LXXV.—*Externally Compensated Hydroxyhydrazino-
hydrindene, its Derivatives, and Resolution into
Optically Active Components.*

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IN spite of the interest attaching to the resolution of externally compensated aldehydes and ketones, very few optically active hydrazines have been prepared, and in no case has a racemic

hydrazine been resolved into its optically active components. Neuberg and Federer (*Ber.*, 1905, **38**, 866) introduced the optically active amyl group into phenylhydrazine, and so obtained an active hydrazine; Kijner (*J. pr. Chem.*, 1895, [ii], **52**, 424) prepared menthomenthylhydrazine from active bromomenthylamine, and from it, by hydrolysis, the corresponding menthylhydrazine.

Bromohydroxyhydrindene has already (Pope and Read, *T.*, 1912, **101**, 758) been converted smoothly and in quantity into the corresponding amine, hydroxyhydrindamine, which is a crystalline compound, forming easily crystallisable salts and derivatives, and is readily resolvable into its optically active components. It was therefore expected that the corresponding hydrazine compound would exhibit similar properties and be resolvable into stereoisomerides, which could then be used for the resolution of externally compensated aldehydes and ketones.

Hydroxyhydrazinohydrindene has the disadvantage of being somewhat unstable in the free state. Its salts when pure and dry are stable, but solutions of them cannot be evaporated to dryness on a water-bath without yielding a considerable quantity of a dark red solid, which melts at 182° and is insoluble in water; solutions can, however, be concentrated to a considerable extent by boiling under diminished pressure, 100 mm. and less, without very appreciable decomposition.

EXPERIMENTAL.

Externally compensated 2-bromo-1-hydroxyhydrindene,

was prepared by the method of Pope and Read (*T.*, 1912, **101**, 760), and the product, after thorough extraction with light petroleum, was dried and used without further purification.

Externally Compensated 1-Hydroxy-2-hydrazinohydrindene,

The best method of preparing this substance appears to be the following. Bromohydroxyhydrindene (50 grams) is mixed with hydrazine hydrate (50 grams) in a flask fitted with a reflux condenser, and gradually heated in an oil-bath. The mixture becomes quite liquid at 90—100°, and a reaction soon sets in so vigorously that the flask has sometimes to be cooled; when the initial vigour has abated, the flask is heated at 135—145° for two hours, and the excess of hydrazine hydrate distilled off under diminished pressure from a water-bath. The residue, when cooled, sets to a solid mass

(70 grams), which, when extracted with warm water, leaves a small quantity of insoluble residue, melting at 202—204°, and consisting of the condensation product of two molecules of bromohydroxyhydrindene with one of hydrazine. The aqueous extract is treated with solid potassium hydroxide (30 grams), and the mixture left to remain all night in a cooled exhausted vessel. The base (about 30 grams) separates as a granular solid, is filtered off through muslin, and is recrystallised from a large quantity of boiling benzene, in which it is moderately soluble. It is very sparingly soluble in cold benzene, chloroform, or ether, insoluble in light petroleum, and readily soluble in alcohol or water. It crystallises in colourless scales, melting at 87—88°, and decomposes on keeping even in an exhausted sealed tube. The following analyses were obtained with material that had been preserved two days and three days respectively:

(1) 0.188 gave 0.443 CO₂ and 0.124 H₂O. C=64.2; H=6.6.

(2) 0.145 „ 0.338 CO₂ „ 0.098 H₂O. C=63.6; H=7.5.

C₉H₁₂ON₂ requires C=65.8; H=7.3 per cent.

When carbon dioxide is passed into benzene or alcoholic solutions of the base a carbonate is precipitated.

dl-1-Hydroxy-2-hydrazinohydrindene Hydrochloride,

This salt is precipitated on mixing alcoholic solutions of the base and hydrogen chloride, and may be prepared more directly by the following process.

