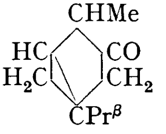
382. *Researches in the Thujone Series. Part I. The Thujones and some Thujyl Alcohols and Thujylamines.*

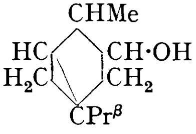
By Andrew G. Short and John Read.

The stereochemical relationship of the so-called "α-thujone" of thuja oil to "β-thujone" of tansy oil is similar to that of *l*-menthone to *d*-*iso*menthone. The stereochemically homogeneous thujones have now been prepared for the first time, and it is proposed to name them *l*-thujone and *d*-*iso*thujone, respectively, and to bring the nomenclature of the derived thujyl alcohols and thujylamines into line with that of the corresponding alcohols and amines in the menthone and carvomenthone series. Two stereochemically pure thujyl alcohols and also two pure thujylamines are described: these are optically active; one of each is derived from *l*-thujone, and its stereoisomeride from *d*-*iso*thujone.

The thujones (I), together with the related thujyl alcohols (II) and thujylamines (III), are substances of pronounced chemical and stereochemical interest; but, in spite of the considerable attention which has been devoted to their study (see, *e.g.*, Wallach, "Terpene und Campher," Leipzig, 1914, 505; Simonsen, "The Terpenes," Cambridge, 1932, **2**, 21 *et seq.*), it is questionable whether any of them, with one possible exception, has hitherto been obtained in a state of stereochemical homogeneity. The thujone molecule contains three dissimilar asymmetric carbon atoms; but since two of these are joined by a diagonal link, which inhibits the *cis-trans* effect, the possibilities of stereoisomerism are reduced to those of a molecular system containing only two dissimilar asymmetric carbon atoms. Thus, the stereoisomerism of the thujones should be similar to that of the menthones and the carvomenthones (J., 1934, 226). The parallelism should hold also for the thujyl alcohols and the thujylamines, each of which types should exist in four pairs of *d*- and *l*-forms.



(I.)



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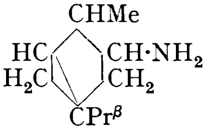

(III.)

Wallach (*Annalen*, 1904, **336**, 365) showed that "α-thujone" was partly converted into "β-thujone" by treatment with alcoholic alkali. It is shown below that the so-called "α-thujone" of thuja oil and the "β-thujone" of tansy oil are related in the same fundamental way as *l*-menthone and *d*-*iso*menthone, and that under appropriate conditions they are capable of existing in dynamic equilibrium. From naturally occurring "α-thujone" having $\alpha_D - 11{\cdot}4°$ (l 1) and "β-thujone" having $\alpha_D + 46{\cdot}2°$ it has proved possible for the first time to prepare two ketones having optimum rotatory powers $\alpha_D - 19{\cdot}9°$ and $+ 72{\cdot}5°$ (cf. Simonsen, *op. cit.*, p. 39). For these substances, which appear to be stereochemically pure, we propose the respective names *l*-thujone and *d*-*iso*thujone, thus opening the way to a systematic nomenclature of the derived alcohols and amines, which are thereby brought into line with the menthols and menthylamines (J., 1934, 1781).* As in the menthone and carvone series (J., 1935, 1139), the *iso*ketone has the higher numerical rotatory power, density, and refractive index.

In presence of alcoholic sodium ethoxide, the two thujones under consideration undergo interconversion (corresponding to the so-called "Beckmann inversion" of *l*-menthone), thereby yielding an equilibrium mixture having a mean value of $\alpha_D + 40{\cdot}0°$ (l 1). The dynamic equilibrium under these conditions may thus be represented as follows:

$$\underset{(35\%)}{l\text{-thujone }(\alpha_D - 19{\cdot}9°)} \rightleftarrows \underset{(65\%)}{d\text{-}iso\text{thujone }(\alpha_D + 72{\cdot}5°)}$$

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* Also with the carvomenthols and carvomenthylamines (J., 1934, 226). The so-called "*Iso-Thujon*" of Wallach (*Annalen*, 1895, **286**, 102), an optically active form of which will be described in a later paper, should be named systematically as a *cyclo*pentenone derivative.

