STEREOISOMERISM OF THE MATRINE ALKALOIDS


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The stereoisomerism of compounds of the matrine series is considered on the basis of the authors' own x-ray structural studies of these alkaloids. A corrected series of eight stereoisomers has been drawn up. It has been shown that the numbers of theoretically possible stereoisomers of matrine is thirty-two.

The molecule of the alkaloid matrine has four asymmetric carbon atoms — C(5), C(6), C(7), and C(11) [1, 2].

This makes the investigations of eight pairs of racemates theoretically possible. The stereoisomerism of these eight alkaloids was first considered in a paper by F. Bohlmann et al. in 1958 [3], and the stereoisomers were subdivided into representatives of the trans and cis series according to the type of linkage of rings A and B.

In 1975, Japanese workers isolated a new stereoisomer of matrine and subsequently established its structure and absolute configuration by x-ray structural analysis [4]. Taking this new compound — (+)-isomatrine — into account, as well, they arranged all the known stereoisomers in the series shown in Fig. 1.

We have previously studied the three-dimensional structures of six stereoisomers (matrine, allomatrine, isosophoridine, sophoridine, tetrahydroneosophoramine, and cis-matrine) by x-ray structural analysis [5-9]. On the basis of the results obtained, a more detailed consideration of the stereoisomerism of the alkaloids of the matrine series is possible.
Ueno et al. [4] ascribed structure (III) in Fig. 1 to sophoridine on the basis of L. I. Begisheva's incorrect results, while the NMR investigations of F. G. Kamaeva [10] and the results of our investigations [6] show that it is represented by structure (VII) shown in the same figure.

Apparently, tetrahydroneosophoramine (THNS), obtained by T. E. Monakhova et al. [11] by the hydrogenation of the alkaloid neosophoramine was unknown to Ueno et al. [4], and therefore they did not consider it. For this A/B-cis stereoisomer of matrine, Monakhova et al. [11], on the basis of chemical facts, proposed a configuration accurately coinciding with that of darvasamine [12] and subsequently confirmed by our x-ray structural investigations [8]. However, the physical constants of THNS and of darvasamine differ sharply, which shows the nonidentity of these compounds. In view of this, it may be assumed that either the configuration of darvasamine has been determined incorrectly or, if it is correct, this is a special case of conformerism — different conformations will correspond to one and the same configuration. Since the structure of darvasamine has not so far been studied by the method of x-ray structural analysis, we shall consider its configuration to be undetermined and put THNS in the series of stereoisomers in place of darvasamine.

In the paper of Ueno et al. [4], the absolute configurations of matrine, allomatrine, and (+)-isomatrine are given in the Cahn–Prelog–Ingold system of symbols [13]. The results that we have obtained indicate that the configuration of the C(7) asymmetric center of these compounds has been determined incorrectly — in matrine and allomatrine it should be S and in (+)-isomatrine it should be R. The C(11) asymmetric center of allomatrine also has the incorrect S configuration.

We have determined the relative configurations of all the stereoisomers studied, taking the configuration of the C(5) asymmetric center as the S configuration. The configurations of the other centers were established relative to the configuration of this center (relative configurations). Consequently, the configurations found correspond to the structures of the actual stereoisomers or to their optical antipode.

Thus, the correct series of matrine stereoisomers consists of six isomers and has the form shown in Fig. 2. In this series, the first four compounds form a trans series with respect to the linkage of rings A and B and the other a cis series.

The series of stereoisomers includes the still unknown compounds (VII) and (VIII). Their theoretical structures and relative configurations (Table 1) can be predicted on the basis of the structures of the known isomers. The system of denoting the conformations — chair C, boat B, and half-chair H — have been adopted from Schwartz [14]. For each of the compounds (VII) and (VIII), the A/B and the A/B-trans configurations are possible.

Table 1 gives the shortened contacts between valence nonbound atoms of the molecule for the given conformation. The conformation with the trans and cis linkages of the A/B rings of compounds (VII) and (VIII) are obtained from the conformations of allomatrine and iso-