Novel Ruthenacarborane–NSAID Conjugates

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Abstract

The significant side effects associated with platinum-based anticancer agents have driven the continuous pursuit of novel, non-platinum-based metal compounds. Ruthenium-based organometallic compounds have emerged as promising alternatives, owing to their distinctive and adaptable biochemical properties. The research efforts are focused on the development of ruthenacarborane-based anticancer drugs. The combination of ruthenium(II) complexes, recognized for their inherent anticancer potential, with carboranes, boron-rich clusters possessing unique chemical and physical characteristics, and NSAIDs, known to inhibit COX, an enzyme overexpressed in tumors, offers a novel approach for cancer therapy. Consequently, combining these three moieties into a single molecule represents a compelling strategy to develop drugs with a dual mode of action. Herein, we report the synthesis of a series of ruthenacarborane-(η6-p-cymene)–NSAID conjugates (4a, 4b, 5b, and 6b) by linking NSAIDs (flurbiprofen, fenoprofen, and ibuprofen) to ruthenacarborane complexes using methylene and ethylene spacers, while maintaining the integrity of the sensitive ester groups present in the system. The synthesized conjugates were thoroughly characterized using multinuclear (1H, 11B, and 13C) NMR spectroscopy. Notably, the conjugates demonstrated low COX inhibition and no cytotoxic potential against different cancer cell lines, probably due to oxidative deactivation confirmed by cyclic voltammetry (CV). This indicates that the conjugation of this type of ruthenacarborane with NSAIDs does not result in novel anticancer drugs.