

SYNLETT Spotlight 269

Camphorsulfonic Acid: A Versatile and Useful Reagent in Organic Synthesis



This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

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Introduction

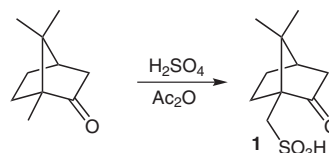
Camphorsulfonic acid (CSA) (or Reychler's acid) **1**, is a white crystalline powder, hygroscopic, very soluble in ethanol and melts at 198 °C.

It is commercially available but it can be easily prepared from camphor by treatment with sulfuric acid and acetic anhydride (Figure 1).¹

CSA is the first C10-substituted camphor derivative obtained,¹ it is frequently used not only in asymmetric synthesis as chiral starting material² (such as its derivative

10-camphorsulfonyl chloride) but also as a useful catalyst in natural product synthesis.³

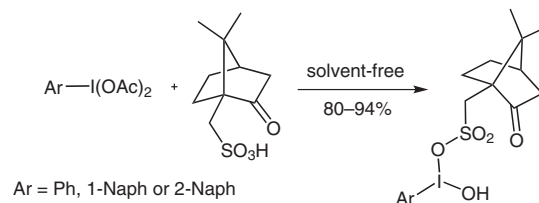
Moreover, CSA is widely used for the diastereomeric salt resolution.^{4,5}



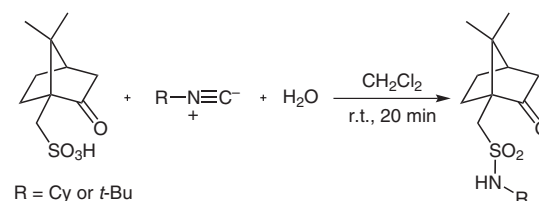
Scheme 1 Preparation of camphorsulfonic acid

Abstracts

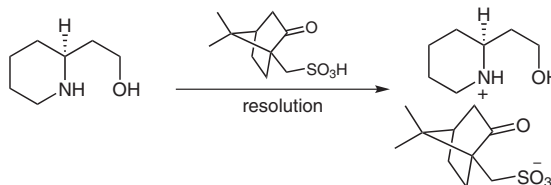
(A) CSA is used in the preparation of hypervalent iodine reagents. These reagents have been used frequently in organic chemistry especially in synthesis. Since these are nonmetallic oxidation agents, toxicity of many transition metals commonly involved in such process is avoided.⁶



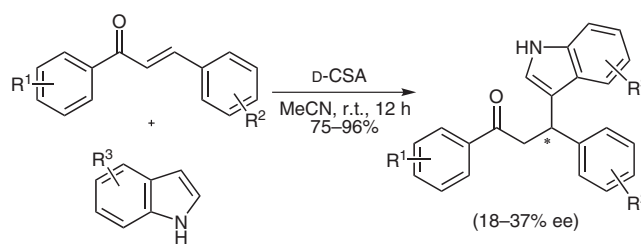
(B) Sulfonamides belong to an important class of pharmaceutical compounds exhibiting a broad wide variety of biological activities. Recently, a novel approach for the synthesis of alkyl and aryl sulfonamides was reported with excellent yields and moderate conditions, consisting on the reaction of CSA, isocyanides and water in dichloromethane at room temperature.⁷



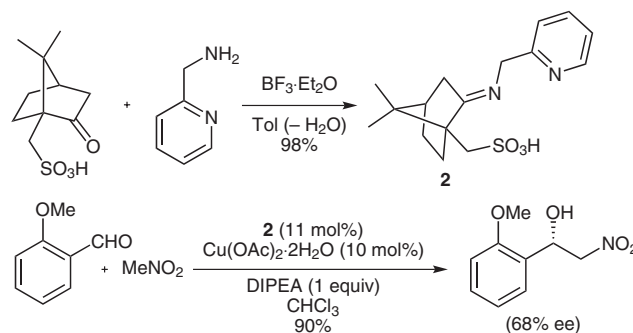
(C) Putrescine, spermidine and spermine are essential polyamines for the growth and function of normal cells. (*S*)-CSA was used on the resolution of 2-piperidineethanol, a chiral starting material for the asymmetric synthesis of (-)-isooncinotine, a 22-membered lactam of spermidine alkaloid.⁸



