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256. A ^{13}C-NMR. Study of *cis-trans* Isomeric Vitamins A, Carotenoids and Related Compounds

by **Gerhard Englert**

F. Hoffmann-La Roche & Co., Ltd., Department of Physics and Physical Chemistry, CH–4002 Basle

(25. VII. 75)

Summary. The ^{1}H-decoupled ^{13}C-NMR. spectra of 35 all-*trans*, 17 mono-*cis* vitamin A compounds (acetates, alcohols, aldehydes, acids and esters) and of one 11,13-di-*cis* compound (11,13-di-*cis* retinol) are reported. Included in this investigation are desmethyl-, desmethylethyl, and aryl-vitamin A analogues and others as well as 30 reference compounds of smaller molecular weight. Furthermore, the ^{13}C-NMR. spectra of 23 β-apo- and other carotenoids were studied. A complete assignment of the signals of all 106 compounds to the specific carbon atoms was achieved by extensive application of lanthanide shift reagents, mainly Yb(dpm)$_3$, by CW-offset and selective ^{1}H-decoupling experiments, by comparison of the shifts of related compounds, and in three cases by utilization of specifically deuteriated compounds (11,12-D_2-retinol and retinyl acetate, 15,15′-D_2-β-carotene). The chemical shift differences between the *cis*- and *trans*-vitamin A compounds and the applicability of the shift reagents for the assignment of the ^{13}C-NMR. spectra are discussed.

Introduction. – ^{13}C-NMR. spectroscopy plays an increasingly important role as a powerful tool for structural elucidation of various classes of compounds, as for example steroids, alkaloids, sugars, and others. Apparently, exceptions to this are vitamin A compounds and carotenoids for which, to the best of our knowledge, only a few publications have appeared most of which only very recently (see [1–5]).

This prompted us to report on our own comprehensive investigations on the ^{13}C-NMR. spectra of vitamins A and related compounds, namely retinoic acids, esters, retinals, retinyl acetates and retinols, including several compounds with 9-*cis*-, 11-*cis*-, 13-*cis*- and in one case, 11,13-di-*cis*-structure as well as some desmethyl, and desmethylethyl analogues. In addition to these compounds with a β-end group (1,1,5-trimethyl-5-cyclohexen-6-yl) related substances were included with a different end group, *e.g.* with a substituted β-group (β-4-keto-, β-3- or β-4-hydroxy-, β-5,6-epoxide- etc.), β-3,4-didehydro-end groups as well as a number of compounds with 5-ring and aryl end groups. Finally, 23 *β-apo-* and other carotenoids were included in this study. Many of these compounds were previously studied by 220 MHz ^{1}H-NMR. spectroscopy [6] [7]. The aim of this ^{13}C-NMR. investigation was to obtain a deeper understanding of the variations in the chemical shifts of the different end groups and of the in-chain carbon atoms, furthermore of the shift changes upon introduction of *cis* double bonds. It is hoped that our results will be helpful in the interpretation of the ^{13}C-NMR. spectra of other carotenoids.

Experimental Part. – *Spectrometer.* – All the spectra were run at 22.63 MHz on a *Bruker* HX 90/15 *Fourier* Transform Spectrometer with *Nicolet* 1083 computer. The D-signal of the deuteriated solvent served as a field lock. The interferograms were accumulated into an 8 K memory. Sweep-widths of 5000 Hz or 6024 Hz were used corresponding to 1.22 Hz per address (0.05 ppm) or 1.47 Hz per address (0.06 ppm). The computer-printed chemical shifts, which were in all cases referenced to the ^{13}C-signal of internal TMS, are, therefore, given rounded to the nearest 0.1 ppm. Exceptions are those compounds which were measured at least 3 times. Here, mean values rounded to the nearest 0.01 ppm are given.

Compounds. – All of the compounds used in this investigation were generously provided by our *Chemical Research Department.* Structure and purity of the samples were checked by ^{1}H-NMR. In many cases their ^{1}H-NMR. data were recently reported [7].

If not otherwise specified, $CDCl_3$ was used as the solvent. In general, the concentrations varied between 0.5 and 1 M, although, in some cases only little of the compound was available yielding correspondingly smaller concentrations down to 0.01 M. The spectra were measured in 0.2–0.4 ml (5 mm insert) or 1–1.5 ml (10 mm insert). The sample temperature was approximately 30° since a stream of nitrogen was used to cool the sample tubes.

Shift reagents. – The lanthanide shift reagents Yb(dpm)$_3$, Eu(dpm)$_3$ and Eu(fod)$_3$ were purchased from *Stohler Isotope Chemicals* and used without further treatment.

Application of shift reagents. – Since the lanthanide-induced shifts (LIS) were the main basis for the assignment of the signals to the specific carbon atoms, some remarks must be made as to the applicability of this technique. In our first experiments, Eu(dpm)$_3$ and Eu(fod)$_3$ were used. However, it was found in agreement with recent reports for other compounds [8] [9], that the LIS-values of carbon atoms near the site of complexation were in some cases mitigated or even changed in sign by large *Fermi* contact contributions, especially in the case of the retinals. The assignments were, therefore, frequently made more difficult or even impossible at first.

Following the proposal of *Gansow et al.* [8] we later successfully utilized Yb(dpm)$_3$ as a shift reagent since with this chelate the contact contribution is evidently largely reduced compared to the Eu-chelates. For future applications it is important to note that in no case have 'wrong-way' shifts with Yb(dpm)$_3$ been directly observed here or indirectly deduced from reductions in the downfield shifts or discrepancies in the assignments.

In all cases where shift reagents were applicable several increasing concentrations of the shift reagent were measured. Mostly 4 to 5 molar ratios R of shift reagent to substrate between approx. 0.1 and 0.5 or 1, if the solubility was high enough, were found sufficient. The signals were traced back by extrapolation to their position in the normal spectrum without shift reagent. Ambiguities in the assignments remained only in a few cases if the lines were too closely spaced in the unshifted spectrum.

In general, the lanthanide-induced shifts were approximately a linear function of the molar ratio R. However, deviations occurred with some solutions at very low concentrations ($R \leq 0.1$) probably due to the presence of traces of water. In other cases some signals were found to deviate from the linear dependance with positive or negative curvature at higher values of R. In the main these were signals of carbon atoms which were close to the site of complexation. This was also accompanied by excessive line broadening, especially with $Yb(dpm)_3$, and identification of those signals was then difficult or even impossible at higher values of R. It should be pointed out that the only purpose here of using shift reagents was to provide as complete an assignment of the ^{13}C-signals as possible. For simplicity it was assumed that the smaller the measured LIS-value, the smaller the position-number of the corresponding carbon atom in the polyene chain should be. Whereas for the all-*trans* compounds the distance increases and hence the LIS decreases with decreasing numbering of the carbon atom, this is not necessarily so for all the *cis*-isomers. As revealed by inspection of molecular models the distance of C(10) in 11-*cis* retinol, for example, from the complexed oxygen could be smaller than that of C(11). However, since these distances all strongly depend on the assumed geometry, namely on the conformation of the different single bonds (s-*trans*, s-*cis* or rotationally averaged structure) including those of the complexed end groups, reliable conclusions do not seem to be possible, at present. This means that the assignments given here of C(10) and C(11) could possibly be reversed in the 11-*cis* compounds. It is intended to follow up this question in more detail in a later publication.

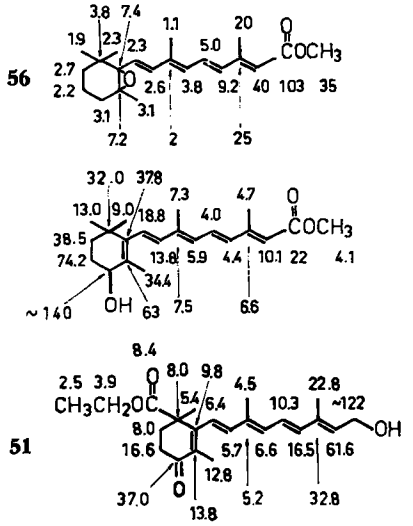
Since we are only using the measured LIS-values qualitatively it was unnecessary to correct them for the diamagnetic complex formation term using $La(dpm)_3$ [10]. This effect is usually negligible compared to the paramagnetic effects, especially at carbon atoms close to the site of complexation.

LIS-values at molar ratios $R = 1$ of up to 190 ppm were measured directly or obtained by extrapolation. These $\delta(1:1)$-values gradually decreased with increasing distance from the site of complexation and could thus be used for the assignment of the signals. In most cases the assignments obtained could be checked since the origin of the different signals from tertiary or quaternary carbon atoms was known from CW-offset ^1H-decoupling experiments. In other cases the assignments were already known from selective decoupling experiments, or from the spectra of the deuteriated compounds. The former check was generally applied. With compounds having only *one* complexation site it was found, as expected, that the magnitude of the LIS of the signal of the quaternary carbon atom C(13) (C(9)) was, in general, between those of the 2 tertiary carbon atoms C(14) and C(12) (C(10) and C(8), respectively). One example, for which a deviation from this rule was observed (δ of C(9) $>$ δ of C(10)) will be given later (see Scheme 2).

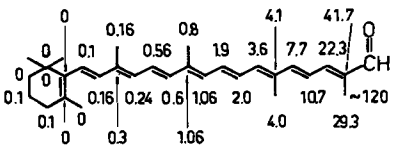
The LIS-values $\delta(1:1)$ extrapolated or measured with $Yb(dpm)_3$ at $R = 1$ were sufficiently large in retinals and retinols to assign all the signals of the in-chain carbons, since even C(7) and C(8) showed, in general, significant LIS-values and LIS-differences.

However, in esters and acetates the effect of complexation was considerably weaker and assignment of the signals of C(7) and C(8) was mostly possible only by analogy or from compounds with –OR functions in the β-end group, *i.e.* from compounds having a second (possibly stronger) complexation site. In these cases decreasing LIS-values were observed starting from both sites of complexation (see examples in Scheme 1).

