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A NEW SYNTHESIS OF VITAMIN A

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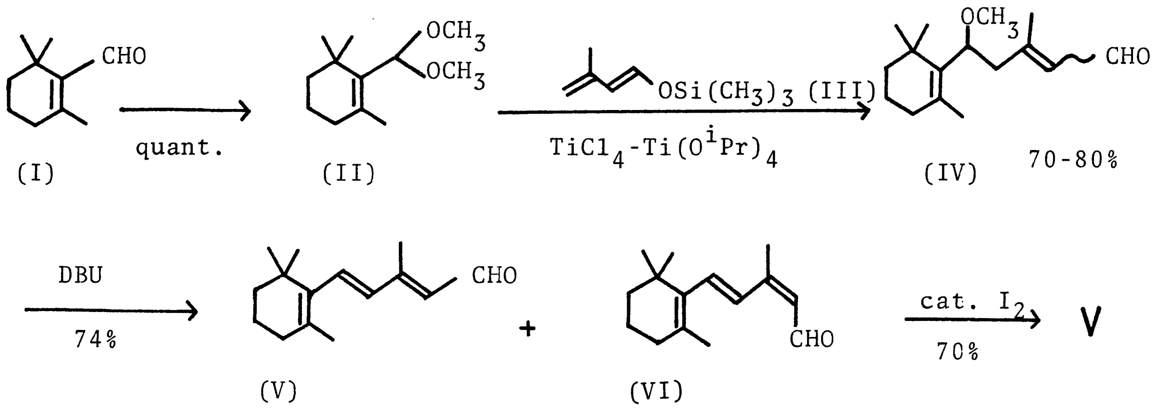
A new synthesis of vitamin A$^{1)}$ was successfully accomplished by reducing retinal, prepared by the reaction of 3-methyl-1-trimethylsiloxy-1,3-butadiene (III) with β-ionylideneacetaldehyde dimethyl acetal (VII) followed by the elimination of methanol with tertiary amine such as 1,5-diazabicyclo[5.4.0]undecene-5. The intermediate, β-ionylideneacetaldehyde (V), was also prepared according to the same procedure starting from β-cyclocitral dimethyl acetal (II).

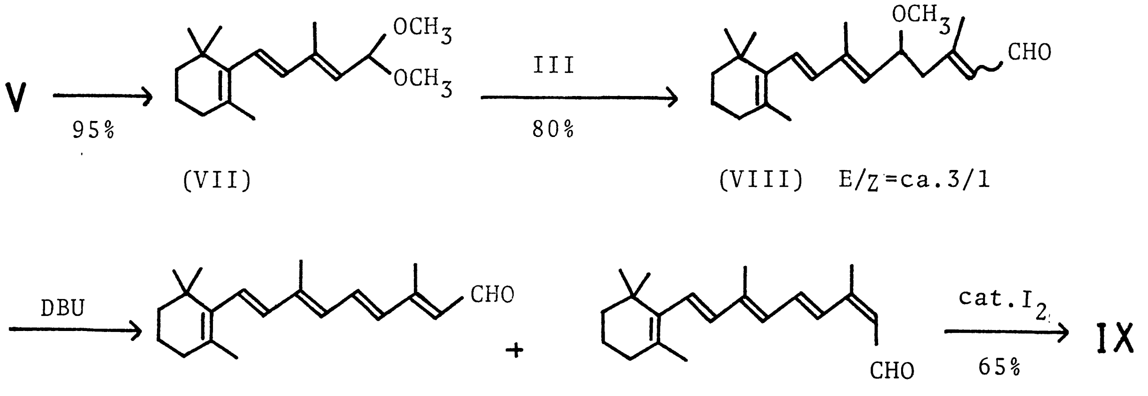
In the preceding papers, a convenient method for the preparation of δ-alkoxy-α,β-unsaturated aldehydes by the reaction of various acetals with dienoxysilane in the coexistence of $TiCl_4$ and $Ti(O^iPr)_4$$^{2)}$ and a new method for the preparation of polyenals from δ-alkoxy-α,β-unsaturated aldehydes by the elimination of alcohol with tertiary amine such as 1,5-diazabicyclo[5.4.0]undecene-5 (DBU) or 1,5-diazabicyclo[4.3.0]nonene-5 (DBN) in the presence of molecular sieves 3A or 4A$^{3)}$ were described.

In this communication, we wish to report a new synthesis of vitamin A starting from β-cyclocitral (I) by the repetition of the above mentioned two preparative methods: β-Cyclocitral (I)$^{4)}$ was converted to its dimethyl acetal (II) on treatment with $HC(OCH_3)_3$-CH_3OH in the presence of d-camphorsulfonic acid at -10°C for 10 min in almost quantitative yield. Dienoxysilane (III) reacted instantaneously with II at -40°C in the presence of $TiCl_4$-$Ti(O^iPr)_4$ to afford δ-methoxy-α,β-unsaturated aldehyde (IV) (E:Z = 3:1 mixture) in 70-80% yield.



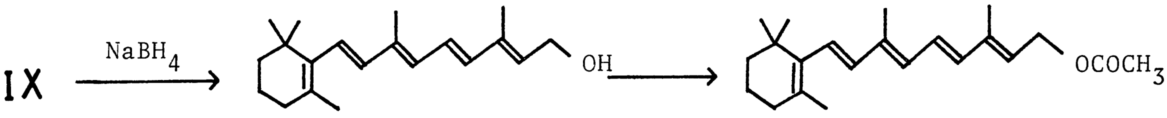
The treatment of IV with DBU (4 equiv) in the presence of molecular sieves 3A for 5 hr in refluxing CH_2Cl_2-CH_3CN (1:1) under an argon atmosphere afforded V and its 2-(Z) isomer (VI) in 56% and 19% yields, respectively. The isomer VI was converted to V in 70% yield on treating with a catalytic amount of iodine[5] in abs. Et_2O-C_6H_6 (1:1) for 4 hr at room temperature.

The synthesis of retinal (IX), a precursor of vitamin A, was also achieved according to the same procedure from V as shown in the following scheme.



(IX) 59% (X) 25%

Retinal (IX) was reduced with sodium borohydride in methanol at -30°C for 1 hr under an argon atmosphere to give vitamin A (XI) in quantitative yield. Acetylation of XI with acetic anhydride-pyridine under an argon atmosphere gave vitamin A acetate (XII) in 71% yield based on IX.



(XI) (XII) 71% based on IX

Spectral data of XII were consistent with those of the authentic sample obtained from commercial source; nmr (δ_{TMS} ppm, CCl_4): 1.00 (s,6H), 1.70 (s,3H), 1.85 (s,3H), 1.90 (s,3H), 1.95 (s,3H), 4.65 (d,2H), 5.55 (t,1H), 5.80 - 6.70 (5H); uv: λ_{max}^{EtOH} 326nm (ε 4.45×10^3); ir: 1740, 1220 cm^{-1}; mass: m/e 328 (M^+).

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