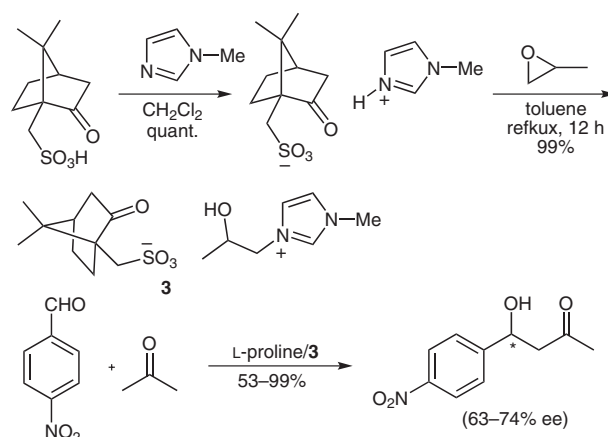
(D) D-CSA, a chiral Brønsted acid, revealed to be a practical and efficient catalyst for the enantioselective Michael-type Friedel–Crafts reactions of indoles with aromatic enones, affording the corresponding β -indolyl ketones with excellent yields and moderate enantioselectivities.⁹



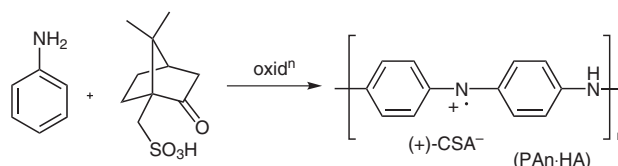
(E) The enantioselective Henry (nitroaldol) reaction between nitromethane and an aromatic aldehyde was successfully catalyzed by copper complexes of chiral iminopyridine, prepared from CSA. High yield and good enantioselectivity were achieved.¹⁰



(F) L-Proline-catalyzed aldol reactions were promoted by a catalytic amount of chiral ionic liquid based on CSA with good chemoselectivity in water as well as in organic solvents.¹¹



(G) Recently, considerable attention has been devoted to active polyanilines (PAn's) due to their potential applications in areas like chiral sensors, electrochemical asymmetric synthesis and chiral separations. (*S*)-CSA has been used as a chiral acid during oxidative polymerization of aniline, in order to induce the optical activity of polyaniline emeraldine salts (PAn-HA).¹²



References

- Reychler, A. *Bull. Soc. Chim.* **1898**, *19*, 120.
- Greene, A. E.; Charbonnier, F. *Tetrahedron Lett.* **1985**, *45*, 5525.
- Lowinger, T. B.; Chu, J.; Spence, P. L. *Tetrahedron Lett.* **1995**, *36*, 8383.
- Elatia, C. R.; Kollaa, N.; Gangulaa, S.; Naredlaa, A.; Vankawalaa, P. J.; Avinigiria, M. L.; Chalamalaa, S.; Sundarama, V.; Mathada, V. T.; Bhattacharyaa, A.; Bandichhor, R. *Tetrahedron Lett.* **2007**, *48*, 8001.
- Kubryk, M.; Hansen, K. B. *Tetrahedron: Asym.* **2006**, *17*, 205.
- Yusubov, M. S.; Wirth, T. *Org. Lett.* **2005**, *7*, 519.
- Shaabani, A.; Soleimani, E.; Rezayan, A. H. *Tetrahedron Lett.* **2007**, *48*, 2185.
- Cheng, H. Y.; Hou, D. R. *Tetrahedron* **2007**, *63*, 3000.
- Zhou, W.; Xu, L. W.; Li, L.; Yang, L.; Xia, C. G. *Eur. J. Org. Chem.* **2006**, 5225.
- Blay, G.; Climent, E.; Fernández, I.; Hernández-Olmos, V.; Pedro, J. R. *Tetrahedron: Asym.* **2007**, *18*, 1603.
- Zhou, W.; Xu, L. W.; Qiu, H. Y.; Lai, G. Q.; Xia, C. G.; Jiang, J. X. *Helv. Chim. Acta* **2008**, *98*, 53.
- Pornputtkul, Y.; Kane-Maguire, L. A. P.; Innis, P. C.; Wallace, G. G. *Chem. Commun.* **2005**, *36*, 4539.