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Regioselective Generation of Iminium Cation by PET Processes: Its *in situ* Trapping by Intramolecular Nucleophiles and Synthesis of Some Biologically Active Heterocycles.#

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Abstract : *Efficient, mild and direct route for regiospecific iminium cation is developed by sequential two electron oxidation of several N-alkylated tertiary amines by photoinduced electron transfer processes. The regiospecificity of iminium cation arises from the deprotonation step of amine radical cation to generate α-amino radical which depends on the stereoelectronic factor subject to kinetic acidity of amine radical cation. Iminium cation is efficiently trapped* insitu *by internal nuleophiles to give cyclic compounds* **14-18** *and* **22a-c**. *Stereoselective synthesis of* **cis** α,α'*-dialkylated piperidines and pyrrolidines* **30a-c** *is achieved by nucleophilic opening of tetrahydro-1,3-oxazines* **22a-c**.

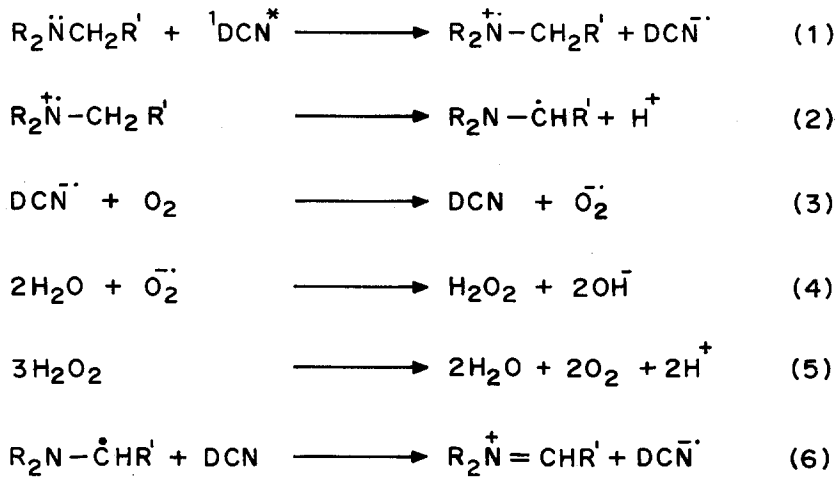
Photoinduced electron transfer (PET) reactions have been attracting considerable attention recently in discovering new and synthetically useful chemical reactions[1,2]. The unique feature of these transformations is that the key reactive intermediates are ion radical species rather than the initially populated excited states. Therefore nature of these reactions are governed by the chemical properties and reactive profiles of ion radicals. Among many other factors, the reactivity of PET generated ion radicals is dependent on solvent polarity[3]. A closely related question is whether the primary intermediate is a solvent separated ion pair (SSIP) or a contact ion pair (CIP). Gould and Farid[4] in their recent study have suggested that in polar solvents such as CH_3CN, electron transfer quenching results in the formation of SSIP directly and in these solvents the fully solvated ions (SSIP) can separate to form free radical ion pair (FRIP)[5]. Thus under these conditions the anion radicals are potentially less reactive with the cation radical than in non-polar solvents in which CIP are more important[6].

PET reaction from arene-amine pair produces arene radical anion and planar amine radical cation[7], which usually undergo intermolecular addition involving α-amino radical formed by efficient deprotonation from amine radical cation at site adjacent to nitrogen. Although further one electron oxidation of these α-amino radicals to produce iminium cation is quite possible due to reduced ionization potential[8], but this is not observed from these systems. Mechanistic studies by Lewis et al[9]., suggested these additions to occur

#Respectfully dedicated to Prof. S. V. Kessar, Department of Chemistry, Panjab University ,Chandigarh, on the occasion of his 60th birth day.

within CIP. Ohashi et al[10]., reported entirely different photoreaction *via* longer lived SSIP between 9,10 dicyanoanthracene (DCA), *tertiary*-amines in CH_3CN (solvent), where addition product of CH_3CN to DCA is observed.

This significant difference in reactivity pattern[10], led us to evolve a concept mainly to explore the synthetic utility of this fundamental process from cyanoarene--amine pair in polar solvents. It was envisaged that SSIP formed between 1,4 dicyanonapthalene (DCN)--amine pair will dissociate into FRIP in the medium of high polarity (CH_3CN:H_2O) where $DCN^{\cdot-}$ would be potentially less reactive towards amine cation radical. Furthermore, deprotonation rate from corresponding amine radical cation to α-aminoradical will be accelerated due to the presence of water in medium. Molecular O_2 dissolved in the solvent would quench the $DCN^{\cdot-}$ to their original ground state, which could participate in the second oxidation step from α-amino radical to give iminium cation similar to electrochemical oxidation[11] as shown in **SCHEME-I.**



