## 323. *Reactions of* αβ-*Unsaturated Cyclic Aldehydes and Ketones. Part V.* dl-*Cryptone and* cis- *and* trans-dl-*Cryptol.*

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*l*-Cryptone is readily racemised by refluxing in ethereal solution with a trace of hydrochloric acid. cis- and trans-dl-*Cryptols* have been isolated from the crude *dl*-cryptol obtained by the reduction of *dl*-cryptone by aluminium *iso*propoxide, the separation being achieved by fractional crystallisation of the α-*naphthylamine* compounds of the mixed 3 : 5-dinitrobenzoates. Derivatives of *dl*-cryptone and the epimeric alcohols are described.

IN previous work (Cooke, Gillespie, and Macbeth, this vol., p. 519) it was shown that the reduction of cryptone by aluminium *iso*propoxide, followed by catalytic hydrogenation, gave *trans*-dihydrocryptol together with some 5% of the *cis*-compound. As no change of configuration can occur during the hydrogenation of the double bond, it seemed probable that the mother-liquors obtained in the crystallisation of the *p*-nitro- or 3 : 5-dinitrobenzoate of crude cryptol would provide a source of the *cis*-alcohol. To simplify the separation, *dl*-cryptone was used as a starting material in the Ponndorf reduction, and use was made of the differing solubilities of the α-naphthylamine compounds of the 3 : 5-dinitrobenzoate (Reichstein, *Helv. Chim. Acta*, 1926, **9**, 799; Sutter, *ibid.*, 1938, **21**, 1266) of *cis*- and *trans*-*dl*-cryptol. In this way the *trans*-alcohol was isolated in good yield, but the process is difficult and tedious and leads to only a small amount of the *cis*-compound. The configuration of the epimers was established by their hydrogenation to the corresponding dihydrocryptols, the isomerism of which was fully explored in the previous work (*loc. cit.*). trans-dl-*Cryptol*, a pleasant smelling, somewhat viscous liquid, b. p. 90°/4 mm., $d_{30^\circ}^{30^\circ}$ 0·9247, $n_D^{20^\circ}$ 1·4761, was characterised by various derivatives, which closely resemble those of *trans*-dihydrocryptol in crystalline form.

cis-dl-*Cryptol* had b. p. 86°/6 mm., $n_D^{20^\circ}$ 1·4752, and $d_{30^\circ}^{30^\circ}$ 0·9282.

## EXPERIMENTAL.

*Racemisation of Cryptone.*—A mixture containing freshly distilled *l*-cryptone (200 g.) having $\alpha_D$ − 61° (homogeneous), ether (200 c.c.), and concentrated hydrochloric acid (10 g.) was heated under reflux on the water-bath for 1·5 hours and, after cooling, was successively washed with water, 1% sodium carbonate solution, and water. After drying (calcium chloride) and removal of the solvent, the residual pale yellow oil, when distilled under reduced pressure, gave a main fraction (174 g.), b. p. 89—90°/4 mm., $\alpha_D$ − 0·24° (homogeneous). Yield, 87%. If the washing to remove hydrochloric acid is omitted, the yield is seriously diminished owing to the greater polymerisation of the ketone during distillation. *dl*-Cryptone has b. p. 78°/2·8 mm., $n_D^{20°}$ 1·4810, $d_{30°}^{30°}$ 0·9393. It gives a *semicarbazone*, which forms transparent plates from methyl alcohol, m. p. 188° (Found: C, 61·3; H, 8·8. $C_{10}H_{17}ON_3$ requires C, 61·5; H, 8·7%), a p-*nitrophenylhydrazone*, which crystallises in fine, felted, yellow needles from methanol, m. p. 160—161° (Found: C, 65·75; H, 6·8. $C_{15}H_{19}O_2N_3$ requires C, 65·9; H, 6·9%), and a 2 : 4-*dinitrophenylhydrazone*, which separates in deep orange-red plates from ethyl alcohol, m. p. 130—131° (Found: C, 56·8; H, 5·6. $C_{15}H_{18}O_4N_4$ requires C, 56·6; H, 5·7%).

