Total Synthesis

International Edition: DOI: 10.1002/anie.201908619
German Edition: DOI: 10.1002/ange.201908619

Concise Access to the Skeleton of Protoilludane Sesquiterpenes through a Photochemical Reaction Cascade: Total Synthesis of Atlanticone C

*Andreas Zech, Christian Jandl, and Thorsten Bach**

Dedicated to Dr. Albrecht Hauff on the occasion of his 65th birthday

Abstract: *In a single photochemical operation ($\lambda \geq 350$ nm) an easily accessible indanone derivative was converted into a structurally complex precursor of the protoilludane sesquiterpenes. The product (60% yield) contains all 15 carbon atoms of the skeleton in the required connectivity and was transformed into the natural product atlanticone C (9 steps, 6% overall yield). In addition, it was shown that other protoilludanes, such as Δ^6-protoilludene and paesslerin A, can be prepared in a concise fashion via the photochemical key intermediate. The photochemical reaction cascade comprises an ortho photocycloaddition, a thermal disrotatory ring opening and a regioselective disrotatory [4π] photocyclization. Open access funding enabled and organized by Projekt DEAL.*

The protiolludane skeleton **A** (Figure 1) represents an intriguing natural product scaffold and is the hallmark of many biologically active sesquiterpenes. A central cyclohexane ring is flanked by a cyclobutane ring with a quaternary carbon center C-3 and by a *gem*-dimethyl-substituted cyclopentane ring at positions C-2 and C-9. The protoilludane

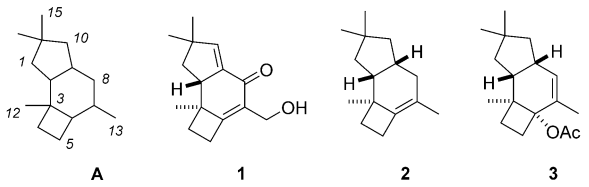
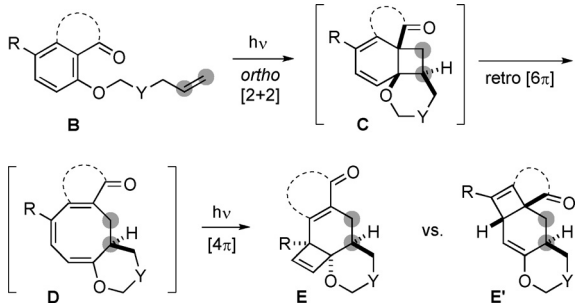


Figure 1. The protoilludane skeleton **A** and representative protoilludane sesquiterpenes: atlanticone C (**1**), Δ^6-protoilludene (**2**), paesslerin A (**3**).

biosynthesis[1] from farnesyl pyrophosphate via cationic intermediates is testimony to the masterful ability of nature to create molecular complexity from simple building blocks. Representative sesquiterpenes with this structure element include atlanticone C (**1**),[2] Δ^6-protoilludene (**2**),[3] and paesslerin A (**3**).[4]

Many synthetic approaches have been described to tackle the challenging core structure of the protoilludanes.[5] One set of syntheses aimed at a construction of the tricyclic skeleton from acyclic or monocyclic precursors in a manner mimicking their biological genesis from humulene.[6] In several other approaches, the rings were built consecutively,[7] with the construction of the cyclobutane ring requiring particular attention. Notable photochemical strategies[8] to secure formation of the four-membered ring include the common [2+2] photocycloaddition[9] but also some less frequently used methods such as the photochemical 1,3-acyl shift reaction of β,γ-unsaturated enones.[10] Our interest in protoilludanes was triggered by recent work[11] on a reaction cascade[12] that is initiated by an *ortho* photocycloaddition and that generates the bicyclo[4.2.0]octane skeleton, a core element of structure **A**, in a single operation. Herein, we disclose a concise access to protoilludane sesquiterpenes that culminated in the first total synthesis of atlanticone C (**1**) and in the stereoselective synthesis of two other advanced intermediates that had been previously converted into Δ^6-protoilludene (**2**) and paesslerin A (**3**).

