4-Phosphoranylidenebutenolide Intermediates in the Synthesis of 4-Ylidenebutenolides and 4-Ylidenetetronic Acids. Synthesis of Alkylidenephthalide Constituents of Celery Odour and Models for Freelingyne

By **David W. Knight** and **Gerald Pattenden,*** Department of Chemistry, The University, Nottingham NG7 2RD

The application of 4-phosphoranylidenebutenolides in the synthesis of 4-ylidenebutenolides and 4-ylidenetetronic acid derivatives is examined. 3-Triphenylphosphoranylidenephthalide (11) reacts stereospecifically with aliphatic aldehydes to product (*E*)-alkylidenephthalides [*e.g.* (13)] and this work has led to the stereocontrolled synthesis of the odorous alkylidenephthalide constituents (4a and b) of celery. By using the ylide (11), the 3-phenacylidenephthalide (14) and the isomeric phthalides (15) and (17) were synthesised.

Condensations of the phosphoranylidenebutenolides (20b) and (26) with aromatic aldehydes have led to the corresponding isomeric arylmethylenebutenolides (27) and (28), and (29) and (30), respectively. Similarly, compounds (20a) and (11) with the 2-furyl-enynal (32) produced the polyunsaturated ylidenebutenolides (33) and (34), and (35) and (36), respectively; these studies have provided a basis for the development of a synthesis of the sesquiterpene freelingyne (2).

4-YLIDENEBUTENOLIDES and 4-ylidenetetronic acids are a group of natural products, many members of which have been discovered in only the past decade. The 4-ylidenebutenolide system (1) is present for example in the acetylenic sesquiterpene freelingyne (2) from *Eremophila freelingii*[1] and in peridinin, the principle carotenoid pigment of dinoflagellates.[2] It is also present in the mould metabolites tetrenolin (3)[3] and patulin,[4] and in bovolide from butter[5] and alkylidenephthalides (4) from celery;[6] several 4-ylidenebutenolides are found in *Compositae* where they co-occur with polyacetylenes.[7] The corresponding 4-ylidenetetronic acid system (5) has been known for a long time as an important structural feature of lichen pigments, *e.g.* vulpinic acid (6).[4] More recently it has been identified in several furan sesterterpenes from sponges of the genus *Ircinia*,[8,9] *e.g.* variabilin

[1] R. A. Massy-Westropp, G. D. Reynolds, and T. M. Spotswood, *Tetrahedron Letters*, 1966, 1939.

[2] H. H. Strain, W. A. Svec, A. Aitzetmüller, M. C. Grandolfo, J. J. Katz, H. Kjøsen, S. Norgård, S. Liaaen-Jensen, F. T. Haxo, P. Wegfahrt, and H. Rapoport, *J. Amer. Chem. Soc.*, 1971, **93** 1823.

[3] G. G. Gallo, C. Coronelli, A. Vigevani, and G. C. Lancini, *Tetrahedron*, 1969, **25**, 5677.

[4] For summary see F. M. Dean, 'Naturally Occurring Oxygen Ring Compounds,' Butterworths, 1963.

[5] G. Lardelli, G. Dijkstra, P. D. Harkes, and J. Boldingh, *Rec. Trav. chim.*, 1966, **85**, 43.

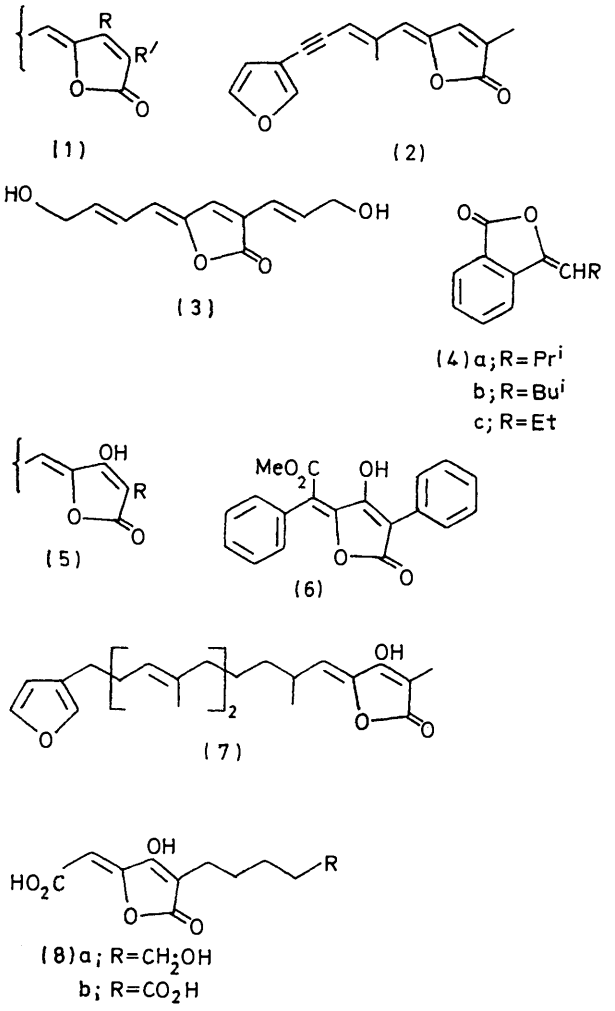
[6] H. J. Gold and C. W. Wilson, tert., *J. Org. Chem.*, 1963, **28**, 985.

[7] F. Bohlmann, T. Burkhardt, and C. Zdero, 'Naturally Occurring Acetylenes,' Academic Press, New York and London, 1973.

