131. The Effect of Electron-Donating and Electron-Withdrawing Substituents on ^{1}H- and ^{13}C-NMR Chemical Shifts of Novel 7′-Aryl-Substituted 7′-Apo-β-carotenes

by **Elli S. Hand, Kenneth A. Belmore**, and **Lowell D. Kispert***

Chemistry Department, Box 870336, University of Alabama, Tuscaloosa, AL 35487, USA

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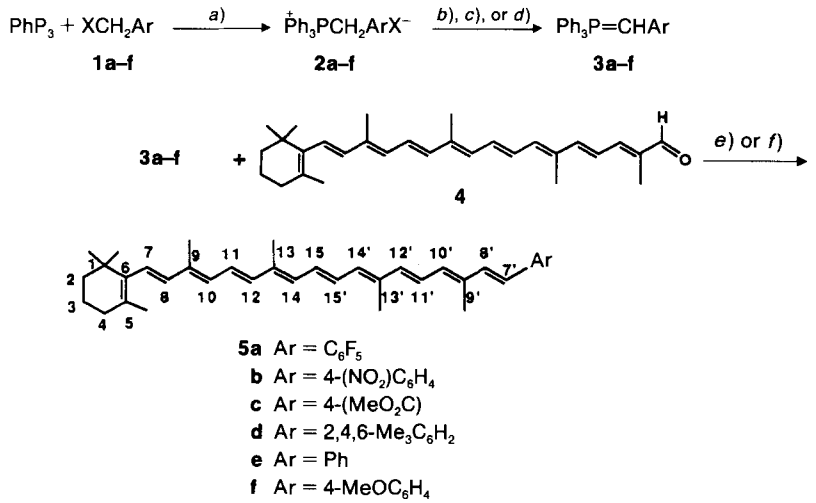
The synthesis of 7′-aryl-7′-apo-β-carotenes, where aryl (Ar) is Ph, 4-$NO_2C_6H_4$, 4-$MeOC_6H_4$, 4-$(MeO_2C)C_6H_4$, C_6F_5, and 2,4,6-$Me_3C_6H_2$, is described. NMR Chemical shifts of all H- and C-atoms are presented, together with specific examples of the spectra. In contrast to ^{1}H chemical shifts which, except for H–C(8′) and H–C(7′), did not differ greatly from those of β,β-carotene, considerable variations in ^{13}C chemical shifts were observed. Signals of the C(α) atoms of the polyene chain [C(β)=C(α)]$_n$Ar were shielded, those of the C(β) atoms were deshielded, with some exceptions when $n = 1$; the effects decreased with increasing n.

Introduction. – Many of the 600-odd known naturally occurring carotenoids have not yet been prepared in the laboratory [1]. The very few that are commercially available have such varied structures that systematic analysis and comparison of their properties is impossible. Electrochemical studies of carotenoids have shown that upon oxidation both a carotenoid cation radical and a carotenoid dication are generated [2]. Further, in the presence of excess carotenoid, an equilibrium is formed between the cation radical, the dication, and the neutral species, and the equilibrium constant depends on the carotenoid [3]. The details of this equilibrium are not understood. As part of an ongoing study of the electrochemical and optical properties of polyenes, a series of 7′-aryl-substituted 7′-apo-β-carotenes was synthesized. These are the 2,3,4,5,6-pentafluoro-, 4-nitro-, 4-(methoxycarbonyl)-, 4-methoxy, and 2,4,6-trimethylphenyl derivatives. The known parent compound [4], 7′-phenyl-7′-apo-β-carotene (**5e**), was also prepared. We report here the synthesis and some of the physical properties of these compounds, including ^{1}H- and ^{13}C-NMR chemical shift assignments of all atoms. It may be noted that unambiguous determination of all chemical shifts has only recently become possible with the advent of powerful 2D-NMR techniques. For the simpler, symmetrical β,β-carotene, this was finally achieved in 1985 [5] [6].

Results and Discussion. – *Syntheses.* Compounds **5a–f** were prepared by the *Wittig* reaction (*Scheme*). The phosphonium salts **2a–f** (*Table 1*) were formed by heating the corresponding benzyl halides **1a–f** with PPh_3 in an aromatic solvent. As expected, reaction of the benzyl bromides **1a–c** was more facile than that of the chlorides [8] [9]. The rate of formation also depended on the nature of the substituent. Thus, the fluoro derivative **2a** began to precipitate as soon as the reagents were mixed at room temperature, the nitro derivative **2b** after *ca.* 15 min at 45°, and the ester **2c** after *ca.* 5 min at 110°; the reaction of the methoxy compound **1f** was the most sluggish.

Scheme



5a Ar = C_6F_5
b Ar = 4-$(NO_2)C_6H_4$
c Ar = 4-(MeO_2C)
d Ar = 2,4,6-$Me_3C_6H_2$
e Ar = Ph
f Ar = 4-$MeOC_6H_4$

a) Aromatic solvent, heat. *b*) BuLi, THF, r.t., 20–60 min. *c*) NaH, THF. *d*) 50% aq. NaOH soln., CH_2Cl_2, r.t. *e*) THF, CH_2Cl_2, r.t. *f*) THF, CH_2Cl_2, 60°.

