Thus, from 310 mg of **17**, 233 mg (66%) of **18** was obtained. The properties of **18** are mp 173–174°; ir 1730 cm^{-1}; nmr 5.3 (s, 1, vinyl), 4.0 (m, 4, ethylene), 1.05 (s, 3), 1.13 (s, 3), 1.20 (s, 3).

Anal. Calcd for $C_{22}H_{32}O_3$: *m/e* 344.2351. Found: *m/e* 344.2349.

17-Ethynyl-8α-methyltestosterone (19).—In 170 ml of spectroquality dioxane under nitrogen in a 500-ml three-neck flask was bubbled acetylene which had been passed through three sulfuric acid wash bottles, one empty trap, one KOH cylinder, and one calcium chloride trap. After 5 min of bubbling, 5.0 g (0.055 mol) of lithium acetylide–EDTA complex[24] (Foote Mineral Co.) was added. The mixture was stirred for 10 min while acetylene bubbling was continued, and then 185 mg (0.54 mmol) of **18** in 120 ml of dioxane was added dropwise over 25 min. Acetylene bubbling was continued for an additional 40 min. The resulting mixture, under nitrogen, was stirred overnight at room temperature (total 22.5 hr), 5 ml of saturated aqueous ammonium chloride solution was carefully added with a micropipette, and 100 ml of a 1:1 mixture of water and concentrated HCl was added. The resulting solution was heated on a steam bath 1.25 hr and cooled and usual work-up gave 205 mg of a yellow oil. The material was purified by preliminary chromatography on neutral alumina (activity IV) and the resulting 120 mg of a yellow semisolid was separated by preparative thin layer chromatography to give 63 mg (36%) of **19** and 20 mg of yellow oil containing **17**. The properties of **19** are mp 230–231°; $[\alpha]^{26}D$ +88° (*c* 0.025); uv max 250 nm (ε 14,100); ir 3350, 1660 cm^{-1}; nmr δ 6.0 (s, 1), 1.33 (s, 3), 1.10 (s, 3), 1.07 (s, 3).

Anal. Calcd for $C_{22}H_{30}O_2$: *m/e* 326.2247. Found: *m/e* 326.2252.

Registry No.—**2**, 17181-88-3; **3**, 31327-29-4; **4**, 31327-30-7; **5**, 31327-31-8; **8**, 31327-32-9; **9**, 31327-33-0; **10**, 31327-34-1; **11**, 31337-76-5; **12**, 31337-75-4; **13**, 31327-35-2; **14**, 31327-36-3; **15**, 31428-83-8; **16a**, 31385-44-1; **17**, 31337-34-5; **18**, 31337-35-6; **19**, 31337-36-7.

Acknowledgments.—The authors are indebted to Dr. Alfred Boris, Endrocrine Section, Hoffmann-La Roche, Inc., for evaluation of the biological activity.

The Stereochemistry of Vinyl Phosphates from the Perkow Reaction and the Phosphorylation of Enolates[1]

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The predominant stereochemistry of vinyl phosphates resultant from the reactions of α-halo ketones with trialkyl phosphites involves the *E* configuration, *i.e.*, $(RO)_2P(=O)O_A{>}C{=}C{<}^{H_B}_{Y}$ for A = Ph, H_A; Y = Ph, alkyl, Cl, Br. The assignment of stereochemistry is based on a combination of nmr spectral effects including (a) the differentiation of cis and trans 1,2-vinyl protons by their J_{HH} coupling constants, (b) a downfield shift for H_B when cis to phosphate and A = Ph in the presence of boron trifluoride etherate, and (c) the application of Tobey–Pascual substituent shielding constants. The phosphorylation of several potassium or lithium enolates with diethyl phosphorochloridate gives predominantly vinyl phosphates. In two cases these also have the *E* configuration. Several vinyl phosphates are found to have $J_{^{31}POCCH}$ coupling constants, trans > cis. Deuteriobenzene solvent induced shifts are briefly discussed.

