

4. Extraction and isolation

The fermented whole broth (50 L) was filtered through cheesecloth to separate into supernatant and mycelia. The supernatant was extracted with ethyl acetate, while the mycelia were extracted with 70% acetone-aqueous. The acetone solution was concentrated under reduced pressure to afford an aqueous solution, which was extracted with ethyl acetate. Both ethyl acetate solutions were combined and concentrated under reduced pressure to give a crude extract (77.7 g). The crude extract was separated into eight fractions on a silica gel column using a step gradient elution of $\text{CHCl}_3/\text{MeOH}$. Fraction 7 was chromatographed on a Sephadex LH-20 column with 50% $\text{CHCl}_3/\text{MeOH}$ to give six fractions, the fourth fraction was purified by semipreparative HPLC (40% $\text{MeOH}/\text{H}_2\text{O}$) to give compound **1** (26 mg). (3*S*, 11*aS*)-3-[(1*H*-Indol-3-yl)methyl]-7, 9-dihydroxy-8-methoxy-2,3,11,11a-tetrahydro-6*H*-pyrazino[1,2-*b*] isoquinoline-1,4-dione (**1**): Amber amorphous solid; $[\alpha]_D^{20}$ -228.7 (c 0.100, MeOH); HRESIMS m/z 408.1574 for $[\text{M} + \text{H}]^+$ (calcd for $\text{C}_{22}\text{H}_{21}\text{N}_3\text{O}_5$, 408.1559); IR (KBr) ν_{max} 3350, 2928, 1658, 1452, 1343, 1246, 1079 cm^{-1} ; UV (λ_{max} , MeOH): 217 (4.30), 269 (3.99); ^1H and ^{13}C NMR ($\text{DMSO}-d_6$, 600 MHz and 150 MHz) see Table 1.

5. Amino acid analysis of hydrolysate of **1**

Compound **1** (1 mg) was dissolved in 6*N* HCl (1.5 ml) and heated to 110 °C for 24 h in a sealed tube. The excess HCl was removed under vacuum. The dry hydrolysate was dissolved in H_2O for chiral HPLC analysis. The chiral HPLC analysis was carried out using a CROWNPAK® CR (+) column [Column Size, 4 × 150 mm; flow rate, 1.2 mL/min; eluent, HClO_4 , PH 2; detection, UV at 210 nm; column temperature, 30 °C]. Retention times of standard L- and D-Try, hydrolysate of **1** were 26.11, 21.82 and 26.12 min, respectively.

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The history of cholinesterase inhibitors: who was Moschnin(e)?

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The synthesis of the first organophosphate cholinesterase inhibitor (tetraethyl pyrophosphate, TEPP) is often credited to the French organic chemist Philippe de Clermont, working in the laboratories of Adolphe Wurtz in Paris. The two de Clermont's publications dealing with TEPP clearly state however that the first synthesis of TEPP was achieved by another student of Wurtz, named Moschnine. While de Clermont is well known, nobody really knows who Moschnine was. This brief communication attempts to give an overview about the life and achievements of the Russian chemist Wladimir Petrovich Moshnin from Moscow.

Most people interested in organophosphorus cholinesterase inhibitors and their history will be familiar with Bo Holmstedt's chapter in Koelle's Textbook "Cholinesterases and Anticholinesterase Agents" published almost half a century ago (Holmstedt, 1963). It contains a superb account of the synthesis of the first organophosphate cholinesterase inhibitor (tetraethyl pyrophosphate, TEPP) by the French organic chemist Philippe de Clermont (1831–1921), working in the laboratories of Adolphe Wurtz (1817–1884) in Paris. Paragraphs from the two de Clermont's publications dealing with TEPP are reproduced by Holmstedt, including de Clermont's statement that TEPP was actually synthesized earlier by another student of Wurtz, named Moschnine (de Clermont, 1853, 1855). Holmstedt concludes his remarks dealing with the very early days of organophosphate chemistry by noting that "Nobody knows who Moschnine was."

Confronted with this blunt statement in my early professional years, I refused to accept the reality and spent time off and on unsuccessfully searching for Mochnine, Moshnin, or Moschnin.

Some twenty years of sporadic and futile search efforts came to an end through my contact with a young Portuguese researcher, Ana Carneiro, author of a Ph.D. thesis entitled "The Research School of Chemistry of Adolphe Wurtz," who not only sent me a copy of her work, but also patiently answered my questions. Through her, I obtained two hints that allowed me to identify the elusive Moschnin (Carneiro 1992).

