Terpenes

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Otto Wallach: Founder of Terpene Chemistry and Nobel Laureate 1910**

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Otto Wallach—Nobel Laureate and Pioneer

Along with polyketides and alkaloids, terpenes are among the most important secondary metabolites, with respect to both their structure and biological activity. Following a simple biogenetic structural principle, the oligomerization of the C_5 building blocks isopentenyl pyrophosphate (IPP) and dimethylallyl pyrophosphate (DMAPP) generates open-chain precursors with terminal pyrophosphate groups from which simple monoterpenes such as menthol and more complex polycyclic natural products such as taxol and cholesterol can be formed in intramolecular reactions. The history of modern terpene chemistry began with structural elucidation of simple monoterpenes, and for a hundred years this area has been directly associated with the name of Otto Wallach[1,2] (Figure 1)—not only because his work begun in 1884 was acknowledged with the Nobel Prize in Chemistry in 1910.

A significant indication of the importance of a class of chemical transformations or the discovery of a certain law is the association of the reaction or law with the name of one or more scientists, not infrequently posthumously. Amongst the named reactions are the Leuckart–Wallach reaction,[3] the reductive amination of carbonyl compounds with ammonium formate, and the Wallach rearrangement,[4] the rearrangement of azoxybenzenes into *p*-hydroxyazobenzenes catalyzed by strong acids (Scheme 1). The less well-known Wallach degradation[5] is a preparatively useful variant of the Favorskii rearrangement. Ring contraction of dihalogenated cyclohexanones (rather than the α-halogenocycloalkanones in the Favorskii rearrangement) yields α-hydroxycycloalkanoic acids which can be degraded oxidatively to ring-contracted cycloalkanones. The name Wallach is also associated with the empirical Wallach rule,[6] according to which racemic crystals are more densely packed than their homochiral counterparts. The generality of this assertion is still a subject of scientific discussion[7] today and confirms Wallach's credo, that—unlike theories—"exact and reliable experimental determinations always retain their value".

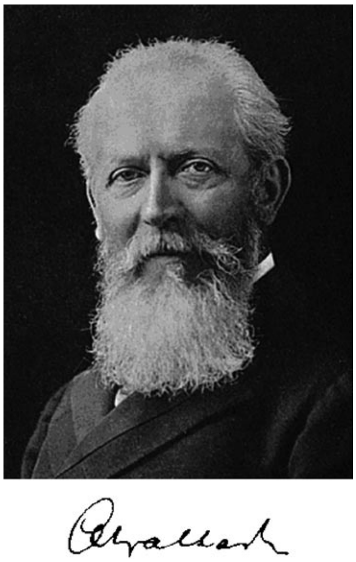
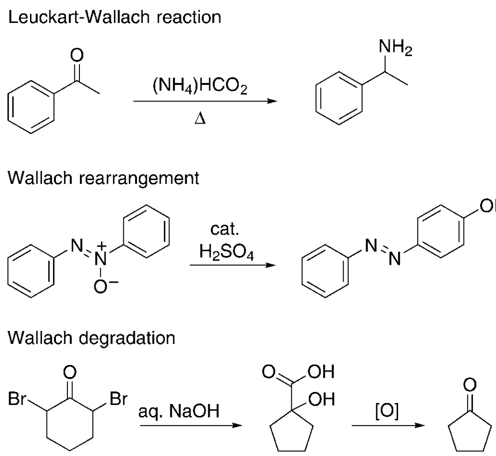


Figure 1. Otto Wallach (signature from Ref. [2a]).



Scheme 1. Named reactions associated with Wallach.

