

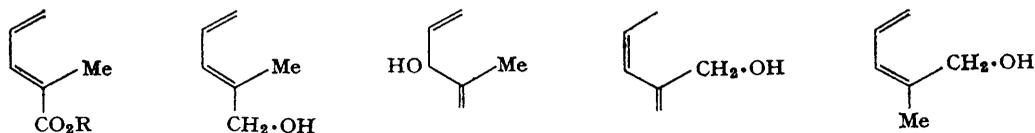
1107. Studies with 2-Methylpenta-2,4-dienoic Acid and Related Compounds.

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The dienoic acid (*Ia*) and its ethyl ester (*Ib*) did not undergo Diels–Alder additions with either *p*-benzoquinone or cyclohex-2-enone. Reduction of the ester (*Ib*) with lithium aluminium hydride gave the unsaturated alcohol (II). The product (II) reported by earlier workers was a mixture of (VII) and other isomers.

HOUSE and RASMUSSEN¹ (cf. ref. 2) stated that methyl 2-methylpenta-2,4-dienoate (*Ib*) prepared by a Wittig reaction is the *trans*-isomer. Reduction of the ethyl ester (*Ic*) with lithium aluminium hydride gave a dienol (II) whose structure was confirmed by catalytic reduction to 2-methylpentanol, also obtained by hydrogenation of the ester (*Ic*) followed by reduction with lithium aluminium hydride. Spectra are consistent with assigned structures.

Our 2-methylpentanol is identical with material prepared by Heilbron, Jones, McCombie, and Weedon³ by hydrogenation of a dienol to which they assigned the structure (II) (stereochemistry unspecified), obtained by acidifying the alcohol (III). Their alcohol (II) formed an adduct with maleic anhydride, but ours does not; it polymerises, making it useless for syntheses⁴ of diterpenoid acids; the α -naphthylurethanes have different melting points.



(*Ia*; R = H)

(II)

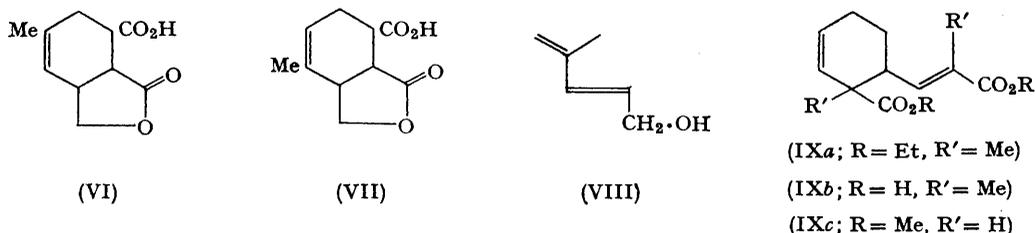
(III)

(IV)

(V)

(*Ib*; R = Me)

(*Ic*; R = Et)



(IXa; R = Et, R' = Me)

(IXb; R = H, R' = Me)

(IXc; R = Me, R' = H)

Two possible explanations of the differences between these dienols are: (a) their alcohol might be the geometrical isomer (V) of ours; (b) in their rearrangement of (III), the intermediate alcohol (II) or (V) was produced and then converted into (IV). We repeated the earlier work³ and confirmed all the results except that (III) rearranges much more rapidly than reported, but this may reflect differences in laboratory temperature. Our spectra confirm the structures of the divinylmethanol (III) and its acetylenic precursor. The rearrangement product contains at least two compounds.

The Diels–Alder adduct of maleic anhydride and the rearrangement product from (III) was converted into its methyl ester which was then hydrogenated. The infrared spectra of the adduct and its derivatives revealed a γ -lactone. The nuclear magnetic resonance spectrum

¹ H. O. House and G. H. Rasmusson, *J. Org. Chem.*, 1961, **26**, 4278.

² L. D. Bergelson and M. M. Shemyakin, *Tetrahedron*, 1963, **19**, 149.

³ I. M. Heilbron, E. R. H. Jones, J. T. McCombie, and B. C. L. Weedon, *J.*, 1945, **84**.

