

CCXC.—*The Optical Resolution of Chlorosulphoacetic Acid.*

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WITH the exception of chlorobromoacetic acid (preceding paper), chlorosulphoacetic acid is the sole substance containing only two carbon atoms in the molecule whose ability to exist in enantiomorphous modifications has been satisfactorily demonstrated. Following inconclusive attempts to resolve chlorosulphoacetic acid with the aid of alkaloids and of *d*-hydroxyhydrindamine (Pope and Read, J., 1908, **93**, 795; 1914, **105**, 814), optically active aqueous solutions of ammonium *d*- and *l*-chlorosulphoacetate were recently prepared by Backer and Burgers (J., 1925, **127**, 233). These authors adopted the method of repeated fractional deposition of an alkaloidal salt from cold water. Aqueous solutions of ammonium *d*-chlorosulphoacetate prepared by decomposing two such fractions of a strychnine salt in the cold, with the calculated quantity of ammonia, exhibited the values  $[M]_D + 18.7^\circ$  and  $+20.5^\circ$ , respectively, the latter value being the highest recorded. Similarly, by the use of cinchonine, an aqueous solution of ammonium *l*-chlorosulphoacetate having the maximum value  $[M]_D - 18.5^\circ$  was obtained. These solutions manifested a slow decline in optical rotatory power when kept, and the ammonium salt racemised completely when evaporated to dryness.

From our related investigations it appeared that a substance so susceptible to racemisation in aqueous solution could scarcely be obtained in optically pure enantiomorphous modifications by means of the procedure adopted by Backer and Burgers (compare J., 1925, **127**, 1573, footnote). These anticipations were borne out as a result of a careful examination of the behaviour in organic solvents of the normal salt of chlorosulphoacetic acid with *l*-hydroxyhydrindamine. By fractional crystallisation from cold dry methyl alcohol, this salt readily yielded pure *l*-hydroxyhydrindamine *d*-chlorosulphoacetate, whilst the very soluble diastereoisomeric salt, *l*-hydroxyhydrindamine *l*-chlorosulphoacetate, remained in the mother-liquor, in association with a certain amount of the first salt. Upon converting *l*-hydroxyhydrindamine *d*-chlorosulphoacetate, *via* the sparingly soluble brucine salt, into ammonium *d*-chlorosulphoacetate, the value  $[M]_D + 31^\circ$  was observed for the last-named salt in dilute aqueous solution, in agreement with the approximate value  $[M]_D + 36^\circ$  calculated from the rotation of *l*-hydroxyhydrindamine *d*-chlorosulphoacetate. The result is in keeping with the comparatively low molecular rotatory powers recorded in our preceding

communications for related substances of simple molecular constitution. On account of the impracticability of recrystallising the impure *l*-hydroxyhydrindamine *l*-chlorosulphoacetate obtained from the mother-liquors, the maximum rotatory power exhibited by the derived ammonium *l*-chlorosulphoacetate was only  $[M]_D -24^\circ$ .

Backer and Burgers noticed that free *d*-chlorosulphoacetic acid, prepared by adding the calculated quantity of dilute sulphuric acid to an aqueous solution of ammonium *d*-chlorosulphoacetate having  $[M]_D +20.5^\circ$ , showed the much higher value  $[M]_D +40^\circ$ . The ammonium salt now described, having  $[M]_D +31^\circ$ , yielded in a corresponding way *d*-chlorosulphoacetic acid having  $[M]_D +76^\circ$ , the enhanced rotatory power being thus even more pronounced. Conversely, the value  $[M]_D +53^\circ$  of a partly racemised acid fell to  $[M]_D +16^\circ$  after exact neutralisation with ammonia.

