[Contribution from the Sterling Chemistry Laboratory, Yale University]

AN EMPIRICAL PRINCIPLE RELATING THE ABSORPTION SPECTRA OF CAROTENOIDS TO THEIR STRUCTURES

ALFRED H. FRYE

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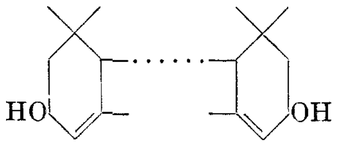
In view of the recent paper by Fieser (1) on this subject, I wish to point out a simple empirical method by which it is possible to predict the absorption maxima of non-carbonyl carotenoids provided certain data are available on analogous compounds. Essentially this method is based on a generalization formulated by Brooker (2) in his work on the cyanine dyes and may be restated in the following manner: in a given solvent the wave lengths of the absorption maxima of an unsymmetrical polyene are approximately the mean values of the corresponding maxima of the two related symmetrical polyenes.

To illustrate the method of calculation, consider γ-carotene (Table II, compound 1). The structure of γ-carotene may formally be regarded as composed of one-half of the lycopene structure (Table I, compound 1) joined to one-half of the β-carotene structure (Table I, compound 2). To calculate the wave length of the absorption maximum of longest wave length of γ-carotene (in carbon disulfide), which shall be called λ_1^{γ}, one-half of the value of the corresponding maximum of lycopene (CS_2) is added to one-half of the corresponding λ_1^{β} value of β-carotene (CS_2). The resulting sum of "half-lambda values" is in substantial agreement with the observed absorption maximum of γ-carotene. In the same way the wave lengths of the other two maxima of γ-carotene, λ_2^{γ} and λ_3^{γ}, may be calculated from the corresponding maxima of lycopene and β-carotene. Table I lists the symmetrical non-carbonyl carotenoids of known structure, and their absorption maxima in carbon disulfide together with their corresponding "half-lambda values". In Table II, the observed absorption maxima in carbon disulfide of the unsymmetrical carotenoids are given and for comparison their calculated absorption maxima. It is seen that the calculated maxima are within 4 mμ of the observed maxima in all cases except rubichrome and mutatoxanthin.

The principle may also be employed indirectly in the case where a carotenoid of given symmetrical structure is unknown. Thus, though a carotenoid of structure I is unknown, its "half-lambda values" may be calculated by subtracting the corresponding "half-lambda values" of zeaxanthin (Table I, compound 6) from the corresponding maxima of lutein (II), (Absolute max. in CS_2, 508, 475, 445 mμ). Thereby one obtains 249.5, 234, and 220 as the "half-lambda values" of I. It is readily seen that a carotenoid of structure I should have absorption



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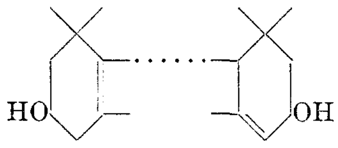

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TABLE I

SYMMETRICAL CAROTENOIDS, THEIR OBSERVED ABSORPTION MAXIMA (CS$_2$) AND CALCULATED "HALF-LAMBDA VALUES"[1]

COMPOUND	OBS. ABS. MAX., (mμ, CS$_2$)			"HALF-LAMBDA VALUES"		
	λ_1	λ_2	λ_3	$\lambda_1/2$	$\lambda_2/2$	$\lambda_3/2$
1. Lycopene	548.	507.5	477.	274.	253.8	238.5
2. β-Carotene	520.	485.	450.	260.	242.5	225.
3. ϵ_1-Carotene	501.	470.		250.5	235.	
4. Dehydrolycopene	601.	557.	520.	300.5	278.5	260.
5. Lycophyll	546.	506.	472.	273.	253.	236.
6. Zeaxanthin	517.	482.	450.	258.5	241.	225.
7. β-Carotene-di-epoxide	502.	472.		251.	236.	
8. Violaxanthin	500.5	469.	440.	250.3	234.5	220.
9. Aurochrome	457.	428.		228.5	214.	
10. Auroxanthin	454.	423.		227.	211.5	

TABLE II

UNSYMMETRICAL CAROTENOIDS, THEIR OBSERVED ABSORPTION MAXIMA (CS$_2$) AND CALCULATED MAXIMA[1]

