



An Expedient Synthesis of tetra-*ortho*-fluoro-azobenzenes *via* Nucleophilic Aromatic Substitutions (S_NAr)

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ABSTRACT

The E to Z photoisomerization of azobenzenes have shown great applicability for the generation of photoswitches, which can be used to prepare chemical probes controlled by light used to study a plethora of biological systems¹. The introduction of four halogens in the positions *ortho* to the azo group allows for the both a red-shift of the $\lambda_{E\to Z}$ as well as a longer half-life for the Z isomer ². In 2016, Trauner and coworkers³ perfomed the synthesis of tetra-*ortho*-chlorinated azobenzenes using directed C-H activation *via* palladium catalysis. In 2021, Sanford and coworkers⁴ used hydrophobic alcohol adducts of fluorides as a source of fluoride anion for S_NAr reactions, allowing for mild reaction conditions that do not require the use anhydrous solvents and reagents. This work uses fluoride-hydrophobic alcohol adducts in S_NAr reactions for the interconversion of tetra-*ortho*-chloro-azobenzenes into their tetra-fluoro counterparts. This methodology allows for a straightforward synthesis of tetra-*ortho*-fluoro-azobenzenes.

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REFERENCES

- 1. Using azobenzene photocontrol to set proteins in motion Bozovic, O.; Jankovic, B.; Hamm, P. Nat. Rev Chem. 2022, 6, 112–124.
- 2. Computational Design and Synthesis of a Deeply Red-Shifted and Bistable Azobenzene. Konrad, D. B.; Savasci, G.; Allmendiger, L.; Ochsenfeld, C.; Ali, A. M.; Trauner, D. J. Am. Chem. Soc. 2020, 142, 6538–6547.
- 3. Synthesis of Redshifted Azobenzene Photoswitches by Late-Stage Functionalization. Konrad, D. B.; Frank J. A.; Trauner, D.; Chem. Eur. J. 2016, 22, 4364–4368.
- 4. Tetramethylammonium Fluoride Alcohol Adducts for S_NAr. Fluorination. Sanford, M. S.; Morales-Cólon, M. T.; See, Y. Y.; Lee, S. J.; Scott, P. J. H.; Bland, D. C.; Org. Lett. **2021**, 23, 4493–4498.