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Photochemistry of Substituted Propiophenones: An Interesting α-and aryl Substituents Effect on Their Photobehaviour[I,II]

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Abstract: *Photochemistry of different α-substituted and phenyl-substituted propiophenones in methanol is investigated with a view to delineate the substituent effect with a special reference to their rearrangement to α-arylpropanoic acids, an important class of nonsteroidal antiinflammatory agents. The results thus obtained bringsforth an important element of their reactivityprofile i.e. the α-chloro-substituent in combination with nuclear alkyl substituents (para > meta) favours 1,2-arylnigration leading to the synthetically useful reaction for α-arylpropanoic acids.*

INTRODUCTION

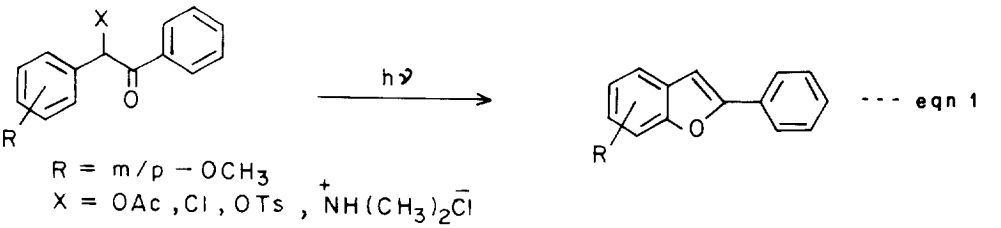
The chemistry of α-substituted propiophenones with a special reference to their transformation into α-aryl propanoic acids, a class of anti-inflammatory agents of current importance has attracted intense attention in the last few years[1,2]. This led to the development of a first photochemical approach for the asymmetric synthesis of S-ibuprofen and S-naproxene[3]. The 1,2-aryl migration involved in the process has been shown to occur through the acetal of the carbonyl group (sp^2 --> sp^3) alone since the S_N2 participation of the aryl group in the parent aryl ketones via the cyclopropane intermediate appears to be disfavoured due to steric strain factor[4].

We have recently reported[3] an efficient direct photo-transformation of *p*-substituted α-chloropropiophenones into α-aryl propanoic acids without prior protection of the carbonyl group. This study has revealed that the excited state (sp^2 --> sp^3) triplets play a profound role in directing the aryl participation, a factor controlling the efficiency of the formation of α-aryl propanoic acids. Especially from the synthetic point of view, this study has led to the discovery of a single step, efficient photo process for ibuprofen.

The mechanistic mode of this rearrangement was probed[3] using a set of optically active α-chloropropiophenones and it emerged that the nature of the carbonyl triplets ($\pi,\pi^*/n,\pi^*$) plays an important role in the chirality transfer. This method finds application in the synthesis of optically active Ibuprofen and ketoprofen,though in moderate optical yields, suggesting that the excited state-induced 1,2-aryl migration is not completely stereospecific.

Despite extensive investigation[5] of the photochemistry of aryl alkyl ketones over the years, the class of α-substituted propiophenones has practically remained unexplored. In this context, our work referred to above as well as a few other reports[6,7] on comparable systems indicate that the photobehaviour is highly sensitive to the inductive effect and pattern of aromatic substituents. For example, an elegant and early contribution by Sheehan and his group[8] on the photochemistry of benzoin ester and desyl compounds leading to disubstituted 2-phenyl benzofurans is noteworthy (eqn. 1). While the *m*-methoxy

substituent greatly enhances the yield of cyclization, the *p*-methoxy group exerts moderate depressing effect on the same process.

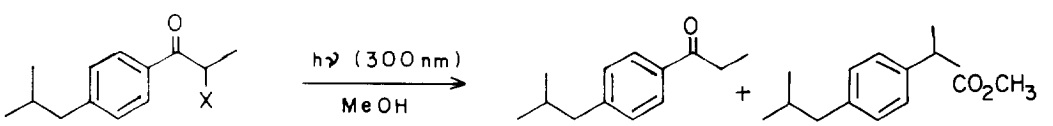


In the last few years, Givens et al[9] have advantageously utilized the efficacious leaving group ability of dialkyl phosphate anion in desyl compounds, to develop cage ligands for oligonucleotides. In this background, α-substituted propiophenones offer unique opportunity to explore the reactions of excited carbonyl group especially with the variation of α- substituents. We wish to present here our interesting findings from such a photoinvestigation and also the results that emerged from the photolysis of *m*-substituted- α-chloropropiophenones. The present findings in conjunction with our previous results help to arrive at a cogent and an unified picture of the photobehaviour of this class of compounds.

RESULTS AND DISCUSSION

Effect of α-substituents: Three *p*-isobutyl α-substitutedpropiophenones **1b** to **1d** were prepared by reported procedures and their identity was established by their spectroscopic data (experimental). A 3% degassed solution of **1** in methanol containing propylene oxide as acid scavenger was irradiated at 300 nm in a Rayonet reactor. The progress of the reaction was monitored by TLC, GLC and after six hours of irradiation, the products were isolated by standard chromatographic techniques. The products in most of the cases were known compounds and their characterization was effected by comparison of their spectral data. The control experiments revealed that these substrates remain totally unreacted in the absence of light.

SCHEME-1



1 5 6

Table 1: Product distribution from the photolysis of α-*p*-isobutyl propiophenones **1a** to **1d**.