trans-dl-*Cryptol.*—After the addition of *dl*-cryptone (90 g.) and dry *iso*propyl alcohol (200 c.c.) to a solution of aluminium *iso*propoxide (aluminium foil, 6 g.; *iso*propyl alcohol, 100 c.c.) the slow constant-volume distillation was continued for 6 hours. The major part of the *iso*propyl alcohol was removed under reduced pressure, and the residue steam-distilled. After extraction of the distillate with ether, drying (anhydrous magnesium sulphate), and removal of the solvent, a residue of crude *dl*-cryptol (79 g.) was obtained. Yield, 88%. Crude *dl*-cryptol (40 g.) was triturated with pyridine (25 c.c.) and *p*-nitrobenzoyl chloride (53 g.) and after 2 hours the pasty mass was ground with 10% sulphuric acid and washed with water, 5% sodium carbonate solution, and water (twice). After steam-distillation the solid residue was crystallised from methanol (norit), and after two further crystallisations from the same solvent pure trans-dl-*cryptol* p-*nitrobenzoate* (26 g.) was isolated in pale yellow needles, m. p. 76·5° (Found: C, 66·3; H, 6·8. $C_{16}H_{19}O_4N$ requires C, 66·4; H, 6·6%). The mother-liquors were reserved as a source of *cis-dl*-cryptol (see below).

*trans-dl*-Cryptol *p*-nitrobenzoate (26 g.) was refluxed for 30 minutes with 5% methyl-alcoholic potassium hydroxide (180 c.c.). After removal of the bulk of the methyl alcohol the *dl*-cryptol was driven over by steam-distillation and a dried (anhydrous magnesium sulphate) ethereal extract of the distillate was, after removal of the solvent, distilled under reduced pressure, trans-dl-*cryptol* being obtained as a clear, somewhat viscous liquid, b. p. 90°/4 mm., $n_D^{20°}$ 1·4761, $d_{30°}^{30°}$ 0·9247 (Found: C, 77·0; H, 11·4. $C_9H_{16}O$ requires C, 77·1; H, 11·5%).

*Configuration of* trans-dl-*Cryptol. Hydrogenation to* trans-*Dihydrocryptol.*—*trans-dl*-Cryptol (2 g.) in absolute alcohol (20 c.c.) with palladised charcoal (1 g.) rapidly absorbed somewhat more than the theoretical amount of hydrogen (320 c.c.) during 12 minutes. After filtration, the product was poured into water and a dried ethereal extract gave, on removal of the solvent, an oil (1·6 g.) which soon solidified on the addition of α-naphthyl *iso*cyanate (2·5 g.). After crystallisation from light petroleum (b. p. 60—90°) the α-naphthylurethane (2 g.) was obtained in light felted needles, m. p. 157·8°, not depressed by authentic *trans*-dihydrocryptol α-naphthylurethane (Cooke, Gillespie, and Macbeth, *loc. cit.*).

*Derivatives of* trans-dl-*Cryptol.*—The alcohol (0·5 g.) and α-naphthyl *iso*cyanate (0·8 g.) in a corked test-tube solidified to a brittle mass of crystals within an hour. trans-dl-*Cryptol α-naphthylurethane* separated in rosettes of needles, m. p. 136°, from light petroleum (Found: C, 77·4; H, 7·5. $C_{20}H_{23}O_2N$ requires C, 77·6; H, 7·5%).

trans-dl-*Cryptol phenylurethane*, similarly prepared and purified, formed fine white needles, m. p. 108° (Found: C, 74·0; H, 8·5; N, 5·3. $C_{16}H_{21}O_2N$ requires C, 74·1; H, 8·2; N, 5·4%).

The alcohol (5 g.) and phthalic anhydride (6 g.) soon dissolved in pyridine (10 c.c.) at 60°. After 3 hours the cooled mixture was poured into 10% sulphuric acid (100 c.c.), and the resulting syrup washed with water and dissolved in 5% sodium carbonate solution (100 c.c.). After ether extraction the alkaline solution was acidified with hydrochloric acid, and the hydrogen phthalate extracted with chloroform. The syrup obtained on evaporation of the dried extract crystallised on trituration with light petroleum, and trans-dl-*cryptol hydrogen phthalate* was obtained in flat plates, m. p. 97—97·5°, when twice crystallised from light petroleum (Found: C, 70·6; H, 7·1. $C_{17}H_{20}O_4$ requires C, 70·8; H, 7·0%).

