Primary Sulfonamide Synthesis Using the Sulfinylamine Reagent N-Sulfinyl-O-[(tert-butyl)hydroxylamine, t-BuONSO

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Preparation of Primary Sulfonamides by t-BuONSO and Organometallics

Selected examples:

- \( \text{BrN} \)NH2, 45% yield
- \( \text{S_N} \)NH2, 74% yield
- \( \text{F} \)\( \text{S_N} \)NH2, 55% yield
- \( \text{S} \)\( \text{S} \)NH2, 72% yield
- \( \text{O} \)\( \text{S} \)NH2, 50% yield
- \( \text{N} \)Boc\( \text{S} \)\( \text{O} \)\( \text{H_2N} \), 59% yield
- Celecoxib, 55% yield

Proposed reaction mechanism:

1. 1.0 equiv \( \text{BuONSO} \) + \( \text{MgBr} \) → \( \text{N-Sulfinyl-O-} \)\( \text{H_2N} \)
2. \( \text{N-Sulfinyl-O-} \)\( \text{H_2N} \) → \( \text{F} \)\( \text{S_N} \)NH2
3. \( \text{F} \)\( \text{S_N} \)NH2 → \( \text{H}^+ \) → \( \text{S_N} \)NH2

Significance: Willis and co-workers report the reaction of readily available organometallic reagents and the novel sulfinylamine reagent t-BuONSO \( [N\text{-sulfinyl-O-(tert-butyl)}] \text{hydroxylamine} \) for the direct synthesis of primary sulfonamides in good yields.

Comment: The authors proposed a reaction mechanism in which, after nucleophilic attack of the Grignard reagent, the sulfonamide A was formed. This intermediate was converted into B, either via a sulfinyl nitrene intermediate or by a concerted N → S O migration. After an intramolecular proton transfer, isobutene was eliminated, giving the anion C, which was quenched after work-up to yield the desired sulfonamide.