According to Backer and Burgers, aqueous solutions of *d*-chlorosulphoacetic acid and ammonium *d*-chlorosulphoacetate underwent complete racemisation when evaporated to dryness. We have succeeded, however, in preparing crystalline specimens of optically active ammonium and benzidine salts of chlorosulphoacetic acid. Upon evaporation to dryness of an aqueous solution of pure ammonium *d*-chlorosulphoacetate, the value of  $[M]_D$  rose from  $+31^\circ$  to  $+60^\circ$ . The optical activity gradually declined to the original value in about 12 hours, and complete racemisation occurred upon then evaporating the solution to dryness; in this instance, the second solution possessed only one-quarter of the concentration of the original solution. Further experiments indicated that complete racemisation attends the slow evaporation of dilute solutions of the optically active ammonium salts, whereas the racemisation is partly or completely masked during the rapid evaporation of stronger solutions. Since the residual material after evaporation to dryness gave no evidence of appreciable hydrolysis, elimination of ammonium chloride, or other chemical change, an indication is afforded of the possible existence of ammonium *d*-chlorosulphoacetate in two dynamically isomeric forms possessing different rotatory powers, the free acid being apparently related more immediately to the ammonium salt possessing the higher optical activity than to the other. Each of the *l*-hydroxyhydrindamine salts, *lBdA* and *lBIA*, exhibited corresponding changes upon evaporation to dryness, the values of  $[M]_D$  changing from  $-85^\circ$  to  $-61^\circ$  and  $-81^\circ$  to  $-111^\circ$ , respectively. Thus, the optical rotatory powers of the ions of the *d*- and *l*-acid apparently received respective increments of 24 and 50 units as a result of the process.

The previous failure to effect the resolution of this acid by means of *d*-hydroxyhydrindamine (*J.*, 1914, 105, 814) must be attributed

to the racemising action of the water present in the hot aqueous alcohol used as solvent; the slight yet distinct fall in the molecular rotatory powers of successive fractions indicates that a partial resolution had indeed taken place, as suggested at the time. Since it is now shown that brucine *l*-chlorosulphoacetate is much less soluble in methyl alcohol than its diastereoisomeride, it appears likely that resolution might also be effected by means of a fractional separation of the brucine salts from this solvent, and we hope to investigate this point more fully.

#### EXPERIMENTAL.

*dl*-Chlorosulphoacetic Acid,  $\text{CHCl}(\text{SO}_3\text{H})\cdot\text{CO}_2\text{H}$ .—The barium salt (80 g.), prepared by Andreasch's method (*Monatsh.*, 1887, 7, 159), was fractionally crystallised from hot water (2000 c.c.), the recrystallised first fraction being taken as pure (Found: Ba, 41.5.  $\text{C}_2\text{HO}_5\text{ClSBa}, \text{H}_2\text{O}$  requires Ba, 41.9%). A suspension of the finely-powdered salt in hot water was treated with the requisite quantity of *N*-sulphuric acid, the concentration of chlorosulphoacetic acid in the filtered solution being then ascertained by titration.

#### *Salts of d-Chlorosulphoacetic Acid.*

##### *l*-Hydroxyhydrindamine *d*-Chlorosulphoacetate, $2\text{C}_9\text{H}_{11}\text{ON}, \text{C}_2\text{H}_3\text{O}_5\text{ClS}$ .

—Upon mixing equivalent weights of *dl*-chlorosulphoacetic acid (8.7 g.) and *l*-hydroxyhydrindamine (14.9 g.) in dry methyl alcohol (300 c.c.), the cold solution deposited a first fraction (4.2 g.) composed of minute, glistening prisms, m. p.  $203^\circ$  (decomp.); 0.2002 g., in solution (20.0 c.c.) in dry methyl alcohol, gave  $\alpha_D - 0.36^\circ$  in a 2-dcm. tube, whence  $[\alpha]_D - 18.0^\circ$  and  $[M]_D - 85^\circ$ . No mutarotation was observed on keeping this solution for 2 days. In a similar way, the mother-liquor yielded three further fractions, all of which were identical with the first fraction in appearance, rotatory power and melting point. The combined fractions, amounting to somewhat more than 40% of the calculated weight of one of the diastereoisomeric salts, underwent no appreciable alteration when fractionally recrystallised from dry methyl alcohol in the same way. The substance was therefore regarded as pure *l*-hydroxyhydrindamine *d*-chlorosulphoacetate (Found: C, 50.4; H, 4.9.  $\text{C}_{20}\text{H}_{25}\text{O}_7\text{N}_2\text{ClS}$  requires C, 50.8; H, 5.3%).