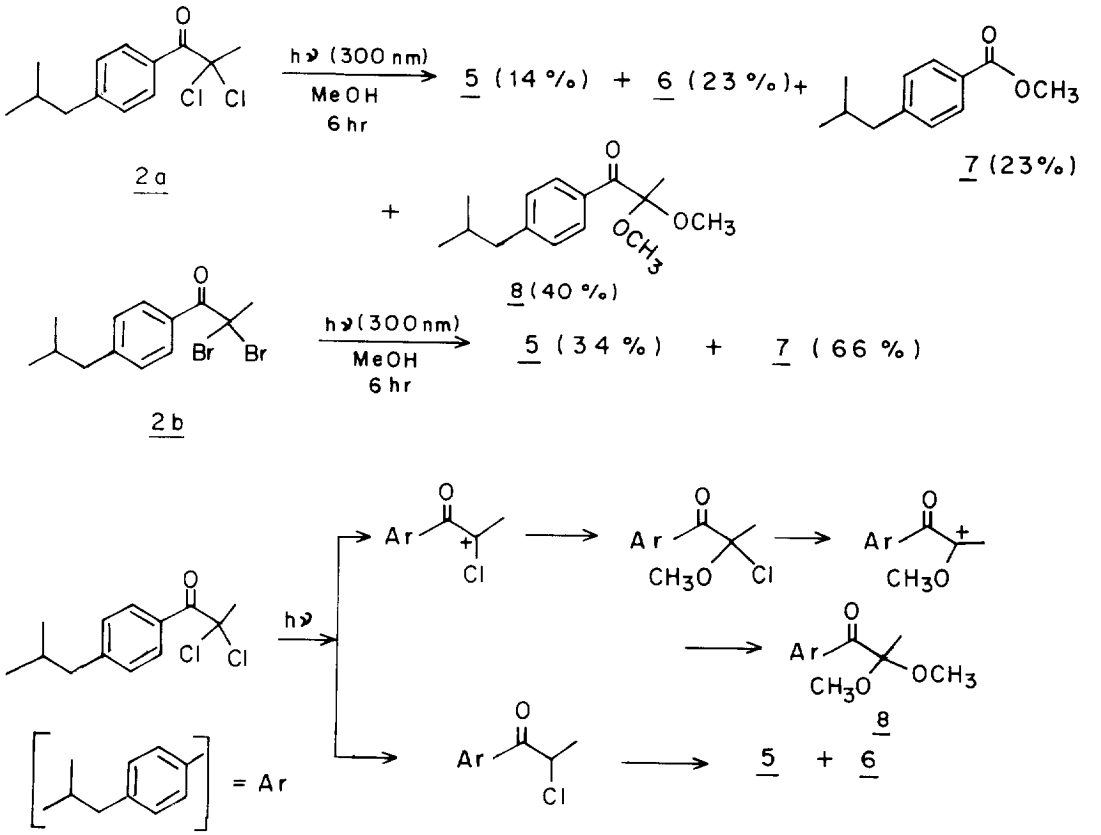
Substrate	X	Conversion	Composition	
		%	**5**	**6**
1a*	Cl	100	25	75
1b	tosyl	100	99	-
1c	#$OCOCH_3$	15	99	-
1d	$N(CH_3)_2$	30	99	-

* The result is abstracted from our previous paper.[3]
\# irradiated at 254 nm

The results arising from the photolysis of **1b** to **1d** have been depicted in scheme 1 and Table 1. At the outset, it is significant to note that all the three substrates **1b** to **1d** have shown a total proclivity for the formation of the reduction product, i.e p-isobutylpropiophenone **5**. The formation of **5** can be easily rationalized by the initial photohomolysis of the C-X bond followed by hydrogen atom transfer. The presently observed photobehaviour is strikingly divergent from that of α-chloro-*p*-isobutyl propiophenone, **1a**, which essentially underwent heterolytic C-X bond cleavage leading to 1,2 aryl migration, furnishing methyl α-(*p*-isobutyl phenyl)propionate **6** as the major product.

We have investigated the photochemistry of α,α-dihalopropiophenones and observed some interesting photobehaviour hitherto unreported. The results obtained from such a study are shown in Scheme 2.

SCHEME - 2



It is interesting to note that there has been a considerable decrease in the quantum of reduction product as well as the 1,2-aryl migration product in the photolysis of **2a** compared to those obtained from the corresponding mono chloroketone **1a**. At the same time, photosolvolysis leading to **8** has turned out to be a major process; it is significant to note that photosolvolysis was conspicuously absent in the photolysis of the corresponding α-chloropropiophenone **1a**[3]. In this context, it may be mentioned that the reductive dechlorination of **2a** to **1a** has been very well one of the competing primary photoprocesses, as observed by us earlier while monitoring the photolysis of **1a**. This also suggests that the observed minor products **5** and **6** arise from the secondary photolysis of mono-chloroketone, which in turn arises from partial reduction of **2a**; monohaloketone formation was detected in aliquotes during the course of photoreaction.

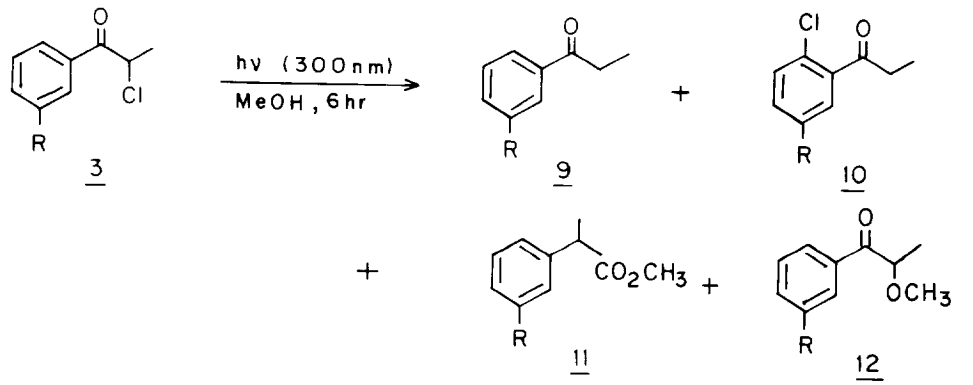
This unique photobehaviour of **2a** leading to **8** contrasting with that of **1a** may be understood in terms of involvement of a facile aryl participation to undergo rearrangement in the case of **1a** and the expulsion of chloride ion in **2a** leading to α-chloro-stabilised carbocation; the latter on nucleophilic capture by methanol may lead to the α,α-chloromethoxy intermediate which undergoes further solvolysis to furnish **8**. Interestingly enough, the solvolysis process as well as 1,2-aryl migration were totally absent in the photolysis of the dibromoketone **2b**. A propensity for radical products resulting from the homolysis of C-Br bond is a typical photobehaviour of alkylbromides[10]. Another common feature is the formation of methylbenzoate, **7** which constitutes the major product from **2b**. In this context, it is relevant to note that Tomioka et al[11a,b] have also observed analogous photobehaviour in α,α,α-trichloroacetophenone and α,α,α-tribromo acetophenone and attributed its formation to the trapping of the photoexcited carbonyl group following α-cleavage by the oxygen present in the medium. A similar process may be operating in the present case as well.

Photolysis of m-substituted-α-chloropropiophenones 3a-3d.

