Stereospecificity in the Migration of a Chiral Phosphinoyl † Group to a Chiral Carbon Atom: *X*-Ray Crystal Structure Determination of Reagent and Product [1]

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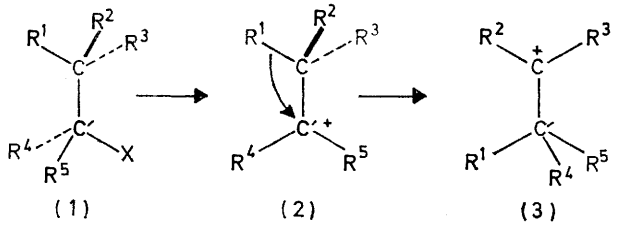
Rearrangement of the toluene-*p*-sulphonate of 3-(methylphenylphosphinoyl)-3-methylbutan-2-ol (10) gave 3-(methylphenylphosphinoyl)-2-methylbut-1-ene (12) in a stereospecific reaction. *X*-Ray crystal-structure determination (by direct methods from diffractometer data) on one diastereoisomer of each of these compounds showed that retention occurred in the migrating chiral phosphinoyl group and inversion in the secondary alkyl migration terminus. The major alcohol (10a) is orthorhombic, space group *Pbca*, with $a = 9{\cdot}067(2)$, $b = 12{\cdot}598(3)$, $c = 21{\cdot}877(5)$ Å, $Z = 8$. The structure was refined to R 0·049 (1596 observed reflections); mean σ in bond lengths 0·008 Å. The olefin (12a) is monoclinic, space group $P2_1/c$, with $a = 15{\cdot}923(12)$, $b = 7{\cdot}352(6)$, $c = 10{\cdot}839(8)$ Å, $\beta = 100{\cdot}94(2)°$, $Z = 4$. The structure was refined to R 0·089 (1024 observed reflections); mean σ in bond lengths 0·013 Å.

THE commonly accepted mechanism for a carbonium ion rearrangement, (1)—(3), requires retention of configuration in the migrating group.[2] This is required by the



(1) (2) (3)

Woodward–Hoffmann rules and has been observed in many reactions,[3] though only recently in a simple carbonium ion rearrangement.[4] If the migration is concerted with loss of the leaving group (4) or faster than C–C′ bond-rotation in the intermediate (2), inversion of configuration will occur at the migration terminus (C′).[5] This follows from the favourable antiperiplanar arrangement of the migrating and leaving groups found in cyclic systems [6] and has been observed in some acyclic systems such as asymmetrically deuteriated neopentyl compounds.[7]

Simple carbonium ion rearrangements often give mixtures of products from substitution and elimination as well as rearrangement pathways. Selectivity between

† In previous, related papers, $H_2P(O)-$ has been named as phosphinyl, but phosphinoyl is to be preferred (I.U.P.A.C. Tentative Nomenclature Rules, Section D).

[1] Preliminary communication, F. H. Allen, O. Kennard, L. Nassimbeni, R. Shepherd, and S. Warren, *Nature*, 1974, **248**, 670.

[2] C. K. Ingold, 'Structure and Mechanism in Organic Chemistry,' Cornell University Press, Ithaca, New York, 1953, pp. 500—511.

[3] E. L. Eliel, 'Stereochemistry of Carbon Compounds,' McGraw Hill, New York, 1962, p. 119.

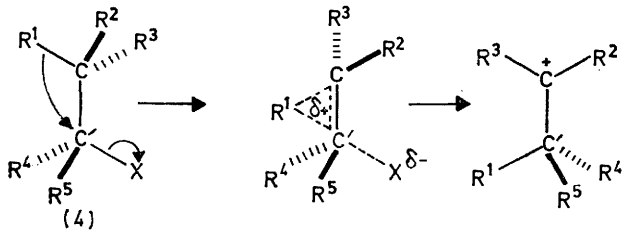
[4] T. Shono, K. Fujita, and S. Kumai, *Tetrahedron Letters*, 1973, 3123.

[5] Ref. 3, p. 142.

[6] E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, 'Conformational Analysis,' Interscience, New York, 1966, p. 105.

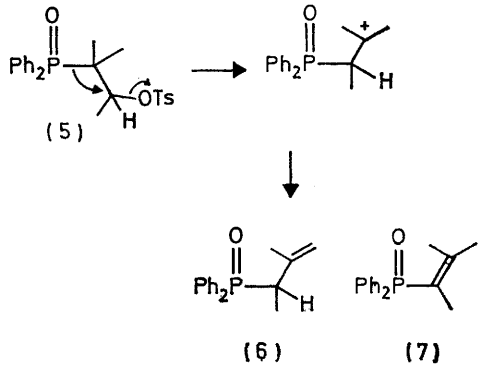
[7] G. Solladié, M. Muskatirovic, and H. S. Mosher, *Chem. Comm.*, 1968, 809.

migrating groups is often rather poor, and low stereospecificity at the migration terminus is often found [8]



(4)

except in rigid bicyclic systems [9] where stereospecificity is inevitable if the reaction is to occur at all. We have



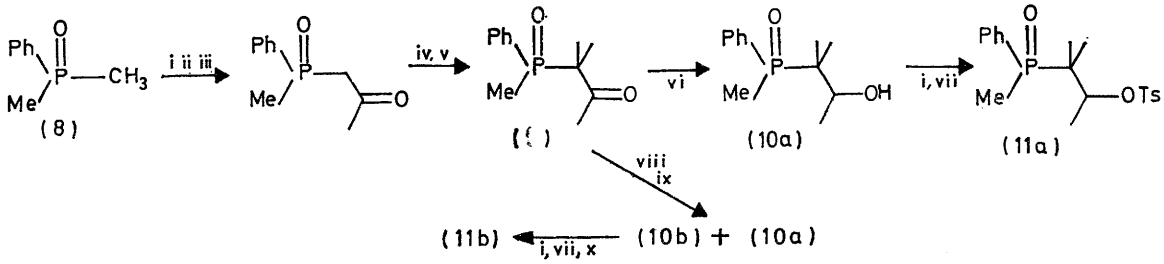
(5) (6) (7)

previously reported [10] that the presence of a phosphinoyl group at the migration origin provides, by contrast, control over these features of the reaction: (i) no substitution or elimination reactions compete with the rearrangement, (ii) only the phosphinoyl group migrates, and (iii) the resultant carbonium ion gives a single olefin in very high yield (>90%).

