

337. *The Synthesis of Some Olefinic Acids using Tetrahydro- β -halogeno-furan and -pyran Derivatives as Intermediates.*

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The preparation of some cyclic β -halogeno-ethers is described. The alkenols obtained by their ring scission are used in syntheses of some alk-4-, -5-, and -6-enoic acids.*

FOR a survey of the intramolecular acylation of alkenoic and ω -aryl-alkenoic acids¹ we needed a general synthesis of acids of type (I; $n = 0-2$), and adopted the ring scission, with sodium, of β -halogeno-ethers (IIa or b) which gives structurally and, in some cases, stereochemically pure alkenols² (III; $n = 0$ or 1); these alkenols were converted into the halides and thence into the required acids.^{2,3} With the exception of tetrahydrofurfuryl chloride, however, we have studied only compounds of type (IIa), as those of type (IIb) are difficult of access.⁴

In this way we have obtained acids of type (I; $n = 0-2$) where $R = R' = H$ and R and/or $R' = Me$. Except for three of these (I; $n = 2$, $R = H$, $R' = Me$; $n = 1$ and 2, $R = R' = Me$), they have been obtained before, but not always by methods free from stereochemical and structural ambiguity. In this respect our method is an improvement.

For the synthesis of pent-4-enoic acid, 3-chlorotetrahydrofuran was obtained by reduction of 2 : 3-dichlorotetrahydrofuran with lithium aluminium hydride (Crombie, Harper, Gold, and Stokes⁵ reported the same reaction using "inverse" addition). Ring scission

* Geneva nomenclature, $CO_2H = 1$.

¹ Ansell and Brown, *Chem. and Ind.*, 1956, 984.

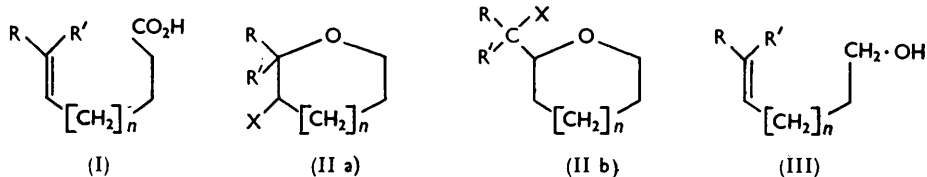
² Crombie and Harper, *J.*, 1950, (a) 1707, (b) 1714.

³ Cf. Linstead and Rydon, *J.*, 1934, 1995; Braude, Linstead, and Wooldridge, *J.*, 1956, 3074.

⁴ Cf. *inter al.*, Eglinton, Jones, and Whiting, *J.*, 1952, 2873.

⁵ Crombie, Harper, Gold, and Stokes, *J.*, 1956, 136.

with sodium gave but-3-en-1-ol,^{5,6} the preparation of which by other methods is difficult.⁷ For conversion of this alcohol by phosphorus tribromide and pyridine into 1-bromobut-1-ene, different authors,^{7,8,9,10} using different techniques, have reported yields ranging from 30% to 78%, the lower yields probably being due, in part, to formation of dibromide (see below); but 4-chlorobut-1-ene is obtained in good yield by use of thionyl chloride in the presence of a catalytic quantity of pyridine,⁹ a method probably owing its success to the



slowness of addition of hydrogen chloride to the isolated double bond (see below). Carboxylation of this halide *via* the Grignard reagent gave pent-4-enoic acid, which has been previously prepared from ethyl allylmalonate¹¹ and by carboxylation of the bromide obtained from cyclopropylmethanol.¹²

For the preparation of hex-5-enoic and hept-6-enoic acid, tetrahydrofurfuryl chloride was required. Its preparation¹³ from the alcohol, pyridine, and thionyl chloride has been improved so that it involves only a catalytic amount of pyridine, with or without benzene as solvent, does not require redistilled alcohol, avoids a tedious extraction, and still gives consistently high yields of easily purified material. From the ring scission product, pent-4-en-1-ol, 5-chloropent-1-ene, and thence hex-5-enoic and hept-6-enoic acid were prepared. Both acids have been previously prepared through alkenylmalonic esters.^{3,10}

Unless $R = R'$ (in I and III), geometrical isomerism can arise. Now stereochemically pure *trans*-alk-4-en-1-ols are obtainable from either *cis*- or *trans*-2-alkyl-3-chlorotetrahydropyrans;^{2a} *trans*-hex-4-en-1-ol, from 3-chloro-2-methyltetrahydropyran,^{2a} was converted into 6-chlorohex-2-ene in 80% yield and thence into *trans*-hept-5-enoic and *trans*-oct-6-enoic acid. The former acid has been previously prepared by carboxylation of the Grignard reagent obtained from 1 : 4 : 5-tribromohexane.¹⁴ The preparation of 6-bromohex-2-ene from hex-4-en-1-ol, using phosphorus tribromide and pyridine, proceeds in only 50% yield, and gives also 15% of a dibromide, probably 1 : 4-dibromohexane. Hunsdiecker¹⁵ reports a similar by-product in the preparation of 1-bromohex-3-ene, but suggests that it is a bromohexanol.

