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Historical Paper

Prelog's Zagreb School of Organic Chemistry (1935 – 1945)*

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This article on Vladimir Prelog and his contribution to the development of organic chemistry in Croatia presents data on his scientific work done in the Department of Organic Chemistry of the Technical Faculty in Zagreb, as well as the scientific research work carried out in collaboration with the Science Laboratory of the pharmaceutical plant »Kaštel« in Zagreb. All the resulting papers were prepared by joint engagement of Professor Prelog's enthusiastic co-workers from the Faculty and »Kaštel«, thus establishing »Prelog's Zagreb School of Organic Chemistry«. It continued its activities even after Professor Prelog's departure for Zürich and had a vital influence on the further development of organic chemistry and biochemistry at the University of Zagreb, research institutions and scientific research laboratories of the chemical and pharmaceutical industries in Croatia.

The 90th birthday of our dear Professor Vladimir Prelog is a great opportunity not only for extending our congratulations and paying our respects to him but also for recalling what he has done for the development of Croatian organic chemistry and pharmaceutical industry during his short scientific activity in Zagreb.

Professor Prelog came to the Technical Faculty in Zagreb in 1935. At that time, I was a freshman and I remember his first lectures on organic chemistry in the summer term of 1935. We got to know Professor Prelog as a brilliant and fascinating lecturer. He rendered his lectures in a clear and

* Dedicated to Professor Vladimir Prelog on the occasion of his 90th birthday.

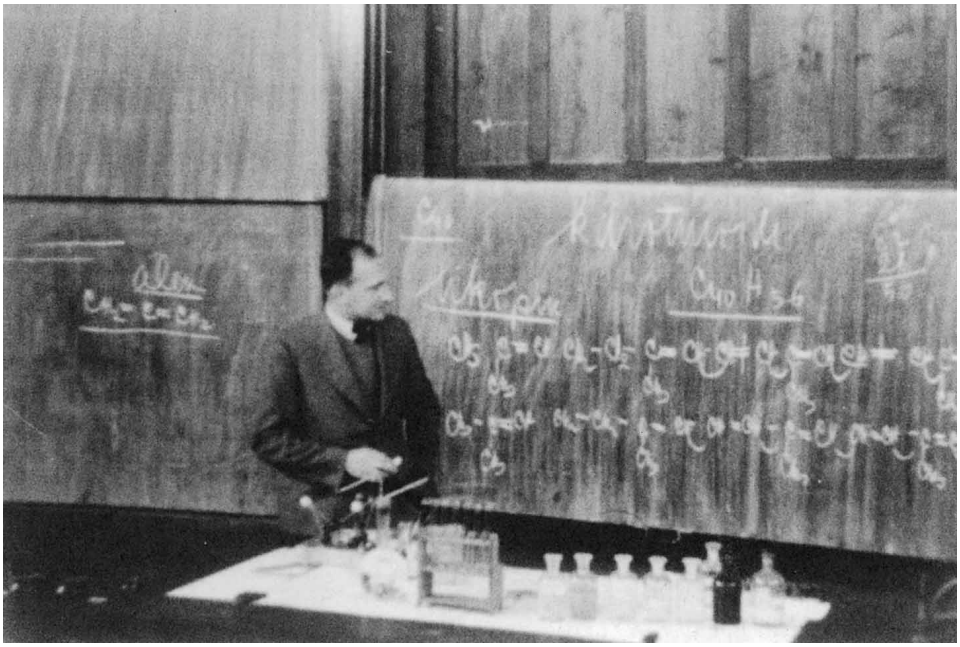

Figure 1. Prelog delivering a lecture on organic chemistry, Zagreb 1936.

witty way, so we listened with interest and memorized his words (Figure 1). It was already at that time that many of us committed ourselves to organic chemistry.

At his lectures, and afterwards in personal contacts during laboratory exercises and doctoral theses, we found out much more about our professor. Vladimir Prelog was born in Sarajevo on July 23, 1906. His father, Milan, was an outstanding historian and university professor. Prelog went to grammar school in Zagreb from 1916 to 1919, then in Osijek for two years (1919–1921), and again in Zagreb from 1921 to 1924. He very early decided to take up chemistry, at secondary school in Osijek, where his excellent chemistry teacher, Ivan Kuria* (Figure 2), encouraged his interest in chemistry. It was in 1921 that, at the age fifteen (Figure 3), with his teacher's help, he published a short communication entitled »Eine Titriervorrichtung« in the prestigious journal *»Chemiker-Zeitung«* (Figure 4).[1]

After his return to Zagreb, Prelog continued corresponding with his chemistry teacher in Osijek. Some of the letters are very touching. For in-

