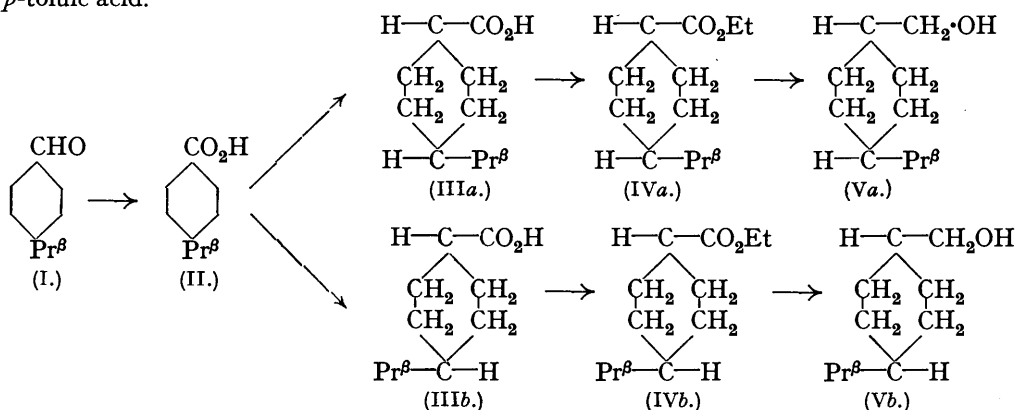


262. *Epimeric Alcohols of the cycloHexane Series. Part II.*
 4-Methyl- and 4-isoPropyl-cyclohexyl-1-carbinols.

By R. G. COOKE and A. KILLEN MACBETH.

cis- and *trans*-Hexahydro-*p*-toluic and hexahydrocuminic acids have been prepared and characterised by the *p*-chloro- and *p*-bromo-phenacyl esters. *cis*-Hexahydrocuminic acid can be prepared by the catalytic hydrogenation of cuminic acid in acetic acid in the presence of platinum oxide, but a small amount of the *trans*-acid is present. The *trans*-hexahydro-acids are readily available by pressure hydrogenation of alkaline solutions of the salts of the corresponding aromatic acids in the presence of Raney nickel. The epimeric 4-methyl- and 4-*isopropyl*-cyclohexylcarbinols have been prepared by the hydrogenation and hydrogenolysis of the esters of the *cis*- and *trans*-hexahydro-acids. The *trans*-alcohols are readily obtained pure, but the *cis*-compounds are contaminated by small amounts of the epimers, and rigid purification of the derivatives is somewhat difficult. All the alcohols have been characterised by crystalline derivatives. Their physical constants are in agreement with the Auwers-Skita rule.

THE relationship of 4-*isopropyl*cyclohexyl-1-carbinols to monocyclic terpene aldehydes, such as phellandral, lends interest to the former compounds, and the synthesis and characterisation of the pure epimeric alcohols were regarded as a necessary preliminary to the study of the hydrogenation of the aldehydes themselves under a variety of conditions. Cuminal (I) was available in quantity as a starting material, and the work carried out is outlined in the following scheme. Similar reactions were also carried out starting with *p*-toluic acid.



trans-Hexahydro-*p*-toluic acid was prepared by the sodium reduction of *p*-toluic acid in amyl alcohol (Einhorn and Willstätter, *Annalen*, 1894, **280**, 160; Perkin and Pickles, *J.*, 1905, **87**, 643), and a solid hexahydrocuminic acid was similarly obtained by Markownikoff (*J. pr. Chem.*, 1898, **57**, 95). The method, however, is laborious and permits the reduction of the acids in only small quantities (10 g.). We have found that the solid *trans*-acids can be obtained much more conveniently by the pressure hydrogenation (150–200 atms., 200°) of their solutions in 10% sodium hydroxide, Raney nickel being used as a catalyst. *trans*-Hexahydro-*p*-toluic acid gives a *p*-chlorophenacyl ester, m. p. 105°, and a *p*-bromophenacyl ester, m. p. 135°. *trans*-Hexahydrocuminic acid (IIIb) is characterised by a *p*-chlorophenacyl ester, m. p. 97.5°, and a *p*-bromophenacyl ester, m. p. 108°.

cis-Hexahydro-*p*-toluic acid has been prepared by Keats (*J.*, 1937, 2003) by catalytic hydrogenation of *p*-toluic acid in acetic acid in the presence of platinum oxide. *cis*-Hexahydrocuminic acid (IIIa), a liquid, b. p. 133°/2.5 mm., n_D^{20} 1.4668, has now been similarly prepared. Both acids, however, contain traces of their *trans*-epimers, for in the purification of their *p*-chloro- and *p*-bromo-phenacyl esters, small amounts of the *trans*-esters were isolated. The *p*-chlorophenacyl esters had m. p. 90° and 61°, and the *p*-bromophenacyl esters m. p. 100° and 85° respectively.