The route to the alk-4-enoic acids requires alk-3-en-1-ols. Preparation of these by ring scission of *cis*-2-alkyl-3-chlorotetrahydrofurans gives a mixture of the *cis*- and *trans*-isomers whilst *trans*-2-alkyl-3-chlorotetrahydrofurans yield mixtures containing mainly *trans*-isomers.^{2b,5} Partial hydrogenation of alk-4-yn-1-ols, which are obtainable, although in poor yield, from 2-alkyl-3-chlorotetrahydrofurans on treatment with sodamide,^{4,5} is an alternative route. We have utilised both routes. Careful fractionation of 3-chlorotetrahydro-2-methylfuran gave the *cis*- and *trans*-isomers in the ratio of 2 : 1 (in agreement with Crombie *et al.*⁵). The latter was converted, *via trans*-pent-3-en-1-ol (87% *trans*⁵),

⁶ Cf. Yur'ev, Voronkov, Gragerov, and Kondrat'eva, *Zhur. obschei Khim.*, 1948, **18**, 1804; Yur'ev and Gragerov, *ibid.*, p. 1811; *Chem. Abs.*, 1949, **43**, 3818.

⁷ Birch and McAllan, *J.*, 1951, 2556.

⁸ Arbusov and Khmel'nitskiĭ, *Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk*, 1952, 766; *Chem. Abs.*, 1953, **47**, 5927; Levina and Viktorova, *Vestnik Moskov. Univ.*, **6**, No. 2, *Ser. Fiz.-Mat. i Estestven. Nauk*, 1951, **1**, 89; *Chem. Abs.*, 1952, **46**, 8605.

⁹ Roberts and Mazur, *J. Amer. Chem. Soc.*, 1951, **73**, 2509.

¹⁰ Gaubert, Linstead, and Rydon, *J.*, 1937, 1971; cf. ref. 3.

¹¹ Linstead and Rydon, *J.*, 1933, 580.

¹² Smith and McKenzie, *J. Org. Chem.*, 1950, **15**, 74.

¹³ Brooks and Snyder, *Org. Synth.*, Coll. Vol. III, 1955, p. 698; cf. ref. 4.

¹⁴ von Braun and Sobecki, *Ber.*, 1911, **44**, 1039.

¹⁵ Hunsdiecker, *Ber.*, 1942, **75**, 460.

into substantially pure *trans*-hex-4-enoic acid,* and the former, with sodamide in liquid ammonia gave pent-3-yn-1-ol in 50–55% yield—substantially higher than that reported as resulting from the *cis-trans*-mixture.^{4,5} Partial hydrogenation of the pentynol gave *cis*-pent-3-en-1-ol which was converted *via* the toluene-*p*-sulphonate and iodide into *cis*-hex-4-enoic acid. This somewhat indirect route was used lest phosphorus tribromide or thionyl chloride should promote acid-catalysed *cis-trans*-isomerisation, as has been observed in the preparation of *cis*-oleyl bromide.¹⁷ That the acid and iodide were stereochemically pure was shown by the absence of an absorption peak at 10.4 μ in their infrared spectra. The *cis*-acid so obtained was identical with that prepared by Crombie and Harper.¹⁶

An alternative route to *trans*-alk-4-enoic acids involves the oxidation of the readily available *trans*-alk-4-en-1-ols. Except, however, in the case of alk-2-en-1-ols, the oxidation of alkenols has rarely been used for the preparation of unsaturated aldehydes or acids. Jacobson,¹⁸ however, has reported the rapid, low-temperature chromic acid oxidation of oct-4-en-1-ol to oct-4-enal in 35% yield. With representative alk-4-en-1-ols, in our hands, this method gave even lower yields of aldehyde, with substantial amounts of ester or lactone. *tert*-Butyl chromate¹⁹ proved equally unsatisfactory, whilst use of the chromium trioxide-pyridine complex²⁰ is limited to compounds of high molecular weight such as steroids.

For the synthesis of acids where R = R' = Me, 4 : 5-dihydro-2-methylfuran was prepared by the dehydrohalogenation of tetrahydrofurfuryl bromide²¹ (attempts to use tetrahydrofurfuryl chloride gave unreproducible yields of tetrahydro-2-methylenefuran⁴), and 5 : 6-dihydro-2-methylpyran from the readily accessible 5 : 6-dihydro-2-methylpyran-3-carboxylic acid.²² The dichloro-compounds obtained by the addition of chlorine to these unsaturated compounds, although sometimes obtained pure, have been reported as unstable.^{23,24} We have found it better to use the dibromides prepared at -50° ; below this temperature the addition product tended to crystallise. The halides were not isolated, but were coupled with methylmagnesium bromide to yield the expected 3-halogenotetrahydro-2 : 2-dimethyl-furan or -pyran. The former product was accompanied by a higher-boiling material corresponding in analysis to a dihalogenotetrahydrodimethylfuran, whilst the latter was accompanied by lower-boiling, halogen-free material corresponding to tetrahydro-2 : 2-dimethylpyran. The formation of these by-products may be rationalised by the annexed scheme, which is given for the pyran series. Montaigne²⁴ records the formation of low-boiling by-product, presumably 2-ethyltetrahydro-2-methylpyran, in the reaction between ethyl Grignard reagent and 2 : 3-dichlorotetrahydro-2-methylpyran.

