Absolute Configuration of Allenes, Conversion of Molecular Dissymmetry into Centrodissymmetry by Heterogeneous Catalytic Hydrogenation

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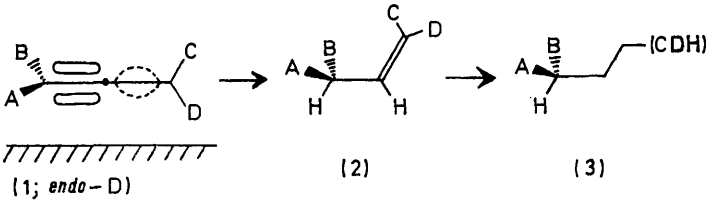
Palladium-catalysed hydrogenation of 4-methylhexa-2,3-dienoic acid and its methyl ester has been studied, by product analysis, over the complete range of hydrogen absorption. 4-Methyl[1-^{14}C]hex-*cis*-2-enoic and 4-methyl[1-^{14}C]hex-3-enoic acid and methyl ester have been employed in co-hydrogenations with the allene, which show that the substantial amount of 4-methylhex-*trans*-2-enoic acid (or ester) formed in the first stage arises neither directly from the allene, nor by isomerisation of the 3-enoic acid, but by stereomutation of 4-methylhex-*cis*-2-enoic acid on the catalyst. The conversion of molecular dissymmetry into centrodissymmetry by catalytic hydrogenation can therefore be used to determine the absolute configuration of allenes.

(−)-Methyl 4-methylhexa-2,3-dienoate gave (−)-(*R*)-methyl 4-methylhexanoate on catalytic semi- and full-hydrogenation and, from analysis of steric effects in the transition state for adsorption, the (−)-allene ester has the *R*-configuration. Semihydrogenation of the (+)-allenic acid, followed by esterification, gave methyl (+)-4-methylhex-2-enoate, oxidised and esterified to (+)-(*S*)-methyl 2-methylbutyrate: this provides a variant of the method. The assumption of *cis*-addition of hydrogen from the catalyst surface is formally proved by hydrogenation of (+)-methyl 4-phenyl-penta-2,3-dienoate of established *S*-configuration.

EXPERIMENTAL approaches to determining the absolute configuration of chiral allenes are limited in number and have been summarised.[1] The results of work described in the previous paper [2] suggest that semihydrogenation of a suitably substituted chiral allene should proceed with conversion of molecular dissymetry into centrodissymmetry and lead to a simple method for the experimental determination of absolute configuration. An optically active allene (1), presenting itself to the catalyst in a sterically favoured orientation [*e.g.* (1; *endo*-D), should lead, by *cis*-addition of hydrogen, to the chiral olefin (2) and the chiral saturated product (3) (Scheme 1). Knowledge of the absolute configuration of the olefin or saturated compound can then be translated to the allene.



SCHEME 1 Conversion of allene dissymmetry into centrodissymmetry by hydrogen addition

As outlined in our preliminary account,[3] the systems selected for investigation were 4-methylhexa-2,3-dienoic acid (4a) [4] and its methyl ester (4b). First, the catalytic hydrogenation (Pd–$BaSO_4$) of the (±)-allenic acid was investigated from a preparative point of view, the products being examined as methyl esters. All five expected hydrogenation products (5)—(9) were isolated

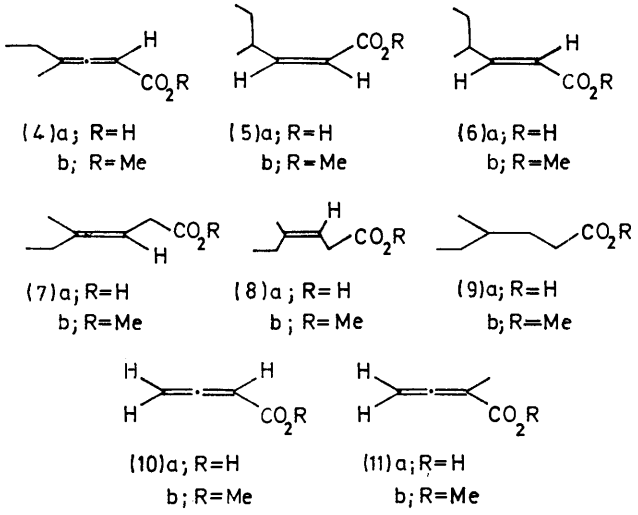
[1] G. Krow, *Topics Stereochem.*, 1970, **5**, 31; see also W. R. Moore, H. W. Anderson, S. D. Clark, and T. M. Ozretich, *J. Amer. Chem. Soc.*, 1971, **93**, 4932.

[2] L. Crombie, P. A. Jenkins, and D. A. Mitchard, preceding paper.

[3] L. Crombie and P. A. Jenkins, *Chem. Comm.*, 1967, 870.

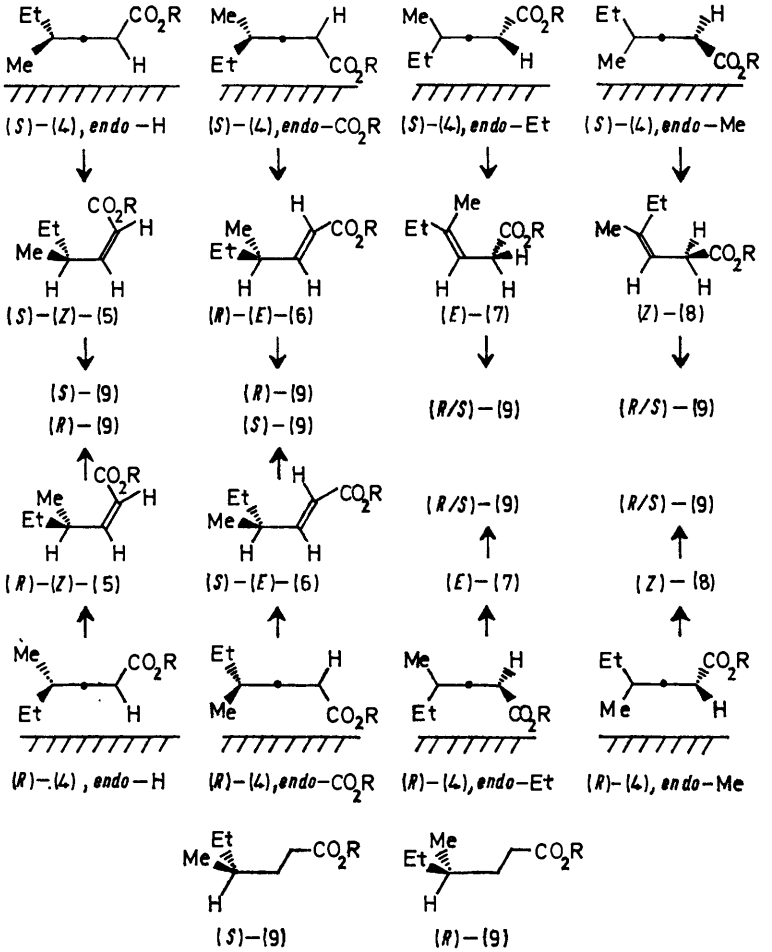
[4] E. R. H. Jones, G. H. Witham, and M. C. Whiting, *J. Chem. Soc.*, 1957, 4628.

by preparative g.l.c. (30% PEGA). The *cis*-olefin (5b), $\nu_{max.}$ 1660 and 694 cm^{-1}, contained an ABX system in the



n.m.r. spectrum with a double doublet at τ 4·05 and a doublet at 4·38 [J_{AB} 11·5, J_{BX} 8·7, J_{AX} *ca.* 0 Hz, consistent with the *cis*(*Z*)-double bond]. The X proton resonated as a multiplet near τ 6·5 consistent with it being *cis* to the ester, and the identity of (5b) was later confirmed by synthesis. The *trans*(*E*)-isomer (6b) was recognised spectroscopically: $\nu_{max.}$ 1672 and 980 cm^{-1}, with an ABX system in the n.m.r., τ 3·20 (dd) and 4·28 (dd) (J_{AB} 15·4, J_{BX} 8·2, J_{AX} *ca.* 0·5 Hz). The J_{AB} value is consistent with a *trans*-disubstituted olefin and the X-proton multiplet was at τ 7·77, an expected higher field position relative to (5b). Components (4b) and (9b) were readily recognised, and the remaining isolate was a mixture of (7b) and (8b), $\nu_{max.}$ 1665 and 825 cm^{-1}. The n.m.r. spectrum showed an AX_2 system with an olefinic proton signal as a triplet at τ 4·29, and a two-proton methylene doublet at 7·33 (J_{AX} 6·2). The broadness of the olefinic signal suggested that this was a *ZE*-mixture of isomers, and later preparative work confirmed this.