The above acids were converted into their ethyl esters by standing in alcoholic solution with sulphuric acid, and the esters were converted into the corresponding carbinols by treatment with hydrogen at 250° under *ca.* 200 atm. in the presence of copper-barium-chromium oxide catalyst for about 10 hours. Under these conditions hydrogenation and hydrogenolysis of the esters occurred, and the resulting carbinols were converted into the acid phthalates which were purified by crystallisation. The carbinols were characterised by the derivatives listed below, and the ease with which those of the *trans*-compounds were obtained pure, compared with the difficulty experienced in the case of the *cis*-derivatives, again suggests the contamination of the latter by traces of the former. *cis*-4-Methylcyclohexyl-1-carbinol: *hydrogen phthalate*, m. p. 127°; *α-naphthylurethane*, m. p. 72—73°. *trans*-4-Methylcyclohexylcarbinol: *hydrogen phthalate*, m. p. 147—148°; *α-naphthylurethane*, m. p. 110·5°; *phenylurethane*, m. p. 82·5°; *p-nitrobenzoate*, m. p. 57°; 3:5-dinitrobenzoate, m. p. 112°. *cis*-4-isoPropylcyclohexyl-1-carbinol (Va): *hydrogen phthalate*, m. p. 107—108°; *p-nitrobenzoate*, m. p. 54—55°, 3:5-dinitrobenzoate, m. p. 72°. *trans*-4-isoPropylcyclohexyl-1-carbinol (Vb): *hydrogen phthalate*, m. p. 107—108°; *p-nitrobenzoate*, m. p. 47·5°; 3:5-dinitrobenzoate, m. p. 95°; *phenylurethane*, m. p. 74°; *α-naphthylurethane*, m. p. 93°.

The refractive indexes and the densities of the *cis*-carbinols are higher than those of the *trans*-compounds and the constants are thus in accordance with the Auwers-Skita rule: *cis*-4-Methylcyclohexyl-1-carbinol, n_D^{20} 1·4617, d_4^{20} 0·9074; *trans*-4-methylcyclohexyl-1-carbinol, n_D^{20} 1·4578, d_4^{20} 0·8962; *cis*-4-isopropylcyclohexyl-1-carbinol, n_D^{20} 1·4682, d_4^{20} 0·9051; *trans*-4-isopropylcyclohexyl-1-carbinol, n_D^{20} 1·4661, d_4^{20} 0·9007.

EXPERIMENTAL.

Cuminic Acid.—This was prepared from cuminal (100 g.) which was vigorously stirred with 10% sodium hydroxide solution (200 c.c.) during addition of hydrogen peroxide (30 c.c., 100-vol.), the reaction vessel being immersed in ice-cold water. Further quantities of alkali and hydrogen peroxide were added during 10 hours, and after standing overnight unchanged cuminal was removed by steam distillation, and the cuminic acid precipitated by acidification after cooling. The crude acid was crystallised (charcoal) from dilute acetic acid, and twice recrystallised from the same solvent.

cis-Hexahydrocuminic Acid.—Cuminic acid was hydrogenated in 10-g. lots in glacial acetic acid (60 c.c.) in the presence of platinum oxide (Adams, 0·5 g.), the flask being continuously shaken and kept hot by a jet of steam. Hydrogen was steadily absorbed during 6 hours, the catalyst being aerated at intervals as necessary. The acetic acid from accumulated reaction products was distilled off under reduced pressure, and the residual *cis*-hexahydrocuminic acid purified by distillation, 45 g. being obtained from 50 g. of cuminic acid. It had b. p. 133°/2·5 mm., n_D^{20} 1·4668 (Found: C, 70·3; H, 10·5. $C_{10}H_{18}O_2$ requires C, 70·55; H, 10·65%). The *p*-chlorophenacyl ester, fine needles, m. p. 61° (Found: Cl, 11·05; $C_{18}H_{23}O_3Cl$ requires Cl, 11·0%), and the *p*-bromophenacyl ester, needles, m. p. 85° (Found: Br, 21·6. $C_{18}H_{23}O_3Br$ requires Br, 21·8%), were both crystallised from dilute alcohol.