The ring scission of 3-chloro- or 3-bromo-tetrahydro-2-methyl-furan or -pyran proceeded equally readily (contrast the low yields obtained²⁵ on ring scission of 2-alkyl-3-bromotetrahydropyrans), to yield 4-methylpent-3-en-1-ol and 5-methylhex-4-en-1-ol, which from their infrared spectra were free from the *isopropenyl* isomer. [Higher yields of the alkenols might have been obtained by ring scission of the *crude* reaction mixtures (cf. refs. 5 and 26).]

* Crombie and Harper²⁵ showed that the acid prepared by this route (*via* 5-bromopent-2-ene) was the pure *trans*-form by comparing it with a sample prepared from (*trans*-)crotyl chloride.¹⁶ Our acid is identical with theirs.

¹⁶ Crombie and Harper, *J.*, 1950, 1152.

¹⁷ Loev and Dawson, *J. Amer. Chem. Soc.*, 1956, **78**, 1180.

¹⁸ Jacobson, *ibid.*, 1950, **72**, 1489.

¹⁹ Oppenauer and Oberrauch, *Anales Asoc. quim. argentina*, 1949, **37**, 246.

²⁰ Poos, Arth, Beyler, and Sarett, *J. Amer. Chem. Soc.*, 1953, **75**, 422; Poos, Johns, and Sarett, *ibid.*, 1955, **77**, 1026.

²¹ Paul and Tchelitcheff, *Bull. Soc. chim. France*, 1950, **17**, 520.

²² Perkin, *J.*, 1887, **51**, 702.

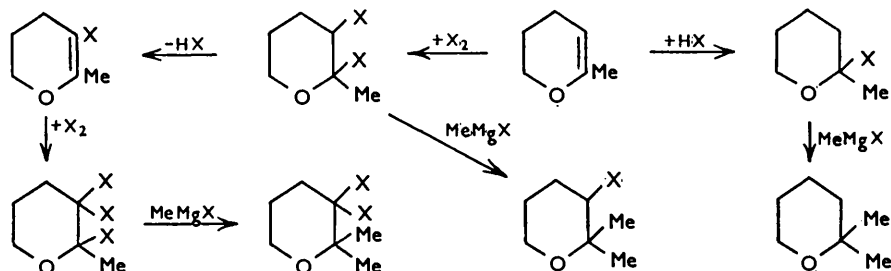
²³ Londergan, Hause, and Schmitz, *J. Amer. Chem. Soc.*, 1953, **74**, 4456.

²⁴ Montaigne, *Ann. Chim. (France)*, 1954, **9**, 310.

²⁵ Brandon, Derfer, and Boord, *J. Amer. Chem. Soc.*, 1950, **72**, 2120.

²⁶ Riobé, *Compt. rend.*, 1955, **240**, 1648.

An attempt to convert 5-methylhex-4-en-1-ol into the chloride by using thionyl chloride and a catalytic amount of pyridine gave instead a good yield of 1 : 5-dichloro-5-methylhexane, formed by addition of the liberated hydrogen chloride to the highly reactive double bond. This alkenol, and the analogous 4-methylpent-3-en-1-ol, reacted normally with toluene-*p*-sulphonyl chloride and pyridine (no hydrogen chloride is actually set free



in this reaction²⁷), to yield the toluene-*p*-sulphonates, which were converted into their iodides as for *cis*-pent-4-en-1-ol. (Attempts to prepare the alkenyl chloride or bromide by using lithium chloride or calcium bromide in boiling ethanol gave only mixtures of the required halide with the ether formed by solvolysis.) Both the iodides and the acids derived from them (5-methylhex-4-enoic, 6-methylhept-5-enoic, and 7-methyloct-6-enoic acid) showed weak infrared absorption at 11.2 μ , indicating the presence of a small amount of the *isopropenyl* isomer. Presumably the isomerisation occurs during formation of the toluene-*p*-sulphonate. 5-Methylhex-4-enoic acid has been previously prepared from isoprene hydrobromide,^{11, 28a} ethyl 5-hydroxy-5-methylhexanoate,^{28b} and, together with 5-methylhex-5-enoic acid,^{28c} by thermal addition of acrylic acid to *isobutene*.^{28d}

The present approach is immediately applicable to the synthesis of compounds derived from more elaborate Grignard reagents, *e.g.*, 2-arylethylmagnesium halides.¹

EXPERIMENTAL

3-Chlorotetrahydrofuran.—2 : 3-Dichlorofuran (306 g.) (prepared by chlorination of tetrahydrofuran in methylene chloride; cf. Crombie and Harper^{2b}) was added during 40 min. to a stirred suspension of lithium aluminium hydride (30 g.; 85% purity) in dry ether (1 l.) so that vigorous refluxing was maintained. The mixture was stirred and heated for a further 1 hr., and then decomposed by water (300 c.c.). The ethereal layer was washed with 10% sodium hydroxide solution and water, and dried (CaCl₂). The product was fractionally distilled through a column (2 × 30 cm.) packed with Dixon gauzes, to yield 3-chlorotetrahydrofuran (186 g., 81%), b. p. 129–130°, n_D^{20} 1.4545. Crombie *et al.*,⁵ record b. p. 59–61°/30 mm., n_D^{20} 1.4532.

