

point is the subject of our further investigations.

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The Absolute Configuration of 2-Hydroxy-2-Methylbutyric Acid

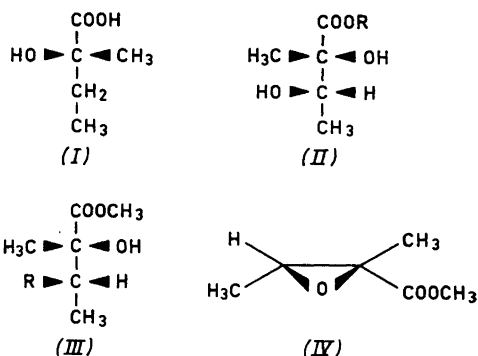
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The absolute configuration is unknown of the simplest, asymmetric, tertiary α -hydroxy-acid, 2-hydroxy-2-methylbutyric acid (2-ethyl-lactic acid), occurring in ester linkage in the *Veratrum* alkaloids protoveratrine A^{1,2} (protoveratrine^{3,4}), deacetylprotoveratrine A⁵ (deacetylprotoveratrine⁶), germerine^{7,8} and germitrine⁸, as well as in the bitter principle glaucarubin⁹. We now report that the naturally derived dextrorotatory acid possesses the (*S*)-configuration (I).

Upon reaction with diazomethane, (+)-*threo*-2,3-dihydroxy-2-methylbutyric acid, to which we recently assigned the (*2R,3S*)-configuration (II, R=H)¹⁰, afforded the corresponding methyl ester (II, R=CH₃)^{*}, b.p. 45°/0.1 mm, n_D^{25} 1.4428, $d_4^{21.5}$ 1.141, $[\alpha]_D^{22}$ -2.5° (neat), which was further converted into the *p*-toluenesulphonate (III, R=*p*-CH₃C₆H₄SO₂O), m.p. 66–67°, $[\alpha]_D^{23}$

* Satisfactory analyses and consistent infrared and NMR-spectra have been obtained for all new compounds reported.



–6.0° (*c* 11.5, CHCl₃). Treatment of the latter with sodium methoxide in methanol yielded a glycidic ester, b.p. 54°/11 mm, n_D^{25} 1.4160, $d_4^{21.5}$ 1.042, $[\alpha]_D^{22}$ +21.1° (neat), possessing the configuration (IV) on basis of the well-established inversion accompanying ring-closure reactions of the present type, induced through nucleophilic displacement. Nucleophilic attack on (IV) with methyl mercaptide, again accompanied by inversion at C-3, afforded the sulphide (III, R=CH₃S), b.p. 100°/10 mm, n_D^{25} 1.4737, d_4^{22} 1.107, $[\alpha]_D^{25}$ -6.7° (neat). Raney nickel hydrogenolysis converted this sulphide into the methyl ester (III, R=H), b.p. 153°, n_D^{25} 1.4137, d_4^{21} 1.002, $[\alpha]_D^{25}$ -6.45° (neat). Lastly, alkaline hydrolysis of the ester yielded (*R*)-2-hydroxy-2-methylbutyric acid, m.p. 73.5–74.5°, $[\alpha]_D^{25}$ -1.5° ± 0.1° (*c* 1.7, H₂O); -6.9° (*c* 1.5, 0.2 N NaOH); -8.5° (*c* 3.0, CHCl₃), *p*-phenylphenacyl ester, m.p. 122°, $[\alpha]_D^{22}$ -2.1° (*c* 3.0, CHCl₃). The melting points agree with literature values^{2,6-9} whilst the optical rotations of the acid are equal in magnitude * but *opposite in sign* to those reported for the dextrorotatory acid of natural

* Except for one set of rotation values⁸ ($[\alpha]_D^{24}$ +4.4° (*c* 1.6, H₂O); +12° (*c* 1.28, 0.2 N NaOH)) which we consider to be somewhat too high. (The original preparation has deteriorated and redeterminations of the reported rotations hence are excluded. Slightly too high polarimeter readings seem to be the only possible source of error (Dr. O. Wintersteiner, private communication)).

derivation^{2,6,7,9}. Hence, the latter possesses the (*S*)-configuration (I).

The present correlation supports the configurational assignment arrived at by application of Prelog's rule¹¹ to the reported preferential synthesis of *dextro* rotatory barium 2-hydroxy-2-methyl-butyrate from (–)-menthyl pyruvate and ethylmagnesium bromide¹².

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The Structures of some Polybromo Substituted Simple Ketones

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In a recent paper it was shown by Rappe and Schotte¹ using NMR-techniques that the two bromo atoms in dibromodiethyl ketone are symmetrically substituted on both sides of the keto group and not unsymmetrically as earlier proposed by Schotte². Among the di-, tri- and tetrabromo compounds of the lower aliphatic ketones several are described in the literature as having unsymmetric structures. As the methods used previously for structure determinations are rather ambiguous owing to possible rearrangements during the procedure³ it is of interest to make a new determination of the structures of these bromo ketones by means of NMR-spectroscopy.

The direct treatment of aliphatic ketones with bromine is reported to give impure products since the liberated hydrogen bromide tends to promote the formation of condensation products⁴. Although several other methods are available, the author made the bromo ketones by an acid catalyzed bromination of ketones dissolved in hydrobromic acid. The ketones used are acetone, methyl ethyl ketone, methyl propyl ketone and diethyl ketone. By using two, three or four equivalents of bromine, the di-, tri- or tetrabromo compound of the corresponding ketone could be obtained. In Table 1 the results of these syntheses are collected, and new structures (based on NMR-spectra) for most of the bromoketones are proposed. In some cases the yield of pure bromo ketone was better than the yield previously reported employing bromination with other methods.

It appears to be a common feature that the two and four bromo atoms in di- and tetrabromo ketones are symmetrically placed one or two on each side of the keto group. The tribromo compounds of symmetrical ketones have two of the bromo atoms on one side and the third on the other. The unsymmetrical ketones give mixtures of the two possible σ -substituted tribromo isomers.

A more detailed account of these works is to be published in *Arkiv för Kemi*.