SCHEME-I

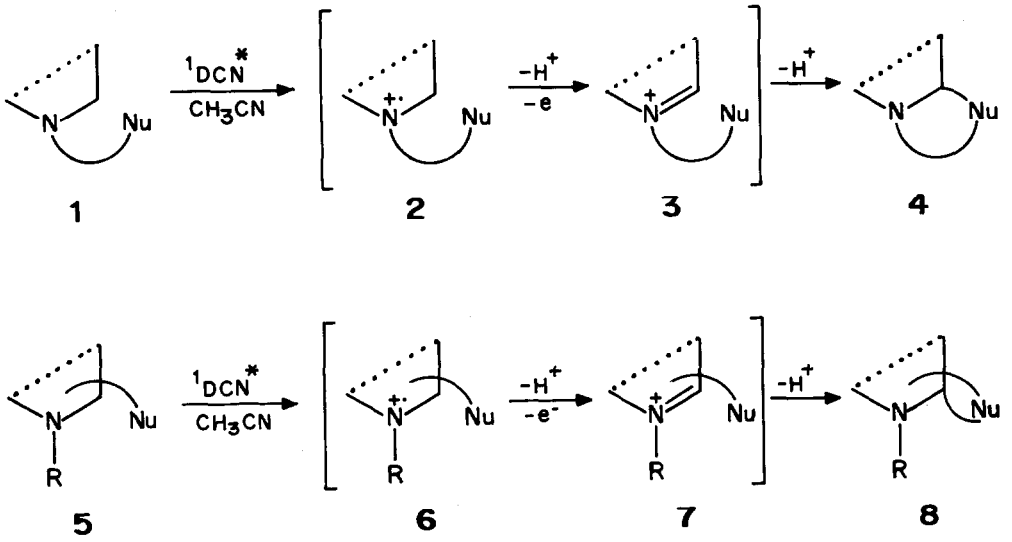
In this way "true sensitized" role of DCN in the process of Electron-Proton-Electron (E-P-E) sequence was realized. The success of this concept in oxidizing N-hydroxylamines to nitrones[12] (from charge transfer stabilized exciplex dissociation of $^1DCN^*$..N-hydroxylamines in CH_3CN:H_2O) encouraged us to apply E-P-E sequence to generate iminium cation. We disclose herein full details of PET generation and *insitu* trapping of iminium cation with internal nucleophiles using $^1DCN^*$ as electron acceptor[13].

RESULTS AND DISCUSSION

Iminium cations are important electrophiles and frequently utilized in preparing biologically active nitrogen heterocycles[14]. The known methods to generate appropriate iminium cation during complex molecule synthesis have been rather tedious and difficult[15]. In our concept, it was anticipated that iminium cation thus generated from unsymmetrical *tertiary*-amines will be highly regiospecific and will depend upon the

orientation of α-deprotonation from amine cation radical. Kinetic acidity which is subject to stereoelectronic factor[9], solvent polarity, basicity of oxidizing agent and oxidation potential of amines will be some of the important parameters which may influence the site of deprotonation.

Initially to gain insight into the regiospecificity of PET generated iminium cations, two types of N-substituted cyclic amines (**1** and **5**) were selected. It was envisaged that E-P-E sequence will produce intermediates **3** and **7** due to stereoelectronic factor which will influence faster rate of proton loss from ring α-CH of corresponding amine cation radical[7]. Presence of internal nucleophile was expected to trap the iminium cation to give important heterocyclic products, **(SCHEME II)**



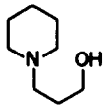
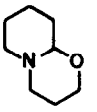
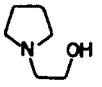
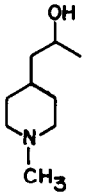
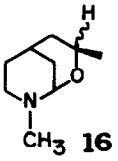
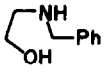
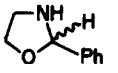
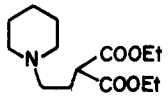
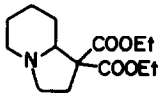
SCHEME-II

To test this, amines (**9-13**) were irradiated (>280 nm) in CH_3CN in the presence of DCN, without prior removal of oxygen, which gave corresponding cyclised compounds (**14-18**) apparently by intramolecular trapping of iminium cation and DCN was recovered quantitatively (>95%) at the end of the reaction.The quantum efficiency of the reaction was estimated by monitoring the loss of starting materials, which gave moderate value of $\phi = 0.02\text{-}0.1$ (**Table-1**). Substrate **11** gave diastereomeric mixture of products. Our attempt to isolate pure diastereomer, however failed.

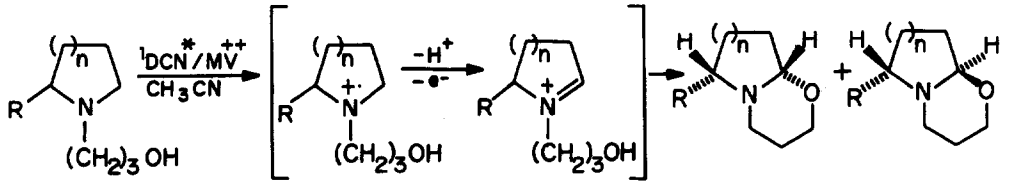
Furthermore, to broaden the scope and to probe the α -deprotonation site from cyclic amines, substrates **19 a-c** were selected where two ring -CH protons are different. PET initiated intramolecular cyclisation of

substrates **19 a-c** gave ring closed products at less substituted α-carbon atom[13b], as a mixture of two

Table 1-PET generation of iminium cation and its in situ intramolecular cyclisation

