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The Longest Polyene

Muhammad Zeeshan,[†] Hans-Richard Sliwka,[*,†] Vassilia Partali,[†] and Ana Martínez[*,‡]

Department of Chemistry, Norwegian University of Science and Technology, Trondheim, Norway, and Instituto de Investigaciones en Materiales, Universidad Nacional Autónoma de México, Circuito Exterior s/n, Coyoacan 04510, México

hrs@nvg.ntnu.no; martina@iim.unam.mx

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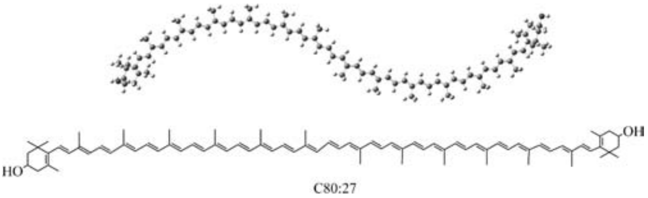
ABSTRACT



C80:27

A microwave assisted Wittig reaction allowed the synthesis, in good yields, of the longest polyene so far recorded with 27 conjugated double bonds. The synthesis of this stable, well-soluble polyene represents a noteworthy step in the direction of ultimate λ_{max}.

Since discovering conjugation in 1899 chemists have struggled with varying success to extend the length of 1,3-butadiene, the elementary conjugated chain of four carbons with two adjacent double bonds, C4:2.[1] All chemists have appended a double bond to butadiene at least one time during their studies and have added the legendary Fieser–Woodward increment of 30 nm when calculating the λ_{max} of a sketched compound. However, in the laboratory, adding C=C units to butadiene leads to an impasse at C8:4 (terminal ene) or C12:5 (terminal methyl).[2,3] Capping the chain ends with phenyl or *tert*-butyl groups induces stability and tolerates chain elongation to C28:8 and C42:13, respectively.[4,5]

Annulenes, another class of polyenes, could not be increased beyond 15 double bonds ([30]annulene C30:15).[6] Five benzene rings can be linearly fused to stable pentacene C22:11; hexacene C26:13 decomposes.[7] Cyclic annulation of benzene (C6:3) rings forms durable polycyclic aromatic hydrocarbons (PAH) reaching via fullerenes and nanotubes an unlimited amount of C=C bonds in graphite.[8] However, the inertness of PAHs, the limiting double bonds in plain polyenes, annulenes, and acenes, complicates investigating their optical, photochemical, and, most topical, semiconductor properties and precludes answering the pertinent question: How many double bonds are required to reach the ultimate λ_{max}? This question is constantly addressed since the concept of conjugation became prevailing and has gathered different answers from extrapolations and molecular calculations.[9–11] Missing is the experimental verification of λ_{ult}, which is hampered by the lack of stable polyenes. The longest naturally occurring polyene offers 14 double bonds.[12] The authentication of arduously HPLC-separated polyenes with 100, 240, or even 1190 C=C bonds (claimed "infinitely long polyacetylenes") failed: these polyenes with λ_{max} around 550 nm express no more than 20 conjugated C=C bonds.[13,14] A laborious synthesis with a molybdenum compound gave a complex product mixture from which a C167:23 ester in a distorted zigzag-conjugated *cis*/*trans* arrangement was isolated by repeated HPLC[15] (Scheme 1S, Supporting Information).

[†] Norwegian University of Science and Technology.

[‡] Universidad Nacional Autónoma de México.

