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PHOTOCHEMICAL SYNTHESIS OF DEHYDROAPORPHANES

N. C. Yang, G. R. Lenz and Arnon Shani*,**

Department of Chemistry, University of Chicago, Chicago, Ill. 60637

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Organic compounds frequently undergo novel photochemical transformation which have been applied as synthetic methods in organic chemistry. One elegant example of such an application is the synthesis of aldosterone by Barton and his coworkers.[1] Stilbene (I) undergoes a rapid cis-trans isomerization under the influence of ultraviolet light, and cis-stilbene then cyclizes to give dihydrophenanthrene(II) upon further irradiation (reaction 1).[2] The reaction has been applied to the synthesis of phenanthrene derivatives.[3] 1-Benzylidene-1,2,3,4-tetrahydroisoquinoline (III) is a substituted stilbene and may undergo a similar reaction to give the dehydroaporphane ring system (IV) (reaction 2). The current communication deals with the photochemical conversion of benzylidene-tetrahydroisoquinoline to dehydroaporphanes.

We found that 2-methyl-1-benzylidene-1,2,3,4-tetrahydroisoquinoline (IIIa, R = CH_3)[4] was remarkably stable toward the influence of ultra-

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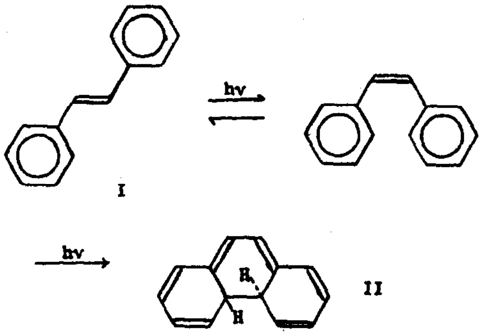
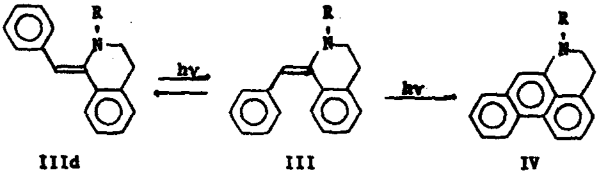


(1)



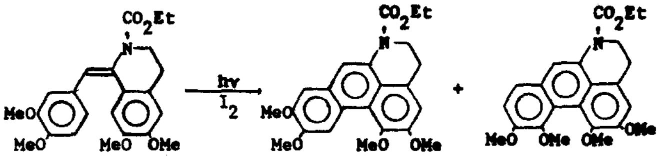
(2)

violet light either in the presence or in the absence of oxidizing agents. Examination of the absorption spectrum of IIIa reveals a transition at 346mμ (log ε, 3.50) which is absent in the characteristic stilbene chromophore. This transition is assigned to the styrylamine system. It is probable that the energy absorbed by the compound will undergo rapid internal conversion to the low-lying excited state of the styrylamine system which then deactivates to the ground state leaving the stilbene system unreacted.[5] If this explanation is correct, the conjugation between the non-bonding p-electron on the nitrogen and the styrene system may be blocked by acylation on the nitrogen and the N-acyl derivative (IIIb, R = COR') will undergo photocyclization to give the aporphane system (IVb, R = COR'). 1-Benzylidene-2-carbethoxy-1,2,3,4-tetrahydroisoquinoline was prepared from the interaction between 1-benzyl-3,4-dihydroisoquinoline[6] and ethyl chlorocarbonate. The compound, m. p. 87-8°, thus prepared was assigned the cis-structure (IIIc, R = $CO_2C_2H_5$) on the basis of its ultraviolet spectrum, λ_{max} 226mμ(log ε, 4.14) and 288mμ(log ε, 3.94). The compound (IIIc) was readily isomerized to the trans-isomer (IIId, R = $CO_2C_2H_5$) under the influence of light, m. p. 97-8°, λ_{max} 231mμ(log ε, 4.05) and 302mμ(log ε, 4.23).[7] At the photostationary state the mixture contains about two portions of the trans isomer to one portion of the cis. The assignment of isomeric structures was verified by their n.m.r. spectra. The CH_3-protons on the carbethoxy group in IIIc were at the normal position for the ester groups, 8.72τ,[8] while the CH_3-protons in IIId were at a higher field, 9.30τ, which may be attributed to the shielding by the phenyl group.