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Schooling and Study

Otto Wallach was born on March 27, 1847 as the youngest of five children in the family of the government official Gustav Wallach and his wife Ottilie (née Thoma) in Königsberg in East Prussia. For professional reasons the family relocated to Potsdam in 1853 where Wallach's father took up the position of Director of the Oberrechnungskammer (public audit office). After attending a private school Wallach entered the Humanistisches Gymnasium in 1856. Through his friendship with Georg Borsche, three years his senior, Wallach was infected by a fascination for chemistry:[1]

"*Georg Borsche however occupied himself with chemistry as an autodidact, devoted all his free time to it, and became skillful at experimentation following the instructions in the only book available at that time for such purposes, 'Stoeckhardts Schule der Chemie'.*[8] *Chemistry exercised an irresistible attraction on me. Soon my room's contents were damaged by many a drop of corrosive acid. Once, during the preparation of oxygen from potassium chlorate, the contents of the cracked retort poured over the spirit lamp of the expensive silver tea service borrowed from my parents and used for heating. But it was highly satisfying when I could produce the green medicine bottle filled with oxygen for experiments and could ignite iron wire in it. My peers in school were rather unimpressed by this hobby, if not dismissive.*"[*]

The love of experimentation and chemical analysis, which may be traced back to his time at school, was a recurring theme throughout Wallach's life and is probably also the key to his approach to the area of terpene chemistry. In addition to the natural sciences Wallach's interests included philosophy, German literature, and contemporary art. After he had concluded his Abitur examinations, Wallach selected the university at which he would study primarily by his desire to quickly gain financial independence. He had heard from his friend Borsche that a doctorate could be gained rapidly in Göttingen. At the end of April 1867 Wallach moved to Göttingen to study chemistry there under Friedrich Wöhler. After just one semester during which Wallach was educated mainly by Wöhler's assistants Hans Hübner and Rudolph Fittig, he enrolled for the winter semester in Berlin to attend lectures from August Wilhelm Hofmann. His hope to be accepted in the Berlin laboratories was not fulfilled because of the lack of laboratory places, and Wallach used the time to hone his practical skills in a forensic laboratory.

In the summer semester of 1868 Wallach returned to Wöhler's laboratories in Göttingen, and there under the guidance of Hübner, he began his work towards a doctorate in December of the same year. Hübner, who had been elected by August Kekulé, was a devotee of his benzene theory published in 1865. Wallach's doctorate work was focused on the isomers produced in the bromination of toluene. During his work Wallach was able to isolate a previously unknown isomer by crystallization, and in an associated scientific dispute with Fittig who doubted its existence he successfully defended his claims. It can only speculated that this experience had a marked influence on Wallach's approach to converting unknown compounds into clearly defined crystalline derivatives and characterizing them. After just five semesters and with the doctorate certificate in hand, Wallach left Göttingen at the beginning of August 1869 "*with the quiet and genuine desire: never to be seen there again. It was to be otherwise.*"[1] He remained in close contact with Hans Hübner until his death in 1884.

In Berlin Wallach worked for a short time as an assistant in Hermann Wichelhaus's private laboratory until Hübner engineered an introduction to August Kekulé. On the May 1, 1870 Wallach took up a private assistant position, today one would say a post-doctorate, with Kekulé in Bonn.

The Time in Bonn

The development of the benzene theory had made Kekulé one of the most highly regarded theoreticians. At this time Theodor Zincke, with whom Wallach very soon became friends, also gained his Habilitation in Kekulé's circle. In December 1871 Wallach received a job offer as an industrial chemist at the Aktiengesellschaft für Anilinfabrikation (later: AGFA), which was located in Rumelsburg close to Berlin. Contact with aggressive chlorine compounds in particular affected him so severely that he had to quit his position after just a short time. After a renewed period in Wichelhaus's laboratories Wallach returned to Bonn in April 1872. After Zinke's internal promotion to associate professor, Kekulé was seeking a new Habilitation candidate and head of organic practical training, and Wallach accepted quickly. In addition to further cultivated scientific discourse with Zincke it was at this time that Wallach began a friendship with Jacobus van't Hoff, who in 1874 published at the same time as Joseph Le Bel a theory on the tetrahedral model of carbon. It can be claimed without exaggerating that during the time of his Habilitation, in January 1873, Wallach resided at the center of modern organic structural chemistry. Wallach dedicated all his energy to his own research and also to the careful and painstaking preparation of experimental lectures. However he commented critically on Zincke's cooperation on Kekulé's textbook.[1]

"*but such receptive work does not suit me, and I have always resisted attempts to accept it for the sake of earning money. The same applies to the frequently rejected suggestions from publishers to write a textbook. Young lecturers should*