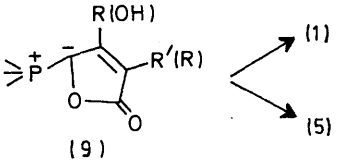
[8] G. Cimino, S. De Stefano, L. Minale, and E. Fattorusso, *Tetrahedron*, 1972, **28**, 333.

[9] F. Cafieri, E. Fattorusso, C. Santacroce, and L. Minale, *Tetrahedron*, 1972, **28**, 1579.

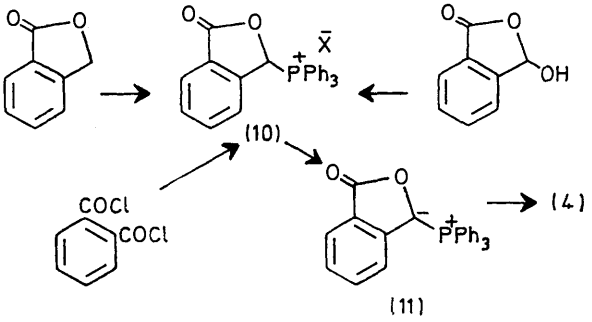
(7),[10] and also in multicolic and multicolosic acids (8a and b) from *Penicillium multicolor*.[11]



Synthetic approaches to 4-ylidenebutenolides from furan,[12] maleic anhydride,[5,13] but-2-enolide,[14] β-butyrolactone,[15] and acetylenic precursors [7,16] have been described, and a few 4-ylidenetetronic acids have been obtained from treatment of propioloylmalonates or *via* elimination from unsaturated enol sulphonates.[17] The unfavourable reaction conditions demanded by some of these approaches, coupled with their lack of stereochemical integrity, makes many of them unsuitable for the stereocontrolled synthesis of sensitive molecules like (2), *etc.* In this paper we describe the application of 4-phosphoranylidenebutenolide intermediates [*viz.* (9)] in the synthesis of 4-ylidenebutenolides and 4-ylidenetetronic acids.* This method has provided a basis for the synthesis of the natural alkylidenephthalide constituents of celery odour, and of model compounds for the acetylenic sesquiterpene freelingyne (2).



We first examined the synthesis of alkylidenephthalides (4) from 3-triphenylphosphoranylidenephthalide (11). The phosphonium bromide (10; X = Br) was prepared from phthalide by bromination with *N*-bromosuccinimide followed by reaction with triphenylphosphine. Two alternative routes to (10) were reported during our investigations, one starting from phthaloyl chloride,[19] the other from 3-hydroxyphthalide.[20] Treatment of the bromide (10; X = Br) with the anion from dimethyl sulphoxide gave a deep red solution of the ylide (11), whose colour was immediately discharged on addition of isobutyraldehyde. Work up produced a 95 : 5 mixture (by n.m.r.) of geometrical isomers of the expected phthalide (4a), which were separated by chromatography. The major isomer was a pale yellow oil which showed a greenish fluorescence; the other was obtained as a crystalline solid, m.p. 93—95°; both isomers possessed a strong celery odour in low concentrations. Assignment of configurations to the isomers, based on ^{1}H n.m.r. data, is made difficult because of the dearth of suitable model

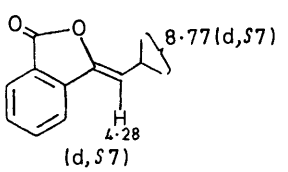


compounds. Calculations, from tables of shift increments for substituted double bonds,[21] although not altogether satisfactory in the case of structure (4), led to the

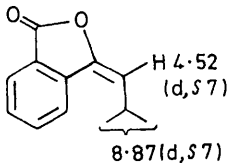
* Corrie,[18] in parallel studies, outlined the application of (20a) in 4-ylidenebutenolide synthesis, while our own work was in progress.

[10] D. J. Faulkner, *Tetrahedron Letters*, 1973, 3821.
[11] J. A. Gudgeon, J. S. E. Holker, and T. J. Simpson, *J.C.S. Chem. Comm.*, 1974, 636.
[12] H. Gilman, R. A. Franz, A. P. Hewlett, and G. F. Wright, *J. Amer. Chem. Soc.*, 1950, **72**, 3.
[13] (*a*) Unilever, N.V., Ger. Pat. 1,072,629 (*Chem. Abs.*, 1961, **55**, 19,949c); (*b*) M. S. Newman and A. S. Smith, *J. Org. Chem.*, 1948, **13**, 592; (*c*) A. P. Gara, R. A. Massy-Westropp, and G. D. Reynolds, *Tetrahedron Letters*, 1969, 4171.
[14] *Cf.* N. Boegman, F. During, and C. F. Garbers, *Chem. Comm.*, 1966, 601 and references cited therein.
[15] K. Yamada, Y. Tokawa, T. Kato, and Y. Hirata, *Tetrahedron*, 1971, **27**, 5445.
[16] J. Castaner and J. Pascual, *J. Chem. Soc.*, 1958, 3962; P. K. Christensen, N. A. Sørensen, I. Bell, E. R. H. Jones, and M. C. Whiting, *Festsch. A. Stoll*, 1957, 545; P. K. Christensen, *Acta Chem. Scand.*, 1957, **11**, 582.
[17] I. Fleming and J. Harley-Mason, *J. Chem. Soc.*, 1963, 4778.
[18] J. E. T. Corrie, *Tetrahedron Letters*, 1971, 4873.
[19] H. Kunzek and K. Rühlmann, *J. Organometallic Chem.*, 1972, **42**, 391.
[20] R. K. Howe, *J. Org. Chem.*, 1973, **38**, 4164.
[21] L. M. Jackman and S. Sternhell, 'Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry,' ch. 3, Pergamon, Oxford, 1969.

conclusion that the predominant isomer has the *E*- and the minor isomer the *Z*-configuration [*i.e.* aryl ring more deshielding than butenolide oxygen; see ^{1}H n.m.r. data associated with formulae (12) and (13)]. Photolysis of



(12)



(13)

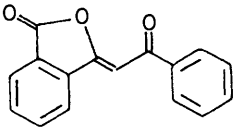
the *E*-isomer (13) in hexane for 1 h produced a 1 : 2 mixture of the *Z*- and *E*-isomers.

