Olefinic Additions with Asymmetric Reactants. Part III. The Resolution and Addition Reactions of 3-Ethylhept-3-en-2-ol. A Partial Asymmetric Synthesis effected by Hydrogenation.*

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(±)-3-Ethylhept-3-en-2-ol has been resolved into its enantiomeric forms. Hydrogenation of the (−)-isomer gave (−)-3-ethylheptan-2-ol; this alcohol on oxidation yielded (+)-3-ethylheptan-2-one, which gave a (+)-semicarbazone (see I—IV). The (+)-ethylheptenol yielded a similar series of compounds having the opposite configurations. A partial asymmetric synthesis is effected by these reactions: a new centre of asymmetry is formed at $C_{(3)}$, with preponderance of one configuration, and the original centre at $C_{(2)}$ is rendered symmetrical. The mechanism and stereochemistry of hydrogenation are discussed; it is concluded that the asymmetric centre controls the conformation in which the molecule is adsorbed at the catalyst surface, and that the subsequent addition of hydrogen is asymmetric by reason of this circumstance.

The reactions of the ethylheptenol with bromine, bromine–sodium methoxide, thiolacetic acid, and toluene-ω-thiol have been investigated.

(±)-3-Ethylhept-3-en-2-ol (I), prepared by the reaction of 2-ethylhex-2-enal with methylmagnesium iodide, has been resolved into its enantiomeric forms by fractional crystallisation of the brucine salt of its hydrogen phthalate. The (+)-hydrogen phthalate, which gave the less soluble salt, was obtained optically pure; on hydrolysis with 5N-potassium hydroxide it yielded (−)-3-ethylhept-3-en-2-ol. A portion of this alcohol was reconverted into its hydrogen phthalate, the specific rotation of which was 10·5% less than that of the original ester; this racemisation is ascribed to the occurrence, to a small extent, of alkyl–oxygen fission during the alkaline hydrolysis (Arcus and Kenyon, *J.*, 1938, 1917). On correction of the observed rotations for this racemisation, the rotatory power of the optically pure alcohol is found to be:

λ	5893	5780	5461	4358	
$[\alpha]^{19}$	−2·09°	−2·14°	−2·16°	−2·80°	(homogeneous)
$[\alpha]^{20}_{5893}$	−14·3° (in CS_2); $[\alpha]^{20}_{5893}$ −6·8° (in $CHCl_3$)				

Hydrogenation.—(−)-3-Ethylhept-3-en-2-ol, on hydrogenation in ethanol with Raney nickel catalyst, gave (−)-3-ethylheptan-2-ol (II); this compound on oxidation with chromic anhydride yielded (+)-3-ethylheptan-2-one (III) which gave a (+)-semicarbazone

$$\underset{\text{(I)}}{CH_3\cdot CH(OH)\cdot CEt{:}CH\cdot C_3H_7} \longrightarrow \underset{\text{(II)}}{CH_3\cdot CH(OH)\cdot CHEt\cdot CH_2\cdot C_3H_7} \longrightarrow$$

$$\underset{\text{(III)}}{CH_3\cdot CO\cdot CHEt\cdot C_4H_9} \longrightarrow \underset{\text{(IV)}}{CH_3\cdot C(:N\cdot NH\cdot CO\cdot NH_2)\cdot CHEt\cdot C_4H_9}$$

(IV). The (+)-ethylheptenol yielded a similar series of compounds having the opposite configurations. A preliminary note has appeared (*Chem. and Ind.*, 1954, 404).

* The papers by Abbott and Arcus (*J.*, 1952, 1515) and Arcus and Strauss (*ibid.*, p. 2669) are regarded as Parts I and II.

These reactions constitute a partial asymmetric synthesis : a new centre of asymmetry is formed at $C_{(3)}$, with preponderance of one configuration, and the original centre at $C_{(2)}$ is rendered symmetrical.

The (−)- and the (+)-ethylheptenol used were respectively 86% and 82% optically pure. The alcohol (II) and the ketone (III) are liquids and were purified by simple distillation; the separation of diastereoisomers or of optical isomers is unlikely during this process (there was no experimental indication of separation), whence the maximum possible optical purity of (III) (*i.e.*, that for 100% asymmetric synthesis) is identical with the optical purity of (I). The percentage asymmetric synthesis is therefore equal to (or greater than) the yield of optically pure semicarbazone obtained from the ketone (III), together with a correction for the optical purity of the original alcohol (I). After the first recrystallisation, the m. p. and rotatory power of the (+)-semicarbazone were constant upon further crystallisation; the (−)-semicarbazone on one recrystallisation had an equal negative rotation; the yields were respectively 65% and 52%, whence the percentage asymmetric synthesis is 76% and 63%.

