1915 Nobel Prize for Chemistry

International Edition: DOI: 10.1002/anie.201505507
German Edition: DOI: 10.1002/ange.201505507

# Richard Willstätter and the 1915 Nobel Prize in Chemistry

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cocaine · Nobel Prize · pigments · Richard Willstätter · total synthesis

In October of 1915, when World War I had spiraled from a "drunken brawl" into a full-blown catastrophe, the Nobel Prize in Chemistry was awarded to Richard Willstätter (Figure 1) "*for his researches on plant pigments, especially chlorophyll*".[1] Around the same time, it was announced that

***Figure 1.*** Richard Willstätter (1872–1942).

the Braggs, father and son, would receive the Prize in Physics "*for their services in the analysis of crystal structure by means of X-rays*" and Romain Rolland the Prize in Literature "*as a tribute […] to the sympathy and love of truth with which he has described different types of human beings*". Medicine and Physiology was not acknowledged that year, perhaps reflecting an inability to agree on a candidate that would not favor one of the war-faring nations. Understandably, 1915, like the year before, did not see a Nobel Prize for Peace either.

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The Nobel Prize must have been a bittersweet coda for what was otherwise a horrible year for Richard Willstätter, a German Jew who had risen to the top echelons of science and civil society. At the end of April, his only son Ludwig, by all accounts a bright and happy child, suddenly fell ill and died of diabetes, possibly diagnosed too late at a time when "*an individual human life carried little weight*".[2] At almost the same time, Germany began to launch chemical warfare on a massive scale by releasing chlorine gas in Flanders—and that at the behest of Fritz Haber, a close friend of Willstätter, with whom he had served as a director at a Kaiser-Wilhelm-Institute in Berlin-Dahlem.[3] In early May, the Lusitania was sunk by a German U-boat, all but ensuring that the US would abandon its formal neutrality and enter the war with its vast resources. Meanwhile, the second Battle of Artois (May 9–June 18, 1915) moved the frontline a mere two kilometers at the expense of 180000 human lives.

Willstätter must have found it difficult to find solace by immersing himself in his work as a chemist. His fertile investigations on the structure and function of chlorophyll, a main justification for his Nobel Prize, and his ongoing studies on the synthesis of cocaine and related alkaloids had come to a sudden halt for lack of co-workers and chemicals. Most of his students and several of his colleagues had been drafted and some had already fallen. Like most prominent chemists in Germany, he became heavily involved in the war effort. At least he could avoid the nastier aspects of chemical warfare, which had ensnared colleagues on both sides of the conflict. Willstätter's team in Berlin worked on the improvement of gas masks and is credited with the development of the "Dreischichtenfilter". Consisting of layers of diatomaceous earth and activated carbon soaked with potassium carbonate, urotropine, and piperazine, this filter proved effective against lethal electrophiles, such as phosgene and mustard gas.[4]

During these dark days, Willstätter must have often reflected on the mostly charmed life that he had led before. Born in 1872 as a son of Jewish merchants in Karlsruhe and growing up in the shadows of the Grand Duke's beautiful palace, Willstätter became an elegant and determined young man who ultimately decided to study chemistry in Munich—then the epicenter of organic chemistry. Following the requisite examinations, he began to pursue graduate studies with Alfred Einhorn, with whom he tried to elucidate the structure of cocaine. With his obvious talent and energy, Richard Willstätter was soon admitted to the inner circle of

  

Adolf von Baeyer, the towering figure of organic chemistry in Munich and the founder of a hugely influential school that also produced Emil Fischer, Heinrich Wieland, and Moses Gomberg, to name but a few. Baeyer remained a lifelong mentor and friend of Richard Willstätter and helped him launch his independent career at the Ludwig-Maximilians-Universität, Munich (LMU). After a few highly productive years, he received a call to the ETH Zurich (1905–1912), followed by a relatively brief stint at the newly established institute in Berlin-Dahlem (1912–1916). In 1916, Willstätter became Baeyer's successor at his Alma Mater, where he remained until his resignation.

Willstätter's work as an assistant professor in Munich was essentially a continuation of his graduate studies on cocaine, the outcome of which he had found unsatisfactory (Figure 2). Cocaine was not only a structural problem that seemed tractable at the time, but it also was a molecule of great medical importance and very much en vogue in the late 19th Century.[6] After Sigmund Freud had unsuccessfully tried to launch his career on cocaine as a remedy for morphinism, his colleague at the University of Vienna, Carl Koller, demonstrated that the alkaloid was an excellent local analgesic for operations on the eye. Unfortunately, Koller (henceforth known as "Coca-Koller") was forced to abandon his promising career as a researcher soon thereafter due to an anti-Semitic incident that resulted in a forbidden duel and his subsequent dismissal.