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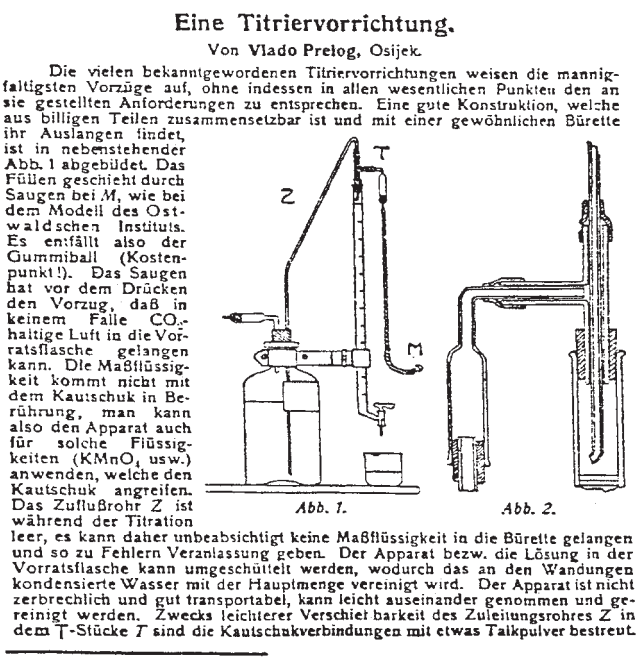
* Ivan Kuria, chemistry teacher at the Osijek grammar school, responsible for Prelog's love of chemistry. After retirement, he volunteered at Pliva to the end of his life.

stance, in his letter of March 16, 1922,[2] Prelog writes about himself: »I am very busy at the moment. In addition to my routine studies, I have enrolled as an extramural student in the crafts school and I spend whole afternoons three times a week learning how to file, hammer and do all the other things that an eager young locksmith should know. I am doing it to be able to, should I feel like it, return to the homeland after finishing my studies. In this way, I also fence myself off such idle pastimes like dancing.« He continues by describing how he spent the winter enjoying winter sports and how he now, in spring, looks forward to bathing, climbing the Triglav and Grintavec mountains and sailing on lakes Bled and Bohinj. He concludes the letter by giving an enthusiastic account of his visit to the Chemical Analytical Institute in Zagreb: »I think this is the best equipped institute in SHS*. This wealth in platinum (a 300 g water beaker), optical instruments (refractometers, spectroscopes, microscopes, *etc., etc.*) and all the analytical devices that God and the German have created – I have nowhere seen anything like that. It is run by Mr. Eisenhut.«

Figure 2. Prof. Ivan Kuria.

Figure 3. Fifteen-year old chemist Vlado.

* The Kingdom of Serbs, Croats and Slovenes.



Eine Titriervorrichtung.

Von Vlado Prelog, Osijek.

Die vielen bekanntgewordenen Titriervorrichtungen weisen die mannigfaltigsten Vorzüge auf, ohne indessen in allen wesentlichen Punkten den an sie gestellten Anforderungen zu entsprechen. Eine gute Konstruktion, welche aus billigen Teilen zusammensetzbar ist und mit einer gewöhnlichen Bürette ihr Auslangen findet, ist in nebenstehender Abb. 1 abgebildet. Das Füllen geschieht durch Saugen bei *M*, wie bei dem Modell des Ostwaldschen Instituts. Es entfällt also der Gummiball (Kostenpunkt!). Das Saugen hat vor dem Drücken den Vorzug, daß in keinem Falle CO_2-haltige Luft in die Vorratsflasche gelangen kann. Die Maßflüssigkeit kommt nicht mit dem Kautschuk in Berührung, man kann also den Apparat auch für solche Flüssigkeiten ($KMnO_4$ usw.) anwenden, welche den Kautschuk angreifen. Das Zuflußrohr *Z* ist während der Titration leer, es kann daher unbeabsichtigt keine Maßflüssigkeit in die Bürette gelangen und so zu Fehlern Veranlassung geben. Der Apparat bezw. die Lösung in der Vorratsflasche kann umgeschüttelt werden, wodurch das an den Wandungen kondensierte Wasser mit der Hauptmenge vereinigt wird. Der Apparat ist nicht zerbrechlich und gut transportabel, kann leicht auseinander genommen und gereinigt werden. Zwecks leichterer Verschiebarkeit des Zuleitungsrohres *Z* in dem T-Stücke *T* sind die Kautschukverbindungen mit etwas Talkpulver bestreut.

Abb. 1. Abb. 2.

Figure 4. Facsimile of Prelog's first paper.

