

**Chemistry.** — *On the Resolution of  $\alpha$ -Phenylpropylamine into Its Optically-active Antipodes* (2nd Part). By F. M. JAEGER and W. FROENTJES.

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§ 1. In a former paper<sup>1)</sup> the preparation of this base and that of its someride *benzedrine*, as well as the resolution of the latter into its antipodes, have been described in detail. In the present one we communicate the results of our investigations concerning the resolution of  *$\alpha$ -phenylpropylamine*:  $C_6H_5 \cdot CH(NH_2) \cdot CH_2 \cdot CH_3$  and of the phenomena therewith observed.

Purest racemic  *$\alpha$ -phenylpropylamine* of the boilingpoint  $62^\circ$ — $63^\circ$  C. under 3 m.M. pressure was converted into its *bi-d-tartrate* and the anhydrous salt obtained subjected to repeated fractional crystallisations from *absolute* alcohol, — first at room-temperature and later in an exsiccator at  $35^\circ$  C., — this being the most adequate temperature for still obtaining well-crystallized fractions from the last mother-liquors. The principal fraction (of  $[\alpha]_D = +22^\circ$ , 5) was thus obtained from the solution at  $18^\circ$  C. and recrystallized from absolute alcohol; but it proved impossible also to isolate the final fraction (of  $[\alpha]_D = +7^\circ$ ) from the mother-liquors in this way. Therefore, — as no other solvent proved to yield better results, we finally made the experiments at  $35^\circ$  C. in the way described. As the difference in solubility of the components proves to be much less than in the case of *benzedrine*; and because their power of crystallisation is rather poor, — the complete resolution happens to be a much more tedious task and involves a greater sacrifice of material than in the case of *benzedrine*; the more so, because the *bi-tartrates*, which in *cold* alcohol are only sparsely soluble, could never be obtained in the form of well-developed crystals, notwithstanding many tentatives were made and after other solvents had been tried. They always were deposited as felt-like, very thin and feathery needles or, from the final mother-liquors, as a slimy aggregation. Moreover, the substance has a disposition to “creep” against the walls of the vessel to a considerable distance above the surface of the solution.

Finally a fraction could be obtained which, after repeated crystallisations, did not change its specific rotation for sodium-light any more. This constantly rotating fraction showed  $[\alpha]_D = +22^\circ,5$ ; its meltingpoint was  $176^\circ$  C.<sup>2)</sup>. The base set free from this salt (boiling at  $67^\circ$  C. under

<sup>1)</sup> F. M. JAEGER and J. A. VAN DIJK, Proc. Ned. Akad. v. Wetensch., Amsterdam, **44**, 26 (1941).

<sup>2)</sup> P. BILLON, Compt. rend. Paris, **182**, 472 (1926). The meltingpoint:  $176^\circ$  C. is  $10^\circ$  higher than that given by BILLON ( $166^\circ$  C.); this again demonstrates the incompleteness of the fission by this author.

5 m.M. pressure), proved to be the *levogyrotory* component. The rotations observed were *less than half* those of *benzedrine*; but they were *not less than 50 % higher* than those indicated by BILLON <sup>2)</sup>, whose resolution evidently must have been still very *incomplete*. The mother-liquors of the final recrystallisations of the mixed *bi-d-tartrates* did not crystallize very well and yielded a kind of semi-colloidal product; but a final fraction thus obtained, showing a (lowest) specific rotation:  $[\alpha]_D = +7.0$  proved to be *homogeneous* and, on further recrystallisations, did no longer alter its rotation any more. This *bi-d-tartrate* showed a meltingpoint of 123° C.; and the base set free from it, proved, indeed, to be the *dextrogyrotory* component, constantly, boiling at 64° C. under a pressure of 4 m.M. The rotatory dispersions of the two antipodes thus observed are given in Tabel II, whilst the same has been done for the *bi-d-tartrates* themselves in Table I.

TABLE I. The Rotatory Dispersion of <i>l-a</i> -Phenylpropylamine- <i>bi-d</i> -Tartrate (176° C.) and of <i>d-a</i> -Phenylpropylamine- <i>bi-d</i> -Tartrate (123° C.) in 2 % aqueous Solutions.		
Wave-length $\lambda$ in A.U.:	Specific Rotations $[\alpha]$ of	
	<i>l-a</i> -Phenylpropylamine- <i>bi-d</i> -tartrate (176° C.):	<i>d-a</i> -Propylamine- <i>bi-d</i> -tartrate (123° C.):
6980	+16.0	—
6730	17.8	+5.2
6480	18.8	5.9
6262	19.8	6.1
6074	20.8	6.5
5893	22.3	7.0
5735	23.6	7.2
5592	24.5	7.7
5463	25.8	8.0
5340	27.1	8.0
5224	28.1	8.0
5126	29.3	8.1
5036	30.1	—
4950	31.5	8.3
4861	32.4	—
4793	35.0	—
4724	36.8	—
4596	39.0	—
4537	42.1	—
4483	(47.0)	—

