Iron Carbonyl Complexes of β -Carotene and Lycopene

MITSUO ICHIKAWA, MINORU TSUTSUI^{1b}, and FREDERICK VOHWINKEL

New York University, Research Division, Department of Chemical Engineering, New York
New York 10453

(Z. Naturforschg. **22 b**, 376—379 [1967]; eingegangen am 22. Oktober 1966)

A metal π -complex of β -carotene has been synthesized as a stable compound which has been found to be a tetrakis (iron tricarbonyl) complex. A structure for this complex is proposed based upon U.V., I.R., and N.M.R. data. Lycopene also forms an iron tricarbonyl π -complex. This appears to be a mixture of tetrakis and pentakis (iron tricarbonyl).

In previous reports in this series, the formation of organometallic π -complexes with biologically significant materials (such as vitamin A acetate¹, acetylgosterol², and esterone³ have been reported. The objective of this research series is the investigation of the possible occurrence of π -complex bonding⁴ in biological media. The significance of biological π -complex bonding has been pointed out previously⁵. Currently the formation of π -complexes of carotenoids such as β -carotene and lycopene with tri-iron dodecacarbonyl have been investigated. Carotenoids containing an extensive eleven conjugated double bond system become interesting ligands from an organometallic point of view.

In a previous paper^{1a}, the π -complex formation of vitamin A acetate (which has five conjugated double bonds) with iron carbonyl compound was discussed. However, linear hydrocarbons containing more than six conjugated double bonds have not been investigated for the possible formation of π -complexes.

β -carotene, triiron dodecacarbonyl (10 mole ratio, 30 mole ratio as $\text{Fe}(\text{CO})_4$), and benzene were refluxed for 63 hours under nitrogen. During the resulting reaction, an iron mirror was formed on the inside wall of the reaction vessel. Metallic iron and unreacted tri-iron dodecacarbonyl were then removed by filtration. The yellow-green filtrate was evaporated to dryness under reduced pressure to give a yellow solid contaminated with a small amount of a black crystalline material. Precipitation from a benzene solution with n-hexane gave fine yellow needles, mp $>350^\circ$, (darkens gradually). This

compound was identified as β -carotene tetrakis (iron tricarbonyl) (I).

The infrared spectra of compound I showed strong peaks at 1970 and 2020 cm^{-1} . This was due to the presence of an iron tricarbonyl group π -complex-bonded to β -carotene¹. In addition, the C—H deformation bond of the *trans*-CH=CH— of β -carotene at 970 cm^{-1} almost disappeared upon π -complex formation. The ultraviolet absorption maxima of conjugated dienes have been shown to shift towards shorter wave lengths upon π -complex formation with an iron tricarbonyl group^{2, 6}. In the case of β -carotene (containing eleven conjugated double bonds) a remarkable shift of absorption maxima was observed upon π -complex formation. The ultraviolet spectra of compound I showed an absorption maximum and a shoulder at 347 $\text{m}\mu$ ($\log \epsilon = 3.11$) and 268 $\text{m}\mu$ ($\log \epsilon = 3.16$), respectively. These positions were further shifted from the two absorption maxima and a shoulder of β -carotene at 478 $\text{m}\mu$ ($\log \epsilon = 4.95$), 448 $\text{m}\mu$ ($\log \epsilon = 5.01$) and 428 $\text{m}\mu$ ($\log \epsilon = 4.188$) while the intensities were greatly decreased. The n.m.r. spectra of compound I was rather complex. Peaks, due to the protons around the six-membered ring of β -carotene, were observed in the n.m.r. spectra of compound I. For the same reason as vitamin A acetate iron tricarbonyl¹, the six-membered ring cannot participate in π -complex formation with the iron tricarbonyl group. The effect of π -complex formation was also observed by the great peak decrease around the =CH— region (3.33, 3.58) and also by the shift of the =CH— peak to the region of an aromatic =CH.

¹ a) Part III: A. NAKAMURA and M. TSUTSUI, J. Med. Chem. **7**, 335 [1964]; Elemental Organic Compounds XIX. —

b) To whom to correspond. Present address: New York University, Dept. of Chemistry, Bronx, N.Y. 10 453.

