HOKKAIDO UNIVERSITY

Title	Splitting and reorientation of pi-conjugation by an unprecedented photo-rearrangement reaction
Author(s)	Inaba, Yuya; Yoneda, Tomoki; Kitagawa, Yuichi; Miyata, Kiyoshi; Hasegawa, Yasuchika; Inokuma, Yasuhide
Citation	Chemical communications, 56(3), 348-351 https://doi.org/10.1039/c9cc09062b
Issue Date	2020-01-11
Doc URL	http://hdl.handle.net/2115/80132
Type	article (author version)
File Information	revised_manuscript_1121.pdf

Instructions for use

Hokkaido University Collection of Scholarly and Academic Papers : HUSCAP

COMMUNICATION

Splitting and Reorientation of π-Conjugation by an Unprecedented Photo-Rearrangement Reaction†

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

Yuya Inaba,[a] Tomoki Yoneda,[a] Yuichi Kitagawa,[a,b] Kiyoshi Miyata,[c] Yasuchika Hasegawa[a,b] and Yasuhide Inokuma*[a,b]

A dodecahexaene analogue cross-conjugated with four carbonyl groups was prepared from an aliphatic tetraketone. Exposure to LED light (>420 nm) led to the splitting of the dodecahexaene conjugation into the two hexatriene subunits, connected through a stereogenic carbon atom. The two triene subunits exhibited excitonic coupling in the UV-Vis absorption and CD spectra.

Retinal, also known as a vitamin A, is produced by oxidative cleavage of β-carotene.[1] Such redistributions of π-conjugation during splitting reactions are important processes for modulating the optical properties of π-systems. Considering the recent upsurge in the synthesis of large π-conjugated organic compounds,[2] such reactions are also considered to have extensive applicability to existing π-systems. However, compared with extension of π-systems, regioselective π-splitting reactions (Fig. 1) remain limited[3] because they require dissociation of stable C–C or C=C covalent bonds. As a representative example, Osuka and co-workers reported a thermal splitting reaction of expanded porphyrins into two contracted porphyrinoids (Fig. 1b)[4]. Recently, Yamago *et al.* reported strain-induced cleavage of cycloparaphenylenes into linear oligophenylene analogues.[5] Focusing on the fragments of π-splitting reactions, two resultant chromophores that have identical or similar excitation energies are expected to show remarkable interchromophore interactions when they are arranged in appropriate orientations.[6] Interchromophore interaction such as excitonic coupling is also an interesting phenomenon that cannot be seen for discrete, single chromophores.

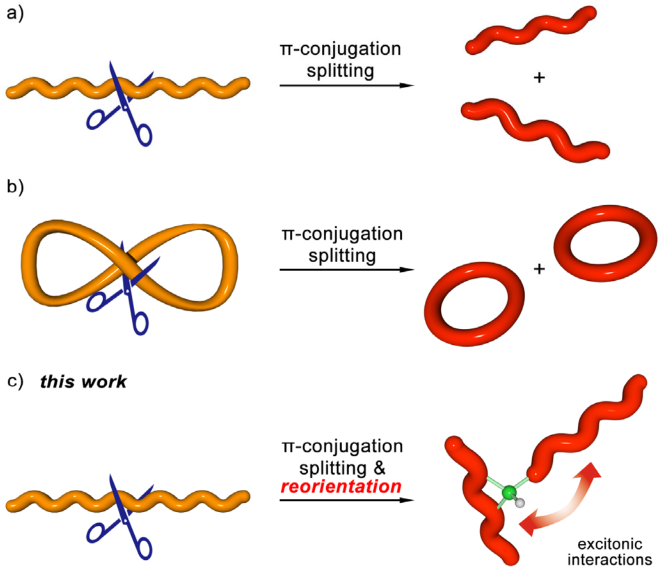


Fig. 1 Schematic diagrams of π-conjugation splitting reactions: a) from a single linear to two linear molecules, b) from macrocyclic to smaller cyclic molecules, and c) splitting and reorientation of a polyene system (this work).

