SYNTHESIS AND STEREOCHEMISTRY OF CHIRAL
2-AZETIDINONES AND 2-AZETIDINETHIONES.
2.* STUDY OF THE CHIROPTICAL PROPERTIES OF SOME
2-AZETIDINONES

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Circular dichroism (CD) spectra were taken for 13 2-azetidinones with one, two, and three asymmetric sites. A possible correlation was found between the sign of the Cotton effect (CE) of the n-π* transition of the amide chromophore with the absolute configuration of the endocyclic stereocenters of 3-methyl-, 4-methyl-, and 3,4-dimethyl-2-azetidinones both with and without an achiral N-α,α-dimethylbenzyl or chiral N-α-methylbenzyl substituent.

The literature data on the chiroptical properties of the simplest monocyclic 2-azetidinones are rather sparse and limited predominantly to derivatives without substituents at the nitrogen atom [2-4] and N-aryl derivatives [5]. Somewhat greater attention has been given to bicyclic models [6, 7] and azetidinones with additional functional groups or heteroatomic substituents [7-9]. A rather extensive series of monocyclic β-lactam stereoisomers became available as the result of our previous study on the chemistry and stereochemistry of chiral 2-azetidinones. These products may be divided into three types:
1) compounds without substituents at the nitrogen atom,
2) lactams containing an achiral α,α-dimethylbenzyl substituent at the nitrogen atom, and
3) azetidinones bearing a chiral α-methylbenzyl group at the nitrogen atom.

The absolute configuration for most of these compounds were established in our previous work [10, 12] as well as by Jensen [2, 14] and Kampe [15]. These findings permit us to evaluate the applicability of various sector rules for stereochemical assignment by analyzing the chiroptical properties of 2-azetidinones.

CIRCULAR DICHROISM SPECTRA OF β-LACTAMS WITH ENDOCYCLIC
ASYMMETRIC CENTERS

In studying the chiral properties of the 2-azetidinones synthesized in our laboratory, we began with their simplest representatives, namely, 3- (I) and 4-methyl-2-azetidinones (II), which lack substituents at the nitrogen atom.

*Communications 1, see ref. [1].

Both enantiomers of II have already been isolated [14, 15] and their CD spectra have been described [2]. Enantiomer (4R)-II [12] was used here for comparison. Both enantiomers of 3-methyl-2-azetidinone I were first obtained in our laboratory [11, 13] although a brief communication concerning the synthesis of racemic β-lactam (R,S)-I without spectral data was published initially by Okano et al. [16].

In order to establish the absolute configuration of the enantiomers of this azetidinone, (+)D-I and (−)D-I, we carried out the hydrolytic cleavage of the β-lactam ring of N-(S)-α-methylbenzyl diastereomer (+)235CD-III, which is related to (−)D-I (see Scheme 1). Subsequent removal of the N-(S)-methylbenzyl substituent in the N-substituted β-amino acid IV obtained in the first step by its hydrogenolysis over Pd(0) leads to the (+)D enantiomer of β-aminoisobutyric acid V, whose (S) configuration has been established by Okamoto et al. [17].

Since none of the transformations in the above scheme affects the asymmetric site at C(3), this permits us to assign absolute configuration (1S,3S)-III and (1'S,2S)-IV to starting isomer (+)235CD-III with specific rotation [α]D = −129.4° and intermediate N-substituted β-amino acid (+)D-IV, respectively. The removal of the chiral substituent at the nitrogen atom in azetidinone (+)235CD-III by the action of sodium in liquid ammonia gives (−)D-I, which is the basis for assigning (3S) configuration to this derivative. Thus, the (+)D enantiomer of 3-methyl-2-azetidinone I has (3R) configuration.

We should note that the chirorotical properties of 3-monosubstituted azetidinones lacking a substituent at the nitrogen atom have not yet been studied. CD spectra have been reported only for two enantiomers of a 3,3-disubstituted β-lactam, namely, 3-methyl-3-cyclopentyl-2-azetidinone (VIa,b), whose absolute configurations are unknown [3].