MAS NMR study of the photoreceptor phytochrome

Rohmer, T.

Publications

T. Rohmer, H. Strauss, J. Hughes, H. de Groot, W. Gärtner, P. Schmieder, and J. Matysik. ^{15}N MAS NMR studies of Cph1 phytochrome: Chromophore dynamics and intramolecular signal transduction. *J Phys Chem B*, 110:20580–20585, **2006**.

E. Roy, T. Rohmer, P. Gast, G. Jeschke, A. Alia, and J. Matysik. Characterization of the Primary Radical Pair in Reaction Centers of *Heliobacillus mobilis* by ^{13}C Photo-CIDNP MAS NMR. *Biochemistry*, 47:4629–4635 **2008**.

T. Rohmer, C. Lang, J. Hughes, L.O. Essen, W. Gärtner, and J. Matysik. Light-induced chromophore activity and signal transduction in phytochromes observed by ^{13}C and ^{15}N magic angle spinning NMR. *Proc Natl Acad Sci USA*, 105:15229–15234, **2008**.

T. Rohmer, C. Lang, C. Bongards, K.B. Sai Sankar Gupta, J. Hughes, W. Gärtner, and J. Matysik. Magic-angle spinning NMR reveals mechanics of chromophore-protein interaction during the Pfr → Pr photoconversion process of phytochrome. *Submitted.*

T. Rohmer, C. Lang, W. Gärtner, J. Hughes, F. Mark, and J. Matysik. CP/MAS NMR study on microcrystaline phycocyanobilin. *Manuscript in preparation.*

T. Rohmer, J. Matysik, and F. Mark. Crystal effects on the geometry and NMR shieldings of bilirubin: A combined NMR spectroscopic and density functional theory study. *Manuscript in preparation.*

T. Rohmer, C. Lang, J. Hughes, W. Gärtner, and J. Matysik. MAS NMR on cyanobacterial and plant phytochromes: A comparison. *Manuscript in preparation.*

Curriculum vitae

In 1996, after obtaining the Baccalauréat in Sciences with specialization Physics and Chemistry at the Lycée Kleber, Strasbourg, France, I joined for three years the preparatory classes to the "Grandes Ecoles" at the Lycée Kleber. I was admitted at the Clermont-Ferrand's Superior National School of Chemistry (Ecole Nationale de Chimie de Clermont-Ferrand), France, where I studied organic and inorganic chemistry, chemical engineering and polymer chemistry. In 2002, I carried out an one-year voluntary internship under the guidance of Dr. Diggelmann and Dr. Lutz at the Syngenta's department of combinatorial chemistry, Basle, Switzerland. Then, I went as Erasmus exchange student to the Dublin City University, Ireland. From April to October 2004, I accomplished my master project "*Analysis of dithiocarbamate pesticides by LC/MS/MS*" under the supervision of Dr. Wanner at the Analysis and Research Center (Centre d'Analyses et de Recherche), Illkirch-Graffenstaden, France. I obtained my Master of Chemistry in October 2004.

In January 2005, I started my PhD project in the Solid-state NMR department led by Prof. Dr. Huub de Groot. Under the supervision of Dr. Jörg Matysik, I worked on the project: "*MAS NMR study of the photoreceptor phytochrome*". During my PhD time, I attended the AMPERE XIII NMR School (2005, Zakopane, Poland), Advanced European Solid-State NMR School in Biological Solids (2007, Brückentinsee, Germany) and the Seminar "Festkörper-NMR-Methoden und Anwendungen in der Materialforschung" (2008, Oberjoch, Germany). The results of my research were presented at international conferences in the form of posters. This includes the Euromar 2005, 2007 and 2008 conferences, the XXII$^{\text{nd}}$ International Conference on Magnetic Resonance in Biological systems, and the 27$^{\text{th}}$, 28$^{\text{th}}$ and 29$^{\text{th}}$ GDCh Annual Discussion Meetings. I presented my work in oral presentations at the 34$^{\text{th}}$ Meeting of the American Society for Photobiology (2008,

Burlingame, United States), the 21st GDCh lecture conference of the Photochemistry group (2008, Bielefeld, Germany), the annual meeting of the study group Theory and Spectroscopy of the chemical society section of the NWO (2009, Lunteren), and as invited speaker at the Small molecule NMR conference (2009, Chamonix, France). The work incorporated in this thesis has led to the *Ernst Award 2009* by the Magnetic Resonance Discussion Group of the German Chemical Society (Gesellschaft Deutscher Chemiker, GDCh).

Bibliography

[1] A. Batschauer. *Photoreceptors and light signalling*. Royal Society of Chemistry, Cambridge, United Kingdom, **2003**.

[2] W.R. Briggs and J.R. Spudich. *Handbook of photosensory receptors*. Wiley, Weinheim, Germany, **2005**.

[3] E. Schäfer and F. Nagy. *Photomorphogenesis in plants and bacteria: Function and signal transduction mechanisms*. Springer, Dordrecht, 3rd edition, **2006**.

[4] W.L. Butler, K.H. Norris, H.W. Siegelman, and S.B. Hendricks. Detection, assay, and preliminary purification of the pigment controlling photoresponsive development of plants. *Proc Natl Acad Sci USA*, 45:1703–1708, **1959**.