This degree of control suggested that the reaction might be concerted and therefore stereospecific. In one case, the rearrangement of the secondary tosylate (5), the chiral migration terminus survives as a chiral centre in the product since the elimination gives the less-crowded olefin (6) and not the more crowded and only weakly (p_π–d_π) conjugated olefin (7). We have shown [10] by deuterium labelling, that this product is indeed formed by diphenylphosphinoyl-migration. We have now used the chiral methylphenylphosphinoyl group to investigate the stereospecificity of the reaction.

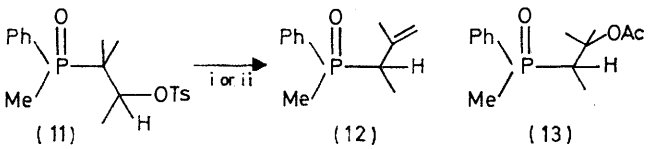
Dimethylphenylphosphine oxide (8) could be selectively lithiated on one methyl group by using one equivalent of n-butyl-lithium. Addition to acetonitrile and methylation gave the ketone (9). Reduction with the sterically demanding lithium tri-t-butoxyaluminium hydride gave >90% of one diastereoisomer (10a) of the alcohol (10) separable from the minor isomer (10b) by fractional crystallisation. The minor alcohol was more difficult to obtain, since even the most favourable conditions (reduction with sodium borohydride in methanol; see Experimental section) gave only a 40 : 60 mixture of (10b) and (10a). This mixture could not easily be separated and was converted into a mixture of tosylates (11a) and (11b); these were separated by preparative t.l.c. to give a pure sample of the minor tosylate (11b). The two tosylates were readily distinguished by their n.m.r. spectra.

Solvolysis of tosylates (11) in formic or acetic acids gave the olefin (12) contaminated by the acetate (13) in acetic acid. The tosylate (11a) gave predominantly one isomer of the olefin (12a): tosylate (11b) gave predominantly the other (12b). The steric course of the reaction was studied by an *X*-ray crystal structure determination



Reagents: i, BuLi; ii, MeCN; iii, H^+, H_2O; iv, NaH; v, MeI; vi, $LiAlH(OBu^t)_3$; vii, TsCl; viii, $NaBH_4$; ix, MeOH; x, t.l.c.

on the major alcohol (10a) and the olefin (12a) derived from it.



(11) (12) (13)

Reagents: i, AcOH; ii, HCO_2H

CRYSTAL STRUCTURE DETERMINATIONS

For both compounds the Laue symmetry and space group were determined by oscillation and Weissenberg photographs. Accurate cell-parameters were obtained from least-squares refinement of 20 2θ values measured on a Picker diffractometer. Intensity data were collected on a Picker four-circle automatic diffractometer equipped with a graphite monochromator using Cu-K_α radiation, λ(mean) 1·54178 Å. The θ—2θ scan technique was employed at a

[8] D. C. Cram and J. E. McCarty, *J. Amer. Chem. Soc.*, 1957, **79**, 2866; D. J. Cram and J. Allinger, *ibid.*, p. 2858; D. J. Cram, H. L. Nyquist, and F. A. A. Elhafez, *ibid.*, p. 2876; A. Streitweiser and W. D. Schaeffer, *ibid.*, pp. 2888, 2893.

[9] J. A. Bersonin, 'Molecular Rearrangements,' ed. P. de Mayo, Interscience, New York, 1963, p. 111.

[10] D. Howells and S. Warren, *J.C.S. Perkin II*, 1973, 1472.

speed of 2° min^{-1} in 2θ, with background counting for 20s at the scan limits. Reflection intensity data were collected with $2\theta < 110°$. Observed reflections had $I > 2\sigma(I)$ where $\sigma^2(I) = S + B + (dS)^2$, and S is the scan count, B the background count corrected to scan time, and d a constant included to account for instrumental instability, its value being determined as 0·02 from a study of the fluctuation of the S values of ' check ' reflections monitored throughout data collection. By use of the above criterion 1596 independent reflections collected from the major alcohol (10a) and 1024 from the olefin (12a) were considered observed. Lorentz and polarization corrections were applied and structure amplitudes and E values derived for both data sets in the usual manner. Both structures were solved by direct methods with programs written by G. M. Sheldrick. The Figures were drawn by use of the program PLUTO written by W. D. S. Motherwell.

TABLE 1

Fractional atomic co-ordinates of the heavy atoms (× 10^4) for the major alcohol (10a)

	x	y	z
P(1)	3461(1)	347(1)	3487(1)
O(1)	4160(3)	−714(2)	3585(1)
O(2)	1188(3)	2145(2)	3596(1)
C(1)	4857(3)	1359(2)	3424(1)
C(2)	6190(4)	1205(3)	3712(2)
C(3)	7315(5)	1950(4)	3658(2)
C(4)	7091(5)	2852(3)	3308(2)
C(5)	5778(5)	2993(3)	3012(2)
C(6)	4666(4)	2269(2)	3067(2)
C(7)	2430(5)	370(4)	2789(2)
C(8)	2250(4)	687(2)	4140(1)
C(9)	859(5)	−4(3)	4075(2)
C(10)	3077(5)	385(4)	4721(2)
C(11)	1873(4)	1879(2)	4160(1)
C(12)	911(5)	2195(3)	4694(2)

TABLE 2

Anisotropic temperature factors * of the heavy atoms (Å² × 10^4) for the major alcohol (10a)

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
P(1)	461(5)	233(5)	416(5)	8(3)	0(4)	25(3)
O(1)	680(15)	280(12)	812(18)	53(10)	52(13)	109(11)
O(2)	656(15)	338(13)	532(14)	34(10)	−18(11)	110(11)
C(1)	454(18)	329(16)	422(16)	−18(13)	39(14)	39(14)
C(2)	615(24)	625(25)	505(21)	63(19)	−23(18)	−24(20)
C(3)	479(23)	1153(39)	678(26)	−161(26)	6(20)	−147(26)
C(4)	732(30)	619(26)	862(30)	−146(22)	269(25)	−202(23)
C(5)	660(27)	498(23)	1040(33)	93(22)	290(25)	−29(20)
C(6)	513(21)	385(18)	799(26)	125(17)	92(20)	13(16)
C(7)	670(26)	535(25)	503(22)	−105(18)	−87(21)	42(23)
C(8)	544(19)	258(15)	419(16)	29(12)	3(14)	−12(14)
C(9)	647(24)	426(20)	716(27)	5(19)	126(21)	−155(19)
C(10)	735(27)	616(26)	511(23)	93(18)	−66(21)	67(23)
C(11)	510(20)	290(15)	470(18)	−32(13)	12(16)	−24(15)
C(12)	780(28)	469(22)	626(26)	−64(18)	156(22)	49(21)

* In the form: $T = exp[-2\pi^2(U_{11}a^{*2}h^2 + U_{22}b^{*2}k^2 + U_{33}c^{*2}l^2 + 2U_{23}b^*c^*kl + 2U_{13}a^*c^*hl + 2U_{12}a^*b^*hk)]$.