⁴ S. K. Roy and D. M. S. Wheeler, *J.*, 1963, 2155.

of the methyl ester showed (a) a double bond to which hydrogen and a methyl group are attached; (b) a methylene group connecting the lactone oxygen to a carbon bearing 1 hydrogen. The spectrum of the dihydro-compound confirmed these; the signal of the vinyl proton disappeared and that of the methyl group shifted to higher field and became a doublet. The only structures for the adduct consistent with its spectroscopy are (VI) and (VII).⁵ Although formation of (VII) would be difficult to explain, we re-prepared it;⁵ in spite of the similarity of melting points it was different from our adduct. Thus, the latter must be (VI) formed from the dienol (VIII). As the rearrangement product was also hydrogenated to 2-methylpentanol, rearrangement had given a mixture of (VIII) and at least one of the dienols (II), (IV), and (V), as confirmed by nuclear magnetic resonance: the methyl group signal is an unsymmetrical doublet, and, more significantly, the signal for the protons of the hydroxymethyl group is a singlet with a small doublet, clearly due to (VIII), beside it. From the intensities of peaks and the yield of (VI) in the Diels–Alder reaction, we concluded that the dienol (VIII) represents about 35% of the rearranged material. The remainder probably consists of (II), (V), and perhaps (IV). We do not think that much (IV) is present because the dienol (II) under the conditions of rearrangement of (III) did not rearrange to other dienols; with stronger acid the product was 2-methylpent-2-enal, formed *via* the $\beta\gamma$ -isomer. Since Heilbron's adduct³ had been formed from (VIII), rather than (II) or (V), we did not attempt to resolve the mixture from (III) into its components. As the rearrangement of (III) gave a mixture (previously³ believed to be essentially one compound), the conclusion⁶ that allylic rearrangements of divinylmethanols initially take place irreversibly and exclusively in one direction is probably untrue. Further, the quantitative results⁷ deduced from the rearrangement of (III), and some related reactions, will need to be modified.

Neither the acid (Ia) nor the ester (Ic) underwent Diels–Alder additions with *p*-benzoquinone or cyclohex-2-enone.⁸ When the ester (Ic) was sealed with *p*-benzoquinone in nitrogen at 150–160°, quinol was formed, presumably by hydrogen transfer⁹ involving oxidation of (Ic). Blank experiments returned benzoquinone; apparently the thermal decomposition of benzoquinone previously reported¹⁰ required air. The ester (Ic) dimerised on heating. We assign structure (IXa) (consistent with our spectral data) by analogy with the structure (IXc) established for the dimer of methyl penta-2,4-dienoate.^{8,11}

We originally hoped that the acids or esters (I) or the alcohol (II) or their geometrical isomers would, by Diels–Alder reaction with benzoquinone, give an adduct suitable for the synthesis of diterpenoid acids. Our work and House and Rasmusson's show that the acids and esters (I), the dienol (II) and (probably) the dienol (V) are not suitable; the geometrical isomers of (Ia) and its esters may be.

EXPERIMENTAL

General directions are in ref. 4. Nuclear magnetic resonance spectra were measured in carbon tetrachloride on a Varian Associates A-60 spectrometer. The Perkin-Elmer model 154 gas chromatography instrument had 12-ft. columns of silicone grease on Chromasorb. Light petroleum had b. p. 30–60°.

Ethyl 6-(2-Ethoxycarbonylprop-1-enyl)-1-methylcyclohex-2-enecarboxylate (IXa).—Ethyl 2-methylpenta-2,4-dienoate (Ic), prepared analogously to the methyl ester,¹ had b. p. 70–71°/10 mm.; λ_{\max} 253 m μ (ϵ 23,000); ν_{\max} 3520, 1692, 1635, 1600, 1375, 1345, 1105, and 995 cm.⁻¹; δ 1.30 (triplet 3 H), 1.93 (singlet 3 H), 4.18 (quartet 2 H), 5.20–5.70 (multiplet 2 H), and 6.32–7.28 (multiplet 2 H).

A solution of the ester (Ic) (2.0 g.) in xylene (5 ml.) containing quinol (trace) was heated in a

⁵ G. W. H. Cheeseman, Sir Ian Heilbron, E. R. H. Jones, F. Sondheimer, and B. C. L. Weedon, *J.*, 1949, 2031.

⁶ E. A. Braude and C. J. Timmons, *J.*, 1950, 2007.

⁷ E. A. Braude, J. A. Coles, E. A. Evans, and C. J. Timmons, *Nature*, 1956, 177, 1167.

⁸ H. O. House and G. H. Rasmusson, *J. Org. Chem.*, 1963, 28, 27.

⁹ L. M. Jackman, *Adv. Org. Chem.*, 1960, 2, 329.

¹⁰ B. Scheid, *Annalen*, 1883, 218, 195; W. N. Hartley and A. G. G. Leonard, *J.*, 1909, 95, 34; H. Stoltzenberg and M. Stoltzenberg-Bergius, *Z. physiol. Chem.*, 1920, 111, 1.