Entry	Substrate	Irr.time (h)	Product	Yield (%)	ϕ Yield (of formation)
9		4·0	 **14**	85	0·1042
10		6·0	 **15**	70	0·0598
11		7·0	 **16**	78	0·0220
12		9·0	 **17**	82	0·0241
13		6·5	 **18**	65	—

diastereomers **22 a-c** (major) and **23 a-c** (minor) in over all 88-92% yield, (**SCHEME III**). Careful analysis by ^{1}H NMR and GC (capillary column, 25mtr, fused silica, methylsilicone) ensured the absence of cyclised



19a-c **20** **21** **22a-c** major **23a-c** minor

19 a n = 2, R = Me
b n = 2, R = n-Butyl
c n 1, R = n-Butyl

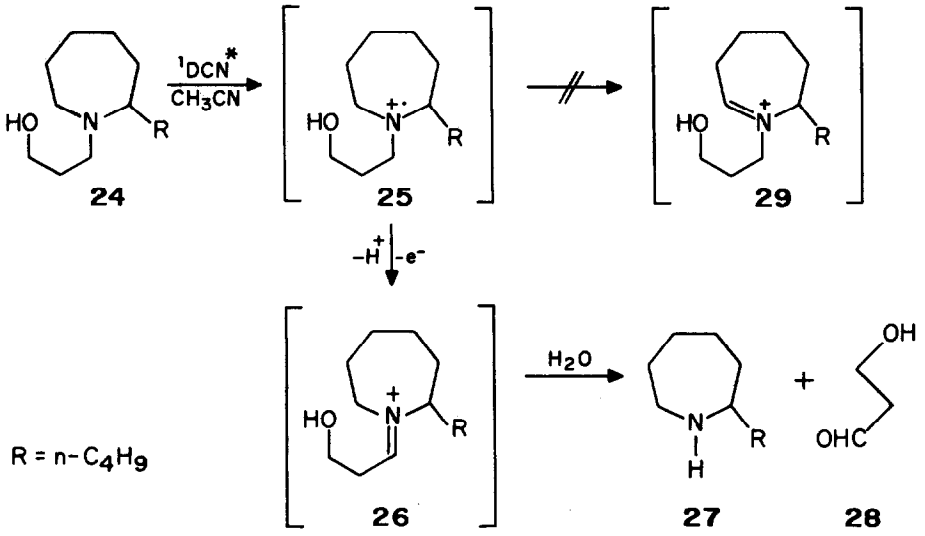
X : Y
96 : 4
95 : 5
93 : 7

SCHEME-III

product with ring closed at the more substituted α-carbon. This cyclisation clearly indicated that there is complete regioselectivity for ring closure towards the less substituted α-carbon of piperidine moiety,

suggesting the faster rate of α-deprotonation to generate least substituted α-amino radical and ultimately regiospecific iminium cation. However, ClO_2 mediated cyclisation of **19a** known to occur via an electron abstraction route[16] is reported to show greater, but not complete preference for ring closure towards the less substituted (ratio 6:1) carbon atom[16]. This difference is attributable to the base strength of the oxidising agent which is likely to influence the orientation of *tertiary*-amine oxidation. Increasing base strength is known to increase the yield of less substituted alkene in E_1 elimination reaction[17]. Wagner et al.,[18] has also reported such an effect for the deprotonation of the *para*-cymene radical cation by trifluroacetophenone radical anion within an exciplex. Although, we do not have any quantitative figure at this moment, but it may be considered that the base strength of $DCN^{\cdot-}$ could be higher than $ClO^{\cdot-}_2$, which makes deprotonation most selective in case of **19a-c** to produce **21a-c**$^+$.

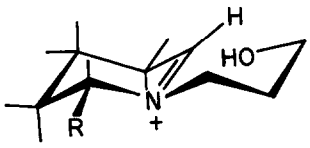
Similarly, we attempted the cyclisation of 2-butyl,N-(1-propanol) hexamethyleneimine (**24**) in similar conditions, but in contrast to our expectations, cleavage products, 2-butyl hexamethyleneimine (**27**) and 3-hydroxy propanal (**28**) were isolated. This suggests the formation of exocyclic iminium cation (**26**), rather than endocyclic iminium cation (**29**), from corresponding amine radical cation (**25**), SCHEME IV. The restriction in endocyclic iminium cation generation here may be postulated again on the basis of flexibility in the conformation of hexamethyleneimine ring of **24** similar to cycloheptane ring systems[19].



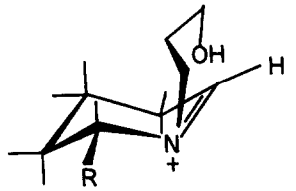
SCHEME-IV

Next we turned our attention, for determining the stereochemistry of cyclised products **22a-c** and **23a-c**. The stereochemical assignment was first deduced for **22a** and **23a** based on the comparison of 9H proton chemical shifts, as reported in literature[20]. The signal for 9H in **22a** appears at δ 4.01 whereas for

23a at δ 4.11 and therefore **22 a-c** (major diastereomers) were assigned as a **cis**. The **cis** stereochemistry of **22 a-c** is likely to emerge due to preferential front side attack of -OH group to iminium cation **A** to avoid steric crowding, as is clear from the structures **A** and **B**. These cyclisations are found to be different from the



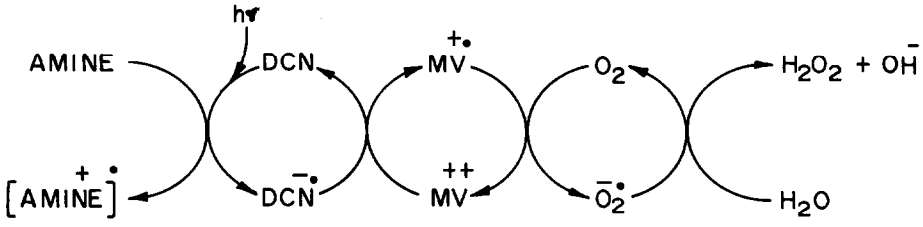
A



B

$Hg(oAc)_2$ oxidative cyclisation of the same amine[15a], where ring closure is dominated at the more substituted α-carbon of piperidine and pyrrolidine moiety.

