45. *The Stereoisomeric* 2 : 3 : 5 : 6-*Tetramethylpiperazines. Part IV.*

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In order to determine the configuration of γ-2 : 3 : 5 : 6-tetramethylpiperazine, attempts have been made to resolve various derivatives of it into optical antimerides; 1-*p*-toluenesulphonyl-γ-2 : 3 : 5 : 6-tetramethylpiperazine (J., 1929, 2896), γ-2 : 3 : 4 : 5 : 6-pentamethylpiperazine, its 1-nitroso- and 1-*p*-toluenesulphonyl derivatives (J., 1932, 1339) have been examined. In all, fourteen salts or derivatives of an unsymmetrical γ-base, $RN<(CHMe)_4>NR'$, with optically active substances have been studied without revealing any sign of resolution. In view of the comparative ease with which the isomeric *dl*-β-base was resolved (J., 1931, 1160) it would appear likely, therefore, that the configuration of γ-2 : 3 : 5 : 6-tetramethylpiperazine is such that derivatives of it, of the type mentioned above, are *meso*-compounds: thus the γ-base is probably represented by formula I or IV (*loc. cit.* and J., 1932, 1336), and it would appear that there is no suitable chemical method of distinguishing between these two configurations.

α-2 : 3 : 5 : 6-Tetramethylpiperazine has also resisted resolution in five cases, but as no unsymmetrical derivatives of this base could be obtained (J., 1932, 1342), and the corresponding pentamethyl base is unknown, work could not be continued in this series.

Salts of p-*Toluenesulphonyl-γ-2 : 3 : 5 : 6-tetramethylpiperazine.*—The d-*camphor-10-sulphonate* was crystallised from EtOH (prisms) and H_2O (long needles). The m. p. was unaccountably variable, 248—251°, 258—260° (Found: N, 5·5. $C_{15}H_{24}O_2N_2S,C_{10}H_{16}O_4S$ requires N, 5·3%). $[\alpha]_{5461}$ + 14·9° in H_2O (c = 0·6).*

The d-α-*bromocamphor-π-sulphonate* was fractionated from EtOH and crystallised in needles, m. p. 256—257° (Found: N, 4·6. $C_{15}H_{24}O_2N_2S,C_{10}H_{15}O_4BrS$ requires N, 4·6%). $[\alpha]_{5461}$ +62·5° in EtOH (c = 1·15).

* All rotations were taken at room temp.

Salts of γ-2 : 3 : 4 : 5 : 6-Pentamethylpiperazine.—The mono-*d*-camphor-10-sulphonate and the mono- and di-*d*-α-bromocamphor-π-sulphonates could not be obtained cryst.

The *di*-d-*camphor*-10-*sulphonate* was fractionated from abs. EtOH : it had m. p. 261° (Found : C, 55·9; H, 8·6. $C_9H_{20}N_2,2C_{10}H_{16}O_4S$ requires C, 56·1; H, 8·4%). $[\alpha]_{5461}$ + 20·0° in H_2O (c = 1·1).

The *d*-tartrate, from equimol. quantities of acid and base, was fractionated from MeOH. It had m. p. 164—165°. $[\alpha]_{5780}$ + 18·5°, $[\alpha]_{5461}$ + 20·3° in H_2O (c = 1·9). Salts suitable for fractionation could not be obtained with base (2 mols.) : acid (1 mol.) or base (1 mol.) : acid (2 mols.).

*γ-2 : 3 : 4 : 5 : 6-Pentamethylpiperazine-*d-*methylenecamphor.*—The base (1 mol.) and *d*-hydroxymethylenecamphor (1 mol.) were boiled together in EtOH during 1 hr. : the mixture, poured into H_2O, gave an oil, a specimen of which, solidified with light petroleum, seeded the whole. It was recrystallised repeatedly from light petroleum (b. p. 60—80°), from which it separated in small prisms, m. p. 123° (Found : C, 75·6; H, 10·7. $C_{20}H_{34}ON_2$ requires C, 75·5; H, 10·7%). $[\alpha]_{5780}$ + 438°, $[\alpha]_{5461}$ + 509° in EtOH (c = 0·47). Several crystns. from acetone did not change these values. The base recovered by the bromine method, was obtained as a *dihydrobromide* (Found : Br, 50·1. $C_9H_{20}N_2,2HBr$ requires Br, 50·3%), which crystallised from EtOH in stout needles, m. p. 268—270°. It was optically inactive, as also was the hydrochloride obtained by treatment with HCl aq. and removal of the hydroxymethylenecamphor in steam.

Salts of the methylenecamphor derivative. The *d*-camphor-10-sulphonate was fractionated from EtOH–acetone. It had m. p. 263—264°. $[\alpha]_{5780}$ + 226°, $[\alpha]_{5461}$ + 266° in H_2O (c = 0·5). The recovered camphor derivative had the same m. p. and rotatory power as before.

