286. *The Resolution of* cis- *and* trans-dl-3-*Carboxy*-1 : 1-*dimethyl*cyclo-*propane*-2-*propionic Acids and of* trans-dl-*Caronic Acid.*

By J. Owen and J. L. Simonsen.

In a recent communication (J., 1932, 1424) we described the synthesis of *cis*- and *trans-dl*-1 : 1-dimethyl-2-γ-ketobutyl*cyclo*propane-3-carboxylic acids, and stated that we proposed to attempt the resolution of these acids into their optical enantiomorphs in order

to compare them with the optically active acids resulting from the oxidation of *d*-Δ^4-carene with potassium permanganate. Unfortunately, the ketonic acids were too weakly acidic to yield satisfactory salts, but we were more successful with the corresponding dibasic acids.

trans-dl-3-Carboxy-1 : 1-dimethyl*cyclo*propane-2-propionic acid combined with nor-*d*-ψ-ephedrine to give the sparingly soluble salt of the trans-l-*acid*, whilst the trans-d-*acid* was obtained by the use of nor-*l*-ψ-ephedrine. Much greater difficulty was experienced in the resolution of the *cis-dl*-acid, but the *d*-form was ultimately obtained with the aid of morphine, the half-molecule method being employed. The purification of the *dimorphine* salt was laborious, since, owing to its sparing solubility, the rotatory power could not be determined, and the progress of the resolution could only be followed by the regeneration of the acid and determination of its rotation. The pure *cis-d*-acid, m. p. 104—105°, $[\alpha]_{5461}$ + 39·0°, was found to be identical in all respects with the acid obtained by Simonsen (J., 1922, **121**, 2297) by the oxidation of *d*-Δ^4-carene. The cis-l-*acid* was prepared from the acid recovered from the more soluble dimorphine salt by crystallisation of the *distrychnine* salt. The half-molecule method was used in this case also, with the modification that only sufficient strychnine was added to combine with the *l*-acid present in the mixture. The distrychnine salt was extremely sparingly soluble, and the optical purity of the salt could only be controlled by regeneration of the cis-l-*acid*, which was ultimately obtained somewhat less pure ($[\alpha]_{5461}$ — 37·8°) than its enantiomorph.

trans-l-Caronic acid has been prepared by Staudinger and Ruzicka (*Helv. Chim. Acta*, 1924, **7**, 201) by the oxidation of chrysanthemum mono- and di-carboxylic acids, and by Gibson and Simonsen (J., 1929, 305, 909) by the oxidation of *d*-Δ^3- and -Δ^4-carenes. We have now prepared the optically pure *d*- and *l*-forms of the acid by the resolution of the *dl*-acid, which was readily effected by the use of nor-*d*- and -*l*-ψ-ephedrines. The acids have m. p. 211—212°, $[\alpha]_{5461}$ + 34·8°, — 34·5°, and it is evident that the lævorotatory acid, m. p. 210°, $[\alpha]_D$ — 33·3°, obtained by Staudinger and Ruzicka, must have been optically pure.

We are indebted to Prof. C. S. Gibson, F.R.S., for kindly presenting us with nor-*l*-ψ-ephedrine and also for many valuable suggestions.

Experimental.

Resolution of cis-dl-3-*Carboxy*-1 : 1-*dimethyl*cyclo*propane*-2-*propionic Acid*.—To a hot solution of the acid (8·9 g.) in water (430 c.c.) and sodium hydroxide solution (2·548*N*; 18 c.c.), morphine (14·5 g.) was added; the cooled solution deposited a crystalline solid (6·4 g.), m. p. 177—178°, and after concentration, two further crops of crystals (2·1 g., m. p. 178—180°; 0·25 g., m. p. 164—167°) were obtained. These were combined and recrystallised twice from dilute alcohol, the *dimorphine* salt of the acid being obtained in needles, m. p. 177—178° (sintering 168°) (Found: C, 66·0; H, 7·1. $C_{43}H_{52}O_{10}N_2,H_2O$ requires C, 66·7; H, 7·0%). The salt was decomposed in the usual manner, and *cis-d*-3-carboxy-1 : 1-dimethyl*cyclo*propane-2-propionic acid crystallised from water in needles, m. p. 104—105° (softening 102°), α_{5461} + 1·01°, $[\alpha]_{5461}$ + 39·0° (*c*, 2·59 in chloroform) (Found: C, 57·8; H, 7·8. Calc. for $C_9H_{14}O_4$: C, 58·0; H, 7·5%). On admixture with a specimen of acid prepared by the oxidation of *d*-Δ^4-carene, no depression of m. p was observed, and the acids appeared identical in all respects.

The acid ($[\alpha]_{5461}$ — 11·62°) recovered from the more soluble dimorphine salt contained approximately 30% of the *l*-acid; to a solution of this (2·9 g.) in water (120 c.c.), sodium hydroxide solution (2·548*N*; 8·8 c.c.) and strychnine (2·88 g.) were added, and the hot filtered solution concentrated to 70 c.c.; on cooling, a strychnine salt (2·5 g.) separated. The *distrychnine* salt (11·2 g.), which was very sparingly soluble in the usual solvents, was recrystallised twice from dilute alcohol, separating in needles, m. p. 189—190° (sintering 185°) [Found: H_2O, 6·9 (over P_2O_5). $C_{51}H_{58}O_8N_4,4H_2O$ requires $3\frac{1}{2}H_2O$, 6·8%. Found, in dried salt: C, 70·6; H, 7·4. $C_{51}H_{58}O_8N_4,\frac{1}{2}H_2O$ requires C, 70·9; H, 6·8%].

cis-l-3-*Carboxy*-1 : 1-*dimethyl*cyclo*propane*-2-*propionic acid*, recovered from the strychnine salt, crystallised from water in needles, m. p. 104—105° (softening 102°), α_{5461} — 1·21°, $[\alpha]_{5461}$ — 37·8° (*c*, 3·204 in chloroform) (Found: C, 57·8; H, 7·5%).