In their pioneering work, Zimmerman and Sandel[12] have demonstrated a strikingly different photobehaviour of aryl substituted benzyl acetates and benzyl chlorides compared with their ground state reactions in aqueous media. It was discovered that *m*-methoxy group selectively enhanced solvolysis compared to the corresponding *p*-OCH_3 isomer; whereas the latter has been shown mostly to lead to radical-derived reduction products: This phenomenon has been explained in terms of the activating effect of the meta group (meta transmission) in the excited-state molecules. Earlier to this, Havinga et al[13] reported a similar type of fascinating *meta* effect in the photochemical hydrolysis of isomeric nitrophenyl phosphate and sulfonate esters. These results prompted us to take up the study of photochemistry of *m*-substituted- α-chloropropiophenones in order to assess whether such a meta effect has any role in their photobehaviour. In the event, this phenomenon would lead to a new methodology for the synthesis of useful antiinflammatory agents such as ketoprofen[3] and phenoprofen[14].

Four differently *m*-substituted- α-chloropropiophenones **3a-d** were selected for the study. These were synthesised by reported methods (experimental) and irradiated in methanol using 300nm light in a Rayonet reactor. Most of the products could be isolated by standard chromatographic techniques and well characterised by their spectral data. The results that ensued from the photolysis of these substrates are shown in Scheme 3(Table 2). A gross comparison of the type of products obtained from the meta-substituted α-chloroketones **3a-d** to those with our earlier results[3] obtained from the corresponding *p*-substituted ketones bringsforth interesting points.

SCHEME 3



It can be noticed that there has been significantly a change in the extent of radical and ionic products, that were obtained from *m*-methyl **3c** compared to those from the corresponding *p*-methyl substituted substrate. While there has been a significant increase in the quantum of reduction product (8 to 33%), the ionic rearranged product is reduced considerably (76 to 66%). Such a result could be attributed to substituent effect on the carbonyl excited state leading to preferential cleavage of C-Cl bond either homolytically or heterolytically. Nonetheless, the alkyl group either in para or in meta position has predominantly led to C-Cl heterolysis; in addition, the meta-alkyl substituent resulted in the C-Cl homolysis to a greater extent.

Table 2: Product distribution from the photolysis of 3a-d.

Substrates	R	Conversion(%)	composition			
			9	**10**	**11**	**12**
3a	*m*-OCH_3	100	13	68	--	19
	**P*-OCH_3	100	12	--	08	70
3b	*m*-OPh	100	70	21	08	-
3c	*m*-CH_3	70	33	--	66	-
	**p*-CH_3	100	8	--	76	-
#3d	*m*-NO_2	20	100	-	-	-

* These results are from our previous paper[3].

\# Photolysis was carried out employing 254nm light.

In this context, similar change in the type of products in going from meta to para substituents reported by Zimmerman[12] et al. referred to earlier in their photolysis of substituted benzyl acetates is noteworthy. An interesting feature of the results from the photolysis of *m*-methoxy ketone **3a** is the dramatic effect of the *m*-methoxy substituent in leading essentially to the reduction products (81%) while the corresponding *p*-OCH_3 substituent led essentially to the solvolysis product **12** . Another significant aspect of the photobehaviour of 3a is the formation of major product **10a**(68%) arising from the selective intramolecular ring chlorination in ortho position to the aryl ketone and para to the OCH_3 substituent. However, similar pronounced effect is not observed in case of *m*-OPh ketone **3b**. The formation of just minor amounts of ionic products viz **11,12**, implies that the characteristic *meta* effect mentioned has no role to play in these *meta* substituted α-chloropropiophenones **3a-3d**. Therefore, the formation of minor rearrangement product leading to phenoprofen **11b** as well as exclusive reductive dechlorination to **9b** in this aryl ketone is not surprising. As expected, *m*-nitroketone **3d** offered essentially reductive dechlorination product **9d**.

Photolysis of phenyl substituted α-methoxy propiophenones:

Another problem that concerns these studies is the genesis of the reduction products **5** and **9** as noted in the above results. That is, these may arise either directly from the primary photoprocess or may arise as the secondary photo products from the solvolysis products such as α-methoxy propiophenones involving Norrish II elimination. We have addressed this problem by examining the photobehaviour of certain α-methoxypropiophenones, **4a-4c**. These substrates were prepared by following the standard procedures and were subjected to photolysis in methanol and results obtained are summarised in scheme-4, Table 3.

SCHEME 4

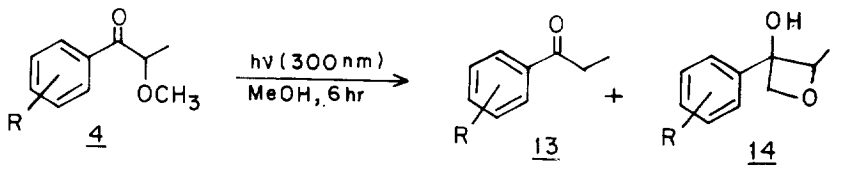


Table 3: Product distribution from the photolysis of **4a-e**

Substrate	R	% conversion	% of photoproducts	
			13	**14**
4a	R=H	95	35	65
4b	*p*-CH_3	100	44	56
4c	*m*-CH_3	100	32	68
4d	*p*-OCH_3	65	50	50
4e	*p*-isobutyl	100	33	66

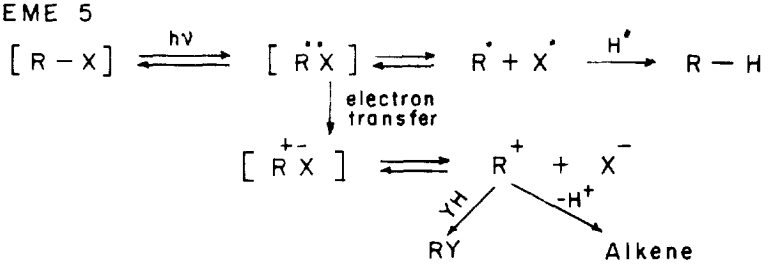
The results show that the photolysis clearly affords both type II elimination and cyclisation products (**13,14**), notably with the predominance of the latter type as a general feature except in the case of **4d** . These results, therefore, suggest that the observed reductive photodechlorination leading to the formation of **5** and **9** in the case of the previously described substrates **1-3**, is a consequence of a direct primary photoprocess; it is not however occurring from the secondary photoprocesses of the methanolysis product as the N-II cyclization leading to oxetanols was totally absent. Another significant aspect of the results from **4a-e** is that the N-II photoprocess is so much overwhelming so that the ring substituent effect is almost not discernable.