cis-Hexahydro-*p*-toluic acid, similarly prepared (compare Keats, *loc. cit.*), required less time for the hydrogenation (4·5 hours) and gave a *p*-chlorophenacyl ester, flat needles, m. p. 90° (Found: Cl, 12·0. $C_{16}H_{19}O_3Cl$ requires Cl, 12·05%), and a *p*-bromophenacyl ester, flaky leaves, m. p. 100° (Found: Br, 23·6. $C_{16}H_{19}O_3Br$ requires Br, 23·6%), both from dilute alcohol.

trans-Hexahydrocuminic acid was conveniently prepared by hydrogenation of cuminic acid (40 g.) in aqueous sodium hydroxide solution (150 c.c., 10%) in the presence of Raney nickel (10 g.) at 200° and a pressure of 150—200 atm. The absorption of hydrogen was completed in 4—5 hours. After removal of nickel from the reaction mixture and acidification with hydrochloric acid, the crude *trans*-hexahydro-acid separated in solid form, and after collection, washing with water, and draining on a porous tile, it was purified by recrystallisation from formic acid; yield of pure acid 65%, m. p. 94°. From dilute alcohol, the *p*-chlorophenacyl ester separated as long plates, m. p. 97·5° (Found: Cl, 11·2. $C_{18}H_{23}O_3Cl$ requires Cl, 11·0%), and the *p*-bromophenacyl ester as glistening leaves, m. p. 108° (Found: Br, 22·0. $C_{18}H_{23}O_3Br$ requires Br, 21·8%).

trans-Hexahydro-*p*-toluic acid, similarly prepared, gave a *p*-chlorophenacyl ester, plates, m. p. 105°, from dilute alcohol (Found: Cl, 11·75. $C_{16}H_{19}O_3Cl$ requires Cl, 12·05%), and a *p*-bromophenacyl ester, plates, m. p. 135° (Found: Br, 23·6. $C_{16}H_{19}O_3Br$ requires Br, 23·6%).

Ethyl cis-hexahydrocuminate was prepared by keeping a solution of the acid (32 g.) in alcohol

(150 c.c.) and sulphuric acid (10 c.c.) for 2 days; the mixture was then heated on the water-bath for an hour, and the major part of the alcohol distilled off. The residue was poured into water, the ester extracted with ether, and after drying with calcium chloride the product was distilled under reduced pressure, b. p. $94^{\circ}/2.5$ mm., n_D^{20} 1.4491 (Found: C, 72.6; H, 11.1. $C_{12}H_{22}O_2$ requires C, 72.65; H, 11.2%). The other esters were prepared similarly or by the Fischer-Speier method: *Ethyl trans-hexahydrocuminate*, b. p. $100^{\circ}/2$ mm. (Found: C, 72.65; H, 10.95. $C_{12}H_{22}O_2$ requires C, 72.6; H, 11.2%); ethyl *cis-hexahydro-p-toluate*, b. p. $64^{\circ}/3$ mm.; ethyl *trans-hexahydro-p-toluate*, b. p. $71^{\circ}/2$ mm.

Hydrogenation-hydrogenolysis of the Esters.—The conversion of the esters into the corresponding carbinols was in all cases carried out by the action of hydrogen at 250° and about 200 atm. pressure, using copper-barium-chromium oxide as the catalyst. About 10% of the catalyst was employed, and for 30–40 g. of the ester the reaction required some 10 hours for completion. After isolation of the carbinol in the usual way, the dried product was converted into the acid phthalate by heating with excess phthalic anhydride for 12–15 hours in a constant-temperature oven at 110° . After being worked up as usual, the phthalates were purified by crystallisation from light petroleum (b. p. 60 – 90°) and the alcohols recovered by steam-distillation of the purified esters in the presence of sodium hydroxide solution (5%, 3 mols.). The distillate was extracted with ether, the extracts dried with anhydrous magnesium sulphate, and the carbinols obtained as pleasant-smelling viscous liquids by distillation under reduced pressure. *cis-4-Methylcyclohexyl-1-carbinol*, b. p. $75^{\circ}/2.5$ mm., n_D^{20} 1.4617, d_4^{20} 0.9074, gave a *hydrogen phthalate*, m. p. 127° , from light petroleum (Found: C, 69.7; H, 7.3. $C_{16}H_{20}O_4$ requires C, 69.5; H, 7.3%), and an α -*naphthylurethane*, glistening plates, m. p. 72 – 73° , from dilute alcohol (Found: C, 76.85; H, 7.7; N, 4.85. $C_{19}H_{23}O_2N$ requires C, 76.7; H, 7.8; N, 4.7%).