COMPOUND	OBS. ABS. MAX., (mμ, CS$_2$)			CALC'D ABS. MAX., (mμ, CS$_2$)		
	λ_1	λ_2	λ_3	λ_1	λ_2	λ_3
1. γ-Carotene	533.5	496.	463.	534.	496.3	463.5
2. δ-Carotene (?)	526.	490.	457.	524.	488.8	
3. α-Carotene	509.	477.		510.5	477.5	
4. Lycoxanthin	547.	507.	473.	547.	506.8	474.5
5. Rubixanthin	533.	494.	461.	532.	494.8	463.5
6. Kryptoxanthin	519.	483.	452.	518.5	483.5	450.
7. Celaxanthin (?)	562.	521.	487.	559.	519.5	485.
8. β-Carotene-mono-epoxide	511.	479.		511.	478.5	
9. α-Carotene-epoxide	503.	471.		501.5	471.	
10. Rubixanthin-epoxide	526.	491.	461.	524.3	488.3	458.5
11. Kryptoxanthin-mono-epoxide	512.	479.		509.5	477.	
12. Antheraxanthin	510.	478.	445.	508.8	475.5	445.
13. Kryptoxanthin-di-epoxide	503.	473.		501.3	470.5	
14. Flavochrome	482.	451.		479.	449.	
15. Mutachrome	489.5	459.		488.8	456.5	
16. Kryptoflavin	490.	459.		487.	455.	
17. Rubichrome	506.	476.		501.	465.3	
18. Mutatoxanthin	488.	459.		485.5	452.5	
19. Luteochrome	482.	451.		479.5	450.	
20. Kryptochrome	456.	424.		455.5	425.5	
21. Lutein-epoxide	501.5	472.		499.8	468.5	
22. Chrysanthemaxanthin	479.	449.		476.5	445.5	

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[1] For the structures assigned to the individual carotenoids see Karrer and Jucker, *Carotenoide*, Verlag Birkhauser, Basel (1948). Absorption maxima are also from this source with the exception of ϵ_1-carotene and rubichrome for which see (7) and (2).

maxima in carbon disulfide close to 499, 468, and 440 mμ. Using these "half-lambda values" of I the absorption maxima of lutein-epoxide and chrysanthemaxanthin (Table II, compounds 21 and 22) were calculated.

TABLE III

SYMMETRICAL CAROTENOIDS, THEIR OBSERVED ABSORPTION MAXIMA AND CALCULATED "HALF-LAMBDA VALUES" IN SOLVENTS OTHER THAN CS_2[1]

COMPOUND	SOLVENT	OBS. ABS. MAX., mμ			"HALF-LAMBDA VALUES"		
		λ_1	λ_2	λ_3	$\lambda_1/2$	$\lambda_2/2$	$\lambda_3/2$
Lycopene	Chloroform	517.	480.	453.	258.5	240.	226.5
Lycopene	Benzene	522.	487.	455.	261.	243.5	227.5
Lycopene	Benzine	506.	475.5	447.	253.	237.8	223.5
Lycopene	Ethanol	503.	472.	443.	251.5	236.	221.5
β-Carotene	Chloroform	497.	466.		248.5	233.	
β-Carotene	Benzine	483.5	452.	426.	241.8	226.	213.
β-Carotene	Hexane	482.	451.		241.	225.5	
ϵ_1-Carotene	Chloroform	483.	452.		241.5	226.	
ϵ_1-Carotene	Pet. ether	470.	439.		235.	218.5	
Lycophyll	Benzene	521.	487.	456.	260.5	243.5	228.
Lycophyll	Benzine	504.	473.	444.	252.	236.5	222.
Lycophyll	Ethanol	505.	474.	444.	252.5	237.	222.
Zeaxanthin	Chloroform	495.	462.	429.	247.5	231.	214.5
Zeaxanthin	Ethanol	483.	451.	423.5	241.5	225.5	211.8
Zeaxanthin	Benzine	483.5	451.5	423.	241.8	225.8	211.5
β-Carotene-di-epoxide	Chloroform	484.	456.		242.	228.	
β-Carotene-di-epoxide	Benzene	485.	456.		242.5	228.	
β-Carotene-di-epoxide	Pet. ether	470.5	443.		235.3	221.5	
Violaxanthin	Chloroform	482.	451.5	424.	241.	225.8	212.
Violaxanthin	Benzine	472.	443.	417.5	236.	221.5	208.8
Violaxanthin	Ethanol	471.5	442.5	417.5	235.8	221.3	208.8
Aurochrome	Benzene	440.			220.		
Aurochrome	Chloroform	428.			214.		
Aurochrome	Pet. ether	437.			218.5		
Auroxanthin	Ethanol	428.	403.	382.	214.	201.5	191.