[*] "George Borsche aber beschäftigte sich mit der Chemie als Autodidakt, widmete ihr alle freie Zeit und verschaffte sich im Experimentieren nach Anleitung des damals für solche Zwecke fast allein vorhandenen Buchs 'Stoeckhardts Schule der Chemie'[8] Fertigkeit. Die Chemie übte auch auf mich eine unwiderstehliche Anziehungskraft aus. Bald wurde mein Stubeninventar durch manchen Tropfen ätzender Säure geschädigt oder es ergoss sich bei der Herstellung von Sauerstoff aus Kaliumchlorat der Inhalt der zersprengten Retorte auf die zum Heizen verwandte silberne Spirituslampe des kostbaren elterlichen Teeservices. Aber es war doch eine große Genugtuung, wenn es gelang, die mit Sauerstoff gefüllte grüne Medizinflasche zu Versuchen vorzeigen zu können und darin einen Eisendraht zum Abbrennen zu bringen. Meine gleichaltrigen Schulgenossen standen diesen Liebhabereien meist sehr kühl, wenn nicht ablehnend gegenüber."

not encumber themselves by taking on lengthy literary tasks."[*]

After Zincke's calling to Marburg University, Wallach was entrusted with the supervision of the inorganic laboratory, and in January 1876 he was promoted to associate professor. Wallach's position as head of the organic laboratory was taken over by Ludwig Claisen, who later also gained his Habilitation in Kekulé's circle. In 1877 Wallach was offered a professorship at the academy in Münster.[9] The negotiations were, however, not led by the appointee but by Kekulé, who did not want Wallach to move. Owing to the better working conditions in Bonn and a sense of obligation to Kekulé following an illness, Wallach remained for the time being in Bonn.[1]

"*My career in Münster would in all events have taken on a different shape than has now come to pass. Whether it would have been more advantageous remains nevertheless most doubtful.*"[**]

When Wallach was offered a chair at the Technische Hochschule in Darmstadt at the end of 1880, he used the opportunity to improve his position in Bonn. In addition to his appointment as "Director of the Pharmaceutical Apparatus" he also managed the chemistry section for all of the natural sciences, which in his view increased his influence on the students of natural sciences. Wallach was subsequently considered for two further chairs. In Zurich in 1884 Arthur Hantzsch was appointed, and in Würzburg in 1885 Emil Fischer received preference at the last moment although the dean had tentatively promised the position to Wallach.[1]

June 1884 can be designated as the beginning of Wallach's important terpene work; at that time Wallach was 37 years old. According to one anecdote Wallach's interest was prompted by a collection of ethereal oils in Kekulé's work room, which had been given to him several years earlier by the company E. Sachsse & Co. (Leipzig) (Figure 2).

Figure 2. Company nameplate: E. Sachsse & Co.[16]

Wallach asked his mentor's permission to investigate the contents in depth, to which he is supposed to have replied smiling ironically: "Yes, if there is anything to be found there." Wallach was soon captivated by this little-researched area, which accompanied him to the end of his scientific work and which was to earn him the highest scientific accolade, the Nobel Prize.

It was already known at the start of Wallach's investigations that monoterpenes had the molecular formula $C_{10}H_{16}$ (corresponding to $C_{10}H_{16}O$ for terpene alcohols and $C_{10}H_{14}O$ for keto compounds). That same year (1884) Emil Fischer began his work on the structural elucidation of glucose,[11] of which likewise only the molecular formula $C_6H_{12}O_6$ was known. Both researchers believed in the tetrahedral model of carbon proposed by van't Hoff and Le Bel and the implicit occurrence of stereoisomeric forms. In particular too the optical inactivity of compounds with a plane of symmetry played an important role in the line of argument of both Fischer and Wallach. A second parallel should also be mentioned: the difficulties in handling these classes of compounds. Whereas Fischer had to struggle with viscous oils, syrups, and caramel-like masses, Wallach's investigations suffered from the chemical instability of numerous terpenes, especially their sensitivity towards oxidation by atmospheric oxygen and their tendency towards isomerization (not to mention rearrangements via nonclassical cations!). For a better understanding of Wallach's systematic approach it is necessary to recall two important pieces of work that predated his terpene studies. As early as 1816 Biot was able to show that turpentine, camphor, and related compounds rotate the plane of polarization of polarized light; the implications were apparent in the work of Pasteur on tartaric acid in combination with the assumption of stereogenic carbon atoms. Furthermore, in 1803 Kindt prepared crystalline pinene hydrochloride $C_{10}H_{17}Cl$ and thus demonstrating a principle way of converting liquid terpenes into solids.