Wave length $\lambda$ in A.U.:	Specific Rotations of		Mean values of the Dispersion:
	<i>d</i> - $\alpha$ -Phenyl- propylamine	<i>l</i> - $\alpha$ -Phenyl- propylamine	
6980	—	—11.7°	(11.7°)
6730	+11.4°	—12.2	11.8
6480	+12.2	—12.7	12.5
6262	+13.0	—13.3	13.2
6074	+13.9	—14.2	14.1
5893	+14.8	—15.1	15.0
5735	+15.7	—16.0	15.9
5592	+16.7	—16.9	16.8
5463	+17.6	—17.9	17.8
5340	+18.4	—18.7	18.6
5224	+19.2	—19.5	19.4
5126	+20.2	—20.4	20.3
5036	+20.9	—21.2	21.1
4950	+21.9	—23.0	22.5
4861	—	—23.8	23.8
4793	—	—24.7	24.7
4724	—	—25.5	25.5
4658	—	—26.3	26.3
4596	—	—27.2	27.2
4537	—	—28.0	28.0
4483	—	—28.8	28.8

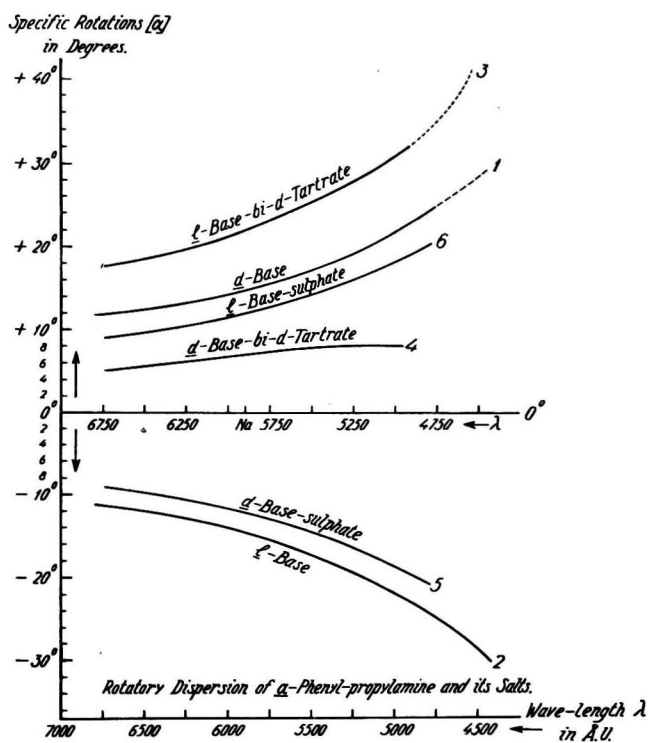


Fig. 1. Rotatory Dispersion of  $\alpha$ -Phenylpropylamine and its Salts.

§ 2. From these data it becomes clear that the two optically active bases, when present in the form of the *bi-tartrates* exhibit a *rotation of the opposite algebraic sign* as compared with that of the free bases themselves: they thus manifest this phenomenon, when they are electrically charged as *ions*. For the purpose of corroborating this conclusions, we have prepared the (anhydrous) *sulphates* <sup>1)</sup> and in Table III we give the corresponding data of the rotatory dispersion for these salts in a 2 % molar (= 1,842 % in weight) aqueous solutions:

TABLE III. The Rotatory Dispersion of the Sulphates of the Optically-active $\alpha$ -Phenylpropylamines in aqueous Solutions.		
Wave-length $\lambda$ in A.U.:	Specific Rotations $[\alpha]$ of $\alpha$ -Phenylpropylamine-sulphates:	
	<i>l</i> - $\alpha$ -Phenylpropylamine-sulphate	<i>d</i> - $\alpha$ -Phenylpropylamine-sulphate
6730	+ 9.4	-10.0
6480	+10.5	-10.7
6262	+11.4	-11.5
6074	+12.0	-12.0
5893	+13.2	-13.5
5735	+14.0	-14.0
5592	+14.4	-14.7
5463	+15.3	-15.3
5340	+16.2	-16.2
5224	+17.2	-16.7
5126	+18.1	-17.2
5036	+19.2	-17.7
4950	+20.2	-18.3
4861	+20.8	-19.5
4793	+21.7	-20.5

<sup>1)</sup> Analysis yielded 25.82 %  $\text{SO}_4$  (calc.: 26.07 %); the salt melts at 200° to 223° C. under partial decomposition. The results, which are graphically represented all-together in Fig. 1, leave no doubt whatsoever about the correctness of the conclusion drawn. The behaviour of the bases, therefore, is in this respect exactly the *opposite* one to that of the isomeric *benzedrine*. Probably the sterical configuration round the asymmetrical carbon-atom in the two isomeric substances may be supposed to be enantiomorphous.