[5] R.D. Vierstra and P.H. Quail. Proteolysis alters the spectral properties of 124 kDa phytochrome from *Avena*. *Planta*, 156:158–165, **1982**.

[6] H.P. Hershey, R.F. Barker, K.B. Idler, J.L. Lissemore, and P.H. Quail. Analysis of cloned DNA and genomic sequences for phytochrome: Complete amino-acid sequences for two gene-products expressed in etiolated *Avena*. *Nucl Acids Res*, 13:8543–8559, **1985**.

[7] B. Karniol, J.R. Wagner, J.M. Walker, and R.D. Vierstra. Phylogenetic analysis of the phytochrome superfamily reveals distinct microbial subfamilies of photoreceptors. *Biochem J*, 392:103–116, **2005**.

[8] E. Giraud, S. Zappa, L. Vuillet, J.M. Adriano, L. Hannibal, J. Fardoux, C. Berthomieu, P. Bouyer, D. Pignol, and A. Vermeglio. A new type of bacteriophytochrome acts in tandem with a classical bacteriophytochrome to control the antennae synthesis in *Rhodopseudomonas palustris*. *J Biol Chem*, 280:32389–32397, **2005**.

[9] S.J. Davis, A.V. Vener, and R.D. Vierstra. Bacteriophytochromes: Phytochrome-like photoreceptors from nonphotosynthetic *eubacteria*. *Science*, 286:2517–2520, **1999**.

[10] Z.Y. Jiang, L.R. Swem, B.G. Rushing, S. Devanathan, G. Tollin, and C.E. Bauer. Bacterial photoreceptor with similarity to photoactive yellow protein and plant phytochromes. *Science*, 285:406–409, **1999**.

[11] K. Evans, J.G. Grossmann, A.P. Fordham-Skelton, and M.Z. Papiz. Small-angle X-ray scattering reveals the solution structure of a bacteriophytochrome in the catalytically active Pr state. *J Mol Biol*, 364:655–666, **2006**.

[12] A.M. Jones and H.P. Erickson. Domain structure of phytochrome from *Avena sativa* visualized by electron microscopy. *Photochem Photobiol*, 49:479–483, **1989**.

[13] M. Nakasako, T. Iwata, K. Inoue, and S. Tokutomi. Light-induced global structural changes in phytochrome A regulating photomorphogenesis in plants. *FEBS J*, 272:603–612, **2005**.

[14] N.C. Rockwell, Y.S. Su, and J.C. Lagarias. Phytochrome structure and signaling mechanisms. *Ann Rev Plant Biol*, 57:837–858, **2006**.

[15] B.L. Montgomery and J.C. Lagarias. Phytochrome ancestry: Sensors of bilins and light. *Trends Plant Sci*, 7:357–366, **2002**.

[16] B. Karniol and R.D. Vierstra. *Photomorphogenesis in plants and bacteria*. Springer, Dordrecht, **2006**.

[17] T. Lamparter, M. Carrascal, N. Michael, E. Martinez, G. Rottwinkel, and J. Abian. The biliverdin chromophore binds covalently to a conserved cysteine residue in the N-terminus of *Agrobacterium* phytochrome agp1. *Biochemistry*, 43:3659–3669, **2004**.

[18] J.R. Wagner, J.S. Brunzelle, K.T. Forest, and R.D. Vierstra. A light-sensing knot revealed by the structure of the chromophore-binding domain of phytochrome. *Nature*, 438:325–331, **2005**.

[19] J. Hahn, H.M. Strauss, F.T. Landgraf, H.F. Gimenez, G. Lochnit, P. Schmieder, and J. Hughes. Probing protein-chromophore interactions in Cph1 phytochrome by mutagenesis. *FEBS J*, 273:1415–1429, **2006**.

[20] J.C. Lagarias and H. Rapoport. Chromopeptides from phytochrome: The structure and linkage of the Pr form of the phytochrome chromophore. *J Am Chem Soc*, 102:4821–4828, **1980**.

[21] T. Lamparter, B. Esteban, and J. Hughes. Phytochrome Cph1 from the cyanobacterium *synechocystis* PCC6803: Purification, assembly, and quaternary structure. *Eur J Biochem*, 268:4720–4730, **2001**.

[22] B. Borucki, H. Otto, G. Rottwinkel, J. Hughes, M.P. Heyn, and T. Lamparter. Mechanism of Cph1 phytochrome assembly from stopped-flow kinetics and circular dichroism. *Biochemistry*, 42:13684–13697, **2003**.

[23] D.M. Arciero, J.L. Dallas, and A.N. Glazer. *In vitro* attachment of bilins to apophycocyanin: Determination of the structures of tryptic bilin peptides derived from the phycocyanobilin adduct. *J Biol Chem*, 263:18350–18357, **1988**.

[24] B. Knipp, M. Müller, N. Metzler-Nolte, T.S. Balaban, S.E. Braslavsky, and K. Schaffner. NMR verification of helical conformations of phycocyanobilin in organic solvents. *Helv Chim Acta*, 81:881–888, **1998**.

[25] A.H. Göller, D. Strehlow, and G. Hermann. The excited-state chemistry of phycocyanobilin: A semiempirical study. *ChemPhysChem*, 6:1259–1268, **2005**.

