

## Vladimir Prelog's Prague Years and My Later Contacts with Him\*

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The circumstances in which V. Prelog studied and worked in Prague, some stories in which he was involved, and the author's reminiscences to his numerous contacts with Prelog are described.

When I was invited to contribute to this »Surprise Festschrift«, I wanted to concentrate on reminiscences of my frequent contacts with Prof. V. Prelog since 1946. I realized, however, that very likely I was the only Czech chemist to have had this opportunity. Vladimir Prelog was very closely connected with Czech chemistry and with Czech chemists: he spent the years 1924–1935 in Prague studying chemistry and concentrating his interests on organic chemistry (especially on the chemistry of natural products) – his whole life's orientation. Here, he met his friends and Kamila Vitek, his lifelong consort of Czech origin. Prague and the Czech milieu was important to V. Prelog and he became important to Czech chemistry. All this is the reason why I feel I should start with a short recapitulation of his Prague period.

It is not easy for me for two reasons:

1. At the time of his stay in Prague, I was a boy of 3–14 years and thus cannot be considered a witness. I simply have to behave like a historian, *i.e.* use the written reports of witnesses; the best of them have been provided by V. Prelog himself;<sup>1,2</sup> they have been repeated several times in literature.

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\* Reminiscences dedicated to Professor Vladimir Prelog on the occasion of his 90th birthday.

2. The true and important witnesses of that time have passed away: E. Votoček (1950)\*, R. Lukeš (1960)\*\*, G. J. Dřiza (1952)\*\*\*, J. Fragner (1977)\*\*\*\* and V. Hanousek (1986)\*\*\*\*\*; only one of them (J. Fragner) has published an article<sup>3</sup> containing useful information.

## I

Vladimir Prelog was 18 years old when he came to Prague in the fall of 1924 and enrolled in the Prague Institute of Chemical Technology (in fact, the Chemical Faculty of the Technical University). He quickly mastered the Czech language but in the first two years he was disappointed in his studies which »seemed to consist of endless details, compounds, and reactions without connection«. Prelog's favoured area were the general problems of the philosophy of science. He overcame this disappointment in the 3rd year of his studies when he became acquainted with Rudolf Lukeš (Figure 1) in the organic chemistry department, headed by Emil Votoček (Figure 2), professor of organic chemistry.

R. Lukeš (9 years older than Prelog) was the professor's assistant in charge of the organic chemical laboratory where practical experiments were carried out. He had just begun to carry out some independent research, when V. Prelog became first his apprentice and later his co-worker. R. Lukeš succeeded in showing to Prelog the attractiveness of experimental organic chemistry, especially in the area of heterocyclic compounds which are structurally close to some natural products, mainly alkaloids. Their first joint study was an investigation of the reaction of *N*-methylsuccinimide with phenylmagnesium bromide.<sup>4</sup> One of the products was 1-methyl-2,5-diphenylpyrrole which formed magnificent crystals. This was probably one of the crucial points in Prelog's life: ...»the awareness that he had created a new substance, something that no hands had previously touched, gave him great pleasure and desire for more such experiences«. He, therefore, spent all his free time assisting Lukeš in his research, which resulted in further original studies: structure of laevulic acid arylamides<sup>5</sup> and reactions of some

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\* Emil Votoček (1872–1950), Professor of organic chemistry at the Prague Institute of Chemical Technology; chemistry of carbohydrates was the main field of his interests.

\*\* Rudolf Lukeš (1897–1960), Disciple of Votoček and his successor to the function of professor of organic chemistry; he founded in Prague a school of the chemistry of heterocyclic compounds.

\*\*\* Gothard Dřiza (1895–1952), Czech chemist and businessman in the field of equipment for chemical laboratories and chemical reagents; his company included a laboratory for small-scale production of rare chemicals.

\*\*\*\* Jiří Fragner (1900–1977), Father of the Czech pharmaceutical research and industry, the first technical director of the natl. company SPOFA.

\*\*\*\*\* Vítězslav Hanousek († 1986), Chemical engineer and specialist in the technology of manufacturing aromatic chemicals and synthetic dyes.



