Carotenoids and Related Compounds. Part XVIII.[1] Synthesis of *cis*- and Di-*cis*-Polyenes by Reactions of the Wittig Type

By **Gerald Pattenden** and **B. C. L. Weedon**, Department of Chemistry, Queen Mary College, London E.1

Some claims to have achieved "*cis*-olefination" have been re-examined.

Attempts to obtain a number of *cis*-allylic Wittig reagents were unsuccessful.

cis-Diethyl 3-methoxycarbonyl-2-methylprop-2-enylphosphonate has been prepared, but its condensation with aldehydes was accompanied by extensive stereomutation. Evidence was obtained for retention of configuration during Wittig reactions with *cis*- and *trans*-citral. Methyl diethylphosphonoacetate condensed with 4-hydroxybut-2-enolide and with its 2- and 3-methyl analogues to give the half esters of the corresponding *cis,trans*-muconates exclusively.

Reaction of 4-hydroxy-3-methylbut-2-enolide with allylic Wittig reagents gave polyene acids with complete retention of (*cis*-) stereochemistry about the αβ-double bond, and a high proportion of *cis*-configuration about the newly formed carbon–carbon double bonds.

The *cis*-11,*cis*-13 isomer of vitamin A acid has been characterised.

SEVERAL natural carotenoids with one or more *cis*-double bonds have been isolated, and there is reason to believe that geometrical isomerism plays an important part in the biosynthesis of carotenoids, and perhaps in some of their biological functions.[2-4] The range of *cis*-carotenoids was greatly extended by the classical stereomutation studies of Zechmeister and his collaborators,[2] and a number of *cis*-compounds have been obtained by partial catalytic hydrogenation of their acetylenic analogues.[5] Central-*cis*-ζ-carotene, prepared by the latter route, proved to be identical with a pigment from *Chlorella* mutants,[4] but all geometrical configurations assigned to other *cis*-carotenoids, both natural ones and those prepared by stereomutation, lack confirmation by synthesis. In this paper we report some model studies on the suitability of the Wittig and related reactions for the unambiguous synthesis of *cis*-polyenes, in particular those with trisubstituted double bonds, since these are not accessible by acetylenic routes and the methods developed in the vitamin A field are of limited scope.[5,6]

A modification of the well known Wittig reaction, resulting in '*cis*-olefination,' was reported by Bergelson and Shemyakin.[7] Although we confirmed their finding [8]

$$\underset{(1)}{Me\cdot[CH_2]_5\cdot CHO} + \underset{(2)}{Ph_3P{:}CH\cdot[CH_2]_9\cdot CO_2Et} \longrightarrow \underset{(3)}{Me\cdot[CH_2]_5\cdot CH{:}CH\cdot[CH_2]_9\cdot CO_2Et}$$

that reaction of heptanal (1) with the Wittig reagent (2) from ethyl 11-iodoundecanoate gives ethyl octadec-*cis*-11-enoate (3) with a stereochemical purity > 90%, we could not obtain the high proportions of *cis*-olefin claimed [7a,9] in the preparation of β-ethylstyrene (6) from either benzylidenetriphenylphosphorane (4) and propionaldehyde (5), or from propylidenetriphenyl phosphorane (8) and benzaldehyde (7), in the presence of amines

$$\underset{(4)}{PhCH{:}PPh_3} + \underset{(5)}{OCHEt} \longrightarrow \underset{(6)}{PhCH{:}CHEt} \longleftarrow \underset{(7)}{PhCHO} + \underset{(8)}{Ph_3P{:}CHEt}$$

and/or lithium salts. In our hands these two reactions gave products in which the proportion of *cis*-olefin did not exceed 45 and 65% respectively. These results agreed well with those reported subsequently by House *et al.*,[10] and with more recent publications by Bergelson and Shemyakin [7b] (Table 1). Wheeler *et al.*[11] were similarly unable to confirm the high proportions of *cis*-stilbene originally reported by the Russian authors for the reaction of the Wittig reagent (4) with benzaldehyde. The reason for these discrepancies is not

TABLE 1

Proportion (%) of *cis*-isomer in β-ethylstyrene from propionaldehyde and benzylidenetriphenylphosphorane

	Authors			
Medium	Bergelson and Shemyakin [7a,9]	Present	House *et al.*[10]	Bergelson and Shemyakin [7b]
Benzene	26	27	23	20
Benzene–aniline	51	38		
Benzene–LiBr...	93	23	23	26
DMF	65	44	44—46	39
DMF–LiBr or NaBr	96	45	46	41

[1] Part XVII, D. F. Schneider and B. C. L. Weedon, *J. Chem. Soc.* (*C*), 1967, 1686.

[2] L. Zechmeister, '*Cis-Trans* Isomeric Carotenoids, Vitamins A and Arylpolyenes,' Springer-Verlag, Vienna, 1962.

[3] B. C. L. Weedon in 'Chemistry and Biochemistry of Plant Pigments,' ed. T. W. Goodwin, Academic Press, London, 1965.

[4] J. B. Davis, L. M. Jackman, P. T. Siddons, and B. C. L. Weedon, *J. Chem. Soc.* (*C*), 1966, 2154.

[5] O. Isler and P. Schudel, *Adv. Org. Chem.*, 1963, **4**, 115.

[6] I. M. Heilbron and B. C. L. Weedon, *Bull. Soc. chim. France*, 1958, **1**, 83.

[7] (*a*) L. D. Bergelson and M. M. Shemyakin, *Tetrahedron*, 1963, **19**, 149; (*b*) L. D. Bergelson and M. M. Shemyakin, *Pure Appl. Chem.*, 1964, **9**, 271; L. D. Bergelson, L. I. Barsukov, and M. M. Shemyakin, *Tetrahedron*, 1967, **23**, 2709.

[8] L. D. Bergelson, V. A. Vaver, V. Yu. Kovtun, L. B. Senyavina, and M. M. Shemyakin, *Zhur. obshchei Khim.*, 1962, **32**, 1802.

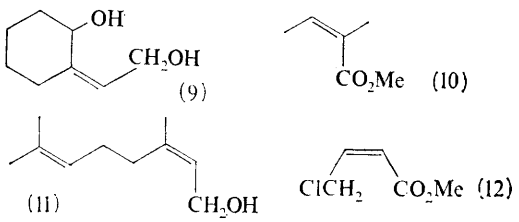
[9] L. D. Bergelson, V. A. Vaver, L. I. Barsukov, and M. M. Shemyakin, *Doklady Akad. Nauk S.S.S.R.*, 1962, **143**, 111.

[10] H. O. House, V. K. Jones, and G. A. Frank, *J. Org. Chem.*, 1964, **29**, 3327; cf. H. O. House and G. H. Rasmussen, *J. Org. Chem.*, 1961, **26**, 4278.

[11] O. H. Wheeler and H. N. Battle de Pabon, *J. Org. Chem.*, 1965, **30**, 1473.

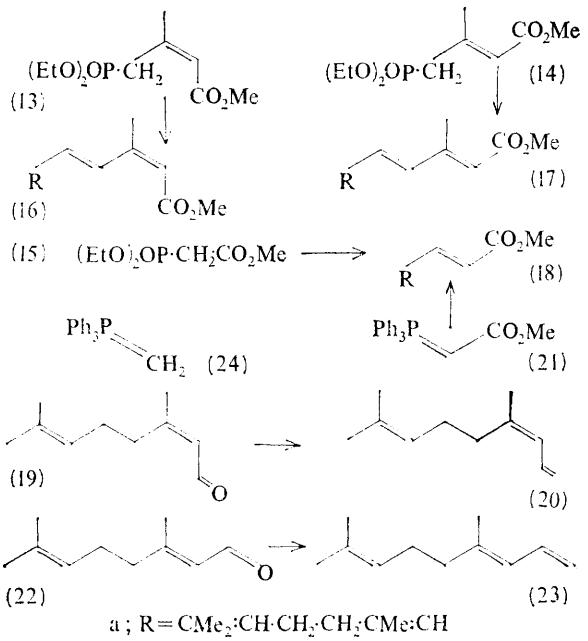
clear, but the possibility that the original reactions were carried out in the presence of impurities capable of co-ordinating strongly with the reagents cannot be excluded. In this connection it is interesting to note the recent claims [12] that reaction of propionaldehyde with the phosphorane (4), or of benzaldehyde with (8), under ' salt-free ' conditions, gives β-ethylstyrene (6) containing 25 and 96%, respectively, of the *cis*-isomer. However, as ' *cis*-olefination ' has not been achieved in reactions of αβ-unsaturated aldehydes with Wittig reagents derived from allylic halides, α-halogeno-ketones or α-halogeno-esters,[7] the method is at present of limited value for the preparation of authentic *cis*-carotenoids. We therefore tried to find out whether *cis*-double bonds already present in either the phosphorus or the carbonyl reagent are preserved during a reaction of the Wittig type.

Although Harrison and Lythgoe [13] observed almost complete retention of configuration during the conversion of the *cis*-allylic alcohol (9) into the corresponding Wittig reagent, and the subsequent condensation of the latter with a ketone, our attempts to prepare *cis*-allylic Wittig reagents from methyl 2-methylisocrotonate (10) following allylic bromination with *N*-bromosuccinimide, from



nerol (11) after treatment with thionyl chloride in triethylamine, and from methyl *cis*-4-chlorocrotonate (12),[10] were unsuccessful. However, the isomeric mixture of diethyl phosphonates [4] derived from methyl 3-bromomethylcrotonate proved to be separable into *cis*- (13) and *trans*- (14) isomers by fractional distillation and preparative g.l.c. The n.m.r. spectra of the isomers resembled each other; both exhibited a doublet of doublets (J_1 1·5 and J_2 3·5 c./sec.) attributable to the olefinic methyl group, and a doublet (J 23·5 c./sec.) attributable to the allylic methylene adjacent to the phosphonate group (the 3·5 and 23·5 c./sec. couplings were shown to be due to phosphorus–proton interactions by appropriate heteronuclear decoupling experiments). With the lower-boiling isomer, which also had the shorter retention time, these absorptions occurred at τ 7·93 and 6·53, respectively, and in the other at 7·70 and 7·31, respectively. Such differences may be ascribed to deshielding by the methoxycarbonyl substituent of groups *cis* to it,[14] and the *cis*-configuration (13) was therefore assigned to the former isomer.

Condensation of the *trans*-phosphonate (14) with benzaldehyde,[15] and with *cis*- (19) and *trans*- (22) citral gave the expected products, shown by n.m.r. spectroscopy [16] to consist entirely of the *trans*-2-esters (17;

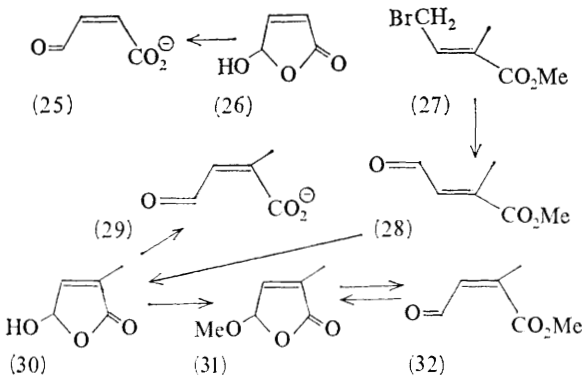


R = Ph) or (17a). However, condensation of the *cis*-phosphonate (13) with benzaldehyde,[15] propionaldehyde, or *trans*-citral (22) was accompanied by extensive stereomutation, and only *ca.* 25% of the resulting esters possessed the *cis*-2-configuration: (16; R = Ph or Et) or (16a).

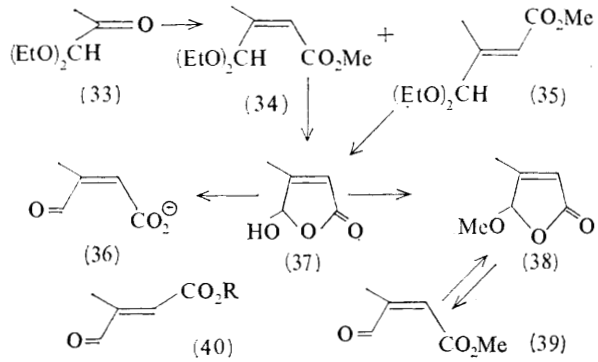
The conjugated triene esters (16a and 17a) derived from citral were not amenable to full stereochemical analysis. A similar situation was encountered with the *trans*-2-esters (18a) obtained by condensation of citral with either the phosphonate (15) [17] or the corresponding Wittig reagents (21).[18] It was therefore not possible to determine whether the stereochemistry of the citrals had been preserved in these reactions. However, retention of the configuration of both *cis*- (19) and *trans*- (22) citral in the reaction with methylenetriphenylphosphorane (24) was clearly demonstrated by g.l.c. analysis of the products (20) and (23) respectively. After the preliminary publication of our results,[19] Bohlmann and Seyberlich [20] reported retention of configuration in Wittig reactions with β-methylthio-αβ-unsaturated aldehydes.

