

C-glycoside synthesis through radical cross-coupling of glycohydrazides

Description

Carbohydrates are among the most abundant and structurally diverse biomolecules in nature, playing central roles in energy storage, molecular recognition and cell signalling. Within this domain, C-glycosides, in which the oxygen atom of the glycosidic bond in O-glycosides is replaced by carbon, have emerged as valuable motifs in medicinal chemistry due to their resistance to enzymatic hydrolysis. Of particular importance are C-aryl glycosides, exemplified by the SGLT2 inhibitors dapagliflozin, canagliflozin and empagliflozin, which are frontline therapies for type 2 diabetes. However, scalable syntheses of C-aryl glycosides have relied traditionally on protected sugar derivatives, lengthy sequences or conventional cross-couplings that often suffer from poor selectivity, limited scope and extensive protecting-group manipulation. The authors present **a redox-neutral radical cross-coupling platform** utilizing glycosyl sulfonyl hydrazides as radical precursors. These specialized reagents are synthesized directly from unprotected native sugars, eliminating early-stage protection steps. Under mild reaction conditions, the glycosyl sulfonyl hydrazides generate anomeric glycosyl radicals. These radicals undergo efficient C–C bond formation without the need for extensive protecting-group manipulation. The method supports stereoretentive radical coupling, allowing chemists to override inherent stereochemical biases and selectively access specific anomers.

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