

ON THE STEREOCHEMISTRY OF PHOTOADDITION BETWEEN α,β -UNSATURATED KETONES AND OLEFINS—II

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(Received in U.S.A. 20 June 1979)

Abstract—Some years ago an empirical rule, which allows the prediction of product stereochemistry in *cis*-photocycloaddition reactions of α,β -unsaturated ketones and olefins was tentatively proposed. Several additional examples, both selected from the literature and synthesized in our laboratory, seem to strengthen the validity of the rule.

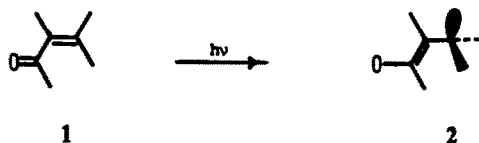
Some time ago¹ we proposed, on the basis of a fairly large number of examples collected in the course of our studies on natural product synthesis, an *empirical rule* which allowed the prediction of the configuration of *cis*-photocyclo adducts between allene and other olefins and α,β -unsaturated ketones.

The rule postulated that the preferred configuration of the excited state determined the configuration of the major photocyclo adduct and its assumed that the geometry of the excited state was (as portrayed in formula 2) trigonal at the α -carbon and pyramidal at the β -carbon. Thus the excited state could, in principle, possess an additional chiral center as compared to the ground state 1. It was further assumed that this additional chiral center would select the more stable one of the two possible epimeric configurations. We emphasized that *no theoretical significance was as yet ascribed to these ideas*, and that they should be regarded for the time being merely as guidelines for an empirical prediction of product stereochemistry.

In the intervening years a few more examples have appeared in the literature. While all of them were compatible with our rule, some of them seemed to us to be quite convincing and hardly explainable in any other way. Thus Ziegler² has shown that compound 3 yields the allene α -adduct 5 in a ratio 14:1 with a minor, presumably diastereoisomeric, product. This seems impressive if contrasted with the photocycloaddition of the system 6→8 which has been demonstrated in many variations¹ to be fully stereospecific from the β -side. The photocycloaddition of the unsubstituted octalone 9 is now known and the allene-adduct 11 has been obtained (stereospecifically) in a 95% yield.³ Another significant result of a new type has been obtained also by Ziegler⁴ who showed that the dimethylcyclohexenone 12 yielded the transoid adduct 14 as a major product in a ratio 4:1 to the minor cisoid isomer. In the same paper the authors pointed out that in cases where it is not easy to estimate the relative stabilities of the two epimeric excited states, one can predict the result of *cis*-photocycloaddition from the result of an alkali metal-ammonia reduction of the same α,β -unsaturated ketone. It is clear that according to our assumptions the excited state in photocycloaddition and the anionic intermediate⁵ in a metal reduction of an α,β -unsaturated ketone should have similar steric properties.

Thus, sodium and ammonia reduction of compound 12 yielded the *trans* and *cis*-dimethylcyclohexanones in a

ratio (84:16) which was similar to the ratio of the two photoadducts. It seems to us however that, while the equilibrium constants between the two diastereoisomeric photo-excited states and anionic intermediates respectively should be similar, there is no reason to expect that they would be numerically identical. Consequently, we have avoided in our further explorations cases of α,β -unsaturated ketones which yield diastereoisomeric metal ammonia reduction products in a ratio near unity. In such a situation a not too large difference in equilibrium constant could in some cases reverse the stereoselectivity of photocycloaddition with respect to metal reduction.



Scheme 1.

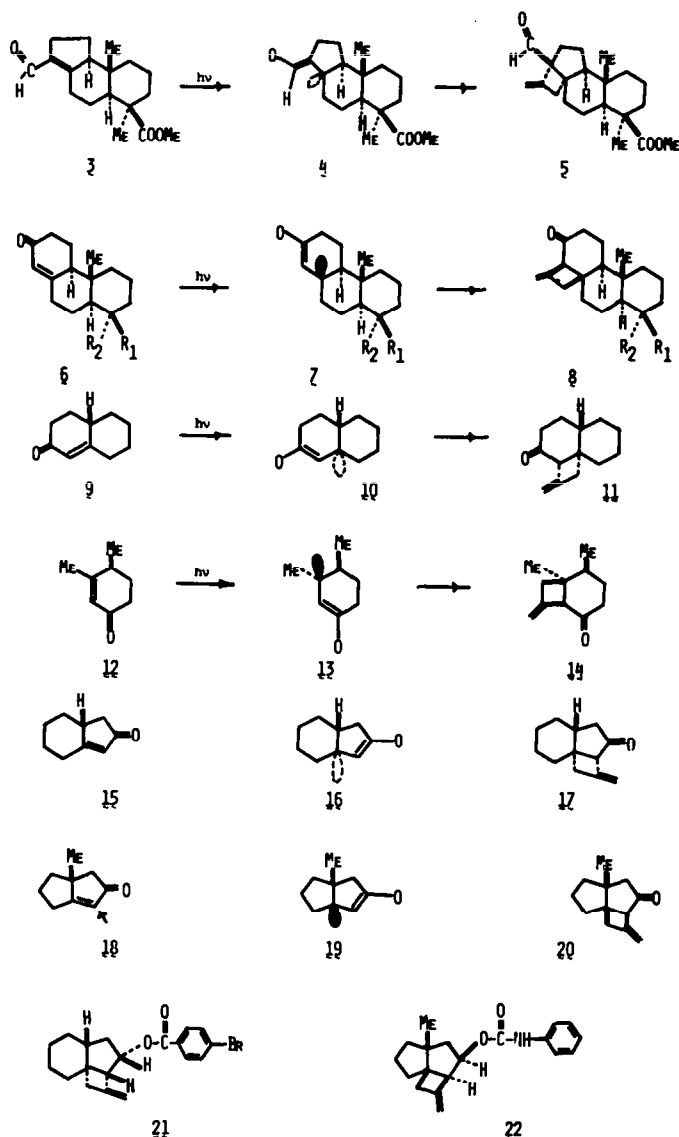
We have now started a small synthetic programme designed to test the addition rule in a variety of different systems.

