It is interesting to note that in the solvolysis of *t*-BuX (where X = Cl, Br, and I) the percent elimination follows the order $Cl^- > Br^- > I^-$, the reverse of what we observe (compound Ia gives less elimination product than compound Id in the same solvent, Table I).[4d] For our system, if the extent of elimination depends on the relative magnitude of k_2 and k_E rather than the intrinsic basicity of the halide ion as we assume, it is easy to see that the ion pair with bromide counterion will give more olefin than the one with chloride counterion since the more concentrated charge on Cl^- will stabilize the ion pair more effectively.

Addition of HCl to styrene in glacial acetic acid has been shown to proceed through the rate-limiting protonation of the C=C bond followed by fast combination of Cl^- ion with the carbonium ion in the tight ion-pair intermediate.[9] Although similar examples of addition of HX to C=C in nonpolar solvents are scarce in the literature,[10] the mechanism proposed for the styrene-HCl system strongly suggests that our proposal that k_E is partly rate limiting in the less polar aqueous dioxane solvents is essentially correct.

Acknowledgment. We thank the National Institutes of Health for financial support of this work (Grant. No. GM 21933).

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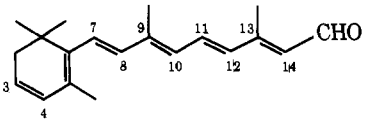
New Geometric Isomers of Vitamin A and Carotenoids. 5. 7-*cis*-3-Dehydroretinal and 7-*cis*-3-Dehydro C_{18} Ketone from Direct Irradiation of the Trans Isomers in Polar Solvents[1]

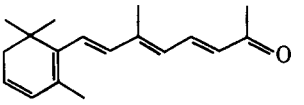
Sir:

In an earlier paper we reported results of photoisomerization of retinal in the aprotic polar solvent acetonitrile giving directly all the mono-cis isomers including the hindered 11-cis and 7-cis.[1] The latter isomers are not formed in nonpolar solvents.[2] The results in polar solvents appear to be consistent with the zwitterionic character of the excited singlet state of polyenes as suggested by recent calculations.[3]

Although all four mono-cis isomers are formed from irradiation of the all-trans isomer of retinal, there appears to be some selectivity preferring formation of the isomer (11-cis) from isomerization near the central most double bond.[4] It occurred to us that this preference may be more profitably used in the 3-dehydrovitamin A series (vitamin A_2) for preparation of the unknown 7-cis isomers,[5] where the 7,8 bond is closer to the central most position in the polyene chain. In this paper we describe results on dehydroretinal (I) and the corresponding C_{18} ketone (II).[6]



I



II

Electronically II is similar to retinal in that it is a pentaene conjugated with a carbonyl group. However, it has the obvious advantage of having one fewer exocyclic double bond, thus reducing the number of possible geometric isomers to eight. Also, the 7,8 and the 9,10 bonds are now the central most double bonds. Therefore we first studied this system.

When a sample of the all-trans isomer of II[7] in acetonitrile was irradiated with light of 360 nm,[8] the appearance of two closely spaced new major peaks in the HPLC chromatogram[9] was immediately detected.[10] The retention time of the first peak was identical with that of 9-*cis*-II. Initially the two peaks (detecting beam 380 nm, not corrected for different molar absorptivities at this wavelength) were of approximately equal magnitude. The two isomers were isolated by preparative HPLC. The ^1H NMR of the minor product was clearly that of 9-*cis*-II and that of the major only consistent with 7-*cis*-II. (Data listed in Table I; see below for a discussion of the ^1H NMR signals characteristic of the geometry). Consistent with the expected blue shift of the UV absorption maximum of the hindered 7-cis that we found when irradiating with light >410 nm (Corning 3-74 filter plates) the amount of the 7-cis isomer reached 60% of the total isomer composition. Although the ratio of isomers did not seem to vary to a great extent when other polar solvents were used (acetone and methanol), formation of the 7-cis isomer was not favored in nonpolar solvents (in hexane 4:1 in favor of the 9-cis isomer).

