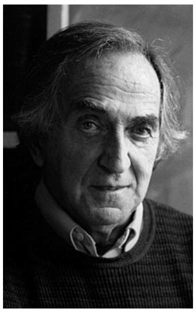
Leslie E. Orgel (1927–2007)

Leslie E. Orgel passed away in October 2007 at age 80. He gained early recognition with his contributions to ligand-field theory; the Orgel diagrams named after him are today still part of the curriculum in inorganic chemistry. He later laid the foundations for a chemical theory on the origin of life, known today as the RNA World hypothesis, with investigations into potential primordial synthetic paths to nucleobases, nucleosides, and nucleotides, and nonenzymatic reactions on RNA templates. Together with his friend Stanley Miller, who also died in 2007, Orgel was one of the most prominent scientists in the area of prebiotic chemistry.



Leslie Orgel was a prodigy. It was said about him that during his chemistry studies in Oxford, he attended very few if any lectures and lab courses, but he achieved his BA with the best possible grade. Directly after his DPhil, he received a research grant from Magdalen College with which he began his scientific career. Jack Dunitz wrote, on the occasion of Orgel's 70th birthday, how their work together on the structure of ferrocene came about, and how Orgel developed a MO model within a few days which explained the structure and stability of ferrocene and above all predicted that bis(benzene)chromium and bis(cyclobutadiene)nickel must be stable compounds.[1] Ferrocene was the subject of a joint paper in *Nature*, in which the term "sandwich complex" was coined.[2]

In the middle of April 1953, Dunitz, Orgel, and Sidney Brenner, who had moved to Oxford, traveled to Cambridge to visit Watson and Crick, who had just built a new version of their DNA model in their laboratory. From this day onwards, Orgel began a continuous transition from theoretical inorganic chemistry to the chemical roots of molecular biology. In 1954/55 he took up the chance with Linus Pauling at Caltech to deepen his knowledge in molecular biology in discussions with the leading experts of this area at the time. In 1956 he returned to England and worked in Cambridge at the Institute for Theoretical Chemistry until 1963. At the end of this creative period, Orgel had, alongside his classic book "*An Introduction to Transition-Metal Chemistry: Ligand Field Theory*",[3] almost 100 publications to show for it. He belonged to the "RNA Tie Club" in Cambridge, which was a young discussion platform with the aim to work on ideas for the decoding of the genetic code and the then unknown role of RNA. There were 24 members (4 for the 4 nucleobases and 20 for the amino acids) who wore wool ties with a double-strand emblem attached.

With his move to the newly founded Salk Institute for Biological Studies in 1964, Orgel concentrated completely on the origins of life. In La Jolla he met Stanley Miller, with whom he wrote "*The Origin of Life on the Earth*",[4] a classic in the area. RNA became the link between prebiotic chemistry and molecular biology. Experiments into the self-constitution of nucleobases, nucleosides, and nucleotides from simple primordial building blocks were as much a part of the program as attempts to form RNA copies by biomimetic paths in the absence of polymerases.

The stepwise achievement of allowing the templated coupling of mononucleoside phosphorimidazolides to proceed chemo- and regioselectively with information transfer[5] was a milestone on the road to molecular replication.[6] All of this work was for Orgel the logical consequence of year-long deliberation, the consequence of which being the replication of RNA or of an even simpler precursor molecule before the evolution of translation machinery could have existed. Even though the term "RNA World" was coined by Walter Gilbert in 1986, a few years after the breakthrough discovery of catalytic RNA (ribozymes) by Cech and Altman, Leslie Orgel, Francis Crick, and Carl Woese established at the end of the 1960s that our current biochemistry based on a sharing of roles by DNA, RNA, and proteins could not have been the prototypical form of life. An archetype with RNA as the carrier of genetic information and at the same time carrier of catalytic function remained as the logical presumption. Jerry Joyce described in his obituary how the discovery of catalytic RNA by Orgel was received: after an animated discussion with Crick and Joyce, Orgel postulated on the same day that a ribosyme functioning as an RNA replicase could have played a key role in the formation of the RNA world. [7]

I knew Orgel as a brilliant, far-sighted, scientifically inquisitive, and highly generous person. In 1984, during my postdoctoral stay in his laboratory, he gave me the freedom to work on a project that was not exactly his line of work. With time, the project became more and more interesting, and I found in Orgel a discussion partner who was as interested as I was in what had just happened. Shortly before my departure, he advised me to further develop and publish the project under my own name. For this generosity I am ever grateful, but regret that we never published together. In June 2006 I met Orgel for the last time at a workshop of the Royal Swedish Academy of Sciences on the origin of life. We were all able to relive once again the unobtrusive humor and brilliant debates of Orgel, who was visibly pleased that this research area, which is so closely tied to his name, has continued to attract much interest.

Orgel will remain a role model to his students. The full relevance of his life's work can only be truly judged once the niche of prebiotic chemistry has developed to become a new mainstream of fundamental research. It is hoped that the general public will understand that the question posed by Orgel on the origin of life is one of the great challenges for future chemistry.

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[7] G. F. Joyce, *Nature* **2007**, *450*, 627.

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