225. *Olefinic Additions with Asymmetric Reactants. Part VII.*[1] *The Hydrogenation of* (±)-3-*Methylenepentan*-2-*ol.*

By C. L. Arcus, Jane M. J. Page, and Joan A. Reid.

Catalytic hydrogenation of (±)-3-methylenepentan-2-ol, in ethanol and in ether, yielded the diastereoisomeric racemates of (±)-3-methylpentan-2-ol in ratios (determined by gas–liquid chromatography) which indicate that 5% and 8%, respectively, of dissymmetric reaction occur. The (2*RS*,3*SR*)-compound (VI + enantiomer) predominates.

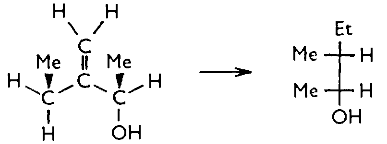
The ratios in which diastereoisomers are formed on hydrogenation of 3-methyl-4-phenylbut-3-en-2-ol[2] (I) and 4-phenylpent-3-en-2-ol[1] (II) have been determined from the areas under the peaks, formed by the diastereoisomers, on gas–liquid chromatograms of the saturated alcohols. (The separation of the diasteroisomeric 3-methyl-4-phenylbutan-2-ols described in Part V[2] was thought to be the first example of gas–liquid chromatographic separation of open-chain diastereoisomers, but an earlier separation, that of the diastereoisomeric 3-phenylbutan-2-ols, was effected by Elphinoff-Felkin and Felkin.[3])

$$\text{*CHMe(OH)·CMe:CHPh} \longrightarrow \text{*CHMe(OH)·*CHMe·CH}_2\text{Ph}$$
(I)

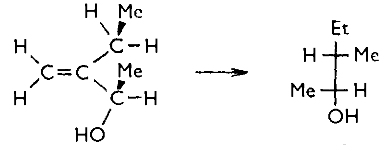
$$\text{*CHMe(OH)·CH:CMePh} \longrightarrow \text{*CHMe(OH)·CH}_2\text{·*CHMePh}$$
(II)

The expression " percentage dissymmetric reaction," equal to $100(a - b)/(a + b)$ where a and b are the amounts of the diastereoisomers formed, was introduced[1] in place of partial asymmetric synthesis as appropriate to the description of results with optically inactive compounds. In the hydrogenation of the olefins (I) and (II), 20% and 54%, respectively, of dissymmetric reaction occurred. The diastereoisomers of the resulting saturated alcohols were not known as compounds of established configuration and physical properties when these hydrogenations were investigated.

(±)-3-Methylenepentan-2-ol has now been hydrogenated, in solution in ethanol and in ether, with W-3 Raney nickel[4] catalyst. The disastereoisomeric products of reaction, (2*RS*,3*RS*)- and (2*RS*,3*SR*)-3-methylpentan-2-ol (V and VI *), are known: they are formed respectively by the reaction of *trans*- and *cis*-2,3-epoxybutane with diethylmagnesium;[5] the mechanism, considered to be a nucleophilic attack with inversion by an anionic ethyl group, leads to the above configurational relations. Further, Gault[6] has found that, in gas–liquid chromatography with a diglycerol–poly(ethylene glycol) stationary



(III) (V)



(IV) (VI)

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* Each of the formulæ (III—VI) represents a pair of enantiomers. Formulæ (III), (IV), and (VII) show the conformation in which the unsaturated alcohol is adsorbed at the catalyst surface, represented by the plane of the paper, as seen from almost vertically above.

The symbolism (2*RS*,3*RS*) denotes an inactive form comprising the (2*R*,3*R*)- and the (2*S*,3*S*)-form; the (2*RS*,3*SR*)-form comprises (2*R*,3*S*) and (2*S*,3*R*). Gault[6] refers to (2*RS*,3*RS*)- and (2*RS*,3*SR*)-3-methylpentan-2-ol, respectively, as the *erythro*- and the *threo*-compound.

[1] Part VI, Arcus and Howard, *J.*, 1961, 670.

[2] Arcus, Cort, Howard, and Le Ba Loc, *J.*, 1960, 1195.

[3] Elphinoff-Felkin and Felkin, *Bull. Soc. chim. France*, 1957, 450.

[4] Pavlic and Adams, *J. Amer. Chem. Soc.*, 1946, **68**, 1471.

[5] Norton and Hass, *J. Amer. Chem. Soc.*, 1936, **58**, 2147.

[6] Gault, *Compt. rend.*, 1960, **250**, 2584.

phase, the (2*RS*,3*RS*)-compound has the shorter retention-time. She also found that the (±)-3-methylpentan-2-ol from the reaction of s-butylmagnesium bromide with acetaldehyde contains the (2*RS*,3*RS*)- and (2*RS*,3*SR*)-form in nearly equal amounts. Use was made of these findings in the preparation of reference specimens for the identification of the present diastereoisomers.