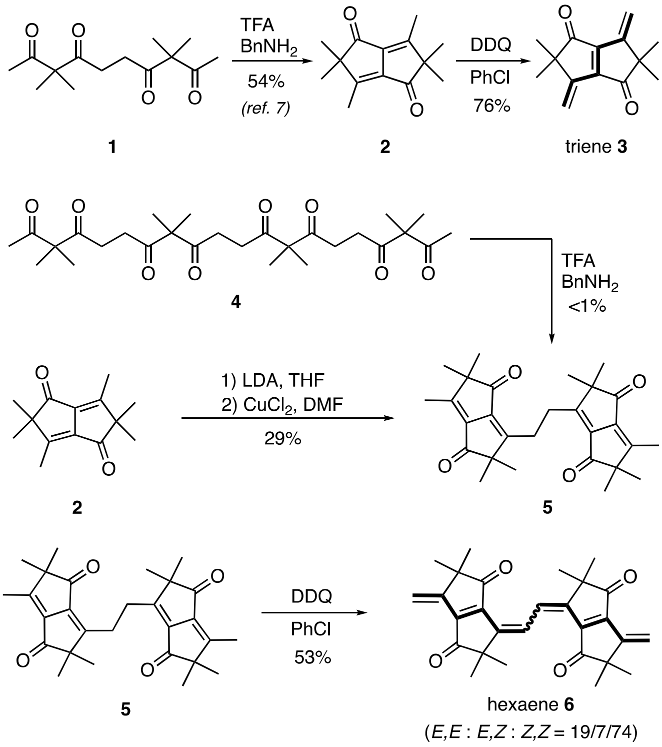
Here we report regioselective π-conjugation splitting reaction of a planar dodecahexaene analogue into an orthogonally arranged bis(triene) with the use of an unprecedented photo-induced rearrangement reaction (Fig. 1c).Starting from 2,5-dihydropentalene-1,4-dione as a stable triene subunit, its conjugated dimer (dodecahexaene) splits into two triene subunits in high yield upon visible light irradiation. Notably, the two triene chromophores were orthogonally arranged in a close proximity by a stereogenic carbon center that was generated in the photo-rearrangement. Therefore, excitonic coupling interactions were clearly observed in the absorption spectrum. Furthermore, because this photo-rearrangement reaction afforded chiral chromophores from achiral hexaene, circular dichroism (CD) signals were observed after optical resolution of enantiomers.

---

[a] *Division of Applied Chemistry, Faculty of Engineering, Hokkaido University, Kita 13, Nishi 8 Kita-ku, Sapporo, Hokkaido 060-8628, Japan*
E-mail: inokuma@eng.hokudai.ac.jp
[b] *Institute for Chemical Reaction Design and Discovery (WPI-ICReDD), Hokkaido University, Kita 21, Nishi 10, Kita-ku, Sapporo, Hokkaido 001-0021, Japan*
[c] *Department of Chemistry, Faculty of Science, Kyushu University, 744 Motooka, Nishi, Fukuoka 819-0395, Japan*

†Electronic supplementary information (ESI) available: Details of the experimental procedure, general information for measurements and materials. CCDC 1954077–1954080. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/x0xx00000x

In this work, we focused on a pentalene-based bicyclic carbon skeleton as a stable hexatriene component. Previously, we have reported an efficient synthesis of 2,2,3,5,5,6-hexamethyl-2,5-dihydropentalene-1,4-dione (**2**) from an aliphatic tetraketone precursor **1**.[7] Upon oxidation using 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ), two allylic methyl positions of **2** were oxidized to give hexatriene analogue **3** bearing two cross-conjugated carbonyl groups in 76% yield (Scheme 1) as a yellow solid. Single crystal X-ray analysis revealed the bond length alternation of **3** (from-end-to-end 1.330, 1.455, 1.352, 1.455, and 1.330 Å; Fig. 2a), which clearly indicated hexatriene-like π-conjugation of the planar pentalene-based bicyclic system.



Scheme 1 Synthesis of hexatriene **3** and dodecahexaene **6** derivatives.

The parent compound **2** is colorless; however, a dichloromethane solution of triene **3** is yellow because the absorption edge of **3** extended up to 380 nm (Fig. 3). Despite the intense absorption band at 300–380 nm, compound **3** did not show *Z* ↔ *E* photoisomerization at the central double bond, because of the rigid bicyclic skeleton. Because this oxidation reaction warrants that compound **2** can be used as a synthon of hexatriene, we attempted to synthesize a dodecahexaene by connecting the pentalene-based subunits. When octaketone **4**[8] was treated under the reaction conditions similar to the synthesis of **2** from tetraketone **1**, a complex mixture containing ethylene-linked pentalene dimer **5** (< 1%) was formed. Because the yield of **5** could not be improved despite many efforts, we alternatively synthesized dimer **5** by an oxidative homo-coupling reaction of monomer **2**. Oxidation of the dienolate species of **2**, generated by the treatment with lithium diisopropylamide (LDA), with $CuCl_2$ afforded dimer **5** in 29% yield after chromatographic separation. Formation of C–C bond at the allylic position of monomer **2** was confirmed by the single crystal X-ray analysis (see ESI).