Prolonged irradiation of IIIc or IIId in methanol in the presence of iodine yielded a new product, IVc (R = $CO_2C_2H_5$), in 65% yield, m. p. 92-3°, mol. wt., 291 (mass spec.), λ_{max} 252mμ(log ε, 3.80), 259mμ(log ε, 3.86) and 304mμ(log ε, 3.40). The structure was confirmed by n.m.r. to be N-carbethoxy-dehydroaporphane, 8.67τ(3H, triplet, $CH_2C\underline{H}_3$), 6.85τ(2H, triplet, benzylic CH_2), 5.91τ(2H, triplet, N-CH_2), 5.68τ(2H, quartet, O-$C\underline{H}_2CH_3$), 2.06-2.86τ(6H, multiplet, aromatic C-H), 1.50τ(2H, doublet, C_1- and C_{11}-H).[9,10]

The N-carbethoxy function was selected in our investigation because of the versatility of its conversion into other functional groups. In a preliminary investigation we found that the corresponding N-benzoyl derivative (IVd, R = COϕ) was extremely resistant toward both acidic and basic hydrolyses. Treatment of IVc with lithium aluminum hydride afforded a mixture, from which dehydroaporphane (IVe, R = H), m. p. 132-3°, ν_{max} 3,333 cm^{-1}, λ_{max} 243mμ(log ε, 4.34), 257mμ(log ε, 4.44) and 325mμ(log ε, 3.82), and N-methyldehydroaporphane (IVf, R = CH_3), m. p. 76-7°, λ_{max} 243mμ(log ε, 4.47), 257mμ(log ε, 4.48) and 324mμ(log ε, 3.93), were isolated. The structures of these compounds were verified by their n.m.r. spectra. Compound IVe exhibits signals at 6.50-7.10 τ(multiplet, 4H, CH_2), 6.07 τ(singlet, 1H, N-H), 3.50 τ(singlet, 1H, C_7-H) and 1.71 τ(doublet, 2H, C_1- and C_{11}-H); compound IVf exhibits signals at 7.09 τ(singlet, 3H, N-CH_3), 6.80-6.90 τ(multiplet, 4H, CH_2), 3.56 τ(singlet, 1H, C_7-H), 2.50-3.15 τ(multiplet, 5H, aromatic C-H), 1.75 τ(doublet, 2H, C_1- and C_{11}-H).

Our investigation indicated that the method may be applicable for the synthesis of aporphane alkaloids in general. A preliminary investigation was carried out with 1-(3,4-dimethoxybenzylidene)-2-carbethoxy-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (V), m.p. 144-6°, mol. wt., 413.45 (mass spec.). N.m.r. analysis indicated that V is a mixture of cis- and trans-isomers (3:2). Irradiation of V in methanol with iodine yielded a mixture, from which 65% of the starting material (V) was recovered and a new compound, VI or N-carbethoxy-dehydro-N-nor-glaucine, was isolated in 25% yield, m.p. 156-7°, mol. wt., 411.44 (mass spec.). The structure of VI was established by its high resolution n.m.r. spectrum, 8.67 τ(triplet, 3H, $CH_2C\underline{H}_3$), 6.86 τ(triplet, 2H, benzylic CH_2), 5.80-6.25 τ(multiplet, 14H, O-CH_3 and N-CH_2), 5.72 τ(quartet, 2H, O-CH_2), 2.99 τ(singlet, 1H, C_3-H), 2.86 τ(singlet, 1H, C_8-H), 2.27 τ (singlet, 1H, C_7-H) and 0.82 τ(singlet, 1H, C_{11}-H). We had so far failed to induce theremaining 10% of the material to crystallize, but the n.m.r. spectrum of this oil indicated that it might be mainly VII.



V VI VII

The conversion of these dehydroaperphanes to aporphanes and the application of this method to synthesize other dehydroaporphanes are now being investigatd.

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