Wallach's first publications from the time in Bonn dealt with the reaction of distilled plant oils with hydrogen halides, halogens, and nitrosyl chloride, and the careful characterization of the addition products thus obtained. In addition to the obligatory melting point, the physical properties included an extensive discussion of the crystalline forms. Wallach reaped the first fruits of his efforts in 1888 with the discovery that a dipentene previously considered an independent terpene was actually a racemic mixture of the enantiomers (+)- and (−)-limonene (Figure 3), which were also characterized by Wallach.[11]

Ordinarius in Göttingen

On the recommendation of Victor Meyer, Wallach finally received a calling to be his successor for the prestigious Wöhler chair in Göttingen in 1889. The move uprooted the 42-year-old from his beloved Bonn environment, and moreover the grandeur of his office did not make it easy to make new friends quickly. Wallach remained a bachelor all his life and his skeptical attitude towards marriage is perhaps best gleaned from his commentary on Kekulé's second marriage:[1]

[*] "Aber solche rezeptiven Arbeiten haben mir nie gelegen und ich habe mich immer der Versuchung erwehrt, sie des Geldverdienens halber anzunehmen. Dasselbe gilt von den häufig zurückgewiesenen Vorschlägen der Verlagsbuchhändler, ein Lehrbuch zu schreiben. Junge Dozenten sollten sich keine Bleigewichte an die Füße binden, indem sie langatmige literarische Aufgaben übernehmen."

[**] "Meine Laufbahn hätte sich bei einer Übersiedlung nach Münster jedenfalls ganz anders gestaltet, als es geschehen ist. Ob günstiger, bleibt immerhin recht zweifelhaft."

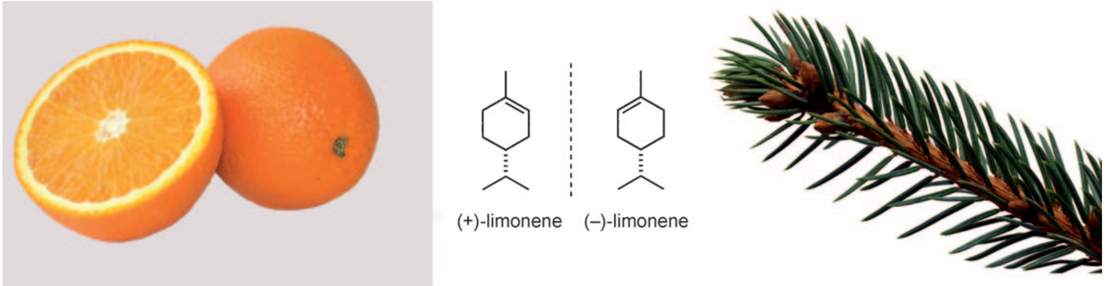

Figure 3. (+)-Limonene can be obtained from orange oil, whereas the enantiomer (−)-limonene occurs in spruce needle oils. Before the elucidation of the stereochemical relationship the racemate was known as dipentene.

"*Now, on the October 7, 1876, came the unfortunate second marriage with his former housekeeper, Fräulein Högel, who instead of lifting the man wore him down. She kept him from his duties of office, and as children were born she exploited him as a childminder, more and more frequently the less the servants endured her. […] A sad example of how a foolish woman can prematurely crush a highly talented man*."[*]

Wallach's terpene program accelerated after his move to Göttingen—doubtlessly through the increase in resources. In 1891 he described his ambitious research goals in detail in a lecture to the Deutsche Chemische Gesellschaft:[12]

1. Clear and definitive features of the properties of all distinct terpenes must be determined such that the chemical individuals can be recognized and differentiated.
2. On the basis of an exact characteristic the behavior and the mutual relationships of the individual hydrocarbons must be determined, especially including their propensity to transform into one another.
3. Finally, based on these investigations, research into the constitution and synthesis of the terpenes should be initiated.

