337. *Reactions of* $\alpha\beta$*-Unsaturated Cyclic Aldehydes and Ketones. Part III. The Reduction of Cryptone.* cis- *and* trans-*Dihydrocryptol.*

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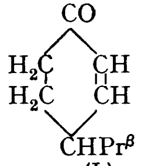
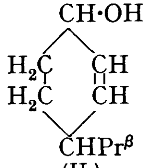
Alcohols derived from *l*-cryptone have been prepared and examined. *l*-Cryptol has previously been described, but has now been further characterised by its lævorotatory *phenyl-* and *a-naphthyl-urethanes.* Dihydrocryptol has been isolated in two forms: one isomer is a main product of the Ponndorf reduction of dihydrocryptone or samples of cryptone from *E. cneorifolia,* and the other is obtained by electrolytic reduction. The alcohols are epimeric, as they both yield dihydrocryptone on oxidation, but although they cannot be regarded as essentially pure, they have both been definitely characterised by the preparation of a series of five crystalline derivatives.

Pure *l*-cryptol on reduction gives a dihydrocryptol substantially the same as that from the Ponndorf reductions, and yielding identical crystalline derivatives. On dehydration *l*-cryptol yields *l*-1-*iso*propyl-$\Delta^{2:4}$-*cyclo*hexadiene.

A STUDY of the alcohols related to naturally occurring carbonyl compounds has been undertaken as a preliminary to the search for the products in the essential oils themselves. With this in view *l*-cryptol (II) and the dihydrocryptols (III *a, b*) derived from *l*-cryptone (I) have now been examined. *cis*- and *trans*-Forms of the saturated alcohol are possible, and the characterisation of these by means of well-defined derivatives has now been achieved.


(I.)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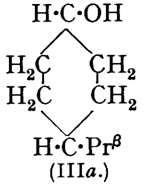
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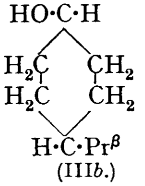
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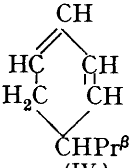
(IV.)

It will be apparent that the epimeric isomerism of the dihydrocryptols (III *a, b*) only arises consequent to the reduction of the carbonyl group, and the stereochemical purity of the sample of cryptone used as a starting material is therefore not a determining factor in the character of the dihydrocryptone formed as a reduction product. Further, the recent observation of Arcus and Kenyon (this vol., p. 698) shows that the Ponndorf reduction of *n*-butylideneacetone to α-methyl-γ-*n*-propylallyl alcohol by aluminium *iso*propoxide yields an identical product from both the *cis*- and the *trans*-form of the ketone, the reagent apparently facilitating the interconversion of geometrical isomerides. It is therefore not surprising to find that substantially the same product was obtained by the Ponndorf reduction of all the samples of cryptone from *E. cneorifolia* which were examined, and also from dihydrocryptone and stereochemically pure *l*-cryptol.

The other form of dihydrocryptol is obtained as a main product in the controlled electrolytic reduction of cryptone, but fractional distillation gives a distillate which still retains a slight optical activity. The alcohols themselves cannot therefore be regarded as sufficiently pure to warrant the consideration of their physical properties as data for configuration determination by the application of the Auwers–Skita rule; but a full examination of methods of preparation and purification of the isomers with this in view is in progress.

The two dihydrocryptols have been characterised by their *phenylurethanes* (m. p.'s 114° and 87—88°), α-*naphthylurethanes* (m. p.'s 159·5° and 113°), p-*nitrobenzoates* (m. p.'s 75·5° and 69·5°), 3 : 5-*dinitrobenzoates* (m. p.'s 124·5° and 112°), and *hydrogen phthalates* (m. p.'s 115° and 129°). The temperatures in parentheses are the corrected m. p.'s for the Ponndorf and the electrolytic alcohol respectively.

On oxidation with Beckmann's chromic acid mixture both dihydrocryptols yield the same ketone, which gives a semicarbazone and a 2 : 4-dinitrophenylhydrazone identical with authentic derivatives of dihydrocryptone (Cahn, Penfold, and Simonsen, J., 1931, 1366; Berry, Macbeth, and Swanson, J., 1937, 988) and the isomerism is therefore a case of *cis-trans* arrangement on reduction of this carbonyl group.

l-Cryptol ($[\alpha]_D^{20°}$ − 45·4°), obtained as the Ponndorf reduction product of cryptone ($[\alpha]_D^{20°}$ − 67·25°), yields a crystalline *phenylurethane* (m. p. 105°) and an α-*naphthylurethane* (m. p. 118°). These are lævorotatory, having respectively specific rotations in alcohol of − 130° (*c*, 1·29) and − 127·5° (*c*, 1·236). Similar derivatives prepared from stereochemically pure *l*-cryptol, $[\alpha]_D^{20°}$ − 142° (alcohol, *c* 3·46) (Galloway, Dewar, and Read, J., 1936, 1595), show that the above α-naphthylurethane was practically optically pure ($[\alpha]_D^{21°}$ − 130·1° in alcohol, *c* 1·614) but that crystallisation of the phenylurethane had not been sufficiently rigorous to give the stereochemically pure compound ($[\alpha]_D^{21°}$ − 147·7° in alcohol, *c* 3·15).