Bromohydroxyhydrindene (40 grams), hydrazine hydrate (20 grams), absolute alcohol (50 grams), and pure quick-lime (20 grams) are mixed and shaken for three days in a stoppered bottle; the product is extracted with boiling absolute alcohol, filtered, cooled, and, if necessary, filtered again. Dry hydrogen chloride is then passed for some time into the cooled solution, and after remaining for two hours, the precipitated hydrochlorides are collected and extracted with a boiling mixture of benzene and alcohol, which leaves hydrazine hydrochloride undissolved; the hydrochloride of the organic base separates readily on allowing this extract to cool. The salt is readily soluble in hot absolute alcohol and water, but sparingly so in cold alcohol, boiling benzene, and ethyl acetate; it crystallises in colourless scales, melting at 165°. It contains two molecules of hydrochloric acid to one of the base, and these are retained even on recrystallisation from water. The aqueous solution does not yield a solid platinichloride with chloroplatinic acid, but

gives a white precipitate with mercuric chloride; it very readily reduces copper sulphate solution:

0.1026 gave 0.1668 CO_2 and 0.0542 H_2O . $\text{C}=44.2$; $\text{H}=5.7$.

0.1961 „ 0.2302 AgCl . $\text{Cl}=29.1$.

$\text{C}_9\text{H}_{12}\text{ON}_2 \cdot 2\text{HCl}$ requires $\text{C}=45.6$; $\text{H}=5.9$; $\text{Cl}=29.9$ per cent.

If the reaction mixture obtained by shaking as above described is extracted with boiling ethyl acetate or benzene, a crystalline precipitate is formed on cooling which crystallises from alcohol or ethyl acetate in white, shining scales, melting at 255° ; this substance is a double compound of the hydrazine with calcium bromide:

0.1542 gave 0.1075 AgBr . $\text{Br}=29.7$.

0.1351 „ 0.0928 AgBr . $\text{Br}=29.2$.

$(\text{C}_9\text{H}_{12}\text{ON}_2)_2 \cdot \text{CaBr}_2$ requires $\text{Br}=30.3$ per cent.

The *sulphate*, $(\text{C}_9\text{H}_{12}\text{ON}_2)_2 \cdot \text{H}_2\text{SO}_4$, is precipitated on mixing an alcoholic solution of the base with twice the calculated quantity of alcoholic sulphuric acid. It crystallises from hot dilute alcohol or water in colourless, hexagonal plates, melting and decomposing at 224° :

0.0987 gave 0.0531 BaSO_4 . $\text{SO}_4=22.1$.

$\text{C}_{18}\text{H}_{26}\text{O}_6\text{N}_4\text{S}$ requires $\text{SO}_4=22.5$ per cent.

The *oxalate*, $\text{C}_9\text{H}_{12}\text{ON}_2 \cdot (\text{CO}_2\text{H})_2$, separates on mixing alcoholic solutions of equivalent proportions of the free base and oxalic acid; after recrystallisation from hot alcohol it is obtained in colourless needles, melting at 173° . It is readily soluble in water, but sparingly so in most organic solvents, except boiling rectified spirit. In both this salt and the hydrochloride the base is diacidic, whereas in the sulphate it is monacidic:

0.1660 gram gave 16.67 c.c. N_2 (moist) at 18° and 762 mm. $\text{N}=11.6$.

$\text{C}_{11}\text{H}_{14}\text{O}_5\text{N}_2$ requires $\text{N}=11.1$ per cent.

The *d*-camphor- β -sulphonate and *d*- α -bromocamphor- π -sulphonate prepared in a manner similar to the above were with difficulty obtained in a crystalline condition, owing to their hygroscopic character; they decomposed on keeping, becoming dark red.

dl-1-Hydroxy-2-benzoylhydrazinohydrindene,

The benzoyl derivative prepared from the hydrochloride by the ordinary Schotten-Baumann process crystallises from a mixture of alcohol and acetone in small white nodules, melting at 196° . Benzoylation in pyridine solution with two molecules of benzoyl chloride yielded only the monobenzoyl derivative:

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0.1184 gave 0.3010 CO_2 and 0.0620 H_2O . $\text{C}=69.4$; $\text{H}=5.9$.

$\text{C}_{16}\text{H}_{16}\text{O}_2\text{N}_2$ requires $\text{C}=71.6$; $\text{H}=5.9$ per cent.

The hydrochloride when heated with acetic anhydride yielded an oil which could not be caused to crystallise; bromohydroxyhydrindene behaves in the same way. The benzenesulphonyl- and *p*-toluenesulphonyl derivatives could not be prepared by the ordinary Schotten-Baumann process, black, uncrystallisable resins being produced.

dl-1-Hydroxy-2-semicarbazinohydrindene,

This compound is obtained in quantitative yield when aqueous solutions of equimolecular proportions of the hydrochloride of the base and potassium cyanate are mixed and left to remain for an hour; it separates as a white, amorphous powder, which crystallises from hot spirit in minute scales, melting at 195° . It dissolves sparingly in most organic solvents, in water or dilute acid, and is moderately soluble in hot alcohol, benzene, or concentrated hydrochloric acid; it is very stable, and its solutions can be evaporated to dryness without decomposition:

0.1255 gave 21.4 c.c. N_2 (moist) at 20° and 758 mm. $\text{N}=19.4$.