Similar condensations between (11) and isovaleraldehyde and between (11) and propionaldehyde also led almost exclusively to the *E*-isomers (>95%) of 3-methylbutylidene- (4b) and propylidene-phthalide (4c), respectively. Like (4a), both (4b) and (4c) had strong celery odours. The observed stereospecificities of the reactions leading to (4) from (11) are remarkable, and complement similar observations made recently;[20] in each case there is clearly a strong kinetic preference for irreversible formation of an *erythro*-betaine intermediate, which once formed collapses rapidly to the *E*-olefin product.

3-Isobutylidene- (4a) and 3-(3-methylbutylidene)-phthalide (4b) have been isolated, along with the corresponding 3a,4-dihydro-compounds, from the celery plant *Apium graveolens* L,[6] and are believed to be responsible for the flavour and odour of celery. Several alkylidenephthalides have been synthesised previously, in a search for a celery flavour/odour substitute, from phthalic anhydride and carboxylic acids or organometallic reagents;[5,22] these reactions have largely led to the more thermodynamically stable *Z*-isomers [*e.g.* (12)]. The natural product (4a) is described as a yellow oil with a green fluorescence.[23] This description corresponds to the isomer synthesised in the present studies, which we have assigned the *E*-configuration. By inference, we would expect the natural product (4b) also to have the *E*-configuration. Both these natural products are thus easily available *via* the phosphorus ylide intermediate (11).

In an extension of our studies with the ylide (11) we also examined the synthesis of 3-phenacylidenephthalide (14) and the benzylidenephthalide (15) from the phosphonium salt (10) and the appropriate carbonyl compounds. 3-Phenacylidenephthalide (14) has been shown recently to be a highly active inhibitor of root geotropism,[24,25] and (15) shows structural features in common with the lichen pigments [*e.g.* (6)]. Condensation between the ylide (11) and phenylglyoxal resulted in attack at both the carbonyl functions in the glyoxal, producing an 8 : 1 mixture of compound (14) and the bis-ylidenephthalide (16). Only one isomer of each of compounds (14) and (16) was isolated, and an unambiguous stereochemical assignment could not be given to either. By contrast, reaction between the ylide (11) and methyl benzoylformate gave a mixture of geometrical isomers (15) and (17) of the expected benzylidenephthalide, whose relative configurations could be deduced from comparative ^{1}H n.m.r. data.

We next turned to the application of 2- and 3-methyl- (20a and b) and 3-methoxy-2-methyl- (26) butenolide ylides as precursors of 4-ylidenebutenolides. For these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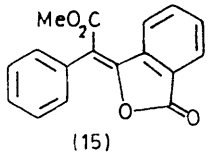

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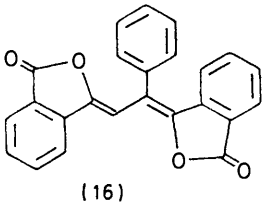
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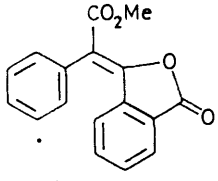


(17)

studies we required the phosphonium salts (19a and b) and (25). The salts (19a and b) were readily prepared from the corresponding lactols (18a and b),[26] respectively, by reaction with thionyl chloride or phosphorus tribromide, and then with triphenylphosphine. While our studies were in progress, Corrie [18] outlined an alternative route to the ylide (20a) from the lactol (18a) by way of 2-methylbut-2-en-4-olide. The phosphonium salt (25) was synthesised as follows from ethyl 2-methylacetoacetate. Bromination produced the 2-bromo-derivative (21),[27] which rearranged in the presence of hydrobromic acid to the 4-bromo-derivative (22). The latter was not isolated, and on heating eliminated ethyl bromide to give 2-methyltetronic acid (23).[28] Methylation of (23) with dimethyl sulphate led to the methyl ether (24), which on sequential reaction with *N*-bromosuccinimide and triphenylphosphine produced the salt (25).

Reactions between anisaldehyde and the ylide (20b) from (19b), and between benzaldehyde and (26), in each case produced mixtures of isomers [(27) and (28), and (29) and (30), respectively] of 4-arylmethylenebut-2-en-4-olides, which were separated by chromatography. The configurations assigned to compounds (27)—(30) followed largely from inspection and comparison of their ^{1}H n.m.r. data (see formulae).

The foregoing syntheses established the general use of

[22] R. Weiss, *Org. Synth.*, Coll. Vol. 2, 1943, p. 61; G. Berti, *Gazzetta*, 1956, **86**, 655; J. Rigaudy and P. Derible, *Bull. Soc. chim. France*, 1965, 3047 (*cf.* the application of Grignard reagents and dialkylcadmiums [23]).

[23] T. Kariyone and S. Schimuzu, *J. Pharm. Soc. Japan*, 1953, **73**, 336.

[24] B. T. Brown, O. Johansen, and W. H. F. Sasse, *Experientia*, 1972, **28**, 1290.

