N-nitro-N-methylaniline-2,6-d_2 were assayed for their deuterium content by the falling-drop method.[14] The sample was burned to water by vaporizing it into a stream of oxygen which carried the vapors first over the decomposition product of silver permanganate (at 550°) and then over the decomposition product of potassium permanganate. The condensed water was diluted quantitatively with ordinary water so that the final sample contained *ca.* 0.4 at. % deuterium. The drop time in isobutyl benzoate was measured and compared with the drop times for standard D_2O–H_2O mixtures to obtain the atom per cent deuterium in the sample. The standard deviation of the measurement was *ca.* ±0.8%. Three determinations were made on each sample.

The isotopic purity of the various samples follows: *p*-iodoaniline-2,6-d_2, 1.82 D atoms; aniline-2,6-d_2, 1.83 D atoms; and N-nitro-N-methylaniline-2,6-d_2, 1.80 D atoms. These results were verified through independent analyses by a commercial laboratory.[15]

Radioactivity Assays.—*p*-Toluidine-2-*t*, 2,6-dibromo-4-toluidine (prepared from the *p*-toluidine-2-*t*), N-nitro-N-methyl-*p*-toluidine-2-*t*, and the rearrangement product, N-methyl-2-nitro-4-toluidine-6-*t*, were assayed for tritium content by liquid scintillation counting. The scintillator solution contained PPO and POPOP dissolved in an ethanol (23%)–toluene (77%) mixture. Carefully weighed samples of the tritiated compounds were dissolved in aliquots of the scintillator solution and the resulting sample solutions were counted.

To correct for differential quenching effects of the various compounds assayed, 1 ml of a solution of ethanol-*t* in toluene was added to each sample after counting and also to a blank containing only scintillator solution. The samples were then recounted. By comparing the increases in activity of the samples to that of the blank, the extent of quenching could be estimated and the actual sample counts could be corrected for this phenomenon.

Relative activities were calculated from the counts per minute per millimole using the average activity of N-nitro-N-methyl-*p*-toluidine as a standard of comparison. The average relative activities follow: *p*-toluidine-2-*t*, 1.03 ± 0.03; 2,6-dibromo-4-toluidine, 0.00 ± 0.00; N-nitro-N-methyl-*p*-toluidine, 1.00 ± 0.02; and N-methyl-2-nitro-4-acetotoluide-6-*t*, 0.52 ± 0.02.

Rates of Rearrangement of Aromatic Nitramines.—The methods described in previous papers[1b,c] in this series were utilized to determine the kinetic constants for the acid-catalyzed rearrangements of N-nitro-N-methylaniline, N-nitro-N-methylaniline-2,6-d_2, N-nitro-N-methyl-*p*-toluidine, and N-nitro-N-methyl-*p*-toluidine-2-*t*.

Spectrophotometric Analysis of Rearrangement Products.—The percentages of *o*- and *p*-nitro-N-methylaniline obtained from N-nitro-N-methylaniline and from N-nitro-N-methylaniline-2,6-d_2 were determined as described previously.[1a] The quoted results (Table I) are the average of two determinations.

Registry No.—N-Nitro-N-methylaniline, 7119-93-9; N-nitro-N-methylaniline-2,6-d_2, 23998-84-7; N-nitro-N-methyl-*p*-toluidine, 23042-30-0; N-nitro-N-methyl-*p*-toluidine-2-*t*, 23998-86-9.

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Absolute Configuration of 1-Methylalkylamines

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During a study of structure–taste relationships of substituted isoasparagines,[1,2] we were surprised to observe a reversal of configurational requirements for sweetness. Thus, in compounds where R_1 was methyl or methoxycarbonyl and R_2 was cyclohexyl or an aromatic ring, only the LL isomer was sweet. However, in the case of R_1 = methyl and R_2 = *n*-butyl or isobutyl the sweet isomer was LD. It seemed highly unlikely that in a biochemical reaction involving complexing between an optically active substrate and an enzyme site conformational specificity could be reversed by a change from cyclohexyl to *n*-butyl when the structural alteration was insulated from the asymmetric carbon by a methylene group. We were led, therefore, to reexamine the absolute configurations previously assigned to 1-methylhexylamine and 1,4-dimethylpentylamine.[3]

$$H_2NCH(CH_2CO_2H)CONHCH(R_1)CH_2R_2$$

For the sake of consistency with the literature, the designations L and D will be retained. It must be understood that for 1-methylalkylamines the assumption is implicit that the methyl group represents the carboxyl group of the corresponding amino acid and the alkyl group represents the amino acid side chain. This is true whether or not the amino acid so described exists in nature or not. The Cahn–Ingold–Prelog[4] system involves a different assumption, namely, agreement on the sequence rules. For amino acids L = *S*, but for the derived 1-methylalkylamines L = *R* which might introduce an element of confusion. However, for some of the compounds to be described the Cahn–Ingold–Prelog designation allows the argument to be followed with greater facility. Both systems will therefore be used in the present work.