By using a series of Hofmann degradations, Willstätter was able to trace cocaine to cycloheptatriene carboxylic acid and then to suberone, thus establishing the crucial insight that cocaine contained a seven-membered carbocycle. He arrived at the correct molecular formula shortly thereafter. According to the scientific standards of his days, the ultimate proof of the structure required a synthesis to complement the analysis. Indeed, Willstätter and his students were able to painstakingly rebuild cocaine from suberone, which was readily available from octanedioic acid (suberoic acid, cork acid).[7] As shown in Figure 3, the ketone was first converted into cycloheptene via aminocycloheptane (**1**), then into cycloheptadiene (via **2**) and cycloheptatriene. The latter underwent addition of hydrogen bromide (→**3**), followed by nucleophilic substitution with dimethylamine and reduction (→**4**). A transannular aminobromination yielded ammonium salt **5**, which was demethylated and underwent elimination to afford tropidine. Conversion of tropidine into *pseudo*-tropine via bromide **6**, followed by oxidation, gave tropinone, which Willstätter had earlier identified as a key intermediate in the series.[8] Tropinone was converted into ecgonine by carboxylation (→**7**) and reduction with dissolved metal. Finally, Fischer esterification with methanol (→ **8**) and benzoylation gave racemic cocaine. Overall, the synthesis did not take place in the linear fashion shown in Figure 3 but occurred in several interlocking phases. The last missing link was the transformation of tropidine into *pseudo*-tropine, which was achieved in 1901. Willstätter was well aware that the whole effort amounted to a "total synthesis". He proudly wrote at the end of his 1901 paper: "*Durch die Umwandlung von Tropidin in ψ-Tropin ist die Synthese der Solanaceen-Alkaloïde Atropin, Atropamin, und Belladonnin, sowie des Cocaalkaloïds Tropacocaïn und die Synthese von racemischem*

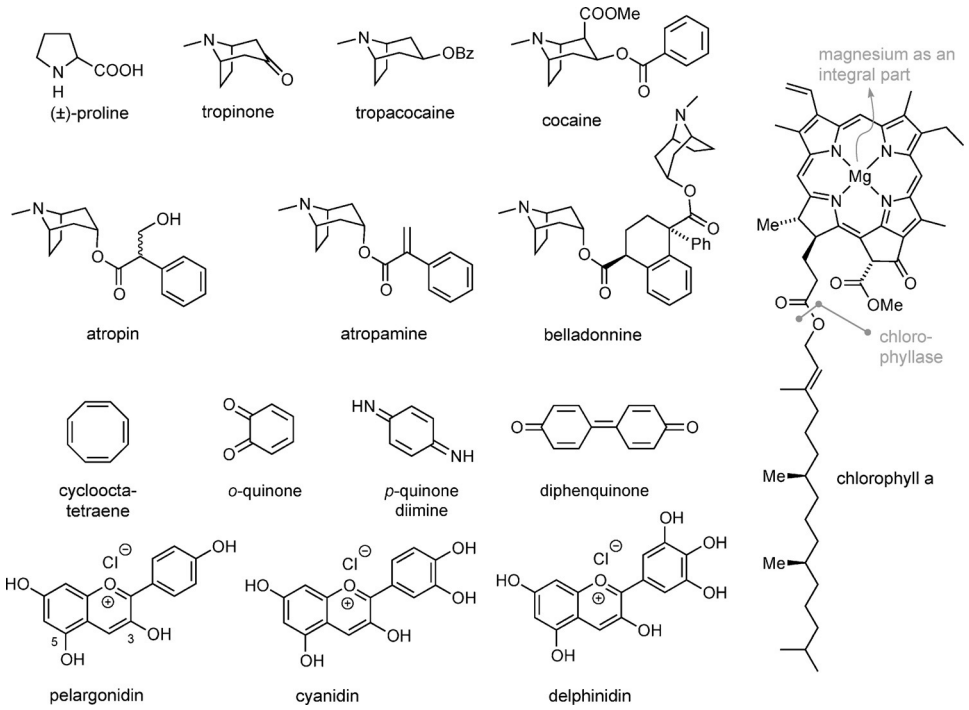


***Figure 2.*** The successes of Richard Willstätter. Besides the first synthesis of proline,[5] he is credited with elucidating and synthesizing several tropane alkaloids, including cocaine, the first synthesis of cyclooctatetraene, *o*-quinone, and *p*-quinone diimine, as well as the elucidation and synthesis of several anthocyanidins. He also contributed substantially to the structural elucidation of chlorophyll, established its magnesium content, and discovered an enzyme, chlorophyllase, which could cleave the molecule into its components.

