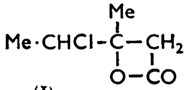
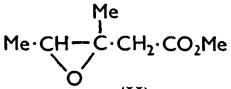
813. *Stereoselective Reaction of Keten with 3-Chlorobutan-2-one; Geometry of the 3-Methylpent-3-enoic Acids.*

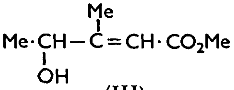
By (Mrs.) R. H. Cornforth.

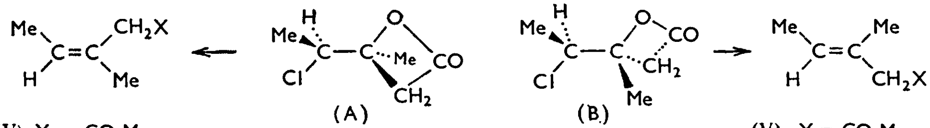
The reaction of keten with 3-chlorobutan-2-one is shown to give, in the ratio 2 : 3, two stereoisomers of 4-chloro-3-methylpentano-3-lactone. These have been isolated and converted into *cis*- and *trans*-3-methylpent-3-enoic acids and the corresponding alcohols. Methyl 3-methylpent-3-enoate prepared by Favorski re-arrangement of 3,4-dibromo-3-methylpentan-2-one is shown to be 75% *trans*. Two other chloro-β-lactones are described.

Grignard reagents and lithium alkyls have been shown to add stereoselectively to aliphatic α-chloro-carbonyl compounds[1]; thus R^4X reacts with $R^1R^2ClC{\cdot}COR^3$ to give a chlorohydrin having a preponderance of molecules where R^4 is *anti* to the larger of the two groups R^1 and R^2 when the chlorine and hydroxyl groups are *anti* to each other. When R^1 and R^2 are hydrogen and alkyl, respectively, stereospecific reduction of the derived iodohydrin gives a mixture of olefins in which 70% has R^4 *trans* to R^2 when the starting material is an α-chloro-aldehyde, and 80—85% when it is an α-chloro-ketone. Sodium borohydride reduction is also 80—85% stereoselective in the expected sense. We were interested in applying this stereoselectivity in the reactions of α-chloro-ketones to a synthesis of optically active mevalonic acid (3,5-dihydroxy-3-methylpentanoic acid) starting from a compound $RO{\cdot}CH_2{\cdot}CHCl{\cdot}COMe$ of known absolute configuration; a highly stereoselective reaction of an α-chloro-ketone with keten in the presence of boron trifluoride would have been admirable for this purpose.


(I)


(II)


$\mathrm{Me{\cdot}CH(OH){-}C(Me){=}CH{\cdot}CO_2Me}$
(III)



(IV) $X = CO_2Me$
(VI) $X = CH_2{\cdot}OH$
(VIII) $X = CH_2{\cdot}OTs$
(X) $X = CO_2H$
(XII) $X = H$

($Ts = p\text{-}C_6H_4Me{\cdot}SO_2$)

(V) $X = CO_2Me$
(VII) $X = CH_2{\cdot}OH$
(IX) $X = CH_2{\cdot}OTs$
(XI) $X = CO_2H$
(XIII) $X = H$

To test the stereoselectivity of the reaction, 3-chlorobutan-2-one was treated with keten

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[1] Cornforth, Cornforth, and Mathew, *J.*, 1959, 112.