(±)-3-Methylpentan-2-ol, mainly (2*RS*,3*RS*), was obtained from a specimen of largely *trans*-2,3-epoxybutane, and the mixed disastereoisomers were prepared by the Grignard reaction. Fractions comprising essentially the total yield of (±)-3-methylpentan-2-ol from the hydrogenations, the reference specimens, and mixtures of the latter with the main fraction of the second hydrogenation, were submitted to gas–liquid chromatography on poly(ethylene glycol) (Table).

The chromatograms for the specimens of (±)-3-methylpentan-2-ol from hydrogenations and the Grignard reactions, also the mixtures ($X + Y$) and ($X + Z$), showed two separate but overlapping peaks, from which the ratio of the retention times, *t*(2*RS*,3*SR*)/*t*(2*RS*,3*RS*), was 1·08 throughout. Those for the methylpentanol from the epoxybutane had a single peak with, on the less-volatile side, a shoulder at a position giving *t*(2*RS*,3*SR*)/*t*(2*RS*,3*RS*) = 1·06 in each case; in confirmation of Gault's finding, the (2*RS*,3*RS*)-compound has the shorter retention time. For given chromatographic conditions, peak area is approximately equal to the product of a constant, peak height, and retention time, and the relation is valid for overlapping peaks.[7] The approximation should be close when applied to diastereoisomers of similar retention times, and this method has been used to determine the relative peak areas of the chromatograms. By application of the diastereoisomer ratios to the weights of the corresponding fractions, and summation of the resultant quantities of (2*RS*,3*RS*)- and (2*RS*,3*SR*)-compound, it is found that 5% and 8% of dissymmetric reaction occurred during hydrogenation in ethanol and in ether, respectively; in both the (2*RS*,3*SR*)-isomer preponderated.

TABLE.

Gas–liquid chromatography of (±)-3-methylpentan-2-ol.

Source of specimen			(2*RS*,3*RS*) (%)	(2*RS*,3*SR*) (%)
Hydrogn. of (±)-3-methylenepentan-2-ol in EtOH:	Fraction 1		51	49
	,, 2		48	52
	,, 3		42	58
Hydrogn. of (±)-3-methylenepentan-2-ol in Et$_2$O:	Fraction 1	(i)	49	51
		(ii)	48	52
	,, 2(X)	(i)	47	53
		(ii)	46	54
	,, 3		43	57
From mainly *trans*-2,3-epoxybutane:	1st Prepn.		75	25
	2nd ,, (Y)		75	25
From Me·CHO and Bu^{s}MgBr:	1st Prepn.		44 *	56
	2nd ,, (Z)		45 *	55
$X + Y$			63(61) †	37(39)
$X + Z$			44(46)	56(54)

* These values are not necessarily identical with the product ratio from the Grignard reaction, since lower and higher fractions were not evaluated.

† The percentages in parentheses are calculated from the weights of X, Y, Z mixed, and their compositions.

In hydrogenation, it is considered [2,8] that the oxygen lone-pairs and the π-electrons of the double bond interact with the nickel surface, and the alkyl substituents become so placed that the olefinic part conforms closely to this surface. Two conformations (III) and (IV) are possible within these premises, and, hydrogenation being considered to be

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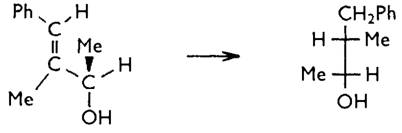
[7] Carroll, *Nature*, 1961, **191**, 377.

[8] Arcus and Smyth, *J.*, 1955, 34.

cis and from below the plane of the paper, the experimental result implies that (IV) is slightly preferred over (III).

N.C.L.-Catalin models of (III) and (IV), and of these conformations with the ethylenic carbon atoms in the sp^3-hydridised state (which they will approach on chemisorption at the nickel surface) have been studied with regard to the packing of the constituent groups, but no outstanding difference was apparent.

For 3-methyl-4-phenylbut-3-en-2-ol, the conformation (VII) was selected [2] as the more probable, since it possesses the wider spacing of the methyl groups (this is so in both sp^2- and sp^3-hydridised models). Hydrogenation of conformation (VII) leads to the configuration (VIII).



(VII) (VIII)

The ascription of this configuration to the major product (the diastereoisomer having the longer retention-time on tritolyl phosphate) has recently been confirmed by Felkin,[9] who has prepared the diastereoisomeric 3-methyl-4-phenylbutan-2-ols by a stereospecific synthesis and ascertained the relationships of their retention times.