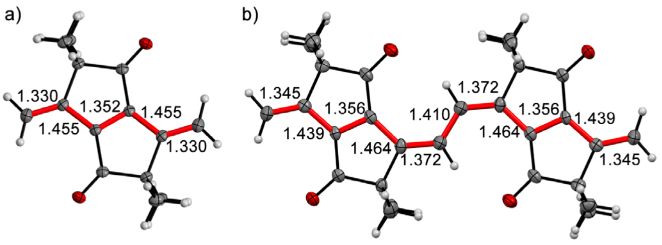


Fig. 2 X-ray crystal structures of a) **3** and b) **6**. Thermal ellipsoids are set at the 50% probability level. Selected distances (in Å) are shown for C–C or C=C bonds highlighted in red.

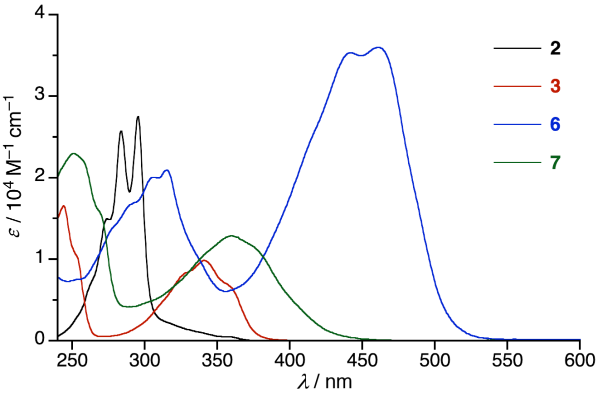
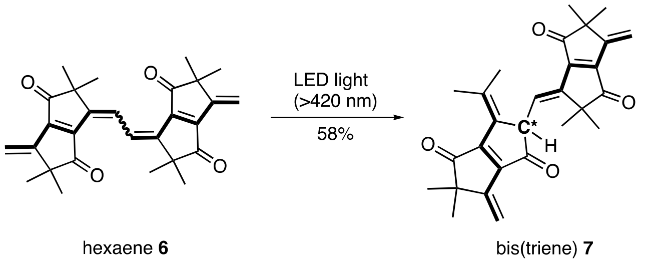


Fig. 3 UV-Vis absorption spectra of compounds **2**, **3**, (*Z*,*Z*)-**6**, and **7** in CH_2Cl_2.

Dimer **5** also underwent DDQ-mediated oxidation to give a dodecahexaene moiety **6** bearing four cross-conjugated carbonyl groups in 53% yield as an orange solid. The as-obtained **6** contained *E,E*, *E,Z*, and *Z,Z* isomers in a 19/7/74 ratio, chromatographic separation on silica gel was unsuccessful because of overlap and rapid photoisomerization even under room light. Repeated recrystallization allowed isolation of the major product (*Z*,*Z*)-**6** as single crystals. X-ray diffraction analysis revealed the planar structure of (*Z*,*Z*)-**6** and its bond length alternation (Fig. 2b), which is typical of the crystal structures of carotenoids.[9] (*Z*,*Z*)-**6** can be classified as a (3*E*,5*Z*,7*Z*,9*E*)-dodecahexaene analogue, in which central two C=C double bonds are able to undergo *Z* ↔ *E* photoisomerization.

Dodecahexaene **6** exhibited an intense visible absorption band at 456 nm in dichloromethane with a molar extinction coefficient of 3.8×10^4 M^{-1} cm^{-1} (Fig. 3). When a $CDCl_3$ solution of as-synthesized **6** was exposed to room light, intensities of proton signals assignable to (*E*,*E*)-**6** and (*E*,*Z*)-**6** gradually increased in the ^1H NMR spectra with concomitant decrease in those for (*Z*,*Z*)-**6**. After 10 h, the system reached a pseudo photo-stationary state with an *E,E* : *E,Z* : *Z,Z* ratio of 41/11/48 (see ESI). DFT calculations indicated that the total energies decreased in the order of (*E*,*Z*)-**6**, (*E*,*E*)-**6**, and (*Z*,*Z*)-**6**, which roughly matched with the observed distribution of diastereomers.