After passing his school-leaving exam in Zagreb, in 1924, Prelog studied chemistry at the Prague Institute of Technology where he, already as a student, started doing research. Thus, we know from his letter of April 3, 1928 to his teacher Ivan Kuria (Figure 5),[3] with whom he always kept in touch, that in the second year of studies he had the good opportunity to engage in organic chemistry, in his spare time from 8 to 12 P.M. In the fourth year, his exams and prescribed exercises kept him very busy, so he could not spend so much time in the laboratory. He writes that he was working on two papers: »One is actually a sequel to the syntheses in the pirrole series and it will be published with Dr. Lukeš, who is a senior assistant lecturer now and also my best friend. The other paper, co-authored by Professor Votoček, deals with the high fatty oxyacids formed by hydrolysis of jalapin and turpeth convolvulin glycosides. Professor Votoček is the leading expert in the field of methylpentoses, which are found in these glycosides. He discovered them there while the fatty acids remained as a by-product. I have undertaken their processing and have already done a great deal of work.«

Prelog concludes the letter by adding: »I would like to take my final by the end of the year, and then I would stay on to get a doctor's degree. Then the army service, and then in search for a better livelihood. You must be aware how difficult these problems are.«

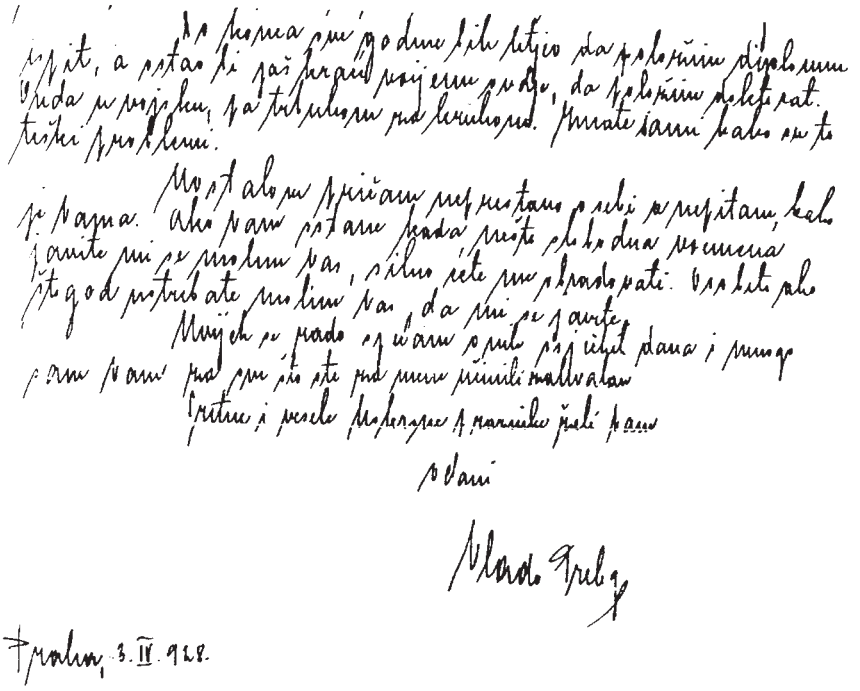


Figure 5. Facsimile of Prelog's letter to his Osijek teacher I. Kuria.

Prelog's wishes came true. He graduated in 1928 and earned his doctor's degree in the shortest possible time, in 1929, *summa cum laude*. After having done his army service in the navy (Tivat in Boka Kotorska), he went back to Prague, where he accepted the job offered him by G. J. Dřiza, a dealer in chemicals. In his laboratory, Prelog carried out syntheses of rare organic chemicals and, in his spare time, also research, which resulted in a number of published papers (see M. Protiva: »Prelog's Prague Years«, in this issue).

Familiar with Prelog's research papers written in Prague, professors of the Chemistry Department of the Technical Faculty in Zagreb, Ivan Marek,* Vladimir Njegovan,** Franjo Hanaman*** and Ivan Plotnikov,**** invited

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* Ivan Marek (1863–1936), professor of organic chemistry at the Institute of Technology (later Technical Faculty) in Zagreb, 1920–1935.

** Vladimir Njegovan (1887–1971), professor of inorganic and analytical chemistry at the Institute of Technology (Technical Faculty) in Zagreb, 1919–1943 and 1945–1951.

*** Franjo Hanaman (1878–1941), professor of inorganic technology and metallurgy at the Institute of Technology (Technical Faculty) in Zagreb, 1919–1941.

**** Ivan Plotnikov (1878–1955), professor of physics and physical chemistry at the Institute of Technology (Technical Faculty) in Zagreb, 1919–1943.

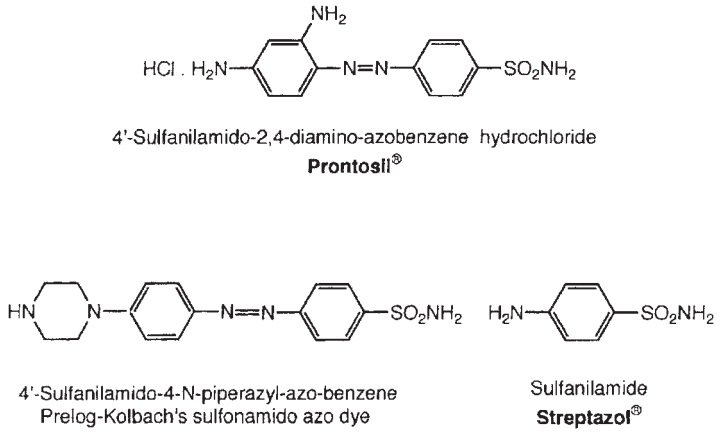


Figure 6. Chemical structures of *Prontosil*®, Prelog's azo dye and sulfanilamide.

the young, but already renowned, organic chemist to succeed Professor Marek as head of the Department of Organic Chemistry.

