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Design of a photosystem to harvest visible-light into electrons: photosensitised one electron redox reactions in organic synthesis

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Abstract: Based on synchronous oxidation-reduction processes, analogous to photosynthetic mechanistic paradigm, a photosystem utilising Ph_3P or ascorbic acid as sacrificial electron donor has been developed to harvest electrons from visible light photons. The utility of such photosystem has been demonstrated by initiating various one-electron reductive -C-C- bond formation reactions. Biologically active PGE_1 and C-Furanosides are synthesised employing this photosystem at a crucial step.

Mimicking natural photosynthetic process or solar energy harvesting technology (refs. 1,2) in organic synthesis is of fundamental interest and vital from an ecological view point. Towards this endeavour, the past decade has witnessed substantial, multidisciplinary research efforts directed towards the conversion of solar light into chemical energy employing photoinduced electron transfer (PET) processes as key approach (ref. 3). Several new and synthetically important organic photoreactions have also been discovered that have employed electron transfer (ET) to or from the substrate in the presence of an electron rich donor or electron poor acceptor (ref. 4). Interestingly, remarkable progress has been made in PET reactions, though the chemistry of the radical cations, generated by the oxidative reactions, remains at the focus (ref. 4). Despite the great synthetic potentials of photosensitised one-electron reductions in organic synthesis, research in this area has been limited, owing to the lack of a suitable photosystem (ref. 5).

Our own interests in this area (ref. 4a), have been centered on the application of PET oxidation reactions from select donors utilising cyanoarenes (ArCN) as light harvesting electron acceptors. The photosensitisation concept has relied on the thermodynamic feasibility of ET from $ArCN^{\cdot-}$ to O_2 followed by disproportionation of $O_2^{\cdot-}$ as shown in Fig-1

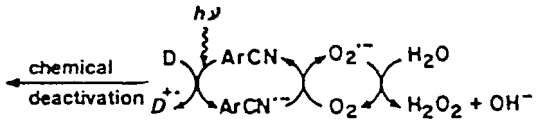


Fig. 1: Mechanism of the PET oxidation of an electron donor D

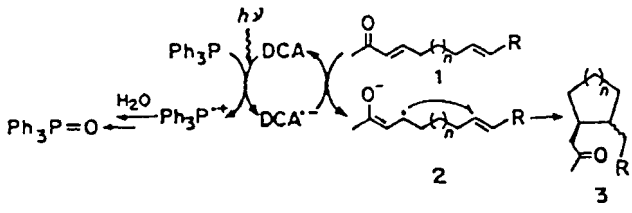


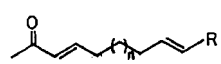
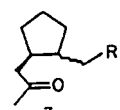
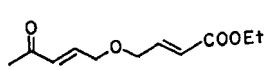
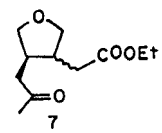
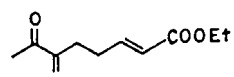
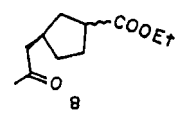
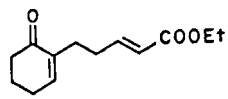
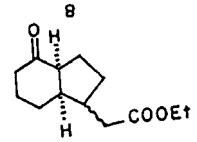
Fig. 2: Mechanism of PET initiated one-electron reduction using Ph_3P as sacrificial electron-donor

Driven by the desire to mimick the photosynthetic mechanistic paradigm (ref. 6) to initiate one electron redox processes in organic reactions and the mechanistic premise of the above photosystem led us to envision that a photosystem comprising of a sacrificial electron donor and ArCN in inert atmosphere should be able to drive a second ET from $ArCN^{\cdot-}$ to another molecule, provided the redox potentials are matched. We are pleased to describe herein our successful effort in developing a photosystem which is capable of harvesting visible light photons into electrons. The harvesting of electrons phenomena from our photosystem has been demonstrated by initiating various one-electron reductive -C-C- bond formation reactions in organic synthesis.