Crystal Data.—(i) *Major alcohol* (10a). $C_{12}H_{19}O_2P$, M = 226·26. Orthorhombic, a = 9·067(2), b = 12·598(3), c = 21·877(5) Å, U = 2498·9(4) Å³, D_m = 1·19, Z = 8, D_c = 1·203 g cm^{-3}, $F(000)$ = 976. Space group *Pbca* (D_{2h}^{15}, No. 61). (ii) *Olefin* (12a). $C_{12}H_{17}OP$, M = 208·24. Monoclinic, a = 15·923(12), b = 7·352(6), c = 10·839(8) β = 100·94(2); U = 1245·8(3) Å³, D_m = 1·10, Z = 4, D_c = 1·110 g cm^{-3}, $F(000)$ = 448. Space group $P2_1/c$ (C_{2h}^5, No. 14).

Refinement and Description of the Major Alcohol Structure (10a).—All the heavy atoms were located from a three-dimensional E map and subsequent electron-density maps. After full-matrix least-squares refinement of the heavy atoms, a difference-Fourier synthesis yielded the positions of all the hydrogen atoms. In the final least-squares refinement, anisotropic temperature factors were applied to the heavy atoms, while the hydrogen atoms were refined independently with isotropic temperature factors. The last cycle of refinement gave R 0·049. Positional and thermal parameters, and principal bond lengths and angles are listed in Tables 1—5. Figures 1 and 2 show the molecule and

TABLE 3

Fractional atomic co-ordinates (× 10^3) and isotropic temperature factors of the hydrogen atoms (Å² × 10^3) for the major alcohol (10a)

	x	y	z	U
H(2)	622(4)	67(3)	393(2)	17(9)
H(3)	834(6)	171(4)	386(2)	68(14)
H(4)	793(4)	346(3)	333(2)	44(11)
H(5)	564(5)	370(4)	276(3)	101(19)
H(6)	372(4)	238(3)	279(2)	46(11)
H(71)	322(4)	27(3)	243(2)	43(11)
H(72)	193(5)	76(3)	276(2)	46(17)
H(73)	180(4)	−26(3)	276(2)	35(11)
H(91)	122(4)	−85(3)	402(1)	21(9)
H(92)	19(6)	40(4)	374(3)	86(17)
H(92)	21(4)	8(3)	450(2)	44(11)
H(101)	249(5)	40(3)	513(2)	56(13)
H(102)	396(4)	72(3)	474(2)	34(11)
H(103)	334(5)	−31(4)	472(3)	72(17)
H(11)	280(4)	222(2)	424(1)	14(8)
H(121)	145(4)	224(3)	512(2)	53(13)
H(122)	64(4)	289(3)	464(2)	28(10)
H(123)	0(4)	179(3)	471(2)	36(11)
H(02)	106(5)	281(3)	355(2)	44(13)

TABLE 4

Bond lengths (Å) for the major alcohol (10a)

P(1)–O(1)	1·495(5)	P(1)–C(7)	1·792(8)
P(1)–C(1)	1·802(7)	P(1)–C(8)	1·851(7)
C(1)–C(2)	1·378(8)	C(8)–C(9)	1·539(9)
C(2)–C(3)	1·391(8)	C(8)–C(10)	1·524(9)
C(3)–C(4)	1·386(9)	C(8)–C(11)	1·540(8)
C(4)–C(5)	1·366(9)	C(11)–O(2)	1·422(7)
C(5)–C(6)	1·365(8)	C(11)–C(12)	1·512(8)
C(6)–C(1)	1·398(7)		
C(2)–H(2)	0·827(37)	C(10)–H(101)	1·041(46)
C(3)–H(3)	1·068(50)	C(10)–H(102)	0·901(40)
C(4)–H(4)	1·086(42)	C(10)–H(103)	0·903(47)
C(5)–H(5)	1·056(51)	C(11)–H(11)	0·961(34)
C(6)–H(6)	1·056(41)	C(12)–H(121)	1·048(44)
C(7)–H(71)	1·070(44)	C(12)–H(122)	0·912(37)
C(7)–H(72)	0·674(43)	C[12)–H(123)	0·975(39)
C(7)–H(73)	0·977(42)	H(02)–O(2)	0·849(43)
C(9)–H(91)	1·121(36)	H(02)–O(1)	1·875(45)
C(9)–H(92)	1·074(57)	O(2)–O(1)	2.715(52)
C(9)–H(93)	1·114(41)		

TABLE 5

Bond angles (°) for the major alcohol (10a)

C(1)–P(1)–O(1)	110·3(3)	C(8)–P(1)–O(1)	110·4(3)
C(7)–P(1)–O(1)	110·9(4)	C(8)–P(1)–C(1)	108·2(3)
C(7)–P(1)–C(1)	106·8(4)	C(8)–P(1)–C(7)	110·1(4)
C(2)–C(1)–P(1)	118·7(4)	C(10)–C(8)–P(1)	107·0(4)
C(6)–C(1)–P(1)	122·5(4)	C(10)–C(8)–C(9)	109·7(5)
C(6)–C(1)–C(2)	118·7(4)	C(11)–C(8)–P(1)	112·4(4)
C(3)–C(2)–C(1)	120·6(5)	C(11)–C(8)–C(9)	111·8(5)
C(4)–C(3)–C(2)	119·5(5)	C(11)–C(8)–C(10)	109·2(5)
C(5)–C(4)–C(3)	119·8(5)	C(12)–C(11)–O(2)	111·0(5)
C(6)–C(5)–C(4)	121·0(5)	C(12)–C(11)–C(8)	114·0(5)
C(5)–C(6)–C(1)	120·4(5)	C(8)–C(11)–O(2)	107·5(4)
C(9)–C(8)–P(1)	106·5(4)	O(2)–H(02)–O(1)	169·9(6)

a packing diagram of the structure. This alcohol (10a) is therefore (2*RS*,P*SR*)-3-(methylphenylphosphinoyl)-3-methylbutan-2-ol.

