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OPTICAL INTERCONVERSION OF ENANTIOMERIC SECONDARY ALCOHOLS USING 2-FLUOROBENZOTHIAZOLIUM SALT

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A convenient method for optical interconversion of enantiomeric secondary alcohols was established according to the following procedures: treatment of optically active 2-alkyloxybenzothiazolium salt, formed in situ from 2-fluoro salt I and optically active secondary alcohols, with trichloroacetic acid to give the corresponding esters with inversion of configuration, and facile hydrolysis of the esters to alcohols with retention.

In the preceding papers, it was demonstrated that 3-ethyl-2-fluorobenzothiazolium tetrafluoroborate(I) reacted with various alcohols to produce highly reactive 2-alkyloxybenzothiazolium salt II, which on treatment with alkali metal halides afforded the corresponding alkyl halides in good yields.[1] The present paper reports further studies on the salt II, and discloses the successful interconversion of optically active secondary alcohols.

It was found that optically active 2-alkoxy salt II, formed in situ from an optically active secondary alcohol and 2-fluoro salt I, reacted in the presence of tertiary amine with a strong acid such as trichloroacetic acid to yield the corresponding ester, which on facile base-catalyzed hydrolysis afforded the alcohol that had an asymmetric carbon atom different in configuration from that of the starting alcohol. Thus the whole sequence makes possible the transformation of the configurationally isomeric secondary alcohols by a simple procedure as is shown in the scheme below.[2] For instance, (S)-(+)-2-octanol was converted to (R)-(-)-2-octanol in overall 70 percent yield by treating the alcohol successively with I and trichloroacetic acid, followed by hydrolysis. The results are summarized in the table.