[12] M. Schlosser, G. Müller, and K. F. Christmann, *Angew. Chem.*, 1966, **78**, 677; M. Schlosser and K. F. Christmann, *Annalen*, 1967, **708**, 1.
[13] I. T. Harrison and B. Lythgoe, *J. Chem. Soc.*, 1958, 843.
[14] L. M. Jackman, ' Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry,' Pergamon, London, 1959.
[15] G. Pattenden and B. C. L. Weedon, following paper.
[16] Cf. J. W. K. Burrell, R. F. Garwood, L. M. Jackman, E. Oskay, and B. C. L. Weedon, *J. Chem. Soc.* (*C*), 1966, 2144.
[17] W. S. Wadsworth and W. D. Emmons, *J. Amer. Chem. Soc.*, 1961, **83**, 1733.
[18] O. Isler, H. Gutmann, M. Montavon, R. Rüegg, G. Ryser, and P. Zeller, *Helv. Chim. Acta*, 1957, **40**, 1242.
[19] G. Pattenden, B. C. L. Weedon, C. F. Garbers, D. F. Schneider, and J. P. van der Merwe, *Chem. Comm.*, 1965, 347.
[20] F. Bohlmann and A. Seyberlich, *Chem. Ber.*, 1966, **99**, 138.

The γ-lactols (26),[21] (30),[22] and (37),[23] are readily converted by alkali into the *cis*-ethylenic aldehydes (25), (29), and (36), respectively. Although the latter are subsequently transformed into their *trans*-isomers when exposed to an excess of alkali, reactions of the lactols with phosphoranes and phosphonates held promise of providing a convenient method for introducing 'unsubstituted' *cis*-double bonds, and their α- and β-methyl derivatives. Moreover, further elaboration of the initial *cis*-polyene could be achieved, if desired, by utilising the carboxy-group incorporated simultaneously.

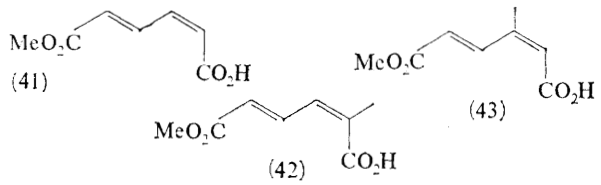


New routes were developed to the α- (30) and β- (37) methyl lactols. A Kröhnke reaction on methyl 4-bromo-2-methylcrotonate (27) yielded the formyl ester (28) which was hydrolysed to give the required α-methyl lactol (30). Condensation of the phosphonate (15) with the diethyl acetal (33) of pyruvaldehyde, and hydrolysis of the resulting isomeric mixture of acetals (34) and (35), readily furnished the β-methyl lactol (37). Treatment of the lactols (30) and (37) with methanolic sulphuric acid gave the corresponding *O*-methyl derivatives, (31)



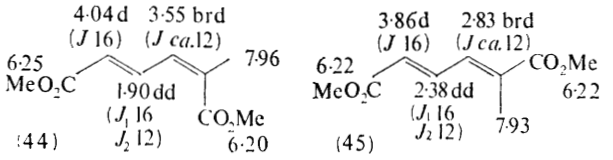
and (38). Reaction of the β-methyl lactol (37) with sodium methoxide, followed by acidification, gave *trans*-β-formylcrotonic acid (40; R = H).[24]

Condensation of the lactols (26), (30), and (37) with the phosphonate (15) in the presence of sodium methoxide gave the known *cis,trans*-half-esters (41),[25] (42),[26] and (43),[27] respectively, with complete retention of the



stereochemistry of the double bonds derived from the lactols, and *trans*-configurations about the newly formed double-bonds. The structures of the products were confirmed by conversions into the corresponding dicarboxylic acids and dimethyl esters, and by n.m.r. and stereomutation studies. In the 'unmethylated' and β-methyl series, our results agreed well with those of Elvidge, Linstead, and their collaborators.[25,27-29] The new syntheses of the α-methyl compounds from the α-methyl lactol (30), and the n.m.r. data now reported for the first time, confirm the stereochemical assignments made by Sugita *et al.*[26]

The n.m.r. properties of the *cis,trans*- and *trans,trans*-1-methylbuta-1,3-diene-1,4-dicarboxylates are summarised in the accompanying formulae (44) and (45) respectively. The olefinic proton bands are readily

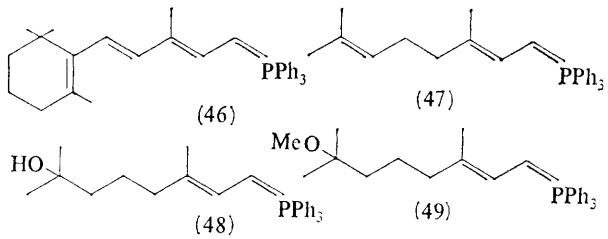


assigned from the observed spin–spin coupling. As with the *cis,trans*-buta-1,3-diene-1,4-dicarboxylates [28] and 2-methylbuta-1,3-diene-1,4-dicarboxylates,[29] the 3-proton signal is observed at lowest field, and the 4-proton is found at higher field than the 2-proton. The observed value (16 c./sec.) of $J_{3,4}$ confirms the *trans*-configuration of the 3,4-double bond in both isomers. The stereochemistry assigned to the 1,2-double bond in the two isomers is based on (i) the absorption of the 3-proton at lower field in the *cis,trans*-isomer than in the *trans,trans*-isomer owing to deshielding by both methoxycarbonyl groups, (ii) the absorption of the 2-proton in the *trans,trans*-isomer at lower fields than in the *cis,trans*-isomer owing to its *cis*-relationship to the 1-methoxycarbonyl group, and (iii) the slight deshielding of the 1-methoxycarbonyl group in the *cis,trans*-isomer, and of the 1-methyl group in the *trans,trans*-isomer, resulting from the situation of these groups with respect to the 3,4-double bond.

[21] H. Fecht, *Ber.*, 1905, **38**, 1272.
[22] C. F. Garbers and J. P. van der Merwe, *J.S. African Chem. Inst.*, 1964, **17**, 149.
[23] W. J. Conradie, C. F. Garbers, and P. S. Steyn, *J. Chem. Soc.*, 1964, 594.
[24] C. F. Garbers, private communication.
[25] J. A. Elvidge, R. P. Linstead, and P. Sims, *J. Chem. Soc.*, 1953, 1793.
[26] T. Sugita, Y. Inouye, and M. Ohno, *J. Agric. Chem. Soc. Japan*, 1958, **22**, 162.
[27] J. A. Elvidge, R. P. Linstead, and P. Sims, *J. Chem. Soc.*, 1951, 3386.
[28] J. A. Elvidge and P. D. Ralph, *J. Chem. Soc.* (*C*), 1966, 387.
[29] J. A. Elvidge, *J. Chem. Soc.*, 1959, 474.

Condensation of the Wittig reagent (21) with the β-methyl lactol (37) also gave the *cis,trans* half-ester (43), though traces of other products (probably artefacts) were also detected.

Condensation of the Wittig reagent (46)[30] from β-ionylideneethyl triphenylphosphonium bromide with the β-methyl lactol (37) gave a mixture of vitamin A acids. The n.m.r. spectrum indicated the presence of two isomers in the ratio 1 : 2. The minor, less soluble



component was isolated and identified as the known *cis*-13(2 *)-isomer (51). By analogy with the products from the corresponding reaction (following paper) of the benzylidene Wittig reagent (4), the main product was assigned the hitherto unknown *cis*-11(4 *), *cis*-13(2 *)-structure (52) containing one ' hindered ' and one ' unhindered ' *cis*-double-bond. At this stage Professor C. F. Garbers (Stellenbosch) informed us that he and his collaborators had isolated the main product from a similar condensation of (37) and (46) by fractional crystallisation. A sample from the South African workers had properties which supported our structural assignment. Its visible light-absorption maximum was at lower wavelength and of lower intensity than those of all other reported forms of vitamin A acid, as would be expected for the first isomer of this acid believed to contain a sterically ' hindered ' double bond. Its n.m.r. spectrum resembled that of the *cis*-13(2 *)-isomer, the principal difference being the absence of the low-field doublet (τ *ca.* 2·3) observed with both the *cis*-13(2 *)- and *cis*-9(6 *),*cis*-13(2 *)-isomers and which is attributable to the 12(4 *)-proton;[31] presumably the 12(4 *) proton in the *cis*-11(4 *),*cis*-13(2 *)-isomer is shielded and absorbs in the region τ 3·0—3·45. Another significant difference is that the band due to the 13(3 *)-methyl occurs at somewhat lower field (7·80 compared with 7·91), probably owing to deshielding by the nearby 9,10(6,7 *)-double-bond. In agreement with this interpretation, the 10(6 *)-proton, which has a similar steric relation to the 13,14(2,3 *)-double-bond, exhibits a doublet (τ 3·66) at lower field than the corresponding absorption in the spectra of either the all-*trans*- (τ 3·85) or *cis*-13(2 *)-isomer (τ 3·75). Analogous deshielding of olefinic protons has previously been observed in the bixin series.[32] The n.m.r. properties of the three isomers of vitamin A acid are summarised in formulae (50—52). The results with the all-*trans*- and mono-*cis*-isomers agree with those published recently by Korver *et al.*,[31] who also give the n.m.r. spectrum of the *cis*-9(6 *),*cis*-13(2 *)-isomer.

Further proof of the proposed configuration for the new isomer came from the observation[19,24] that iodine-catalysed isomerisation in ether at 20° for 3 min., gave the *cis*-13(2 *)-isomer in excellent yield. Moreover, under conditions known to cause stereomutation of the *cis*-13(2 *)-, but not the *cis*-9(6 *)-acid, the new isomer yielded all-*trans* vitamin A acid (50).

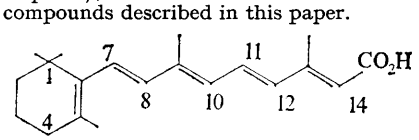
Condensation of the geranyl Wittig reagent (47),[33] and of the related methoxy-reagent (49),[34,35] with the β-methyl lactol (37) also gave a stereoisomeric mixtures of acids. Comparison of the n.m.r. spectra of these mixtures with that of the corresponding product in the vitamin A acid series again indicated the presence of *cis*-2- [3-methyl *ca.* 7·94; 4-proton *ca.* 2·32 (d, *J* 15 c./sec.)] and *cis*-2,*cis*-4- (3-methyl *ca.* 7·85) isomers in the approximate ratio 1 : 2.

Condensation of the geranyl (47) and the hydroxy-(48)[34,36] Wittig reagents with the *O*-methyl derivative (38) gave the corresponding conjugated trienoates. Examination of the n.m.r. spectra of these mixtures of esters showed the presence of *cis*-2- (56 and 59) and *cis*-2,*cis*-4- (57 and 60) isomers, but (in marked contrast to the acids from the β-methyl lactol) in the approximate ratio 2 : 1. Mild iodine-catalysed stereomutation of the mixture from the geranyl reagent gave a product containing 90% of the *cis*-2-isomer (56), and 10% of the *cis*-2,*cis*-4-isomer (57). Further stereomutation led to the formation of some *trans*-2-isomers (55).

Reaction of the same two Wittig reagents with the *trans*-formyl ester (40; R = Me) gave the expected conjugated trienoates as mixtures of the *cis*-4- and all-*trans*-isomers. The latter (55 and 58) were readily isolated after iodine-catalysed stereomutation of the mixtures. No significant difference could be detected between the product from the geranyl Wittig reagent (47) and (40; R = Me) after stereomutation, and that formed by condensation of *trans*-citral (22) with the *trans*-phosphonate (14).

The assignments of the n.m.r. bands from the mixtures of conjugated trienoic acids and their esters are shown in

* The conventional numbering of vitamin A derivatives is ndicated in the accompanying formula. The figures given in parentheses in the text refer to the alternative numbering (carboxy-group as 1); these are included to facilitate comparisons with other compounds described in this paper.



