142. Synthesis, Isolation, and NMR-Spectroscopic Characterization of Fourteen (*Z*)-Isomers of Lycopene and of Some Acetylenic Didehydro- and Tetradehydrolycopenes

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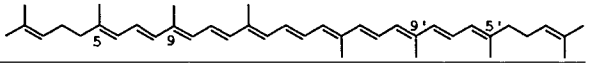
Eight (*Z*)-isomers of lycopene were prepared by stereocontrolled syntheses and fully characterized by ^{1}H-NMR, ^{13}C-NMR, mass, and UV/VIS spectroscopy: (5*Z*)-, (7*Z*)-, (15*Z*)-, (5*Z*,5′*Z*)-, (7*Z*,7′*Z*)-, (7*Z*,9*Z*)-, (9*Z*,9′*Z*)-, and (7*Z*,9*Z*,7′*Z*,9′*Z*)-lycopene. Six additional (*Z*)-isomers, namely (9*Z*)-, (13*Z*)-, (5*Z*,9′*Z*)-, (9*Z*,13′*Z*)-, (5*Z*,9*Z*,5′*Z*)-, and (5*Z*,13*Z*,5′*Z*)-lycopene, were isolated in small quantities from isomer mixtures by semiprep. HPLC and were identified by ^{1}H-NMR spectroscopy.

1. Introduction. – *Zechmeister*'s standard work on *cis-trans* isomeric carotenoids published in 1962 [1] lists over 40 lycopene isomers which were either isolated from nature or obtained by stereomutation experiments and synthesis. Regrettably, the spectroscopic techniques available at that time did not allow for a definite assignment of (*E*/*Z*)-geometry to these isomers. Years later, structure elucidation of (*E*/*Z*)-isomeric carotenoids became greatly facilitated by the progress in high-resolution NMR spectroscopy [2]. An illustrative example is prolycopene, a pigment first isolated in 1941 by *Zechmeister* and coworkers [3] from ripe fruits of the Tangerine tomato and proposed to be a (poly-*Z*)-isomer of lycopene. In 1979, the (7*Z*,9*Z*,7′*Z*,9′*Z*)-geometry of this intriguing carotenoid was independently established by *Englert et al.* [4] and *Pattenden et al.* [5], using advanced ^{1}H- and ^{13}C-NMR spectroscopy.

Synthesis, characterization, and HPLC data of (5*Z*)- and (5*Z*,5′*Z*)-lycopene were reported by *Eugster* and coworkers [6] [7] in context of their extensive investigation of the biological ring closure of (5*E*)- and (5*Z*)-ψ-end groups to cyclic end groups.

This paper summarizes the results of our investigation of the 15 (*E*/*Z*)-isomeric lycopenes listed in *Table 1*. The nine isomers **1**–**9** were prepared by total synthesis and

Table 1. *(E/Z)-Isomeric Lycopenes* **1**–**15**



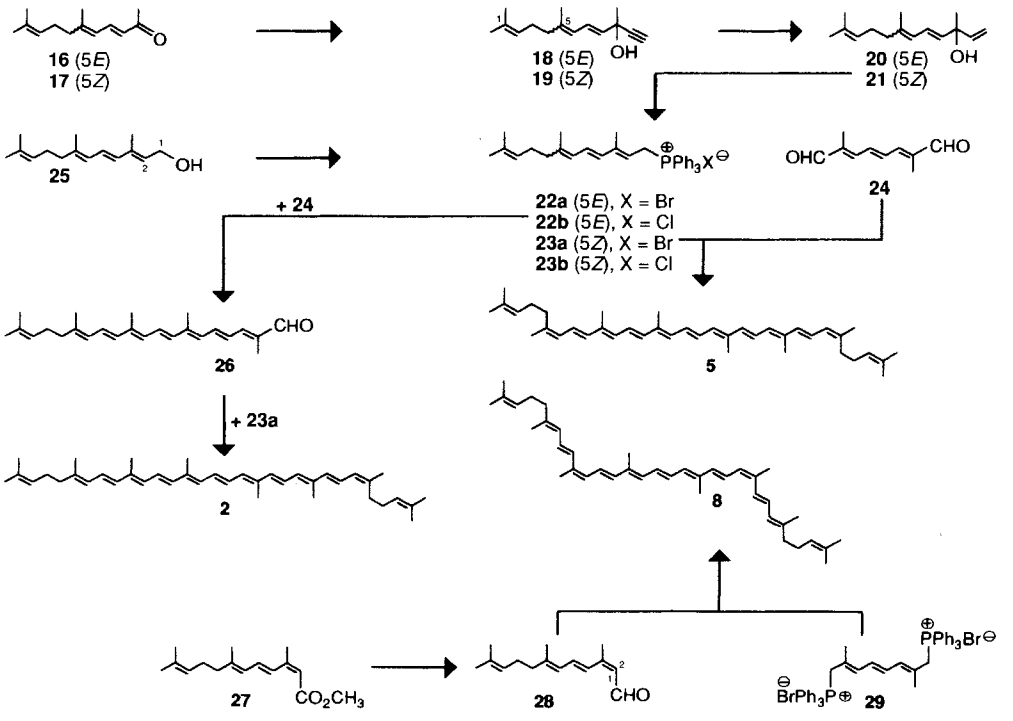
Total synthesis		Isolation by HPLC	
1	(all-*E*)	**10**	(9*Z*)
2	(5*Z*)	**11**	(13*Z*)
3	(7*Z*)	**12**	(5*Z*,9′*Z*)
4	(15*Z*)	**13**	(9*Z*,13′*Z*)
5	(5*Z*,5′*Z*)	**14**	(5*Z*,9*Z*,5′*Z*)
6	(7*Z*,7′*Z*)	**15**	(5*Z*,13*Z*,5′*Z*)
7	(7*Z*,9*Z*)		
8	(9*Z*,9′*Z*)		
9	(7*Z*,9*Z*,7′*Z*,9′*Z*)		

fully characterized by ^{1}H- and ^{13}C-NMR, UV/VIS, mass, and IR spectroscopy. In addition, the six (*Z*)-isomers **10–15** were isolated in small amounts between a few μg and up to *ca.* 100 μg from isomeric mixtures and unequivocally identified by ^{1}H-NMR spectra.

2. Synthesis. – The stereocontrolled synthesis of a carotenoid polyene chain with one or more (*Z*)-double bonds remains a challenging task for the preparative chemist [8]. The *Wittig* condensation, considered as the most versatile coupling reaction in polyene chemistry, generally leads to mixtures of (*E*)- and (*Z*)-isomers with regard to the newly formed double bonds. Additional difficulties arise from the frequently observed stereomutation of intermediate α,β-unsaturated phosphonium ylides and from the general tendency of carotenoids to isomerize. Despite these drawbacks, we applied the $C_{15} + C_{10} + C_{15}$ *Wittig* scheme to the syntheses of the lycopene isomers **2–9** (*Table 1*), with the exception of (15*Z*)-lycopene (**4**) which was prepared by the $C_{10} + C_{20} + C_{10}$ *Wittig* route described by *Isler et al.* [9]. Particular care was taken to prepare and use stereochemically pure phosphonium salts and polyene aldehydes for the *Wittig* condensation, to avoid the formation of complex isomeric mixtures which would have rendered the purification very difficult. Thus, the synthesized (*Z*)-isomers of lycopene could all be purified by crystallization and were obtained in 50 mg to g quantities with HPLC purities ranging from 92 to 98 area-% (except 86 area-% for **7**).

For the preparation of (5*Z*)-lycopene (**2**) and (5*Z*,5′*Z*)-lycopene (**5**) previously synthesized by *Eugster* and *Zumbrunn* [6], a shorter and more efficient synthetic route was

Scheme 1



elaborated (*Scheme 1*). First, the conversion of (all-*E*)- and (5*Z*)-9-vinyl-ψ-ionol[1]) (**20** and **21**, resp.) to the corresponding C_{15}-phosphonium salts was examined[2]). These substrates were prepared by C_2-elongation of (all-*E*)- and (5*Z*)-ψ-ionone (**16** and **17**, resp.) [10] *via* **18** and **19**, respectively. Treatment of **20** with $PPh_3 \cdot HBr$ in MeOH at room temperature led, however, to a complex mixture of stereoisomeric and, presumably, regioisomeric phosphonium salts. HPLC Analysis of the crude product showed the presence of the primary *Wittig* salts **22a** and **23a** (*ca.* 1:1), demonstrating that stereomutation at C(5)=C(6) had occurred to a substantial degree. When the corresponding (5*Z*)-isomer **21** was reacted with $PPh_3 \cdot HBr$ under the same conditions, a qualitatively similar mixture of phosphonium salts was obtained. Interestingly, it was the phosphonium salt **23a** which preferentially precipitated from both reaction mixtures after dissolution in AcOEt; the (5*Z*,7*E*,9*E*)-geometry of the recrystallized compound was established by ^1H- and ^{13}C-NMR spectroscopy. Starting with commercially available ψ-ionone, a 1:2 mixture of the isomers **16** and **17**, larger amounts of **23a** were prepared by this expeditious route.

The condensation of C_{15}-phosphonium salt **23a** (2.6 equiv.) with C_{10}-dialdehyde **24** was studied next with special attention given to the possibility that the intermediate phosphonium ylide may undergo an unwanted stereomutation. Fortunately, the *Wittig* reaction, carried out with NaOMe in CH_2Cl_2, afforded (5*Z*,5′*Z*)-lycopene (**5**) with retention of the (*Z*)-configuration of the terminal conjugated double bond.

First attempts to prepare the phosphonium salt **22** with defined (all-*E*)-geometry from the known (all-*E*)-4,5-didehydrofarnesol[1]) (**25**) [13], either with $PPh_3 \cdot HBr$ [13] or by mesylation with $MeSO_2Cl/Et_3N$ and treatment with PPh_3, led again to complex mixtures including isomerization of the polyene chain (in [13], **25**, but not **22a**, was spectroscopically characterized). A surprising solution to this problem was finally found by reacting (all-*E*)-9-vinyl-ψ-ionol (**20**) with PPh_3 in AcOH. Under these conditions, stereomutation at C(5) and formation of regioisomeric compounds were suppressed to a large extent. After AcO/Cl anion exchange, (all-*E*)-phosphonium chloride **22b** was isolated as amorphous solid [14]. Condensation of **22b** with an equimolar amount of the C_{10}-dialdehyde **24** in presence of NaOMe yielded pure (all-*E*)-12′-apo-ψ-caroten-12′-al (**26**) [11b], after recrystallization from hexane. Finally, a second *Wittig* reaction of **26** with phosphonium salt **23a** afforded pure (5*Z*)-lycopene (**2**).

For the preparation of (9*Z*,9′*Z*)-lycopene (**8**), an inverse *Wittig* strategy of reacting (2*Z*)-4,5-didehydrofarnesal[1]) (**28**) with the C_{10}-diphosphonium salt **29** [15] was chosen. The requisite (2*Z*)-aldehyde **28** was obtained from the known methyl (2*Z*)-4,5-didehydrofarnesoate[1]) (**27**) [16] by reduction with diisobutylaluminium hydride (DIBAH) and oxidation with MnO_2. Condensation of **28** with the preformed dianion of the diphosphonium salt **29** gave an isomeric mixture from which pure (9*Z*,9′*Z*)-lycopene (**8**) was isolated in modest yield after isomerization and crystallization from hexane.