  

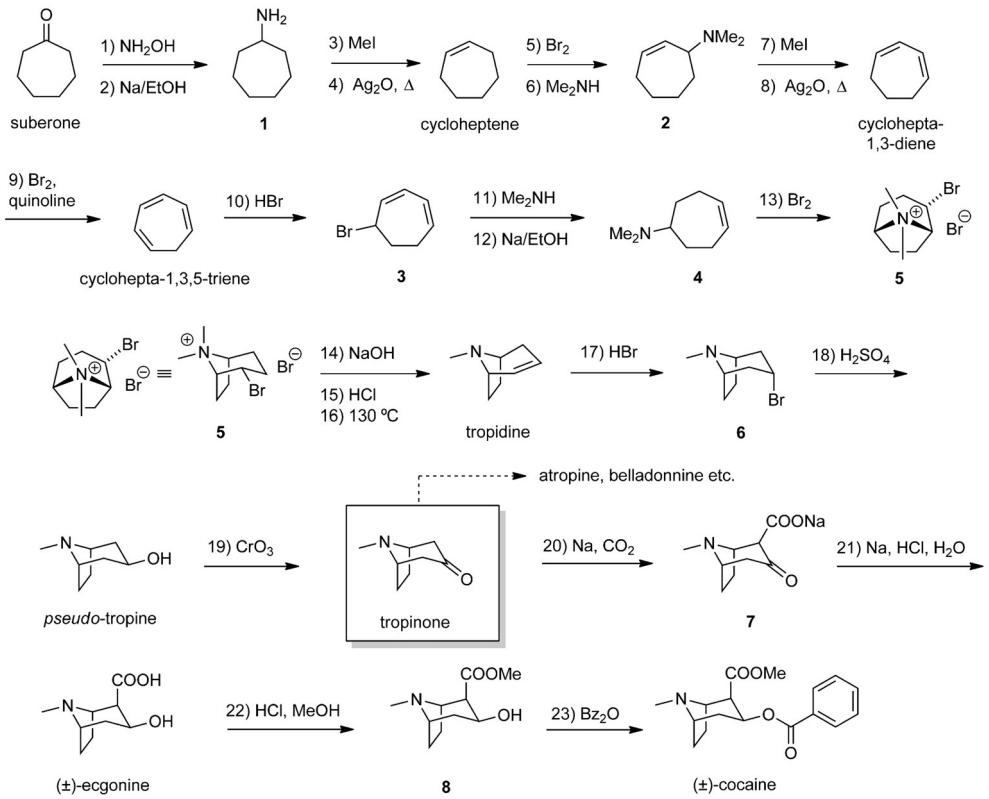


***Figure 3.*** Willstätter's virtually protecting-group-free 1901 synthesis of racemic cocaine.

*Cocaïn vollständig geworden.*" ("*Through conversion of tropidine into ψ-tropine, the syntheses of the Solanaceae alkaloids atropine, atropamine, and belladonnine, as well as of the Coca alkaloid tropacocaine, and the synthesis of racemic cocaine have become total.*")[7]

Unusually for his time, Willstätter was not only interested in natural products and associated drugs but also in molecules that would advance the theory of organic chemistry. In a literal extension of his investigations on highly unsaturated cycloheptenes, he turned to compounds with eight-membered rings. These studies resulted in his seminal synthesis of cyclooctatetraene, whose marked difference to benzene he immediately noted (Figure 4).[9] Using the alkaloid *pseudo*-pelletierine, which could be isolated in large quantities from the root bark of pomegranate trees, as an "awesome starting material" ("*herrliches Ausgangsmaterial*"), he was able to arrive at cycloocta-1,3,5-triene (**11**) through reduction, dehydration (→ **9**), and twofold Hofmann elimination (→**10**→**11**). Bromination of **11**, followed by nucleophilic substitution with dimethylamine, which had served him so well in the tropane series, then gave the diamine **12**, which once again underwent twofold Hofmann elimination to yield cyclooctatetraene. Lingering doubts about the viability of this simple route and the identity of cyclooctatetraene were finally laid to rest in 1947, when Arthur Cope repeated Willstätter's experiment and confirmed his results.[10] In the meantime, Walther Reppe had obtained the same material through the nickel-catalyzed tetramerization of acetylene.[11]

Trying to grasp the essence of benzene and its derivatives, Willstätter next attempted to synthesize the lower homologue in the $(CH{=}CH)_n$ series, namely cyclobutadiene.[12] For reasons all too clear to the modern reader, this endeavor failed.

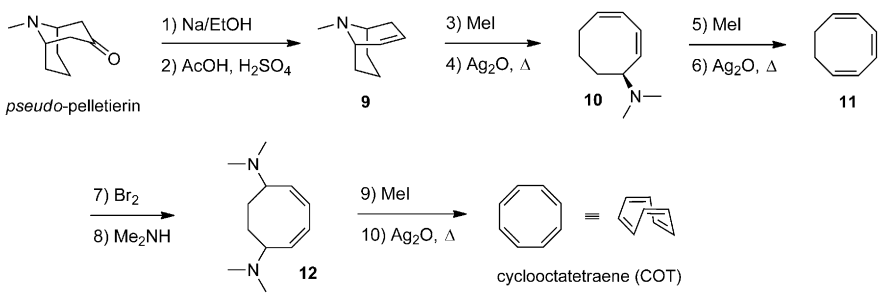


***Figure 4.*** Willstätter's synthesis of cyclooctatetraene from *pseudo*-pelletierine.

  

Less well-known, but equally important are Willstätter's investigations of quinones and quinone imines, in particular his correct formulation of *o*-quinones and their relationship to catechols (Figure 2).[13] His studies on purpurogallin, the oxidative dimerization product of pyrogallol, provided some important insights but yielded an incorrect structural formula.

