STILBENE PHOTOCYCLIZATION. SYNTHESIS OF CEPHARANONE B

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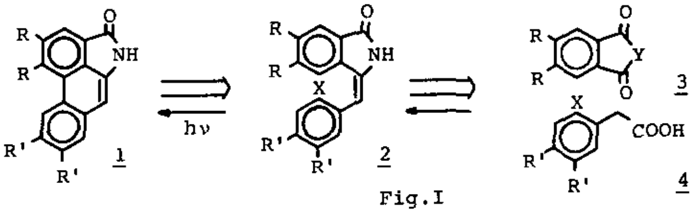
Abstract- The photocyclization of enamides of type 2 is investigated. Photochemical electrocyclization did not take place due to an ineffectiveness of overlapping of the hexatriene system. However, radical induced cyclization gave a satisfactory result.

As a continuation to our studies on the synthesis of aporphine alkaloids and related compounds, we recently became interested in the highly oxidized members of this alkaloid group, namely oxoaporphines, 4,5-dioxoaporphines and aristolactams[1]. We should now like to report on the synthetic studies[2] leading to the latter class of compounds.

We soon realized that disconnection of the strategic bond of aristolactams 1 leads to an enamide synthon 2 (Fig.I). Furthermore, in the synthetic sense, photochemical cyclization of enamides[3,4] is now a well stablished method for achieving formation of polycyclic compounds. Further disconnection of the key enamide 2 suggested synthons 3 and 4 as being probably the most accessible ones.



a) R=OMe; R'=H

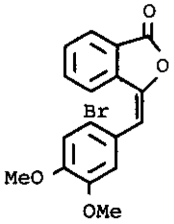
b) R=R'=OMe

Fig.I

Therefore we planned to carry out a short and efficient synthesis of aristolactams 1 by simply generating the key enamide 2 through a Perkin condensation[5] (3+4→2), followed by photocyclization to the desired aristolactams. Previous work[6a,b] on the photochemical cyclization of isatinylidene and indanylidene ring derivatives was somewhat disappointing. It showed that these systems do not suffer photochemical ring closure. The structure feature which prevents the cyclization was assumed to be the presence of the exocyclic double bond to a fused five-membered ring although no conclusive proof for this was actually found. Consequently,we suspected that the desired electrocyclization of 2(X=H)to aristolactams would not take place.Instead we trusted in the photocyclization of o-bromo enamides,a reaction which has been mechanistically rationalized on the basis of a charge tranfer mechanism. In fact, Umezawa et al.[7] achieved the cyclization of N-(o-bromopiperonyl)indolenine in 67% yield.

Thus we prepared phthalimidine 2b(X=Br)[8] by a Perkin condensation of the appropriate o-bromophenylacetic acid 4b and m-hemipinic anhydride 3b(Y=O)[9] followed by treatment with $AcONH_4$/AcOH. However, phthalimidine 2b(X=Br) on irradiation under argon(450 W Hanovia lamp,48 hr) did not afford any cyclized product. The only observation was that of cis-trans isomerization. Furthermore irradiation of phthalide 5[8] did not give the desired phenanthrene derivative.

Several rules governing photocyclization of stilbene derivatives have been proposed[10]. However, as Laarhoven et al.[11] pointed out, besides F_{r*} (sum of free valence indices for the first excited state of the atoms involved in C-C bond formation) other factors are also of decisive importance. In fact, bearing in mind the assumption of Kumler and Dybas[6a] we looked at the Dreiding models which showed that the distance between the carbono C_1 and C_6 of the hexatriene system was much further apart in 6 (X=H; Y=NR; Z=O) than in 7 . We therefore believe that electrocyclization of stilbene derivatives such as 6(Y=C or heteroatom;X=H or Br; Z=2H or O) will not take place due to the ineffectiveness of overlapping of the extremes of the hexatriene system. Consequently, we thought of aryl iodides 2(X=I) as being the alternative to submit to photocyclization. Kupchan et al.[12] indeed used aryl iodides to promote radical induced cyclization of stilbene systems[13].On the other hand, it has been stablished[14] that only those stilbene systems 8(X=H) which do not cyclized under photochemical excitation will give rise to direct coupling with the carbon bearing the iodine atom 8(X=I).



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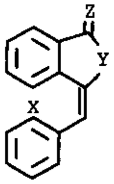

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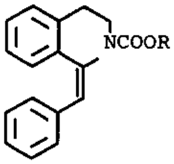

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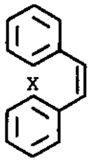

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Therefore, we prepared the iodo-enamide 2a(X=I)[8] from m-hemipinic anhydride 3a(Y=O)[9] and o-iodo phenylacetic acid 4a[15] using the same method as for 2b(X=Br). When a dilute benzene solution of iodo-enamide 2a(X=I) was irradiated (45 W Hanovia lamp, 12 hr) cepharanone B 1a was now obtained in 25% yield. It showed mp 249-251°C(from n-butanol) and identical spectroscopic properties to those reported[16]. Thus, in our opinion iodo-enamides of type 2 and related stilbene compounds are the alternative to achieve a satisfactory cyclization.

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