Although the two hydrogenations above differ in that the 3-methyl group in the product was originally present as such in (VII), but as a methylene group in (IV), it is noteworthy that the preponderating products (VI) and (VIII) are both (2*RS*,3*SR*)-isomers.

EXPERIMENTAL

M. p.s are corrected.

α-Ethylacraldehyde and hence 3-methylenepentan-2-ol were prepared by the methods of Marvel, Myers, and Saunders.[10] Condensation of n-butyraldehyde (318 ml.) with formaldehyde (334 ml. of 36% w/v solution) in the presence of dimethylamine hydrochloride (364 g.) gave α-ethylacraldehyde (177 g.), b. p. 92°, n_D^{25} 1·4216. Reaction of this aldehyde (84 g.) in ether (450 ml.) with methylmagnesium bromide (from magnesium, 29·7 g., and methyl bromide, 121 g.) in ether (910 ml.) yielded 3-methylenepentan-2-ol (83 g.), b. p. 76—76·5°/72 mm., n_D^{25} 1·4350 (Found: C, 72·1; H, 11·85. Calc. for $C_6H_{12}O$: C, 72·0; H, 12·1%). Its chromatogram showed a single peak. 1-*Methyl-2-methylenebutyl* N-1-*naphthylcarbamate*, recrystallised from light petroleum (b. p. 40—60°), had m. p. 56—57° (Found: C, 75·5; H, 7·2; N, 5·4. $C_{17}H_{19}NO_2$ requires C, 75·8; H, 7·1; N, 5·2%).

3-Methylenepentan-2-ol (14·0 g.), in 99% ethanol (100 ml.), was hydrogenated in the presence of W-3 Raney nickel (0·9 g.); the maximum temperature and pressure were 35° and 96 atm.; the time of stirring was 3 hr. Next day the solution was filtered and concentrated, and the product twice distilled. Three fractions of 3-methylpentan-2-ol were collected: (1) (0·63 g.), b. p. 73—73·5°/67 mm., n_D^{25} 1·4170; (2) (7·25 g.), b. p. 73·5—74°/67 mm., n_D^{26} 1·4177; and (3) (0·75 g.), b. p. 74°/67 mm., n_D^{26} 1·4176 [Found, for (2): C, 70·85; H, 13·6. Calc. for $C_6H_{14}O$: C, 70·55; H, 13·8%].

The methylpentanol tended to co-distil with ethanol, but much less so with ether; the latter was therefore used as solvent in the second hydrogenation. 3-Methylenepentan-2-ol (50·2 g.) in ether (sodium-dried; 200 ml.) was hydrogenated in the presence of W-3 Raney nickel (2·8 g., wet with ethanol) with stirring for 6½ and 9½ hr. on successive days; the maximum temperature and pressure were 35° and 79 atm. The ether was distilled through a 15 cm. column of glass helices. Three fractions of 3-methylpentan-2-ol were collected: (1) (3·6 g.), b. p. up to 72°/64 mm., n_D^{25} 1·4124; (2) (33·5 g.), b. p. 72—73°/64 mm., n_D^{25} 1·4180; and (3) (9·6 g.), b. p. 73°/64 mm., n_D^{25} 1·4180.

A specimen of 2,3-epoxybutane, largely *trans* from infrared analysis, was kindly supplied by the Distillers Company. It was dried (K_2CO_3) and distilled; the central fraction, b. p. 54·5—55·5°, n_D^{25} 1·3708 (42·5 g., 0·59 mole, in 45 ml. of ether) was allowed to react with an ethereal

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[9] Felkin, personal communication.

[10] Marvel, Myers, and Saunders, *J. Amer. Chem. Soc.*, 1948, **70**, 1694.

solution of diethylmagnesium (480 ml. containing, by titration, 0·40 mole) by the procedure of Norton and Hass,[5] and gave 3-methylpentan-2-ol (18·2 g.), b. p. 72·5—74°/69 mm., n_D^{25} 1·4180 (Found: C, 69·9; H, 13·5%).

Acetaldehyde (30 ml.) in chilled ether (30 ml.) was added with stirring to ice-cooled s-butylmagnesium bromide (from magnesium, 8·95 g., and s-butyl bromide, 50 g.) in ether (75 ml.). The mixture was then boiled for 45 min., cooled, and added to ice and dilute sulphuric acid. The ethereal extract, washed with water and dried (K_2CO_3), yielded 3-methylpentan-2-ol (3·5 g.), b. p. 73—74°/66 mm., n_D^{25} 1·4177 (Found: C, 70·3; H, 13·5%).

A Pye argon chromatograph was used, and the conditions were: Column, 120 cm. Temp., 75°. Packing: 10% poly(ethylene glycol)-400 on 100—120 mesh Celite. Rate of flow: 40 ml./min.

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