Arenes **B** (Scheme 1), which have a carbonyl group in *ortho* position to an alkenyloxy group, are known to undergo an initial [2+2] photocycloadditon at the arene (*ortho* photo-

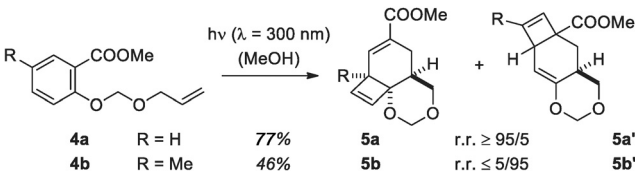


Scheme 1. A Photochemical reaction cascade triggered by an *ortho* photocycloaddition of salicylic acid derivatives **B** to give the constitutional isomers **E** and **E′** (gray circles indicate the carbon atoms of the former olefinic double bond).

[*] M. Sc. A. Zech, Dr. C. Jandl, Prof. Dr. T. Bach
Department Chemie and Catalysis Research Center (CRC)
Technische Universität München
Lichtenbergstr. 4, 85747 Garching (Germany)
E-mail: thorsten.bach@ch.tum.de
Homepage: http://www.oc1.ch.tum.de/home_en/
Supporting information and the ORCID identification number(s) for the author(s) of this article can be found under: https://doi.org/10.1002/anie.201908619.

cycloaddition[13,14]). Products **C** are unstable and form cyclooctatrienes **D** through a disrotatory ring opening. In some cases, these products have been isolated[15] but the most frequent reaction pathway is a consecutive disrotatory [4π] cyclization, which can lead to products **E** or **E′** depending upon the substitution pattern within the tether.[16]

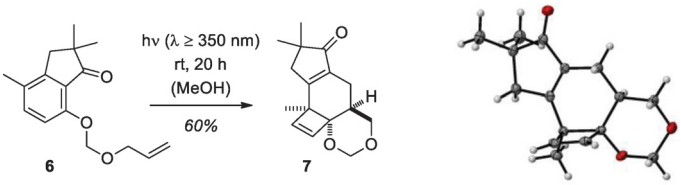
Following up on earlier work by Wagner and co-workers,[17] we have recently found that several salicylates and salicyclic acid derivatives deliver clean formation of products **E** if irradiated at $\lambda = 300$ nm in methanol solution.[11] Given the structural similarity of **E** with the biyclo[4.2.0]cyclooctane part of structure **A**, we reasoned that a substituent Y = O would facilitate a ring opening of the former tether and would secure the introduction of the hydroxy group required at position C-13 of the natural product atlanticone C. Regarding the other variable R in structure **E**, a late-stage introduction of the C-12 methyl group did not seem feasible. It was thus mandatory to introduce this substituent already in the starting material, that is, into the *meta* position of the salicylate. The respective salicylic acid is readily available through a Kolbe–Schmitt reaction,[18] and substrate **4b** (Scheme 2) was synthesized in three steps and an overall yield of 77% from *para*-cresol (see the Supporting Information). The results of its photochemical reaction were disappointing, however. While the unsubstituted salicylate **4a** had given the desired product **5a** in 65% yield in previous work,[11] substrate **4b** delivered an inseparable mixture of diastereoisomers in only 46% yield under identical reaction conditions with a strict preference for the opposite regioisomer. Attempts to alter this reaction outcome by changing the light source or the solvent remained unsuccessful. Apparently, a larger R group (R = Me instead of R = H) avoids the sterically encumbered position at the quaternary carbon center and the [4π] ring closure to the linear product **5b′** becomes competitive.



4a	R = H	*77%*	**5a**	r.r. ≥ 95/5	**5a'**
4b	R = Me	*46%*	**5b**	r.r. ≤ 5/95	**5b'**

Scheme 2. Photochemical reaction of methyl salicylates **4** to give regioisomeric products **5** and **5′** (r.r. = regioisomeric ratio).