Prelog, who had always wanted to work in an academic laboratory, promptly accepted the offer. At the end of 1934, he came to Zagreb, with his wife Kamila neé Vitek, where he assumed the duty of head of the Department, first as assistant professor, and since 1941 as associate professor.

According to Professor Prelog,[4] the working conditions were more than modest. The laboratory was not equipped for preparatory work in organic chemistry because Professor Marek was predominantly engaged on organic elemental analysis, and the other units of the Chemistry Department also tended towards analytics. In industrial laboratories, chemical engineers mainly analyzed raw materials and finished products, and very few worked in the production. Hence, there was no incentive for preparatory work. Nobody was actually against scientific research at that time, but the budget was so small that it only just covered tuition while research funds depended on the resourcefulness of those who wanted to do research. Prelog was disappointed with the situation and his enthusiasm dwindled. However, it soon came back when he received an offer for scientific cooperation from Dr. Eugen Ladany, director and co-owner of the small pharmaceutical company »Kaštel« in Zagreb. Prelog did not hesitate in accepting the offer, since it enabled him to do scientific research as he had always wanted to. He described briefly and clearly the agreement on cooperation:[4] »We agreed that Kaštel would set up a research laboratory. The chemical section of the laboratory would work on the procedures for the production of medically interesting compounds, while the pharmacological section would test their biological and therapeutical properties. Kaštel will help me fit out the Department of Organic Chemistry at the Faculty, where I will also deal with medically in-

teresting compounds, something that I have always wanted to do. Our short-term plan is to design procedures for the production of known, profit making medicines, and the long-term one to discover new, original, biologically active and medically interesting compounds.» He continued: »My first concern was to provide a real content for these abstract plans. In 1935, Domagk's *Prontosil*® (4'-sulfanilamido-2,4-diamino-azobenzene hydrochloride), the first efficient agent against bacterial infections, received great acclaim in the field of medical chemistry (Figure 6). I proposed as our short-range goal to copy *Prontosil*®, but in a way so as not to get into conflict with the powerful German chemical industry. At the same time, I was approached by the Prague student, Dragutin Kolbach, an engineer, who wished to work on his doctoral thesis with me. I suggested he should prepare a series of azo dyes related to *Prontosil*®. Out of his compounds, 4'-sulfanilamido-4-*N*-piperazyl-azo-benzene (Figure 6) showed good characteristics and, after some tests, we decided to produce it commercially.

Figure 7. Facsimile of one of »Kaštel« advertisements, Zagreb, 1939.

When the first steps in this direction were undertaken, a paper written by Daniel Bovet and Francoise Nitti of the Pasteur Institute in Paris appeared in 1936, in which the authors demonstrated that *Prontosil*® underwent to reductive splitting in mammals and that its antibacterial effect derives from the product of this splitling, *i.e.* sulfanilamide (Figure 6) (starting material for *Prontosil*® allied azo dyes). As sulfanilamide was not patent protected, after an incredibly short time, in 1937, »Kaštel« launched it on the market under the name. *Streptazol*® (Figure 7). It was a miracle drug until resistant strains of pathogenic bacteria appeared. Its huge success contributed a lot to »Kaštel« extending its support to our research cooperation.«

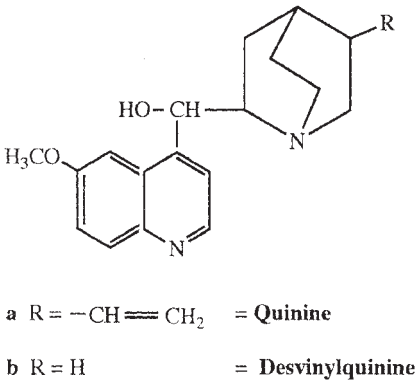
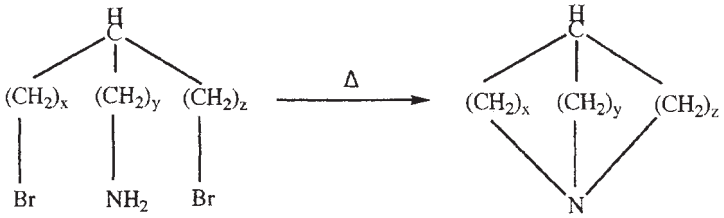


Figure 8. Chemical structures of quinine and desvinylquinine.