In the thujone series the equilibrium lies further to the right than in the menthone series (J., 1927, 1278). From the nature of this equilibrium it follows that natural " α- " and " β-thujone " are mixtures of these two dynamic stereoisomerides; further, that either of the pure ketones, or any mixture of the two, will yield identical mixtures of products when submitted under like conditions to such reactions as reduction with sodium and alcohol or amination by heating with ammonium formate. Owing to their facile interconversion, the stereochemically pure ketones cannot be prepared by hydrolysing the pure semicarbazones. Thus, Wallach (*Annalen*, 1904, **336**, 261) gave the value $[\alpha]_D + 59{\cdot}83°$ for a thujone semicarbazone, m. p. 186—188°, in methyl alcohol solution : the thujone derived from this by hydrolysis with phthalic anhydride had $\alpha_D - 9{\cdot}33°$, $[\alpha]_D - 10{\cdot}23°$. Paolini (*Ann. Chim. Appl.*, 1925, **15**, 414), in a similar way, obtained a ketone having $[\alpha]_D + 10{\cdot}23°$. The pure ketones described in this paper were obtained by oxidising a stereochemically pure thujyl and *iso*thujyl alcohol with Beckmann's reagent.

As yet, only one thujyl and one *iso*thujyl alcohol appear to have been isolated in a state of stereochemical purity. A crystalline l-*thujyl alcohol*, m. p. 66—67°, $[\alpha]_D - 20{\cdot}5°$ (methyl alcohol), was obtained by fractionally crystallising the mixed *p*-nitrobenzoates of hydrogenated " α-thujone " : when oxidised, it gave *l*-thujone, $\alpha_D - 19{\cdot}9°$ (*l* 1). Similarly, the *p*-nitro- or 3 : 5-dinitro-benzoates of the mixture of alcohols formed on reducing " α- " or " β-thujone " with sodium and alcohol yielded a liquid d-iso*thujyl alcohol*, b. p. 103°/16 mm., $\alpha_D + 106{\cdot}7°$: this was oxidised to *d-iso*thujone, $\alpha_D + 72{\cdot}46°$. The same alcohol has apparently been obtained by Paolini (*Atti R. Accad. Lincei*, 1911, [v], **20**, I, 765), and by Tschugaev and Fomin (*Ber.*, 1912, **45**, 1293), by applying the phthalate method to the reduction products of thujones. On the present evidence, the stereochemical homogeneity of the so-called " δ-thujyl alcohol," $[\alpha]_D + 50{\cdot}01°$, obtained in a similar way by Paolini and Divizia (*Atti R. Accad. Lincei*, 1912, [v], **21**, I, 570), and also described as a natural product by Paolini and Lomanaco (*ibid.*, 1914, [v], **23**, II, 123), cannot be regarded as established, owing to lack of information concerning the optical rotation of the derived thujone.

No homogeneous thujylamine has hitherto been isolated (Simonsen, *op. cit.*, p. 41). By reducing the liquid oxime of *l*-thujone with sodium and alcohol and fractionally crystallising the derived mixture of thujylamine hydrochlorides, we have been able to isolate a stereochemically pure l-*thujylamine*, having $\alpha_D^{17°} - 24{\cdot}32°$ (*l* 1). The crystalline oxime of *d-iso*thujylamine, when treated similarly, yielded d-iso*thujylamine*, with $\alpha_D^{13°} + 94{\cdot}82°$. In reaction with nitrous acid these bases yielded complex mixtures of decomposition products which did not appear to contain any thujyl alcohols. The close correspondence existing between the optical rotatory powers of *l*-thujyl alcohol and *l*-thujylamine, on the one hand, and those of *d-iso*thujyl alcohol and *d-iso*thujylamine, on the other, falls into line with the relationships observed for menthols and menthylamines (J., 1934, 1781). This evidence, taken in conjunction with the preparative methods, points to the stereochemical equivalence of these two alcohol–amine pairs in the thujone series.

From their close analogy to the menthones and carvomenthones, it follows that either *l*- or *d-iso*-thujone when heated with ammonium formate under like conditions would yield an identical mixture of the formyl derivatives of the four related optically active thujylamines, including *l*- and *d-iso*thujylamine (J., 1927, 2168; 1934, 231); it has not proved possible, however, to isolate any individual thujylamine, beyond a small amount of *d-iso*thujylamine, from the product of this reaction. Moreover, the derived mixture of stereoisomeric thujylamines appeared to furnish no thujyl alcohol in reaction with nitrous acid, a result which indicates that this reagent cannot be used at all in deaminating a thujylamine to a thujyl alcohol. Nor can such alcohols be obtained from *l*-thujyl- or *d-iso*thujyl-trimethylammonium hydroxide (cf. piperitylamine; J., 1930, 2779), since these substances when heated yield almost exclusively the corresponding tertiary amines. This observation conflicts with the statement of Tschugaev (*Ber.*, 1901, **34**, 2276) that thujenes are the main products of the pyrolysis, and agrees with the views of Hugh and Kon (J., 1927, 2594) on the stability of a ring-system of the general character here concerned.