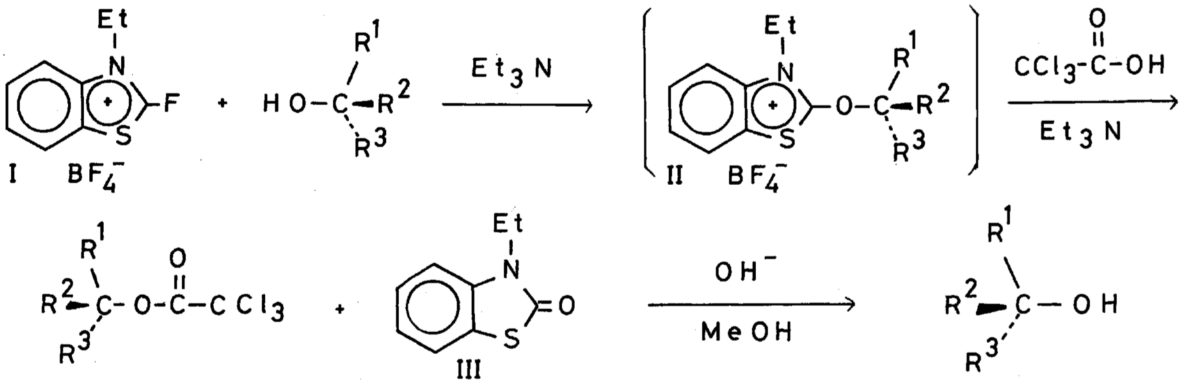


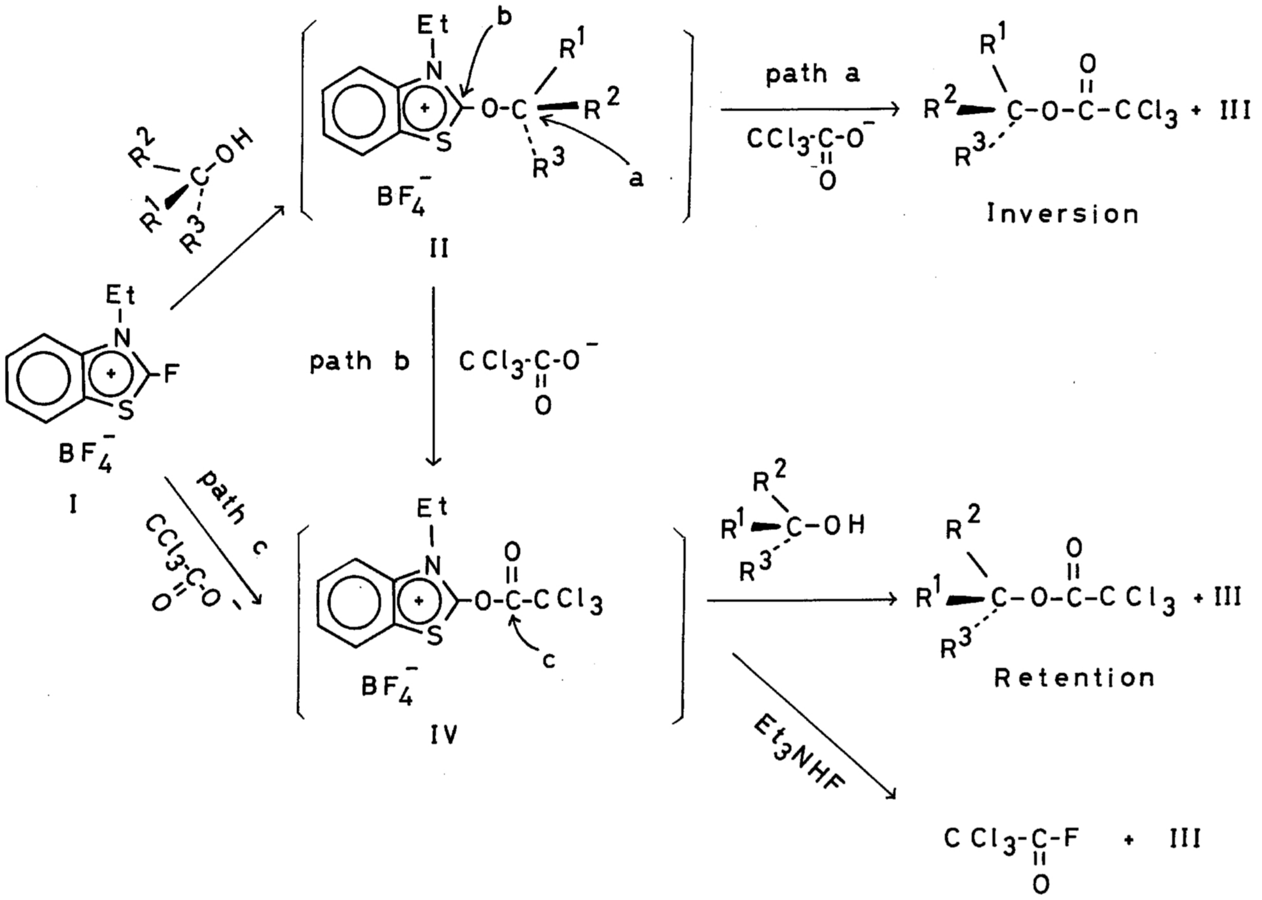
Table Optical Interconversion of Secondary Alcohol[3]

Entry No.	Starting Alcohol	$[\alpha]_D^{24}$ [a]	Yield (%)	Ester $[\alpha]_D^{24}$ (CH_2Cl_2)	Product Alcohol Yield (%)	$[\alpha]_D^{24}$	Inversed Isomer (%)
1	(S)-(+)-2-butanol	+9.4° (c 11.3, $CHCl_3$)	74	-12.8° (c 12.3)	81[b]	-7.8° (c 8.3, $CHCl_3$)	92
2	(R)-(-)-2-butanol	-9.7 (c 9.3, $CHCl_3$)	83	+14.3 (c 17.7)	84[b]	+8.6 (c 7.5, $CHCl_3$)	95
3	(S)-(+)-2-octanol	+12.3 (c 8.8, ether)	70	-10.3 (c 19.6)	quant.	-11.2 (c 8.6, ether)	98
4	(R)-(-)-2-octanol	-12.0 (c 9.5, ether)	61	+10.5 (c 19.9)	quant.	+10.2 (c 8.7, ether)	95
5	(S)-(+)-3-nonanol	+9.6 (c 8.3, $CHCl_3$)	64	-0.10 (c 10.3)	98	-7.4 (c 8.1, $CHCl_3$)	89
· · ·	· · ·	· · ·	· · ·	· · ·	· · ·	· · ·	
6	(R)-(-)-2-octanol	-12.0 (c 9.5, ether)	73[c]	-11.6 (c 15.9)	quant.	-12.1 (c 11.9, ether)	0

a) Optical rotation measurements were performed in a 0.1 dm cell by the automatic polarimeter. b) 2-Butanol was obtained by an ester exchange reaction; sodium metal (200 mg, 8.7 mmol) was dissolved in 2,2'-(ethylenedioxy)diethanol (10 ml), and to this was added optically active s-butyl trichloroacetate (700 mg, 3.2 mmol). 2-Butanol was distilled in vacuo directly from the reaction mixture, and purified by redistillation. c) This ester was prepared by the inverse addition of the acid and the alcohol to the 2-fluoro-salt I. See text.

