209. *Unsaturated Lactones. Part I. (Researches on Acetylenic Compounds. Part X.) A New Route to Growth-inhibitory αβ-Ethylenic γ- and δ-Lactones.*

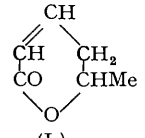
By L. J. Haynes and E. R. H. Jones.

Certain aspects of the literature concerning growth-inhibitory substances present in animal and plant tissues are briefly reviewed. It seems probable, though not yet established with certainty, that the natural active agents are αβ-unsaturated lactones. The methods employed for the synthesis of such compounds are discussed and a new general procedure for the preparation of αβ-unsaturated γ- and δ-lactones from acetylenic hydroxy-acids is described. A number of lactones synthesised by this route are evaluated according to their inhibitory effects on the germination of cress seeds.

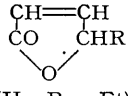
Unsaturated lactone groupings are frequently encountered as characteristic structural features of many naturally occurring compounds exhibiting diverse types of physiological action. Attention has been drawn to this structural similarity, observed for example in the heart aglycones, fish poisons of the furocoumarin type, antibiotics such as penicillic acid, patulin, etc., by several workers (Houben–Weyl, " Die Methoden der Organischen Chemie," Leipzig, 1930, III, 682; Oxford, *Ann. Rev. Biochem.*, 1945, **14**, 749; Lauger, Martin, and Muller, *Helv. Chim. Acta*, 1944, **27**, 892; Veldstra, *Enzymologia*, 1944, **11**, 373). The scope and siguificance of this correlation have been considerably extended and emphasised by the discovery by Medawar, Robinson, and Robinson (*Nature*, 1943, **151**, 195) that an unsaturated lactone is also effective in controlling the differential growth of animal tissues. Moreover, Kuhn, Jerchel, Moewus, Müller, and Lettré (*Naturwiss.*, 1943, **31**, 468) have observed that a similar lactone, and some related compounds, also exert growth inhibitory effects in the plant kingdom, especially on seed and pollen germination.

Heaton (*J. Path. Bact.*, 1926, **29**, 293; 1929, **32**, 565) demonstrated the presence, in tissue extracts of most adult mammalian organs and also in malt, of a substance which inhibited the growth *in vitro* of explanted chick fibroblasts at concentrations at which the proliferation of epithelial tissues proceeded unchecked. He suggested that the cessation in adults of connective tissue growth, as contrasted with the continued reproduction of epithelial tissue, was to be attributed to the controlling action of this differential growth inhibitor. This work has since been confirmed by Brues, Jackson, and Aub (*Proc. Soc. Exp. Biol. Med.*, 1936, **34**, 270) and by Medawar (*Quart. J. Exp. Physiol.*, 1937, **27**, 147), the last showing that its action extended to all mesenchyme derivatives and that the factor was also present in a variety of ungerminated cereals and in oranges.

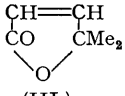
By vigorous steam distillation of a commercial malt extract, Medawar, Robinson, and Robinson (*loc. cit.*) isolated a small quantity of a material, exhibiting the differential growth inhibitory action, for which they suggested the formula $C_6H_8O_2$ and an unsaturated lactone structure. The lactone (I) of pent-1-en-4-ol-1-carboxylic acid (δ-$\Delta^{\alpha\beta}$-hexenolactone) was synthesised in small yield by condensation of acetaldol with malonic acid and was shown to possess growth-inhibitory properties, although to a less marked degree than the product isolated from malt.



(I.)



(II; R = Et)
(VI; R = *n*-Pr)
(VII; R = Me)



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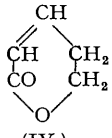

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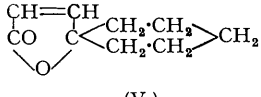

(V.)

A dextrorotatory lactone (the so-called parasorbic acid) to which structure (I) was assigned had been isolated from the berries of the mountain ash (*Sorbus aucuparia*) (Hofmann, *Annalen*, 1859, **110**, 129; Doebner, *Ber.*, 1894, **27**, 344). Kuhn and Jerchel (*Ber.*, 1943, **76**, 413; see also Veldstra, Thesis, Utrecht, 1935) rigidly established the structure of this compound as (I) rather than (II) by hydrogenation to δ-hexolactone, and they synthesised the *dl*-lactone by treatment of 3 : 5-dibromohexoic acid (obtained by the addition of hydrogen bromide to sorbic acid) with hot water. Following the observations of Medawar, Robinson, and Robinson, the action of the *dl*-lactone on the growth of chick fibroblasts *in vitro* was examined (Kuhn, Jerchel, *et al.*, *loc. cit.*) and the synthetic *dl*-compound was found to possess practically the same activity as the natural *d*-parasorbic acid.