The late M. E. Selleck in this Laboratory, in agreement with Birch and McAllan,⁷ found that the preparation of this alcohol from trioxymethylene and allyl chloride or bromide gives a poor yield (5–10%). (Cf. however Linstead and Rydon³ who report a 45% yield.) The alternative preparation⁷ by dehydration of butane-1 : 3-diol necessitates a careful fractional distillation.

Tetrahydrofurfuryl Chloride.—Thionyl chloride (170 g., 1.43 moles) was added slowly, with stirring, to an ice-cooled mixture of tetrahydrofurfuryl alcohol (133 g., 1.30 moles), pyridine (0.7 c.c.), and benzene (160 c.c.). When about one-half of the reagent had been added (30 min.), evolution of gas began; the remainder was then run in rapidly, without cooling, and the mixture was cautiously heated to gentle reflux, with continuous stirring. This was maintained till

²⁷ Edgell and Parts, *J. Amer. Chem. Soc.*, 1955, **77**, 4899.

²⁸ (a) Simon, Kaufmann, and Schinz, *Helv. Chim. Acta*, 1946, **29**, 1133; (b) Samokhvalov, Miropol'skaya, Vakulova, and Preobrazhenskii, *Doklady Akad. Nauk S.S.S.R.*, 1952, **84**, 1179; *Chem. Abs.*, 1953, **47**, 3277; (c) Eschenmoser and Frey, *Helv. Chim. Acta*, 1952, **35**, 1660; (d) Albisetti, Fisher, Hogsed, and Joyce, *J. Amer. Chem. Soc.*, 1956, **78**, 2637.

acid gases were no longer freely liberated (45 min.), the mixture was then cooled and poured on excess of ice. After thorough washing (water, 5% aqueous sodium carbonate, and water) and drying (MgSO_4), the solvent was fractionated through a short column, and the residue distilled, to give tetrahydrofurfuryl chloride (115 g., 74%), b. p. 43—44°/13 mm., n_D^{17} 1.4566. Eglinton, Jones, and Whiting⁴ record b. p. 55—56°/20 mm., n_D^{20} 1.4552.

Larger runs (up to 15 moles) were most conveniently effected without a solvent; the yields were the same.

5-Chloropent-2-ene.—This halide, b. p. 104—105°, $n_D^{18.5}$ 1.4309, was prepared in 65% yield on a 4-molar scale from pent-4-en-1-ol as for tetrahydrofurfuryl chloride. Paul²⁹ records b. p. 105°/747 mm., n_D^{19} 1.4305.

Hex-5-enoic Acid.—A solution of the Grignard reagent prepared from 5-chloropent-2-ene (42 g., 0.40 mole) and magnesium (10 g., 0.42 g.-atom) in ether (200 c.c.) was poured on a large excess of stirred, finely powdered solid carbon dioxide. After most of the carbon dioxide had evaporated, water (300 c.c.) and light petroleum (b. p. 40—60°; 200 c.c.) were added, followed by sufficient 10*N*-hydrochloric acid (24 c.c., 0.24 mole) to give two clear phases. The organic layer was separated and the aqueous phase extracted with light petroleum (3 × 100 c.c.). The combined petroleum solutions were extracted with a saturated solution of sodium hydrogen carbonate (42 g., 0.5 mole), and the alkaline solution so obtained back-extracted with light petroleum and then acidified at 0° by stirring it with an equal volume of light petroleum and cautiously adding 5*N*-hydrochloric acid (100 c.c.). After extraction, etc., as before, distillation gave hex-5-enoic acid (34 g., 74%), b. p. 95—96°/7 mm., n_D^{20} 1.4338. Linstead and Rydon³ record b. p. 107°/17 mm., n_D^{20} 1.4343.

cis- and trans-3-Chlorotetrahydro-2-methylfuran.—The crude reaction product²⁶ from 2 : 3-dichlorotetrahydrofuran (784 g., 5.56 moles) and methylmagnesium bromide (from 168 g. of magnesium) was fractionated through a column (total reflux, variable take-off; 2.5 × 90 cm.; packed with 1/16" Dixon gauze rings). *trans*-3-Chlorotetrahydro-2-methylfuran (178 g., 27%), b. p. 129—131°, n_D^{20} 1.4412—1.4425, was collected, followed by an intermediate cut (32 g., 5%), and then the *cis*-isomer (278 g., 42%), b. p. 145—146°. (This last cut quickly darkened on storage.) Total yield, 74%; proportion of *trans*-isomer in product, 39% (Crombie *et al.*^{26, 5} report for the *trans*-isomer, b. p. 130°, n_D^{19} 1.4424, and for the *cis*, b. p. 147°, with 35% of *trans*-isomer in the product).