EXPERIMENTAL.

Ketones.

1. " *α-Thujone.*"—Thuja oil (150 g.), with $d_{16^\circ}^{16^\circ}$ 0·9300, $n_D^{16^\circ}$ 1·4641, $\alpha_D^{16^\circ}$ − 11·39° (*l* 1), after two successive fractional distillations yielded " α-thujone " (75—85 g.) having b. p. 80—82°/20 mm., $n_D^{16^\circ}$ 1·4585, $\alpha_D^{16^\circ}$ − 15·43° (*l* 1); this fraction still contained small amounts of *l*-fenchone and other impurities, including *l*-bornyl esters.

2. " *β-Thujone.*"—Tansy oil (150 g.), with $n_D^{16^\circ}$ 1·4610, $\alpha_D^{16^\circ}$ + 38·03° (*l* 1), upon similar treatment furnished " β-thujone " (70—75 g.) having b. p. 74—76°/14 mm., $n_D^{16^\circ}$ 1·4564, $\alpha_D^{15^\circ}$ + 46·21° (*l* 1). Another specimen (150 g.) gave a corresponding fraction (60—65 g.) having b. p. 84—85°/18 mm., $n_D^{20^\circ}$ 1·4568, $\alpha_D^{16^\circ}$ + 40·46° (*l* 1). Small quantities of *l*-camphor were isolated from these fractions upon oxidising the thujone to carvacrol with ferric chloride and glacial acetic acid (semicarbazone, m. p. 237°, $[\alpha]_D^{15^\circ}$ + 36·0° [*c* 1, chloroform]; *d*-camphorsemicarbazone, m. p. 237°, $[\alpha]_D^{15^\circ}$ − 36·0°).

3. l-*Thujone.*—*l*-Thujyl alcohol, m. p. 66—67°, $[\alpha]_D^{16^\circ}$ − 20·5° (*c* 1, methyl alcohol), obtained by hydrogenating " α- " or " β-thujone," as described below, was oxidised with chromic acid by Beckmann's method (*Annalen*, 1889, **250**, 335), the use of alkali being avoided in purifying the product. The resulting *l*-thujone was a clear, mobile liquid with a characteristic odour, b. p. 74·5°/9 mm., $d_{4^\circ}^{25^\circ}$ 0·9109, $n_D^{25^\circ}$ 1·4490, $[R_L]_D$ 44·77 (calc. for $C_{10}H_{16}O$, 44·11), $\alpha_D^{18^\circ}$ − 19·94° (*l* 1, homogeneous).

l-*Thujone* 2 : 4-*dinitrophenylhydrazone* separated from methyl alcohol in long, red-gold needles, m. p. 117°, $[\alpha]_D^{16^\circ}$ + 44·0° (*c* 1, chloroform) (Found : C, 58·2; H, 6·1. $C_{16}H_{20}O_4N_4$ requires C, 57·8; H, 6·1%). The semicarbazone crystallised from aqueous methyl alcohol in fine needles, m. p. 186—188°, $[\alpha]_D^{14^\circ}$ + 42·0° (*c* 1, methyl alcohol) (cf. Wallach, *Annalen*, 1904, **336**, 261). The same derivatives were obtained from crude " α-thujone " after repeated fractional crystallisations of the crude products.

4. d-iso*Thujone.*—*d-iso*Thujyl alcohol, b. p. 103°/16 mm., $\alpha_D^{14^\circ}$ + 106·7° (*l* 1), obtained by reducing " α- " or " β-thujone " with sodium and alcohol as described below, was oxidised with Beckmann's reagent, an ethereal extract of the product being washed three times with water and dried over sodium sulphate. The resulting ketone was a clear, mobile liquid with the typical odour of thujone, b. p. 76°/10 mm., $d_{4^\circ}^{25^\circ}$ 0·9135, $n_D^{25^\circ}$ 1·4500, $[R_L]_D$ 44·72 (calc. for $C_{10}H_{16}O$, 44·11), $\alpha_D^{15^\circ}$ + 72·46° (*l* 1, homogeneous). Wallach (*Annalen*, 1904, **336**, 267) and Haller (*Compt. rend.*, 1905, **140**, 627) gave the respective values, $[\alpha]_D$ + 76·16° (in ether) and + 74·3° (homogeneous, *d* 0·9206). The rotatory power of the ketone is enhanced considerably in ethereal solution, and Haller's specimen seems to have been isolated by fractional distillation alone; so that neither of these specimens can be accepted as stereochemically pure.

d-iso*Thujone* 2 : 4-*dinitrophenylhydrazone*, prepared by the method of Brady (J., 1931, 756), was obtained from methyl alcohol in small red-gold needles, m. p. 116°, $[\alpha]_D^{16^\circ}$ + 161° (*c* 1, chloroform) (Found : C, 58·0; H, 6·0. $C_{16}H_{20}O_4N_4$ requires C, 57·8; H, 6·1%). The semicarbazone crystallised from aqueous methyl alcohol in long needles, m. p. 172°, $[\alpha]_D^{15^\circ}$ + 222·0° (*c* 1, methyl alcohol) (cf. Wallach, *loc. cit.*). The same ketonic derivatives were obtained by fractionally crystallising the crude products furnished directly by " β-thujone ".