L-Leucine has been related to 1,3-dimethylbutylamine having a positive rotation in methanol.[5] This amine is the closest analog to higher 1-methylalkylamines that can be derived from a naturally occurring amino acid. Resolution of 1,3-dimethylbutylamine, 1-methylhexylamine, and 1,4-dimethylpentylamine was achieved by fractional crystallization of the L-(+)-tartrates.[6] The bases were regenerated and distilled and rotations measured both neat and in methanol. The neat rotations were all negative; 1,3-dimethylbutylamine had a positive rotation in methanol while 1-methylhexylamine and 1,4-dimethylpentylamine had negative rotations in methanol. Treatment of resolved 1,3-dimethylbutylamine with *p*-toluenesulfonyl chloride in pyridine gave an amide identical with that obtained from L-leucine.

As further evidence for absolute configuration of the seven-carbon amines, partial resolution[7,8] of 2-phenylbutyric acid was carried out. The absolute configuration of this acid is *S*-(+).[7] If an excess of an optically inactive acid is caused to react with an optically active amine and the transition state is similar to the final product, then the resulting mixture of diastereoisomeric amides will contain an excess of the amide representing the least hindered transition state. The product can be analyzed easily by isolating unreacted

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acid and finding its sign of rotation. This acid is the isomer giving the most hindered transition state and, if the absolute configuration of the acid is known, the absolute configuration of the amine can often be deduced.

Coupling of the three amines with an excess of 2-phenylbutyric acid gave, in each case, recovered acid with a positive neat rotation and positive rotation in methanol. Since the structural changes among the three amines are not likely to alter group interactions in the 2-phenylbutyramides, 1-methylhexylamine and 1,4-dimethylpentylamine have the same absolute configuration as 1,3-dimethylbutylamine, namely *R*-(−) referred to neat rotations. As was mentioned above, in this series of amines *R* = L and taste turned out to be a reliable guide to absolute configuration.

Experimental Section

Elemental analyses were done under the direction of E. Zielinski and rotations under the direction of A. J. Damascus. Melting points were determined in a stirred bath and are uncorrected.

Resolutions.—1,3-Dimethylbutylamine (101 g, 1.0 mol) and 150 g (1.0 mol) of L-(+)-tartaric acid were dissolved in 600 ml of methanol, and the solution allowed to stand overnight at room temperature. The product (98.2 g) was crystallized three times from 2.5 parts of methanol to yield 41.2 g of the tartrate salt, mp 128–131°, $[\alpha]^{28}D$ +21.0° (*c* 1, MeOH). *Anal.* Calcd for $C_{10}H_{21}NO_6 \cdot {}^1/_3H_2O$: C, 46.68; H, 8.49; N, 5.44. Found: C, 46.91; H, 8.50; N, 5.46.

The above tartrate (30.2 g, 0.12 mol) was suspended in 150 ml of ether plus 50 ml of water. Sodium hydroxide (50%, 20 ml, 0.36 mol) was added and the mixture shaken vigorously. The ether layer was washed with 25 ml of 5 *M* potassium carbonate, and dried over anhydrous potassium carbonate; the ether was distilled. The residue was fractionated to yield 9.96 g (82%) of 1,3-dimethylbutylamine: bp 106–107°; $[\alpha]^{25}D$ −11.2° (neat), +3.5° (*c* 1, MeOH) [lit.[9] −10.7° (neat)]. *Anal.* Calcd for $C_6H_{15}N$: N, 13.84. Found: N, 13.65.

1-Methylhexylamine tartrate had mp 109–110°; $[\alpha]^{26}D$ +19.0° (*c* 1, MeOH). *Anal.* Calcd for $C_{11}H_{23}NO_6$: C, 49.80; H, 8.74; N, 5.28. Found: C, 49.53; H, 8.90; N, 5.12.

The free base had bp 140°; $[\alpha]^{25}D$ −6.7° (neat), −0.8° (*c* 10, MeOH). *Anal.* Calcd for $C_7H_{17}N$: N, 12.16. Found: N, 12.21.

1,4-Dimethylpentylamine tartrate had mp 142–144°; $[\alpha]^{28}D$ +19.5° (*c* 1, MeOH). *Anal.* Calcd for $C_{11}H_{23}NO_6$: C, 49.80; H, 8.74; N, 5.28. Found: C, 49.79; H, 8.90; N, 5.12.