The salt dissolves readily in water, fairly readily in warm methyl alcohol, less readily in ethyl alcohol or glacial acetic acid, and is only sparingly soluble in most of the other common organic solvents. When a solution in dry methyl alcohol was evaporated to dryness on the water-bath and the *l*-hydroxyhydrindamine *d*-chlorosulpho-

acetate then redissolved in the cold solvent, the original values  $[\alpha]_D - 18.0^\circ$ ,  $[M]_D - 85^\circ$  declined to  $[\alpha]_D - 12.5^\circ$ ,  $[M]_D - 59^\circ$ . In water, 0.2001 g. made up to 20.0 c.c., gave  $\alpha_D - 0.36^\circ$  in a 2-dcm. tube, whence  $[\alpha]_D - 18.0^\circ$  and  $[M]_D - 85^\circ$ . No mutarotation was observed on keeping this solution for 2 days, but upon evaporating it to dryness on the water-bath and redissolving the crystalline residue in cold water, the observed value for the solution, made up to 20 c.c., was  $\alpha_D - 0.26^\circ$ , whence  $[\alpha]_D - 13.0^\circ$  and  $[M]_D - 61^\circ$ . Upon dissolving 0.1350 g. of the salt similarly in glacial acetic acid, with gentle warming, the values  $\alpha_D - 0.26^\circ$ ,  $[\alpha]_D - 19.2^\circ$ ,  $[M]_D - 91^\circ$  were recorded, but no observations of possible mutarotation could be made, owing to the rapid crystallisation of the material in the polarimeter tube.

*Brucine d-Chlorosulphoacetate.*—To a cold solution of *l*-hydroxy-hydrindamine *d*-chlorosulphoacetate (1.4 g.) in water (40 c.c.) was added a solution of the calculated weight of brucine (2.8 g.) in water (30 c.c.) containing a corresponding quantity of hydrochloric acid. Brucine *d*-chlorosulphoacetate (2.4 g.) was deposited slowly as hard, glistening prisms, with an average length of about 5 mm. The salt, m. p.  $196^\circ$  (slight decomp.), is sparingly soluble in water, glacial acetic acid, or chloroform, but it dissolves readily in methyl alcohol. A solution in methyl alcohol, containing 0.2036 g. in 20.0 c.c., gave  $\alpha_D - 0.04^\circ$ , whence  $[\alpha]_D - 2^\circ$ .

*Ammonium d-Chlorosulphoacetate*,  $\text{CHCl}(\text{SO}_3\text{NH}_4)\cdot\text{CO}\cdot\text{ONH}_4\cdot\text{H}_2\text{O}$ .—To an aqueous suspension of powdered brucine *d*-chlorosulphoacetate (about 4 g.) was added gradually at the ordinary temperature the calculated quantity of *N*-ammonia, together with a little chloroform, admixture being effected by shaking. The chloroform solution of the alkaloid was removed, and the aqueous layer extracted three times with the same solvent. The neutral aqueous solution, made up forthwith to 20.0 c.c., gave  $\alpha_{5461} + 1.20^\circ$  and  $\alpha_D + 1.02^\circ$  ( $l = 2$ ). By subsequently evaporating an aliquot part of the aqueous solution to dryness, the total weight of ammonium salt ( $M = 226.5$ ) present in 20.0 c.c. was found to be 0.7376 g., whence  $[\alpha]_{5461} + 16.3^\circ$ ,  $[M]_{5461} + 37^\circ$ , and  $[\alpha]_D + 13.8^\circ$ ,  $[M]_D + 31^\circ$ ; the rotatory dispersion  $\text{Hg}_{5461}/\text{Na}_D$  is thus 1.177. These readings remained unaltered after the solution had been kept for 24 hours.