Pent-3-yn-1-ol.—*cis*-3-Chlorotetrahydro-2-methylfuran (121 g., 1.0 mole) was added dropwise during 30 min. to a stirred suspension of sodamide (from 80 g. of sodium and a catalytic quantity of ferric nitrate) in liquid ammonia (2.5 l.). After a further 15 hours' stirring, ammonium chloride (150 g.) was added, followed by sufficient water (*ca.* 500 c.c.) to give two clear phases. The product was continuously-extracted with ether, the dried (MgSO_4) solution evaporated, and the residue distilled, to give the required alkynol (46 g., 55%), b. p. 152—153°, n_D^{20} 1.4540. Crombie and Harper³⁰ report b. p. 154—157°, n_D^{20} 1.4554. Slightly lower yields (50%) were obtained in 0.4-mole runs.

cis-1-Iodopent-3-ene.—Pent-3-en-1-ol (44 g., 0.51 mole) (from pent-3-yn-1-ol by hydrogenation over Lindlar catalyst; cf. ref. 30) was added during 40 min. to a stirred slurry of toluene-*p*-sulphonyl chloride (108 g., 0.5 mole) in pyridine (53 c.c.) at 20° ± 2°. After a further 2 hours' stirring at room temperature the mixture was poured on ice, and the precipitated oil extracted with ether, washed with excess of 25% sulphuric acid, water, saturated aqueous sodium hydrogen carbonate, and water, and dried (K_2CO_3). Evaporation gave *cis*-pent-3-enyl toluene-*p*-sulphonate (110 g.). This, together with sodium iodide (77 g., 0.51 mole), was stirred in acetone (750 c.c.) under reflux for 2 hr. After cooling to 0°, the precipitated sodium toluene-*p*-sulphonate was filtered off and washed with ether, and the solvents were evaporated. The residue was washed with 10% aqueous sodium thiosulphate and water, dried (MgSO_4), and distilled, to yield *cis*-1-iodopent-3-ene (60 g., 67%), b. p. 53—55°/15 mm., n_D^{20} 1.5227. Goethals³¹ records b. p. 53.6°/20 mm., n_D^{20} 1.5153. The α -*naphthalide* of *cis*-hex-4-enoic acid (prepared *via* the Grignard reagent) formed needles (from aqueous alcohol), m. p. 104—105° (Found: C, 80.2; H, 6.9; N, 5.7. $\text{C}_{16}\text{H}_{17}\text{ON}$ requires C, 80.3; H, 7.2; N, 5.85%).

trans-1-Chloropent-3-ene.—This halide, b. p. 108—109°, n_D^{20} 1.4360, was prepared in 75% yield from *trans*-pent-3-en-1-ol²⁶ as for tetrahydrofurfuryl chloride. Goethals³¹ records b. p.

²⁹ Paul, *Ann. Chim. (France)*, 1932, **18**, 338.

³⁰ Crombie and Harper, *J.*, 1950, 873.

³¹ Goethals, *Bull. Soc. chim. belges*, 1937, **46**, 409.

107—107.5°/755 mm., n_D^{20} 1.4310, for 1-chloropent-3-ene. The α -naphthalide of *trans*-hex-4-enoic acid (prepared as above) formed needles (from aqueous alcohol), m. p. 134—135° (Found : C, 80.3; H, 7.1; N, 6.1%).

cis- and *trans*-Hex-4-enoic Acid.—These acids were prepared as for hex-5-enoic acid from *cis*-1-iodopent-3-ene (in 38% yield) and *trans*-1-chloropent-3-ene (in 68% yield) and had respectively : b. p. 112—113°/17 mm., n_D^{20} 1.4406 (*p*-bromophenacyl ester, m. p. 51—52°); b. p. 110—111°/17—18 mm., n_D^{20} 1.4385, m. p. -2° to +1° (*p*-bromophenacyl ester, m. p. 81—82°). Crombie and Harper¹⁶ record for the *cis*-isomer, b. p. 106°/14 mm., n_D^{20} 1.4403 (*p*-bromophenacyl ester, m. p. 55°), and for the *trans*-isomer b. p. 108—109°/19 mm., m. p. -1° to +1°, n_D^{20} 1.4387 (*p*-bromophenacyl ester, m. p. 82.5°).

trans-6-Bromohex-2-ene.—Hex-4-en-1-ol^{2a} (212 g., 2.12 moles) and pyridine (47 g., 0.60 mole) were added dropwise with stirring during 2 hr. to phosphorus tribromide (229 g., 0.85 mole) at -5°, then left at room temperature for 18 hr., after which volatile material (b. p. < 120°/20 mm.) was distilled off. The distillate was washed (water, 10% sodium carbonate solution, and water), dried (MgSO₄), and fractionally distilled, to yield *trans*-6-bromohex-2-ene (204 g., 59%), b. p. 48—51°/20 mm., n_D^{20} 1.4680 (Ansell and Selleck³² found b. p. 42°/12 mm., n_D^{20} 1.4695), together with a dibromohexane (42 g., 15%), b. p. 97—98°/11 mm., n_D^{20} 1.5054 (Found : C, 29.7; H, 5.0. Calc. for C₆H₁₂Br₂ : C, 29.5; H, 5.0%) (cf. 1 : 4-dibromohexane,³³ b. p. 98.2—98.4°/11—12 mm., n_D^{15} 1.5084, and 1 : 5-dibromohexane,³⁴ b. p. 106—107°/15 mm., n_D^{15} 1.5072).

trans-6-Chlorohex-2-ene.—This chloride, b. p. 134—135°, n_D^{20} 1.4418, was prepared as for tetrahydrofurfuryl chloride, from *trans*-hex-4-en-1-ol in a 79% yield, on a 3-molar scale (Found : C, 61.2; H, 9.2. C₆H₁₁Cl requires C, 60.7; H, 9.4%). The α -naphthalide of *trans*-hept-5-enoic acid (prepared *via* the Grignard reagent) formed felted needles (from aqueous alcohol), m. p. 89—90° (Found : C, 80.9; H, 7.7; N, 5.55. C₁₇H₁₉ON requires C, 80.6; H, 7.6; N, 5.5%).

trans-Hept-5-enoic acid.—This acid, b. p. 121—122°/17 mm., n_D^{20} 1.4424, was prepared as for hex-5-enoic acid from the preceding chloride in a 59% yield on a 1-molar scale (Found : C, 66.2; H, 9.5. Calc. for C₇H₁₂O₂ : C, 65.6; H, 9.45%); Braun and Sobceki¹⁴ give b. p. 117°/11 mm. Its *p*-bromophenacyl ester, plates (from aqueous alcohol), has m. p. 62—63° (Found : C, 55.6; H, 5.5. C₁₃H₁₇O₃Br requires C, 55.4; H, 5.3%).