(±)-3-Ethylhept-3-en-2-ol was hydrogenated to (±)-3-ethylheptan-2-ol, which was converted into the 4-diphenylylcarbamate; recrystallisation of this derivative gave one compound only. This result indicates that hydrogenation yields a single diastereoisomeric racemate : if the configurations at $C_{(2)}$ and $C_{(3)}$ are designated by *d*, *l*, and *d'*, *l'*, respectively, then either (*dd'* + *ll'*)- or (*dl'* + *ld'*)-3-ethylheptan-2-ol is formed. Thus, as inferred from the results obtained with the optically active ethylheptenols, the configuration existing at $C_{(2)}$ controls the formation of that at $C_{(3)}$.

Stereochemistry of the Hydrogenation.—Recrystallisation of the semicarbazone and 2 : 4-dinitrophenylhydrazone of 2-ethylhex-2-enal, and of (±)-2-ethyl-1-methylhex-2-enyl * 4-diphenylylcarbamate, yielded in each instance only one compound. (±)-3-Ethylhept-3-en-2-ol on oxidation gave (±)-3-ethylhept-3-en-2-one, the semicarbazone of which was similarly a single entity. It is concluded that 2-ethylhex-2-enal, 3-ethylhept-3-en-2-ol, and 3-ethylhept-3-en-2-one are each a single geometrical isomer, and that very probably the same geometrical configuration has been retained during the conversion of aldehyde into secondary alcohol, and of the latter into ketone. We are informed by the manufacturers (Messrs. British Industrial Solvents Limited) that the 2-ethylhex-2-enal is prepared by the self-condensation of *n*-butyraldehyde; a similar condensation of acetaldehyde yields crotonaldehyde, and Blacet, Young, and Roof (*J. Amer. Chem. Soc.*, 1937, **59**, 608) conclude that purified commercial crotonaldehyde consists solely of the *trans*-isomeride. It is probable, therefore, that the present compounds have the aldehyde group, and groups derived from it, *trans* to the *n*-propyl group.

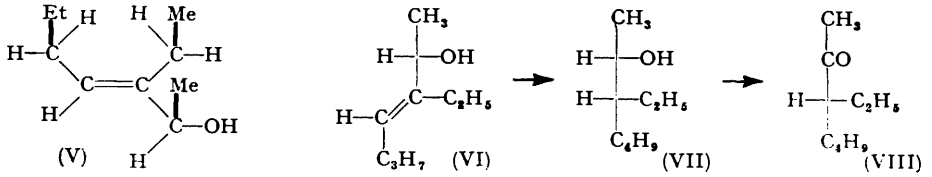
From a discussion of the stereochemistry of hydrogenation, Linstead, Doering, Davis, Levine, and Whetstone (*J. Amer. Chem. Soc.*, 1942, **64**, 1985) conclude, with regard to the " substrate " molecule, that the side which becomes attached to the metallic surface is, in general, that which conforms most closely to a plane, and that reaction proceeds by the addition of hydrogen atoms to this side of the molecule. The latter condition implies *cis*-hydrogenation; von Wessely and Welleba (*Ber.*, 1941, **74**, 777) have found *cis*-αβ-dimethylstilbene to give *meso*-βγ-diphenylbutane on hydrogenation, and the *trans*-compound, also *trans*-diethylstilbœstrol and its dimethyl ether, to yield the racemic dihydro-compounds; the configurations of these products are those which arise from *cis*-addition of hydrogen.

It is inferred that the most probable course for the hydrogenation of 3-ethylhept-3-en-2-ol is *cis*-addition at that side of the double bond which is adjacent to the nickel surface. Adsorption of the molecule most probably occurs by interaction of the lone-pairs of the oxygen atom, as well as of the π-electrons of the double bond, with the catalyst. A model of the ethylheptenol showed there to be one conformation of the molecule which conforms more closely to a plane than does any other, namely, that represented in (V). Conformation (V) has been adopted for the present discussion, but the mechanism proposed is not dependent on this particular conformation. The hydrogenation of (V) is represented in

* The alkyl radical derived from 3-ethylhept-3-en-2-ol is designated 2-ethyl-1-methylhex-2-enyl.

the Fischer formulæ (VI) and (VII), addition being to the surface of the paper; oxidation of (VII) yields 3-ethylheptan-2-one having configuration (VIII).