Figure 1. Rudolf Lukeš (1897–1960).



Figure 2. Emil Votoček (1872–1950).

hydropyrrole derivatives with the Grignard reagent from 1,4-dibromobenzene.<sup>6</sup> V. Prelog finished his regular studies in the shortest possible time (eight semesters) – he received his degree in chemical engineering in 1928. His friendship with R. Lukeš was strong and lasting.

The next step of Prelog's studies in Prague was his attainment of the doctor's degree in chemical sciences. The theme of the thesis was not chosen by R. Lukeš but by Prof. E. Votoček who assigned him the problem of clarifying the structure of the aglycone of the glycoside rhamnoconvolvuline. V. Prelog quickly determined that the aglycone was 3,12-dihydroxypalmitic acid<sup>7</sup> and successfully passed his doctoral examination in June 1929.

J. Fragner<sup>3</sup> gives a vivid description of the place in which Prelog carried out his experiments leading to the degree: it was a doctoral laboratory called »Dáblík« (»the infernal lab«). The equipment was primitive and the atmosphere more or less terrible. The general mood was normally good but sometimes – especially when the products were unwilling to crystallize – even this was bad; this was corrected by the production of giant capillary tubes (R. Lukeš was a master in glasswork). In such days of tension, Prof. Votoček did not appear in the lab; he had his own informant on the situation and was of the opinion that difficulties had to be solved by those who had them.

There are two stories in which V. Prelog was involved. Once it went so far that Prof. E. Votoček wanted to ban Prelog from the lab for ever; he obviously had no idea that he was dealing with a future Nobel laureate. The

reason of Votoček's rage was a minor accident: with a glass rod, Prelog broke a flask containing the valuable methyl 3,12-dihydroxypalmitate which was placed in an oil bath. Hearing this, the enraged professor expelled the young man from the lab declaring that he never wanted to see him there. It was R. Lukeš who found a solution: the whole content of the oil bath was saponified with sodium hydroxide solution, the aqueous layer was acidified, the free acid isolated, purified and esterified. Prof. Votoček was surprised but reconciled and annulled his verdict with obvious relief since he liked Prelog very much.

In another story, R. Lukeš was the protagonist, with V. Prelog assisting him. R. Lukeš complained to V. Prelog that the professor (*i.e.* E. Votoček) evidently disliked him. V. Prelog could not understand why, but there was no time for discussion. At the same moment, Votoček entered the »infernial lab« in his best mood and asked the young chemists whether anybody could tell him how to synthesize an epigram. Nobody wanted to answer the strange question and Votoček explained that it was rather easy: »it was just necessary to take a gram and epimerize it.« Most of the present applauded the nice joke and the professor was happy. But, at that moment, the disturbing voice of R. Lukeš resounded in the lab: »I do not think, Sir, that this method would work«. And Votoček, astonished by this arrogance, asked: »What do you mean?«. And Lukeš explained: »To transform a gram into an epigram, it is necessary first to oxidize it with hypobromous acid to the gramonic acid which is then transformed to gramonolactone. This may be epimerized to epigramonolactone and only its reduction with sodium amalgam results in the required epigram.« After a moment of icy silence, the vain professor left the laboratory and did not appear for more than a week. And Prelog remarked to Lukeš: »And you are surprised that he dislikes you?«

In 1929, when Prelog finished his studies, economic depression reached its top and no academic positions were available. For this reason, he gladly accepted the offer of G. J. Dříza, a colleague of R. Lukeš, who was planning to start a laboratory for the production of rare chemicals and needed someone to head it. V. Prelog, thus, spent the next five years in Prague and after fulfilling his duties, he was able to continue his scientific work concentrated mainly on piperidine and piperazine derivatives, partly using diethanolamine as starting material. A special study was devoted to the characterization and identification of sapogenin from sugar beet as oleanolic acid.<sup>8</sup> Part of the experiments dealing with *N,N*-bis-(2-halogenoethyl)amines and their chemistry<sup>9-11</sup> were carried out in collaboration with his superior G. J. Dříza and were used as the basis for his doctoral thesis. V. Prelog had, thus, unofficially his first doctoral student; Prof. Votoček was the official supervisor.