Our photosystem (Fig.2), designed for this purpose, employs Ph_3P as sacrificial electron donor, 9,10-dicyanoanthracene (DCA) as visible light absorbing electron acceptor and α, β-unsaturated ketones (**1**) as secondary one electron acceptor. The selection of **1** as secondary electron acceptors are made because of its matching redox potentials for electron acceptance from $DCA^{\cdot-}$ and to explore the interesting synthetic avenues of free-radical reactions. The established PET phenomena (ref. 7) between Ph_3P and $^1ArCN^*$ and the efficient transformation of $Ph_3P^{+\cdot}$ to stable Ph_3PO by reaction with water led us to select Ph_3P as the sacrificial electron donor. Considering the efficient transformation of $Ph_3P^{+\cdot}$ to Ph_3PO in aqueous solvent, it was anticipated that Ph_3P would be an ideal substrate for controlling the impact of electron transfer, the intrinsic limitations of PET processes (ref. 3).

The feasibility of ET from $DCA^{\cdot-}$ to **1** is evaluated by estimating the Gibb's free energy (ΔG_{et} = -42.43 to -47.25 KJmol^{-1}) change employing the redox potentials of $DCA^{\cdot-}$ (-0.89ev) (ref. 8) and **1** (-0.40ev) (ref. 9) according to the equation $\Delta G_{et} = E^{1/2}_{(ox)} - E^{1/2}_{(red)}$. To monitor the suitability of the above photosystem for initiating one electron reductive cyclisation of **1**, a solution of Ph_3P (2.1 mmol), DCA (1.4 mmol) and **1** (3.60 mmol) in aqueous acetonitrile containing small amount of i-PrOH as hydrogen donor, was irradiated with visible light (λ = 405 nm) (ref. 10) which provided cyclisation product **3** in very high yield (ref. 9). The product **3** may obviously be considered to be formed via the free radical initiation at the β-position of the enone moiety of **1**. The major diastereomer of **3** has the *trans*-configuration. An alternative route for the formation of **3** involving first [2+2] cycloaddition followed by one-electron reductive -C-C- bond cleavage (ref. 11) can be ruled out, since **1** does not absorb light under the present experimental conditions. The quantum yield ($\phi_{1\text{-}3}$ = 0.060) for the formation of **3** clearly indicates that it is not arising through the radical chain reactions. Since the transformation of Ph_3P to Ph_3PO involves two electron process, it provides two successive electrons for reduction and therefore, only one molecule of Ph_3P is required for the reduction of two molecules of **1**. To generalise this transformation for synthetic utility, a number of substrates of type **1** were subjected to one electron reductive cyclisations and the results are given in Table-I.

Table-I Photosensitised one electron reductive cyclisation of α,β-unsaturated ketones tethered with activated olefins

Enones	Products[a] (ϕ)[b]	Time of Irrad. (h)	Yield (*trans*:*cis*)[c]
 1	 3		
n = 1, R = COOEt		28	98 (85:15)
n = 1, R = CN		31	97 (80:20)
n = 2, R = CN		42	94 (68:32)
n = 2, R = COOEt		40	95 (75:25)
 4	 7	30	80 (78:22)
 5	 8	30	85 (80:20)
 6	 9	30	70 (85:15)

a) Characterised by ^{1}H NMR, ^{13}C NMR and mass spectral data

b) Quantum Yields were estimated using Applied Photophysics instrument and employing uranyl oxalate as chemical actinometer

c) Ratios measured by gas chromatography (capillary column, cross-linked methyl silicone, 25 m)