Table 1. *Reaction Conditions and Physical Data for Compounds* **2**

2	X	Ar	Conditions			M.p.	Yield
			Solv.[a])	Time [h]	Temp. [°C]	[°C]	[%]
a	Br	C_6F_5	Xyl.	18	115	243–244[b])	100
b	Br	4-$(NO_2)C_6H_4$	C_6H_6	20	60	> 265	92
c	Br	4-$(COOMe)C_6H_4$	Tol.	18	110	245–248 dec.	92
d	Cl	2,4,6-$Me_3C_6H_2$	C_6H_6	48	70	229–230	80
e	Cl	Ph	Tol.	19[c])	110	> 275	85
			Xyl.	20[c])	138		
f	Cl	4-$MeOC_6H_4$	Tol.	50	110	243 dec.	85

[a]) Xyl. = xylenes, Tol. = toluene. [b]) [7]: M.p. 240–241°. [c]) After 19 h, toluene was displaced with xylenes and heating was continued for 20 h.

In situ generation of the ylides **3a, b, d–f** in THF with BuLi (*Method A*, *Exper. Part*) proceeded smoothly, as indicated by the rapid disappearance of the insoluble salts **2** and the formation of deeply colored solutions. The ylide containing the ester moiety, **3c**, was prepared with NaOMe, generated by reaction of NaH with anhydrous MeOH in THF (*Method B*). Reaction of 8′-apo-β-caroten-8′-al (**4**) with the ylide **3a**, whose precursor **2a** formed most easily, was the slowest. Qualitatively, the rates increased in the order **5a** to **5f**, as indicated by TLC monitoring. Reaction times (*Table 2*), which are a less reliable measure since in general the reactions were worked up prior to total disappearance of **4**, especially in the case of **5e**, show a similar trend. Compound **5e** was also prepared under phase-transfer conditions, using CH_2Cl_2 and aq. NaOH solution (*Method C*); the phosphonium salt served as the transfer reagent [10].

Table 2. *Reaction Conditions and Physical Data for Compounds* **5**

5	Method (time, eluant[a]))	R[a])[b])	Yield [%]	M.p. [°C]	Color	EI-HR-MS (m/z)		
						Formula	calc.	found
a (7′*E*)	*A* (3 d, I)	0.8 (III)	63	182	red-brown	$C_{37}H_{41}F_5$	580.313	580.318
b (7′*E*)	*A* (2 d, II and 1)	0.5 (II)	54	177–179	slate gray	$C_{37}H_{45}NO_2$	535.345	535.347
c (7′*E*)	*B* (2 d, I)	0.8 (I)	53	168–172	deep red	$C_{39}H_{48}O_2$	548.365	548.366
d (7′*E*)	*A* (1 h, I)	0.8 (III)	73	*ca.* 155	dark red	$C_{40}H_{52}$	532.407	532.403
e (7′*E*)	*A* (1 h, III)	0.7 (III)	28[c])	159–161[d])	bronze	$C_{37}H_{46}$	490.360	490.362
(7′*Z*)[e])	*C* (3.5 h)	0.75 (III)	21	–	bronze	–	–	–
f (7′*E*)	*A* (4 h, II)	0.65 (II)	33	183–184	brick red	$C_{38}H_{48}O$	520.371	520.370

[a]) Chromatography solvents: I, benzene; II, benzene/hexane 1:1; III, benzene/hexane 1:5.
[b]) TLC on silica gel.
[c]) An additional amount (40%) consisted of *ca.* 80% (*Z*)- and 20% (*E*)-isomers.
[d]) [4]: M.p. 158°.
[e]) Contaminated with *ca.* 10% (*E*)-isomer.

In addition to the (all-*E*)-products (*i.e.* (7′*E*)), varying amounts of the sterically hindered (7′*Z*)-isomers were also formed. Although the isomers could not be separated by column chromatography, the (*Z*)-isomers were more soluble in MeOH and much more soluble in hexane than the corresponding (*E*)-isomers. Both isomers of **5e** were isolated from the phase-transfer reaction, which appeared to give relatively larger amounts of the (*Z*)-isomer than were formed using *Method A*. TLC's of all crude products showed a spot slightly above that due to the (7′*E*)-isomer, which was faint for compounds **5a–c**, but intense and larger for **5d–f**. By analogy to the TLC behavior of the isomers of **5e**, the faster migrating materials are, therefore, likely to have the (*Z*)-structure. The fact that high stereoselectivity occurred in the slow reactions suggests that relatively larger amounts of the (*E*)-isomers of **5d–f** might be obtainable by carrying out the reactions at lower temperatures.

All compounds **5** gradually decomposed at room temperature, especially when exposed to light and/or air, and were less stable in solution than in the solid state. Silica gel also enhanced the rate of decomposition. The fluoro and nitro derivatives **5a, b** were more stable than the others. The geometries of compounds **5** were indicated by ^{1}H-NMR data. Elemental compositions were establish by high-resolution mass spectroscopy (*Table 2*) and, for **5a, b, f**, by elemental analysis.

MS Fragmentation patterns were not very reproducible, but all compounds showed m/z peaks expected for the radical cations formed by extrusion of toluene and xylene from the polyene chain [11]. Peaks due to $C_5H_9^+$, formed by cleavage of the β end group, and the tropylium and methyltropylium ions were generally intense. Substituted tropylium ions, derived from the terminal aryl substituents, were observed for **5a** (m/z 181 (61%, $C_7F_5H_2^+$)), **5d** (m/z 133 (100%, $C_{10}H_{13}^+$)), and **5f** (m/z 121 (100%, $C_8H_9O^+$)), but not for **5b** and **5c**.

