ORGANIC LETTERS

2003
Vol. 5, No. 15
2675−2678

Structure Elucidation of Polyene Systems with Extensive Charge Delocalization—Carbocations from Allylic Carotenols

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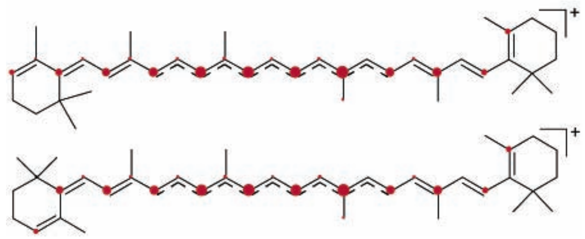
Received June 3, 2003

ABSTRACT



The structures of two diastereomeric cations, readily prepared from *β,β*-caroten-4-ol (1) by treatment with trifluoroacetic acid, have been determined by NIR and NMR spectroscopy, resulting in the complete structure elucidation of the most extensively delocalized carbocations so far described. Higher partial charge was observed toward the center of the polyene chain (larger filled red circles). Bond reversion occurs in the central region of the molecule.

In the carotenoid field the elimination of allylic hydroxy or alkoxy groups in acidified chloroform, resulting in products with prolonged chromophore, has become a useful diagnostic reaction.[1] This reaction, performed in 0.03 N HCl/$CHCl_3$, was first introduced in 1951 by Karrer's school[2] and later standardized.[3] The reaction was early employed for isocryptoxanthin (**1**, *β*,*β*-caroten-4-ol), providing isocarotene (**2**, 4′,5′-didehydro-4,5′-*retro*-*β*,*β*-carotene).[4] The reaction has been considered to proceed via a hypothetic, rearranged allylic carbocation, Scheme 1.[1,5]

Recently we have characterized in detail a dication prepared from *β*,*β*-carotene (**3**) by treatment with BF_3-etherates.[6] A modern reinvestigation of the reaction referred to in Scheme 1 has led to a complete structure elucidation of the most charge delocalized carbocation (over 23 carbon atoms) so far described.

(4*RS*)-Isocryptoxanthin (**1**) was prepared by $NaBH_4$-reduction of echinenone (*β*,*β*-caroten-4-one). The standard reaction in 0.03 N HCl in $CHCl_3$ was monitored by vis−NIR spectroscopy, and the reaction mixture was analyzed by HPLC. At room temperature, a weak absorption around 1010 nm was detected and assigned to the intermediate carbocation. This cation intermediate was more pronounced at −20 °C. However, the reaction proceeded to the elimination products isocarotene (**2**) and some 3,4-didehydro-*β*,*β*-carotene. Strongly *E*/*Z* isomerized isocarotene (**2**), established by HPLC analysis, was consistent with cationic intermediates.

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[1] Liaaen-Jensen, S. In *Carotenoids*; Isler, O., Ed.; Birkhaüser: Basel, 1971; pp 61−188.

[2] Karrer, P.; Leumann, E. *Helv. Chim. Acta* **1951**, *34*, 445−453.

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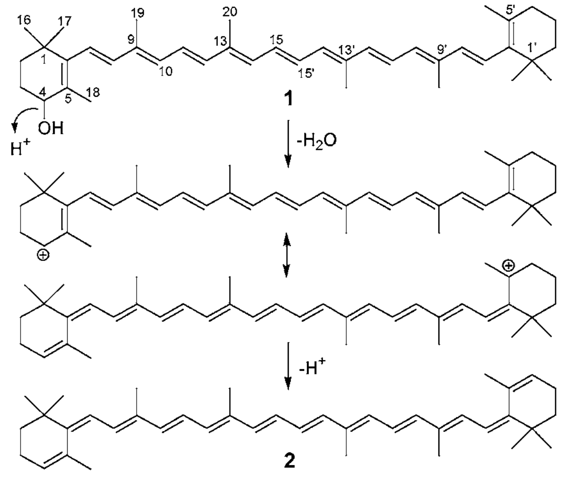
10.1021/ol034987w CCC: $25.00

Scheme 1



When isocryptoxanthin (**1**) was reacted with 13 mM trifluoroacetic acid in CH_2Cl_2 at −20 °C, a fast and quantitative conversion of **1** to a colorless (black at high concentration) solution of cation **4** was observed, with λ_{max} 1028 nm in the same region as carotenoid radical cations,[7] Figure 1. The small differences in λ_{max} for **4** in CH_2Cl_2 and $CHCl_3$ are ascribed to different solvents and counterions. The stability of the cation **4** was monitored by its NIR absorption at −20 °C, demonstrating a decrease in intensity at λ_{max} of <10% during 3 h.

