Table I. Rate Constants and Isotope Effects for Reaction of *N*-Methylacridinium Ion with Hydride Donors **2**, **3**, **T-4**, and **5** in Acetonitrile at 30 °C [Literature Values in Brackets]

hydride donor	k, M^{-1} s^{-1}	k_H/k_D	Y_H/Y_D
2-H,H	79.9 ± 0.9		
2-H,D		[2.76 ± 0.15[a]] [3.70 ± 0.18[a,b]]	[4.0 ± 0.2[a]]
2-D,D	19.5 ± 0.1	4.11 ± 0.05	
3-H,H	0.762 ± 0.013		
3-H,D	0.447 ± 0.007	4.95[c] [2.0 ± 0.2[d]]	[7.6 ± 0.3[d]]
3-D,D	0.149 ± 0.003	5.09 ± 0.15	
T-4-H,H	0.051 ± 0.002		
T-4-H,H	0.103 ± 0.005[e]		
5-H,H	2.90 ± 0.02[e]		
5-H,D		[3.30 ± 0.44[f]]	[6.2[f]]
5-D,D	0.655 ± 0.012[e]	4.43 ± 0.08	

[a] Reference 8. [b] $Mg(ClO_4)_2$ added (1.20×10^{-3} M). [c] This value is calculated from the rates of **3**-H,H, **3**-H,D, and **3**-D,D[g]; the secondary kinetic isotope effect is 1.03. Assumption of a secondary kinetic isotope effect of unity gives $k_H/k_D = 5.77$. [d] Reference 9. [e] Temperature 50.0 ± 0.1 °C. [f] Reference 10. [g] By mass spectral analysis, all dideuterated compounds were greater than 99% authentic.

of ref 10, the reaction of eq 3 is kinetically significant such that the measured ratio of **4**-H,H to **4**-H,D in ref 10 does not reflect the "true" value of Y_H/Y_D due to isotope scrambling caused by reaction in the reverse direction. A more detailed study including the effect of the reverse rates is currently in progress.

The present study has shown that mechanistic arguments based upon the supposed differences in k_H/k_D and Y_H/Y_D are invalid and should not be used to infer electron transfer in the hydride reductions of dihydronicotinamides.

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Registry No. 1, 13367-81-2; **2**-H,H, 952-92-1; **2**-D,D, 60172-94-3; **3**-H,H, 17260-79-6; **3**-H,D, 79798-57-5; **3**-D,D, 83077-37-6; **4**-H,D, 83077-38-7; T-**4**-H,H, 83077-39-8; **5**-H,H, 83077-40-1; **5**-D,D, 83077-41-2; D_2, 7782-39-0; NADH, 58-68-4.

Facile Stereospecific Synthesis of α-Fluoro-β-amino Acids

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Fluorinated analogues of bioactive compounds are finding increasing use as chemical probes for biomedical research, as radiographic tools, and as therapeutic agents of increasing lipid permeability and metabolic stability.[1]

Although β-amino acids occur fairly widely in nature,[2] only a few of them have been synthesized so far. α-Fluoro-β-alanine (a metabolite of the antitumor drug 5-fluorouracil) has been prepared in several steps from either fluoromalonic or from fluorooxaloacetic acid esters,[3,4] β-(fluoromethyl)-β-alanine (an inhibitor of γ-aminobutyric acid transaminase) has been synthesized by means of a series of reactions starting from fluoroacetonitrile,[5] and ω-perfluorinated β-amino acids have been obtained through the amination of ω-perfluorinated α-bromo acids,[6] probably via an elimination–addition mechanism.

In this communication we report a novel and stereospecific method for the preparation of α-fluoro-β-amino acids from β-hydroxy-α-amino acids. The method involves fluorination of *N*,*N*-dibenzyl derivatives of β-hydroxy-α-amino acid esters with (diethylamino)sulfur trifluoride (DAST) to the rearranged *N*,*N*-dibenzyl-α-fluoro-β-amino acid esters. Specifically, treatment of *N*,*N*-dibenzyl-L-serine benzyl ester (**1**)[7] with DAST[8] provided

