

Citation:

<i>x</i> Sulpho-propionic acid and its resolution into optically active isomerides, in:
KNAW, Proceedings, 17 II, 1914, pp. 653-658

The nitrogroup attached to the nitrogen atom of the nitramine is evidently not essential for the reaction.

Further, the spectrum of trinitrobenzene with alkali, though much differing from that of the other alkaline solutions, has yet its absorption in about the same part $\left(\frac{1}{\lambda} \text{ 1800—2500}\right)$.

We may thus conclude, that in all these cases the coloration is produced by a reaction of the base with one or more nitrogroups of the nucleus.

Finally it has been shown, that the presence of a strong acid, as well as the introduction of acyl radicals, completely expels the absorption bands of picrylmethylamide.

Chemistry. — " *α -Sulpho-propionic acid and its resolution into optically active isomerides*". By Prof. A. P. N. FRANCHIMONT and Dr. H. J. BACKER.

(Communicated in the meeting of September 26, 1914).

Already in 1902 a great number of diverse chemical and biochemical methods were tried by the first of us to separate the α -sulphopropionic acid $\text{CH}_3(\text{SO}_3\text{H})\text{CHCO}_2\text{H}$ prepared by him ¹⁾ from propionic anhydride and sulphuric acid, into the two optical isomerides that one might expect according to theory. Not a single one, however, had given the desired result, although sometimes strychnine salts with a different rotating power were obtained, but after their conversion into ammonium salts these always appeared to be inactive.

As SWARTS ²⁾ had stated that he certainly had obtained from fluorochlorobromoacetic acid strychnine salts with varying rotating power, but had not succeeded in isolating the optically active acids. and as also PONCHER ³⁾, who tried to effect a separation of bromochloromethanesulphonic acid by means of cinchonine, only obtained rotating ammonium and barium salts, but no acids, it appeared as if with such simple acids the tendency to form racemic mixtures or compounds was very great and likewise the velocity of conversion. This was provisionally also assumed in the case of α -sulphopropionic acid (methylsulphoacetic acid) and the experiments were discontinued in consequence.

Still with lactic acid (methyloxyacetic acid) PURDIE and WALKER ⁴⁾

¹⁾ Rec. d. Tr. ch. d. P.B. 7. p. 27 (1888).

²⁾ Bull. Ac. Belg. (3) 31. p. 25 (1896).

³⁾ Bull. Soc. ch. (3) 27. p. 438 (1903).

⁴⁾ J. ch. Soc. 61. p. 754 (1892).

and with α -bromopropionic acid (methylbromoacetic acid) RAMBERG ¹⁾ had obtained decided results, but on the other hand, POPE and READ ²⁾ did not succeed in resolving the chlorosulphoacetic acid. The question now arose whether perhaps the sulphogroup created the difficulty, i. e. causes the rapid racemisation. This became less probable after POPE and READ ³⁾ had succeeded in splitting the chloriodomethanesulphonic acid and had found that the optically active acids thus obtained were not so readily transformed into the racemic mixture. Hence, the investigation of sulphopropionic acid was at once again taken in hand.

Both chlorosulphoacetic acid and methylsulphoacetic acid (α -sulphopropionic acid) are dibasic and thus can form acid salts. Moreover, the two groups that cause the acid reaction, have a different composition, the one being a carboxyl- and the other a sulphoxyl-group, and of different strength, so that as the sulphoxyl is stronger acid, salts will presumably contain the carboxyl-group in the free and the sulphoxyl-group in the combined state.

Whereas, previously, chiefly the neutral and mixed metallic salts and the neutral strychnine salt had been experimented with, the acid strychnine salt was now employed and the desired result was obtained at once.

α -Sulphopropionic acid itself was hitherto only known as a viscous syrup, whilst sulphoacetic acid had been obtained in crystals; therefore we have tried also to obtain α -sulphopropionic acid in a crystallized condition.

A dilute solution of the acid prepared by decomposition of the barium salt with the theoretical quantity of sulphuric acid was concentrated by partial freezing and draining by suction. The strong solution was placed in vacuo first over sulphuric acid and then over P_2O_5 . The viscous residue was kept for a day in an ice safe at about 0° , when gradually large crystals were formed. The acid thus obtained contains one mol. of water and is exceedingly hygroscopic. In order to determine its melting point a little apparatus was constructed, consisting of two tubes communicating with a transverse tube, one of which contained P_2O_5 and the other the α -sulphopropionic acid. After the apparatus had been evacuated and sealed, it was allowed to stand for a few days. The m. p. of the α -sulphopropionic acid was then found to be $100^\circ.5$, therefore, higher than that of sulphoacetic acid, which is stated to be $84^\circ-86^\circ$.

¹⁾ Ber. d. D. ch. G. 33. p. 3354 (1900).

²⁾ J. ch. Soc. 93. p. 795 (1908).

³⁾ J. ch. Soc. 105. p. 811 (1914).