This cooperation enabled Prelog to upgrade the equipment in his Department, so he could organize laboratory work with some young associates and resume research activities that he had started in Prague. These are chemotherapeutic agents for some common diseases, syntheses in the field of cinchona bark alkaloids and bicyclic bases that constitute the skeleton of some alkaloids. Quinine was still the most important antimalarial agent at that time. Its constitution was already known (Figure 8), but its spacial structure, configuration and synthesis were still unknown. Due to the modest working conditions, work on the synthesis was chosen for being simpler and less costly than that on the configuration. A satisfactory procedure was known for the synthesis of the quinoline part whereas no adequate method existed for the preparation of quinuclidine, which is actually a tertiary amine with a nitrogen atom at the branching point.

With a group of co-workers (Krešimir Balenović,[39,40] Krunoslav Božičević,[25] Eugen Cerkovnikov,[10,13,14,16,20,22,33,36] Eugen Guštak,[28] Suzana Heimbach-Juhász,[20,22,24,26,32,33] Dragutin Kolbach,[13] Miho Piantanida,[13] Adolf Režek,[13,32] Bruno Schönbaum,[35] Rativoj Seiwerth,[26,28] Nikola Šoštarić,[34] Pavao



a X = 2, Y = 2, Z = 2 ; **Quinuclidine**
b X = 4, Y = 0, Z = 4 ; **Norlupinane**
c X = 5, Y = 0, Z = 3 ; **Norlupinane B**
c X = 4, Y = 0, Z = 3 ; **δ-Coniceine**

Figure 9. Prelog's synthesis of quinuclidine, norlupinane, norlupinane B and δ-coniceine by the method of double intramolecular alkylation.

Štern[37] and Georgij Ustričev[16]), Prelog dedicated his efforts to the synthesis of quinuclidine and a whole series of allied bases with nitrogen at the branching point. Several methods were developed for the preparation of these compounds, the most efficient of which was the so called Prelog's method of double intramolecular alkylation, which enabled syntheses of the already known as well as new bicyclic amines (Figure 9), which are interesting not only because their skeleton is incorporated in alkaloids but also from the aspect of stereo-chemistry. Preparation of these amines was patented by »Kaštel«.

After gaining experience in the syntheses of quinuclidine and the allied bicyclic amines, V. Prelog, R. Seiwerth, V. Hahn and E. Cerkovnikov[27] moved on to the synthesis of compounds similar to quinine. The aim of the research was to develop methods for the preparation of various compounds with the rubane skeleton (Figure 10 a), representative samples of which would be tested for antimalarial activity. The compounds prepared (Figures 10 b, c, d, e, f) were tested for antimalarial activity but showed no activity.

Then, V. Prelog, R. Seiwerth, Suzana Heimbach-Juhácz and P. Štern[37,38] prepared a simple quinine analogon in which the vinyl group was replaced by hydrogen, desvinylquinine (Figure 8 b). By reduction of 6-methoxy-ruban-9-ol, a diastereoisomeric pair was obtained as the main product, which was in experiments with animals shown to have the same activity as the not easily available quinine, Thus, it was proven that the vinyl group is not indispensable for antimalarial activity.

In their further research on quina-alkaloids, V. Prelog and M. Proštenik[53] succeeded in partial synthesis of quinotoxine (Figure 11 a) from the still unknown homomeroquinene (Figure 11 b), prepared by decomposition of cinchonine *via* cinchotoxine. This was an additional step to the total synthesis of quinine.

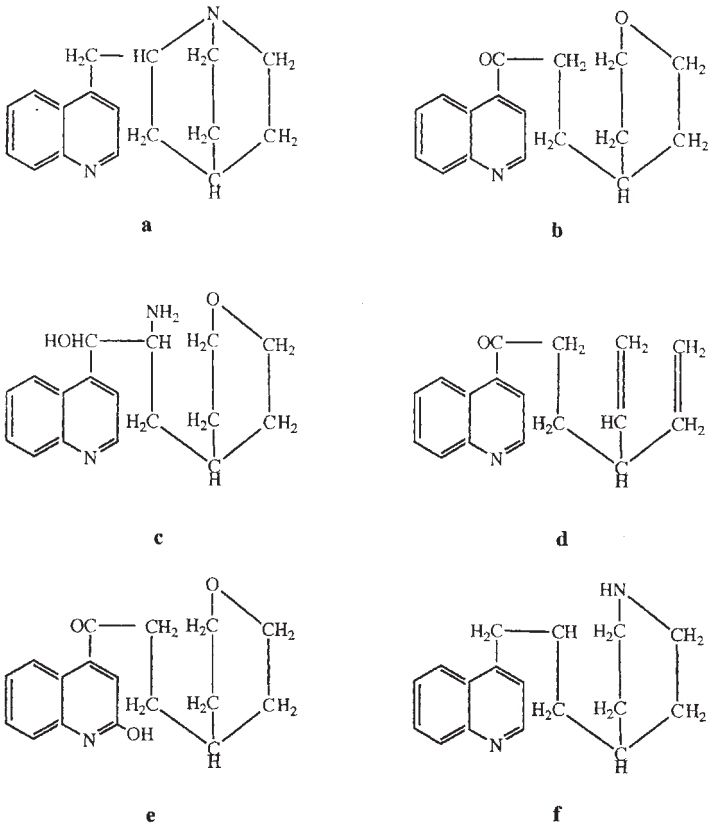


Figure 10. Chemical structures of rubane (a) and its related compounds (c–f), synthesized and tested by Prelog and co-workers.