Scheme 1. *Compounds* **56**, **50** *and* **51** *with more than one possible site of complexation*: $Yb(dpm)_3$ induced downfield shifts in ppm of the ^{13}C-NMR. signals extrapolated to equimolar concentration of substrate (approx. 1M in $CDCl_3$) and shift reagent ($R = 1$). **56** Extrapolated from $R = 0.67$; C=O from $R = 0.33$. **50** Extrapolated from $R = 0.67$; C(4) from $R = 0.2$. **51** Extrapolated from $R = 0.33$; C(15) tentative value only due to excessive line broadening, obtained from $R \sim 0.1$.



Scheme 2. *Yb(dpm)₃-induced chemical shifts* $\delta(1:1)$ *in ppm for all*-trans-*β-apo-8′-carotenal* (**87**; 0.87 M in $CDCl_3$) *extrapolated from* $R = 0.8$



Results. – The ^{13}C-chemical shifts and the assignments for the compounds studied in this work are collected in Tables 1, 2 and 3. Table 1 contains the compounds with the lower molecular weight than vitamin A which served as reference compounds for the assignment of the carbon atoms of the different end groups. Table 2, on the other hand, contains all the vitamins A and related compounds. Here, the compounds were ordered in the following manner: all-*trans* compounds with different end groups,

followed by 13-*cis*-, 11-*cis*-, 9-*cis*-compounds and one 11,13-di-*cis*-compound. Table 3 presents the results obtained for some *β-apo-* and other carotenoids.

The assignments can not be justified in detail. They were based on the application of the following techniques and criteria (see also last column of Tables 1, 2 and 3):

(a) The relative magnitude of the lanthanide-induced shift, mostly of $Yb(dpm)_3$, directly reflects the distance of the specific carbon atom from the complexation site;

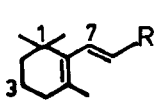
(b) CW-offset ^1H-decoupling and broad-band decoupling with reduced rf power led to the recognition of the different types of carbon atoms (quaternary, tertiary, secondary, and primary carbon atoms);

(c) Assessment of substituent effects, *i.e.* of shift changes upon alteration of the chemical structure (changes of the end groups, replacement of one or two of the in-chain methyl groups, *cis-trans* effects) and comparison of the spectra of related compounds;

(d) In three cases (all-*trans*-11,12-D_2-retinol and -retinyl acetate, 15,15'-D_2-β-carotene) dideuterio compounds were available. Here, the signals of C(11), C(12) and of C(15), C(15'), respectively, were unobservable;

(e) Application of selective ^1H-decoupling was also possible in some cases. However, in many instances the chemical shift differences in the ^1H-NMR. spectra at

Basic Chemical Structures contained in Table 1:



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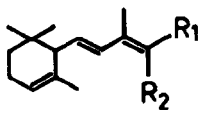

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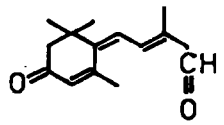

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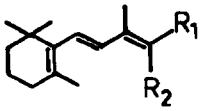

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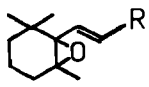

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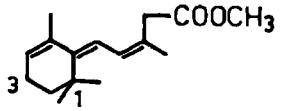

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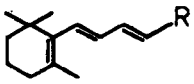

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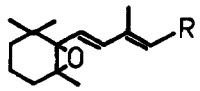

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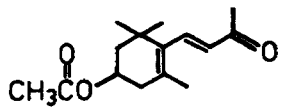

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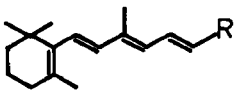

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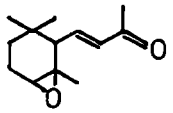

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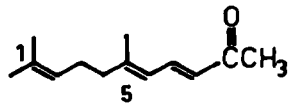

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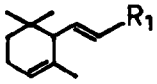

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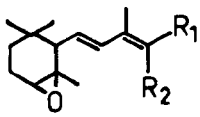

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5–cis

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Table 1: *^{13}C-NMR. chemical shifts of*

No.	R	End group						In-chain		
		1	2	3	4	5	6	7	8	9
1	R = COOH	34.1	40.0	19.0	33.7	136.0[1])	136.7[1])	146.6	121.1	–
2	R = $COCH_3$	34.1	39.8	18.9	33.6	136.0[1])	135.6[1])	142.8	131.7	–
3	$R_1 = R_2 = H$	34.3	39.8	19.5	33.0	128.8	137.7	127.5	136.0	142.3
4	$R_1 = CH_3$; $R_2 = H$	34.3	39.8	19.5	33.0	128.2	138.2	125.0	137.9	135.0
5	$R_1 = H$; $R_2 = CH_3$	34.3	39.8	19.5	33.0	128.7	138.4	127.0	130.2	133.4
6	$R_1 = CH_2OH$; $R_2 = H$	34.2	39.7	19.4	32.9	129.7	137.7	126.6	137.3	136.1
7	$R_1 = CH_2OAc$; $R_2 = H$	34.2	39.7	19.3	33.0	129.1	137.5	127.8	136.6	139.0
8	$R_1 = CH(OC_2H_5)_2$; $R_2 = H$	34.1	39.4	19.4	33.0	129.0	137.9[1])	127.7[2])	137.0	137.7[1])
9	$R_1 = CHO$; $R_2 = H$	34.1	39.7	19.4	33.4	132.5	137.2	135.4	135.7	154.6
10	$R_1 = H$; $R_2 = CHO$	34.3	39.8	19.2	33.3	132.4	137.4	136.4	128.0[1])	154.6
11	$R_1 = COOH$; $R_2 = H$	34.4	39.8	19.3	33.2	131.5	137.3	134.6[1])	136.2[1])	155.2
12	$R_1 = H$; $R_2 = COOH$	34.2	40.0	19.2	33.5	132.7	137.3	135.4	129.9	154.1
13	R = COOH	34.2	39.9	19.1	33.5	133.6	137.1	141.6	130.3	147.9
14	R = COOH	34.3	39.8	19.3	33.2	130.9	137.6	131.5	136.6	145.4
15	R = $COCH_3$	32.6	31.3	23.1	122.6	132.0	54.3	148.7	132.4	–
16	R = $CHCH_3$–CHO	32.0	31.7	23.1	121.2	133.7	54.7	127.7	135.5	50.0
17	$R_1 = COOH$; $R_2 = H$	32.8	31.8	23.2	121.9	133.5	55.1	139.2	135.0	154.9
18	$R_1 = COOC_2H_5$; $R_2 = H$	32.6	31.8	23.1	121.6	133.4	54.9	137.8	135.0	152.1
19	$R_1 = H$; $R_2 = COOH$	32.6	32.0	23.2	121.5	133.7	55.3	140.5	129.3	153.4
20	$R_1 = H$; $R_2 = COOC_2H_5$	32.5	31.9	23.2	121.3	133.8	55.2	139.4	129.3	150.7
21	R = $COCH_3$	33.5	35.6	17.0	29.8	65.6	70.4	142.4	132.7	–
22	R = $COOC_2H_5$	33.9	35.9	17.1	30.2	65.5	71.0	136.4[1])	131.5[1])	150.8
23	–	28.7	31.2	21.7	59.2	58.5	52.3	146.0	133.8	–
24	$R_1 = COOC_2H_5$; $R_2 = H$	31.6	29.4	22.1	59.7	59.7	53.1	134.9[1])	136.3[1])	152.2
25	$R_1 = H$; $R_2 = COOC_2H_5$	31.4	29.3	22.1	59.6	59.4	53.6	136.3[1])	130.5[1])	151.0
26	–	41.9	52.3	197.4	122.4	153.5[1])	152.5[1])	130.8	143.7	139.9
27	–	34.9	40.6	22.9	127.7	134.1	144.6	119.1	126.6	130.0
28	–	36.5	44.1	67.6	38.7	131.2	135.8	141.7	132.6	–
29	–	132.2	123.3	26.4	40.5	150.8	123.8	139.4	128.5	–
30	–	132.5	123.3	27.0	33.0	150.9	124.7	139.2	128.3	–

[a]) CW offset ^1H-decoupling; [b]) selective ^1H-decoupling; [c]) $Eu(fod)_3$; [d]) $Yb(dpm)_3$; [e]) $Eu(dpm)_3$;
[i]) Corresponding assignments may be interchanged.

some related compounds. Solvent: $CDCl_3$

			Methyls				Others	Remarks
10	11	12	1,1–		5–	9–		
–	–	–	28.7	28.7	21.6	–	COO: 172.9	a
–	–	–	28.8	28.8	21.6	–	CO: 197.9; CH_3: 27.1	a
114.8	–	–	28.9	28.9	21.5	18.4	–	a
124.0	–	–	29.0	29.0	21.6	12.0	10-CH_3: 13.8	a
123.2	–	–	29.0	29.0	21.7	20.4	10-CH_3: 13.0	a
129.1	–	–	28.9	28.9	21.5	12.4	OCH_2: 59.0	a
123.1	–	–	28.9	28.9	21.6	12.5	OCH_2: 61.3; CO: 170.8; CH_3: 20.9	a, c
127.4[2])	98.7	–	29.0	29.0	21.6	13.0	OCH_2: 60.3; CH_3: 15.4	a
128.7	–	–	28.9	28.9	21.6	12.9	CO: 190.9	a, b, d
127.8[1])	–	–	29.0	29.0	21.8	21.1	CO: 189.6	a, e
117.5	–	–	29.0	29.0	21.6	14.0	CO: 172.6	a
115.6	–	–	29.0	29.0	21.8	21.0	CO: 172.3	a
118.5	–	–	28.9	28.9	21.6	–	CO: 172.8	a
127.7	142.8	119.2	29.0	29.0	21.6	13.0	CO: 172.7	a
–	–	–	26.9	27.7	22.8	–	CO: 197.9; CH_3: 26.9(?)	a
–	–	–	27.0	27.5	22.7	13.6	CO: 201.2	a, d
117.2	–	–	27.2	27.7	23.0	14.4	CO: 172.5	a
118.1	–	–	27.0	27.6	22.9	14.0	CO: 167.0; OCH_2: 59.4; CH_3: 14.4	a, d
115.5	–	–	27.1	27.7	22.9	21.4	CO: 171.6	a
116.2	–	–	27.1	27.7	22.9	21.2	CO: 166.2; OCH_2: 59.5; CH_3: 14.4	a
–	–	–	25.9	25.9	20.8	–	CO: 196.8; CH_3: 27.9	a, d
119.6	–	–	26.0	26.0	21.0	14.0	CO: 166.0(?); OCH_2: 59.6; CH_3: 14.3	a
–	–	–	27.3	27.9	23.9	–	CO: 197.9; CH_3: 26.4	a, d
118.5	–	–	27.2	28.3	24.1	14.2[2])	CO: 167.0; OCH_2: 59.7; CH_3: 14.4[2])	a
116.5	–	–	27.3	28.2	24.1	14.3	CO: 166.2; OCH_2: 59.4; CH_3: 14.3	a
–	–	–	28.0	28.0	25.1	9.3	CO: 194.2	a
37.4	–	–	28.9	28.9	21.7	25.1	CO: 171.4; CH_3: 51.7	a, d
–	–	–	28.3	29.5	21.2	–	OCO: 170.4; CH_3: 21.2; CO: 197.8; CH_3: 27.2	a, d
–	–	–	17.7(c)	25.7(tr)	17.5	–	CO: 198.3; CH_3: 27.4	a, d
–	–	–	17.6(c)	25.6(tr)	24.6	–	CO: 198.2; CH_3: 27.3	a, d

