

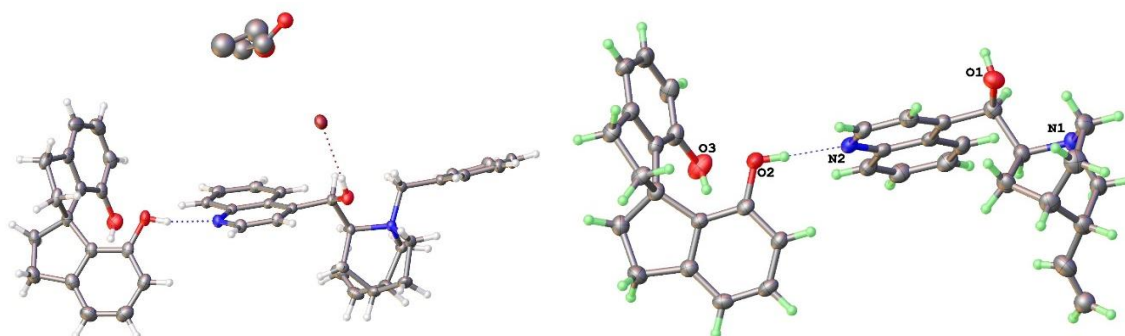
Resolution of SPINOL by cinchona alkaloids and application of high throughput screening by solvent assist grinding

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SPINOL (1,1'-spirobiindan-7,7'-diol) is a useful chiral ligand used in asymmetric catalysis.[1] Originally prepared itself by a chiral catalysis, it was later resolved using an inclusion complex technique pioneered by Toda.[2] Thus the N-benzylcinchonidinium chloride or bromide salt could co-crystallize with SPINOL.[3] The use of enantiomeric neutral cocrystals for resolution was also well established, thus we also attempted to resolve SPINOL by screening for co-crystal formation. This included using the neutral alkaloid bases from the Cinchona family. Solvent-assisting grinding was applied in screening of diastereomeric solid formation with N-benzylcinchonidinium bromide and cinchonidine. Other than the reported "inclusion complex", a new inclusion complex with a solvate, which resolved the opposite hand of (R)-SPINOL, was discovered when screening with N-benzylcinchonidinium bromide. Also a 1:1 co-crystal with cinchonidine itself was readily formed and found to contain predominantly R-SPINOL. These phases were characterized by single X-ray diffraction, and the optical purity was determined by chiral HPLC. A single recrystallization improved the % ee to the required 99% level. The isolation of both hands is facilitated since recrystallization of the chiral SPINOL from the supernatant solution can rapidly afford an enantiopure sample since SPINOL forms a conglomerate when crystallizing from methanol.



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References

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