Scheme I

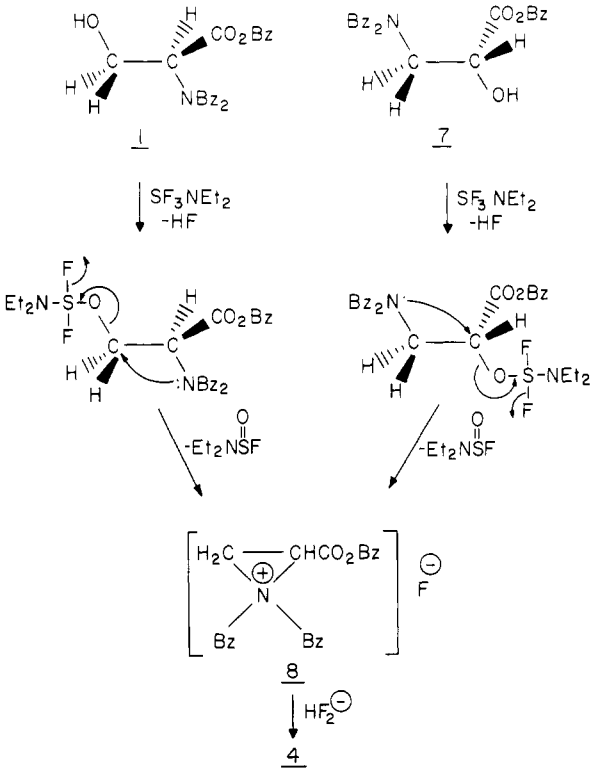

Table I. Preparation of α-Fluoro-β-amino Acids from *N*,*N*-Dibenzyl Derivatives of β-Hydroxy-α-amino Acids and DAST

product	yield,[a] %	mp, °C	^1H NMR, δ[b] CHF	^1H NMR, δ[b] CHN
4	90	80-81[c]	4.88 (dt, *J* = 49.0, 4.0)	2.93 (dd, *J* = 24.5, 4.0)
5A	60[d]	oil	4.86 (dd, *J* = 49.0, 3.8)	3.35 (m, *J* = 31.1, 7.0, 3.8)
5B	90	oil	5.21 (dd, *J* = 50.2, 3.8)	3.32 (m, *J* = 25.8, 6.9, 3.8)
6A	90	oil	5.18 (dd, *J* = 47.8, 2.6)	2.90 (dm, *J* = 33.2, 8.8, 2.6)
6B	90	83-84[c]	5.40 (d, *J* = 48.1)	2.88 (dd, *J* = 29.6, 10.0)

[a] The yields given are of isolated compounds. [b] The chemical shifts are in ppm from internal Me_4Si; the spectra were run at 270 MHz in $CDCl_3$ solutions; *J* values are in hertz. [c] Recrystallization solvent was ether–hexane. [d] Isomeric (*2R*,*3R*)-2-(dibenzylamino)-3-fluorobutyric acid benzyl ester was also isolated in 26% yield.

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(3) E. D. Bergmann and S. Cohen, *J. Chem. Soc.*, **4669** (1961).

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(5) P. Bey, M. Jung, and F. Gerhart, European Patent Application 24965 (1981) *Chem. Abstrs.*, **95**, 62710*b* (1981).

(6) H. M. Walborsky, M. E. Baum, and D. F. Loncrini, *J. Am. Chem. Soc.*, **77**, 3637 (1955).

(7) L. Velluz, G. Amiard, and R. Heynaes, *Bull. Soc. Chim. Fr.*, 201 (1955).

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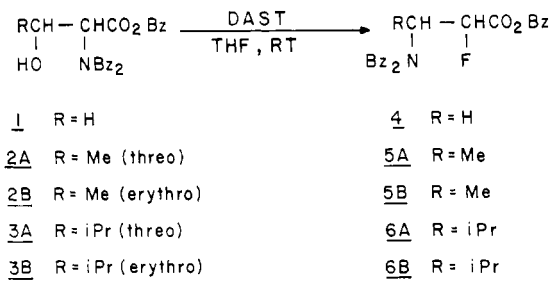

N,N-dibenzyl-α-fluoro-β-alanine benzyl ester (**4**, Scheme I) in 90% yield.[9] The structure of **4** was established by ^1H and ^{19}F NMR, IR, and mass spectrometry. Hydrogenolysis of **4** over Pd/C 10% catalyst gave optically active α-fluoro-β-alanine, $[\alpha]_D$ +29.1° (*c* 1.05, H_2O).[10]

So that stereospecificity of the reaction could be examined, the diastereoisomeric threonine and allothreonine derivatives **2A** and **2B**, respectively, were subjected to the same reaction conditions (the products and yields are given in Table I). Inspection of the NMR spectra of the rearranged fluorinated products obtained indicated that only one diastereoisomer from each reaction (**5A** and **5B**) was formed. The stereochemical purity of the products was confirmed by GLC analysis of their *N*-trifluoroacetyl isopropyl ester derivatives. On the basis of the NMR data of **5A** and **5B** and particularly the chemical shifts of the α hydrogen, we have assigned the threo configuration to the compound with the signal of higher field (**5A**) and the erythro configuration to the one of lower field (**5B**). In order to confirm this assignment, we subjected the monobenzyl derivative of **5A** to X-ray analysis. The crystal structure established the compound to have the threo configuration.[11]