On dehydration by potassium hydrogen sulphate *l*-cryptol yields a lævorotatory diene, which gives a beautifully crystalline lævorotatory *adduct* with maleic anhydride, and so appears to be *l*-1-*iso*propyl-$\Delta^{2:4}$-*cyclo*hexadiene (IV). This structure was confirmed by oxidation of the diene to *iso*propylsuccinic acid, which was identified as the acid anilide. The optical activity of the diene is variable, racemisation evidently occurring to varying degrees during different dehydration experiments.

EXPERIMENTAL.

l-*Cryptol* (l-4-iso*Propyl-*Δ^2*-cyclohexen-*1*-ol*).—A sample of cryptone (90 g.) having $\alpha_D^{20^\circ}$ — 67·25° (homogeneous) was reduced by Ponndorf's method with aluminium (6 g.) dissolved in dry *iso*propyl alcohol (300 c.c.), the constant-volume distillation being continued until the distillate no longer gave a test for acetone with 3 : 5-dinitrobenzoyl chloride (7 hours). The excess of *iso*propyl alcohol was distilled off, and the residue subjected to steam-distillation. An ethereal extract of the distillate, after treatment with sodium sulphite solution to remove unreduced ketone (nil), washing, and drying, yielded on distillation 66 g. of *l*-cryptol, b. p. 82—83°/2 mm., $n_D^{20^\circ}$ 1·4780, $d_{15^\circ}^{20^\circ}$ 0·9354, $d_{15^\circ}^{15^\circ}$ 0·9388. It had α_D — 42·5° (homogeneous), which gives a specific rotation $[\alpha]_D^{20^\circ}$ — 45·4°. We did not observe the formation of the *iso*propyl ether of the unsaturated alcohol such as has been reported by Lund (*Ber.*, 1937, **70**, 1520) in the case of the unsaturated ketones which he examined.

Cryptol α-Naphthylurethane.—Condensation readily occurred when equivalent amounts of freshly distilled cryptol (α_D — 42°, homogeneous) and α-naphthyl *iso*cyanate were mixed in a dry conical flask plugged with cotton wool. Crystallisation soon began and the mixture set to a solid mass. (The reaction mixture should not be heated, as partial dehydration of the alcohol occurs with the formation of a large proportion of *s*-di-α-naphthylurea together with the urethane. With old samples of the alcohol the formation of the urea was also observed.) *Cryptol α-naphthylurethane* crystallised from light petroleum as colonies of fine white needles, m. p. 118°, $[\alpha]_D^{20^\circ}$ — 127·5° * in alcohol (*c*, 1·236) (Found: C, 77·8; H, 7·3; N, 4·5. $C_{20}H_{23}O_2N$ requires C, 77·6; H, 7·5; N, 4·5%).

Cryptol phenylurethane, prepared similarly to the above, crystallised from light petroleum in rosettes of long white needles, m. p. 105°, $[\alpha]_D^{20^\circ}$ — 130° * in alcohol (*c*, 1·29) (Found: C, 74·4; H, 8·1; N, 5·4. $C_{16}H_{21}O_2N$ requires C, 74·1; H, 8·2; N, 5·4%).

Dehydration of Cryptol.—Cryptol (25 g.; α_D — 38·4°) was heated under reflux at 120° with potassium hydrogen sulphate (30 g.). The oil collected by steam-distillation and extraction with ether gave on distillation a main fraction (10 g.), b. p. 30—31°/4 mm., $n_D^{15^\circ}$ 1·4842, $d_{15^\circ}^{15^\circ}$ 0·8531, $\alpha_D^{15^\circ}$ — 59·94° (homogeneous), whence $[\alpha]_D^{15^\circ}$ — 70·24°. A small amount (1·8 g.) of higher b. p. 38°/2 mm., having $n_D^{15^\circ}$ 1·5028, $d_{15^\circ}^{15^\circ}$ 0·8731, and $[\alpha]_D^{15^\circ}$ — 11·68°, was also collected. In a second experiment with the same quantities of materials a main fraction, b. p. 35—36°/6 mm., $n_D^{20^\circ}$ 1·4775, $[\alpha]_D^{20^\circ}$ — 82·2°, was collected.

