The results showed the 1,4-diazabicyclo[2.2.1]heptane structure proposed by Pettit.[2,3]

Two cycles of isotropic least squares for all atoms reduced the R factor to 18% and one cycle of full-matrix anisotropic least squares gave an R value of 14.6%. Bond distances and angles are given in Figure 1 (a second set of data taken with Ni-filtered Cu radiation gave an R factor of 13.1% after one cycle of anisotropic least squares). A list of atomic coordinates for this structure is given in Table I.

New Compounds

Synthesis of Enantiomeric Chloroacetylcarnitine Chlorides

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Convincing experimental evidence exists for the role of (*R*)-(−)-carnitine in enzyme-mediated transport of activated acyl groups across mitochondrial and possibly other membranes.[1-6] Further, the structural similarity of carnitine (**1**) and acetylcarnitine (**2**) to choline and acetylcholine, respectively, the possible biotransformation of **1** and **2** to β-methylcholine,[7] and the use of **1** in the clinic,[8] point to possible therapeutic potential[9] and/or pharmacologic utility of these types of biological molecules or related derivatives. We report a convenient synthesis of (*R*)-(−)-, (*S*)-(+)-, and racemic chloroacetylcarnitine chlorides (**3**),[10] which have been investigated for cholinergic activity,[12,13] and in tissue culture.[14]

$$(CH_3)_3N^+CH_2CHO{-}X$$
$$\qquad\qquad\quad |$$
$$\qquad\qquad CH_2COO^-$$

1, X = H
2, X = $COCH_3$
3, HCl, X = $COCH_2Cl$

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(10) (*R*)-(−)-Bromoacetylcarnitine has been synthesized,[11] but the yield was not reported and purity was ascertained only by chemical assay and by tlc. This derivative in the presence of CoA has been demonstrated to be a reversible inhibitor of acetyl-CoA:L-carnitine *O*-acetyltransferase [E.C. 2.3.1.7]; in the absence of CoA it is an irreversible inhibitor, which is postulated to act by an active-site-directed mechanism.[11]

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(12) R. T. Louis-Ferdinand, K. R. Cutroneo, D. C. Kosegarten, R. C. Vasavada, J. G. Turcotte, and D. R. DeFanti, *J. Pharm. Pharmacol.*, **22**, 704 (1970).

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(14) (*RS*)-**3**, (*R*)-(−)-**3**, and (*S*)-(+)-**3** showed modest and comparable inhibition of murine leukemic lymphoblast (L5178Y) growth in culture, indicating that these quaternary ammonium salts may cross the plasma membrane; radioactive **1** has been shown to be progressively taken up by intact Ehrlich ascites tumor cells.[15]

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Experimental Section[16]

(*R*)-(−)-**Chloroacetylcarnitine Chloride (3).**—A mixt of 1.0 g (0.005 mole) of (*R*)-(−)-carnitine chloride, 0.9 g (0.005 mole) of chloroacetaic anhydride, and 0.1 g of *p*-TsOH was stirred at 70–75° for 75 min. The syrupy reaction mixt then was cooled to 25°, washed with Et_2O (3 × 5 ml), and taken up in 3.5 ml of *i*-PrOH. After standing 2–3 hr at 25°, and overnight at 5°, 0.85 g (62%)[18] of a cryst product was obtd. One recrystn from EtOH–*i*-PrOH afforded white crystals: mp 186–188°; $[\alpha]^{22}D$ −27.7° (*c* 8.03, H_2O); tlc (silica) R_f 0.07, CH_3CN–CH_3OH–NH_3 (10:5:2); ir (μ, Nujol) 5.69 (C=O, ester), 5.89 (C=O, acid); pmr (δ, D_2O) 2.91 (2, d), 3.2 (9, s), 3.81 (2, m), 4.32 (2, s), 5.67 (1, m). *Anal.* ($C_9H_{17}Cl_2NO_4$), C, H, N, Cl.

(*S*)-(+)-**Chloroacetylcarnitine chloride** (**3**) was obtained in 62% yield:[18] mp 186–188°; $[\alpha]^{22}D$ +29.8° (*c* 8.89, H_2O). *Anal.* C, H, N, Cl.

(*RS*)-**Chloroacetylcarnitine chloride** (**3**) with *p*-TsOH·H_2O as catalyst was obtained in 66% yield,[18] mp 179°. *Anal.* C, H, N, Cl.

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(16) (*R*)-(−)-Carnitine chloride, $[\alpha]^{22}D$ −21.7° (lit.[17] −23.7°), (*S*)-(+)-carnitine chloride, $[\alpha]^{22}D$ +23.1° (lit.[17] +23.6°), and (*RS*)-carnitine chloride were obtd from Nutritional Biochemicals Co., Cleveland, Ohio 44128. (*R*)-(−)-**3**, (*S*)-(+)-**3**, and (*RS*)-**3** were prepd using the same method and only details of the synthesis of (*R*)-(−)-**3** are given. Optically active precursors and products were found to be extremely hygroscopic, and it was necessary to use *anhyd* *p*-TsOH as catalyst and to scrupulously exclude moisture in order to obtain cryst products—operations requiring moisture-free conditions were carried out in a Labconco controlled atm glove box. The ir and pmr spectra of each compd were consistent with the expected structure and are reported for (*R*)-(−)-**3**. Melting points were detd with a Thomas-Hoover Uni-Melt capillary melting point apparatus and are uncorrected. Where analyses are indicated only by the symbols of the elements, anal. results obtained for those elements were within ±0.4% of the theor values; analyses by Micro-Analysis, Inc., Marshallton, Wilmington, Del.

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(18) Yields by this method approach those reported[19] using three different methods designed to improve yields of O-acylation of (*RS*)-carnitine chloride.

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3-Amino-4-hydroxy-L(−)-butyramide Hydrochloride[1]

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In the current investigation of compounds related to asparagine for antitumor activity, 3-amino-4-hydroxy-

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