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

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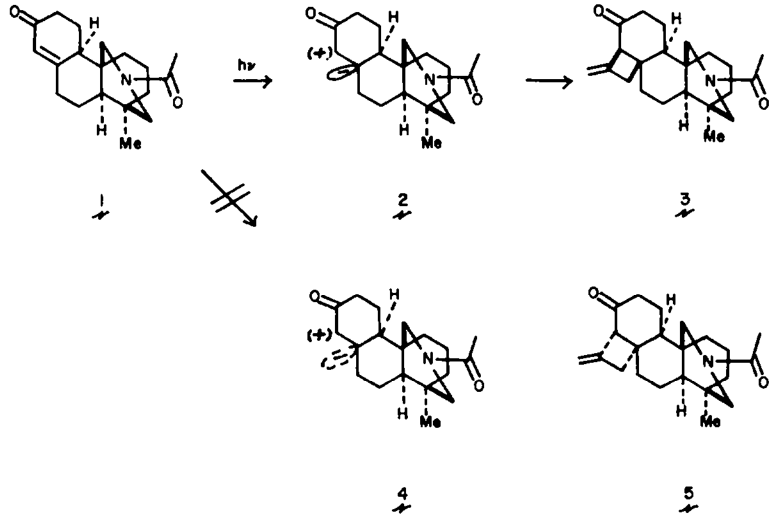
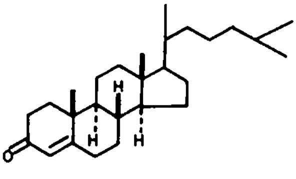
Abstract—The stereochemistry of the photoaddition between α,β-unsaturated ketones and olefins is discussed. It is shown that the stereochemistry of the product is determined by the relative stability of the excited state. This stability can be judged by the application of the principles of conformational analysis, coupled with the assumption that the β-carbon of the excited state is pyramidal and can select the more stable configuration. Many examples derived mainly from synthetic work performed at the University of New Brunswick during the last ten years are in agreement with these assumptions.

During the last 10 yr we have utilized many times the photoaddition of allene and other olefins to α,β-unsaturated ketones in the course of the construction of polycyclic bridged natural products.

We wish to disclose now a general rule which allows to predict the stereochemistry of such photoadducts. It should be pointed out that while the rule works reliably and must consequently have some physical basis, the suggested explanation is tentative and we regard it merely as a starting point to a proper theoretical treatment.

We have encountered the first case of this type of steric control in our synthesis of Atisine.[1] The α,β-unsaturated ketone 1 gave on irradiation with allene the product 3 with complete stereospecificity in almost quantitative yield.

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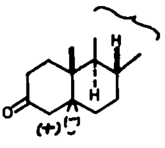
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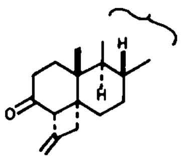
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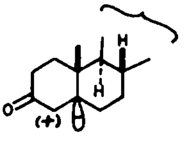
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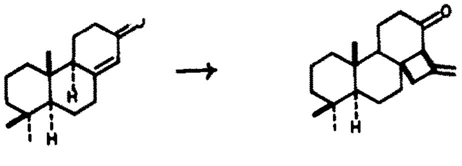
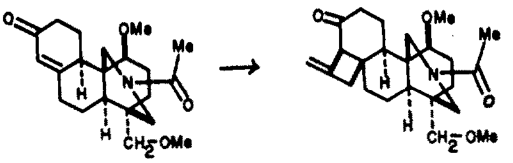
10 → 11



12 → 13



14 → 15

If we examine the models of the product 3 and its stereoisomer 5, we get the impression that compound 5 is less crowded and energetically more favorable than the product 3. Also from the point of view of steric hindrance to the approach of allene to the ketone 1 an approach from the α side leading to 5 seems to be easier. Consequently, neither the stability of the product nor the steric hindrance to the approach of the reagent can explain the complete stereospecificity observed. It seemed to us that the preferred stereochemistry of the excited state might be the crucial controlling factor.