[30] H. Pommer, *Angew. Chem.*, 1960, **72**, 811, 911.
[31] P. K. Korver, C. Kruk, P. J. van der Haak, J. L. Baas, and H. O. Huisman, *Tetrahedron*, 1966, **22**, 277; cf. C. von Planta, U. Schwieter, J. Chopard-dit-Jean, R. Rüegg, M. Kofler, and O. Isler, *Helv. Chim. Acta*, 1962, **45**, 548.
[32] M. S. Barber, A. Hardisson, L. M. Jackmann, and B. C. L. Weedon, *J. Chem. Soc.*, 1961, 1625.
[33] O. Isler, H. Gutman, H. Lindlar, M. Montavon, R. Rüegg, G. Ryser, and P. Zeller, *Helv. Chim. Acta*, 1956, **39**, 463.
[34] J. D. Surmatis and A. Ofner, *J. Org. Chem.*, 1963, **28**, 2735.
[35] M. S. Barber, L. M. Jackman, P. S. Manchand, and B. C. L. Weedon, *J. Chem. Soc.* (*C*), 1966, 2166.
[36] R. Bonnett, A. A. Spark, and B. C. L. Weedon, *Acta Chem. Scand.*, 1964, **18**, 1739.

formulae (**53**—**62**). The features, already discussed, which differentiate the vitamin A acids, are also evident in the other series. Unfortunately, it was not possible (at 60 Mc./sec.) to determine accurately the absorption due to the protons of the γδ-*cis* double bonds in any of these compounds.

The studies now reported indicated that the stereochemistry of the *cis*-aldehydes formed from the three lactols (**26**), (**30**), and (**37**), and the *O*-methyl derivative (**38**), like that of the *trans*-aldehyde (**40**; R = Me), was fully retained during condensations of the Wittig type (provided that exposure to an excess of base was avoided). There were, however, considerable differences in the reactions studied concerning the stereochemistry of the newly formed double-bonds; these are summarised below:

(i) In the phosphonate condensations, the newly formed double-bond was *trans*, as expected by analogy with previously published results with diethyl phosphonates and aliphatic or aromatic aldehydes.[37a]

(ii) The double bond formed during the reactions of the β-methyl lactol (**37**) with the phosphorane (**21**) had predominantly the *trans*-configuration.

(iii) Reaction of the allylic Wittig reagents (**47**) and (**48**) with the *trans*-formyl ester (**40**; R = Me) gave the all-*trans*-products together with smaller amounts of the *cis*-**4**-isomers.

(iv) Similar reactions with the *O*-methyl derivative (**38**), effectively the *cis*-formyl ester (**39**), gave products in which *ca.* 30% of the newly formed (γδ-) double bonds had the *cis*-configuration.

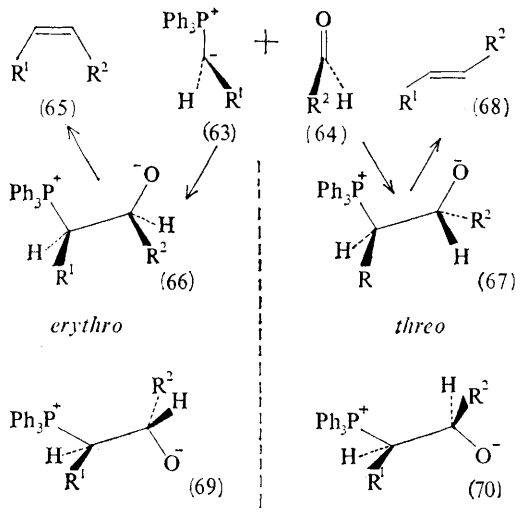
(v) Reaction of the β-methyl lactol (**37**) with allylic Wittig reagents gave products in which a remarkably

[37] (*a*) D. H. Wadsworth, O. E. Schupp, E. J. Seus, and J. A. Ford, *J. Org. Chem.*, 1965, **30**, 680; (*b*) A. J. Speziale and D. E. Bissing, *J. Amer. Chem. Soc.*, 1963, **85**, 3878.

high proportion (>60%) of the newly formed double-bonds had the *cis*-configuration.

The high proportion of the newly formed double-bonds with the *cis*-configuration from the reactions of allylic Wittig reagents with the *O*-methyl derivative (38), and in particular with the β-methyl lactol (37), resulting in di-*cis*-products, is surprising. The adoption of a *cis*-configuration about all the (γδ-) double bonds in question involves considerable steric interaction between the β-methyl groups and the ε-hydrogen atoms.[2,3] Hitherto the only general method for preparing such ' sterically hindered ' *cis*-double-bonds has been by partial catalytic reduction of the corresponding acetylenes.[3,5] Fortunately the formation of high proportions of these di-*cis*-products does not invalidate the use of the β-methyl lactol (37) and its *O*-methyl derivative (38) for the synthesis of αβ-*cis*-polyene acids or esters; as has been demonstrated with (52), (57), and the phenyl analogue,[15] the di-*cis*-isomer may be converted into the required mono-*cis*-isomer by preferential stereomutation of the ' sterically hindered ' double bond.

Our findings on the reactions of different phosphoranes with the β-methyl lactol (37) and its *O*-methyl derivative (38) may be rationalised by extension of previous views on the stereochemistry of the Wittig reaction.[7,10,37b] The initial combination of an aldehyde (64) with a phosphorane (63) can occur in two ways to give either the *erythro*- or the *threo*-form of the corresponding betaine, which subsequently collapses with the formation of the *cis*- (65) and *trans*- (68) olefin, respectively, and triphenylphosphine oxide. In the absence of suitable ligands, the eclipsed conformations (66) and (67) are



preferred for the betaine owing to the electrostatic attraction between the two charged groups. In this conformation the *threo*-betaine (67) is the less sterically hindered, and thus more likely to form. The *trans*-configuration is therefore favoured for the resulting olefin. Such factors are probably involved in the reactions summarised under (iii) and (iv) above.

It has been suggested that the staggered forms, (69) and (70), of the betaine are stabilised under appropriate conditions by solvation with polar solvents and co-ordination of the positively charged phosphorus atom with a Lewis base, or of the negatively charged oxygen atom with a Lewis acid.[7,10] If, as the result of one or more of these factors, the staggered conformations become important, the initial combination of the aldehyde and phosphorane will favour the *erythro*-form (69), which is now the less sterically hindered. In the subsequent formation of the olefin, presumably after rotation to give the eclipsed conformation (66), the proportions of the *cis*-isomer will be correspondingly enhanced. Many reactions leading to partial or substantial ' *cis*-olefination,' such as those discussed at the beginning of this paper, may be explained along these lines.

Turning to the betaines involved in the reaction of phosphoranes with the *cis*-aldehyde (36) derived from the β-methyl-lactol (37), a study of models suggests that interaction between the positively charged phosphorus atom and the carboxylate ion contributes to the stabilisation of the staggered conformations (69) and (70) (see also discussion in following paper). This would enhance the proportion of the *erythro*-form of the betaine in the initial combination, since the *erythro*-form (69) is again less sterically hindered than the *threo*-form in the staggered conformation (70). Such factors would promote the proportion of *cis*-double-bond to be produced subsequently.

Of the phosphoranes studied, only the methoxycarbonyl phosphorane (21) did not give an appreciable proportion of *cis*-configuration about the new double bond on reaction with the β-methyl lactol (37). This is consistent with many previous observations with related Wittig reagents.[7,10a,10b,37b] Bergelson and Shemyakin [7] attributed failure to achieve ' *cis*-olefination ' with reagents such as (21) to a strong preference for the *threo*-conformation (67) in the intermediate betaine as the result of polar interactions involving the methoxycarbonyl, or similar, substituent in the phosphorane. House *et al.*[10] and Speziale *et al.*,[37b] on the other hand, point out that the phosphoranes concerned are ' stable ' owing to electron withdrawal by the methoxycarbonyl, or related, substituent, and suggest that betaine formation with these phosphoranes is reversible. Subsequent reaction would then be expected to proceed almost entirely through the *threo*-form (67) of the betaine to give the *trans*-olefin since, as pointed out earlier, the eclipsed conformation required immediately prior to olefin formation is less sterically hindered in the *threo*- than in the *erythro*-form.

EXPERIMENTAL

Melting points are corrected. As far as possible all operations were carried out in an atmosphere of nitrogen. Those involving *cis*-polyenes were conducted at room temperature in diffuse light, or in the dark. Solutions of *cis*-polyenes were dried over magnesium sulphate, and evaporated under reduced pressure in the dark. Alumina

for chromatography was washed and graded.[38] DMF refers to commercial dimethylformamide from British Drug Houses, Ltd. It was used without purification except where otherwise indicated.

Only the main i.r. absorption bands are given. Unless otherwise stated, n.m.r. spectra were determined with a Varian A60 instrument for dilute solutions in deuteriochloroform, with tetramethylsilane as an internal standard. Bands were sharp singlets, except where one of the following designations is used: br, broad; d, doublet; dd, doublet of doublets; dm, doublet of multiplets; dt, doublet of triplets; m, multiplet; q, quartet; t, triplet; td, triplet of doublets. Band positions are given on the τ scale and coupling constants (J) in c./sec.; many of the assignments are summarised on the appropriate formulae. Relative intensities are not normally quoted as these had the expected values.

Proportions of geometrical isomers present in mixtures of polyene carboxylic acids or their esters were calculated from the relative intensities of the bands due to the β-methyl groups in the different isomers. Since the absorption due to the β-methyl group in the acid (54) overlapped that due to the methylene protons, the analysis of the mixture of (53) and (54) was confirmed by comparing the intensity of the doublet at 2·32 (J 15), due to the 4-proton in the *cis*-2-isomer, with that of the broad band at 4·90 due to the 10-proton in both isomers; the same procedure was followed with mixtures of the corresponding methyl esters.

Octadec-cis-11-*enoic Acid* (with D. W. L. Allen).—Ethyl 11-bromoundecanoate[39] (23·5 g.) was added to a suspension of sodium iodide (18 g., 50% excess) in methyl ethyl ketone. The mixture was stirred and boiled under reflux for 11 hr., then cooled to 20° and filtered. The filtrate was evaporated (to 50 ml.), diluted with benzene (250 ml.), washed with aqueous sodium thiosulphate, dried, and evaporated (to 100 ml.). Triphenylphosphine (25·2 g.) was added and the mixture was boiled under reflux for 12 hr. and then cooled. Most of the solvent was evaporated off and the residue was triturated with ether to give 10-ethoxycarbonyldecyltriphenylphosphonium iodide (31·4 g., 65%) as a glass which slowly crystallised, m.p. 116—118° (lit.,[8] 114—116°).

The phosphonium iodide (18·1 g.) in DMF (30 ml.) was added (10 min.) to a cooled (3—5°) and stirred suspension of sodium ethoxide (1·7 g.) in DMF (5 ml.). Stirring was continued for 30 min. at 3—5° and then for 30 min. at 20°. Heptanal (2·28 g.) in DMF (10 ml.) was added slowly (2 hr.), and the mixture was stirred at 20° for 2 hr. and then kept for 20 hr. The solvent was evaporated under reduced pressure, and the residue was extracted with ether. The extract was evaporated, and the residue was treated with a large volume of light petroleum (b.p. 60—80°). The triphenylphosphine oxide (m.p. and mixed m.p. 153—155°) which had separated was collected, and the petroleum solution was filtered through a short column of alumina to remove the residual phosphine oxide. Distillation gave ethyl octadec-11-enoate (3·3 g., 55%), $\nu_{max.}$ (film) 1730 cm.$^{-1}$.

The ethyl ester was hydrolysed with boiling aqueous methanolic sodium hydroxide and the sodium salt was separated at 0°. Thorough extraction of the latter with ether and acidification of the residue, gave octadec-*cis*-11-enoic acid (2·1 g.), $n_D^{21.5}$ 1·4581, $\nu_{max.}$ (liq. film) 1700 cm.$^{-1}$ (lit.,[8] n_D^{20} 1·4583). Treatment with ethereal diazomethane gave the methyl ester, b.p. 134—136°/0·2 mm., n_D^{22} 1·4522, $\nu_{max.}$ (liq. film) 1730 cm.$^{-1}$ (lit.,[8] b.p. 162—164°/1 mm., n_D^{20} 1·4527). Determination of the intensity of absorption (in CS_2) at 965 cm.$^{-1}$ by the method of Shreve and Heether,[40] with methyl oleate and methyl elaidate as standards, indicated that the ester contained 5—7% of the *trans*-isomer. In the olefinic proton region, the n.m.r. spectrum of the ester closely resembled that of methyl oleate, and differed from that of methyl elaidate.