The most remarkable feature of Wallach's research program is that it is aimed to establish connections between all monoterpenes as the initial stage and the actual goal, structural elucidation (research of the constitution) and total synthesis of terpenes, is at the end of the line. A plausible alternative would have been to concentrate on one or two representative monoterpenes like many of his contemporaries did. This ingenious gambit allowed Wallach to construct what was for that time a unique collection of substances and data solely by derivatization (by using the then quite primitive synthetic methods) and based on available physical parameters such as boiling point, density, and optical behavior (rotation and refractive index), and extended by melting point, shape, and appearance of crystalline derivatives.

[*] "Nun kam am 7.10.1876 die unglückliche zweite Heirat mit seiner bisherigen Hausdame, Fräulein Högel, die den Mann, statt zu heben, herunterzog. Sie hielt ihn von seinen Amtspflichten zurück, und als Kinder zur Welt kamen, nutzte sie ihn als Kinderwärter aus, immer vollständiger, je weniger die Dienstboten bei ihr aushielten. […] Ein trauriges Beispiel, wie eine törichte Frau einen hochbegabten Mann vor der Zeit knicken kann."

Subsequently Wallach focused on the rearrangements and interconversions of individual terpenes. The famous Figure 4 shows the state of knowledge of the interconversions ("transitions") of terpenes in 1891.

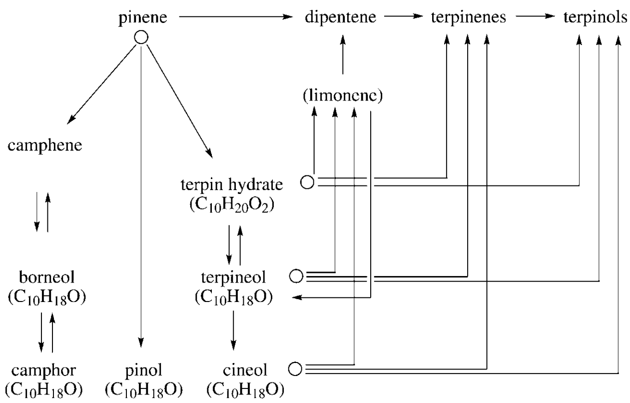

Figure 4. Transformations in the terpene series (O. Wallach, 1891).[17]

Actual structural elucidation first came to the fore of Wallach's work towards 1893, most likely because he was feeling the hot breath of competition on the back of his neck. At this time the presence of a bridging cyclohexane ring in camphor and pinene (Figure 5) was generally accepted, but it was Julius Bredt of Bonn University who published the correct structure of camphor in 1893 after a series of elegant degradation experiments.[13] Wallach engaged in what was at times vigorous scientific skirmishes, mainly with Friedrich-Wilhelm Semmler, Georg Wagner, and Julius Wilhelm Brühl. The latter made fundamental contributions to modern spectroscopic structure elucidation, especially through his work on molecular refraction. Wallach, however, lent little credence to structural predictions based solely on spectroscopic data and frequently commented derisively on Brühl's work in his publications.

On the other hand, following the work of Bredt, Wagner had published the correct structure of pinene in 1894,[14] but rejected it the following year in favor of another structure. The original structure from 1894 was finally confirmed by Adolf von Baeyer in 1896. Wallach played the role of a critically commenting observer during these discoveries.