This principle has been employed in the calculation of the absorption maxima of carotenoids in solvents other than carbon disulfide where the requisite data are available. Table III gives the observed absorption maxima and the corresponding "half-lambda values" for symmetrical carotenoids in various solvents, while in Table IV the observed and calculated absorption maxima of unsymmetrical carotenoids in such solvents are given. Again it is seen that there is reasonable agreement between the calculated and observed maxima, however

TABLE IV

UNSYMMETRICAL CAROTENOIDS, THEIR OBSERVED AND CALCULATED ABSORPTION MAXIMA IN SOLVENTS OTHER THAN CS_2[1]

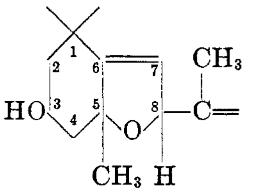
COMPOUND	SOLVENT	OBS. ABS. MAX., mμ			CALC'D ABS. MAX., mμ		
		λ_1	λ_2	λ_3	λ_1	λ_2	λ_3
γ-Carotene	Chloroform	508.5	475.	446.	507.	473.	
γ-Carotene	Hexane	494.	462.	431.	494.	463.3	
δ-Carotene	Chloroform	503.	470.	440.	500.	466.	
δ-Carotene	Hexane	490.	458.	428.	488.	456.3	
α-Carotene	Chloroform	485.	454.		490.	459.	
α-Carotene	Benzine	478.	447.5		476.	440.	
Lycoxanthin	Benzene	521.	487.	456.	521.5	487.	455.5
Lycoxanthin	Ethanol	505.	474.	444.	503.5	473.	443.5
Lycoxanthin	Benzine	504.	473.	444.	505.	474.3	445.5
Rubixanthin	Chloroform	509.	474.	439.	506.	471.	441.
Rubixanthin	Ethanol	496.	463.	433.	493.	461.5	433.3
Rubixanthin	Benzine	495.5	463.	432.	494.8	463.6	435.
Kryptoxanthin	Chloroform	497.	463.	433.	496.	464.	
Kryptoxanthin	Benzine	485.5	452.	424.	482.8	451.3	
β-Carotene-mono-epoxide	Chloroform	492.	459.		491.5	461.	
β-Carotene-mono-epoxide	Pet. ether	478.	447.		476.3	447.	
α-Carotene-epoxide	Chloroform	483.	454.		483.5	454.	
α-Carotene-epoxide	Pet. ether	471.	442.		470.3	440.	
Kryptoxanthin-mono-epoxide	Chloroform	488.	456.		489.5	459.	
Rubixanthin-epoxide	Chloroform	504.	474.		499.5	465.8	438.5
Antheraxanthin	Chloroform	490.5	460.5		488.5	456.8	426.5
Kryptoxanthin-di-epoxide	Chloroform	482.	453.		483.5	453.8	
Flavochrome	Chloroform	461.	433.		455.		
Mutatochrome	Chloroform	469.	438.		462.5		
Mutatochrome	Pet. ether	456.	427.		459.		
Kryptoflavin	Chloroform	468.	438.		461.5		
Rubichrome	Ethanol	480.	448.		465.5	437.5	412.5
Mutatoxanthin	Ethanol	457.	427.		455.5	427.	402.8

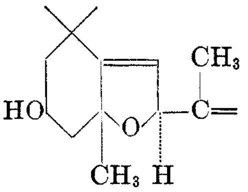
discrepancies of more than 4 mμ are somewhat more frequent. Thus for mutatoxanthin in ethanol the observed maxima are at 457 and 427 mμ, while the calculated values are 455.5, 427 and 402.8 mμ.[2] For rubichrome, on the other hand, with maxima at 480 and 448 mμ (3), the calculated maxima are 465.5, 437.5, and 412.5 mμ. In view of the more frequent deviation between the calculated and observed maxima in solvents other than carbon disulfide, it would appear that the application of this principle in those solvents is somewhat less trustworthy. However in certain of the calculations absorption data in petroleum ether, benzine, and hexane have been taken as equivalent since the requisite data in one of these solvents is lacking. This is justifiable in view of the slight variation of absorption maxima in these solvents.