Such a programme can be profitably conducted with undergraduate students or masters degree candidates since it gives purpose to the normally boring tasks of an undergraduate laboratory. The selection of suitable systems together with data on the outcome of their metal reduction has been recently facilitated by the publication of the excellent summarizing article by Drury Caine.⁶

We now wish to disclose our first two syntheses which seem quite relevant to us.

The system 15 has been reported to yield on reduction with Li/NH_3 almost exclusively the *trans* dihydro derivative (*trans*:*cis* ratio 99:1).⁶ Photoaddition of allene to compound 15 under our standard conditions¹ gave 75% of a single oily product to which the stereo structure 17 was tentatively assigned [IR (CCl_4): 1740, 1760 cm^{-1} ($\text{C}=\text{O}$, $\text{C}=\text{CH}_2$); NMR (CDCl_3): multiplets $\tau = 5.0, 5.15$ (1H each, $=\text{CH}_2$); $m/e = 126$].

Reduction of the adduct 17 with NaBH_4 yielded a single secondary alcohol which gave a crystalline (m.p. = 68–70°) *p*-bromobenzoate. The crystal and molecular structure of this material was determined by Dr. Peter S. White in our department⁷ and found to correspond to the formula 21.



Scheme 2.

The second system which we have studied was the α,β -unsaturated ketone 18.⁹ Metal reduction of this particular compound has not been reported, but it is fairly clear that the cisoid species 19 must be the more stable one. In agreement with this assumption, a similar compound (18 with the angular Me displaced to the position indicated by the arrow) is known⁶ to yield exclusively the cisoid reduction product with Li/NH_3 . Photoaddition of allene under our standard conditions to compound 18

yielded 85% of a single adduct presumably 20 [IR (CHCl_3): 1735, 1668 cm^{-1} ($\text{C}=\text{O}$, $\text{>C}=\text{CH}_2$); NMR (CDCl_3): multiplet centered at $\tau = 5.08$ (2H, $\text{>C}=\text{CH}_2$); $m/e = 176$].

Reduction of compound 20 with NaBH_4 and treatment of the resulting single alcohol with phenylisocyanate gave a crystalline (m.p. 93–4°) phenyl urethane which was recrystallized from *n*-hexane. The crystal and molecular structure of this material was determined by Ahmed and Przybylska⁸ (National Research Council, Ottawa) and it corresponds to the formula 22.

We believe that continuing studies of this type (and we hope that they will be joined by other workers) will soon demonstrate if the addition rule has general validity or not. If the rule has general or almost general validity it must also have a physical basis and it will be up to the theorists to either make our interpretation theoretically respectable or provide a better one.[†]

In conclusion, we should like to point out that pairs of systems as for example 17 and 20 which are specially

[†]At the insistence of a referee, we answer the criticism levelled at the addition rule by Loufty and de Mayo.¹⁰ We have stated repeatedly in this and the previous article, that until we have more examples and the validity of the empirical rule is generally accepted, we do not wish to discuss its physical basis. Consequently, we feel that it is our privilege to answer the theoretical objections of Loufty and de Mayo by a "no comment". On the other hand, the claim that a "steric hindrance to approach rule" can make the same predictions as ours is patently incorrect. A survey of the systems published in this and the previous article is quite sufficient to rule out this possibility.

designed to illustrate the operation of the principle and are chosen in such a manner that both metal reduction and photoaddition are practically stereospecific may be expected to achieve a faster and more convincing solution of the problem than examples chosen at random.

Acknowledgements—We wish to thank Dr. F. R. Ahmed and Dr. M. Przybylska (N.R.C., Ottawa) and Dr. Peter S. White from our Department for the solution of the crystal structures. We also thank the N.S.E.R.C., Ottawa for an operating grant and the Canada Council for a Killam Memorial Scholarship to one of us (K.W.).

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