Finally, the implications of the steric course of the present hydrogenation may be summarised, without reference to particular configurations, as follows: Were adsorption, and hence addition, to occur with equal ease at either side of the double bond, then a single optical isomer of 3-ethylhept-3-en-2-ol would yield (±)-3-ethylheptan-2-one, and no asymmetric synthesis could result. Hence the asymmetric carbon atom must determine the configuration in which the molecule is adsorbed, *i.e.*, asymmetric adsorption precedes, and leads to, asymmetric addition of hydrogen.



An asymmetric synthesis effected by hydrogenation has been recorded by Vavon and Jakubowicz (*Bull. Soc. chim.*, 1933, **53**, 1111), who reduced the β-methylcinnamates of six optically active alcohols. Hydrolysis of the saturated esters yielded, in each instance, optically active β-phenylbutyric acid; the highest degree of asymmetric synthesis (20%) was obtained with the menthyl ester:

$$CMePh{:}CH{\cdot}CO_2R \longrightarrow CHMePh{\cdot}CH_2{\cdot}CO_2R \longrightarrow CHMePh{\cdot}CH_2{\cdot}CO_2H$$

Lipkin and Stewart (*J. Amer. Chem. Soc.*, 1939, **61**, 3295), in the hydrogenation of hydrocinchonine β-methylcinnamate, obtained 9% asymmetric synthesis.

Substantially less asymmetric synthesis occurs during the reduction of the β-methylcinnamic esters than in the present hydrogenations. This may be due to the separation of the ethylenic group from the asymmetric centre by two symmetrical atoms in the methylcinnamates; in 3-ethylhept-3-en-2-ol these structures are adjacent.

Reaction at a metal surface may also have occurred in an asymmetric synthesis which is not a hydrogenation. The Reformatsky reaction (1) has been found by Reid and Turner

$$COMePh + Br{\cdot}Zn{\cdot}CH_2{\cdot}CO_2R \longrightarrow CMePh(OH){\cdot}CH_2{\cdot}CO_2R \longrightarrow CMePh(OH){\cdot}CH_2{\cdot}CO_2H \quad (1)$$
(R = menthyl)

(*J.*, 1949, 3365; 1950, 3694) to yield β-hydroxy-β-phenylbutyric acid having a rotatory power approximately one-third that of the optically-pure acid. Metallic zinc (50% excess) was present throughout the reaction, and it is now suggested that much of the interaction, and particularly that leading to asymmetric synthesis, takes place at the zinc surface. The following mechanism would lead to a substantial degree of asymmetric synthesis: the molecule $Br^- {}^+Zn{\cdot}CH_2{\cdot}CO{\cdot}O{\cdot}C_{10}H_{19}$ is adsorbed at the zinc surface in a configuration determined by the menthyl group; for minimum energy of activation, a molecule of acetophenone has to approach with carbonyl, methyl, and phenyl groups in a definite relationship to the adsorbed molecule. The new asymmetric centre will then be formed with a preponderance of one configuration.

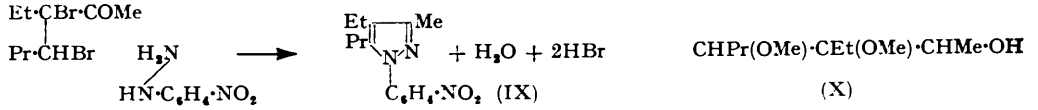
Other Addition Reactions.—Asymmetric syntheses have been effected by Kenyon and Partridge (*J.*, 1936, 1313) and Balfe, Kenyon, and Waddan (*J.*, 1954, 1366) through the addition of bromine to optically active pent-3-en-2-ol, 1-phenylbut-1-en-3-ol, and 1-phenylpent-1-en-3-ol, followed by oxidation of the dibromo-alcohol to the dibromo-ketone:

$$CHR{:}CR'{\cdot}CHR''{\cdot}OH \longrightarrow CHRBr{\cdot}CR'Br{\cdot}CHR''{\cdot}OH \longrightarrow CHRBr{\cdot}CR'Br{\cdot}COR''$$

