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# HOW ZEBRAFISH MODELS ARE RESHAPING MODERN TRANSLATIONAL NEUROSCIENCE AND DRUG DISCOVERY RESEARCH*

**Key words:** zebrafish, neuroscience, drug screening.

The zebrafish (Danio rerio) is a small freshwater teleost fish that has become a new powerful aquatic vertebrate model organism in preclinical biomedical research and drug screening. Zebrafish possess all major neurotransmitter receptors, transporters and enzymes, as well as express rich behavioral repertoire, thereby offering a wide spectrum of CNS disease models. However, our understanding of zebrafish role as a new emerging mainstream model in neuroscience research is still limited. For example, zebrafish behavior has long been mistakenly viewed as "primitive" or "reflex-driven", resulting in incomplete utilization of the major advantages of this species for CNS disease modeling or drug discovery – 1) phenotypic robustness, 2) ease of experimental manipulations, 3) high-throughput potential, and 4) high relevance to the 3Rs principles of humane animal experimentation. Here, we will discuss zebrafish models relevant to several important human disorders, including epilepsy, autism, stress/depression, anxiety and addiction, to demonstrate excellent future of this model organism in biological psychiatry research. Furthermore, zebrafish are highly sensitive to all major classes of neurotropic drugs (including antipsychotics, anxiolytics, antidepressants, sedatives/anesthetics, stimulants, hallucinogens, antiepileptics) and are well-suited to various high-throughput applications (due to their high fecundity, rapid external development, transparency, fast drug intake, and robust behavioral and physiological phenotypes in both larval and adult fish). Finally, zebrafish emerge as an excellent model for neurogenetic analyses, as they have 25 pairs of chromosomes containing 26,000 protein-coding genes, with the overall genetic homology to mammals and humans around 75 %, and nearly 85 % of shared genes

known to be associated with human disease. Collectively, this calls for a wider use of zebrafish models as a powerful promising model organism for neuroscience and drug discovery research.

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## REGIODIVERGENT DIPOLAR CYCLOADDITION BASED ON PYRROLE-2,3-DIONES

**Keywords:** 2,3-dihydro-2,3-pyrroldiones, dipolarophiles, dipolar cycload-ditions.

It was previously demonstrated, that thermal decarbonylation of *N*-substituted 2,3-dihydro-2,3-pyrroldiones afforded imidoylketenes, whose chemical behavior largely depends on the nature of substituents at *N*-1.

It was discovered that *N*-(diphenylenamino)pyrrolediones experienced facile CO-extrusion at elevated temperatures and the resulting a zwitterionic dihydropyrazolone species, which can be represented by enolate-iminium 1,4-dipole resonance form. In the absence of dipolarophiles, the products of [4+4]-cyclodimerization – bis(pyrazolo)dioxadiazocines – were formed in high yields. To this end, we generated the ketenes in the presence of alkyl vinyl ethers, aldehydes, ketenes, nitriles and isocyanides targeting products of dipolar cycloadditions.