² Ibidem, *ibid.* **6**, 796 [1963].

³ Ibidem, Z. Naturforschg. **18 b**, 666 [1963].

⁴ The bonding between a transition metal atom and organic π -ligand.

⁵ a) M. TSUTSUI, Chem. Engng. News **39**, No. 16, 42 [1961].

b) Ibidem, Z. Chem. **2**, 214 [1962].

⁶ B. F. HALLAM and P. L. PAUSON, J. chem. Soc. [London] **1958**, 642.

The formation of iron tricarbonyl complexes have been reported through bonding with two adjacent conjugated double bonds in the cisoid form on the same plane⁷. Although β -carotene has eleven conjugated double bonds, two double bonds in the cyclic rings may be considered unavailable for π -complex formation since, in compounds with β -end groups, steric hindrance between the gem-dimethyl group and the polyene chain forces the latter out of the plane of the cyclic double bond⁸ and, consequently, conjugation between the cyclic double bond and the polyene chain is restricted. Upon π -complex formation between vitamin A acetate and triiron dodecacarbonyl, the cyclic double bond is not used for π -complex formation¹. The n.m.r. spectrum of the gem-dimethyl group of compound I showed a very sharp singlet peak at 9.12. It indicates that no iron tricarbonyl was attached to the cyclic double bond in this compound. It was also reported that the cyclic bond in β -ionylidene is not involved in π -complex formation with iron pentacarbonyl⁹.

Fig. 1.

Thus, nine double bonds in a conjugated system may be considered to form π -complexes with iron tricarbonyl groups. A maximum of four iron tri-

carbonyl groups can possibly be introduced into the β -carotene molecule. There are three distinct arrangements possible, [A], [B], and/or [C].

Fig. 2.

On the basis of stereochemical considerations, it has been concluded that only double bonds of the type $-\text{C}(\text{CH}_3)=\text{CH}-$ and the double bond in the center of a carotenoid molecule can take part in *cis-trans* isomerization¹⁰.

In the case of β -carotene, only the 9, 10), (13, 14), 15, 15'), (13', 14') and (9', 10') double bonds can be involved in *cis-trans* isomerism.

The existence of structure [C] can be excluded by stereochemical considerations using stereo-models; the three isomers of type A and one of type B are possible. It is well known that the isomerization of β -carotene results in the formation of neo- β -carotene- μ and neo- β -carotene-B as the main products¹¹. By electronic absorption spectra, infra-

⁷ a) M. A. BENNETT, Chem. Review **62**, 611 [1962]; b) E. O. FISCHER and H. WERNER, Angew. Chem. **75**, 57 [1963]; c) R. PETTITT, G. EMERSON, and J. MAHLER, J. chem. Educat. **40**, 175 [1963].

⁸ a) BRANDE, TONES, RICHARDSON, SONDHEIMER, and TOOGOOD, J. chem. Soc. [London] **1949**, 1890; b) OROSHNIK, KARMAS, and MEBANE, J. Amer. chem. Soc. **74**, 295 [1952]; c) BRANDE, BRUUN, WEEDON, and WOODS, J. chem. J. chem. Soc. **1952**, 1419.

⁹ M. CAIS and N. MAOZ, J. Organomet. Chem. **5**, 3110 [1966].

¹⁰ a) L. ZEICHMEISTER, L. PAULING and coworkers, J. Amer. chem. Soc. **65**, 1940 [1943]; b) L. ZEICHMEISTER, Chem. Reviews **34**, 267 [1944].

¹¹ L. ZEICHMEISTER and A. POLGAR, J. Amer. chem. Soc. **64**, 1856 [1942].

red analysis, and thermal stability, it is concluded that neo- μ and neo- β possibly have 9,10-*cis*, and 9,10; 13',14'-*di-cis* structures, respectively.

The structure [A-1], therefore, most probably represents compound I.

Lycopene

Fig. 3.