β-*Ethylstyrene* (6).—The phosphorane was prepared from benzyltriphenylphosphonium bromide (15 mmoles),[41] m.p. 299—301°, or chloride (15 mmoles),[42] m.p. >307°, in either benzene (100 ml.) or DMF (100 ml. unless otherwise indicated) by the addition of ethereal butyl-lithium (*ca.* 10 ml., 1 equiv.) in the former solvent or of sodium ethoxide [normally in ethanol (*ca.* 5 ml.)] in the latter. In some experiments a fine suspension of lithium bromide, prepared by neutralising a solution of butyl-lithium (15 mmoles) in benzene (100 ml.) and ether (10 ml.) with anhydrous hydrogen bromide, or aniline, was added to the phosphorane solution. Freshly distilled propionaldehyde (10 mmoles) was added rapidly. Isolation of the products in the usual way and distillation gave β-ethylstyrene, b.p. 92—99°/20 mm. The proportions of *cis*- and *trans*-isomers were determined by g.l.c. (polyethylene glycol adipate; 98°). The results of typical experiments are summarised in Table 2.

TABLE 2

Formation of β-ethylstyrene from propionaldehyde and benzylidenetriphenylphosphorane

Wittig salt	Solvent	Base	Conditions [a]	Yield (%)	Proportion (%) of *cis*-olefin
Bromide	C_6H_6	BuLi	80°/3 hr.	57	27
Bromide	C_6H_6	BuLi	LiBr (15 mmoles) added; 80°/3 hr.	53	23
Bromide	C_6H_6	BuLi	$PhNH_2$ (10 mmoles) added; 80°3 hr.	53	38
Bromide	DMF	EtONa		74	45
Chloride	DMF	EtONa	80°/1 hr.	50	42
Chloride	DMF	EtONa		60	41
Chloride	DMF [b]	EtONa		65	41
Chloride	DMF [c]	EtONa	Base and aldehyde added at −25°	65	43
Chloride	DMF [c]	EtONa	Base and aldehyde added at 0°	62	42
Chloride	DMF [c,d]	EtONa [e]	Base added at 0°	60	40

[a] Reaction mixtures were stirred at 20° for 20 hr.; only subsequent heating, if any, is listed. [b] 20 ml. [c] 50 ml. [d] Dried and redistilled. [e] Solid.

Reaction of the phosphorane prepared from n-propyltriphenylphosphonium bromide, m.p. 238—239° (15 mmoles) in DMF (100 ml.) and sodium ethoxide (15 mmoles) in ethanol (5 ml.) with benzaldehyde (10 mmoles) at 20° for 20 hr. gave (75%) β-ethylstyrene which contained 65% of the *cis*-isomer.

Attempted Preparations of cis-*Allylic Wittig Reagents*.—

[38] G. W. H. Cheeseman, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 1949, 3120; H. Brockmann and H. Schodder, *Ber.*, 1941, **74**, 73.

[39] R. E. Bowman, *J. Chem. Soc.*, 1950, 177.

[40] O. D. Shreve and M. R. Heether, *Analyt. Chem.*, 1950, **22**, 1261.

[41] Badische Anilin u. Soda-Fabrik, B.P. 812, 522 (*Chem. Abs.*, 1959, **53**, 19,975f).

[42] K. Friedrich and H. G. Henning, *Chem. Ber.*, 1959, **92**, 2756.

(*a*) A mixture of methyl 2-methylisocrotonate [43] (3·5 g.), *N*-bromosuccinimide (5·5 g.), and carbon tetrachloride (15 ml.) was boiled under reflux for 3 hr. The succinimide was filtered off, and the filtrate and washings were concentrated under reduced pressure to leave the crude bromide (4 g.) as a pale brown oil. Its retention time (silicone; 140°) and n.m.r. spectrum (CCl_4) were identical with those of methyl 4-bromo-2-methylcrotonate. The crude bromide (4 g.) was added, during 30 min., to a stirred solution of triphenylphosphine (6·2 g.) in dry benzene (30 ml.) at 40°. The mixture was stirred at 20° for 24 hr., and the benzene was then evaporated off under reduced pressure to leave the phosphonium salt as a glassy solid; this was dissolved in boiling acetonitrile (10 ml.) and added to hot ethyl acetate (25 ml.). When the solution was cooled (*trans*-3-methoxycarbonyl-3-methylprop-2-enyl)triphenylphosphonium bromide (4·0 g.) crystallised; m.p. and mixed m.p. 191—192° (decomp.) (lit.,[44] 187—187·5°).

(*b*) Thionyl chloride (7·2 ml.) in chloroform (50 ml.) was added slowly (1 hr.) to a cooled (0°) and stirred solution of nerol (15·4 g.) and triethylamine (12·12 g.) in chloroform (50 ml.). The mixture was stirred at 20° for 30 min. and then evaporated to dryness under reduced pressure. Extraction of the residue with ether, and evaporation of the extract left the crude chloride (13 g.). Reaction with triphenylphosphine (20 g.) in benzene (150 ml.) at 20° for 7 days, evaporation, and trituration of the residue with ether gave a solid (5·8 g.), m.p. *ca.* 176°, from which no pure product could be isolated; its n.m.r. spectrum ($CDCl_3$) indicated the presence of both cyclic and alicyclic derivatives. Under identical conditions geraniol (15·4 g.) was converted into *geranyltriphenylphosphonium chloride* (11·7 g.), m.p. 194—195° (from methylene chloride–ethyl acetate), τ 2·0—2·5 (aryl H), 5·0br (olefinic H), 5·48 (dd, J_1 8, J_2 15, $\text{:CH·C}H_2\overset{+}{\text{P}}$), 7·95—8·34 ($\text{:C·CH}_2\text{·CH}_2\text{·C:}$), 8·43 and 8·47 ($Me_2C$:), and 8·63 (d, J 4, β-Me) (Found: C, 77·25; H, 7·2; Cl, 8·35; P. 7·2. $C_{28}H_{32}ClP$ requires C, 77·3; H, 7·4; Cl, 8·2; P, 7·1%). The corresponding bromide [33] exhibited a similar n.m.r. spectrum. (7-Hydroxy-3,7-dimethyloct-2-enyl)triphenylphosphonium bromide [34,36] had τ 2·0—2·5, 4·90br, 5·51 (dd, J_1 8, J_2 15), 8·05br (allylic CH_2), 8·65 (other CH_2 and β-Me), and 8·86 (Me_2C).

(*c*) Methyl 4-chlorocrotonate was prepared, and separated into *cis*- and *trans*-forms, as described by House *et al.*[10] The *cis*-isomer had τ 3·62 (dt, J_1 11, J_2 6, β-H), 4·1 (dt, J_1 11, J_2 1, α-H), 5·32 (dd, J_1 1, J_2 6, $\text{ClCH}_2\text{·CH:}$), and 6·25 (OMe); the *trans* isomer exhibited the corresponding bands at 2·95 (dt, J_1 15, J_2 6), 3·88 (dt, J_1 15, J_2 1), 5·82 (dd, J_1 1, J_2 6), and 6·33. Neither isomer reacted appreciably with triphenylphosphine in benzene at 20° during 2 weeks. When the reaction was carried out at 70° for 36 hr. both isomers gave (trans-3-*methoxycarbonylprop*-2-*enyl*)*triphenylphosphonium chloride* (42 and 35% respectively), which gave needles, m.p. and mixed m.p. 170—171° (from acetonitrile–ethyl acetate), $\nu_{max.}$ ($CHCl_3$) 1712, 1650, 1000, and 990 cm.$^{-1}$, τ 2·23 (m, aryl H), 3·50 (m, olefinic H), 4·78 (dd, J_1 6, J_2 16, $\overset{+}{\text{P}}CH_2$), and 6·34 (OMe) (Found: C, 66·6; H, 5·9; Cl, 8·0. $C_{23}H_{22}ClO_2P,H_2O$ requires C, 66·6; H, 5·8; Cl, 8·5%).

cis- and trans-*Diethyl* 3-*Methoxycarbonyl*-2-*methylprop*-2-*enylphosphonate* (13 and 14) (cf. ref. 4).—Methyl 3-bromomethylcrotonate (74·7 g.) was added slowly (30 min.) to triethyl phosphite (64 g.) at 100—110°. The mixture was heated to 150° during 30 min. and maintained at this temperature for 1 hr. Distillation of the residue gave the isomeric phosphonates (74 g., 80%) as a liquid, b.p. 115—125°/0·06 mm., $n_D^{22·5}$ 1·4600; n.m.r. and g.l.c. (polyethylene glycol adipate, 175°) showed the *cis–trans* ratio to be *ca.* 2 : 3. Fractional distillation through a Stedman column (18 × 2 cm.) gave *ca.* 90% concentrates of the individual isomers. These stereochemical purities were raised to >98% by preparative g.l.c. (silicone; 220°) and redistillation.

The *cis*-phosphonate, which had the lower retention time, had b.p. 82° (bath)/10^{-2} mm., n_D^{21} 1·4591, $\lambda_{max.}$ (95% EtOH) 218·5 mμ (ε 10,900), $\nu_{max.}$ (film) 1710vs, 1645s, 1250vs, 1160vs, 1050vs, 1030vs, 885m, 845m, and 800m—w, τ 4·17br (d, J 5, C:CH·), 5·89 (q, J 7 c.p.s.) (O·CH_2Me), 6·31 (OMe), 6·53 (d, J 23·5, CH_2·PO<), 7·93 (dd, J 1·5 and 3·5, MeC:C), 8·71 (t, J 7, O·CH_2Me) (Found: C, 48·0; H, 7·8; P, 12·55. $C_{10}H_{19}PO_5$ requires C, 48·0; H, 7·6; P, 12·4%.)

The *trans*-phosphonate had b.p. 102° (bath)/10^{-2} mm., n_D^{21} 1·4619, $\lambda_{max.}$ (95% EtOH) 219·5 mμ (ε 13,400) $\nu_{max.}$ (film) 1710vs, 1645s, 1250vs, 1215vs, 1150vs, 1050vs, 1030vs, 885m—w, 860w, 840w, and 780 (m—w), τ 4·17br (d, J 5)(C:CH·), 5·87 (q, J 7, O·CH_2Me), 6·30 (OMe), 7·31 (d, J 23·5, ·CH_2·PO), 7·70 (dd, J 1·5 and 3·5) (MeC:C), and 8·69 (t, J 7, O·CH_2·Me) (Found: C, 47·85; H, 7·7; P, 12·6%).

Methyl 3-*Methylhepta*-2,4-*dienoate* (16; R = Et).—A solution of sodium methoxide (from sodium, 130 mg.) in methanol (2 ml.) was added, during 10 min., to a stirred solution of *cis*-diethyl 3-methoxycarbonyl-2-methylprop-2-enylphosphonate (1·25 g.) (>95% stereochemical purity) and propionaldehyde (0·29 g.) in DMF (10 ml.). The mixture was stirred for 2 hr., then diluted with water and extracted with light petroleum (b.p. 40—60°). The extract was washed (H_2O), dried, and evaporated, to give an oil (650 mg., 83%); the relative intensities of the β-methyl bands at τ 8·01 and 7·72 indicated the presence of *cis*- and *trans*-2-esters in the ratio *ca.* 1: 3. Distillation (b.p. 160—168°/18 mm.), and preparative g.l.c. (silicone; 150°), gave the *ester* as a mixture of *cis*-2,*trans*-4- and *trans*-2,*trans*-4-isomers b.p. 120° (bath)/8 mm., $n_D^{22·5}$ 1·5000, $\lambda_{max.}$ (95% EtOH) 264 mμ (ε 24,400), $\nu_{max.}$ (liq. film) 1710, 1640, 1615, and 970 cm.$^{-1}$, τ 6·31 (OMe), 7·5—8·0 (CH_2), 7·72 (d, J 1·5), 8·01 (d, J *ca.* 1·5, MeC:), and 8·96 (t, J 7, MeC) (Found: C, 70·3; H, 9·0. $C_9H_{14}O_2$ requires C, 70·1; H, 9·15%). The relative intensity of the n.m.r. bands at 8·01 and 7·72 was unchanged after purification. Only partial separation of the isomers could be achieved by g.l.c. with various stationary phases.

cis- *and* trans-*Citral* (19 and 22).—Commercial citral [*cis–trans* ratio (g.l.c.[16]) *ca.* 1: 3] was redistilled, and the two isomers were separated by preparative g.l.c. (polyethylene glycol adipate; 110°).

cis-Citral (eluted first) had n_D^{17} 1·4904, $\lambda_{max.}$ (EtOH) 238 mμ, $\nu_{max.}$ (liq. film) 1670 and 1622 cm.$^{-1}$, τ 0·07 (d, J 8, CHO), 4·14 (d, J 8, α-H), 4·92 (m C:CH·CH_2), 7·25—7·9 (·CH_2·CH_2·), 8·02 (d, J 1·5, β-Me), and 8·34 and 8·40 (CMe_2C).

trans-Citral had n_D^{17} 1·4878, $\lambda_{max.}$ (EtOH) 236 mμ, $\nu_{max.}$ (liq. film) 1670 and 1625 cm.$^{-1}$, τ 0·03 (d, J 8), 4·13 (d, J 8), 4·94 (m), 7·7—7·85 (CH_2·CH_2), 7·81 (d, J 1·5, β-Me), and 8·34 and 8·40.