A quantitative study of the hydrogenation products from allenes (4a and b) during the absorption of 0—2 mol. equiv. of hydrogen is summarised in Figures 1 and 2: geometrical isomers [(7b) and (8b)] could not, however, be separated with the analytical column employed (10% PEGA). Table 1 shows the position at the end of the first stage of the hydrogenation. Selectivity of attack on the ester is excellent, but diminished for the



SCHEME 2 Stereochemical consequences of 1,2-*cis*-addition of hydrogen to (*S*)- and (*R*)-4-methylhexa-2-3-dienoic acid and ester

acid. Neither the high regioselectivity, nor stereoselectivity of attack found for the mono- and 1,1-disubstituted allenic acids [(10a) and (11a)] and esters [(10b) and (11b)] [2] is characteristic of this trisubstituted allenic acid and ester. Stereoselectivity for the production of the *cis*(*Z*)-olefin (5a) in the acid is particularly poor.

The eight significant orientations of the (*R*)/(*S*)-allene molecules towards the catalyst are shown in Scheme 2. In Figures 1 and 2 and Table 1 a striking feature is the

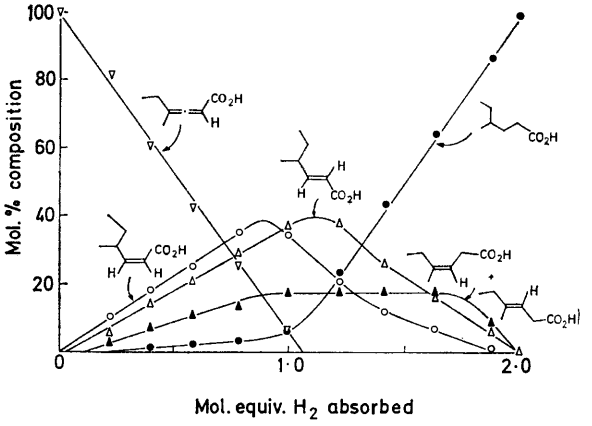


FIGURE 1 Hydrogenation (Pd) of 4-methylhexa-2,3-dienoic acid

amount of *trans*(*E*)-4-methylhex-2-enoic acid or ester (6) produced, even in the early stages of hydrogenation. stable Δ^2 (*E*)-(6). Finally, *trans*(*E*)-(6), may arise by stereomutation of ' half hydrogenated ' forms of *cis*(*Z*)-(6) on the catalyst. There are indeed indications that

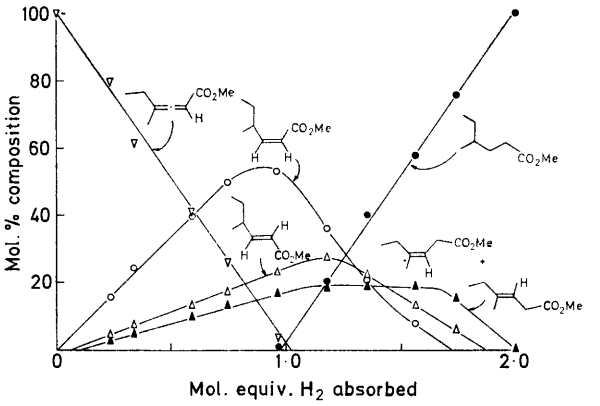


FIGURE 2 Hydrogenation (Pd) of methyl 4-methylhexa-2,3-dienoate

this is happening from Figure 1, where small amounts of saturated material are being formed throughout the first stage. Radiotracer experiments were therefore set up to track the source of (*E*)-(6) during the absorption of the first mol. equiv. of hydrogen.

Stereomutation of *cis*(*Z*)-(5a) into *trans*(*E*)-(6a) during the first stage of the hydrogenation of the allene (4a) could be observed if [^{14}C]-*cis*(*Z*)-(5a) were introduced at the beginning of the hydrogenation and its subsequent

TABLE 1

Product analysis at 1 mol. equiv. absorption of hydrogen (end of first stage)

	Products (%) at end of first stage								
		Olefins				Max. (%)			
Allene hydrogenated	Allene (4)	(5)	(6)	(7) (8)	Satd. (9)	(6) in Stage 2	Sel.[a] (%)	Ss.[a,b] (%)	Rs.[a] (%)
(±)-Acid (4a)	6	34	36	18	6	40	94	49 [c]	80
(±)-Ester (4b)	2	53	26	17	2	28	98	67	82
(−)-Acid (4a)	7	32	34	20	7	36	93	48 [c]	77
(−)-Ester (4b)	2	56	22	18	2	25	98	72	81

[a] As previously defined. [b] Stereoselectivity relates to the production of (5). [c] *trans*-Isomer predominates.

TABLE 2

Measured distances from a plane surface of the carbon termini of the reactant double bonds in 4-methylhexa-2,3-dienoic acid and ester

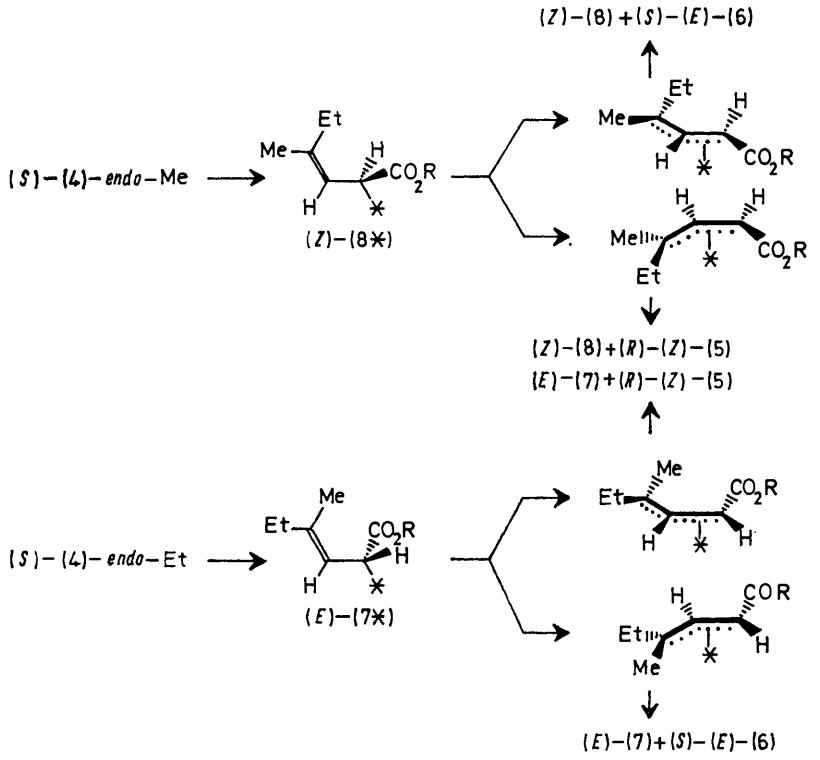
	Orientation of allene to surface							
	(4; *endo*-H)		(4; *endo*-CO_2R)		(4; *endo*-Et)		(4; *endo*-Me)	
	d_1	d_2	d_1	d_2	d_1	d_2	d_1	d_2
Allene (4a or b)	1·80	1·90	2·15	2·80	1·65	2·20	1·65	2·20