[26] F. Thümmler, W. Rüdiger, E. Cmiel, and S. Schneider. Chromopeptides from phytochrome and phycocyanin: NMR studies of the Pfr and Pr chromophore of phytochrome and *E*,*Z* isomeric chromophores of phycocyanin. *Z Naturforsch A*, 38:359–368, **1983**.

[27] F. Andel, J.C. Lagarias, and R.A. Mathies. Resonance Raman analysis of chromophore structure in the Lumi-R photoproduct of phytochrome. *Biochemistry*, 35:15997–16008, **1996**.

[28] Y. Mizutani, S. Tokutomi, and T. Kitagawa. Resonance Raman-spectra of the intermediates in phototransformation of large phytochrome - deprotonation of the chromophore in the bleached intermediate. *Biochemistry*, 33:153–158, **1994**.

[29] W. Rüdiger, F. Thümmler, E. Cmiel, and S. Schneider. Chromophore structure of the physiologically active form Pfr of phytochrome. *Proc Natl Acad Sci USA*, 80:6244–6248, **1983**.

[30] F. Andel, K.C. Hasson, F. Gai, P.A. Anfinrud, and R.A. Mathies. Femtosecond time-resolved spectroscopy of the primary photochemistry of phytochrome. *Biospectroscopy*, 3:421–433, **1997**.

[31] M. Bischoff, G. Hermann, S. Rentsch, and D. Strehlow. First steps in the phytochrome phototransformation: A comparative femtosecond study on the forward Pr $\longrightarrow$ Pfr and back reaction Pfr $\longrightarrow$ Pr. *Biochemistry*, 40:181–186, **2001**.

[32] M. Bischoff, G. Hermann, S. Rentsch, D. Strehlow, S. Winter, and H. Chosrowjan. Excited-state processes in phycocyanobilin studied by femtosecond spectroscopy. *J Phys Chem B*, 104:1810–1816, **2000**.

[33] K. Heyne, J. Herbst, D. Stehlik, B. Esteban, T. Lamparter, J. Hughes, and R. Diller. Ultrafast dynamics of phytochrome from the cyanobacterium *Synechocystis* reconstituted with phycocyanobilin and phycoerythrobilin. *Biophys J*, 82:1004–1016, **2002**.

[34] C. Schumann, R. Gross, N. Michael, T. Lamparter, and R. Diller. Subpicosecond mid-infrared spectroscopy of phytochrome Agp1 from *Agrobacterium tumefaciens*. *ChemPhysChem*, 8(11):1657–1663, **2007**.

[35] C. Schumann, R. Gross, M.M.N. Wolf, R. Diller, N. Michael, and T. Lamparter. Subpicosecond midinfrared spectroscopy of the Pfr reaction of phytochrome Agp1 from *Agrobacterium tumefaciens*. *Biophys J*, 94:3189–3197, **2008**.

[36] M.G. Müller, I. Lindner, I. Martin, W. Gärtner, and A.R. Holzwarth. Femtosecond kinetics of photoconversion of the higher plant photoreceptor phytochrome carrying native and modified chromophores. *Biophys J*, 94:4370–4382, **2008**.

[37] T. Lamparter, F. Mittmann, W. Gärtner, T. Börner, E. Hartmann, and J. Hughes. Characterization of recombinant phytochrome from the cyanobacterium *Synechocystis*. *Proc Natl Acad Sci USA*, 94:11792–11797, **1997**.

[38] T. Gensch, M.S. Churio, S.E. Braslavsky, and K. Schaffner. Primary quantum yield and volume change of phytochrome: A phototransformation determined by laser-induced optoacoustic spectroscopy. *Photochem Photobiol*, 63:719–725, **1996**.

[39] H. Foerstendorf, C. Benda, W. Gärtner, M. Storf, H. Scheer, and F. Siebert. FTIR studies of phytochrome photoreactions reveal the C=O bands of the chromophore: Consequences for its protonation states, conformation, and protein interaction. *Biochemistry*, 40:14952–14959, **2001**.

[40] H. Foerstendorf, E. Mummert, E. Schäfer, H. Scheer, and F. Siebert. Fourier-transform infrared spectroscopy of phytochrome: Difference spectra of the intermediates of the photoreactions. *Biochemistry*, 35:10793–10799, **1996**.

[41] C. Kneip, D. Mozley, P. Hildebrandt, W. Gärtner, S.E. Braslavsky, and K. Schaffner. Effect of chromophore exchange on the resonance Raman spectra of recombinant phytochromes. *FEBS Lett*, 414:23–26, **1997**.

[42] A. Remberg, I. Lindner, T. Lamparter, J. Hughes, C. Kneip, P. Hildebrandt, S.E. Braslavsky, W. Gärtner, and K. Schaffner. Raman spectroscopic and light-induced kinetic characterization of a recombinant phytochrome of the cyanobacterium *Synechocystis*. *Biochemistry*, 36:13389–13395, **1997**.

[43] J. Matysik, P. Hildebrandt, W. Schlamann, S.E. Braslavsky, and K. Schaffner. Fourier-transform resonance Raman-spectroscopy of intermediates of the phytochrome photocycle. *Biochemistry*, 34:10497–10507, **1995**.