The *d*-α-bromocamphor-π-sulphonate, crystallised from acetone, had m. p. 257°. $[\alpha]_{5780}$ + 239°, $[\alpha]_{5461}$ + 278° in H_2O (c = 0·5).

Salts of 1-*Nitroso-γ-2 : 3 : 4 : 5 : 6-pentamethylpiperazine.*—The *d*-camphor-10-sulphonate was fractionated from acetone containing a little H_2O. It had m. p. 213—215° (decomp.). $[\alpha]_{5780}$ + 12·3°, $[\alpha]_{5461}$ + 15·2° in H_2O (c = 3·5). The recovered nitroso-derivative was inactive.

The d-α-*bromocamphor-π-sulphonate* crystallised from EtOH in needles, m. p. 207° (Found : N, 8·5. $C_9H_{19}ON_3,C_{10}H_{15}O_4BrS$ requires N, 8·5%). $[\alpha]_{5780}$ + 58·2°, $[\alpha]_{5461}$ + 68·5° in H_2O (c = 2·2).

Salts of p-*Toluenesulphonyl-γ-2 : 3 : 4 : 5 : 6-pentamethylpiperazine.*—The *d*-camphor-10-sulphonate crystallised from H_2O in prisms, m. p. 208—211°. $[\alpha]_{5780}$ + 24·4°, $[\alpha]_{5461}$ + 28·4° in $CHCl_3$ (c = 4·25).

The *d*-α-bromocamphor-π-sulphonate crystallised from warm H_2O (hot sat. solutions deposited an oil) in long needles, m. p. 204—205°. $[\alpha]_{5461}$ + 63·6° in EtOH (c = 1·4).

The *d*-α-chlorocamphor-π-sulphonate crystallised from hot H_2O in needles, m. p. 215—216°. $[\alpha]_{5461}$ + 49·5° in EtOH (c = 1·3).

The *d*-tartrate crystallised from acetone, containing about 20% of H_2O, in needles, m. p. 174—175°. $[\alpha]_{5780}$ + 9·4°, $[\alpha]_{5461}$ + 9·7° in H_2O.

Salts of α-2 : 3 : 5 : 6-Tetramethylpiperazine.—The *mono*-d-*camphor*-10-*sulphonate* was fractionated from $CHCl_3$–C_6H_6 (eq. vols.). It crystallised in needles, m. p. 113—114° (Found : S, 8·8. $C_8H_{18}N_2,C_{10}H_{16}O_4S$ requires S, 8·6%). $[\alpha]_{5461}$ + 17·4° in H_2O, + 35·8° in $CHCl_3$ (c = 1·2).

The *di*-d-*camphor*-10-*sulphonate* was fractionated from H_2O. It had no m. p. below 320° (Found : C, 55·5; H, 8·3; S, 10·9. $C_8H_{18}N_2,2C_{10}H_{16}O_4S$ requires C, 55·5; H, 8·3; S, 10·6%). $[\alpha]_{5780}$ + 19·5°, $[\alpha]_{5461}$ + 23·8° in H_2O (c = 1·5).

The *mono*-d-α-*bromocamphor-π-sulphonate* crystallised from H_2O in needles, m. p. 230—231° (Found : Br, 17·8. $C_8H_{18}N_2,C_{10}H_{15}O_4BrS$ requires Br, 17·7%). $[\alpha]_{5780}$ + 62·3°, $[\alpha]_{5461}$ +73·0° in H_2O (c = 1·1).

The *di*-d-α-*bromocamphor-π-sulphonate* crystallised from H_2O in needles. No m. p. below 320° (Found : Br, 21·0. $C_8H_{18}N_2,2C_{10}H_{15}O_4BrS$ requires Br, 20·9%). $[\alpha]_{5780}$ + 76·5°, $[\alpha]_{5461}$ + 89·7° in H_2O (c = 2·2).

α-2 : 3 : 5 : 6-*Tetramethylpiperazinedi*-d-*methylenecamphor* was prepared by boiling an alc. solution of the base (1 mol.) and *d*-hydroxymethylenecamphor (2 mols.). After 2 hr. the separated crystals were removed by filtration, and the mother-liquor boiled during a further 6—7 hr.; on being cooled, the solution deposited a further crop of crystals. The product was fractionated both from diacetone alcohol (plates) and from xylene (needles). It had m. p. 320° Found : C, 76·95; H, 9·75. $C_{30}H_{46}O_2N_2$ requires C, 77·2; H, 9·9%). $[\alpha]_{5780}$ + 691°, $[\alpha]_{5461}$ + 822° in $CHCl_3$ (c = 0·8). The hydrobromide of the base, recovered by the bromine method, was optically inactive.

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