The term " blastocholine " was given by Köckemann (*Ber. deut. bot. Ges.*, 1934, **52**, 523) to a material of unknown structure, present in various ripe fruits, which suppressed the germination of cress seeds (*Lepidium sativum*). Blastocholine was found to be both ether and water soluble, insoluble in light petroleum, and stable at 100° in aqueous solution but sensitive to peroxide and alkalis. Köckemann noted the similarity in chemical and physical properties with the auxins, but he showed that blastocholine exhibited no auxin-like activity. Kuhn, Jerchel, *et al.* (*loc. cit.*) showed that both the natural and the synthetic lactone (I) completely inhibit the germination of cress seeds at a concentration of 0·1% and although germination occurs at 0·01% the root lengths are definitely less than those of the controls. With coumarin, at this latter concentration, only 2% of the seeds germinate. It had previously been observed by Cameron (*J. Physical Chem.*, 1910, **14**, 422) that both coumarin and daphnetin prevent the growth of wheat, and Sigmund (*Biochem. Z.*, 1914, **62**, 339) had noted the inhibitory effect of aesculetin and daphnetin on seed germination. Veldstra and Havinga (*Rec. Trav. chim.*, 1943, **62**, 841) have confirmed and extended the results of Kuhn, Jerchel, *et al.*, showing that the isomeric lactone (II) and β-angelicalactone exert similar inhibitory properties, and that 5 : 6- and 7 : 8-benzcoumarins exhibit definite inhibitory effects. It should be noted that the concentrations at which these lactones are effective are very much higher than those required to produce comparable effects with substituted phenoxyacetic acids, etc. (Slade, Templeman, and Sexton, *Nature*, 1945, **155**, 497; Templeman and Sexton, *ibid.*, 1945, **156**, 630).

Certain suggestions have been made as to the possible mode of action of these unsaturated lactones, but it should be emphasised that as yet there is no certainty (as was pointed out by Medawar, Robinson, and Robinson, *loc. cit.*) that hexenolactone (I) is the actual natural growth inhibitor present in either plant extracts [cf. Köckemann, *loc. cit.*; Larsen, *Planta* (*Z. wiss. Biol.*), 1939, **30**, 160] or animal tissues. Medawar *et al.* (*loc. cit.*) suggested the possibility that the growth inhibitory material might interfere with pantothenic acid metabolism,

Light-absorption Data for Unsaturated Lactones.

(in alcoholic solutions)

	λ A.	ε.		λ A.	ε.
(I)	2110	10,000	Compare:		
(III)	2130 *	7,000	$CH_3 \cdot CH(OH) \cdot CH_2 \cdot CH{=}CH \cdot CO_2Et$...	2150	10,000
(IV)	2140	8,000	$CH_2OH \cdot CH_2 \cdot CH{=}CH \cdot CO_2Et$	2130	9,500
(V)	2140	10,000	$CH_3 \cdot CH(OH) \cdot CH_2 \cdot C{\equiv}C \cdot CO_2Et$	2160	6,000
(VI)	2140 *	8,000	$CH_2OH \cdot CH_2 \cdot C{\equiv}C \cdot CO_2Et$	2130	5,000
(VII)	2140	10,000			

* Maxima, in other cases end absorption only.

but the presence of this acid was found to have no effect on the activity of hexenolactone. Hauschka (*Nature*, 1944, **154**, 769) who employed the flat-worm, *Dugesia tigrina* [which develops a characteristic Y-shaped lesion in M/20,000-hexenolactone (I) solutions], in extensive biological tests, observed that α- and β-alanine and glutathione exerted protective influences at certain concentrations. In later studies (Hauschka, Toennies, and Swain, *Science*, 1945, **101**, 383) the appreciable hexenolactone antagonism found with cysteine led to the postulate that it interfered with thiol metabolism essential to enzyme function. Evidence was produced to show that a direct and reversible interaction occurs between cysteine and the lactone (I) (cf. Geiger and Conn, *J. Amer. Chem. Soc.*, 1945, **67**, 112; Cavallito and Haskell, *ibid.*, p. 1991). Veldstra and Havinga (*loc. cit.*; *Enzymologia*, 1943—1945, **11**, 373) believe that unsaturated lactones function as permeability regulators for protoplasmic membranes, in this way antagonising the action of the plant growth hormones, and they have shown that in the pea test coumarin counteracts the effect of naphthaleneacetic acid.