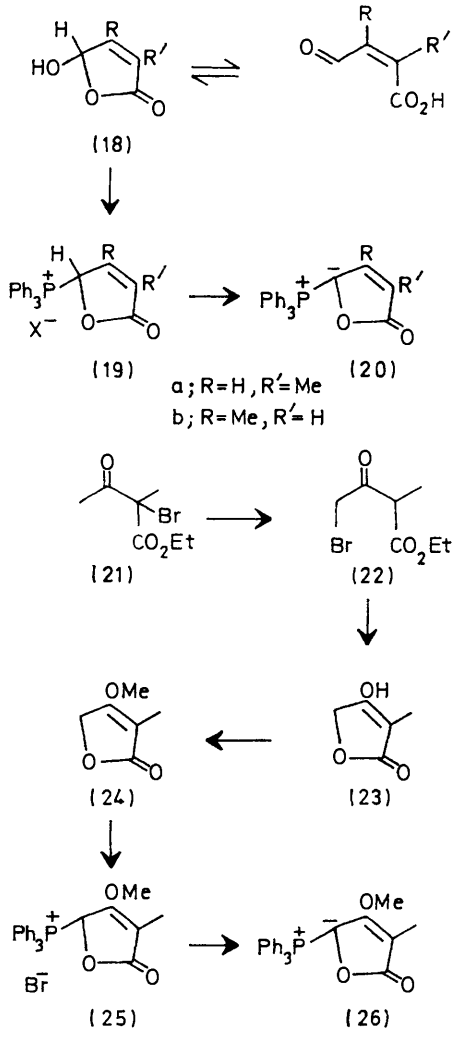
[25] B. T. Brown, O. Johansen, G. F. Katekar, and W. H. F. Sasse, *Pesticide Sci.*, 1973, **4**, 473.

[26] G. Pattenden and B. C. L. Weedon, *J. Chem. Soc.*, 1968, 1984.

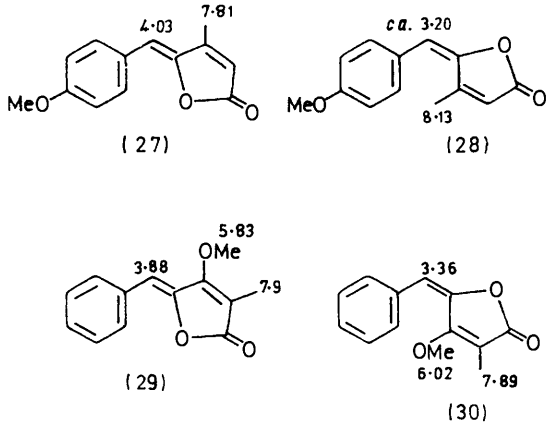
[27] M. Conrad, *Ber.*, 1896, **29** (**1**), 1042.

[28] *Cf.* E. B. Reid, R. B. Fortenbaugh, and H. R. Patterson, *J. Org. Chem.*, 1950, **15**, 572.

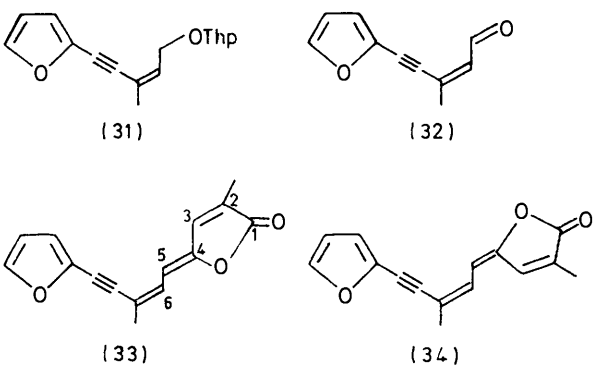
phosphoranylidenebutenolide intermediates in the preparation of 4-ylidenebut-2-en-4-olides. The application



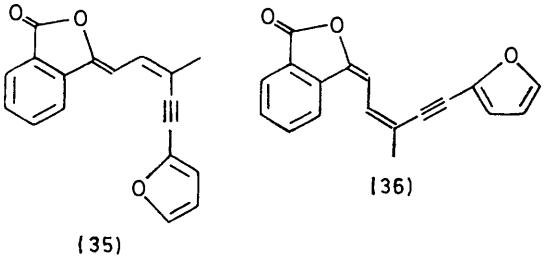
of this approach to models (33) and (35) for the synthesis of natural freelingyne (2) was made *via* the enynal (32)



and the salts (19a) and (10). The enynal (32) was synthesised from the tetrahydropyranyl ether (31),[29] by acidic hydrolysis and oxidation of the resulting alcohol with manganese dioxide. Wittig condensation between (32) and the ylide (20a) derived from (19a) led to a mixture of geometrical isomers of (33) from which the



(4*Z*,6*Z*)- (33) and (4*E*,6*Z*)- (34) isomers were separated by chromatography and crystallisation. The configurations assigned to these isomers followed (*a*) from their method of synthesis *i.e.* *Z*-αβ-unsaturated aldehydes retain their stereochemistry during condensations with phosphorus ylides [26] and (*b*) from comparison of their ^{1}H n.m.r. data with those of the corresponding isomers of freelingyne (2) (see following paper). In a similar manner, reaction between the aldehyde (32) and the ylide (11) led to a mixture of isomers (35) and (36) of the expected ylidenephthalide, whose configurations, once again, were inferred from their ^{1}H n.m.r. data. The application of the phosphoranylidenebutenolide (20a) towards the total



synthesis of natural freelingyne is described in the accompanying paper.

EXPERIMENTAL

M.p.s are corrected. ^{1}H N.m.r. spectra were determined with a Perkin-Elmer R10 or a Varian HA-100 spectrometer, with tetramethylsilane as internal standard. Bands were singlets except where stated otherwise; splittings (*S*) are in Hz. Molecular weights were determined from mass spectra, measured with an A.E.I. MS 902 spectrometer. All solvents for chromatography were redistilled, and all organic solutions were dried over anhydrous magnesium sulphate.