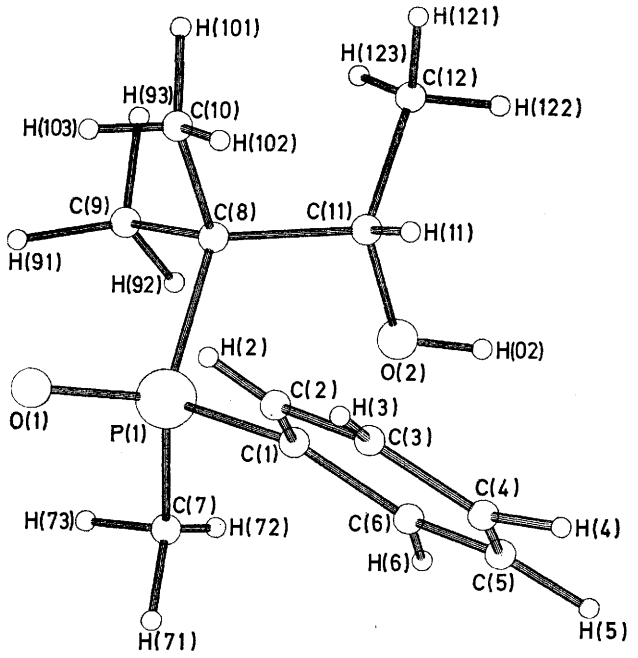


FIGURE 1 Molecular structure of the major alcohol (10a)

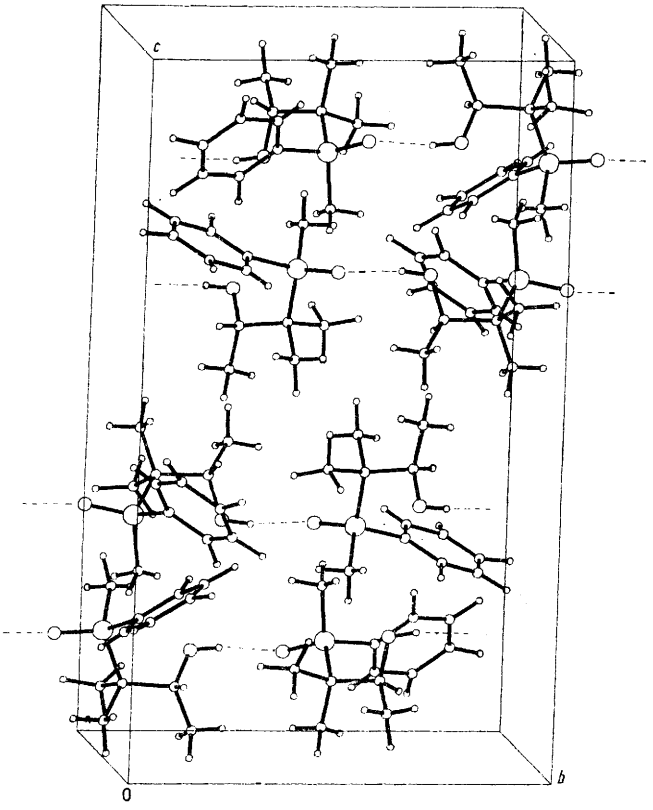


FIGURE 2 Packing diagram for the major alcohol (10a)

An interesting feature of the structure is the hydrogen bond O–H · · · O=P. The distances H · · · O and O · · · O are 1·875(41) and 2·715(46) Å, while the angle O–H · · · O is 169·9°(6). Each molecule is hydrogen bonded to two others forming a ribbon-like structure orientated approximately parallel to the *b* axis of the crystal. This is shown in Figure 2 where the hydrogen bonds are indicated by broken lines.

Refinements and Description of the Olefin (12a).—The compound decomposes slowly on exposure to air. A suitable crystal was therefore mounted in a Lindemann glass capillary. Despite this precaution the decomposition could not be checked altogether and data collection was stopped after some 80% of all possible reflections had been collected owing

TABLE 6

Fractional atomic co-ordinates of the heavy atoms ($\times 10^4$) for the olefin (12a)

	x	*y*	*z*
P(1)	2883(1)	2220(2)	3976(2)
O(1)	3005(3)	2309(7)	5374(6)
C(1)	1920(4)	1025(9)	3283(9)
C(2)	1695(5)	732(10)	2006(10)
C(3)	953(6)	−261(12)	1548(11)
C(4)	428(5)	−931(11)	2359(13)
C(5)	658(6)	−605(11)	3642(13)
C(6)	1430(5)	369(11)	4115(9)
C(7)	3746(4)	1049(11)	3432(8)
C(8)	2823(4)	4393(9)	3201(7)
C(9)	2040(5)	5475(11)	3393(10)
C(10)	3649(4)	5460(10)	3591(8)
C(11)	3877(6)	6198(14)	4827(9)
C(12)	4167(5)	5681(14)	2731(10)

TABLE 7

Anisotropic temperature factors * of the heavy atoms (Å^2 × 10^3) for the olefin (12a)

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
P(1)	60(1)	50(1)	59(3)	3(1)	16(1)	3(1)
O(1)	115(5)	80(4)	27(5)	3(2)	17(3)	−1(3)
C(1)	49(4)	53(4)	62(7)	6(4)	26(4)	2(3)
C(2)	66(5)	70(5)	69(7)	9(4)	17(5)	−7(4)
C(3)	95(7)	76(6)	112(10)	−6(5)	−11(6)	−5(5)
C(4)	55(5)	60(5)	151(11)	5(6)	25(6)	−5(4)
C(5)	89(7)	59(5)	148(11)	11(6)	73(7)	1(4)
C(6)	89(6)	61(5)	87(8)	−1(4)	8(5)	4(5)
C(7)	58(4)	71(5)	72(8)	5(4)	22(4)	10(4)
C(8)	63(4)	55(4)	44(6)	−3(3)	19(3)	1(3)
C(9)	58(5)	65(5)	137(9)	13(5)	33(5)	19(4)
C(10)	61(4)	55(4)	77(7)	5(4)	5(5)	−2(4)
C(11)	106(7)	101(7)	81(8)	5(6)	−8(6)	−33(6)
C(12)	71(6)	116(8)	111(10)	16(6)	49(6)	−15(5)

* See footnote to Table 2.