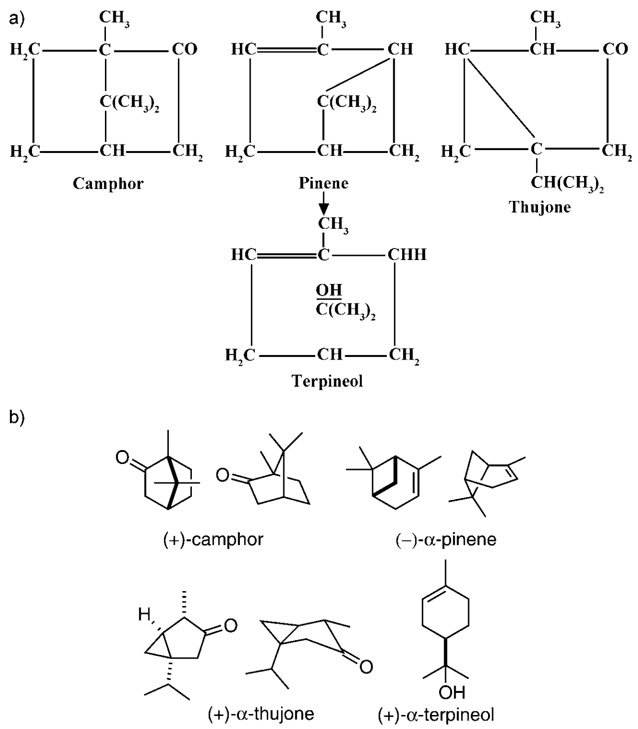

Figure 5. The terpenes camphor, pinene, thujone, and terpineol: a) historical representation from Wallach's Nobel lecture; b) current representations.

In addition to important work on acyclic terpenes such as citral, citronellal, and geraniol, Semmler had also deduced the correct structures of menthol and pulegone. In 1895 Wallach once more took part actively in events and published contemporaneously with Ferdinand Tiemann und Friedrich-Wilhelm Semmler the structure of α-terpineol, important on account of its central position amongst the terpenes. Thus at the end of 1895 the structures of the most important terpenes had been elucidated, and Walach's supremacy in this area slowly declined.

Book Publication and the Nobel Prize

In 1905, with his 60th birthday on the horizon, Wallach began to collect his work as an oeuvre in book form. Its appearance almost coincided with Wallach's 100th paper in *Liebigs Annalen* and the 25th anniversary of his terpene work, which his students deemed a suitable reason to hold a private celebration for their teacher. On the August 4, 1909 they presented Wallach with a festschrift and a marble bust sculpted by Adolph von Donndorf.

The title of the Wallach's Opus summum "*Terpenes and Camphors*" which he dedicated to his students referred to terminology introduced by Berzelius. According to this, ethereal oils such as terpentine that remain liquid even at low temperatures are called "terpenes" and solids like camphor itself "camphors".

In 1909 Wallach eas appointed president of the Deutsche Chemische Gesellschaft (today: Gesellschaft Deutscher Chemiker, GDCh) and became an honorary member in 1912. On the return trip from a lecture tour in England Wallach learned of the award of the Nobel Prize:[1]

"*When I bought an evening paper in Hannover and read it on the last step of the journey to Göttingen I found the unbelievable report that I had been awarded the Nobel Prize for 1910. At home I received the confirmatory telegram from Stockholm. An official letter from the secretary of the Swedish Academy, Aurivillus, and a private letter from Arrhenius brought further confirmation.*"[*]

The award presentation took place on December 10 in the Swedish Academy in the presence of King Gustav V. Wallach's Nobel lecture discussed the history of flavors and fragrances with special acknowledgement of Jöns Jacob Berzelius and other Swedish chemists. After a short historical outline on the isolation and characterization of the terpenes Wallach closed with a description of the economic importance of terpene research. Through Wallach's investigations a previously empirically working branch of industry of the fragrance industry was placed on a scientific footing. It is not surprising that the work of Wallach coincided with the blossoming of the German fragrance industry in which many of his students found positions after obtaining their doctorates.

During his stay in Göttingen Wallach maintained excellent contacts with England, where his work and he himself found considerable recognition; for example, he was appointed an Honorary Fellow of the Chemical Society (1908). In 1909 he received an honorary doctorate from the University of Manchester, and in 1912 he was awarded the Davy Medal of the Royal Society, the highest British scientific award for chemists. Scientifically he worked together mainly with William Henry Perkin, Jr., and Wallach's most famous student is the British Nobel laureate Walter Norman Haworth, who received the Nobel Prize in 1937 together with the Swiss terpene chemist Paul Karrer. Whereas Haworth was honored for his contributions to the structure of carbohydrates and vitamin C, Karrer received the award for his pioneering work on plant pigments. The carotenoids he investigated were tetraterpenoids, and so Karrer's Nobel Prize can also be considered to be linked to the pioneering work of Wallach.