The reactions of α-halo ketones with trialkyl phosphites lead to either ketophosphonates or, more usually, to vinyl phosphates (Perkow reaction).[3] The stereoisomerism of these vinyl phosphates has been previously discussed,[4] although rigorous assignment of structure has often been lacking. In one case, an unambiguous assignment[4c] was unfortunately inverted by error.[3a] We now report that the stereochemistry of vinyl phosphates can be determined, in a number of cases, by a combination of nmr techniques including the assignment of cis and trans groups on an ethylene by the method of Tobey[5a] and Pascual.[5b] We have also phosphorylated several enolates to give mainly vinyl phosphates whose stereochemistry can be correlated with those obtained from the Perkow reaction. Although some enolates have previously been phosphorylated on oxygen,[3a] the resultant vinyl phosphates have not previously been correlated with those arising from the Perkow reaction.[5c]

Results and Discussion

Phosphorylation of Enolates.—A number of potassium or lithium enolates were prepared under kinetic control conditions by the reaction of potassium or lithium triphenylmethide with the respective ketone (Scheme I).[6] Reaction of these enolates with diethyl phosphorochloridate gives the vinyl phosphate as the exclusive product (Table I) except in the case of acetophenone where some ketophosphonate (11%) is also formed. Equilibrium control formation of several enolates[6b] gave the same results.

Our phosphorylation results parallel the reactions of enolates with acetyl chloride or chlorotrimethylsilane in that bond formation occurs on oxygen in most cases.[6,7] The small yield of **16** could arise from either direct C-phosphorylation of the enolate or from the

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(2) To whom correspondence should be addressed.

(3) (a) F. W. Lichtenthaler, *Chem. Rev.*, **61**, 607 (1961); (b) P. A. Chopard, V. M. Clark, R. F. Hudson, and A. J. Kirby, *Tetrahedron*, **21**, 1961 (1965); (c) I. J. Borowitz, M. Anschel, and S. Firstenberg, *J. Org. Chem.*, **32**, 1723 (1967).

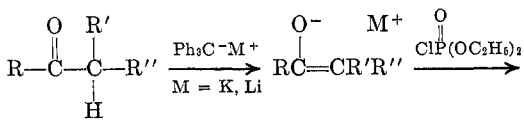
(4) (a) J. C. Craig, M. D. Bergenthal, I. Fleming, and J. Harley-Mason, *Angew. Chem., Int. Ed. Engl.*, **8**, 429 (1969); (b) J. C. Craig and M. Moyle, *J. Chem. Soc.*, 3712 (1963); (c) A. R. Stiles, C. A. Reilly, G. R. Pollard, C. H. Tieman, L. F. Ward, D. D. Philips, S. B. Soloway, and R. R. Whetstone, *J. Org. Chem.*, **26**, 3960 (1961).

(5) (a) S. W. Tobey, *ibid.*, **34**, 1281 (1969); (b) C. Pascual, J. Meier, and W. Simon, *Helv. Chim. Acta*, **49**, 164 (1966); (c) for recent work on the stereochemistry of the thiophosphorylation of enolates, see B. Miller, H. Margulies, T. Drabb, Jr., and R. Wayne, *Tetrahedron Lett.*, 3801, 3805 (1970).

(6) (a) H. O. House, "Modern Synthetic Reactions," W. A. Benjamin, New York, N. Y., 1965, pp 272–275; (b) H. O. House, L. J. Czuba, M. Gall, and H. D. Olmstead, *J. Org. Chem.*, **34**, 2324 (1969).

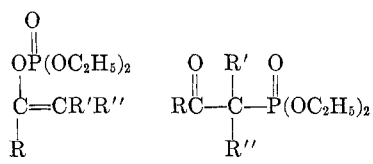
(7) G. Stork and P. F. Hudrlik, *J. Amer. Chem. Soc.*, **90**, 4462 (1968).

SCHEME I



1, R = Ph; R′ = R″ = H
2, R = Ph; R′ = CH_3; R″ = H
3, R = Ph; R′ = R″ = CH_3
4, R = Ph; R′ = Ph; R″ = H
5, R, R′ = $-(CH_2)_4-$; R″ = H

6
7
8
9
10



11
12a,b
13
14a,b
15

16, R′ = R″ H
17, R′ = CH_3; R″ = H

TABLE I

PHOSPHORYLATION OF ENOLATES WITH DIETHYL PHOSPHOROCHLORIDATE

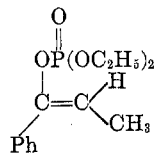
Ketone	Procedure[a]	Yields, %[b] Keto-phosphonate	Vinyl phosphate
Acetophenone	A	16, 11	11, 61
Propiophenone	B,C		12, 75,[c] 47[d]
Isobutyrophenone	A		13, 58
Benzyl phenyl ketone	B,C		14, 41,[c] 47[d]
Cyclohexanone	A		15, 62

[a] See Experimental Section for reaction conditions. [b] Determined by vpc or nmr methods (see Experimental Section). [c] Kinetic control conditions. [d] Equilibrium control conditions.