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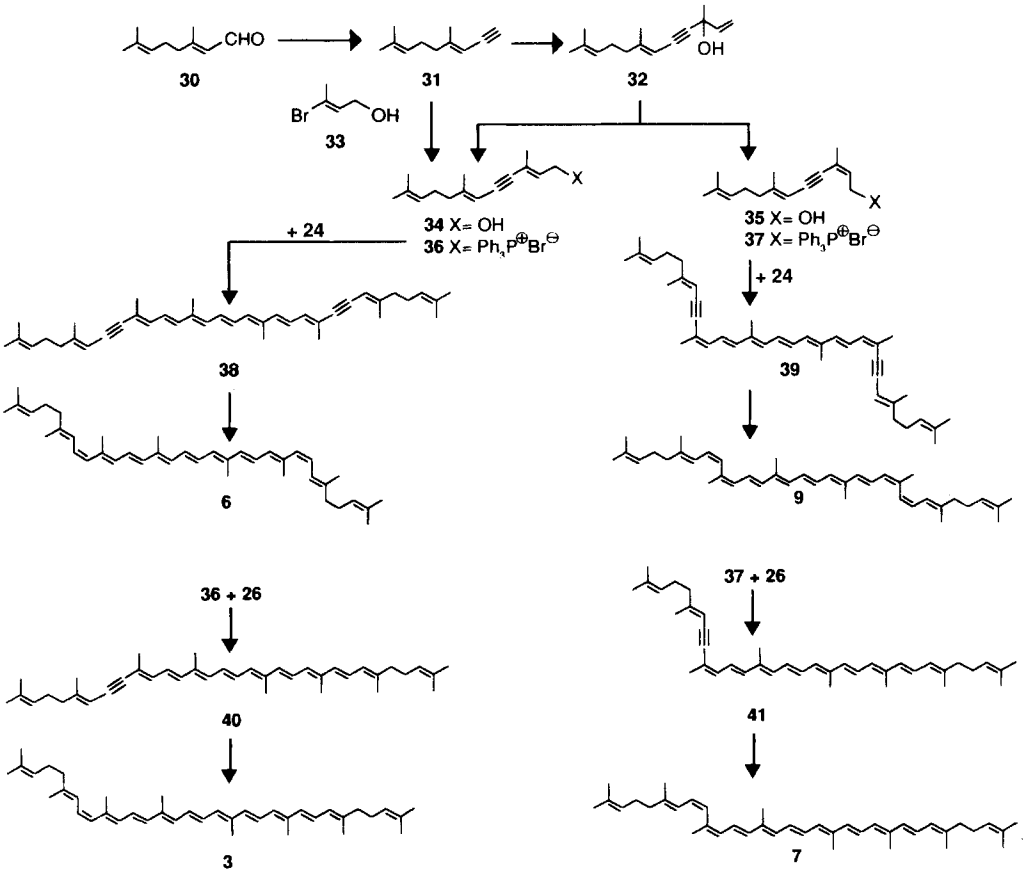
[1]) Carotenoid numbering is used throughout the *General Part*, except for **25**, **27**, and **28**; for systematic names, see *Exper. Part.*

[2]) Phosphonium-salt formation from vinyl-ψ-ionol (presumably a mixture **20**/**21**) and $PPh_3 \cdot HX$ was reported without spectroscopic characterization [11] and without configurational assignment to an isolated crystalline salt [12].

Scheme 2



The syntheses of the lycopene isomers **3**, **6**, **7**, and **9** are based on a strategy of forming the requisite disubstituted (7*Z*)- and (7*Z*,7′*Z*)-double bonds, respectively, in the last step by semihydrogenation of the corresponding acetylenic C_{40}-precursors (*Scheme 2*). Starting material for these substrates was (*E*)-citral (**30**) which was converted to the known acetylenic hydrocarbon **31** [17] by a standard C_1-elongation method [18]. Addition of **31** to methyl vinyl ketone in presence of LiBr afforded the tertiary alcohol **32**. Allylic rearrangement in AcOH/NaOAc and subsequent saponification of the formed acetate with KOH gave a mixture of the two isomeric alcohols **34** and **35** in a 1:2 ratio. The latter were separated by chromatography, converted with PBr_3 to the corresponding bromides, and reacted with PPh_3 to yield, without observable isomerization, the *Wittig* salts **36** and **37**. Later, a more efficient method for the preparation of (all-*E*)-alcohol **34** was found in the coupling reaction of **31** with the known (*E*)-3-bromobut-2-en-1-ol (**33**) [19]. C–C Bond formation was carried out in presence of catalytic amounts of $[Pd(PPh_3)_4]$ and CuI in Me_2NH/C_6H_6 [20] and afforded in high yield alcohol **34**. *Wittig* reaction of the phosphonium salt **36** with the C_{10}-dialdehyde **24** with BuLi as base, followed by thermal isomerization, gave pure (all-*E*)-7,8,7′,8′-tetradehydrolycopene (**38**). In the final step, the

two triple bonds of **38** were hydrogenated over desactivated Pd on $CaCO_3$ to yield pure (7*Z*,7′*Z*)-lycopene (**6**).

The analogous reaction sequence was followed in the synthesis of (7*Z*,9*Z*,7′*Z*,9′*Z*)-lycopene (= prolycopene; **9**). The last steps and intermediates of our route [21] **35** → **37** → **39** → **9** coincide with the reported total synthesis of prolycopene which was independently accomplished by *Pattenden* and *Robson* [22]. However, our different experimental conditions resulted in a significantly higher yield in the *Wittig* condensation **37** → **39** and the semihydrogenation step **39** → **9**.

Condensation of the phosphonium salt **36** with 12′-apolycopenal (**26**) was again carried out with BuLi as base and led to the configurationally pure C_{40}-precursor **40**. Semihydrogenation of the single triple bond over *Lindlar* catalyst in presence of quinoline gave a clean conversion to (7*Z*)-lycopene (**3**). The rather sensitive (7*Z*,9*Z*)-lycopene (**7**) was prepared in the same manner utilizing the isomeric phosphonium salt **37**.

3. HPLC and Isolation of Isomers. – An analytical separation of (all-*E*)-, (5*Z*)-, and (5*Z*,5′*Z*)-lycopene by high performance liquid chromatography (HPLC) was previously achieved by *Eugster* and coworkers [7] on a *Spherisorb-ODS* column with MeCN/THF 92:8. Our own investigation resulted in a highly efficient HPLC method which separates the above mentioned and many other (*Z*)-isomers of lycopene. The system is based on *Nucleosil 300-5* as stationary phase and hexane/*N*-ethyldiisopropylamine 2000:1 as mo-

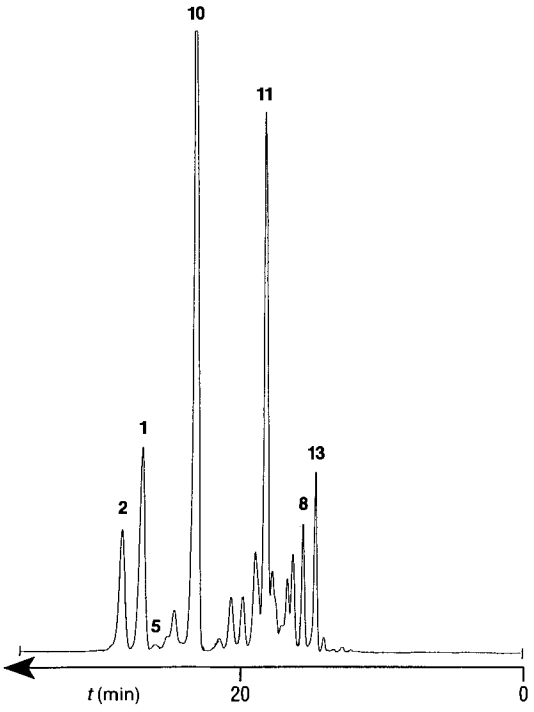


Fig. 1. *HPLC of a mother liquor obtained after stereomutation of (all-*E*)-lycopene* (**1**). *Nucleosil 300-5*, hexane/Et(i-Pr)$_2$N (0.05%).

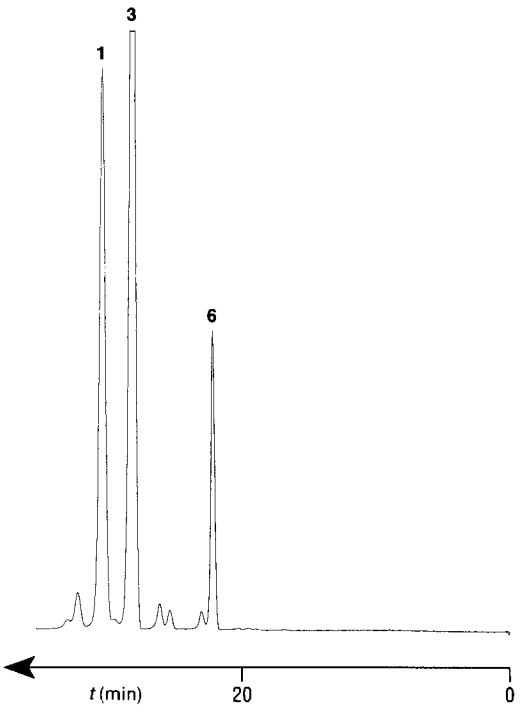


Fig. 2. *HPLC of the product formed in the* Wittig *reaction of (geranyl)triphenylphosphonium bromide and crocetindialdehyde. Nucleosil 300-5*, hexane/Et(i-Pr)$_2$N (0.05%).

bile phase. It was used for the isolation of small quantities of the (*Z*)-isomeric lycopenes **10**–**15** listed in *Table 1* (only a few μg of **13** and between 10–100 μg of the remaining five isomers were isolated for spectroscopic investigation). *Fig. 1* presents the HPLC analysis of a mother liquor obtained by isomerizing (all-*E*)-lycopene (**1**) in refluxing heptane, followed by filtration. From such a mixture, the isomers **10** (9*Z*), **11** (13*Z*) [23], and **13** (9*Z*,13′*Z*) were separated and their structures determined by ^{1}H-NMR spectroscopy (tentative assignments of the (9*Z*)- and/or (13*Z*)-geometry based on IR and/or UV/VIS data were reported, *e.g.* [23]).

Identification of the peaks of the isomers **1**, **2**, **5**, and **8** was carried out by spiking experiments using the corresponding synthetic reference compounds. For the isomers **1**, **2**, and **8**, the assignments were recently confirmed by the UV/VIS spectra measured with a photodiode-array HPLC detector.

The lycopene isomers **14** (5*Z*,9*Z*,5′*Z*) and **15** (5*Z*, 13*Z*,5′*Z*) were isolated from a mother liquor obtained after analogous thermal stereomutation of (5*Z*,5′*Z*)-lycopene (**5**), while (5*Z*,9′*Z*)-lycopene (**12**) was isolated from a mixture obtained in the course of the synthesis of (5*Z*)-lycopene (**2**).

The HPLC profile shown in *Fig. 2* presents a mixture of the lycopene isomers **1** (all-*E*), **3** (7*Z*), and **6** (7*Z*,7′*Z*) as formed in the *Wittig* reaction of geranyltriphenylphosphonium bromide with crocetindialdehyde [9] in presence of NaOMe in CH_2Cl_2.

4. Spectroscopic Studies. – *NMR Spectra.* All compounds in this investigation were fully characterized by ^{1}H-NMR and, in part, by ^{13}C-NMR. In all cases where the assignments of the ^{1}H-NMR spectra were not straightforward, a combination of 1D and particularly of 2D techniques was routinely applied in order to unambiguously verify the assignments and thus the molecular structures. This included 1D techniques such as nuclear *Overhauser* effect (NOE) difference experiments, double INDOR difference (DID) [24], *i.e.* a simple and efficient method for the elucidation of *J*-connectivities in crowded ^{1}H-NMR spectra of carotenoids [2], homonuclear COSY, DEPT, heteronuclear ^{1}H,^{13}C-COSY tuned to one-bond and to multiple-bond C,H couplings, ^{1}H-double quantum 2D [25], and rotating-frame nuclear *Overhauser* 2D spectroscopy (ROESY) [26]. Typical experimental conditions for these experiments are given in the *Exper. Part.* The complete assignments of the ^{1}H-NMR signals of the lycopenes **1**–**15**, the dehydrolycopenes **38**–**41**, and (all-*E*)-15,15′-didehydrolycopene are given in *Table 2*. The corresponding ^{13}C-NMR assignments of nine lycopenes and five dehydrolycopenes, which were available in sufficiently large quantities, are collected in *Table 3*. In the last row of either *Table*, the different types of 1D and 2D experiments used to derive the assignments are indicated.

^{1}H-NMR. A stereomutation (*E*) → (*Z*) at C(7)=C(8) or C(11)=C(12) (and/or C(7′)=C(8′) or C(11′)=C(12′)) is readily identified by inspection of the value of the corresponding ^3J(H,H) which is for carotenoids in the range of 11.5 and 12.8 Hz for (*Z*)-bonds and between 13.5 and 16.8 Hz for (*E*)-bonds. The determination of all other sites of stereomutation mainly relies on the observed chemical-shift difference of the individual protons (and C-atoms) caused by stereomutation.

We previously showed that in the ^{1}H-NMR spectra, this so-called isomerization shifts $\Delta\delta = \delta((Z)) - \delta((E))$ (in ppm) for the different protons are indeed very characteristic and informative for the position of the stereomutated bond(s). From more than 40 geometrical (mono-*Z*)- and (di-*Z*)-isomers of several types of C_{40} carotenoids, a number of experimental rules were derived [2] which later helped in the identification of numerous other geometrical isomers, *e.g.* of astaxanthin diacetate [27], β,β-carotene [28], and zeaxanthin [29]. The $\Delta\delta$ values observed for the isomers of lycopene were included in *Tables 2* and *3*, since they are thought to be relevant for the confirmation of the individual structures.