[44] A.J. Fischer and J.C. Lagarias. Harnessing phytochrome's glowing potential. *Proc Natl Acad Sci USA*, 101:17334–17339, **2004**.

[45] Y. Oka, T. Matsushita, N. Mochizuki, T. Suzuki, S. Tokutomi, and A. Nagatani. Functional analysis of a 450-amino acid N-terminal fragment of phytochrome B in *Arabidopsis*. *Plant Cell*, 16:2104–2116, **2004**.

[46] I. Lindner, S.E. Braslavsky, K. Schaffner, and W. Gärtner. Model studies of phytochrome photochromism: Protein-mediated photoisomerization of a linear tetrapyrrole in the absence of covalent bonding. *Angew Chem Intl Ed Engl*, 39:3269–3271, **2000**.

[47] C.M. Park, J.Y. Shim, S.S. Yang, J.G. Kang, J.I. Kim, Z. Luka, and P.S. Song. Chromophore-apoprotein interactions in *Synechocystis* sp. PCC6803 phytochrome Cph1. *Biochemistry*, 39:6349–6356, **2000**.

[48] S.H. Wu and J.C. Lagarias. Defining the bilin lyase domain: Lessons from the extended phytochrome superfamily. *Biochemistry*, 39:13487–13495, **2000**.

[49] A. Remberg, P. Schmidt, S.E. Braslavsky, W. Gärtner, and K. Schaffner. Differential effects of mutations in the chromophore pocket of recombinant phytochrome on chromoprotein assembly and Pr-to-Pfr photoconversion. *Eur J Biochem*, 266:201–208, **1999**.

[50] I. Lindner, B. Knipp, S.E. Braslavsky, W. Gärtner, and K. Schaffner. A novel chromophore selectively modifies the spectral properties of one of the two stable states of the plant photoreceptor phytochrome. *Angew Chem Intl Ed Engl*, 37:1843–1846, **1998**.

[51] J.R. Wagner, J.R. Zhang, J.S. Brunzelle, R.D. Vierstra, and K.T. Forest. High resolution structure of *Deinococcus* bacteriophytochrome yields new insights into phytochrome architecture and evolution. *J Biol Chem*, 282:12298–12309, **2007**.

[52] X. Yang, E.A. Stojkovic, J. Kuk, and K. Moffat. Crystal structure of the chromophore binding domain of an unusual bacteriophytochrome, RpBphP3, reveals residues that modulate photoconversion. *Proc Natl Acad Sci USA*, 104:12571–12576, **2007**.

[53] L.O. Essen, J. Mailliet, and J. Hughes. The structure of a complete phytochrome sensory module in the Pr ground state. *Proc Natl Acad Sci USA*, 105:14709–14714, **2008**.

[54] P. Schwinté, H. Foerstendorf, Z. Hussain, W. Gärtner, M.A. Mroginski, P. Hildebrandt, and F. Siebert. FTIR study of the photoinduced processes of plant phytochrome phyA using isotope-labeled bilins and density functional theory calculations. *Biophys J*, 95:1256–1267, **2008**.

[55] X. Yang, J. Kuk, and K. Moffat. Crystal structure of *Pseudomonas aeruginosa* bacteriophytochrome: Photoconversion and signal transduction. *Proc Natl Acad Sci USA*, 105:14715–14720, **2008**.

[56] A. Abraham. *Principles of nuclear magnetism*. Oxford University Press, Oxford, United Kingdom, **1961**.

[57] M.J. Duer. *Introduction to solid-state NMR spectroscopy*. Blackwell Publishing Ltd., Oxford, United Kingdom, **2004**.

[58] K. Schmidt-Rohr and W. Spiess. *Multidimensional solid-state NMR and polymers*. Acamdemic Press Ltd., London, United Kingdom, **1994**.

[59] E.R. Andrew, A. Bradbury, and R.G. Eades. Nuclear magnetic resonance spectra from a crystal rotated at high speed. *Nature*, 182:1659–1659, **1958**.

[60] W. Kessemeier and R.E. Norberg. Pulsed nuclear magnetic resonance in rotating solids. *Phys Rev*, 155:321–337, **1967**.

[61] I.J. Lowe. Free induction decays of rotating solids. *Phys Rev Lett*, 2:285–287, **1959**.

[62] S.R. Hartmann and E.L. Hahn. Nuclear double resonance in rotating frame. *Phys Rev*, 128:2042–2053, **1962**.

[63] K. Takegoshi, S. Nakamura, and T. Terao. ^{13}C-^{1}H dipolar-driven ^{13}C-^{13}C recoupling without ^{13}C RF irradiation in nuclear magnetic resonance of rotating solids. *J Chem Phys*, 118:2325–2341, **2003**.

[64] K. Takegoshi, S. Nakamura, and T. Terao. ^{13}C-^{1}H dipolar-assisted rotational resonance in magic angle spinning NMR. *Chem Phys Lett*, 344:631–637, **2001**.

[65] A.E. Bennett, C.M. Rienstra, M. Auger, K.V. Lakshmi, and R. G. Griffin. Heteronuclear decoupling in rotating solids. *J Chem Phys*, 103:6951–6958, **1995**.