in the presence of boron trifluoride: this gave a crystalline mixture of 4-chloro-3-methylpentano-3-lactones (I) which was converted into a mixture of methyl *cis*- and *trans*-3,4-epoxy-3-methylpentanoate (II) by cautious treatment with less than one equivalent of sodium methoxide in methanol; if the reaction mixture is allowed to become alkaline re-arrangement [2] readily occurs to methyl 4-hydroxy-3-methylpent-2-enoate (III). This reaction is naturally interpreted as an opening of the β-lactone ring by attack of methoxide ion on the carbonyl group; formation of the epoxide from the resulting chlorohydrin anion occurs in a second step, with inversion at the halogen-bearing carbon. The iodohydrins from the mixture of epoxy-esters were reduced by stannous chloride–phosphorus oxychloride–pyridine to a mixture of methyl *cis*- and *trans*-3-methylpent-3-enoate (IV and V); reduction with lithium aluminium hydride gave the alcohols (VI and VII), the toluene-*p*-sulphonates of which (VIII and IX) were further reduced by lithium aluminium hydride to a mixture of *cis*- and *trans*-3-methylpent-2-enes (XII and XIII). This mixture was shown, by comparison of infrared spectra,[1] to contain about 60% of the *trans*-form. Thus the reaction of 3-chlorobutan-2-one with keten is much less stereoselective than with organometallic reagents and the degree of selectivity was not sufficient for the proposed synthesis of mevalonic acid. Possibly keten is effectively smaller than an organometallic reagent in solution and therefore less subject to steric hindrance; an organometallic reagent presumably reacts as an ether solvate, but this is not necessarily true of keten.

The literature on the 3-methylpent-3-enoic acids (X and XI) presents a rather unsatisfactory picture. Kon, Linstead, and Wright [3] studied the isomeric αβ- and βγ-unsaturated acids obtained by dehydration of 3-hydroxy-3-methylpentanoic acid and its ester; the acids were separated by partial esterification. After equilibration of the αβ-unsaturated acids with alkali, partial esterification gave an ester which on hydrolysis gave an acid of m. p. 1°; this was assumed to be pure 3-methylpent-*cis*-3-enoic acid. On the other hand, when the product from dehydration of ethyl 3-hydroxy-3-methylpentanoate with phosphoric oxide was hydrolysed and partially esterified, the resulting βγ-unsaturated ester could be hydrolysed to give, on crystallisation, an acid of m. p. 35°; this was assigned the *trans*-configuration. No derivatives were described and the assignments of configuration were purely provisional. Now Wagner [4] claimed to have obtained methyl 3-methyl-*trans*-pent-3-enoate stereochemically pure by Favorski re-arrangement of 3,4-dibromo-3-methylpentan-2-one obtained from 3-methylpent-3-en-2-one of unspecified geometry; he did not isolate the parent acid but made derivatives (amide, anilide, and *p*-toluidide) which he compared with derivatives of " *cis* "- and " *trans* "-3-methylpent-3-enoic acids prepared according to Kon, Linstead, and Wright; he accepted their provisional assignment of structure as fact. Undoubtedly the anilide and *p*-toluidide were identical with those from the acid of m. p. 35° accepted as *trans*, and thus Wagner's ester is likely to consist predominantly of this form; but the isolation of pure re-crystallised derivatives, unless in quantitative yield, does not indicate stereochemical homogeneity of the starting material. The weight of further evidence is in favour of the *trans*-configuration for the acid, m. p. 35°, as assigned by Kon, Linstead, and Wright. Thus, Ansell and Gadsby [5] reduced Wagner's ester to the corresponding alcohol and converted this into its homologue, 4-methylhex-4-en-1-ol; from this specimen and from the hexenol obtained by scission with sodium of 3-chlorotetrahydro-2,3-dimethylpyran the same α-napthylurethane was obtained by reaction with α-naphthyl isocyanate and recrystallisation of the products. This correlation was considered proof of the stereochemical homogeneity of the ring-scisson product. A *trans*-configuration for the latter was supported by theoretical consideration of the mechanism of ring scisson and by the fact that tiglic and angelic acid can both be converted *via* the derived allylic bromides into a hexenol in which, as judged by preparation of derivatives,

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[2] Rambaud, *Compt. rend.*, 1945, **220**, 742.
[3] Kon, Linstead, and Wright, *J.*, 1934, 599.
[4] Wagner, *J. Amer. Chem. Soc.*, 1949, **71**, 3214.
[5] Ansell and Gadsby, *J.*, 1958, 3388.