90 MHz were rather too small in order to help much in the differentiation between different possible assignments;

(f) In a few cases, direct comparison with other work was possible. However, with the exception of [2] and [11] other solvents were used (dioxane: [4]; carbon tetrachloride: [3]; acetone-d_6 and cyclohexane-d_{12}: [5]). Therefore, some smaller discrepancies in the assignments could be due to solvent effects and will not be discussed further in this paper. It should be pointed out that small variations ($\sim$1 ppm) of the chemical shifts with the concentration even in the same solvent ($CDCl_3$) have been observed in the course of our study so that a direct comparison of the shifts obtained in other solvents was impossible in cases where 2 or more signals were relatively close to each other.

Although in [2] and [11] $CDCl_3$ was used as a solvent some discrepancies in the assignment were observed. In [2] assignments for all-*trans*-retinal (**34**), β-apo-8'-carotenal (**87**) (in part), axerophthene (**31**) and β-carotene (**88**) were given. The former two spectra were shown in graphical form only. Similarly, the spectra of all-*trans*-, 13-*cis*- and 9-*cis*-retinyl acetate (**33**, **67** and **77**) and of β-carotene (**88**) were very recently assigned by *Weedon et al.* [11]. In this work only the 13-*cis*-compound shows several deviations from our assignments. Since these were mainly based on the application of shift reagents and the reasoning for the assignments given in [2] and [11] were not explicitly given a detailed discussion of the discrepancies is not feasible, at present.

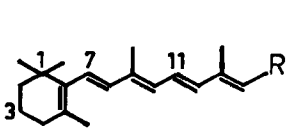
In order to demonstrate the advantage of $Yb(dpm)_3$, compared to $Eu(dpm)_3$ and $Eu(fod)_3$, as a method for the assignment of the in-chain carbon atoms, we collected in Table 4 the extrapolated LIS-values $\delta(1:1)$ for 4 isomeric retinals and 6 retinols. In one case (13-*cis*-retinal) LIS-values for the ^{1}H-resonance obtained with $Eu(dpm)_3$ are included. Here, no evidence for a significant contact contribution is qualitatively seen, in contrast to the ^{13}C-NMR.

If one compares first the $Yb(dpm)_3$-induced relevant ^{13}C-NMR. shifts with $\delta \geqslant 1$ ppm of the 4 retinals one can see, as expected, a steady decrease of the $\delta(1:1)$-values with increasing distance from the complexed aldehydic group ($\delta \sim 76$ to 160 ppm) along the polyene chain until C(7), the $\delta(1:1)$-value of which is still smaller than that of C(8). This led to the assignment of all these carbon atoms of the polyene chain as well as to the assignment of the H_3C–C(9) and H_3C–C(13) carbon atoms. The small upfield shifts of the carbons of the β-end group of the 13-*cis*-isomer as well as some 'irregularities' in vitamin A_2-aldehyde (**53**: C(4), C(5) and C(6)) are not understood.

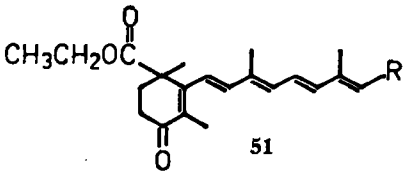
More important for our discussion is the observation that the use of Eu-complexes with the retinals (all-*trans* and 13-*cis*) partly led to upfield shifts or reduced downfield shifts at the even-numbered carbon atoms of the polyene chain (C(14), C(12), C(10), C(8)). This can only be explained by the assumption of strong contact contributions and alternating spin-densities with decreasing amplitude along the conjugated chain.

With the retinols, on the other hand, which are also very strongly complexed ($\delta(1:1) \sim 190$ ppm of C(15) in all-*trans* retinol), application of Eu-shift reagents did not result in 'wrong-way' shifts, *i.e.* the assignments of the in-chain carbon atoms and of the methyl carbon atoms from the relative magnitude of the Eu-induced

Basic Chemical Structures contained in Table 2:



31–38



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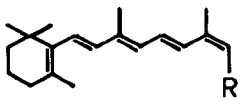
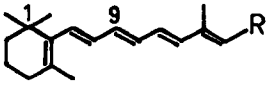


66–70



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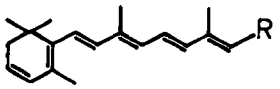

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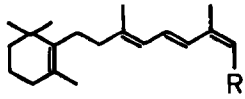

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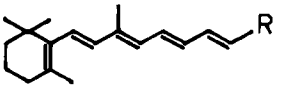

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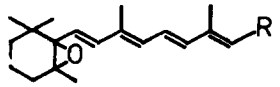

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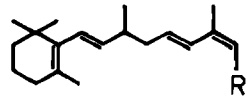

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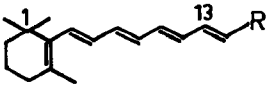

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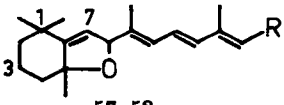

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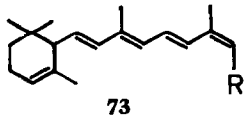

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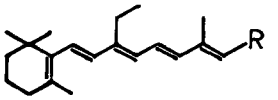

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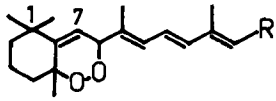

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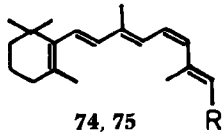

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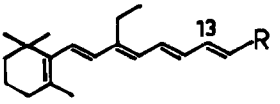

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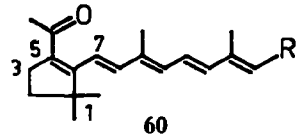

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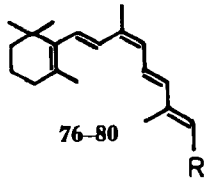
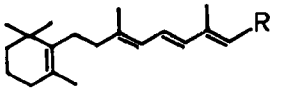


76–80



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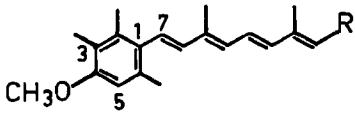

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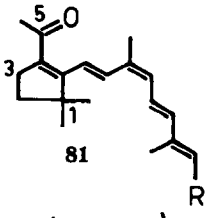

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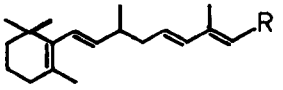

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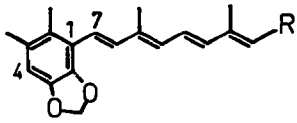

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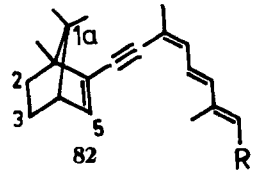

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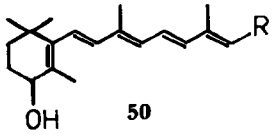

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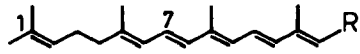

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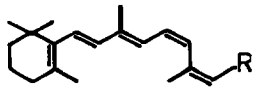

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Table 2: *^{13}C-NMR. chemical shifts of all-trans and cis vitamins A*