Although the photosystem as shown in Fig.2 represents the success of our basic concept of harvesting photons into electrons to trigger one electron redox processes, yet it lacks in the novelty as synthetic methodology due to constant build up of Ph_3PO. Our zest to design a perfect photosystem that could have wider acceptability as methodology led us to develop another photosystem consisting of D-D-A*-A tetrad assembly where DCA is the visible-light harvesting electron acceptor, DMN (1,5-dimethoxynaphthalene) as primary electron donor and ascorbic acid as sacrificial electron donor. Various α,β-unsaturated ketones and aldehydes functioned as usual the secondary electron acceptors. This improved photosystem (ref. 12) (Fig.3) is again based upon the thermodynamic feasibility of ET between each interacting partners which is established by estimating negative ΔG_{et} values from the redox potentials of respective components. For illustrations, evaluation of diffusion controlled fluorescence quenching rate constants (K_{qet} = 1.27 x 10^{10} M^{-1} s^{-1}) of DCA (λ_{ex} = 430 nm, λ_{em} = 461 nm) at variable concentration of DMN and estimation of exergonic ΔG_{et} values (-68.42 kJM^{-1}) for radical ion formation through Weller equation (ref. 13), unequivocally suggests the occurrence of PET

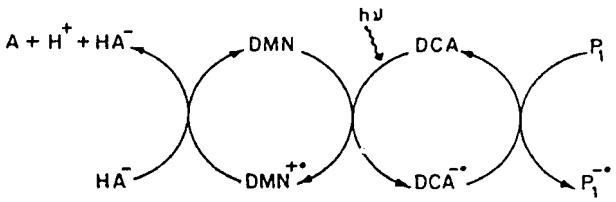
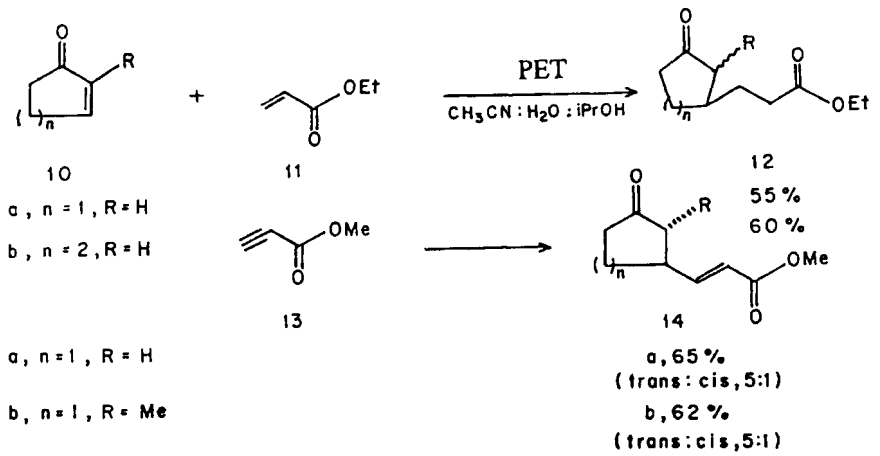


Fig. 3 : Mechanism of PET initiated one-electron reductions from an improved photosystem consisting of D-D-A*-A tetrad assembly

phenomenon between these two substrates. Similarly, ET feasibility from ascorbic acid to $DMN^{+\cdot}$ have been evaluated by estimating ΔG_{et}(-18.81 kJM^{-1}) employing equation $\Delta G_{et} = E^{1/2}_{(ox)} - E^{1/2}_{(red)}$. The $E^{1/2}_{(ox)}$ of ascorbic acid (1.084 ev Vs SCE) has been estimated by cyclic voltametry. The transformation of ascorbate ion to the dehydroascorbic acid and proton after donation of an electron to $DMN^{+\cdot}$ is precedented from the literature report (ref. 14).