An acid strychnine salt was obtained by evaporating an aqueous solution of the acid with the equimolecular quantity of strychnine on a steam-bath until crystallisation set in. The large crystals that had separated were purified by repeated crystallisation from water; their composition then was $C_3H_6O_5S + C_{21}H_{22}O_2N_2 + H_2O$. They, however, proved to be not the acid strychnine salt of the inactive (racemic) α -sulphopropionic acid, but of the dextrorotatory acid. On heating, they are decomposed at about 250° with evolution of gas and formation of a brown liquid.

As in the case of all other compounds described here, the rotating power was determined in aqueous solution with sodium light at 20° . By concentration c is meant the number of grams of anhydrous active substance per 100 cc. solution. The specific rotation $[\alpha]$ is likewise calculated on the anhydrous substance. The molecular rotation has, of course, the same value for the anhydrous and the hydrated crystalline substance.

For the acid strychnine salt was found at $c = 1.938$, $[\alpha]_D^{20} = -14^\circ.6$ and $[M]_D^{20} = -71^\circ.4$.

By way of comparing, strychnine hydrochloride was also investigated and at $c = 1.297$ was found: $[\alpha] = -30^\circ.2$ and $[M] = -112^\circ.1$.

The acid strychnine salt of α -sulphopropionic acid investigated is, therefore, presumably that of the dextrorotatory acid.

In order to obtain this acid, the acid strychnine salt was first decomposed with the theoretical quantity of barium hydroxide¹⁾. After complete separation of the strychnine by extracting the drained off liquid with chloroform, the neutral barium salt was precipitated by addition of alcohol. This salt is *laevorotatory*.

For $c = 1.764$ was found $[\alpha] = -4^\circ.96$ and $[M] = -14^\circ.4$.

From this salt the active α -sulphopropionic acid was liberated by

¹⁾ This value agrees fairly well with the constant $[M] = -114^\circ$ found by POPE and READ for a somewhat different concentration. J. Chem. Soc. **105**, p. 820 (1914).

²⁾ The acid strychnine α -sulphopropionate can be titrated with baryta water and a suitable indicator such as methyl-red which is sensitive to feeble bases. It may also be titrated with litmus to violet-blue. If however, phenolphthalein is used which is but little sensitive to weak bases such as strychnine, the colour does not appear until also the second acid group combined to the strychnine has been neutralised by the inorganic base. As the change in colour is fairly sharp, both with methyl-red and phenolphthalein, the titration forms an interesting application of the theory of indicators. Still more remarkable becomes the experiment, when both indicators are used simultaneously. The methyl-red passes into yellow after addition of a semi-molecule of barium hydroxide, the phenolphthalein then being still colourless; so soon, however, one mol. has been added, the violet colour of the phenolphthalein salt appears, unaffected by the pale yellow colour of the methyl-red.

the theoretical quantity of sulphuric acid and its rotatory power was then determined.

For $c=0.645$ was found $[\alpha]=+31^{\circ}.6$ and $[M]=+48^{\circ}.7$.

In another preparation was found for $c=1.85$, $[\alpha]=+32^{\circ}.0$ and $[M]=+49^{\circ}.2$.

Therefore, it is the *dextrorotatory* acid, whose neutral barium salt is *laevorotatory*.

It was now tried to obtain also this dextrorotatory acid in the solid condition. The solution was, therefore, concentrated in vacuo first over sulphuric acid and then over P_2O_5 . The viscous mass did not crystallize on cooling, but did so slowly after a trace of the racemic compound had been introduced. The crystals are exceedingly hygroscopic, melt between 81° and 82° and contain one mol. of water.

As the *neutral* barium salt of the *dextro* α -sulphopropionic acid rotates in the opposite direction of the free acid, it became of importance to investigate also the *acid* salt. For this was found at $c=0.776$

$$[\alpha]=+18^{\circ}.0 \text{ and } [M]=+79^{\circ}.8 \text{ or } =2 \times 39^{\circ}.9^1).$$

The acid potassium salt gave at $c=0.516$ the values:

$$[\alpha]=+23^{\circ}.8. [M]=+45^{\circ}.7.$$

The *acid* metallic salts of *dextro* α -sulphopropionic acid are, therefore, *dextrorotatory* like the acid itself. The racemisation of *dextro* α -sulphopropionic acid and its salts was also tried.

The aqueous solution, at $c=0.645$, when heated for six hours at 100° , suffered no appreciable racemisation, the rotation remaining unchanged.

A solution of the barium salt at $c=1.28$ after being heated for eight hours at 150° was racemised to the extent of 80% .

A solution of the potassium salt at $c=0.64$, which also contained 2% of free potassium hydroxide, was completely racemised after being heated for eight hours at 180° . An excess of free base thus seems to accelerate the racemisation²⁾, although also the temperature, the

¹⁾ As the molecule of the acid barium salt contains two groups of the sulphopropionic acid, it may for the sake of comparison with the other rotations be written more conveniently $[M]=2 \times 39^{\circ}.9$.