Scheme 2 shows that if produced by direct 1,2-*cis*-hydrogenation of the optically active allene (4) in the *endo*-CO_2R presentation, its chirality will be opposite to that of the *cis*(*Z*)-isomer (5) arising from allene of the same chirality. On the other hand, models (*cf.* Table 2) indicate that the *endo*-CO_2R is much the most hindered of the four presentations of the allene and there are three other possible modes of formation of *trans*(*E*)-(6). One of these is its production *via* a π-allyl intermediate as shown in Scheme 3. Another is the isomerisation of the (*E*)- and (*Z*)-Δ^3-compounds (7) and (8) to give the more fate followed. Transference of label to *trans*(*E*)-(6a) would be observed if stereomutation occurred. A similar transfer experiment could show if formation of (6a) is *via* (7) and (8). 4-Methyl[1-^{14}C]hex-2-ynoic acid (12) was therefore prepared as shown in Scheme 4. Catalytic hydrogenation gave the [1-^{14}C]-(±)-*cis*-acid (5a), which was also esterified to give the corresponding methyl ester (5b). Base-catalysed isomerisation [5] of (5a) was then used to obtain a *ZE*-mixture of 4-methyl-[1-^{14}C]hex-3-enoic acids (7a) and (8a): the mixture of

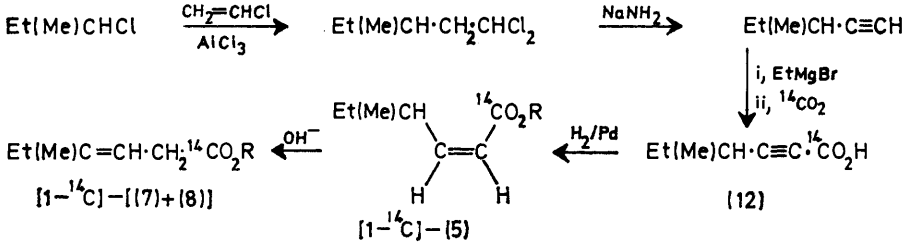
[5] R. P. Linstead and J. T. W. Mann, *J. Chem. Soc.*, 1930, 2064.

Δ^2- and Δ^3-isomers produced in the isomerisation was separated by selective esterification followed by preparative g.l.c.

The allenic acid (4a) was co-hydrogenated with (Tables 3—6). Results (Tables 5 and 6) demonstrate that the Δ^3-acids [(7a) and (8a)] and esters [(7b) and (8b)] remain virtually unisomerised and unhydrogenated throughout the first stage of the hydrogenation. On



SCHEME 3 Stereochemical consequences of π-allyl formation



SCHEME 4

[1-^{14}C]-(5a) and also with [1-^{14}C]-[(7a) + (8a)]: similar experiments were carried out with the methyl esters.

TABLE 3

Hydrogenation of allenic acid (±)-(4a) with added [1-^{14}C]-*cis* (*Z*)-(5a)

Mol. equiv. H_2 absorbed	^{14}C Relative activities				
	(4a)	(5a)	(6a)	(7a) + (8a)	(9a)
0·000	0·000	1·000			
0·527	0·000	0·832	0·164	0·000	0·013
1·000		0·690	0·181	0·000	0·128
1·482		0·295	0·222	0·000	0·471

The hydrogenations were stopped after absorption of 0·5, 1·0, and 1·5 mol. equiv. of hydrogen in each case, and the products were separated by preparative g.l.c. The radioactivity of each component was measured

the other hand, Table 3 shows that in the experiment with added [1-^{14}C]-*cis*(*Z*)-(5a), there is marked stereomutation into [1-^{14}C]-*trans*(*E*)-(6a) during the first stage. Furthermore, the hydrogenation is rather unspecific and radioactivity is also being transferred into the saturated acid (9a) during the first stage. A similar transfer

TABLE 4

Hydrogenation of allenic ester (±)-(4b) with added [1-^{14}C]-*cis*(*Z*)-(5b)

Mol. equiv. H_2 absorbed	^{14}C Relative activities				
	(4b)	(5b)	(6b)	(7b) + (8b)	(9b)
0·000	0·000	1·000			
0·505	0·000	0·892	0·109	0·000	
1·000		0·858	0·141	0·000	
1·486		0·597	0·253	0·000	0·143

of radioactivity from [1-^{14}C]-*cis*(*Z*)-(5b) into [1-^{14}C]-*trans*(*E*)-(6b) occurs in the ester experiment (Table 4), though it is less marked and the reaction proceeds with excellent selectivity and no (9b) was found in the first stage.

TABLE 5

Hydrogenation of allenic acid (±)-(4a) with added [1-^{14}C]-[(7a) + (8a)]

Mol. equiv. H_2 absorbed	^{14}C Relative activities				
	(4a)	(5a)	(6a)	(7a) + (8a)	(9a)
0·000	0·000			1·000	
0·511	0·000	0·000	0·000	0·997	
1·000	0·000	0·000	0·000	0·993	
1·498		0·000	0·000	0·833	0·164

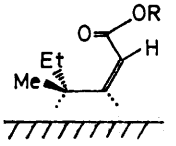
TABLE 6

Hydrogenation of allenic ester (±)-(4b) with added [1-^{14}C]-[(7b) + (8b)]

Mol. equiv. H_2 absorbed	^{14}C Relative activities				
	(4b)	(5b)	(6b)	(7b) + (8b)	(9b)
0·000	0·000			1·000	
0·488	0·000	0·000	0·000	0·986	
1·029		0·000	0·000	0·991	0·009
1·541		0·000	0·000	0·892	0·089

The molar activity of the radioactive *cis*-isomer (5) decreases during the reaction because of dilution by non-radioactive *cis*-(5) being formed from allene (4) by hydrogenation. After making suitable corrections for this, an estimate of the amount of *cis*(*Z*)-(5) converted into *trans*(*E*)-(6) can be made. In the first half of the first stage (*i.e.* during absorption of 0 to *ca.* 0·5 mol. equiv. of hydrogen), 97·0% of *trans*-acid (6a) and 99·1% of *trans*-ester (6b) arise by stereomutation of the corresponding *cis*-compounds (5a and b). From the data for 1·0 mol. equiv. of hydrogen absorbed, the corresponding results are 90·1 and 100%. However, ignoring the formation at this stage of saturated material (9) of unestablished origin makes the latter estimate less accurate in the case of the acid.