Two main methods have previously been employed for the synthesis of simple unsaturated lactones. (*a*) Conversion of keto-acids into βγ- or γδ-ethylenic lactones by heating with either acetyl chloride or acetic anhydride (see, *e.g.*, Lukes, *Coll. Czech. Chem. Comm.*, 1929, **1**, 461; Kuhn and Jerchel, *loc. cit.*; Desai, *J.*, 1932, 1079; Qadrat-I-Khuda, *J.*, 1929, 1913; Swain, Todd, and Waring, *J.*, 1944, 548; Wolff, *Annalen*, 1885, **229**, 249; Thiele, Tischbein, and Lossow, *ibid.*, 1901, **319**, 180; Gilmour, *J.*, 1914, **105**, 73; Jacobs and Scott, *J. Biol. Chem.*, 1931, **93**, 139; Cavallito and Haskell, *loc. cit.*). The βγ-unsaturated γ-lactones can generally be isomerised to the more stable αβ-unsaturated compounds by heating with bases, *e.g.*, triethylamine (*e.g.*, Thiele *et al.*, *loc. cit.*; Lukes, *loc. cit.*; Pauly, Gilmour, and Will, *Annalen*, 1914, **403**, 152). (*b*) Simultaneous hydrolysis and dehydrobromination of dibromo-acids, usually on boiling with water or sodium carbonate solution (see, *e.g.*, Lespieau, *Bull. Soc. chim.*, 1905, **33**, 466; Kuhn and Jerchel, *loc. cit.*; Jacobs and Scott, *J. Biol. Chem.*, 1930, **87**, 601; Cavallito and Haskell, *loc. cit.*).

Recently a third method has been extensively exploited for the synthesis of substances containing a β-substituted αβ-unsaturated γ-lactone structure (β-substituted $\Delta^{\alpha\beta}$-butenolides), such as is present in the heart aglycones (Paist, Blout, Uhle, and Elderfield, *J. Org. Chem.*, 1941, **6**, 273). This method consists of the application of the Reformatsky reaction, using bromoacetate, to α-methoxy- or -acetoxy-ketones, the γ-lactones being obtained on hydrolysis (Ruzicka, Reichstein, and Fürst, *Helv. Chim. Acta*, 1941, **24**, 76; Ruzicka, Plattner, and Fürst, *ibid.*, p. 716 and many later papers; Elderfield *et al.*, *J. Org. Chem.*, 1941, **6**, 260, 270, 273, 289; 1942, **7**, 362, 374, 383, 444).

None of these methods is especially convenient for the synthesis of αβ-unsaturated δ-lactones. It has now been found that the semi-hydrogenation of acetylenic hydroxy-acids (Haynes and Jones, this vol., p. 503)

provides a useful route to αβ-unsaturated lactones; syntheses of typical γ- and δ-lactones are illustrated below.

$$Me_2CO + HC{\equiv}CH \longrightarrow Me_2C(OH)\cdot C{\equiv}CH \longrightarrow Me_2C(OH)\cdot C{\equiv}C\cdot CO_2H \longrightarrow \text{(III.)}$$

$$\begin{array}{l} CH_2\cdot CH_2 \\ \diagdown\,O\,\diagup \end{array} + HC{\equiv}CH \longrightarrow HO\cdot CH_2\cdot CH_2\cdot C{\equiv}CH \longrightarrow HO\cdot CH_2\cdot CH_2\cdot C{\equiv}C\cdot CO_2H \longrightarrow \text{(IV.)}$$

The partial hydrogenation proceeds readily in methanol solution employing a 5% palladium–barium sulphate catalyst; Raney nickel is insufficiently selective for this purpose. In order to avoid contamination of the product with saturated lactone, it has been found preferable to interrupt the hydrogenation after up to about 90% of the theoretical amount of hydrogen has been absorbed. Distillation of the residue obtained after removal of catalyst and solvent gives the lactones directly in yields of 65—80%, the non-distillable residue consisting of unhydrogenated acid together with polymeric lactone formed by intermolecular dehydration. Although it is convenient to use the crude acetylenic hydroxy-acids obtained by carboxylation of the ethynylcarbinols (Haynes and Jones, *loc. cit.*), care has to be taken to avoid contamination with sulphur compounds, and purification of the " AnalaR " benzene employed in the Grignard reactions by shaking at room temperature with Raney nickel (*e.g.*, Bougault, Cattelain, and Chabrier, *Bull. Soc. chim.*, 1940, **7**, 780) was found to be a useful precaution. In two cases the alternative procedure of semihydrogenating the esters of the acetylenic hydroxy-acids to the corresponding *ethylenic hydroxy-esters*, followed by acidic hydrolysis to the lactones (I and IV), has also been employed. The overall yields, however, are lower than those obtained by the more direct route.