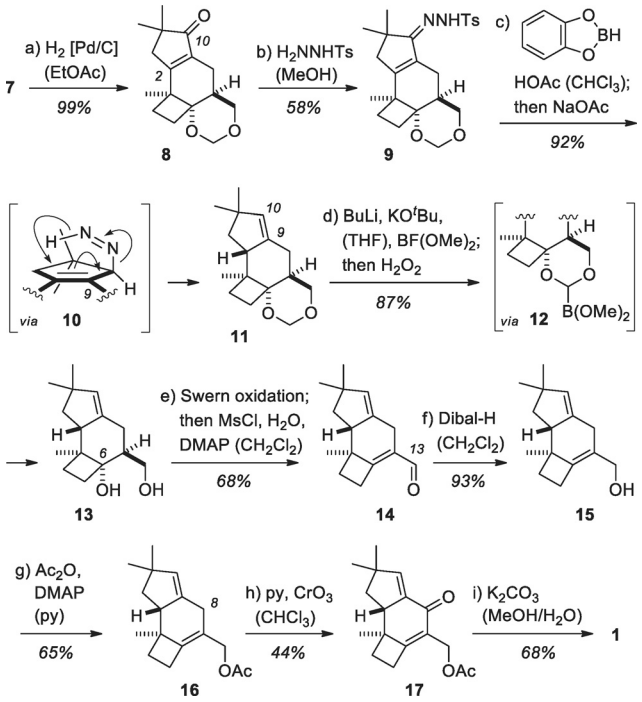
Inspection of molecular models indicated that a cyclic carbonyl compound, that is, a ketone, might enforce the desired reaction pathway, delivering a product **E** with an even higher structural similarity to skeleton **A**. However, there was no precedence for the *ortho* photocycloaddition of cyclic aromatic ketones, and many photochemical reaction pathways are conceivable for the keto group both in a potential substrate and its product. Despite these concerns, we decided to investigate this topic more closely, and ketone **6** (Scheme 3) was easily synthesized from *para*-methyl anisole in four steps and an overall yield of 57% (see the Supporting Information). Gratifyingly, this substrate could be successfully taken into the desired photochemical reaction cascade without notable decomposition. Careful optimization eventually led to conditions under which the desired product **7** was reproducibly formed in yields of 60%. In order to avoid undesirable consecutive reactions of enone **7** an $Fe_2(SO_4)_3$ solution ($c = 300\ mg\,L^{-1}$) in 0.01M aqueous HCl[19] was employed to filter the desired wavelength region from fluorescent lamps emitting at a maximum of $\lambda = 350$ nm.[20] Parallel to extensive NMR analyses the structure of crystalline diastereomerically pure product **7** was secured by X-ray crystallography.[21]



Scheme 3. Successful photochemical reaction cascade of ketone **6** to tetracyclic product **7**, the structure of which was elucidated by single crystal X-ray crystallography.

The transformation of ketone **7** to atlanticone C (**1**) required the adjustment of the oxidation state at several carbon atoms and the introduction of the stereogenic center at carbon atom C-2. The tetracyclic skeleton directs an attack of a given reagent to the bottom face, which made it impossible to secure the relative configuration at C-2 by a direct reduction. After hydrogenation of the cyclobutene to a cyclobutane ring, it was therefore attempted to employ the functional group at position C-10 in intermediate **8** (Scheme 4) as a directing group. Ketone reduction was diastereoselective but subsequent attempts to perform a directed hydrogenation of the allylic alcohol[22] remained unsuccessful. Instead, the ketone was converted into hydrazone **9** by condensation[23] with *N*-tosylhydrazine (58% yield, 36% of unreacted starting material). Subsequent reduction according to the method of Kabalka et al.[24] not only delivered the hydride from the correct diastereotopic face via intermediate **10** but also established the double bond in product **11** at the desired position C-9/C-10.

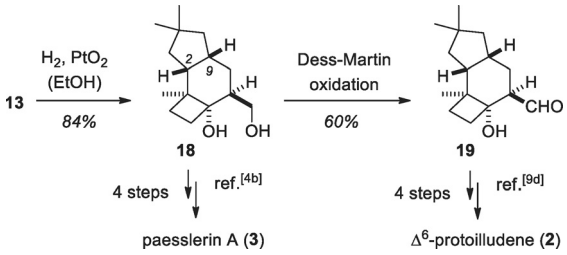
In order to adjust the oxidation state at positions C-6, C-7, and C-8, the 1,3-dioxane ring of intermediate **11** had to be opened. Reported procedures for the ring opening of methylene acetals[25] require acidic conditions, which turned out to be not perfectly compatible with the substrate. For example, the yield of deprotection with trifluoroacetic acid anhydride and acetic acid in CH_2Cl_2[26] was only 36%. We therefore turned to a somewhat unusual method that makes use of the relative high acidity of the methylene protons and of the high stability of substrate **11** towards base. Treatment with the Schlosser–Lochmann base BuLi/KO^{t}Bu and a subsequent quench with $BF(OMe)_2{\cdot}OEt_2$[27] delivered product **13** after oxidative work-up. It is likely that the deprotection proceeds via boronate **12**, which upon oxidative hydrolysis splits into diol **13** and formic acid. Since several known dehydration methods were not applicable to diol **13**, we followed a procedure reported by Furukawa et al.,[9d] according to which a 6-hydroxy C-13 protoilludane aldehyde can be dehydrated by treatment with MsCl, water, and DMAP. Reduction of aldehyde **14** to alcohol **15** and acetylation to