The excited state of α,β-unsaturated ketones (presumably n–π^*) has been represented by Corey[2] with the β-carbon charged negatively relative to the α-carbon. Such a representation is in agreement with the regiospecificity of most photochemical additions as well as with theoretical calculations of Hoffmann.[cf. 2]

In conformity with these proposals we represent the excited state with an orbital and a negative charge on the β-carbon. We postulate now that the β-carbon may invert and select the more stable configuration. *However, we must emphasize, that we do not wish to enter into a discussion of the charge distribution in the excited state.*

Any model of the excited state with a pyramidal carbon in the β-position coupled with the assumption that this carbon may invert and assume the more stable configuration would agree equally well with our results. The excited state of the ketone 1 may consequently select either the configuration 2 or 4. Clearly the trans-anti-trans configuration corresponding to 2 is the more stable one.

Since all the photoadditions were carried out at −70°C we can assume that the less stable configuration 4 was present only in a negligible concentration and this situation is responsible for the exclusive formation of the product 3.

In order to obtain some preliminary verification of our assumptions we have investigated the photoaddition of allene to cholestenone 6.

Our prediction in this case is that 9 should be formed exclusively since the excited state 7 is energetically preferred to the excited state 8.

In fact a single product was obtained and the structure and configuration 9 was rigorously proved for it.[3]

A few years later several cases similar to those first two were encountered in the synthesis of ishwarane,[4] (10 → 11) trachylobane[5] (12 → 13) and talatisamine[6] (14 → 15).

In all these cases the expected products (11, 13 and 15) were obtained stereospecifically and in high yield.

The first example of a somewhat different type which nevertheless also fits our assumption was encountered in our synthesis of napelline.[7] The α,β-unsaturated ketone 16 added vinyl acetate stereospecifically and gave the product 18 in high yield. While the orientation of the vinyl acetate in the adduct is unusual the stereochemistry is the expected one. The excited state 17 with the equatorial methyl group is more stable than its epimer in which the same methyl group is axial.

In the synthesis of the Lycopodium alkaloid annotinine[8] the tricyclic vinylogous imide 19 gave the single photoadduct 21 with allene in high yield. The preferential stability of the excited state 20 as compared to its cisoid epimer may again explain this complete steric control.

In the synthesis of epilycopodine compound 22 underwent a high yield stereospecific photocyclization to the product 23.[9]

It is clear that the configuration 24 of the excited state in which both the methyl and nitrogen substituents may be equatorial is more stable than the diastereoisomeric configuration, which must have one of these groups axial. As a consequence the cyclization occurs exclusively trans to the methyl group.

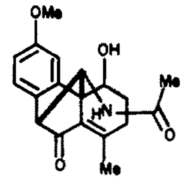
In spite of the agreement of prediction and experiment in the cases quoted we were reluctant to generalize the foregoing conclusions since several of the systems were of a similar type.

A quite different case was reported last year by Ziegler and Kloek.[10]

The excited state of the indene aldehyde 25 must clearly prefer the cisoid configuration 26 and thus the adduct 27 is formed on irradiation with allene.

We have encountered at about the same time in connection with some model studies for diterpene alkaloid synthesis the following two examples. The two epimeric compounds 28 and 31 prefer the excited states 29 and 32 respectively with the cyclohexane ring annelated to the bicycloheptene system either exo-exo (29) or endo-endo (32). Allene addition was in both cases completely stereospecific and the two adducts are portrayed by the stereostructures 30[11] and 33.[12] The structure of both products followed from X-ray analysis performed on suitable derivatives by Dr. M. Przybylska and Dr. F. R. Ahmed at the National Research Council Laboratories, Ottawa. The structure of the adduct 30 is specially significant. In this case our rule enabled us to make the seemingly improbable prediction that the allene will add to the sterically much more hindered endo face of compound 28.