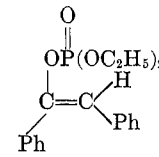
reaction of excess enolate with the O-phosphorylated product. The latter pathway is involved in the C-acylation of enolates.[6a] Evidence for direct C-phosphorylation was found as follows. Treatment of the potassium enolate of acetophenone (**6**) with diethyl phenylvinyl phosphate (**11**) or diethyl cyclohexenyl phosphate (**15**) does not lead to any C-phosphorylation or other discernable reaction.[8]

The demonstration of O-phosphorylation of enolates serves as further evidence against the involvement of enolate halophosphonium ion pairs in the Perkow reaction.[3b,c] If α-halo ketones reacted with trialkyl phosphites *via* attack on halogen, the resultant ion pairs should then interact to give O-phosphorylation. The Perkow reaction, however, results in ketophosphonate formation from α-bromoacetophenone and α-bromopropiophenone, in major and minor yields, respectively.[9]

The formation of vinyl phosphates **12** and **14** by the O-phosphorylation of enolates under kinetic or equilibrium control conditions leads to only one of the two possible isomers in each case. These isomers have now been shown to have the *E* configurations[10] **12a** and **14a**. While we do not have direct evidence,[11] **14a** may be more stable than the *trans*-stilbene **14b**.



12a



14a

Thus both (*E*)-1-(4-morpholino)-1,2-diphenylethylene[12] and (*E*)-1-toluenesulfonyl-1,2-diphenylethylene[13] (both *cis*-stilbene derivatives) are more stable than the corresponding *trans*-stilbene isomers.

Our finding of stereospecific phosphorylation under both kinetic and equilibrium control conditions is in contrast to the acetylation[14] and trimethylsilylation[6b] of potassium enolates in glyme wherein opposing ratios of isomeric products are formed under the two sets of conditions. Although the 1,2-diphenylethylene system may be a special case, the 1-phenyl-2-methylethylene system should be more typical and comparable to known cases.[6b] The effects of solvent, cation, substrate, and other factors on the stereochemistry of the phosphorylation of enolates need to be further investigated.[5c]

Stereochemistry of the Perkow Reaction.—Table II indicates nmr data obtained on vinyl phosphates formed in the reactions of α-halo ketones, α,α-dihalo ketones, and α-haloaldehydes with triethyl phosphite (TEP) or trimethyl phosphite (TMP). In many of the cases, one isomeric vinyl phosphate predominates or is the sole product. This isomer is identical (for **12** and **14**) with the one formed in the phosphorylation of the corresponding enolate.

Our initial attempts at determining the stereochemistry of the predominant isomer **14a** by the nuclear Overhauser effect[15] or by reductive conversion to the corresponding stilbene[16] failed. Thus reaction of the dimethyl 1,2-diphenylvinyl phosphate mixture **14c,d** with lithium and ammonia under various conditions gave *trans*-stilbene as the sole product; *i.e.*, equilibration to the more stable *trans*-stilbenyl carbanion occurs under the reaction conditions.[17] While this method might work for other cases, especially those that have been used in the Board olefin synthesis,[18] we needed other methods for phenyl-substituted olefins.

Several attempts at the unambiguous synthesis of a vinyl phosphate of known stereochemistry also failed. Thus we could not phosphorylate the erythro bromohydrin **19** derived from *trans*-stilbene epoxide (**18a**,

(8) House, *et al.*, have similarly shown that silyl ethers do not undergo trans silylation with enolate anions.[6b]

(9) Data and a summary of arguments relevant to the mechanism of the Perkow reaction have been presented.[3c]

(10) J. E. Blackwood, C. L. Gladys, K. L. Loening, A. E. Petrarca, and J. E. Rush, *J. Amer. Chem. Soc.*, **90**, 509 (1968).

(11) (a) Attempted isomerization of **14a,b** or **14a** with iodine in various solvents gave no change or led to the destruction of the vinyl phosphate(s). We had previously argued that the enolate of phenyl benzyl ketone should be more stable as a *trans*-stilbene derivative.[11b] It now appears that both kinetic and equilibrium control conditions lead to a phosphorylated *cis*-stilbene derivative. (b) I. J. Borowitz, P. E. Rusek, and R. Virkhaus, *J. Org. Chem.*, **34**, 1595 (1969).

(12) M. E. Munk and Y. K. Kim, *ibid.*, **30**, 3705 (1965).