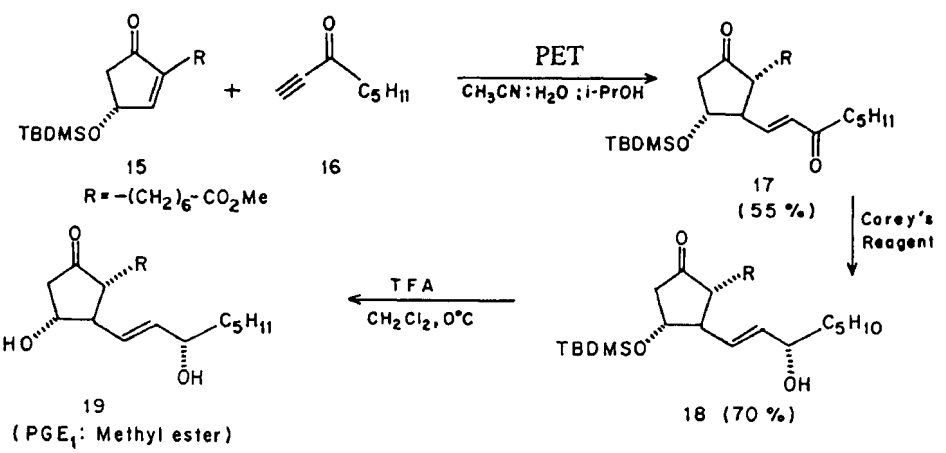
The efficient activation of α,β-unsaturated ketones to produce an allylic radical and its success in the intramolecular cyclisations encouraged us to evaluate its applicability for the intermolecular coupling of enones and activated olefins. Subjecting a mixture of cycloalkenones (**10a-b**) and ethyl acrylate (**11**) under PET redox reaction conditions led to the unprecedented coupling product **12** in 55-60 % yield (Scheme-I).



Scheme-I : PET promoted coupling of activated olefins

This coupling represents a new dimension in -C-C- bond formation reaction between the two activated olefins. The coupling of methylpropiolate (**13**) with **10-a** gave thermodynamic more stable *trans*-isomer (**14-a**). Furthermore, the reaction **10-c** with **13** gave **14-b** in 95% diastereomeric purity.

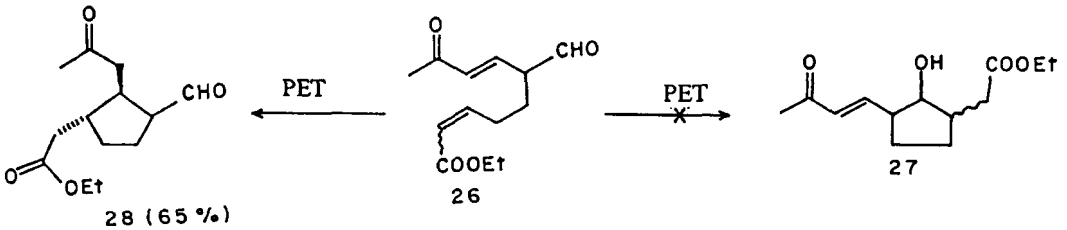
The excellent streoselectivity observed during the coupling of **10-c** with **13** encouraged us to extend this reaction for the synthesis of biologically active protaglandins (ref. 15) (**19**). Our synthetic approach involves the coupling of optically pure (ref. 16) **15** with **16** as key step (Scheme-II). The PET initiated coupling of



Scheme-II : Approach towards the synthesis of Prostaglandins

15 with **16** followed by its purification gave **17** in approximately 55 % yield. The enantioselective reduction of the enone moiety of **17** utilising Corey's (ref. 17) oxazaborolidine reagent produced **18** in 80 % yield. The silylether deprotection of **18** by stirring in methylene chloride at 0°C in the presence of trifluoroacetic acid gave PGE_1 as methyl ester (**19**).