Table 2. *^{1}H-NMR Data of Isomeric Lycopenes* **1**–**15**, *Dehydrolycopenes* **38**–**41**, *and (all-*E*)-15,15′-Didehydrolycopene.* δ in ppm; shift differences $\Delta\delta = \delta((Z)) - \delta((E))$ for $|\Delta\delta| > 0.02$ ppm. Solvent $CDCl_3$.

	Lycopenes																	
	1 (all-*E*)	**2** (5*Z*)		**3** (7*Z*)		**10** (9*Z*)		**11** (13*Z*)		**4** (15*Z*)		**5** (5*Z*,5′*Z*)		**6** (7*Z*,7′*Z*)		**8** (9*Z*,9′*Z*)		**12** (5*Z*,9′*Z*)	
	δ	δ	$\Delta\delta$	δ	$\Delta\delta$	δ	$\Delta\delta$	δ	$\Delta\delta$	δ	$\Delta\delta$	δ	$\Delta\delta$	δ	$\Delta\delta$	δ	$\Delta\delta$	δ	$\Delta\delta$
H–C(2)	5.11	5.15	0.04	5.11		5.12		5.11		5.11		5.15	0.04	5.12		5.12		5.15	0.04
H–C(2′)		5.11		5.11		5.12		5.11										5.12	
2 H–C(3)	*ca.* 2.11	*ca.* 2.13		*ca.* 2.13		*ca.* 2.13		*ca.* 2.12		*ca.* 2.12		*ca.* 2.13		*ca.* 2.13		*ca.* 2.13		*ca.* 2.13	
2 H–C(3′)		*ca.* 2.12		*ca.* 2.11		*ca.* 2.11		*ca.* 2.12										*ca.* 2.13	
2 H–C(4)	*ca.* 2.11	2.23	0.12	*ca.* 2.13		*ca.* 2.13		*ca.* 2.12		*ca.* 2.12		*ca.* 2.24	0.13	*ca.* 2.13		*ca.* 2.13		*ca.* 2.23	0.12
2 H–C(4′)		*ca.* 2.12		*ca.* 2.11		*ca.* 2.11		*ca.* 2.12										*ca.* 2.12	
H–C(6)	5.95	5.94		6.44	0.49	6.03	0.08	5.97		5.97		5.94		6.44	0.49	6.04	0.09	5.94	
H–C(6′)		5.95		5.96		5.95		5.95										6.03	0.08
H–C(7)	6.49	6.49		6.16	–0.33	6.51		6.51		6.50		6.49		6.16	–0.33	6.51		6.48	
H–C(7′)		6.49		6.49		6.49		6.49										6.52	0.03
H–C(8)	6.25	6.22	–0.03	5.86	–0.39	6.70	0.54	6.26		6.27		6.22	–0.03	5.86	–0.39	6.79	0.54	6.22	–0.03
H–C(8′)		6.25		6.25		6.25		6.25										6.79	0.54
H–C(10)	6.18	*ca.* 6.18		6.24	0.06	6.04	–0.14	6.23	0.05	6.20		6.18		6.23	0.05	6.05	–0.13	6.18	
H–C(10′)		*ca.* 6.18		6.19		6.18		6.19										6.04	–0.14
H–C(11)	6.64	6.63		6.60	–0.04	6.80	0.16	6.64		6.67	0.03	6.63		6.60	–0.04	6.80	0.16	6.63	
H–C(11′)		6.63		6.64		6.63		6.63										6.80	0.16
H–C(12)	6.35	6.35		6.36		6.28	–0.07	6.88	0.53	6.43	0.08	6.35		6.36		6.29	–0.06	6.35	
H–C(12′)		6.35		6.36		6.35		6.36										6.28	–0.07
H–C(14)	6.25	6.25		6.26		*ca.* 6.25		6.11	–0.14	6.68	0.43	6.25		6.25		6.25		*ca.* 6.24	
H–C(14′)		6.25		6.26		*ca.* 6.25		6.25										*ca.* 6.24	
H–C(15)	6.62	6.63		*ca.* 6.64		6.62		6.80	0.18	6.40	–0.22	6.63		6.63		6.63		6.62	
H–C(15′)		6.63		*ca.* 6.64		6.62		6.56										6.62	
Me(16)	1.688	1.684		1.696		1.694		1.689		1.692		1.686		1.697		1.695		*ca.* 1.687	
Me(16′)		1.684		1.689		1.690		1.689										*ca.* 1.691	
Me(17)	1.612	1.622		1.615		1.620		1.616		1.619		1.624		1.615		1.622		1.622	
Me(17′)		1.612		1.615		1.616		1.616										1.622	
Me(18)	1.818	1.818		1.786	–0.03	1.820		*ca.* 1.821		1.825		1.825		1.788		1.829		1.824	
Me(18′)		1.814		1.819		1.827		*ca.* 1.821										1.824	
Me(19)	1.968	1.949		2.077	0.11	*ca.* 1.967		1.960[h])		1.978		1.953		2.079	0.11	1.971		1.950	
Me(19′)		*ca.* 1.963		*ca.* 1.97		*ca.* 1.967		1.967[h])										1.965	
Me(20)	1.968	*ca.* 1.963		*ca.* 1.97		1.979		1.974[h])		1.969		1.966		1.976		1.979		1.965	
Me(20′)		*ca.* 1.963		*ca.* 1.97		*ca.* 1.967		1.989[h])										1.977	
Techniques	[a])[b])			[b])[c])[d])[e])		[a])		[c])		[d])		[b])[f])		[e])		[a])[e])		[d])	

[a]) Double resonance technique. [b]) NOE difference experiment. [c]) DID technique; ^{1}H,^{1}H-COSY. [d]) Magnitude. [e]) Phase-sensitive technique. [f]) Double-quantum 2D experiment. [g]) 2D ROESY technique. [h]) Corresponding assignments may be interchanged.

Table 2 (cont.)

	Lycopenes										*7,8,7′,8′-Tetra-dehydro-lycopenes*			*7,8-Di-dehydro-lycopenes*			*15,15′-Di-dehydro-lycopene*
	7 (7Z,9Z)		**9** (7Z,9Z,7′Z,9′Z)		**13** (9Z,13′Z)		**14** (5Z,9Z,5′Z)		**15** (5Z,13Z,5′Z)		**38** (all-*E*)	**39** (9Z,9′Z)		**40** (all-*E*)	**41** (9Z)		(all-*E*)
	δ	*Δδ*	*δ*	*Δδ*	*δ*	*Δδ*	*δ*	*Δδ*	*δ*	*Δδ*	*δ*	*δ*	*Δδ*	*δ*	*δ*	*Δδ*	*δ*
H–C(2)	5.07	–0.04	5.07	–0.04	5.12		5.15	0.04	5.15	0.04	5.09	5.10		5.09	5.11		5.11
H–C(2′)	5.11				5.12		5.15		5.15					5.11	5.11		
2 H–C(3)	*ca.* 2.06	–0.05	*ca.* 2.07	–0.04	*ca.* 2.13		*ca.* 2.12		*ca.* 2.12		*ca.* 2.13	*ca.* 2.16	0.03	*ca.* 2.13	*ca.* 2.16	0.03	*ca.* 2.11
2 H–C(3′)	*ca.* 2.11				*ca.* 2.13		*ca.* 2.12		*ca.* 2.12					*ca.* 2.11	*ca.* 2.11		
2 H–C(4)	*ca.* 2.06	–0.05	*ca.* 2.07	–0.04	*ca.* 2.13		*ca.* 2.24	0.13	*ca.* 2.24	0.13	*ca.* 2.13	*ca.* 2.16	0.03	*ca.* 2.13	*ca.* 2.16	0.03	*ca.* 2.11
2 H–C(4′)	*ca.* 2.11				*ca.* 2.13		*ca.* 2.24	0.13	*ca.* 2.24	0.13				*ca.* 2.11	*ca.* 2.11		
H–C(6)	6.12	0.17	6.11	0.16	6.03	0.08	6.03	0.08	5.96		5.45	5.52	0.07	5.45	5.53	0.08	5.96
H–C(6′)	5.95				5.97		5.94		5.95					5.95	5.96		
H–C(7)	6.31	–0.18	6.30	–0.19	*ca.* 6.51		6.50		6.51		–	–	–	–	–		6.52
H–C(7′)	6.49				*ca.* 6.51		6.49		6.49					6.49	6.49		
H–C(8)	6.03	–0.22	6.02	–0.23	6.79	0.54	6.76	0.51	6.23		–	–	–	–	–		6.25
H–C(8′)	6.25				6.26		6.23		6.24					6.25	6.26		
H–C(10)	6.04	–0.14	6.03	–0.15	6.05	–0.13	6.04	–0.14	6.22	0.04	6.46	6.29	–0.17	6.45	6.30	–0.15	6.16
H–C(10′)	6.18				6.23	+0.05	6.18		6.18					6.18	6.19		
H–C(11)	6.48	0.16	6.47	–0.17	6.79	0.15	6.79	0.15	6.63		6.51	6.80	0.29	6.50	6.79	0.29	6.69
H–C(11′)	6.63				6.64		6.63		6.63					6.64	6.64		
H–C(12)	6.26	0.09	6.26	–0.09	6.28	–0.07	6.28	–0.07	6.89	0.54	6.34	6.34		6.34	6.36		6.34
H–C(12′)	6.35				6.88	0.53	6.35		6.36					6.35	6.36		
H–C(14)	6.21	–0.03	6.20	–0.05	6.23		*ca.* 6.25		6.11	–0.14	6.27	6.25		6.27	6.26		5.72
H–C(14′)	6.24				6.10	–0.15	*ca.* 6.25		6.25					6.25	6.26		
H–C(15)	*ca.* 6.61		6.58	–0.04	6.59	–0.03	6.63		6.81	0.19	6.64	6.62		*ca.* 6.63	6.63		–
H–C(15′)	*ca.* 6.61				6.79	0.16	6.63		6.56	–0.06				*ca.* 6.63	6.63		
Me(16)	1.653	–0.04	1.651	–0.04	1.692		1.687		1.690		1.686	1.691		1.685	1.693		1.688
Me(16′)	1.688				1.692		1.687		1.690					1.685	1.689		
Me(17)	1.563	–0.05	1.561	–0.05	1.619		1.625		1.628		1.607	1.613		1.607	1.616		1.614
Me(17′)	1.615				1.619		1.625		1.628					1.612	1.616		
Me(18)	1.802		1.799		1.825		1.845	0.03	1.832		1.924	1.981	0.06	1.922	1.985	0.06	1.823
Me(18′)	1.819				1.825		1.827		1.829					1.816	1.820		
Me(19)	2.003	0.04	1.999	0.03	1.986[h])		1.955		1.961		1.992	1.975		1.986	1.978		1.978
Me(19′)	1.965				1.970[h])		1.955		1.954					1.966	1.968		
Me(20)	1.879	–0.09	1.871	–0.10	1.970[h])		1.976[h])		1.971		1.952	1.945		1.945	1.951		2.107
Me(20′)	1.965				1.970[h])		1.967[h])		1.961					1.966	1.948		
Techniques	[e])		[b])[d])[g])				[d])[f])		[d])		[d])			[d])[e])	[d])		

Table 3. *^{13}C-NMR Data of Isomeric Lycopenes* **1**–**9**, *Dehydrolycopenes* **38**–**41**, *and (all-*E*)-15,15′-Didehydrolycopene.* δ in ppm; shift differences $\Delta\delta = \delta((Z)) - \delta((E))$ for $|\Delta\delta| > 0.05$ ppm. Solvent $CDCl_3$.