Triphenyl(phthalidyl)phosphonium Bromide (10; X = Br).—A solution of 3-bromophthalide [30] (3·5 g) and triphenylphosphine (4·3 g) in benzene (75 ml) was boiled under reflux for 12 h, then cooled and evaporated to dryness *in vacuo*. Crystallisation of the solid residue from ethanol

[29] D. W. Knight and G. Pattenden, following paper.
[30] I. A. Koten and R. J. Sauer, *Org. Synth.*, 1962, **42**, 26.

gave the *salt* (6 g, 80%), m.p. 237° (lit.,[20] 258—260°), $\nu_{max.}$ 1790 cm^{-1}, τ 0·2br (C*H*–$\overset{+}{P}$<) and 1·9—2·7 (19H, m) (Found: C, 65·4; H, 4·4; Br, 17·0; P, 6·7. $C_{26}H_{20}BrO_2P$ requires C, 65·7; H, 4·2; Br, 16·8; P, 6·5%).

The corresponding phosphonium chloride (10; X = Cl), prepared as described previously,[19] showed m.p. 238—240° (lit.,[19] 239—241°), τ 0·02br (C*H*–$\overset{+}{P}$<) and 1·9—2·9 (19H, m).

Preparation of 4-Ylidenebutenolides, 4-Ylidenetetronic Acid Derivatives, and 3-Ylidenephthalides; General Procedure.—A solution of the phosphonium salt (0·01 mol) in dry dimethyl sulphoxide (DMSO) (5 ml) was added to a stirred solution of the anion prepared from DMSO [with sodium hydride (0·01 mol)] [31] in DMSO (20 ml) under nitrogen. The mixture was stirred at 25° for *ca.* 1 h, and then treated during 5 min with the carbonyl compound (0·009 mol), either neat or in solution in DMSO (2 ml). After stirring at 25° for 1 h [20 h in the case of (32) and (19a); u.v.–visible monitoring], the mixture was poured onto iced water (*ca.* 200 ml) and then extracted with ether (3 × 100 ml). The combined extracts were washed with water, then dried and evaporated. Isomerically homogenous samples of the Wittig reaction products were then obtained by column or preparative layer chromatography on silica gel by using the eluants specified.

(E)-3-(2-*Methylpropylidene*)*phthalide* (13).—By the general procedure, the ylide from the phthalidylphosphonium chloride and isobutyraldehyde produced a 95 : 5 mixture of the (*E*)- and (*Z*)-phthalides (65%), which, after separation and purification by chromatography in benzene gave (i) the (E)-*phthalide*, a pale yellow oil, with a greenish fluorescence, $\nu_{max.}$ (film) 1785 and 1690 cm^{-1}, τ 2·1—2·6 (4H, m), 4·52 (d, *S* 7, :C*H*·CH), 6·85 (m, :CH·C*H*), and 8·87 (d, *S* 7, CH*Me*$_2$) (Found: C, 76·2; H, 6·6. $C_{12}H_{12}O_2$ requires C, 76·6; H, 6·4%); and (ii) the (*Z*)-phthalide (eluted second), m.p. 93—95° (lit.,[23] 97°), $\nu_{max.}$ (CCl_4) 1790 and 1678 cm^{-1}, τ 2·1—2·6 (4H, m), 4·28 (d, *S* 7, :C*H*·CH), 6·8 (m, :CH·C*H*), and 8·77 (d, *S* 7, CH*Me*$_2$), *m/e* 188 (M^+, $C_{12}H_{12}O_2$).

Irradiation of the (*E*)-phthalide in hexane for 1 h with a medium-presssure mercury lamp (Hanovia), led to a 1 : 2 mixture of the *Z*- and *E*-isomers (n.m.r. monitoring); prolonged irradiation produced polymeric material.

(E)-3-(3-*Methylbutylidene*)*phthalide* (4b).—By the general procedure, the ylide from the phthalidylphosphonium bromide and isovaleraldehyde produced a 95 : 5 mixture of the (*E*)- and (*Z*)-phthalide (*ca.* 70%) which, after separation and purification by chromatography in benzene, gave (i) the (*E*)-phthalide, an oil, $\nu_{max.}$ ($CHCl_3$) 1773 and 1680 cm^{-1}, τ 2·1—2·6 (4H, m), 4·37 (t, *S* 7, :C*H*·CH$_2$), 7·66 (dd, *S ca.* 7, :CH·C*H*$_2$), 7·8—8·6 (m, C*H*Me$_2$), and 9·04 (d, *S* 7, CH*Me*$_2$), *m/e* 202 (M^+, $C_{13}H_{14}O_2$); and (ii) the (*Z*)-phthalide, an oil (eluted second), $\nu_{max.}$ 1773 and 1665 cm^{-1}, τ 2·1—2·6 (4H, m), 4·2 (t, *S* 7, :C*H*·CH$_2$), 7·58 (dd, *S ca.* 7, :CH·C*H*$_2$), 7·85—8·5 (m, C*H*Me$_2$), and 9·01 (d, *S* 7, CH*Me*$_2$), *m/e* 202.

(E)-3-*Propylidenephthalide* (4c).—By the general procedure, the ylide from the phthlidylphosphonium bromide and propionaldehyde produced the phthalide (55%), which was purified by chromatography in benzene and showed $\nu_{max.}$ 1780 and 1685 cm^{-1}, τ 2·0—2·7 (4H, m), 4·4 (t, *S* 7, :C*H*·CH$_2$), 7·53 (dq, *S ca.* 7, :CH·C*H*$_2$), and 8·86 (t, *S* 7, CH$_2$·C*H*$_3$), *m/e* 174 (M^+, $C_{11}H_{10}O_2$). The (*Z*)-phthalide was not detected.