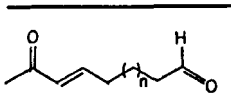
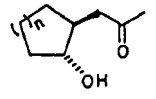
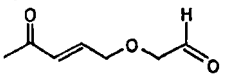
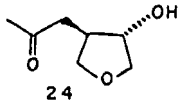
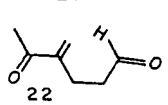
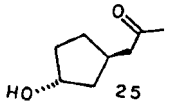
Due to significant difference in the redox potentials of α, β-unsaturated ketones compared with simple ketones and aldehydes, we envisaged that our photosystem could be utilised for the selective redox reactions of enone moiety in the presence of ketones as the selectivity in the radical ion formation in the case of two potential donor/acceptor depends upon the magnitude of the ΔG_{et} values (ref. 18). Furthermore, we envisioned that selective reductive activation of enone functionality, suitably tethered with an aldehyde, could undergo stereoselective intramolecular cyclisation reaction to produce bioactive cycloalkanoids (ref. 19). PET



Scheme-III : Support for the selectivity of α, β-unsaturated ketones activation

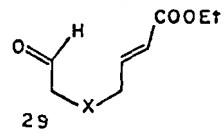
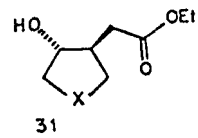
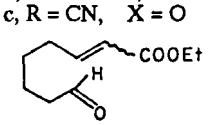
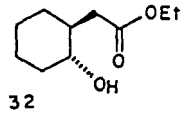
reductive activation of a series of enones suitably linked with aldehydes (e.g.**20-22**) as listed in Table-II gave corresponding cycloalkanols (**23-25**) in synthetically good yields (60-85 %). To provide, exclusive support for the selective activation of enone moiety during the cyclisations of the above substrates, compound **26** was synthesised with a view that enone activation would give **28** as product while ketone activation would lead to the formation of **27**. PET activation of **26** gave **28** (65 %) exclusively supporting the fact that our photosystem leads to the selective activation of enone moiety in the presence of aldehydes(Scheme -III).

Table-II : Selective β-activation of α, β-unsaturated ketones in the presence of aldehydes and their intramolecular cyclisations

Entry	Product[a] (major)	Yields (%)[b] (isolated)
 20	 23	
a, n = 1		85
b, n = 2		78
 21	 24	75
 22	 25	70

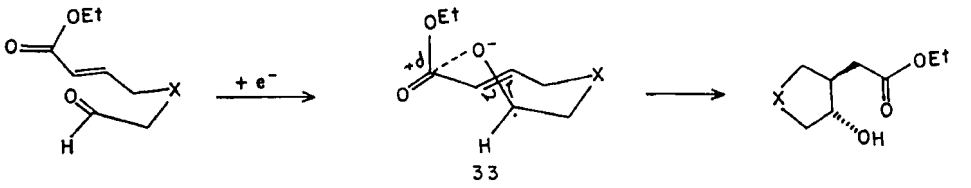
a) Characterised by ^1H NMR, ^{13}C NMR and mass spectral data
b) Yields not optimised

Table-III : Photosensitised generation and cyclisation of ketyl radicals

Entry	Product[a,b] (major)	Yields (%)[c] (isolated)
 29	 31	
a, R = COOEt, X = CH_2	de : 95%	82
b, R = COOEt, X = O	de : 92%	80
c, R = CN, X = O	de : 93%	78
 30	 32 de : 92%	70

a) Characterised by ^1H NMR, ^{13}C NMR and mass spectral data
b) diastereomeric ratio measured by capillary GC analysis
c) Yields not optimised