The free base had bp 133°; $[\alpha]^{25}D$ −7.2° (neat), −0.6° (*c* 10, MeOH). *Anal.* Calcd for $C_7H_{17}N$: N, 12.16. Found: N, 12.48.

N-*p*-Toluenesulfonyl-L-1,3-dimethylbutylamine.—L-Leucinol N-*p*-toluenesulfonamide O-*p*-toluenesulfonate[5] (8.50 g, 0.02 mol), mp 105–107°, $[\alpha]^{25}D$ −54.1° (*c* 1, MeOH), was reduced with $LiAlH_4$ in refluxing ether. Crystallization of the crude product from *n*-pentane gave the desired amide, 3.29 g (65%), mp 65–67°, $[\alpha]^{25}D$ +3.8° (*c* 1, MeOH); lit.[5] mp 62–63°, $[\alpha]^{18}D$ +1.4° (*c* 0.8, EtOH).

Resolved 1,3-dimethylbutylamine (1.0 g, 0.01 mol) was treated with *p*-toluenesulfonyl chloride in pyridine. Crystallization of the crude product from *n*-pentane yielded the toluenesulfonamide, 2.03 g (80%), mp 65–67°, $[\alpha]^{28}D$ +4.5° (*c* 1, MeOH).

Anal. Calcd for $C_{13}H_{21}NO_2S$: C, 61.14; H, 8.29; N, 5.49; S, 12.56. Found: C, 61.45; H, 8.14; N, 5.78; S, 12.73.

Asymmetric Syntheses.—Racemic 2-phenylbutyric acid (9.84 g, 0.06 mol) was dissolved in 50 ml of methylene chloride, and 4.04 g (0.04 mol) of resolved 1,3-dimethylbutylamine was added. The mixture was stirred in an ice bath and 8.24 g (0.04 mol) of dicyclohexylcarbodiimide in 40 ml of methylene chloride was added. After stirring 0.5 hr at room temperature, the dicyclohexylurea was removed by filtration and the methylene chloride distilled. The residue was dissolved in ether and extracted with 50 ml of 1 *N* sodium hydroxide. The basic extract was acidified with hydrochloric acid and the unreacted 2-phenylbutyric acid taken up in ether; the ether extract was washed twice with water, dried over sodium sulfate, and distilled. The residue was dried overnight at room temperature under vacuum. Recovered 2-phenylbutyric acid (3.40 g, 0.0207 mol) had $[\alpha]^{27}D$ +7.4° (neat), +6.3° (*c* 10, MeOH).

When optically active 1-methylhexylamine was used, unreacted 2-phenylbutyric acid showed $[\alpha]^{26}D$ +7.3° (neat), +5.7° (*c* 10, MeOH).

When optically active 1,4-dimethylpentylamine was used, unreacted 2-phenylbutyric acid had $[\alpha]^{27}D$ +8.4° (neat), +6.5° (*c* 10, MeOH).

Registry No.—1-Methylhexylamine, 6240-90-0; 1-methylhexylamine tartrate, 24118-68-1; 1,4-dimethylpentylamine, 24110-97-2; 1,4-dimethylpentylamine tartrate, 24215-84-7; 1,3-dimethylbutylamine tartrate, 24118-69-2; 1,3-dimethylbutylamine toluene sulfonamide, 24118-70-5.

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Reaction of Perfluoro Olefins with Bromine Trifluoride in Bromine

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Bromine trifluoride has been used as a source of BrF in organic reactions; however, the references are few.[3,4] Chambers, *et al.*,[5] have reported the addition of BrF to hexafluoropropene to give the 2-bromo derivative. No information is available concerning such reactions with more complex perfluoro olefins. The present investigation concerns the reactions of bromine trifluoride in bromine with some perfluoroheptenes and hexenes. Davis and Larsen,[6] using BrF_3 in the presence of a large excess of Br_2, have replaced Br by F in bromofluoroethanes. In the present study no perfluoroalkanes were found. The major products of the reactive olefins are the perfluoroalkyl monobromides.

Perfluoroheptene-1 gave almost exclusively perfluoro-2-bromoheptane (87%). Other fractions isolated in small amounts were perfluoro-*trans*-2-bromoheptene-2 (4%) and perfluoro-*trans*-2-bromohexene-2 (9%). Perfluoroheptane and 1-bromoheptane were absent in the crude product as shown by vpc analysis. Perfluoroheptene-2,[7] synthesized by treating perfluoroheptene-1 with cesium fluoride,[8] gave a mixture of 50:50 perfluoro-2-bromo- and -3-bromoheptanes.

The reaction of BrF_3 in Br_2 with the three isomeric

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