$\text{C}_9\text{H}_{13}\text{O}_2\text{N}_3$ requires $\text{N}=20.1$ per cent.

On dissolving the semicarbazide in concentrated sulphuric acid some blackening occurs, but, if the solution is left for two hours and then poured into water and filtered, a yellow solution with a green fluorescence is obtained. This may contain the compound:

and, if so, the hydroxy- and hydrazino-groups in the parent substance are probably in the *cis*-position.

On attempting to prepare the thiosemicarbazide by a similar method no solid separated, and on evaporating the solution the main product was the thiocyanate, which crystallises in colourless rosettes, melting at 112° , and turning pink on keeping.

dl-1-Hydroxy-2-anisylidenehydrazinohydrindene,

The hydrochloride of the base is dissolved in a solution containing rather more than two molecular equivalents of sodium acetate and a little acetic acid. The calculated weight of anisaldehyde is then

added to the hot solution, which is well shaken and heated in a boiling-water bath for two hours. On cooling, the hydrazone separates as a solid mass, which is collected, washed with ether, and recrystallised first from hot alcohol, and then from hot benzene, from which it separates in small, flat, yellow scales, melting at 168° :

0.1436 gave 12.6 c.c. N_2 (moist) at 17° and 744 mm. $N=9.97$.

$C_{17}H_{18}O_2N_2$ requires $N=9.92$ per cent.

dl-1-Hydroxy-2-cinnamylidenehydrazinohydrindene was prepared in a similar way, but this compound separated in the cold as an orange-yellow solid, which seemed somewhat unstable, and was difficult to purify. It was precipitated as a yellow powder from its alcoholic solution by light petroleum, and melted at 124° :

0.1175 gave 0.3328 CO_2 and 0.0575 H_2O . $C=77.3$; $H=5.5$.

$C_{18}H_{18}ON_2$ requires $C=77.7$; $H=6.4$ per cent.

dl-1-Hydroxy-2-benzylidenehydrazinohydrindene was prepared similarly to the anisic compound; it crystallises from hot rectified spirit in small, white needles, melting at 107° .

The vanillylidene compound, prepared as above, was very difficult to purify; it was recrystallised from a hot mixture of methyl alcohol and benzene, and separated in small, yellow scales, melting at 161° :

0.1316 gave 10.67 c.c. N_2 (moist) at 16° and 746 mm. $N=9.28$.

$C_{17}H_{18}O_3N_2$ requires $N=9.39$ per cent.

The salicylidene compound prepared similarly crystallised from hot spirit in shining, yellow scales, melting at 213° .

The piperonylidene compound was, like that of vanillin, very difficult to purify; it was recrystallised several times, and finally separated from benzene in yellow scales, melting at 201° :

0.1053 gave 8.6 c.c. N_2 (moist) at 17° and 755 mm. $N=9.58$.

$C_{17}H_{16}O_3N_2$ requires $N=9.46$ per cent.

The nitropiperonylidene compound was easily prepared in a very good yield by the usual method. It was recrystallised twice from hot rectified spirit, and obtained in orange-red needles, melting at 142° :

0.1590 gave 16.67 c.c. N_2 (moist) at 20° and 758 mm. $N=11.9$.

$C_{17}H_{15}O_5N_3$ requires $N=12.3$ per cent.

The benzoylmethylene compound prepared in the usual manner was obtained in a very poor yield; after precipitation by light petroleum from its solution in rectified spirit, it melted at 96° .

Neither dextrose nor lævulose precipitated hydrazones on being treated in the above manner, nor when left in contact with an alcoholic solution of the free base. An attempt to prepare an

osazone by the usual method only yielded tarry decomposition products.