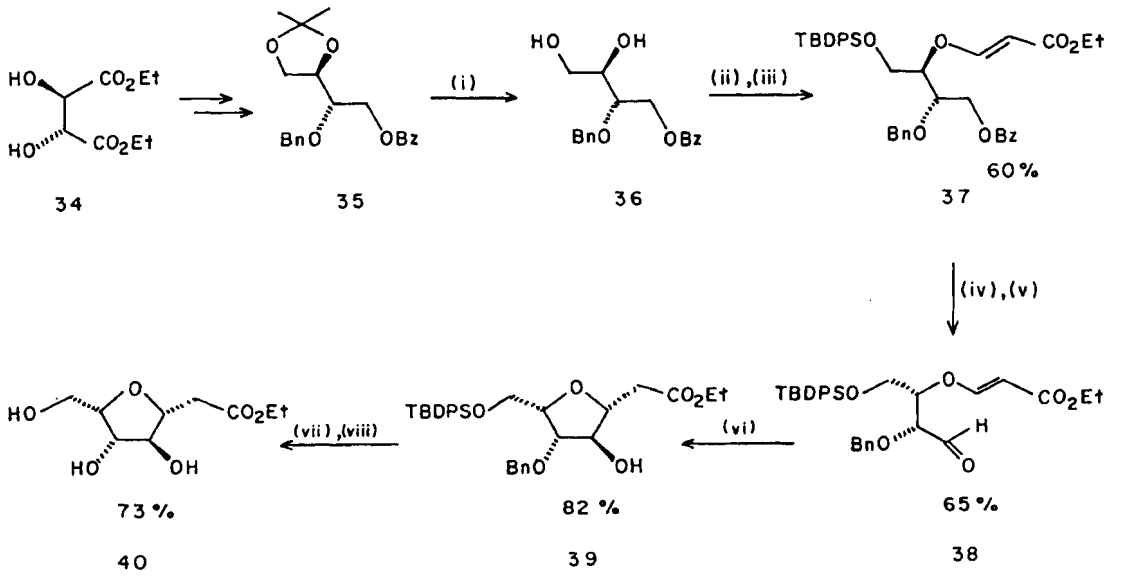
Ketyl radicals have found diverse application recently in synthesis of bioactive cyclopentanoids (ref. 19). These radicals have normally been generated by reduction using various metal salts (ref. 20) and photoreduction (ref. 21) employing 254 nm light. However, these methodologies have always produced cycloalkanols as mixture of diastereomers. Considering the synthetic significance of this intermediate, we decided to extend our approach as an alternative strategy for the generation of ketyl radicals for intramolecular cyclisation reactions. Various examples (**29a-c, 30**), as listed in Table-III, underwent cyclisations to produce cyclopentanols (**31a-c, 32**) in high diastereomeric purity (92-95 %). We believe that the high diastereoselectivity observed in these cyclisations is due to the involvement of a rigid chair-like transition state (**33**, Fig.4) produced by the interaction of enolate moiety with the ester moiety.



33

Fig. 4 : Visualisation of Diastereoselectivity

We extended this cyclisation strategy for synthesis of C-furanoside (**40**), an important class of compounds as precursors to C-nucleoside antibiotics and other more complex natural products. Generally, these are made from reducing sugars via Wittig reaction with stabilised ylides followed by intramolecular Michael addition of hydroxyl group (ref. 22). However, this method generally yields mixture of stereoisomer at the "anomeric" carbon centre. Our strategy to synthesis C-furanoside (**40**) involves the intramolecular cyclisation of ketyl radical, generated from **38**. The precursor compound **38** is obtained following simple steps from (+)-tartaric acid (**34**). The details of our synthetic strategy is outlined in Scheme-IV.



i) PTSA, MeOH ii) TBDPSCl, imidazole, pyridine iii) ethyl propiolate, NMM, DCM iv) K_2CO_3, MeOH
v) Swern oxidation vi) PET vii)H_2, Pd/C, MeOH viii) PTSA, MeOH, reflux

Scheme-IV : Synthesis of C-Furanosides

In summary, we have designed a photosystem based on synchronous one electron oxidation-reduction process analogous to photosynthetic mechanistic paradigm to harvest visible-light photons into electrons whose applicability has been demonstrated to trigger various one-electron redox reactions in organic chemistry. Synthetic application of such photosystem is expected to add new dimensions to the evergrowing demands of developing ecologically friendly "Green Chemistry"

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