An overview of the results obtained from the photolysis of differently substituted propiophenones reported[3] by us previously and those discussed in this paper will be extremely interesting. *P*-substituted α-chloropropiophenones furnished products arising from both the homolysis and heterolysis of C-Cl bond; α-tosyl,α-dimethylamino and *p*-isobutyl-α-acetoxypropiophenones gave products exclusively from C-X homolysis. Between the α,α-dichloro and α,α-dibromo *p*-isobutylpropiophenones, only the former furnished the product from C-Cl heterolysis. In the meta-substituted series, the α-substituent was the chloro group and the photolysis of all the substrates led again to both radical and ionic products. An important feature that emerges from the above gross analysis is the distinctly characteristic tendency of the C-Cl bond towards heterolytic cleavage, a feature conspicuously absent with the other substituents. This unique photobehaviour of the α-chloroketo moiety is rather intriguing and needs to be understood.

Mechanistic Aspects :

Photochemistry of alkyl halides has been extensively studied over the years and the generally accepted mechanism suggested by Kropp et al[15] involves an initial homolytic cleavage of the C-X bond followed by competing electron transfer within the resulting caged radical pair and diffusion from the cage (scheme 5).

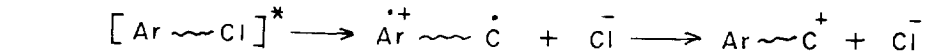
SCHEME 5



Morrison and co-workers[16] have made significant contribution especially in photolytic cleavage of remote functional leaving groups in poly functional molecules such as exo/endo 2-benzonorbornyl chlorides and sulphonate esters. A remarkably large exo:endo reactivity ratio(700:1) is attributed to the stereoelectronic aspects of the remote activation due to the aromatic ring of the benzo systems. These authors suggested a mechanism which incorporated both direct heterolytic fission as well as a homolytic

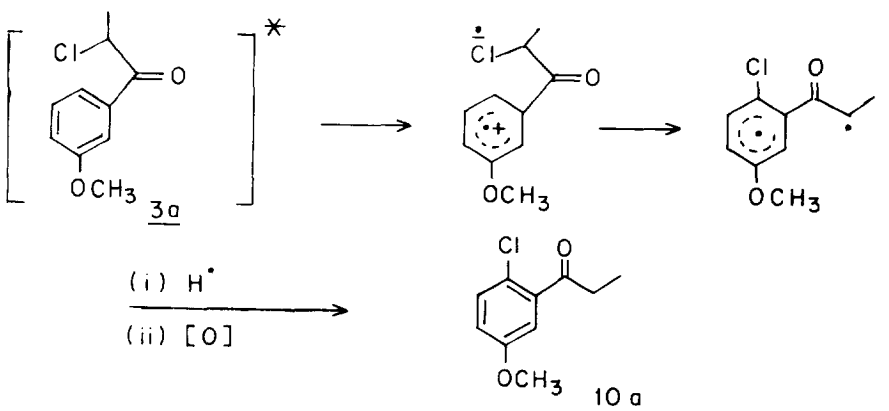
fission to a polarized radical pair followed by electron transfer leading to ion pair. Cristol and co-workers[17] in their photolytic study of related systems made an indepth investigation on a variety of rigid benzo systems with chlorides and mesylates as leaving groups. These authors proposed that the C-X cleavage proceeds via an "intimate ion radical pair" namely $R\cdot Cl\cdots > R^{+}Cl^{-}$ which may then dissociate to a pair of radicals or a pair of ions depending on the polarity of the medium. Activation of the C-Cl bond in these substrates was suggested to occur via an electron transfer from the $\pi\rightarrow\pi^{*}$ state of the aromatic ring to the C-Cl σ^{*}-orbital (scheme 6).

SCHEME 6



Viewed in this background, it becomes clear that the activation of the α-C-Cl bond in propiophenones examined in the present study is due to the aryl ketone chromophore since we observed no evidence of photoreactivity upon the irradiation of propiophenone dimethylketal[3]. Our quenching studies have supported the involvement of triplet state and further elaborated the role of specific excited states on the primary photoprocesses of reductive dechlorination, 1,2 aryl migration and solvolysis. The homolytic and heterolytic cleavage of α-C-Cl bond leading to radical and ionic product could therefore be rationalised implicating the mechanistic concept largely due to Kropp and Morrison, referred to above. The interesting intramolecular selective transfer of chlorine into the aromatic ring in the case of *m*-methoxy-α-Chloropropiophenone (scheme 3) may be accounted on the lines of electron transfer from the aromatic ring proposed by Cristol (scheme 7). At this stage, we are not sure whether solvolysis and 1,2 aryl migration products from the other substrates could involve radical cations of the type (scheme 6) wherein back electron transfer leads to α-keto cations.

SCHEME 7



In conclusion, the present work extends our earlier photochemical studies on p-substituted- α-chloropropiophenones wherein the problem of the mode of 1,2 aryl migration was addressed. The work described in this paper on the photochemistry of α- and meta substituted propiophenones helps further in the understanding the photobehaviour of this class of ketones. In addition, some of the transformations may be synthetically useful.

EXPERIMENTAL

UV absorption spectra were recorded on Carl Zeiss UV-VIS model 44069.

IR spectra were recorded as smears or nujol mulls(solids) on Perkin-Elmer Infracord model 137-E.

Proton Magnetic Resonance (**^{1}H-NMR**) were recorded on Varian T-60, FT-80A, Bruker FT-90, MSL-200 instrument. All spectra were taken in $CDCl_3$ and chemical shifts are reported in parts per millon(ppm) downfield from TMS as the internal standard.

The mass spectra (**MS**) were recorded on a CEC mass spectrometer model 21-110B, using an ionization potential of 70eV.

GLC analyses were carried on a Hewlett Packard Gas Chromatograph 5793, with the following columns:

(i) Carbowax (5%,6'x1/8",Aluminium column)

(ii) OV-101 (5%,6'x1/8",Aluminium column)

(iii) HP-1 (1m x 0.53mm x 2.65µm, Fused silica capillary column).

Usual work-up refers to extraction of the reaction mixture with a suitable organic solvent, washing the organic layer with water, followed by brine and drying over anhydrous Na^2SO^4.