5. *Inversion Experiments with* l- *and* d-iso-*Thujone.*—Each pure ketone (1·25 g.) was dissolved separately in a solution of sodium (0·25 g.) in absolute alcohol (6 c.c.) and kept at room temperature for 24 hours, after which the ketone was recovered and distilled under diminished pressure. Under these conditions the optical rotatory power of *l*-thujone changes from $\alpha_D^{18^\circ}$ − 19·94° to $\alpha_D^{17^\circ}$ + 38·22°, and that of *d-iso*thujone from $\alpha_D^{15^\circ}$ + 72·46° to $\alpha_D^{14^\circ}$ + 41·8° (*l* 1).

When the above *d-iso*thujone semicarbazone was hydrolysed with hot 20% oxalic acid solution, the recovered ketone had $\alpha_D^{15^\circ}$ + 54·83° (*l* 1), $n_D^{17^\circ}$ 1·4501. A similar inversion has been observed for " α-thujone " (Wallach, *Annalen*, 1904, **336**, 263; Paolini, *Ann. Chim. Appl.*, 1925, **15**, 414).

Alcohols.

1. l-*Thujyl Alcohol.*—The specimens of " α-thujone " mentioned above were submitted to two further fractional distillations under diminished pressure. The material thus obtained had b. p. 72—74°/8 mm., $n_D^{17^\circ}$ 1·4590, $\alpha_D^{15^\circ}$ − 13·05° (*l* 1), and was still contaminated with *l*-fenchone. By hydrogenation in *cyclo*hexane solution at 65—70° under an over-pressure of 3 atm. in presence of an active hydrogenating catalyst, it was possible to effect selective reduction, so that the fenchone remained unaltered when 85% of the amount of hydrogen calculated for pure thujone had been absorbed. The crude product had $n_D^{21^\circ}$ 1·4638, $\alpha_D^{17^\circ}$ + 1·96° (*l* 1). It was esterified in dry pyridine (50 g. in 250 c.c.) with *p*-nitrobenzoyl chloride (69 g.; 1·1 mols,), which was added

slowly with stirring. When isolated according to the usual method (J., 1934, 315), the crude ester was somewhat oily, but after twelve recrystallisations from methyl alcohol it yielded pure l-*thujyl* p-*nitrobenzoate* (7·1 g.) consisting of glistening plates, m. p. 101°, $[\alpha]_{\mathrm{D}}^{15^\circ}$ − 32·25° (*c* 2, chloroform) (Found : C, 67·5; H, 6·8. $C_{17}H_{21}O_4N$ requires C, 67·3; H, 7·0%).

When boiled for 30 minutes with 5% methyl-alcoholic potassium hydroxide (1·2 mols.), the ester yielded l-*thujyl alcohol*, which crystallised from methyl alcohol in long, fine needles, m. p. 66—67°, $[\alpha]_{\mathrm{D}}^{16^\circ}$ − 20·5° (*c* 1, methyl alcohol), $[\alpha]_{\mathrm{D}}^{15^\circ}$ − 22·5° (*c* 1, ethyl alcohol) (Found : C, 78·0; H, 11·9. $C_{10}H_{18}O$ requires C, 77·9; H, 11·8%). The 3 : 5-*dinitrobenzoate* separated from methyl alcohol in long, fine needles, m. p. 106°, $[\alpha]_{\mathrm{D}}^{19^\circ}$ − 24·5° (*c* 2, chloroform) (Found : C, 58·6; H, 5·6. $C_{17}H_{20}O_6N_2$ requires C, 58·6; H, 5·8%).

A typical product obtained by hydrogenating " β-thujone " under similar conditions had $n_{\mathrm{D}}^{12^\circ}$ 1·4692, $\alpha_{\mathrm{D}}^{13^\circ}$ + 36·21° (*l* 1). The derived nitrobenzoates crystallised with great reluctance, and it was impracticable to isolate any single substance from the mixture of esters thus produced.