the alcohol from the scission was the major component: in the reaction sequence used, the thermodynamically more stable *trans*-configuration would be expected to predominate. Also, Loftfield [6] has put forward a convincing stereospecific mechanism for the Favorski re-arrangement; since one would expect Wagner's starting material, 3-methylpent-3-en-2-one, to be predominantly *trans*, the derived methyl 3-methylpent-3-enoate should also be predominantly *trans*. This is now proved to be so; methyl 3-methylpent-3-enoate prepared according to Wagner was hydrolysed to the corresponding acid, which was liquid at room temperature and therefore could not be pure " *trans* "-acid, m. p. 35°; the acid was reduced by lithium aluminium hydride, and the methanesulphonate of the 3-methylpent-3-en-1-ol further reduced by lithium aluminium hydride to 3-methylpent-2-ene, which was shown by comparison of infrared spectra to be about 75% *trans*. Thus Wagner's ester and Ansell and Gadsby's 3-methylpent-*trans*-3-en-1-ol (and the corresponding *cis*-isomer which they obtained by a series of reactions designed to invert the geometry of the double bond) must also be about 75% stereochemically pure (equal yields being assumed from both isomers in the various transformations).

There seems little ground for the assumption that the acid of m. p. 1° is stereochemically pure; Wagner assumed that it was and described three derivatives (amide, anilide, and *p*-toluidide), only the last of which gave any substantial depression on admixture with the corresponding derivative of the *trans*-acid or of the Favorski re-arrangement product.

The mixture of 4-chloro-3-methylpentano-3-lactones, if it could be separated into its stereoisomers, offered a means of preparing stereochemically pure samples of *cis*- and *trans*-3-methylpent-3-enoic acids and the corresponding alcohols. By chromatography on silica gel two crystalline forms (A), m. p. 71—72°, and (B) m. p. 56—57°, were obtained, the latter being present in larger amount. The melting point of the original mixture (36—38°) was that of a 2 : 3 mixture of A and B (see Table 2). The infrared spectra of these two mixtures were also very similar. Since the mixture of lactones can be converted into a mixture of 3-methylpent-2-enes containing 60% of the *trans*-isomer it may be assumed that (A) is the form giving rise to the *cis*- and (B) that giving rise to the *trans*-olefin. Lactones (A) and (B) were converted respectively into the *cis*- and *trans*-isomers of methyl 3,4-epoxy-3-methylpentanoate and of methyl 3-methylpent-3-enoate; the infrared spectrum of a mixture of 2 parts of the *cis*- and 3 parts of the *trans*-3-methylpent-3-enoate was also very similar to that of the unsaturated ester from the original lactone mixture. Hydrolysis of the *cis*- and *trans*-esters gave 3-methylpent-*cis*-3-enoic, m. p. 14·5—15·5°, and 3-methylpent-*trans*-3-enoic acid, m. p. 35°. Melting points of these acids and their derivatives are assembled in Table 1. Examination of the data shows that the assignment of the *trans*-configuration to the acid, m. p. 35°, by Kon, Linstead, and Wright was correct but that the acid, m. p. 1°, was obviously a mixture. Since Wagner succeeded in isolating one pure *cis*-derivative (the *p*-toluidide) from this mixture it is presumably richer in the *cis*- than the *trans*-acid. Wagner's re-arrangement product furnished pure *trans*-anilide and -*p*-toluidide

TABLE 1. *3-Methylpent-3-enoic acids and derivatives.*

Source of acid	M. p.	Amide, m. p.		Anilide, m. p.		*p*-Toluidide, m. p.	
Pure *cis* from chloro-lactone A	14·5—15·5°	138—139°	mixed 125—127	111—112·5°	mixed 96—98	100—101°	mixed 75
Pure *trans* from chloro-lactone B	35	136—137		98—99		91—92	
" *trans* " prepd. by Wagner according to Kon *et al.*	35	—		100—101	mixed 97—98	91·5—92·5	mixed 70
" *cis* " prepd. by Wagner according to Kon *et al.*	1 (Kon *et al.*)	126—127	mixed 127—130	99—100		100·5—101·5	mixed 70
Favorski re-arr. product (Wagner)	—	130—131		99—100		91—92	