The structure of the C_5 carbinol produced by the reaction of propylene oxide with sodium acetylide in liquid ammonia has been definitely established as pent-1-yn-4-ol, by hydrogenation to methylpropylcarbinol, oxidised subsequently to methyl propyl ketone.

Apart from the limitation imposed on the synthesis of δ-lactones by the availability of oxides, this synthetic method is of general applicability for the γ- and δ-substituted compounds. It has the additional advantage that, by utilising the additive properties of the acetylenic acids, β-amino-, -alkoxyl, -mercapto- and similar substituents can readily be introduced and a range of such γ- and δ-lactones has been made in this manner.

Light-absorption data for the various lactones described in this paper are given in the accompanying Table. It will be noted that, as has been observed by other workers (*inter al.*, Ruzicka, Plattner, and Heusser, *Helv. Chim. Acta*, 1942, **25**, 435; 1944, **27**, 186), αβ-unsaturated lactones exhibit high-intensity absorption at the extreme end of the usual ultra-violet range, maxima only being discernible in certain cases. Similar absorption properties have been found for αβ-ethylenic and αβ-acetylenic esters, but in the latter case the intensities are considerably lower.

These lactones are at present being examined by Dr. Medawar for their selective growth-inhibitory properties on explanted chick fibroblasts. Their effects on the inhibition of the germination of cress seeds are tabulated below.

Effect of Unsaturated Lactones on the Germination of Cress Seeds.

	Concentration, g. per c.c.				
	1 : 2000.	1 : 4000.	1 : 8000.	1 : 16,000.	1 : 32,000.
	Seeds germinated (%).				
(I)	0	0	88	100	96 *
(IV)	0	0	0	80	100 *
(VII)	0	64	96	96	96
(VI)	16	76	92	100	100
(III)	80	100	92	100	100
(V)	32	64	84	100	100

All tests were carried out in 8 cm. Petri dishes, 25 seeds being uniformly distributed on a filter paper moistened with 5 c.c. of solution. The solutions were made up in a 0·3% sodium phosphate buffer solution (pH 7) all tests being controlled by blank determinations using an equal volume of the buffer solution. The percentage of seeds germinated was noted after 72 hours, germination being allowed to proceed at room temperature in the absence of direct sunlight. In all cases, except those marked with an asterisk, the root and stem growth of the germinated seeds was less than in the blank experiments.

Experimental.

Pent-1-yn-4-ol [cf. Kreimeier, U.S.P. 2,106,182 (1938)].—To a solution of sodium acetylide in liquid ammonia (6 l.), prepared from sodium (230 g.) (Heilbron, Jones, and Weedon, *J.*, 1945, 83), propylene oxide (725 g.) which had been freshly distilled through a 24 cm. Dufton column, was added during one hour. The acetylene flow (*ca.* 100 c.c. per minute) was maintained for a further 2 hours and then stopped; the reaction mixture was stirred for 24 hours and then the reaction was interrupted by the gradual addition of ammonium chloride (600 g.) during one hour. After addition of ether (2 l.) the mixture was stirred for a further 30 minutes to complete the decomposition of the sodio-compound. The ammonia was allowed to evaporate overnight and the residual suspension of salt extracted thoroughly with ether. Evaporation of the dried (Na_2SO_4) ethereal solution gave a residue which on distillation in nitrogen gave pent-1-yn-4-ol (305 g.), b. p. 74·6°/100 mm., $n_D^{16°}$ 1·4406 (Found: C, 71·6; H, 9·55. Calc. for C_5H_8O: C, 71·4; H, 9·6%). (Kreimeier, *loc. cit.*, describes methyl-β-ethynylethanol, b. p. 125—130°, $n_D^{25°}$ 1·4225.)