Prolonged visible light irradiation (>420 nm) of dodecahexaene **6** in degassed chloroform by a LED light caused splitting of the π-conjugated system and rearrangement of pentalene-based carbon skeleton (Scheme 2). Upon visible irradiation, the orange color of the solution was gradually degraded over 10 h. The ^{1}H NMR spectroscopy showed the formation of non-symmetric product **7** in 80% yield based on an internal standard (isolated yield: 58%). It should be noted that other peaks assignable to other diastereomers of **7** were not found in ^{1}H NMR spectra during the reaction. The Atmospheric Pressure Chemical Ionization (APCI)-TOF mass analysis of **7** indicated the chemical formula to be $C_{28}H_{30}O_4$, which is exactly the same as that of **6**. Whereas the starting material **6** has six vinylic protons, only five were observed in the ^{1}H NMR spectrum of **7**. A methine proton was observed at 4.47 ppm in $CDCl_3$ as a doublet which coupled to a vinyl proton at 6.21 ppm with a coupling constant of 10.6 Hz. In the HMQC spectrum, the methine proton showed correlation with *sp*^{3}-hybridized carbon at 58.4 ppm. Furthermore, two of the eight methyl groups were shifted down-field to 2.36 and 1.87 ppm, indicating the formation of an isopropylidene group.



Scheme 2 Photo-induced rearrangement of hexaene **6** into bis(triene) **7**.

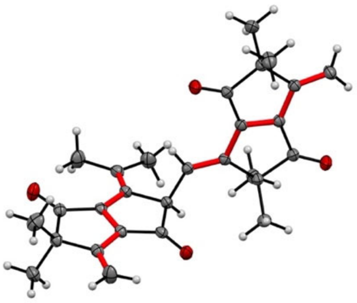


Fig. 4 Crystal structure of photo-rearranged product **7**. Two hexatriene moieties are highlighted in red. Only the R-form in racemic crystal is shown.

Single crystal X-ray analysis of **7** unambiguously confirmed the splitting and redistribution of the hexaene π-conjugation of **6** into two triene moieties arranged in an orthogonal fashion. Photo-product **7** crystallized in a centrosymmetric space group *P*2$_1$/*c* in its racemic form. One of two pentalene-based subunits was identical to that in **6**; however, the other contained a stereogenic *sp*^{3}-carbon center and an isopropylidene group. Nonetheless, a hexatriene-like π-conjugation with the two cross-conjugated carbonyl groups was preserved. The center-to-center distance of the two triene subunits was 6.21 Å, and the dihedral angle of the mean planes of two pentalene-based subunits was 79.7°. The through-bond π-conjugation between the two triene moieties was cleaved at the bridging *sp*^{3}-carbon atom; however, the observed orientation is advantageous for inducing interchromophore interactions.

Although the detailed mechanism is unclear, this photo-induced rearrangement reaction can be explained by a Norrish type I-like α-cleavage reaction at an internal carbonyl group (see ESI). As observed for 5,5-dimethylcyclopent-2-en-1-one,[10] a substructure of **6**, a ketene intermediate can be generated by photo-induced α-cleavage at the quaternary *sp*^{3}-carbon side. Single bond rotation and a subsequent ring closing reaction form a stereogenic *sp*^{3}-carbon-embedded five-membered ring bearing the isopropylidene group. As the crystal structure and NMR spectrum of **7** indicated that the *E*-isomer with respect to the double bond attached with chiral carbon was exclusibely obtained under the given conditions, the visible light-induced photo-rearrangement reaction occurred on (*E*,*Z*)-**6**, or (*E*,*E*)-**6** that were generated by photoisomerization of (*Z*,*Z*)-**6**. Notably, the regioselective transformation of **6** into **7** was observed only under visible light (>420 nm) irradiation. UV irradiation of dichloromethane solution of **6** produced a complex mixture of photo-products, presumably due to further photo-reactions of **7** by UV-excitation.

The π-splitting reaction of **6** led to drastic changes in optical properties of the chromophores. Because the π-conjugation length is shortened, UV-Vis absorption spectrum of rearranged product **7** hypsochromically shifted compared with **6** (Fig. 3). While hexaene (*Z*,*Z*)-**6** and its *E*/*Z* mixture (*E*,*E* : *E*,*Z*, : *Z*,*Z* = 19/7/74) showed visible fluorescence emission at 567 nm (quantum yield: 5%; lifetime 2.2 ns) and 568 nm (quantum yield: 3%; lifetime 2.1 ns), respectively, rearranged product **7** was virtually non-fluorescent as well as its component chromophore **3**. These observations matched well with the TD-DFT calculation results: while the lowest energy transition for **6** corresponded to the allowed transition of the dodecahexaene moiety, those of **7** and **3** were forbidden transitions.