No.	R	End group						In-chain				
		1	2	3	4	5	6	7	8	9	10	11
	all-trans											
31	CH_3	34.1	39.4	19.3	33.2	128.9	138.1	127.1[1]	137.6	135.4	130.7	125.9[1]
32a	CH_2OH	34.2	39.8	19.4	33.1	128.9	137.9	126.5	137.7	135.6	130.2	124.8
32b	CH_2OH	34.2	39.6	19.3	33.0	128.6	137.7	126.2	137.7	135.3	130.3	124.7
32c	11,12-D_2 CH_2OH	34.2	39.7	19.3	33.0	128.6	137.7	126.2	137.7	135.3	130.2	–
33a	CH_2OAc	34.30	39.78	19.35	33.10	129.26	137.95	127.00	137.66	136.46	130.02	125.82
33b	11,12-D_2 CH_2OAc	34.30	39.80	19.36	33.11	129.26	137.90	127.00	137.62	136.50	129.86	–
34	CHO	34.1	39.6	19.3	33.2	130.3	137.6	129.6[1]	137.1	141.1	129.4[1]	132.4
35	COOH	34.5	40.0	19.5	33.3	129.8	138.0	128.7	137.6	139.3	129.8	131.1
36	$COOCH_3$	34.32	39.77	19.32	33.17	129.84	137.77	128.64	137.31	139.35	129.50	130.92
37	$COOCH_2$—C≡CH	34.3	39.8	19.3	33.2	130.3	137.7	128.9	137.3	139.8	129.4	131.5
38	CONH—CH_2CH_3	34.3	39.8	19.4	33.1	129.7	137.7	128.2	137.5	138.5	129.7[1]	129.5[1]
39	COOH	34.2	39.9	19.2	33.4	131.4	137.5	134.5	133.0	138.1	130.4	135.9
40	$COOCH_3$	34.2	39.9	19.2	33.3	131.0	137.5	134.1	133.0	137.5	130.5	135.1
41	COOH	34.3	39.8	19.3	33.2	130.3	137.0	129.3[1]	137.0	141.3	129.1[1]	138.2
42	$COOCH_3$	34.3	39.7	19.2	33.0	130.1	137.7	129.4[1]	137.1	140.7	129.1[1]	137.3
43	COOH	34.2	39.9	19.2	33.4	131.7	137.5	135.3	132.8	139.1	129.9	142.2
44	$COOCH_3$	34.1	39.8	19.1	33.3	131.4	137.3	134.7	132.7	138.4	130.0	141.1
45	COOH	34.4	39.8	19.4	33.1	129.9	138.0	128.4[1]	135.8[2]	146.7	128.8[1]	131.4
46	COOH	34.4	39.7	19.4	33.2	130.2	137.8	129.4[1]	135.5	148.0	128.0	138.0
47	$COOCH_3$	34.4	39.7	19.3	33.1	129.9	137.8	129.0	135.6	147.2	128.1	136.9
48	COOH	35.1	40.0	19.6	32.9	127.5	136.8	27.6	40.9	145.4	131.9	124.4
49	$COOCH_3$	34.0	39.6	19.5	32.7	127.7	137.7	126.7	139.1	37.8	40.8	135.7[1]
50	$COOCH_3$	34.8	34.8	28.6	70.0	130.6	141.4	127.8	138.3	139.0	130.2	130.8
51	CH_2OH	46.8	34.5	33.3	197.5	132.1	152.6	123.8	140.4	134.8	135.5	124.2
52	CH_2OH	33.9	39.9	124.7	129.9	126.5	138.5	125.4	137.1	135.7	130.8	124.9
53	CHO	34.0	40.0	125.0	130.0	127.7	138.2	128.3	136.4	140.9	130.0	132.3
54	CH_2OAc	33.8	35.9	17.2	30.2	65.3	71.2	131.1	137.2	134.9	125.4	124.5
55	CHO	33.9	35.8	17.1	30.1	65.5	71.1	127.4	136.8	139.4	130.3	132.0
56	$COOCH_3$	33.8	35.9	17.1	30.2	65.3	71.1	130.6	137.0	137.8	126.2	130.6
57	COOH	34.7	41.3	20.4	41.3	88.0	154.9	118.5[1]	87.2	143.3	125.6	131.2
58	$COOCH_3$	34.7	41.5	20.4	41.3	87.8	154.9	118.5	87.2	142.7	125.7	130.5
59	$COOCH_2CH_3$	35.4	41.2	18.9	35.7	79.8	149.7	115.7	82.7	141.3	127.5	130.2
60	COOH	47.8	40.4	31.1	137.3	198.5	156.0	123.5	138.8	138.8	130.0	133.4

and related compounds. Solvent: $CDCl_3$, (if not otherwise specified).

			Methyls					Others	Remarks
12	13	14	1,1–		5–	9–	13–		
138.0	134.6	122.6	29.0	29.0	21.7	12.7	12.1	CH_3: 14.0	a
136.5	136.2	130.6	29.0	29.0	21.7	12.5	12.6	OCH_2: 59.1	a
136.5	136.0	130.5	29.0	29.0	21.6	12.4	12.5	OCH_2: 58.9	a, c, d, f
–	136.2	130.3	29.0	29.0	21.6	12.5	12.5	OCH_2: 59.0	f
135.89	139.02	124.60	29.00	29.00	21.67	12.73	12.73	OCH_2: 61.27; CO: 170.66; CH_3: 20.88	a, b, c
–	138.96	124.42	28.96	28.96	21.68	12.73	12.73	OCH_2: 61.20; CO: 170.59; CH_3: 20.87	
134.5	154.5	128.9	29.0	29.0	21.7	13.0	13.0	CO: 190.7	a, c, e
135.5	153.2	118.5	29.0	29.0	21.6	12.9	13.9	CO: 168.6	a, g
135.15	152.76	118.18	28.98	28.98	21.68	12.85	13.86	CO: 167.33; CH_3: 50.73	a, c, e
134.9	154.1	117.2	29.0	29.0	21.7	12.9	14.0	CO: 165.9; CH_2: 51.1; –C≡: 78.4; ≡CH: 74.3	a, d
135.8	148.1	121.8	29.0	29.0	21.7	12.8	13.6	CO: 167.2; CH_2: 34.3; CH_3: 14.9	a
134.5	155.0	118.0	29.0	29.0	21.8	–	14.0	CO: 172.6	a
134.7	152.6	118.3	29.0	29.0	21.7	–	13.8	CO: 167.3; CH_3: 50.8	a, c
129.7[1]	147.1	119.0	29.0	29.0	21.7	12.8	–	CO: 172.0	a
129.4	145.1	119.3	29.0	29.0	21.7	12.8	–	CO: 167.6; CH_3: 51.3	a, c
128.8	146.9	119.1	29.0	29.0	21.7	–	–	CO: 172.5	a
129.0	144.7	119.6	28.9	28.9	21.7	–	–	CO: 167.3; CH_3: 51.2	a, c
135.2[2]	155.1	117.9	29.1	29.1	21.7	–	14.2	CO: 172.5; 9-CH_2: 20.5; CH_3: 14.4	a
129.5[1]	147.2	118.9	29.0	29.0	21.7	–	–	CO: 172.7; 9-CH_2: 20.5; CH_3: 14.5	a
129.6	145.1	119.4	29.0	29.0	21.7	–	–	CO: 167.4; OCH_3: 51.2; 9-CH_2: 20.4; CH_3: 14.4	a, c
133.4	155.4	117.2	28.7	28.7	19.8	17.3	14.1	CO: 172.3	a
134.9[1]	152.6	117.4	28.8	28.8	21.7	20.4	14.0	CO: 167.5; OCH_3: 50.7	a
135.6	152.7	118.4	27.7	29.1	18.6	12.8	13.9	CO: 167.4; OCH_3: 50.9	a, c
139.5	135.7	132.9	22.7	–	12.3	12.5	12.5	1-CO: 175.9; CH_2: 61.1; CH_3: 14.1; 15-CH_2: 59.2	a, c
136.7	136.4	130.6	26.7	26.7	20.2	12.6	12.6	OCH_2: 59.2	a, c
134.8	154.3	129.0	26.8	26.8	20.3	12.9	13.1	CO: 190.5	a, c
136.6	138.8	125.1	25.9	25.9	21.1	12.9	12.7	OCH_2: 61.2; CO: 170.6; CH_3: 20.9	a, c
135.3	154.1	129.2	25.9	25.9	21.1	13.1	13.1	CO: 190.7	a
135.9	152.5	118.6	25.9	25.9	21.1	13.1	13.8	CO: 167.2; CH_3: 50.7	a, c
135.3	154.9	118.2[1]	26.0	26.0	30.7	13.0	14.1	CO: 172.2	a
135.5	152.8	118.4	26.0	26.0	30.7	13.0	13.9	CO: 167.5; OCH_3: 50.9	a, d
136.2	152.2	119.2	25.7	27.8	30.7	15.0	13.8	CO: 167.0; OCH_2: 59.6; CH_3: 14.4	a
137.3	151.1	120.7	27.4	27.4	30.2	12.5	13.6	CO: 168.1	a, g

Table 2: continued

No.	R	End group						In-chain				
		1	2	3	4	5	6	7	8	9	10	11
	all-trans											
61	CHO	129.8	135.9	122.9	156.5	110.3	133.9	129.6	137.9	140.7	130.1	132.2
62	$CONHCH_2CH_3$	130.0	135.8	122.7	156.2	110.1	133.8	128.0	138.2	138.0	130.5	129.1
63	$CON(CH_2CH_3)_2$	129.8	135.3	122.3	156.0	109.8	133.3	127.8[1]	138.1	136.9	130.5	127.5[1]
64	COOH	119.2	129.0[1]	126.6[1]	109.1	143.5[2]	148.8[2]	122.8	137.6	138.8	130.1	131.8
65	CH_2OAc	131.6	124.0	26.8	40.2	139.5	125.7	125.1	135.2	136.7	130.6	125.9
	13-cis											
66a	CH_2OH	34.3	39.8	19.4	33.1	129.3	137.9	127.1	137.6	136.8	130.2	127.1
66b	CH_2OH	34.2	39.6	19.3	33.0	128.8	137.8	126.7	137.6	136.1	130.5	126.7
67a	CH_2OAc	34.3	39.8	19.4	33.1	129.4	137.9	127.4	137.6	137.3	130.2	127.8
67b	CH_2OAc	34.2	39.7	19.3	33.0	129.0	137.8	127.0	137.6	136.6	130.4	127.4
68	CHO	34.3	39.7	19.3	33.2	130.3	137.6	129.6	137.0	141.3	129.4	133.4
69	COOH	34.4	40.0	19.4	33.3	130.1	137.9	128.9	137.4	140.3	130.3	132.9
70	$COOCH_3$	34.3	39.7	19.4	33.2	129.9	137.7	128.5	137.5	139.6	130.4	132.1
71	COOH	35.1	40.1	19.6	32.9	127.5	136.8	27.6	40.9	145.7	133.2	125.2
72	$COOCH_3$	34.0	39.6	19.5	32.7	127.7	137.8	126.5	139.3	37.8	41.0	137.5
73	COOH	32.7	31.8	23.2	121.1	134.1	55.0	129.8[1]	135.9	139.8	133.2[2]	132.8[2]
	11-cis											
74	CH_2OH	34.3	39.7	19.4	33.1	129.1	138.0	127.1	138.1	137.1	126.4	125.2
75a	CH_2OAc	34.3	39.7	19.3	33.1	129.2	138.0	127.2	138.0	137.4	126.2	125.7
75b	CH_2OAc	34.2	39.6	19.3	33.0	128.7	138.0	126.4	137.8	136.8	126.8	125.6
	9-cis											
76a	CH_2OH	34.3	39.8	19.4	33.2	129.4	138.2	128.6[1]	130.0	134.8	128.7[1]	124.0
76b	CH_2OH	34.1	39.6	19.2	33.0	128.8	138.1	128.0	130.0	134.0	128.8	123.7
77a	CH_2OAc	34.3	39.8	19.4	33.2	129.4	138.1	128.6	130.0	135.1	128.6	124.7
77b	CH_2OAc	34.2	39.6	19.3	33.0	129.0	138.1	128.7	130.0	134.5	128.3	124.6[1]
78	CHO	34.1	39.7	19.3	33.2	130.4	138.1	131.1	129.4	140.0	127.9	131.2
79	COOH	33.9	39.3	18.9	32.7	129.4	137.3[1]	129.6[2]	129.0[2]	137.6[1]	128.1	129.6[2]
80	$COOCH_3$	34.3	39.7	19.4	33.2	130.0	138.1	130.2	129.6[1]	138.3	128.1	129.9[1]
81	$COOCH_2CH_3$	48.0	40.3	31.5	137.9	199.3	156.3	124.8	130.9	137.9	129.0	131.3
82	CHO	55.8[1]	31.2	24.9	52.5	141.5	132.2	94.1[2]	92.8[2]	124.6	134.4[3]	133.8
	11,13-di-cis											
83	CH_2OH	34.3	39.8	19.4	33.1	129.3	137.9	127.5	137.8	137.3	126.2	126.8

Remarks: [a] CW offset ^1H-decoupling, [b] selective ^1H-decoupling, [c] $Yb(dpm)_3$, [d] $Eu(dpm)_3$, [e] $Eu(fod)_3$, [f] $CCl_4 + CDCl_3$ 4:1, [g] $CDCl_3$ + dioxane 1:1, [h] $CDCl_3$ + DMSO-d_6 1:1, [i] Corresponding signals may be interchanged; preferred assignment given.