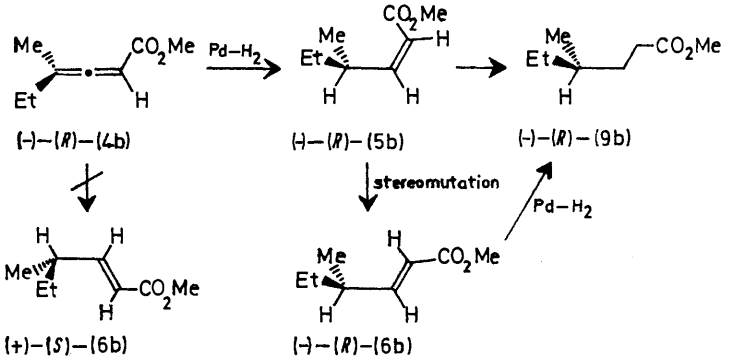
These results thus show that stereomutation (5) ⟶ (6) accounts for almost all the latter present at the end of the first stage. In the formation of *trans*-olefins (6), the π-allyl route (Scheme 3), or direct hydrogenation of the allene in the hindered (4; *endo*-CO_2R) orientation, can, at most, be only minor pathways. It was pointed out earlier [2] that allene hydrogenation was unstereospecific in a case in which the transition state leading to rehybridised absorption was internally sterically strained (despite least-hindered presentation of the allene to the catalyst). This is also the case in the present example [*cf.* (13)], and may result in incomplete coverage of the



(13)

catalyst surface by allene in the first stage. Competitive adsorption and stereomutation of *cis*-olefin (5) can thereby occur.

The radiochemical work thus clears the ground for using hydrogenation to convert allenic molecular dissymmetry into centrodissymmetry. A clear pattern of overall *cis*-1,2-hydrogenation from the least hindered side emerges, and any π-allyl rearrangement is small or absent: there is no $\Delta^3 \longrightarrow \Delta^2$ isomerisation to consider, and the *trans*-olefin (6) is a stereomutation product of (5). The allenic acid (±)-(4a) was therefore resolved (using quinine, the only one of eleven bases to produce a crystalline salt) to give (−)-(4a), m.p. 44—45°, $[\alpha]_D^{24}$ −36·1° (±0·2°), and esterified to give (−)-(4b), $[\alpha]_D^{24}$ −29·4° (±0·1°). Partially resolved (+)-(4a), $[\alpha]_D^{24}$ +21·7° (±0·2°) was also obtained.



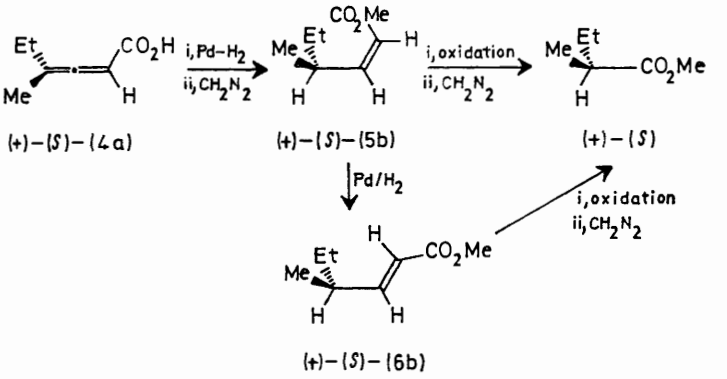
SCHEME 5

The allenic acid (−)-(4a) and its methyl ester (−)-(4b) were each hydrogenated with g.l.c. analysis of the products formed between 0 and 2 mol. equiv. of hydrogen absorption in the usual way. Table 1 summarises the analytical situation at the end of the first stage, and the figures agree satisfactorily with those for the (±)-acid (4a) and its (±)-ester (4b). A larger sample of the (−)-ester was then semihydrogenated and the products were isolated by preparative g.l.c.: optical rotations are given in Table 7. The separated (−)-(5b) was then further hydrogenated to give (−)-methyl 4-methylhexanoate $[\alpha]_D^{21}$ −7·4° (±0·2°) (lit.,[6] $[\alpha]_D^{25}$ +8·03° for the enantiomorph; 96% retention of configuration). The absolute configuration of the anteiso-acid (−)-(9b)

[6] C. Djerassi and L. E. Geller, *J. Amer. Chem. Soc.*, 1959, **81**, 2789.

is known to be *R* [6] so (—)-(5b) is also *R*. On the basis of the latter being formed by 1,2-*cis*-addition of hydrogen to the 3,4-double bond from the less hindered side of the allene (—)-(4b) (*endo*-H approach), the allene also has the *R*-configuration (Scheme 5).

Had the *trans*(*Z*)-olefin (6b), also formed in the hydrogenation, been produced direct by 3,4-*cis*-hydrogenation of the (—)-allene (4b) in its hindered (*endo*-CO_2Me) approach to the catalyst, it would have been produced in the (+)-(*S*)-*trans*-configuration. In fact (6b) isolated in this experiment, although partly racemised, was (—)-(*R*)-, and on hydrogenation gave (—)-(*R*)-(9b), $[\alpha]_D^{24}$ —3·6° (±0·2°).



SCHEME 6

The partially resolved (+)-allenic acid (4a) was also semihydrogenated (Table 7) and after esterification (+)-(5b) was isolated. This was oxidised (O_3–H_2O_2) and methylated to give (+)-methyl 2-methylbutyrate, $[\alpha]_D^{23}$ +5·1° of known *S*-configuration [7] (lit.,[8] $[\alpha]_D^{25}$ +23·1°) (Scheme 6). The allene configuration is thus confirmed. (+)-*trans*(*Z*)-Ester (6b) obtained in this experiment was also oxidatively degraded and gave (+)-(*S*)-methyl 2-methylbutyrate, $[\alpha]_D^{24}$ +2·0° (±0·5°). Again the result agrees with the experiments on the (—)-allenic ester (4b) and also with the radiochemical finding on the origins of (6b) from (5b), though considerable racemisation apparently accompanies stereomutation.

TABLE 7

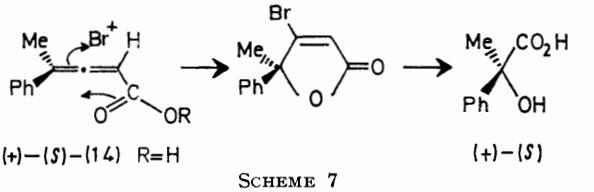
Optical rotations of products isolated by g.l.c. after addition of 1 mol equiv. of hydrogen to chiral allenes

Allene hydrogenated	(5)	(6)	(7) + (8)	(9)
(—)-Ester (4b) [a] $[\alpha]_D$	−9·8° (±0·2°)	−5·0° (±0·4°)	0°	−2·8° (±0·4°)
(+)-Acid (4a) [b,c] $[\alpha]_D$	+5·5° (±0·2°)	+1·8° (±0·5°)	0°	+1·4° (±0·3°)

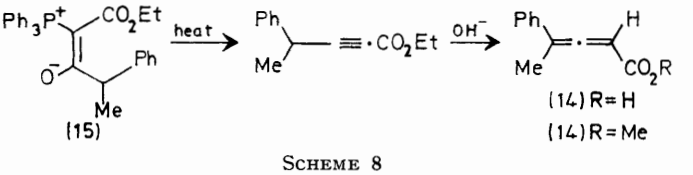
[a] $[\alpha]_D$ −29·4° (±0·1°). [b] $[\alpha]_D$ +21·7° (±0·1°). [c] Rotations as methyl esters.

This treatment assumes, as generally accepted, that hydrogen adds to the allene from the catalyst side. The postulate that hydrogen adds from the solution side to an activated unsaturated molecule adsorbed on a catalyst has, sometimes, been made,[9] and one piece of evidence for addition from the catalyst side is the observation that *trans*- and *cis*-cyclononene are hydrogenated readily, although in the former the conformation of the ring completely blocks the side of the molecule away from the catalyst.[10] An allene of known absolute configuration, 4-phenylpenta-2,3-dienoic acid,[11] was therefore prepared and studied by the hydrogenation method.

The assumption of *cis*-addition of hydrogen from the catalyst face is confirmed if the latter gives an absolute configuration in agreement with that already arrived at (Scheme 7).[11] (±)-4-Phenylpenta-2,3-dienoic acid (14; R = H) [11] was made by pyrolysis of the betaine (15),[12] followed by isomerisation of the resulting acetylene with base (Scheme 8). The allene was resolved with (—)-phenylethylamine to give (+)-(14; R = H), $[\alpha]_D^{25}$ +316°, m.p. 100—101°, and partially resolved (—)-(14; R = H), $[\alpha]_D^{25}$ —107°: the former was converted into the methyl ester.