Scheme 4. Synthesis of atlanticone C (**1**), exact conditions and yields: a) H_2 (1 atm), 10 mol% Pd/C, (EtOAc), rt, 1 h, 99%; b) H_2NHNTs (1.5 equiv.), 10 mol% H_2SO_4, (MeOH), 65 °C, 24 h, 58% (91% based on conversion); c) catecholborane (4.0 equiv.), HOAc (8.0 equiv), ($CHCl_3$/THF), −40 °C, 3 h, then NaOAc·3 H_2O (16 equiv.), −40 °C→52 °C, 16 h, 92%; d) BuLi (10 equiv.), KO^{t}Bu (10 equiv.), (THF/hexane), −78 °C, 1 h, then $BF(OMe)_2$·OEt_2 (16.6 equiv.), 5 min, then 10 M NaOH (100 equiv.), 30% H_2O_2 (100 equiv.), −78 °C→rt, 18 h, 87%; e) $(COCl)_2$ (2.0 equiv.), DMSO (5.0 equiv.), (CH_2Cl_2/DMSO) −78 °C, 15 min; NEt_3 (10 equiv.), −78 °C→−40 °C, 30 min, short work-up (see Supporting Information), then MsCl (7.25 equiv.), DMAP (3.63 equiv.), H_2O (2.9 equiv.), (CH_2Cl_2), rt, 3 h, 68% over two steps; f) Dibal-H (1.2 equiv.), (CH_2Cl_2), −78 °C, 1 h, 93%; g) Ac_2O (5.0 equiv.), 10 mol% DMAP, (py), rt, 30 min, 65%; h) py (75 equiv.), CrO_3 (20 equiv.), (CH_2Cl_2), rt, 3 h, 44%; i) K_2CO_3 (8.0 equiv.), ($MeOH/H_2O$), rt, 40 min, 68%. Ts = *para*-toluenesulfonyl, Ms = methanesulfonyl, DMAP = 4-dimethylaminopyridine, Dibal-H = diisobutylaluminum hydride.

ester **16** proceeded uneventfully. However, the allylic acetate **16** proved to be a labile compound, presumably due to its high electophilicity. In this regard, it was fortunate that oxygenation at the C-8 methylene group could be executed with pyridine and CrO_3. Saponification of acetate **17** resulted in the formation of the desired alcohol **1**. The spectroscopic data of synthetic product **1** perfectly matched the data reported for atlanticone C[2] and thus support the structural assignment of this natural product (see the Supporting Information for a comparison).

Compounds **18** and **19** (Scheme 5) were prepared as an additional exercise to illustrate the broad applicability of the photochemical reaction cascade to protoilludane synthesis. Compound **18** had been reported previously in the context of the total synthesis of paesslerin A (**3**) and had been obtained in 15 steps and 2% yield from 5,5-dimethylcyclopent-2-enone.[4b] Compound **19** had been described as a precursor of Δ^6-protoilludene (**2**) and had been prepared from methyl



Scheme 5. Diastereoselective conversion of protoilludane precursor **13** into products **18** and **19**, which have previously served as intermediates in the total synthesis of natural products **2** and **3**.

4,4-dimethyl-2-oxocyclopentane-1-carboxylate in 19 steps and 4% yield.[9d]

The starting material for our synthetic approach was diol **13**, which could be diastereoselectively hydrogenated to establish the stereogenic center at carbon atom C-9 and deliver product **18**. The facial diastereoselectivity is in line with previous work on Pt-catalyzed hydrogenation reactions.[28] It is likely that the concave structure of the hexahydro-1*H*-indene directs the attack *cis* to the existing stereogenic center at C-2. The overall yield for product **18** starting from *para*-methylanisole, the precursor of ketone **6** (see above), was 13% over 9 steps. Dess–Martin oxidation of alcohol **18** delivered ketone **19** in an overall yield of 8% over 10 steps.