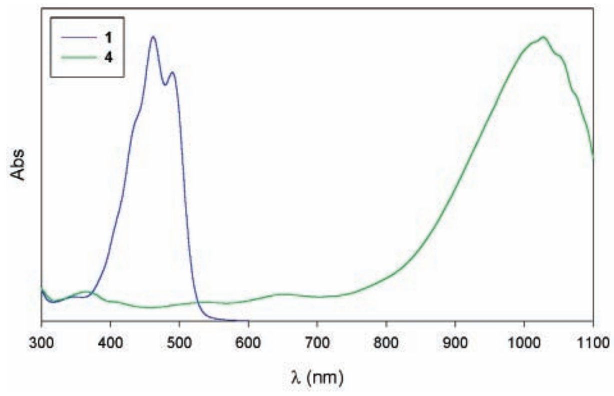


Figure 1. Absorption spectra of isocryptoxanthin (**1**) and the monocation **4** in CH_2Cl_2.

Detailed NMR analysis (400 and 500 MHz, CD_2Cl_2, −10 °C) using CF_3COOD as acid was carried out, including ^1H, $^1H-^1H$ COSY, ROESY, $^1H-^{13}C$ HSQC, and $^1H-^{13}C$ HMBC spectra.

It was evident that the cation **4** had an unsymmetrical structure and consisted of two isomers **4a** and **4b** in a ca. 2:1 ratio. ^1H and ^{13}C NMR chemical shifts of **4a** and of β,β-carotene (**3**)[8] and isocarotene (**2a**)[8] used as models are given in Table 1, as well as shift differences between the cation **4a** and the relevant model.

Table 1. ^1H and ^{13}C Chemical Shifts for Monocation **4a** and Shift Changes Relative to **2** or **3** in CD_2Cl_2 Solution

	δ_H (ppm)			δ_C (ppm)		
	4a	ref[a]	Δ	**4a**	ref[a]	Δ
1				36.5	35.1	1.4
2	1.58[d]	1.50	0.08	40.1	40.8	−0.7
3	2.24[d]	2.12	0.12	23.6	23.0	0.6
4	6.20	5.78	0.42	138.3	128.6	9.7
5				135.6	134.1	1.5
6				160.3	146.1	14.2
7	6.60	6.39	0.21	122.6	120.3	2.3
8	7.56	6.79	0.77	147.7	130.4	17.3
9				139.4	135.5	3.9
10	7.29	6.44	0.85	158.7	138.9	19.8
11	7.00	6.63[b]	0.37	127.4	124.3	3.1
12	7.41	6.35	1.06	161.7	137.3	24.4
13				141.1	136.4	4.7
14	7.27	6.25	1.02	158.4	132.4	26.0
15	7.00	6.63	0.37	132.4	130.0	2.4
16	1.35	1.31	0.04	29.5	29.0?	0.5
17	1.35	1.31	0.04	29.5	29.0?	0.5
18	1.96	1.92	0.04	21.6	21.7	−0.1
19	2.07	1.97	0.10	12.0	12.1	−0.1
20	2.13	1.97	0.16	12.7	12.8	−0.1
1′				34.7	34.4	0.3
2′	1.48[d]	1.46	0.02	39.9	39.8	0.1
3′	1.61[d]	1.62	−0.01	19.0	19.4	−0.4
4′	2.12[d]	2.02	0.10	34.4	33.2	1.2
5′				139.9	129.3	10.6
6′				138.7	138.0	0.7
7′	6.90	6.16	0.74	138.2	126.7	11.5
8′	6.49	6.15	0.34	137.0	137.8	−0.8
9′				154.6	136.0	18.6
10′	6.54	6.15	0.39	133.6	130.8	2.8
11′	7.70	6.65	1.05	143.5	125.1	18.4
12′	6.74	6.35	0.39	137.8	137.3	0.5
13′				163.9	136.4	27.5
14′	6.82	6.25	0.57	136.8	132.4	4.4
15′	7.75	6.63	1.12	154.3	130.0	24.3
16′	1.08	1.03	0.05	29.0	29.0	0.0
17′	1.08	1.03	0.05	29.0	29.0	0.0
18′	1.82	1.72	0.10	22.2	21.7	0.5
19′	2.21	1.97	0.24	13.8	12.8	1.0
20′	2.34	1.97	0.37	14.5	12.8	1.7
Σ			12.42[c]			254.2