Willstätter was very fond of his work on tropane alkaloids and hydrocarbons, which occupied him until the end of his career. His most famous and influential work, however, concerned a different topic, which he began to investigate in earnest after his move to Zurich: the plant pigments that surround us in everyday life, in particular chlorophyll and the beautiful colors of flowers and fruits.[14] These had eluded chemists for decades until Willstätter, with his rigorous approach toward purification and analysis, entered the field. He was able to identify the colorants of geraniums, cornflowers, blueberries, roses, pomegranate seeds, grapes, blackcurrant, etc. as glycosides of certain flavylium ions, such as pelargonidine, cyanidine, and delphinidine (Figure 2). Elucidating the structure and chemistry of these anthocyanins, and their glycosides, the anthocyanidins, must have provided no small measure of satisfaction for Willstätter, who was an avid gardener throughout his life and was partial to red wine.

As before, he complemented his structural studies with syntheses, in this case of the aglycons, since selective glycosylation methods were not available. These systematic studies culminated in 1924 with syntheses of anthocyanidins that are elegant and efficient even by today's standards (Figure 5a).[15] The synthesis of cyanidine started with phloroglucinol carbaldehyde (**13**), which underwent acylation and Perkin reaction to yield the methoxycoumarin **14**. Ester cleavage and methylation then gave compound **15**, which underwent addition of aryl Grignard reagent **16**. Subsequent acidification and ionization afforded flavylium chloride **17**. Global demethylation and conversion into the chloride salt then gave the anthocyanidin cyanidin. Other members of the series, such as pelargonidin, were available through variation of the aryl Grignard reagent. In addition, Willstätter and his students clarified the puzzling observation that virtually the same compound could account for different colors depending on the pH value of its source (Figure 5b). At low pH values, the flavylium cation predominates, which turns into the so-called anhydrobase as the pH value nears neutrality. Further deprotonation produces an anionic species that is also brightly colored, albeit with a bathochromically shifted absorption spectrum. At even higher pH values, the addition of a hydroxide ion to the *p*-quinone methide moiety produced a colorless chromenol anion that ultimately opens to the corresponding chalcone (not shown). Although these pH ranges do not necessarily reflect the physiological reality of plants, where metal complexes can form with the anthocyanidins, these studies indicated how a single pigment, such as cyanidin, could account for the very different colors of cornflowers, blackberries, blueberries, raspberries, cherries, red cabbage, and roses.

Already in Munich, Willstätter and his students also began to work on chlorophyll, whose importance for plant life had been recognized but whose nature had also eluded chemists.[14] This was mostly due to the fact that "chlorophyll" consisted of closely related lipophilic molecules of fairly large molecular weight that were not tractable with the purification methods of the day, namely crystallization and distillation. Although Tswett had introduced the principle of chromatography in 1906, it was not widely adopted until well into the