			Methyls					Others	Remarks
12	13	14	1,1–		5–	9–	13–		
135.1	154.2	129.1	–	–	–	13.1	13.1	CO: 190.6; CH_3: 21.4; 17.4; 11.8	a, c
136.9	147.7	122.4	–	–	–	12.9	13.5	CH_3: 21.4; 17.4; 11.9; CO: 167.1; OCH_3: 55.4; NCH_2: 34.2; CH_3: 13.5	a, c
136.2	144.6	121.9	–	–	–	12.7	14.0	CH_3: 21.2; 17.3; 11.8; CO: 166.3; OCH_3: 55.4; NCH_2: 40; CH_3: 13.6	a, d, f
136.4	150.9	120.2	–	–	–	12.4	13.5	CH_3: 15.1; 20.5; OCH_2O: 100.3; CO: 167.8	a, h
136.0	139.1	124.7	17.7(c)	25.6(tr)	16.9	12.8	12.7	OCH_2: 61.3; CO: 170.7; CH_3: 20.9	a, c
128.6[1]	135.6	128.7[1]	29.0	29.0	21.6	12.7	20.4	OCH_2: 58.4	a, c
128.6	135.0	128.8	29.0	29.0	21.6	12.6	20.3	OCH_2: 58.1	a, d, f
128.1	137.9	122.8	29.0	29.0	21.6	12.8	20.3	OCH_2: 60.3; CO: 170.9; CH_3: 20.9	a, c
128.2	137.4	123.2	29.0	29.0	21.6	12.6	20.3	OCH_2: 59.8; CO: 169.3; CH_3: 20.5	a, c, f
126.5	154.2	127.7	29.0	29.0	21.7	13.0	21.1	CO: 189.6	a, c
129.4	153.3	115.9	29.0	29.0	21.6	12.9	21.1	CO: 171.4	a
129.5	151.1	116.2	29.0	29.0	21.7	12.8	20.8	CO: 166.5; OCH_3: 50.7	a, c
127.5	153.9	115.4	28.7	28.7	19.9	17.2	21.1	CO: 171.5	–
129.1	151.2	115.6	28.8	28.8	21.4	20.8	21.0	CO: 166.5	a
129.2[1]	153.4	115.8	27.1	27.7	23.0	13.3	21.1	CO: 171.6	a
132.6	136.1	130.5	29.0	29.0	21.7	12.2	17.1	OCH_2: 59.4	a, c
132.1	138.4	124.9	29.0	29.0	21.7	12.2	17.2	OCH_2: 61.2; CO: 170.7; CH_3: 20.8	a, c
132.1	137.8	125.1	29.0	29.0	21.6	12.2	17.1	OCH_2: 60.7; CO: 169.3; CH_3: 20.5	a, e, f
135.7	136.7	130.0	29.0	29.0	21.8	20.7	12.7	OCH_2: 59.4	a, c
135.7	136.1	130.1	29.0	29.0	21.7	20.7	12.5	OCH_2: 59.0	a, d, f
135.1	139.0	124.5	29.1	29.1	21.8	20.7	12.7	OCH_2: 61.2; CO: 170.7; CH_3: 20.8	a, c
135.2	138.5	124.4[1]	29.0	29.0	21.7	20.6	12.6	OCH_2: 60.7; CO: 169.4; CH_3: 20.6	a, f
133.8	154.3	128.9	29.0	29.0	21.8	20.9	13.2	CO: 190.6	a, c
134.7	151.2	119.6	28.8	28.8	21.6	20.5	13.4	CO: 167.8	a, h
134.5	152.3	118.2	29.1	29.1	21.8	20.9	13.9	CO: 167.4	a, c
136.0	151.9	119.6	27.5	27.5	30.3	20.3	13.7	CO: 166.8; CH_2: 59.6; CH_3: 14.3	a, d
135.0[3]	155.0	118.7	12.1	–	–	23.7	14.0	C-1a: 56.6[1]); CH_3: 19.6; CO: 172.6	a, b
128.2	135.7	127.9	29.0	29.0	21.7	12.5	23.9	OCH_2: 60.6	a, c

shifts were in accordance with those derived from $Yb(dpm)_3$-experiments. However, as is seen from a comparison of Yb- and Eu-induced shifts near the site of complexation, the ratios of both figures are not constant along the polyene chain. This means, that even with the retinols relevant contact contributions of the Eu-complexes are likely to be present. It is thus again demonstrated that use of Eu-shift reagents for the calculation of *quantitative* structural information may lead to erroneous results. This is especially true for the retinals where a stronger delocalization of the unpaired electron spin may presumably occur by transmission through the π-system of the conjugated polyene *via* the conjugated carbonyl group.

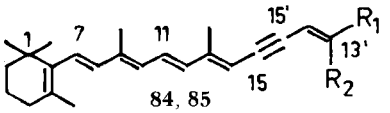
With the different retinyl acetates investigated in the course of our study similar results were obtained which will, however, not be discussed here in detail. In the case of all-*trans*-, 13-*cis*-, 11-*cis*-, and 9-*cis*-retinyl acetates application of $Eu(fod)_3$ again led to the observation of reduced downfield shifts due to contact contributions. So it was found that the $\delta(1:1)$-values of C(14) were in all cases smaller than those of the quaternary C(13) and smaller contact contributions were also discernible along the conjugated chain as far as C(7) or C(8).

The magnitude of the downfield shifts by $Yb(dpm)_3$ of the olefinic carbon atoms of the acetates was considerably weaker than with the retinols and retinals, probably partly due to the fact that the complexation takes place now at the more distant C=O group rather than at the –OH or CHO-group. The $\delta(1:1)$-values in ppm of the C=O carbon atom (and of C(15)) of the all-*trans*-, 13-*cis*-, 11-*cis*-, and 9-*cis*-retinyl acetates were ~ 65 (20.6), ~ 61 (19.6), ~ 84 (29.4), and 123 (42.8), respectively. As was already mentioned the assignment of carbon atoms more remote from the site of complexation, namely of C(7), C(8), and in some cases even of C(10) had to be achieved by analogy to the retinols, since the $\delta(1:1)$-values encountered were too small for a clear differentiation.

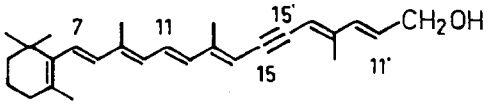
A similar situation occurred with the different retinoic esters where some of the assignments had to be done by comparison with the corresponding retinals. The $Yb(dpm)_3$-induced downfield shifts of the (C=O)-carbon atoms of the different isomers were, in general, smaller than those obtained with the retinals. The $\delta(1:1)$-values observed for C(15) (C(14)) of all-*trans*-, 13-*cis*-, and 9-*cis*-retinoic acid methyl esters were 101 (41), 73.4 (30.6) and 89 (30.6) ppm, respectively. Interestingly, the absence of the 13-methyl group in all-*trans*-13-desmethyl compounds scarcely affected these values (91 and 42 ppm in the 13-desmethyl compound; 107 and 55.5 ppm in the 9-ethyl-13-desmethyl retinoic acid methyl ester). Evidently, the strength of the complexation is not significantly altered by the absence of the 13-methyl group. As with the other classes of vitamins A, the use of Eu-shift reagents did in some cases clearly lead to the observation of contact contributions.

So far compounds with only one site of complexation have been discussed. In *Scheme 1* we present examples of the $Yb(dpm)_3$-induced shifts $\delta(1:1)$ in ppm of compounds with 2 and 3 sites of complexation (**56**, **50** and **51**). A comparison of the $\delta(1:1)$-values obtained by extrapolation from $R = 0.67$ (compound **56** and **50**) and $R = 0.33$ (**51**) of shift reagent to substrate shows, in agreement with expectation, that complexation is strongest at the OH-group and weakest at the sterically hindered epoxide. The magnitude of the LIS decreases with increasing distance from the site of strongest complexation and finally increases again, approaching the second site

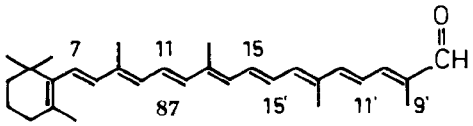
Basic Chemical Structures contained in Table 3:



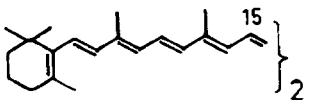
84, 85



86



87

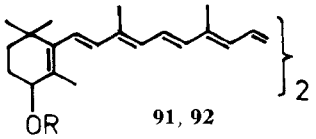


88a

88b: 15,15′-D_2-

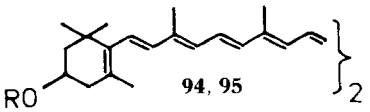
89: 15,15′-cis-

90: 15,15′-didehydro-

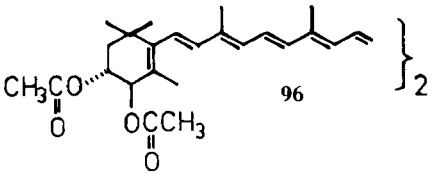


91, 92

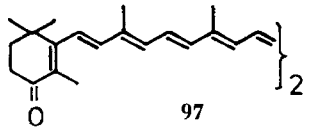
93: 15,15′-didehydro-



94, 95

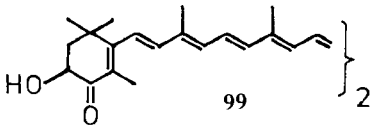


96



97

98: 15,15′-didehydro-



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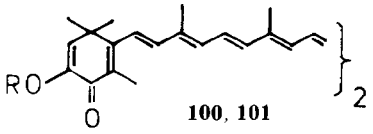
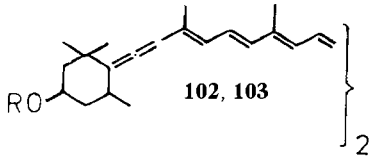
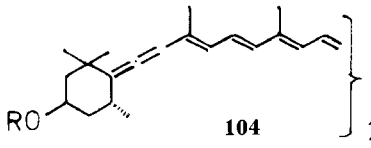


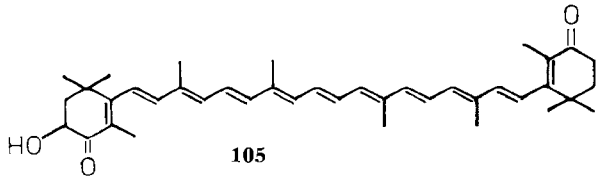
100, 101



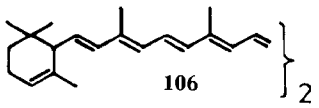
102, 103



104



105



106

Table 3: *^{13}C-NMR. chemical shifts* (in ppm) *for some β-apo- and*

No.	R	End group						In-chain				
		1,1′	2,2′	3,3′	4,4′	5,5′	6,6′	7,7′	8,8′	9,9′	10,10′	11,11′
84	R_1: CHO	34.3	39.7	19.3	33.2	129.9	137.8	128.3	137.4	138.9	129.9	129.2
	R_2: CH_3	–	–	–	–	–	–	–	–	–	–	–
85	R_1: CH_3	34.3	39.8	19.4	33.2	129.8	137.9	128.2	137.5	138.7	129.9	128.8
	R_2: CHO	–	–	–	–	–	–	–	–	–	–	–
86	–	34.3	39.8	19.4	33.2	129.5	137.5	127.5	137.5	137.9	130.1	127.3
		–	–	–	–	–	–	–	–	–	–	130.1
87	–	34.3	39.7	19.3	33.1	129.4	137.8	127.1	137.5	136.6	130.7	126.1
		–	–	–	–	–	–	–	194.0	135.0	148.9	122.5
88a	–	34.4	39.8	19.4	33.2	129.3	138.0	126.7	137.8	136.0	130.8	125.1
88b	–	34.4	39.9	19.4	33.2	129.3	138.1	126.7	137.8	136.0	130.9	124.7
89	–	34.4	39.9	19.4	33.2	129.3	138.1	126.8	137.8[1]	136.1	130.8	125.4[2]
90	–	34.4	39.9	19.4	33.2	129.5	138.0	127.1[1]	137.6	137.4	130.2	127.4[1]
91	CH_3	34.7	34.7	23.2	79.1	128.6	142.3	125.7	138.7	135.4	131.6	124.8
92	Ac	34.7[1]	34.8[1]	25.3	72.6	126.0	144.2	125.1	139.1	135.1	132.0	124.8
93	H	34.9	34.9	28.8	68.8	130.7	141.4	126.6[1]	138.6	136.9	131.1	127.0[1]
94	H	37.1	48.7	65.1	42.7	126.2	137.9	125.7	138.5	135.7	131.3	125.0
95	CH_3	36.7	44.6	73.7	39.3	126.2	137.8	125.7	138.4	135.6	131.3	124.9
96	–	36.6	41.4	70.8[1]	75.4[1]	124.6	142.7	124.0	139.8	134.8	132.5	124.7
97	–	35.7	37.5	34.2	198.8	129.8	160.9	124.0	141.2	134.6	134.4	124.6
98	–	35.7	37.4	34.2	198.9	129.9	160.8	124.7	140.9	136.1	133.7	126.6
99	–	36.8	45.6	69.2	200.3	126.9	162.4	123.3	142.2	134.7	135.1	124.6
100	H	39.3	125.5	144.6	182.5	128.5	161.4	123.1	142.4	134.7	135.4	124.7
101	Ac	39.9	141.8	143.1	179.7	130.5	158.0	122.7	142.3	134.4	135.2	124.6
102	H	35.9	50.7	67.1	45.2	29.8	118.8	201.2	103.6	134.0	128.1	125.4
103	Ac	35.5	45.2	70.0	40.9	29.3	117.9	200.6	103.4	133.3	128.0	125.0
104	H	34.7	46.7	67.3	42.8	30.0	119.7	200.8	103.1	134.0	127.7	125.1
105	–	36.9	45.6	69.2	200.3	127.0	162.1	123.3	142.3	134.8	135.2	124.6
		35.8	37.6	34.3	199.0	130.0	161.0	124.2	141.2	134.8	134.4	124.8
106	–	32.6	31.8	23.1	120.7	134.5	55.0	130.0	136.2	135.5	131.0	124.9

[a]) CW-offset ^{1}H-decoupling, [b]) $Yb(dpm)_3$, [c]) $CDCl_3$ + dioxane approx. 3:1, [d]) selective ^{1}H-decoupling, [e]) $CDCl_3$ + CH_3OH approx. 3:1, [f]) The chemical shifts given in [7] should be corrected by multiplication with 0.975, [g]) Assignment in agreement with ref. [2] with the exception of C-13 and C-9 which are reversed here in agreement with compounds **91**, **92**, **95** and **96**.

other carotenoids. Solvent: $CDCl_3$ (if not otherwise specified).

12,12′	13,13′	14,14′	15,15′	Methyls 1,1′–	5,5′–	9,9′–	13,13′–	Others	Remarks
134.1	150.4	109.0	107.2	29.0	29.0	21.7	12.8	15.5		a, b
193.2	146.4	128.3	94.2	–	–	–	–	11.7		
134.1	150.0	108.8	99.6	29.0	29.0	21.8	12.9	15.6		a, b
191.7	144.3	126.0	92.6	–	–	–	–	15.2		
134.8	146.8	110.3	96.9	29.0	29.0	21.7	12.8	15.3		a, b
133.7	145.2	111.2	96.9	–	–	–	–	15.3	OCH_2: 62.4	
136.8	138.5	131.8	132.9	29.0	29.0	21.7	12.7	12.9		a, b
145.7	135.0	137.5	129.0	–	–	–	9.5	12.6		
137.3	136.4	132.4	130.0	29.0	29.0	21.7	12.8	12.8		a, f, g
137.3	136.4	132.4	–	29.1	29.1	21.7	12.8	12.8		f
137.5[1]	137.1	126.8	125.6[2]	29.1	29.1	21.7	12.8	12.6		a
135.0	146.5	110.6	98.2	29.0	29.0	21.7	12.8	15.3		a
137.7	136.3	132.6	130.1	29.0	27.5	18.9	12.7	12.8	OCH_2: 56.6	a, b
138.0	136.3	132.8	130.1	28.9	27.4	18.4	12.7	12.8	CO: 170.7; CH_3: 21.1	a, b
135.5	146.5	110.9	98.3	29.1	27.8	18.6	12.7	15.3		a, c
137.6	136.4	132.6	130.1	30.4	28.8	21.6	12.8	12.8		a
137.5	136.3	132.6	130.1	30.3	28.7	21.6	12.7	12.7		a, b
138.2	136.3	132.9	130.2	29.8	27.9	16.8	12.7	12.7	CO: 170.1+170.5; CH_3: 20.8+21.0	a, b
139.2	136.5	133.5	130.5	27.7	27.7	13.8	12.5	12.7		a, b, d
136.9	146.5	111.8	98.6	27.7	27.7	13.8	12.7	15.3		a, b
139.7	136.7	133.8	130.7	30.8	26.2	13.9	12.6	12.8		a
139.8	136.7	133.8	130.8	28.2	28.2	13.6	12.6	12.8		a
139.7	136.6	133.8	130.7	27.5	27.5	13.6	12.5	12.8	CO: 168.5; CH_3: 20.4	a, b
136.9	136.6	132.5	130.2	31.1	27.5	19.9	14.3	12.9		e
136.7	136.2	132.2	139.9	30.7	27.2	19.7	14.1	12.7	CO: 170.4; CH_3: 21.2	a, b
136.6	136.4	132.1	129.9	31.5	25.9	19.9	14.2	12.9		
139.8	136.8	133.9	130.8	30.8	26.2	13.9	12.6	12.8		
139.3	136.5	133.5	130.5	27.8	27.8	14.0	12.6	12.8		
137.1	136.4	132.3	130.2	27.6	27.1	23.0	13.1	12.8		a

i) Corresponding assignments may be interchanged

of weaker complexation. An irregular sequence is observed with C(7) and C(8) of compound **56**. Here, the two signals were assigned by analogy with compounds with β-end groups such that C(8) is lowfield of C(7) (see below). The unexpected Yb-shifts may be at least partly caused by the special steric conditions of the 5,6-epoxide together with a hindered rotation of the end group around the C(7) and C(8) single bond.

The LIS-values of compound **50** and **51**, on the other hand, clearly confirm the assignment of C(8) downfield of C(7) in all compounds with β-end group. Furthermore, in **50** the relative assignment of C(5) as upfield compared to C(6) is clear.

The assignment of the signals of C(2), C(3) and C(4) of the β-end groups with the first at lowest and the second carbon atom at highest field [1] is confirmed by an assessment of the additional shifts of these carbon atoms, caused by introduction of the HO–C(4) group as in **50**. In a hydroxy substituted cyclohexane, the α-, β- and γ-contributions of this group to the ^{13}C-NMR. shifts of the different carbon atoms are approximately +43, +8 and −3 ppm, respectively. With these values the predicted shifts of the unsubstituted β-ring should be roughly 27 (C(4)), 21 (C(3)) and 38 ppm (C(2)). The same relative order and approximate shifts of 33, 19.3 and 39.5 ppm were observed for the β-end groups. In addition, the assignment of C(4) was confirmed in several cases by selective ^{1}H-decoupling experiments.