[a] **2a** used as reference for positions 1−11 and 16−19; **3** used for the rest of the molecule. Data from ref 8, except H-11. [b] From ref 11. [c] Counting methylene protons twice and methyl protons three times. [d] Methylene protons pairwise same chemical shifts.

The total ^1H (12.42 ppm) and ^{13}C (254.2 ppm) shift difference of **4a** relative to **2a** (C-1−C-11 and C-16,17,18,-

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(7) Konovalov, V. V.; Kispert, L. D. *J. Chem. Soc., Perkin Trans. 2* **1999**, *4*, 901−910.

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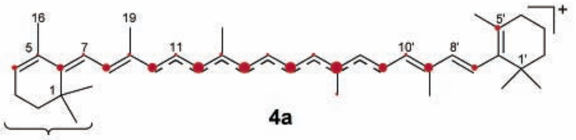
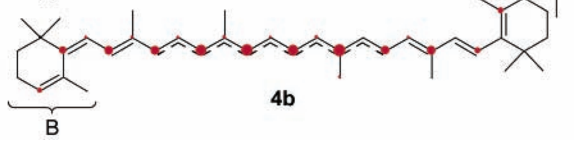
19) or **3** (rest of the molecule) was consistent with a monocarbocation.[6,9,10] The ^{13}C chemical shift differences, Table 1, were used to identify the charge distribution in **4a**. The charge was mainly located in the central region; $\Delta\delta_C >$ 18 ppm at C-10, 12, 14, 15′, 13′, 11′, and 9′; $\Delta\delta_C >$ 9 ppm also includes C-4, 6, 8, 5′, and 7′. Larger filled red circles (structures **4a** and **4b**) indicate higher charge density. Judged by the chemical shift and coupling pattern, **4a** contained an olefinic proton at C-4. A double bond at C-8,9 was concluded from the long-range coupling of Me-19 to H-8 in the COSY spectrum and the s-*trans* coupling of 13.4 Hz for H-7,8.

A common β-end group, extended from C-1′ to C-10′, followed from the *trans* H-7′,8′ coupling constant (J = 16.0 Hz) and long-range coupling of Me-19′ to H-10′. Consequently, bond reversion (dotted bonds) must take place within the C-10−C-11′ region in **4a**.



4a



4b

The isomer **4b** differed from **4a** in chemical shifts mainly in the C-1−C-10 region, as predicted for opposite configuration of the exocyclic C-6,7 double bond. ^{1}H and ^{13}C chemical shifts for this isomer and shift changes relative to relevant models are given in Table 2.

Table 2. ^{1}H and ^{13}C Chemical Shifts for Monocation **4b** and Shift Changes Relative to **2** or **3** in CD_2Cl_2 Solution[a]

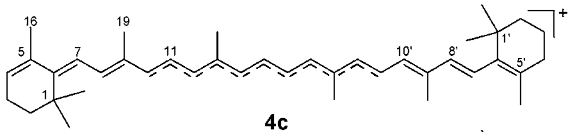
	δ_H (ppm)			δ_C (ppm)		
	4b	ref[b]	Δ	**4b**	ref[b]	Δ
1				38.2	36.3	1.9
2	1.57[d]	1.49	0.08	36.5	37.2	−0.7
3	2.30[d]	2.12	0.18	24.4	23.9	0.5
4	6.04	5.64	0.40	138.7	129.8	8.9
5				132.9	132.5	0.4
6				162.7	147.4	15.3
7	6.65	6.38	0.27	121.7	118.6	3.1
8	7.49	6.69	0.80	149.5	131.0	18.5
16	1.16	1.12	0.04	28.1	28.0	0.1
17	1.16	1.12	0.04	28.1	28.0	0.1
18	2.15	2.09	0.06	26.0	25.5	0.5
Σ			12.66[c]			255.4

[a] Chemical shifts in positions not given in Table 2 are the same as for **4a** given in Table 1. [b] **2b** used as reference for positions 1−8 and 16−18; data from ref 8. [c] Counting methylene protons twice and methyl protons three times. [d] Methylene protons pairwise same chemical shifts.