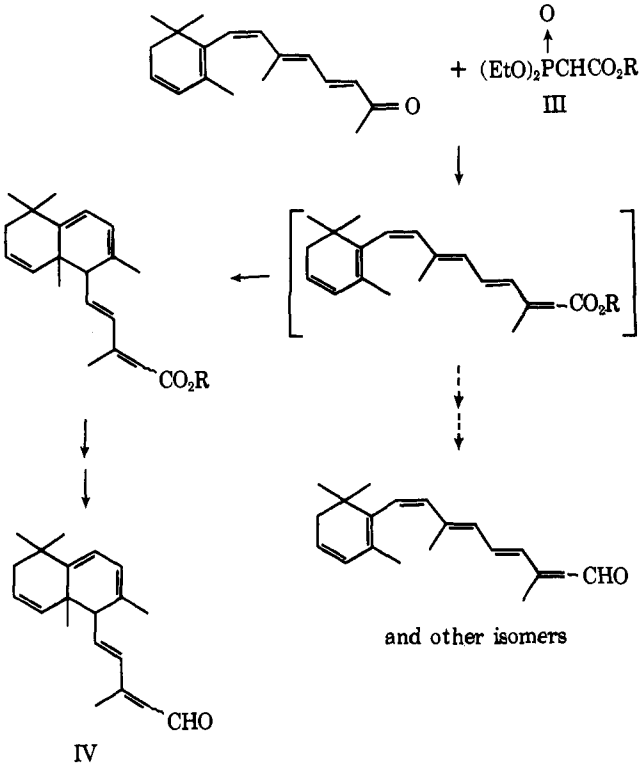
The 7-cis C_{18} ketone II is an obvious precursor to the 7-cis isomers of vitamin A_2. Unfortunately we found this compound surprisingly unreactive toward the C_2 phosphonate III in the Horner reaction. No reaction was detected when an irradiated mixture of II and the C_2 phosphonate was stirred in THF with lithium diisopropyl amide at room temperature for 5 h. At 55 °C the Horner reaction proceeded at a moderate rate. However, although 7-*cis*-II appeared stable at this temperature, the resultant condensation products apparently were not. Thus, we found the eventual retinal mixture obtained after treating the retinoate mixture consecutively with $LiAlH_4$ and MnO_2 containing little of the 7-cis isomer[11] (by the absence of a strong high field CH_3-5 peak in the ^1H NMR spectrum[12] and by comparison of 1c retention time with authentic 7-*cis*-I; see below). Preparative 1c yielded only the all-trans, 9-cis, and 13-cis isomers of dehydroretinal (assignment based on their ^1H NMR spectra, data in Table I)[13] and another minor deconjugated aldehyde with its ^1H NMR spectrum consistent with the cyclized structure IV. Therefore 7-*cis*-retinoate obtained from the Horner reaction must have undergone 6e electrocyclization[14] and/or geometric isomerization at 55 °C.

We next turned to direct irradiation of dehydroretinal I. When a mixture of 13-cis and all-trans isomers of the aldehyde was irradiated in acetonitrile first with light >380 nm (Corning

Table I. ^{1}H NMR Signals of Isomer of Dehydroretinal (I) And Dehydro C_{18} Ketone (II)[a]

Compd	CH_3-5	CH_3-9	CH_3-13	H-3	H-4	H-7	H-8	H-10	H-11	H-12	H-14	H-15	$J_{7,8}$	$J_{11,12}$
all-trans-I	1.87	2.04	2.33	5.74	5.85	6.33	6.33	6.22	7.15	6.38	5.97	10.10	?	15.0
all-trans-I[b]	1.87	2.05	2.32	5.72	5.86	6.31	6.31	6.21	7.14	6.37		10.09		
7-*cis*-I	1.58	1.96	2.31	5.78	5.80	5.98	6.18	6.26	7.07	6.34	5.96	10.06	12.5	14.9
9-*cis*-I	1.81	2.03	2.29	5.74	5.84	6.34	6.80	6.12	7.21	6.32	5.96	10.11	15.8	15.0
13-*cis*-I	1.87	2.03	2.14	5.74	5.84	6.33	6.33	6.25	7.03	7.29	5.86	10.16	?	15.0
all-trans-II	1.86	2.06	2.28	5.77	5.84	6.40	6.32	6.19	7.57	6.17			16.2	15.2
all-trans-II[c]	1.84					6.30	6.30	6.13	7.46	6.07				
7-*cis*-II	1.57	1.98	2.28	5.76	5.80	6.01	6.15	6.25	7.48	6.13			11.8	15.4
9-*cis*-II	1.90	2.04	2.27	5.80	5.86	6.40	6.81	6.08	7.63	6.11			15.9	14.6
9-*cis*-II[c]	1.90					6.28	6.85	6.03	7.51	6.01				