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[6] Loftfield, *J. Amer. Chem. Soc.*, 1951, **73**, 4707.

but the amide was not pure *trans*. The composition of Wagner's ester (75% *trans*) was also confirmed by comparison of the spectrum of the derived alcohol with those of mixtures of pure *cis*- and *trans*-alcohol (VI) and (VII). The pure alcohols were prepared by reduction of the esters (IV) and (V) with lithium aluminium hydride; their α-naphthylurethanes had higher melting points than those prepared by Ansell and Gadsby from the alcohols derived from Wagner's ester.

In drawing conclusions about the stereochemical composition of the mixture of chloro-lactones (I) and of Wagner's ester from the composition of the final olefin mixture it has been assumed that the two isomers give equal yields in the various transformations. This assumption seems reasonable, and after the separation of the chloro-lactone mixture into the two pure forms (A) and (B) supporting evidence was available from mixed m. p.'s and infrared spectra of mixtures of (A) and (B) and also from infrared spectra of mixtures of the derived *cis*- and *trans*-unsaturated esters and alcohols. The assignment of *cis*- and *trans*-configurations rests ultimately on the composition of the derived 3-methylpent-2-enes. The hypothesis that the proportions of *cis*- and *trans*-isomers in, *e.g.*, Wagner's ester could have become reversed in transformation to the methylpentenes requires too great a difference in yields to be seriously entertained.

Because of the unexpected crystallinity of the 4-chloro-3-methylpentano-3-lactones, the β-lactones from chloroacetone and 3-chloropentanone were also examined; that from chloroacetone was crystalline, m. p. 25°, but the mixture from 3-chloropentan-2-one was liquid and could not be separated into crystalline isomers by chromatography. Pyrolysis of 4-chloro-3-methylpentano-3-lactone at 150—160° gave a good yield of 3-chloro-2-methylbut-1-ene, but none of these chloro-β-lactones was decarboxylated in water, as was β-methylbutyro-β-lactone.[7]

EXPERIMENTAL

4-Chloro-3-methylpentano-3-lactone; Isomers A and B.—A solution of 3-chlorobutan-2-one (21·3 g.) in dry ether (25 c.c.) was cooled to −15°, boron trifluoride–ether complex (0·6 c.c.) was added, and keten (slightly more than 0·2 mole) was passed in; the internal temperature rose to 5—10°. The mixture was diluted with more ether, washed with saturated sodium hydrogen carbonate solution (40 c.c.) and saturated sodium chloride solution, dried ($MgSO_4$), and evaporated at low pressure. The residue crystallised from dry ether (80 c.c.) at −70°, to give 25 g. (84%) of colourless *4-chloro-3-methylpentano-3-lactone*, m. p. 36—38° (Found: C, 48·5; H, 6·4; Cl, 23·9. $C_6H_9O_2Cl$ requires C, 48·5; H, 6·1; Cl, 23·9%). A few crystals left on a watch-glass evaporated overnight. The chloro-lactone (2 g.) was pyrolysed at 150—160° to give 1·3 g. of distillate; redistillation gave 3-chloro-2-methylbut-1-ene (1·0 g., 76%), b. p. 92—94°, n_D^{22} 1·4310 (Found: C, 57·1; H, 8·6. Calc. for C_5H_9OCl: C, 57·4; H, 8·6%). Burgin *et al.*[8] give b. p. 93·8°, n_D^{20} 1·4304.