General procedure for the photochemical reactions of substituted propiophenones

A 3% solution of the substrate in dry methanol (0.60g. in 20 ml) was degassed by passing N_2 gas for 5 minutes, followed by addition of propylene oxide (1-2 ml, wherever indicated) and irradiated in a Rayonet photochemical reactor with 254/300 nm light. The progress of the reaction was monitored by periodic thin layer chromatography of aliquotes at different intervals of time. Generally, after an irradiation for six hours, the solvent was evaporated and the residue distilled under reduced pressure. The products were separated either by column chromatography on silica gel or preparative TLC. As most of the products were well known compounds, their identification could be easily done by a direct comparison of their spectral data. In many instances, the products could be characterised by peak accentuation technique in GLC with authentic samples.

Preparation of the substrates 1b-1d

p-Isobutyl-α-tosylpropiophenone (1b): This substrate was prepared by following a reported procedure.[14] A solution of (1.96g, 0.007M) of silver *p*-toluenesulfonate and a *p*-isobutyl-α-bromopropiophenone[11] (1.345g, 0.005M) in 20 ml of acetonitrile was heated under reflux for 40 hours. The solution was filtered and the solvent was stripped off in vacuo. The residue obtained was purified by crystallization from ethanol. Yield 1.26g.(70%), m.p. 64-65°C. **IR** (CCl_4) : 2960, 1700, 1600, 1380, 1235, 1180, 1020, 930 and 820 cm^{-1}. **^{1}H-NMR** 0.90 (d, 6H), 1.60 (d, 3H), 1.68-2.10(m, 1H), 2.40 (s, 3H), 2.52 (d, 2H), 5.70 (q, 1H), 7.10 (d, 2H), 7.20 (d, 2H), 7.60 (d, 2H), 7.70 (d, 2H). **Anal. Calcd. for** $C_{20}H_{24}O_4S$: C, 66.66; H, 6.66; Found: C, 66.30; H, 6.75.

p-Isobutyl-α-acetoxypropiophenone (1c): p-isobutyl-α-hydroxypropiophenone:[2] (2.06g, 0.01M) and dry pyridine (1.185g, 0.015M) were taken in 10 ml dry CH_2Cl_2 followed by addition of acetyl chloride (1.17g, 0.015M) in 10 ml dry CH_2Cl_2 with continuous stirring for 3 hr. A standard work-up yielded a product. **b.p.** 175-180 (bath)/3mm. Yield: 1.92g.(77%). **IR** (Neat): 2940, 1740, 1690, 1600, 1370, 1230, 1130, 1090, 1040, 980 and 860 cm^{-1}. **^{1}H-NMR**: 0.90 (d, 6H), 1.50 (d, 3H), 1.60-2.10(m, 1H), 2.05 (s, 3H), 2.50 (d, 2H), 5.90 (q, 1H), 7.20 (d, 2H), 7.80 (d, 2H). **Anal. calcd. for** $C_{15}H_{20}O_3$: C, 72.58; H, 8.06. **Found**: C, 72.76; H, 8.41.

p-isobutyl-α-N,N-dimethylaminopropiophenone (1d): A mixture of α-bromo(*p*-isobutyl)propiophenone (2.69g,.01M), dimethylammonium chloride (1.25g,.015M), anhydrous K_2CO_3 (2.76g, 0.02M) and tributyl ammonium hydrogen sulphate (30 mg) was taken in 30 ml CH_2Cl_2 and stirred overnight under anhydrous condition. The reaction was quenched by adding 50 ml water. Organic layer was separated. A normal work-up gave a product. **b.p.** 107-8°C/1.5mm, Yield 1.51g.(65%). **IR** (Neat): 2960, 1680, 1605, 1440, 1370, 1230, 1180, 1100, 1040 and 830 cm^{-1}. **^{1}H-NMR**: 0.90 (d, 6H), 1.28 (d, 3H), 1.68-2.08(m, 1H), 2.32 (s, 6H), 2.52 (d, 2H), 4.08 (q, 1H), 7.28 (d, 2H), 7.95 (d. 2H). **Anal. calcd. for** $C_{15}H_{23}NO$: C, 77.25; H, 9.87; N, 6.00. **Found**: C, 77.42; H, 9.98; N, 5.70.

The UV spectral data of 1a-1d.(solvent methanol)

Compound	X	λ_{max} - nm (ε)		
1a	-Cl	207 (8982)	262 (10778)	304 (449)
1b	-OTS	212 (15184)	245 (16360)	310 (519)
1c	-OAC	215 (5317)	255 (12744)	300 (91)
1d	$-N(Me)_2$	212 (9475)	255 (15801)	300 (921)

Photolysis of 1a to 1d: The photolysis was carried out as described in the general procedure with the addition of propylene oxide as an acid scavanger. However, in the case of **1d**, the propylene oxide was not added. The products were separated by preparative TLC (silica gel-benzene).

Photoproduct of (1a)

p-isobutylpropiophenone (5): **IR** (Neat): 1690 cm^{-1}; **^{1}H-NMR**: 0.91 (d, 3H), 1.22 (t, 3H), 1.60-2.10(m, 1H), 2.53 (d, 2H), 2.98 (q, 2H), 7.20 (d, 2H), 7.90 (d, 2H).

Methyl α(p-isobutylphenyl)propionate (6): **IR** (Neat): 1745 cm^{-1}; **^{1}H-NMR**: 0.88 (d, 6H), 1.43 (d, 3H), 1.60-2.05(m, 1H), 2.4(d, 2H). 3.56(s, 3H), 3.60(q, 1H), 7.10(m, 4H). **MS** m/z (%): 220 (M^+, 38), 177(43), 162(49), 145(21), 131(19), 118(100), 105(25), 91(34), 77(17).

Photoproduct of **1b-1d** is *p*-isobutyl propiophenone **5** only. The spectral data is given above.