SCHEME 7



SCHEME 8

The product composition diagram for the absorption of 0—2 mol. equiv. of hydrogen by (±)-4-phenylpenta-2,3-dienoic acid is shown in Figure 3. Products were identified by preliminary preparative g.l.c. as described in the Experimental section, but separation of methyl

[7] M. Winitz, S. M. Birnbaum, and J. P. Greenstein, *J. Amer. Chem. Soc.*, 1955, **77**, 3106.
[8] K. Freudenberg and W. Lwowski, *Annalen*, 1955, **594**, 76.
[9] R. L. Burwell, jun., *Chem. Rev.*, 1957, **57**, 895.
[10] A. T. Blomquist, C. H. Liu, and J. C. Bohrer, *J. Amer. Chem. Soc.*, 1952, **74**, 3643.
[11] K. Shingu, S. Hagishita, and M. Nagakawa, *Tetrahedron Letters*, 1967, 4371.
[12] G. Markl, *Chem. Ber.*, 1961, 3005.

(*Z*)-4-phenylpent-2-enoate and methyl (*Z*)-4-phenylpent-3-enoate was not achieved: n.m.r. analysis indicates their relative proportions to be *ca.* 2 : 3. Saturated

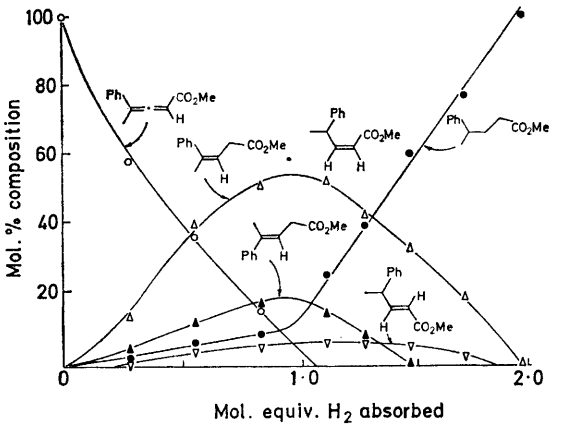
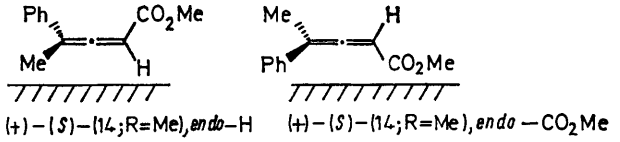


FIGURE 3 Hydrogenation (Pd) of methyl 4-phenylpenta-2,3-dienoate

ester was formed during the first stage and the selectivity at the end of the first stage was 87%: the stereoselectivity for production of methyl (*Z*)-*cis*-4-phenylpent-2-enoate was *ca.* 77% and the regioselectivity towards production of 2,3-olefins *ca.* 35%.

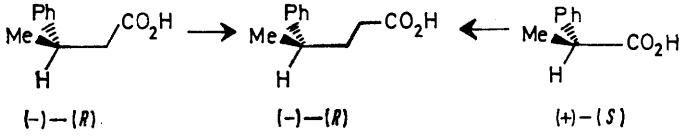
In the light of our earlier study, only two approaches to the catalyst will lead to conversion of molecular dissymmetry into centrodissymmetry and of these that involving the *endo*-CO_2Me (Scheme 9) will be highly



SCHEME 9

hindered. (+)-Methyl 4-phenylpenta-2,3-dienoate, $[\alpha]_D^{26}$ +146°, derived from (+)-acid, $[\alpha]_D^{26}$ +212° by diazomethane esterification, was therefore hydrogenated to give (−)-methyl 4-phenylpentanoate, $[\alpha]_D^{20}$ −0·8° (±0·1°). Similarly (−)-4-phenylpenta-2,3-dienoic acid, $[\alpha]_D^{25}$ −107°, gave (+)-4-phenylpentanoic acid, $[\alpha]_D^{23}$ +0·5° (±0·1°). The absolute configuration of (−)-(*R*)-4-phenylpentanoic acid was determined by Levene,[13] who obtained it, $[\alpha]_D^{25}$ −1·06°, by synthesis from (−)-(*R*)-3-phenylbutanoic acid. We have confirmed this by partially resolving 2-phenylpropionic acid [14] to give (−)-(*R*)-acid, $[\alpha]_D^{23\cdot5}$ −46°, which *via* reduction with lithium aluminium hydride and standard chain-lengthening gave (+)-(*S*)-4-phenylpentanoic acid, $[\alpha]_D^{24}$ +1·2°, esterified to the (+)-(*S*)-methyl ester (Scheme 10).

It follows that 3,4-*cis*-addition of hydrogen from the catalyst side to (+)-methyl 4-phenylpenta-2,3-dienoate (14; R = Me) in the *endo*-H orientation (Scheme 9) will generate (−)-(*R*)-methyl 4-phenylpentanoate, and the (+)-allenic ester itself should have the *S*-configuration. This agrees with Shingu's assignment and is also in accord with Lowe's polarisability rule.[15]



SCHEME 10

EXPERIMENTAL

4-Methylhexa-2,3-dienoic Acid.—Nickel carbonyl (30 ml), sodium acetate (32 g), acetic acid (24 g), and water (6 ml) were refluxed and 3-chloro-3-methylpent-1-yne (23 g) was added slowly. The excess of nickel carbonyl was removed by codistillation with ether and destroyed by slow addition of bromine water. Ether and water were added and the acid was worked up *via* 10% potassium carbonate and distilled; b.p. 90—92° at 0·5 mmHg, n_D^{18} 1·4805 (lit.,[4] b.p. 92—94° at 0·05 mmHg, n_D^{20} 1·4731). *4-Methylhexa-2,3-dienoic acid* (4·4 g, 17%) had m.p. 39—40° [from light petroleum (b.p. 30—40°)] (Found: C, 66·7; H, 7·9. $C_7H_{10}O_2$ requires C, 66·6; H, 8·0%), $\nu_{max.}$ 1964 and 856 cm^{-1}, $\lambda_{max.}$ (EtOH) 215·5 nm (ε 6000), τ −0·97 (1H, s), 4·47 (1H, sextet, *J* 3·0 Hz), 7·89 (2H, dq, *J* 3·0 and 7·2 Hz), 8·18 (3H, d, *J* 3·0 Hz), and 8·94 (t, *J* 7·2 Hz).

The *methyl ester* (CH_2N_2) (Found: C, 68·9; H, 8·7. $C_8H_{10}O_2$ requires C, 68·55; H, 8·65%) had b.p. 68—69° at 9 mmHg, n_D^{21} 1·4691, $\nu_{max.}$ 1692 and 825 cm^{-1}.

Resolution of 4-Methylhexa-2,3-dienoic Acid.—Quinine (15 g) in hot ethyl acetate (300 ml) was added to the acid (10 g) in hot ethyl acetate (100 ml). The product which crystallised was recrystallised to constant rotation; m.p. 101—102°, $[\alpha]_D^{25}$ −113·5° (±0·1°) (*c* 0·7 in $CHCl_3$). Decomposition (dil. HCl) gave (−)-*4-methylhexa-2,3-dienoic acid* (2·7 g, 54%), m.p. 44—45°, $[\alpha]_D^{24}$ −36·1° (±0·1°) (*c* 0·34 in $CHCl_3$) (Found: C, 66·9; H, 7·9. $C_7H_{10}O_2$ requires C, 66·6; H, 8·0%). The mother liquor from the resolution gave, on work-up, the partially resolved (+)-acid, m.p. 34—35°, $[\alpha]_D^{24}$ +21·7° (±0·1°) (*c* 1·36 in $CHCl_3$) (Found: C, 66·9; H, 7·95%).