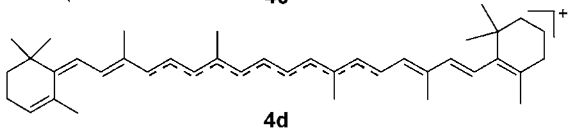
The total NMR evidence is thus accommodated with **4** being a mixture of the stereoisomers **4a** and **4b** differing in the configuration of the exocyclic C-6,7 double bond caused by restricted rotation of the ring. The effect of this *E*/*Z* isomerization on the charge distribution in the two diastereomeric cations **4a** and **4b** is reflected by the difference in chemical shift data, Tables 1 and 2.

Rotation also of the C-6′,7′ single bond of the monocation **4** was observed by a sharp singlet at δ_H 1.38 ppm, constituting 20% of the geminal dimethyl groups of the β-end group. Support for this assignment was obtained from the HMBC spectrum, giving the following carbon chemical shifts: 30.3 ppm (C-16′,17′), 34.4 ppm (C-1′), and 135.9 ppm (C-6′).

Structures **4c** and **4d** for these less populated conformers of the monocation **4** are shown. For **4c**, all polyene single bonds are in the s-*trans* configuration, giving the best overlap of π orbitals. This would therefore be the structure expected to provide maximum charge delocalization. It is interesting to note that the C-6′,7′ s-*trans* conformation of the β-end group has only been encountered in the ionized state.



4c



4d

The monocation **4** in CH_2Cl_2 solution was reacted with water as a nucleophile in aqueous acetone at −10 °C, pigment recovery 88%. The reaction mixture was analyzed by HPLC/vis, revealing the formation of strongly *E*/*Z* isomerized isocryptoxanthin (**1**, 89% of total recovered) and isocarotene (**2**, ca. 5%). Both **4a** and **4b** will provide **1** with a C-6,7 s-*cis* bond. All carotenoids with the common β-end group exist in this preferred conformation.[8,12]

Isocarotene was originally assigned the structure **2**. More recent NMR studies including NOE experiments have demonstrated that the C-6,7 *E* (*trans*) end group A dominated over the C-6,7 *Z* (*cis*) end groups B in a 3:1 ratio in $CDCl_3$.[11] This means that **2** consisted of three diastereomers with end groups A,A (**2a**, 56%), B,B (**2b**, 6%), and A,B (**2c**, 38%). The formation of products **2** (as **2a**, **2b**, **2c**) and **1** from the cations **4a** and **4b** may readily be rationalized.

The smooth formation of the cations **4** by treatment of the allylic carotenol isocryptoxanthin (**1**) with CF_3COOH in CH_2Cl_2 demonstrates a preferential and selective protonation of the hydroxy group, followed by elimination of water to produce the cations **4**. No protonation of the polyene chain was noted. It has been shown previously that treatment of unsubstituted β,β-carotene (**3**) with CF_3COOH at −20 °C

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results in protonation of the polyene chain,[7,13] as determined by ^{1}H, ^{1}H−^{1}H COSY, and HSQC NMR (600 MHz, $CDCl_3$, −20 °C) analysis.[13]

Work on the cation prepared from isozeaxanthin (*β*,*β*-carotene-4,4′-diol) with suitable acids is in progress.

The charge distribution of the monocation **4**, which is the longest charged polyene system structurally elucidated, may be of relevance for the understanding of conductivity properties of doped carotenoids[14] and conducting organic polymers. The NMR chemical shifts and indirect coupling constants should serve as reference data for extensive empirical force-field and ab initio calculations of these large polyenyl carbocations.

Acknowledgment. We thank Hoffmann-La Roche, Basel, for a sample of synthetic echinenone and for a research grant to S.L.J.

Supporting Information Available: NMR spectra of isocryptoxanthin and the monocations. This material is available free of charge via the Internet at http://pubs.acs.org.

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