Ethyl trans-Hex-4-enylmalonate.—*trans*-6-Chlorohex-2-ene (166 g., 1.4 moles) was added during 30 min. to a warm, stirred solution of sodiomalonic ester [from ethyl malonate (216 g.) and sodium (30 g.) in alcohol (300 c.c.)], in the solution then stirred and boiled for 10 hr. After cooling, the precipitated salt was filtered off and washed with alcohol. Distillation of the combined alcoholic solutions gave *ethyl trans*-hex-4-enylmalonate (254 g. 75%), b. p. 143—144°/10 mm., n_D^{20} 1.4402 (Found : C 64.7; H, 9.3. C₁₃H₂₂O₄ requires C, 64.4; H, 9.15%).

trans-Hex-4-enylmalonic Acid.—The above ester (242 g., 1 mole) was added with stirring to a cold solution of potassium hydroxide (267 g.) in water (350 c.c.), followed by sufficient alcohol to produce homogeneity. After 24 hr. at room temperature the solution was cooled to 0° and made just acid to Congo-red with concentrated hydrochloric acid. The precipitated *trans*-acid was extracted with ether, the solvent removed, and the residual oil desiccated *in vacuo* over silica gel; it solidified. Crystallisation from benzene gave the pure acid (130 g., 70%), m. p. 115—116° (Found : C, 57.9; H, 7.3. C₉H₁₄O₄ requires C, 58.05; H, 7.6%).

trans-Oct-6-enoic Acid.—The above malonic acid (65 g., 0.35 mole) was decarboxylated at 150—160° for 5 hr. The product was dissolved in saturated sodium hydrogen carbonate solution and, after extraction with ether, the solution was acidified under light petroleum as described for hex-5-enoic acid. The final distillation gave *trans*-oct-6-enoic acid (42 g., 85%), b. p. 147—148°/23 mm., 74—76°/1 mm., n_D^{20} 1.4455 (Found : C, 67.3; H, 9.7. C₈H₁₄O₂ requires C, 67.6; H, 9.9). Its *p*-bromophenacyl ester formed plates (from alcohol), m. p. 70—71° (Found : C, 56.5; H, 5.4; Br, 23.8. C₁₈H₁₉O₃Br requires C, 56.6; H, 5.7; Br, 23.6%), and the *phenylhydrazide* plates (from aqueous alcohol), m. p. 94—95° (Found : C, 72.7; H, 8.2; N, 11.9. C₁₄H₂₀ON₂ requires C, 72.4; H, 8.7; N, 12.1%).

3-Chlorotetrahydro-2 : 2-dimethylfuran.—A solution of 4 : 5-dihydro-2-methylfuran³¹ (126 g., 1.5 moles) in ether (370 c.c.) was cooled to -60° and chlorine passed in until 103 g. (1.45 moles) were absorbed (*ca.* 45 min.). The resulting white solution was added from a cooled dropping funnel to a stirred solution of methylmagnesium bromide (from 45 g. of magnesium) in ether

³² Ansell and Selleck, unpublished work.

³³ Glacé, *Compt. rend.*, 1944, **218**, 283.

³⁴ Paul, *Bull. Soc. chim. France*, 1938, **5**, 919.

(1400 c.c.) at such a rate (*ca.* 30 min.) that gentle refluxing was maintained. The mixture was stirred for a further 15 min., then poured on crushed ice and ammonium chloride (43 g., 0.8 mole). On vigorous stirring two clear phases were obtained; the ethereal solution was separated and the aqueous layer extracted with ether. Distillation of the dried (MgSO_4) combined extracts gave 3-chlorotetrahydro-2:2-dimethylfuran (60 g., 30%), b. p. 47—49°/19 mm., n_D^{21} 1.4450 (Found: C, 53.8; H, 8.35; Cl, 26.6. $\text{C}_6\text{H}_{11}\text{OCl}$ requires C, 53.6; H, 8.2; Cl, 26.4%), and 3:3-dichlorotetrahydro-2:2-dimethylfuran (44 g., 17%), b. p. 88—89°/19 mm., n_D^{20} 1.4791 (Found: C, 43.3; H, 6.35. $\text{C}_6\text{H}_{10}\text{OCl}_2$ requires C, 43.6; H, 6.0%). The latter compound darkened slowly. Use of methylene chloride in the chlorination stage, or of an even larger excess of Grignard reagent in the coupling reaction, did not materially improve the yield or alter the relative amounts of the products.