Photolysis of α,α-dihaloketones 2a, 2b

Preparation of p-isobutyl-α,α-dichloropropiophenone (2a): This compound was prepared by a known[16] procedure. A solution of (5.61g, .025M) of α-chloro *p*-isobutylpropiophenone in 50 ml of dimethyl formamide was heated to 80°C and Cl_2 was slowly bubbled for 45 minutes. The reaction mixture was poured into 2N HCl (100 ml) and extracted repeatedly with CCl_4. The organic layer was washed by water followed by brine and dried over anhydrous Na_2SO_4. The solvent was removed in vacuo and residue was distilled. **b.p.** 160-61°C/15mm. Yield 5.93g. (92%). **IR** (Neat): 2950, 1690, 1610, 1380, 1265, 1190, 1080, 970 and 870 cm^{-1}. **^{1}H-NMR**: 0.90(d, 6H), 1.60-2.05(m, 1H), 2.25(s, 3H), 2.50(d, 2H), 7.20(d, 2H), 8.20(d, 2H). **Anal. calcd. for** $C_{13}H_{16}Cl_2O$: C, 60.23; H, 6.17; Cl, 27.41. **Found**: C, 60.56; H, 6.44; Cl, 27.02.

p-isobutyl-α,α-dibromopropiophenone (2b) Bromine (32.2g, 0.20M) was added dropwise over a period of 1 hr. into a solution of *p*-isobutylpropiophenone[10] (19g, 0.10M) in CCl_4 (50 ml). After stirring for 3h, the reaction mixture was poured into cooled 10% sodium meta bisulphite solution (100 ml). The organic layer was separated and washed successively with saturated $NaHCO_3$, water and brine. The usual work-up afforded **2b. b.p.** 111-12°C/2mm, Yield 29.30g. (84%). **IR** (Neat): 2980, 1690, 1610, 1430, 1380, 1250, 1140, 1070, 960 and 860 cm^{-1}. **^{1}H-NMR**: 0.90(d, 6H), 1.60-2.05(m, 1H), 2.50(d, 2H), 2.65(s, 3H), 7.10(d, 2H), 8.20(d, 2H). **Anal. calcd. for** $C_{13}H_{16}Br_2O$: C, 44.82; H, 4.59; Br, 45.97. **Found**: C, 44.95; H, 5.05, Br, 45.64.

The UV spectral data of **2a** and **2b** are furnished below:

2a: λ_{max} - nm (ε): 210(6229), 268(13606), 328(409)

2b: 210(7094), 272(12030), 330(488).

Photoproducts from 2a and 2b: The photolysis was carried out as described in the general procedure with the addition of propylene oxide as acid scavenger. The products were separated by preparative TLC (silica gel-benzene).

p-isobutylpropiophenone (5): Spectral data (Vide supra)

Methyl-α(p-isobutylphenyl)propionate (6): Spectral data (Vide supra)

Methyl(p-isobutyl)benzoate (7): **IR** (Neat) 1735 cm^{-1}; **^{1}H-NMR**: 0.90(d, 6H), 1.60-2.05(m, 1H), 2.50(d, 2H), 3.80(s, 3H), 7.20(d, 2H), 7.90(d, 2H). When this compound was hydrolysed, *p*-isobutyl benzoic acid was obtained and its spectral data comparable with reported.[3]

p-Isobutyl-α . α-dimethoxypropiophenone (8a): **IR** (neat): 1690 cm^{-1}. **^{1}H-NMR**: 0.90(d, 6H), 1.55(s, 3H), 1.60-2.05(m, 1H), 2.50(d, 2H), 3.30(s, 6H), 7.10(d, 2H), 8.00(d, 2H). **MS** m/z (%): 250 (M^+, 2), 219(20), 207(7), 161(40), 118(22), 89(100).

Photolysis of m-substituted-α-chloropropiophenones 3a-3d

Preparation of 3a to 3d: Treatment of *m*-substituted benzaldehyde (0.05M) with Grignard reagent prepared from ethyl bromide (10.90g,0.1M) and Mg turnings (2.4g,0.1M) under standard conditions afforded the secondary alcohol.

Substituent at the meta position	b.p.	Yield %
$-OCH_3$	131-32°C/15mm	90
-OPh	145-46°C/1.5mm	92
$-CH_3$	87-90°C/6mm	88

Oxidation of the secondary alcohols to the corresponding *m*-substituted propiophenone. The secondary alcohol (0.042M) when subjected to Brown's reagent[18] (prepared by dissolving 5g. of sodium dichromate in 15 ml of water, followed by addition of 4 ml of conc. H_2SO_4 and diluted to 25 ml) was oxidised to the corresponding ketone.

Compound R	b.p.	Yield %
$-OCH_3$	135-40°C/15mm	91
-OPh	135-36°C/1mm	90
$-CH_3$	108-109°C/6mm	91

α-Chlorination of the above ketones to 3a-3d

α-chlorination was performed by reported procedure.[19a,b] A mixture of hydrated copper (II) chloride (0.096M), LiCl (0.048M) was taken in 40 ml DMF, the temperature was raised to 80-90°C,and the ketone (0.04M) in 15 ml DMF was added in one lot. Temperature of the reaction mixture was maintained between 80-90°C for specified hours (Table) with constant stirring. The reaction mixture after cooling to room temperature was poured into dilute HCl (200 ml), extracted with ether (3x50 ml). The combined organic layer was washed with dil. HCl, followed by saturated $NaHCO_3$. The pure α-chloro ketone was obtained by column chromatography (Silica gel - Benzene), followed by distillation.

Compound	R	Reflux time(hr.)	b.p./m.p.	Yield %
3a	$-OCH_3$	6	120-21°C/4mm	74
3b	-OPh	15	156-57°C/1.5mm	58
3c	$-CH_3$	4	185-90°C/40mm	66
3d	$-NO_2$	15	42-43°C	51

m-nitropropiophenone was obtained by nitration of propiophenone following a reported procedure.[20] Spectral data of α-chloro (*m*-substituted) propiophenones **3a-3d** are as follows:

m-Methoxy-α-chloropropiophenone (3a): **IR** (Neat): 2920, 2820, 1695, 1600, 1590, 1490, 1450, 1420, 1270, 1050, 750 cm^{-1}. **^{1}H-NMR**: 1.70 (d, 3H), 3.83 (s, 3H), 5.10 (q, 1H), 6.90-7.60 (m, 4H). **Anal. calcd. for** $C_{10}H_{11}ClO_2$: C, 60.45; H, 5.54, Cl, 17.88. **Found**: C, 60.80; H, 5.36; Cl, 17.51.

