Toxicity of phosphor esters: Willy Lange (1900–1976) and Gerda von Krueger (1907–after 1970)

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In 1851 Williamson serendipitously discovered a new and efficient way to produce ethers using ethyl iodide and potassium salts. Based on this new synthetic approach, the Frenchman Philippe de Clermont and the Muscovite Wladimir Moschnin, both élèves de Adolphe Wurtz in his Paris School of Chemistry, achieved the synthesis of the first ester of pyrophosphoric acid (TEPP). de Clermont “tasted” the new compound and although TEPP is a potent cholinesterase inhibitor he failed to recognize its toxicity. Almost a century later, in 1932, Willy Lange (1900–1976) and his graduate student Gerda v. Krueger (1907–after 1970) described the toxicity of organophosphonates. While the classic paper of the two “Über Ester der Monofluorphosphorsäure” is cited by almost everybody working in the field, little is known about Lange and almost nothing about v. Krueger. This brief communication attempts to shed some light on the life of both.

1. Introduction

The synthesis of the first ester of phosphoric acid (organophosphate) is widely attributed to the Frenchman Philippe de Clermont (1831–1921) and the Muscovite Wladimir Moschnin (died 1889). These two noblemen were both élèves de Adolphe Wurtz (1817–1884) in his Paris school of chemistry (Holmstedt, 1963; Carneiro 1992) and probably knew each other from Giessen, Germany, where their chemistry studies briefly overlapped in the summer semester of 1852 (Petroianu 2008). Each of them independently synthesized tetraethyl pyrophosphate (TEPP) by reaction of the silver salt of pyrophosphoric acid with ethyl iodide (Williamson method, Williamson 1851, 1852). While only de Clermont published his TEPP-related work, he acknowledged Moschnin’s earlier success (de Clermont 1854, 1855).

TEPP’s prominence is related to the extreme toxicity of most organophosphates, the substance class to which TEPP belongs. TEPP is considered nowadays to be the first organophosphate inhibitor of cholinesterases. Of course neither the toxicity nor the mode of action of the new compound was known at the time, as evidenced by de Clermont’s willingness to taste his product, which he describes as a sticky liquid with a burning taste and a peculiar odor (“un liquide visqueux d’une saveur brulante (et) d’une odeur particulière”). It would be almost a century later, in 1932, that Willy Lange (Fig. 1) and his graduate student Gerda v. Krueger, working on the synthesis of esters of monophosphonic acid would recognize the toxicity of this class of compounds: “the fumes of these compounds have a pleasant, slightly aromatic odor. But a few minutes after inhalation there is a feeling of pressure to the larynx and difficulty in breathing. Then a disturbance of consciousness develops, as well as blurred vision and a painful over-sensitiveness of the eyes to light. Only after several hours do the problems wear off. They are apparently not caused by acidic products of a possible decomposition, but by the esters themselves. The effects are produced by very small amounts.” (Lange and von Krueger 1932, Fig. 2).

While the paper the two published “Über Ester der Monofluorphosphorsäure” is cited by almost everybody working in the field, little is known about the authors. This brief communication attempts to shed some light on the life of the two.


The city of Itzehoe in Holstein at the northern tip of Germany is in the vicinity of “Loher Heide” a tract of land used since 1867 by the Royal Prussian Army as artillery training grounds. Itzehoe was since 1891 also the garrison city for the 9th Field Artillery Regiment. It is January 11th, 1907 that Gerda Anne-Marie Minna Elisabeth v. Krueger is born in Itzehoe (Fig. 3); her father is the artillery officer Alfred v. Krueger while her mother Wilhelma is a born Krichauff.

2.1. Mother’s family

The Krichauffs were a large and prominent Northern German/South Danish family related by marriage to the Alsen cement dynasty. Otto Friedrich Alsen and his homonymous son established 1863 the Portland Cement factory in Itzehoe, one of the early German industrial success stories and the major employer in Itzehoe. The younger Otto Friedrich (1805–1872) marries 1833 Henriette Wilhelmine Dorothea Schmidt, the daughter of a ship owner from Flensburg. One of their daughters, Mina Alsen (died 1917), marries Carl Christian W.E. Krichauff (1848–1899) who joins the management of the cement factory. Their son Willy Alsen (1872–1932) establishes 1899 the Portland Cement factory in Itzehoe, one of the early German industrial success stories and the major employer in Itzehoe. The younger Otto Friedrich (1805–1872) marries 1833 Henriette Wilhelmine Dorothea Schmidt, the daughter of a ship owner from Flensburg. One of their daughters, Mina Alsen (died 1917), marries Carl Christian W.E. Krichauff (1848–1899) who joins the management of the cement factory.