The above mixture of stereoisomers (10 g.) in cyclohexane (300 c.c.) was added to a column of silica gel (B.D.H.) (500 g.) and eluted with cyclohexane–benzene (50 : 50), the eluate being collected in 100 c.c. portions. Fractions 1—13 gave on evaporation 3·6 g. (a), m. p. 53—56°; thereafter the m. p. dropped to 36—39° (fraction 20), then rose to 59—67° (fraction 27). The solvent was changed to benzene after fraction 30. Fractions 27—33 gave on evaporation 1·2 g. (b), m. p. 60—65°, fractions 34—37 gave 1·4 g. (c), m. p. 65—70°, and fractions 38—40 gave 0·25 g. (d), m. p. 67—70°. Total recovery from the column was 8·75 g. Material (a), recrystallised from cyclohexane (20 c.c.), gave 3·2 g. of lactone, m. p. 56—57° (Found: C, 48·5; H, 6·1%); materials (b), (c), and (d), recrystallised from cyclohexane, gave 2·7 g., of lactone, m. p. 70—71°, raised to 71—72° by a second recrystallisation (Found: C, 48·5; H, 6·2%). Three recrystallisations of fractions 14—19 and 21—26 gave respectively 0·5 g., m. p. 55—56°, and 0·6 g., m. p. 70—71°. Since conversion into 3-methylpent-2-ene, described below, gave a mixture predominantly *trans*, it may be assumed that the isomer, m. p. 56—57°, has structure (B) and the isomer, m. p. 71—72°, structure (A). The infrared spectrum of a 2 : 3 mixture of (A)

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[7] Gresham, Jansen, Shaver, and Beears, *ibid.*, 1954, **76**, 486.

[8] Burgin, Engs, Groll, and Hearne, *Ind. Eng. Chem.*, 1939, **31**, 1414.

and (B) was very similar to that of the original mixture. The annexed Table of mixed m. p.s also indicates that the original mixture is composed of (A) and (B) in the ratio 2 : 3.

TABLE 2. *M. p.s of mixtures of* (*A*), *m. p.* 71—72°, *and* (*B*), *m. p.* 56—57°.

Ratio A : B	1 : 3	3 : 7	1 : 2	2 : 3	1 : 1	2 : 1
M. p.	39—45°	37—42°	37—42°	36—39°	40—49°	50—60°

Methyl 3,4-*Epoxy*-3-*methylpentanoate* (*Mixture of Geometrical Isomers*).—A solution of the mixture of chloro-β-lactones (10 g.) in dry methanol (20 c.c.) was heated in a water-bath at 55—60°. Evaporation (to avoid excessive volumes) was encouraged by rapid stirring during titration with 2N-sodium methoxide (Cresol Red as indicator); the reaction, at first very rapid, gradually became more sluggish and care was taken to prevent the solution remaining even faintly alkaline for any length of time. The titration was stopped short of the theoretical (32·7 instead of 33·7 c.c.; time 45 min.). The solution was filtered from sodium chloride and evaporated; the residue was taken up in ether, filtered, recovered by evaporation, and distilled, giving *methyl* 3,4-*epoxy*-3-*methylpentanoate* (6·6 g., 64%), b. p. 72—78° (mostly 74—75°)/16 mm. (Found: C, 58·0; H, 8·3. $C_7H_{12}O_2$ requires C, 58·3; H, 8·3%), and 1·9 g. of material, b. p. 110—120°/16 mm. (Found: C, 58·6; H, 8·4%). The higher-boiling fraction is isomeric with the epoxy-ester; infrared and ultraviolet absorption spectra [$\nu_{max.}$ 3400 (OH) and 1720 cm.$^{-1}$ (ester); $\lambda_{max.}$ (in EtOH) 2180 Å (ε 13,500)] confirmed its structure as *methyl* 4-*hydroxy*-3-*methylpent*-2-*enoate*. In some experiments, when the reaction mixture was allowed to become too alkaline, this product predominated.