3-Bromotetrahydro-2:2-dimethylfuran.—A stirred solution of 4:5-dihydro-2-methylfuran (152 g., 1.81 moles) in ether (400 c.c.) was cooled to -55° and treated dropwise with dry bromine until (after *ca.* 40 min.) flocks of solidified bromine remained undissolved. About 202 g. (1.30 moles) of bromine were thus used. The white suspension was added to methylmagnesium bromide and worked up, as for 3-chlorotetrahydro-2:2-dimethylfuran, to yield 3-bromotetrahydro-2:2-dimethylfuran (145 g., 45%), b. p. 58—60°/14 mm., n_D^{20} 1.4741 (Found: Br, 44.9. $\text{C}_6\text{H}_{11}\text{OBr}$ requires Br, 44.6%), and 3:3-dibromotetrahydro-2:2-dimethylfuran (95 g., 20%), b. p. 66—70°/0.3—0.5 mm. (too unstable to be obtained analytically pure).

4-Methylpent-3-en-1-ol.—A solution (50 c.c.) of 3-halogenotetrahydro-2:2-dimethylfuran (1.0 mole) in ether (500 c.c.) was added to a stirred suspension of sodium sand (51 g.) in ether (100 ml.). After a few minutes, reaction set in; the remainder of the solution was then added at such a rate that vigorous refluxing was maintained and the viscous mixture was stirred under reflux for a further 1 hr. Water was then added until two clear phases were obtained; the ethereal layer was separated, the aqueous phase extracted with ether, and the combined extracts were dried (MgSO_4) and fractionated, to give 85—87% yields of 4-methylpent-3-en-1-ol, b. p. 157—158° (62—63°/13 mm.), n_D^{19} 1.4452. Willimann and Schintz³⁵ give b. p. 98—100°/130 mm., n_D^{21} 1.4432; Bruylants and Dewael³⁶ give b. p. 157°, n_D^{20} 1.4455.

5-Iodo-2-methylpent-2-ene.—This iodide was prepared in 63—75% yield (0.5-molar scale) from 4-methylpent-3-en-1-ol via the toluene-*p*-sulphonate, as for *cis*-1-iodopent-3-ene. Distillation from silver powder gave a colourless product, b. p. 62—63°/13 mm., n_D^{17} 1.5246 (Found: C, 34.3; H, 5.5; I, 60.8. $\text{C}_6\text{H}_{11}\text{I}$ requires C, 34.3; H, 5.3; I, 60.4%). A compound ascribed this structure is reported³⁷ to have b. p. 176—180° (decomp.). The derived *thiuronium picrate*, yellow rhombs (from alcohol), had m. p. 136—137° (Found: C, 40.4; H, 4.7; N, 18.4. $\text{C}_{13}\text{H}_{17}\text{O}_7\text{N}_3\text{S}$ requires C, 40.3; H, 4.4; N, 18.1%). The α -naphthalide of 5-methylhex-4-enoic acid (prepared *via* the Grignard reagent) formed needles [from light petroleum (b. p. 100—120°)], m. p. 115—116° (Found: C, 80.2; H, 7.3; N, 5.9. $\text{C}_{17}\text{H}_{19}\text{ON}$ requires C, 80.6; H, 7.6; N, 5.5%).

5-Methylhex-4-enoic Acid.—This acid, obtained in 61% yield (on 1-molar scale) from 5-iodo-2-methylpent-2-ene as for hex-5-enoic acid, had b. p. 98—99°/5 mm., m. p. -29° to -28° , n_D^{20} 1.4470. Linstead and Rydon¹¹ record b. p. 105°/5 mm., m. p. -33° , n_D^{20} 1.4461.

3-Chlorotetrahydro-2:2-dimethylpyran.—This compound, prepared in 38—45% yield (on a 1—2-molar scale) from 3:4-dihydro-6-methylpyran^{23,24} as for 3-chlorotetrahydro-2:2-dimethylfuran, had b. p. 56—57°/10 mm., n_D^{20} 1.4606 (Found: C, 56.2; H, 9.0. $\text{C}_7\text{H}_{13}\text{OCl}$ requires C, 56.6; H, 8.8%). It was accompanied by a small amount of camphoraceous-smelling material of low b. p., which was halogen-free, saturated towards hydrogen in the presence of Adams catalyst, but decolorised bromine in carbon tetrachloride. A sample redistilled from sodium had b. p. 121—122°, n_D^{16} 1.4272 (Found: C, 73.7; H, 12.7. Calc. for $\text{C}_7\text{H}_{14}\text{O}$: C, 73.6; H, 12.4%). For tetrahydro-2:2-dimethylpyran Smith *et al.*³⁸ report b. p. 118—120°, n_D^{20} 1.4300.

3-Bromotetrahydro-2:2-dimethylpyran.—This compound, prepared in 55—61% yield (on a 1—2-molar scale) from 3:4-dihydro-6-methylpyran as for 3-bromotetrahydro-2:2-dimethylfuran, had b. p. 83—84°/20 mm., n_D^{20} 1.4884 (Found: Br, 41.9. $\text{C}_7\text{H}_{13}\text{OBr}$ requires Br, 42.4%).

³⁵ Willimann and Schinz, *Helv. Chim. Acta*, 1952, **35**, 2401.

³⁶ Bruylants and Dewael, *Bull. Sci. Acad. Roy. Belg.*, 1928, **14**, 140.

