UDC 547.94

SPATIAL STRUCTURE OF SOPHORIDINE AND SOPHORIDINIC ACID

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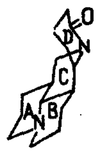
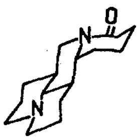
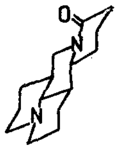
Isomers of matrine containing cis-C/D-linked rings, like perhydrophenanthrene [1] can exist in two spatial forms. In agreement with this, natural sophoridine [2] may correspond to one of the conformational formulas (I) or (II).



I

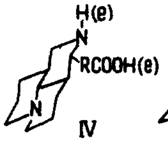


II

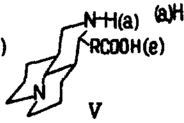


III

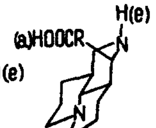
To determine the configuration of sophoridine, we have studied some reactions of sophoridinic acid, which would have one of the formulas given—(V) or (VI)—according to whether the configuration of sophoridine is that of (I) or (II).



IV



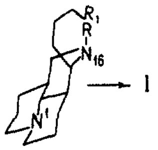
V



VI

The most stable isomer of matrine, allomatrine (III), must be represented by formula (IV). From a comparison of the configuration of the acids (V) and (VI), it can be seen that (V) differs from (IV) by the location of hydrogen at N_{16}—in (V) it is axial and in (IV) equatorial. If we obtain an N-substituted derivative of sophoridinic acid with a voluminous substituent, then in the case of (V) the latter, replacing axial hydrogen, must occupy the equatorial position, i.e., change into a derivative of (IV), which cannot be said of (VI), since it differs from (IV) by the location of the radical with the acid group.

When sophoridine was heated with concentrated hydrochloric acid, the hydrochloride of sophoridinic acid was obtained, and from this it was possible to isolate free sophoridinic acid. Then, by benzoylation of ethyl sophoridinate (VII) and subsequent saponification of the ester group we obtained N-benzoylsophoridinic acid (IX).



VI ($R=H, R_1=-COOH$)
VII ($R=H, R_1=-COOC_2H_5$)
VIII ($R=-COC_6H_5, R_1=-COOC_2H_5$)
IX ($R=-COC_6H_5, R_1=-COOH$)

The thermal treatment of the hydrochlorides of both sophoridinic acid (VI) and its N-benzoyl derivative (IX) led to the formation of sophoridine (I) and not of allomatrine (III). This shows unambiguously that sophoridinic acid is represented by the configurational formula (VI) and sophoridine by (I).

Experimental

Sophoridinic acid dihydrochloride. A mixture of 2.0 g of sophoridine (mp 109° C) and 10 ml of concentrated hydrochloric acid was heated for 5 hr. The residue, after evaporation, was washed several times with acetone and recrystallized from a mixture of acetone and ethanol (1 : 1), mp 243–245° C.

Found, %: C 51.64, 51.83; H 8.56, 8.44; N 7.83, 7.72; Cl 20.63, 20.90. Calculated for $C_{15}H_{26}N_2O_2 \cdot 2HCl \cdot 0.5\ H_2O$, %: C 51.72; H 8.19; N 8.00; Cl 20.40.

Sophoridinic acid. A solution of ethanolic potassium hydroxide was added to 0.55 g of sophoridinic acid dihydrochloride in 3 ml of absolute ethanol until the reaction was neutral. After the potassium chloride had been filtered off, the ethanol was distilled off from the reaction mixture; the residue crystallized in the form of a foamy mass with mp 65–67° C.

The dipicrate of sophoridinic acid had mp 168° C (from aqueous ethanol).

Found, %: N 14.93, 14.89. Calculated for $C_{27}H_{32}N_8O_{16}$, %: N 15.48.

Ethyl sophoridinate. A solution of 2.0 g of sophoridinic acid dihydrochloride in absolute ethanol was treated with two drops of concentrated sulfuric acid, and hydrogen chloride was passed through the solution to saturation. After 20 hr, the reaction mixture was boiled for 1 hr and the ethanol was distilled off. The residue was dissolved in water and the solution was saturated with potassium carbonate and extracted with ether.

Distillation of the solvent yielded 0.6 g of ethyl sophoridinate in the form of an oil; the hydrochloride had mp 250–251° C (from ethanol) and the picrate mp 195–195.5° C (from water).

Ethyl N-benzoylsophoridinate. A solution of benzoyl chloride in dry benzene was added to 0.5 g of ethyl sophoridinate in 3 ml of dry benzene. The reaction product was extracted with water and then from the aqueous solution with ether. After drying and the elimination of the solvent, 0.73 g was obtained of a viscous oily substance with R_f 0.98 [1-butanol–water–HCl (100 : 27 : 15)] which solidified to a resinous mass on trituration with acetone.

Found, %: C 71.60, 71.99; H 8.81, 8.81; N 7.39, 7.60. Calculated for $C_{24}H_{34}N_2O_3$, %: C 72.37; H 8.54; N 7.04.

N-Benzoylsophoridinic acid hydrochloride. A solution of 0.6 g of ethyl N-benzoylsophoridinate in 25% hydrochloric acid was evaporated to dryness, and the residue was triturated with dry acetone and recrystallized from absolute ethanol, mp 267–268° C.

Found, %: C 64.43, 64.22; H 7.78, 7.69; N 6.39, 6.52; Cl 8.93, 8.64. Calculated for $C_{22}H_{31}N_2O_3 \cdot HCl$, %: C 64.94; H 7.62; N 6.88; Cl 8.73.

Thermal treatment of sophoridinic and N-benzoylsophoridinic acid hydrochlorides. The hydrochlorides (0.2 g) were heated in an atmosphere of nitrogen to their melting points (245 and 268° C, respectively) for 30 min.

The contents of the tubes were dissolved in water and the solutions were made alkaline with potassium carbonate and extracted with ether. After evaporation of the solvent, in both cases, crystals with mp 108° C (sophoridine) were obtained.

Conclusion

It has been established that sophoridine and sophoridinic acid have the syn-cis configuration.

REFERENCES

1. R. P. Linstead and R. R. Whetstone, J. Chem. Soc., 1428, 1950.
2. F. Rulko and N. F. Proskurnina, ZhOKh, 31, 308, 1961.

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