The dehydration evidently proceeds with the formation of *l*-1-*iso*propyl-$\Delta^{2:4}$-*cyclo*hexadiene, as the oil (3 g.), when refluxed with maleic anhydride (1·5 g.) and ether (6 c.c.), gave a crystalline *adduct* which after two recrystallisations from methyl alcohol was obtained in long white needles, m. p. 133°, $[\alpha]_D^{20^\circ}$ — 29·16° (chloroform, *c*, 2·709) (Found: C, 70·65; H, 7·25. $C_{13}H_{16}O_3$ requires C, 70·85; H, 7·3%).

The structure of *l*-1-*iso*propyl-$\Delta^{2:4}$-*cyclo*hexadiene was confirmed by its oxidation to *iso*propylsuccinic acid. The diene (2·5 g.), dissolved in a little acetone, was added to a well-stirred solution of potassium permanganate (2·5 g.) in water (50 c.c.) cooled in ice. Rapid oxidation took place with rise in temperature. A further quantity of water (45 c.c.) was added, followed gradually by finely powdered permanganate until oxidation was complete. After filtration, and washing of the manganese sludge, the combined filtrates were evaporated to small bulk, acidified with sulphuric acid, and extracted with ether (8 times). To the residual oil (2 g.) in water (20 c.c.) with sulphuric acid (20%, 20 c.c.), lead peroxide (5 g.) was gradually added with continuous stirring. Carbon dioxide was evolved and after filtration of the lead salt at the end of the reaction (½ hour) the filtrate was repeatedly extracted with ether. After removal of the solvent crude *iso*propylsuccinic anhydride (0·7 g.) was obtained on distillation under reduced pressure. It gave a crude acid anilide on the addition of aniline (0·4 g.) in benzene (3 c.c.) to a solution of the anhydride in the same solvent (3 c.c.). After recrystallisation (four times) from benzene it had m. p. 142°, not depressed by authentic *iso*propylsuccinic acid anilide prepared from α-phellandrene (Semmler, *Ber.*, 1903, **36**, 1751).

Hydrogenation of Pure l-*Cryptol.*—A sample of optically crude *l*-cryptol (53 g.), prepared as above and having $\alpha_D^{20^\circ}$ — 43°, was converted into the *p*-nitrobenzoate, which was repeatedly crystallised from methyl alcohol until the m. p. and rotation were no longer affected (Galloway, Dewar, and Read, *loc. cit.*). Hydrolysis by 5% methyl-alcoholic potassium hydroxide, followed by steam-distillation, ether extraction of the distillate, and distillation under reduced pressure, gave pure *l*-cryptol (22 g.), b. p. 72°/2 mm., $d_{20^\circ}^{20^\circ}$ 0·9346, $n_D^{20^\circ}$ 1·4788, $[\alpha]_D^{20^\circ}$ — 133° (homogeneous), $[\alpha]_D^{20^\circ}$ — 142° (alcohol, *c* 3·46). It gave a phenylurethane and an α-naphthylurethane having

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* See below.

the m. p.'s given above, and in alcoholic solution the former had $[\alpha]_D^{21^\circ}$ − 147·7° (*c*, 3·15) and the latter $[\alpha]_D^{21^\circ}$ − 130·1° (*c*, 1·614).

On hydrogenation in alcoholic solution in the presence of palladised charcoal, after being worked up in the usual way, a sample of dihydrocryptol was obtained with substantially the same physical constants as those given in the case of the Ponndorf reductions below, and yielding an α-naphthylurethane and a *p*-nitrobenzoate identical with those described (see below).

On dehydration by potassium hydrogen sulphate pure *l*-cryptol gave the diene, b. p. 30°/4 mm., $n_D^{20^\circ}$ 1·4806, α_D − 37·7°. The optical activity cannot therefore be regarded as a reliable value, as under the experimental conditions of dehydration it is evidently subject to change.

Dihydrocryptol (4-iso*Propyl*cyclo*hexan*-1-*ol*).—*l*-Cryptol (50 g.) as prepared above was catalytically reduced at the ordinary temperature in the presence of palladised charcoal (6 g.) and absolute alcohol (450 c.c.). After being worked up in the usual way, the reduced alcohol (33 g.) was obtained as a clear, somewhat viscous liquid, b. p. 84—85°/5 mm., $n_D^{20^\circ}$ 1·4667, $d_{15^\circ}^{15^\circ}$ 0·9209. It was optically inactive.