Methyl Propyl Ketone.—A solution of pent-1-yn-4-ol (2 g.) in methyl acetate (10 c.c.) was shaken with hydrogen in the presence of platinic oxide (50 mg.) until absorption was complete. (Uptake 1135 c.c. at 16°/765 mm., equivalent to 2·0 mol.) Distillation of the residue after removal of catalyst and solvent gave methylpropylcarbinol (1·6 g.) b. p. 118°, $n_D^{20°}$ 1·4052 (Sherrill, Baldwin, and Hass, *J. Amer. Chem. Soc.*, 1929, **51**, 3036, give b. p. 119·5°, $n_D^{20°}$ 1·4060). The α-naphthylurethane separated from light petroleum in spheroids, m. p. 75—76° (Adamson and Kenner, *J.*, 1934, 842, give m. p. 74·5°). Oxidation of the hydrogenation product with chromic acid in acetic acid solution gave methyl propyl ketone, b. p. 102—104°, $n_D^{18.5°}$ 1·3920 (Ceuterick, *Bull. Soc. chim. Belg.*, 1936, **45**, 555, gives b. p. 102—103°, $n_D^{20°}$ 1·39012). The 2 : 4-dinitrophenylhydrazone crystallised from ethanol in glistening orange plates, m. p. 143·5—144·5° (Campbell, *Analyst*, 1936, **61**, 393, gives m. p. 143—144°) undepressed on admixture with an authentic specimen.

Lactone of Pent-1-en-4-ol-1-carboxylic Acid (δ-Hexenolactone) (I).—(*a*). A solution of pent-1-yn-4-ol-1-carboxylic acid (42 g.; Haynes and Jones, *loc. cit.*) in methanol (110 c.c.) was shaken with hydrogen in presence of a palladium–barium sulphate catalyst (1·5 g., 5% Pd; Schmidt, *Ber.*, 1919, **52**, 409; Shriner and Adams, *J. Amer. Chem. Soc.*, 1924, **46**, 1683) and hydrogenation was interrupted after the absorption of 6·6 l. of hydrogen (theoretical for semihydrogenation, 7·77 l.). The catalyst was filtered off and the solvent evaporated from the filtrate after addition of benzene (50 c.c.). Distillation of the residue gave the lactone of pent-1-en-4-ol-1-carboxylic acid (24·5 g.), b. p. 110°/15 mm., $n_D^{19°}$ 1·4730 (Kuhn and Jerchel, *loc. cit.*, give b. p. 103—105°/14 mm., $n_D^{18°}$ 1·475) (Found : C, 64·45; H, 7·4. Calc. for $C_6H_8O_2$: C, 64·3; H, 7·2%).

(*b*) Ethyl pent-1-yn-4-ol-1-carboxylate (8 g.; Haynes and Jones, *loc. cit.*) in ethyl acetate (25 c.c.) was hydrogenated in the presence of a palladium–barium sulphate catalyst (0·5 g.; 5% Pd) the hydrogenation being interrupted after the absorption of 0·7 l. of gas. Distillation of the residue after removal of catalyst and solvent gave *ethyl pent-1-en-4-ol-1-carboxylate* (5 g.), b. p. 54°/0·02 mm., $n_D^{20°}$ 1·4583 (Found : C, 60·5; H, 9·1. $C_8H_{14}O_3$ requires C, 60·7; H, 8·9%). Unchanged acetylenic ester (2·6 g.) was recovered in the higher boiling fraction. The ethylenic hydroxy-ester (3 g.) was refluxed with dilute hydrochloric acid (50 c.c.; 1%) for 1 hour. Isolation by the usual procedure gave the lactone (1·2 g.), b. p. 44°/0·05 mm., $n_D^{20.5°}$ 1·4723.

But-1-yn-4-ol-1-carboxylic Acid.—But-1-yn-4-ol (35 g.; Macallum, U.S.P. 2,125,384; Kreimeier, *loc. cit.*) was carboxylated by the general method described by Haynes and Jones (*loc. cit.*). The Grignard complex separated as a white powder from the benzene solution. *But-1-yn-4-ol-1-carboxylic acid* (18·5 g.; 32·5% conversion) was obtained as a very hygroscopic solid which sublimed at 55° (bath temp.)/10^{-4} mm., m. p. 65° (Found : C, 52·2; H, 5·4. $C_5H_6O_3$ requires C, 52·65; H, 5·3%). Light absorption : $\epsilon = 5000$ at 2130A. The *ethyl* ester, prepared by the general method, had b. p. 90°/0·2 mm., $n_D^{14°}$ 1·4714 (Found : C, 59·0; H, 7·25. $C_7H_{10}O_3$ requires C, 59·15; H, 7·1%).