The same reaction was also used with *threo*- and *erythro*-3-hydroxyleucine[12] derivatives (**3A** and **3B**, respectively) in order to produce the rearranged fluorinated products **6A** and **6B**, respectively. The stereochemical purity of the diastereoisomers **6A** and **6B** was shown by HPLC analysis (over silica SI 100, with CH_2Cl_2/hexane (2/3, v/v) as eluent). The assignment of the configuration was based on NMR data (similar to the previous case): **6A**, the threo configuration; **6B** the erythro configuration.

The stereospecificity of this reaction may be rationalized by the intermediacy of an aziridinium ion. The latter is probably formed by initial attack of DAST on the hydroxy group of the amino acid[13] and subsequent cyclization. Opening of the aziridinium ion by fluoride attack at the carbon atom α to the carboxyl group yields the rearranged product.

Support for the suggested mechanism was obtained when fluorination of the D-isoserine[14] derivative **7** with DAST provided α-fluoro-β-alanine in identical yield and optical activity as obtained from L-serine, implying a common intermediate (**8**).

In addition, the isolation of both (2*R*,3*R*)-2-dibenzyl-amino)-3-fluorobutyric acid benzyl ester (26%) and α-fluoro-β-amino acid **5A** (60%) from fluorination of *N,N*-dibenzyl-L-threonine benzyl ester (**2A**) (see Table I) strongly suggests ring opening at either the β or the α positions of the aziridinium intermediate.[15]

The formation of aziridinium ion intermediates in rearrangement reactions[16] and the participation of a carbonyl group in enhancing S_N2 attack at the α-carbon atom[17] are known. However, no case of opening of aziridinium ions at the carbon atom adjacent to the carbonyl group has, to our knowledge, been reported.

This method thus provides a useful route for the formation of α-fluoro-β-amino acids from β-hydroxy-α-amino acids in high stereospecificity and high yield. Further experiments are in progress to determine the detailed mechanism and stereochemical pathway of this rearrangement.

Registry No. 1, 82770-40-9; **2a**, 82770-41-0; **2b**, 82770-42-1; **3a**, 82770-43-2; **3b**, 82770-44-3; **4**, 82770-45-4; **5a**, 82770-46-5; **5b**, 82770-47-6; **6a**, 82770-48-7; **6b**, 82770-49-8; **7**, 82770-50-1; DAST, 38078-09-0; (3*R*,3*R*)-2-(*N*,*N*-dibenzylamino)-3-fluorobutyric acid, 82770-51-2.

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(9) A solution of **1** (1.875 g, 5 mmol) in dry THF (10 mL) was added for 20 min to a stirred solution of DAST (0.72 mL, 5.5 mmol) in dry THF (10 mL) at room temperature. The reaction mixture was stirred for a further 30 min, and then ice was added to destroy the excess DAST. The mixture was diluted with EtOAc, washed with 5% $NaHCO_3$, and concentrated in vacuo. Chromatography of the residue on silica gel (with 3.5% EtOAc in hexane as eluent) yielded 1.750 g of the rearranged fluorinated product **4**.
(10) The optical purity of **4** is under current investigation.
(11) The full X-ray structure has been established by Dr. F. Frolow and will be reported in a forthcoming publication.
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Synthesis and Structure of Novel Mononuclear and Binuclear Zerovalent Platinum Complexes Involving Coordination by Tin Centers To Give Heteropolymetallic Arrays of Three or Five Atoms. A Unique Bridging Function for Bivalent Tin and a New Class of Platinum(0) Dimers

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Metal cluster chemistry is currently an extremely active area of research. This may be attributed[1,2] to (a) the importance of the contribution to bonding theory that has accrued through characterization of novel polyhedral geometries and (b) the potential significance in relation to catalytic applications of the incorporation into a single molecular framework of metal centers having different coordination properties. We describe representatives of two new types of heteropolymetallic species containing platinum and tin, which are related to one another by demonstrating tetrahedral coordination geometry characteristic of zerovalent platinum. Both also embody bivalent tin centers, in one structure as electron-pair donor sites in terminally bound ligating groups and in the other in a highly unusual bridging configuration, i.e., as a bridging stannylene.[3] So far as we are

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