5 C.c. of the solution were rapidly evaporated to dryness on a boiling water-bath, the crystalline residue being finally dried in a steam-oven. The resulting 0.1844 g. of ammonium salt, when redissolved in cold water, made up to 20.0 c.c., gave at once  $\alpha_D + 0.49^\circ$  ( $l = 2$ ), whence  $[\alpha]_D + 26.6^\circ$  and  $[M]_D + 60^\circ$ , and  $\alpha_D + 0.35^\circ$ ,  $+ 0.29^\circ$ , and  $+ 0.24^\circ$  after 8 minutes, 6 hours, and 12 hours, respectively, the corresponding values of  $[M]_D$  being  $+ 43^\circ$ ,  $+ 36^\circ$ ,

and  $+29^\circ$ . The solution was then evaporated to dryness; the crystalline residue when redissolved in water exhibited no measurable optical activity.

Another measured volume (10.0 c.c.) of the original solution of ammonium *d*-chlorosulphoacetate, having  $[M]_D +31^\circ$ , was treated with the calculated quantity of *N*-sulphuric acid (2 equivs.) and made up to 20.0 c.c. with water. The solution, containing 0.2841 g. of *d*-chlorosulphoacetic acid, gave  $\alpha_D +1.24^\circ$  ( $l = 2$ ), whence the values  $[\alpha]_D +43.6^\circ$  and  $[M]_D +76^\circ$  are derived for the free acid in dilute aqueous solution containing ammonium sulphate. When the solution was boiled for  $\frac{1}{2}$  minute and cooled rapidly, the reading  $\alpha_D$  fell to  $+1.02^\circ$ , whence  $[\alpha]_D +35.8^\circ$  and  $[M]_D +62^\circ$ ; after 18 hours, the value  $\alpha_D +0.87^\circ$  was observed, corresponding to  $[\alpha]_D +30.5^\circ$  and  $[M]_D +53^\circ$ . The solution was finally treated with the calculated quantity of *N*-ammonia and made up to 30.0 c.c. with water;  $\alpha_D$  was then  $+0.17^\circ$ , so that the dissolved ammonium *d*-chlorosulphoacetate had  $[\alpha]_D +6.9^\circ$  and  $[M]_D +16^\circ$ .

Ammonium *d*-chlorosulphoacetate crystallises in hard, glistening needles. It dissolves readily in water, but is practically insoluble in alcohol or acetone. An aqueous solution was rapidly evaporated to dryness, and the crystalline residue washed with methyl alcohol; it then decomposed at  $207^\circ$ . Ammonium *dl*-chlorosulphoacetate, after similar treatment, decomposed at  $201^\circ$ . In each instance, the redissolved salt gave only a slight opalescence when treated with dilute nitric acid and silver nitrate. Ammonium *d*-chlorosulphoacetate, obtained in the manner indicated, appears to resemble barium *dl*-chlorosulphoacetate and free chlorosulphoacetic acid by containing one molecular proportion of combined water (Found:  $\text{NH}_3$ , by absorption in standard acid, 14.7.  $\text{C}_2\text{H}_9\text{O}_5\text{N}_2\text{ClS}\cdot\text{H}_2\text{O}$  requires  $\text{NH}_3$ , 15.0%). A similar statement applies to ammonium *dl*-chlorosulphoacetate, which gave identical analytical results.