The part of Dříza's company in Prague-Holešovice, headed by V. Prelog,<sup>12</sup> consisted of two laboratories for preparative work, an analytical laboratory, a room for water distillation, a library and an office. The laboratories were

quite well equipped and the library had, in addition to *Beilstein's Handbuch*, three most important journals (*Berichte der Deutschen Chemischen Gesellschaft*, *Chemisches Zentralblatt* and *Chemical Abstracts*). The social climate was excellent, the co-workers considered Prelog an outstanding colleague and advisor rather as a superior. Twice a month, discussion panels were held – very probably attended by R. Lukeš. The manufacturing program (small scale) of the unit was very diversified. In an article on the outsets of the Prague's pharmaceutical factory Interpharma, J. Tamchyna<sup>13</sup> mentioned that the analgesic *Dinarcon* (14-hydroxydihydrocodeinone) was developed in cooperation with V. Prelog during his stay in Prague.

The adamantane story<sup>2</sup> was another important event that happened during that time. While investigating the hydrocarbons of the rock-oil from Hodonin in Moravia, S. Landa (1932) of the Institute of Fuels of the Prague Institute of Chemical Technology isolated a saturated hydrocarbon C<sub>10</sub>H<sub>16</sub> melting at 266 °C, rather volatile and very stable, forming very nice tetrahedral crystals. It was named adamantane because the crystals were similar to those of the diamond. V. Prelog<sup>2,14</sup> recalls the moment when R. Lukeš intuitively in his and Landa's presence suggested the correct formula of the *sym*-tricyclodecane for adamantane and, at the same time, its synthesis starting from bicyclo (3.3.1)nonane derivatives.<sup>15</sup> S. Landa<sup>16</sup> then published a report on the discovery of adamantane for which he gave the correct structure on the basis of scarce data but not mentioning the priority of Lukeš's idea; he asserted that the structure was supported by a primitive X-ray analysis. Several years later, V. Prelog together with R. Seiwerth<sup>14</sup> confirmed the correctness of the adamantane structure by two syntheses, carried out in Zagreb. This work brought him international recognition. For a detailed description of the background of the whole story, *cf.* J. Markvart,<sup>17</sup> F. Petruš and B. Hájek<sup>18</sup> and R. Seiwerth in this issue.

In 1935, V. Prelog left Prague and accepted the post of an assistant professor at the University of Zagreb. For some time, however, he continued publishing his papers in the Czech journal "Collection".

## II

In the second part of my reminiscences, I certainly have no intention to reproduce V. Prelog's biography. On the other hand, our rather regular encounters and other personal contacts in a way reflect his life's career from the viewpoint of his position, development of his scientific work, working possibilities, contacts with Prague *etc.*

It was at the end of the war that I came across the name of V. Prelog and his publications in chemical literature. I first met him in May 1946 in Basle as a member of a small Czech delegation participating there in a bio-

chemical conference.<sup>19</sup> At that opportunity, we visited in Zürich the world-known »Laboratorium fur organische Chemie« of The Swiss Federal Institute of Technology. Prof. Prelog offered K. Wiesner and me to spend some time in his laboratories as post-graduate students.

At the end of March 1947, Prof. V. Prelog visited Prague and gave a series of three lectures:<sup>20</sup>

- On steroids in animal tissues,
- On multimembered rings, and
- On approaches to the structure of strychnine.

After the second lecture, a colloquium was devoted to general discussion in which Prof. Prelog answered with humour and in perfect Czech many questions dealing with all research phases in an organic chemistry laboratory. After the third lecture (held at the Prague Institute of Chemical Technology, *i.e.* in the new building of the Institute where Prof. Prelog graduated in 1928), a touching meeting of Prof. Prelog and his old teacher, Prof. E. Votoček, came about. This was my second meeting with Prof. Prelog and on that occasion the term of my future stay at the E. T. H. in Zürich was agreed upon in the presence of my superiors, J. Fragner and M. Herold.