	Lycopenes											
	1 (all-*E*)	**2** (5*Z*)		**3** (7*Z*)		**4** (15*Z*)		**5** (5*Z*,5′*Z*)		**6** (7*Z*,7′*Z*)		**8** (9*Z*,9′*Z*)	
	δ	δ	$\Delta\delta$	δ	$\Delta\delta$	δ	$\Delta\delta$	δ	$\Delta\delta$	δ	$\Delta\delta$	δ	$\Delta\delta$
C(1)	131.64	131.96		131.76		131.81		131.96		131.73		131.80	
C(1′)		131.69		131.76									
C(2)	124.12	124.05[d])		124.00[d])		123.85		124.05		124.02		123.9	
C(2′)		124.01[d])		123.97[d])									
C(3)	26.83	26.91		26.61		26.62		26.91		26.62		26.71	
C(3′)		26.74		26.70									
C(4)	40.30	32.84	–7.5	40.50		40.22		32.84	–7.5	40.50		40.28	
C(4′)		40.26		40.24									
C(5)	139.30	139.40		140.85	1.60	139.63		139.65		140.77	1.5	140.38	1.1
C(5′)		139.62		139.51									
C(6)	125.94	126.63	0.7	122.43	–3.5	125.59		126.83	0.9	122.46	–3.5	125.83	
C(6′)		125.82		125.74									
C(7)	124.87	124.64		125.00		124.82		124.69		125.00		126.31	1.4
C(7′)		124.81		124.82									
C(8)	135.54	135.19		131.55	–4.0	135.33		135.19		131.57	–4.0	127.28	–8.2
C(8′)		135.87		135.41									
C(9)	136.15	136.14		136.22		136.31		136.14		136.23		134.58	–1.6
C(9′)		136.14		136.18									
C(10)	131.64	131.61		132.54	0.9	131.49		131.53		132.56	0.9	129.97	–1.7
C(10′)		131.53		131.55									
C(11)	125.21	125.16		124.91		125.45		125.17		124.91		123.9	–1.3
C(11′)		125.16		125.17									
C(12)	137.46	137.37[e])		137.55		137.53		137.37		137.56		136.69	–0.8
C(12′)		137.40[e])		137.36									
C(13)	136.54	136.53		136.52[e])		137.24	0.7	136.53		136.50		136.40	
C(13′)		136.53		136.56[e])									
C(14)	132.71	132.69		132.66		126.98	–5.7	132.67		132.65		132.45	
C(14′)		132.69		132.66									
C(15)	130.17	130.11		130.07[f])		125.56	–4.6	130.11		130.08		129.98	
C(15′)		130.11		130.10[f])									
C(16)	25.66	25.70		25.70		25.76		25.71		25.72		25.71	
C(16′)		25.70		25.70									
C(17)	17.70	17.65		17.71		17.73		17.66		17.72		17.71	
C(17′)		17.70		17.71									
C(18)	16.97	24.18	7.2	16.46	–0.5	16.97		24.14	7.2	16.46	–0.5	17.00	
C(18′)		16.97		16.97									
C(19)	12.90	12.90		17.42	4.5	12.94		12.91		17.41	4.5	20.82	7.9
C(19′)		12.90		12.91									
C(20)	12.81	12.80		12.80		12.52		12.81		12.82		12.88	
C(20′)		12.80		12.80									
Techniques	[a])[b])[c])	[b])[c])		[a])[b])[c])		[b])[c])		[b])[c])		[b])[c])		[b])[c])	

[a]) DEPT spectrum. [b]) One-bond ^{1}H,^{13}C-COSY. [c]) Multiple-bond ^{1}H,^{13}C-COSY. [d])[e])[f]) Corresponding assignments may be interchanged.

Table 3 (cont.)

	Lycopenes				*7,8,7′,8′-Tetradehydro-lycopenes*			*7,8-Didehydro-lycopenes*			*15,15′-Didehydro-lycopene*
	7 (7Z,9Z)		**9** (7Z,9Z,7′Z,9′Z)		**38** (all-*E*)	**39** (9Z,9′Z)		**40** (all-*E*)	**41** (9Z)		(all-*E*)
	δ	*Δδ*	*δ*	*Δδ*	*δ*	*δ*	*Δδ*	*δ*	*δ*	*Δδ*	*δ*
C(1)	131.72		131.72		132.31	132.15		132.08	132.16		131.78
C(1′)	131.72							131.72	131.72		
C(2)	123.99		123.99		123.47	123.48		123.53	123.48		123.94
C(2′)	123.99							123.99	124.00		
C(3)	26.72		26.72		26.34	26.38		26.39	26.38		26.69
C(3′)	26.72							26.72	26.72		
C(4)	40.35		40.35		38.86	38.92		38.88	38.92		40.25
C(4′)	40.25							40.26	40.26		
C(5)	140.90	1.6	140.89	1.6	151.90	151.95		151.72	151.94		140.04
C(5′)	139.39							139.54	139.47		
C(6)	122.53	–3.4	122.52	–3.4	105.19	105.40		105.31	105.40		125.67
C(6′)	125.78							125.78	125.78		
C(7)	126.22	1.4	126.25	1.4	89.12	94.86	5.7	89.11	94.86	5.8	125.47
C(7′)	124.76							124.90	124.85		
C(8)	125.96	–9.6	125.97	–9.6	96.79	92.41	–4.4	96.91	92.43	–4.5	135.19
C(8′)	135.45							135.42	135.43		
C(9)	135.63	–0.5	135.53	–0.6	118.99	119.81	0.8	118.86	119.73	0.9	137.64
C(9′)	136.05							136.31	136.21		
C(10)	129.87	–1.8	129.86	–1.8	135.39	135.61		135.45	135.64		130.86
C(10′)	131.59							131.55	131.56		
C(11)	126.38	1.2	126.19	1.0	124.30	127.19	2.9	124.12	127.10	3.0	127.19
C(11′)	125.05							125.37	125.25		
C(12)	136.09	–1.4	136.12	–1.3	138.09	137.26	0.8	138.18	137.3[d])	0.9	135.04
C(12′)	137.42							137.31	137.35[d])		
C(13)	136.63[d])		136.37		136.44	136.49		136.06	136.34		146.63
C(13′)	136.26[d])							136.92	136.69		
C(14)	132.01	–0.7	131.99	–0.7	133.48	133.00	–0.5	133.65	133.1		110.64
C(14′)	132.67							132.53	132.57		
C(15)	129.71		129.75		130.37	130.17		130.62	130.30		98.39
C(15′)	130.15							129.88	129.97		
C(16)	25.66		25.66		25.71	25.69		25.7	25.70		25.70
C(16′)	25.70							25.7	25.70		
C(17)	17.63		17.63		17.72	17.72		17.71	17.71		17.71
C(17′)	17.71							17.71	17.71		
C(18)	16.61		16.61		19.43	19.54		19.42	19.54		17.00
C(18′)	16.96							16.98	16.97		
C(19)	24.73	11.8	24.72	11.8	17.99	23.53	5.5	17.96	23.53	5.6	12.96
C(19′)	12.90							12.91	12.91		
C(20)	12.72		12.70		12.76	12.73		12.74	12.73		15.29
C(20′)	12.78							12.81	12.80		
Techniques[b][c])			[a][b][c])		[a][b][c])	[a][c])		[a][b][c])	[b][c])		[b][c])

It is important to note that larger $\Delta\delta$ values are, in general, only found for protons (and C-atoms) close to the site of stereomutation. As a consequence, isomers with two or more stereomutated bonds behave fairly additive, if their (*Z*)-bonds are sufficiently separated from each other (see *Tables 2* and *3*).

The most prominent feature in ^{1}H-NMR is the strong downfield shift of $\Delta\delta \approx 0.5$ ppm of H–C(6) in (7*Z*)-, of H–C(8) in (9*Z*)-, and of H–C(12) in (13*Z*)-isomers which are, therefore, readily identified (see **3**, **6**, **8**, **10**, and **11** in *Table 2*). Moreover, (15*Z*)-isomerization interchanges the relative position of the signals of H–C(15,15′) and H–C(14,14′). The latter signals are readily distinguished from those of H–C(15,15′) by their additional broadening due to coupling to Me(20,20′).

Isomers with stereomutated C(5)=C(6) bonds show only minor shift changes, but the downfield shift of 2 H–C(4) ($\Delta\delta = 0.13$) is sufficiently indicative and limited to this case (see **2**, **5**, **12**, **14**, and **15**).

The $\Delta\delta$ values of prolycopene (**9**) behave, as an exception, completely unexpected, since relevant shift changes are observable at all positions except for Me(18,18′) (see *Table 2*). The derivation of this (tetra-*Z*)-structure was previously mainly based on 270-MHz NOE difference experiments [4]. In the meantime, all ^{1}H- and ^{13}C-NMR assignments were carefully checked by 2D ROESY and ^{1}H,^{13}C-COSY tuned to one-bond and multiple-bond *J*(C,H) coupling constants. Particularly the long-range hetero-correlation experiment provided important structural information, since each proton is coupled *via* two- and three-bond couplings to neighboring C-atoms. From these experiments, it is concluded that the previous assignments were correct [4]. The unexpected $\Delta\delta$ values could, in principle, be speculatively explained by the assumption that the structure of this isomer significantly deviates from planarity with a relevant back-folding of the end of the molecule upon the center part.

To investigate this hypothesis, we measured a 2D ^{1}H,^{1}H-ROESY spectrum of **9** (see *Exper. Part*). However, no unexpected through-space contacts were found, although a long accumulation time and a relatively high concentration were used. All unambiguous through-space contacts between individual protons are presented by arrows in *Fig. 3*. They confirm the structure and the assignment of the ^{1}H-NMR signals; however, no through-space contacts between protons of the outer and central parts of the molecule were detectable. Hence, no evidence for a relevant back-folding of the outer parts of the molecule was found.

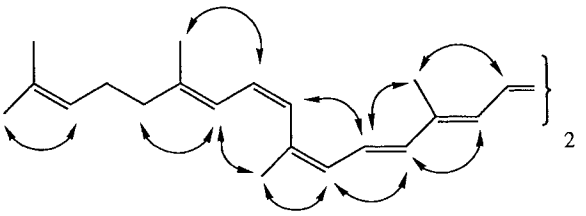


Fig. 3. *Results from the 400-MHz 2D ^{1}H,^{1}H-ROESY* (see *Exper. Part*) *of (7Z,9Z,7′Z,9′Z)-lycopene* (**9**). Each double-headed arrow represents two medium or strong ^{1}H,^{1}H cross peaks and hence a corresponding through-space contact revealing the proximity of the two protons or groups of protons.

^{13}C-NMR. The full assignments of the ^{13}C-NMR signals were based mainly on ^{1}H,^{13}C-COSY 2D experiments. The isomerization shifts $\Delta\delta$ were found as expected. Particularly strong effects of $\Delta\delta$, *i.e. ca.* −8 to −9.6 ppm, were observed for C(4) in (5*Z*)- and C(8) in (9*Z*)-isomers. In contrast to the ^{1}H-NMR, $\Delta\delta$ values of the Me C-atoms are also very indicative as seen for isomers **2** and **5** (C(18,18′)) and **3**, **6**, **7**, and **9** (C(19,19′)).

In the ^{13}C-NMR spectrum, prolycopene (**9**) shows no irregular behavior, since relevant $\Delta\delta$ values are confined to a narrow range close to the stereomutated bonds, except for a minor deviation at C(14,14′).

UV/VIS Data. The UV/VIS spectra of the nine geometrical lycopene isomers **1**–**9** prepared by synthesis were determined in hexane containing 2% of CH_2Cl_2 (see *Table 4*).

As expected, the absorption maxima and minima as well as the molar absorption coefficients ε of the (all-*E*)-, (5*Z*)-, and (5*Z*,5′*Z*)-isomers **1**, **2**, and **5**, respectively, are not distinguishable. The presumably planar, 'unhindered' (9*Z*,9′*Z*)-lycopene (**8**) retains the pronounced fine structure of **1**, but a hypsochromic shift of 10 to 12 nm is observed. Another interesting aspect of this study concerns the UV/VIS spectra of the four isomeric lycopenes **3**, **6**, **7**, and **9** which possess one or two sterically hindered (*Z*)-double bonds in position 7 and 7′, respectively. The

Table 4. *UV/VIS Data (hexane/2% CH_2Cl_2) of Isomeric Lycopenes* **1**–**9**. λ_{max} (incl. shoulders) and λ_{min} in nm and molar absorption coefficients $\varepsilon \cdot 10^{-3}$ in parentheses.