On mixing an alcoholic solution of the externally compensated hydrazine, which had been recrystallised from benzene, with an alcoholic solution of the equimolecular proportion of *d*-tartaric acid, the *d*-tartrates were precipitated, being almost insoluble in rectified spirit. After five recrystallisations from boiling aqueous alcohol, the mixture was found to be resolved, the less soluble component being the salt *lBdA*, containing the *l*-base. This salt is sparingly soluble in cold water, very sparingly soluble in cold alcohol, and readily soluble in hot water and boiling dilute alcohol, from which latter solvent it separates in very fine colourless needles, melting at 195–196°:

0.1002 gave 0.1856 CO₂ and 0.0624 H₂O. C=50.5; H=6.6.

C₁₈H₁₈O₉N₂ requires C=49.6; H=5.7 per cent.

	0.2406 gram in water.			0.2854 gram in water.		
	Hg _{green} .	Hg _{yellow} .	N _{ayellow} .	Hg _{green} .	Hg _{yellow} .	
α	- 0.125°	- 0.085°	0°	- 0.15°	- 0.10°	
$[\alpha]$	3.90	2.66	0	3.94	2.62	
$[M]$	12.2	8.34	0	12.4	8.2	

Mean values, $[M]$: Hg_{green} - 12.3°; Hg_{yellow} - 8.27°.

Rotatory dispersion: Hg_{green}/Hg_{yellow}=1.48. No mutarotation was observed.

The solutions were made up to 30 c.c., and measured in 4-dcm. tubes at 20°, except where otherwise stated.

This salt was not obtained in a pure state. On leaving the solutions, from which the more sparingly soluble salt had been separated, to remain, a further crop of crystals was obtained; the less soluble portion was removed from this by fractional recrystallisation, and finally a salt was obtained, melting at 168–169°, this being unchanged by further recrystallisation. The following rotations were observed with two specimens prepared in this way:

	0.177 gram in water.	0.320 gram in water.	
	Hg _{green} .	Hg _{green} .	Hg _{yellow} .
α	+ 0.60°	+ 1.16°	+ 1.05°
$[\alpha]$	25.4	27.2	24.6
$[M]$	79.8	85.4	75.9

0.1791 gave 0.3200 CO₂ and 0.0945 H₂O. C=48.7; H=5.8.

C₁₃H₁₈O₉N₂ requires C=49.6; H=5.7 per cent.

The resolution by means of tartaric acid could not be effected by the equilibrium method. On dissolving one molecular proportion of the tartrate and of the hydrochloride in hot water or hot dilute alcohol and allowing the solution to cool, the first crystals that separated contained both salts, *lBdA* and *dBdA*, and the hydrochloride recovered from the solution showed only a very slight activity.

1-1-Hydroxy-2-semicarbazinohydrindene,

The compound separated on mixing warm aqueous solutions of the active tartrate and potassium cyanate; it was recrystallised from rectified spirit, and obtained in shining scales, melting at 196°:

0.1202 gave 0.2515 CO₂ and 0.0633 H₂O. C=57.1; H=5.8.

C₁₀H₁₃O₂N₃ requires C=58.2; H=5.8 per cent.

0.1530 gram, in rectified spirit, gave for Hg_{green} light, α-0.30°; whence [α]-14.7° and [M]-28.6°.

No mutarotation was observed.

1-1-Hydroxy-2-hydrazinohydrindene Oxalate,

The tartrate of the *l*-base was mixed in hot water with the calculated quantity of crystalline barium hydroxide; the precipitated barium tartrate was removed by filtration, the calculated quantity of oxalic acid added, and the solution left to cool. The oxalate then separated in colourless rosettes, melting at 178°; it crystallises from dilute alcohol in needles:

0.1095 gave 0.2055 CO₂ and 0.0563 H₂O. C=51.2; H=5.66.

C₁₁H₁₄O₅N₂ requires C=51.9; H=5.5 per cent.

0.1126 gram in water.

	Hg _{green} .	Hg _{yellow} .	Na _{yellow} .
α	-0.33°	-0.265°	-0.21°
[α]	21.98	17.65	13.98
[M]	55.82	44.82	35.53

Rotatory dispersions: 1.24; 1.26.

The rotatory dispersion Hg_{yellow}/Na_{yellow} is remarkably high; no mutarotation was observed.

The tartrates of the active bases could not be used for the direct preparation of hydrazones, as on heating a solution of the tartrate in presence of sodium acetate and acetic acid with either nitro-

piperaldehyde or anisaldehyde a tarry mass resulted; a similar result was obtained in alcoholic solution. The oxalates would seem to be more suitable for the preparation of the hydrazones.

In conclusion I wish to thank Prof. Pope for suggesting this work, and for the interest he has taken in it.

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