3-*Phenacylidenephthalide* (14).—By the general procedure, the ylide derived from the salt (10; X = Br) was treated with phenylglyoxal to produce, after chromatography in chloroform, (i) the phthalide (*ca.* 40%) (eluted second) as yellow needles, m.p. 165—166° (lit.,[25] 164·5—167°), $\lambda_{max.}$ ($CHCl_3$) 287·5, 299, and 320·5 nm, $\nu_{max.}$ (KBr) 1770, 1680, and 1648 cm^{-1}, τ 1·9—2·8 (9H, m) and 3·20 (:CH·CO) (Found: C, 76·8; H, 4·2. Calc. for $C_{16}H_{10}O_3$: C, 76·8; H, 4·0%), *m/e* 250 (19%, $C_{16}H_{10}O_3$), 222 (6), 194 (2), 173 (40), 165 (6), 105 (100), 89 (42), and 77 (62); (ii) 3-(α-*phthalidylbenzylidene*)*phthalide* (16) (*ca.* 5%) (eluted first) as yellow cubes, m.p. 240—242°, $\lambda_{max.}$ 304, 418, and 441 nm, $\nu_{max.}$ (KBr) 1766, 1668, and 1610 cm^{-1}, τ 1·6—2·7 (14H, m) and 3·15 (:C*H*·CPh:) (Found: M^+, 366·0914. $C_{24}H_{14}O_4$ requires *M*, 366·0892), *m/e* 366 (58%), 289 (26), 233 (8), 176 (8), 129 (11), 106 (10), 105 (100), 104 (13), 101 (14), 97 (14), and 77 (55).

(Z)- *and* (E)-3-(α-*Methoxycarbonylbenzylidene*)*phthalide* [(15) *and* (17)].—By the general procedure, the ylide derived from the salt (10; X = Br) reacted with methyl benzoylformate to produce, after chromatography in chloroform, (i) the (E)-*isomer* (17) (0·93 g, 33%) (eluted first), which crystallised from methanol as golden yellow needles, m.p. 121°, $\lambda_{max.}$ ($CHCl_3$) 329 and 290 nm, $\nu_{max.}$ (KBr) 1775, 1720, and 1640 cm^{-1}, τ 2·0—2·85 (9H, m) and 6·15 (OMe) (Found: C, 72·7; H, 4·2. $C_{17}H_{12}O_4$ requires C, 72·9; H, 4·3%); and (ii) the (Z)-*isomer* (0·8 g, 30%) (eluted second), which crystallised from methanol as golden yellow needles, m.p. 221—223° (with softening at 180°), $\lambda_{max.}$ 323sh, 311, and 278 nm, $\nu_{max.}$ (KBr) 1770, 1705, and 1601 cm^{-1}, τ 2·12 (1H, dd, *S* 6 and 2), 2·4—2·8 (7H, m), 3·61 (1H, dd, *S* 6 and 2), and 6·2 (OMe) (Found: C, 72·6; H, 4·5%).

2,5-*Dihydro*-3-*methyl*-5-*oxofuran*-2-*yl*(*triphenyl*)*phosphonium Chloride* (19b; X = Cl).—A mixture of 4-hydroxy-3-methylbut-2-en-4-olide [26] (2·9 g) and freshly distilled thionyl chloride (3·5 g) was heated at 60° for 3 h and then distilled to give the corresponding chloride (1·7 g, 53%), b.p. 100—104° at 20 mmHg, $\nu_{max.}$ 1800 and 1655 cm^{-1}, τ 3·53 (CHCl), 4·0 (q, *S ca.* 1, :CH), and 7·78 (d, *S ca.* 1, :CMe). A solution of the chloride (1·5 g) and triphenylphosphine (2·7 g) in dry benzene (100 ml) was boiled under reflux for 18 h, and then evaporated to dryness. The residue was triturated with dry ether, and then dried *in vacuo* to give the salt as a deliquescent glass, $\nu_{max.}$ 1795 and 1640 cm^{-1}, τ 0·56 (m, CH–$\overset{+}{P}$<), 1·9—2·7 (15H, m), 4·05 (m, :CH), and 7·96 (:CMe), which was used without further purification.

2,5-*Dihydro*-4-*methyl*-5-*oxofuran*-2-*yl*(*triphenyl*)*phosphonium Bromide* (19a; X = Br).—A solution of phosphorus tribromide (2 g) in ether (5 ml) was added, during 20 min, to a stirred solution of 4-hydroxy-2-methylbut-2-en-4-olide [26] (2·3 g) in ether (10 ml) containing pyridine (0·5 ml) at 0°. The mixture was warmed to 25° during 1 h, and was then poured into water (30 ml) and extracted with ether. The extracts were washed successively with 6N-hydrochloric acid and saturated sodium chloride solution, then dried and evaporated to give the corresponding bromide (1 g, 40%) as a yellow unstable oil, τ 2·7 (m, CHBr), 3·1 (m, :CH), and 8·0 (m, :CMe). A solution of the bromide (0·8 g) and triphenylphosphine (2 g) in dry benzene (25 ml) was boiled under reflux for 20 h, and then evaporated to dryness. The residue was triturated with ether, and then dried *in vacuo* to give the salt (1·4 g) as a deliquescent solid, $\nu_{max.}$ 1780 and 1650 cm^{-1}, τ 1·03 (m, CH–$\overset{+}{P}$<), 2·0—2·8 (15H, m), 4·4 (m, :CH), and 8·25 (:CMe), which was used without further purification.