First, she pointed the way to Charles Friedel's introductory remarks to Wurtz's book *La Theorie Atomique* (1886).

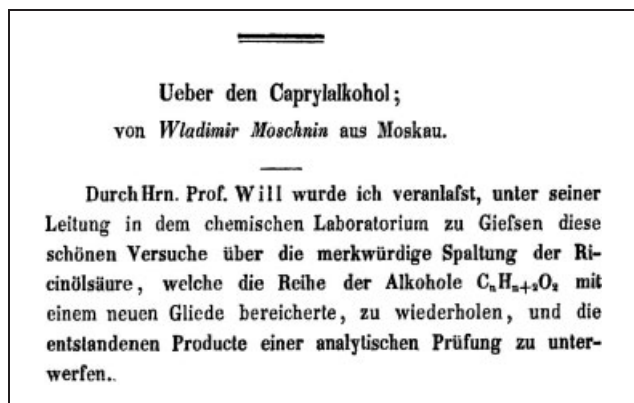


Fig. 1: The 1853 paper on capryl alcohol (octanol) authored by Moschnin, possibly the only organic chemistry paper he ever published

(These remarks also served as an obituary for Wurtz, who had died two years earlier.) Friedel (1832–1899) pointed out that on the occasion of Wurtz's election to the French Senate, his former students (*élèves*) presented him with a bronze statuette by Louis Ernest Barrias (1841–1905) representing the French artist Bernard Palissy (1510–1589). On the base or pedestal of the statuette were engraved the names of the one hundred and eleven Wurtz *élèves*. Friedel lists them all, among them that of Moschnin, including his (to me) hitherto unknown initials, W.P. (Friedel, 1886).

More importantly, Ana Carneiro quotes a paper on capryl alcohol (octanol) authored by Moschnin, possibly the only organic chemistry paper he ever published (Moschnin 1853, Fig. 1).

The publication, written in German, was authored by a "Wladimir Moschnin" from Moscow and reports on work done in Giessen, Germany, under the supervision of Professor Will. At the time (1852–1853), Heinrich Will (1812–1890) was the "Ausserordentlicher Professor" at the "Grossherzoglichen Hessischen Ludewigs Universitaet"; he was soon to follow Justus von Liebig (1803–1873) as Director of the Chemistry Laboratory. The superb archives of Giessen University allowed me to trace Moschnin's presence in Giessen.

He enrolled as a chemistry student in the summer semester of 1852 and rented accommodation in the house of the widow Bott. Interestingly enough, Philippe de Clermont was also a student in Giessen at the same time, so the two most probably have known each other. While de Clermont left Giessen after that summer, Moschnin stayed on for two more terms, but changed his accommodation (to the house of the merchant Hasst).

When exactly Moschnin joined Wurtz in Paris is not known, but most probably it happened around 1853–1854 (Carneiro 1992). The only known traces of his presence in Paris are the pedestal of the Barrias bronze and the double mention in de Clermont's papers.

After returning to Russia in the late 1850's or early 1860's, Moschnin was awarded a Master's Degree for work performed abroad by the Department of Chemistry of the Imperial Moscow University, headed by Professor N.E. Lyaskovskiy (1816–1871). Oddly enough, Lyaskovskiy was interested in (among other things) the presence of straight-chain carboxylic acids (capronic, caprylic and capric) in cheese, while Moschnin's single known publication dealt with capryl alcohol.

Moschnin taught chemistry at the Alexandrine Orphan Military (Cadet Corps) School, which in 1863 merged with the Aleksandrovskiy Military School (Fig. 2).



Fig. 2: The Aleksandrovskiy Military School where Moshnin taught chemistry

By and large, Moschnin's position in Russian chemistry was deemed important enough to prompt Mendeleev (1834–1907) to mention his name together with those of other, better known contemporary chemists: Voskresenski, Khodenev, Lyaskovskiy, Ilin, Shishkov and Sokolov (Mladentsev and Tischenko 1938; Dmitriev 2007). Moschnin's subsequent activities were less related to bench work and more in line with his aristocratic origins, wealth, and status in Muscovite society. His interests spanned science, business and culture.

