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A COMPARISON OF THE FORMULAS PROPOSED FOR HETEROXANTHIN

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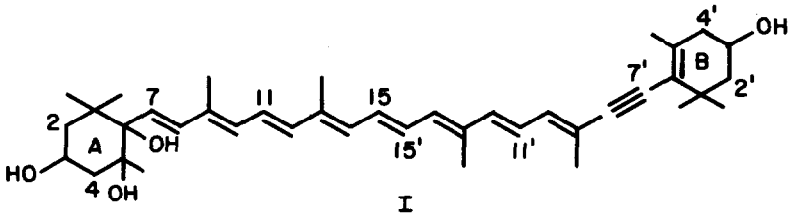
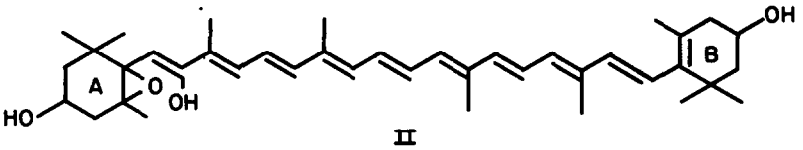
Summary: Current observations on heteroxanthin (obtained from Tribonema and Vaucheria) provide further support for the structure as 3,5,6,3'-tetrahydroxy-5,6-dihydro-7',8'-didehydro-β-carotene.

Recently, two different molecular structures have been proposed for heteroxanthin. Preparations isolated primarily from Tribonema aequale have been reported as 3,5,6,3'-tetrahydroxy-5,6-dihydro-7',8'-didehydro-β-carotene(I).[1,2] Preparations from Vaucheria have been reported as 3,3',8-trihydroxy-5,6-epoxy-β-carotene(II).[3]



I



II

Preparations of heteroxanthin from Vaucheria and Tribonema have now been found to exhibit identical physical and chemical properties.[2] Mixtures of the two preparations could not be separated by various chromatographic procedures. With several chromatographic systems, both preparations were more sorbed than the trihydroxy neoxanthin.[2]

Additional physical measurements provide further support for (I). They also provide a basis for the direct comparison of (I) and (II).

Mass spectral fragmentation patterns support (I). Some of the observed fragments, which correspond to loss of terminal rings, were $C_9H_{17}O_3$, $C_{10}H_{18}O_3$,

$C_{11}H_{19}O_3$ and $C_{13}H_{22}O_3$. The loss of $C_9H_{17}O_3$ and $C_{10}H_{18}O_3$ occur as splitting at C6-C7 and C7-C8 (IA). With (II) these total fragments could be lost by the splitting at C6-C7 and C7-C8 with a concurrent loss of water from ring B or from the -OH on C8. A splitting at C8-C9 in I results in the direct loss of $C_{11}H_{19}O_3$, the fragment observed. The analogous splitting in II would yield a fragment of $C_{11}H_{17}O_3$, two hydrogen atoms short. If this occurred with the concurrent loss of water the resulting fragment lost would be $C_{11}H_{19}O_4$. This fragment was not observed. Similar conclusions are reached when the splitting at C9-C10 is considered. From (I) the expected fragment $C_{13}H_{22}O_3$ is the one observed. The loss with formula II should be either $C_{13}H_{20}O_3$ or, with water, $C_{13}H_{22}O_4$, neither of which was found. All these fragmentation patterns, which have been extensively studied, support (I).

From the MS results, but one hydroxyl group occurs at the other (B) end of the molecule, and the acetylene unit is probably at C7'-C8'. Splitting at C6'-C7' should be inhibited by the acetylene unit of (I). Splitting at C7'-C8' of (I) should also be inhibited by the acetylene unit of (I), but (II) should yield M-$C_{10}H_{17}O$, not found. This peak has been found in all compounds containing a β ring (IIB). Splitting at C8'-C9' of (I) should yield M-$C_{11}H_{15}O$, found, but (II) should yield M-$C_{11}H_{17}O$, not found.