My third »meeting« with Prof. Prelog lasted 6 months, *i.e.* from May to October 1947, during my post-graduate stay in his laboratory at the E. T. H. in Zürich.<sup>19</sup> There, I had all rights and duties of the E. T. H. students and was in daily contact with Prof. Prelog, who, himself, introduced me to the craft – or art – of experimental organic chemistry from the preparation of an experiment to the isolation of the products and preparation of the samples for analysis. My stay started with four very pleasant days in Ascona (near Lugano), where I was invited by the Prelogs together with K. Wiesner, his wife and E. Knobloch. Back in Zürich, I got a place in the laboratory together with K. Wiesner and two Swiss colleagues. In June, F. Šorm came from Prague and spent three months with us in the same laboratory. There were three different topics of my experimental work:

- Catalytic hydrogenation of julolidine and separation of the mixture of hexahydrojulolidines obtained by fractional crystallization of the picrates; homogeneous picrates of stereoisomers A and B were obtained,
- An attempt to prepare dipeptides in aqueous medium which did not give useful results, and
- Synthesis of a greater amount of racemic phenylalanine and its resolution with brucine to enantiomers.

I had no more time to continue this work and my products were used by Z. Vejdšek, my Czech successor in Prelog's laboratory. The stay in Zürich enabled me to become acquainted not only with the Institute's Director Prof. L. Ružička, but also with the other important persons there, especially Pl.



A. Plattner, O. Jeger, E. Hardegger, G. Buechi, A. Fürst *etc.*, which later proved important for my further career. I attended all colloquia at the Institute and came in touch with several distinguished guests from abroad. I had the rare opportunity to work in the atmosphere of one of the most important centres of the chemistry of natural products and, thanks to Prof. Prelog, I returned to Prague with sufficient knowledge and experience to form a proper methodical basis for the experimental work of the team I led in Prague.

The following eight »dark« years made it impossible for me to keep up personal contacts with Prof. Prelog; correspondence was the only way. At the beginning of 1949, Prof. Prelog decided to publish our results on the hydrogenation of julolidine; I sent him the experimental part and my only paper with Prof. Prelog appeared.<sup>21</sup>

In August 1950, I proposed – with J. Staněk – to Prof. O Tomiček, at that time Chairman of the Prague section of the Czech. Chemical Society, to elect Prof. Prelog an honorary member of our Society. The proposal was motivated by his studies and activity in Prague, by his firm friendly relations to Czech chemists, and by his scientific achievements. Our proposal was accepted by the General Meeting of the Czech. Chemical Society in Brno (Sept. 1950) and the Honorary Membership was conferred on him.<sup>22,23</sup>

After eight years of hard political conditions in our country, I was at last allowed to attend the 14th International Congress of Pure and Applied Chemistry in July 1955, which took place in Zürich. Landing in Zürich, I could not resist a strong emotion realizing that I was coming to a free country. After the arrival, I was almost constantly in contact with Prof. Prelog. It was really a memorable congress with several hundreds of participants, most of them the cream in the organic chemical field. The most memorable event for me, to which I was invited thanks to Prof. Prelog's kindness, was the informal reception organized by Prof. Ružička in the Institute's Library for about 150 selected participants, where it was possible to meet and speak with anybody without any inhibition.

In April 1956, I sent Prof. Prelog a copy of my monograph on antihistamine agents. Prof. Prelog replied in a letter that very early, as a coworker of the company Kaštel in Zagreb, he had also been involved in the synthesis of potential antihistaminics and wished me success in our efforts. In July 1957, *i.e.* approximately at the time he became head of the Organic Department in Zürich, we shortly met in Paris at the 16th International Congress of Pure and Applied Chemistry. The following year we exchanged letters on the possibility of accepting some younger Czech chemists for a short (one year) post-graduate study at the E. T. H. Institute in Zürich. Prof. Prelog's standpoint was negative and justified by the strong anticommunist mood in Switzerland after the events in Hungary in 1956. Nine years later, we again discussed the possibility of scholarships for young chemists in Zürich. In principle, Prof. Prelog did not disagree but there were several obstacles:

state scholarships were granted exclusively to Swiss chemists; American scholarships were rare and granted only to those warranting the highest quality and prospects for the work progress; the growing danger of misuse of scholarships by students wishing to emigrate from unfree countries (this was considered by Prof. Prelog as a failure of his efforts to increase the scientific level in such countries).

