Organic synthesis *via* photoinduced hydrogen and electron transfer reactions

S V KESSAR

Department of Chemistry, Panjab University, Chandigarh 160014, India

Abstract. Synthetic utility of photoinduced intramolecular hydrogen transfer reactions of ketones, amides, imines, nitrites and nitro compounds is highlighted by illustrative examples. Role of light-initiated electron transfer from amines, mercaptans, aryl groups and from lithiated ketones, amides and imines in reactions of synthetic interest is discussed.

Keywords. Ketones; amides; imines; nitrites; nitro compounds; photocyclisation; benzophenanthridines; berberines; aporphines.

1. Introduction

Adsorption of light by an organic molecule promotes it to a relatively high energy state and therein lies the strength as well as the weakness of photochemistry as a synthetic tool. Whereas a desired reaction pathway which is thermally inaccessible can become available in the excited state many side reactions may also occur from it. Nevertheless, numerous photoreactions showing good stereo-, regio, and chemoselectivity have been discovered. The present article is intended to highlight the utility of such reactions for synthesis of complex organic molecules. It is limited only to transformations which involve intramolecular hydrogen or electron transfer as the primary photoprocess. Thus many photoreactions of proven synthetic utility like cycloadditions, electrocyclic ring closures and rearrangements (Wender and Howbert 1982; Oppolzer and Godel 1978; Schulty *et al* 1977; Ninomiya and Naito 1981) are not covered. Further, the examples are chosen primarily from author's own area of interest *viz* the photochemistry of nitrogen containing functional groups.

2. Hydrogen transfer reactions

On irradiation, functional groups containing oxygen, sulphur and nitrogen multiple bonds can abstract hydrogen from a suitable donor inter or intramolecularly. The latter process is often followed by fragmentation or ring closures of synthetic importance as illustrated below for some classes of compounds.

2.1 *Ketones*

Photoreactions based on intramolecular hydrogen abstraction are efficient and synthetically useful if a six-membered transition state is involved (Quinkert *et al* 1980). However factors like framework rigidity (Paquette *et al* 1983), solvent-induced folding (Breslow *et al* 1973) and complexation (Gotschi and Eschenmoser 1973) can force

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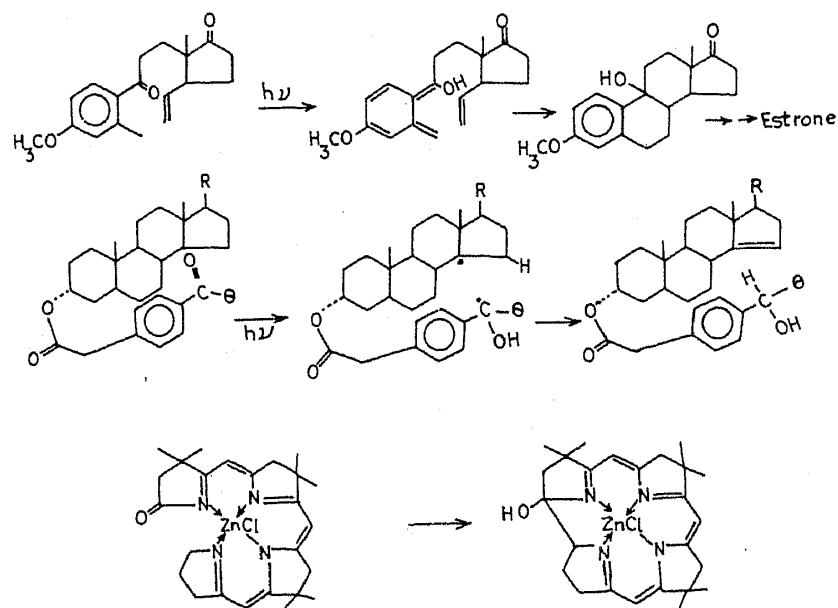
distant hydrogen atoms into a disposition favourable for abstraction resulting in 'remote functionalization'.