To enhance the synthetic scope of this reaction, methyl viologen (MV^{++}) was used as electron relay during photolysis[21]. This accelerated the reaction rate significantly. The reaction completed within 3-4h which otherwise took 6-9h. After irradiation, and removal of solvent, the MV^{++} was quantitatively recovered by triturating and decanting the reaction mixture with benzene. Chromatographic purification of the benzene portion of the reaction mixture over neutral alumina gave corresponding cyclised products, and DCN quantitatively. To explain the role of MV^{++}, a plausible schematic ET steps are shown in, **SCHEME-V**.



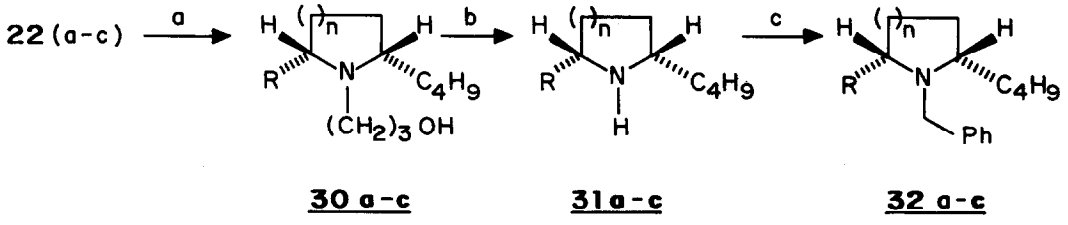
DCN = DICYANO NAPTHALENE ; MV^{++} = METHYL VIOLOGEN

SCHEME - V

From respective reduction potentials of ground state O_2 ($O_2/O_2^{\cdot-}$=-0.78 eV)[1c] and MV^{++} ($MV^{++}/MV^{+\cdot}$=-0.45 eV)[22] it is probable that the anion radical of DCN ($DCN/DCN^{\cdot-}$=-1.28 eV)[23] transfers its electron preferentially

to MV^{++} to produce $MV^{+\cdot}$ and ground state DCN which participates in further electron abstraction process from α-amino radical[24]. The $MV^{+\cdot}$ is subsequently oxidized rapidly by atmospheric oxygen possibly producing $O_2^{-\cdot}$ which in aqueous solution dismutates via hydrogen peroxide[25]. The above argument is supported from the fact that reaction does not proceed in inert atmosphere as well as in dry acetonitrile.

The easy accessibility of **22 a-c** from the above approach led us to utilize them as precursors for the synthesis of α, α'-dialkyl piperidines and pyrrolidines by their nucleophilic opening along the lines reported earlier[26]. Both **cis** and **trans** α, α'-dialkyl piperidines and pyrrolidines are widely distributed alkaloids, associated with significant biological activity[27]. A number of synthetic routes have appeared over the years for these alkaloids[28], but most of these methodologies end up giving mixture of both **cis** and **trans** compounds. We anticipated that nucleophilic opening of **22 a-c** will give only **cis** α, α'-dialkylated products. To this end, **22 a-c** were reacted with n-butyl magnesium bromide in ether at -20°C, and usual workup followed by chromatographic purification gave **30 a-c** in 94-96% yield. Compounds **30 a-c** were characterized by ^1H, ^{13}C NMR and mass spectral data. The **cis** stereochemistry of the **30 a-c** was suggested on the basis of observed C_2 symmetry in the ^{13}C NMR spectra of **30 b** and **c**, which is further confirmed by observing characteristic singlet for benzylic protons in ^1H NMR spectrum of N-benzylated derivatives **32 a-c**[29], derived as shown in **SCHEME-VI.**



30 a-c **31 a-c** **32 a-c**

a) n-C_4H_9 Mg Br / ETHER, -20°C; b) (i) α-CHLOROETHYL CHLOROFORMATE/ (CH_2Cl_2) / REFLUX. (ii) MeOH / REFLUX, 1h; c) BENZYLBROMIDE / CH_3CN/ REFLUX, 12h

SCHEME-VI

The N-dealkylation of **30 a-c** was achieved by following Olofson et al[30]., procedure (50 to 62% yield).

Acknowledgement: We (G.K and P.Y.R) are thankful to CSIR, for financial support.

EXPERIMENTAL

General

The chemicals and reagents used in this study were commercial grade pure, and some of them were used after further purification. 2-Methyl piperidine and 3-Chloro-1-propanol were obtained from Fluka, and used after distillation. Methyl viologen dichloride hydrate (Aldrich), was used as such. Dicyanonapthalene (DCN) was prepared by standard procedure[31]. The chromatography was performed using either aluminum oxide (Neutral, activity grade III) or silicagel (Acme India, finer than 200 mesh). The solvents used during experiments were purified unless otherwise stated by standard literature procedure.