The catalytic hydrogenation of the thujones is affected markedly by the conditions. Thus, the hydrogenation of " α-thujone " was not always so profitable as indicated above. A completely hydrogenated specimen, with $n_{\mathrm{D}}^{13^\circ}$ 1·4654, $\alpha_{\mathrm{D}}^{13^\circ}$ − 7·0° (*l* 1), yielded with 3 : 5-dinitrobenzoyl chloride a product which after ten recrystallisations from aqueous methyl alcohol furnished a fraction having m. p. 80°, $[\alpha]_{\mathrm{D}}^{16^\circ}$ − 15·25° (*c* 2, chloroform). The derived alcohol had b. p. 99°/10 mm., $n_{\mathrm{D}}^{15^\circ}$ 1·4628, $\alpha_{\mathrm{D}}^{14^\circ}$ − 12·6° (*l* 1), and gave an apparently homogeneous *p*-nitrobenzoate with m. p. 71°, $[\alpha]_{\mathrm{D}}^{15^\circ}$ − 24° (*c* 2, chloroform). However, when kept for some months in the refrigerator, this alcohol deposited crystalline material identical with *l*-thujyl alcohol described above.

In another experiment, in which the hydrogenation of " α-thujone " was retarded through the presence of a catalyst poison, the crude product had $n_{\mathrm{D}}^{14^\circ}$ 1·4700, $\alpha_{\mathrm{D}}^{14^\circ}$ + 7·29° (*l* 1). The value of $[\alpha]_{\mathrm{D}}^{16^\circ}$ for the derived 3 : 5-dinitrobenzoate changed only from + 3·0° to − 2·75° (*c* 2, chloroform) after six recrystallisations from methyl alcohol, and the separation of a homogeneous ester had to be abandoned.

2. d-iso*Thujyl Alcohol*.—Coarse pieces of sodium (37·5 g.) were added gradually to a boiling solution of " α-thujone " (50 g.) in dry ethyl alcohol (300 c.c.; reflux, sand-bath). When all the sodium had dissolved, the mixture was cooled, diluted with ice-water, neutralised with concentrated hydrochloric acid, and extracted with ether. The mixture of alcohols thus obtained (40 g.) was a clear, viscous, sweet-smelling liquid, b. p. 97—99°/15 mm., $n_{\mathrm{D}}^{18^\circ}$ 1·4693, $\alpha_{\mathrm{D}}^{16^\circ}$ + 39·82° (*l* 1). " β-Thujone " furnished a practically identical product (cf. Wallach, *Annalen*, 1892, **272**, 109; Semmler, *Ber.*, 1892, **25**, 3344).

The latter material (100 g.) was treated in dry pyridine (500 c.c.) with 3 : 5-dinitrobenzoyl chloride (167 g.; 1·1 mols.). After remaining overnight, the mixture was poured into 50% hydrochloric acid (1000 c.c.) and extracted with chloroform. The extract was washed with sodium hydroxide solution and steam-distilled. The non-volatile residue, when extracted with ether, furnished a clear yellow syrup which slowly crystallised to a hard mass. After one recrystallisation from aqueous methyl alcohol the ester had m. p. 75°, $[\alpha]_{\mathrm{D}}^{14^\circ}$ + 63·25° (*c* 2, chloroform). Thirteen further recrystallisations furnished a fraction of pure d-iso*thujyl* 3 : 5-*dinitrobenzoate*, which was not altered by further recrystallisation; it consisted of long, colourless needles, m. p. 92°, $[\alpha]_{\mathrm{D}}^{17^\circ}$ + 96·75° (*c* 2, chloroform) (Found : C, 58·5; H, 5·6%). When hydrolysed with boiling methyl-alcoholic potassium hydroxide, this ester (8·7 g.) yielded d-iso*thujyl alcohol* (3·2 g.), which was purified by steam-distillation, followed by distillation under diminished pressure; it was a sweet-smelling, viscous liquid, b. p. 103°/16 mm., $n_{\mathrm{D}}^{16\cdot5^\circ}$ 1·4627, $\alpha_{\mathrm{D}}^{14^\circ}$ + 106·70° (*l* 1).