[a] Varian XL-100; solvent, $CDCl_3$; chemical shift, δ, in parts per million; coupling constants in hertz. [b] In CCl_4. Data of W. Vetter, G. Englert, V. Rigassi, and U. Schwieter in "Carotenoids", O. Isler, Ed., Birkhäuser Verlag, Basle, 1971, p 216. [c] In CCl_4. Data of ref 6.



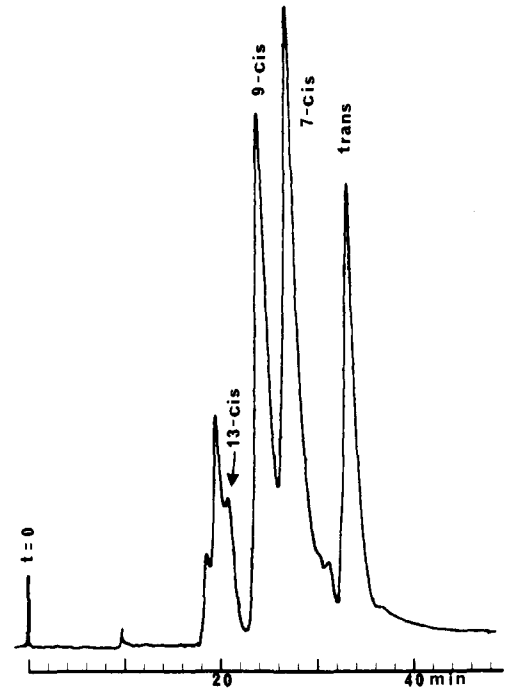


Figure 1. HPLC chromatogram of an irradiated mixture of 3-dehydroretinal (Du Pont 830 1c and Varian VARICHROM detector, 400 nm). The minor isomers with shorter retention time have not been isolated.

0-51 filter plate), the appearance of two new major peaks (area ratio of 2:1 at 400 nm) in the HPLC chromatogram was again observed. Formation of these new isomers was accompanied by a rapid decrease of the 13-cis and more slowly of the all-trans isomers. By comparison of 1c retention times, the product associated with the larger peak was identified to be 9-*cis*-dehydroretinal. When changed to light of longer wavelengths, >480 nm (Corning 3-71 filter plate), the relative amounts of the minor peak increased. After 3 h, it surpassed that of 9-cis. An 1c chromatogram of the mixture is shown in Figure 1. The new isomer was isolated by preparative HPLC. Its ^{1}H NMR spectrum is shown in Figure 2 and data are listed in Table I. The high field CH_3-5 signal and the magnitude of $J_{7,8}$ agree with the 7-cis geometry, and the large $J_{11,12}$ with the 11-trans geometry. The low field CH_3-13 and the high field H-8 signals indicate, respectively, the 13-trans and the 9-trans geometry.[13] The compound is therefore 7-*cis*-dehydroretinal.

In spite of the fact that dehydroretinal is also a visual chromophore (in porphyropsin),[15] unlike the retinal system, little photochemical studies have been reported. Our preliminary results suggest similar dependence in the dehydro series of isomer composition on solvent polarity. For example, in hexane 7-cis is only a minor product in the photolysate. This

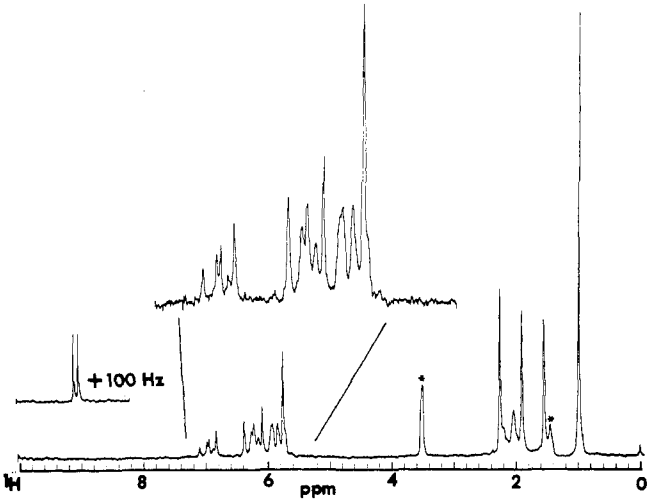


Figure 2. ^{1}H NMR spectrum of 7-*cis*-3-dehydroretinal (Varian XL-100; solvent, 5% dioxane-d_8 in CCl_4). The peaks with * are solvent impurities.