NMR Spectral Analysis. In all compounds **5**, 13 of the 14 olefinic protons give rise to ^{1}H-NMR signals within 0.50 ppm of each other; in the spectrum of **5d** (*Fig. 1*) all olefinic signals fall within this range. Thus, even at relatively high frequency (360 MHz), extensive overlap occurs (*Figs. 1–6*). The spectrum of the ester **5c** (not shown) is similar to that of the unsubstituted phenyl compound **5e** (*Fig. 2*). It is noted that the chemical shift of the

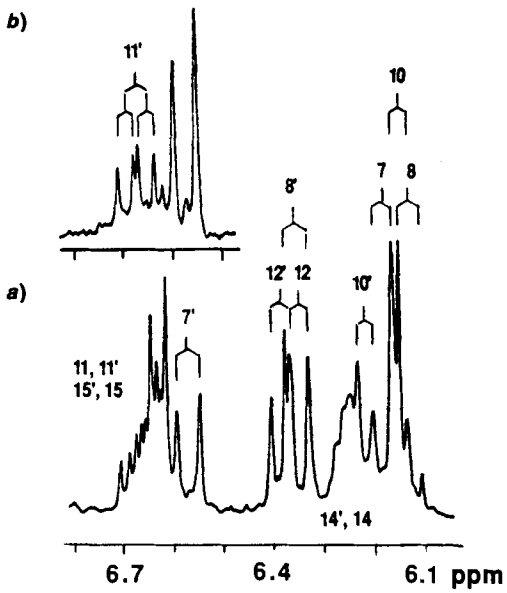


Fig. 1. *^{1}H-NMR Spectra of* **5d** (*ca.* 25 mg/ml $CDCl_3$): a) *olefinic region and* b) *NOE difference spectrum* (irradiation at 2.06 ppm)

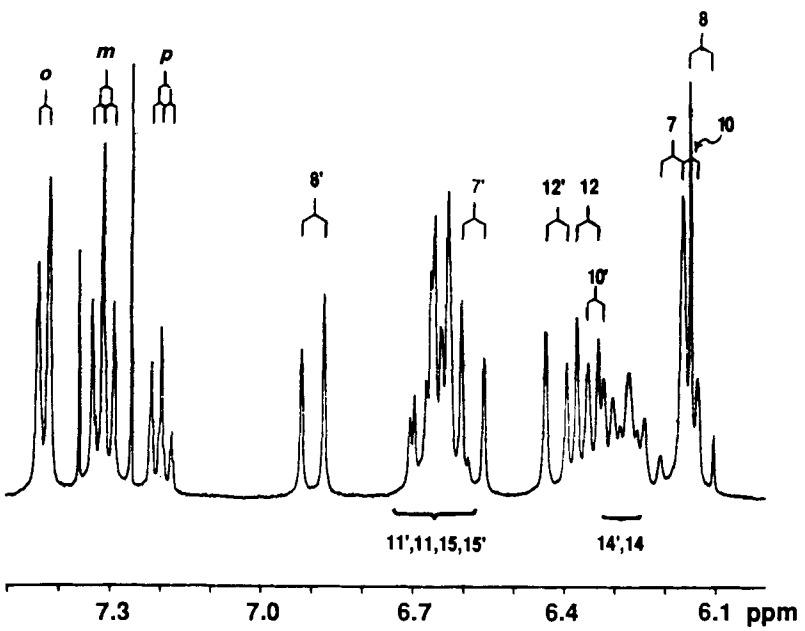


Fig. 2. *Low-field ^{1}H-NMR spectral region of* **5e** ((7′*E*); 18 mg/ml $CDCl_3$). The *s* at 7.37 ppm is due to benzene.

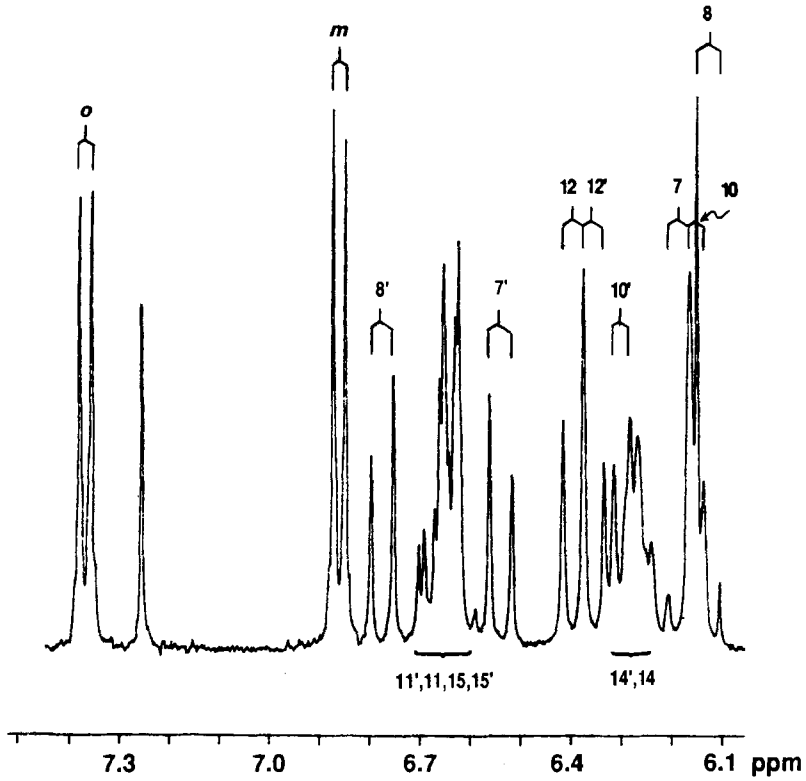


Fig. 3. *Low-field ^{1}H-NMR spectral region of* **5f** (20 mg/ml $CDCl_3$)