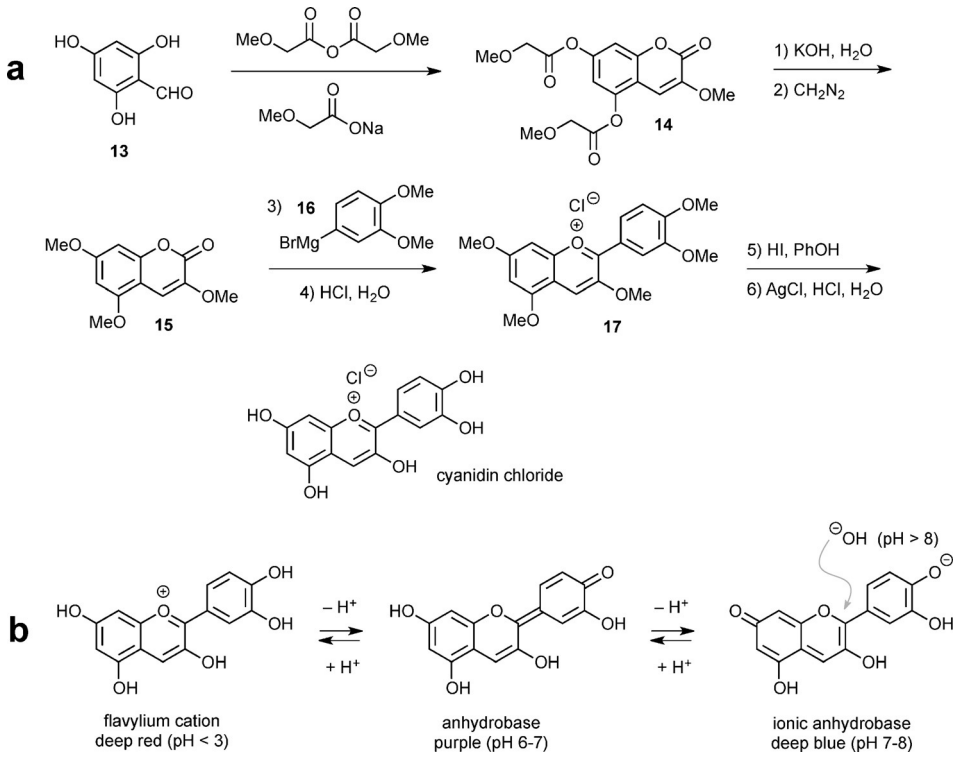


***Figure 5.*** Willstätter's work on the anthocyanins. a) The 1924 synthesis of cyanidin. b) pH-dependence of its color.

  

20th century, when Willstätter's student Richard Kuhn picked up and refined the method.[16] Willstätter's crucial insight was that chlorophyll could be cleaved into a lipid side chain (phytol) and chlorin-type tetrapyrroles that were amenable to crystallization and purification. This enabled the determination of the molecular formula and proved that magnesium was an integral part of the molecule and not a contamination. His meticulous studies ultimately enabled the full structure elucidation by Hans Fischer in 1940, which Willstätter himself and his students could not complete.[17] In addition, Willstätter's investigations established that chlorophylls, with small variations, occurred across all photosynthetic plants and algae, thus making it likely that they were central to photosynthesis. The mechanistic role of the chlorophylls was ultimately clarified through crystallization and structure elucidation of the photosynthetic center by Deisenhofer, Michel, and Huber in the early 1980s.[18] As such, three Nobel Prizes in Chemistry are associated with both chlorophyll and Munich.

In the course of his investigations on chlorophyll and photosynthesis, Willstätter isolated the enzyme chlorophyllase, which could cleave the pigments into a tetrapyrrole carboxylic acid and phytol under very mild conditions. This sparked his interest in enzymes and enzymatic catalysis, which occupied the later phase of his career. Unfortunately, his studies on this subject were not as fruitful as the previous ones on alkaloids and pigments, which provided a considerable amount of frustration to a man accustomed to a high level of success.

In 1924, at the age of 52 and in good health, Richard Willstätter announced his resignation from the most prestigious chair in chemistry in Germany. Much has been speculated about his motivations, and the rising anti-Semitism in Munich in the early 1920s is usually cited as the major cause.[1,19] It is true that parts of the faculty at the Ludwig-Maximilians-Universität were deeply anti-Semitic, but they were far from the majority and certainly not the dominant voice in the Department of Chemistry, where colleagues such as Heinrich Wieland or Kazimierz Fajans set the tone. At the student level, Willstätter had regularly to deal with anti-Semitic manifestations, such as the degrading posters cited in his autobiography.[19] It cannot have eluded him that one of his brightest students, Richard Kuhn, whom he graduated summa cum laude in 1922, sympathized with the nationalist movement. It should be noted, however, that Willstätter's resignation came at a time when the Nazi party numbered around 20000 and was seen as more of a fringe movement. That it would come to power through democratic elections nine years later and establish a dictatorship immediately thereafter was foreseen by few.

It can be argued that the rising anti-Semitism, within the university and beyond, was only one of the factors that drove Richard Willstätter into early retirement.[20] Like Emil Fischer, who had committed suicide in 1919, he was deeply distressed by World War I and the private losses he suffered during that time. He was clearly loyal to the monarchy and he was offended by the idea that the war was caused solely by German militarism and aggressiveness. Accordingly, he signed the "Manifesto of the 93", a misfired attempt by German intellectuals to deny responsibility that was typical of the propaganda in the early phase of the war. Other signees included Emil Fischer, Fritz Haber, Ernst Haeckel, Wilhelm Ostwald, Max Planck, Max Reinhart, Wilhelm Röntgen, and Wilhelm Wundt.[21]

In addition to this, Willstätter found it difficult to regain traction as a scientist after the war. He must have felt, at times, that his best days as a researcher were over. In 1917, a certain Robert Robinson published a one-step synthesis of tropinone, Willstätter's signature molecule. This study made Willstätter's efforts look a bit outdated.[22,23] It did not help that Willstätter himself seems to have developed ideas along similar lines. He was always gracious toward Robinson but, as a highly competitive man, he could not help noting in his autobiography that because of the war and the incompetence of one of his co-workers "… *the long planned condensation of succinic dialdehyde with acetone dicarboxylic acid never took place. […] At the very same time (my German Patent was filed in January of 1917 and the work was disclosed publically in front of the Bavarian Academy in July of 1917), we carried out the synthesis of tropinone carboxylic ester from our Dahlem succinyl diacetic ester [that is, diethyl 3,6-dioxooctanedioate, see Figure 6]*."[24] Willstätter returned to succinic dialdehyde a few years later when he combined it with methylamine and the monomethyl ester of acetone dicarboxylic acid to make racemic cocaine and its diastereomers, which he then resolved and tested for biological activity. This four-step synthesis, repeated and optimized by Casale in 1987,[25] could have found practical applications if cocaine were not so cheaply available from Coca shrubs.