¹¹ K. Alder and W. Vogt, *Annalen*, 1950, 570, 190.

sealed tube in nitrogen for 70 hr. at 140°. The dimeric ester (IXa) after work up had b. p. 90—92°/0.2 mm.; λ_{\max} 219 m μ (ϵ 14,100); ν_{\max} 1705, 1650, 1375, and 1105 cm.⁻¹; δ 1.0—2.3 (complex structure 17 H), 3.80—4.40 (multiplet 4 H), 5.65 (multiplet 2 H), and 6.62 (doublet 1 H).

Alkaline hydrolysis of the diester (IXa) (0.2 g.), gave the corresponding *diacid* (IXb) which, after isolation by extraction with ethyl acetate, crystallized from ether—light petroleum in needles (0.1 g.), m. p. 202—205°; λ_{\max} 220 m μ , (ϵ 14,100); ν_{\max} 3600—2300, 1690, 1645, 1460, 1420, 1395, 1280, 1255, 1130, 1075, 1020, 950, and 755 cm.⁻¹ (Found: C, 64.2; H, 7.0; O, 28.4. C₁₂H₁₆O₄ requires C, 64.3; H, 7.2; O, 28.5%).

trans-2-Methylpenta-2,4-dienol (II).—Lithium aluminium hydride in ether was added slowly to a solution of the ester (Ic) (3.2 g.) and quinol (trace) in ether. When the mixture had been stirred for 38 hr. at room temperature, it was treated at 0° with water, and filtered. The residue was refluxed with ether and the combined ethereal solutions were dried (Na₂SO₄). The ether was removed under reduced pressure; the *dienol* (II) distilled at 67—68°/10 mm. (yield 2.0 g.); λ_{\max} 231 m μ (ϵ 23,100), ν_{\max} 3580, 3440, 1662, 1610, 1460, 1385, 1145, 995, 955, and 910 cm.⁻¹; ν_{\max} (pure) 3300, 3080, 3040, 2900, 2860, 1810, 1662, 1609, 1455, 1425, 1390, 1295, 1215, 1150, 1075, 995, 960, 945, 910 (sh), 905, and 825 cm.⁻¹; δ 1.75 (singlet 3 H), 3.32 (singlet 1 H), 3.95 (singlet 2 H), 4.95 (single 1 H), 5.20 (quartet 1 H), and 5.80—6.90 (multiplet 2 H); vapour-phase chromatography at 175° showed one peak (retention time 6.8 min.). The α -naphthylurethane of the alcohol crystallized from light petroleum in needles, m. p. 87—88°; ν_{\max} 3455, 1935, 1730, 1605, 1585, 1495, 1350, 1325, 1105, 1000, 975, 910, and 875 cm.⁻¹ (Found: C, 76.2; H, 6.0; N, 5.4. C₁₇H₁₇NO₂ requires C, 76.4; H, 6.4; N, 5.2%). The α -naphthylurethane of Heilbron's dienol (ref. 3) had m. p. 59—60°.

The dienol, on catalytic hydrogenation, gave 2-methylpentanol, δ 0.6—2.0 (complex 11 H), 3.3 (doublet 2 H), 4.0 (broad 1 H), identified by its α -naphthylurethane, m. p. 73—75°, which was identical (infrared spectra and mixed m. p.) with an authentic sample.³

Rearrangement of the Dienol (II).—The dienol (II) (1.0 g.) and quinol (trace) were stirred in nitrogen with aqueous sulphuric acid (4%) for 64 hr. at room temperature. The product, isolated by extraction with ether, distilled at 38—40°/10 mm. to yield 2-methylpent-2-enal (0.35 g.); λ_{\max} 229 m μ (ϵ 13,100) and 315 m μ (ϵ 31); ν_{\max} 1680, 1645, 1365, 1310, and 1000 cm.⁻¹; δ 1.12 (triplet 3 H), 1.71 (singlet 3 H), 2.36 (multiplet 2 H), 6.38 (triplet 1 H), and 9.43 (singlet 1 H); vapour-phase chromatography at 170° showed a single peak (retention time 6.4 min.). The dinitrophenylhydrazone (deep-red plates from methanol) had m. p. 162—163° (lit.,¹² 159°), λ_{\max} 375 m μ (ϵ 28,600) (Found C, 52.0; H, 5.0; N, 20.3. Calc. for C₁₂H₁₄N₄O₄: C, 51.8; H, 5.1; N, 20.1%).