Table 3. *^{1}H-NMR Chemical-Shift Differences* (ppm) *of Olefinic Protons of (all-*E*)-7'-Aryl-7'-apo-β-carotenes and β,β-Carotene*[a])

	5a	5b	5c	5e	5f	5d
H–C(15)	0.05	0.07	0.03	0.00	0.00	–0.01
H–C(14')	0.06	0.07	0.05	0.01	–0.01	0.00
H–C(12')	0.11	0.12	0.08	0.06	0.03	0.02
H–C(11')	–0.01	0.00	0.00	0.00	0.01	0.01
H–C(10')	0.24	0.28	0.22	0.17	0.14	0.05
H–C(8')	1.04	0.90	0.84	0.76	0.63	0.21
H–C(7')	0.19	0.38	0.38	0.37	0.34	0.37

[a]) In the symmetrical *β,β*-carotene, *δ* values of primed and non-primed atoms are identical. Other chemical shifts of **5a–d** were the same (±0.01 ppm) as those reported for *β,β*-carotene [5], except for Me–C(9'): **5a**, 2.03; **5b**, 2.05; **5c**, 2.04; **5d**, 2.06; **5e**, 2.05; **5f**, 2.03; *β,β*-carotene, 1.98 ppm.

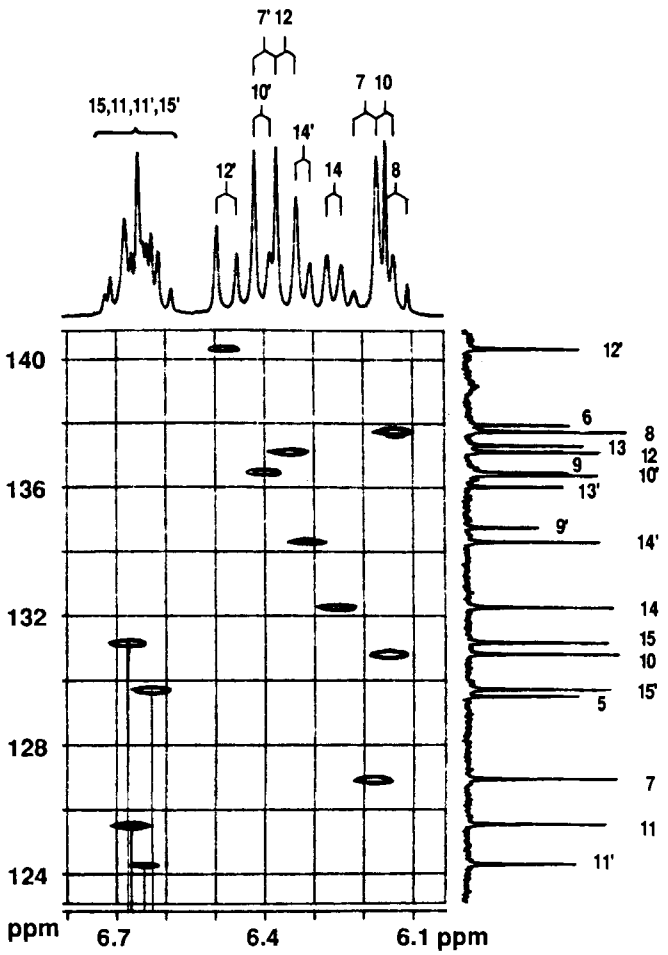


Fig. 4. *Selected portion of a HETCOR plot of* **5a** (13 mg/ml $CDCl_3$). Projections along the axes are 1D spectra obtained at 360 MHz for ^1H and 90 MHz for ^{13}C. The spectra contain additional olefinic signals at 141.76 (C(8')), 110.81 (C(7')), and 7.18 (*d*, H–C(8')) ppm.

H–C(8')'s reflects the electron-withdrawing properties of the substitutents. A combination of 1D and 2D techniques is used to establish the assignments shown, and the chemical-shift changes as compared to β,β-carotene are listed in *Tables 3* and *4*.