2.2 Amides

As compared to ketones carboxylic acid derivatives show less proclivity for hydrogen abstraction (Coyle 1978) but rich photochemistry is associated with imides (Kanaoka 1978). In α-ketoamides also hydrogen abstraction is facile and may be followed by a ring closure to a β-lactam (Henry-Logan and Chen 1973; Johansson et al 1976) or a α-lactone (Aoyama et al 1983).

The diradical initially formed from a α-ketoamide can also undergo a Norrish type-II fragmentation (Aoyama et al 1981) but in the case of tetrahydroisoquinoline derivatives further oxidation of the nitrogenous segment is observed (Kessar et al 1978). This aromatisation is of mechanistic and synthetic interest due to complications observed during dehydrogenation (Sainsbury et al 1969). The vinalogous benzamides with an ortho aldehydic group furnish, on irradiation, amino-lactones, presumably through a 1,5 hydrogen transfer (unpublished results from this laboratory).

2.3 Amines and imines

Many a claimed photoreductions of Schiff bases have been shown to be caused through 'chemical sensitisation' by carbonyl impurities (Padwa 1977; Pratt 1977).

The lack of photoinitiated hydrogen abstraction in imines has been variously attributed to energy dissipation through rapid cis-trans isomerisation, $\pi\pi^*$ character of the excited state or the lower strength of the incipient NH bond (Padwa 1977; Pratt 1977; Ohta and Tokumaru 1974). Whatever the reasons for the absence of this photoreactivity in imines, the methodology dependent on it is not available for heterocyclic synthesis. However, recently it has been shown that certain α-ketoimines do undergo phototransformations leading to spirobenzyl isoquinoline and berberine
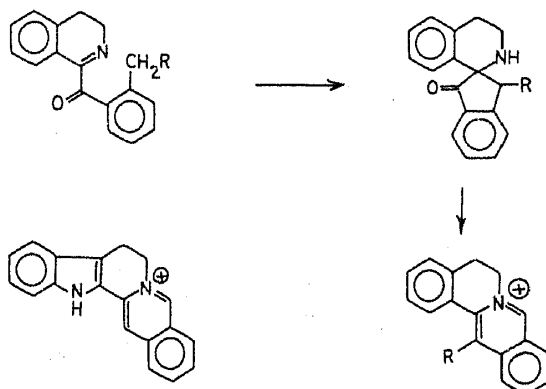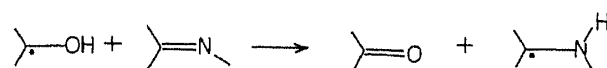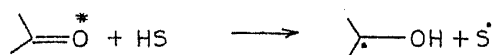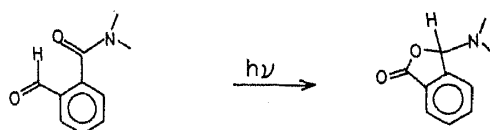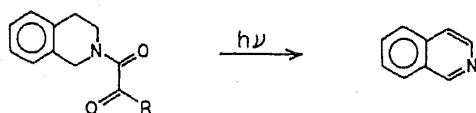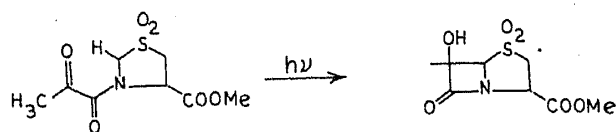
alkaloids (Kessar *et al* 1978). The procedure has been extended to synthesis of indole alkaloids also (Hirai *et al* 1983).

The above reaction when used in conjuction with a known photodegradation of berberine derivatives (Wu *et al* 1978) can bring about an intriguing transposition of D ring substituents of these alkaloids (Kessar *et al* 1982). Mechanisms of both the involved photoreactions have been investigated by deuterium labelling experiments (Kessar *et al* 1982).

2.4 *Nitrites and nitro compounds*

Barton reaction (Barton and Akhtar 1962) is an outstanding example of the synthetic utility of photochemical reactions, although here the hydrogen abstraction step may not be occurring on the excited state surface.

