CCXXV.—*Studies in the Penthian Series. Part IV. The Four Stereoisomeric Oxides of Benzamidobenzpenthiene.*

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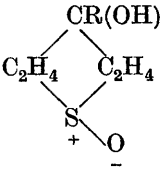
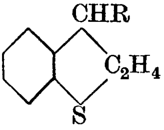
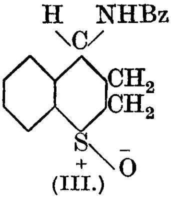
IN Part III (J., 1929, 2832) an account was given of the *cis-trans* isomerism of certain penthian-4-ol oxides (I), of which the molecules are symmetrical about a plane. The investigation has now been extended to a similar case where this element of symmetry was absent, so that enantiomorphism could arise, a suitable substance of the type (II) being selected which should give rise on oxidation to two sulphoxides each resolvable into a pair of optically active forms.


(I.)


(II.)


(III.)

An attempt to prepare the hydroxy-carboxylic acid from thiachromanone (benzpenthienone) through its cyanohydrin was unsuccessful, for the ketone did not, even under the most favourable conditions, combine with hydrocyanic acid to an appreciable extent, thus resembling α-ketotetrahydronaphthalene (Lapworth and Manske, J., 1928, 2548).

A substance of the required type was finally obtained as follows. Thiachromanone was converted by reduction of its *oxime* into aminobenzpenthiene, which was resolved into its optical antipodes by means of *d*- and *l*-α-bromocamphor-π-sulphonic acids. The crystalline d- and l-*benzamidobenzpenthienes* each yielded by oxidation with hydrogen peroxide a pair of stereoisomeric *oxides* (III), which were separated in a state of optical purity. The two dl-*oxides* were similarly prepared by oxidation of dl-*benzamidobenzpenthiene*.

The m. p. of each *dl*-compound is lower than that of the active form except in the case of the sulphone derived from acetamidobenzpenthiene (see table).

	Benzamidobenzpenthienes (rotatory powers in 1% chloroform solution).			*Acetamidobenzpenthienes.*	
	d.	*dl.*	*l.*	*dl.*	*l.*
M. p. ...	170°	158°	170°	159°	199°
$[\alpha]_D$	+100·5°	—	−99·6°	—	−190·5° *
	d-α-Oxide.	*dl*-α-Oxide.	*l*-α-Oxide.		
M. p. ...	220·5°	210·5°	220·5°		
$[\alpha]_D$	+176°	—	−177°		
	d-β-Oxide.	*dl*-β-Oxide.	*l*-β-Oxide.		
M. p. ...	204°	180·5°	204°		
$[\alpha]_D$	−106°	—	+105·5°		
	d-Dioxide.	*dl*-Dioxide.	*l*-Dioxide.	*dl*-Dioxide.	*l*-Dioxide.
M. p. ...	237°	202·5°	237°	240°	239°
$[\alpha]_D$	+ 44·5°	—	− 43°	—	− 69° *

* In ethyl alcohol.

EXPERIMENTAL.

Action of Hydrocyanic Acid and of Hydroxylamine on Thiachromanone.—Thiachromanone (m. p. 28°; see Arndt, *Ber.*, 1923, **56**, 1269) was recovered unchanged after several attempts to convert it into the cyanohydrin, in one of which a large excess of hydrocyanic acid was distilled into a cold concentrated alcoholic solution of the ketone containing potassium cyanide, and the mixture was acidified after standing for several hours.

An aqueous-alcoholic solution of thiachromanone (16·2 g.), hydroxylamine hydrochloride (7 g.), and potassium hydroxide (30 g.) was kept over-night. Unchanged ketone was extracted with ether, and the oxime then removed in ether after acidification with acetic acid. The product (18·5 g.) recovered by evaporation of the dried ethereal solution was crystallised successively from 50% alcohol and petroleum (b. p. 70—80°), *thiachromanoneoxime* being obtained in colourless plates, m. p. 98—100° (Found : N, 7·9. C_9H_9ONS requires N, 7·8%).