A problem quite different from the chemistry of cinchona bark alkaloids was the first synthesis of adamantane. The diamond lattice contains a special tricylcic carbon skeleton made up of ten carbon atoms. Organic compounds with such skeletons were named diamondoid *(diamond-like)* compounds. The simplest representative of such compounds is the hydrocarbon $C_{10}H_{16}$, symmetrical tricyclodecane (Figure 12 d), which Landa and Macháček isolated in 1933 from petroleum in the vicinity of Hodonin in Moravia and named adamantane* (Figure 12 d).

The first synthesis of adamantane was carried out by Prelog and Seiwerth in 1941, using bicyclo-[3,3,1]-nonane[41] as starting material. By condensation of disodium dimethyl ester salt of bicyclo-[1,3,3]-nonandion-

* αδαμαξ, the invincible, wherefrom the word DIAMOND and ADAMANTANE were formed.

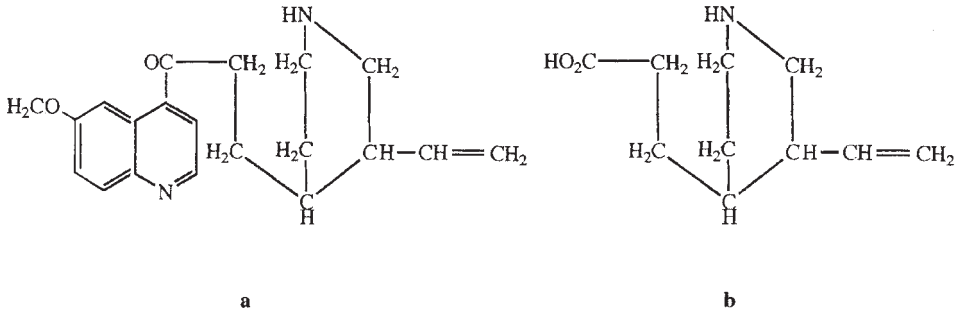


Figure 11. Partial synthesis of quinotoxine.

(2,6)-dicarboxylic acid-(3,7) (**12a**) with dibromomethane, a dimethyl ester of adamantandion-(2,6)-dicarboxylic acid-(1,5) (**12b**) was prepared. Its hydrolysis gave adamantandion-(2,6)-dicarboxylic acid-(1,5), which was by the Wolff-Kishner reduction transformed into adamantane dicarboxylic acid-(1,3) (**12c**).

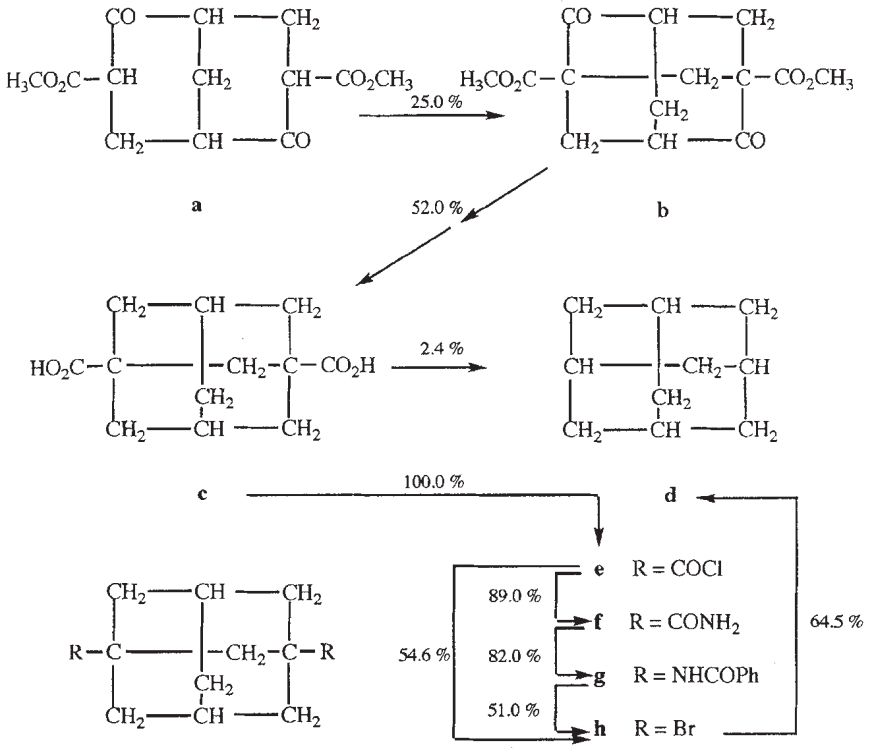


Figure 12. Prelog-Seiwerth's syntheses of adamantane.