In August 1962, Prof. F. Šorm was the main organizer of the 2nd International Symposium on the Chemistry of Natural Products in Prague, which was very successful and attended by many outstanding scientists in the field.<sup>24</sup> Prof. V. Prelog came with his wife and I took part in welcoming them. The topic of Prelog's lecture was »stereochemistry and reactivity of medium size ring compounds«. A Symposium Dinner was held at the Smetana Hall in the centre of Prague and there I parted with the Prelogs, who left Prague before the official end of the Symposium.

In 1966, Prof. Prelog celebrated his 60th birthday, which was mentioned in a short article.<sup>25</sup> Describing his qualities and achievements, I stressed the fact that he was not only a brilliant chemist but also a splendid man who was able to assist his co-workers and friends to solve their personal problems and unable to cause grief. On that occasion, Prof. Prelog was awarded the Hanuš medal by the Czech. Chemical Society.<sup>26</sup>

In October 1975, Prof. Prelog was awarded the Nobel prize,<sup>27</sup> the highest appraisal of his scientific achievements. I congratulated him and my colleagues in Prague published two articles<sup>15,28</sup> about this memorable event.

Since then and out of a number of encounters we have had, I would like to mention just one from 1978. Despite a signed petition in Zürich which the Czechoslovak government might not have liked, Prelog obtained a visa and arrived in Prague at the beginning of November. The next day, he was received with great ceremony in the main lecture hall of the Prague Institute of Chemical Technology, and then awarded the Emil Votoček Medal of the Institute. He then gave a lecture on natural and synthetic ionophores, notably boromycin. In the evening, the distinguished guests visited me at home and we had a wonderful time together. I had the opportunity to show Prof. Prelog my chemical library, including the *Beilsteins Handbuch* and numerous volumes of *Chemisches Zentralblatt* which had formerly been part of Dříza's library and probably used by Prof. Prelog every day some 50 years before. The next day, we went to Liblice where Prof. Prelog opened the Meeting on Stereochemistry, organized by the Czech. Chemical Society, with his lecture »Second thoughts about the specification of molecular chirality«. It was only during our next meeting that I heard about the shameful scene at the Prague Airport where the police delayed the flight in order to inspect very carefully Prelog's luggage. This was probably the reason why the Prelogs refused to accept any further invitation to Prague, even after 1989.



In 1986, Prof. Prelog celebrated his 80th birthday and I was happy to be able to attend the celebration, in June in Zagreb and then in September in Zürich. The jubilee was remembered by O. Červinka<sup>29</sup> and V. Herout<sup>30</sup> who again emphasized the importance of Prof. Prelog for Czech chemistry. Five years later, Prof. Prelog was visited in Zürich by a delegation from the Prague Institute of Chemical Technology which conferred on him the honorary doctor's degree of this Institute.<sup>31</sup>

Now, the moment has come for me to wish Prof. Vladimir Prelog good health and continued interest in the topics that have accompanied him throughout his life. At the end, I would like to say what my short stay in Prof. Prelog's laboratory in Zürich in 1947 and the following contacts meant for my life. They have influenced all my life. Whenever and wherever I met chemists in the world, and mentioned that I belong to the group of Prelog's students and friends, I was immediately one of them because one or more of them have been connected with E. T. H. or directly with Prof. Prelog. The doors opened which otherwise would have been closed. The acquaintance with Prof. Prelog was one of the chances that have definitely affected my life. I thank him.