Resolution of trans-dl-3-*Carboxy*-1 : 1-*dimethyl*cyclo*propane*-2-*propionic Acid*.—To a hot solu-

tion of nor-*d*-ψ-ephedrine (11·7 g.) in acetone (160 c.c.) the *trans*-acid (7·3 g.) was added, and the filtered solution kept for 48 hours; the needles which separated (4·8 g., m. p. 191—193°) were recrystallised twice from water (60 c.c.), and the *di-nor*-d-*ψ-ephedrine* salt of the acid was obtained in needles, which, after drying in a vacuum, had m. p. 192—193° (sintering 187°), α_{5461} + 0·535°, $[\alpha]_{5461}$ + 18·16° (*c*, 2·876 in methyl alcohol). The rotatory power was unaltered by further crystallisation (Found: C, 64·3; H, 8·1. $C_{27}H_{40}O_6N_2,H_2O$ requires C, 64·0; H, 8·3%).

trans-l-3-*Carboxy*-1 : 1-*dimethyl*cyclo*propane-2-propionic acid*, regenerated from the salt, crystallised from water in prisms, m. p. 112°, α_{5461} − 1·52°, $[\alpha]_{5461}$ − 37·1° (*c*, 4·1 in ethyl acetate) (Found: C, 57·9; H, 7·8%). The sodium salt of the acid was dextrorotatory in water, α_{5461} + 0·29°, $[\alpha]_{5461}$ + 11·6° (*c*, 2·496).

From the more soluble di-nor-*d*-ψ-ephedrine salt, the *trans*-acid ($[\alpha]_{5461}$ + 8·7°) was recovered and treated with nor-*l*-ψ-ephedrine under the conditions described above. The *di-nor*-l-*ψ-ephedrine* salt of the *trans-d*-acid separated very rapidly, and after crystallisation from water had m. p. 192—193°, α_{5461} − 0·45°, $[\alpha]_{5461}$ − 18·5° (*c*, 2·428 in methyl alcohol) (Found: C, 64·5; H, 8·2%). The trans-d-*acid*, after recrystallisation from water, had m. p. 112°, α_{5461} + 1·09°, $[\alpha]_{5461}$ + 37·4° (*c*, 2·912 in ethyl acetate) (Found: C, 58·1; H, 7·4%).

Resolution of trans-dl-*Caronic Acid*.—To nor-*d*-ψ-ephedrine (4·7 g.; 1 mol.) in acetone (65 c.c.) *trans-dl*-caronic acid (4·86 g.; 1 mol.) was added, and the hot solution filtered. The solid (*A*, 1·85 g.) (rosettes of needles, m. p. 198—200°) which separated on cooling was collected, the solvent removed from the filtrate, and the gummy residue dissolved in hot ethyl alcohol (35 c.c.), needles (*B*, 1·8 g.) (m. p. 197—200°) being deposited on cooling. (Filtrate *C*, see below.) The solid *A* was recrystallised from alcohol and then had m. p. 198—200°, α_{5461} + 0·56°, $[\alpha]_{5461}$ + 38·0° (*c*, 1·474 in water), and after further crystallisation the salt was obtained in fine needles, m. p. 199—200° (sintering 195°), α_{5461} + 0·59°, $[\alpha]_{5461}$ + 38·5° (*c*, 1·53 in water). A further quantity of the same salt ($[\alpha]_{5461}$ + 38·0°) was obtained by recrystallisation of *B* from ethyl alcohol (Found: C, 62·1; H, 7·7. $C_{16}H_{23}O_5N$ requires C, 62·1; H, 7·4%).

trans-l-*Caronic acid*, prepared by decomposition of the salt, crystallised from water in long needles, m. p. 211—212°, α_{5461} − 0·6°, $[\alpha]_{5461}$ − 34·5° (*c*, 1·74 in alcohol) (Found: C, 53·3; H, 6·6. $C_7H_{10}O_4$ requires C, 53·2; H, 6·3%).

From the filtrate, *C*, the alcohol was removed, and the crude *d*-acid recovered. The acid (2·84 g.) was added to an acetone (35 c.c.) solution of nor-*l*-ψ-ephedrine (2·8 g.), and the deposited *salt* was purified as described above; it crystallised in needles, m. p. 199—200° (sintering 195°), α_{5461} − 0·54°, $[\alpha]_{5461}$ − 38·5° (*c*, 1·404 in water) (Found: C, 62·2; H, 7·8%).

trans-d-*Caronic acid* crystallised from water in long needles, m. p. 211—212°, α_{5461} + 0·56°, $[\alpha]_{5461}$ + 34·8° (*c*, 1·61 in alcohol) (Found: C, 53·1; H, 6·4%).

One of us (J. O.) acknowledges a grant from the Council of the Department of Scientific and Industrial Research.

UNIVERSITY COLLEGE OF NORTH WALES, BANGOR. [*Received, July 14th*, 1933.]