Interestingly, the two methyl carbon atoms at C(1) of the β-5,6-epoxide analogue (**56**) were accidently equivalent. Addition of a shift reagent, however, led to a splitting and two different δ(1:1)-values. With 4-hydroxy compound **50**, the signal at the two non-equivalent methyl carbon atoms showed different downfield shifts, the larger one presumably must be assigned to the methyl group *cis* to the OH-group.

In conclusion it may be seen that application of shift reagents can still be very helpful with compounds possessing several sites of complexation, since even here the assignment of the ^{13}C-signals can be considerably simplified.

β-Apo- and other Carotenoids. – In the course of this work a number of β-apo-carotenoids and other carotenoids were also studied in order to test the limits of the applicability of Yb(dpm)$_3$ as a tool for the assignment of the ^{13}C-signals of these more complex molecules. As a result, it was found that in favourable cases relevant LIS-differences of the carbon atoms of the conjugated polyene chain can clearly be detected even 8 conjugated double bonds away from the complexed end group. Thus it was possible to assign all signals of the 18 olefinic carbon atoms of all-*trans*-β-apo-8'-carotenal (**87**) solely from the observed LIS-values although 13 signals of the 18 appear very closely spaced in the range between 126 and 138.5 ppm. The resulting assignments together with those of 22 further compounds, the assignments of which were also partly based on the application of Yb(dpm)$_3$, are presented in Table 3 (see last column).

As an example the Yb(dpm)$_3$-induced δ(1:1)-values obtained for all-*trans*-β-apo-8'-carotenal (**87**) by linear extrapolation from the last measurement at R = 0.8 are presented in *Scheme 2*. The assignments given in Table 3 were based on the observation that the δ(1:1)-values gradually decrease, as expected, with increasing distance from the complexed aldehyde group. Small irregularities in this behaviour were exceptionally observed only for the quaternary carbon atoms C(9) and C(13), the

δ(1:1)-values of which were slightly too large compared to those of the preceeding carbon atoms C(10) and C(14), respectively. Furthermore, the LIS-differences of the 2 carbon atoms of each individual (C=C)-unit seem to be relatively small compared to those of the connected (=C–C=)-units. Since a quantitative treatment of these effects is outside the scope of this study, these observations will not be discussed further.

Similarly favourable conditions for the assignment of most of the ^{13}C-signals were also met in all-*trans*-15,15'-didehydro-β-apo-12'-carotenal (**84**), where again clear LIS-differences enabled all the polyene carbon atoms to be assigned including C(7). With the corresponding 13'-*cis*-isomer (**85**), on the other hand, significant LIS-differences were measured only as far as C(13), and the carbon atoms C(7) to C(12) the signals of which showed small negative δ (1:1)-values, had to be assigned by analogy with the *trans* compound. The reasons for this behaviour are not understood.

It has already been pointed out elsewhere [2] that carbonyl groups exert a relatively strong influence on the chemical shifts of even very remote carbon atoms. It seems likely that this is caused both by a linear electric field effect, such as was postulated to account for the spectra of unsaturated fatty acids [12], and, in conjugated systems, by an even more important direct bond polarization effect *via* a contribution of other mesomeric forms. Both result in alternating charge densities along the polyene chain causing the signals of the α,γ- etc. carbon atoms to fall at relatively high fields, and those of the β-,δ-, etc. carbon atoms at lower field. The long-range nature of these effects has been demonstrated in several cases in the course of this study. For example, in β-apo-8'-carotenal (**87**) the carbon atoms C(15) and C(15') still show a chemical shift difference of $\Delta\delta = 3.9$ ppm although the mean value of both shifts (130.95) is close to the chemical shift of C(15) and C(15') of β-carotene (**88**; 130.0 ppm). This effect of carbonyl and carboxyl groups has to be taken into account when comparisons are made between the chemical shifts of specific carbon atoms in compounds of different chemical structure (Tables 1, 2 and 3).

Effects of *cis/trans* isomerism on ^{13}C-shifts. – From our previous analysis of the ^{1}H-NMR. spectra of *cis/trans* isomeric vitamins A and related compounds [7] the following conclusions were drawn:

(1) If one subtracts possible shift contributions of carbonyl and carboxyl end groups to the chemical shifts of the olefinic protons in *trans* compounds H–C(11) is particularly strongly deshielded. Its low-field shift was explained by a strong steric interaction with the hydrogen atoms of the H_3C–C(9) group. This was experimentally proven by the upfield shift of H–C(11) by 0.3 to 0.4 ppm with the 9-desmethyl analogues (see Table 6 of [7]). Interestingly, the ^{1}H-chemical shift of H–C(7) was practically unaffected by the presence of the H_3C–C(9) group. Similarly, the H–C(11) shift was practically identical in the 13-desmethyl compounds pointing to the fact that the two latter steric interactions should be small or fully compensated by other effects.

(2) In all the *cis* isomers, where new strong steric interactions between approaching hydrogen atoms were to be expected, downfield shifts of up to 0.5 ppm were observed (see Table 7 of [7]). Conversely, the reduction of specific steric compressions in the *cis* isomer gave rise to corresponding upfield shifts in the ^{1}H-NMR. spectra.

Downfield shifts of ^{1}H-NMR. signals caused by steric effects have been treated theoretically by *Cheney* [13] and *Cheney & Grant* [14] in terms of a sterically-induced

charge polarization in the C–H bond produced by the component of the H–H repulsive force along the C–H bond. This polarization effect formally produces a decrease of the electron density at the proton. At the same time, a corresponding increase of the electron density at the attached carbon should occur. Therefore, the downfield shift of the ^{1}H-NMR. signal should be accompanied by an upfield shift of the ^{13}C-NMR. signal if the physical model given above is assumed to be correct.

This general rule was recently discussed in detail for the ^{1}H-NMR. spectra of all-*trans*, 9-*cis*- and 13-*cis*-retinal [15] as well as for the ^{13}C-NMR. spectra of the retinals [4] [5]. The main features of this rule could also be applied to the compounds investigated here. However, a strict reversal of ^{1}H- and ^{13}C-shift behaviour was not observable in all cases. This is probably partly due to the fact that a quantitative separation of the steric effects from other substituent effects can not always easily be achieved in ^{13}C-NMR. spectra. This is seen, for example, from a comparison of the chemical shifts of the methyl esters of retinoic acid and its 9- and 13-desmethyl as well as its 9,13-di-

Table 4: *Lanthanide induced shifts* $\delta(1:1)$ *in ppm, extrapolated to equimolar ratio of substrate*

	Isomer		Nucleus observed	Shift Reagent	Position						
					1	2	3	4	5	6	7
Retinals	**34**	all-trans	^{13}C	Yb(dpm)$_3$	1.0	0.7	0.8	0.9	1.2	1.1	2.0
			^{13}C	Eu(fod)$_3$	1.0	0.8	0.6	0.6	2.0	0.2	3.4
	68	13-cis	^{13}C	Yb(dpm)$_3$	– 0.4	– 0.4	– 0.5	– 0.6	– 0.4	– 0.4	0.3
			^{13}C	Eu(dpm)$_3$	0.4	0.2	0.2	0.2	1.2	– 0.2	2.4
			^{1}H	Eu(dpm)$_3$	–	–	–	–	–	–	0.2
	78	9-cis	^{13}C	Yb(dpm)$_3$	1.1	0.4	0.4	0.5	0.8	0.7	1.3
	53	A_2-aldehyde (all-trans)	^{13}C	Yb(dpm)$_3$	1.4	1.2	1.4	1.2	1.8	1.4	1.8
Retinols	**32**	all-trans	^{13}C	Yb(dpm)$_3$	1.0	0.8	0.6	0.6	1.2	1.4	2.0
			^{13}C	Eu(dpm)$_3$	0.2	0.2	0.2	0.2	0.3	0.4	0.7
	66	13-cis	^{13}C	Yb(dpm)$_3$	0	0	– 0.3	0	– 0.4	0?	0.7
			^{13}C	Eu(dpm)$_3$	0	0	– 0.1	– 0.1	– 0.1	0	0.4
	74	11-cis	^{13}C	Yb(dpm)$_3$	0.3	– 0.3	– 0.5	– 0.7	0.2	0.5	1.2
	76	9-cis	^{13}C	Yb(dpm)$_3$	1.0	0.8	0.9	0.5	1.2	1.5	1.9
			^{13}C	Eu(dpm)$_3$	0.4	0.3	0.4	0.4	0.6	0.6	0.9
	83	11,13-di-cis	^{13}C	Yb(dpm)$_3$	– 0.6	– 0.9	– 0.9	– 0.9	– 0.6	– 0.1	1.5
	52	A_2-alcohol (all-trans)	^{13}C	Yb(dpm)$_3$	1.2	1.0	0.9	1.0	1.3	1.3	1.8

[a]) 4:1

desmethyl analogues. Replacement of the H–C(9) (compound **40**) by the H_3C–C(9) group (**36**) leads to upfield shifts of C(7) (−5.5 ppm), C(10) (−1 ppm) and C(11) (4.2 ppm), whereas downfield shifts are observed for C(8) (+4.3 ppm), C(9) (+1.8 ppm) and C(12) (+0.4 ppm). From these shift changes, the upfield shifts in **36** of C(7) and C(11) can be attributed at least partly to the steric interaction with the H_3C–C(9) hydrogen atoms. Correspondingly, the replacement of the H–C(13) (**42**) by a H_3C–C(13) group (**36**) leads to an upfield shift of C(9) (−1.4 ppm), C(11) (−6.4 ppm) and C(14) (−1.1 ppm), whereas downfield shifts are observed for C(12) (+5.7 ppm) and C(13) (+7.7 ppm). Interestingly, the latter value is considerably larger than the previous one for the H_3C–C(9) group. The strong upfield shift of C(11) is now presumably caused mainly by the steric effect of the H_3C–C(13) hydrogen atoms

In the 9,13-di-desmethyl analogue (**44**) the effects found are approximately additive with upfield shifts of C(7) (−6.1 ppm), C(10) (−0.5 ppm), C(11) (−10.2 ppm) and C(14) (−1.4 ppm) and downfield shifts at C(8) (+4.6 ppm), C(9) (+0.9 ppm), C(12)

and shift reagent for retinals and retinols. Negative numbers correspond to upfield shifts.

