CLXXXV.—*The Triazo-group. Part V. Resolution of
α-Triazopropionic Acid.*

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WHILE examining the properties of α-triazocamphor, or camphoryl-azoimide (Trans., 1905, 87, 826), we were impressed by the high specific rotatory power displayed by solutions in benzene, ethyl alcohol, acetone, and chloroform; with a concentration of 1 per cent., α-triazocamphor in these media gave $[\alpha]_D - 351^\circ$, -284° , -279° , and -246° respectively, values which are not approached by any known

derivative of the general formula $C_8H_{14} \begin{smallmatrix} \diagup CHX \\ | \\ CO \end{smallmatrix}$. Moreover, whilst camphor, α -chlorocamphor, α -bromocamphor, and α -iodocamphor are dextrorotatory to the extent of $[\alpha]_D$ 42°, 96°, 135°, and 160° respectively, α -triazocamphor resembles nitrocamphor in being lævoro-rotatory.

It would be reasonable to suppose from this comparison that the triazo-group is capable of exerting on the optical activity of a molecule in which it is attached to the asymmetric carbon atom an influence much more powerful than that of the halogen elements, and, in view of the general chemical resemblance between these latter and the complex in question, it became of interest to study other triazo-derivatives in which rotatory power is liable to be affected by this group. The case of α -triazocamphor being complicated by the presence of three asymmetric carbon atoms, we were led to select the simplest available molecule, namely, α -triazopropionic acid, and have resolved the racemic material (this vol., 671) by means of brucine, the salt of this alkaloid with *l*- α -triazopropionic acid crystallising readily from concentrated aqueous solutions of the racemic acid which have been neutralised with the base. Contrary to expectation, however, the influence of the triazo-group appears to be very slight, since the liquid acid has $[\alpha]_D -2.27^\circ$, which is raised to $[\alpha]_D -28.9^\circ$ by dissolution in ether. This comparatively insignificant optical activity is another illustration of the wide divergence between the effect of an azoimide complex when replacing hydrogen in a cycloid system and its influence in the aliphatic series, the asymmetric triazo-compound taking a normal position among the typical α -substituted derivatives of propionic acid. Optical data concerning these are curiously incomplete and conflicting, but we believe the following to represent existing information on the subject:

Acid.	$[\alpha]_D$.	$[\alpha]_D$ in water.	$[\alpha]_D$ of Ethyl ester.
α -Chloropropionic	unknown	unknown	19.9°
α -Bromopropionic	45°	unknown	37° to 46°
α -Hydroxypropionic	unknown	2.5° to 2.0°	14.5°
α -Aminopropionic	(solid)	2.7°	less than 1°
α -Triazopropionic	-2.27°	4.8° to 3.0°	18.2°

Keeping in view the tendency displayed by this class of compounds to undergo racemisation, the conditions likely to bring about this change have been, as far as possible, excluded in preparing *l*- α -triazopropionic acid, and, assuming the precautions to have been successful, it has been established that:

(a) The rotation of triazopropionic acid is very low compared with that of bromopropionic acid.

(b) The rotation of the free acid is opposite in sign to that of its ion, as in the case of lactic acid.

(c) The ester has a specific rotatory power comparable with that of lactic and chloropropionic esters, but much lower than that of bromopropionic ester.

(d) The rotation of the amide is not only much greater than that of the ester, but is opposite in sign.

(e) Replacing the triazo-complex by the amino-group leads to alanine of activity opposite to that of the original material.

The problem of referring *l*-α-triazopropionic acid to the corresponding alanine presented some difficulty at first, owing to the preclusion of alkaline reducing agents; aluminium amalgam was finally chosen, and, although no definite result was reached on reducing the ester, an aqueous solution of ammonium *l*-α-triazopropionate was found to yield *d*-alanine, a specimen of which was isolated in the form of its β-naphthalenesulphonic derivative. Through the kindness of Geheimrath Professor Emil Fischer, to whom we are indebted for several grams of *d*-alanine prepared from silk, we have been able to make a direct comparison of the β-naphthalenesulphonic derivatives from both sources, the original description (Fischer and Bergell, *Ber.*, 1902, 35, 3781) giving no information as to optical activity.

The question whether the change in direction of rotation on passing from triazopropionic acid to alanine is another case of the Walden inversion, cannot, of course, be determined until some process is devised for effecting the converse transformation.

EXPERIMENTAL.

l-α-Triazopropionic Acid, $\text{CH}_3 \cdot \text{CHN}_3 \cdot \text{CO}_2\text{H}$.