Its decarboxylation in the presence of Cu-bronze at 400 °C gave adamantane (**12d**) in a poor yield of 2.4% (total yield 0.16%). By another, more abundant synthesis,[47] adamantane dicarboxylic acid-(1,3) (**12c**) was transformed *via* dichloride **12e** into diamide **12f**. The latter was diverted into 1.3-diaminoadamantane by a reaction with sodium hypobromite. From its dibenzoil derivate (**12g**) with phosphorus-pentabromide, 1,3-dibromineadamantane (**12h**) was obtained, and by catalytic hydration of the latter in the presence of Raney-nickel, adamantane (**12d**) was obtained in a total yield of 3.12%. Dibromo-derivate **12h** was also easily obtained by diversion of the silver salt of adamantane carboxylic acid **12c** with bromine, which is a further simplification of adamantane synthesis (4.73%). Properties of thus synthetically obtained adamantane fully corresponded to the values that Landa and Maháček[5] had reported for natural adamantane.

All the above trials were done with a small group of enthusiastic co-workers under very modest working conditions. I vividly recall the instance when the Professor procured an oil pump for high vacuum and installed it himself. A celebration broke out in the laboratory and the pump was cherished dearly. Since the Professor worked with us in the laboratory, we could learn a great deal from him. He showed us how, using the appliances available, we could make apparatus that was applicable even to very sensitive and complex reactions. Our professor was a real master of glass processing, so he taught us how to bend glass tubes at different angles and make various small flasks, distillation apparatus, stirring rods, *etc*. He taught us to love our work, to be filled with joy at newly synthesized compounds, obtained in the form of clear oily liquids or beautiful crystals, and the joy reached its peak when it was confirmed by analysis that we had attained just that compound that we had wanted. Despite meagre funds and potentials, Prelog's group worked with satisfaction and was very efficient. In a period of seven years, 48 research papers and eight patents were published, as well as five dissertations under Prelog's supervision. It is interesting to note that, with his ten papers, Prelog's group was the team with the largest number of papers published in the prestigious journal *»Berichte der Deutschen Chemischen Gessellschaft«* in 1941.

The commercial success of *Streptazol*® speeding up considerably the fitting out of a research laboratory at »Kaštel« and the training of promising experts for such work. After the first successes, the »Kaštel« research team became so strong that a research department with three laboratories (chemical, pharmacological ad bacteriological) was founded at »Kaštel« in 1938. The research department staff included: V. Hahn, E. Rajner and E. Cerkovnikov, chemists, P. Štern, a pharmacologist, and J. Kolačny, a bacteriologist. In this department, following Prelog's long-term plan, new barbituric acid derivatives[7] were synthesized, as well as a number of new compounds that were tested for antimalarial[l27,37,38,51,52] and spasmolytic[42,43,44] activity. Among the new 4-aminopiperidine derivatives, marked spasmolytic activity was manifested by 4-dimethylamino-1-phenyl-piperidine. The compound was subjected to further tests, which were necessary before its launching on the market. At the same time, the research group was developing methods for the production of some

Figure 13. Prelog's Zagreb school of organic chemistry. Some of his co-workers on the occasion of his birthday celebration in 1939 (sitting from left to right: M. Piantanida, A. Režek, Nina Cerkovnikov, Suzana Heimbach-Juhász, V. Prelog and E. Rajner; standing from the left: R. Seiwerth, K. Juhácz, V. Hahn, P. Štern, K. Božičević, D. Kolbach, B. Schwirtlich, E. Cerkovnikov, I. Corubolo and Lj. Trinajstić).

already known medicines. *Streptazol*® was immediately followed by sulfapyridine (*Plurazol*®), which was soon abandoned because of toxicity. Methods were developed for the production of *Eucistine*® (3-phenyl-1-azo-2,6-diaminopyridine), the classical analeptic, nicotinic acid diethylamide (*Leptamin*®) as well as calcium levulinate (*Eukalcin*®) for calcium therapy. Thus Prelog and his collaborators founded the synthetic production and organized scientific research in the factory »Kaštel«, which was actually the beginning of the research institute of the present day »Pliva«.

By this cooperation with »Kaštel«, Prelog demonstrated that cooperation between university and industrial research laboratories could be very successful, though this was a rather sensitive and complex relationship. Their cooperation was based on mutual trust, good will and benefits to both sides, the limits of whose respective potentials were well known to each other. Prelog succeeded in establishing a full mutual understanding while his associates, both from the faculty and from »Kaštel«, founded **Prelog's Zagreb School of Organic Chemistry** (Figure 13).