8	9	10	11	12	13	14	15	1,1-CH_3	5-CH_3	9-CH_3	13-CH_3	Solvent
2.1	4.0	4.6	8.8	12.4	25.8	47.2	~130	1.0	1.3	2.7	15.6	$CDCl_3$
1.0	6.0	− 0.8	8.4	− 2.8	17.2	− 25.8	52.8	0.6	0.2	0.2	2.4	$CDCl_3$
1.3	2.3	3.4	8.0	16.2	25.2	~44.6	~120	− 0.4	− 0.6	1.8	12,2	$CDCl_3$
− 0.6	4.6	− 0.6	7.4	0.8	17.0	− 22.2	~60	0	− 0.2	0.2	0.6	$CDCl_3$
0	–	1.0	2.5	7.5	–	15.5	23.3	0	− 0.2	0.9	4.4	$CDCl_3$
1.6	2.5	2.8	5.1	7.1	15.0	27.7	~76	0.1	0.9	1.4	9.5	$CDCl_3$
2.8	5.0	5.6	11.0	14.8	31.0	57.0	~160	1.4	1.8	3.4	19.4	$CDCl_3$
2.4	4.0	5.7	10.4	22.4	34.6	61.0	~190	0.8	1.2	3.4	23.0	$CCl_4/CDCl_3$[a])
0.7	1.2	1.6	2.6	4.6	5.4	9.2	~52	0.2	0.2	1.0	7.3	$CCl_4/CDCl_3$[a])
0.9	2.8	5.9	11.7	23.2	32.0	57.4	~96?	0	0	2.7	15.5	$CDCl_3$
0.7	1.5	2.8	5.4	10.7	13.3	14.8	~73.2	0	− 0.1	1.3	6.6	$CCl_4/CDCl_3$[a])
1.2	1.7	3.1	3.5	5.2	10.4	18.5	~59.4	0.2	0.2	3.5	22.0	$CDCl_3$
2.8	3.5	5.3	9.2	15.0	30.6	56.1	~112	1.2	1.5	2.3	21.6	$CDCl_3$
1.3	1.3	2.3	3.0	5.6	9.9	11.8	60.0	0	0.6	1.1	9.6	$CCl_4/CDCl_3$[a])
4.0	7.2	13.1	16.2	23.1	32.6	62.1	75.0	− 0.7	− 0.4	4.0	15.5	$CDCl_3$
2.5	3.8	5.8	10.2	16.8	34.0	62.8	~63	1.2	1.2	3.2	24.0	$CDCl_3$

Table 5. *Significant chemical shift differences* δ_{cis}–δ_{trans} (abs. value > 0.6 ppm) *of the* ^{13}C-*NMR. signals of the vitamins A and related compounds.* If not otherwise specified, $CDCl_3$ was used as a solvent. Positive shifts mean downfield in the *cis* compound.

Isomers			R	C-7	C-8	C-9	C-10	C-11	C-12	C-13	C-14	C-15	9-CH_3	13-CH_3
13-cis:	**66–32**		$-CH_2OH$	–	–	1.2	–	2.3	– 7.9	– 0.6	– 1.9	– 0.7	–	7.8
	67–33		$-CH_2OAc$	–	–	0.9	–	2.0	– 7.8	– 1.1	– 1.8	– 0.9	–	7.6
	68–34		–CHO	–	–	–	–	1.0	– 8.0	–	– 1.2	– 1.1	–	8.1
	69–35		–COOH[a])	(–)	(–)	(1.0)	(–)	(1.8)	(– 6.1)	(–)	(– 2.6)	(– 2.8)	(–)	(7.2)
	70–36		$-COOCH_3$	–	–	–	0.9	1.2	– 5.7	– 1.7	– 2.0	– 0.8	–	6.9
	71–48	7,8-dihydro	–COOH	–	–	–	1.3	0.8	– 5.9	– 1.5	– 1.8	– 0.8	–	7.0
	72–49	9,10-dihydro	$-COOCH_3$	–	–	–	–	1.8	– 5.8	– 1.4	– 1.8	– 1.0	–	7.0
11-cis:	**74–32**		$-CH_2OH$	–	–	1.5	– 3.8	–	– 3.9	–	–	–	–	4.5
	75–33		$-CH_2OAc$	–	–	0.9	– 3.8	–	– 3.8	–	–	–	–	4.5
9-cis:	**76–32**		$-CH_2OH$	2.1	– 7.7	– 0.8	– 1.5	– 0.8	– 0.8	–	–	–	8.2	–
	77–33		$-CH_2OAc$	1.6	– 7.7	– 1.4	– 1.4	– 1.1	– 0.8	–	–	–	8.0	–
	78–34		–CHO	1.5	– 7.7	– 1.1	– 1.5	– 1.2	– 0.7	–	–	–	7.9	–
	79–35		–COOH[a])	(0.9)	(– 8.6)	(– 1.7)	(– 1.7)	(– 1.5)	(– 0.8)	(– 2.0)	(1.1)	(– 0.8)	(7.6)	(–)
	80–36		$-COOCH_3$	1.6	– 7.7	– 1.0	– 1.4	– 1.0	– 0.7	–	–	–	8.0	–
	81–61		–COOR[b])	(1.3)	(– 7.9)	(– 0.9)	(– 1.0)	(– 2.1)	(– 1.3)	(0.8)	(– 1.1)	(– 1.3)	(7.8)	(–)
11,13-di-cis:	**83–32**		$-CH_2OH$	1.0	–	1.7	– 4.0	2.0	– 8.3	–	– 2.7	1.5	–	11.3

[a]) Approximate values due to the use of different solvents; see Table 2.

[b]) Approximate values. Use of different solvents and compounds: trans = $-COOCH_3$; cis = $-COOCH_2CH_3$.

(+6.1 ppm) and C(13) (+8.1 ppm). The detailed interpretation of all these shift changes in terms of steric and substituent contributions seems, therefore, to be more complicated and not in all cases directly related to the effects observed in the ^{1}H-NMR. spectra [7].

A much better separation of the effects of steric crowding on the ^{13}C-NMR. spectra is, however, readily obtained from the changes of the chemical shifts produced by *cis*-isomerization of the different double bonds.

Table 5 presents the chemical shift differences $\Delta\delta = \delta_{cis} - \delta_{trans}$ of the different types of *cis* and *trans* isomers computed from the data contained in Table 2. Only differences of $\Delta\delta > 0.6$ ppm were taken into account. The values found for the 13-*cis* and 9-*cis* retinals are in reasonable agreement with those measured in dioxane [4]. From the values measured for the different 13-*cis* isomers it is seen that, as expected, strong upfield shifts occur with C(12) and corresponding downfield shifts with the H_3C–C(13) carbon signals resulting from the relief of steric interaction at the latter and introduction of steric interaction at the former upon going from the trans to the 13-*cis* structure.

The different $\Delta\delta$-values of C(12) of the acids and esters compared with the aldehydes are not unexpected. Recent ^{1}H-NMR. investigations on a number of α,β-unsaturated aldehydes, ketones, esters and amides [16] suggest that in analogy to these compounds the C=O group of the retinals will be predominantly oriented in an s-*trans* configuration of the 14,15-single bond, whereas esters will presumably exist as a mixture of s-*trans* and s-*cis* forms depending on the steric conditions. The different $\Delta\delta$-values are thus attributed to a different average orientation of the C=O group in both classes of compounds. The same $\Delta\delta$ of C(12) in the 13-*cis*-retinals, -retinols and -retinyl acetates points to an equal contribution of the steric effect independent of the nature of the attached end group.

In the 9-*cis* compound stronger variations of the steric interactions are to be expected for C(8) and H_3C–C(9) in agreement with the experimental observation.

In 11-*cis* compounds one would expect, if a planar structure with 12-s-*cis* or 12-s-*trans* of the polyene chain is assumed, mainly a strong upfield shift of C(10), since the *cis*-orientation of the H_3C–C(13) with respect to the substituent at C(14) is the same as in the all-*trans* compounds. In the 12-s-*cis* structure, an additional upfield shift of C(14) should occur.

Interestingly, the observed $\Delta\delta$-value of C(10) is less ($\sim$ 4 ppm) than expected (6–8 ppm) and no relevant effect was observed for C(14). This can be interpreted in terms of an increased conformational mobility, in solution, about the C(12)–C(13) single bond in the 11-*cis* isomer by which part of the sterical crowding will be reduced. [5]. This qualitative interpretation is in accordance with recent spectroscopic and theoretical evidence on the geometry in solution of 11-*cis*-retinal which was very recently discussed in detail [17].

In 11,13-di-*cis*-retinol, the same $\Delta\delta$ of C(10) is observed (–4 ppm) as in the 11-*cis* compound. In addition, C(12) gives a 'normal' $\Delta\delta$ of –8 ppm presumably by interaction with the H_2C–C(15) group, as was observed in 13-*cis*-retinol. The $\Delta\delta$ of the H_3C–C(13) signal in this compound is approximately additively shifted downfield by 11.3 ppm compared to 4.5 ppm in 11-*cis* and 7.8 ppm in 13-*cis*. It is believed that the particularly large shift difference of the H_3C–C(13) as observed in the 11,13-di-*cis*-

retinol could be helpful in the identification of corresponding di-*cis* subunits in poly-*cis* isomeric carotenoids.

For a further detailed discussion of the smaller *cis/trans* effects we refer to [5]. It is felt that a quantitative separation of the chemical shift differences into sterical effects and those due to the end groups would be desirable before further reliable deductions can be drawn.

Conclusions. – In the course of this study the ^{13}C-NMR. spectra of 106 compounds, mainly vitamins A and analogues as well as carotenoids are reported and completely assigned. The utility of the lanthanide shift reagents, especially of Yb $(dpm)_3$ for the assignment of the rather complicated ^{13}C-NMR. spectra of these compounds is demonstrated. It is believed that these data will serve as a comprehensive basis for further interpretation of the ^{13}C-NMR. spectra of other compounds of this type.

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