Prolycopene, a Tetra-*cis* Carotene with Two Hindered *cis* Double Bonds

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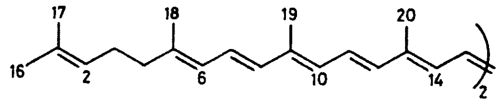
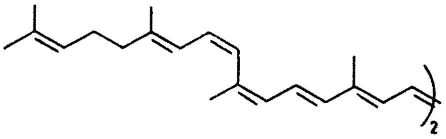
Summary Prolycopene is shown to be 7,9,7′,9′-tetra-*cis*-ψ,ψ-carotene by application of ^{1}H-n.m.r. spectroscopy at 270 and 360 MHz and by ^{13}C-n.m.r. spectroscopy.

Prolycopene was first isolated by Zechmeister[1] from tangerine tomatoes and subsequently from a number of other plants.[2] It was shown[2] to be a poly-*cis* isomer o lycopene (**1**) with an unusual visible absorption spectrum where the absorption maximum was at 35 nm shorter wavelength than the corresponding all-*trans* isomer. The number and position of the *cis* double bonds were not ascertained. We report here the complete assignment of stereochemistry of this novel carotene.



(1)



(2)

A previous examination of the ^{1}H-n.m.r. spectrum showed that the molecule was probably symmetric with significant changes of the chemical shifts of two of the in-chain methyl group signals.[3] In the meantime, these results were confirmed by the spectra run at 270 and eventually at 360 MHz. Here it was possible to make a complete assignment of all the signals by means of the appropriate decoupling experiments. A complete assignment of the 220 MHz spectrum of all-*trans*-lycopene has already been reported.[4] Reinvestigation of this spectrum at 270 MHz and additional decoupling experiments fully confirmed the previous assignments. A comparison of the data of the all-*trans* compound and its poly-*cis* isomer allowed some important conclusions to be drawn concerning the structure of the latter. The relevant ^{1}H-n.m.r. data of both compounds are collected in Table 1.

TABLE 1. 270 MHz ^{1}H-N.m.r. data (δ values; J in Hz) of lycopene and prolycopene; solvent $CDCl_3$. Chemical shift differences $\Delta = \delta_{cis} - \delta_{trans}$ in p.p.m.

	H–2	H–3/H–4	H–6	H–7	H–8	H–10	H–11	H–12	H–14	H–15
Lycopene	5·11	*ca.* 2·11	5·95	6·49	6·25	6·19	6·64	6·35	6·23	6·63
Prolycopene	5·08	*ca.* 2·06	6·11	6·30	6·02	6·04	6·48	6·26	6·20	6·58
Δ	−0·03	*ca.* −0·05	0·16	−0·19	−0·22	−0·16	−0·16	−0·09	−0·03	−0·05

	H–16	H–17	H–18	H–19	H–20	$J_{6,7}$	$J_{7,8}$	$J_{10,11}$	$J_{11,12}$
Lycopene	1·69	1·62	1·82	1·97	1·97	11·4	15	11·5	14·8
Prolycopene	1·65	1·56	1·80	2·00	1·87	*ca.* 11·5	*ca.* 11·5	11·3	14·7
Δ	−0·04	−0·06	−0·02	0·03	−0·10				

In the spectrum of prolycopene, the characteristic AA′BB′ spectrum of the 14,14′- and 15,15′-protons showed only minor chemical shift changes compared to the all-*trans* isomer. Hence it was concluded that the 15(15′) double bond was *trans*. Decoupling experiments were used to relate the protons at 2 to 3, 16 and 17; 4 to 6; 11 to 10 and 12; 14 to 20; and 19 to 10.† In this way it was shown that ${}^{3}J_{7,8}$ = *ca.* 11·7 Hz and ${}^{3}J_{11,12}$ = *ca.* 15 Hz. Hence the 7(8) double bond is hindered *cis* and the 11(12)-double bond is *trans*.

Although the ^{13}C-n.m.r. spectrum of prolycopene was not yet completely assignable (see Table 2) the stereochemistry of the trisubstituted double bonds 5(6), 9(10), and 13(14) could be unequivocally deduced.

TABLE 2. ^{13}C-N.m.r. shifts δ in p.p.m. and assignment of the signals of lycopene (*ca.* 33 °C) and prolycopene (10 °C). Relevant chemical shift differences $\Delta = \delta_{cis} - \delta_{trans} \geqslant 0{\cdot}4$ p.p.m. between both spectra; 68 MHz, solvent $CDCl_3$.

	C–1	C–2	C–3	C–4	C–5	C–6	C–7	C–8	C–9	C–10
Lycopene	131·64	124·12	26·83	40·30	139·30	125·94	124·87	135·54	136·15	131·64
Prolycopene	131·77	123·92	26·66	40·34	140·99	122·43	126·13[a]	126·15[a]	135·50	129·72[b]
$\Delta = \delta_{cis} - \delta_{trans}$	—	—	—	—	1·7	−3·5	1·3	−9·4	−0·7	−1·9

	C–11	C–12	C–13	C–14	C–15	C–16	C–17	C–18	C–19	C–20
Lycopene	125·21	137·46	136·54	132·71	130·17	25·66	17·70	16·97	12·90	12·81
Prolycopene	125·82	136·10	136·36	132·00	129·86[b]	25·69	17·64	16·61	24·79	12·71
$\Delta = \delta_{cis} - \delta_{trans}$	0·6	−1·4	—	−0·7	—	—	—	−0·4	11·9	—

[a,b] Corresponding assignments may be interchanged.

A *cis* configuration about a double bond in a carotenoid is associated with characteristic shifts in the ^{13}C (and ^{1}H) n.m.r. bands of neighbouring positions.[5,6] Since the 11(12) and 15(15′) double bonds were known to be *trans*, a ^{13}C methyl signal at δ 12·7 p.p.m., at nearly the same position as the signal in all-*trans*-lycopene, was assigned to an in-chain methyl group on a *trans*-double bond at 13(14). A *trans* 5(6)-double bond was revealed by signals at δ 16·6 and 40·3 p.p.m. attributable to the methyl at C-5 and the 4-methylene group, respectively (*cf.* all-*trans*-lycopene, δ 17·0 and 40·3 p.p.m., respectively). A signal at δ 24·8 was assigned to the methyl at C-9; the downfield shift of 11·9 p.p.m. from the corresponding signal (δ 12·9) in the all-*trans*-isomer appears to be typical for such structural sub-units with two consecutive *cis* bonds as was recently reported for 11,13-di-*cis* retinol (Δ = 11·3 p.p.m.) and analogues (Δ = 11·5 p.p.m.).[6]

Hence it is concluded that prolycopene is 7,9,7′,9′-tetra-*cis*-lycopene (**2**). The dramatic change in the visible

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† Owing to the symmetry of the molecule the following statements also relate to protons at positions with primed numbers.

spectrum is clearly due to the presence of two hindered *cis* double bonds.[7] Work is in progress to confirm this stereochemistry by the synthesis of this compound.

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