All the compounds were characterized by IR, ^{1}H & ^{13}C NMR, Mass and GC-MS spectroscopy. Nuclear Magnetic Resonance spectra obtained for ^{1}H and ^{13}C were recorded on BRUKER 200MHz, VARIAN GEMINI 200MHz and FT 80MHz, in $CDCl_3$, using tetramethyl silane as internal reference. Chemical shifts are given on δ (ppm) scale, the coupling constants (J values) are reported in Hertz. Infrared spectra were recorded on Perkin-Elmer model 283B, and values are reported in cm^{-1}. Mass spectra were recorded on VG-MICRO MASS 7070 model, GC-MS was done on FINNIGAN MAT and GC analysis were performed by using carbowax 20m (14%, 10'x1/8"), OV-17 (10%, 10'x1/8") and methyl-silicone (fused silica, 25m) capillary columns.

Equipment used for photolysis were 450-W Hanovia medium pressure mercury lamp, Pyrex filtered immersion well and reaction vessels (ACE glass USA), and quantum yields were determined using Rayonet photoreactor equipped with RPR 300nm lamps.

Quantum yield measurement:

For the quantum yield measurement samples were prepared by pipetting out 5ml of acetonitrile sample solution in to Pyrex test tube containing ($3.404x10^{-2}$M) of compound **9** and ($3.37x10^{-4}$M) of DCN. The irradiation was performed in Rayonet reactor consisting RUL 3000 A° lamps in "merry go-round" apparatus for short intervals of time to bring about 8-10% conversion. Uranyl oxalate actionometry was used to monitor the intensity of the light[32]. The quantitative loss of starting material was monitored by GC (column 10% SE-30 8'x1/8"). The quantum yield of the reaction was measured at donor concentration (**10-12**) of $4.13x10^{-2}$, $2.45x10^{-2}$, $2.69x10^{-2}$ respectively, and concentration of the DCN was $3.37x10^{-4}$ fixed.

General method for synthesis of 2-butyl cyclic amines.

The synthesis was accomplished in four steps.

a). The *tertiary*-butyl carbazate (6.6g, 50mmol) was dissolved into a mixture of acetic acid (20ml) and water (40ml). To the resulting solution $NaNo_2$ (3.8g,55mmol) was added portion wise at 0°C with stirring. After 30 minutes of stirring, reaction mixture was diluted with 40ml of water and oily layer was extracted with ether (3x50ml). The combined extracts were washed successively with water and 1M $NaHCO_3$, dried over anhydrous Na_2SO_4 and concentrated to offer brown oily liquid of t-butyl azidoformate (Boc-N_3,90%), which was used without further purification.

b) To a solution of appropriate cyclic amine (80mmol) and triethylamine (100mmol) in dioxane (40ml), Boc-N_3 (80mmol, in 20ml of dioxne) was added. The mixture was stirred until a clear solution resulted. After evaporation of dioxane, the residue was extracted twice with ether, washed with brine, dried over anhydrous Na_2SO_4, and concentrated to result N-Boc protected cyclic amines as clear liquids which were purified by distillation under reduced pressure.

c) A solution of N-Boc protected cyclicamines (13.6mmol) in 30ml of dry ether were cooled to -78°C and treated with TMEDA (31.2mmol) followed by *sec*-butylithium (1.5M, 10.8ml, 16.4mmol). After stirring the reaction mixture for 3.5h at-78°C, *n*-butyl bromide (16.4mmol) was added slowly, then allowed to warm to room temperature and diluted with 3ml of water. The aqueous layer was extracted with ether (30mlx4), combined etherial extracts were dried over Na_2SO_4 and concentrated to give 2-butyl, N-Boc cyclic amines as clear liquids, which was purified by column, using hexane:acetone (12:1) as eluent.

d) To the solution of 2-butyl,N-Boc cyclic amines (24mmol) in dry DCM (35ml), trifluroaceticacid (72mmol) was added slowly, and stirring was continued at room temperature for about 2h, then reaction mixture was basified (adjusted to pH=10) with 10% NaOH solution. The aqueous layer was extracted three times with DCM, and combined extracts were dried over anhydrous Na_2SO_4, concentrated to give (80-85%) of 2-butyl cyclicamines as a clear liquids.

D. General method for preparation of cyclic amino alcohols 9,10,19 (a-c) and 24.

3-chloro-1-propanol (210 mmol), was added dropwise with stirring to a refluxing solution of appropriate cyclic amine (220mmol) in dry acetonitrile containing anhydrous K_2CO_3 (180mmol). After 20h of reflux, reaction mixture was allowed to cool to room temperature, and solid material was filtered off, washed with EtOAc, combined filtrates were concentrated and distilled under reduced pressure to offer pure compounds **9,10,19** (**a-c**) and **24** as clear liquids.

i). N-(1-propanol) piperidine (9).
Yield 84%; b.p (125°C/30mm): **^{1}H NMR** (90 MHz): 1.41-1.85(m, 8H), 2.32-2.67(m, 6H), 3.82(t, J=5.2, 2H), 5.07(1H, OH) D_2O exchangeable. **IR** (Neat): 3500, 2900, 2800, 1300 and 1200.; **Mass** : (m/z:144).