With a shorter reaction time (20 hr.) and more-dilute sulphuric acid (2%), starting material was recovered. When the reaction mixture was kept for 56 hr. in 4% sulphuric acid the product was a mixture; the spectra (u.v., i.r., and n.m.r.) showed clearly that besides 2-methylpent-2-enal, the $\beta\gamma$ -isomer, 2-methylpent-3-enal, was also present (about 40%).

2-Methylpent-1-en-4-yn-3-ol. This, prepared by the method of Heilbron *et al.*,³ had b. p. 73—75°/50 mm. (lit.,³ 74°/50 mm.); ν_{\max} 3600, 2112, 1650, 1425, 1372, 1000, and 905 cm.⁻¹; δ (pure) 1.82 (split singlet 3 H), 2.65 (doublet 1 H), 4.40 (singlet 1 H), 4.80 and 4.90 (2 H), and 5.20 (1 H); vapour-phase chromatography at 175° showed retention time 3.2 min., purity better than 99%.

2-Methylpenta-1,4-dien-3-ol (III).—The previous compound was hydrogenated in the presence of a poisoned palladium catalyst; the divinylmethanol (III) had b. p. 66—67°/50 mm. (lit.,³ 66°/50 mm.); ν_{\max} 3600, 3450, 1850, 1820, 1650, 1425, 1375, 988, and 905 cm.⁻¹; δ 1.63 (singlet, 3 H), 3.5 (singlet 1 H), 4.45 (doublet 1 H), 4.8 (split singlet 1 H), 4.95—6.1 (multiplet 4 H); vapour-phase chromatography at 174° showed 1 peak, retention time 2.8 min. (purity 99%).

The α -naphthylurethane crystallized from light petroleum in needles, m.p. 88—89° (lit.,³ 88—89°); ν_{\max} 3440, 1730, 1640, 1600, 1575, 1475, 1370, 1345, 1100, 1000, 962, and 910 cm.⁻¹

Acid-catalyzed Rearrangement of the Alcohol (III).—The alcohol (III) (1 g.) was stirred at room temperature (25°) with aqueous sulphuric acid (2%; 10 ml.) containing a trace of quinol in nitrogen for 6½ hr. The mixture was saturated with sodium chloride and the product extracted with ether. Removal of solvent followed by distillation gave the product (0.42 g.), b. p. 76—77°/16 mm., (lit.,³ 72—74°/15 mm.); λ_{\max} 228 m μ (ϵ 25,800); ν_{\max} 3615, 3440, 1815, 1657, 1612, 1455, 1382, 992, 972, and 900 cm.⁻¹; ν_{\max} (pure) 3300, 3080, 2900, 2840, 1660, 1615 (sh), 1605, 1460, 1425, 1385, 1215, 1150, 1075, 995, 975, 905, and 820 cm.⁻¹; δ 1.75 (doublet 3 H), 3.8 (singlet 1 H) 4.0 (singlet and doublet 2 H), 4.95 (split singlet, 1 H), 5.2 (quartet 1 H), 5.75—6.9 (multiplet 2 H).

¹² Sir Ian Heilbron, "Dictionary of Organic Compounds," O.U.P., New York, 1953, Vol. III, 377.

The α -naphthylurethane crystallized in needles (from light petroleum), m. p. 59—60° (lit.,³ 59—60°); ν_{\max} . 3420, 1925, 1725, 1655, 1627, 1600, 1580, 1490, 1395, 1345, 1315, 1100, 995, 965, and 960 cm^{-1} .

The product, on hydrogenation, gave 2-methylpentanol identified by its α -naphthylurethane, identical with a sample from Sir Ewart Jones³ and with the urethane we obtained from the hydrogenation product of (II). When the rearrangement reaction was kept longer a carbonyl-containing product was obtained in addition to the dienol.