Even more frustrating must have been Willstätter's attempts to clarify the structure of proteins and enzymes and understand the nature of enzymatic catalysis. His approach toward structure elucidation—to purify and crystallize—was unfortunately not successful with the proteins he chose. It had served him well with the alkaloids, the anthocyanins and anthocyanidins, and even the chlorophylls, but it was a failure once he turned toward enzymes that were familiar to him, such as chlorphyllase. He did make significant advances in protein purification using adsorption on silica gel and metal salts, but his samples stubbornly refused to undergo crystallization. That he had simply picked the wrong target became clear when Sumner published his work on crystalline Jack bean urease in 1926, a breakthrough result that earned Sumner the Nobel Prize in 1946 (Figure 6d).[26]

Willstätter can hardly be blamed for structures that turned out to be wrong or were unlikely on theoretical grounds (Figure 6a). His formula for purpurogallin[27] and his futile attempts to synthesize cyclobutadiene[12] simply reflect the poor understanding of aromaticity in his days. Erich Hückel's ideas were not formulated until the early 1930s and resonated little with synthetic chemists until the 1950s.[28]

Willstätter seems to have struggled with more contemporary ideas regarding chemical structure and bonding. His clinging to the formula of flavylium salts with a "tetravalent oxygen" (Figure 6b), which he still used in his 1942 autobiography, indicates that the octet rule and G. N. Lewis' ideas never took firm hold in his mind. It may also reflect the fact that he saw "tetravalent oxygen" as his first original discovery

  

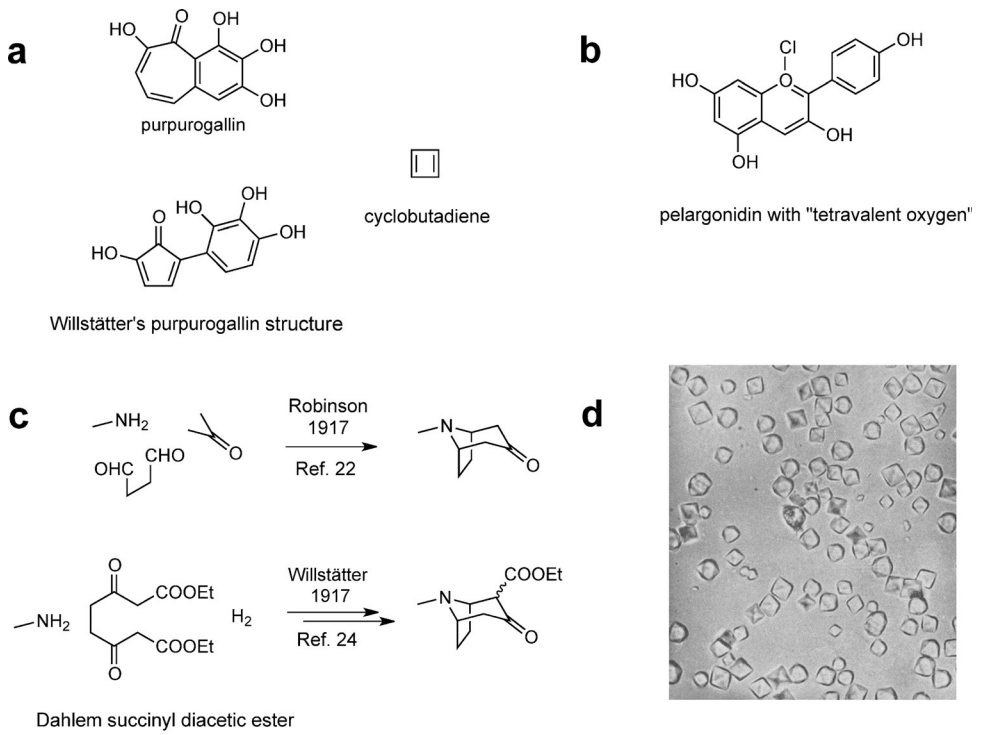


***Figure 6.*** Willstätter shortcomings and "failures". a) His formula of purpurogallin and his attempt to synthesize cyclobutadiene reflect the poor understanding of aromaticity in the early 1900s. b) His formula of pelargonidine with "tetravalent oxygen". c) Robinson's celebrated one-step synthesis of tropinone, which Willstätter claims to have "thought of" as well, and his 1917 patent on cocaine. d) Sumner's crystallization of Jack bean urease paved the way for modern protein biochemistry and enzymology. The photograph is taken from Sumner's original paper.[26]

and that he felt a bit cheated by his mentor Adolf von Baeyer, who took the credit for this concept. On the other hand, Willstätter himself was not shy of claiming his co-workers' results and moving aggressively into fields established by other researchers. This was particularly true for local anesthetics, which Willstätter's teacher Alfred Einhorn had pioneered on the basis of certain (erroneous) ideas about the structure of cocaine. At a time when scientists considered fields ("Arbeitsgebiete") as their fiefdoms and expressly reserved the right to methodically reap the fruits of their discoveries,[29] this did not earn him universal admiration.

