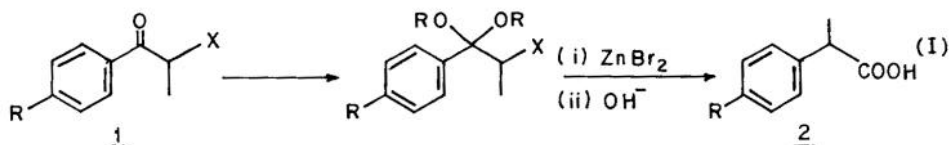


LIGHT-MEDIATED DIRECT TRANSFORMATION OF 2-CHLORO-PROPIOPHENONES INTO 2-ARYLPROPIONIC ACIDS[#]

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Abstract: A strategy based on photochemical 1,2-aryl migration as the pivotal step allows efficient transformation of 2-chloro-propiofenones into 2-arylpropionic acids. A noticeable substituent-directed excited state control on the rearrangement process has been observed.

The synthesis of 2-arylpropionic acids, an important class of non-steroidal anti-inflammatory agents has emerged as an area of intense research. Though the record¹ is full of numerous methods, a satisfactory solution to the problem of direct transformation² of 2-halo-propiofenones **1** into 2-arylpropionic acids **2** has still remained unaccomplished. An examination of the structural features of **1** revealed³ that the sp^2 carbonyl carbon geometry constrains the attainment of the spirocyclopropyl-like transition state implied in the rearrangement. A recourse chosen in current practical processes, therefore, involves masking the carbonyl function as an acetal ($sp^2 \rightarrow sp^3$) for the rearrangement to occur (eqn.I). It is in this context that an analogous change in the excited carbonyl carbon was

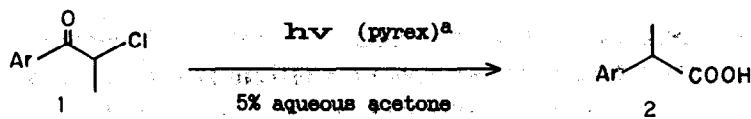


envisaged to promote the rearrangement and we have now found that such is indeed the case. This communication describes our preliminary findings on the interesting alkyl-aryl ketone excited state-mediated 1,2-aryl shift in **1** (X=Cl) leading to a convenient and direct route for **2** in moderate to high yields (Table-I). Depending upon the nature of the substituent, competing photoreduction and nucleophilic substitution reactions also occur leading to propiofenones and the corresponding 2-hydroxy derivatives respectively

At the outset, the substituent effect in the photoreaction appears to be the manifestation of relative contributions of the lowest excited triplet states ($n \rightarrow \pi^*$, $\pi \rightarrow \pi^*$) involved, a phenomenon now well recognized in alkyl-aryl ketone photochemistry⁴.

In effect, we have demonstrated that 2-arylpropionic acids are readily accessible in high yields, directly in one step, especially from p-alkyl-2-chloro-propiofenones, by a new photochemical approach which is clean, convenient and also environmentally safe.

Table-I: Photoinduced Transformation of 2-Chloro-propiophenones into 2-Arylpropionic acids.



Entry	1 (Ar)	2 (Yield ^b (%))
a	Phenyl	58 ^c
b	p-Methyl-Phenyl	84 ^d
c	p-Ethyl-Phenyl	82 ^d
d	p-n-Propyl-Phenyl	84 ^d
e	p iso-Butyl-Phenyl	74 ^d
f	p-t-Butyl-Phenyl	78 ^d
g	p-Chloro-Phenyl	45 ^c
h	Biphenyl	40 ^c
i	p-Methoxy-Phenyl	32 ^{e,f}

^aGeneral procedure: A solution of Chloro-ketone (10mmol), in 250ml of 5% aq. acetone containing 5ml propylene oxide (HCl scavenger), was irradiated with a medium pressure (Hg) lamp (200W, Hanovia, Pyrex filter) under nitrogen, in a standard immersion well photoreactor for 3 hours⁵. The reaction mixture was concentrated, extracted with ether and the acid was isolated by standard extractive alkali workup and identified by comparison with authentic products^{6,7}. Column chromatography of the neutral material over silica gel afforded the reduction and nucleophilic substitution products. ^bIsolated yields. ^{c,d,e}In addition, the corresponding propiophenones were isolated in 25%, 5%, and 10% yield respectively⁸. ^f2-Hydroxy-p-methoxy-propiophenone was isolated in 50% yield⁸.

Acknowledgements: The authors wish to thank Dr.M.S.Wadia (University of Poona) for stimulating discussions. One of us (DGK) thanks CSIR, India, for fellowship.

References and Notes

NCL.Communication No. 4982

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