The (−)-*methyl ester* (CH_2N_2) had b.p. 70—72° at 11 mmHg, n_D^{18} 1·4704, $[\alpha]_D^{24}$ −29·4° (±0·1°) (*c* 0·48 in $CHCl_3$), $[\alpha]_D^{24}$ −52·6° (±0·1°) (neat liquid) (Found: C, 68·7; H, 8·7. $C_8H_{12}O_2$ requires C, 68·5; H, 8·6%).

Hydrogenation of (−)-Methyl 4-Methylhexa-2,3-dienoate.—The ester (1·3 g) was semihydrogenated and the product worked up by preparative g.l.c. to give (−)-methyl 4-methylhex-*cis*-2-enoate, $[\alpha]_D^{23}$ −9·8° (±0·2°) (*c* 0·89 in $CHCl_3$), (−)-methyl 4-methylhex-*trans*-2-enoate, $[\alpha]_D^{22}$ −5·0° (±0·4°) (*c* 0·12 in $CHCl_3$), methyl 4-methylhex-3-enoate, $[\alpha]_D^{22}$ 0°, and (−)-methyl 4-methylhexanoate, $[\alpha]_D^{22}$ −2·8° (±0·4°) (*c* 0·42 in $CHCl_3$).

[13] P. A. Levene and R. E. Marker, *J. Biol. Chem.*, 1935, **110**, 329.

[14] K. Pettersson, *Arkiv. Kemi*, 1956, **10**, 283 (*Chem. Abs.*, 1957, **51**, 8039).

[15] G. Lowe, *Chem. Comm.*, 1965, 411; R. Moore, H. W. Anderson, and S. D. Clark, *J. Amer. Chem. Soc.*, 1973, **95**, 835.

The (−)-methyl 4-methylhex-*cis*-2-enoate (240 mg) was fully hydrogenated to give (−)-methyl 4-methylhexanoate, $[\alpha]_D^{21}$ −7·4° (±0·2°) (*c* 0·2 in $CHCl_3$) after distillation (lit.,[6] $[\alpha]_D^{25}$ +8·03° for the enantiomer).

(−)-Methyl 4-methylhex-*trans*-2-enoate was similarly hydrogenated to give (−)-methyl 4-methylhexanoate, $[\alpha]_D^{21}$ −3·6° (±0·2°) (*c* 0·1 in $CHCl_3$).

Hydrogenation of (+)-4-*Methylhexa*-2,3-*dienoic Acid*.—The acid (1·0 g) was semihydrogenated and worked up by preparative g.l.c. to give, on esterification, (+)-methyl 4-methylhex-*cis*-2-enoate, $[\alpha]_D^{23}$ +5·5° (±0·2°) (*c* 1·1 in $CHCl_3$), (+)-methyl 4-methylhex-*trans*-2-enoate, $[\alpha]_D^{23}$ +1·8° (±0·5°) (*c* 0·7 in $CHCl_3$), methyl 4-methylhex-3-enoate, $[\alpha]_D^{23}$ 0°, and (+)-methyl 4-methylhexanoate, $[\alpha]_D^{23}$ +1·4° (±0·3°) (*c* 0·7 in $CHCl_3$).

Ozonolysis of (+)-*Methyl* 4-*Methylhex*-cis- *and* trans-2-*enoates*.—Ozone was passed for 2·5 h through the *cis*-ester (300 mg) in methylene chloride (5 ml), with cooling (acetone–solid CO_2). The solution was stirred with a mixture of aqueous 10% sodium hydrogen carbonate (10 ml) and hydrogen peroxide (30%; 10 ml) for 4 h and then refluxed. The acid was recovered by acidification and continuous extraction with ether, esterified, and purified by preparative g.l.c. to give (+)-methyl 2-methylbutyrate, $[\alpha]_D^{23}$ +5·1° (±0·2°) (*c* 0·7 in $CHCl_3$) (lit.,[8] $[\alpha]_D^{25}$ +23·1°). Its g.l.c. retention time was identical with that of authentic (+)-methyl 2-methylbutyrate.

The (+)-*trans*-ester on similar ozonolysis gave (+)-methyl 2-methylbutyrate, $[\alpha]_D^{24}$ +2·0° (±0·5°).

4-*Methyl*[1-^{14}C]*hex*-2-*ynoic Acid*.—1,1-Dichloro-3-methylpentane, b.p. 90—92° at 100 mmHg, n_D^{24} 1·4405 (lit.,[16] b.p. 92° at 100 mmHg, n_D^{20} 1·4426), was prepared (31%) by treating 2-chlorobutane and aluminium chloride with vinyl chloride at −30°. It was dehydrohalogenated with sodamide in paraffin at 140° to give 3-methylpent-1-yne (36%), b.p. 56—57°, n_D^{21} 1·3908 (lit.,[17] b.p. 57·7°, n_D^{20} 1·3916). 3-Methylpent-1-yne (11 g) was treated in ether with ethylmagnesium bromide and carboxylated with $^{14}CO_2$ [from $Ba^{14}CO_3$ (1 mCi)] to give 4-*methyl*[1-^{14}C]*hex*-2-*ynoic acid* (10·5 g, 62%) (Found: C, 66·7; H, 8·2. $C_7H_{10}O_2$ requires C, 66·6; H, 8·2%), b.p. 73—74° at 0·2 mmHg, n_D^{19} 1·4563.

4-*Methyl*[1-^{14}C]*hex*-cis-2-*enoic Acid*.—Semihydrogenation of 4-methyl[1-^{14}C]hex-2-ynoic acid (10·4 g) over 5% palladium–barium sulphate in n-pentane gave 4-*methyl*-[1-^{14}C]*hex*-cis-2-*enoic acid* (7·8 g, 74%), b.p. 73—75° at 1 mmHg, n_D^{20} 1·4484 (Found: C, 65·7; H, 9·2. $C_7H_{12}O_2$ requires C, 65·6; H, 9·4%), which was purified by preparative g.l.c. (polyethylene glycol adipate; 140°). It had $\nu_{max.}$ 1698, 1641, and 725 cm^{-1}, τ −1·04 (1H, s), 3·92 (dd, *J* 11·5 and 9·5 Hz), 4·14 (d, *J* 11·5 Hz), 6·52 (1H, m), 8·68 (2H, dq, *J* 6·0 and 6·2 Hz), 8·96 (d, *J* 6·2 Hz), and 9·09 (t, *J* 6 Hz). The *methyl ester* (Found: C, 67·7; H, 9·8. $C_8H_{14}O_2$ requires C, 67·6; H, 9·95%) had b.p. 64—65° at 15 mmHg, n_D^{20} 1·4317. It was prepared with diazomethane and purified by preparative g.l.c. (PEGA; 80°); $\nu_{max.}$ 1728, 1660, and 694 cm^{-1}.

4-*Methyl*[1-^{14}C]*hex*-3-*enoic Acid*.—4-Methyl[1-^{14}C]hex-*cis*-2-enoic acid (5·0 g) was heated at 100° with 25% potassium hydroxide (10 ml) for 20 h, and then acidified and extracted continuously with ether. The product was partially esterified [5] and treated with aqueous sodium carbonate, and the ester was collected. Hydrolysis of the ester (10% potassium hydroxide) gave 4-methyl[1-^{14}C]hex-3-enoic acid (2·0 g, 40%), b.p. 105—106° at 8 mmHg, n_D^{20} 1·4498 (lit.,[5] 118° at 13 mmHg, $n_D^{17\cdot4}$ 1·4510). Final purification was by preparative g.l.c. (PEGA; 140°). *Methyl* 4-*methyl*-[1-^{14}C]*hex*-3-*enoate* (Found: C, 67·4; H, 9·75. $C_8H_{14}O_2$ requires C, 67·6; H, 9·95%) had b.p. 71—72° at 15 mmHg, n_D^{20} 1·4346 and was purified by preparative g.l.c. (PEGA; 80°).