Lactone of But-1-en-4-ol-1-carboxylic Acid (IV).—(*a*) A solution of the above acid (15 g.) in methanol (50 c.c.) was shaken with hydrogen in presence of palladium–barium sulphate catalyst (2 g.; 5% Pd). The hydrogenation was interrupted after 2·90 l. of hydrogen had been absorbed (theoretical for semihydrogenation, 3·21 l.). Removal of catalyst and solvent after the addition of benzene gave the *lactone* (7·9 g.), b. p. 103°/10 mm., $n_D^{17°}$ 1·4827 (Found : C, 59·9; H, 6·3. $C_5H_6O_2$ requires C, 61·2; H, 6·15%).

(*b*) A solution of ethyl but-1-yn-4-ol-1-carboxylate (11 g.) in ethyl acetate (25 c.c.) was hydrogenated in presence of palladium–barium sulphate catalyst (0·5 g.; 5% Pd), the experiment being interrupted after 1·67 l. of gas had been absorbed (theoretical for semihydrogenation, 1·75 l.). Removal of catalyst and solvent gave *ethyl but-1-en-4-ol-1-carboxylate* (9·8 g.), b. p. 120°/14 mm., $n_D^{16°}$ 1·4632 (Found : C, 58·55; H, 8·4. $C_7H_{12}O_3$ requires C, 58·3; H, 8·4%). The ethylenic hydroxy-ester (9 g.) was refluxed with N-hydrochloric acid (60 c.c.) for 1 hour. Isolation by the usual procedure gave the lactone (2·8 g.), b. p. 98°/10 mm., $n_D^{19°}$ 1·4807.

Lactone of 2-(1′-Hydroxycyclohexyl)acrylic Acid (V).—2-(1′-Hydroxycyclohexyl)propiolic acid (10 g.; Haynes and Jones, *loc. cit.*) in methanol (50 c.c.) was hydrogenated in the presence of palladium–barium sulphate (0·5 g.; 5% Pd), the experiment being interrupted after 1·35 l. hydrogen had been absorbed (theoretical for semihydrogenation, 1·43 l.). The catalyst was filtered off and the solvent evaporated from the filtrate after the addition of benzene. The residue on distillation gave the lactone (7·6 g.), b. p. 84°/0·1 mm., $n_D^{16°}$ 1·4972 (Found : C, 70·85; H, 7·9. $C_9H_{12}O_2$ requires C, 71·0; H, 7·95%).

Lactone of Hex-1-en-3-ol-1-carboxylic Acid (VI).—Hex-1-yn-3-ol-1-carboxylic acid (32 g.; Haynes and Jones, *loc. cit.*) in methanol (100 c.c.) was hydrogenated in presence of palladium–barium sulphate (2 g.; 5% Pd), the experiment being interrupted after the absorption of 5·39 l. of gas (theoretical, 5·99 l.). Isolation by the usual procedure gave the lactone (23·1 g.), b. p. 73°/0·05 mm., $n_D^{18°}$ 1·4596 (Found : C, 66·35; H, 8·25. $C_7H_{10}O_2$ requires C, 66·65; H, 8·0%).

Lactone of 3-Methylbut-1-en-3-ol-1-carboxylic Acid (III).—3-Methylbut-1-yn-3-ol-1-carboxylic acid (21·3 g.; Haynes and Jones, *loc. cit.*) in methanol (100 c.c.) was hydrogenated in the presence of palladium–barium sulphate (2 g.; 5% Pd) until 3·57 l. of gas had been absorbed (theoretical, 3·97 l.). Isolation by the usual procedure gave the lactone (11·4 g.), b. p. 80°/10 mm., $n_D^{18°}$ 1·4470 (Fittig and Geisler, *Annalen*, 1881, **208**, 49, give b. p. 210°; Jacobs and Scott, *J. Biol. Chem.*, 1930, **87**, 601, give b. p. 127°/72 mm.).

Lactone of But-1-en-3-ol-1-carboxylic Acid (VII).—But-1-yn-3-ol-1-carboxylic acid (10 g.; Haynes and Jones, *loc. cit.*) in methanol (50 c.c.) was hydrogenated in the presence of a palladium–barium sulphate catalyst (0·5 g.; 5% Pd) until 1·8 l. of gas had been absorbed (theoretical, 1·96 l.). Isolation by the usual procedure gave the lactone of but-1-en-3-ol-1-carboxylic acid (β-angelicalactone) (6 g.), b. p. 84°/10 mm., $n_D^{21°}$ 1·4532 (Jacobs and Scott, *J. Biol. Chem.*, 1930, **87**, 601, give b. p. 84·5°/12 mm.).

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