^1H-NMR Chemical shifts of H–C(7), H–C(8), and H–C(10) can be directly assigned, since H–C(7) and H–C(8) typically give rise to an *AB* pattern with a large coupling constant ($J(7,8) = 16.4$ Hz), which overlaps with the H–C(10) *d* ($J(10,11) \approx 12$ Hz) near 6.15 ppm so that a total of five signals are observed for these 3 *d*'s. Nuclear *Overhauser* enhancement (NOE) studies confirm the identification of H–C(7) and H–C(8) and, in general, permit identification of only 3 other olefinic protons. An example of an NOE difference spectrum is shown in *Fig. 1b*: the protons of single chain Me group (δ 2.06 ppm) of the trimethylphenyl compound **5d** were irradiated. Since enhancement is observed for a *d* (H–C(7) or H–C(7')) and a *dd* H–C(11) or H–C(11'), the irradiated protons can only be due to either CH_3–C(9) or CH_3–C(9'). Because H–C(7) is known to resonate at higher field, CH_3–C(9) is

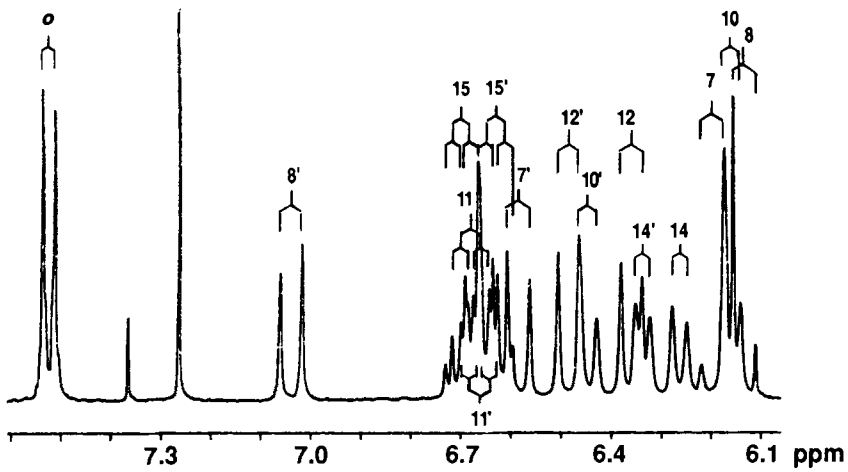


Fig. 5. *Selected portion of the* ^{1}*H-NMR spectrum of* **5b** (18 mg/ml $CDCl_3$). The *d* due to H–C(3′) and H–C(5′) (8.17 ppm) is not shown; the small *s* at 7.37 ppm is due to benzene.

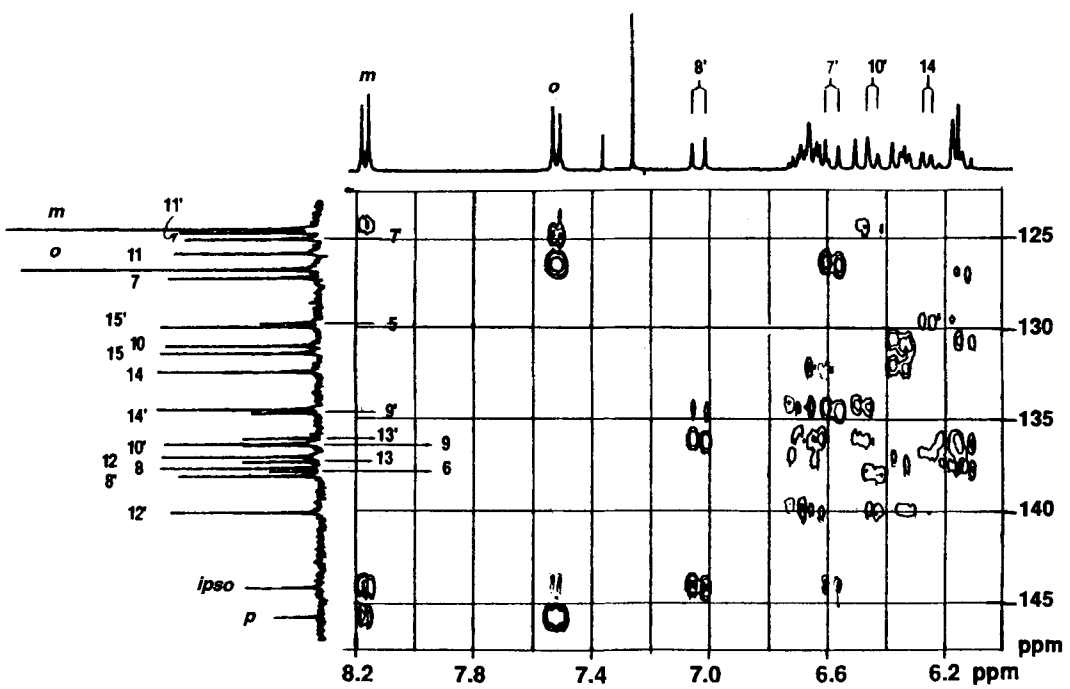


Fig. 6. *Contour plot of a selected portion of the* $^{13}C,^1H$ *HMBC spectrum of* **5b** (20 mg/ml $CDCl_3$). Projections along the axes are 1D spectra determined at 360 MHz for ^{1}H and 90 MHz for ^{13}C.