TABLE 8

Fractional atomic co-ordinates ($\times 10^3$) and isotropic temperature factors of the hydrogen atoms (Å^2 × 10^3) for the olefin (12a)

	x	*y*	*z*	*U*
H(2)	209(1)	124(1)	137(1)	54(25)
H(3)	77(1)	−49(1)	55(1)	168(59)
H(4)	−14(1)	−170(1)	199(1)	33(18)
H(5)	25(1)	−107(1)	428(1)	36(19)
H(6)	163(1)	59(1)	511(1)	18(18)
H(71)	362(0)	102(1)	242(1)	41(24)
H(72)	379(0)	−33(1)	379(1)	69(28)
H(73)	434(0)	176(1)	377(1)	35(19)
H(8)	275(0)	415(1)	220(1)	84(34)
H(91)	151(1)	462(1)	296(1)	105(15)
H(92)	204(1)	560(1)	438(1)	105(15)
H(93)	197(1)	680(1)	296(1)	105(15)
H(11)	335(1)	689(1)	513(1)	105(15)
H(112)	414(1)	520(1)	552(1)	105(15)
H(113)	436(1)	717(1)	472(1)	105(15)
H(121)	476(1)	643(1)	298(1)	76(36)
H(122)	398(1)	511(1)	180(1)	77(37)

to serious fall off in the intensities of the ' check ' reflections. The heavy atoms were located from three-dimensional E maps and electron-density maps. However, owing to the rather poor quality of the data the hydrogen atoms could not be refined independently. Refinement was therefore carried out with anisotropic temperature factors applied to the heavy atoms, but with the hydrogen atoms positionally constrained at a distance of 1·08 Å from the carbon atoms to which they were attached.[11] The last cycle of refinement yielded R 0·089. Positional and thermal parameters, and principal bond lengths and angles are listed in Tables 6—10; Figures 3 and 4 show the molecule and a packing diagram of the structure. The olefin (12a) is (3*RS*,P*SR*)-3-methylphenylphosphinoyl-2-methylbut-1-ene.

TABLE 9

Bond lengths (Å) for the olefin (12a)

P(1)–O(1)	1·492(9)	P(1)–C(7)	1·812(11)
P(1)–C(1)	1·803(11)	P(1)–C(8)	1·799(11)
C(1)–C(2)	1·380(13)	C(5)–C(6)	1·432(15)
C(1)–C(6)	1·385(14)	C(8)–C(9)	1·527(13)
C(2)–C(3)	1·397(15)	C(8)–C(10)	1·520(12)
C(3)–C(4)	1·412(16)	C(10)–C(11)	1·428(14)
C(4)–C(5)	1·390(15)	C(10)–C(12)	1·367(13)

TABLE 10

Bond angles (°) for the olefin (12a)

C(1)–P(1)–O(1)	112·4(6)	C(8)–P(1)–O(1)	114·8(4)
C(7)–P(1)–O(1)	113·0(6)	C(8)–P(1)–C(1)	105·8(5)
C(7)–P(1)–C(1)	105·7(6)	C(8)–P(1)–C(7)	104·3(5)
C(2)–C(1)–P(1)	122·1(6)	C(5)–C(6)–C(1)	119·5(10)
C(6)–C(1)–P(1)	116·0(8)	C(9)–C(8)–P(1)	111·8(7)
C(6)–C(1)–C(2)	121·9(9)	C(10)–C(8)–P(1)	111·3(7)
C(3)–C(2)–C(1)	118·6(10)	C(10)–C(8)–C(9)	112·3(8)
C(4)–C(3)–C(2)	121·5(11)	C(11)–C(10)–C(8)	120·6(9)
C(5)–C(4)–C(3)	119·2(10)	C(12)–C(10)–C(8)	118·3(9)
C(6)–C(5)–C(4)	119·3(10)	C(12)–C(10)–C(11)	121·0(9)

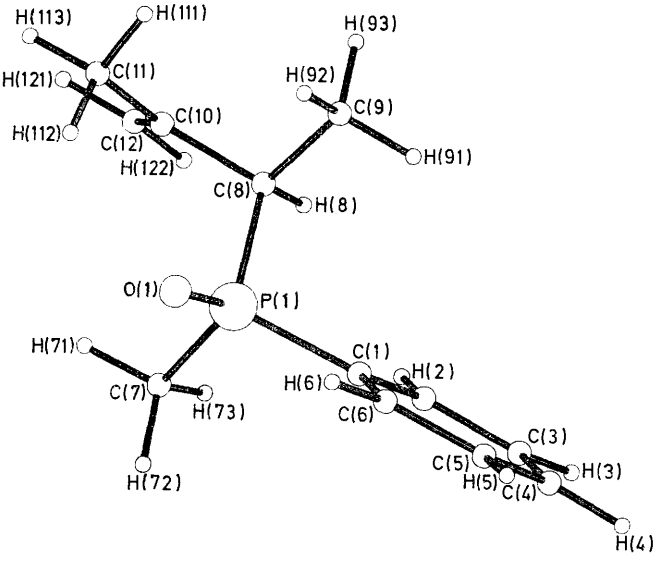


FIGURE 3 Molecular structure of the olefin (12a)

DISCUSSION

In formic acid, the only products are the two olefins: the proportion of the minor isomer increasing in each case with time. This suggested that epimerisation of starting material or product occurred under the reaction conditions. The starting tosylates did not in fact epimerise in formic acid at 75°, but the olefin (12a) did, to the extent that *ca.* 20% of the minor isomer (12b) was produced in 3 h. The amount of minor olefin formed during the reaction (also 3 h) was 15% and the reaction is thus completely stereospecific.

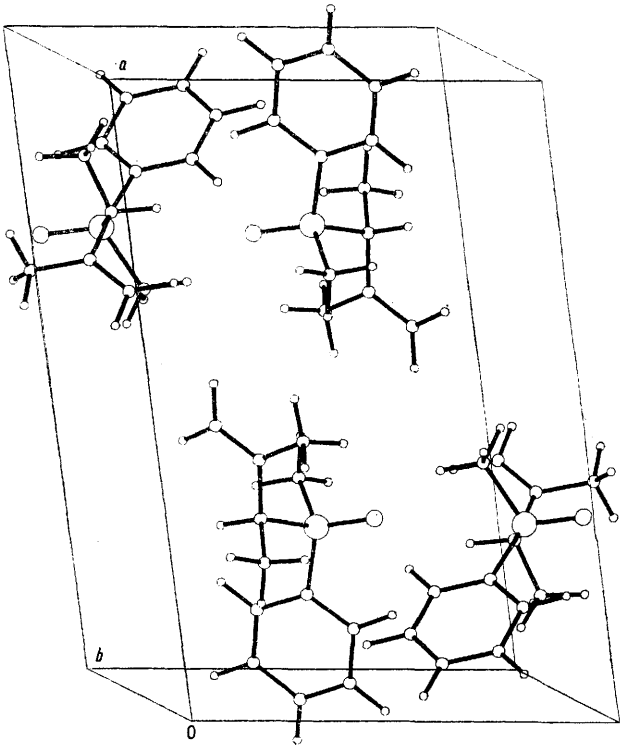
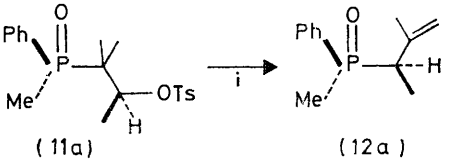


