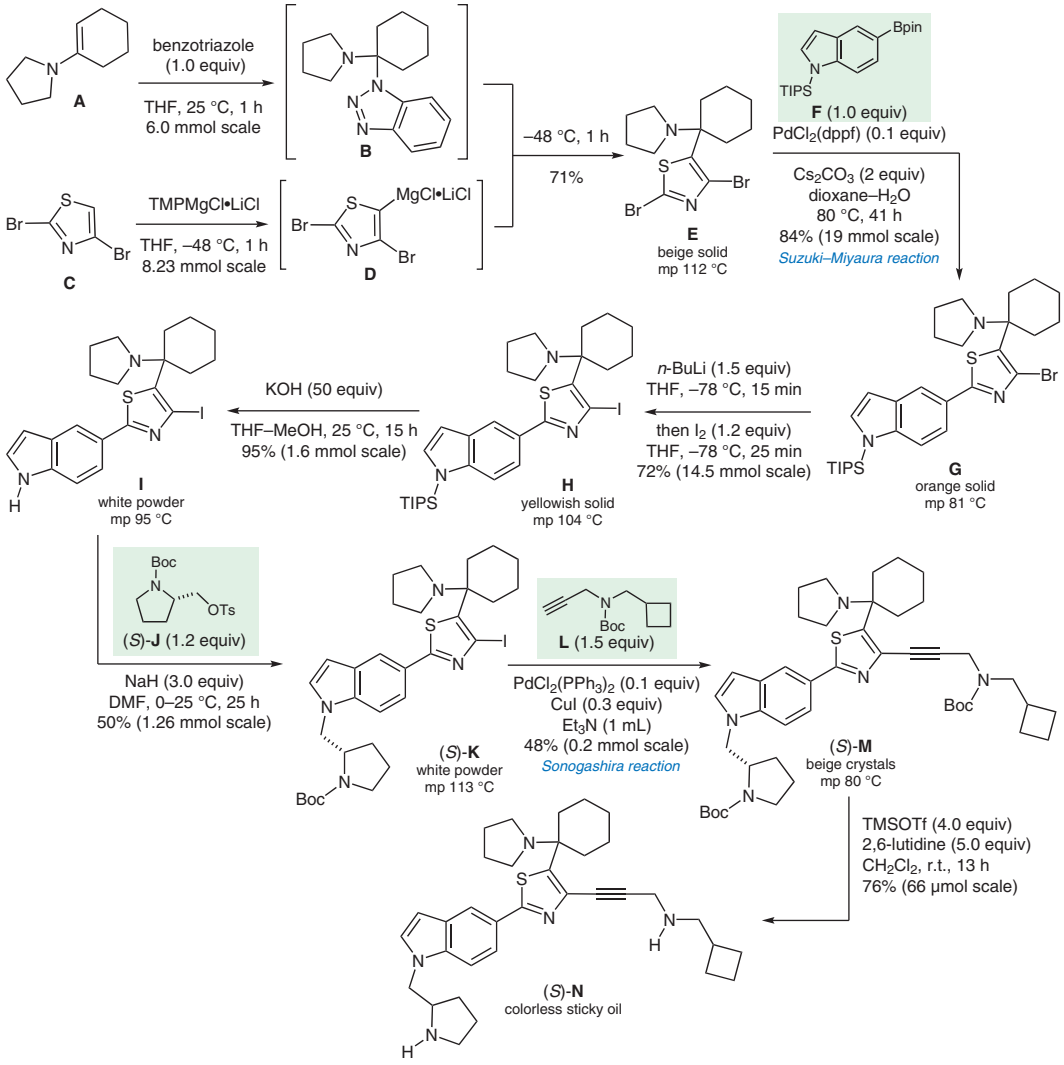
R. DE GASPARO, O. HALGAS, D. HARANGOZO, M. KAISER*, E. F. PAI*, R. L. KRAUTH-SIEGEL, F. DIEDERICH* (ETH ZURICH, SWITZERLAND)

Targeting a Large Active Site: Structure-Based Design of Nanomolar Inhibitors of *Trypanosoma brucei* Trypanothione Reductase
Chem. Eur. J. **2019**, *25*, 11416–11421.

Nanomolar Inhibitor of *Trypanosoma brucei* Trypanothione Reductase



Significance: The parasitic protozoa responsible for trypanosomiasis, Chagas' disease, and leishmaniasis require the reduction of trypanothione disulfide to trypanothione, which the parasites use in several essential processes. Target molecule **N** is the strongest competitive inhibitor in vitro of trypanothione reductase from *Trypanosoma cruzi* reported to date.

Comment: Note the construction of highly hindered amine **E** by nucleophilic substitution of benzotriazole from *N*,*N*-acetal **B** by the organomagnesium reagent **D**.

Review: For a Review on properties and synthetic utility of N-substituted benzotriazoles, see A. R. Katritzky, X. Lan, J. Z. Yang *Chem. Rev.* **1998**, *98*, 409–548.

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Category

Synthesis of Natural Products and Potential Drugs

Key words

trypanothione reductase inhibitor

benzotriazole

***N*,*N*-acetal**

tertiary amine

Suzuki–Miyaura coupling

Sonogashira coupling

Synfact of the Month

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