Not only were the contacts with England cut short with the start of the First World War; many of Wallach's doctoral students did not return from the war and this had a severe impact on his research program:[15]

"*The […] work […] suffered a disruption before it was completed at the start of the war. It was […] however held back in the hope that my co-workers would soon be able to take up the research again under my supervision and carry it out in the*

[*] "Als ich mir in Hannover eine Abendzeitung gekauft hatte und darin auf dem letzten Weg nach Göttingen las, fand ich die mir unglaubliche Notiz, dass mir der Nobelpreis für 1910 verliehen sei. Zu Haus empfing mich das bestätigende Telegramm aus Stockholm. Ein offizieller Brief von dem Sekretär der Schwedischen Akademie, Aurivillus und ein Privatbrief von Arrhenius brachten weitere Bestätigung."

planned way; since this expectation has not been fulfilled I will no longer postpone the publication […]."[*]

Walbach retired shortly after the outbreak of the war (1915); he placed the leadership of the institute in the hands of Adolf Windhaus, who himself was awarded the Nobel Prize for Chemistry in 1928 for work in the area of steroids and vitamins. In total 214 students gained their doctorates under Wallach, of these 30 in Bonn and 5 further after his retirement. Otto Wallach died on February 26, 1931 in Göttingen and lies at rest in the Göttingen municipal cemetery.

The University of Göttingen awards the Wallach Prize to young scientists for exceptional final degree dissertations. In commemoration of the ground-breaking work of Otto Wallach and in recognition of its significance for the fragrance industry the Otto Wallach Medal (Figure 6) has been awarded by the Gesellschaft Deutscher Chemiker since 1966 to European researchers for exceptional accomplishments in the area of terpene and pheromone chemistry. However, this prize, established by the company DRAGOCO, has been temporarily suspended since its merger with Haarmann& Reimer to the new company Symrise and the associated change in orientation. The list of the previous prize winners:

Figure 6. Otto Wallach Medal. The obverse (left) show the structural formulas of isoprene, β-pinene, and α-terpinene.

1966 Walter Hückel, Tübingen
1969 Guy-Henri Ourisson, Strasbourg/Frankreich
1974 Ferdinand Bohlmann, Berlin
1977 Hermann Eggerer, München
1981 Günther Ohloff, Genf/Schweiz
1986 Hans-Jürgen Bestmann, Erlangen
1988 Erich Hecker, Heidelberg
1991 Wolfgang Oppolzer, Genf/Schweiz
1996 Wittko Francke, Hamburg
1999 Peter Welzel, Leipzig
2002 Pierre Potier, Gif-sur-Yvette/Frankreich

Compared to other important achievements in natural product chemistry at the end of the 19th century Wallach's pioneering role in terpene chemistry is often not appropriately appreciated. For many undergraduates and postgraduates the history of terpenes begins with the no less impressive work of Leopold Ruzicka (Nobel Prize in Chemistry, 1939), who in particular distinguished himself for the structural elucidation of higher terpenes (sesquiterpenes, diterpenes, etc.) and the further development of the empirical isoprene rule. Only later were Feodor Lynen and Konrad Bloch able to elucidate the biosynthesis of the terpenes in detail; for this they were awarded the Nobel Prize in Physiology or Medicine in 1964. It is frequently forgotten, however, that just 20 years after the publication of the tetrahedral model of carbon the structures of bicyclic terpenes were determined, mainly through the pivotal contributions of Wallach, and this ultimately concluded the triumph of structural theory.

Attempts are occasionally made to compare Wallach with other greats of his time such as Adolf von Baeyer and Emil Fischer. All three were without doubt excellent experimentalists whose approach to complex structural chemistry problem is still exemplary. Fischer's work on the structure of monosaccharides in particular is today still part of the curriculum because of the fascinating logical reasoning. Whereas, however, Fischer and von Baeyer themselves harvested the fruits of their work and hypothesized, speculation was foreign to Wallach. He indeed stands as one of the greatest analytical organic chemists of his time, but he shied away from making structural suggestions because of the danger of being proven wrong—Wallach was all the more critical of incorrect structural suggestions of his rivals.