solvent dependence and conditions for preparation of the visually important 11-cis isomer will be examined in more detail.[16] Also under investigation is possible existence of 7-cis analogues of porphyropsin.

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(7) Prepared by bromination with NBS of the C_{18} ketone followed by dehydrobromination. The product mixture contained the trans and the 9-cis isomers in a 6:1 ratio. They were readily separated on silica gel columns.
(8) Irradiation was carried out either with a high-pressure Hg arc lamp coupled with a Schoeffel monochromator, bandwidth 25 nm (analytical scale), or with a 550-W Hanovia medium-pressure Hg lamp with appropriate cutoff filter plates (preparative).
(9) All of the HPLC work were done on a $\frac{1}{2}$ in. Altex 5-μ Lichrosorb column. Hexane containing 5–10% of ether was the solvent.
(10) Two minor peaks of shorter retention time were also observed. In analogy to the parent C_{18} ketone,[6] we tentatively assigned these to the 11-cis and 9,11-cis isomers.
(11) The retention time of a small peak in the HPLC chromatogram of the aldehyde mixture was identical with that of 7-*cis*-I (see text).
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(13) The ^{1}H NMR signals in the dehydro series generally follow the parent retinal isomers. Therefore, the 7,8 and 11,12 geometry can be deduced from their coupling constants and the chemical shifts of CH_3-5, CH_3-13, and H-8 reliably indicate, respectively, the 7,8, 13,14, and 9,10 geometry. See, e.g., D. Patel, *Nature*, **221**, 825 (1969), and R. Rowan III, A. Warshel, B. D. Sykes, and M. Karplus, *Biochemistry*, **13**, 970 (1974).
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(16) A minor product with retention time close to that of the 13-cis isomer (see Figure 1) could be the 11-cis isomer.

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Acid–Base Reactions of the Metallocubanes. Synthesis and Structural Characterization of $Cu_{10}[S_2CCH(COO\text{-}t\text{-}C_4H_9)_2]_6[S_2CC(COO\text{-}t\text{-}C_4H_9)_2]_2$, a Ten Copper Atom Aggregate

Sir:

The pronounced tendency of Cu^I ions toward the formation of clusters with sulfur ligands is well established. A remarkable variety in composition and structures occurs in these clusters where the molecular architecture is based on the existence of cores such as Cu_4S_6,[1] Cu_4S_8,[2] Cu_5S_6,[3] Cu_5S_7,[4] and Cu_8S_{12}.[5] With the exception of the Cu^I, Cu^{II} mixed valence clusters obtained with β,β-dimethylcysteamine,[6] $[Cu_{14}L_{12}Cl]^{7+}$ ($L = [SC(CH_3)_2CH_2NH_2]^-$), and D-penicillamine,[7] $[Cu_{14}L_{12}Cl]^{5-}$ ($L = [SC(CH_3)_2CHCOO]^{2-}$), there exist no other copper cluster compounds which contain more than eight copper atoms in a molecular unit.

In an attempt to evaluate the importance of various ligand characteristics that may affect the structural and chemical properties of copper clusters with sulfur ligands, we have undertaken a study of the $[Cu_8L_6]^{4-}$ cubanes.[5b,8] The coordinated 1,1-dithiolate ligands in these clusters undergo facile protonation and sulfur addition[9] reactions that make it possible to alter the electronic and structural properties of the ligands.