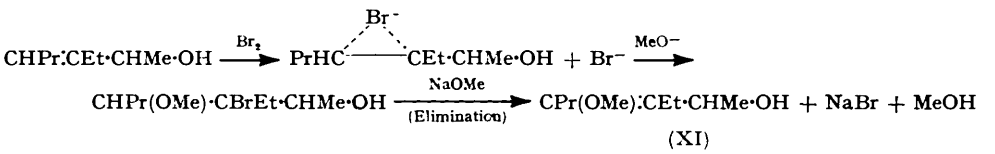
These reactions (R = Pr^n; R′ = Et; R″ = Me) have been applied to (+)-3-ethylhept-3-en-2-ol of 27% optical purity; the (+)-dibromo-alcohol on oxidation with chromic anhydride gave 3 : 4-dibromo-3-ethylheptan-2-one having a small positive rotation; on distillation it became practically optically inactive. This dibromo-ketone, and also that

prepared from the (±)-ethylheptenol, condensed with *p*-nitrophenylhydrazine to yield 4-ethyl-3-methyl-1-*p*-nitrophenyl-5-*n*-propylpyrazole (IX). It appears improbable that the compound is the isomeric 4-ethyl-5-methyl-1-*p*-nitrophenyl-3-*n*-propylpyrazole because this molecule, unlike (IX), cannot be formed by simple eliminations.

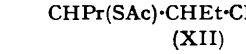
The stereochemical result of the bromine addition is inconclusive, and, in view of the difficulty in purification of the dibromo-ketone, a liquid racemising on distillation, and of preparing a solid derivative in the formation of which the dibromo-ketone does not undergo non-carbonyl reactions, the problem is somewhat intractable. Further addition reactions (below) have been investigated, but each potential asymmetric synthesis fails at some stage before the formation of a ketone.



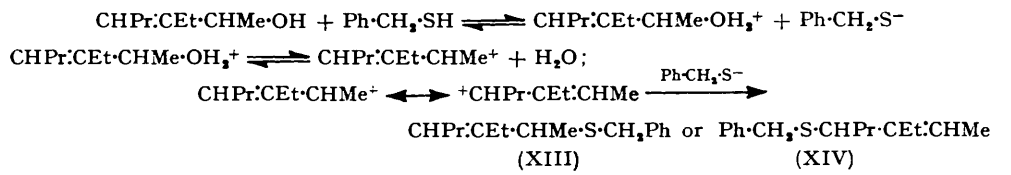
In an attempt to prepare the dimethoxy-alcohol (X), bromine was added to a solution of (±)-3-ethylhept-3-en-2-ol in methanolic sodium methoxide; there was obtained an unsaturated compound which gave analyses correct for an ethylmethoxyheptenol. This compound is most probably (±)-3-ethyl-4-methoxyhept-3-en-2-ol (XI), formed as follows:



The addition of thiolacetic acid to (±)-3-ethylhept-3-en-2-ol proceeded readily at 100° in the presence of benzoyl peroxide, and yielded (±)-4-acetylthio-3-ethylheptan-2-ol (XII). The acetylthio-group is considered to have added at the β-position to the carbinol group because such addition has been observed by Brown, Jones, and Pinder (*J.*, 1951, 2123) for the peroxide-catalysed reaction of allyl and 1-methylallyl alcohol with thiolacetic acid.



The interaction of toluene-ω-thiol and (±)-3-ethylhept-3-en-2-ol yielded an unsaturated compound, containing no oxygen, which gave analyses correct for (±)-2-benzylthio-3-ethylhept-3-ene (XIII) or for the isomeric thioether (±)-4-benzylthio-3-ethylhept-2-ene (XIV). The occurrence of alkyl–oxygen fission during the hydrolysis of the hydrogen phthalate indicates the ethylmethylhexenyl group to have some capacity for separation as a carbonium ion, and the thio-ether is probably formed by an alkylation according to the following equations; the intermediate mesomeric cation may yield either (XIII) or (XIV):



Under the conditions above, thiolacetic acid added smoothly to 2-ethylhex-2-enal; by analogy with the addition of thiolacetic acid to other αβ-unsaturated aldehydes (Brown, Jones, and Pinder, *loc. cit.*), the acetylthio-group is considered to have combined at the β-carbon atom, giving 3-acetylthio-2-ethylhexanal CHPr(SAc)·CHEt·CHO.

Bromine added readily to the 2 : 4-dinitrophenylhydrazone of 2-ethylhex-2-enal, to yield that of 2 : 3-dibromo-2-ethylhexanal. The reaction demonstrates that 2-ethylhex-2-enal 2 : 4-dinitrophenylhydrazone has the assigned structure, and has not rearranged into the isomeric 1-(2 : 4-dinitrophenyl)-4-ethyl-5-*n*-propyl-Δ^2-pyrazoline.