In conclusion, we have discovered a concise access to protoilludane sesquiterpenes from a substituted indanone. The reaction cascade establishes the correct constitution of the carbocyclic skeleton and also secures its relative configuration. In order to access more complex protoilludanes, it will be necessary to install further functional groups in the starting material or in the products. It is envisaged, for example, that the cyclobutene ring of photoproduct **7** could be employed to install hydroxy groups at positions C-4 and C-5, which are frequently encountered in protoilludanes.[29] Another intriguing topic relates to the control of the absolute configuration, which could be achieved either by starting from chiral enantiopure substrates or through enantioselective photochemical reactions.[30]

Acknowledgements

This project was supported by the *Deutsche Forschungsgemeinschaft* (Ba 1372/22-1) and by the TUM Graduate School. Open access funding enabled and organized by Projekt DEAL.

Conflict of interest

The authors declare no conflict of interest.

Keywords: carbocycles · photochemistry · reduction · terpenoids · total synthesis

How to cite: *Angew. Chem. Int. Ed.* **2019**, *58*, 14629 – 14632
Angew. Chem. **2019**, *131*, 14771 – 14774

[1] Review: M. B. Quin, C. M. Flynn, C. Schmidt-Dannert, *Nat. Prod. Rep.* **2014**, *31*, 1449 – 1473.
[2] M. Clericuzio, M. Mella, L. Toma, P. V. Finzi, G. Vidari, *Eur. J. Org. Chem.* **2002**, 988 – 994.
[3] S. Nozoe, H. Kobayashi, S. Urano, J. Furukawa, *Tetrahedron Lett.* **1977**, *18*, 1381 – 1384.
[4] a) M. F. Rodríguez Brasco, A. M. Seldes, J. A. Palermo, *Org. Lett.* **2001**, *3*, 1415 – 1417; b) Y. Mogi, K. Inanaga, H. Tokuyama, M. Ihara, Y. Yamaoka, K.-i. Yamada, K. Takasu, *Org. Lett.* **2019**, *21*, 3954 – 3958.
[5] Review: P. Siengalewicz, J. Mulzer, U. Rinner, *Eur. J. Org. Chem.* **2011**, 7041 – 7055.
[6] Examples: a) E. P. Johnson, K. P. C. Vollhardt, *J. Am. Chem. Soc.* **1991**, *113*, 381 – 382; b) M. R. Elliott, A.-L. Dhimane, M. Malacria, *J. Am. Chem. Soc.* **1997**, *119*, 3427 – 3428; c) M. Kögl, L. Brecker, R. Warrass, J. Mulzer, *Angew. Chem. Int. Ed.* **2007**, *46*, 9320 – 9322; *Angew. Chem.* **2007**, *119*, 9480 – 9482; d) L. Zu, M. Xu, M. W. Lodewyk, D. E. Cane, R. J. Peters, D. J. Tantillo, *J. Am. Chem. Soc.* **2012**, *134*, 11369 – 11371; e) A. Pitaval, D. Leboeuf, J. Ceccon, A. M. Echavarren, *Org. Lett.* **2013**, *15*, 4580 – 4583.
[7] Examples: a) M. F. Semmelhack, S. Tomoda, *J. Am. Chem. Soc.* **1981**, *103*, 2427 – 2428; b) M. F. Semmelhack, S. Tomoda, H. Nagaoka, S. D. Boettger, K. M. Hurst, *J. Am. Chem. Soc.* **1982**, *104*, 747 – 759; c) W. Oppolzer, A. Nakao, *Tetrahedron Lett.* **1986**, *27*, 5471 – 5474; d) T. V. Hansen, L. Skattebø, Y. Stenstrøm, *Tetrahedron* **2003**, *59*, 3461 – 3466; e) M. T. Hovey, D. T. Cohen, D. M. Walden, P. H.-Y. Cheong, K. A. Scheidt, *Angew. Chem. Int. Ed.* **2017**, *56*, 9864 – 9867; *Angew. Chem.* **2017**, *129*, 9996 – 9999.