Dihydrocryptol p-*nitrobenzoate* was prepared by the action of *p*-nitrobenzoyl chloride on the alcohol in presence of pyridine. It crystallised from methyl alcohol in long needles, m. p. 75·5° (Found: C, 66·0; H, 7·2; N, 4·75. $C_{16}H_{21}O_4N$ requires C, 65·95; H, 7·25; N, 4·8%).

Dihydrocryptol 3 : 5-*dinitrobenzoate* was prepared by the interaction of the alcohol and 3 : 5-dinitrobenzoyl chloride in the presence of pyridine. After being washed with dilute acid, water, dilute sodium carbonate solution, and water, it was crystallised several times from alcohol, yielding needles, m. p. 124·5° (Found: C, 57·3; H, 6·0; N, 8·3. $C_{16}H_{20}O_6N_2$ requires C, 57·1; H, 6·0; N, 8·3%).

Dihydrocryptol phenylurethane. Crystallisation began about ½ hour after a mixture of equivalent parts of phenyl *iso*cyanate and dihydrocryptol had been set aside in a small conical flask plugged with cotton-wool. After standing overnight, the solid mass was dissolved in light petroleum (b. p. 60—90°) and crystallised. After recrystallisation from the same solvent the *phenylurethane* was obtained in fine, long, felted needles, m. p. 114° (Found: C, 73·8; H, 8·9; N, 5·37. $C_{16}H_{23}O_2N$ requires C, 73·6; H, 8·9; N, 5·36%).

Dihydrocryptol α-naphthylurethane, obtained similarly to the above, crystallised from light petroleum in stellate masses of fine needles, m. p. 159·5° (Found: C, 77·1; H, 8·1; N, 4·52. $C_{20}H_{25}O_2N$ requires C, 77·1; H, 8·1; N, 4·5%).

Dihydrocryptol hydrogen phthalate. The alcohol (9 g.) was heated with finely powdered phthalic anhydride (10 g.) at 110° for 15 hours and the resultant liquid whilst still hot was poured into 5% sodium carbonate solution (100 c.c.). The small portion remaining undissolved was extracted with ether and on acidification of the aqueous solution with concentrated hydrochloric acid an oil separated which soon crystallised. The separated solid, after drying and recrystallisation from light petroleum (b. p. 60—90°), was obtained in pearly plates, m. p. 115° (Found: C, 70·5; H, 7·55. $C_{17}H_{22}O_4$ requires C, 70·3; H, 7·6%).

Dihydrocryptol was also prepared by the catalytic reduction of cryptone to dihydrocryptone by palladised charcoal and the conversion of the latter by Ponndorf reduction. The product gave a phenylurethane and an α-naphthylurethane identical with the above. The same isomeric alcohol is thus evidently produced by both procedures.

Electrolytic Reduction of Cryptone.—In a typical experiment cryptone (125 c.c.), dissolved in alcohol (95%, 250 c.c.) containing nickel sulphate (1·5 g.) and sulphuric acid (10%, 50 c.c.), was placed in the cathode compartment of a cell, the anode compartment consisting of a porous pot containing a cylindrical platinum electrode immersed in 10% sulphuric acid. The cathode was a sheet of freshly etched nickel (2 sq. dm. area) enveloping the porous pot at such a distance that the voltage was some 14 v. with a current of 8 amp. flowing. The current was passed for about 12 hours, the temperature being maintained at 34—36° by a cooling coil in the cathode compartment. Sulphuric acid was added as required during the reduction, at the end of which the mixture was poured into a large volume of water. After standing, the separated oil was drawn off, the water extracted with ether, and the oil, together with that recovered from the extract, steam-distilled. An ethereal extract of the distillate gave no colour with phenolphthalein on shaking with neutral sodium sulphite, showing the absence of cryptone. Dihydrocryptone was removed from the ethereal extract by shaking with sodium bisulphite solution (35%, 500 c.c.). After standing for 24 hours, the liquid was filtered (pump), and the bisulphite cake thoroughly treated with ether to remove dihydrocryptol. After drying and removal of the ether the crude dihydrocryptol (50 c.c.) was distilled, and the following fractions collected. The optical activity of the fractions shows that a trace of optically active impurity is not removed by the fractionation (compare Cahn, Penfold, and Simonsen, J., 1931, 1369). Fractional crystallisation of the derivatives shows that the alcohol is a mixed product containing some of the Ponndorf reduction isomer:

	Vol., c.c.	$n_D^{20°}$.	α_D.
Up to 65°/0·8 mm.	3	1·4669	−1·50°
65—66°/0·7 mm.	30	1·4691	+2·75
66—68°/0·8 mm.	6	1·4696	+2·26
Over 68°/0·8 mm.	6	1·4710	−0·74

The mixed yields of dihydrocryptone obtained in the electrolytic reductions, when distilled under reduced pressure, gave a main fraction, b. p. 60°/1·9 mm., from which the usual derivatives were prepared.