	λ_{max} ($\varepsilon \cdot 10^{-3}$)	λ_{min} ($\varepsilon \cdot 10^{-3}$)	λ_{max} ($\varepsilon \cdot 10^{-3}$)	λ_{min} ($\varepsilon \cdot 10^{-3}$)	λ_{max} ($\varepsilon \cdot 10^{-3}$)	λ_{max} ($\varepsilon \cdot 10^{-3}$)
1 (all-*E*)	502 (172)	487 (102)	470 (187)	453 (109)	443 (123)	362 (12)
2 (5*Z*)	502 (169)	487 (101)	470 (184)	453 (108)	443 (121)	362 (12)
5 (5*Z*, 5′*Z*)	502 (167)	487 (100)	470 (182)	453 (107)	443 (121)	362 (14)
8 (9*Z*, 9′*Z*)	490 (151)	476 (87)	459 (168)	443 (98)	433 (113)	360 (16)
3 (7*Z*)	499 (129)	486 (104)	469 (154)	449 (111)	443 (112)	362 (13)
6 (7*Z*, 7′*Z*)	493 (97)	487 (96)	466 (128)		444 (sh, 106)	364 (sh)
7 (7*Z*, 9*Z*)	470 (115)	457 (100)	444 (115)		422 (sh, 76)	
9 (7*Z*, 9*Z*, 7′*Z*, 9′*Z*)	461 (sh, 70)		437 (105)		417 (sh, 90)	
4 (15*Z*)	499 (87)	485 (65)	468 (110)	451 (75)	441 (82)	360 (77)

change from the (all-*E*)-configuration to the (7*Z*)-geometry of isomer **3** results in a less marked fine structure and a decrease of the molar absorption coefficient ε. Both effects are strongly intensified in the symmetrical (7*Z*,7′*Z*)-lycopene (**6**). Basically, the same loss of fine structure and decrease of extinction coefficient ε is observed by comparing the UV/VIS of (all-*E*)-lycopene (**1**) with those of the (7*Z*,9*Z*)-[3]) and (7*Z*,9*Z*,7′*Z*,9′*Z*)-isomers **7** and **9**, respectively. Furthermore, a very strong hypsochromic shift is observed in this latter series. None of the above mentioned (*Z*)-isomers exhibits a significant subsidiary peak at *ca.* 360 nm (the so-called '*cis*-peak') which is a salient feature in the UV/VIS spectrum of (15*Z*)-lycopene (**4**).

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Experimental Part

(In collaboration with *Paul Jauslin*)

General. All reactions were carried out under Ar utilizing dry solvents of high purity. Except for compound **28**, chromatography was carried out on silica gel *60* (0.063–0.20 mm and 0.040–0.063 mm, *Merck*); FC = flash chromatography. HPLC Separations. *Method 1: Nucleosil-300-5* column (50 × 0.4 cm), hexane/0.05% (*v*/*v*) *N*-ethyldiisopropylamine, flow 0.6 ml/min, monitoring wavelength 469 nm; *Method 2: Spherisorb-S5-W* column (25 × 0.4 cm), hexane/2.5% (*v*/*v*) i-PrOAc, flow 1 ml/min, monitoring wavelength 428 nm; *Method 3: LiChrospher-100-CH-18/2* (*Merck* Cat. No. 50377) column (25 × 0.4 cm), MeCN/H_2O 13:7 containing 0.4% (*w*/*v*) $Bu_4N(HSO_4)$ and 0.2% (*w*/*v*) sodium dodecyl sulfate, flow 1 ml/min, column temp. 50°, monitoring wavelength 254 nm; the mixture of lycopene isomers shown in *Fig. 1* was obtained by heating (all-*E*)-lycopene (**1**; 1.0 g) in refluxing heptane (10 ml) in presence of a trace of Br_2 (*ca.* 10 µg) for 16 h, followed by cooling to 2° and filtration of the suspension (analysis of the filtrate according to *Method 1*). M.p.: not corrected. UV/VIS Spectra: *Uvikon 810* instrument; λ_{max} (ε) in nm; at r.t. IR Spectra: *Nicolet 170-SX*, FT-IR spectrometer; in cm^{-1}. NMR Spectra: *Bruker AC-250, AM-400*, and *AM-500* spectrometer with *Aspect 3000* computer, process controller, and 160 Mbyte disk, corresponding to ^1H frequencies of 250, 400, and 500 MHz, and ^{13}C frequencies of 62.5, 100.6, and 125 MHz; $CDCl_3$ with internal TMS as standard; measuring temp. *ca.* 26°, if not otherwise specified; standard *Bruker* DISNMR software and microprogramms; typical experimental conditions for phase-sensitive COSY: 400 MHz, 0.4 mg of **7** in 0.6 ml of $CDCl_3$, 2K data points in t_2, 300 experiments in t_1, zero-filling in t_1 to 2K, 800 Hz spectral width in F_1 and F_2 (olef. range), shifted sine-bell windows in t_2 and t_1 (SSB2 = SSB2 = 8), 0.78 and 0.78 Hz/pt digital resolution, 1.25 relaxation delay, acquisition times 1.28 and 0.15s, 80 scans and 2 dummy scans per experiment, total acquisition time 13.5 h; for magnitude COSY: 500 MHz, temp. 4°, 20 mg of **4** in 0.6 ml of $CDCl_3$, 2K data points in F_2, 512 experiments in t_1, zero-filling to 4K and 2K, 1000 Hz spectral width in both directions (olef. range), sine-bell windows, 0.49 and 0.49 Hz/pt digital resolution, 1.0s relaxation delay, acquisition times 1.02

[3]) According to the UV/VIS spectra, poly-*cis*-lycopene I described by *Zechmeister* and *Pinckard* in [30] is probably identical with (7*Z*,9*Z*)-lycopene (**7**).

and 0.255s in t_2 and t_1, 16 scans and 2 dummy scans, total acquisition time 5.3 h; for double-quantum 2D (magnitude, [25]): 400 MHz, 0.23 mg of **14** in 0.3 ml of $CDCl_3$, 1K data points in t_2, 250 experiments in t_1, zero-filling to 4K and 1K, 800 and 1600 Hz spectral width (olef. range), *Lorentz-Gauss* window in t_2 (LB = –5, GB = 0.2), trapezoidal window in t_1 (30, 250), 0.39 and 1.56 Hz/pt, 2s relaxation delay, delay tuned to 25 Hz coupling constant (10 ms), 320 scans per experiment, total acquisition time 65 h; for ^{13}C-detected ^{1}H, ^{13}C-COSY: 100.6 and 400 MHz, *ca.* 20 mg of **8** in 0.6 ml of $CDCl_3$; *a*) one-bond experiment (^1J(C,H) = 140 Hz): 4K data points in t_2, 180 experiments in t_1, zero-filling in t_1 to 512, 18518, and 3520 Hz spectral width, trapezoidal windows (30, 600), digital resolution 9.0 and 6.9 Hz/pt, 1.0s relaxation delay, 3.6 and 2 ms polarisation transfer delays, 24 scans and 2 dummy scans per experiment, total acquisition time 1.5 h; *b*) long-range experiment ($^{2,3}J$(C,H) = 8.3 Hz); same conditions as above, except 1.2-s relaxation time, delays 60 and 38 ms, 96 scans and 2 dummy scans, total acquisition time *ca.* 6 h; for 1D nuclear *Overhauser* difference: exper. conditions as in [4]; for 2D ROESY [26]: **9** in 0.6 ml of $CDCl_3$, 400 MHz, 4K data points in t_2, 800 experiments in t_1, zero-filling in t_1 to 4K, 5000 Hz spectral width, cosine-square windows, 2.44 Hz/pt digital resolution in both directions, 3s relaxation delay, co-addition of FID's with 0.3 and 0.6s mixing time, duty cycle 0.08 (1.9 KHz), 48 scans per experiment, 47 h total acquisition time. Mass Spectra: updated *MS9* (*AEI*, Manchester, GB) for EI at 70 eV; in *m/z* (%).

1. *(all-*E*)-3,7,11-Trimethyldodeca-4,6,10-trien-1-yn-3-ol* (**18**). Lithium acetylide was prepared by passing acetylene gas into a soln. of Li (0.27 g, 39 mmol) in liq. NH_3 (25 ml). The NH_3 was evaporated and gradually replaced by THF (30 ml). (5*E*,7*E*)-ψ-Ionone [10] (**16**; 5.0 g, 26 mmol; GC: 94.4%) in THF (10 ml) was added at 10° over 10 min, the mixture stirred for additional 5 min and quenched with ice-water. AcOH (5 ml) and Et_2O (5 ml) were added, the org. layer was separated, the aq. phase extracted with Et_2O, and the combined org. phase washed with sat. $NaHCO_3$ soln. and brine, dried, and evaporated. The residual oil was distilled: 4.6 g (81%) of **18**. Colorless liquid. B.p. 78–81°/0.03 Torr. GC: 86.0%. An anal. sample was prepared by chromatography (silica gel, hexane/AcOEt 95:5 (0.1% Et_3N)) and bulb-to-bulb distillation. GC: 93.1%. IR (film): 3385*s*, 3306*s*, 2113*w*, 1654*m*, 1107*s*, 1059*s*, 964*s*. ^{1}H-NMR (250 MHz, $CDCl_3$): 1.60 (*s*, Me–C(3)); 1.61 (*s*, Me–C(11)); 1.69 (*s*, 3H–C(12)); 1.80 (*s*, Me–C(7)); *ca.* 2.1 (*m*, 2H–C(8), 2H–C(9)); 2.13 (*s*, OH); 2.60 (*s*, H–C(1)); 5.09 (*m*, H–C(10)); 5.68 (*d*, *J* = 15, H–C(4)); 5.85 (*d*, *J* = 11, H–C(6)); 6.77 (*dd*, *J* = 15, 11, H–C(5)). MS: 218 (8, M^+), 203 (2), 69 (100). Anal. calc. for $C_{15}H_{22}O$ (218.34): C 82.52, H 10.16; found C 82.54, H 10.23.

2. *(all-*E*)-3,7,11-Trimethyldodeca-1,4,6,10-tetraen-3-ol* (**20**) [31]. A mixture of **18** (4.0 g, 18.3 mmol), *Lindlar* catalyst (type A; 0.22 g), 2,2′-(ethylenedithio)bis(ethanol) (2.3 mg), and Et_3N (0.25 ml) in CH_2Cl_2 (70 ml) was hydrogenated at r.t./1 bar H_2, until the uptake of H_2 ceased. The suspension was filtered and the filtrate evaporated: 3.7 g (92%) of **20**. Labile liquid. IR (film): 3389*s*, 1654*m*, 991*s*, 967*s*, 919*s*. ^{1}H-NMR (250 MHz, $CDCl_3$): 1.41 (*s*, Me–C(3)); 1.61 (*s*, Me–C(11)); 1.68 (*s*, 3H–C(12)); 1.77 (*s*, Me–C(7)); *ca.* 2.1 (*m*, 2H–C(8), 2H–C(9)); 5.08 (*dd*, *J* = 11, 1, H–C(1)); *ca.* 5.10 (*m*, H–C(10)); 5.26 (*dd*, *J* = 17, 1, H–C(1)); 5.68 (*d*, *J* = 15, H–C(4)); 5.84 (*d*, *J* = 11, H–C(6)); 5.99 (*dd*, *J* = 17, 11, H–C(2)); 6.47 (*dd*, *J* = 15, 11, H–C(5)). MS: 220 (5, M^+), 177 (5), 43 (100).

3. *(4*E,6Z*)-3,7,11-Trimethyldodeca-4,6,10-trien-1-yn-3-ol* (**19**). Lithium acetylide was prepared from Li (1.62 g, 0.233 mol) and acetylene in liq. NH_3 (150 ml) and, after evaporation of NH_3 and replacement by THF (190 ml), treated with a soln. of (5*Z*,7*E*)-ψ-ionone [10] (**17**); 30.0 g, 0.156 mol; GC: 90.7%) in THF (30 ml) at 10°. Workup as described in *Exper. 1* followed by distillation afforded 30.2 g (89%) of **19**. Colorless liquid. B.p. 74–76°/0.06 Torr. GC: 86.3%. IR (film): 3389*s*, 3307*s*, 2113w, 1654*m*, 1108*s*, 1059*s*, 964*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.58, 1.61 (2*s*, Me–C(3), Me–C(11)); 1.68 (*s*, 3H–C(12)); 1.80 (*s*, Me–C(7)); 2.07 (*s*, 1OH); 2.1–2.2 (*m*, 2H–C(8)), 2H–C(9)); 2.58 (*s*, H–C(1)); 5.12 (*m*, H–C(10)); 5.65 (*d*, *J* = 15, H–C(4)); 5.83 (*d*, *J* = 11, H–C(6)); 6.75 (*dd*, *J* = 15, 11, H–C(5)). MS: 218 (2, M^+), 185 (11), 69 (100). Anal. calc. for $C_{15}H_{22}O$ (218.34): C 82.52, H 10.16; found: C 82.23, H 10.41.

