Synthesis of *cis*- and Di-*cis*-Polyenes by Reactions of the Wittig Type. A New Isomer of Vitamin A Acid

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FEW methods are available for the controlled synthesis of polyenes possessing a *cis*-configuration about a methyl-substituted double bond. A study was therefore initiated of the reaction of Wittig and similar reagents with α- and β-methyl-αβ-unsaturated aldehydes.

Reaction of citral *a* and *b* with methylenetriphenylphosphoran (I; R = H) gave the trienes (II) and (III) with complete retention of the *trans*- and *cis*-configurations in the starting materials.

Condensation of the phosphonate (IV) with the hydroxybutenolides (V*a*)[1] and (V*b*)[2] under alkaline

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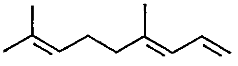
[1] Obtained by acid hydrolysis of methyl *trans*-β-formylcrotonate, or by oxidation of 3-methylbut-2-enolide, *cf.* W. J. Conradie, C. F. Garbers, and P. S. Steyn, *J. Chem. Soc.*, 1964, 594.

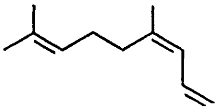
[2] Obtained by the photochemical oxidation of 3-methylfuran (C. F. Garbers and J. P. van der Merwe, *J. S. African Chem. Inst.*, 1964, **17**, 149), or by acid hydrolysis of methyl *trans*-3-formyl-2-methylacrylate (G. Pattenden and B. C. L. Weedon, unpublished results).

conditions led (~90%) exclusively to the *cis*-2, *trans*-4-isomer (VI, R = CO_2Me) of the expected product.

Reaction of the hydroxybutenolide (V*a*) with various phosphorans in ether likewise gave products in which the *cis*-configuration of the butenolide double bond was preserved (Table). However, except where R = CO_2Me, the main isomer produced also had a *cis*-configuration about the newly formed double bond.

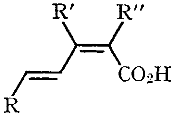
RCH=PPh_3
(I)


(II)

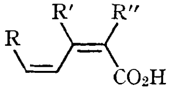

(III)

$MeO_2C{\cdot}CH_2PO(OEt)_2$
(IV)

(V)

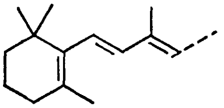


(VI)



(VII)

a, R' = Me, R'' = H, *b*, R' = H, R'' = Me, *c*, R' = Me, R'' = H, R =



Although several instances have been reported of a Wittig reaction favouring the formation of a *cis*-olefin, the high yields of "hindered" *cis*-isomers in the present studies were unexpected. Bergelson and Shemyakin have claimed[3] that "*cis*-olefination" can be achieved in many Wittig reactions by carrying out the condensation under appropriate conditions in the presence of a Lewis base,* though an important exception is provided by the reagent I, R = CO_2Me. If the carboxylate group derived from the hydroxybutenolide (V*a*) is regarded as an intramolecular Lewis base, extension of the general concepts of Bergelson and Shemyakin provide a plausible explanation of the present results.

Fractional crystallisation of the mixture of vitamin A acids prepared from the hydroxybutenolide (V*a*) gave the hitherto unknown *cis*-2, *cis*-4 isomer (VII*c*); m.p. 128° (from MeOH); λ_{max} (96% EtOH) 346 mμ, ϵ 25,900; τ 7·80.†

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* We were unable to obtain the very high proportions of *cis*-isomer originally claimed[3] in syntheses of 1-phenylbut-1-ene; our results were in excellent agreement with those reported subsequently by House *et al.*,[4] and the modified claims of Bergelson and Shemyakin.[5] We have, however, confirmed (in collaboration with Mr. D. Allen) that the synthesis reported[6] for octadec-11-enoic acid gives almost entirely (92—95%) the *cis*-isomer.

† N.m.r. spectra were determined on a Varian A60 spectrometer using dilute solutions in deuterochloroform and tetramethylsilane as an internal standard. Only bands due to β-methyl groups are quoted.

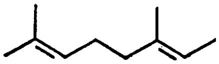
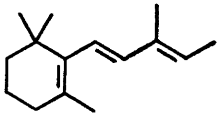
[3] L. D. Bergelson and M. M. Shemyakin, *Tetrahedron*, 1963, **19**, 149.

[4] H. O. House, V. K. Jones, and G. A. Frank, *J. Org. Chem.*, 1964, **29**, 3327.

[5] L. D. Bergelson and M. M. Shemyakin, *Pure Appl. Chem.*, 1964, **9**, 271.

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

TABLE. *Reaction of phosphorans with the hydroxybutenolide* (*V*a)

Phosphoran (I) R	Total yield (%) of isomers	Product Content (%) of isomers*		
		di-*cis* (VII*a*)	mono-*cis* (VI*a*)	all-*trans*
Ph	94—99	60	40	0
$-CO_2Me$	65—73	0	97	3†
	70—75	55	45	0
	68—75	64	36	0

* Determined by C–3 methyl band intensities in the n.m.r. spectra.
† Possibly formed by stereomutation.

Iodine-catalysed isomerisation of the di-*cis* acid in ether at 20° for 3 min. gave the known[7] *cis*-2 isomer (VI*c*) in excellent yield; λ_{max} 355 mμ; τ 7·91. Under conditions known[7,8] to cause stereomutation of the *cis*-2, but not the *cis*-6 acid, the *cis*-2, *cis*-4 isomer yielded all-*trans* vitamin A acid, τ 7·63.

Details of these and related studies will be published separately by the British and South African authors.

(*Received, June 25th,* 1965; *Com.* 397.)

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[7] C. D. Robeson, J. D. Cawley, L. Weisler, M. H. Stern, C. C. Eddinger, and A. J. Chechak, *J. Amer. Chem. Soc.*, 1955, **77**, 4111.

[8] H. Pommer, *Angew. Chem.*, 1960, **72**, 811.