m-Phenoxy-α-Chloropropiophenone (3b): **IR** (Neat): 3020, 2990, 2920, 1690, 1590, 1490, 1430, 1250, 890, 740 cm^{-1}. **^{1}H-NMR**: 1.70 (d, 2H), 5.10 (q, 1H), 6.90-7.70(m, 9H). **Anal. calcd. for** $C_{15}H_{13}ClO_2$: C, 69.27; H, 4.99; Cl, 13.62. **Found**: C, 69.27; H, 5.17; Cl, 13.75.

m-Methyl-α-chloropropiophenones (3c): **IR** (Neat): 2920, 2980, 1690, 1600, 1580, 1490, 1250, 1160, 750 cm^{-1}. **^{1}H-NMR**: 1.73 (d, 3H), 2.40 (s, 3H), 5.22 (q, 1H), 7.22-7.95(m, 4H). **Anal. calcd. for** $C_{10}H_{11}ClO$: C, 65.75; H, 6.02; Cl, 19.45. **Found**: C, 65.38; H, 6.12; Cl, 19.21.

m-Nitro-α-chloropropiophenone (3d): **IR** (Nujol): 3100, 2920, 1690, 1600, 1520, 1440, 1360, 1240, 1190, 1070, 810, 710 cm^{-1}. **^{1}H-NMR**: 1.70 (d, 3H), 5.15 (q, 1H), 7.50-8.90(m, 4H). **Anal. calcd. for** $C_9H_8ClNO_3$: C, 50.58; H, 3.74; Cl, 16.62; N, 6.55. **Found**: C, 50.13; H, 3.61; Cl, 16.90; N, 6.25.

The UV Spectral Data of 3a-3d (Solvent methanol)

Compound	R	λ_{max} - nm (ε)		
3a	$-OCH_3$	218 (4241)	255 (7297)	315 (1883)
3b	-OPh	226 (19428)	250 (9694)	300 (2649)
3c	$-CH_3$	210 (13300)	252 (12528)	300 (1538)
3d	$-NO_2$	210 (8695)	234 (15312)	300 (855)

Photoproducts: Photolyses of **3a-3d** were carried out as described previously with the addition of 1,2 ml of propylene oxide and the products were isolated by preparative TLC (silica gel-benzene).

Products from m-methoxy-α-chloropropiophenone (3a)

m-methoxy propiophenone (9a): **IR** (Neat): 1695 cm^{-1}; **^{1}H-NMR**: 1.16 (t, 3H), 2.86 (q, 2H), 3.76 (s, 3H), 6.76-7.56(m, 4H).

2-chloro, 5-methoxypropiophenone (10a): **IR** (neat): 1690 cm^{-1}; **^{1}H-NMR**: 1.15 (t, 3H), 2.85 (q, 2H), 370 (s, 3H), 6.70-7.25(m, 3H); **MS** m/z (%): 198 (M^+, 44), 200 (M^{+2}, 14), 169(100), 171(34), 141(41), 143(12), 126(38), 128(12).

m-methoxy-α-methoxypropiophenone (12a): **IR** (neat) 1700 cm^{-1}; **^{1}H-NMR**: 1.46 (d, 3H), 3.33 (s, 3H), 3.82 (s, 3H), 4.57 (q, 1H), 7.00-7.66(m, 4H). Identity of this compound was further confirmed by peak accentuation technique with the authentic sample prepared by following the procedure described later.

Photoproducts of m-phenoxy-α-chloropropiophenone (3b)

m-phenoxy propiophenone (9b): **IR** (Neat): 1690 cm^{-1}; **^{1}H-NMR**: 1.20 (t, 3H), 2.92 (q, 2H), 6.12-7.44(m, 9H).

2-chloro, 5-phenoxypropiophenone (10b): **IR** (neat): 1690 cm^{-1}; **^{1}H-NMR**: 1.22 (t, 3H), 2.97 (q, 2H), 6.82-7.73 (m, 8H). **MS** m/z (%): (M^+), 260(60), M^{+2}, 262(20), 231(100), 233(33), 203(50), 205(17), 77(54).

Methyl-α-(m-phenoxyphenyl)propionate (11b): **IR** (Neat): 1740 cm^{-1}; **^{1}H-NMR**: 1.40 (d, 3H), 3.68 (s, 3H), 3.88 (q, 1H), 6.88-7.56(m, 9H); **MS**: m/z (%): 256 (M^+, 60), 197(100), 119(25), 104(45), 91(68), 77(62). **MS** m/z (%): 164 (M^+, 3%), 119(100), 105(15), 91(60), 77(32).

Photoproduct of m-methyl-α-chloropropiophenone (3c)

m-Methylpropiophenone (9c): **IR** (Neat): 1690 cm^{-1}; **^{1}H-NMR**: 1.16 (t, 3H), 2.40 (s, 3H), 2.86 (q, 2H), 7.13-7.73(m, 4H).

Methyl-α(m-methylphenyl)propionate (11c): **IR** (neat): 1735 cm^{-1}; **^{1}H-NMR**: 1.48 (d, 3H), 2.32 (s, 3H), 3.68 (s, 3H), 3.72 (q, 1H), 7.08-7.88 (m, 4H). **MS** m/z (%): 178 (M^+, 3%), 119(100), 1.5(15), 91(60), 77(32).

Photoproduct of m-nitroα-chloropropiophenone (3d)

m-nitro propiophenone (9d): **IR** (nujol): 1690 cm^{-1}; **^{1}H-NMR**: 1.23 (t, 3H), 3.03 (q, 2H), 7.40-8.60(m, 4H).

Photolysis of phenylsubstituted-α-methoxypropiophenones 4a-e

Preparation of 4a-e

General Procedure: The α-hydroxy ketals were prepared as described in the preparation of α-acetoxy *p*-isobutyl propiophenone **1c** (Section-A). (0.02M) of the α-hydroxy ketal in THF (15 ml) was added dropwise to a suspension of NaH (0.025M) in THF (25 ml) at 0°C. After 10 minutes, CH_3I (0.025M) in THF (10 ml) was added slowly over a period of 15 minutes. Stirring was continued for 3 hr. The reaction was quenched by adding ice cold water (50 ml) and extracted repeatedly with ether (3x25 ml). The residue obtained after the removal of solvent was taken in CH_2Cl_2 and treated with 5% H_2SO_4 to get the required deprotected α-methoxy ketones. The crude product obtained was purified by distillation under diminished pressure. b.p and yields are mentioned below.