4. *(4*E,6Z*)-3,7,11-Trimethyldodeca-1,4,6,10-tetraen-3-ol* (**21**). A mixture of **19** (4.37 g, 20 mmol), *Lindlar* catalyst (type *A*, 0.23 g), 2,2′-(ethylenedithio)bis(ethanol) (2.4 mg) and Et_3N (0.26 ml) in CH_2Cl_2 (70 ml) was hydrogenated at r.t./1 bar H_2, until H_2 uptake ceased. The suspension was filtered and the filtrate evaporated: 4.42 g (100%) of **21**. Labile oil. IR (film): 3372*s*, 1653*m*, 992*s*, 966*s*, 919*s*. ^{1}H-NMR (80 MHz, $CDCl_3$): 1.41 (*s*, Me–C(3)); 1.62 (*s*, Me–C(11)); 1.69 (*s*, 3H–C(12)); 1.80 (*s*, Me–C(7)); 2.1–2.2 (*m*, 2H–C(8), 2H–C(9)); 5.10 (*dd*, *J* = 11, 1, H–C(1)); 5.27 (*dd*, *J* = 17, 1, H–C(1)); 5.70 (*d*, *J* = 15, H–C(4)); 5.86 (*d*, *J* = 11, H–C(6)); 6.05 (*dd*, *J* = 17, 11, H–C(2)); 6.53 (*dd*, *J* = 15, 11, H–C(5)). MS: 220 (10, M^+), 177 (8), 43 (100).

5. *Triphenyl[(2*E,4E,6Z*)-3,7,11-trimethyldodeca-2,4,6,10-tetraenyl]phosphonium Bromide* (**23a**). Mixture **20**/**21** (1:2; 85 g, 0.386 mol; prepared from commercial (5*E*/*Z*,7*E*)-ψ-ionone as described in *Exper. 1* and *2*) was added at 15° over 30 min to a stirred suspension of $Ph_3P \cdot HBr$ (132 g, 0.385 mol) in MeOH (500 ml). The mixture was stirred at r.t. overnight and then evaporated. The residue was taken up in AcOEt (750 ml) and stirred at r.t. for 1 h

and at 0° for 30 min. The precipitate was collected by centrifugation and washed with AcOEt to give 34 g of a yellowish solid (m.p. 175–176°; HPLC: 72%). The product was dissolved in warm EtOH (80 ml), AcOEt (1.3 l) slowly added, and the resulting suspension stirred at 0° for 30 min. The filtered and washed precipitate was recrystallized 3 times in the same manner to afford 17.8 g (8.5%) of **23a**. White crystals. M.p. 206°. HPLC (*Method 3*): 93.2%. IR (KBr): 1635*m*, 1618*m*, 1437*s*, 1112*s*, 956*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.45 (*d*, *J* = 4, Me–C(3)); 1.59 (*s*, Me–C(11)); 1.66 (*s*, 3 H–C(12)); 1.79 (*s*, Me–C(7)); 2.04–2.2 (*m*, 2 H–C(8), 2 H–C(9)); 4.80 (*dd*, *J* = 16, 8, 2 H–C(1)); 5.09 (*m*, H–C(10)); 5.33 (*td*, *J* = 8, 8, H–C(2)); 5.81 (*d*, *J* = 11, H–C(6)); 6.02 (*d*, *J* = 15, H–C(4)); 6.34 (*ddd*, *J* = 15, 11, 2, H–C(5)); 7.65–7.9 (*m*, 15 arom. H). ^{13}C-NMR (100.6 MHz, $CDCl_3$; ^{1}H,^{13}C-COSY): 13.28 (*d*, *J* = 2, Me–C(3)); 17.64 (Me–C(11)); 24.08 (Me–C(7)); 25.45 (*d*, *J* = 53, C(1)); 25.72 (C(12)); 26.76 (C(9)); 32.72 (C(8)); 112.95 (*d*, *J* = 12, C(2)); 123.74 (C(10)); 125.56 (C(6)); 126.38 (*d*, *J* = 5, C(5)); 132.05 (C(11)); 132.71 (*d*, *J* = 6, C(4)); 141.63 (C(7)); 143.80 (*d*, *J* = 14, C(3)); arom. C-atoms: 118.18 (*d*, *J* = 85, C(1′)); 130.39 (*d*, *J* = 12.5, C(3′), C(5′)); 133.93 (*d*, *J* = 9.5, C(2′), C(6′)); 135.08 (*d*, *J* = 2.6, C(4′)). Anal. calc. for $C_{33}H_{38}BrP$ (545.55): C 72.65, H 7.02, Br 14.65; found: C 72.48, H 7.28, Br 14.60

6. *Triphenyl[(all-*E*)-3,7,11-trimethyldodeca-2,4,6,10-tetraenyl]phosphonium Chloride* (**22b**). At 60°, **20** (25.8 g. 0.117 mmol) in hexane (15 ml) was added over 10 min to PPh_3 (52.5 g, 0.20 mol) in AcOH (525 ml). The mixture was stirred at 60° for 2.5 h, then taken up in CH_2Cl_2 (500 ml), and treated 6 times with 2% aq. NaCl soln. (6 × 500 ml) to effect the anion exchange of AcO^- by Cl^-. The org. phase was evaporated and the residue partitioned between hexane (200 ml) and MeOH/H_2O 4:1 (300 ml). The MeOH/H_2O phase was evaporated and the residue taken up in MeOH/CH_2Cl_2 10:1, diluted with AcOEt and stirred at 0° for 16 h. The formed precipitate (5 g of **22b**/**23b**) was filtered off, the filtrate evaporated, and the residual phosphonium salt crystallized from $ClCH_2CH_2Cl$/AcOEt (5 h at 0°): 25 g (39%) of **22b**. Colorless amorphous solid. HPLC (*Method 3*): 90% (*ca.* 1% **23b**). H_2O content: 10% (*Karl-Fischer* titration). ^{1}H-NMR (250 MHz, $CDCl_3$): 1.46 (*d*, *J* = 4, Me–C(3)); 1.60 (*s*, Me–C(11)); 1.68 (*s*, 3 H–C(12)); 1.76 (*s*, Me–C(7)); 2.07 (br. *s*, 2 H–C(8), 2 H–C(9)); 4.90 (*dd*, *J* = 16, 8, 2 H–C(1)); 5.08 (*m*, H–C(10)); 5.35 (*td*, *J* ≈ 7, 7, H–C(2)); 5.82 (*d*, *J* ≈ 11, H–C(6)); 6.06 (*d*, *J* = 15, H–C(4)); 6.35 (*m*, H–C(5)); *ca.* 7.6–8.0 (*m*, 15 arom. H).

7. *(5*Z*,5′*Z*)-Lycopene* (**5**). NaOMe in MeOH (7 ml, 3M NaOMe, 21 mmol) was added over 30 min to a stirred soln. of **23a** (10.91 g, 20 mmol) and 2,7-dimethylocta-2,4,6-trienedial (**24**; 1.263 g, 7.7 mmol) in CH_2Cl_2 (55 ml) at −5°. The mixture was stirred for 30 min at 0° and evaporated, and the residue taken up in CH_2Cl_2 (130 ml). Then, CH_2Cl_2 was distilled off over a *Claisen* distilling head, while MeOH (130 ml) was simultaneously added. The resulting suspension was stirred for 30 min at 0° and the precipitate collected, washed with MeOH, and dried *in vacuo*. The isolated product (4.0 g, m.p. 148–149°) was purified by 2 additional recrystallizations from CH_2Cl_2/MeOH (solvent exchange): 2.89 g (70%) of **5**. Deep-red crystals. M.p. 152–153°. HPLC (*Method 1*): 97.7%. UV/VIS: *Table 4*. IR (KBr): 1628*m*, 1441*m*, 1369*m*, 969*s*. ^{1}H-NMR: *Table 2*. ^{13}C-NMR: *Table 3*. MS: 536 (25, M^+), 467 (2), 444 (3), 430 (4), 69 (100). Anal. calc. for $C_{40}H_{56}$ (536.89): C 89.49, H 10.51; found: C 89.16, H 10.38.

8. *(all-*E*)-12′-Apo-ψ-caroten-12′-al* (**26**). NaOMe in MeOH (10 ml, 3M NaOMe, 30 mmol) was added over 10 min to a stirred soln. of **22b** (15.03 g, 30 mmol) and **24** (4.93 g, 30 mmol) in CH_2Cl_2 (75 ml) at 0°. The mixture was stirred at 0° for 10 min, evaporated and partitioned between hexane/AcOEt 4:1 (150 ml) and MeOH/H_2O 4:1 (40 ml). The hexane/AcOEt layer was washed with MeOH/H_2O 4:1, dried ($MgSO_4$), and evaporated. Chromatography (silica gel, hexane/AcOEt 7:3) gave 8.3 g of a dark oil which was dissolved in CH_2Cl_2 (8 ml). Hexane (170 ml) was added, the CH_2Cl_2 evaporated, and the suspension stirred at 0° for 1 h. The precipitate was filtered off (5.05 g, m.p. 99–102°) and recrystallized from CH_2Cl_2/hexane: 4.32 g (41%) of **26**. Red crystals. M.p. 105°. HPLC (*Method 2*): 96.4%. UV/VIS (hexane): 455 (70000), 429 (85000). IR (KBr): 1661*s*, 1607*s*, 961*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.62 (*s*, Me(17)); 1.69 (*s*, Me(16)); 1.83 (*s*, Me(18)); 1.88 (*s*, Me(20′)); 1.99 (*s*, Me(19)); 2.04 (*s*, Me(20)); 2.12 (br. *s*, 2 H–C(3), 2 H–C(4)); 5.11 (*m*, H–C(2)); 5.96 (*d*, *J* = 11, H–C(6)); 6.20 (*d*, *J* = 12, H–C(10)); 6.25 (*d*, *J* = 15, H–C(8)); 6.30 (*d*, *J* = 12, H–C(14)); 6.37 (*d*, *J* = 15, H–C(12)); 6.55 (*dd*, *J* = 15, 11, H–C(7)); 6.68 (*dd*, *J* = 14, 12, H–C(15′)); 6.78 (*dd*, *J* = 15, 12, H–C(11)); 6.96 (*d*, *J* = 12, H–C(14′)); 7.03 (*dd*, *J* = 14, 12, H–C(15)); 9.45 (*s*, CHO). ^{13}C-NMR (100.6 MHz, $CDCl_3$; assignments based on ^{1}H,^{13}C-COSY tuned to one-bond and multiple-bond couplings): 9.58 (C(20′)); 12.98, 13.01 (C(19), C(20)); 17.00 (C(18)); 17.70 (C(17)); 25.69 (C(16)); 26.67 (C(3)); 40.26 (C(4)); 123.90 (C(2)); 125.69 (C(6)); 125.85 (C(7)); 127.29 (C(15′)); 127.75 (C(11)); 130.96 (C(14)); 131.04 (C(10)); 131.73 (C(1)); 135.10 (C(8)); 136.41 (C(12)); 136.77 (C(13′)); 137.72 (C(15)); 138.08 (C(9)); 140.35 (C(5)); 141.75 (C(13)); 148.86 (C(14′)); 194.29 (C(12′)). MS: 350 (100, M^+), 281 (30), 69 (80). Anal. calc. for $C_{25}H_{34}O$ (350.55): C 85.66, H 9.78; found: C 85.47, H 10.04.

9. *(5*Z*)-Lycopene* (**2**). NaOMe in MeOH (4.3 ml, 3M NaOMe, 12.9 mmol) was added over 10 min to a stirred soln. of phosphonium salt **23a** (6.49 g, 11.9 mmol) and **26** (3.0 g, 8.6 mmol) in CH_2Cl_2 (85 ml) at −5°. The mixture

was stirred at r.t. for 30 min. Then, CH_2Cl_2 was distilled off over a *Claisen* distilling head, while MeOH (85 ml) was simultaneously added. The suspension was stirred at 0° for 30 min, the precipitate filtered off, washed with MeOH, and dried *in vacuo*. Two additional recrystallizations from CH_2Cl_2/MeOH (solvent exchange) yielded 3.64 g (79%) of **2**. Red crystals. M.p. 143°. HPLC (*Method 1*): 95.6%. UV/VIS: *Table 4*. IR (KBr): 1629*m*, 1443*m*, 1375*m*, 959*s*. ^{1}H-NMR: *Table 2*. ^{13}C-NMR: *Table 3*. MS: 536 (20, M^+), 467 (2), 444 (3), 430 (4), 69 (100).