Another aspect that may have contributed to Richard Willstätter's decision to step down so early was the fact that he could afford it economically. He was a popular and highly paid consultant for the German and Swiss chemical industry (e.g. for Bayer, Böhringer, Merck, and Sandoz) and, as a holder of several lucrative patents, a man of considerable wealth. He received several prestigious calls, such as an offer to return to Berlin (as Emil Fischer's successor), head the Siemens research laboratories, move to the newly established Rockefeller Institute in Madrid (at the invitation of Ramón y Cajal) or the University of Chicago, all of which he declined. He preferred life as a gentleman of leisure in Munich, running a small research program with his co-worker Margarete Rohdewald by telephone. After his resignation, he built a villa in a modern style in the most fashionable neighborhood (Thomas Mann lived nearby), which housed his vast library and art collection. This, of course, made him a prime target for the Nazis, who harassed and humiliated him after they came to power in 1933 and tried to arrest him following the Kristallnacht in 1938. As a consequence of lucky circumstances—he was in his beloved garden when the Gestapo showed up—he avoided detection and imprisonment in Dachau. After an unsuccessful attempt to flee to Switzerland via Lake Bodensee, he was finally able to leave the Reich with the help of his loyal students, although not without leaving behind most of his possessions.[30] Settling in Muralto on the shores of Lago Maggiore, he found the time and energy to complete his autobiography. This book, simply entitled "Aus meinem Leben" ("From My Life"), is one of the most beautifully written scientific autobiographies and should appeal to everyone interested in the history of science and the 20th Century.[31] It discusses Willstätter's discoveries, his family life, his friendship with Adolf von Baeyer and Fritz Haber, and the circumstances of his emigration in much greater detail than can be provided here. Although it has the usual shortcomings of an autobiography, it remains the best and most easily accessible source on his life and his times.

Richard Willstätter died in August of 1942, aged 70, at a time when victory over the Nazis was by no means assured (the battle of Stalingrad took place in the winter thereafter). Several of his discoveries, such as the anthocyanidins, cyclooctatetraene, the *ortho*-quinones, and the structure of cocaine, now belong to the canon of organic chemistry and will forever be associated with his name. Although he was at times too ambitious, he will always remain a model of a scientist who successfully operated in vastly different fields. His students and postdoctoral colleagues were equally diverse: they include Rudolf Pummerer (born as an Austrian and naturalized as a German), Riko Majima (Japanese), Kazimierz

  

Fajans (Polish), Arthur Stoll (Swiss), Lázló Zechmeister (Hungarian), Richard Kuhn (Austrian), and Roger Adams (American). With his rigorous scientific style and his uncanny ability to pick important scientific problems, he remains a huge inspiration for his successors. His legacy looms large in Zurich and Munich, which has largely recovered from the disasters that befell Richard Willstätter and his contemporaries and has regained much of its former beauty (Figure 7). Every spring, when the English Garden in the center of the city turns green, and every fall when newly synthesized anthocyanins account for red and orange colors, one should pause for a moment to think of this great man.

***Figure 7.*** The colors of Richard Willstätter. Top: The English Garden in the center of Munich in May with chlorophyll (and carotene) in full display. Bottom: The same in October, with anthocyanins dominating the scene.

## Acknowledgements

I thank Prof. Wolfgang Steglich, Prof. Heinz Langhals, Dr. David Barber, Dr. Oliver Thorn-Seshold, and Dr. Henry Toombs-Ruane for critical reading and valuable suggestions.