FIGURE 4 Packing diagram of the olefin (12a)

In acetic acid, very little epimerisation occurs: the tosylates are not epimerised at all, and the olefin (12a) formed only 5% of its epimer (12b) after 12 h in acetic acid at 75°. After the same time, nearly 8% of the epimer is formed during this reaction and while it is difficult to be accurate about these small amounts, the reaction in acetic acid seems to be at least 95% stereospecific.

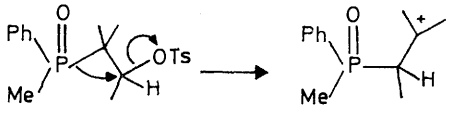
The rearrangement then is nearly completely stereospecific: the tosylate (11a) gives only olefin (12a). Inversion has occurred at the migration terminus and retention at the migrating phosphorus atom. The most likely interpretation of this result is that all three bond-making and -breaking processes (14) are concerted. It is possible, but unlikely, that the secondary cation (16) is



Reagents: i, RCO_2H at 75 °C.

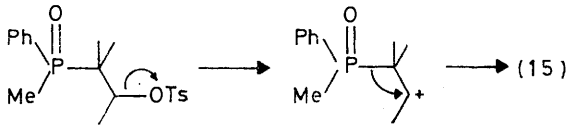
[11] F. H. Allen, O. Kennard, and G. M. Sheldrick, in preparation.

formed and that rearrangement occurs more quickly than C–C bond rotation. What is clearly confirmed is that



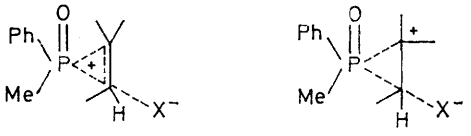
(14) (15)

the formation of the new P–C bond and the cleavage of the original P–C bond are concerted processes in spite of



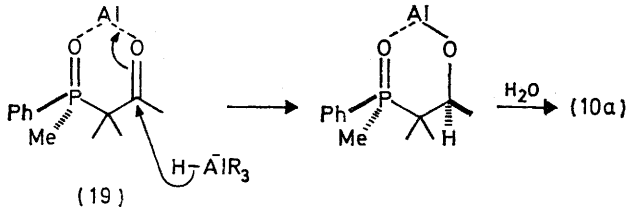
(16)

the inability of the migrating group to support the positive charge in a transition state such as (17). It may be that the two processes, P–C bond-making and -breaking, are exactly concerted so that no positive charge at all is generated on the phosphorus atom. The transition state would then be (18).



(17) (18)

One further stereochemical point deserves comment. The stereoselectivity (>90%) shown in the reduction of the ketone (9) by $LiAlH(OBu^t)_3$ is remarkable, considering that selectivity must be based on the chiral phosphorus atom which is two atoms away from the carbonyl group. The possible explanation is that a chelate (19) is formed which is attacked by hydride most easily opposite the larger phenyl substituent.



(19)

EXPERIMENTAL

Dimethylphenylphosphine Oxide (8).—Phenylphosphonic dichloride prepared from thionyl chloride and phenylphosphonic acid [12] (19·5 g), in dry ether (100 ml) was added under nitrogen to methylmagnesium iodide, made from methyl iodide (28·4 g) and magnesium turnings (5 g), in dry ether (200 ml) at such a rate that the ether gently boiled. The addition was stopped when the solution became slightly yellow (further addition produced a red impurity which caused difficulty in purification) and the mixture set aside for 30 min. Aqueous ammonium chloride solution (200 ml) was added and the mixture stirred for 30 min. The aqueous layer was separated and extracted with chloroform (5 × 100 ml). The combined chloroform layers were dried (Na_2SO_4) and evaporated under reduced pressure to give the hygroscopic phosphine oxide (13·0 g, 85%), which was purified by recrystallisation from ethyl acetate–light petroleum (b.p. 60—80°) or by vacuum sublimation. I.r. and n.m.r. spectra are the same as those reported; [13] mass spectrum shows *m/e* 154 (M^+, 55%), 139 ($PhPOMe^+$, 100), 77 (Ph^+ and Me_2PO^+, 50), and 47 (PO^+, 62).

1-(*Methylphenylphosphinoyl*)*propan*-2-*one*.— Butyl-lithium (29·3 ml; 15% in hexane) was added under nitrogen to dimethylphenylphosphine oxide (10·25 g) in dry tetrahydrofuran (250 ml). A 20% solution of acetonitrile in tetrahydrofuran saturated with lithium bromide was added with stirring until the red colour was discharged. After 30 min aqueous ammonium chloride solution (100 ml) was added, the pH checked (it must be <7), and the solution extracted with chloroform (3 × 100 ml). The combined organic layers were dried (Na_2SO_4) and evaporated under reduced pressure. The residue was dissolved in chloroform (50 ml) and passed down a column of alumina (200 g Gr-1 neutral Wöelm). Fractional crystallisation from chloroform–light petroleum (b.p. 60—80°) gave recovered dimethylphenylphosphine oxide (5·4 g, 52%) and the *ketone* (7·6 g, 34%) as white crystals, m.p. 83—84 °C; $\nu_{max.}$ 1720 (ketone), 1438 (PPh), and 1175 (P=O) cm^{-1}; τ ($CDCl_3$) 2·1—2·7 (5H, m, P–Ph), 6·66 and 6·84 (2H, ABP system, J_{AB} 12, J_{AP} 14, J_{BP} 16 Hz, PCH_2*), 7·73 (3H, s, MeCO), and 8·17 (3H, d, J_{PH} 13 Hz, PMe); *m/e* 196 (M^+, 20%), 153 ($MePhPO{\cdot}CH_2^+$, 60), 139 ($MePhPO^+$, 100), and 77 (Ph^+, 30) (Found: C, 61·0; H, 6·6; P, 16·1. $C_{10}H_{13}O_2P$ requires C, 61·3; H, 6·7; P, 16·3%). This ketone gave a crystalline semicarbazone (from chloroform-di-isopropyl ether after column chromatography on alumina), which was used to make the first crystalline sample of the ketone.

