

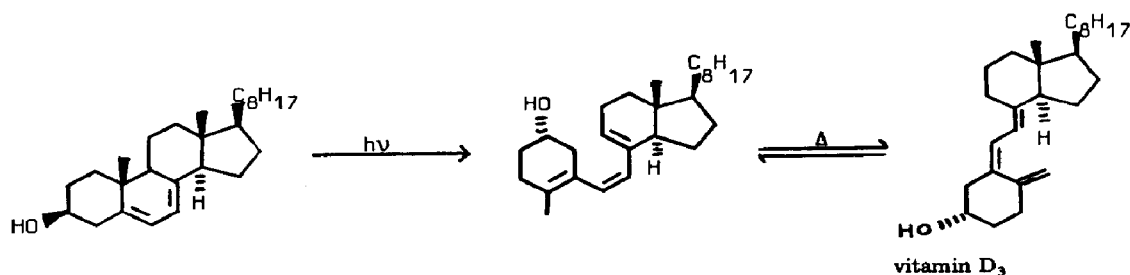
RELEVANCE OF PHOTOCHEMICAL TRANSFORMATIONS TO THE LABORATORY SYNTHESIS OF BIOLOGICALLY INTERESTING MOLECULES

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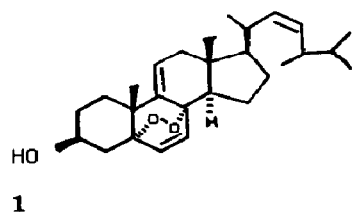
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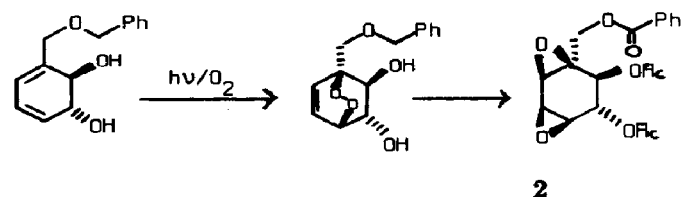
Photochemistry has played a key role in very many laboratories concerned with the synthesis of biologically active molecules. Some 30 years ago the preparation of vitamin D₃ was investigated. The important step involved a photochemical cyclohexadiene to hexatriene rearrangement:



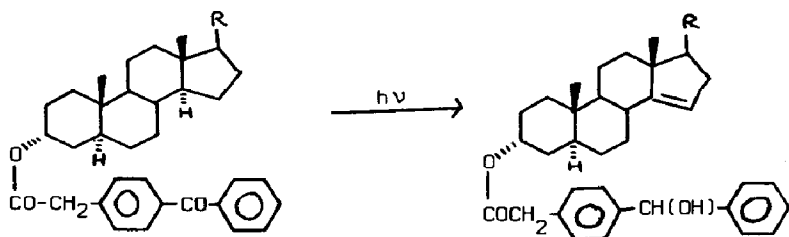
In the same era photogeneration of singlet oxygen was used by Jones *et al.* in the preparation of dehydroergosterol peroxide 1:



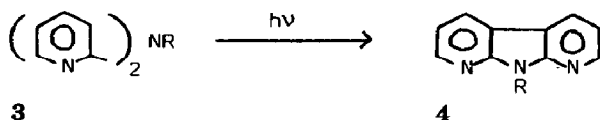
This material was used in a number of imaginative ways by the Manchester group and by collaborators at Greenford. More recently a similar process has been used to prepare crotepoxide 2 (Ph ≡ phenyl; Ac ≡ acetyl):



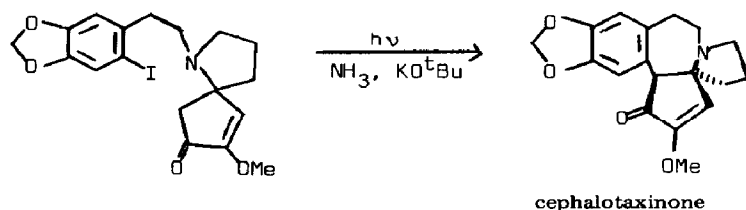
In the 1960s Barton's brilliant research demonstrated how a C(18) methyl group in the steroid skeleton could be functionalized through a photo-oxidation involving a remote nitrite ester moiety. A synthesis of aldosterone was achieved in this way. Breslow used the same philosophy in the preparation of a Δ_{14} steroid by photoactivation of a benzophenone group attached to the hydroxyl group at C(3):