Definitive evidence that supports (I) but not (II) depends upon the appearance of specific MS fragments as illustrated in tabular form:

Fragment	Compound	(I)	(II)	Result
M-80	Epoxide splitting	Not expected	Expected	Not found
M-106, C_8H_{10}	Xylene from chain	Not expected	Expected	Not found
M-143, $C_8H_{15}O_2$	From 5,6-di-OH ring	Expected	Not expected	Found
M-153, $C_{10}H_{17}O$	From β ring	Not expected	Expected	Not found
M-161, $C_8H_{15}O_2+H_2O$	From 5,6-di-OH ring	Expected	Not expected	Found

From studies of a 5,6 diol (azafrin),[4] the formation of an M-143 $C_8H_{15}O_2$ fragment from heteroxanthin[1] indicates that hydroxy groups must occur at C5 and

C6 as in (I). Similarly, the formation of a pyrrylium ion m/e 181[1] is expected from a 3,5,6-trihydroxy ring,[1] also as in (I). This assignment of the location of the three hydroxy groups in (IA) is supported by the NMR.

The NMR data[1,2] support (I) not (II). Half the molecule (B) of (I) is like the half molecule of diadinoxanthin and diatoxanthin with a 3-hydroxy-β-ring adjoining the conjugated system through an acetylenic bond. The half molecule (B) of (II) is like the half molecule of diatoxanthin and zeaxanthin with a 3-hydroxy-β-ring adjoining the conjugated olefinic system. The tabulated results for the τ values (observed in C_5D_5N, ref. H.M.S.) indicate that one half molecule of heteroxanthin is like that of (B) in (I) not like that of (B) in (II).

Location of CH_3-	1	1	5	9	13
Heteroxanthin (τ)	8.87	8.79	8.15	8.06	8.15
Diadinoxanthin (as IB) (τ)	8.87	8.79	8.14	8.04	8.14
Diatoxanthin (as IB) (τ)	8.87	8.79	8.14	8.04	8.14
Zeaxanthin (as IIB) (τ)	8.97	8.98	8.33	8.12	8.10
Diatoxanthin (as IIB) (τ)	8.96	8.96	8.31	8.15	8.05

The electronic spectrum of heteroxanthin in ethanol is not shifted by HCl.[2,3] This indicates the absence of a 5,6-epoxide unless its rearrangement is prevented by an anomalous structure. Because of scattering in the KBr pellets containing carotenoids, the weak absorption in the IR by the acetylenic group was often unobservable.[2]

The -OH at C8 in (II) represents an improbable structure. As formulated, it is an allylic enol of an 8-ketonic compound. Experience with 8-ketonic carotenoids has provided no indication that the corresponding enols are stable. If (II) were to isomerize (with acid) to the corresponding ketone, the electronic spectrum would be altered to that of a ketonic pigment approximating that of fucoxanthin or siphonaxanthin.

Acylation and silylation results show that two hydroxyl groups of heteroxanthin are remarkably inert.[1] Although the hydroxyl at C6 of (IA) is formally

allylic, it is so isolated by the polyene chain, the saturated ring, and the methyl groups at C1 and C5 that it might not exhibit typical allylic properties (as absence of ether formation with methanol plus HCl,[1,2] as observed[1,2,3]).

The limited quantities of heteroxanthin have restricted chemical investigation of the vicinal hydroxyl groups. With azafrin, however, the hydroxyl at C6 is so isolated that it resists methylation with methyl iodide[5]. Moreover, the vicinal hydroxyl groups of heteroxanthin may occur in stereoisomeric modifications that inhibit their mutual chemical reactions. The hydroxyl at C8 in II, by contrast, should exhibit the usual properties of a tertiary alcohol, which were not observed[1].

From these results and comparisons, (I) is a supportable structure for heteroxanthin. (II) is untenable.

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1. H. H. Strain, K. Aitzetmüller, W. A. Svec, and J. J. Katz: Chem. Commun. 876 (1970).
2. H. H. Strain, F. L. Benton, M. C. Grandolfo, K. Aitzetmüller, W. A. Svec, and J. J. Katz: Phytochem. 9, 2561 (1970).
3. H. Nitsche: Tetrahedron Letters 38, 3345 (1970).
4. C. R. Enzell, G. W. Francis, and S. Liaaen-Jensen: Acta Chem. Scand. 23, 727 (1969).
5. H. Müller and P. Karrer: Helv. Chim. Acta 48, 291 (1965).