The reduction product obtained from " α-thujone " yielded a crude *p*-nitrobenzoate which after six recrystallisations from methyl alcohol, followed by seven from aqueous methyl alcohol, gave d-iso*thujyl* p-*nitrobenzoate* in long, colourless needles, m. p. 78°, $[\alpha]_{\mathrm{D}}^{13^\circ}$ + 107·0° (*c* 1, chloroform) (Found : C, 67·5; H, 6·8. $C_{17}H_{21}O_4N$ requires C, 67·3; H, 7·0%). The derived *d-iso*thujyl alcohol had b. p. 88°/6 mm., $n_{\mathrm{D}}^{14^\circ}$ 1·4630, $\alpha_{\mathrm{D}}^{14^\circ}$ + 108·84° (*l* 1); it yielded a 3 : 5-dinitrobenzoate with m. p. 92°, $[\alpha]_{\mathrm{D}}^{17^\circ}$ + 96·75° (*c* 2, chloroform). The melting point was unaffected when this ester was admixed with *d-iso*thujyl 3 : 5-dinitrobenzoate, m. p. 92°, obtained from " β-thujone," as described above. *d-iso*Thujyl alcohol obtained from either " α-thujone " or " β-thujone " yielded upon oxidation *d-iso*thujone, with $\alpha_{\mathrm{D}}^{15^\circ}$ + 72·46° (*l* 1), as described above.

3. No sensible reduction occurred when " α-thujone " or " β-thujone " was treated in dry *iso*propyl alcohol with aluminium *iso*propoxide at 130° for 48 hours, according to the method of Ponndorf (*Z. angew. Chem.*, 1926, **39**, 138).

Amines.

1. l-*Thujylamine.*—A solution in aqueous methyl alcohol of " α-thujone " (50 g.), hydroxylamine hydrochloride (25·2 g.), and sodium acetate crystals (30·2 g.) was kept for a week at room temperature, and then diluted largely with water and extracted with ether. After fractional distillation under diminished pressure the extract yielded crude *l*-thujone oxime, b. p. 131—132°/12 mm., α_D from − 33·8° to − 25·3° (*l* 1) (cf. *Ber.*, 1892, **25**, 3344; *Annalen*, 1904, **336**, 267). The derived *p*-nitrobenzoate crystallised from aqueous methyl alcohol in long, brownish needles, m. p. 107—108°, $[\alpha]_D^{12^\circ}$ − 35·25° (*c* 2, chloroform).

A solution of the oxime (50 g.) in dry ethyl alcohol (750 c.c.) was reduced at the boiling point with sodium (75 g.). The product was diluted with water and steam-distilled, the distillate being then neutralised with hydrochloric acid, evaporated to small bulk, extracted with ether, and evaporated to dryness. The yield of crude thujylamine hydrochloride thus obtained was equal to the weight of oxime used. Two recrystallisations from hot absolute alcohol–acetone gave pure *l*-thujylamine hydrochloride in glistening leaflets, m. p. 248—249° (decomp.), $[\alpha]_D^{16^\circ}$ −15·75° (*c* 2, water).

Free *l*-thujylamine was obtained from the hydrochloride as a colourless, viscid liquid with a strong odour of decaying fish, b. p. 81·5°/15·5 mm., $n_D^{19^\circ}$ 1·4673, $\alpha_D^{17^\circ}$ − 24·32° (*l* 1). It absorbed carbon dioxide from the air, forming a white crystalline deposit. The formyl derivative, prepared by distilling the formate under diminished pressure, was a waxy solid, m. p. 40°, $[\alpha]_D^{15^\circ}$ − 51·11° (*c* 1·7, chloroform). The acetyl and benzoyl derivatives were syrups. p-*Nitrobenzoyl*-l-*thujylamine* formed long needles from aqueous methyl alcohol, m. p. 146·5°, $[\alpha]_D^{15^\circ}$ − 51·25° (*c* 2, chloroform) (Found : C, 67·4; H, 6·9. $C_{17}H_{22}O_3N_2$ requires C, 67·6; H, 7·3%).

The following derivatives were also prepared : *p*-toluenesulphonyl, brownish leaflets, m. p. 120°, $[\alpha]_D^{15^\circ}$ − 7·75° (*c* 2, chloroform); carbimide, long needles, m. p. 141—142°, $[\alpha]_D^{15^\circ}$ − 41·0° (*c* 1, chloroform); formate, glistening needles, m. p. 110°, $[\alpha]_D^{16^\circ}$ − 15·5° (*c* 1, water); hydrogen oxalate, glistening plates, m. p. 218—220°, $[\alpha]_D^{15^\circ}$ − 6·0° (*c* 0·9, water); hydrogen *d*-tartrate, fine needles, m. p. 194°, $[\alpha]_D^{15^\circ}$ + 3·5° (*c* 1, water). The *salicylidene* derivative formed lemon-yellow plates from methyl alcohol, m. p. 66°, $[\alpha]_D^{15^\circ}$ − 7·03° (*c* 2, chloroform); it showed anomalous rotatory dispersion, but was not phototropic (J., 1927, 2174) (Found : C, 79·7; H, 8·8. $C_{17}H_{23}ON$ requires C, 79·3; H, 9·0%).