[43] R. E. Buckles and G. V. Mock, *J. Org. Chem.*, 1950, **15**, 680.

[44] E. Buchta and F. Andree, *Chem. Ber.*, 1960, **93**, 1349.

Methyl 5,9-*dimethyldeca*-2,4,8-*trienoate* (18a).—(*a*) A solution of sodium methoxide [from sodium (0·25 g.)] in methanol (20 ml.) was added slowly (15 min.) to a stirred solution of methyl diethylphosphonoacetate [17] (2·3 g.) and redistilled commercial citral (1·52 g.) in DMF (30 ml.); the rate of addition was such that the temperature did not exceed 30°. The mixture was stirred for a further 1 hr., and then diluted with ice–water and extracted with ether. The combined ethereal extracts were washed with water, then dried and evaporated. Distillation of the residue gave the *ester* (1·53 g., 75%) as a mixture of *trans*-2,*cis*-4- and *trans*-2,*trans*-4-isomers, b.p. 76°/0·02 mm., n_D^{21} 1·5100, $\lambda_{max.}$ (EtOH) 277 mμ (ε 20,800), $\nu_{max.}$ (liq. film) 1715, 1640, 1612, 985, and 730 cm.$^{-1}$, τ 2·40 (dd, J_1 16, J_2 12, β-H), 4·02 (d, J 12, γ-H), 4·23 (d, J 16, α-H), 4·92 (m, C:C*H*·CH_2), 6·28 (OMe), 7·86 (CH_2·CH_2), 8·12 (δ-Me), and 8·34 and 8·40 (CMe_2:C) (Found: C, 74·9; H, 9·6. $C_{13}H_{20}O_2$ requires C, 75·0; H, 9·6%). Attempts to separate the isomers by g.l.c. were unsuccessful.

(*b*) A solution of redistilled commercial citral (200 mg.) and (methoxycarbonyl)methyltriphenylphosphorane [18] (600 mg.) in dry chloroform (75 ml.) was stirred at 20° for 48 hr.; the course of the reaction was followed by the i.r. spectra of aliquot portions in chloroform by use of the band at 1618 cm.$^{-1}$ characteristic of the phosphorane and the band at 1715 cm.$^{-1}$ exhibited by the product. Evaporation of the solution to dryness, and chromatography of the residue in light petroleum (b.p. 40—60°) on alumina (IV), gave the ester (165 mg., 69%) as an oil, $n_D^{20·5}$ 1·5140, $\lambda_{max.}$ (EtOH) 278 mμ (ε 19,400). The i.r. and n.m.r. spectra were identical with those of the mixture obtained by method (*a*).

cis- *and* trans-4,8-*Dimethylnona*-1,3,7-*triene* (20 and 23).—(*a*) An equivalent of butyl-lithium in hexane was added, during 2 min., to a stirred suspension of methyltriphenylphosphonium bromide [45] (735 mg.) in ether (70 ml.). The mixture was stirred at 20° for 20 min., and then redistilled commercial citral (200 mg.) in ether (5 ml.) was added. The resulting pale yellow suspension was stirred at 20° for 2 hr., then diluted with water and extracted with ether. The extracts were washed (H_2O), dried, and evaporated.

The residual oily solid was triturated with light petroleum (b.p. 40—60°), and the supernatant liquid was decanted from the solid (Ph_3PO), filtered through a short column of alumina (IV), dried, and evaporated, to give a mixture of the *cis*- and *trans*-isomers of the hydrocarbon as a colourless oil (105 mg., 51%), n_D^{19} 1·4836, $\lambda_{max.}$ (95% EtOH) 236 mμ (ε 19,300), $\nu_{max.}$ (liq. film) 1645, 1600, 990, and 902 cm.$^{-1}$; the n.m.r. spectrum was very similar to those of the individual isomers; g.l.c. (squalane; 75°) showed two peaks only, in the ratio 1 : 3.

(*b*) Repetition of reaction (*a*) with *trans*-citral in place of the isomeric mixture of citrals gave a colourless oil (120 mg., 60%); g.l.c. (squalane; 75°) showed only one peak. Purification by preparative g.l.c. (silicone; 125°) gave the trans-*hydrocarbon*, n_D^{20} 1·4826, $\lambda_{max.}$ (95% EtOH) 236 mμ (ε 21,100), $\nu_{max.}$ (liq. film) 1645, 1600, 990, and 902 cm.$^{-1}$, τ 3·45 (td, J_1 10, J_2 10, J_3 16, 2-H), 4·19 (dm, J_1 10, 3-H), 5·0 (m, 1-H and 7-H), 7·88—7·94 (CH_2·CH_2), 8·25 (4-Me), and 8·34 and 8·40 (CMe_2:C) (Found: C, 88·05; H, 12·25. $C_{11}H_{18}$ requires C, 87·9; H, 12·1%).

(*c*) A similar reaction with *cis*-citral (170 mg.) gave a colourless oil (90 mg., 54%); g.l.c. (squalane; 75°) showed only one peak, with a retention time less than that of the product from (*b*). Purification by preparative g.l.c. (silicone; 125°) gave the cis-*hydrocarbon*, n_D^{20} 1·4798, $\lambda_{max.}$ (95% EtOH) 236 mμ (ε 18,200), $\nu_{max.}$ (liq. film) 1645, 1600, 990, and 902 cm.$^{-1}$ τ 3·45 (td, J_1 10, J_2 10, J_3 16), 4·19 (dm, J_1 10), 5·0 (m) 7·84, 8·22, 8·34, and 8·40 (Found: C, 87·7; H, 12·05%).

Methyl trans-3-*Formyl*-2-*methylacrylate* (28).—A mixture of methyl 2-methylcrotonate (130 g.), *N*-bromosuccinimide (203 g.), and dry carbon tetrachloride (1 l) was boiled under reflux for 18 hr., then cooled. Isolation of the product in the usual manner gave methyl 4-bromo-2-methylcrotonate (168 g., 77%), b.p. 96—102°/18 mm., n_D^{22} 1·4950 (lit.,[46] b.p. 90—94°/10 mm.).

Pyridine (85 ml.) was added, during 15 min., to a stirred solution of methyl 4-bromo-2-methylcrotonate (165 g.) in benzene (150 ml.). A mildly exothermic reaction set in, and an oily solid separated. The mixture was kept at 70° for 2 hr., and then at 20° overnight. *p*-Nitrosodimethylaniline (128 g.) in methanol (1200 ml.) was added. The mixture was cooled (0°), and N-sodium hydroxide (850 ml.) was added during 2·5 hr. with vigorous stirring. The mixture was stirred at 0° for a further 2 hr., and then at 20° for 2 hr. The crystalline product which had separated was filtered off, and the filtrate was then evaporated under reduced pressure to give more crude product as a brown oil; both samples were hydrolysed together in the next stage. Recrystallisation of a small amount of the solid gave the *nitrone* as orange-brown needles, m.p. 173·5—174° (Found: C, 64·0; H, 7·0; N, 10·75; O, 18·3. $C_{14}H_{18}N_2O_3$ requires C, 64·1; H, 6·8; N, 10·7; O, 18·3%).

6N-Sulphuric acid (1 l.) was added, over 3 hr., to a stirred and cooled (0—5°) solution of the nitrone in ether (1 l.). The mixture was stirred at 5—10° for a further 2 hr., and then thoroughly extracted with ether (5 × 500 ml.). The ethereal extracts were washed with sodium hydrogen carbonate solution, then with water, and dried. Evaporation of the ether and distillation of the residue gave the *formyl ester* (30 g., 28%) as a colourless liquid, b.p. 114—118°/15 mm., n_D^{20} 1·4690, $\nu_{max.}$ (film) 1720 (CO_2Me) and 1682 (CHO) cm.$^{-1}$.

4-*Hydroxy*-2-*methylbut*-2-*enolide* (30).—A mixture of methyl *trans*-3-formyl-2-methylacrylate (29 g.) and 6N-hydrochloric acid (100 ml.) was boiled under reflux for 3·5 hr.; every 45 min. about 10 ml. was distilled from the mixture to remove the methanol formed. The resulting mixture was evaporated under reduced pressure, water (50 ml.) was then added, and the solution was again concentrated; addition of water and evaporation was repeated three times. Distillation of the residue (14 g.) gave the butenolide (8·5 g., 35%) as an oil, b.p. 90—92°/0·07 mm., which rapidly solidified to a hard mass of crystals, m.p. 68—71°. A small portion recrystallised from ether had m.p. 72—74°, $\nu_{max.}$ ($CHCl_3$) 3300, 1760, and 1660 cm.$^{-1}$, τ 3·11, 3·88, 4·66, and 8·1 (all m, relative intensities *ca.* 1 : 1 : 1 : 3. With aqueous Brady's reagent it formed a 2,4-dinitrophenylhydrazone, m.p. 228—230° (from methanol). The butenolide was identical (m.p. and mixed m.p., i.r., and n.m.r.) with a sample supplied by Professor C. F. Garbers, prepared from 3-methylfuran.[22]

4-*Methoxy*-2-*methylbut*-2-*enolide* (31).—A mixture of 4-hydroxy-2-methylbut-2-enolide (1·5 g.), methanol (30 ml.), and sulphuric acid (0·2 ml.) was stirred at 20° for 24 hr. The mixture was diluted with ice–water, and the product

[45] G. Wittig and U. Schöllkopf, *Chem. Ber.*, 1954, **87**, 1318.
[46] R. E. Buckles, G. V. Mock, and L. Locatell, *Chem. Rev.*, 1955, **55**, 659.

was extracted with ether. Evaporation of the washed (H_2O) and dried extracts, and distillation of the residue, gave the *ether* (0·85 g., 52%) as a colourless liquid, b.p. 38°/0·02 mm., n_D^{21} 1·4511. A sample purified by preparative g.l.c. (Ucon-polar, 170°) had b.p. 60° (bath)/0·5 mm., $n_D^{21\cdot5}$ 1·4508, $\nu_{max.}$ (liq. film) 2820, 1780, 1760, and 1660 cm.$^{-1}$; τ 3·17(m), 4·26(m), 6·44, and 8·05(m) (relative intensities *ca.* 1 : 1 : 3 : 3) (Found: C, 56·45; H, 6·2. $C_6H_8O_3$ requires C, 56·2; H, 6·3%).

4-*Hydroxy*-3-*methylbut*-2-*enolide* (37).— (a) *From* 3-*methylcrotonic acid*. Esterification of 3-methylcrotonic acid with methanolic sulphuric acid, and treatment of the resulting ester in carbon tetrachloride with *N*-bromosuccinimide, gave methyl 3-bromomethylcrotonate. The latter (122 g.) was submitted to a Kröhnke reaction, as described by Sisido *et al.*,[47] to give methyl *trans*-3-formylcrotonate (45 g.), b.p. 71—73°/12 mm., n_D^{19} 1·4670, $\nu_{max.}$ (liq. film) 1720 (CO_2Me) and 1690 (CHO) cm.$^{-1}$, τ 0·38 (CHO), 3·43 (m, α-H), 6·18 (OMe), and 7·85 (d, *J* 2, β-Me) (lit.,[47] b.p. 56—57°/7 mm.). (No *cis*-isomer could be detected by n.m.r. spectroscopy). Hydrolysis of the formyl ester (44·5 g.) as described by Conradie *et al.*[23] gave the butenolide (33·2 g.) as a viscous oil, b.p. 130—132°/0·02 mm., which solidified; it gave prisms, m.p. 44—46° [from ether–light petroleum (b.p. 40—60°)], $\nu_{max.}$ ($CHCl_3$) 3300, 1760, and 1650 cm.$^{-1}$, τ 3·95br (γ-H and OH), 4·16 (m, α-H), 7·90 (d, *J* 1·5, β-Me), relative intensities *ca.* 2 : 1 : 3 (no signal in the CHO region) (lit.,[23] m.p. 45—46°). The overall yield from 3-methylcrotonic acid was 30%.