The alcohol (1 g.) in pyridine (5 c.c.) was triturated with 3 : 5-dinitrobenzoyl chloride (1·8 g.) and after 2 hours the product was worked up in the usual way. Crystallisation from methanol (twice) gave trans-dl-*cryptol* 3 : 5-*dinitrobenzoate* in thin plates, m. p. 108° (Found: C, 57·3;

H, 5·6; N, 8·3. $C_{16}H_{18}O_6N_2$ requires C, 57·5; H, 5·4; N, 8·4%). This ester (1·4 g.) in ether (10 c.c.), when added to α-naphthylamine (1·0 g.) in 80% alcohol (30 c.c.), gave an immediate orange-red precipitate, which was filtered off and washed with 50% alcohol. After drying overnight in a desiccator, the trans-dl-*cryptol* 3 : 5-*dinitrobenzoate–α-naphthylamine* compound crystallised from light petroleum (b. p. 60—90°) in fragile, orange needles, m. p. 140° (Found : C, 65·2; H, 5·8; N, 8·7. $C_{16}H_{18}O_6N_2,C_{10}H_7{\cdot}NH_2$ requires C, 65·4; H, 5·7; N, 8·8%), practically insoluble in cold light petroleum, moderately readily soluble in hot, and easily soluble in cold benzene, ether, or chloroform. Boiling with aqueous alcohol dissolves the compound, but later the free dinitrobenzoate is precipitated owing to partial dissociation.

cis-dl-*Cryptol.*—Preliminary experiments with the crude cryptol recovered on hydrolysis of the mother-liquors from the crystallisation of *trans-dl*-cryptol *p*-nitrobenzoate (above) showed that the α-naphthylamine compound of the crude 3 : 5-dinitrobenzoate, when dissolved in light petroleum, gave a crystalline product on cooling to 35° which on recrystallisation (twice) from the same solvent gave an α-naphthylamine compound, m. p. 135—139°. This yielded practically pure *trans-dl*-cryptol 3 : 5-dinitrobenzoate on treatment with dilute hydrochloric acid. On further cooling of the original solution, crops of crystals collected at 26° and at 0° melted over a wide range even after several recrystallisations, and yielded with acid a mixture of *cis*- and *trans*-cryptol 3 : 5-dinitrobenzoates. After considerable concentration of the mother-liquor an α-naphthylamine compound separated on refrigeration, from which *cis-dl*-cryptol 3 : 5-dinitrobenzoate could be obtained. As the *trans*-compound thus evidently carries down with it quantities of the more soluble *cis*-derivative in the intermediate crystallisations, and as purification of these could not be achieved by further crystallisation, the following procedure was ultimately adopted. Mother-liquors from the *p*-nitrobenzoate crystallisations (4·5 l.) were concentrated to 500 c.c. and heated under reflux for 1 hour after the addition of potassium hydroxide (100 g.). Steam-distillation of the product, and ether extraction of the distillate, gave crude cryptol (118 g.), which was converted into the 3 : 5-dinitrobenzoate in the usual way, pyridine (100 c.c.) and 3 : 5-dinitrobenzoyl chloride (190 g.) being used. The crude ester, dissolved in ether (1 l.), was slowly poured into a solution of α-naphthylamine (120 g.) in 80% alcohol (2 l.), and the red precipitate collected and dried overnight in a desiccator (260 g.). This was extracted with light petroleum mixed with 10% of benzene, and after filtration from an insoluble residue, the crop of crystals obtained on cooling to 35° was collected (105 g.). Recrystallisation from light petroleum (b. p. 60—90°) gave an α-naphthylamine compound (72 g.), m. p. 135—138°, from which *trans-dl*-cryptol 3 : 5-dinitrobenzoate was regenerated (addition of excess of dilute hydrochloric acid to a methyl-alcoholic solution). The latter on recrystallisation from methanol (thrice) gave the pure ester identical with that previously described. The α-naphthylamine compound obtained on complete evaporation of the light petroleum–benzene solution was repeatedly refluxed with light petroleum (60—90°); the crystals obtained on cooling the extracts to 35° and then to 0° were separately collected. The former were worked up for the *trans-dl*-cryptol ester as above, and the latter were again extracted, two crops collected, and the process repeated. The accumulated mother-liquors from all these extractions (some 30 l.) were concentrated by distillation; the concentrate yielded clusters of orange-red needles, m. p. 96—99°, and 97—99° after recrystallisation. The product (11 g.), when dissolved in methyl alcohol, gave, on the addition of dilute hydrochloric acid, an oil which soon solidified. The crude ester (7·5 g., m. p. 92—94°) on recrystallisation from methanol gave cis-dl-*cryptol* 3 : 5-*dinitrobenzoate* in slender, flat needles, m. p. 96·5° (Found : C, 57·3; H, 5·8; N, 8·45. $C_{16}H_{18}O_6N_2$ requires C, 57·5; H, 5·4; N, 8·4%).