[66] M. Lee and W.I. Goldburg. Nuclear magnetic resonance line narrowing by a rotating RF field. *Phys Rev*, 140:1261–1271, **1965**.

[67] A. Bielecki, A.C. Kolbert, and M.H. Levitt. Frequency-switched pulse sequences: Homonuclear decoupling and dilute spin NMR in solids. *Chem Phys Lett*, 155:341–346, **1989**.

[68] B.J. van Rossum, H. Förster, and H.J.M. de Groot. High-field and high-speed CP/MAS ^{13}C NMR heteronuclear dipolar-correlation spectroscopy of solids with frequency-switched Lee-Goldburg homonuclear decoupling. *J Magn Res*, 124:516–519, **1997**.

[69] M.D. Maines. The heme oxygenase system: A regulator of second messenger gases. *Ann Rev Pharm Tox*, 37:517–554, **1997**.

[70] R.F. Troxler and L. Bogorad. Studies on formation of phycocyanin porphyrins and a blue phycobilin by wild-type and mutant strains of *cyanidium caldarium*. *Plant Physiol*, 41:491–499, **1966**.

[71] J. Hughes, T. Lamparter, F. Mittmann, E. Hartmann, W. Gärtner, A. Wilde, and T. Börner. A prokaryotic phytochrome. *Nature*, 386:663–663, **1997**.

[72] J. Crusats, A. Delgado, J.A. Farrera, R. Rubires, and J.M. Ribó. Solution structure of mesobilirubin XIIIα bridged between the propionic acid substituents. *Monatsh Chem*, 129:741–753, **1998**.

[73] H. Marko, N. Müller, and H. Falk. NMR investigations of the biliverdin-apomyoglobin complex. *Eur J Biochem*, 193:573–580, **1990**.

[74] S.E. Braslavsky, D. Schneider, K. Heihoff, S. Nonell, P.F. Aramendia, and K. Schaffner. Phytochrome models: Photophysics and photochemistry of phycocyanobilin dimethyl ester. *J Am Chem Soc*, 113:7322–7334, **1991**.

[75] A.H. Göller, D. Strehlow, and G. Hermann. Conformational flexibility of phycocyanobilin: An AM1 semiempirical study. *ChemPhysChem*, 2:665–671, **2001**.

[76] B. Dietzek, R. Maksimenka, G. Hermann, W. Kiefer, J. Popp, and M. Schmitt. The excited-state dynamics of phycocyanobilin in dependence on the excitation wavelength. *ChemPhysChem*, 5:1171–1177, **2004**.

[77] H. Falk. *The Chemistry of Linear Oligopyrroles and Bile Pigments*. Springer-Verlag, **1989**.

[78] D.D. Laws, H.M.L. Bitter, and A. Jerschow. Solid-state NMR spectroscopic methods in chemistry. *Angew Chem Intl Ed Engl*, 41:3096–3129, **2002**.

[79] I. de Boer, J. Matysik, M. Amakawa, S. Yagai, H. Tamiaki, A.R. Holzwarth, and H.J.M. de Groot. MAS NMR structure of a microcrystalline Cd-bacteriochlorophyll *d* analogue. *J Am Chem Soc*, 125:13374–13375, **2003**.

[80] A.B. Siemer, A.A. Arnold, C. Ritter, T. Westfeld, M. Ernst, R. Riek, and B.H. Meier. Observation of highly flexible residues in amyloid fibrils of the HET-s prion. *J Am Chem Soc*, 128:13224–13228, **2006**.

[81] F. Castellani, B. van Rossum, A. Diehl, M. Schubert, K. Rehbein, and H. Oschkinat. Structure of a protein determined by solid-state magic angle spinning NMR spectroscopy. *Nature*, 420:98–102, **2002**.

[82] A.J. van Gammeren, F.B. Hulsbergen, J.G. Hollander, and H.J.M. de Groot. Residual backbone and side-chain ^{13}C-^{13}C and ^{15}N resonance assignments of the intrinsic transmembrane light-harvesting-2 protein complex by solid-state magic angle spinning NMR spectroscopy. *J Biomol NMR*, 31:279–293, **2005**.

[83] Alia, J. Matysik, C. Soede-Huijbregts, M. Baldus, J. Raap, J. Lugtenburg, P. Gast, H.J. van Gorkom, A.J. Hoff, and H.J.M. de Groot. Ultrahigh field MAS NMR dipolar correlation spectroscopy of the histidine residues in light-harvesting complex II from photosynthetic bacteria reveals partial internal

charge transfer in the B850/His complex. *J Am Chem Soc*, 123:4803–4809, **2001**.

[84] Y.F. Wei, A.C. de Dios, and A.E. McDermott. Solid-state ^{15}N NMR chemical shift anisotropy of histidines: Experimental and theoretical studies of hydrogen bonding. *J Am Chem Soc*, 121:10389–10394, **1999**.

[85] W.S. Sheldrick. Crystal and molecular structure of biliverdin dimethyl ester. *J Chem Soc, Perkin Trans 2*, pages 1457–1462, **1976**.

[86] U. Wagner, C. Kratky, H. Falk, and H. Woss. Crystal structure and conformation of 10-aryl-bilatrienes. *Monatsh Chem*, 122:749–758, **1991**.