Figure 14. Prof. Prelog with his old co-workers at the opening ceremony of the Pliva Institute, autumn 1952 (from the left: E. Rajner, R. Seiwerth, D. Kolbach, V. Prelog and E. Guštak).

The war, however, put an end to these activities. During the war, scientific research was almost impossible. »Kaštel« was made a state company and all research was discontinued. Under such confused and uncertain circumstances, Prelog took a sabbatical. He had received invitations by the president of the German Chemical Society, Richard Kuhn, to give a few lectures at Heidelberg and by Leopold Ružička to come to Zürich. He decided to go to Zürich and it was after the war that he also gave a lecture at Heidelberg. On Prelog's suggestion, R. Seiwerth was appointed his deputy during the sabbatical. As the »short sabbatical« was extended, Seiwerth ran the tuition and the Department throughout the war, until 1945, but Prelog did not return. He stayed on in Zürich after the war.

Though Prelog's work at the faculty and in pharmaceutical industry was interrupted by his departure for Switzerland at the end of 1941, his Zagreb school of organic chemistry continued its activities and development. After the war, Prelog's former students and co-workers assumed responsible duties at faculties, research institutions and in industry, they set up new research laboratories and educated a new generation of organic chemists. Pro-

Figure 15. Prelog's Zagreb school of organic chemistry. Prof. Prelog and Mrs. Prelog with organic chemists at dinner at Hotel Esplanade, 1973 (sitting from the left: Mrs. J. Guštak, Mrs. Z. Štefanec, Mrs. Prelog and Mrs. N. Bregant; standing from the left: B. Glunčić, B. Gašpert, P. Mildner, R. Marušić, D. Kolbach, M. Laćan, E. Guštak, Professor Prelog, S. Borčić, R. Seiwerth, K. Balenović and S. Đokić).

fessor Prelog has been continually monitoring the development of his school and has always stayed in touch with his former associates. He occasionally comes to Zagreb to visit his family, and he readily accepts invitations to give lectures and attend scientific and professional gatherings, as well as various celebrations. When he comes, he always finds time to meet his old associates from Zagreb, as well as those who worked with him in Zürich* (Figures 14, 15 and 16). Prelog also arranges for our young organic chemists to spend some time working in his ETH Laboratory. »Exchange of experience is the best form of cooperation«, Prelog used to say. This practice is systematically carried out even now when he is retired.

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* The following chemists have worked with Professor Prelog in Zürich where they acquired »organic polish«: Dušan Dvornik, Stanko Borčić, Mirko Ternbach, Berislav Glunčić, Branimir Gašpert, Vitomir Šunjić, Radoslav Marušić, Mladen Žinić, Krunoslav Kovačević, Stjepan Mutak, Miljenko Dumić and Miće Kovačević.

Figure 16. Prelog's Zagreb school of organic chemistry. Prof. Prelog and Mrs. Prelog with his former Zagreb and Zürich associates at the Pliva Club, on May 22, 1989 (sitting from the left: R. Seiwerth, D. Kolbach, Professor Prelog, Mrs. Prelog and M. Prošteník: standing from the left: M. Dumić, S. Mutak, B. Glunčić, K. Kovačević, B. Gašpert, M. Žinić, M. Kovačević, S. Borčić, V. Šunjić and S. Đokić).

This ensures uninterrupted work and rejuvenation of Prelog's Zagreb school of organic chemistry. We are, therefore, grateful to our Professor Prelog for all that he has done for our chemistry and for our future.

Acknowledgement. – I am grateful to my colleague Dr. Miljenko Dumić for correcting and editing the manuscript.

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SAŽETAK

Prelogova škola organske kemije u Zagrebu

Rativoj Seiwerth

U ovom prikazu o Vladimiru Prelogu i njegovom doprinosu razvitku organske kemije u Hrvatskoj izneseni su podaci o znanstvenim radovima izvedenima u Zavodu za organsku kemiju Tehničkog fakulteta u Zagrebu, kao i znanstveno-istraživačkim radovima izvedenima u suradnji sa Znanstvenim laboratorijem farmaceutske tvornice »Kaštel« u Zagrebu. Svi ti radovi nastali su zajedničkim radom oduševljenih suradnika prof. Preloga s fakulteta i tvornice »Kaštel«, stvarajući time »Prelogovu školu organske kemije u Zagrebu«. Ona je i nakon odlaska prof. Preloga u Zürich nastavila radom i bitno utjecala na daljnji razvoj organske kemije i biokemije na visokim školama, znanstvenim ustanovama i znanstveno-istraživačkim laboratorijima organsko kemijske i farmaceutske industrije u Hrvatskoj.