Reduction of Thiachromanoneoxime.—A solution of the oxime (25 g.) in glacial acetic acid (250 c.c.) was violently agitated during the addition of zinc dust (70—80 g.). Next day, most of the acetic acid was removed from the filtered solution in steam, an excess of ammonia added, the base extracted with ether, and the extracts dried over sodium sulphate and evaporated. 4-Aminobenzpenthiene, thus isolated as a brown oil which could not be distilled unchanged, was characterised by the preparation of the *picrate*, which formed small yellow granules from water or monoclinic plates from alcohol, m. p. 220° (decomp.) (Found : N, 14·2. $C_{15}H_{14}O_7N_4S$ requires N, 14·2%). The hydrochloride, obtained from the base and hydrogen chloride in dry benzene (yield, 77% of that calculated from the oxime), was an almost colourless, microcrystalline powder, very soluble in alcohol and in water; it could not be purified and the crude salt was used for subsequent experiments. dl-4-*Acetamidobenzpenthiene* crystallised from petroleum (b. p. 90—120°) in fine needles with a straight extinction; m. p. 157—159° (Found : N, 6·9. $C_{11}H_{13}ONS$ requires N, 6·9%). Oxidation of this substance with hydrogen peroxide in boiling glacial acetic acid furnished dl-4-*acetamidobenzpenthiene dioxide*, which was crystallised successively from xylene, methyl ethyl ketone, and water, from which it separated in colourless monoclinic prismatic needles, m. p. 238·5—240° (Found : C, 55·2; H, 5·5. $C_{11}H_{13}O_3NS$ requires C, 55·2; H, 5·4%). This substance is somewhat easily soluble in water or ethyl alcohol.

dl-4-*Benzamidobenzpenthiene* crystallised from alcohol in fine colourless needles with a straight extinction; m. p. 158° (Found : C, 71·9; H, 5·8; N, 5·1; S, 12·1. $C_{16}H_{15}ONS$ requires C, 71·4; H, 5·6; N, 5·2; S, 11·9%). It was oxidised by hydrogen peroxide in boiling acetic acid to the corresponding sulphone, dl-4-*benzamidobenzpenthiene dioxide*, which crystallised from methyl ethyl ketone or xylene in colourless needles, m. p. 201—202·5° (Found : N, 4·9. $C_{16}H_{15}O_3NS$ requires N, 4·7%).

Oxidation of dl-4-*Benzamidobenzpenthiene to a Pair of Oxides.*—To the sulphide (3·35 g.) in the minimum of glacial acetic acid, hydrogen peroxide (1·71 g. of 24·8% solution) was slowly added with agitation. The mixture, after standing over-night, was freed from acetic acid, and the crude product (3·5 g.) was separated very easily by crystallisation from alcohol into two isomeric sulphoxides. dl-4-*Benzamidobenzpenthiene α-oxide* separated first; it crystallised from methyl ethyl ketone in minute needles resembling cotton-wool (1·2 g.), m. p. 210·5° (Found : C, 67·6; H, 5·5. $C_{16}H_{15}O_2NS$ requires C, 67·4; H, 5·3%).

dl-4-*Benzamidobenzpenthiene* β-*oxide* was obtained by evaporation of the alcoholic mother-liquor. It crystallised in contact with methyl ethyl ketone, was fractionally crystallised from this solvent, and finally obtained in small prisms (0·5 g.) from xylene; m. p. 180·5° (Found: C, 67·3; H, 5·6%). It was very readily soluble in ethyl alcohol, but less soluble in cold methyl ethyl ketone. Mixed with an equal weight of the α-isomeride, it melted at 163—181°.

Resolution of dl-*Aminobenzpenthiene into its Active Components.*—The tartrate, malate, and camphor-10-sulphonate of the base did not give a ready resolution, but the *d*-α-bromocamphor-π-sulphonate was found to be suitable.

The hydrochloride of the *dl*-base (60 g.) and ammonium *d*-bromocamphorsulphonate (97·5 g.) were separately dissolved in hot water and mixed (2900 c.c.). A little oily deposit was removed by filtration, and the solution concentrated to half its bulk; a salt (30 g.) then separated having $[\alpha]_D$ + 41·5° in 0·903% aqueous solution, and a further crop (16·3 g.) had $[\alpha]_D$ + 63·4°. By fractional crystallisation to constant rotation the pure l-*aminobenzpenthiene* d-*bromocamphorsulphonate* was isolated, which formed highly refractive, orthorhombic plates from water (Found: N, 2·9. $C_{19}H_{26}O_4NBrS_2$ requires N, 2·9%). In water (*c* 1·01), $[\alpha]_D$ = + 27·2°, unchanged on recrystallisation.

Benzoylation of the liberated lævo-base yielded l-4-*benzamidobenzpenthiene*, which crystallised from ethyl alcohol in colourless needles, m. p. 170° (Found: N, 5·4. $C_{16}H_{15}ONS$ requires N, 5·2%); $[\alpha]_D$ − 99·6° in 1·316% chloroform solution. This benzoyl compound was oxidised by hydrogen peroxide in hot glacial acetic acid to l-4-*benzamidobenzpenthiene dioxide*, which crystallised from xylene in colourless needles, m. p. 237° (Found: N, 4·7. $C_{16}H_{15}O_3NS$ requires N, 4·7%); $[\alpha]_D$ − 43·0° in 0·562% solution in chloroform. The liberated *l*-base was also acetylated: l-*acetamidobenzpenthiene* crystallised from petroleum (b. p. 90—120°) in colourless needles, m. p. 199° (Found: N, 6·8. $C_{11}H_{13}ONS$ requires N, 6·8%); $[\alpha]_D$ − 190·5° for a 0·698% solution in ethyl alcohol. It was oxidised by hydrogen peroxide in hot glacial acetic acid to l-*acetamidobenzpenthiene dioxide*, which separated from water in fine needles, m. p. 239° (not depressed by admixture of the *dl*-compound) (Found: C, 55·4; H, 5·3. $C_{11}H_{13}O_3NS$ requires C, 55·2; H, 5·4%); $[\alpha]_D$ − 69·0° in 1·372% alcoholic solution.

