

BRIDGING TIME RESOLVED KINETICS WITH *IN VIVO* DRUG DELIVERY: PROOF-OF-CONCEPT FROM Pt DIOLEFIN COMPLEXES?

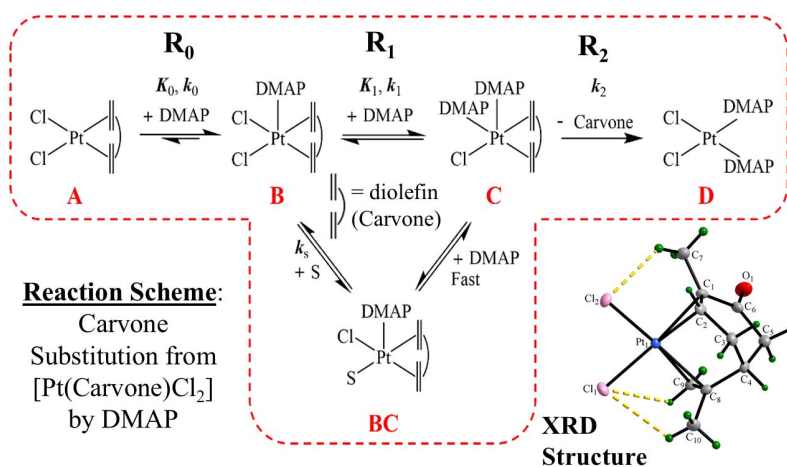
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Detailed *in vitro* kinetic and mechanistic studies is important for understanding *in vivo* reactivity of medicinal and chemotherapeutic entities. Thus, potential ways of agent-delivery to specific sites, i.e., more clarity of dynamic factors affecting uptake/ biodistribution of agents are relevant [1,2]. Readily available natural terpene compounds with biological activity such as limonene and analogs are known, containing olefinic entities for potentially coordination to soft transition metals. Carvone, a diolefinic terpene boasts antibacterial, antifungal, antiparasitic, antineuraminidase, antioxidant, anti-inflammatory and anticancer activities [3].

[Pt((R)-Carvone)Cl₂] was thus synthesized and characterized via NMR spectroscopy and single crystal X-ray diffraction (see Figure) [4,5]. The complex, analogous to cis-platin, exhibits a square-planar geometry with carvone coordinated as a 2x η^2 bidentate ligand and two chlorido ligands in the remaining cis positions.

A detailed kinetic study utilising UV/Vis and ¹H NMR analysed the mechanism of the Pt(II) complex with strong pyridine-like nucleophiles such as DMAP [5]. Five reactions (only 3 shown: R₀, R₁, R₂) were observed from time-resolved data, requiring advanced concepts to analyse. Quite large negative ΔS^\ddagger values for both R₁ and R₂ were obtained: R₂ [$\Delta H^\ddagger > 90\%$ of ΔG^\ddagger ; ΔH^\ddagger driven] vs. R₁ (51% entropy driven); the system becoming more ordered as DMAP is incorporated.



Some implications of the detailed kinetics studied, the rate law derived, and the mechanism will be presented.

[1] Roodt A, Alberto A, Frei A, Mokoloko PP, Bolliger RK, Brink A, Kama DV. **US Patent**; 11,690,923; 2023.

[2] Yadav P, Blacque O, Roodt A, Zelder F. **Inorg. Chem. Front.**; 8(19): 4313-4323; 2021.

[3] Bouyahya A, Mechchate H, Benali T, Ghchime R, Charfi S, Balahbib A, Burkov P, Shariati MA, Lorenzo JM, Omari NE. **Biomolecules**; 11: 1803 (26pp); 2021.

[4] Bezuidenhout, Z, Roodt, A. **J. Coord. Chem.**; 78(1-3): 208-224; 2025.

[5] Bezuidenhout, Z. **MSc Dissertation**; University of the Free State, July 2021.