163. *The Configuration of Heterocyclic Compounds. Part IV. The Optical Resolution of* 10-*Phenylphenoxarsine*-2-*carboxylic Acid.*

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In Parts I and II (J., 1934, 1170; 1935, 1268) the resolutions of 10-methyl- and 10-ethylphenoxarsine-2-carboxylic acid were described. It was necessary to discover if the 10-aryl analogues could exhibit optical activity, and we therefore attempted the preparation of 10-phenylphenoxarsine-2-carboxylic acid. The synthetic method used for the alkyl compounds failed in the sense that treatment of 10-chlorophenoxarsine-2-carboxylic acid with phenylmagnesium bromide under various conditions gave no isolable quantity of the 10-phenyl acid. This difficulty was overcome by oxidising 10-phenyl-2-methylphenoxarsine (J., 1935, 1051) to 10-*phenylphenoxarsine*-10-*oxide*-2-*carboxylic acid* and reducing this, 10-*phenylphenoxarsine*-2-*carboxylic acid* being obtained.

Partial resolution of the l-α-*phenylethylamine* salt of this acid took place readily in alcoholic solution. The complete resolution, which presented considerable difficulty, was accomplished with results which are summarised below (rotations in ethyl alcohol) :

	M. p.	$[\alpha]^{20^\circ}_{5791}$.	$[\alpha]^{20^\circ}_{5461}$.
d-Acid	189—190°	+223·1°	+260·7°
dl-Acid	208—209	0	0
l-Acid	189—190	−223·2	−260·9

Attention is drawn to the high specific rotation of the new acid as compared with that of the methyl analogue, which has $[\alpha]^{20^\circ}_{5791}$ ± 96° in ethyl alcohol.

10-Phenylphenoxarsine has high optical stability. An ethyl-alcoholic solution of the *l*-acid lost none of its activity when it was heated for four hours in a closed tube at 100°. Oxidation of the *l*-acid to 10-phenylphenoxarsine-10-oxide-2-carboxylic acid was accompanied by complete loss of activity, although the oxide acid should be capable of optical activity even if the molecule is not possessed of a " folded " configuration. The resolution of the oxide acid is being attempted.

Experimental.

10-*Phenylphenoxarsine*-10-*oxide*-2-*carboxylic Acid.*—A suspension of 12 g. of 10-phenyl-2-methylphenoxarsine in a solution of 20 g. of potassium permanganate in 1200 c.c. of water was vigorously stirred at about 95° until oxidation ceased (1—2 hours). The resulting mixture was poured into excess of cold water saturated with sulphur dioxide and the *acid* precipitated was filtered off. It was dissolved in boiling alcohol, and excess of hot water added; 7 g. of small leaflets, m. p. 320°, then separated (Found : C, 60·0; H, 3·9. $C_{19}H_{13}O_4As$ requires C, 60·0; H, 3·45%).

dl-10-*Phenylphenoxarsine*-2-*carboxylic acid* was obtained by dissolving the oxide acid (19 g.) in chloroform, adding dilute hydrochloric acid and a little iodine, and passing sulphur dioxide through the warmed mixture for about an hour, the chloroform being allowed to evaporate gradually but completely. The precipitated *acid* was collected and crystallised from alcohol, 14·5 g. of hexagonal plates, m. p. 206—207°, being obtained. Recrystallisation from benzene raised the m. p. to 208—209° (Found : C, 62·6; H, 3·7. $C_{19}H_{13}O_3As$ requires C, 62·65; H, 3·6%).

The acid separates from alcoholic solutions at 0—10° with alcohol of crystallisation, the product melting below 100° with loss of solvent of crystallisation. The sodium salt of the acid is sparingly soluble in aqueous sodium hydroxide, from which it can be caused to separate as leaflets.

Reduction of small quantities of the oxide acid may readily be effected without the use of chloroform, since it is appreciably soluble in dilute hydrochloric acid, no doubt as the hydroxychloride.