(13) S. J. Cristol and P. Pappas, *ibid.*, **28**, 2066 (1963).

(14) H. O. House and V. Kramer, *ibid.*, **28**, 3362 (1963).

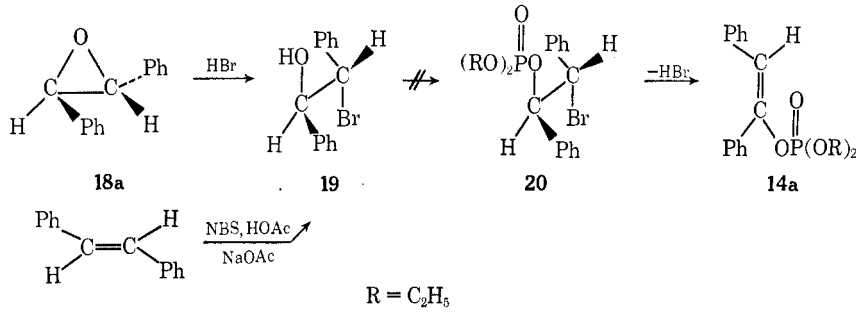
(15) Performed by Mr. Hara of JEOLCO on JEOLCO 60- and 100-MHz nmr spectrometers.

(16) Alicyclic vinyl phosphates have thus been reduced to olefins: (a) M. Fetizon, M. Jurison, and N. T. Anh, *Chem. Commun.*, 112 (1969); (b) R. E. Ireland and G. Pfister, *Tetrahedron Lett.*, 2145 (1969).

(17) D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press, New York, N. Y., 1965, pp 130–135.

(18) M. C. Hoff, K. W. Greenlee, and C. E. Boord, *J. Amer. Chem. Soc.*, **73**, 3329 (1951).

SCHEME II



18a 19 20 14a

(Scheme II). Attempts to directly convert **18a** to the corresponding phosphorylated chlorohydrin also failed. It had been hoped to then convert **20** to **14a** by a trans elimination.[19]

The successful approach to the stereochemical problem involved noting the changes in the nmr chemical shift for the vinyl proton β to the phosphate upon changing the solvent from diethyl ether to boron trifluoride etherate in diethyl ether. Ordinarily, a phosphate group behaves as an electron-donating group and it shields trans β-vinyl protons more than cis β-vinyl protons (see below for an estimate of this effect). Greater shielding (or deshielding) of trans vicinal vinyl protons as opposed to cis vicinal vinyl protons is found for a number of groups.[5a,b] A Lewis acid, such as boron trifluoride, should cause an increase of the net positive charge on phosphorus (of a vinyl phosphate) because of coordination with the PO "double bond." Such coordination compounds are well known.[20] The effect of this coordination should be a deshielding one for both cis and trans β-vinyl protons since the phosphate group will now be less electron donating. Whether the resultant change will be felt more by cis or trans β-vinyl protons is open to argument. Our results (Table II) indicate that the observed effect depends mainly upon the vicinal shielding (or deshielding) properties of the group geminal to phosphate. When this group is phenyl, the overall effect of boron trifluoride coordination of PO is a greater deshielding of the cis β-vinyl proton as opposed to the trans β-vinyl proton. That this overall effect may be due to the phenyl group, which shields trans and deshields cis β-vinyl protons,[5a,b] can be seen by comparing the results for **12a,b**, **14a,b**, **14c,d**, **38**, and **39** with those for the *gem*-methyl compounds **40–42**. In the latter set, boron trifluoride causes a relatively greater deshielding of the trans β-vinyl proton. Since many of the vinyl phosphates of interest to us had either *gem*-phenyl groups or were of otherwise determinable stereochemistry, the deshielding of cis β-vinyl protons by boron trifluoride for many cases could be used without ambiguity. In support of the proposal that boron trifluoride is coordinating with the oxygen of PO, we note a general deshielding of the methylene group of OC_2H_5 in all of the diethyl phosphates studied. Some of the data is included in Table II.