*Benzidine d-chlorosulphoacetate* separated in almost quantitative yield upon mixing solutions in glacial acetic acid of *l*-hydroxyhydrindamine *d*-chlorosulphoacetate and benzidine acetate. The salt is practically insoluble in the usual organic solvents, but it dissolves appreciably in hot water, from which the racemised salt separates, on cooling, in long, glistening needles, decomposing at  $245^\circ$ . Owing to its sparing solubility in cold water, the optical activity of the original separation was established by examining an almost saturated solution in a 4-dcm. tube in mercury green light. A solution containing 0.0858 g. in 30.0 c.c. gave  $\alpha_{5461} +0.18^\circ$ , whence  $[\alpha]_{5461} +15.7^\circ$ . The optical activity slowly diminished, and vanished when the solution was evaporated to dryness.

*Salts of l-Chlorosulphoacetic Acid.*

*l-Hydroxyhydrindamine l-Chlorosulphoacetate.*—The mother-liquor from the fourth fraction of *l*-hydroxyhydrindamine *d*-chlorosulphoacetate, described above, when kept at the ordinary temperature for several days yielded a somewhat sticky, semi-solid mass; this became dry and pulverable after further keeping in a desiccator. From the method of preparation, the material evidently consisted of *l*-hydroxyhydrindamine *l*-chlorosulphoacetate contaminated with a certain amount of *l*-hydroxyhydrindamine *d*-chlorosulphoacetate; owing, however, to its ready solubility and its reluctance to crystallise, a satisfactory purification of the salt was impracticable. When made up to 20.0 c.c. in dry methyl alcohol, 0.2004 g. gave  $\alpha_D -0.48^\circ$  ( $l = 2$ ), whence  $[\alpha]_D -24.0^\circ$  and  $[M]_D -113^\circ$ . Similarly, for 0.2001 g. in water, the value observed was  $\alpha_D -0.34^\circ$ , whence  $[\alpha]_D -17.0^\circ$  and  $[M]_D -81^\circ$ . The residue obtained by evaporating this solution to dryness gave the following values when redissolved in cold water and made up again to 20.0 c.c. :  $\alpha_D -0.47^\circ$ ,  $[\alpha]_D -23.5^\circ$ ,  $[M]_D -111^\circ$ .

*Brucine l-Chlorosulphoacetate.*—The above *l*-hydroxyhydrindamine salt, when treated with brucine acetate in the manner already indicated, yielded a separation of small, colourless prisms, which decomposed slightly at  $206^\circ$  and completely at  $235^\circ$ , without melting. The material, which evidently consisted of brucine *l*-chlorosulphoacetate contaminated with the diastereoisomeric salt, differed from the latter by reason of its slight solubility in methyl alcohol; it was sparingly soluble in water, glacial acetic acid, or chloroform.

*Ammonium l-Chlorosulphoacetate.*—Crude brucine *l*-chlorosulphoacetate was decomposed with dilute ammonia in the manner described above. The resulting aqueous solution, containing 1.2601 g. of the ammonium salt in 30.0 c.c., gave  $\alpha_D -0.74^\circ$  ( $l = 2$ ), whence  $[\alpha]_D -9.6^\circ$ ,  $[M]_D -20^\circ$ . After 2 days, the values were  $\alpha_D -0.61^\circ$ ,  $[\alpha]_D -8.0^\circ$ ,  $[M]_D -16.5^\circ$ . When the solution was evaporated to dryness on the water-bath the optical activity vanished.

A specimen of the ammonium salt prepared from brucine *l*-chlorosulphoacetate which had been purified by extraction with boiling methyl alcohol had  $[\alpha]_D -10.6^\circ$  and  $[M]_D -24^\circ$ , the former being the highest specific rotation observed for ammonium *l*-chlorosulphoacetate.

An aqueous solution of another specimen of the ammonium salt, containing 1.3 g. in 20 c.c. and having  $[M]_D -12^\circ$ , was divided into two equal parts. On evaporating the first part to dryness as rapidly as possible on the water-bath, the value of  $[M]_D$  declined to  $-8^\circ$ ; the second part, when evaporated similarly to a syrupy consistency, showed  $[M]_D -11^\circ$  when re-examined. The racemisation was

accelerated considerably in solutions containing small amounts of free ammonia.

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