Methyl 3-*Methylpent*-3-*enoate* (*Mixture of Geometrical Isomers*).—The epoxy-ester mixture (29·5 g.) was added to sodium iodide (60 g.) and sodium acetate (6 g.) in propionic acid (240 c.c.) and acetic acid (80 c.c.) at −20°. After 2 hr. the mixture was warmed to 0°, another 20 g. of sodium iodide were added, and the mixture was kept at 0° for a further 2 hr. It was then poured (with stirring) into ether and excess of aqueous sodium hydrogen carbonate. The ether was washed with aqueous sodium hydrogen sulphite and water, dried ($MgSO_4$), and evaporated at low pressure. The iodohydrin (51 g.) was added to anhydrous stannous chloride (52 g.) in pyridine (200 c.c.) at 0° and treated cautiously with phosphoryl chloride (15 c.c.) in pyridine (50 c.c.). The mixture was allowed to warm to a maximum temperature of 50° during solidification. After 3 hr. ether was added, the mixture was filtered, and the residue washed with ether. The ethereal solution was cooled in ice-water and made just acid to Methyl Orange with dilute hydrochloric acid; after separation, the ether layer was treated with water and small quantities of iodine until the brown colour persisted, then washed with sodium thiosulphate–sodium carbonate solution and dried ($MgSO_4$), and the ether was distilled off through a fractionating column. The residue was distilled, to give methyl 3-methylpent-3-enoate (17·5 g., 67%), b. p. 49—52°/16 mm. (Found: C, 65·7; H, 9·8. Calc. for $C_7H_{12}O_2$: C, 65·7; H, 9·4%).

3-*Methylpent*-2-*ene* (*Mixture of Geometrical Isomers*).—Methyl 3-methylpent-3-enoate (17 g.), obtained as above, was reduced with lithium aluminium hydride (8 g.) in ether (220 c.c.), essentially as described by Ansell and Gadsby,[5] to give 3-methylpent-3-en-1-ol (10·6 g., 80%), b. p. 58—60°/16 mm., n_D^{20} 1·4470. The toluene-*p*-sulphonate (11·6 g.), prepared according to Ansell and Gadsby's directions, in dry peroxide-free dibutyl ether (20 c.c.) was added dropwise during 1 hr. to lithium aluminium hydride (2 g.) in the same solvent (70 c.c.) with stirring; the temperature rose to 34—36°. After the addition the mixture was heated and stirred for 2·5 hr. at 45°, cooled in ice-water, and decomposed by water (10 c.c.). Next day the mixture was filtered, the residue washed with dibutyl ether, and the filtrate (which was neutral to litmus) distilled through a Widmer column. The distillate (6·75 g., b. p. $\ngtr$138°) gave a slight reaction with dinitrophenylhydrazine and was therefore shaken with a strong solution of semicarbazide acetate for 30 min., washed with water, aqueous sodium hydrogen carbonate, and water again, dried (KOH), and distilled from a flask with an indented neck. The distillate up to 90° (2·4 g.) was left over calcium chloride overnight (to remove any butyl alcohol) and distilled over sodium; 3-methylpent-2-ene (1·92 g.; b. p. 68—73°) was thus obtained. The infrared spectrum was almost identical with that of a 2 : 3 mixture of *cis*- and *trans*-3-methylpent-2-ene.[1]