Prof. Stork who has very kindly read a prepublication copy of this article pointed out that in analogy to his work on the lithium–ammonia reduction of α,β-unsaturated ketones[13] there may be cases in which the excited state will not select the most stable (as judged by conforma-



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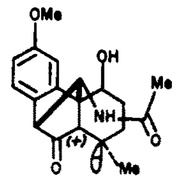

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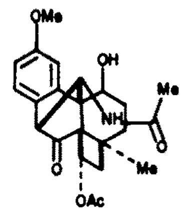

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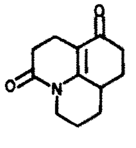

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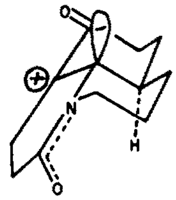

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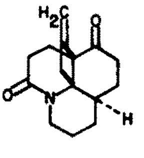

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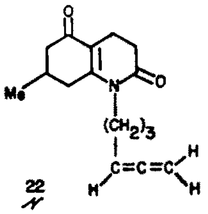

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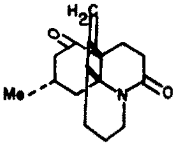

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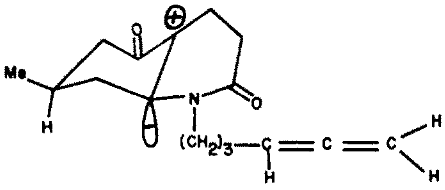

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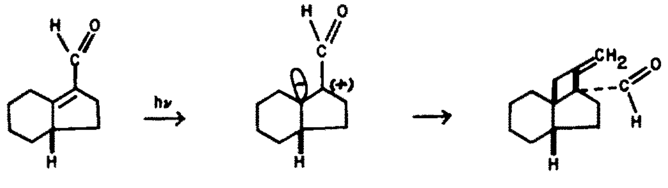

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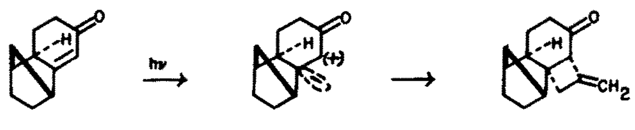
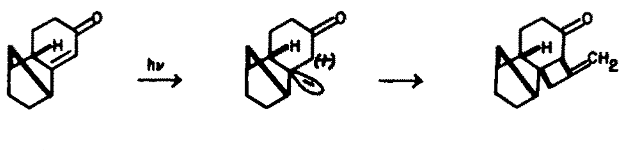


28 29 30



31 32 33

tional analysis) configuration, because in that particular configuration orbital overlap is impossible. In none of the examples reported by us is this effect present and the experimental study of α,β-unsaturated ketones similar to those described by Stork and Darling[13] provides a further opportunity to define the nature of the excited state.

In the preceding discussion we have interpreted the selection of the more stable configuration by assuming that the β-carbon of the excited state is pyramidal and that the more and less stable configuration of this species are in equilibrium.

It is clear that this is not the only way in which the selection of configuration may operate.

It is conceivable that the excited state is planar and that the β-carbon is pyramidalized in the process of the reaction with the olefin.

In such an event the energy of pyramidalization could be related to the stability of the corresponding pyramidal isomer and the process of configuration-selection would be kinetically controlled. Clearly it is not possible to derive such details merely by product analysis. The famous controversy about nonclassical carbonium ions may serve as an example. On the other hand we hope that our generalization might stimulate further experimental and theoretical studies and thus contribute to the ultimate clarification of the problem.

Acknowledgements—I wish to thank Profs. Roald Hoffmann and Gilbert Stork for valuable discussions, Dr. Maria Przybylska and Dr. F. R. Ahmed for the X-ray structure determination of two of our adducts, and the National Research Council of Canada, Ottawa, the Hoffmann–La Roche Company, Nutley, New Jersey, and Vaudreuil, Quebec, for continuous support of these studies over the period of many years.

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