(b) *From methylglyoxal diethyl acetal* (33) (with B. O. Brown).—A solution of sodium methoxide [from sodium (1·2 g.)] in methanol (30 ml.) was added, during 1 hr., to a stirred solution of the diethyl acetal of methylglyoxal (7·3 g.) and methyl diethylphosphonoacetate[17] (11·5 g.) in DMF (80 ml.) at 35—40°. The mixture was stirred at 20° for 4 hr., then diluted with water and extracted with ether. The extracts were washed (H_2O) and dried. Distillation gave the diethyl acetal of methyl 3-formylcrotonate (9·1 g., 90%) as a mixture of *cis*- and *trans*-isomers, b.p. 116—122°/12 mm., $n_D^{22\cdot5}$ 1·4396, $\lambda_{max.}$ (EtOH) 215 mμ, $\nu_{max.}$ (liq. film) 1720 (ester C=O), 1660 (C=C), 1060, and 1110 (acetal) cm.$^{-1}$. The relative intensity of the n.m.r. bands at τ 8·04 and 7·82 showed that the product was a mixture of *cis*- and *trans*-isomers in the ratio *ca.* 1 : 2.

The mixture of acetals (4·5 g.) was boiled under reflux with 6N-hydrochloric acid (50 ml.) for 3 hr.; every 45 min. about 5 ml. was distilled from the mixture to remove the alcohols formed. The resulting mixture was evaporated under reduced pressure, water (35 ml.) was added, and the solution was again evaporated; the addition of water and evaporation was repeated three times. Distillation of the residue gave 4-hydroxy-3-methylbut-2-enolide (1·75 g., 72%) as a viscous oil, b.p. 106—110°/0·01 mm., which solidified; m.p. 43—46°, i.r. and n.m.r. spectra identical with those of the material from (a), overall yield was 65%.

4-*Methoxy*-3-*methylbut*-2-*enolide* (38).—A mixture of 4-hydroxy-3-methylbut-2-enolide (2·25 g.), methanol (50 ml.), and sulphuric acid (0·2 ml.) was stirred at 20° for 15 hr. The mixture was then poured into water and the aqueous mixture was thoroughly extracted with ether. The extracts were washed (H_2O), dried, and evaporated. Distillation of the residue gave the *ether* (1·7 g., 68%) as a colourless liquid, b.p. 54—56°/0·14 mm., n_D^{21} 1·4563, $\nu_{max.}$ (liq. film) 2820, 1785, and 1760 cm.$^{-1}$, τ 4·12 (m, α-H), 4·33 (m, γ-H), 6·46 (OMe), 7·93 (m, β-Me) (Found: C, 55·8; H, 6·6. $C_6H_8O_3$ requires C, 56·2; H, 6·3%). Only one peak was observed on g.l.c. analysis (polyethylene glycol adipate; 120°).

trans-β-*Formylcrotonic acid*[24] (40; R = H).—A solution of sodium methoxide [from sodium (1·84 g.)] in methanol (25 ml.) was added to a solution of 4-hydroxy-3-methylbut-2-enolide (4·6 g.) in methanol (20 ml.) and the mixture was kept at 20° for 1 hr. It was then diluted with water, acidified with conc. hydrochloric acid, saturated with ammonium chloride, and extracted with ether. The extracts were dried and evaporated. Recrystallisation of the solid residue (4·2 g.) from ether gave the acid, m.p. 67—68°, $\lambda_{max.}$ (EtOH) 229 mμ (ε 11,300), $\nu_{max.}$ ($CHCl_3$) 1700 and 1645 cm.$^{-1}$, τ 0·35 (CHO), 3·41 (m, α-H), 7·85 (d, *J* 1·5, β-Me) (lit.,[48] m.p. 66°).

5-*Methoxycarbonylpenta*-cis-2,trans-4-*dienotic Acid* (41).—Sodium methoxide [from sodium (0·25 g.)] in methanol (20 ml.), and 4-hydroxybut-2-enolide[21] (0·5 g.) in ether (20 ml.), were added, simultaneously but separately, during 10 min., to a stirred solution of methyl diethylphosphonoacetate[17] (1·15 g.) in ether (50 ml.) at 20°. The solution was stirred for a further 45 min., then diluted with water and acidified with dilute sulphuric acid. The mixture was thoroughly extracted with ether, and the extracts were washed with dilute sodium carbonate solution. The aqueous phase was separated, then acidified with dilute sulphuric acid, and extracted with ether. The extract was washed (H_2O), dried, and evaporated to give colourless crystals (665 mg., 85%) of the *cis,trans* half-ester, which gave needles, m.p. 100—101° (from benzene), $\lambda_{max.}$ (EtOH) 261·5 mμ (ε 24,700), $\nu_{max.}$ (Nujol) 1715 (CO_2Me), 1690 (CO_2H), 1640, 1605, 890, 845, and 770 cm.$^{-1}$, τ 1·55 (dd, J_1 11, J_2 15, γ-H), 3·22 (dd, J_1 and J_2 both 11, β-H), 3·83 (d, *J* 15, δ-H), 4·00 (d, *J* 11, α-H), and 6·20 (OMe) (lit.,[25] m.p. 101°).

Buta-cis-1,trans-3-*diene*-1,4-*dicarboxylic Acid*.—A solution of the half ester just described (250 mg.) in 10% sodium hydroxide (2 ml.) was warmed (*ca.* 80°) for 10 min., then cooled and acidified (conc. hydrochloric acid). The precipitate was collected and gave the dicarboxylic acid (195 mg., 88%) as prismatic needles, m.p. 190—191° (from hot water), $\lambda_{max.}$ (EtOH) 261 mμ (ε 22,700), $\nu_{max.}$ (Nujol) 895, 842, and 752 cm.$^{-1}$ (lit.,[25] m.p. 190—191°).

Dimethyl Buta-cis-1,trans-3-*diene*-1,4-*dicarboxylate*.—(*a*) The half ester (100 mg.) described above was treated with a small excess of ethereal diazomethane. Evaporation of the solution and crystallisation of the residue from aqueous methanol gave the dimethyl ester in almost quantitative yield as feathery needles, m.p. 72—73°, $\lambda_{max.}$ (EtOH) 263 mμ (ε 25,800), $\nu_{max.}$ (Nujol) 1725, 1705, 895, 840, and 750 cm.$^{-1}$, τ 1·58 (dd, J_1 11, J_2 15, γ-H), 3·37 (dd, J_1 and J_2 both 11, β-H), 3·91 (d, *J* 15, δ-H), 4·04 (d, *J* 11, α-H), and 6·23 (both OMe) (lit.,[25] m.p. 75°).

(*b*) Similar treatment of the *cis,trans*-butadienedicarboxylic acid gave the same dimethyl ester, m.p. and mixed m.p. 72—73°.

(*c*) The crude product, m.p. 92—94°, from the butenolide–phosphonate condensation was esterified with diazomethane in the usual manner to give the crude di-ester as a solid, m.p. 70—74°, $\lambda_{max.}$ (EtOH) 263 mμ, n.m.r. spectrum identical with that of a purified sample of the product from (*a*).

[47] K. Sisido, K. Kondô, H. Nozaki, M. Tuda, and Y. Udô, *J. Amer. Chem. Soc.*, 1960, **82**, 2286.
[48] H. Pommer and W. Sarnecki, D.R.P. 1,068,709.

Buta-trans-1,-trans-3-*diene*-1,4-*dicarboxylic Acid*.—A solution of the *cis,trans*-dicarboxylic acid (50 mg.) in methanol (2·5 ml.) containing a trace of iodine was illuminated with a 100 w light at a distance of 1 ft. for 90 min.; after 35 min. solid began to separate and continued to do so for a further 30 min. The all-*trans* acid (44 mg.) was filtered off; m.p. 296—298°, $\lambda_{max.}$ (EtOH) 261 mμ (ε 26,100), $\nu_{max.}$ (Nujol) 1020 and 870 cm.$^{-1}$ (lit.,[25] m.p. 297—300°).

5-*Methoxycarbonyl*-2-*methylpenta*-cis-2,trans-4-*dienoic Acid* (42).—A solution of sodium methoxide [from sodium (0·24 g.)] in methanol (10 ml.), and one of 4-hydroxy-2-methylbut-2-enolide (0·57 g.) in ether (20 ml.), were added, simultaneously but separately, during 15 min., to a stirred solution of methyl diethylphosphonoacetate [17] (1·15 g.) in ether (60 ml.) at 20°. The solution was stirred for a further 45 min., then diluted with water and acidified with 2N-sulphuric acid. The mixture was thoroughly extracted with ether, and the extracts were combined and washed with dilute sodium carbonate solution. The aqueous phase was separated, then acidified with 2N-sulphuric acid, and extracted with ether. The extract was washed (H_2O), dried, and evaporated to give a colourless crystalline solid (0·75 g., 88%) m.p. 119—122° which gave the half-ester as feathery needles, m.p. 124—125° (from benzene), $\lambda_{max.}$ (EtOH) 271·5 mμ (ε 25,700), $\nu_{max.}$ (Nujol) 1710 (CO_2Me), 1680 (CO_2H), 1622, 1590, 985, 928, 870, 838, and 778 cm.$^{-1}$, τ 1·77 (dd, J_1 16, J_2 *ca.* 12, γ-H), 3·42br (d, *J ca.* 12, β-H), 3·98 (d, *J* 16, δ-H), 6·22 (OMe), 7·91 (α-Me) (lit.,[26] m.p. 121°).

1-*Methylbuta*-cis-1,trans-3-*diene*-1,4-*dicarboxylic Acid*.—A solution of the half-ester (42) (200 mg.) in 10% sodium hydroxide (2 ml.) was kept at 20° for 45 min., and then acidified (conc. hydrochloric acid). The precipitate was collected, washed with ice–water, and dried. It gave the acid (105 mg.) as micro-needles, m.p. 180—181° (from ethanol), $\lambda_{max.}$ (EtOH) 270 mμ (ε 23,700), $\nu_{max.}$ (Nujol) 995, 923, 828, and 778 cm.$^{-1}$ (lit.,[26] m.p. 172°).

Dimethyl 1-*Methylbuta*-cis-1,trans-3-*diene*-1,4-*dicarboxylate* (44).—(*a*) The above dicarboxylic acid (100 mg.) was treated with a small excess of ethereal diazomethane. Evaporation of the solution and crystallisation of the residue from methanol gave the dimethyl ester (75 mg.), m.p. 57—59°, $\lambda_{max.}$ (EtOH) 272 mμ (ε 25,100), $\nu_{max.}$ (Nujol) 920, 862, and 778 cm.$^{-1}$, τ, see formula (44) (lit.,[26] m.p. 60°).

(*b*) Similar treatment of the half ester (42) also gave the dimethyl ester, m.p. and mixed m.p. 57—59°.

(*c*) The crude product, m.p. 119—122°, from the butenolide–phosphonate condensation was esterified with diazomethane to give the crude dimethyl ester as a solid, m.p. 53—57°, $\lambda_{max.}$ (EtOH) 272 mμ (ε 22,400) $\nu_{max.}$ (Nujol) 920, 862, and 778 cm.$^{-1}$, n.m.r. spectrum identical with that of a purified sample of the diester from (*a*).

1-*Methylbuta*-trans-1,trans-3-*diene*-1,4-*dicarboxylic Acid*.—A solution of 1-methylbuta-*cis*-1,*trans*-3-diene-1,4-dicarboxylic acid (130 mg.) in 20% sodium hydroxide (5 ml.) was boiled under reflux for 4 hr., then cooled and acidified with 50% sulphuric acid. The precipitate was filtered off and dried, and gave the *trans,trans*-acid (60 mg.) as needles, m.p. 282—283° (decomp.) (from ethanol), $\lambda_{max.}$ (EtOH) 273·5 mμ (ε 28,600), $\nu_{max.}$ (Nujol) 988 and 824 cm.$^{-1}$ (lit.,[26] m.p. 273°).