The corresponding chloride was also prepared (50%), as described for the 3-methyl analogue, but this did not react to any appreciable extent with triphenylphosphine.

[31] E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, 1962, **84**, 866.

2-*Methoxy*-2-*methylbut*-2-*en*-4-*olide* (24) [*with* R. HAWKES].—3-Methyltetronic acid (23) was prepared from ethyl 2-methylacetoacetate by bromination to give the α-bromoacetate [τ 6·47 (q, *S* 7, C*H*·CH$_3$), 7·75 (COMe), and 8·65 (d, *S* 7, CH*Me*)], rearrangement to the γ-bromo-acetate, and spontaneous thermal cyclisation, largely according to the procedures outlined by Conrad [27] and by Reid *et al.*[28] It showed m.p. 179—181° $\lambda_{max.}$ 228 nm, $\nu_{max.}$ ($CHCl_3$) 2700 and and 1600 cm^{-1}, τ −0·73 (OH), 5·5 (m, CH_2), and 8·4 (Me).

A solution of 2-methyltetronic acid (5·7 g) and anhydrous potassium carbonate (6·9 g) in dry acetone (100 ml) was stirred and heated at reflux temperature, and treated during 0·25 h with dimethyl sulphate (4·8 ml). The mixture was heated under reflux for 2 h, then cooled and filtered. Evaporation left the *ether* (*ca.* 65%), a pale yellow oil, $\nu_{max.}$ 1743 and 1665 cm^{-1}, τ 5·33 (m, (CH_2), 6·03 (OMe), and 8·25 (m, :CMe) (Found: M^+, 128·0562. $C_8H_8O_3$ requires M, 128·0473).

2,5-*Dihydro*-3-*methoxy*-4-*methyl*-5-*oxofuran*-2-*yl*(*triphenyl*)*phosphonium Bromide* (25) [*with* R. HAWKES].—A mixture of 3-methoxy-2-methylbut-2-en-4-olide (2·6 g) and *N*-bromosuccinimide (3·6 g) in dry carbon tetrachloride (100 ml) was boiled under reflux for 3·5 h, then cooled and filtered. Evaporation of the filtrate *in vacuo* left the corresponding 4-bromobutenolide (3·8 g) as a yellow oil, $\nu_{max.}$ (CCl_4) 1760 and 1678 cm^{-1}, τ 3·27 (CHBr), 5·86 (OMe), and 8·1 (:CMe). A solution of the bromide (3·1 g) and triphenylphosphine (4·2 g) in dry benzene (30 ml) was stirred at 25° for 24 h and then evaporated to dryness. The residue was triturated with ether and then dried *in vacuo* to give the salt (5·7 g) as a highly deliquescent powder, $\nu_{max.}$ 1755 and 1675 cm^{-1}.

(Z)-4-(4-*Methoxybenzylidene*)-3-*methylbut*-2-*en*-4-*olide* (27).—By the general procedure, the ylide from the phosphonium chloride (19b; X = Cl) (2·5 g) with 4-methoxybenzaldehyde (1 g) gave, after chromatography in 1 : 1 benzene–ether, (i) the (Z)-*butenolide* (27) as yellow needles, m.p. 121—122°, $\lambda_{max.}$ (EtOH) 350 nm, $\nu_{max.}$ (KBr) 1760sh, 1745, 1655, and 1600 cm^{-1}, τ 2·26 (2H, d, *S* 9), 3·13 (2H, d, *S* 9), 4·03 (ArC*H*:), 4·13 (q, *S ca.* 1, :CH·CO), 6·22 (OMe), and 7·81 (d, *S ca.* 1, :CMe) (Found: C, 72·2; H, 5·8. $C_{13}H_{12}O_3$ requires C, 72·2; H, 5·55%); and (ii) a 1 : 1 mixture of the *Z*- and *E*-isomers, τ 8·13 and 7·81.

(Z)- *and* (E)-4-*Benzylidene*-3-*methoxy*-2-*methylbut*-2-*en*-4-*olide* [(29) *and* (30)].—By the general procedure, the ylide from phosphonium salt (25) (2·35 g) with benzaldehyde (0·5 ml) gave, after chromatography in chloroform, (i) the (Z)-*benzylidenebut*-2-*enolide* (0·1 g) (eluted first), which crystallised from chloroform–light petroleum (b.p. 60—80°) as needles, m.p. 138—139°, $\lambda_{max.}$ ($CHCl_3$) 321 nm, $\nu_{max.}$ (KBr) 1750, 1635, 970, 764, and 690 cm^{-1}, τ 2·14—2·4 (2H), 2·55—2·8 (3H), 3·88 (PhC*H*:), 5·83 (OMe), and 7·9 (:CMe) (Found: C, 72·1; H, 6·0. $C_{13}H_{12}O_3$ requires C, 72·2; H, 5·6%); and (ii) the (E)-*isomer* (0·2 g) (eluted second), which crystallised from chloroform–light petroleum (b.p. 60—80°) as needles, m.p. 101—102°, $\lambda_{max.}$ 310 nm, $\nu_{max.}$ (KBr) 1760, 1665, 1620, 987, 772, and 702 cm^{-1}, τ 2·5—2·8 (5H, m), 3·36 (PhC*H*:), 6·02 (OMe), and 7·89 (:CMe) (Found: C, 72·0; H, 5·8%).

A significant amount (*ca.* 0·4 g) of triphenylphosphine was eluted before the (*Z*)-isomer.