Experimental

Rotations of undiluted liquid compounds are for *l*, 0·5; those of solutions are for *l*, 1·0.

A solution of 2-ethylhex-2-enal in ether was dried (Na_2SO_4) and distilled: the aldehyde had b. p. 65—66°/16 mm., n_D^{20} 1·4459. Its semicarbazone formed needles, m. p. 153° (Found: C, 58·9; H, 9·1; N, 22·9. Calc. for $C_9H_{17}ON_3$: C, 58·9; H, 9·3; N, 23·0%), from aqueous ethanol; Grignard and Fluchaire (*Ann. Chim.*, 1928, **9**, 17) record m. p. 147°. Its 2:4-dinitrophenylhydrazone formed orange plates, m. p. 124° (Found: C, 55·1; H, 5·9; N, 18·1. Calc. for $C_{14}H_{18}O_4N_4$: C, 54·9; H, 5·9; N, 18·3%), from acetic acid; Morgan and Hardy (*Chem. and Ind.*, 1933, 518) record m. p. 124—125°.

The ethylheptenol was prepared by a modification of Grignard and Vestermann's method (*Bull. Soc. chim.*, 1925, **37**, 425). To a solution of methylmagnesium iodide [prepared from magnesium (32 g.), methyl iodide (190 g.), and ether (300 ml.)], cooled in ice and salt, a solution of 2-ethylhex-2-enal (172 g.) in ether (200 ml.) was added during 2 hr. The complex was decomposed with ammonium chloride; the ethereal solution was washed with aqueous sodium hydrogen carbonate and with aqueous sodium hydrogen sulphite, dried (Na_2SO_4), and evaporated. The product, on distillation from potassium carbonate (1 g.), yielded (±)-3-ethylhept-3-en-2-ol (159 g.), b. p. 78—80°/15 mm., n_D^{20} 1·4490, d_4^{20} 0·845, $[R]_D$ 45·09 (Calc.: 44·82).

The ethylheptenol (1·0 g.) and 4-diphenylyl *iso*cyanate (1·25 g.) were heated for 3 hr. at 80°, and the product was extracted with light petroleum (b. p. 40—60°). The extract was chilled to −10°: a solid separated which, on recrystallisation, yielded (±)-*2-ethyl-1-methylhex-2-enyl 4-diphenylylcarbamate* (1·6 g.), needles, m. p. 74—75° (Found: C, 78·2; H, 8·1; N, 4·4. $C_{22}H_{27}O_2N$ requires C, 78·3; H, 8·1; N, 4·2%).

The ethylheptenol (2·0 g.) was oxidised as described below for (±)-3-ethylheptan-2-ol, but at 100°; it yielded (±)-*3-ethylhept-3-en-2-one* (1·8 g.), b. p. 65—66°/14 mm., n_D^{20} 1·4428 (Found: C, 77·2; H, 11·4. $C_9H_{16}O$ requires C, 77·1; H, 11·4%) [*semicarbazone*, needles (from ethanol), m. p. 180—181° (Found: C, 60·8; H, 9·6; N, 20·9. $C_{10}H_{19}ON_3$ requires C, 60·9; H, 9·7; N, 21·3%)].

Resolution of (±)-*3-Ethylhept-3-en-2-ol.*—This alcohol (132 g.) was kept for 6 hr. at 50° with phthalic anhydride (135 g.) and pyridine (85 g.); the viscous product was diluted with acetone, acidified with dilute hydrochloric acid, and poured on ice. The oil which separated was dissolved in ether; the solution was extracted with aqueous sodium hydrogen carbonate; the latter was acidified and extracted with ether; the extract was dried (Na_2SO_4) and evaporated by the passage of a stream of dry air, with final evaporation under reduced pressure: there was obtained (±)-*2-ethyl-1-methylhex-2-enyl hydrogen phthalate* (262 g.), a colourless oil (Found: equiv., 302. $C_{17}H_{22}O_4$ requires equiv., 290).