³⁷ Kishner and Klawikordow, *J. Russ. Phys. Chem. Soc.*, 1911, **43**, 595; *Chem. Zentr.*, 1911, **82**, 363; Favorskaya and Fridman, *J. Gen. Chem. (U.S.S.R.)*, 1945, **15**, 421; *Chem. Abs.*, 1946, **40**, 4655.

³⁸ Smith, Norton, and Ballard, *J. Amer. Chem. Soc.*, 1951, **73**, 5273.

5-Methylhex-4-en-1-ol.—Ring scission of either 3-bromo- or 3-chloro-tetrahydro-2:2-dimethylpyran (1 mole) as for 3-chlorotetrahydro-2:2-dimethylfuran gave *5-methylhex-4-en-1-ol* (78–84%), b. p. 82–83°/20 mm., n_D^{19} 1.4520 (Found: C, 73.1; H, 12.3. $C_7H_{14}O$ requires C, 73.6; H, 12.4%). The α -*naphthylurethane* formed needles [from light petroleum (b. p. 80–100°)], m. p. 62–63° (Found: N, 5.2. $C_{18}H_{21}O_2N$ requires N, 4.9%).

2:6-Dichloro-2-methylhexane.—Treatment of *5-methylhex-4-en-1-ol* (80 g., 0.4 mole) with thionyl chloride as for tetrahydrofurfuryl alcohol gave *2:6-dichloro-2-methylhexane* (72 g., 72%), b. p. 86–87°/15 mm., n_D^{20} 1.4539 (Found: C, 49.8; H, 8.50; Cl, 41.7. $C_7H_{14}Cl_2$ requires C, 49.7; H, 8.4; Cl, 41.9%). This compound gave an immediate precipitate when shaken with aqueous silver nitrate solution.

6-Iodo-2-methylhex-2-ene.—This *iodide*, prepared in 62–73% yield (0.5-molar scale) from *5-methylhex-4-en-1-ol* as for *cis-1-iodopent-3-ene*, had b. p. 80–82°/13 mm., 50–52°/5 mm., n_D^{16} 1.5180 (Found: C, 37.4; H, 6.0; I, 57.2. $C_7H_{13}I$ requires C, 37.5; H, 5.9; I, 56.6%). The derived *thiuronium picrate* formed bright yellow laths (from alcohol), m. p. 138–139° (Found: C, 41.9; H, 4.9; N, 16.9. $C_{14}H_{19}O_7N_2S$ requires C, 41.9; H, 4.8; N, 17.4%). The α -*naphthalide* of *6-methylhept-5-enoic acid* formed needles (from methyl alcohol), m. p. 117–118° (Found: N, 5.3. $C_{18}H_{21}ON$ requires N, 5.2%).

6-Methylhept-5-enoic Acid.—This *acid*, prepared in 36% yield from the preceding *iodide* (0.3 mole) as for *hex-5-enoic acid*, had b. p. 129–130°/12 mm., 88–92°/0.5–1 mm., n_D^{20} 1.4502 (Found: C, 67.4; H, 9.8. $C_8H_{14}O_2$ requires C, 67.6; H, 9.9%), and gave a *p-bromophenacyl ester*, plates (from alcohol), m. p. 50–51° (Found: C, 56.9; H, 5.8. $C_{16}H_{18}O_3Br$ requires C, 56.6; H, 5.7%), and a *phenylhydrazide*, plates (from alcohol), m. p. 84–85° (Found: C, 72.6; H, 8.4; N, 12.1. $C_{14}H_{20}ON_2$ requires C, 72.4; H, 8.7; N, 12.1%).

Ethyl 5-Methylhex-4-enylmalonate.—This *ester*, b. p. 144–145°/10 mm., n_D^{11} 1.4489, was prepared in 75% yield from *6-iodo-2-methylhex-2-ene* (0.4 mole) as for ethyl *trans-hex-4-enylmalonate* (Found: C, 65.9; H, 9.5. $C_{14}H_{24}O_4$ requires C, 65.6; H, 9.4%).

5-Methylhex-4-enylmalonic Acid.—This *acid*, needles [from benzene–light petroleum (b. p. 40–60°)], m. p. 78–79°, was prepared in 69% yield from the corresponding ester (0.3 mole) as for *trans-hex-4-enylmalonic acid* (Found: C, 60.4; H, 8.1. $C_{10}H_{16}O_4$ requires C, 60.0; H, 8.05%).

7-Methyloct-6-enoic Acid.—This *acid*, b. p. 99–101°/0.7 mm., n_D^{20} 1.4513, was prepared in 84% yield from the above malonic acid (0.2 mole) as for *trans-oct-6-enoic acid* (Found: C, 69.1; H, 10.4. $C_9H_{16}O_2$ requires C, 69.2; H, 10.3%). Its *phenylhydrazide*, plates (from aqueous alcohol), had m. p. 87–88° (Found: C, 72.7; H, 8.75; N, 11.1. $C_{18}H_{22}ON_2$ requires C, 73.1; H, 9.0; N, 11.4%), and the *p-bromophenacyl ester* formed needles (from methanol), m. p. 56–57° (Found: C, 58.0; H, 6.4. $C_{17}H_{21}O_3Br$ requires C, 57.8; H, 6.0%).

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