[8] Reviews: a) M. D. Kärkäs, J. A. Porco, Jr., C. R. J. Stephenson, *Chem. Rev.* **2016**, *116*, 9683 – 9747; b) T. Bach, J. P. Hehn, *Angew. Chem. Int. Ed.* **2011**, *50*, 1000 – 1045; *Angew. Chem.* **2011**, *123*, 1032 – 1077; c) N. Hoffmann, *Chem. Rev.* **2008**, *108*, 1052 – 1103.
[9] a) T. Matsumoto, K. Miyano, S. Kagawa, S. Yu, J.-I. Ogawa, A. Ichihara, *Tetrahedron Lett.* **1971**, *12*, 3521 – 3524; b) Y. Ohfune, H. Shirahama, T. Matsumoto, *Tetrahedron Lett.* **1975**, *16*, 4377 – 4380; c) H. Takeshita, H. Iwabuchi, I. Kouno, M. Iino, D. Nomura, *Chem. Lett.* **1979**, *8*, 649 – 652; d) J. Furukawa, N. Morisaki, H. Kobayashi, S. Iwasaki, S. Nozoe, S. Okuda, *Chem. Pharm. Bull.* **1985**, *33*, 440 – 443.
[10] a) B. D. Schwartz, E. Matoušová, R. White, M. G. Banwell, A. C. Willis, *Org. Lett.* **2013**, *15*, 1934 – 1937; b) E. L. Chang, B. Bolte, P. Lan, A. C. Willis, M. G. Banwell, *J. Org. Chem.* **2016**, *81*, 2078 – 2086.
[11] A. Zech, T. Bach, *J. Org. Chem.* **2018**, *83*, 3069 – 3077.
[12] Selected recent examples of photochemical reaction cascades: a) S. Pusch, D. Schollmeyer, T. Opatz, *Org. Lett.* **2016**, *18*, 3043 – 3045; b) P. J. Koovits, J. P. Knowles, K. I. Booker-Milburn, *Org. Lett.* **2016**, *18*, 5608 – 5611; c) Ł. Woźniak, G. Magagnano, P. Melchiorre, *Angew. Chem. Int. Ed.* **2018**, *57*, 1068 – 1072; *Angew. Chem.* **2018**, *130*, 1080 – 1084; d) J. Buendia, Z. Chang, H. Eijsberg, R. Guillot, A. Frongia, F. Secci, J. Xie, S. Robin, T. Boddaert, D. J. Aitken, *Angew. Chem. Int. Ed.* **2018**, *57*, 6592 – 6596; *Angew. Chem.* **2018**, *130*, 6702 – 6706; e) M. J. James, J. L. Schwarz, F. Strieth-Kalthoff, B. Wibbeling, F. Glorius, *J. Am. Chem. Soc.* **2018**, *140*, 8624 – 8628.
[13] a) H. J. F. Angus, D. Bryce-Smith, *Proc. Chem. Soc.* **1959**, 326 – 327; b) J. G. Atkinson, D. E. Ayer, G. Büchi, E. W. Robb, *J. Am. Chem. Soc.* **1963**, *85*, 2257 – 2263; c) K. E. Wilzbach, L. Kaplan, *J. Am. Chem. Soc.* **1971**, *93*, 2073 – 2074.
[14] Reviews: a) R. Remy, C. G. Bochet, *Chem. Rev.* **2016**, *116*, 9816 – 9849; b) N. Hoffmann, *Photochem. Photobiol. Sci.* **2012**, *11*, 1613 – 1641; c) U. Streit, C. G. Bochet, *Beilstein J. Org. Chem.* **2011**, *7*, 525 – 542; d) N. Hoffmann, *Synthesis* **2004**, 481 – 495; e) J. Cornelisse, R. de Haan in *Molecular and Supramolecular Photochemistry, Vol. 8* (Eds.: V. Ramamurthy, K. Schanze), Dekker, New York, **2001**, pp. 1 – 126; f) P. J. Wagner, *Acc. Chem. Res.* **2001**, *34*, 1 – 8.
[15] a) K. B. Cosstick, M. G. B. Drew, A. Gilbert, *J. Chem. Soc. Chem. Commun.* **1987**, 1867 – 1868; b) P. J. Wagner, K. McMahon, *J. Am. Chem. Soc.* **1994**, *116*, 10827 – 10828; c) P. J. Wagner, J.-I. Lee, *Tetrahedron Lett.* **2002**, *43*, 3569 – 3571.