Table 4. *^{13}C-NMR Chemical-Shift Differences* (ppm) *of Compounds* **5a–f** (all *E*) *and β,β-Carotene*[a])

	5a	**5b**	**5c**	**5e**	**5d**	**5f**
C(7′)	−15.93	−2.01	−0.69	+0.61	−1.10	+0.22
C(9′)	−1.30	−1.45	−1.03	−0.61	−0.48	−0.36
C(11′)	−0.86	−0.74	−0.48	−0.25	−0.32	−0.10
C(13′)	−0.50	−0.48	−0.34	−0.18	−0.19	−0.07
C(15′)	−0.38	−0.38	−0.26	−0.16	−0.15	−0.10
C(14)	−0.22	−0.23	−0.14	−0.09	−0.07	−0.04
C(12)	−0.22	−0.25	−0.17	−0.13	−0.09	−0.09
C(10)	−0.11	−0.13	−0.09	−0.07	−0.05	−0.05
C(8)	−0.09	−0.12	−0.08	−0.07	−0.05	−0.06
C(6)	−0.14	−0.17	−0.14	−0.15	−0.09	−0.14
C(5)	0.10	0.11	0.07	0.04	0.00	+0.02
C(7)	0.16	0.17	0.09	0.00	−0.04	−0.04
C(9)	0.41	0.37	0.23	0.11	0.04	0.05
C(11)	0.40	0.43	0.26	0.10	0.04	0.02
C(13)	0.80	0.85	0.55	0.27	0.15	0.13
C(15)	1.07	1.11	0.74	0.34	0.21	0.14
C(14′)	1.83	1.91	1.30	0.69	0.41	0.39
C(12′)	3.00	2.90	1.96	0.99	0.67	0.45
C(10′)	5.48	5.44	3.95	2.33	1.24	1.37
C(8′)	3.94	0.34	−1.66	−4.17	0.71	−6.09

[a]) Negative values indicate upfield shifts, compared to those of *β,β*-carotene from [5], except that values of C(9) and C(13) are interchanged [6].

eliminated. Thus, the irradiated protons are due Me group is Me–C(9′) and the enhanced signals must be due to H–C(11′) and H–C(7′). Decoupling experiments (irradiation of H–C(7′)) then lead to the identification of H–C(8′). Only the signals at *ca.* 6.6–6.7 ppm (4 H) are enhanced when the protons of the remaining 3 chain Me groups (*ca.* 1.97 ppm) are irradiated. These signals are, therefore, attributed to H–C(11), H–C(11′), H–C(15), and H–C(15′) in all compounds. In the case of **5b**, **c**, **e**, **f**, irradiation of the H_o's of Ar could also be used to identify H–C(7′) and H–C(8′). ^{1}H,^{1}H Correlation (COSY) spectra, determined for **5a**, **e**, confirm the assignments of H–C(7′), H–C(8′), and H–C(11) (coupled to H–C(10); but, due to extensive overlap of the other cross-peaks, such spectra are only marginally useful for other chemical-shift determinations.

The ^{13}C-NMR spectra, on the other hand, display separate signals for nearly all of the 37–40 C-atoms of **5a–f**. As expected, the geminal CH_3 and the C_o and C_m signals coincide. For **5c** signals of C(10) and C(15) and of C(8′) and C(13′) coincide, and for **5f** those of C(8) and C(12′). Heteroatom correlation (HETCOR) and longrange ^{1}H,^{13}C coupling correlation (hetero multiple-bond correlation, HMBC) are used for unambiguous determination of the ^{13}C and the remaining ^{1}H chemical shifts. HETCOR Spectra, exemplified by the partial spectrum of **5a** (*Fig. 4*), provide the chemical shifts of those C-atoms that are directly bonded to the identified protons. Signals due to quaternary C-atoms are of lower intensity (no cross-peaks). In addition, chemical shifts of H's whose signals severely overlap can be evaluated from the cross-peaks, since their shape reflects the frequency range of the proton *m*'s. The centers of the cross-peaks are taken as the chemical shifts (see vertical lines in *Fig. 4*).

For the HMBC spectra, the pulse-sequence parameters were chosen so that 9-Hz (primarily three-bond) coupling gives rise to the most intense cross-peaks. As an example, the olefinic and aromatic spectral regions of the nitro compound **5b**, together with the identification of all ^{13}C-signals and a few of the ^{1}H-signals, are shown in *Fig. 6* (complete ^{1}H-signal assignments in *Fig. 5*). Starting with the established ^{1}H and ^{13}C chemical shifts, the connectivity is derived as follows. Each H_m vicinal to the NO_2 group shows three-bond coupling to the distal C_m's and to C_{ipso}, which is identified by its other strong (three-bond) cross-peak with H–C(8′) and weaker (two-bond) cross-peaks with the H_o's and H–C(7′). The lowest-field signal can only be due to C_p coupled with both the H_m's and the H_o's. Two additional cross-peaks of the H_o's must be due to three-bond coupling to the distal C_o's and to C(7′). These assignments are in accord with the chemical shifts of the C_o's and C(7′) already known from HETCOR. HMBC shows H–C(8′)/C_{ipso}, H–C(8′)/C(10′), and H–C(8′)/C(9′) cross-peaks, so that H–C(10′) can be assigned from the HETCOR spectrum. In turn, HMBC shows H–C(10′)/(C(8′) and H–C(10′)/C(12′) (140 ppm)