Compound	R	b.p.	Yield %
4a	-H	118-20°C(bath)/6mm	80
4b	*p*-CH_3-	138-40°C(bath)/8mm	82
4c	*m*-CH_3-	110-12°C/6mm	86
4d	*p*-OCH_3-	128-30°C(bath)/1mm	72
4e	*p*-isobutyl-	175-78°C/6mm	80

α-methoxy propiophenone (4a): **IR** (Neat): 2990, 2940, 1700, 1600, 1460, 1250, 1220, 1140, 980, 720 cm^{-1}; **^{1}H-NMR**: 1.45 (d, 3H), 3.30 (s, 3H), 4.50 (q, 1H), 7.20-8.10(m, 5H). **Anal. calcd. for** $C_{10}H_{12}O_2$: C, 73.10; H, 7.31. **Found**: C, 72.71; H, 6.96.

p-methyl-α-methoxypropiophenone (4b): **IR** (Neat): 2990, 2940, 1700, 1610, 1450, 1240, 1220, 1140, 980, 850 and 780 cm^{-1}. **^{1}H-NMR**: 1.40 (d, 3H), 2.36 (s, 3H), 3.26 (s, 3H), 4.33 (q, 1H), 7.13 (d, 2H), 7.90 (d, 2H). **Anal. calcd. for** $C_{11}H_{14}O_2$: C, 74.15; H, 7.86. **Found**: C, 74.53; H, 7.87.

m-methyl-α-methoxypropiophenone (4c): **IR** (Neat): 3000, 2980, 1710, 1620, 1600, 1480, 1280, 1150, 1000, 790 cm^{-1}. **^{1}H-NMR**: 1.36 (d, 3H), 2.36 (s, 3H), 3.23 (s, 3H), 4.33 (q, 1H), 7.10-7.90(m, 4H). **Anal. calcd. for** $C_{11}H_{14}O_2$: C, 74.15; H, 7.86. **Found**: C, 73.73; H, 7.78.

p-methoxy-α-methoxypropiophenone (4d): **IR** (Neat): 2990, 2940, 1700, 1610, 1520, 1470, 1320, 1270, 1050, 980, 860 and 770 cm^{-1}. **^{1}H-NMR**: 1.37 (d, 3H), 3.24 (s, 3H), 3.75 (s, 3H), 4.48 (q, 1H), 7.46 (d, 2H), 7.91 (d, 2H). **Anal. calcd. for** $C_{11}H_{14}O_3$: C, 68.41; H, 7.21. **Found**: C, 67.72; H, 7.31.

p-isobutyl-α-methoxypropiophenone (4e): **IR** (Neat): 2990, 1710, 1640, 1490, 1440, 1390, 1260, 1210, 1150, 1000, 890 and 790 cm^{-1}. **^{1}H-NMR**: 0.93 (d, 3H), 1.46 (d, 3H), 1.73-1.85(m, 1H), 2.04 (d, 2H), 3.35 (s, 3H), 4.60 (q, 1H), 7.20 (d, 2H), 7.88 (d, 2H). **Anal. calcd for** $C_{14}H_{20}O_2$: C, 76.36; H, 9.09. **Found**: C, 76.59; H, 9.40.

Photolyses of **4a-e** were carried out as described before, without adding propylene oxide. Photoproducts were separated by column chromatography (silica gel. 5% ethyl acetate in pet.ether).

The identity of products **13a**, **13b**, **13c**, **13d**, **13e** was established by peak accentuation technique with authentic samples and also by their spectral data comparison with reported[21a,b] spectral data of the compounds **14a-e** is as follows:

2-Methyl-3-phenyloxetanol-3 (14a): **IR** (neat): 3400 cm^{-1}. **^{1}H-NMR**: 1.45 (d, 3H), 2.55 (s, 1H exchangeable with D_2O), 4.60 (d, 1H), 4.85 (d, 1H), 5.15 (q, 1H), 7.10-7.65 (m, 5H). **Mass** m/z (%): 134(64), 133(79), 120(100), 105(45), 77(13).
2-Methyl-3-(p-methylphenyl)oxetanol-3 (14b): **IR** (neat): 3400 cm^{-1}. **^{1}H-NMR**: 1.45 (d, 3H), 2.35 (s, 3H), 2.55 (br s, 1H, exchangeable with D_2O), 4.60 (d, 1H), 4.80 (d, 1H), 5.00 (q, 1H), 7.10 (d, 2H), 7.50 (d, 2H), **Mass** m/z (%): 148(21), 134(100), 119(88), 91(48).
2-Methyl-3-(m-methylphenyl)oxetanol-3 (14c): **IR** (Neat): 3400 cm^{-1}. **^{1}H-NMR**: 1.44 (d, 3H), 2.32 (s, 3H), 2.56 (s, 1H, exchangeable with D_2O), 4.64 (d, 1H), 4.92 (d, 1H), 5.12 (q, 1H), 7.07-7.52 (m, 4H). **Mass**: m/z, 148(21), 134(100), 119(79), 92(70).
2-Methyl-3-(p-methoxyphenyl)oxetanol-3 (14d): Solid **m.p.** 80-81° (recrystallised by ethanol). **IR** (Nujol): 3400 cm^{-1}. **^{1}H-NMR**: 1.44 (d, 3H), 2.56 (broad s, 1H, exchangeable with D_2O), 3.77 (s, 3H), 4.62 (d, 1H), 4.84 (d, 1H), 5.04 (q, 1H), 6.88 (d, 2H), 7.37 (d, 2H). **Mass** m/z (%): 163(11), 164(8), 150(79), 135(100), 107(16), 77(38).
2-Methyl-3-(p-isobutylphenyl)oxetanol-3 (14e): **IR** (Neat): 3400 cm^{-1}. **^{1}H-NMR**: 0.88 (d, 6H), 1.46 (d, 2H), 1.64-2.00 (m, 1H) and also **^{1}H** broad singlet merged here), 4.60 (d, 1H), 4.86 (d, 1H), 5.02 (q, 1H), 7.04 (d, 2H), 7.15 (d, 2H). **Mass** m/z (%): 190(7), 176(47), 161(17), 147(26), 133(100), 91(12).

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II. Abstracted from Ph.D thesis entitled *"Photochemical studies of α-substituted propiophenones and construction of bicyclo[m.3.0] bridged alkenes:Thermal rearrangement of spirocyclic vinylcyclopropanes"* submitted by G.M.Nazeruddin to the University of Poona in April 1995.

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