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were supposed to reside in the Villa Clara (Talstrasse No. 16, Itzehoe) a superb purpose built “designer home” but he passes away shortly before the construction is finished. Minna will reside in the villa until her death whereupon the house is donated to the city contingent on being used for non-profit purposes. The building survived the war and can be visited.

Their daughter Wilhelma Therese Marie Isidora Krichauff (born in Itzehoe, January 14th, 1882) is the mother of Gerda.

2.2. Father’s family

In 1825, Carl Eduard Robert Krueger (*1797 in Hamburg, †1868), a retired Royal Prussian army captain who served in the Napoleonic liberation wars (Befreiungskriegen), becomes a civil servant (Domaenen Rent Meister and 1837 Amtsrath) in Marienburg; with this position goes an official residence located in the Teutonic Marienburg (Malbork) Castle in Western Prussia. The castle was founded in 1274 by the Teutonic Order during their government of Prussia and is located on the Southeastern bank of the river Nogat. After the Marienburg period the family moves 1848 to Wittenberg where the father joins the University administration (Universitaetsverwalter).

While little is known about his private life, his passion for organ music is well documented; he was instrumental in arranging funding for Friedrich Ladegast (1818–1905), probably the best...
organ-builder of the time, to build the organ in Wittenberg. He passes away at age seventy after suffering a stroke. He is survived by his wife Emma (born Bever) and their seven children (four daughters).

Best known is the fourth child, Carl Nikolaus Adalbert (1832–1896), born in Marienburg Castle who becomes a Professor of Astronomy in Kiel. Also born in the Castle on September 3rd 1835 is Robert Adolf Hermann (1835–1917) who joins the Royal Prussian army. The battle of Mossunle (February 2nd, 1864) in the opening days of the Second Danish-German War was a turning point in the career of Second Lieutenant Krueger from the 3rd Artillery Brigade, Adjutant to Colonel Colomer, the Chief of Artillery: for bravery during the battle Hermann Robert Adolf Krueger1 (1835–1917) was elevated to nobility on March 10th 1864 (Briclade) by King Wilhelm I of Prussia. The subsequent military career was steep; the final position being that of the commanding officer of the Pommeranian Field Artillery Regiment Nr. 2. Since 1886 in the rank of a colonel. 1890 Hermann von Krueger retired from active duty in the rank of a General Major.

September 3rd 1867 he married in Muenster Katharina Bernhardine Marie Boele (*Unna, Oct 9th, 1841–1883 Stralsund) hailing from a prominent catholic family from Westphalia. Re-assigned to the 10th Field Artillery Regiment (First Hanoveran) in Hannover two children are born there: Alfred Eduard Marie v. Krueger, Gerda’s father, (March 21st, 1872, Bache) and Elisabeth (born June 5th, 1872). Both will remain at the same address until December 1957 when she moves to Berlin as residing in Wilmersdorf, Dueseldorfer street # 1.

Alfred Eduard Marie v. Krueger follows the family’s military and artillery tradition: From 1896 to 1899 second-lieutenant v. Krueger is adjutant of the commanding officer of the 3rd unit (III. Abteilung) of the 9th Field Artillery Regiment (Schleswig) (Schleswig-Holstein Regiment Nr. 9, 1901 renamed Regiment General Field Marshall Count Waldsee). 1907–1908, in the meanwhile promoted to captain, v. Krueger is commanding officer (Batterie Chef) of the 3rd mobile battery (fahrende Batterie) in Itzehoe. After 1910 Alfred v. Krueger, now a retired captain, is recorded in the address book of Berlin as residing in Wilmersdorf, Dueseldorfer street # 1. Starting 1923 Alfred v. Krueger is listed as a retired major. Since 1933 he is recorded in the address book of Berlin as residing in Friedenau, Bache2 street # 3; Gerda resides at the same address until December 1957 when she moves to Wohnung 1, Schützallee 108 in Berlin 37 (Zehlendorf) where she remains at least until 1970.

During the early years in Gerda’s life (up to 1917) her grand- father the General Major also resided in Berlin, in Friedenau, Kaiserralleu Nr. 74, of the best addresses in the Capital at the time.

