Journal of Labelled Compounds and Radiopharmaceuticals
J. Labelled Cpd. Radiopharm. **44**, 43-45 (2001)

Synthesis and Characterization of [2-^{3}H] (1R,2S)-(-)-2-Amino-1,2-diphenylethanol

Judith A. Egan and Crist N. Filer*

Perkin Elmer Life Sciences
549 Albany St.
Boston, Massachusetts 02118

SUMMARY

(R)-(-) Benzoin oxime **2** was catalytically tritiated to afford [2-^{3}H] (1R,2S)-(-)-2-amino-1,2-diphenylethanol **1** in 92% ee.

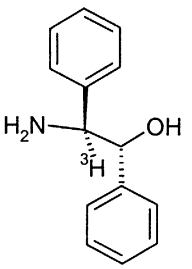
Key Words: Tritium, Oxime, Enantioselective Reduction

DISCUSSION

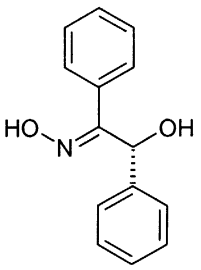
1,2-Diphenylaminoalcohols have played a significant role as chiral auxiliaries and scaffolding for chiral reagents (1) as well as stationary phases for chiral HPLC (2). We were called upon to prepare [^{3}H] (1R,2S)-(-)-2-amino-1,2-diphenylethanol **1** with an optical purity in excess of 90% ee and reasoned that an efficient way to accomplish this would be the reductive tritiation of an appropriate chiral benzoin oxime. Harada and Shiono (3) had earlier studied the stereoselectivity of the catalytic hydrogenation of benzoin oxime and reported the predominance of an *erythro* product. They suggested that the stereoselective nature of the hydrogenation resulted from oxime chelation with the palladium catalyst. Davis (4) improved upon the stereoselectivity of the reduction and reported that the catalytic hydrogenation of (S)-(+) benzoin oxime afforded (1S,2R)-(+)-2-amino-1,2-diphenylethanol in high optical purity, especially under mildly acidic conditions. Attempts to reduce this oxime with metal hydrides were not as successful This result encouraged us to prepare and utilize the corresponding (R)-(-) benzoin oxime **2** as a precursor for our target compound. At the time we were required to prepare (R)-(-) benzoin using the procedure of Davis (5) but it is now commercially available (6). The oxime **2** was easily prepared (4) and catalytically reduced with tritium gas using the conditions of Davis to afford

Received 13 September 2000
Accepted 22 September 2000

after purification [2-^{3}H] (1R,2S)-(-)-2-amino-1,2-diphenylethanol **1** with a specific activity of 6.5 Ci/mmol and 98% radiochemical purity by non chiral reverse phase HPLC. Using Marfey's reagent as a derivatizing agent, it was also demonstrated by HPLC that the product contained 96% [2-^{3}H] (1R,2S)-(-)-2-amino-1,2-diphenylethanol **1** and 4% [2-^{3}H] (1S,2R)-(+)-2-amino-1,2-diphenylethanol. This observed 92% ee paralleled the observation of Davis for the catalytic hydrogenation of the (S)-(+)-benzoin oxime and was sufficient for our work. Catalytic tritiations of other chiral alpha hydroxy oximes may prove useful to prepare the corresponding chiral amino alcohols.



1



2

EXPERIMENTAL

Evaporations were carried out on a Buchi rotary evaporator *in vacuo* at bath temperatures less than 40°C. TLC was performed on Analtech plates coated with silica gel (250 microns for analytical and 500 microns for preparative). Autoradiography was performed at 0°C after spraying with PPO and exposing the plates to x-ray film. TLC plates were also scanned (~ 3 min.) for radioactivity (~ 10 μCi). Preparative and analytical HPLC was performed with peak detection done simultaneously by UV (280 nm) and a liquid scintillation flow monitor.

[2-^{3}H] (1R,2S)-(-)-2-Amino-1,2-diphenylethanol (1) Oxime **2** (25 mg, 0.11 mmol) in 1 mL of ethanol with 15 μL of conc. HCl was reduced with tritium gas and 10 mg of 5% palladium on charcoal at room temperature for 2 h. After the reduction, labile tritium was removed by ethanol vacuum transfer affording 340 mCi of crude product. The product was purified by preparative TLC eluting with chloroform : methanol (7:1) with authentic standard (Aldrich Cat. #33,189-9) allowed to run in a side lane. The desired product was identified by UV visualization. The silica support was scraped from the plate and eluted with a minimum of ethanol to afford 119 mCi of product **1**. Compound **1** was found to be 97.2% radiochemically pure by TLC (chloroform: methanol (9:1)) and 98% radiochemically pure by reverse phase HPLC (1% triethylammonium acetate (pH = 4) : acetonitrile (3:1)) and co-chromatographed with authentic cold standard. A portion of the product was derivatized with Marfey's reagent (Aldrich Cat. # 36,605-6) and reexamined by reverse phase HPLC (1% triethylammonium acetate

(pH = 4) : acetonitrile (1:1)). By this method 96% of the sample was found to coelute with the derivatized (-) enantiomer and the remaining 4% coeluted with the derivatized (+) enantiomer (Aldrich Cat. # 33,188-0). The specific activity was measured by mass spectral analysis to be 6.5 Ci/mmol.

ACKNOWLEDGMENT

We would like to thank Dr. Thomas Rodgers (Perkin Elmer) for preparing oxime **2** and acknowledge helpful discussions with Prof. Franklin A. Davis of Drexel University.

REFERENCES

1. Yaozhong J. et al. *Tetrahedron Asymmetry* **5:** 1211-1214 (1994).
2. Yuki Y. et al. *J. Chrom.* **400:** 65-75 (1987).
3. Harada K. et al. *Bull. Chem. Soc. Japan* **57:** 1040-1045 (1984).
4. Davis F. A. et al. *J. Org. Chem.* **54:** 2021-2024 (1989).
5. Davis F. A. et al. *J. Org. Chem.* **51:** 4083-4085 (1986).
6. Aldrich Chemical Company, Catalogue Item 45,994-1