[87] H. Falk, K. Grubmayr, K. Magauer, N. Müller, and U. Zrunek. On the chemistry of pyrrole pigments. Phytochrome model studies: The tautomerism at N-22-N-23 of unsymmetrically substituted bilatrienes and 2,3-dihydrobilatrienes. *Israel J Chem*, 23:187–194, **1983**.

[88] M. Hölzl, A. Jarosik, and K. Grubmayr. Inducing *anti*-conformers of biliverdin chromophores by reducing sterical hindrance. *Monatsh Chem*, 136:747–754, **2005**.

[89] C. Kneip, P. Hildebrandt, K. Nemeth, F. Mark, and K. Schaffner. Interpretation of the resonance Raman spectra of linear tetrapyrroles based on DFT calculations. *Chem Phys Lett*, 311:479–484, **1999**.

[90] C. Kratky, H. Falk, K. Grubmayr, and U. Zrunek. On the molecular-structure of the phytochrome chromophore: X-ray-analysis of two 2,3-dihydrobilatriene-abc derivatives. *Monatsh Chem*, 116:761–776, **1985**.

[91] U.G. Wagner, C. Kratky, H. Falk, and G. Kapl. Synthesis and X-ray crystal-structure of a 15*E*-dihydrobilatriene-abc-derivate. *Monatsh Chem*, 117:1413–1422, **1986**.

[92] A.D. Becke. A new mixing of Hartree-Fock and local density-functional theories. *J Chem Phys*, 98:1372–1377, **1993**.

[93] M.J. Frisch, G.W. Trucks, H.B. Schlegel, G.E. Scuseria, M.A. Robb, J.R. Cheeseman, J.A. Montgomery Jr., T. Vreven, K.N. Kudin, J.C. Burant, J.M. Millam, S.S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G.A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J.E. Knox, H.P. Hratchian, J.B. Cross, C. Adamo, J. Jaramillo, R. Gomperts, R.E. Stratmann, O. Yazyev, A.J. Austin, R. Cammi, C. Pomelli, J.W. Ochterski, P.Y. Ayala, K. Morokuma, G.A. Voth, P. Salvador, J.J. Dannenberg, V.G. Zakrzewski, S. Dapprich, A.D. Daniels, M.C.

Strain, O. Farkas, D.K. Malick, A.D. Rabuck, K. Raghavachari, J.B. Foresman, J.V. Ortiz, Q. Cui, A.G. Baboul, S. Clifford, J. Cioslowski, B.B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R.L. Martin, D.J. Fox, T. Keith, M.A. Al-Laham, C.Y. Peng, A. Nanayakkara, M. Challacombe, P.M.W. Gill, B. Johnson, W. Chen, M.W. Wong, C. Gonzalez, and J.A. Pople. Gaussian 03, Revision C.02, Gaussian, Inc., Wallingford CT, 2004.

[94] H.M. Strauss, J. Hughes, and P. Schmieder. Heteronuclear solution-state NMR studies of the chromophore in cyanobacterial phytochrome Cph1. *Biochemistry*, 44:8244–8250, **2005**.

[95] M. Baldus, D.G. Geurts, S. Hediger, and B.H. Meier. Efficient ^{15}N-^{13}C polarization transfer by adiabatic-passage Hartmann-Hahn cross polarization. *J Magn Res*, 118:140–144, **1996**.

[96] S.E. Braslavsky, W. Gärtner, and K. Schaffner. Phytochrome photoconversion. *Plant Cell Environ*, 20:700–706, **1997**.

[97] S.P.A. Fodor, J.C. Lagarias, and R.A. Mathies. Resonance Raman analysis of the Pr and Pfr forms of phytochrome. *Biochemistry*, 29:11141–11146, **1990**.

[98] J.R. Wagner, J.R. Zhang, D. von Stetten, M. Günther, D.H. Murgida, M.A. Mroginski, J.M. Walker, K.T. Forest, P. Hildebrandt, and R.D. Vierstra. Mutational analysis of *Deinococcus radiodurans* bacteriophytochrome reveals key amino acids necessary for the photochromicity and proton exchange cycle of phytochromes. *J Biol Chem*, 283:12212–12226, **2008**.

[99] H. Heise, W. Hoyer, S. Becker, O.C. Andronesi, D. Riedel, and M. Baldus. Molecular-level secondary structure, polymorphism, and dynamics of full-length α-synuclein fibrils studied by solid-state NMR. *Proc Natl Acad Sci USA*, 102:15871–15876, **2005**.

[100] P. Schmidt, T. Gensch, A. Remberg, W. Gärtner, S.E. Braslavsky, and K. Schaffner. The complexity of the Pr to Pfr phototransformation kinetics is an intrinsic property of native phytochrome. *Photochem Photobiol*, 68:754–761, **1998**.

[101] V.A. Sineshchekov. Extreme dehydration of plant tissues irreversibly converts the major and variable phyA' into the minor and conserved phyA". *J Photochem Photobiol*, 85:85–91, **2006**.

[102] J. Hahn, R. Kuhne, and P. Schmieder. Solution-state ^{15}N NMR spectroscopic study of α-C-phycocyanin: Implications for the structure of the chromophore-binding pocket of the cyanobacterial phytochrome Cph1. *ChemBioChem*, 8:2249–2255, **2007**.