ii). N-ethanol pyrrolidine (10).
Yield 85%; b.P (55°C/6mm): **^{1}H NMR** (90 MHz): 1.41-1.81(m, 4H), 2.24-2.58(m, 6H), 3.32(t, J=4.8, 2H), 3.90(s,1H, OH); **IR** (Neat): 3500, 900, 2800, 1225 and 1050. **Mass**: (m/z155).

iii). 2-Methyl,N-(1-propanol)piperidine (19a).
Yield 82%; b.p (110°C/0.4mm): **^{1}H NMR** (90 MHz): 1.12(d, J=6.6, 3H), 1.21-1.54(m, 6H), 1.60-1.85(m, 4H), 2.40-2.95(m, 3H), 3.84(t, J=5.8, 2H); **^{13}C NMR** (200 MHz) 16.16, 27.45, 27.88, 29.20, 29.73, 50.48, 54.67, 59.13, 63.44.; **IR** (Neat) : 3600, 2950, 2850, 1350, 1150 and 1020.; **Mass** : 157, 142, 112, 98, 84.

iv). 2-Butyl, N-(1-propanol)piperidine (19b).
Yield 88%; b.p (126-128°C/0.4mm); **^{1}H NMR** (200 MHz): 0.95 (t, J=6.2, 3H), 1.45-1.85(m, 9H), 1.20-1.40(m, 6H), 2.15-2.20(m, 3H), 2.82-3.05(m, 2H), 3.84 (t J= 5.6, 2H); **^{13}C NMR** (200 MHz); 13.72, 22.15, 22.74, 24.00, 27.10, 27.95, 29.00, 29.72, 50.32, 53.52, 60.75, 64.31.; **IR** (Neat): 3500, 2900, 2800, 1350, and 1220.; **Mass** : 199, 142, 98, 84.

v). 2-Butyl,N-(1-proponol) pyrrolidine (19c).
Yield 84%; b.p (118-122°C/0.4mm); **^{1}H NMR** (200 MHz): 0.90(t, J=6.1, 3H), 1.15-1.30(m, 6H), 1.45-2.15(br, 9H), 2.28-2.34(m,1H), 2.95-3.04(m, 1H) 3.30(p, J=5.1, 1H), 2.82-3.71(m, 2H); **^{13}CNMR** (200 MHz): 13.85, 21.51, 22.93, 28.52, 28.95, 30.00, 33.55, 33.92, 54.60, 66.22, 65.20; *IR* (Neat) :3600, 2900, 2800, 1225, and 1050.; **Mass** : 185, 128, 84, 70.

vi). 2-Butyl,N-(1-Propanol) Hexamethyleneimine (24).
Yield 88%; b.p (128-130°C/0.4mm) ; **^{1}H NMR** (200 MHz): 0.9(t, J=6.2, 3H), 1.21-1.40(m, 6H), 1.45-1.75 (m, 10H), 2.55-2.95(m, 6H) 3.82(t,J=3.8, 2H); **^{13}C NMR** (200 MHz): 13.88, 22.74, 24.52, 26.81, 27.72, 28.29, 29.10, 31.69, 32.33, 48.94, 63.25, 64.81.; **Mass** : 212, 156, 112.

II Synthesis of 1-Methyl,4-(2-propanol)piperidine (11).

The compound **11** was prepared in three steps starting from commercially available 1-Methyl-4-piperidone and chloroacetone by following literature procedure[33].

a). preparation of dimethyl-1-oxopropyl phosphate.

To 43.3g (290mmol) of triethyl phosphite in 500ml of two neck R.B flask, freshly distilled iodoacetone (52.2g, 285mmol) was added slowly through pressure equalizer addition funnel with stirring at 0-5°C. After complete addition, reaction mixture was allowed to warm spontaneously, to about 35°C. Reaction mixture was allowed to stirr for additional 2h, then product was distilled off under reduced pressure, which offered 15.5g (30%) of dimethyl-1-oxopropyl phosphate,(**11**) ; b.p 83-84°C /4mm.

^{1}H NMR (90 MHz) : 1.34 (t, J=6.5, 6H), 2.32(s, 3H), 2.96(s,1H), 3.22(s,1H), 4.16(m,4H); **IR** (Neat): 1717, 1258, and 1165.

b). To a stirring solution of dimethyl-1-oxopropyl phosphate (10g, 50mmol), KOH (2.88g,50mmol) in aqueous ethanol (4:1), 1-Methyl-4-piperidone (5.45ml, 46mmol) was added. After 3h of stirring at room temperature, ethanol was evaporated, residue was extracted with ether and dried over anhydrous Na_2SO_4, which on removal of organic layer gave 5.2g (75%) of crude product, (mixture of α,β and β,γ unsaturated ketones), which was purified by distillation.; b.p 57-58°C/5mm.

^{1}H NMR (90 MHz): 1.90-2.00 (m,6H), 2.01(s, 3H), 2.11-2.26(m, 3H).; **IR** (Neat): 2900, 2800, 1710, and 1255.

c). Reduction of 1-Methyl,4(2-propanone) piperidine.