Due to the rearrangement reaction, the triene chromophores in compound **7** were positioned in close proximity influencing its UV-Vis absorption spectrum (Fig. 3) through excitonic interaction. Although the conjugation length of **7** is similar to that of monomer **3**, the absorption bands of **7** were markedly red-shifted and slightly broadened. In spite of having an additional effect of the terminal methyl groups at one triene segment in the overall absorption spectrum of **7**, the presence of excitonic coupling between two chromophores was also indicated from the spectral shape.[6] We analysed the spectrum using molecular exciton theory with the Holstein-type vibronic Hamiltonian[11] (See ESI). The total excitonic coupling was estimated to be 540 cm^{-1}. The coupling likely originated from Dexter-type interaction rather than Förster-type interaction, which is consistent with the well-established theory of excitonic interactions.[12]

Because compound **7** is chiral, we further evaluated the excitonic interactions between two hexatriene species using CD spectroscopy. The two enantiomers of **7** were successfully resolved by HPLC with a cellulose-based chiral column. The racemic **7** was CD silent; however, the first fraction eluted at

13.1 min exhibited positive CD signals at 415 nm and 347 nm (Fig. 5). The mirror-image spectrum was observed for the second fraction eluted at a retention time of 17.0 min. TD-DFT calculation results at the B3LYP/6-31G(d,p) level suggested that the stereochemistry of the first and second fractions were *R* and *S*, respectively. These observations clearly showed that the photo-rearrangement reaction converted the achiral dodecahexaene derivative into two π-conjugated fragments having a chiral orientation, which induces excitonic coupling interactions.

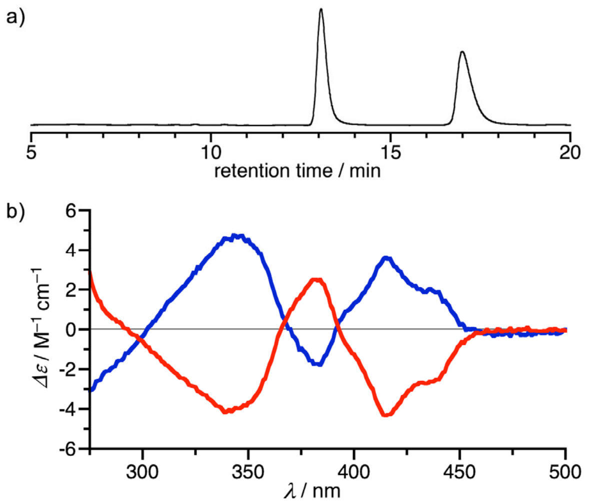


Fig. 5 a) Chiral HPLC chromatogram for optical resolution of racemic compound **7** (detection by absorption at 254 nm). b) CD spectra of the first (blue) and the second (red) fractions in dichloromethane.

In summary, we have demonstrated a photo-induced π-conjugation splitting and reorientation of a pentalene-based dodecahexaene system as a novel approach for π-conjugation redistribution. Because the two resultant chromophores were held in a chiral orientation by a stereogenic *sp*^{3}-carbon atom, excitonic interactions were observed in the UV-vis absorption and CD spectra. As a result, drastic structural and optical property changes were achieved by the π-conjugation redistribution reaction. Because π-conjugated carbon materials such as polyenes and nanographenes have been extensively synthesized by organometallic means, our π-splitting and reorientation strategy will contribute to the reconstruction of existing π-conjugated systems. In this sense, the introduction of cross-conjugated carbonyl groups to a conjugated carbon skeleton may play an important role in regioselectively cleave the conjugation.

This work was supported by Grant-in-Aid for Young Scientists (A) (No. 17H04872) and by the Asahi Glass Foundation, of which Y.I. is the principal investigator. K.M. thanks JSPS KAKENHI (Nos. JP17H06375, JP18H05170, JP18H05981, JP19K15508), and Qdai-jump Research (QR) Program Wakaba Challenge. Institute for Chemical Reaction Design and Discovery (ICReDD) was established by World Premier International Research Initiative (WPI), MEXT, Japan.

Conflicts of interest

There are no conflicts to declare.