Preliminary experiments with cinchonine, bornylamine, and brucine indicated the last-named alkaloid as the one best calculated to effect satisfactory resolution of α-triazopropionic acid. An aqueous solution of cinchonine triazopropionate did not deposit crystals during many days, and concentration led to the separation of an oil even when conducted at the temperature of the laboratory; bornylamine formed a crystalline salt, but only in solutions so concentrated that the mother liquor was syrupy.

Two hundred and forty grams of brucine were mixed with 200 c.c. of water, and to the paste were added 70 grams of racemic α-triazopropionic acid, which quickly dissolved the alkaloid; crystallisation began almost immediately, and yielded 120 grams of brucine *l*-triazopropionate.

propionate, having $[\alpha]_D -25.6^\circ$. Recrystallisation from 120 grams of boiling water gave 90 grams of salt, which was further recrystallised from 500 c.c. of hot absolute alcohol; 70 grams of rectangular plates were thus obtained, having $[\alpha]_D -26.3^\circ$, this rotation being raised only one-tenth of a degree by another recrystallisation from 75 grams of boiling water, the final quantity of salt amounting to 62 grams. The specific rotatory power, $[\alpha]_D -26.4^\circ$, for brucine *l*-triazopropionate having been confirmed by another experiment, involving 100 grams of brucine and 30 grams of racemic α -triazopropionic acid, the specimen was regarded as an individual salt, and employed in preparing the active acid. Seventy-five grams were dissolved in warm water, treated with excess of ammonia, filtered from brucine, and extracted twice with chloroform to remove any remaining alkaloid. The aqueous solution of ammonium triazopropionate was then treated with 100 grams of sulphuric acid, diluted to 25 per cent., saturated with solid ammonium sulphate, and extracted five or six times with ether; after drying the solvent with sodium sulphate, evaporation was conducted without heating the acid, which was left in a vacuum desiccator until constant in weight, 15 grams remaining in the form of a colourless oil.

l-Triazopropionic acid has the appearance, odour, and chemical properties of the racemic substance, and the specific gravity is 1.2293 compared with water at 21° , which corresponds very nearly with that of the inactive material, 1.2247 at 25° ; in a 2-dm. tube the specimen gave $\alpha_D -5.35'$ at 21° , whence $[\alpha]_D -2.27^\circ$. A solution containing 4.1327 grams of the acid made up to 25 c.c. with ether at 23° gave $[\alpha]_D -9.33'$ in the 2-dm. tube, whence $[\alpha]_D -28.9^\circ$. The aqueous solution, however, is dextrorotatory, one containing 5.2136 grams of acid made up to 25 c.c. at 21° giving $\alpha_D 2.0'$ in the 2-dm. tube, whence $[\alpha]_D 4.8^\circ$; the same solution diluted to 50 c.c. gave $\alpha_D 0.38'$, whence $[\alpha]_D 3.0^\circ$.

The brucine salt dissolves readily in its own weight of boiling water, from which it crystallises in large, transparent, rectangular plates; it requires about five times its weight of absolute alcohol for dissolution, and is only sparingly soluble in the cold medium:

0.3183 gave 37.6 c.c. N_2 at 20° and 761 mm. $N = 13.53$.

$C_{23}H_{26}O_4N_2, C_8H_5O_2N_3$ requires $N = 13.75$ per cent.

The substance has not a definite melting point, but evolves gas at about 150° . It displays mutarotation, a solution containing 1.0005 grams made up to 25 c.c. with water giving $\alpha_D -1.50'$ in a 2-dm. tube, increasing to $-2.07'$ during half an hour on the water-bath; the initial and permanent values for the specific rotatory power are, therefore, $[\alpha]_D -22.9^\circ$ and -26.4° respectively. From this it appears that the

triazopropionic ion is dextrorotatory, and is therefore opposite in sign to the free acid, for, on calculating the contribution of the brucinium ion, this is found to be approximately $-2^{\circ}27'$, whence the contribution of the triazopropionic ion must be dextrorotatory, even supposing the undissolved salt to contain water of crystallisation, the possibility of which is suggested by the above analysis. This conclusion was confirmed by dissolving 20 grams of brucine *l*-α-triazopropionate in water, adding excess of ammonia, extracting three times with chloroform, concentrating to 100 c.c., and examining the aqueous solution in the polarimeter, when the ammonium *l*-α-triazopropionate was found to be dextrorotatory to the extent of 1° , which would correspond with an approximate value of 11° for the ion.

Ethyl l-α-Triazopropionate, $\text{CH}_3 \cdot \text{CHN}_3 \cdot \text{CO}_2 \cdot \text{C}_2\text{H}_5$.