**How to cite:** *Angew. Chem. Int. Ed.* **2015**, *54*, 11910–11916
*Angew. Chem.* **2015**, *127*, 12078–12085

[1] The Nobel Prize in Chemistry 1915". http://Nobelprize.org. Nobel Media AB 2014. http://www.nobelprize.org/nobel_prizes/chemistry/laureates/1915/.
[2] R. Willstätter, *Aus meinem Leben*, *2nd ed.*, Verlag Chemie, Weinheim, **1973**, p. 232.
[3] D. Stolzenberg, *Fritz Haber*: *Chemiker*, *Nobelpreisträger*, *Deutscher*, *Jude*, Wiley-VCH, Weinheim, **1994**.
[4] D. Martinez, *Der Gaskrieg 1914–1918*: *Entwicklung*, *Herstellung und Einsatz chemischer Kampfstoffe*, Bernard & Graefe, Bonn, **1996**.
[5] R. Willstätter, *Ber. Dtsch. Chem. Ges.* **1900**, *33*, 1160.
[6] H. Markel, *The Anatomy of Addiction*, *Sigmund Freud*, *William Halsted and the Miracle Drug Cocaine*, Pantheon Books, New York, **2011**.
[7] R. Willstätter, *Chem. Ber.* **1901**, *34*, 3163.
[8] R. Willstätter, *Chem. Ber.* **1896**, *29*, 392.
[9] R. Willstätter, E. Waser, *Chem. Ber.* **1911**, *44*, 3423.
[10] A. C. Cope, G. Overberger, *J. Am. Chem. Soc.* **1947**, *69*, 976.
[11] W. Reppe, O. Schlichting, K. Klager, T. Toepel, *Justus Liebigs Ann. Chem.* **1948**, *560*, 1.
[12] R. Willstätter, W. von Schmadel, *Chem. Ber.* **1905**, *38*, 1992.
[13] R. Willstätter, R. Pfannenstiel, *Chem. Ber.* **1904**, *37*, 4744.
[14] Richard Willstätter—Nobel Lecture: On Plant Pigments". http://Nobelprize.org. Nobel Media AB 2014. http://www.nobelprize.org/nobel_prizes/chemistry/laureates/1915/willstatter-lecture.html.
[15] R. Willstätter, L. Zechmeister, W. Kindler, *Chem. Ber.* **1924**, *57*, 1938.
[16] R. Kuhn, E. Lederer, W. Kindler, *Chem. Ber.* **1933**, *66*, 488.
[17] Hans Fischer—Nobel Lecture: On Haemin and the Relationships between Haemin and Chlorophyll". http://Nobelprize.org. Nobel Media AB 2014. http://www.nobelprize.org/nobel_prizes/chemistry/laureates/1930/fischer-lecture.html.
[18] a) Johann Deisenhofer—Nobel Lecture: "The Photosynthetic Reaction Centre from the Purple Bacterium Rhodopseudomonas Viridis". Nobelprize.org. Nobel Media AB 2014. http://www.nobelprize.org/nobel_prizes/chemistry/laureates/1988/deisenhofer-lecture.html; b) Robert Huber—Nobel Lecture: "A Structural Basis of Light Energy and Electron Transfer in Biology". Nobelprize.org. Nobel Media AB 2014. http://www.nobelprize.org/nobel_prizes/chemistry/laureates/1988/huber-lecture.html; c) Hartmut Michel—Nobel Lecture: "The Photosynthetic Reaction Centre from the Purple Bacterium Rhodopseudomonas Viridis". Nobelprize.org. Nobel Media AB 2014. http://www.nobelprize.org/nobel_prizes/chemistry/laureates/1988/michel-lecture.html.
[19] R. Willstätter, *Aus meinem Leben*, *2nd ed.*, Verlag Chemie, Weinheim, **1973**, p. 338 ff.
[20] F. Litten, *Studien zur Geschichte der Mathematik und der Naturwissenschaften*, Heft 32; München (Institut für Geschichte der Naturwissenschaften) **1999**, VII, 88.
[21] J. von Ungern-Sternberg, W. von Ungern-Sternberg. *Menschen und Strukturen. Historisch-sozialwissenschaftliche Studien*, Bd. 21, 2., erw. Aufl., Peter Lang, **2013**.
[22] R. Robinson, *J. Chem. Soc.* **1917**, *111*, 762.
[23] A. J. Humphrey, D. O'Hagan, *Nat. Prod. Rep.* **2001**, *18*, 494.
[24] R. Willstätter, *Aus meinem Leben*, *2nd ed.*, Verlag Chemie, Weinheim, **1973**, p. 448 f.
[25] J. F. Casale, *Forensic Sci. Int.* **1987**, *33*, 275.
[26] J. B. Sumner, *J. Biol. Chem.* **1926**, *69*, 435.
[27] R. Willstätter, H. Hess, *Justus Liebigs Ann. Chem.* **1923**, *430*, 269.
[28] E. Hückel, *Z. Phys.* **1931**, *76*, 204.
[29] O. Diels, K. Alder, *Justus Liebigs Ann. Chem.* **1928**, *460*, 98.
[30] *Heinrich Wieland*: *Naturforscher*, *Nobelpreisträger und Willstätters Uhr* (Eds.: S. Wieland, A.-B. Hertkorn, F. Dunkel), Wiley-VCH, Weinheim, **2008**.
[31] R. Willstätter, *Aus meinem Leben*, *2nd ed.*, Verlag Chemie, Weinheim, **1973**. English version: R. Willstätter, *From My Life*, W. A. Benjamin, New York, **1965**.

Received: June 15, 2015
Published online: August 20, 2015

  