When methylated in dry methyl alcohol in presence of sodium methoxide and an excess of methyl iodide (cf. J., 1930, 2777), *l*-thujylamine yielded l-*thujyltrimethylammonium iodide*, which crystallised from hot water in small prisms, m. p. 269° (decomp.), $[\alpha]_D^{15\cdot5^\circ}$ − 30·75° (*c* 2, chloroform) (Found, by titration : I, 39·0. $C_{13}H_{26}NI$ requires I, 39·3%). The derived hydroxide was obtained as a brittle solid mass which absorbed water and carbon dioxide rapidly from the air (cf. *Ber.*, 1901, **34**, 2276). When heated in an oil-bath, it melted at 140° and decomposed at 150—160°, yielding *N*-dimethyl-*l*-thujylamine as a colourless liquid with a strong basic odour, b. p. 88°/11 mm., $n_D^{20^\circ}$ 1·4615, $\alpha_D^{18^\circ}$ − 14·12° (*l* 1). The *picrate* of this base separated from alcohol in flat, yellow plates, m. p. 137—138°, $[\alpha]_D^{18}$ − 40·5° (*c* 1, chloroform) (Found : C, 52·8; H, 6·2. $C_{12}H_{23}N,C_6H_3O_7N_3$ requires C, 52·7; H, 6·4%). The methiodide, formed by warming the base with methyl iodide, was identical with *l*-thujyltrimethylammonium iodide, described above. A very small amount of a neutral oil was formed in the pyrolysis of the quaternary ammonium hydroxide.

Solutions of *l*-thujylamine in excess of dilute hydrochloric acid yielded no thujyl alcohol when treated with sodium nitrite solution : the oily product contained terpenes and other decomposition products, as in the case of *d-iso*thujylamine (*vide infra*).

2. d-iso*Thujylamine.*—"β-Thujone " (550 g.), when oximated in the way described above for " α-thujone," yielded a viscid syrup (381 g.), which slowly crystallised to a mass of long, colourless needles, m. p. 53°, b. p. 120—121°/6·5 mm., $[\alpha]_D^{12^\circ}$ + 98·14° (*c* 2, ethyl alcohol) (cf. *Annalen*, 1904, **336**, 247, 267). In order to secure satisfactory results, a ketone of high rotatory power must be used. The *p*-nitrobenzoate of *d-iso*thujone oxime crystallised from aqueous methyl alcohol in coarse pale yellow needles, m. p. 72°, $[\alpha]_D^{12^\circ}$ + 32·5° (*c* 2, chloroform).

Reduction of the oxime (300 g.) with sodium and alcohol, and subsequent treatment as outlined above, led to crude *d-iso*thujylamine hydrochloride (310 g.). Two recrystallisations from boiling absolute alcohol, to which acetone had been added, gave the pure salt (92 g.) in glistening needles, m. p. above 255°, $[\alpha]_D^{10^\circ}$ + 79·0° (*c* 2, water).

*d-iso*Thujylamine was a colourless, mobile liquid, with a sweetish and not particularly unpleasant odour, b. p. 75·5°/11 mm., $\alpha_D^{13^\circ}$ + 94·82° (*l* 1), $n_D^{12^\circ}$ 1·4641. Its absorption of carbon dioxide from the air resembled that of *l*-thujylamine, but it was more rapid. The following derivatives were prepared: formyl, waxy solid, m. p. 51°, $[\alpha]_D^{14°}$ + 114° (*c* 1, chloroform); acetyl, long needles, m. p. 68—69°, b. p. 163·5°/6·5 mm., $[\alpha]_D^{15°}$ + 112·5° (*c* 1, chloroform); *benzoyl*-d-iso*thujylamine*, soft needles, m. p. 131·5°, $[\alpha]_D^{15°}$ + 90·5° (*c* 1, chloroform) (Found: C, 79·3; H, 8·8. $C_{17}H_{23}ON$ requires C, 79·3; H, 8·9%); p-*nitrobenzoyl* derivative, yellowish needles, m. p. 147°, $[\alpha]_D^{15°}$ + 77·0° (*c* 1, chloroform) (Found: C, 68·0; H, 7·2. $C_{17}H_{22}O_3N_2$ requires C, 67·6; H, 7·3%); 3 : 5-dinitrobenzoyl, soft yellow needles, m. p. 173·5°, $[\alpha]_D^{15}$ + 68·0° (*c* 1, chloroform); *p*-toluenesulphonyl, flat, brownish needles, m. p. 154·5°, $[\alpha]_D^{15°}$ + 92·5° (*c* 1, chloroform); carbimide, oil; formate, long needles, m. p. 143°, $[\alpha]_D^{12°}$ + 74·25° (*c* 1, water); hydrogen oxalate, soft needles, m. p. 167°, $[\alpha]_D^{14°}$ + 62·5° (*c* 1, water); hydrogen *d*-tartrate, glistening plates, m. p. 197·5°, $[\alpha]_D^{14°}$ + 64·0° (*c* 1, water). The salicylidene derivative was an oil.