Resolution of 10-*Phenylphenoxarsine*-2-*carboxylic Acid.*—The acid (30 g.) and 10 g. of *l*-α-phenylethylamine were dissolved together in 1400 c.c. of hot ethyl alcohol. The solution was allowed to cool, the crystalline material removed, and the mother-liquor evaporated, this process being repeated so that six crops were obtained by successive reduction of the volume. The first (15·3 g.) had $[\alpha]^{20^\circ}_{5791}$ +31·2° in methyl alcohol ($\alpha^{20^\circ}_{5791}$ + 0·91°; $l = 2$; $c = 1·458$). The second (3·5 g.) had $[\alpha]^{20^\circ}_{5791}$ − 27·1°; the third (6·5 g.) had $[\alpha]^{20^\circ}_{5791}$ − 29·4°; the fourth (9·1 g.) had $[\alpha]^{20^\circ}_{5791}$ − 18·9°; the fifth (0·7 g.) had $[\alpha]^{20^\circ}_{5791}$ − 46·6°; and the sixth (0·6 g.) had $[\alpha]^{20^\circ}_{5791}$ − 13·3°.

The first crop was recrystallised five times from ethyl alcohol, and 1·9 g. of salt were obtained with $[\alpha]^{20^\circ}_{5791}$ + 184·3°. Further crystallisation did not alter this value.

Successive recrystallisations of the other crops gave salts, the specific rotations of which varied from + 12·2° to − 79·4°. By combining crops with approximately the same rotation and recrystallising them many times there was finally obtained a pure salt of the *l*-acid, with $[\alpha]^{20^\circ}_{5791}$ − 191·2°.

l-α-*Phenylethylamine* d-10-*phenylphenoxarsine*-2-*carboxylate* crystallises from ethyl alcohol in clusters of needles, m. p. 208—209°, and has $[\alpha]^{20^\circ}_{5791}$ + 184·3° and $[\alpha]^{20^\circ}_{5461}$ + 214·5° in methyl alcohol ($l = 2$; $c = 1·354$; $\alpha^{20^\circ}_{5791} = + 4·99°$; $\alpha^{20^\circ}_{5461} = + 5·62°$) (Found : C, 67·1; H, 5·3. $C_{27}H_{24}O_3NAs$ requires C, 66·8 ; H, 5·0%).

l-α-*Phenylethylamine* l-10-*phenylphenoxarsine*-2-*carboxylate* crystallises from ethyl alcohol in very slender needles, m. p. 199—200°, and has $[\alpha]^{20^\circ}_{5791}$ − 191·2° and $[\alpha]^{20^\circ}_{5461}$ − 222·7° in methyl alcohol ($l = 2$; $c = 1·441$; $\alpha^{20^\circ}_{5791}$ − 5·51°; $\alpha^{20^\circ}_{5461}$ − 6·42°) (Found : C, 67·25; H, 5·2%).

The salts were decomposed by pouring a methyl-alcoholic solution into dilute hydrochloric acid, and the precipitated acids collected.

d-10-*Phenylphenoxarsine*-2-*carboxylic acid* crystallises in long glistening needles from ethyl alcohol. It melts at 189—190° and has $[\alpha]^{20^\circ}_{5791}$ + 223·1° and $[\alpha]^{20^\circ}_{5461}$ + 260·7° in ethyl alcohol ($l = 2$; $c = 0·865$; $\alpha^{20^\circ}_{5791} = + 3·86°$; $\alpha^{20^\circ}_{5461} = + 4·51°$) (Found : C, 62·5; H, 3·8%).

l-10-*Phenylphenoxarsine*-2-*carboxylic acid* has m. p. 189—190°, and $[\alpha]^{20^\circ}_{5791}$ − 223·2° and $[\alpha]^{20^\circ}_{5461}$ − 260·9° in ethyl alcohol ($l = 2$; $c = 0·934$; $\alpha^{20^\circ}_{5791}$ − 4·17°; $\alpha^{20^\circ}_{5461}$ − 4·875°) (Found : C, 62·1; H, 4·0%).

The *l*-acid was oxidised at room temperature with alkaline permanganate solution. A solution in aqueous ammonia of the oxide acid obtained was optically inactive.

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