Slight excess of silver oxide was mixed with the active acid dissolved in ether, and, without separating the salt from unchanged oxide, considerable excess of ethyl iodide was added and left in contact, with frequent shaking, during thirty-six hours at the laboratory temperature. It was hoped in this way to avoid any risk of racemisation, and the esterification appearing to be complete, silver iodide was filtered, and a gentle current of dry air passed through the liquid while maintained under 20 mm. pressure. The limpid residue, which had the characteristic odour of the racemic ester, after remaining several days in a darkened desiccator was distilled under 5 mm. pressure, when it boiled steadily at 49° . The specific gravity was 1.063 compared with water at 22° , and the rotatory power at this temperature was $\alpha_D -38^{\circ}42'$ in the 2-dcm. tube, whence $[\alpha]_D -18.2^{\circ}$. A 12 per cent. solution in ether had practically the same rotation, 3.0093 grams made up to 25 c.c. giving $\alpha_D -4^{\circ}27'$ in the 2-dcm. tube, whence $[\alpha]_D -18.5^{\circ}$.

l-α-Triazopropionamide, $\text{CH}_3 \cdot \text{CHN}_3 \cdot \text{CO} \cdot \text{NH}_2$.

Three grams of the active ester were shaken with concentrated aqueous ammonia during six hours, becoming thereby transformed into lustrous crystals of the amide; crystallisation from benzene gave snow-white needles melting at 85° , higher by 6° than the point at which the racemic compound fuses. Although derived from the levorotatory acid, the amide is dextrorotatory, a solution containing 1.0175 grams made up to 25 c.c. with water giving $\alpha_D 4^{\circ}0'$ in the 2-dcm. tube, whence $[\alpha]_D 49.1^{\circ}$; 0.8986 gram made up to 20 c.c. with acetone gave $\alpha_D 9^{\circ}0'$ in the same tube, whence $[\alpha]_D 100.1^{\circ}$.

Reduction of Triazopropionic Acid to Alanine.

Many preliminary experiments with the racemic acid and its ester were directed towards replacing the triazo-group by the amino-radicle, and the selection of aluminium amalgam as reducing agent followed. Two grams of inactive α -triazopropionic ester were diluted with 50 c.c. of ether, and treated with 5 grams of amalgamated aluminium gravel added in small quantities during six hours, drops of water being introduced occasionally while the liquid was cooled externally. The ethereal solution of alanine ester was then filtered from alumina and mixed with 2 grams of picric acid in ether; the solvent, on evaporation, deposited a pale red oil, which became crystalline when stirred with a few drops of water, and, on recrystallisation from warm water, which deposited one gram of lustrous, pale yellow needles, the substance melted and decomposed at 167° :

0.2310 gave 33.0 c.c. N_2 at 24° and 759 mm. $N = 16.00$.

$C_5H_{11}O_2N, C_6H_5O_7N_3$ requires $N = 16.19$ per cent.

The melting point recorded for the picrate of ethyl α -amino-propionate by Emil Fischer is 168° .

Three grams of the *l*-ester diluted with 50 c.c. of ether were then reduced with 10 grams of aluminium amalgam, and, on concentrating the filtrate and washings to 20 c.c., the solution was found to be still laevorotatory, although the rotation had diminished to about $35'$. This experiment being indecisive, however, owing to the possibility of the activity being due to unattacked triazopropionic ester, an aqueous solution of ammonium *l*-triazopropionate was reduced with the same agent, which furnished an inactive solution becoming dextrorotatory on adding hydrochloric acid; the result suggested the formation of *d*-alanine, which has $[\alpha]_D 2.7^{\circ}$ in water and $[\alpha]_D 10.4^{\circ}$ in the form of hydrochloride (Fischer and Raske, *Ber.*, 1907, **40**, 3720), but might equally well have arisen from unchanged *l*-triazopropionic acid, this being dextrorotatory in water. Accordingly, the liquid was neutralised with normal potassium hydroxide and agitated with excess of β -naphthalenesulphonyl chloride in ether during four hours, one molecular proportion of alkali being added after each hour; the colourless derivative obtained on acidifying the alkaline liquid with hydrochloric acid was recrystallised from boiling water, and, after being dried in the desiccator, melted at 112° . A direct polarimetric comparison between this product and the β -naphthalenesulphonic derivative of *d*-alanine was then made, the requisite amount of normal potash diluted with water being used as the solvent; in concentration approximating to 2.5 per cent., the specimen from *l*- α -triazopropionic acid gave $[\alpha]_D - 57.7^{\circ}$, whilst that from *d*-alanine gave $[\alpha]_D - 50.6^{\circ}$, a value perhaps a few

degrees too low because of the horny condition of the material, which it was therefore difficult to dry completely. The transformation

was thus established.

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