It had been anticipated that a cis β-vinyl proton would show little change for $\Delta = \delta_{CCl_4} - \delta_{C_6D_6}$ (other than a general effect experienced by all groups including TMS) since it is close to the bulky phosphate group. Furthermore benzene molecules were expected to orient themselves so as to be away from the negative (oxygen) end of the PO dipole. A trans β-vinyl proton was expected to show an upfield shift due to increased shielding by benzene molecules forming a "collision complex" at this "far end" of the molecule.[21]

The anticipated preferential shielding of a trans β-vinyl proton was found for **14**, **40**, and the related phosphorylated species **41** and **42**. The *gem*-phenyl phosphates **11** (and related species **38**, **39**), **12**, **31**, and **32**, however, exhibit a deshielding of the trans β-vinyl proton and a shielding of the cis β-vinyl proton. Our data indicate that factors additional to steric ones have to be considered. These may include the relative orientation of the phosphate group in various vinyl phosphates, an attraction of benzene molecules to the positive phosphorus, and a repulsion from the negative oxygen of the PO group. As evidence for the orientation of benzene molecules away from the oxygen end of PO, we cite the relatively greater shielding of methyl (+0.25 ppm) than methylene (+0.12 ppm) in the ethoxy group of **11**. Similar benzene solvent effects have been noted with esters[21c] and ketones.[21d]

The magnitude of our nmr effects was established for several cases of known stereochemistry (Table II). The deshielding of the cis β-vinyl proton in **15**, **22**, and **24** by BF_3 coordination with PO was found to be −0.145, −0.26, and −0.32 ppm, respectively. The geminal proton values for **22** and **24** were less affected (+0.03 and −0.06 ppm). The $\Delta = \delta_{CCl_4} - \delta_{C_6D_6}$ shifts were negative for **15**, **22**, and **24** (−0.24, −0.06, and −0.01 ppm). The reactions of α-bromoacetaldehyde (**21**) or α-chlorobutyraldehyde (**23**) with TMP gave the trans *E*-vinyl phosphates **22** and **24**, respectively, as established by the J_{HH} vinyl proton coupling constants of 12 and 12.6 Hz.[22]

Assuming that the above nmr effects hold for other vinyl phosphates, we conclude that α-chlorobenzyl phenyl ketone (**25**) reacts with TEP to give a 65:35 ratio of the *E*:*Z* isomers **14a** and **14b**. Similarly TMP gives **14c** and **14d**, with **14c** predominating. Phosphorylation

(19) Such an approach has been widely used to synthesize ethylenes of known stereochemistry.[12,13]

(20) (a) A. B. Burg and W. E. McKee, *J. Amer. Chem. Soc.*, **73**, 4590 (1951); (b) A. V. Topchiev, S. V. Z. Zangorodnii, and Y. M. Paushkin, "Boron Trifluoride and Its Compounds as Catalysts in Organic Chemistry," Pergamon Press, New York, N. Y., 1959, pp 82–84.

(21) Benzene solvent shifts for vinyl halides, acids, and esters have been found to be largest for trans β-vinyl protons: (a) F. Hruska, D. W. McBride, and T. Schaefer, *Can. J. Chem.*, **45**, 1081 (1967); (b) J. Ronague and D. H. Williams, *J. Chem. Soc.*, 2642 (1967); (c) A. Kemula and R. T. Iwamoto, *J. Phys. Chem.*, **72**, 2764 (1968); (d) M. Fétizon, J. Goré, P. Laszlo, and B. Waegell, *J. Org. Chem.*, **31**, 4047 (1966).

(22) Cis 1,2-divinyl proton coupling constants of vinyl phosphates are 4.1–5.8 Hz and trans constants are 11.1–13.2 Hz. See J. P. Ferris, G. Goldstein, and D. J. Beaulieu, *J. Amer. Chem. Soc.*, **92**, 6598 (1970), and references therein.