The simplified representation of Fischer and von Baeyer as visionary characters and Wallach as a craftsman certainly falls short of the mark. It is not possible to resist the impression that during the discussion in Kekulé's office (or shortly before) when he asked permission to become involved with the ethereal oils that Wallach recognized that he was the right person in the right place—in other words it was his destiny to bring order to the area of terpenes! And not just for single substances but for the entire group of natural products. This decision also meant for Wallach a change in research area. In my opinion Wallach's vision manifested itself in the ambitious three-stage research plan announced before the Chemische Gesellschaft. That Wallach did not fulfill all stages of his plan himself is of secondary importance.

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[*] "Die […] Arbeiten […] erlitten vor vollkommener Durchführung bei Kriegsbeginn eine Unterbrechung. Sie wurden […] aber in der Hoffnung zurückgehalten, dass meine Mitarbeiter bald in der Lage sein würden, die unter meiner Leitung begonnenen Untersuchungen wieder aufzunehmen und in geplanter Weise durchzuführen; da diese Erwartung sich nicht erfüllt hat, will ich die Veröffentlichung […] nicht länger aufschieben."

[1] *Otto Wallach 1847–1931. Chemiker und Nobelpreisträger. Lebenserinnerungen*, published and annotated by G. Beer, H. Remane, Verlag für Wissenschafts- und Regionalgeschichte, Berlin, **2000**.
[2] a) W. Hückel, *Chem. Ber.* **1961**, *94*, VII–CVIII; b) L. Ruzicka, *J. Chem. Soc.* **1932**, 1582–1597.
[3] a) R. Leuckart, *Ber. Dtsch. Chem. Ges.* **1885**, *18*, 2341–2344; b) O. Wallach, *Justus Liebigs Ann. Chem.* **1893**, *272*, 99–122.
[4] a) O. Wallach, E. Belli, *Ber. Dtsch. Chem. Ges.* **1880**, *13*, 525–527; b) E. Buncel, *Acc. Chem. Res.* **1975**, *8*, 132–139.
[5] O. Wallach, *Justus Liebigs Ann. Chem.* **1918**, *414*, 296–336.
[6] O. Wallach, *Justus Liebigs Ann. Chem.* **1895**, *286*, 90–143.

[7] a) T. Friscic, L. Fabian, J. C. Burley, D. G. Reid, M. J. Duer, W. Jones, *Chem. Commun.* **2008**, 1644 – 1646; b) C. P. Brock, W. B. Schweizer, J. D. Dunitz, *J. Am. Chem. Soc.* **1991**, *113*, 9811 – 9820.

[8] Julius Adolph Stöckhardt's "*Die Schule der Chemie oder Erster Unterricht in der Chemie. Zum Schulgebrauch und zur Selbstbelehrung, insbesondere für angehende Apotheker, Landwirthe, Gewerbetreibende etc.*" appeared between 1846 and 1881 in a total of 19 editions and at that time contributed to the popularization of chemistry.

[9] Münster achieved full university status only in 1902.

[10] K. Roth, S. Hoeft-Schleeh, *Chem. Unserer Zeit* **2002**, *36*, 390 – 402.

[11] O. Wallach, *Justus Liebigs Ann. Chem.* **1888**, *246*, 221 – 239.

[12] Communicated in the lecture before the Deutsche Chemische Gesellschaft (today: Gesellschaft Deutscher Chemiker, GDCh) on 23rd February, 1891.

[13] a) J. Bredt, *Ber. Dtsch. Chem. Ges.* **1893**, *26*, 3047 – 3057; b) G. B. Kauffman, *J. Chem. Educ.* **1983**, *60*, 341 – 342.

[14] G. Wagner, *Ber. Dtsch. Chem. Ges.* **1894**, *27*, 1636 – 1654.

[15] O. Wallach, *Justus Liebigs Ann. Chem.* **1918**, *414*, 271 – 296.

[16] Advertisment in Industrie Compass **1919**, Band I, 1248/V, Austrian National Library.

[17] Otto Wallach, *Terpene und Campher, Zusammenfassung eigener Untersuchungen auf dem Gebiet der alicyclischen Kohlenstoffverbindungen*, 2nd ed., Verlag Veit & Co., Leipzig, **1914**..