3-(*Methylphenylphosphinoyl*)-3-*methylbutan*-2-*one* (9).— The above ketone (2·5 g) and methyl iodide were dissolved in dry tetrahydrofuran (100 ml) and sodium hydride (1·02 g from 60% suspension in oil, washed with light petroleum) added in small portions under nitrogen. The reaction mixture was stirred for 30 min, and aqueous ammonium chloride solution (100 ml) added, with enough sodium thiosulphate solution to remove iodine. The solution was extracted with chloroform (3 × 100 ml), dried (Na_2SO_4), and evaporated. Recrystallisation from carbon tetrachloride–light petroleum (b.p. 60—80°) gave white crystals of the *ketone* (9) (2·1 g, 74%), m.p. 113—115 °C; $\nu_{max.}$ 1690 (ketone), 1440 (PPh), and 1170 (P=O) cm^{-1}; τ ($CDCl_3$) 2·1—2·7 (5H, m, PPh), 7·77 (3H, s, MeCO), 8·20 (3H, d, J_{PH} 12 Hz, PMe), 8·57 (3H, d, J_{PH} 14 Hz, $PCMe_2$*), and 8·69 (3H, d, J_{PH} 15 Hz, $PCMe_2$*); *m/e* 224 (M^+, 12%), 182 (42), 157 (100), 139 (55, $MePhPO^+$), 125 (25), and 77 (16) (Found: C, 64·7; H, 7·6; P, 13·6. $C_{12}H_{17}O_2P$ requires C, 46·3; H, 7·6; P, 13·8%).

(2RS,*P*SR)-3-(*Methylphenylphosphinoyl*)-3-*methylbutan*-2-*ol* (10a).—The ketone (9) (1 g) in dry tetrahydrofuran (50 ml) at −65 °C was treated with lithium tri-t-butoxyaluminium hydride [14] (2·3 g) under nitrogen and the reaction mixture kept at −65 °C for 8 h. Chloroform (100 ml) and dilute HCl (50 ml) were added, and the aqueous layer was separated and further extracted with chloroform (2 × 50 ml). The combined chloroform extracts were dried and evaporated to

* Diastereotopic because of the chiral phosphinoyl group.

[12] A. Michaelis, *Annalen*, 1876, **181**, 265.

[13] P. Haake, R. D. Cook, and G. H. Hurst, *J. Amer. Chem. Soc.*, 1967, **89**, 2650.

[14] L. F. Fieser and M. Fieser, ' Reagents for Organic Synthesis,' vol. 1, Wiley, New York, 1967, p. 620.

give a crystalline mixture [>90% of the (2*RS*,P*SR*)-isomer (10a) by the n.m.r. spectrum of the tosylates]. Fractional crystallisation (di-isopropyl ether–chloroform) gave the pure (2RS,*P*SR)-*alcohol* (10a) (500 mg, 49%), m.p. 138—139 °C; $\nu_{max.}$ 3350 (br, OH), 1440 (PPh), and 1150 (P=O) cm^{-1}; τ ($CDCl_3$) 2·1—2·7 (5H, m, PPh), 5·98 (1H, AX_3P system, J_{PH} 14, J_{HH} 7 Hz, PCC*H*Me), 8·14 (3H, d, J_{PH} 12 Hz, PMe), 8·85 (3H, d, J_{HH} 7 Hz, *Me*CH), 8·90 (3H, d, J_{PH} 16 Hz, $PCMe_2$*), and 9·02 (3H, d, J_{PH} 16 Hz, $PCMe_2$*), *m/e* 226 (M^+, 0·3%) 182 (100, $PhMePO{\cdot}CHMe_2$), 140 (41, PhMePOH), 125 (29, $PhPOH^+$), 85 (43, *M* − $PhMePOH_2$), 93 (63), *m** 107·8 (182→140), and 111·6 (140→125) (Found: C, 63·7; H, 7·7; P, 13·7. $C_{12}H_{19}O_2P$ requires C, 63·4; H, 8·2; P, 13·9%).

Re-crystallisation from di-isopropyl ether–chloroform gave a crystal used in the *X*-ray crystal-structure determination.

Reduction of the Ketone (9) *with Various Reducing Agents.*—Different conditions and reducing agents gave different proportions of the two diastereoisomeric alcohols:

Reagents	Temp. (°C)	Time (h)	Ratio (2*RS*,P*SR*) : (2*RS*,P*RS*) alcohols produced
$NaBH_4$, MeOH	25	0·5	60 : 40
$LiBH_4$, THF	25	0·5	65 : 35
$LiBH_4$, THF	−78	3	80 : 20
$LiAlH(OBu^t)_3$, THF	25	0·5	70 : 30
$LiAlH(OBu^t)_3$, THF	−65	8	90 : 10

(2RS,*P*SR)-2-(*Methylphenylphosphinoyl*)-1,2-*dimethylpropyl Toluene*-p-*sulphonate* (11a).—A solution of the pure (2*RS*,P*SR*)-alcohol (10a) (226 mg) in tetrahydrofuran (10 ml) was stirred at 0 °C with n-butyl-lithium (440 μl of 15% solution in hexane). After 5 min toluene-*p*-sulphonyl chloride (200·5 mg) in tetrahydrofuran (5 ml) was added and the mixture stirred at 0 °C for 0·5 h. Chloroform (50 ml) and saturated aqueous sodium hydrogen carbonate solution (50 ml) were added, and the aqueous layer was separated and further extracted with chloroform (2 × 25 ml). The combined chloroform layers were dried (Na_2SO_4) and evaporated. The residue was recrystallised from ethyl acetate–light petroleum (b.p. 60—80 °C) to give the tosylate (11a) (260 mg, 67%), m.p. 124—125 °C; $\nu_{max.}$ 1440 (PPh) and 1165 (P=O) cm^{-1}; τ ($CDCl_3$) 2·1—2·8 (9H, m, ArH, $MeC_6H_4SO_2$–), 5·46 (1H, AX_3P system, J_{PH} 12, J_{HX} 6 Hz, PC·C*H*·Me·OTs), 7·56 (3H, s, *Me*$C_6H_4SO_2$), 8·17 (3H, d, J_{PH} 13 Hz, PMe), 8·53 (3H, d, J_{HH} 6 Hz, *Me*CHOTs), 8·83 (3H, d, J_{PH} 13 Hz, $PCMe_2$*), and 8·99 (3H, d, J_{PH} 16 Hz, $PCMe_2$*) (Found: C, 59·9; H, 6·4; P, 8·2. $C_{19}H_{25}O_4PS$ requires C, 59·9; H, 6·6; P, 8·1%); *m/e* 380 (M^+, 0·03%), 208 (65, *M* − TsOH), 193 (38, 208 — Me), 139 (100, $PhMePO^+$), 125 (47), *m** 179·2 (208→193), and 111·6 (140→125).

