C2 MODIFICATION OF QUINAZOLINE DERIVATIVES VIA AZIDE-TETRAZOLE TAUTOMERISM

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Quinazoline derivatives exhibit a broad range of biological activities, finding use as anticancer, antimicrobial, antimalarial, and antiviral agents. Numerous 2-amino-6,7-dimethoxyquinazoline analogs are extensively employed as α_1-adrenoreceptor blockers and in recent years quinazoline-based OLED materials have also gained attention[1–3].

Several methods of selective C4 position modification are known, but the modification of the C2 position is still challenging[4].

In this research, we employ the sulfonyl group dance[5] to achieve 4-azido-2-sulfonylquinazolines, which inverse the regioselectivity and further undergo C2 substitution, yielding 2-amino-4-azidoquinazolines. The regioselectivity of the transformation was proven by chemical synthesis, NMR, and X-ray crystallography.

Furthermore, we show the applications for these products in the synthesis of phosphoronylidenes, fluorescent 4-triazolylquinazolines, and the development of a novel synthesis pathway toward α_1-adrenoreceptor blockers terazosin and prazosin.

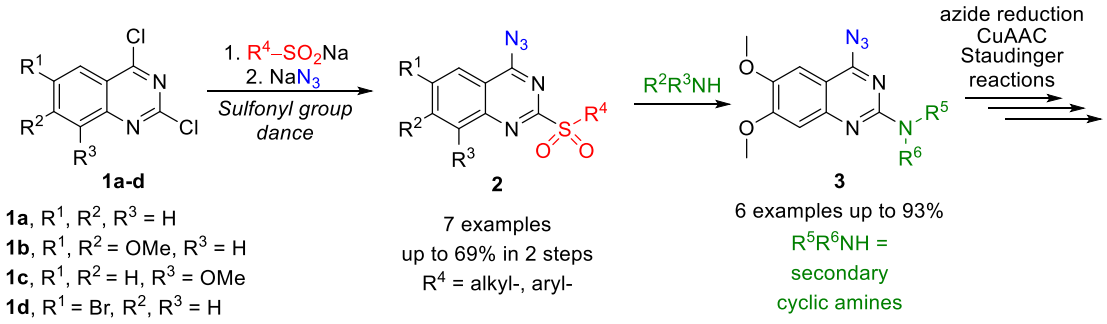

Fig. 1. Inversion of the regioselectivity of the quinazoline core via sulfonyl group dance.

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