[103] M. Stanek and K. Grubmayr. Protonated 2,3-dihydrobilindiones: Models for the chromophores of phycocyanin and the red absorbing form of phytochrome. *Chem Eur J*, 4:1653–1659, **1998**.

[104] T. Rohmer, H. Strauss, J. Hughes, H. de Groot, W. Gärtner, P. Schmieder, and J. Matysik. ^{15}N MAS NMR studies of Cph1 phytochrome: Chromophore dynamics and intramolecular signal transduction. *J Phys Chem B*, 110:20580–20585, **2006**.

[105] G. Filippini and A. Gavezzotti. The crystal-structure of 1,3,5-triamino-2,4,6-trinitrobenzene - centrosymmetric or noncentrosymmetric. *Chem Phys Lett*, 231:86–92, **1994**.

[106] H. Foerstendorf, T. Lamparter, J. Hughes, W. Gärtner, and F. Siebert. The photoreactions of recombinant phytochrome from the cyanobacterium *Synechocystis*: A low-temperature UV-Vis and FTIR spectroscopic study. *Photochem Photobiol*, 71:655–661, **2000**.

[107] W.L. DeLano. The PyMOL molecular graphics system. www.pymol.org, **2002**.

[108] L. Yu. *Solitons and polarons in conduction polymers*. World Scientific, Singapore, **1988**.

[109] J.H. Koek. *Synthesis and spectroscopy of tetrapyrrol systems related to biliprotein chromophores*. PhD thesis, Leiden University, 1987.

[110] D. Mozley, A. Remberg, and W. Gärtner. Large-scale generation of affinity purified recombinant phytochrome chromopeptide. *Photochem Photobiol*, 66:710–715, **1997**.

[111] H.M. Strauss, P. Schmieder, and J. Hughes. Light-dependent dimerisation in the N-terminal sensory module of cyanobacterial phytochrome 1. *FEBS Lett*, 579:3970–3974, **2005**.

[112] P. Eilfeld, P. Eilfeld, J. Vogel, and R. Maurer. Evidence for a sequential pathway from Pr to Pfr of the phototransformation of 124-kDa oat phytochrome. *Photochem Photobiol*, 45:825–830, **1987**.

[113] P. Eilfeld and W. Rüdiger. Absorption spectra of phytochrome intermediates. *Z Naturforsch*, 40:109–114, **1985**.

[114] R.D. Scurlock, C.H. Evans, S.E. Braslavsky, and K. Schaffner. A phytochrome phototransformation study using two-laser/two-color flash-photolysis: Analysis of the decay mechanism of I(700). *Photochem Photobiol*, 58:106–115, **1993**.

[115] W. Gärtner and S.E. Braslavsky. *Photoreceptors and light signalling,*, volume 3, chapter The Phytochromes: Spectroscopy and Function, pages 136–180. Royal Society Chemistry, Cambridge, United Kingdom, D.P. Häder and G. Jori edition, **2003**.

[116] P. Schwinté, W. Gärtner, S. Sharda, M.A. Mroginski, P. Hildebrandt, and F. Siebert. The photoreactions of recombinant phytochrome CphA from the cyanobacterium *Calothrix* PCC7601: A low-temperature UV-Vis and FTIR study. *Photochem Photobiol*, 85:239–249, **2009**.

[117] M. Concistrè, A. Gansmüller, N. McLean, O.G. Johannessen, I.M. Montesinos, P.H.M. Bovee-Geurts, P. Verdegem, J. Lugtenburg, R.C.D. Brown, W.J. de Grip, and M.H. Levitt. Double-quantum ^{13}C nuclear magnetic resonance of bathorhodopsin, the first photointermediate in mammalian vision. *J Am Chem Soc*, 130:10490–10491, **2008**.

[118] M.L. Mak-Jurkauskas, V.S. Bajaj, M.K. Hornstein, M. Belenky, R.G. Griffin, and J. Herzfeld. Energy transformations early in the bacteriorhodopsin photocycle revealed by DNP-enhanced solid-state NMR. *Proc Natl Acad Sci USA*, 105:883–888, **2008**.

[119] A.V. Cherepanov, E.V. Doroshenko, J. Matysik, S. de Vries, and H.J.M. de Groot. The associative nature of adenylyl transfer catalyzed by T4 DNA ligase. *Proc Natl Acad Sci USA*, 105:8563–8568, **2008**.

[120] T. Rohmer, C. Lang, J. Hughes, L.O. Essen, W. Gärtner, and J. Matysik. Light-induced chromophore activity and signal transduction in phytochromes observed by ^{13}C and ^{15}N magic-angle spinning NMR. *Proc Natl Acad Sci USA*, 105:15229–15234, **2008**.

[121] U. Robben, I. Lindner, and W. Gärtner. New open-chain tetrapyrroles as chromophores in the plant photoreceptor phytochrome. *J Am Chem Soc*, 130:11303–11311, **2008**.

[122] J. Dasgupta, R.R. Frontiera, K.C. Taylor, J.C. Lagarias, and R.A. Mathies. Ultrafast excited-state isomerization in phytochrome revealed by femtosecond stimulated Raman spectroscopy. *Proc Natl Acad Sci USA*, 106:1784–1789, **2009**.