Notes and references

1 a) T. Moore, *Biochem. J.* 1930, **24**, 696–702; b) J. Lintig, K. Vogt, *J. Biol. Chem.* 2000, **275**, 11915–11920.

2 Y. Segawa, T. Maekawa, K. Itami, *Angew. Chem. Int. Ed.*, 2015, 54, 66–81; *Angew. Chem.* 2015, **127**, 68–83.

3 a) R. R. Nani, J. A. Kelley, J. Ivanic, M. Schhermann, *Chem. Sci.* 2015, **6**, 6556–6563; b) S. Saito, K. Furukawa, A. Osuka, *J. Am. Chem. Soc.* 2010, **132**, 2128–2129; c) D. Ajami, O. Oeckler, R. Herges, *Nature*, 2003, **426**, 819–821; d) A. Wojtkielewicz, J. Maj, A. Dzieszkowska, J. W. Morzycki, *Tetrahedron*, 2011, **67**, 6868–6875; e) F. Vögtle, E. Schmohel, M. Nieger, *J. Chem. Soc. Chem. Commun.*, 1993, 760–762.

4 a) Y. Tanaka, W. Hoshino, S. Shimizu, K. Youfu, N. Aratani, N. Maruyama, S. Fujita, A. Osuka, *J. Am. Chem. Soc.* 2004, **126**, 3046–3047; b) S. Saito, K. S. Kim, Z. S. Yoon, D. Kim, A. Osuka, *Angew. Chem. Int. Ed.* 2007, **46**, 5591–5593; *Angew. Chem.* 2007, **119**, 5687–5689.

5 E. Kayahara, T. Hayashi, K. Takeuchi, F. Ozawa, K. Ashida, S. Ogoshi, S. Yamago, *Angew. Chem. Int. Ed.* 2018, **57**, 11418–11421; *Angew. Chem.* 2018, **130**, 11588–11591.

6 a) J. Hernando, M. van der Schaaf, E. M. H. P. van Dijk, M. Sauer, M. F. García-Parajó, N. F. van Hulst, *J. Phys. Chem. A*, 2003, **107**, 43–52; b) A. Osuka, K. Maruyama, *J. Am. Chem. Soc.* 1988, **110**, 4454–4456; c) S. Tretiak, W. M. Zhang, V. Chernyak, S. Mukamel, *Proc. Natl. Acad. Sci. USA*, 1999, **96**, 13003–13008.

7 Y. Saito, M. Higuchi, S. Yoshioka, H. Senboku, Y. Inokuma, *Chem. Commun.* 2018, **54**, 6788–6791.

8 a) M. Uesaka, Y. Saito, S. Yoshioka, Y. Domoto, M. Fujita, Y. Inokuma, *Commun. Chem.* 2018, **1**, 23; b) Y. Manabe, M. Uesaka, T. Yoneda, Y. Inokuma, *J. Org. Chem.*, 2019, **84**, 9957–9964.

9 a) G.Bartalucci, S. Fisher, J. R. Helliwell, M. Helliwell, S. Liaaen-Jensen, J. E. Warren, J. Wilkinson, *Acta Cryst.*, 2009, **B65**, 238–247; b) G. Bartalucci, C. Delroy, S. Fisher, M. Helliwell, S. Liaaen-Jensen, *Acta Cryst.*, 2008, **C64**, o128–o131; c) G. Bartalucci, J. Coppin, S. Fisher, G. Hall, J. R. Helliwell, M. Helliwell, S. Liaaen-Jensen, *Acta Cryst.*, 2007, **B63**, 328–337.

10 a) W. C. Agosta, A. B. Smith III, *J. Am. Chem. Soc.* 1971, **93**, 5513–5520; b) W. C. Agosta, A. B. Smith III, A. S. Kende, R. G. Eilerman, J. Benham, *Tetrahedron Lett.* 1969, **52**, 4517–4520.

11 a) F. C. Spano, *J. Chem. Phys.* 2002, **116**, 5877-5891; b) K. Miyata, S. Tanaka, Y. Ishino, K. Watanabe, T. Uemura, J. Takeya, T. Sugimoto, Y. Matsumoto, *Phys. Rev. B* 2015, **91**, 195306.

12 a) G. D. Scholes, K. P. Ghiggino, *J. Phys. Chem.* 1994, **98**, 4580–4590; b) M. Kasha, H. R. Rawls, M. A, El-Bayoumi, *Pure Appl. Chem.* 1965, **11**, 371–392.