10. *(2Z,4E,6E)-3,7,11-Trimethyldodeca-2,4,6,10-tetraenal* (**28**). DIBAH (12.5 ml, 1.2M in toluene, 15 mmol) was added at 0° over 15 min to methyl (2*Z*,4*E*,6*E*)-3,7,11-trimethyldodeca-2,4,6,10-tetraenoate [16] (**27**; 1.49 g, 6.0 mmol) in THF (70 ml). Then, H_2O (30 ml) was carefully added, the mixture stirred at r.t. for 1 h and filtered, the filter cake washed with AcOEt, the aq. phase reextracted with AcOEt, and the combined org. phase dried ($MgSO_4$). After evaporation of the solvents, the crude allylic alcohol was dissolved in AcOEt (90 ml) and treated with activated MnO_2 (13 g, 150 mmol) at r.t. for 1.5 h. The slurry was filtered, the filtrate concentrated, and the residue chromatographed (aluminium oxide (neutral, act. III; *Camag*), hexane/AcOEt 7:3 (+0.1% Et_3N)): 1.13 g (86%) of **28** as yellowish, labile oil, which was used without further purification. IR (film): 1663*s*, 1631*s*, 1600*s*, 957*s*. ^{1}H-NMR (270 MHz, $CDCl_3$): 1.62 (*s*, Me–C(11)); 1.69 (*s*, 3 H–C(12)); 1.88 (*s*, Me–C(7)); 2.12 (*s*, Me–C(3)); *ca.* 2.16 (*m*, 2 H–C(8), 2 H–C(9)); *ca.* 5.10 (*m*, H–C(10)); 5.82 (*d*, J = 8, H–C(2)); 6.05 (*d*, J = 11, H–C(6)); 6.89 (*dd*, J = 15, 11, H–C(5)); 7.17 (*d*, J = 15, H–C(4)); 10.20 (*d*, J = 8, CHO). MS: 218 (12, M^+), 149 (35), 69 (100).

11. *(9Z,9'Z)-Lycopene* (**8**). BuLi (3.1 ml, 1.6M in hexane, 5.0 mmol) was added at 0° to (i-Pr)$_2$NH (501 mg, 5.0 mmol) in THF (25 ml) and the soln. cooled to −78°. Bis-phosphonium salt **29** [15] (1.82 g, 2.2 mmol) was added and the mixture stirred at −35° for 10 min and at 20° for 10 min. Aldehyde **28** (1.08 g, 4.95 mmol) in THF (2.5 ml) was added in one lot and the mixture stirred at r.t. for 1 h and then evaporated. Chromatography (silica gel, hexane/CH_2Cl_2 2:1), isomerization in refluxing hexane, and crystallization at −20° gave, in two crops, 143 mg (12%) of **8**, m.p. 132°. Recrystallization from hexane yielded 97 mg (8%) of **8**. Red crystals. M.p. 135°. HPLC (*Method 1*): 93.3%. UV/VIS: *Table 4*. IR (KBr): 1629*m*, 1438*m*, 1376*m*, 962*s*. ^{1}H-NMR: *Table 2*. ^{13}C-NMR: *Table 3*. MS: 536 (26, M^+), 467 (2), 444 (2), 430 (3), 69 (100).

12. *(E)-4,8-Dimethylnona-3,7-dien-1-yne* (**31**). BuLi (224 ml, 1.6M in hexane, 0.358 mol) was added at 0–4° over 90 min to a stirred suspension of (chloromethyl)triphenylphosphonium chloride (134 g, 0.386 mol) in THF (700 ml). Then, a soln. of (*E*)-citral (**30**; 42 g, 0.276 mol) in THF (140 ml) was added at 0° over 30 min. After stirring at r.t. for 15 min, the mixture was filtered and partitioned between brine and hexane. The dried hexane soln. was concentrated and the residue distilled to afford 39.6 g (78%) of (1*E*/*Z*,3*E*)-1-chloro-4,8-dimethylnona-1,3,7-triene as colorless liquid, b.p. 43–44°/0.1 Torr. This compound (37 g, 0.20 mol) was dissolved in THF (750 ml) and MeLi (310 ml, 1.6M in Et_2O, 0.50 mol) added at 0° over 20 min. The mixture was stirred at 0° for 90 min and then worked up in the usual way. Distillation of the crude product yielded 23.5 g (79%) of **31**. Colorless liquid. B.p. 84–86°/18 Torr ([17]: b.p. 75°/15 Torr). GC: 96%. IR (film): 3308*s*, 2098*m*, 1628*m*, 1444*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.60 (*s*, Me–C(8)); 1.69 (*s*, 3 H–C(9)); 1.92 (*s*, Me–C(4)); *ca.* 2.11 (*m*, 2 H–C(5), 2 H–C(6)); 3.02 (*d*, J = 2, H–C(1)); 5.07 (*m*, H–C(7)); 5.27 (*m*, H–C(3)). MS: 148 (1, M^+), 133 (25), 69 (100). Anal. calc. for $C_{11}H_{16}$ (148.25): C 89.12, H 10.88; found: C 88.63, H 10.67.

13. *(E)-3,7,11-Trimethyldodeca-1,6,10-trien-4-yn-3-ol* (**32**). BuLi (25 ml, 1.6M in hexane, 40 mmol) was added at −20° over 20 min to a soln. of **31** (5.93 g, 40 mmol) in THF (80 ml). After addition of dry LiBr (3.47 g, 40 mmol) and stirring of the mixture at −20° for 10 min, a soln. of methyl vinyl ketone (4.67 g, 67 mmol) in THF (20 ml) was added at −20° over 30 min. The mixture was allowed to warm to r.t. over 1 h and poured into ice-cold brine. The aq. phase was extracted with Et_2O and the combined org. phase dried and evaporated. Chromatography (silica gel, hexane/AcOEt 7:3 (+0.1% Et_3N)) and distillation gave 6.5 g (74%) of **32**. Colorless oil. B.p. 85–86°/0.01 Torr. GC: 94%. IR (film): 3382*s*, 2210*m*, 1629*m*, 987*m*, 924*s*. ^{1}H-NMR (250 MHz, $CDCl_3$): 1.59 (*s*, Me–C(3), Me–C(11)); 1.69 (*s*, 3 H–C(12)); 1.89 (*d*, J = 1, Me–C(7)); 2.09 (*s*, 1 OH); *ca.* 2.11 (*m*, 2 H–C(8), 2 H–C(9)); 5.06 (*m*, H–C(10)); 5.12 (*dd*, J = 10, 1, H–C(1)); 5.32 (br. *s*, H–C(6)); 5.52 (*dd*, J = 17, 1, H–C(1)); 6.02 (*dd*, J = 17, 10, H–C(2)). MS: 218 (1, M^+), 203 (12), 69 (100). Anal. calc. for $C_{15}H_{22}O$ (218.34): C 82.52, H 10.16; found: C 82.22, H 10.23.

14. *(2Z,6E)- and (all-E)-3,7,11-Trimethyldodeca-2,6,10-trien-4-yn-1-ol* (**35** and **34**, resp.). A mixture of **32** (10.0 g, 46 mmol) and anh. NaOAc (30 g, 0.37 mol) in AcOH (120 ml) was stirred at 60° for 4 h. The soln. was partitioned between H_2O and AcOEt, the AcOEt phase washed with H_2O and sat. $NaHCO_3$ soln., dried (Na_2SO_4), and concentrated. The crude acetate was purified by FC (silica gel, hexane/AcOEt 19:1 (+0.1% Et_3N)). The obtained oil (9.6 g) was dissolved in MeOH (180 ml) and saponified by addition of a KOH soln. (5.70 g, 85%, 87 mmol) in H_2O (35 ml) over 15 min at 20°. Most of the MeOH was evaporated, the mixture partitioned between

H_2O and AcOEt, and the aq. layer extracted with AcOEt. The AcOEt extracts were washed with brine, dried (Na_2SO_4), and evaporated: 7.7 g of crude **35**/**34** 2:1. Extensive chromatography (silica gel, hexane/AcOEt 4:1 (+0.1% Et_3N)) gave 3.59 g (36%) of **35** [22] and 1.42 g (14%) of **34** as colorless liquids.

35: GC: 97.3%. IR (film): 3336*s*, 2180*m*, 1617*m*, 1003*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.61 (*s*, Me–C(11); 1.69 (*s*, 3 H–C(12)); 1.92 (*s*, Me–C(3), Me–C(7)); *ca.* 2.13 (*m*, 2 H–C(8), 2 H–C(9)); 4.34 (*d*, J = 7, 2 H–C(1)); 5.08 (*m*, H–C(10)); 5.43 (*s*, H–C(6)); 5.83 (*m*, H–C(2)). MS: 218 (15, M^+), 149 (24), 69 (100). Anal. calc. for $C_{15}H_{22}O$ (218.34): C 82.52, H 10.16; found: C 82.22, H 10.24.

34: GC: 94.2%. IR (film): 3335*s*, 2180*m*, 1617*m*, 1003*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.35 (br. *s*, OH); 1.60 (*s*, Me–C(11)); 1.68 (*s*, 3 H–C(12)); 1.87, 1.90 (2*s*, Me–C(3), Me–C(7)); *ca.* 2.12 (*m*, 2 H–C(8), 2 H–C(9)); 4.24 (*d*, J = 7, H–C(1)); 5.08 (*m*, H–C(10)); 5.39 (*s*, H–C(6)); 5.97 (*t*, J = 7, H–C(2)). MS: 218 (34, M^+), 149 (25), 69 (100). Anal. calc. for $C_{15}H_{22}O$ (218.34): C 82.52, H 10.16; found: C 82.25, H 10.22.

15. *(all-*E*)-3,7,11-Trimethyldodeca-2,6,10-trien-4-yn-1-ol* (**34**). To a stirred soln. of (*E*)-3-bromobut-2-en-1-ol [19] (**33**; 11.7 g, 77 mmol) in C_6H_6/Et_2NH 1:1 (150 ml) was added [$Pd(Ph_3P)_4$] (1.12 g, 1 mmol) and CuI (0.46 g, 2.4 mmol). Then, a soln. of **31** (12.06 g, 81 mmol) in Et_2NH (150 ml) was slowly added at r.t. The mixture was stirred for 5 h, evaporated to ¼ of its original volume, and partitioned between Et_2O and sat. NH_4Cl soln. The org. phase was washed with H_2O and brine, dried (Na_2SO_4), and evaporated. Chromatography (silica gel, hexane/AcOEt 4:1 (+0.1% Et_3N)) afforded 13.2 g (78%) of **34**. GC: 96.4%. The substance was identical in all respects (NMR, IR, MS, GC, DC) with the compound described above.

16. *Triphenyl[(2*Z*,6*E*)-3,7,11-trimethyldodeca-2,6,10-trien-4-ynyl]phosphonium Bromide* (**37**). A soln. of PBr_3 (1.22 g, 4.5 mmol) in AcOEt (1.4 ml) was added over 5 min to a cooled (−20°) soln. of **35** (1.40 g, 6.4 mmol) in AcOEt (5 ml), DMF (1.5 ml), and pyridine (0.015 ml). The mixture was stirred at −20° for 1 h, at 0° for 20 min, and then partitioned between hexane and ice-water. The org. phase was washed with sat. $NaHCO_3$ soln. and brine, dried (Na_2SO_4), and evaporated. Then, the crude bromide (1.50 g) was dissolved in AcOEt (10 ml), PPh_3 (1.57 g, 6.0 mmol) was added and the mixture stirred at r.t. in the dark for 16 h. The resulting suspension was diluted with Et_2O and the precipitate filtered off and dried: 2.06 g (59%) of **37**. White powder. M.p. 99–102°. HPLC (*Method 3*): 92.3%. IR (KBr): 2757*w*, 2180*w*, 1437*s*, 745*m*, 691*m*. ^{1}H-NMR (270 MHz, $CDCl_3$): 1.60 (*s*, Me–C(11)); 1.69 (*s*, 3 H–C(12)); 1.72 (*s*, Me–C(7)); 1.83 (*d*, J = 6, Me–C(3)); *ca.* 2.09 (*m*, 2 H–C(8), 2 H–C(9)); 4.92 (*dd*, J = 15, 8, 2 H–C(1)); 5.04 (*m*, H–C(10)); 5.22 (*s*, H–C(6)); 5.65 (*m*, H–C(2)); 7.6–7.9 (*m*, 15 arom. H). Anal. calc. for $C_{33}H_{36}BrP$ (543.53): C 72.92, H 6.68, Br 14.70; found: C 72.66, H 6.59, Br 14.46.