cross-peaks, and knowledge of the C(12′) chemical shift leads to that of H–C(12′) (HETCOR). C(12′) also shows long-range coupling with two other protons, H–C(11′) (whose chemical shift is known from NOE), and H–C(14′) (6.33 ppm), so that C(14′) is identified (HETCOR). HMBC links C(14′) with two protons, H–C(12′) (*d*) and H–C(15) (*m*), which is then linked C(15) by HETCOR. Since the cross-peak of C(15) overlaps with H–C(12)/C(10), and C(15) is expected to show three-bond coupling with only H–C(14′), H–C(12) and H–C(14′) must overlap. This conclusion is in accord with the previous assignment of H–C(14′). Assignment of C(5) follows from the weak cross-peak H–C(7)/C(5) and strong signals (not shown) due to H–C(4)/C(5) and CH_3–C(5)/C(5). These Me protons (1.72 ppm) also show long-range coupling to C(6) (137.90 ppm) which, in turn, also shows a cross-peak with H–C(8) (*Fig. 6*). CH_3–C(9′) (2.05 ppm, not shown) is coupled to the (already assigned) C(8′), C(9′), and C(10′) atoms. Of the remaining three chain Me groups, CH_3–C(9) resonates at slightly higher field (1.97 ppm) than the other two, since these protons show long-range coupling (not shown) with C(10) and a quaternary C-atom, which must, therefore, be C(9). The latter also shows cross-peaks with H–C(7), H–C(8), and/or H–C(10) (*Fig. 6*). The cross-peak (*d*) of H–C(12) at 137.35 ppm identifies C(13), and the remaining quaternary ^{13}C-signal can only be due to C(13′) (136.02 ppm).

Chemical shifts of compounds **5a**, **d**, **f** were deduced as described for **5b**. Comparison of the data reveal certain trends that were then utilized in the analyses of the spectra of **5c**, **e**, for which HMBC spectra were not determined. First, apparent first-order coupling constants of corresponding protons are similar; approximate values are: $J(7,8;7',8') \approx 16$, $J(10,11;10',11') \approx 10$–12, $J(11,12;11',12') \approx 15$, $J(14,15;14',15') \approx 10$, and $J(15,15') \approx 14$ Hz). Except for $J(7,8)$, the coupling constants $J(11,12;11',12')$ are considerably larger than the others, so that the *d*'s due to H–C(12), H–C(12′), and H–C(10′) can be identified, even in regions of overlap. Second, for the paired *d*'s of H–C(7′)/H–C(8′) in compounds **5a**, **b**, **f** the chemical shift of H–C(8′) is greater than that of H–C(7′). Third, for a given pair with non-primed and corresponding primed C-atoms, δ(non-primed) > δ(primed) for odd-numbered C-atoms, whereas the opposite is true for even-numbered C-atoms. That is, those atoms that bear formal a positive charge in the resonance structures, *i.e.* $+C(\beta)^{\delta+}=C(\alpha)-_n Ar^{\delta-}$ are deshielded; the others are shielded. Fourth, compared to β,β-carotene, in general, C(β) atoms are deshielded (*Table 4*), while C(α) atoms are shielded. Both effects decrease in a regular, albeit nonlinear manner similar to the shift changes reported for apo-β-carotenals [12]. Exceptions are the chemical shifts of C(7′) and C(8′), which are subject to anisotropy effects (of the Ar substitutent) that differ from those in β,β-carotene. The fact that all substituents, whether electron-donating or electron-withdrawing in the classical sense, cause shifts in the same direction suggests that changes in the polyene chain C electron densities are similar. Correlations of ^{13}C chemical shifts and electron densities (AM1 calculations) in these compounds are currently under investigation. A correspondence of these properties has already been demonstrated for aldehyde **4** and 7′,7′-dicyano-7′-apo-β-carotene [13].

^{1}H-NMR Data of the minor isomer of **5e** are consistent with the (7′*Z*)-structure that is expected on chemical grounds. Thus, the observed high-field shift of one CH_3 signal (1.70 *vs.* 2.05 ppm) is expected if *Me*–C(9′) lies above the plane of the Ph ring. Further, the *d*'s due to H–C(7′) and H–C(8′) in the (*E*)-isomer (6.57 and 6.90 ppm) are shifted upfield (6.43 and 6.27 ppm) in the (*Z*)-isomer, as is observed in the spectra of other (*E*/*Z*)-isomers [11] [15].

Finally, the electron-acceptor/donor substituents have a remarkable influence on the formation of carotenoid cation radicals in solution. Studies of the equilibrium $Car^{2+} + Car \rightleftharpoons 2\ Car^{+\cdot}$ (Car = carotenoid) show that $K = 23$, 9, 7, 1, 0.02, and 0.004 for **5a**, **5b**, **5c**, **5e**, **5f**, and **5d**, respectively [14]. The tendency of cation-radical formation is favored for carotenoids with strong electron-withdrawing substituents, while the forma-

tion of carotenoid dications is favored for donor substituents. The oxidation potential also increases with the strength of the electron-withdrawing group.

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Experimental Part

1. *General.* Compound **4** was obtained from *Roche Vitamins and Fine Chemicals* as a 20% oil suspension; the oil was removed by repeated trituration with hexane. Solvents were purchased from *Fisher Scientific*; silica gel *60* (70–230 mesh) for column chromatography (LC) and TLC plates ('Kieselgel' *60* F_{254}, 0.2 mm) from *EM Science*, and reagents from *Aldrich*. N_2 (*Matheson*, prepurified) was passed through a column of *ca.* 2 × 6″ *Drierite* and 2 × 1″ 3-Å *Linde* sieves. THF was distilled under N_2 from sodium benzophenone ketyl just prior to use; CH_2Cl_2 was dried over 4-Å molecular sieves. All manipulations were carried out as rapidly as possible in near-darkness, and solvents were evaporated at < 35° under reduced pressure. Purified products were stored at 4° over *Drierite* or at −20° in ampoules sealed under vacuum (10^{-4} Torr). NMR Spectra: *ca.* 0.04M $CDCl_3$ solns. and Me_4Si as internal standard (δ(H), δ(C) = 0.0 ppm), *Bruker-AM360* (^{1}H, 360.13 MHz; ^{13}C, 90.56 MHz, 5-mm ^{1}H/^{13}C dual probe) instrument. The COSY [16], HETCOR [17], and HMBC [18] spectra were obtained according to standard procedures using the pulse sequences reported previously [13]. Mass Spectra: *VG-Autospec-E* spectrometer, EI mode, 70 eV; perfluoro carbon oil for HR-MS.