## REFERENCES

1. V. Prelog, *Gedanken nach 118 Semestern Chemiestudium, Chemie und Gesellschaft*, Forum Philippinum 1983, p. 57. Wissenschaftliche Verlagsgesellschaft, Stuttgart, 1984.
2. V. Prelog, *My 132 Semesters of Chemistry Studies*, in: J. I. Seeman (Ed.), *Profiles, Pathways, and Dreams*, American Chemical Society, Washington, DC 1991, pp. 7–20.
3. J. Fagner, *Chem. Listy* **70** (1976) 1032.
4. R. Lukeš and V. Prelog, *Chem. Listy* **22** (1928) 244; *Proc. Czech. Acad. (II)* **36** (1927) 41; *Collect. Czech. Chem. Commun.* **1** (1929) 334.
5. R. Lukeš and V. Prelog, *Chem. Listy* **24** (1930) 251; **25** (1931) 76 and 101; *Proc. Czech. Acad. (II)* **39** (1930) 3; **40** (1931) 39; *Collect. Czech. Chem. Commun.* **1** (1929) 282 and 617.
6. R. Lukeš and V. Prelog, *Chem. Listy* **24** (1930) 277; *Proc. Czech. Acad.* **39** (1930) 4.
7. E. Votoček and V. Prelog, *Chem. Listy* **25** (1931) 489; *Collect. Czech. Chem. Commun.* **1** (1929) 55.
8. V. Prelog, *Chem. Listy* **25** (1931) 393; *Collect. Czech. Chem. Commun.* **2** (1930) 414; **5** (1933) 165; *Proc. Czech. Acad. (II)* **40** (1931) 44.
9. V. Prelog, G. Dříza, and V. Hanousek, *Collect. Czech. Chem. Commun.* **3** (1931) 578.
10. V. Prelog and G. J. Dříza, *Collect. Czech. Chem. Commun.* **4** (1932) 32.
11. V. Prelog and G. J. Dříza, *Collect. Czech. Chem. Commun.* **5** (1933) 497.
12. V. Gryc, *Přispěvky k Historii Čs. Chemického Průmyslu* **10** (1982) 159.
13. J. Tamchyna, *Přispěvky k Historii Čs. Chemického Průmyslu* **20** (1991) 190.
14. V. Prelog and R. Seiwert, *Ber. Dtsch. Chem. Ges.* **74** (1941) 1644 and 1769.
15. O. Červinka and M. Ferles, *Chem. Listy* **70** (1976) 435.

16. S. Landa, V. Macháček, and J. Mžourek, *Chem. Listy* **27** (1933) 415; *Collect. Czech. Chem. Commun.* **5** (1933) 1.
17. J. Markvart, *Dějiny Věd a Techniky* **23** (1990) 1.
18. F. Petřů and B. Hájek, *O Vývoji České Chemie*, Orbis, Praha, 1954, pp. 94 and 134.
19. M. Protiva, *Chem. Listy* **40** (1946) 147; **85** (1991) 1020.
20. Anonym, *Chem. Listy* **41** (1947) 148.
21. M. Protiva and V. Prelog, *Helv. Chim. Acta* **32** (1949) 621.
22. R. Lukeš and J. Staněk, *Chem. Listy* **44** (1950) 242.
23. O. Hanč, *100 Let Československé Společnosti Chemické, Její Dějiny a Vývoj*, Academia, Praha, 1966, p. 71.
24. V. Herout, *Chem. Listy* **57** (1963) 217.
25. M. Protiva, *Chem. Listy* **60** (1966) 934.
26. O. Hanč and J. Tomko, *Československá Společnost Chemická 1966–1975*, Academia, Praha, 1980, p. 25.
27. L. K. James (Ed.), *Nobel Laureates in Chemistry 1901-1992*, American Chemical Society, 1993, p. 378.
28. O. Červinka, *Sborník VŠCHT v Praze, A*, **16** (1977) 45.
29. O. Červinka, *Chem. Listy* **80** (1986) 659.
30. V. Herout, *Chem. Listy* **80** (1986) 662.
31. O. Červinka, *Chem. Listy* **86** (1992) 68.

## SAŽETAK

### Praške godine Vladimira Preloga i moji kasniji kontakti s njim

*Miroslav Protiva*

Opisane su okolnosti u kojima je V. Prelog studirao i radio u Pragu, i neka zbivanja u kojima je sudjelovao, kao i autorova sjećanja na njegove brojne kontakte s Prelogom.