A typical experimental procedure is described below: to a stirred suspension of I (1.92 g, 7.2 mmol) in dry CH_2Cl_2 (5 ml) was added a mixture of (R)-(-)-2-octanol (930 mg, 7.2 mmol, $[\alpha]_D^{24}$ -12.0° (c 9.4, ether)) and triethylamine (727 mg, 7.2 mmol) in CH_2Cl_2 (10 ml) at -65°C under an argon atmosphere, and the solution was stirred at -60 ∿ -50°C for one hour. A mixture of trichloroacetic acid (1.17 g, 7.2 mmol) and triethylamine (727 mg, 7.2 mmol) in CH_2Cl_2 (8 ml) was added at -50°C and the reaction mixture was warmed to room temperature over a period of 3 hours. The usual work-up and separation by column chromatography yielded (+)-2-octyl trichloroacetate: 1.20 g (61%),[4] $[\alpha]_D^{23}$ +10.5° (c 19.9 CH_2Cl_2). The ester (1.02 g, 3.7 mmol) was hydrolysed in aqueous methanol containing potasium hydroxide to give (S)-(+)-2-octanol (478 mg, quant.), which was purified by distillation. Yield: 418 mg (87%), $[\alpha]_D^{22}$ +10.2° (c 8.7, ether).

Following observations should be mentioned with this ester forming reaction: (1) The yield and optical purity of the esters depended on the nature of the neucleophiles[5] and on the solvents used.[6] (2) Successive treatment of 2-fluoro salt I first with the acid then with an optically active alcohol gave an ester with complete retention of the configuration (see Entry 6 of the table and path c in the scheme below). (3) In some cases, the presence of the acid fluoride in the reaction mixture was detected by ir spectroscopy. These observations can be reasonably accommodated in the scheme shown below.



There can be considered two alternative pathways (a and b) for the reaction of 2-alkoxy salt II with a carboxylate anion. Path a is an S_N2 type reaction at the asymmetric carbon, which leads to an ester of inverted configuration, whereas path b is an addition-elimination process at 2-position of the ring to produce 2-acyloxybenzothiazolium salt IV, which on reaction with an alcohol or a fluoride ion gives an ester of retained configuration or acid fluoride, respectively. The latter process seems responsible for partial loss of optical purity observed in the products.

It is noted that the present procedure using 2-fluoro salt I and trichloroacetic acid is a simple and convenient method for the optical interconversion of secondary alcohols at a specific position.7)

Further investigations are now in progress.

References and Notes

1) a) T. Mukaiyama and K. Hojo, Chem. Lett., 267 (1976).
   b) K. Hojo and T. Mukaiyama, ibid., 619 (1976).

2) Inversion of configuration was also observed in esterification (formate and benzoate) using triphenylphosphine-diethyl azodicarboxylate.
   a) O. Mitsunobu and M. Eguchi, Bull. Chem. Soc. Japan, 44, 3427 (1971).
   b) A. K. Bose, B. Lal, W. A. Hoffman III, and M. S. Manhas, Tetrahedron Lett., 1619 (1973).

3) All compounds exhibited nmr and ir spectra in agreement with assigned structures.

4) The alcohol recovered in this step (16%) showed $[\alpha]_D^{23}$ -11.9° (c 8.2, ether), identical with that of the starting alcohol.

5) Use of weak acids such as formic, acetic, and benzoic acid produced low yields of esters (with recovered alcohols), where extensive racemization of the esters was observed. These results suggest that weak acids tend to attack the 2-position of the ring carbon in 2-alkoxy salt II. Hydrolysis of the optically active salt II gave the original alcohol of retained configuration and 1-ethyl-2-benzothiazolinone(III).

6) For example in the case of Entry 3 of the table, following yield (%) of the ester was obtained in solvents: $CHCl_3$ (85), CH_2Cl_2 (70), THF (31), and acetone (30). The optical rotation of the ester prepared in $CHCl_3$ showed somewhat lower value than that of the ester produced in CH_2Cl_2.

7) A conventional method employs tosylation with tosyl chloride (retntion), reaction with a carboxylate anion (inversion), and hydrolysis (retention). Important findings related to the present work was that optically active 2-alkoxy salt II underwent reaction with p-toluenesulfonic acid in the presence of base such as triethylamine to yield a corresponding tosylate of inverted configuration. For instance from (S)-(+)-2-butanol, $[\alpha]_D^{24}$ +9.4° (c 11.3, $CHCl_3$) and (R)-(-)-2-octanol, $[\alpha]_D^{20}$ -9.7° (neat), the corresponding tosylates were obtained in 49 and 44 percent yield; the tosylates showed $[\alpha]_D^{24}$ -11.1° (c 9.3, acetone), and +5.1° (c 10.1, acetone) respectively. Reported rotations of (+)-2-butyl and (+)-2-octyl tosylate are $[\alpha]_D$ (neat) +11.1°,[8] and +7.3°,[9] respectively.

8) J. Kenyon, H. Phillips, and V. P. Pittman, J. Chem. Soc., 1072 (1935).

9) H. Phillips, J. Chem. Soc., 2552 (1925).

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