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THE CONVERSION OF
2-FORMYL-3-KETO-9-METHYL-$\Delta^{1,4}$-HEXAHYDRONAPHTHALENE
INTO A PERHYDROAZULENE DERIVATIVE

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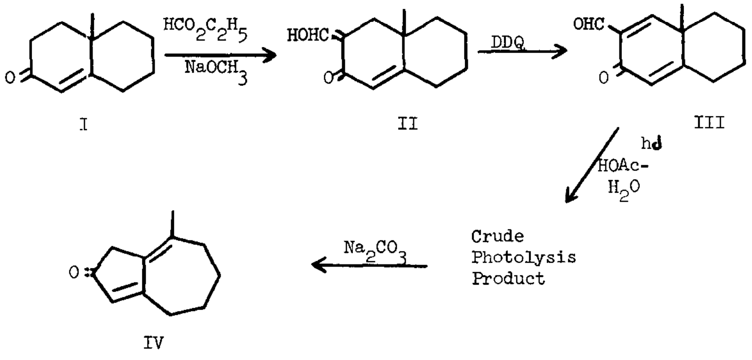
We have found that on irradiation in aqueous acetic acid followed by base catalyzed deformylation of the crude photo-product, the 2-formyl dienone III is converted into the 5/7-fused dienone IV in ca. 70% overall yield.

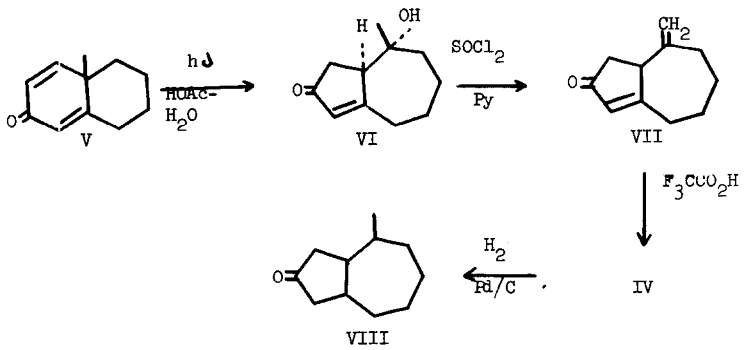
Compound III was prepared from the octalone I (1) by a procedure similar to that employed by Edwards et al. (2) for the preparation of 2-formyl-$\Delta^{1,4}$-3-keto steroids. Condensation of I with ethyl formate in the presence of sodium methoxide and reaction of the hydroxymethylene derivative II [b.p. 116-118° (0.5mm.); 75% yield; λ_{max}^{EtOH} 250 (ϵ10,500) and 306 mμ (ϵ5,600); $\lambda_{max}^{EtOH + NaOH}$ 240 (ϵ11,700) and 360 mμ (ϵ8,000); Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 75.06; H, 8.60] with 2,3-dichloro-5,6-dicyanobenzoquinone (3) in dioxane gave III [m.p. 82.5-84.0°; 76% yield; λ_{max}^{EtOH} 220 (ϵ11,900) and 244 mμ (ϵ11,000); $\lambda_{max}^{EtOH + NaOH}$ 242 (ϵ12,000) and 347 mμ (ϵ9,600); $\lambda_{max}^{CHCl_3}$ 5.87, 6.00, 6.16, and 6.24 μ; $\delta_{TMS}^{CCl_4}$ 1.38 (s, 3H), 1.25-2.65 (broad adsorption, 8H), 6.06 (m, 1H), 7.40 (s, 1H), and 10.10 p.p.m. (s, 1H); Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.60; H, 7.54].



A 1% solution of III in 45% aqueous acetic acid was irradiated for 3.5 hr. at room temperature using a 450-watt Hanovia high-pressure mercury lamp fitted with a Pyrex filter, and after addition of toluene the solvents were removed under reduced pressure using a rotatory evaporator on a steam bath. The resulting crude photo-product, a viscous brown oil, was dissolved in a 1% solution of sodium carbonate in 1:1 water-dioxane and warmed for 12 hr. on a steam bath. Extraction of the basic solution with ether, washing and drying, and evaporation of the ether under reduced pressure gave IV [b.p. 123-127° (bath temperature) (0.9mm.); Anal. Calcd for $C_{11}H_{14}O$: C, 81.44; H, 8.70. Found: C, 81.62; H, 8.87] in 70% yield from III. The 2,4-dinitrophenylhydrazone derivative of IV showed m.p. 174.5-175.3°; Anal. Calcd for $C_{17}H_{18}N_4O_4$: C, 59.64; H, 5.30; N, 16.37. Found: C, 59.41; H, 5.28; N, 16.24.

The structural assignment of IV is supported by spectral and chemical evidence. The product showed infrared absorption ($CHCl_3$) at 5.99 (conjugated carbonyl) and 6.40 μ (conjugated double bond) and ultraviolet absorption (95% ethanol) at 300 mμ (ϵ10,900) (4) . The n.m.r. spectrum of the product showed the presence of an olefinic methyl group (C-10 CH_3), a methylene group (C-2) allylic and α to the carbonyl group, and one vinyl proton (C-4 H), as indicated by single peaks at $\delta_{TMS}^{CCl_4}$ 1.85 (3H), 2.83 (2H), and 5.86 p.p.m. (1H).