The above ester (3 g.) was refluxed (20 minutes) with 5% methyl-alcoholic potassium hydroxide (30 c.c.), and the product steam-distilled. The distillate was extracted with ether (four times); the dried extract yielded *cis-dl*-cryptol (1·1 g.), b. p. 86°/6 mm., $n_{\mathrm{D}}^{20^\circ}$ 1·4752, $d_{30^\circ}^{30^\circ}$ 0·9282.

*Configuration of* cis-dl-*Cryptol. Hydrogenation to* cis-*Dihydrocryptol.*—*cis-dl*-Cryptol (0·08 g. in ether (10 c.c.) was hydrogenated with hydrogen and palladised charcoal, and the residual oil after filtration and evaporation of the ether was mixed with α-naphthyl *iso*cyanate (0·1 g.) and left for several hours. The viscous product was taken up in light petroleum (b. p. 30—60°) and after filtration from traces of di-α-naphthylurea the solvent was allowed to evaporate at room temperature. The residue consisted solely of small, hard nodules, which crystallised from light petroleum in the same characteristic form (0·14 g.). It had m. p. 112—113°, unchanged on admixture with authentic *cis*-dihydrocryptol α-naphthylurethane (Cooke, Gillespie, and Macbeth, *loc. cit.*).

*Derivatives of* cis-dl-*Cryptol.*—*cis-dl*-Cryptol (0·15 g.) and α-naphthylurethane (0·2 g.), on standing in a corked test-tube, gave a partly crystalline product, which, when dissolved in light petroleum (b. p. 30—60°), yielded fine felted needles of cis-dl-*cryptol α-naphthylurethane*, m. p. 105·5°, unchanged on further crystallisation (Found : N, 4·55. $C_{20}H_{23}O_2N$ requires N, 4·5%). This was the least soluble and most readily crystallised of the derivatives examined.

The alcohol (0·18 g.) in pyridine (2 c.c.) was treated with *p*-nitrobenzoyl chloride (0·23 g.) and after some hours the crude ester obtained by the usual treatment was dissolved in a little methanol and cooled in a freezing mixture. The precipitated mass of fine plates, when recrystallised by slow evaporation of a methyl-alcoholic solution in a refrigerator gave cis-dl-*cryptol* p-*nitrobenzoate* in small clusters of well-defined transparent plates, m. p. 34·5—35·5° (Found : N, 4·7. $C_{16}H_{19}O_4N$ requires N, 4·85%).

*cis-dl*-Cryptol 3 : 5-dinitrobenzoate (0·3 g.) in ether (3 c.c.), when added to a solution of α-naphthylamine (0·15 g.) in 80% alcohol (6 c.c.), gave an orange-red precipitate, which, after being washed with 50% alcohol and dried, was recrystallised from light petroleum (b. p. 60—90°) and norit. The cis-dl-*cryptol* 3 : 5-*dinitrobenzoate–α-naphthylamine* compound separated in deep orange-red, felted, needles, m. p. 102—104°, unaltered by further crystallisation (Found : N, 8·8. $C_{16}H_{18}O_6N_2,C_{10}H_7{\cdot}NH_2$ requires N, 8·8%).

iso*Propyl Alcohol for Ponndorf Reductions.*—Our present technique in the treatment of commercial *iso*propyl alcohol for Ponndorf reductions may be of interest to other workers, as it gives a product which dissolves aluminium foil, dusted with a little mercuric chloride, on short refluxing (25—30 minutes). The commercial alcohol is stored over good-quality, coarsely powdered quicklime, and is drawn off as required and refluxed (2 l.) with calcium (5—10 g.) for 2 hours, the condenser being fitted with a calcium chloride-tube. The alcohol is then distilled into a 2 l. flask containing some aluminium *iso*propoxide in *iso*propyl alcohol, and is simultaneously distilled off and collected in a thoroughly dry receiver.

The distillates collected during the Ponndorf reductions may be recovered for future use by fractionation until the temperature at the head of the column reaches 80°. The flask residue is added to the *iso*propoxide flask above, together with some amalgamated aluminium foil (1—2 g.) and refluxed for 1 hour before distillation. (If the commercial alcohol contains much acetone, it is similarly treated.) The distillate yields negative acetone tests and quickly dissolves aluminium foil.

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