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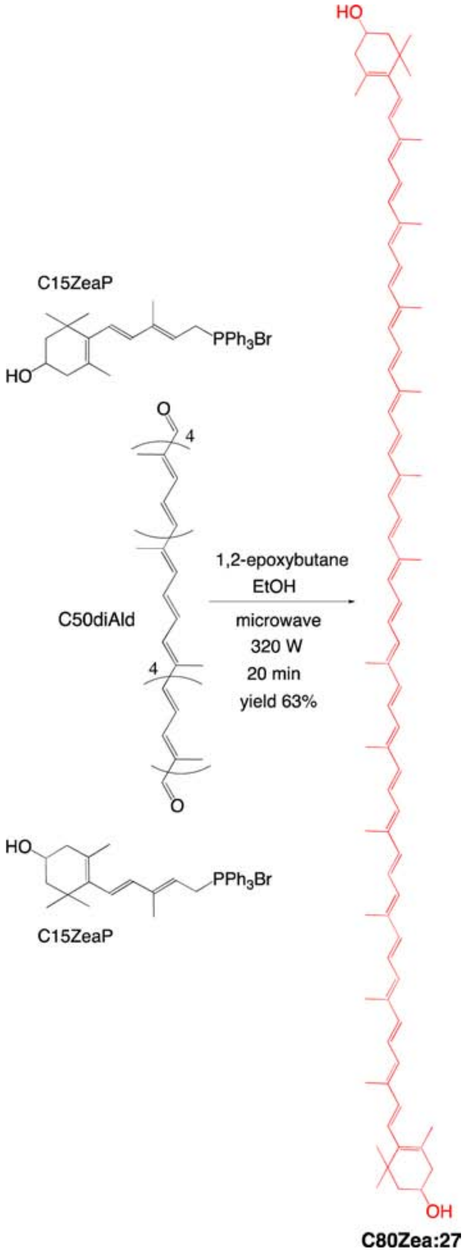
Since plain polyenes, annulenes, and acenes are not expandable, elongation synthesis has to rely on stabilized chains. Stable polyenes appear in nature as methyl branched, and many are, in addition, terminated with cyclohexenyl groups in the carotenoid series. All references to previous attempts demonstrate that chain lengthening of carotenoids is, so far, the only compelling recourse to predefined long polyenes. The Wittig reaction provides an efficient synthesis to carotenoids.[16] Even so, the preparation of long-chain carotenoids under classical Wittig conditions always attends substantial decomposition; the stability of polyenes decreases with increasing length. A C70:23 carotenoid decomposed at low temperatures under argon.[17] Not surprisingly, the dictum expressed in 1951 by Karrer and Eugster still reigns over carotenoid chemistry: 'The synthesis of dodecapreno-*β*,*β*-carotene (C60:19) appears to represent the limit of our method.'[18]

We have now taken a great stride toward λ_{ult}. We found that the reaction time can substantially be reduced and yields increased when the Wittig reaction is performed with microwave irradiation. Shorter reaction times prevent the formation of byproducts and result in in stable compounds. The microwave Wittig synthesis facilitated the addition of ylide C15ZeaP with C50-dialdehyde (C50diAld) to blue C80-zeaxanthin in 63% yield (Scheme 1). C50diAld was obtained by several sequences: two protected C5P aldehydes and C20diAld gave C30diAld, which reacted with two other C5P units to C40diAld and consecutively to C50diAld (Scheme 2).

Although the short wavelength part of the vis-spectrum of C80Zea:27 deviates from the habitual C40Zea:11 shape (Figure 1) it conforms to the fine structure seen with C60:19-carotene.[18,19] Nevertheless, since the polyene chain may be sensitive to spatial variations the occurrence of *cis*-(*Z*)-isomers cannot be excluded; after all, more than one million isomers are theoretically expected.[20] On the other hand, the short high-temperature microwave reaction favors the formation of the all *trans*-(*E*)-isomer;[21] the longer the polyene, the more the *trans*-isomer is stabilized.[4,22] The absence of spectral changes after the classical *cis* → *trans* isomerization experiment with light and I_2[23] supports the predominance of the all-*trans*-isomer (Figure 1S, Supporting Information).

Scheme 1. Microwave Assisted Wittig Synthesis of C80Zea:27



Molecular modeling with time-dependent density functional theory (TDDFT) using the M06-2X functional[24] in combination with the 6-311g basic set outlined the geometry of C80Zea and then generated the absorption spectra in CH_2Cl_2 with the polarizable continuum model. The molecule appeared with an in-plane bended structure typical for carotenoids (Figure 2).