Extension of this principle to carbonyl carotenoids is unsatisfactory for, though the introduction of a carbonyl group produces a bathochromic shift, no simple regularity is apparent. In part this may be due to keto-enol equilibrium of the substance in solution.

In view of the potential usefulness of this principle in problems of structure in the carotenoid field, where, oddly enough, it does not appear to have been applied, it is of interest to seek explanations for deviations between observed and calculated maxima. Brooker (2) has proposed several empirical rules to explain deviations found in the cyanine dyes, while Sklar (4) and Herzfeld and Sklar (5) have treated the problem of the unsymmetrical cyanine dyes using quantum mechanics. Small deviations may, of course, be attributed to experimental error but should not exceed 2 mμ. A second aspect that must be considered is the effect of *cis-trans* isomerism. Prolycopene, a naturally occurring stereoisomer of the all-*trans* lycopene, has in all probability six double bonds with *cis*-configuration and its absorption spectrum in carbon disulfide shows maxima at 500.5 and 469.5 mμ. This constitutes a hypsochromic shift of 47.5 and 38 mμ. However, in general, the presence of a single *cis*-double bond in a carotenoid will effect a shift of the maximum of longest wave length of −5 mμ (±1 mμ) (6). The agreement between the observed maxima and the calculated maxima is corroboratory evidence for simular stereo-configuration in the symmetrical and unsymmetrical carotenoids.

Since the basic structures of rubichrome (3) and mutatoxanthin (7) are well substantiated one might anticipate that the discrepancies between the calculated and observed maxima might be explained on stereochemical grounds, but since the calculated values are *less* than the observed values it does not seem probable that *cis*-isomerization has appeared in the polyene chain. Nor is it probable that the relative stereo-configuration in the furanoid-oxide ring at C_5 and C_8 could account for the discrepancy. It is significant in this connection that the





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[2] Only two maxima are reported for rubichrome; *cf.* ref. (2).

second maximum of rubichrome shows a subnormal decrease in wave length from rubixanthin from which it may be derived. In general the introduction of a furanoid-oxide ring into a carotenoid causes a hypsochromic shift of 24–26 mμ in the wave length of the second maximum. The decrease in the case of rubichrome is only 18 mμ. Though it is true that the introduction of the furanoid-oxide ring has shortened the polyene chain by one vinyl group, this is an unlikely explanation since in the majority of similar compounds the agreement between the calculated and observed absorption maxima is good. A more probable explanation is perhaps to be found in the theoretical equation of Herzfeld and Sklar (5),

$$2\Delta\ E_N = [(e_1 - e_2)^2 + (\alpha\sigma N_1)^2]^{\frac{1}{2}} + [(e_1 - e_2)^2 + (\alpha\sigma N_2)^2]^{\frac{1}{2}}$$

which also affords an explanation of Brooker's "sensitivity rule" (2). That rule pertains to the greater deviations found with the more unsymmetrical cyanine dyes. Accordingly one would expect a corresponding deviation in the yet unknown furanoid oxide of γ-carotene.

Though Winterstein (8) did not succeed in isolating in the crystalline state the carotenoid which he called δ-carotene, on the basis of its behavior he assumed it to be a hydrocarbon and suggested that its structure might be that of α-carotene with an opened ionone ring. More recently Haxo (9) has reported the presence of a carotenoid in *Neurospora crassa* having an absorption spectrum similar to that of Winterstein's substance. If one assumes for δ-carotene (Table II, compound 2) an unsymmetrical structure formed from one-half of the lycopene structure together with one-half of the ϵ_1-carotene structure, the calculated maxima for that structure are in agreement with those for Winterstein's compound, not only in carbon disulfide but in chloroform and hexane as well, albeit such a structure is inconsistent with Winterstein's reported vitamin A activity. It is also of interest in this connection that the hydrocarbon carotenoid neurosporene isolated by Haxo (9) having maxima at 502.5, 470.5 and 439.5 mμ are in close agreement with the maxima of ϵ_1-carotene recently synthesized by Karrer and Eugster (10) and very probably neurosporene is a component stereoisomer of ϵ_1-carotene.

New Haven, Connecticut

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