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Novel bexarotene esters - synthesis and spectroscopic characterization

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Abstract. Bexarotene (Bex), a selective retinoid X receptor (RXR) agonist with established anticancer activity, is clinically constrained by poor aqueous solubility and unfavorable pharmacokinetics. This study aims to explore structural modification through the synthesis of Bex ester derivatives in order to improve physicochemical stability and expand its pharmaceutical applicability. Conventional esterification of Bex with thionyl chloride ($SOCl_2$) produces numerous by-products, which complicates purification and reduces yield. To overcome these challenges, an alternative and optimized synthetic route is applied, utilizing oxalyl chloride in primary alcohol media to generate four Bex esters: methyl (E1) and ethyl (E2), which are previously reported compounds, and two novel derivatives, propyl (E3) and butyl (E4). Reaction progression and purity are monitored by thin-layer chromatography (TLC), while the final products are isolated under controlled vacuum evaporation conditions. Structural confirmation and spectral profiling are performed using attenuated total reflectance Fourier-transform infrared spectroscopy (ATR-FTIR) and ultraviolet-visible (UV-Vis) spectroscopy. The IR spectra reveal characteristic carbonyl signals near 1717 cm^{-1}, confirming ester bond formation, while UV-Vis measurements demonstrate preserved electronic transitions of Bex with absorption maxima around 204 and 262–264 nm. A validated UV-Vis method for quantitative determination of Bex shows excellent linearity ($R^2 = 0.9976$), precision (RSD < 0.64%), and sensitivity (LOD = 0.3 μg/mL). The synthesized esters display distinct solubility profiles and yields up to 81.5%, highlighting the relevance of this approach as a cleaner and more efficient alternative to conventional routes. These results establish a versatile synthetic platform and open avenues for future studies focused on advanced Bex derivatives, prodrug design, and improved drug delivery strategies.

***Keywords*:** bexarotene esters; TLC; spectroscopy; qualitative analysis; quantitative determination.

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