²⁾ This would agree with the rule given by ROTHE Ber. d. D. ch. G. 46. p. 845, (1914), that active carboxylic acids, the α -carbon atom of which is asymmetric and carries a hydrogen atom, are readily racemised under the influence of alkalies. He tries to explain this by assuming that, owing to the base, enol formation takes place in the molecule, thus causing the asymmetric carbon atom to disappear temporarily.

concentration and the duration of the reaction may exert an influence.

In the motherliquor, from which the acid strychnine salt of the *dextro*-acid had deposited, there should still be present that of the *laevo*-acid, this being more soluble. On addition of acetone a precipitate was obtained which could be recrystallized from absolute alcohol. Of course, it still contains a trifle of the less soluble salt of the antipode, but yet in one of the preparations it was obtained in a fairly pure condition.

For the rotating power at $c = 1.658$ was found $[\alpha] = -27^\circ.7$ and $[M] = -135^\circ$. The concentration does not seem to exert a great influence on the specific rotation, for, at $c = 8.424$ was found $[\alpha] = -27^\circ.4$ and $[M] = -134^\circ$.

From this acid strychnine salt of the *l*-acid the neutral ammonium salt was prepared. This gave for $c = 3.113$ the values $[\alpha] = +7^\circ.9$ and $[M] = +14^\circ.8$. The neutral ammonium salt of the *l*-acid is therefore, dextrorotatory.

If to a solution of the ammonium salt is slowly added dilute sulphuric acid, the dextrorotation diminishes, becomes zero and then changes to a laevorotation, which finally remains constant, as soon as all the organic acid has been liberated. The rotation for the *l*-acid, at $c = 2.449$, amounted to $[\alpha] = -29^\circ.8$ and $[M] = -45^\circ.8$.

Although we have not prepared the *l*- α -sulphopropionic acid in a pure and solid condition, it appears from the experiments in quite a

	<i>d</i> -acid		<i>l</i> -acid	
	$[\alpha]_D^{20}$	$[M]_D^{20}$	$[\alpha]_D^{20}$	$[M]_D^{20}$
α -sulphopropionic acid $C_3H_5O_2S$	+ 32.7	+ 49.2	- 29.8	- 45.8
acid potassium salt $C_3H_5O_2SK$	+ 23.8	+ 45.7		
acid barium salt $(C_3H_5O_2S)_2Ba$	+ 18.0	+ 79.8		
acid strychnine salt		$= 2 \times 39.9$		
$C_3H_5O_2S.C_{21}H_{22}O_2N_2$	- 14.6	- 71.4	- 27.7	- 135
neutral ammonium salt				
$C_3H_5O_2S(NH_4)$			+ 7.9	+ 14.8
neutral barium salt $C_3H_5O_2SBa$	- 4.96	- 14.4		

satisfactory manner that a resolution has been effected of the racemic α -sulphopropionic acid.

The specific and molecular rotations of the compounds investigated are united in the subjoined table. It should, however, be remarked that the values of the *l*-acid and its derivatives are less trustworthy because the acid has not been quite pure.

It deserves notice that the molecular rotation of the α -sulphopropionic acid ($49^{\circ}.2$) is certainly somewhat stronger than that of the α -bromopropionic acid ¹⁾ ($44^{\circ}.4$) although the bromine atom (80) differs but little in weight from the sulpho-group (81); still this may perhaps support the view that the weight of the group influences the rotatory power. If for instance, we compare with the rotation of α -ethylpropionic acid ²⁾ ($18^{\circ}.2$) we notice that both the rotation and the weight of the group (29) are less.

More interesting seems the fact that the rotation of the neutral metallic salts is much less than, and of an opposite sign to that of the acid metallic salts and the acids themselves, particularly in connexion with what has been stated at the commencement, namely that it concerns here a dibasic acid with two groups of different ionisibility which cause the acid functions.

Although the phenomenon that salts of optically active acids possess a rotatory power contrary to that of the acids themselves was observed previously, for instance with lactic and glyceric acids, the example now found seems a more simple one, because there are not present any groups that can react on each other, and because it may be called highly improbable that in the circumstances stated the carboxyl- and the sulphonyl-group should react on each other. Consequently, the rotation will, probably, be less dependent on concentration, temperature, age of solution etc.

In conclusion, it may be remarked that the laevorotation of the acid strychnine salt of the *d*- α -sulphopropionic acid as compared with that of strychnine hydrochloride, amounts to about as much less as the dextrorotation of the acid metallic salts.

¹⁾ RAMBERG. Liebig's Ann. 370. p. 234 (1909) gives $[\alpha] = 29^{\circ}.0$, whence $[M] = 44^{\circ}.4$.

²⁾ SCHÜTZ & MARCKWALD. Ber. d. D. ch. G. 29. p. 59 (1896) $[\alpha] = 17^{\circ}.85$, hence $[M] = 18^{\circ}.2$.