Dimethyl 1-*Methylbuta*-trans-1,trans-3-*diene*-1,4-*dicarboxylate* (45).—The above dicarboxylic acid (40 mg.) was treated with a small excess of ethereal diazomethane. Evaporation of the solution gave the di-ester, m.p. 51—53°, $\lambda_{max.}$ (EtOH) 275·5 mμ (ε 28,100), $\nu_{max.}$ (Nujol) 975, 882, and 760 cm.$^{-1}$, τ, see formula (45) (lit.,[26] m.p. 55·5°).

5-*Methoxycarbonyl*-3-*methylpenta*-cis-2,trans-4-*dienoic Acid* (43).—(*a*) A solution of sodium methoxide [from sodium (0·24 g.)] in methanol (15 ml.), and one of 4-hydroxy-3-methylbut-2-enolide (0·57 g.) in ether (20 ml.), were added, simultaneously but separately, during 10 min., to a stirred solution of methyl diethylphosphonoacetate [17] (1·15 g.) in ether (50 ml.). The solution was stirred for a further 10 min., then diluted with water and acidified with 2N-sulphuric acid. The mixture was thoroughly extracted with ether, and the extracts were combined and washed with dilute sodium carbonate solution. The aqueous phase was separated, acidified with 2N-sulphuric acid, and extracted with ether. The extracts were washed (H_2O), dried, and evaporated to give the half-ester (0·78 g., 92%) as a colourless crystalline solid, m.p. 131—133°, unchanged when crystallised from benzene, $\lambda_{max.}$ (EtOH) 266 mμ (ε 22,400), $\nu_{max.}$ (Nujol) 1710 (CO_2Me), 1680 (CO_2H), 1625, 1595, 1010, 995, 985, 900, and 885 cm.$^{-1}$, $\nu_{max.}$ ($CHCl_3$) 998 and 895 cm.$^{-1}$, τ 1·37 (d, *J* 16, γ-H), 3·80 (d, *J* 16, δ-H), 4·02 (m, α-H), 6·20 (OMe), and 7·91 (d, *J* 1·5, β-Me), i.r. and n.m.r. spectra were identical with those of a sample, m.p. 132—134°, prepared by the method of Elvidge *et al.*,[27] who give m.p. 126—127°; the mixed m.p. was not depressed.

(*b*) A solution of sodium methoxide [from sodium (0·46 g.)] in methanol (15 ml.) was added, during 30 min., to a vigorously stirred suspension of methoxycarbonylmethyltriphenylphosphonium bromide [18] (6·8 g.) in ether (100 ml.). The mixture was stirred for a further 1 hr., and then 4-hydroxy-3-methylbut-2-enolide (1·14 g.) in ether (10 ml.) was introduced during 30 min. The mixture was stirred at 20° for 90 min., and then diluted with water. The unreacted phosphorane (*ca.* 1·6 g.), m.p. and mixed m.p. 157—160°, which separated was filtered off, and the filtrate was thoroughly extracted with ether. The aqueous phase was separated, then acidified with 20% sulphuric acid and extracted with ether. The extracts were washed (H_2O), dried, and evaporated to give the crude half-esters as an oil (1·25 g., 73%) which partly solidified; $\lambda_{max.}$ (EtOH) 266 mμ ($E_{1\,cm.}^{1\%}$ 1110), $\nu_{max.}$ (Nujol) 1710, 1680, 1630, 1595, 1012, 990, 985, 900, and 885 cm.$^{-1}$. The first ether extract contained no acid; evaporation gave only triphenylphosphine oxide (*ca.* 2·4 g., 80—85%). A sample of the crude half-ester was treated with a small excess of ethereal diazomethane. Evaporation left an oil, $\lambda_{max.}$ (EtOH) 267 mμ; its n.m.r. spectrum (CS_2) showed three olefinic methyl bands at τ 7·76, 8·0, and 8·14 with relative intensities which indicated the presence of *ca.* 3% of the *trans,trans*-dicarboxylate, *ca.* 87% of the *cis*-2,*trans*-4 isomer, and *ca.* 10% of another product.

2-*Methylbuta*-cis-1,trans-3-*diene*-1,4-*dicarboxylic Acid*.—A solution of the half-ester (43) (250 mg.) in 10% sodium hydroxide solution (3 ml.) was kept at 20° for 1 hr., and then acidified (conc. hydrochloric acid). The precipitate was collected, washed with ice–water, and dried, and gave the acid (110 mg.) as needles, m.p. 177—179° (from ethanol), $\lambda_{max.}$ (EtOH) 263 mμ, $\nu_{max.}$ (Nujol) 1190, 995, and 893 cm.$^{-1}$ (lit.,[27] m.p. 178°).

Dimethyl 2-*Methylbuta*-cis-1,trans-3-*diene*-1,4-*dicarboxylate*.—(*a*) The above dicarboxylic acid (50 mg.) was treated with a small excess of ethereal diazomethane. Evaporation left the dimethyl ester as an oil, $\lambda_{max.}$ (EtOH) 267·5 mμ (ε 20,900), $\nu_{max.}$ (liq. film) 995 and 892 cm.$^{-1}$, τ (CS_2) 1·53

(d, J 16, γ-H), 3·93 (d, J 16, δ-H), 4·16 (m, α-H), 6·33 (OMe), 6·36 (OMe), and 8·0 (d, J 1·5, β-Me) (lit.,[27] m.p. 37°).

(*b*) The crude product, m.p. 131—133°, from the butenolide–phosphonate condensation was esterified with diazomethane to give the dimethyl ester as an oil, $\lambda_{max.}$ (EtOH) 267·5 mμ, n.m.r. spectrum identical with that of the diester both from (*a*) and from an authentic specimen of the *cis,trans*-half-ester.

2-Methylbuta-trans-1,trans-3-*diene*-1,4-*dicarboxylic Acid*.—A solution of the corresponding *cis,trans*-acid (50 mg.) in 20% sodium hydroxide solution (2 ml.) was boiled under reflux for 4 hr., then cooled, acidified with 50% sulphuric acid, and extracted with ether. The extracts were washed (H_2O), and evaporated. The residue gave the *trans,trans*-acid (22 mg.), m.p. 226—228° (from benzene), $\lambda_{max.}$ (EtOH) 265 mμ, $\nu_{max.}$ (Nujol) 1180, 982, 895, and 865 cm.$^{-1}$ (lit.,[27] m.p. 229—230°).

Dimethyl 2-Methylbuta-trans-1,trans-3-*diene*-1,4-*dicarboxylate*.—The above dicarboxylic acid (20 mg.) was treated with a small excess of ethereal diazomethane. Evaporation of the solution left the di-ester, m.p. 50—54°, $\lambda_{max.}$ (EtOH) 267 mμ, τ (CS_2) 2·80 (d, J 16, γ-H), 3·89 (d, J 16, δ-H), 4·03 (m, α-H), 6·33 (both OMe), and 7·76 (d, J 1·5, β-Me) (lit.,[27] m.p. 55—56°).

cis-13- *and* cis-11,cis-13-*Vitamin A Acid* (51 and 52).—A solution of vinyl-β-ionol [49] (1·53 g.) and triphenylphosphonium bromide [34] (2·4 g.) in methanol (50 ml.) was stirred at 20° for 48 hr. The methanol was removed under reduced pressure and the oily residue was washed several times with ether. Solvents were removed under high vacuum to leave the triphenylphosphonium salt [30] as a glassy solid which was used without further purification.

A solution of sodium methoxide [from sodium (0·23 g.)] in methanol (10 ml.) was added, during 10 min., to a stirred suspension of the above phosphonium salt in ether (400 ml.). A deep red colour, characteristic of the phosphorane, developed during 20 min., and then 4-hydroxy-3-methylbut-2-enolide (0·4 g.) in ether (20 ml.) was added as quickly as possible. The mixture, which became pale orange in colour almost immediately, was stirred at 20° for 2 hr., then diluted with ice–water, and extracted with ether. The aqueous solution was separated and acidified with 2N-sulphuric acid, and the acidic products were extracted with ether. The extracts were washed with water, dried, and evaporated to leave the mixture of isomers (0·68—0·78 g., 66—75%) as an orange oil, $\lambda_{max.}$ (95% (EtOH) 347 mμ ($E_1^{1\%}_{cm.}$ 910); the n.m.r. spectrum, and the relative intensity of absorptions at τ 7·80 and 7·91, showed that the product contained *ca.* 64% of the *cis*-11,*cis*-13- and *ca.* 36% of the *cis*-13-isomer of vitamin A acid. The crystals which slowly separated from the isomer mixture were collected. Recrystallisation from methanol gave *cis*-13-vitamin A acid as orange-red cubes, m.p. 172—173°, $\lambda_{max.}$ (95% EtOH) 354 mμ (ε 37,600), τ, see formula (51) (lit.,[50] m.p. 174—175°).

The *cis*-11,*cis*-13-isomer supplied by Professor C. F. Garbers had m.p. 128°, $\lambda_{max.}$ (95% EtOH) 346 mμ (ε 25,900) [19,24] τ, see formula (52).

All-trans-*Vitamin A Acid* (50).—The isomer mixture (820 mg.) from the preceding experiment, in ether (7 ml.), was treated with a solution of iodine (7 mg.) in benzene (7 ml.), and the solution was kept in daylight for 7 hr. The solution was cooled, and the crystals (370 mg., 34%) which separated were filtered off and gave all-*trans*-vitamin A acid as yellow needles, m.p. 179—180° (from ethanol), $\lambda_{max.}$ (95% EtOH) 349·5 mμ (ε 43,100), τ, see formula (50) (lit.,[50] m.p. 180—181°).

The 3,7,11-Trimethyldodeca-2,4,6,10-tetraenoic Acids and their Methyl Esters (53—57).—(*a*) A solution of sodium methoxide [from sodium (0·46 g.)] in methanol (20 ml.) was added, during 10 min., to a stirred suspension of geranyltriphenylphosphonium chloride (4·34 g.) in ether (400 ml.). The mixture was stirred for 45 min., and then 4-hydroxy-3-methylbut-2-enolide (0·57 g.) in ether (20 ml.) was added as quickly as possible. The mixture was stirred for a further 1 hr., then diluted with water and extracted thoroughly with ether. The aqueous phase was separated, then acidified with 2N-sulphuric acid, and the acidic products were extracted with ether. The extracts were washed with water, dried, and evaporated to leave the tetraenoic acids (0·85 g., 70%) as a pale yellow oil, n_D^{22} 1·5728, $\lambda_{max.}$ (95% EtOH) 297—310 mμ ($E_1^{1\%}_{cm.}$ 950), $\nu_{max.}$ (liq. film) 1680, 1603, 1580sh, 975, 940, and 862 cm.$^{-1}$. The n.m.r. spectrum [for band positions see formulae (53) and (54)] indicated that the product was a mixture of the *cis*-2,*trans*-4,*trans*-6- and the *cis*-2,*cis*-4,*trans*-6-isomers in the approximate ratio 1 : 2.

(*b*) Substitution of geranyltriphenylphosphonium bromide [33] for the chloride in reaction (*a*) gave a mixture of the same isomeric acids in about the same proportions.

(*c*) The isomeric mixture (100 mg.) of tetraenoic acids from (*a*) in ether (25 ml.) containing a small crystal of iodine, was exposed to a 100 w light at a distance of 1 ft. for 5 min. The solution was washed with aqueous sodium thiosulphate, dried, and evaporated to leave a pale yellow oil (*ca.* 60 mg.), n_D^{20} 1·5736, $\lambda_{max.}$ (EtOH) 309 mμ. The relative intensities of the n.m.r. bands at τ 7·68, 7·94, and 7·83 indicated the presence of *ca.* 10% of the all-*trans*-, *ca.* 75% of the *cis*-2,*trans*-4,*trans*-6-, and *ca.* 15% of the *cis*-2,*cis*-4,*trans*-6-isomer.