[123] W.M. Gong, B. Hao, and M.K. Chan. New mechanistic insights from structural studies of the oxygen-sensing domain of *Bradyrhizobium japonicum* FixL. *Biochemistry*, 39:3955–3962, **2000**.

[124] E. Daviso, G. Jeschke, and J. Matysik. *Biophysical Techniques in Photosynthesis*, volume 26 of *Advances in Photosynthesis and Respiration*, chapter Photo-CIDNP Magic Angle Spinning NMR, page 385–399. Springer Publishers, Dordrecht, **2008**.

[125] A.F.L. Creemers, S. Kiihne, P.H.M. Bovee-Geurts, W.J. de Grip, J. Lugtenburg, and H.J.M. de Groot. H-1 and C-13 MAS NMR evidence for pronounced ligand-protein interactions involving the ionone ring of the retinylidene chromophore in rhodopsin. *Proc Natl Acad Sci USA*, 99:9101–9106, **2002**.

[126] S.R. Kiihne, A.F.L. Creemers, W.J. de Grip, P.H.M. Bovee-Geurts, J. Lugtenburg, and H.J.M. de Groot. Selective interface detection: Mapping binding site contacts in membrane proteins by NMR spectroscopy. *J Am Chem Soc*, 127:5734–5735, **2005**.

[127] M.A. Verhoeven, P.H.M. Bovee-Geurts, H.J.M. de Groot, J. Lugtenburg, and W.J. de Grip. Methyl substituents at the 11 or 12 position of retinal profoundly and differentially affect photochemistry and signalling activity of rhodopsin. *J Mol Biol*, 363:98–113, **2006**.

[128] A. Bifone, H.J.M. de Groot, and F. Buda. Ab initio molecular dynamics of rhodopsin. *Pure Appl Chem*, 69:2105–2110, **1997**.

[129] A. Cembran, F. Bernardi, M. Olivucci, and M. Garavelli. Excited-state singlet manifold and oscillatory features of a nonatetraeniminium retinal chromophore model. *J Am Chem Soc*, 125:12509–12519, **2003**.

[130] P.J.E. Verdegem, M. Helmle, J. Lugtenburg, and H.J.M. de Groot. Internuclear distance measurements up to 0.44 nm for retinals in the solid state with 1-D rotational resonance C-13 MAS NMR spectroscopy. *J Am Chem Soc*, 119:169–174, **1997**.

[131] H. Görner and H.J. Kuhn. *Advances in Photochemistry*, volume 19, chapter *Cis-trans* photoisomerization of stilbenes and stilbene-like molecules. Wiley InterScience, **1995**.

[132] H. Falk, K. Grubmayr, E. Haslinger, T. Schlederer, and K. Thirring. Chemistry of pyrrole pigments: Diastereomeric (geometrically isomeric) biliverdindimethylesters-structure, configuration and conformation. *Monatsh Chem*, 109:1451–1473, **1978**.

[133] K. Smit, J. Matysik, P. Hildebrandt, and F. Mark. Vibrational analysis of biliverdin dimethyl ester. *J Phys Chem*, 97:11887–11900, **1993**.

[134] J. Matysik, P. Hildebrandt, K. Smit, F. Mark, W. Gärtner, S.E. Braslavsky, K. Schaffner, and B. Schrader. Raman spectroscopic analysis of isomers of biliverdin dimethyl ester. *J Pharm Biomed Anal*, 15:1319–1324, **1997**.

[135] B. Durbeej. On the primary event of phytochrome: quantum chemical comparison of photoreactions at C-4, C-10 and C-15. *Phys Chem Chem Phys*, 11:1354–1361, **2009**.

[136] X.L. Yao, K. Schmidt-Rohr, and M. Hong. Medium- and long-distance H-1-C-13 heteronuclear correlation NMR in solids. *J Magn Reson*, 149:139–143, **2001**.

[137] N. Khaneja and N.C. Nielsen. Triple oscillating field technique for accurate distance measurements by solid-state NMR. *J Chem Phys*, 128, **2008**.

[138] S.R. Kiihne, A.F.L. Creemers, J. Lugtenburg, and H.J.M. de Groot. Accurate CSA measurements from uniformly isotopically labeled biomolecules at high magnetic field. *J Magn Reson*, 172:1–8, **2005**.

[139] T. Kakiuchi, H. Kato, K.P. Jayasundera, T. Higashi, K. Watabe, D. Sawamoto, H. Kinoshita, and K. Inomata. Total syntheses of ±-phycocyanobilin and its derivatives bearing a photoreactive group at D ring. *Chem Lett*, pages 1001–1002, **1998**.

[140] A. Gossauer and W. Hirsch. Syntheses of bile-pigments: Total synthesis of racemic phycocyanobilin (phycobiliverdin) and of a homophycobiliverdin. *Liebigs Ann Chem*, pages 1496–1513, **1974**.

[141] Y. Makhynya, Z. Hussain, T. Bauschlicher, P. Schwinté, F. Siebert, and W. Gärtner. Synthesis of selectively ^{13}C-labelled bilin compounds. *Eur J Org Chem*, pages 1287–1293, **2007**.