17. *Triphenyl[(2*E*,6*E*)-3,7,11-trimethyldodeca-2,6,10-trien-4-ynyl]phosphonium Bromide* (**36**). A soln. of PBr_3 (5.61 g, 21 mmol) in AcOEt (7 ml) was added over 5 min at −20° to a stirred soln. of **34** (6.55 g, 30 mmol) in AcOEt (20 ml), DMF (7 ml), and pyridine (0.07 ml). The mixture was stirred at −20° for 30 min, at 0° for 30 min, and worked up as described in *Exper. 16*. The crude bromide (7.6 g) was dissolved in AcOEt (55 ml), PPh_3 (7.94 g, 30 mmol) was added and the mixture stirred at r.t. for 17 h. The resulting suspension was diluted with AcOEt (50 ml) and the solid collected by filtration yielding 12.8 g (78%) of **36** as white powder, m.p. 147–148°. The product was dissolved in CH_2Cl_2 (20 ml), AcOEt (540 ml) was slowly added and the suspension stirred at 0° for 30 min and then filtered: 11.7 g (72%) of white crystalline **36**. M.p. 150–151°. HPLC (*Method 3*): 96.9%. IR (KBr): 2180*w*, 1437*s*, 744*m*, 690*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.56 (*d*, J = 4, Me–C(3)); 1.59 (*s*, Me–C(11)); 1.67 (*s*, 3 H–C(12)); 1.84 (*s*, Me–C(7)); *ca.* 2.10 (*m*, 2 H–C(8), 2 H–C(9)); 4.87 (*dd*, J = 8, 16, 2 H–C(1)); 5.05 (*m*, H–C(10)); 5.32 (*s*, H–C(6)); 5.65 (*m*, H–C(2)); 7.65–7.9 (*m*, 15 arom. H). Anal. calc. for $C_{33}H_{36}BrP$ (543.53): C 72.92, H 6.68, Br 14.70; found: C 72.67, H 6.78, Br 14.73.

18. *(all-*E*)-7,8,7′,8′-Tetradehydrolycopene* (**38**). BuLi (5 ml, 1.6M in hexane, 8.0 mmol) was added over 5 min at −78° to **36** (4.35 g, 8.0 mmol) in THF (40 ml). After stirring at −78° for 5 min and at −10° for 3 min, **24** (493 mg, 3.0 mmol) was added in one lot. The mixture was stirred at r.t. for 30 min and then evaporated. The residue was chromatographed (silica gel, hexane/CH_2Cl_2 2:1) to yield a semisolid compound (1.65 g) which was isomerized in refluxing hexane for 2 h and cooled to −20°. The precipitate was filtered off and dried: 0.960 g (60%) of **38**. Red-orange crystals. M.p. 131°. HPLC (*Method 1*): 97.8%. UV/VIS (hexane/2% CH_2Cl_2): 480 (123000), 451 (144000), 428 (sh, 109000). IR (KBr): 2165*w*, 1619*w*, 1442*m*, 962*s*. ^{1}H-NMR: *Table 2*. ^{13}C-NMR: *Table 3*. MS: 532 (15, M^+), 463 (2), 69 (100). Anal. calc. for $C_{40}H_{52}$ (532.86): C 90.16, H 9.84; found: C 90.11, H 10.01.

19. *(7*Z*,7′*Z*)-Lycopene* (**6**). A mixture of **38** (300 mg, 0.56 mmol), Pd/$CaCO_3$ (300 mg), and 2,2′-(ethylenedithio)bis(ethanol) (1.5 mg, added in 0.15 ml THF) in hexane (20 ml) was hydrogenated at 5 bar H_2/r.t. for 4 h. CH_2Cl_2 (10 ml) was added, the mixture filtered, the filtrate evaporated, the residue (306 mg) dissolved in CH_2Cl_2 (2 ml), hexane (5 ml) added, and the CH_2Cl_2 evaporated. The precipitate was filtered off, washed with hexane, and dried: 199 mg (66%) of **6**. Red-orange crystals. M.p. 133°. HPLC (*Method 1*): 95.5%. UV/VIS: *Table 4*. IR (KBr):

1621*m*, 1440*m*, 967*s*. ^{1}H-NMR: *Table 2*. ^{13}C-NMR: *Table 3*. MS: 536 (20, M^+), 467 (2), 444 (2), 69 (100). Anal. calc. for $C_{40}H_{56}$ (536.89): C 89.49, H 10.51; found: C 89.20, H 10.35.

20. *(9Z,9'Z)-7,8,7',8'-Tetradehydrolycopene* (**39**). BuLi (5.8 ml, 1.6M in hexane, 9.3 mmol) was added over 5 min at −78° to **37** (5.02 g, 9.3 mmol) in THF (45 ml). The mixture was stirred at −78° for 5 min, then the temp. raised quickly to −10°, and **24** (0.572 g, 3.5 mmol) added in one lot. Stirring at r.t. was continued for 30 min, the mixture evaporated and the residue chromatographed (silica gel, hexane/CH_2Cl_2 2:1): crude **39** (1.9 g) as a mixture of isomers. Isomerization in refluxing hexane and crystallization at 0° gave in 3 crops 0.95 g (51%) of **39**, m.p. 117–119°. Two recrystallizations from hexane afforded 0.815 g (44%) of **39**. Orange crystals. M.p. 117–118° ([22]: m.p. 110°). HPLC (*Method 3*): 95.1%. UV/VIS (hexane/2% CH_2Cl_2): 470 (116000), 441 (131000), 418 (90000). IR (KBr): 2170*w*, 1620*w*, 1442*m*, 962*s*. ^{1}H-NMR: *Table 2*. ^{13}C-NMR: *Table 3*. MS: 532 (12, M^+), 463 (2), 69 (100). Anal. calc. for $C_{40}H_{52}$ (532.86): C 90.16, H 9.84; found: C 90.20, H 10.04.

21. *(7Z,9Z,7'Z,9'Z)-Lycopene* (= *Prolycopene*; **9**). *Lindlar* catalyst (type *A*, 500 mg) in hexane/CH_2Cl_2 9:1 (25 ml) was pre-hydrogenated at r.t. for 20 min. Then, a soln. of **39** (196 mg, 0.37 mmol) in hexane/CH_2Cl_2 9:1 (25 ml) and quinoline (0.2 ml) was added. The mixture was hydrogenated at 1 bar H_2/r.t. in the dark. After 30 min (the rate of H_2 uptake had decreased markedly), the mixture was filtered and evaporated and the residue chromatographed (silica gel, hexane/CH_2Cl_2 2:1). The product (200 mg) was first recrystallized from hexane (2.5 ml, 35°→−20°, m.p. 108–109°) and then from CH_2Cl_2/MeOH (1:10, 7 ml): 86 mg (44%) of **9** as red-orange crystals. M.p. 109°. HPLC (*Method 1*): 95.1%. UV/VIS: *Table 4*. IR (KBr): 1620*m*, 1442*m*, 961*s*. ^{1}H-NMR: *Table 2*. ^{13}C-NMR: *Table 3*. MS: 536 (20, M^+), 467 (2), 444 (2), 69 (100). Anal. calc. for $C_{40}H_{56}$ (536.89): C 89.49, H 10.51; found: C 89.46, H 10.70.

22. *(all-E)-7,8-Didehydrolycopene* (**40**). BuLi (2.5 ml, 1.6M in hexane, 4.0 mmol) was added at −78° over 3 min to **36** (2.2 g, 4.0 mmol) in THF (60 ml) and the mixture stirred at −78° for 5 min. The internal temp. was quickly brought to −10°, and a soln. of **26** (946 mg, 2.7 mmol) in CH_2Cl_2 (6 ml) was added over 1 min. The mixture was stirred at r.t. for 20 min and then worked up and isomerized as described in *Exper. 20* to give, in 2 crops, 1.00 g (69%) of **40**, m.p. 143°. Recrystallization from hexane yielded 916 mg (63%) of **40**. Red crystals. M.p. 145°. HPLC (*Method 1*): 98.4%. UV/VIS (hexane/2% CH_2Cl_2): 492 (143000), 461 (165000), 436 (112000). IR (KBr): 2169*w*, 1626*w*, 1443*m*, 964*s*. ^{1}H-NMR: *Table 2*. ^{13}C-NMR: *Table 3*. MS: 534 (20, M^+), 465 (3), 428 (3), 69 (100). Anal. calc. for $C_{40}H_{54}$ (534.87): C 89.82, H 10.18; found: C 89.07, H 10.25.

23. *(7Z)-Lycopene* (**3**). Compound **40** (428 mg, 0.80 mmol) was hydrogenated at 1 bar H_2/r.t. over *Lindlar* catalyst (type *A*, 1 g) in hexane/CH_2Cl_2 4:1 (100 ml) in presence of quinoline (0.4 ml). H_2 uptake ceased after 1 h. The filtered soln. was evaporated and chromatographed (silica gel, hexane/CH_2Cl_2 2:1). Recrystallization of the solid product from hexane afforded 274 mg (64%) of **3**. Red crystals. M.p. 126°. HPLC (*Method 1*): 93.4%. UV/VIS: *Table 4*. IR (KBr): 1624*w*, 1444*m*, 955*s*. ^{1}H-NMR: *Table 2*. ^{13}C-NMR: *Table 3*. MS: 536 (20, M^+), 430 (9), 69 (100). Anal. calc. for $C_{40}H_{56}$ (536.89): C 89.49, H 10.51; found: C 89.66, H 10.65.

24. *(9Z)-7,8-Didehydrolycopene* (**41**). BuLi (1.15 ml, 1.6M in hexane, 1.84 mmol) was added over 3 min at −78° to a soln. of **37** (1.0 g, 1.84 mmol) in THF (30 ml). The mixture was stirred at −78° for 5 min, then quickly brought to −10°, and treated with a soln. of **26** (0.435 g, 1.24 mmol) in CH_2Cl_2 (3 ml). The mixture was stirred at r.t. for 15 min, then worked up and isomerized as described in *Exper. 20* to give 415 mg (62%) of **41**, m.p. 96°. Recrystallization from hexane afforded 224 mg (34%) of **41**. Red-orange crystals. M.p. 103–104°. HPLC (*Method 1*): 98.1%. UV/VIS (hexane): 486 (134000), 455 (147000), 430 (97000). IR (KBr): 2160*w*, 1626*w*, 1441*m*, 965*s*. ^{1}H-NMR: *Table 2*. ^{13}C-NMR: *Table 3*. MS: 534 (12, M^+), 465 (2), 69 (100). Anal. calc. for $C_{40}H_{54}$ (534.87): C 89.82, H 10.18; found: C 89.69, H 10.41.

25. *(7Z,9Z)-Lycopene* (**7**). Compound **41** (78 mg, 0.15 mmol) was hydrogenated at 1 bar H_2/r.t. over *Lindlar* catalyst (type *A*, 170 mg) in hexane/CH_2Cl_2 9:1 (16 ml) in presence of quinoline (0.07 ml). After 30 min, H_2 uptake ceased, and the filtered soln. was evaporated and the residue chromatographed (silica gel, hexane/CH_2Cl_2 2:1). Recrystallization from CH_2Cl_2/MeOH (solvent exchange) gave 49 mg (63%) of 7. Sensitive, red-orange crystals. M.p. 78–79°. HPLC (*Method 1*): 86.1%. UV/VIS: *Table 4*. IR (KBr): 1630*w*, 1444*m*, 961*s*. ^{1}H-NMR: *Table 2*. ^{13}C-NMR: *Table 3*. MS: 536 (11, M^+), 69 (100).

26. *(all-E)-15,15'-Didehydrolycopene* was prepared as described in [9]. M.p. 192–194°. HPLC (*Method 1*): 95.4%. UV/VIS (hexane/2% CH_2Cl_2): 481 (119000), 451 (136000), 431 (sh, 108000). IR (KBr): 2140*w*, 1628*m*, 1440*s*, 967*s*. ^{1}H-NMR: *Table 2*. ^{13}C-NMR: *Table 3*. MS: 534 (10, M^+), 465 (4), 69 (100). Anal. calc. for $C_{40}H_{54}$ (534.87): C 89.82, H 10.18; found: C 89.79, H 10.33.

27. *(15Z)-Lycopene* (**4**) was prepared as described in [9]. M.p. *ca.* 100°. HPLC (*Method 1*): 93.8%. UV/VIS: *Table 4*. IR (KBr): 1631*m*, 1444*m*, 958*s*. ^{1}H-NMR: *Table 2*. ^{13}C-NMR: *Table 3*. MS: 536 (15, M^+), 467 (1), 444 (2), 430 (3), 69 (100).

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