Counting Techniques.—An end-window Geiger counter with Panax scaler was used and all samples were planchette counted, after combustion, as infinitely thick films of barium carbonate (standard area 2·1 cm^2) to statistical errors of <1%.

Determination of trans-*Disubstituted Olefins being formed by Stereomutation*.—Mixtures (*ca.* 1 : 1) of the allenic acid (or ester) with each [^{14}C]olefinic acid (or ester) were hydrogenated: samples were removed after *ca.* 0·5, 1·0, and 1·5 mol. equiv. of hydrogen had been absorbed. Mixture compositions were determined by g.l.c. and the mixtures were then separated by preparative g.l.c., a sample of each component being counted as above. The product of count rate and mol. proportion of each component in the hydrogenation system gives an ' experimental activity ' since all contain the same number of carbon atoms and are counted as barium carbonate. The ratios of ' experimental activities ' are the same as the ratios of molar activities of hydrogenation products to those of radioactive starting materials and are referred to as ' relative activities.'

Making the assumption that all the *trans*-olefin arises by stereomutation of the *cis*-isomer, a value for the expected relative activity of *trans*-olefin can be calculated as follows: Y mol of allene are present at the commencement of the hydrogenation and X mol of [1-^{14}C]-*cis*-olefinic acid are added. If A (mol % × mol H_2 absorbed) = area under the *cis*-olefin formation curve up to the absorption of N mol of hydrogen, the mean amount of *cis*-olefin formed during hydrogenation = A/N mol % = $AY/100N$ mol. Thus, total mean amount of *cis*-olefin present in the radiochemical hydrogenation up to the absorption of N mol of hydrogen = $X + (AY/100N)$ mol. If the count rate of the planchet made from [1-^{14}C]-*cis*-olefin at the start of the experiment = P counts per 100 s, the mean dilution of count during the absorption of N mol of hydrogen = $PX/[X + (AY/100N)]$ counts per 100 s.

Similarly, if B (mol % × mol H_2 absorbed) = area under the *trans*-olefin formation curve up to the absorption of N mol of hydrogen, the mean amount of *trans*-olefin formed during hydrogenation = B/N mol % = $B(X + Y)/100N$ mol.

The ' experimental activity ' (count rate × mol. proportion) for *trans*-olefin = $[B(X + Y)/100N]\{PX/[X + (AY/100N)]\}$.

The ' experimental activity ' of the *cis*-olefin added at the start of the experiment = PX.

So the ' relative activity ' of the *trans*-olefin = $BPX(X + Y)/[100N(X + AY/100N)PX] = B(X + Y)/(100NX + AY)$.

Thus, from the radioactive *cis*-olefin added in known amount at the start of the experiment, and the mean rate of formation of unlabelled *cis*-olefin from allene together with the mean rate of *trans*-olefin from the *cis*-olefin which is being continuously diluted by unlabelled olefin coming from the allene, a calculated value for the relative activity of the *trans*-olefin may be obtained. It is based on the assumption that all the *trans*-olefin formed

[16] P. Pomerantz, A. Foakson, T. W. Mears, S. Rothberg, and F. L. Howard, *J. Res. Nat. Bur. Stand.*, 1954, **52**, 51.
[17] H. Rupe, *Annalen*, 1909, **369**, 311.

is coming from *cis*-olefin by stereomutation and none direct from the allene by hydrogenation. If the relative activity of the *trans*-olefin is now measured experimentally, the % of *trans*-olefin formed by the stereomutation of *cis*-precursor

$$= \frac{\text{experimental ' relative activity ' (EA)}}{\text{calculated ' relative activity ' (CA)}} \times 100$$

The data relevant to the experiments reported in Tables 3 and 4 are in Table 8.

TABLE 8

Compounds	X	Y	A	B	N	EA	CA	% *trans*
(5a) and (6a)	$3{\cdot}67 \times 10^{-3}$	$7{\cdot}92 \times 10^{-3}$	7·86	3·73	0·527	0·164	0·169	97·0
Table 3	$7{\cdot}06 \times 10^{-3}$	$7{\cdot}42 \times 10^{-3}$	21·31	12·02	1·000	0·181	0·201	90·1
(5b) and (6b)	$2{\cdot}11 \times 10^{-3}$	$5{\cdot}58 \times 10^{-3}$	8·24	2·19	0·505	0·109	0·110	99·1
Table 4	$1{\cdot}91 \times 10^{-3}$	$5{\cdot}27 \times 10^{-3}$	31·91	7·06	1·000	0·141	0·141	100·0

4-Phenylpenta-2,3-dienoic Acid.—2-Phenylpropanol was oxidised to 2-phenylpropionic (hydratropic) acid [18] and converted into the acid chloride,[17] b.p. 62—64° at 1 mmHg, with thionyl chloride. Ethoxycarbonylmethyltriphenylphosphonium bromide [19] was converted into ethoxycarbonylmethylenetriphenylphosphorane,[20] m.p. 118°, by aqueous sodium hydroxide.

2-Phenylpropionyl chloride (33·7 g) in benzene (200 ml) was added dropwise to ethoxycarbonylmethylenetriphenylphosphorane (139·2 g) in benzene (1 l) and the mixture was stirred (5 h) and filtered. Evaporation of the filtrate gave *1-ethoxycarbonyl-3-phenyl-1-triphenylphosphoniobut-1-en-3-olate* (15) (84·8 g, 89%), m.p. 160° (from methanol–water) (Found: C, 77·5; H, 6·2. $C_{31}H_{29}O_3P$ requires C, 77·5; H, 6·0%). The betaine (70·3 g) was heated at 0·1 mmHg in a Woods metal bath [12] and the distillate, b.p. *ca.* 280° at 0·1 mmHg, collected and dissolved in methanol. Concentrated sodium hydroxide solution was added and the mixture was kept for 24 h. Methanol was removed under vacuum and water added. The precipitated triphenylphosphine oxide was filtered off and the filtrate was acidified to give *4-phenylpenta-2,3-dienoic acid* (15 g, 59%), m.p. 120—121° (Found: C, 75·6; H, 5·9. $C_{11}H_{10}O_2$ requires C, 75·8; H, 5·8%), $\nu_{max.}$ 3200, 1960, 1680, and 850 cm^{-1}, τ −1·28 (1H, s), 2·68 (5H, s), 4·12 (1H, q, *J* 3 Hz), and 7·81 (3H, d, *J* 3 Hz).

Esterification at −80° with diazomethane (0·9 equiv.) gave *methyl 4-phenylpenta-2,3-dienoate*, b.p. 70° at 0·7 mmHg (Found: C, 76·9; H, 6·1. $C_{12}H_{12}O_2$ requires C, 76·6; H, 6·4%), $\nu_{max.}$ 1950 and 1730 cm^{-1}.