trans-4-Methylcyclohexyl-1-carbinol had b. p. $74^{\circ}/3$ mm., n_D^{20} 1.4578, d_4^{20} 0.8962. The *hydrogen phthalate*, recrystallised from light petroleum, had m. p. 147 – 148° (Found: C, 69.4; H, 7.25. $C_{16}H_{20}O_4$ requires C, 69.5; H, 7.3%); the *p-nitrobenzoate* separated as practically colourless laths, m. p. 57° , from methyl alcohol (Found: N, 5.0. $C_{15}H_{19}O_4N$ requires N, 5.0%); the 3 : 5-*dinitrobenzoate*, pale yellow needles from ethyl alcohol, m. p. 112° (Found: C, 56.0; H, 5.6; N, 8.4. $C_{15}H_{18}O_6N_2$ requires C, 55.85; H, 5.65; N, 8.7%); the *phenylurethane*, glistening plates from light petroleum, m. p. 82.5° (Found: C, 73.1; H, 8.6; N, 5.8. $C_{15}H_{21}O_2N$ requires C, 72.8; H, 8.6; N, 5.65%); the α -*naphthylurethane*, needles from light petroleum, m. p. 110.5° (Found: C, 76.8; H, 7.55; N, 4.85. $C_{19}H_{23}O_2N$ requires C, 76.7; H, 7.8; N, 4.7%).

cis-4-isoPropylcyclohexyl-1-carbinol had b. p. $101^{\circ}/2$ mm., n_D^{20} 1.4682, d_4^{20} 0.9051 (Found: C, 76.95; H, 12.7. $C_{10}H_{20}O$ requires C, 76.85; H, 12.9%); *hydrogen phthalate*, from light petroleum, m. p. 107 – 108° (Found: C, 70.8; H, 7.9. $C_{18}H_{24}O_4$ requires C, 71.0; H, 7.95%); *p-nitrobenzoate*, very pale yellow glistening flakes from methyl alcohol, m. p. 54 – 55° (Found: C, 66.5; H, 7.5; N, 4.7. $C_{17}H_{23}O_4N$ requires C, 66.8; H, 7.6; N, 4.6%); 3 : 5-*dinitrobenzoate*, pale yellow needles from methyl alcohol, m. p. 72° (Found: C, 58.4; H, 6.4; N, 8.2. $C_{17}H_{22}O_6N_2$ requires C, 58.25; H, 6.35; N, 8.0%); α -*naphthylurethane*, m. p. 72 – 73° , needles from light petroleum (Found: C, 77.4; H, 8.5; N, 4.4. $C_{21}H_{27}O_2N$ requires C, 77.5; H, 8.35; N, 4.3%).

trans-4-isoPropylcyclohexyl-1-carbinol had b. p. $98^{\circ}/2$ mm., n_D^{20} 1.4661, d_4^{20} 0.9007 (Found: C, 76.5; H, 12.85. $C_{10}H_{20}O$ requires C, 76.85; H, 12.9%); the *hydrogen phthalate*, crystallised from light petroleum, had m. p. 107 – 108° , which is the same as the ester of the *cis*-carbinol, but a mixed m. p. showed marked depression (Found: C, 71.0; H, 7.7. $C_{18}H_{24}O_4$ requires C, 71.0; H, 7.95%). The *p-nitrobenzoate* separated as practically colourless, long plates from dilute methyl alcohol, m. p. 47.5° (Found: C, 67.1; H, 7.7; N, 4.8. $C_{17}H_{23}O_4N$ requires C, 66.8; H, 7.6; N, 4.6%); 3 : 5-*dinitrobenzoate*, characteristic curved laths from dilute methyl alcohol, m. p. 95° (Found: C, 58.05; H, 6.1; N, 8.05. $C_{17}H_{22}O_6N_2$ requires C, 58.25; H, 6.35; N, 8.0%); *phenylurethane*, flakes from light petroleum, m. p. 74° (Found: C, 74.0; H, 8.8; N, 5.1. $C_{17}H_{25}O_2N$ requires C, 74.1; H, 9.15; N, 5.1%); α -*naphthylurethane*, needles from light petroleum, m. p. 93° (Found: C, 77.8; H, 8.4; N, 4.1. $C_{21}H_{27}O_2N$ requires C, 77.5; H, 8.35; N, 4.3%).

One of us (R. G. C.) is indebted to the Commonwealth Government for a Federal Research Grant which enabled him to participate in the work.