The crops of salt from the crystallisation having $[\alpha]_D > + 60°$ were shaken with aqueous ammonia and the base was removed in ether, recovered by evaporation, dissolved in benzene, and thrown out as the hydrochloride. This was mixed with an equivalent of ammonium *l*-bromocamphorsulphonate in aqueous solution and the salts were fractionally crystallised as before. *d*-Aminobenzpenthiene *l*-bromocamphorsulphonate was then isolated quite readily, $[\alpha]_D$ − 27·2°.

After several weeks' standing, there was collected from the mother-liquor a small quantity of l-*aminobenzpenthiene* l-*bromocamphorsulphonate*, which crystallised in stout prisms or prismatic needles from water (Found : C, 47·9; H, 5·9. $C_{19}H_{26}O_4NBrS_2$ requires C, 47·9; H, 5·5%); $[\alpha]_D$ − 90·0° in 0·6892% aqueous solution, in agreement with the value to be expected for this salt. The antipode of this salt was not isolated.

The *d*-base was liberated from the pure salt and readily converted into d-4-*benzamidobenzpenthiene*, which crystallised in fine needles, m. p. 190°, from paraffin (b. p. 90—120°) (Found : C, 71·9; H, 5·7; N, 5·3. $C_{16}H_{15}ONS$ requires C, 71·4; H, 5·6; N, 5·2%); $[\alpha]_D$ + 116·0° in 0·856% solution in alcohol and + 100·5° in 2·2808% solution in chloroform.

Oxidation of this benzoyl derivative by hydrogen peroxide in hot glacial acetic acid yielded d-4-*benzamidobenzpenthiene dioxide*, which crystallised from absolute alcohol and from xylene in colourless needles, m. p. 237° (Found : N, 4·8. $C_{16}H_{15}O_3NS$ requires N, 4·7%); $[\alpha]_D$ + 44·5° in 0·788% chloroform solution.

Oxidation of d-4-*Benzamidobenzpenthiene to a Pair of Sulphoxides.*—*d*-Benzamidobenzpenthiene (7·1 g.) was oxidised in glacial acetic acid by addition of hydrogen peroxide (3·9 g. of 22·9% solution) with agitation. After 12 hours, the mixture was diluted and neutralised, giving 6·7 g. of product; a further 0·95 g. was obtained by extraction of the liquid with chloroform. The mixture after crystallisation from xylene melted at 177—205°. Separation of the two isomerides was effected by crystallisation from 33% aqueous alcohol and from water.

d-*Benzamidobenzpenthiene α-oxide* (yield, 1·5 g.) crystallised from water in elongated plates with a straight extinction; m. p. 220·5° (Found : C, 67·4; H, 5·25; N, 5·1. $C_{16}H_{15}O_2NS$ requires C, 67·4; H, 5·3; N, 4·9%); $[\alpha]_D$ + 176° in 2·006% chloroform solution. This substance is more soluble in cold water than the isomeride, which is also much less soluble in chloroform. Both are far more soluble in alcohol than the *dl*-compounds.

d-*Benzamidobenzpenthiene β-oxide* was isolated (yield, 1 g.) by crystallising the lower-melting crops of crystals from methyl ethyl ketone. It formed long plates with straight extinction; m. p. 204° (Found : C, 67·0; H, 5·3; N, 5·2; S, 11·0%); $[\alpha]_D$ − 106° in 0·7264% solution in chloroform. A mixture with the α-oxide melted at 177—198°. The proportion in which these two substances were formed appears to be α : β = 3 : 1.

Oxidation of l-*Benzamidobenzpenthiene*.—This was carried out as with the enantiomorph. Crystallisation from methyl ethyl ketone did not separate the products readily, but these were finally obtained by crystallising the separate crops from water. l-4-*Benzamidobenzpenthiene* α-*oxide* crystallised from water, methyl ethyl ketone or ethyl acetate in long plates with a straight extinction; m. p. 220·5° (Found: C, 67·2; H, 5·2%); $[\alpha]_D - 177°$ in 1·211% solution in chloroform. l-4-*Benzamidobenzpenthiene* β-*oxide* (Found: C, 67·2; H, 5·6%) had $[\alpha]_D + 105·5°$ in 1·003% solution in chloroform. From 4·25 g. of sulphide, 1·8 g. of α- and 0·9 g. of β-oxide were isolated.

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