Resolution of (±)-4-Phenylpenta-2,3-dienoic Acid.—(−)-Phenethylamine (1·55 g) in ethyl acetate (5 ml) was added to 4-phenylpenta-2,3-dienoic acid (2·2 g) in warm ethyl acetate (20 ml). After refrigeration (4 days), the crystals were separated and recrystallised to constant rotation from ethyl acetate; m.p. 129·5—130°, $[\alpha]_D^{22}$ +240° (*c* 1·1 in MeOH) (1·3 g). Decomposition of the salt gave (+)-4-phenylpenta-2,3-dienoic acid (0·6 g, 55%), m.p. 100—101°, $[\alpha]_D^{25}$ +316° (±0·3°) (*c* 1·1 in EtOH) (Found: C, 75·7; H, 5·8. Calc. for $C_{11}H_{10}O_2$: C, 75·8; H, 5·8%) (lit.,[11] m.p. 101—102°, $[\alpha]_D$ +318°), τ −1·2 (1H, s), 2·64 (5H), 4·12 (1H, q, *J* 3 Hz), and 7·81 (3H, d, *J* 3 Hz).

Work-up of the mother liquors gave partially resolved (−)-4-phenylpenta-2,3-dienoic acid, m.p. 115°, $[\alpha]_D^{25}$ −107° (±0·3°) (*c* 1·0 in EtOH) (Found: C, 76·0; H, 5·9%).

(+)-Methyl 4-phenylpenta-2,3-dienoate was prepared (CH_2N_2) from a sample of acid of $[\alpha]_D^{26}$ +212° (*c* 1·0 in EtOH) and had $[\alpha]_D^{26}$ +146° (±0·1°) (*c* 2·0 in EtOH) (Found: C, 76·4; H, 6·7%).

Hydrogenation of (+)-Methyl 4-Phenylpenta-2,3-dienoate.—The ester, $[\alpha]_D^{24}$ +146°, absorbed 2 mol. equiv. of hydrogen over a palladium catalyst and gave (−)-*methyl 4-phenylpentanoate*, b.p. 100° at mmHg, $[\alpha]_D^{20}$ −0·8° (±0·1°) (*c* 1 in EtOH) (Found: C, 74·8; H, 8·15. $C_{12}H_{16}O_2$ requires C, 74·9; H, 8·4%).

Hydrogenation of (−)-4-Phenylpenta-2,3-dienoic Acid.—The (−)-acid, $[\alpha]_D^{25}$ −107° absorbed 2 mol. equiv. of hydrogen over a palladium catalyst and gave (+)-4-phenylpentanoic acid, b.p. 150° at 5 mmHg, $[\alpha]_D^{23}$ +0·5° (±0·1°) (*c* 1·5 in EtOH) (lit.,[13] for enantiomorph, b.p. 137° at 1 mmHg, $[\alpha]_D^{25}$ −1·06°) (Found: C, 74·05; H, 8·0. Calc. for $C_{11}H_{14}O_2$: C, 74·1; H, 7·9%).

Separation and Identification of the Products from Semi-hydrogenation of (±)-4-Phenylpenta-2,3-dienoate.—The allene was hydrogenated over Pd–$BaSO_4$ until one mol. equiv. of hydrogen had been absorbed. The products were separated by preparative g.l.c. (30% diethylene glycol succinate on Chromosorb P; 135°; 20 ft × $\frac{3}{8}$ in column). Methyl 4-phenylpentanoate was identified by its n.m.r. spectrum and from the fact that it was the product of full hydrogenation of the allene. Methyl 4-phenylpent-*trans*-2-enoate, $\nu_{max.}$ 1660 and 980 cm^{-1}, showed τ 8·55 (3H, d, *J* 7 Hz), 6·3 (4H, OMe and sat. CH), 4·18 (1H, dd, *J* 16 and 2 Hz), 2·85 (1H, dd, *J* 16 and 7 Hz), and 2·7 (5H). Methyl 4-phenylpent-3-enoate had $\nu_{max.}$ 770 cm^{-1}, $\lambda_{max.}$ (EtOH) 243 nm (ε 10,280), τ 2·65 (5H, m), 4·05 (1H, tq, *J* 7 and 1·5 Hz), 6·3 (3H, s), 6·75 (2H, d, *J* 7 Hz), and 7·95 (3H, d, *J* 1·5 Hz). The n.m.r. spectrum of a fourth fraction indicated that it was a mixture of the other geometrical isomer of methyl 4-phenylpent-3-enoate with methyl 4-phenylpent-*cis*-2-enoate (*ca.* 3 : 2 based on the Me signals), the two remaining unidentified hydrogenation products. The n.m.r. spectrum of methyl 4-phenylpent-3-enoate in the mixture had the PhMeC=C*H*·CH_2·CO_2Me signal as a triple quartet at τ 4·38, *i.e.* 20 Hz upfield of the triple quartet τ 4·05 of the pure isomer. This suggests that the pure isomer has the *E*-configuration and the isomer in the mixture is *Z*, by comparison with the τ values of the vinyl protons of α-methylstyrene (Varian Catalog No. 232).

On an analytical column of polyethylene glycol adipate at 120° the following retention times (min) were observed: methyl 4-phenylpentanoate 16, methyl (3*Z*)-4-phenylpent-3-enoate plus methyl (2*Z*)-4-phenylpent-2-enoate 18, methyl (2*E*)-4-phenylpent-2-enoate 29, methyl (3*E*)-4-phenylpent-3-enoate 39, methyl 4-phenylpenta-2,3-dienoate 44.

Configurational Correlation of (+)-Methyl 4-Phenylpentanoate with (−)-Methyl 2-Phenylpropionate.—(−)-2-Phenylpropionic acid, b.p. 150° at 10 mmHg, $[\alpha]_D^{23\cdot5}$ −46° (±0·2°) (*c* 0·5 in $CHCl_3$), was obtained by partial resolution with (−)-phenethylamine (lit.,[21] b.p. 152° at 16 mmHg, $[\alpha]_D^{25}$

[18] E. L. Eliel and J. D. Freeman, *J. Amer. Chem. Soc.*, 1952, **74**, 923.

[19] G. Wittig and W. Haag, *Chem. Ber.*, 1955, **88**, 1654.

[20] O. Isler, H. Gutmann, M. Montavon, R. Ruegg, G. Ryser, and P. Zeller, *Helv. Chim. Acta*, 1957, 1242.

[21] ' Dictionary of Organic Compounds,' 4th edn., Eyre and Spottiswoode, London, 1965.

$-58°$), and converted into the methyl ester, $[\alpha]_D^{25}$ $-48·0°$ ($\pm 0·2°$) (*c* 0·5 in $CHCl_3$). It was reduced with lithium aluminium hydride to give (+)-2-phenylpropan-1-ol, $[\alpha]_D^{23·5}$ $+10·0°$ ($\pm 0·2°$) (*c* 1·0 in $CHCl_3$) (lit.,[22] $[\alpha]_D^{27}$ $+9·07°$) and this was converted into (+)-1-bromo-2-phenylpropane, $[\alpha]_D^{23}$ $+9·0°$ ($\pm 0·1°$) (*c* 0·3 in $CHCl_3$), by phosphorus tribromide and pyridine at 0° (lit.,[22] for the enantiomeric bromo-compound, $[\alpha]_D^{20}$ $-2·56°$). Malonic ester synthesis then gave (+)-4-phenylpentanoic acid, b.p. 130° at 1 mmHg, $[\alpha]_D^{24}$ $+1·2°$ ($\pm 0·2°$) (*c* 0·5 in $CHCl_3$) (Found: C, 74·2; H, 7·5. Calc. for $C_{11}H_{14}O_2$: C, 74·1; H, 7·9%) (lit.,[13] for the enantiomeric acid, $[\alpha]_D^{24}$ $-1·06°$). Esterification (CH_2N_2) gave (+)-methyl 4-phenylpentanoate, $[\alpha]_D^{24}$ $+0·6°$ ($\pm 0·2°$) (*c* 1·1 in EtOH).

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[4/2201 *Received*, 25*th October*, 1974]

[22] P. A. Levene, R. E. Marker, and A. Rothen, *J. Biol. Chem.*, 1933, **100**, 589.