Nitro compounds also serve as useful photolabile amino protecting groups (Rajashekharan Pillai 1980) as shown below.
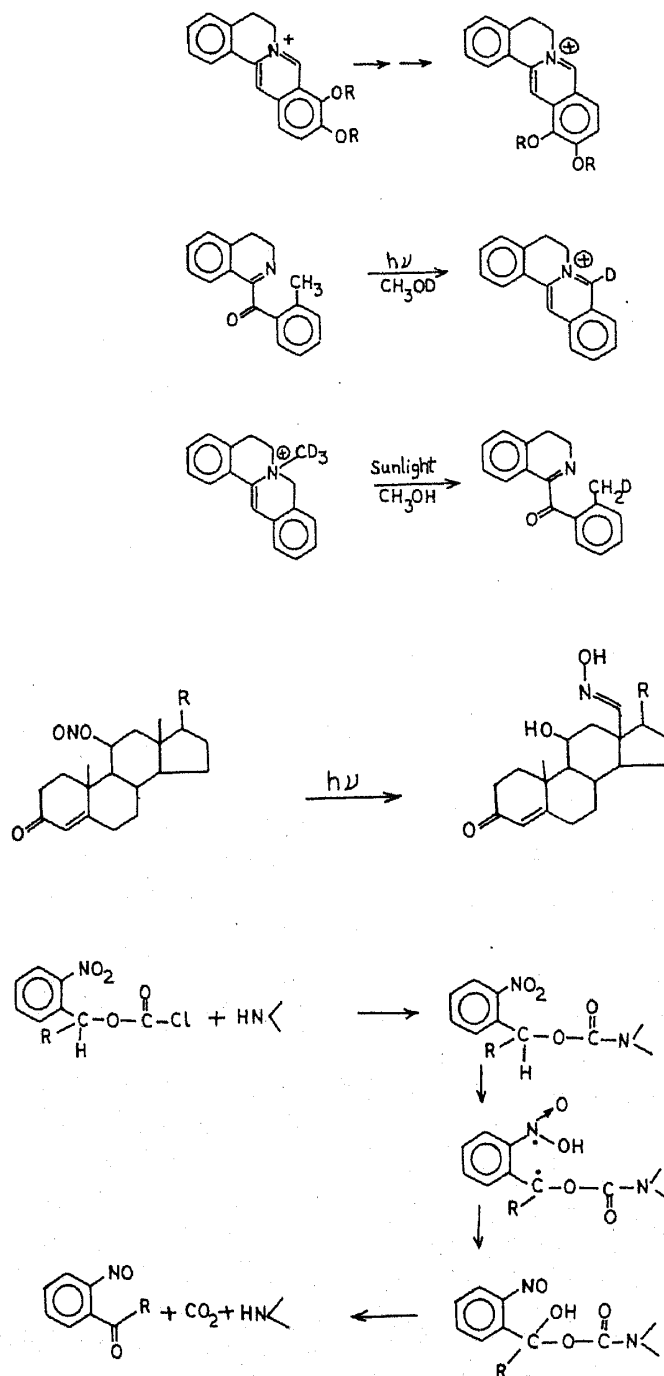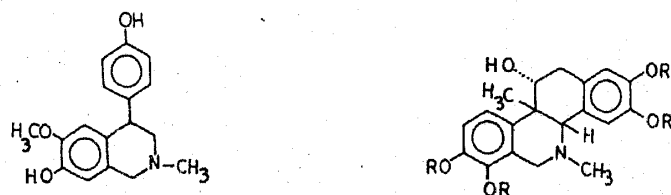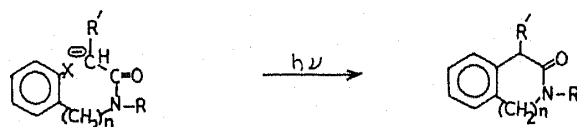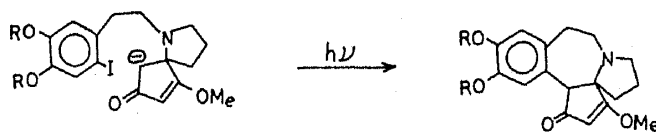
3. Electron transfer reactions

In photoinduced electron transfer reactions, back electron transfer is an energy wasting process. Nature has its own mechanism for overcoming it and in artificial solar energy utilisation also ingenious procedures have been devised to minimise it (Whitten 1980). For a synthetically efficient reaction, electron transfer should be followed by a fast event like loss of a nucleofuge from the receptor or of a proton from the donor. A few such examples involving different functional groups are given below.