To a solution of above α,β and β,γ-unsaturated ketone (5.8g, 32.6mmol) in methanol (50ml), 1M KOH solution (100ml) was added with stirring. After 5 minutes **Ni/Al** alloy (40g) was added over a period of 1h in portions, and stirring was continued for a further one 1h after complete addition of Ni/Al alloy. Then contents were filtered off through sintered funnel and washed twice with CH_2Cl_2. The filtrate was extracted three times with CH_2Cl_2, combined extracts dried over Na_2SO_4, concentrated and distilled to offer 4g (80%) of compound **11** (b.p 64-70°C/0.5mm) as clear liquid.

^{1}H NMR (90 MHz): 1.00-1.38(m, 2H), 1.50-1.69(m, 2H), 1.74-1.86(m, 2H), l2.12(s, 3H), 2.63-2.79(m,2H), 3.0(1H, OH), 3.72-3.82(m, 1H).; **IR** (Neat) :3500, 2800, 1250 and 1050.; **Mass**: m/z:157.

III Preparation of N-benzyl-2-amino ethanol (12).

To a stirring solution of 2-amino ethanol (10g, 163.9mmol) in dry DMF (10ml), distilled benzylchloride (10.3g, 81.7mmol in 10ml of DMF) was added slowly. After 1h of reflux, resulting mixture was allowed to cool to room temperature, excess aminoethanol was removed under reduced pressure. The crude salt was neutralised (pH=8) by using 1N KOH solution. The aqueous layer was extracted with EtOAc and dried over anhydrous Na_2SO_4. On concentration followed by distillation gave 7.9g (80%) of pure **12** as a clear liquid. b.p 120°C/0.4mm.

^{1}H NMR (90 MHz): 2.32-2.58(m, 3H), 3.80(t, J=5.6,2H), 4.02(s,2H), 7.01-7.10(m,4H), 6.25(1H, OH).; **IR** (Neat): 3500, 2900, 2800, 1510, 1480, 1210.; **Mass**: (m/z: 151)

IV. Preparation of 1(3,3-diethyl carboxy propyl)piperidine (13).

To 1.02g (35m mol) of NaH (80% in mineral oil) in evacuated system, 10ml of THF and HMPA (8:2) was added. After 5 minutes of stirring, diethylmalanoate 5.5g (35m mol) was added at a moderate rate and stirring was continued for further 30 minutes. When evolution of hydrogen was stoped, 5g (34mmol) of 1-(2-Chloroethyl) piperidine was added. The resulting mixture was refluxed for 6h, allowed to cool to room temperature, and quenched with saturated NH_4Cl solution. The aqueous layer was extracted with ether (3x40ml), extracts was washed with brine and dried over Na_2SO_4. Concentration followed by distillation offered 2.9g (62%) of pure compound **13** as a clear liquid.

^{1}H NMR (90 MHz): 1.26(t,J= 7.1, 6H), 1.29-1.62(m, 6H), 2.10-2.32(m, 6H), 3.42(t, J=6.5, 1H), 4.10-4.22(m, 4H); **IR** (Neat) : 2900, 1750, 1530, 1440, 1200, and 1030.; **Mass**: (m/z, 171).

General method of photolysis :

a). In absence of Methyl Viologen.

Acetonitrile (500ml) solution containing 2g (10mmol) of compounds (**9-13**) and 0.150g (0.842mmol) of DCN was irradiated using 450-W Hanovia medium pressure mercury lamp, with Pyrex filter, at ambient temperature without removing dissolved air. The reaction progress was monitored by VPC (10% OV-17, 8' X 1/8''). After 4-9h of irradiation, GC chromatography showed complete disappearance of starting material. After removal of solvent the compounds were purified as mentioned below and DCN was recovered back (>98%).

b). In presence of Methyl Viologen.

Here irradiation was performed same as above, but additional catalytic amount (40mg) of methyl viologen was added in 500ml irradiating solution. During irradiation the colour of the reaction changes from blue to brown which subsequently disappears when photolysis was discontinued. After 3-4h of irradiation starting material was completely disappeared. Photolysis was discontinued and acetonitrile solution was removed under reduced pressure at low temperature. To the residue, 2ml of benzene was added and precipitate (methyl viologen and some of DCN) was filtered off and washed twice with benzene (2X2ml). Filtrate was concentrated and chromotographed using ether:pentane (1:9) as an eluent to give cyclised products as a pure liquids and DCN was recovered quantitatively.

14). Yield 84%.; ^{1}H NMR (90 MHz): 1.36-1.86(m,7H), 1.96-2.38(m,3H), 2.59-2.94(m, 2H), 3.29-3.53(m, 2H), 3.71-4.09(m, 1H).; **IR** (Neat): 2800, 2700, 1200, and 1000 ; **Mass** : (m/z: 141).

15). Yield 70%.; ^{1}**H NMR** (90 MHz): 1.20-2.45(m, 8H), 2.48-2.98(m, 2H), 3.10-3.57(m, 1H); **IR** (Neat) :2800, 2700, 1200, 1000 and 750.; **Mass** : (m/z :113)

16). Yield 73%.; ^{1}**H NMR** (90 MHz): 1.67-1.86(m, 3H), 1.98-2.08(m, 2H), 2.36(s, 3H), 2.72-2.83(m, 2H), 3.80-3.87(m, 1H), 3.91-3.95(m, H).; **IR**(Neat) : 2900, 2800, 1200, and 1020.; **Mass** : (m/z: 155).