[16] Examples: a) S. Y. Al-Qaradawi, K. B. Cosstick, A. Gilbert, *J. Chem. Soc. Perkin Trans. 1* **1992**, 1145 – 1148; b) J. M. Nuss, J. P. Chinn, M. M. Murphy, *J. Am. Chem. Soc.* **1995**, *117*, 6801 – 6802; c) W. Saeyens, R. Busson, J. Van der Eycken, P. Herdewijn, D. De Keukeleire, *Chem. Commun.* **1997**, 817 – 818; d) N. Hoffmann, J.-P. Pete, *J. Org. Chem.* **1997**, *62*, 6952 – 6960; e) N. Hoffmann, J.-P. Pete, *Tetrahedron Lett.* **1998**, *39*, 5027 – 5030; f) N. Hoffmann, J.-P. Pete, *Synthesis* **2001**, 1236 – 1242.
[17] P. J. Wagner, R. P. Smart, *Tetrahedron Lett.* **1995**, *36*, 5135 – 5138.
[18] D. Cameron, H. Jeskey, O. Baine, *J. Org. Chem.* **1950**, *15*, 233 – 236.
[19] a) S. F. Pellicori, *Appl. Opt.* **1964**, *3*, 361 – 366; b) S. Poplata, A. Bauer, G. Storch, T. Bach, *Chem. Eur. J.* **2019**, *25*, 8135 – 8148.
[20] For the detailed emission spectra of the lamps ($\lambda = 300$ nm, $\lambda = 350$ nm), see the Supporting Information.
[21] CCDC 1939717 (**7**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.
[22] R. H. Crabtree, M. W. Davis, *J. Org. Chem.* **1986**, *51*, 2655 – 2661.
[23] Review: H. Wang, Y.-H. Deng, Z. Shao, *Synthesis* **2018**, *50*, 2281 – 2306.
[24] a) G. W. Kabalka, R. Hutchins, N. R. Natale, D. T. C. Yang, V. Broach, *Org. Synth.* **1979**, *59*, 42 – 47; b) M. L. Shrestha, W. Qi, M. C. McIntosh, *J. Org. Chem.* **2017**, *82*, 8359 – 8370.
[25] P. G. M. Wuts, *Greene's Protective Groups in Organic Synthesis*, 5th ed., Wiley, Hoboken, **2014**, pp. 385 – 388.
[26] a) J. L. Gras, H. Pellissier, R. Nouguier, *J. Org. Chem.* **1989**, *54*, 5675 – 5677; b) A. Boto, D. Hernández, R. Hernández, E. Suárez, *J. Org. Chem.* **2006**, *71*, 1938 – 1948.
[27] a) K. Fujita, M. Schlosser, *Helv. Chim. Acta* **1982**, *65*, 1258 – 1263; b) R. W. Hoffmann, G. Feussner, H. J. Zeiss, S. Schulz, *J. Organomet. Chem.* **1980**, *187*, 321 – 329.
[28] a) A. S. Narzullaev, M. S. Yunusov, S. Y. Yunusov, *Chem. Nat. Compd.* **1973**, *9*, 424 – 425; b) M. Tori, K. Nakashima, M. Seike, Y. Asakawa, A. D. Wright, G. M. König, O. Sticher, *Tetrahedron Lett.* **1994**, *35*, 3105 – 3106.
[29] a) T. C. McMorris, M. S. R. Nair, M. Anchel, *J. Am. Chem. Soc.* **1967**, *89*, 4562 – 4563; b) S. L. Midland, R. R. Izac, R. M. Wing, A. I. Zaki, D. E. Munnecke, J. J. Sims, *Tetrahedron Lett.* **1982**, *23*, 2515 – 2518; c) A. Arnone, R. Cardillo, G. Nasini, *Phytochemistry* **1986**, *25*, 471 – 474.
[30] Review: R. Brimioulle, D. Lenhart, M. M. Maturi, T. Bach, *Angew. Chem. Int. Ed.* **2015**, *54*, 3872 – 3890; *Angew. Chem.* **2015**, *127*, 3944 – 3963.

Manuscript received: July 11, 2019
Version of record online: September 3, 2019