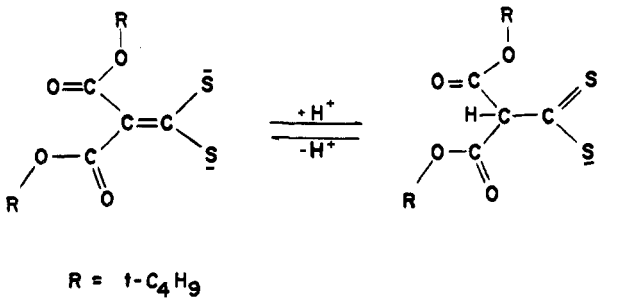

Figure 1. Structure and acid–base behavior of the *t*-Bu-DED, $[S_2CC(COO\text{-}t\text{-}C_4H_9)_2]^{2-}$, ligand.

In this communication we report on the acid–base behavior of the $[Cu_8(t\text{-Bu-DED})_6]^{4-}$ cluster (I) (*t*-Bu-DED = $S_2CC(COO\text{-}t\text{-}C_4H_9)_2$) (Figure 1) and the crystal and molecular structure of one of the proton addition products, $Cu_{10}(t\text{-Bu-DEDH})_6(t\text{-Bu-DED})_2$.

The reaction of $K_2(t\text{-Bu-DED})$[10] with $Cu(CH_3CN)_4ClO_4$[11] in acetonitrile in 1:1 molar ratio affords I as a potassium salt which upon recrystallization from an acetone–pentane mixture is obtained as orange crystals, mp 180 °C dec. Anal. Calcd for $K_4Cu_8S_{12}O_{24}C_{72}H_{108}$: C, 35.91; H, 4.52. Found: C, 35.70; H, 4.88. Cation exchange in I is accomplished readily in warm acetonitrile, CH_3CN, upon the addition of tetraalkylammonium or tetraarylphosphonium chlorides. The apparent molecular weight of the $BzPh_3P$ salt of I in 1,2-dichloroethane solution varies as a function of concentration. At concentrations >0.08 M, however, the apparent molecular weight is 3600 ± 70 and stays constant. This value indicates complete ionic association at higher concentrations and agrees well with the calculated molecular weight of 3666 for the $(BzPh_3P)_2Cu_8(t\text{-Bu-DED})_6$ cluster.

A potentiometric titration of I with $HClO_4$ in CH_3CN shows inflections at 1 and 6 equiv of acid/mol of I. Addition of 1 equiv of HCl (0.1 M in CH_3CN) to a solution of I (0.5 mmol in a minimum amount of CH_3CN) results in the formation of a dark green solution. Addition of 3 equiv of Ph_4PCl[12] to this solution, followed by solvent removal, results in the formation of a dark green crude solid contaminated with KCl. The solid mixture is extracted with $CHCl_3$. The green $CHCl_3$ solution upon addition of CS_2 gives dark green crystals of $(Ph_4P)_3Cu_8(t\text{-Bu-DED})_5(t\text{-Bu-DEDH})$ (II), mp 164 °C dec, in 83% yield. Anal. Calcd for $Cu_8S_{12}P_3O_{24}C_{144}H_{169}$: C, 52.90; H, 5.21; Cu, 15.6. Found: C, 52.10; H, 5.25; Cu, 15.5. Addition of a standard Bu_4NOH solution to a solution of II results in the formation of the cluster anion of I in a quantitative yield. A preliminary structure determination of the Bu_4N^+ "salt" of II clearly shows the Cu_8 cube in a Cu_8S_{12} core similar to those observed previously in other structures.[5b,8] Additions of 2 or 1 equiv of acid to I or II, respectively, result in violet solutions. Following a procedure similar to the one described previously, and employing $BzPh_3P^+$ [12] as a counterion, purple crystals of $(BzPh_3P)_2Cu_8(t\text{-Bu-DED})_4)(t\text{-Bu-DEDH})_2$ (III), mp 125 °C dec, can be isolated in 54% yield. Anal. Calcd for $Cu_8S_{12}P_2O_{24}C_{122}H_{154}$: C, 49.51; H, 5.25; S, 13.00; P, 2.09; Cu, 17.2. Found: C, 49.51; H, 5.19; S, 13.8; P, 2.13; Cu, 17.0. Quantitative conversion of the anion in III to the cluster anions of II or I is accomplished by the addition of 1 or 2 equiv of base, respectively.

Addition of 3 equiv of acid to I results in the formation of a red-brown solution which contains III and a red by-product. This by-product becomes the major product in the reaction of