3.1 Ketones and amides

Even carbonyl triplets with a $\pi\pi^*$ character which are generally unreactive in hydrogen abstraction can be efficiently reduced by amines through electron transfer followed by proton transfer (Cohen *et al* 1973). Unfortunately, in the case of aminoketones intramolecular proton transfer is inefficient (Wagner and Ersfeld 1976) and not many reactions of synthetic import have been reported. However, electron transfer from a sulphur atom followed by intramolecular proton transfer has been invoked to explain the formation of medium and large ring systems on irradiation of certain imides (Sato *et al* 1976).

A mechanism involving electron transfer from the nitrogen atom has also been proposed for γ-hydrogen abstraction in α-ketoamides (Aoyama *et al* 1983). Evidence for bimolecular electron transfer in pyruvates has been adduced recently (Davidson *et al* 1983).

Light-promoted electron transfer from enolate anions to aryl halides has been invoked to explain the photoinduced S_{RN^1} reactions (Bunnet 1978). An intramolecular
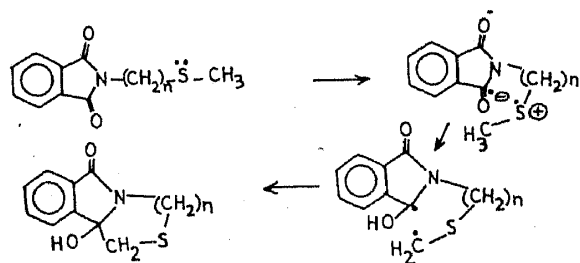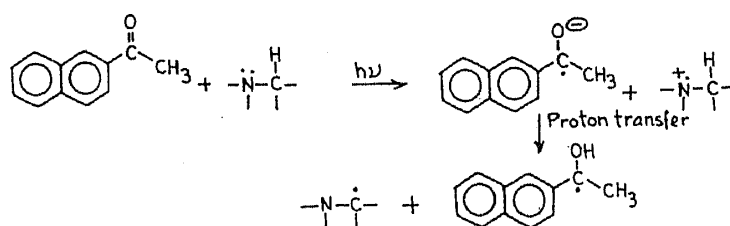
version has been used in the synthesis of cephalotoxin (Semmelhack and Bargar 1980) and other medium-sized ring compounds (Semmelhack and Bargar 1977). Electron transfer-mediated cyclisation of metalated amides constitutes the key step in the synthesis of cherylline and corynoline-type alkaloids (Kessar *et al* 1981).

Witkop reaction which is very useful for synthesis of benzazepinones is claimed to entail electron transfer in the reverse direction *i.e.* from the aromatic moiety to the chlorocarbonyl function (Yonemitsu *et al* 1968; Hamada *et al* 1977).

3.2   *Amines, imines and enamines*

Metalated imines have been found to undergo photocyclisation (unpublished results from this laboratory) in a manner similar to that of carbonyl enolates. This reaction can open up convenient routes to many alkaloidal structures.