(2RS,*P*RS)-2-(*Methylphenylphosphinoyl*)-1,2-*dimethylpropyl Toluene*-p-*sulphonate* (11b).—The ketone (9) (300 mg) in methanol (15 ml) at room temperature was stirred with sodium borohydride (100 mg). Aqueous ammonium chloride solution (25 ml) was added and the mixture extracted with chloroform (4 × 25 ml). The combined chloroform extracts were dried ($MgSO_4$) and evaporated to give an oily mixture of the diastereoisomeric alcohols (10) (303 mg, 100%). This mixture was converted into the mixed toluene-*p*-sulphonates, as before, and separated by preparative t.l.c. (silica, eluted with ethyl acetate) to give the (2*RS*,P*RS*)-tosylate (11b); τ ($CDCl_3$) 2·2—2·7 (9H, m, PPh, $MeC_6H_4SO_2$), 4·96 (1H, q, J_{PH}, J_{HH} 7 Hz, PCC*H*Me), 7·77 (3H, s, *Me*$C_6H_4SO_2$), 8·31 (3H, d, J_{PH} 13 Hz, PMe), 8·60 (3H, d, J_{HH} 7 Hz, CH*Me*OTs), 8·90 (3H, d, J_{PH} 16 Hz, $PCMe_2$*), and 9·02 (3H, d, J_{PH} 15 Hz, $PCMe_2$*).

Solvolysis of the Tosylates of Alcohols (10).—Solutions of the tosylates (0·1M) in formic or acetic acids were kept at 75 °C for 12 (AcOH, *ca.* 6 half-lives) or 3 h (HCO_2H). Solvent was removed under reduced pressure, saturated aqueous sodium hydrogen carbonate solution (25 ml–200 mg tosylate) added, and the mixture extracted with chloroform (3 × 25 ml–200 mg tosylate). The combined chloroform extracts were dried (Na_2SO_4) and evaporated and the crystalline residue recrystallised from light petroleum (b.p. 100—120 °C) to give 3-(*methylphenylphosphinoyl*)-2-*methylbut*-1-*ene* (12) [100% from formolysis, 80% from acetolysis, the other 20% in this case being the acetate (13)]. The (3*RS*,P*SR*)-tosylate gave (3*RS*,P*SR*)-olefin (12a), m.p. 77—79 °C; $\nu_{max.}$ 1640 (C=C), 1440 (PPh), and 1175 (P=O) cm^{-1}; τ ($CDCl_3$) 2·2—2·7 (5H, m, PPh), 5·0 (1H, m, C=CH), 5·1 (1H, m, C=CH), 7·36 (1H, AX_3P, J_{PH} 101, J_{HX} 7 Hz, PC*H*Me), 8·11 (3H, br s, allylic coupling, MeC=C), 8·34 (3H, d, J_{PH} 13 Hz, PMe), and 8·81 (3H, dd, J_{PH} 16, J_{HH} 7 Hz, PCH*Me*); *m/e* 208 (M^+, 100%), 193 (69), 140 (PhMePOH, 81), 125 (30), *m** 179·3 (208→193), and 111·6 (140→125) (Found: C, 69·6; H, 8·0; P, 15·0. $C_{12}H_{17}OP$ requires C, 69·3; H, 8·2; P, 14·9%). The (2*RS*,P*RS*)-tosylate (11b) gave the (3*RS*,P*RS*)-olefin (12b); τ ($CDCl_3$) 2·2—2·6 (5H, m, PPh), 5·13 (1H, m, C=CH), 5·3 (1H, m, C=CH), 7·30 (1H, AX_3P system, J_{HP} 14, J_{HH} 6 Hz, PC*H*Me) 8·28 (3H, d, J_{PH} 12 Hz, PMe), and 8·34 (3H, dd, J_{PH} 16, J_{HH} 6 Hz, PCH*Me*).

By-products and Epimerisation during Acetolysis of Tosylates (11).—The n.m.r. spectrum of the reaction mixture revealed a small amount of a by-product [τ 7·99 (s); $\nu_{max.}$ 1720 cm^{-1}] presumably an acetate. This compound could not easily be separated by t.l.c. so a sample of the reaction mixture was treated with sodium borohydride to convert the acetate into an alcohol; preparative t.l.c. now gave a very small amount of an alcohol whose n.m.r. and mass spectra were consistent with the rearranged structure 3-(methylphenylphosphinoyl)-2-methylbutan-2-ol; τ ($CDCl_3$) 2·3—2·6 (5H, m, PhP), 4·7br (1H, s, OH), 6·4 (1H, m, P*CH*Me), 8·21 (3H, d, J_{PH} 13 Hz, PMe), 8·74br (6H, s, CMe_2), and 9·11 (3H, m, PCH*Me*); *m/e* 226 (M^+, 1%), 211 (*M* − Me, 79), 196 (*M* − Me_2, 22), 168 (PhMePO·Et, 28), 140 (PhMePOH, 100), 125 ($PhPOH^+$, 79), *m** 107·8 (182→140), 116·7 (168→140), and 111·6 (140→125).

The olefin produced was epimerised by amounts varying according to reaction time, *ca.* 8% of the other diastereoisomer being formed in *ca.* 12 h. A sample of pure olefin (12a) in acetic acid at 75 °C epimerised slowly, *ca.* 5% of the other diastereoisomer being formed after 12 h. An n.m.r. spectrum of the tosylate isolated from the reaction mixture after one half-life showed no trace (<1%) of epimerisation.

By-products and Epimerisation During Formolysis of Tosylates (11).—No by-products could be detected by n.m.r. or t.l.c. in this reaction mixture but again a variable amount of the other diastereoisomer was formed, *ca.* 15% after 3 h. A sample of pure olefin (12a) in formic acid at 75° contained 20% of the other isomer after 3 h. No epimerisation of the starting material occurred under these conditions.

[4/599 *Received, 25th March,* 1974]