Brucine (308 g.) was cautiously added to a solution of the hydrogen phthalate (225 g.) in hot acetone (1 l.). Heating was continued until a clear solution was obtained, and, on cooling, the alkaloidal salt separated. After ten recrystallisations from acetone, the brucine salt (24 g.) of (+)-2-ethyl-1-methylhex-2-enyl hydrogen phthalate was obtained as rosettes of needles, m. p. 168—169°; the rotatory power of the hydrogen phthalate derived from the salt remained constant when this crop was subjected to two further recrystallisations. A total of 35 g. of the optically pure salt, $[\alpha]_{5893}^{20}$ −8·2° (*c*, 2·91 in $COMe_2$), was obtained; it was suspended in acetone and acidified with dilute hydrochloric acid; the whole was extracted with ether, which was washed with dilute hydrochloric acid, and with water, dried (Na_2SO_4), and evaporated as above. It yielded (+)-*2-ethyl-1-methylhex-2-enyl hydrogen phthalate* (14 g.), a colourless oil, n_D^{20} 1·5060, α_{5893}^{20} +8·41°, $[\alpha]_{5893}^{20}$ +18·1° (*c*, 4·19 in $CHCl_3$) (Found: equiv., 294).

The mother-liquors rich in the brucine salt of the (−)-hydrogen phthalate were concentrated, filtered from solid alkaloidal salt, acidified, and extracted with ether. The extract was shaken with aqueous sodium hydrogen carbonate, which was then extracted with ether, acidified, and again extracted. This last extract yielded (−)-2-ethyl-1-methylhex-2-enyl hydrogen phthalate (9 g.), having $[\alpha]_{5893}^{18}$ −17·6° (*c*, 2·61 in $CHCl_3$).

The (+)-hydrogen phthalate (14 g.) was heated under reflux with 5N-potassium hydroxide (25 ml.) for ½ hr. at 100°. Steam-distillation yielded (−)-3-ethylhept-3-en-2-ol (6·8 g.), b. p. 80—81°/15 mm., n_D^{20} 1·4497, d_4^{20} 0·845, α_{5893}^{19} −0·79°, α_{5780}^{19} −0·81°, α_{5461}^{19} −0·82°, α_{4358}^{19} −1·06°; $[\alpha]_{5893}^{20}$ −12·8° (*c*, 3·05 in CS_2); $[\alpha]_{5893}^{20}$ −6·1° (*c*, 2·46 in $CHCl_3$). A portion of the alcohol was reconverted into the hydrogen phthalate, which had $[\alpha]_{5893}^{20}$ +16·2° (*c*, 4·11 in $CHCl_3$).

Similar hydrolysis of the (−)-hydrogen phthalate (9 g.) yielded (+)-3-ethylhep-3-en-2-ol (3·8 g.), b. p. 81—82·5°/16 mm., α_{5893}^{19} +0·75°, $[\alpha]_{5893}^{20}$ +12·4° (*c*, 3·05 in CS_2).

Hydrogenation of 3-*Ethylhept*-3-*en*-2-*ol*.—A solution of (±)-3-ethylhept-3-en-2-ol (11·5 g.) in ethanol (100 ml.) was stirred with Raney nickel (4 g.); hydrogen was supplied, and the autoclave heated. Maximum temperature and pressure, 130° and 170 lb./sq. in., were attained after 4 hr.; the whole was then allowed to cool. The ethanolic solution yielded (±)-3-*ethylheptan*-2-*ol* (8·2 g.), b. p. 91—92°/22 mm., n_D^{20} 1·4308 (Found: C, 74·9; H, 13·9. $C_9H_{20}O$ requires C, 75·0; H, 13·9%). It did not decolorise a solution of bromine in carbon tetrachloride; each product from the attempted addition reactions (below) was so tested for unsaturation.

The ethylheptanol (0·5 g.) and 1-naphthyl *iso*cyanate (0·6 g.), heated at 100° for 1 hr., gave (±)-2-*ethyl*-1-*methylhexyl* 1-*naphthylcarbamate* (0·3 g.), needles, m. p. 48°, from light petroleum (b. p. 40—60°) (Found: C, 76·3; H, 8·5; N, 4·6. $C_{20}H_{27}O_2N$ requires C, 76·6; H, 8·7; N, 4·5%).

The ethylheptanol (3·0 g.) and 4-diphenylyl *iso*cyanate (4·2 g.) were similarly heated; the product was extracted with light petroleum and gave a carbamate (6·9 g.) which was four times recrystallised by chilling its solution in light petroleum (b. p. 40—60°) to −15°. It yielded (±)-2-*ethyl*-1-*methylhexyl* 4-*diphenylylcarbamate* (3·9 g.), needles, m. p. 103° (Found: C, 78·2; H, 8·6; N, 4·0. $C_{22}H_{29}O_2N$ requires C, 77·9; H, 8·6; N, 4·1%); there was no indication of the presence of an isomeric urethane.