Reaction of the Rearrangement Product with Maleic Anhydride.—The reaction was carried out as previously described.³ The product 1,3,3a,4,5,7a-hexahydro-6-methyl-3-oxoisobenzofuran-4-carboxylic acid (VI) (0.45 g. from 1.3 g. of dienol) crystallized from methanol-ether-light petroleum and had m. p. 183—184° (lit.,³ 181—182°); ν_{\max} . (KBr) 3500—2600, 1769, 1697, 1672, 1490, 1450, 1435, 1385, 1322, 1280, 1240, 1220, 1195, 1180, 1157, 1132, 1120, 1055, 995, 970, 917, 882, 852, 715, and 675 cm^{-1} ; δ (in deuterated tetrahydrofuran) 1.7 (singlet 3 H), 2.18 (doublet 2 H), 2.5—3.7 (multiplet 3 H), 3.85—4.45 (AB quartet with further splitting of 2 peaks, 2 H), 5.35 (broad peak 1 H), and 8.75 (broad peak 1 H) (Found: C, 61.3; H, 6.1; O, 32.5. Calc. for $\text{C}_{10}\text{H}_{12}\text{O}_4$: C, 61.2; H, 6.2; O, 32.6%). The adduct in methanol was methylated with diazomethane. The *methyl ester* crystallized from ether in needles, m. p. 90.5—91°; ν_{\max} . 2910, 1775, 1740, 1672, 1450, 1385, 1347, 1325, 1312, 1280, 1170, 1140, 1120, 1020, 1000, and 965 cm^{-1} ; δ 1.7 (singlet 3 H), 2.8 (doublet 2 H), 2.5—3.6 (multiplet 3 H), 3.75 (singlet 3 H), 3.8—4.5 (AB quartet with 2 peaks further split, 2 H), and 5.32 (broad peak 1 H) (Found: C, 62.8; H, 6.6; O, 30.4. $\text{C}_{11}\text{H}_{14}\text{O}_4$ requires C, 62.8; H, 6.7; O, 30.4%).

Methyl Dihydro-ester.—The methyl ester of (VI) (100 mg.) in ethyl acetate was hydrogenated in the presence of palladized charcoal until the uptake of hydrogen stopped. The product *methyl octahydro-6-methyl-3-oxoisobenzofuran-4-carboxylate* (100 mg.; m. p. 83—86°) crystallized from ether-light petroleum in needles, m. p. 85—86°; ν_{\max} . 2910, 1772, 1737, 1462, 1380, 1337, 1132, 1080, 1017, and 984 cm^{-1} ; δ 1.0 (doublet 3 H), 1.1—3.0 (multiplet 7 H), 3.25 (triplet 1 H), 3.8 (singlet 3 H), 3.85—4.5 (AB quartet with further splitting of 2 peaks, 2 H), (Found: C, 62.4; H, 7.6; O, 30.1. $\text{C}_{11}\text{H}_{16}\text{O}_4$ requires C, 62.25; H, 7.6; O, 30.15%).

trans-3-Methylpenta-2,4-dienol.—By hydrogenation of *trans*-3-methylpent-2-en-4-yn-1-ol, this was obtained as a colourless oil, b. p. 79—80°/32 mm. (lit.⁵ 68—71°/15 mm.); ν_{\max} . (in carbon tetrachloride) 3612, 3338, 2970, 2930, 2880, 1804, 1608, 1446, 1412, 1381, 1296, 1180, 1084, 1060, 989, 900, and 856 cm^{-1} ; δ 1.72 (singlet 3 H), 4.16 (doublet 2 H), 4.38 (singlet 1 H), 4.88—5.25 (quartet 2 H), 5.59 (triplet 1 H), and 6.13—6.60 (quartet 1 H).

1,3,3a,4,5,7a-Hexahydro-7-methyl-3-oxoisobenzofuran-4-carboxylic Acid (VII).—The adduct of the above dienol and maleic anhydride crystallized from methanol in rhombs, m. p. 181.5—182.5° (lit.,⁵ 182—183°) [m. p. depressed on addition of adduct (VI)]; ν_{\max} . (KBr disc) 3500—2600, 1761, 1708, 1473, 1451, 1375, 1326, 1311, 1288, 1254, 1216, 1194, 1167, 1129, 1093, 1061, 1035, 1017, 995, 980, 957, 874, 815, 779, 742, 682, and 639 cm^{-1} . The adduct in methanol was methylated with diazomethane. The *methyl ester* crystallized from ether-light petroleum in needles, m. p. 76—77°, ν_{\max} . (KBr disc) 3500—2600, 1776, 1732, 1475, 1448, 1436, 1392, 1380, 1361, 1329, 1304, 1280, 1237, 1211, 1166, 1156, 1131, 1089, 1061, 1039, 1023, 1007, 981, 908, 881, 867, 809, 789, 751, 743, 730, 683, and 640 cm^{-1} ; δ (CDCl_3) 1.75 (singlet 3 H), 2.1—2.5 (multiplet 2 H), 2.6—3.7 (multiplet 3 H), 3.76 (singlet 3 H), 4.0—4.6 (multiplet, probably AB quartet with further splitting, 2 H) (Found: C, 62.5; H, 6.8; O, 30.35. $\text{C}_{11}\text{H}_{14}\text{O}_4$ requires C, 62.8; H, 6.7; O, 30.4%).

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