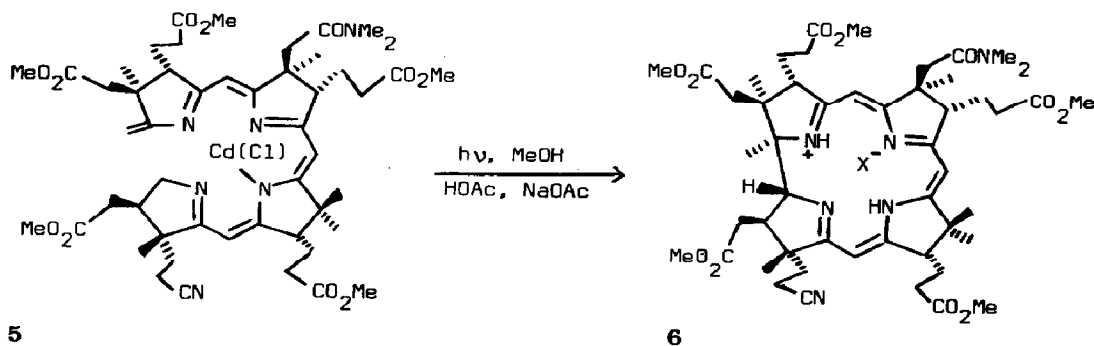
Photochemistry has been used to gain access to a wide variety of interesting heterocyclic systems which may be difficult to synthesize by thermal methods. Thus the dipyridylamine **3** can be transformed into the azacarboline **4**:



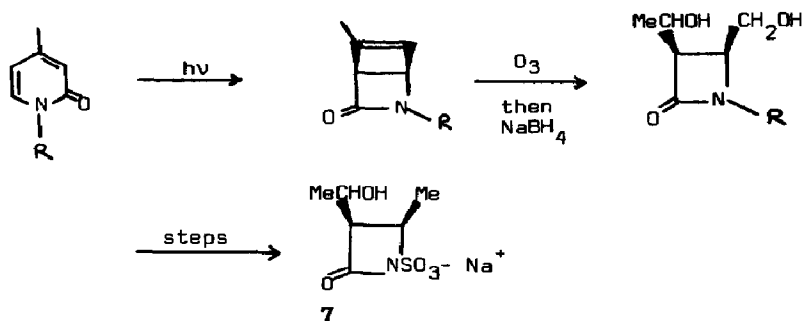
while the photochemical substitution of an aryl halide by an enolate anion has been utilized in an elegant synthesis of cephalotaxinone (KO^tBu \equiv potassium *tert*-butoxide; Me \equiv methyl):



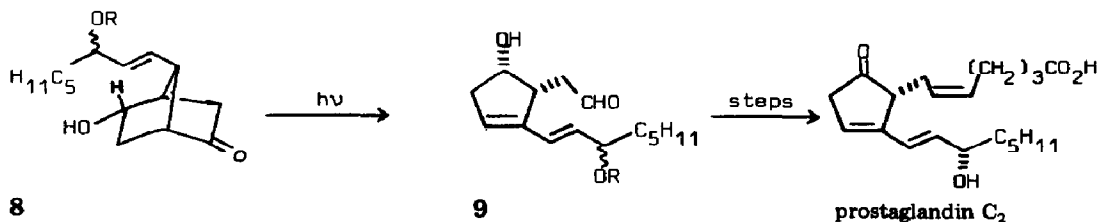
Perhaps the most esoteric example of heterocyclic synthesis involving a photon-induced reaction is Eschenmoser's preparation of the corrin **6** from the cadmium complex **5** by a 1,16 shift of a hydrogen atom:



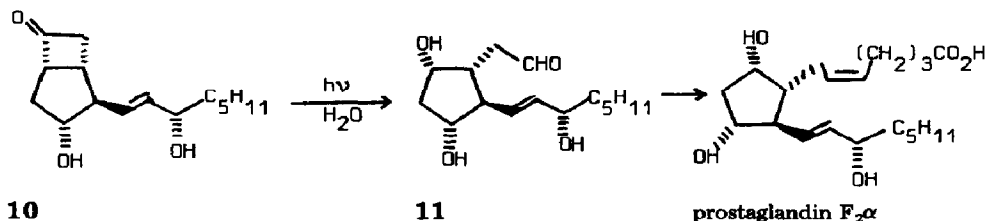
In more recent years Brennan has shown that the photolysis of pyridones can be used to prepare β -lactams such as the thienamycin-aztreonam hybrid structure 7:



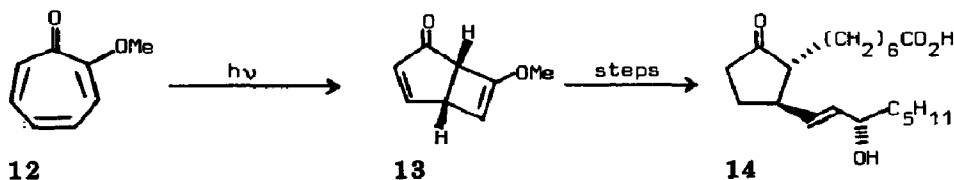
In the Glaxo laboratories at Ware, Newton *et al.* have capitalized on the detailed and wide ranging research of Yates to convert the readily prepared norbornanone 8 into an intermediate 9 *en route* to prostaglandin C₂:



The same group used information from Turro's work on the photochemistry of cyclobutanones to gain access to other prostaglandins. Thus the ketone 10 was photolysed in an aqueous medium to give the hydroxyaldehyde 11, a late stage precursor to prostaglandin F_{2 α} :



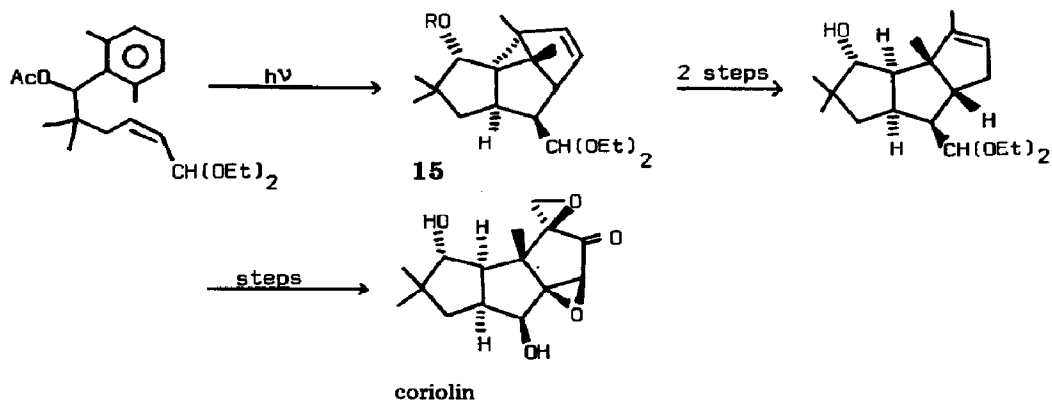
In Crabbe's synthesis of 11-deoxyprostaglandin E₁ 14, the intriguing photochemical transformation of the α -tropolone derivative 12 into the bicyclic ketone 13 represents the first step in a multistep procedure:



The above examples (which are chosen in a very subjective way and reflect our parochial interests) serve to illustrate that the synthetic organic chemist will use a photochemical transformation as a key step in a long

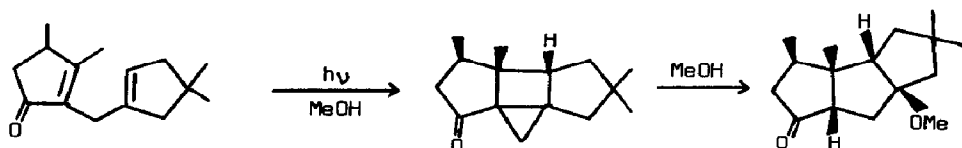
synthetic sequence when the photon-induced process has been fully researched on suitable model systems and the advantages and the limitations of the process are well documented. Three other areas of research can be cited to substantiate these points.