3-*Methylpent*-trans-3-*enoic Acid*.—The chloro-lactone (B) (6·5 g.) was converted as described above into *methyl* trans-3,4-*epoxy*-3-*methylpentanoate* (4·9 g., 78%), b. p. 69—72°/16 mm., n_D^{21} 1·4230 (Found: C, 57·9; H. 8·5%). Reduction of the derived iodohydrin (8·4 g. from 4·5 g.) gave *methyl* 3-*methylpent*-trans-3-*enoate* (3·2 g.), b. p. 48—49°/16 mm., n_D^{21} 1·4318 (Found: C, 65·8; H, 9·6%). Hydrolysis of the ester (500 mg.) with 2N-sodium hydroxide (3 c.c.) and methanol (3 c.c.) at room temperature for several days gave 3-methylpent-*trans*-3-enoic acid (442 mg.; m. p. 34—35°); recrystallisation from light petroleum (b. p. 40—60°) at 2° did not raise the m. p. The *amide* was prepared from the ester and saturated methanolic ammonia at 36° (5 weeks); it formed plates, m. p. 136—137° raised to 137—138° on one recrystallisation from benzene (Found: C, 63·8; H, 10·0. $C_6H_{11}ON$ requires C, 63·7; H, 9·7%). The anilide, prepared from the acid and aniline with dicyclohexylcarbodi-imide, had m. p. 98—99°, not raised by recrystallisation from light petroleum (b. p. 60—80°). The *p*-toluidide prepared in a similar manner had m. p. 89—90°, raised to 91—92° after two crystallisations from light petroleum (b. p. 60—80°). M. p.s recorded in the literature are given in Table 1.

3-*Methylpent*-trans-3-*en*-1-*ol*.—Reduction of methyl 3-methylpent-*trans*-3-enoate (1·3 g.) by lithium aluminium hydride gave 3-methylpent-*trans*-3-en-1-ol (0·91 g.), b. p. 58°/15 mm., n_D^{21} 1·4480 (Found: C, 71·6; H, 12·1. Calc. for $C_6H_{12}O$: C, 71·9; H, 12·1%); the α-naphthylurethane, recrystallised from light petroleum (b. p. 60—80°), had m. p. 81—82: (Found: C, 75·7; H, 7·1. Calc. for $C_{17}H_{19}O_2N$: C, 75·8; H, 7·1%). Ansell and Gadsby [5] gave m. p. 78—78·5° for the α-napthylurethane of material shown below to be only 75% *trans*.

3-*Methylpent*-cis-3-*enoic Acid*.—The chloro-lactone (A) (9·6 g.) gave *methyl* cis-3,4-*epoxy*-3-*methylpentanoate* (5·8 g.), b. p. 65—67°/16 mm., n_D^{21} 1·4230 (Found: C, 58·1; H, 8·5%). Reduction of the derived iodohydrin (9·1 g. from 5 g.) gave *methyl* 3-*methylpent*-cis-3-*enoate*, (3·5 g.; b. p. 43—44°/16 mm., n_D^{21} 1·4298 (Found: C, 65·9; H, 9·4%). Hydrolysis of the ester (500 mg.) gave liquid 3-*methylpent*-cis-3-*enoic acid* (425 mg.), which distilled at about 40°/0·005 mm. and then had m. p. 14·5—15·5°, not raised by recrystallisation from ether at −70° (Found: C, 69·9; H, 9·0. $C_6H_{10}O_2$ required C, 63·1; H, 8·8%). The *amide* formed plates (from benzene), m. p. 138—139° (Found: N, 12·0. $C_6H_{11}ON$ requires N, 12·3%). The *anilide*, recrystallised from light petroleum (b. p. 60—80°) had m. p. 111—112·5° (Found: C, 76·0; H, 8·1. $C_{12}H_{15}ON$ requires C, 76·2; H, 7·9%). The *p*-toluidide had m. p. 100—101° after recrystallisation from light petroleum (b. p. 60—80°) (Found: C, 76·6; H, 8·3. Calc. for $C_{13}H_{17}ON$: C, 76·8; H, 8·4%). Earlier data and m. p.'s for mixtures are given in Table 1.

The infrared spectrum of methyl 3-methylpent-3-enoate prepared from the mixture of chloro-lactones corresponded to that of a mixture of pure *cis*- and *trans*-esters in the proportion 2 : 3.