As for lycopene, pentairon pentadecacarbonyl complexes are expected to be formed since steric hindrance of gem methyl groups with the two end double bonds is not a restricting factor. The reaction of lycopene with triiron dodecacarbonyl (25 mole ratio as $\text{Fe}(\text{CO})_4$) was achieved by refluxing in a benzene solution for 144 hours. A greenish-yellow supernatant liquid was evaporated to dryness under reduced pressure. The extraction of the evaporated residue with *n*-pentane gave an orange yellow solution. A yellow residue was subsequently obtained by evaporation. Further purification was accomplished by reprecipitation using benzene and *n*-pentane. After repeated reprecipitation, the elemental analysis did not reveal increased purity. The analytical data always fell between the calculated values for lycopene $-4\text{Fe}(\text{CO})_3$ and $-5\text{Fe}(\text{CO})_3$. Similar analytical data was obtained when reacting for short periods. The infrared spectra of the compound obtained here (II) showed peaks at 1970 and 2030 cm^{-1} which is almost the same as that of compound I. In this case, also, the CH deformation band of *trans*- $\text{CH}=\text{CH}-$ at 970 cm^{-1} is greatly decreased by π -complex formation. Compound II may consist of a mixture of lycopene tetrairon dodecacarbonyl isomers and lycopene pentairon pentadecacarbonyl isomers.

Attempts to synthesize β -carotene complexes with less than four iron tricarbonyl groups have been tried. It was, however, very difficult to isolate the complexes (as isomeric mixtures) in spite of many efforts. These efforts always resulted in mixed complexes of β -carotene containing different numbers of iron tricarbonyl groups. The purification of vitamin A acetate iron tricarbonyl mixtures was successful using an alumina column chromatograph technique. However, this technique was undesirable here because of marked evolution of a gas from the

column. This was probably due to the decomposition of iron tricarbonyl groups.

Experimental

The β -carotene used was a commercial product of Eastman Organic Chemicals; and the lycopene was a product of Hoffman-LaRoche Inc. Triiron-dodecacarbonyl was prepared by KING's method¹². Infrared spectra were measured on a Perkin-Elmer Infracord, 137 B, in *n*-ujol. The ultraviolet spectra were determined by the use of a Bausch & Lomb Spectronic 505 measured in spectrograde hexane. The n.m.r. spectra were taken on a Varian A-60 in deuterio benzene using tetramethylsilane as an internal standard. Elemental analysis was done by Schwarzkoff Microanalytical Laboratory, N. Y.

Reaction of β -carotene with Triiron Dodecacarbonyl

β -carotene (537 mg, 1 mmole), tritiron dodecacarbonyl (5037 mg, 10 mmoles) and benzene (100 ml) were refluxed under nitrogen for 63 hours. During the reaction, a shiny metal was deposited on the wall of the Schlenk tube used as the reaction vessel. As the reaction proceeded, the mirror intensity increased. After cooling, metallic iron and unreacted triiron dodecacarbonyl were removed by filtration. The green filtrate was evaporated to dryness under reduced pressure to yield a bright yellow solid contaminated with a small amount of a black crystalline material (Ca 400 mg). No oily product was observed. The solid material was treated with 150 ml. of *n*-hexane and filtered to remove any insoluble black material. The filtrate was evaporated to ca. 60 ml. under reduced pressure and the precipitate was collected on a sintered glass filter and washed three times with 30 ml. of *n*-hexane to give canary yellow solid. Additional contaminating black material (which is soluble in *n*-hexane) was removed by thorough washing with *n*-hexane. For further purification, the solid was dissolved in a small amount of benzene, filtered to remove any insoluble material, and reprecipitated by adding a large amount of *n*-hexane. The solution was concentrated by evaporation to effect crystallization. This was stored in a refrigerator at -5°C . and the solid was collected and washed with *n*-hexane (92 mg). This purification procedure was repeated three times to give fine yellow microscopic needles, $\text{mg} > 350^\circ\text{C}$. (darkens gradually).