During ¼ hr., chromic anhydride (0·95 g.) was added portionwise with shaking to a solution of (±)-3-ethylheptan-2-ol (2·0 g.) in glacial acetic acid (5 ml.) at 80°. The whole, after cooling, was poured into water and extracted with ether. The extract was washed with aqueous sodium carbonate and dried (Na_2SO_4); it yielded (±)-3-*ethylheptan*-2-*one* (1·6 g.), b. p. 66°/16 mm., n_D^{20} 1·4206 (Found: C, 76·2; H, 12·7. $C_9H_{18}O$ requires C, 76·0; H, 12·8%). The *semicarbazone*, needles, m. p. 86°, from ethanol, was prepared by keeping the reactants overnight at room temperature (Found: C, 60·6; H, 10·6; N, 20·8. $C_{10}H_{21}ON_3$ requires C, 60·3; H, 10·6; N, 21·1%).

(−)-3-Ethylhept-3-en-2-ol (8·8 g., freshly distilled, α_{5893}^{18} −0·76°) was hydrogenated by the method described for the (±)-alcohol except that the maximum temperature and pressure were 96° and 109 lb./sq. in.; it yielded (−)-3-ethylheptan-2-ol (5·8 g.), b. p. 80—81°/12 mm., n_D^{20} 1·4312, d_4^{20} 0·821, α_{5893}^{19} −0·58°. Oxidation, as above, of the (−)-ethylheptanol (4·5 g.) gave (+)-3-ethylheptan-2-one (4·0 g.), b. p. 74—75°/16 mm., n_D^{20} 1·4211, α_{5893}^{19} +0·51°. The *semicarbazone*, needles (4·1 g.), derived from this ketone (3·5 g.) had m. p. 90—91°, $[\alpha]_{5893}^{19}$ +2·1° (*c*, 3·33 in $CHCl_3$); after recrystallisation from aqueous alcohol it (3·2 g.) had m. p. 91—92°, $[\alpha]_{5893}^{19}$ +2·2° (*c*, 3·93 in $CHCl_3$) (Found: C, 60·2; H, 10·8; N, 20·7%). Further recrystallisation resulted in no significant change in m. p. or specific rotation.

Hydrogenation (max. temp. and pressure: 120° and 140 lb./sq. in.) of (+)-3-ethylhept-3-en-2-ol (3·2 g., α_{5893}^{20} +0·72°) gave (+)-3-ethylheptan-2-ol (2·7 g.), b. p. 82—84°/16 mm., n_D^{20} 1·4310, α_{5893}^{20} +0·44°. The whole of this alcohol was oxidised, and yielded (−)-3-*ethylheptan*-2-*one* (1·8 g.), b. p. 73—75°/16 mm., n_D^{20} 1·4207, α_{5893}^{23} −0·31° (Found: C, 75·6; H, 12·3%). The *semicarbazone* (1·9 g.) prepared from this ketone (1·8 g.) had m. p. 86—89°, $[\alpha]_{5893}^{20}$ −2·1° (*c*, 3·33 in $CHCl_3$); after recrystallisation from aqueous alcohol it (1·3 g.) had m. p. 90—91°, $[\alpha]_{5893}^{20}$ −2·2° (*c*, 3·93 in $CHCl_3$) (Found: C, 60·4; H, 10·7; N, 20·9%).

Addition Reactions of 3-*Ethylhept*-3-*en*-2-*ol and* 2-*Ethylhex*-2-*enal*.—Bromine (3·45 g.) in chloroform (10 ml.) was added dropwise (½ hr.) to an ice-cooled solution of (±)-3-ethylhept-3-en-2-ol (3·0 g.) in chloroform (10 ml.). After the passage of a stream of dry air and final evaporation under reduced pressure, there remained (±)-3 : 4-dibromo-3-ethylheptan-2-ol (6·5 g.), a yellow oil, n_D^{20} 1·5121, which could not be distilled without decomposition. The dibromo-alcohol (6·5 g.), on oxidation with chromic anhydride (1·45 g.) at 70° by the method described for (±)-3-ethylheptan-2-ol, yielded (±)-3 : 4-*dibromo*-3-*ethylheptan*-2-*one* (5·9 g.), a lachrymatory yellow liquid, b. p. 72—74°/1 mm., n_D^{20} 1·5046 (Found: Br, 53·8. $C_9H_{16}OBr_2$ requires Br, 53·4%). The dibromo-ketone (1·5 g.), *p*-nitrophenylhydrazine (0·75 g.), and pyridine (1·0 g.) were heated for 3 hr. at 100°. The product was cooled, diluted with methanol, and poured into ice and dilute hydrochloric acid; the oil which separated solidified, and, after recrystallisation from aqueous acetic acid, gave 4-*ethyl*-3-*methyl*-1-p-*nitrophenyl*-5-n-*propylpyrazole* (0·3 g.), brown needles, m. p. 131° (Found: C, 66·7; H, 7·2; N, 15·6. $C_{15}H_{19}O_2N_3$ requires C, 66·2; H, 7·0; N, 15·4%).