Dihydrocryptol (Electrolytic) Derivatives.—(a) The *phenylurethane* was formed when equivalent quantities of the alcohol and phenyl *iso*cyanate were mixed. A little of the syrupy product was triturated with light petroleum, whereby crystallisation was induced; on nucleation, the whole syrup soon solidified. Recrystallised from light petroleum, the phenylurethane formed white needles, m. p. 87—88°, markedly depressed by the phenylurethane of the dihydrocryptol described above. The present product was much more soluble in light petroleum (Found: C, 73·8; H, 8·75; N, 5·3, 5·3. $C_{16}H_{23}O_2N$ requires C, 73·6; H, 8·9; N, 5·4%).

(b) The *α-naphthylurethane*, prepared from equivalent quantities of α-naphthyl *iso*cyanate and the alcohol, showed the same reluctance to crystallise as noted above. Recrystallisation from light petroleum gave a fraction (needles), which on further purification had m. p. 159·5°, not depressed by the α-naphthylurethane described above. A main product (more soluble) was isolated in small hard granular clumps, which on further purification continued to separate in this characteristic form and had m. p. 113°, markedly depressed by the other form (Found: C, 77·3; H, 8·1. $C_{20}H_{25}O_2N$ requires C, 77·1; H, 8·1%).

(c) The p-*nitrobenzoate* was obtained by trituration of equivalent quantities of the alcohol and *p*-nitrobenzoyl chloride with excess of pyridine in a warmed mortar. After 3 hours, the product was worked up, and obtained, after several recrystallisations from methyl alcohol, in pale yellow plates, m. p. 69·5°, markedly lowered by the corresponding derivative (needles) from the Ponndorf alcohol (Found: C, 65·8; H, 7·2. $C_{16}H_{21}O_4N$ requires C, 65·95; H, 7·25%).

(d) The 3 : 5-*dinitrobenzoate* was prepared in a similar way and crystallised from alcohol and finally from 90% spirit, forming flat, almost colourless needles, m. p. 112°. It was exceedingly difficult to separate the two isomeric forms in this case (Found: C, 56·9; H, 5·8. $C_{16}H_{20}O_6N_2$ requires C, 57·1; H, 6·0%).

(e) The *hydrogen phthalate* was prepared by heating the electrolytic alcohol (6 g.) at 100—120° for 15 hours with phthalic anhydride (7 g.). The hot mixture was poured into 5% sodium carbonate solution (60 c.c.) and worked up as described above. Fractional crystallisation from light petroleum yielded the hydrogen phthalate as a main product in large needles, m. p. 129°. It can also crystallise in plates having the same m. p. The m. p. of a mixture with the hydrogen phthalate described above, or with phthalic anhydride, was greatly depressed (Found: C, 70·2; H, 7·5. $C_{17}H_{22}O_4$ requires C, 70·3; H, 7·6%).

Oxidation of Dihydrocryptol.—Both the dihydrocryptols described above were converted on oxidation into the same ketone, which was identified as dihydrocryptone. The dihydrocryptol of the Ponndorf reduction type (4·5 g.), when added to 40 c.c. of Beckmann's chromic acid mixture (*Annalen*, 1889, **250**, 335) at 35°, formed a black addition compound on shaking and the temperature rose quickly to 55°, with the liberation of the ketone. After successive washing of an ethereal extract with 5% sodium carbonate solution and water and drying, a residual oil (3·5 g.) was obtained on removal of the solvent. This had b. p. 56°/1·3 mm., $n_D^{19°}$ 1·4570, and gave a semicarbazone, m. p. 188—189°, and a 2 : 4-dinitrophenylhydrazone in lath-like orange plates, m. p. 119·5—120°, identical with the derivatives of dihydrocryptone (Berry, Macbeth, and Swanson, *loc. cit.*). A similar oxidation was carried out with the dihydrocryptol (1·6 g.) prepared by hydrolysis of the hydrogen phthalate derived from the electrolytically reduced alcohol. The residual oil (1·1 g.) gave two derivatives identical with those above.

One of the authors (T. B. S.) is indebted to the Federal Research Grant of the Commonwealth Government for help which enabled him to participate in the work.

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[*Received, August* 12*th*, 1938.]