Anal. Calcd. for $\text{C}_{40}\text{H}_{56} \cdot 4\text{Fe}(\text{CO})_3$: C, 56.97; H, 5.15; Fe, 20.38; mol. wt., 1096.4, Found: C, 56.82; H, 5.22; Fe, 20.30; mol. wt., 1060.

Reaction of Lycopene with Triiron Dodecacarbonyl

Lycopene (540 mg, 1.0 mmole) and triiron dodecacarbonyl (4.20 g, 25/3 mmoles) were refluxed under nitrogen for 144 hours. During the reaction, an iron

¹² R. B. KING, "Inorg. Synthesis", Vol. 7, 193, McGraw-Hill Co., New York 1963.

mirror was formed on the wall of the reaction vessel. An insoluble black material was removed by centrifugation. The supernatant solution was then evaporated to dryness under reduced pressure. The dried residue was extracted with *n*-pentane in a Soxhlet apparatus. For further purification, the yellow residue obtained by evaporating the orange-yellow extract was completely dissolved once in ca. 10 ml of benzene using a Schlenk tube for centrifugation. It was then concentrated to a thick paste into which 20 ml. of pentane were added. After thorough shaking, the solution was evaporated to ca. 5 ml. and the solid material was obtained by centrifugation. The above purification procedure was repeated twice to give a yellow solid (A), mp $> 350^\circ\text{C}$. (The color changed gradually to black at about 230°C .)

Anal. Found: C, 55.39; H, 4.92; Fe, 20.27.

Solid (A) was reprecipitated in the same manner as described above to give yellow solid (B), mp $> 350^\circ$ (darkens about 230°C .)

Anal Found: C, 55.79; H, 5.27; Fe, 20.73 (ash).

The first, second, third and fourth supernatant solutions were combined and the above purification procedure was applied three times to give a yellow solid, mp $> 350^\circ\text{C}$ (darkens about 220°C).

Anal Found: C, 55.01; H, 5.24; Fe, 21.82 (ash).

Calcd. for $\text{C}_{40}\text{H}_{56} \cdot n \text{Fe}(\text{CO})_3$

	C	H	Fe
$\text{C}_{40}\text{H}_{56} \cdot 4 \text{Fe}(\text{CO})_3$	56.96	5.15	20.38
$\text{C}_{40}\text{H}_{56} \cdot 5 \text{Fe}(\text{CO})_3$	53.43	4.57	22.59

Nuclear Magnetic Resonance Results

Table I shows the peak position, splitting, relative ratio of the areas, and assignment of protons to β -

carotene and its tetrairon dodecacarbonyl π -complexes (I). A high resolution was not obtained because sufficient concentration could not be reached using deuterobenzene. In the spectra of compound I, the peak between $\tau = 3$ and 4 (I) was greatly decreased.

Peak Position (τ)	Splitting	Relative Ratio of Area	Assignment
2.79			$=\text{CH}-$ (in C_6H_6)
3.33	v. broad	3	$=\text{CH}-$
3.58	v. broad	5	$=\text{CH}-$
8.00	multi	18	$=\text{CH}-$ (μ), and olefinic CH_3
8.37	v. broad	6	olefinic CH_3 (terminal)
8.77	S	12	$=\text{CH}-$
9.08	S	12	gem- CH_3
2.73		μ	$=\text{CH}-$ (C_6H_6)
3.58	broad	1	$=\text{CH}-$
7.74	broad	6	$=\text{CH}-$ (μ)
7.91	broad	2	$=\text{CH}-$ (μ)
8.13	broad	12	olefinic $-\text{CH}_3$
8.53	broad	6	olefinic CH_3 (terminal)
8.64	broad	6	$-\text{CH}_2-$
8.74	broad	4	$-\text{CH}_2-$
8.94	broad	2	$-\text{CH}_2-$
9.12	S	12	gem- CH_3

Table I. Peak position, splitting, relative ratio of the areas, and assignment of protons to β -carotene and its tetrairon dodecacarbonyl π -complexes.

The authors wish to express their appreciation for financial support to The National Institute of Health, United States Public Health Service, Grant RG-8921, and to Hoffman-La Roche for samples of lycopene.