(Z)-5-(2-*Furyl*)-3-*methylpent*-2-*en*-4-*ynal* (32).—(*Z*)-5-(2-Furyl)-3-methyl-1-(tetrahydropyran-2-yloxy)pent-2-en-4-yne [29] was treated with hydrochloric acid as described for the (*E*)-5-(3-furyl)-2-methyl-enyne analogue (see following paper). Chromatography produced the alcohol (77%) as an oil, $\lambda_{max.}$ ($CHCl_3$) 303 and 387 nm, $\nu_{max.}$ 3400 and 2205 cm^{-1}, τ 2·64 (d, *S* 2, O·C*H*:CH), 3·43 [dd, *S* 3·5 and 0·5, C*H*:C(O)C:], 3·64 (dd, *S* 2 and 1, O·CH:C*H*), 4·1 (tq, *S* 7·5 and 1, :C*H*·CH_2), 5·66 (dd, *S*2 and 7, CH_2·OH), 6·99 (OH), and 8·08 (d, *S* 1, Me) (Found: M^+, 162·0666. $C_{10}H_{10}O_2$ requires M, 162·0681).

Oxidation of the alcohol, as described for the *E*-5-(3-furyl)-2-methyl-enynol (see following paper) gave the aldehyde (80%), an oil, $\lambda_{max.}$ 333 nm, $\nu_{max.}$ 2220 and 1682 cm^{-1}, τ −0·16 (d, *S* 7·5, CHO), 2·5 (d, *S* 2, O·C*H*:CH), 3·22 [d, *S* 3, CH:C(O)C:], 3·54 (dd, *S* 2 and 1·5, O·CH:C*H*), 3·82 (dq, *S* 7·5 and 1·5, :C*H*·CHO), and 7·81 (d, *S* 1·5, Me) (Found: M^+, 160·0516. $C_{10}H_8O_2$ requires M, 160·0524).

(4Z) *and* (4E)-*Isomers of* (6Z)-9-(2-*Furyl*)-2,7-*dimethylnona*-2,4,6-*trien*-8-*yn*-4-*olide* [(33) *and* (34)].—By the general procedure, the ylide from the salt (19a; X = Br) (0·5 g) with the enynal (32) gave, after chromatography in chloroform, (i) the (Z)-*isomer* (33) (28 mg) (eluted first), which crystallised from benzene as yellow rhombs, m.p. 82—84°, $\lambda_{max.}$ ($CHCl_3$) 386 nm, $\nu_{max.}$ ($CHCl_3$) 2205, 1762, 1593, 1563, 1497, 1457, 1385, 1320, 1160, 1132, 1064, 1020, 991, 948, 917, and 898 cm^{-1}, τ 2·63 (dd, *S* 2·3 and 0·9, O·C*H*:CH), 3·0 (q, *S* 1·4, C*H*:CMe·CO), 3·27 (dq, *S* 12 and 1·3, ·CMe:C*H*·CH), 3·42 [dd, *S* 3 and 0·9, :C·C(O):CH], 3·63 (dd, *S* 3 and 2·3, O·CH:C*H*·CH), 3·9 (d, *S* 12, :C*H*·CH·CMe), 7·92 (:CMe·CO), and 8·01 (:C·CMe) (Found: M^+, 240·0786. $C_{15}H_{12}O_3$ requires M, 240·07861); and (ii) the (E)-*isomer* (34) (75 mg) (eluted second), which crystallised from benzene as yellow needles, m.p. 141—143°, $\lambda_{max.}$ ($CHCl_3$) 383 nm, $\nu_{max.}$ ($CHCl_3$) 2205, 1757, 1590, 1568, 1497, 1392, 1350, 1306, 1162, 1128, 1072, 997, 941, 917, and 874 cm^{-1}, τ 2·62—2·67 (m, OCH:C*H* and C*H*:CMe·CO), 3·38 (d, *S* 12, :C*H*·CH:CMe), 3·42 [m, :C·C(O):C*H*], 3·6 (dq, *S* 12 and 1, ·CMe:C*H*·CH), 3·65 (m, O·CH:C*H*·CH), 7·95 (:CMe·CO), and 8·0 (:C·CMe) (Found: M^+, 240·0783).

(Z)- *and* (E)-*Isomers* of 3-[(2Z)-5-(2-*Furyl*)-3-*methylpent*-2-*en*-4-*ynylidene*]*phthalide* [(35) *and* (36)].—By the general procedure, the ylide from the salt (10; X = Cl) (0·57 g) with the enynal (32) gave, after chromatography in benzene–chloroform (4 : 1), (i) the (Z)-*isomer* (35) (17 mg) (eluted first), a labile red oil, $\lambda_{max.}$ ($CHCl_3$) 385 nm, $\nu_{max.}$ 2200 and 1780 cm^{-1}, τ 2·0—3·2 (m, 4 × aryl :CH + furan α-H + ·CMe:C*H*·C*H*:), 3·35 [m, :C·C(O):CH], 3·58 (m, O·CH:C*H*·CH:), and 7·88 (Me) (Found: M^+, 276·0786. $C_{18}H_{12}O_3$ requires M, 276·0786); and (ii) the (E)-*isomer* (0·14 g) (eluted second), which crystallised from ethyl acetate–methanol as bronze rhombs, m.p. 146—147°, $\lambda_{max.}$ ($CHCl_3$) 385 nm, $\nu_{max.}$ (KBr) 1775 cm^{-1}, τ 2·0—2·8 m (4 × aryl :CH + furan α-H), 3·1 (·CMe:C*H*·C*H*:), 3·35 [d, *S* 2, :C·C(O):C*H*], 3·6 (dd, *S ca.* 2 and *ca.* 4, O·CH:C*H*·CH), and 7·84 (Me) (Found: M^+, 276·0798).

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