17). Yield 83%.; ^{1}**H NMR** (90 MHz): 3.65-3.71(m, 2H), 3.82-3.89(m, 2H), 4.35-4.45(m, 2H), 7.28-7.41(m, 5H).; **IR** (Neat): 2900, 2800, 1500, 1400 and 1000.; **Mass** : (m/z: 149).

18). Yield 65%.; ^{1}**H NMR** (90 MHz): 1.28(t, 6H), 1.49-1.84(m, 6H), 1.91-2.15(m, 3H), 2.45-2.52(m, 1H), 2.59-2.73(m, 2H), 3.14(dd, J=7.2 and 6.9, 1H), 4.16 (q, 4H).; **IR** (Neat) : 2900, 2800, 1740, 1150 and 1050.; **Mass** : (m/z: 269).

22 a). Yield 92%.; ^{1}**H NMR** (90 MHz): 0.9(d, J=6.2, 3H), 1.30-1.80(m, 8H), 2.00-2.18(m, 2H), 3.30-3.44(m, 3H) 4.02-4.10(m, 1H).; **IR** (Neat): 2900, 2800, 1200 and 1020.; **Mass** : 155, 140, 120,110, 97, 84.

22 b). Yield 90%.; ^{1}**H NMR** (200 MHz): 0.91(t,J=6.4, 3H), 1.21-1.40(m, 6H), 1.52-1.80(m, 8H), 1.91-2.14(m, 2H), 3.22-3.85(m, 3H), 3.92-4.08(m, 1H).; **IR** (Neat) : 2900, 2800, 1350, 1230 and 1060; **Mass**: 197, 169, 140, 84.

22 c). Yield 88%; ^{1}**H NMR** (200 MHz) : 0.85-0.90(m, 3H), 1.18-2.20(m, 13H) 3.12-3.18(m, 2H), 3.48-3.52(m, 1H), 3.62-3.66(m, 1H), 4.02-4.08(m, 1H).; ^{13}**C NMR** (200 MHz) : 13.93, 19.37, 22.89, 28.34, 28.51, 30.25, 34.25, 42.72, 56.48, 67.05, 92.28.; **IR**(Neat): 2900, 2800, 1350, 1260 and 1020.; Mass : 183, 149, 129.

General method for synthesis of 30 a-c.

To the stirring solution of n-butyl magnesium bromide (6mmol) in ether at -20°C, tetrahydro-1,3-Oxazines (**22a-c**, 2.5 mmol) was added. After 30 minutes of stirring at room temperature, reaction was quenched with saturated NH_4Cl solution. The aqueous layer was extracted with ether and dried over Na_2SO_4 and concentrated to offer the crude products **30 (a-c)** as clear liquids (98%), which was purified by column chromtogrphy (silicagel), using acetone,hexane (1:9) as eluent.

30a. Yield 94%; ^{1}**H NMR** (200 MHz): 0.9 (t, J=6.9, 2H), 1.20-1.85 (m, 17H), 2.08-2.14(m, 1H), 2.44-2.52 (m, 1H), 2.60-2.65(m, 1H), 2.82(t, J=7.2, 2H), 3.81(t, J=6.1, 2H); ^{13}**C NMR** (200 MHz) : (*No C_2 Symmetry*) ;13.13, 20.00, 22.00, 22.50, 27.60, 28.25, 28.87, 31.19, 32.87, 46.30, 56.76, 61.72, 62.56. ; **IR** (Neat) : 3500 (br), 2800, 2900, 1350, 1280 and 1060; **Mass**: 213, 198,168,156,112.

30b. Yield 96%.; ^{1}**H NMR** (200 MHz): 0.82(t, J=6.8, 6H), 1.11-1.32(m, 12H), 1.56 (m, 3H), 1.62-1.74(m, 6H), 2.48-2.54(m, 2H), 2.70(t, J=6.6, 2H), 3.75(t, J=5.6, 2H).; ^{13}**C NMR** (200 MHz): (*C_2 symmetry*);17.00, 21.00, 21.52, 23.34, 24.82, 25.10, 26.81, 43.32, 61.10, 62.00.; **IR** (Neat): 3500 (br), 2900, 2800, 1350, and 1230.;**Mass** :255, 199, 198, 140.

30c. Yield 94%; ^{1}**H NMR** (200 MHz) 0.8-1.00(m, 6H), 1.20-1.44(m, 12H), 1.65-1.90(m, 4H), 2.05(s, 2H), 2.81(t, J=6.2, 2H), 3.85(t, J=5.4, 2H); ^{13}**C NMR** (200 MHz): (*C_2 symmetry*); 13.97, 22.75, 28.88, 29.13, 29.54, 35.42, 55.37, 64.43, 67.77; **IR** (Neat) : 3500 (br), 2900, 1220 and 1020; **Mass**: 241, 198, 165, 164, 140.

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24. However, the direct participation of MV^{++} in electron abstraction from α-amino radical for iminium cation generation (as shown below) can not be ruled out at this point.
$$R_2N\text{-}\dot{C}HR' + MV^{++} \rightarrow R_2\overset{+}{N}{=}CHR' + MV^{+}\cdot$$
It may be possible that this step is occuring *via* more than one route.

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