The conversion of the 5/7-fused hydroxy ketone VI into IV offers further support for the structure of IV. Using the conditions described by Kropp and Erman (5) for synthesis of the 6-methyl derivative (steroid numbering), VI was prepared on irradiation of the dienone V (6) in <u>ca</u>. 10% yield. Compound VI showed m.p. 108.5-109.5°; λ_{max}^{EtOH} 237 mμ (ϵ13,000); $\lambda_{max}^{CHCl_3}$ 2.88, 5.97, and 6.25 μ; $\delta_{TMS}^{CDCl_3}$ 0.92 (s, 3H, C-10CH_3), and 5.62 p.p.m. (m, 1H, C-4H); <u>Anal</u>. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.45; H, 9.09. The spectral properties of VI are in close agreement with those reported (5) for its 6-methyl derivative. Treatment of VI with thionyl chloride in pyridine (7) gave a crude reaction product having an n.m.r. spectrum consistent with the structure VII. When VII (as an approximately 20% solution in carbon tetrachloride) was treated with a catalytic amount of trifluoracetic acid, it was slowly isomerized (monitored by n.m.r.) into a substance having n.m.r. and infrared spectra identical to that of IV.

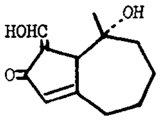


Reduction of IV and determination of the number of exchangeable hydrogen atoms α to the carbonyl group in the saturated ketone product were used to establish the position of the carbonyl group in IV. Hydrogenation of IV over palladium on charcoal gave VIII (stereochemistry unknown) [b.p. 95-102° (bath temperature) (0.7mm.); $\lambda_{max}^{CCl_4}$ 5.74 mμ (cyclopentanone); $\delta_{TMS}^{CCl_4}$ 0.92 (d, J = 7 c.p.s., C-10CH$_3$), 1.25-2.65 p.p.m. (broad absorption), and no vinyl protons; Anal. Calcd for $C_{11}H_{18}O$: C, 79.47; H, 10.91. Found: C, 80.05; H, 10.99]. Equilibration of VIII with deuterium oxide using potassium carbonate as the catalyst yielded a partially deuterated material (ca. 95% one component by v.p.c. analysis). A sample, collected by v.p.c., showed: direct deuterium analysis by the falling-drop method: atom % D, Calcd: 22.22. Found: 18.75 (ca. 84% deuterium substitution based on an incorporation of four deuterium atoms); Anal. Calcd for $C_{11}H_{14}D_4O$; C, 77.58; weight H_2O + D_2O (from a 3.205-mg. sample), 3.127 mg. Found: C, 78.08;

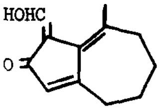
weight $H_2O + D_2O$, 3.056 mg.

The mass spectrum of the sample in the region of the molecular weight showed peaks at m/e 166, 167, 168, 169, 170, and 171 indicative of the presence of approximately 2% $C_{11}H_{18}O$, 6% $C_{11}H_{17}DO$, 21% $C_{11}H_{16}D_2O$, 40% $C_{11}H_{15}D_3O$, and 31% $C_{11}H_{14}D_4O$. These data show that compound VIII is capable of exchanging four hydrogen atoms and this clearly establishes the location of the carbonyl group at C-3 in IV.

The structure of the photo-product that gives rise to IV on base treatment has not been established, since all attempts at purification of the oil obtained after photolysis of III have led either to its conversion into IV or to decomposition. The oil showed solubility in 10% sodium hydroxide and gave positive ferric chloride and Tollens' tests indicating the presence of an enolizable β-keto aldehyde grouping. Based on present evidence and probable precursors of IV, we suggest IX (or its tautomeric or internal hemiacetal form) or X (or its tautomeric form) as the likely major components of the photolysis mixture. Further studies to check this point are in progress.



IX



X

The nature of the influence of the formyl group on the rearrangement of III has not been determined. Although the formation of the 5/7-fused ring system can be rationalized easily in terms of generally accepted pathways for the rearrangement of ring A unsubstituted and alkyl-substituted cyclohexadienones in aqueous acid, (5,8) in view of the chromophoric nature of the formyl group such an interpretation in this case may not be tenable. A previous study (9) has shown that irradiation of a 2-formyl steroidal dienone in dioxane with light at 2537 Å does not give the expected lumiproduct and that irradiation with unfiltered light gives a complex mixture of mainly phenolic products. A study of the influence of the nature of the medium on the course of the rearrangement of III as well as the behavior of cyclohexadienones having chromophoric groups other than formyl at C-2 is in progress.

It should be pointed out that the yield of 5/7-fused dienone obtained in the conversion of III into IV is considerably greater than that of 5/7-fused hydroxy ketone products obtained on irradiation of ring A unsubstituted cyclohexadienones such as V and its 6-methyl derivative (5) in aqueous acid. Thus the procedure of irradiation of a 2-formyl cyclohexadienone in aqueous acid and removal of the formyl group after photolysis appears to be useful for the synthesis of certain ring A unsubstituted perhydroazulenes.

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