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GEOMETRIC CONFIGURATION OF THE ISOMERIC 2-AMINO-TRANS-2-DECALINCARBOXYLIC ACIDS

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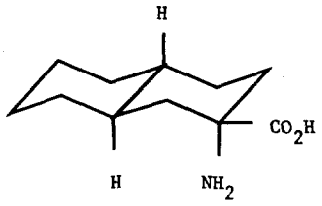
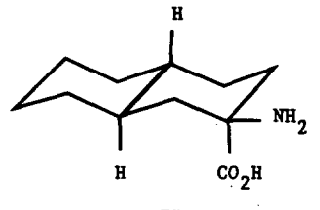
Munday[1] postulated that conformationally rigid alkyl-1-aminocyclohexanecarboxylic acids produced upon hydrolysis of their Bucherer-Lieb hydantoins possess carboxyl and amino functions locked in the equatorial and axial positions, respectively. Their conformational isomers, prepared *via* the Strecker cyanate method, were assigned the reverse configuration. Cremlyn and Chisholm[2] arrived at the opposite conclusion in an investigation of the amino acids derived from the Bucherer-Lieb and Strecker *trans*-2-decalinspiro-5'-hydantoins, leaving in doubt which interpretation is correct.[3] We wish to report some new evidence that, in contrast to the earlier report,[2] supports (I) as the product of Bucherer-Lieb synthesis of 2-amino-*trans*-2-decalincarboxylic acid.



I



II

Recent work has shown that α-chymotrypsin (CT) catalyzes the hydrolysis of equatorial *trans*-2-decalincarboxylic acid *p*-nitrophenyl ester (EQ-NPE) 1000 times faster than its axial analog.[4] The CT assisted hydrolysis rate of *p*-nitrophenyl 1,2,3,4-tetrahydro-2-naphthoate (tetrahydro-NPE) equals that of EQ-NPE, establishing that the enzymatically preferred conformation of the ester function of the non-rigid tetrahydro-2-naphthoates is equatorial. This suggested that by measuring the reactivity of CT towards the two geometrically isomeric *p*-nitrophenyl 2-acetamido-*trans*-2-decalincarboxylates (Bucherer-NPE and Strecker-NPE) and comparing their rates to that of *p*-nitrophenyl 2-acetamido-1,2,3,4-tetrahydro-2-naphthoate (amidotetrahydro-NPE) an assignment of configuration to the decalin amino acids and their parent hydantoins might be possible.

Racemic Bucherer-NPE, m.p. 150.5-151.5°, and racemic amidotetrahydro-NPE, m.p. 141.5-143°, were prepared using the dicyclohexylcarbodiimide (DCC) method. Strecker-NPE could not be synthesized; the N-acetylated amino acid resisted esterification using DCC in a variety of solvents. The ratio k_c/K_m was used to compare the reactivity of CT towards Bucherer-NPE and amidotetrahydro-NPE. This parameter provides one unequivocal measure of the specificity of the enzyme for a given substrate.[5] Progress of the enzymatic hydrolyses in pH 5.4, 0.05 M acetate buffer, 20% methanol, was monitored by following the production of p-nitrophenol at 330 nm. The kinetic behavior of both racemic esters indicated a low stereochemical preference by CT for one optical isomer. k_c/K_m values reported here used data obtained from the initial portions of the O.D. vs time curves. With amidotetrahydro-NPE k_c/K_m was evaluated under turnover[4] conditions ($K_m \approx S_0 > E_0$): $E_0 = 9.85 \times 10^{-7}$ M; $S_0 = 8.89\text{-}97.8 \times 10^{-6}$ M (18 point Lineweaver-Burk plot); $k_c/K_m = 2{,}670 \pm 250\ M^{-1}\ sec^{-1}$. An acylation[4] procedure ($E_0 \gg S_0$) produced a second-order rate constant equal to k_c/K_m for the Bucherer-NPE: $E_0 = 8.70\text{-}20.3 \times 10^{-6}$ M; $S_0 = 3.60\text{-}7.14 \times 10^{-6}$ M (12 experiments); $k_c/K_m = 2307 \pm 213\ M^{-1}\ sec^{-1}$.

The nearly identical reactivity of CT towards Bucherer-NPE and amidotetrahydro-NPE closely parallels the results found with EQ-NPE and tetrahydro-NPE.[4] Extrapolation of the available data to a common set of conditions also reveals that the value of k_c/K_m for all four esters is quite similar. The data support the idea that in Bucherer-Lieb 2-amino-trans-2-decalincarboxylic acid the carboxyl group is equatorial and the amino function is axial. Our inability to produce Strecker-NPE is consistent with the assignment of structure (II) to the Strecker amino acid. It is known that an axial carboxyl in trans-2-decalincarboxylic acid is sterically less accessible to reaction than the equatorial isomer[6] and that DCC esterifications often fail with sterically hindered amino acids.[7]

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