(*d*) The isomeric mixture (200 mg.) of acids from (*a*) was treated with a small excess of ethereal diazomethane. The solution was washed with dilute sodium carbonate solution, then with water, and dried. Evaporation left a mixture of esters (160 mg.) as a pale yellow oil, n_D^{20} 1·5582, $\lambda_{max.}$ (EtOH) 317 mμ, $\nu_{max.}$ (liq. film) 1708, 1603, 1578, 1052, 975, 922, and 860 cm.$^{-1}$. (The i.r. spectrum was similar to that of the ester obtained from the chloro-Wittig reagent and 4-methoxy-3-methylbut-2-enolide.) The relative intensity of the n.m.r. bands at τ 7·98 and at 8·2 indicated that the product consisted of the *cis*-2,*trans*-4,*trans*-6- and the *cis*-2,*cis*-4,*trans*-6-esters in the approximate ratio 2 : 3.

(*e*) A solution of sodium methoxide [from sodium (0·3 g.)] in methanol (10 ml.) was added, during 10 min., to a stirred suspension of geranyltriphenylphosphonium chloride (2·2 g.) in ether (300 ml.). The mixture was stirred for 45 min., and then 4-methoxy-3-methylbut-2-enolide (0·32 g.) in ether (10 ml.) was added during 10 min. The mixture was stirred for a further 90 min., then diluted with water, and extracted with ether. The extracts were washed (H_2O), dried, and evaporated. Light petroleum (b.p. 60—80°) was added to the residue, and the triphenylphosphine oxide which was precipitated was filtered off. The filtrate was dried and evaporated to leave a pale yellow oil (450 mg., 70%), n_D^{22} 1·5576. Distillation gave the esters as a mixture of isomers, b.p. 110° (bath)/0·04 mm., n_D^{22}

[49] H. Pommer and W. Sarnecki, D.R.P. 1,059,900 and 1,068,702; cf. P. S. Manchand, R. Rüegg, U. Schwieter, P. T. Siddons, and B. C. L. Weedon, *J. Chem. Soc.*, 1965, 2019.

[50] C. D. Robeson, J. D. Cawley, L. Weisler, M. H. Steyn, C. C. Eddington, and A. J. Chechak, *J. Amer. Chem. Soc.*, 1955, **77**, 4111.

1·5590, $\lambda_{max.}$ (95% EtOH) 317 mμ ($E^{1\%}_{1\,cm.}$ 1090), $\nu_{max.}$ (liq. film) 1708, 1605, 1580, 1052, 975, 922, and 860 cm.$^{-1}$ (Found: C, 77·2; H, 9·7. Calc. for $C_{16}H_{24}O_2$: C, 77·4; H, 9·7%). The n.m.r. spectrum [for band positions see formulae (56) and (57)] both before and after distillation, indicated the presence of *ca.* 65% of the *cis*-2,*trans*-4,*trans*-6- and *ca.* 35% of the *cis*-2,*cis*-4,*trans*-6-isomers.

(*f*) The isomeric mixture (100 mg.) of esters from (*e*) in ether (25 ml.), containing a small crystal of iodine, was exposed to a 100 w light at a distance of 1 ft. for 5 min. The solution was washed with sodium thiosulphate solution, dried, and evaporated to leave an oil (*ca.* 75 mg.), n_D^{20} 1·5580. The n.m.r. spectrum indicated that the product was a mixture of the *cis*-2,*trans*-4,*trans*-6- and *cis*-2,*cis*-4,*trans*-6-isomers of the ester in the approximate ratio 9 : 1.

(*g*) The isomeric mixture (100 mg.) of esters from (*e*) in ether (25 ml.) containing a trace of iodine was exposed to a 100 w light at a distance of 1 ft. for 20 min. The product gave an oil, the n.m.r. spectrum of which showed the presence of *ca.* 15% of the all-*trans*-, *ca.* 75% of the *cis*-2,*trans*-4,*trans*-6-, and *ca.* 10% of the *cis*-2,*cis*-4,*trans*-6-isomer of the ester.

(*h*) A solution of sodium methoxide [from sodium 0·3 g.)] in methanol (10 ml.) was added, during 10 min., to a vigorously stirred suspension of geranyl triphenylphosphonium chloride (5·0 g.) in ether (300 ml.). The mixture was stirred for 30 min., and then methyl *trans*-β-formylcrotonate [47] (0·96 g.) in ether (20 ml.) was added during 10 min. The mixture was stirred for a further 1 hr., then diluted with water and extracted with ether. The extracts were washed (H_2O), dried, and evaporated. The residue was diluted with light petroleum (b.p. 60—80°), and the triphenylphosphine oxide which was precipitated was filtered off. The filtrate was dried and evaporated; only one β-methyl band (τ 7·68) was observed in the n.m.r. spectrum, but the complexity of the spectrum in the olefinic proton region indicated the presence of both *cis*-4- and *trans*-4-isomers. The residue (1·6 g., 85%) was dissolved in ether, a trace of iodine was added, and the solution was kept in daylight for 20 min. The product gave the all-*trans* ester, b.p. 100° (bath)/0·014 mm., n_D^{22} 1·5584, $\lambda_{max.}$ (95% EtOH) 313 mμ (ε 31,800), $\nu_{max.}$ (liq. film) 1710, 1605, 1360, 1040, 965, 930, 880, and 838 cm.$^{-1}$, τ, see formula (55) (Found: C, 77·3; H, 9·55. Calc. for $C_{16}H_{24}O_2$: C, 77·4; H, 9·7%).

(*i*) Substitution of geranyltriphenylphosphonium bromide for the chloride in reaction (*h*) led to the same (all-*trans*) product.

(*j*) A solution of sodium methoxide [from sodium (40 mg.)] in methanol (2 ml.) was added, during 2 min., to a stirred solution of *trans*-diethyl 3-methoxycarbonyl-2-methylprop-2-enylphosphonate (365 mg.) and *trans*-citral (200 mg.) in DMF (15 ml.). The mixture was stirred for 6 hr., then diluted with water, and extracted with light petroleum (b.p. 40—60°). The extract was washed (H_2O), dried, and evaporated. Distillation of the residue gave the all-*trans*-ester (210 mg., 70%), b.p. 110° (bath)/0·02 mm., n_D^{21} 1·5598, $\lambda_{max.}$ (95% EtOH) 313 mμ, $\nu_{max.}$ (liq. film) 1710, 1605, 1360, 1040, 965, 930, 882, and 835 cm.$^{-1}$, τ, see formula (55) (Found: C, 77·2; H, 9·5. Calc. for $C_{16}H_{24}O_2$: C, 77·4; H, 9·7%), i.r. and n.m.r. spectra were identical with those of the product from (*h*).

(*k*) Reaction (*j*) was repeated with use of the *trans*-phosphonate (120 mg.), *cis*-citral (70 mg.), and sodium methoxide [from sodium (15 mg.)] in methanol (1 ml.) and DMF (10 ml.). The resulting ester (65 mg.) had b.p. 120° (bath)/0·04 mm., n_D^{20} 1·5592, $\lambda_{max.}$ (95% EtOH) 313 mμ, i.r. (liq. film) and n.m.r. spectra virtually identical with those of the product from (*j*). Analysis of the products by g.l.c. gave erratic results.

(*l*) A solution of sodium methoxide [from sodium (30 mg.)] in methanol (2 ml.) was added, during 15 min., to a stirred solution of *cis*-diethyl 3-methoxycarbonyl-2-methylprop-2-enylphosphonate (290 mg.) and *trans*-citral (150 mg.) in DMF (10 ml.). The mixture was stirred for 7 hr., then diluted with water. Isolation of the product as in (*j*) gave an oil (180 mg., 72%), b.p. 100—105° (bath)/0·012 mm., n_D^{20} 1·5590, $\lambda_{max.}$ (EtOH) 314 mμ, $\nu_{max.}$ (liq. film) 1710, 1605, 1360, 1040, 965, 930, 882, and 835 cm.$^{-1}$. The n.m.r. spectrum indicated that the product was a mixture of the *trans*-2- and *cis*-2-esters in the approximate ratio 3 : 1.

The Methyl 11-*Hydroxy*-3,7,11-*trimethyldodeca*-2,4,6-*trienoates* (58—60).—(*a*) A solution of sodium methoxide [from sodium (0·25 g.)] in methanol (10 ml.) was added, during 10 min., to a stirred suspension of (7-hydroxy-3,7-dimethyloct-2-enyl)triphenylphosphonium bromide [34,36] (1·6 g.) in ether (300 ml.). The mixture was stirred for 45 min., and then 4-methoxy-3-methylbut-2-enolide (0·2 g.) in ether (20 ml.) was added, dropwise, during 30 min. The mixture was stirred for a further 30 min., then diluted with water, and the product was isolated in the usual way. Distillation gave the isomeric mixture of esters as an oil (0·27 g., 63%), b.p. 120—130° (bath)/0·05 mm., n_D^{22} 1·5589, $\lambda_{max.}$ (95% EtOH) 317 mμ ($E^{1\%}_{1\,cm.}$ 1010), $\nu_{max.}$ (liq. film) 3400, 1710, 1610, 1580, 1050, 975, 930, and 860 cm.$^{-1}$ (Found: C, 72·8; H, 9·75. Calc. for $C_{16}H_{26}O_3$: C, 72·2; H, 9·8%). The n.m.r. spectrum [for bands see formulae (59) and (60)] indicated that the mixture consisted of the *cis*-2,*trans*-4,*trans*-6- and the *cis*-2,*cis*-4,*trans*-6-isomers in the ratio *ca.* 3 : 2.

(*b*) A solution of sodium methoxide [from sodium 0·18 g.)] in methanol (10 ml.) was added during 10 min. to a vigorously stirred suspension of (7-hydroxy-3,7-dimethyloct-2-enyl)triphenylphosphonium bromide [34,36] (3·75 g.) in ether (300 ml.). The mixture was stirred for 45 min., and then methyl *trans*-β-formylcrotonate [47] (0·64 g.) in ether (25 ml.) was added during 30 min. The mixture was stirred for a further 1 hr., then diluted with water and neutralised with 2N-sulphuric acid. The mixture was extracted with ether, and the extracts were washed with water, dried, and evaporated. The residue was triturated with light petroleum (b.p. 60—80°), and the separated triphenylphosphine oxide was removed. The petroleum solution was dried and evaporated; only one β-methyl band (τ 7·69) was observed, but the complexity of the n.m.r. spectrum in the olefinic proton region indicated that both *cis*-4- and *trans*-4-isomers were present. The residue, in ether containing a trace of iodine, was exposed to daylight for 20 min. The product gave the *all*-trans-*ester* (1·05 g., 77%) as an oil, b.p. 125—130° (bath)/0·014 mm., n_D^{26} 1·5474, $\lambda_{max.}$ (95% EtOH) 313 mμ (ε 28,900), $\nu_{max.}$ (liq. film) 3400 1710, 1603, 1040, 965, 930, 880, and 838 cm.$^{-1}$, τ, see formula (58) (Found: C, 72·45; H, 9·7. $C_{16}H_{26}O_3$ requires C, 72·2; H, 9·8%).

The 11-*Methoxy*-3,7,11-*trimethyldodeca*-2,4,6-*trienoic Acids and their Methyl Esters*.—(*a*) Reaction of (7-methoxy-3,7-dimethyloct-2-enyl)triphenylphosphonium bromide [34,35] (2·5 g.) with 4-hydroxy-3-methylbut-2-enolide (0·3 g.) in the usual manner gave the methoxy-acids (0·43 g., 65%) as a golden-yellow oil, $\lambda_{max.}$ (EtOH) 307 mμ, $\nu_{max.}$ (film) 1680, 1605, 975, 940, and 860 cm.$^{-1}$. The n.m.r. spectrum indicated the presence of *cis*-2,*trans*-4,*trans*-6- and *cis*-

2,*cis*-4,*trans*-6-isomers (β-Me bands at τ 7·95 and 7·85 respectively) in the ratio *ca.* 2 : 3.

(*b*) The isomeric mixture of acids obtained in (*a*) was treated with a slight excess of ethereal diazomethane. Evaporation left a mixture of the corresponding esters, n_D^{22} 1·5527, $\lambda_{max.}$ (EtOH) 315 mμ, $\nu_{max.}$ (liq. film) 1710, 1605, 1580, 1080, 1050, 975, 925, and 860 cm.$^{-1}$. The n.m.r. spectrum indicated the presence of the *cis*-2,*trans*-4,*trans*-6- and *cis*-2,*cis*-4,*trans*-6-isomers in the ratio *ca.* 2 : 3; for band assignments see formulae (61) and (62).

We thank Dr. D. Shaw for the n.m.r. experiments involving heteronuclear decoupling. We also thank the S.R.C. for a Research Studentship (to G. P.).

[8/161 *Received, February 5th,* 1968]