3-*Methylpent*-cis-3-*en*-1-*ol*.—Reduction of methyl 3-methylpent-*cis*-3-enoate (1·7 g.) with lithium aluminium hydride gave 3-methylpent-*cis*-3-en-1-ol (1·1 g.), b. p. 56—57°/16 mm., n_D^{21} 1·4466 (Found: C, 71·8; H, 12·0%). The α-naphthylurethane had m. p. 111—112° after recrystallisation from light petroleum (b. p. 60—80°). Ansell and Gadsby [5] gave m. p. 105° for the α-napthylurethane of the "*cis*"-alcohol derived from the "*trans*"-alcohol now shown to be only 75% *trans*.

Determination of the Stereochemical Composition of Wagner's Methyl 3-*Methylpent*-trans-3-*enoate*.—Methyl 3-methylpent-3-enoate prepared by Wagner's method [4] was hydrolysed at room temperature with a slight excess of 2N-methanolic potassium hydroxide diluted with an equal volume of water. The 3-methylpent-3-enoic acid obtained distilled at 50—52°/0·05 mm. and its ultraviolet absorption spectrum showed that it contained no αβ-isomer. It solidified at 0° but was liquid at room temperature. Reduction of the acid (12 g.) by lithium aluminium hydride in ether gave 3-methylpent-3-en-1-ol (7·7 g.), b. p. 58—62° (mostly 58—59°)/16 mm., n_D^{20} 1·4466. The alcohol (3·5 g.) was added slowly, with stirring, to methanesulphonyl chloride (8 g.; two-fold excess) and pyridine (7·6 g.) at 5° at a rate to keep the temperature at 10—12°; the mixture was stirred without cooling for 1 hr. longer. Next day it was poured on ice and extracted with ether; the ether was washed with dilute sulphuric acid, sodium hydrogen carbonate solution, and water, dried, and evaporated. The *methanesulphonate* (4·7 g.) distilled at 84—86°/0·03 mm. (Found: C, 46·8; H, 7·8. $C_7H_{14}O_3S$ requires C, 47·2; H, 7·9%); it was reduced, as described above for the toluene-*p*-sulphonate, by means of lithium aluminium hydride (1 g.) in dibutyl ether (35 c.c.). The distillate boiling up to 138° (3·9 g.) smelt very strongly of thiol; it was therefore washed repeatedly with sodium hydroxide and water and dried. Distillation from a flask with an indented neck gave 1·04 g. of b. p. up to 90°; this was redistilled over sodium to give 0·8 g. of 3-methylpent-2-ene, b. p. 67—70°. The infrared spectrum corresponded to that of a mixture of 3-methylpent-2-enes containing 75% of the *trans*-isomer. The infrared spectrum of the intermediate alcohol also corresponded with that of a 3 : 1 mixture of *trans*- and *cis*-alcohols.

γ-*Chloro*-β-*methylbutyro*-β-*lactone*.—Chloroacetone (20·75 g.) in dry ether (18 c.c.) was cooled to −15°, boron trifluoride–ether complex (0·6 c.c.) added, and a slight excess of keten passed in. The mixture was worked up as described above. The residue after evaporation of the ether did not crystallise; on distillation it gave lactone (22·9 g.), b. p. 36—42°/0·003 mm. Recrystallisation from dry ether (50 c.c.) at −70° gave *γ-chloro-β-methylbutyro-β-lactone* (18·5 g.), m. p. 24—25° (Found: C, 44·4; H, 5·1. $C_5H_7O_2Cl$ requires C, 44·6; H. 5·2%).

4-*Chloro*-3-*methylhexano*-3-*lactone*.—From 3-chloropentan-2-one (14·85 g.), treated as for chloroacetone (above), a product was obtained which was heated to 40°/0·01 mm. to remove unchanged ketone. The residue (9·4 g.) did not crystallise. Chromatography of a portion, as described for 4-chloro-3-methylpentano-3-lactone, did not give crystalline fractions. The eluate was distilled to give 4-*chloro*-3-*methylhexano*-3-*lactone*, b. p. 45—50°/0·001 mm. (Found: C, 52·0; H, 6·6. $C_7H_{11}O_2Cl$ requires C, 51·7; H, 6·8%). This is presumably a mixture of stereoisomers.

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