By the above procedures, (+)-3-ethylhept-3-en-2-ol (2·2 g., α_{5893}^{20} +0·24°) yielded (+)-3 : 4-dibromo-3-ethylheptan-2-ol (4·6 g.), n_D^{20} 1·5158, $[\alpha]_{5893}^{20}$ +13·3° (*c*, 3·16 in CS_2), which gave 3 : 4-dibromo-3-ethylheptan-2-one: the undistilled ketone (4·1 g.) had n_D^{20} 1·5038, α_{5893}^{21} +0·11° (*c*, 3·36 in CS_2); after distillation it (3·4 g.) had b. p. 68—70°/0·2 mm., n_D^{20} 1·5034, α_{5893}^{20} −0·01°

(*c*, 3·46 in CS_2), and yielded the substituted pyrazole, m. p. 131° alone and when mixed with the analysed specimen.

Sodium (2·3 g.) was allowed to react with methanol (50 ml.; distilled from CaO), to which was then added (±)-3-ethylhept-3-en-2-ol (7·2 g.); after the dropwise addition of a solution of bromine (8·0 g.) in methanol (50 ml.), the whole was heated under reflux for 2 hr. It was poured into water and extracted with ether, which yielded (±)-*3-ethyl-4-methoxyhept-3-en-2-ol* (6·2 g.), b. p. 99°/24 mm., n_D^{20} 1·4444 (Found: C, 70·1; H, 11·4; Br, nil. $C_{10}H_{20}O_2$ requires C, 69·8; H, 11·5%).

(±)-3-Ethylhept-3-en-2-ol (2·0 g.) and thiolacetic acid (1·2 g.) were heated with a few mg. of benzoyl peroxide at 100° for 3 hr. The product on redistillation yielded (±)-*4-acetylthio-3-ethylheptan-2-ol* (2·3 g.), b. p. 86—87°/1 mm., n_D^{20} 1·4700 (Found: C, 60·4; H, 9·9; S, 14·5. $C_{11}H_{22}O_2S$ requires C, 60·5; H, 10·1; S, 14·7%).

(±)-3-Ethylhept-3-en-2-ol (2·0 g.) and toluene-ω-thiol (1·9 g.) were similarly heated for 5 hr.; fractionation of the product yielded (±)-*2-benzylthio-3-ethylhept-3-ene* (1·6 g.), b. p. 111°/1·5 mm., n_D^{20} 1·4820 (Found: C, 77·6; H, 9·6; S, 12·8. $C_{16}H_{24}S$ requires C, 77·5; H, 9·7; S, 12·9%).

2-Ethylhex-2-enal (2·0 g.) and thiolacetic acid (1·2 g.) were similarly heated for 4 hr. The product on redistillation gave *3-acetylthio-2-ethylhexanal* (2·0 g.), b. p. 79—80°/0·5 mm., n_D^{20} 1·4811 (Found: C, 59·0; H, 8·7; S, 16·0. $C_{10}H_{18}O_2S$ requires C, 59·3; H, 8·9; S, 15·9%) [2 : 4-*dinitrophenylhydrazone*, yellow plates (from *cyclo*hexane), m. p. 80—81° (Found: C, 50·0; H, 5·8; N, 14·2; S, 8·3. $C_{16}H_{22}O_5N_4S$ requires C, 50·2; H, 5·8; N, 14·6; S, 8·4%)].

Bromine (0·35 g.) in chloroform (5 ml.) was added dropwise during 10 min. to a solution of 2-ethylhex-2-enal 2 : 4-dinitrophenylhydrazone (0·5 g.) in chloroform (20 ml.). The solvent was evaporated under reduced pressure; the product, on recrystallisation from *cyclo*hexane, yielded 2 : *3-dibromo-2-ethylhexanal* 2 : 4-*dinitrophenylhydrazone* (0·4 g.), yellow needles, m. p. 131—132° (Found: C, 36·1; H, 3·8; N, 11·6; Br, 34·6. $C_{14}H_{18}O_4N_4Br_2$ requires C, 36·1; H, 3·9; N, 12·0; Br, 34·3%).

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