d-iso*Thujyltrimethylammonium iodide* crystallised from hot water in long needles, m. p. 260° (decomp.), $[\alpha]_D^{15°}$ + 47·0° (*c* 1, chloroform) (Found, by titration: I, 39·0. $C_{13}H_{26}NI$ requires I, 39·3%). The derived hydroxide resembled the corresponding derivative of *l*-thujylamine; when heated to 160°, it yielded *N*-dimethyl-*d*-isothujylamine, b. p. 79°/11 mm., $n_D^{12·5°}$ 1·4600, $\alpha_D^{13°}$ + 124·64° (*l* 1) [Found, for the *platinichloride*, m. p. 173—174° (decomp.): Pt, 25·3. $2C_{12}H_{23}N,H_2PtCl_6$ requires Pt, 25·3%]. The picrate separated from rectified spirit in yellow needles, m. p. 158°, $[\alpha]_D^{19°}$ + 21·0° (*c* 1, chloroform); the methiodide was identical with the above *d-iso*thujyltrimethylammonium iodide. A small amount of a neutral liquid, formed in the decomposition of the quaternary ammonium hydroxide, having $n_D^{17·5°}$ 1·4527, and smelling of aniseed, possibly contained thujene.

Deamination of *d-iso*thujylamine with nitrous acid yielded a yellow oil with a terpene-like odour, $\alpha_D^{12°}$ + 28·06° (*l* 1), $n_D^{12°}$ 1·4643, the bulk of which distilled up to 80°/8 mm. The oil decolourised bromine, and underwent esterification to a small extent, but did not appear to contain any thujyl alcohols.

3. When " α-thujone " (190 g.) was heated with solid ammonium formate (250 g.), ultimately at 200° for several hours, in an apparatus permitting of the escape and condensation of volatile products, it was found possible to extract a dark brown syrup (200 g.) from the product with chloroform. Distillation of the syrup under diminished pressure gave a main fraction (115 g.) consisting of a pale yellow, viscid liquid, b. p. 175°/11 mm., $n_D^{18°}$ 1·4877, $\alpha_D^{14°}$ + 27·04° (*l* 1); a practically identical product was obtained from " β-thujone." No crystallisation was induced by seeding the viscid product with the formyl derivatives of *l*- and *d-iso*-thujylamine.

The material was boiled with ten times its weight of 10% methyl-alcoholic hydrogen chloride for 12 hours. Steam-distillation of the basified product yielded a basic oil, b. p. 72—74°/15 mm., $n_D^{16°}$ 1·4672, $\alpha_D^{16°}$ + 19·62° (*l* 1). The only pure substance obtained from this product, after it had been treated in various ways, was a small quantity of *d-iso*thujylamine formate, prepared by repeated fractional crystallisation of the mixed formates. Deamination with nitrous acid yielded an oil which appeared to contain thujene but failed to yield any crystalline ester of a thujyl or other alcohol.

A non-saponifiable residue from the treatment with methyl-alcoholic hydrogen chloride was obtained as a somewhat viscid liquid, b. p. 181—182°/9 mm., $n_D^{16°}$ 1·4875, $d_{16°}^{16°}$ 0·9219, $\alpha_D^{14°}$ + 23·5° (*l* 1). This was basic to litmus, and when shaken with dilute hydrochloric acid became coated with an insoluble layer of a salt. No crystalline derivative could be obtained from this material, which appeared to consist essentially of *dithujylamines*, with properties similar to those of dicarvomenthylamines (J., 1934, 232) (Found: C, 81·5; H, 11·8; N, 5·4. $C_{20}H_{35}N$ requires C, 83·0; H, 12·2; N, 4·8%).

A similar mixture of *dimenthylamines*, obtained as a by-product of the reaction between *l*-menthone and ammonium formate (J., 1927, 2168), had b. p. 176°/10 mm., $n_D^{16°}$ 1·4821, $\alpha_D^{15°}$ −9·96° (*l* 1) (Found: C, 81·2; H, 13·0; N, 5·1. $C_{20}H_{39}N$ requires C, 81·9; H, 13·3; N, 4·8%).

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