2. *Benzyltriphenylphosphonium Halides* **2a–f.** A stirred soln. of the benzyl halide **1a–f** (*ca.* 10 mmol) and Ph_3P (1.05 equiv.) in dry benzene, toluene, or xylenes (50 ml), protected against moisture (*Drierite*), was heated until no further precipitate seemed to form. The cooled mixture was filtered, and the colorless product **2a–f** was triturated with benzene (3 × 10 ml) followed by hexane, dried *in vacuo*, and stored over *Drierite*. Conditions, yields, and melting points: *Table 1.*

3. *7′-Aryl-7′-apo-β-carotenes* **5a–f.** 3.1. *Method A*: *7′-(Pentafluorophenyl)-7′-apo-β-carotene* (**5a**, (all-*E*)). A stirred mixture of **2a** (0.63 g, 1.2 mmol) and THF under N_2 was treated dropwise with 2.5M BuLi in hexane (0.50 ml, 1.04 equiv.) during *ca.* 1 min. The clear, yellow soln. was stirred for 20 min and covered with Al foil, and a soln. of **4** (0.42 g, 1 mmol) in CH_2Cl_2 (10 ml) was added with a syringe. The soln. was stirred at r.t. for 3 d and then evaporated. The residue was triturated with MeOH (1 × 30 ml, 3 × 5 ml) and at once subjected to LC (silica gel (50 g), C_6H_6): **5a**, which contained *ca.* 0.5 mol H_2O (by ^{1}H-NMR). Data: *Table 2.* Anal. calc. for $C_{37}H_{41}F_5 + 0.5\ H_2O$ (589.735): C 75.36, H 7.18; found: C 75.43 and 75.35, H 7.07 and 7.07.

7′-(4-Nitrophenyl)-(**5b**, (all-*E*)), *7′-(2,4,6-trimethylphenyl)-*(**5d**, (all-*E*)), *7′-phenyl-*(**5e**), and *7′-(4-methoxyphenyl)-7′-apo-β-carotene* (**5f**, (all-*E*)) were similarly prepared, but larger amounts of BuLi (sufficient to obtain a clear soln. of the phosphorane) were added; for specifics, see *Table 2.* **5b**: Anal. calc. for $C_{37}H_{45}NO_2$ (535.774): C 82.95, H 8.47, N 2.61; found: C 82.78 and 82.71, H 8.49 and 8.50, N 2.64.

Compound **5f**, purified as above, was dissolved in $CHCl_3$ and precipitated by gradual addition of MeOH. Anal. calc. for $C_{38}H_{48}O + 0.1\ CHCl_3$ (537.74): C 85.90, H 9.10; found: C 85.99 and 85.91, H 9.10 and 9.11.

3.2. *Method B*: *7′-[(4-Methoxycarbonyl)phenyl]-7′-apo-β-carotene* (**5c**, (all-*E*)). NaH (0.10 g, 2.6 mmol; 60% mineral-oil dispersion) was rinsed with hexane under N_2, treated with THF (40 ml), **2c** (1.0 g, 2.0 mmol), and anh. MeOH (0.10 ml), and stirred at 55° for 18 h. 15-Crown-5 (3 drops) was added, followed after 2 h by **4** (0.42 g, 1 mmol). The mixture was stirred at 55–60° for 2 d, and then worked up as in *Method A.*

3.3. *Method C*: *7′-Phenyl-7′-apo-β-carotene* (**5e**). Aq. NaOH soln. (50%, 0.75 ml) was added dropwise during 1 min to a stirred soln. of **2e** (0.40 g, 1.0 mmol) and **4** (0.30 g, 0.7 mmol) in CH_2Cl_2 (10 ml). After 1 h, an additional amount of **2e** (0.2 g, 0.5 mmol; 2.1 equiv., total) was added and stirring continued for 2.5 h. CH_2Cl_2 (40 ml) and ice and H_2O (*ca.* 50 g) were then added. The org. layer was washed with cold H_2O (2 × 50 ml), dried ($MgSO_4$), and evaporated. The residue was extracted with several portions of C_6H_6/hexane 1:4 (25 ml, total) and the extract partly evaporated and then subjected to LC (silica gel (60 g), C_6H_6/hexane 1:4): **5a** (130 mg, 37%), (7′*Z*)/all-*E*) *ca.* 2:1. The major portion of the (all-*E*)-isomer (38 mg, 11%) was insoluble in hexane (5 ml). The hexane-soluble part was dissolved in C_6H_6 (1 ml) and then treated dropwise with MeOH (5 ml): (7′*Z*)/(all-*E*) mixture *ca.* 9:1 (74 mg, 21%).

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