Although the nucleophilicity of the enamine carbon atom is well established, photocyclisation based on intramolecular electron transfer to aryl halides could not be induced in these compounds (unpublished results from this laboratory). In contrast, irradiation of the corresponding aromatic amines leads to ready ring closure (Mizuno *et al* 1973). Based on this observation, efficient syntheses of chelilutine and sanguilutine were carried out (Kessar *et al* 1977) to settle the controversy regarding the placement of alkoxy groups in this set of alkaloids (Ishii *et al* 1975). This route has been extended to
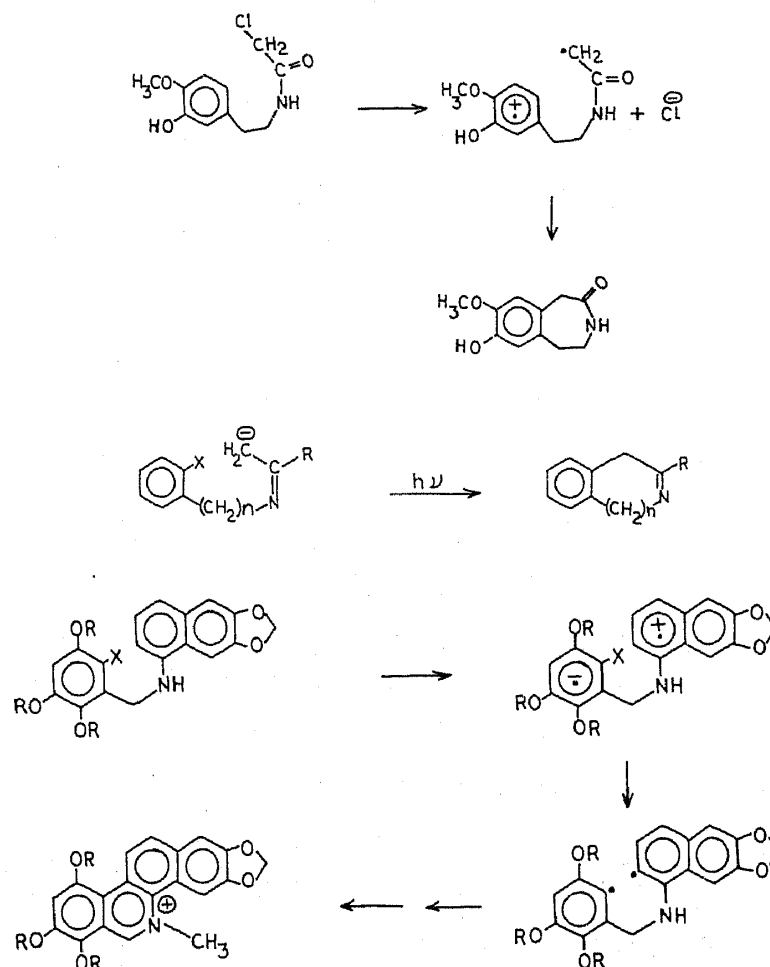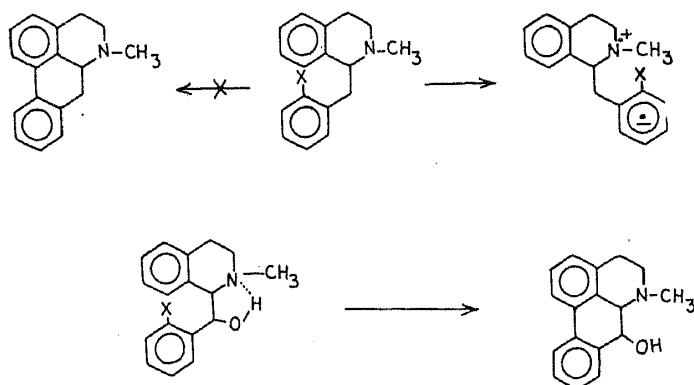
the synthesis of macarpine which carries six alkoxy groups on the benzophenanthridine nucleus (Takao *et al* 1981).

Finally, success of certain photoreactions may hinge on preventing the electron transfer process. For example, lack of aporphine formation on irradiation of ortho-halogenated benzylisoquinolines has been ascribed to a deleterious electron transfer from the nitrogen atom (Kessar *et al* 1981). A strategem for preventing this, and for locking the aryl moieties in close proximity, is based on introduction of a hydrogen bonding group. Synthesis of oliveridine and related alkaloids could thus be achieved readily (Kessar *et al* 1980; Kessar *et al* 1983).

Acknowledgements

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