He was an active member (elected full member on October 3rd, 1870) of the Imperial Society of Amateurs of Natural Science, Anthropology and Ethnography, one of the early learned societies, founded in Moscow in 1863. In the Proceedings [published from volume 1: 1866 to volume 128: 1914] Moschnin's many contributions are recorded. Best known is his speech delivered on 17 (29) March of 1880 in support of Pavel Yablochkov (1847–1894) and his "electric candle" (a type of electric carbon-arc lamp that was in competition with Edison's filament lamp). In the minutes of the meeting it was noted that: "V.P. Moshnin focused the attention of the meeting on the fact that American advertisements about ... inventions made supposedly by Edison in the area of electrical illumination, induce the public into error about the real state of this question, and impede the success of the already developed methods of electrical illumination, including – Yablochkov's method". The functioning of Yablochkov's



Fig. 3: Around 1880, the Moschnin family moved to a new home on the Karetniy Row No. 3 (Каретный ряд). This new location also housed the so-called Moshninka Theater where cultural events were organized

electric candle was demonstrated, as street illumination, during the Paris Exhibition of 1878, on the Avenue de l'Opéra.

In 1889, the Natural Science branch of the Society established a prize bearing the name of Vladimir P Moshnin (премия имени В. П. Мошнина): The fund had a capitalization of 8000 rubles, while the prize itself was 300 rubles. Among the contributors to the fund were Nadejda Konstantinovna (Moschnin's wife) and Konstantine Vladimirovich (his son). The prize was to be awarded to chemists and to physicists. One of the first laureates was N. P. Kasterin (1869–1947), who was awarded the Prize twice, in 1892 for studies regarding the surface tension of liquids at high temperatures and in 1898 for work on the reflection of acoustic waves by metallic bodies at low temperatures. Kasterin also received in 1895 the Rastsvetov Prize from Moscow University for the determination of the capillary constant and of the contact angle of drops; Rastsvetov (1823–1902) was the Chairman of the Anthropological Branch and Vice-Chairman of the Society of Amateurs of Natural Science, Anthropology and Ethnography.



Fig. 4: Vladimir's son (Konstantin; 1861–1921) who graduated from the Imperial Moscow Technical School (ИМТУ) in 1882 as a mechanical engineer

Other recipients of the Moshnin Prize are E. I. Spitalski (electrochemistry), W. A. Michelson (thermal radiation), I. F. Usagin (transformation of currents, awarded 1897), K. A. Krasuski (chemistry, awarded 1901), W. D. Zernov (air oscillation, awarded 1904), and I. I. Ostromyslenskiy (synthetic rubber, awarded 1910).

Moschnin was a high-ranking civil servant (Class IV in the Tsarist hierarchy) with the title of "Actual State Counselor", the civilian equivalent of a major general. As such, he had the privilege to be addressed as "Your Excellency" (Ваше превосходительство) and enjoyed hereditary nobility.

Following the tenure of A. P. Shipov (1864–1875) as Chairman of Nizhny Novgorod Fairground Committee, Moschnin filled that post from 1875 to 1881. This was a very prestigious and influential position at the time.

Around 1880, the Moschnin family moved from their property on the Vvedenskiy alley to a new home on the Karetnyi Row (Каретный ряд). This new location also housed the so-called Moshninka Theater where cultural events were organized (Fig. 3). Moschnin became a major figure in Moscow artistic circles.

Details about his family are scant. His father was (probably) Peter Nikitich Moshnin, a well-off Moscow merchant. With his wife Nadejda Konstantinovna, Vladimir had a son (Konstantin; 1861–1921) who graduated from the Imperial Moscow Technical School (ИМТУ) in 1882 as a mechanical engineer (Fig. 4).

Konstantin (and Moshnin's widow Nadejda) lived in the Karetnyi Row house in Moscow and taught (like his father before him) at the Aleksandrovskiy Military School. Konstantin's claim to fame is based on his contribution to dog breeding for hunting purposes, the editorship of a hunting journal and his support for cultural activities at the Karetnyi Row estate.

Vladimir Petrovich Moschnin died in 1899 or 1900.

It is highly unlikely that Vladimir was related to the (much better known) Moshnin family from Sarov. They gave Orthodoxy one of its most popular saints, Saint Seraphim of Sarov, whose worldly name was Prohor Isidorovitch Moshnin (1758–1833).

While this short biographical note does not exhaustively answer the question "who was Moschnin?" it should satisfy the idle curiosity of most researchers. For those wishing to know more, it gives some direction about where to look.

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