The distinct alignment with positive and negative amplitudes hinders C80Zea to extend to twice the length of the barely curved C40Zea[25] (C80Zea $l_{\text{calc}} = 63$ Å, C40Zea $l_{\text{calc}} = 40$ Å). The prolonged conjugation is expressed by an adjustment of the bond lengths (calculated range in C80Zea: C=C 1.3697–1.3887 Å, C—C 1.4347–1.4898 Å, C80Zea mid C=C (31,31′) = 1.3836 Å, measured in

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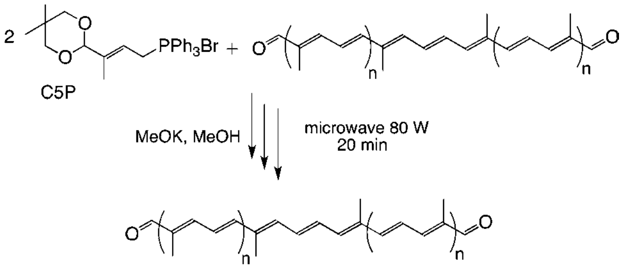
Scheme 2. Synthesis of C50-Dialdehyde



Starting aldehyde n = 1 C20diAld, intermediate aldehydes n = 2 C30diAld and n = 3 C40diAld, final aldehyde n = 4 C50diAld.

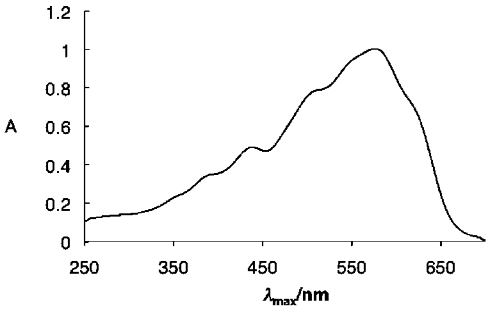


Figure 1. Vis-spectrum of *trans*-C80Zea:27, λ_{max} = 576 nm (CH_2Cl_2).

Figure 2. Calculated structure of *trans*-C80Zea:27.

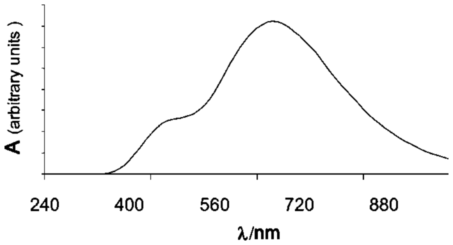


Figure 3. Calculted vis-spectrum of *trans*-C80Zea:27, λ_{max} = 672 nm (CH_2Cl_2).

C40Zea: C═C 1.3216−1.3666 Å, C—C 1.4255−1.4737 Å, mid C═C (15,15′) = 1.3416 Å).[25]

Long-chain polyenes point not only to synthetic complications but also to obstacles for theoretical calculations. The λ_{max} of the computed spectrum (672 nm, CH_2Cl_2) deviates considerably from experimental λ_{max} = 576 nm (CH_2Cl_2); the calculation overestimated the absorption by 3.7 nm for each conjugated C═C bond (the ring double bonds are not fully conjugated with the chain bonds due to sterical deviation). Spectral prediction of polyenes, including C40Zea, is susceptible to inaccuracies,[26] although TDDFT schemes operate with lower average errors than ZINDO/S and M06-2X performs better than other functionals.[24,26] The calculated spectrum of *trans*-C80Zea shows an absorption shoulder in the lower wavelength range (Figure 3) in agreement with the recorded data. The spectrum of the 31,31′-*cis*-isomer is quite different in shape (Figure S2, Supporting Information), thus supporting the experimentally indicated absence of *cis*-isomers.

The microwave Wittig reaction has surpassed the solution-based method heading to C80Zea:27, a noteworthy step in the direction of ultimate λ_{max}. This long, well-defined polyene, when modified at the peripheral rings, is moreover a likely candidate for molecular wire studies.[27−29]

Despite recently refined molecular modeling methods, the errors in spectra calculation of polyenes are still noticeable. The insolubility in current solvents of dialdehydes with more than C50 prevents going beyond C80Zea:27 with Wittig reactions based on prefabricated synthons (Schemes 1, 2). The challenge is now to develop a synthesis for carotenoids even longer than C80Zea:27; maximal elongated, soluble, and stable polyenes will be attained with shorter dialdehydes CndiAld (n < 50) and longer Wittig salts CnZeaP n > 15.

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Supporting Information Available. Schemes, figures, experimental details, and characterization. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.

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