2.3. School years

The early school years of Gerda are listed in detail in the curriculum vitae (Lebenslauf) included in her doctoral thesis. She writes: “I attended the private pre-school of Ms. M.”


2 Friedrich Bache (1841–1917) secret chancellery council, was a politician from Berlin-Friedenau. During his life time (1910) the local council decided to honor him by renaming the street # 12 to Bache street.

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Fig. 5: Gerda von Krueger's name appears in the impressum (legal disclosure) of the "Chemisches Zentralblatt" first 1942, then 1943.

Baumgarten (1896–1943) is accepted as an extraordinary member of the Society. In 1948 she becomes an ordinary member of the Society (1848); she leaves the Society in June 1970 (Fig. 4). The Doctoral examination is June 1st, 1933; the thesis is reviewed by PD Lange and Professor Wilhelm Schlenk (1879–1943, Tidwell 2001).

Gerda von Krueger’s vita during the war years is fuzzy: after receiving the doctoral degree she leaves the university and we find her 1938 reviewing for "Fette und Seifen", the official journal of the "German Society for Fat Research" (Deutsche Gesellschaft für Fettforschung) in Münster, Westphalia. She publishes two papers (one dealing with products derived from whales to be used for illumination, the other one dealing with shaving products [Rasiermittel]); on both papers the address of the author is given as being Münster in Westphalia (v. Krueger 1938 a, b). In the early forties she returns to Berlin where she joins the editorial team of "Chemisches Zentralblatt". We find her name in the impressum (legal disclosure) of the "Chemisches Zentralblatt" first 1942, than 1943 (Fig. 5; top row), than again 1948 (middle row), 1950 (bottom row), and then finally 1966. Especially in the years immediately after the war her contribution to the journal was impressive, reviewing and abstracting literally dozens if not hundreds of papers. In 1954 her name also appears in the impressum of "Angewandte Chemie" (Applied Chemistry).

3. Willy Lange (1900 – 1976)

Nothing is known to me about Lange’s family or school years. Born in Berlin October 31st, 1900, he studied chemistry at the Friedrich-Wilhelms-University of Berlin, Germany. His Ph.D. thesis accepted 1923 had two components and was titled was "I. Ueber die bei der Einwirkung von konzentrierter Schwefelsäure auf Fluorspat sich abspielenden Reaktionen" and "II. Beiträge zur Kenntnis der Fluoridionsäuren" or "I. About the action of concentrated sulfuric acid on fluorapat" and "II. Contributions to the knowledge of fluorosulfonic acid". 

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Fluor spar (fluorite) is a mineral composed of calcium fluoride. Subsequently he became assistant to Professor Wilhelm Traube and was awarded the “venia legendi” in 1930 and thus became a Privatdozent. Gerda von Knueger must have been his first (if not only) doctoral student. In 1925 he married a colleague from the Chemical Institute, Lilli Baerman (1901–1982). Due to the race policies of the time, he had to leave academia and eventually emigrated to America Lange became first Research Associate and then Associate Professor at the University of Cincinnati [UC] in Ohio while subsequently moving to The Procter & Gamble Company (P&G) in the same city as a Research Chemist (1940), Head of oil research section 1945 and eventually Associate Director of Research (1956). Upon his retirement from P&G in 1965 he returned to UC as a Research Professor (Fig. 6).

Dr. Lange was the 1958 recipient of the Cincinnati Section, American Chemical Society (ACS) Eminent Chemist Award. He was a member of the ACS, the American Oil Chemists Society, the American Chemical Society (ACS)'s National Historic Chemical Landmark Program, the Collectors Club of New York (Philately). While this short communication does not exhaustively answer the questions “who was Lange?” or “who was von Knueger?” it should satisfy the idle curiosity of most researchers. For those wishing to know more, it gives some direction for future investigations.

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References


Fig. 6: Application letter to the University of Cincinnati dated September 15th, 1965 containing a reference to his main contribution to science. The letter gives also the address at which Dr. and Mrs. Lange resided and ends with Willy Lange’s signature.

We reside at 2832 Roberts Avenue Mt. Airy.
Sincerely yours,
Willy Lange

PROOFREAD: (at that time unknown), I discovered the fluorophosphate esters of which stimulated large-scale research in industrial laboratories and thus became the forerunners of the modern phosphorus-containing systemic insecticides. Political reasons forced me to leave the academic career. I became...