The elegant synthesis of the cytotoxic agent coriolin by Wender utilized an intramolecular 1,3 cycloaddition of a photoexcited benzene nucleus to an alkene moiety in one of the early steps to furnish the polycyclic acetal **15** which possesses many of the stereochemical features of the natural product (Et \equiv ethyl):

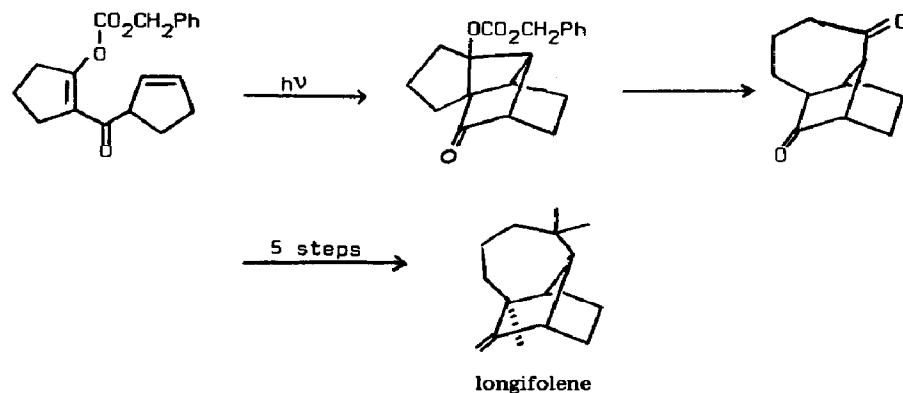


Wender was able to plan this synthesis using the extensive data provided by the earlier research of Gilbert and Bryce-Smith.

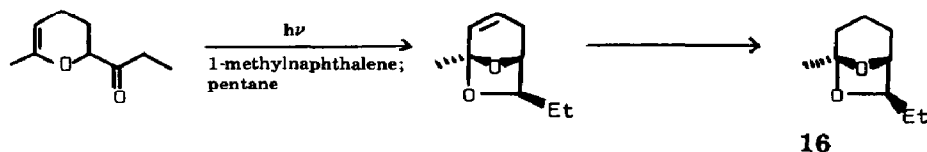
The photochemical [2 + 2] addition of an alkene to an enone system is well known and this reaction was employed by Pattenden in another successful approach to the hirsutane system:



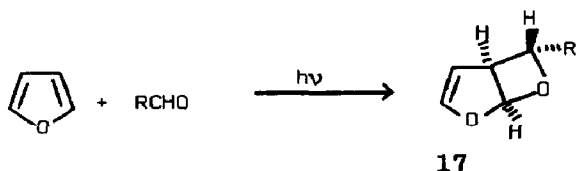
Oppolzer has used a similar pathway to prepare longifolene:



The Paterno-Büchi reaction involving the cycloaddition of an alkene moiety and a carbonyl group is well established and the parameters have been well defined. It has been used recently in a short synthesis of *exo*-brevicomine 16 the sex attractant of the western pine beetle:



Finally the addition of an aldehyde to the double bond in a furan ring has also been used recently to provide acetals 17 *en route* to sugars and the macrolide antibiotics:



Over the last 10 years photochemical transformations have featured with increasing frequency as key steps in the synthesis of complex molecules. In addition, many other chemists have used solution photochemistry to promote bromination adjacent to a carbonyl group or an alkene unit, to oxidize an alkene via the generation of singlet oxygen and the ene reaction and to isomerize an alkene or azo compound. Nevertheless, there are a considerable number of organic chemists who still regard photochemistry with suspicion in the belief that photochemically driven reactions invariably give a multitude of products and that finding conditions to provide the required product would require much work and knowledge of the tricks of the photochemist's trade.

The availability of reactors suitable for medium-scale work (*e.g.* falling film systems, carousel reactors etc.) coupled with the increasing number of examples of routes to complex molecules involving a photochemical process should ensure that in the future the more conservative chemists will see the light.