, 49.2, 40.75, 39.0, 31.40, 31.28, 29.67, 29.30, 25.53, 23.43, 21.22, 20.50; IR (neat) 3450 (br), 2950, 2866, 2824, 1955, 1450, 1366, 1127, 1046 cm^{-1}.

1-Propadienyl-2-[4-carboethoxy-3(*E*)-butenyl]cyclopentanol (47). The acetal **46** was deprotected by following the experimental procedure as described for the preparation of compound (**32**), and the crude aldehyde was used as such for the Wittig reaction in an identical manner as described for **21a**: yield 48%; 200 MHz ^{1}H NMR ($CDCl_3$) δ 6.96 (1H, dt, J = 15.6, 7 Hz), 5.82 (1H, dt, J = 15.6, 1.4 Hz), 5.25 (1H, m), 4.94 (2H, d, J = 6.5 Hz), 4.17 (2H, q, J = 7 Hz), 2.23 (2H, m), 2.0−1.34 (10H, m), 1.28 (3H, t, J = 7 Hz); 50 MHz ^{13}C NMR ($CDCl_3$) δ 205.62, 166.45, 149.27, 121.06, 97.8, 79.48, 78.17, 59.91, 48.56, 40.73, 30.89, 29.32, 26.85, 21.09, 14.06; IR (neat) 3472 (br), 2941, 2862, 1955, 1719, 1651, 1450, 1369, 1274, 1183, 1048 cm^{-1}.

Synthesis of 48. Compound **47** (0.9 g, 3.6 mmol) dissolved in an aqueous acid mixture (50% AcOH, 5% H_2SO_4; 9 mL) was charged into a 50 mL RB flask fitted with a condenser and immediately heated in an oil bath at 80 °C for 3 min. The reaction was stopped by cooling into an ice bath and neutralized by adjusting to slightly alkaline condition by adding NaOH solution (5 M). The mixture was extracted with hexanes (3 × 30 mL). The combined organic layer was washed with water and a saturated brine solution, dried over Na_2SO_4, and concentrated in vacuo. Silica gel column chromatographic purification of the concentrate using petroleum ether:EtOAc (10:1) as eluent gave a clear gummy liquid (0.58 g, 64%): 200 MHz ^{1}H NMR ($CDCl_3$) δ 6.98 (1H, m), 6.3−6.1 (1H, m), 5.85 (1H, m), 4.18 (2H, m), 3.3−2.08 (8H, m), 2.03−1.13 (9H, m); 75 MHz ^{13}C NMR ($CDCl_3$, major isomer) δ 197.53, 169.83, 166.07, 147.96, 121.5, 119.24, 59.80, 45.79, 33.28, 31.63, 30.99, 30.86, 29.76, 23.94, 13.93; IR (neat) 2954, 2926, 2876, 1728, 1711, 1692, 1615, 1442, 1376, 1272, 1195, 1178, 1042, 986 cm^{-1}; MS *m*/*e* (relative intensity) 251 (M^+ + 1, 2), 250 (M^+, 3), 207 (5), 204 (15), 176 (12), 161 (45), 137 (97), 119 (75), 114 (88), 105 (38), 95 (73), 91 (80), 81 (100), 68 (60), 55 (91).

1-(2-Oxopropane)-2-carboethoxymethylbicyclo[3.3.0]octane (49): yield 61%; 200 MHz ^{1}H NMR ($CDCl_3$) δ 4.12 (2H, q, J = 7.1 Hz), 2.67−2.38 (3H, m), 2.35−2.15 (3H, m), 2.13 (3H, s), 2.08−1.82 (2H, m), 1.75 (2H, m), 1.58 (1H, m), 1.40 (3H, m), 1.35−1.02 (5H, m); ^{13}C NMR ($CDCl_3$) δ 208.93, 173.86, 60.37, 54.23, 52.43, 49.09, 44.12, 35.85, 35.30, 34.67, 32.32, 31.54 (2C), 26.33, 14.43; IR (neat) 2943, 2866, 1736, 1716, 1450, 1365, 1276, 1165, 1031 cm^{-1}; MS *m*/*e* (relative intensity) 253 (M^+ + 1), 252 (M^+), 207 (9), 194 (30), 148 (17), 120 (61), 107 (100), 91 (22), 79 (35), 67 (20), 55 (15). HRMS (EI): 207.1397 [(M^+ − OEt), calcd for $C_{13}H_{19}O_2$ 207.1385].

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Supporting Information Available: Crystal data, data collection, and solution and refinement data for **25b** (3 pages). See any current masthead page for orderingand Internet access instructions.

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