Desymmetrization of meso-Diols via Covalent Substrate Binding Catalysis

**Significance:** The desymmetrization of meso-diols is a highly useful asymmetric transformation since it can provide synthetically valuable intermediates with theoretically quantitative yields. The authors utilized catalysts 1 as a substrate-binding module as well as a silyl chloride activator. High enantioselectivity was obtained for cyclic and acyclic meso-diols (er up to 97.5:2.5). Also, the substituent adjacent to the imidazole group affects the enantioselectivity dramatically and displays strong match/mismatch effects on the enantioselectivity.

**Comment:** The presented method features a highly elegant substrate activation mode. As a part of the proposed catalytic cycle, the authors detected a reversible covalent bond equilibrium between catalyst and diol adduct 2 (Keq = 0.20). Also, from the X-ray crystal structure obtained with 4-bromobenzyl alcohol and 1c, the configuration of adduct 2 was assigned as depicted in the Scheme (highlighted in red), although the observed diastereomeric ratio of 2 was low (dr = 60:40). Further detailed investigations on the catalytic intermediates (2 or 3) are anticipated.

**Selected examples:**

- **1a:** er = 70:30 (20% yield)
- **1b:** er = 42:58 (25% yield)
- **1c:** er = 98.5:1.5 (84% yield)
- **1d:** er = 52:48 (5% yield)

**Proposed catalytic cycle:**

1. TBSCI (2 equiv), base (1.2 equiv)
2. **HO**OTBS
3. + meso-diol
4. MeOH
5. SiR3Cl, base
6. **MeOH**
7. + meso-diol
8. **HO**OSiR3

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