TABLE II
VINYL PHOSPHATE SPECTRAL DATA

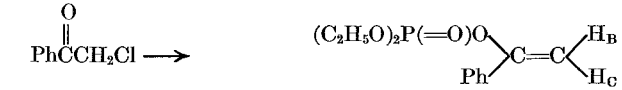
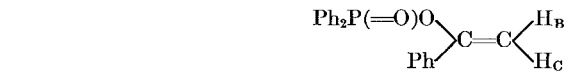
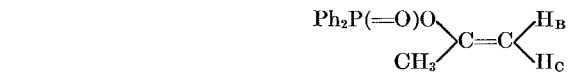
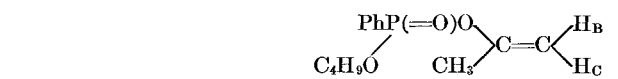
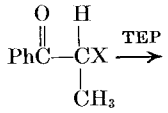
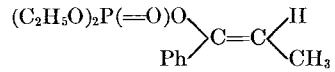
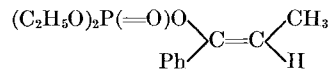
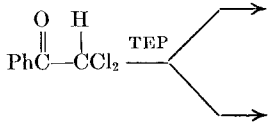
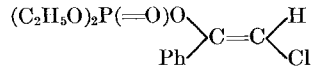
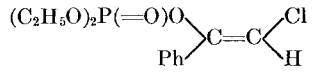
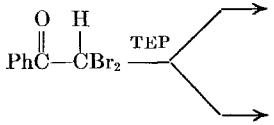
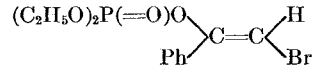
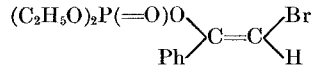
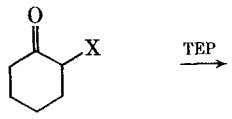
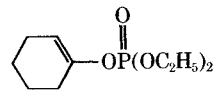
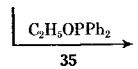
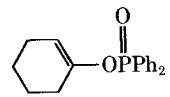
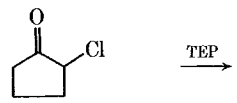
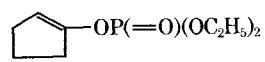
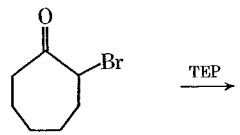
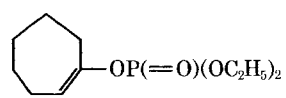
Origin	Compd	Isomer ratio	β-Vinyl H nmr: $-\delta_{Et_2O}$	$\Delta = \delta_{Et_2O} - \delta_{BF_3\cdot Et_2O}$	$-\delta_{CCl_4}$	$\Delta = \delta_{CCl_4} - \delta_{C_6D_6}$	J_{POCCH}, Hz	Other data
25 → TEP	14a (*E*)	65[a]	6.42	−0.28	6.33	−0.15	1.0	Uv λ_{max}^{EtOH} 221 nm (4.16), 283.5 (4.25)
25 → TEP	14b (*Z*)	35[a]	6.79	−0.02	6.69	+0.30	2.5	Ir (CCl_4) 1605, 1645 cm^{-1}
25 → TMP	14c (*E*)	65	6.42	−0.25	6.34	−0.05	1.0	^{31}P nmr +4.0 ppm
	14d (*Z*)	35	6.75	−0.04	6.67	+0.28		
26 + TEP or 9 + $ClPO(OC_2H_5)_2$ →	14a		6.40	−0.26	6.32	−0.05		Uv λ_{max}^{EtOH} 221 nm (4.09), 283.5 (4.31)
25 or 26 →	 36		6.22	−0.19	6.19	−0.05	*Ca.* 1.0	Uv λ_{max}^{EtOH} 274 nm (4.29), 283 (4.28); ^{31}P nmr −27.5 ppm
 →	 11		5.24	−0.28 −0.01	5.21	+0.02 −0.29	2.3 (Et_2O), 2.1 (CCl_4)	
		OCH_2				+0.12		
		CH_3				+0.25		
	 38							
		H_B	5.05	−0.29	5.04	+0.07[b]	1.0	
		H_C	5.28	−0.06	5.21	−0.36	2.0	
	 39							
		H_B	5.18	−0.21	5.12	+0.02[b]	1.5	
		H_C	5.20	0.00	5.20	−0.30	2.5	
		OCH_2		−0.30		0.00		
		CH_3				+0.20		
 →	40							
		H_B	4.71	−0.09	4.68	−0.22[b]		
		H_C	4.40	−0.31	4.45	+0.10		
		OCH_2		−0.34		+0.10		
		CH_2CH_3				+0.32		
		Vinyl CH_3		−0.09		+0.14		
	 41							
		H_B	4.75	−0.05	4.60	−0.29[b]	~1.0	
		H_C	4.37	−0.31	4.22	+0.10	2.5	
		Vinyl CH_3			1.90	+0.14		
	 42							
		H_B	4.70	−0.07	4.67	−0.20[b]		
		H_C	4.35	−0.27	4.35	+0.07		
		OCH_2	4.09	−0.28	4.03	+0.02		
		Vinyl CH_3	1.85	−0.09	1.85	+0.03		

TABLE II (*Continued*)

Origin	Compd	Isomer ratio	β-Vinyl H nmr: $-\delta_{Et_2O}$	$\Delta = \delta_{Et_2O} - \delta_{BF_3\cdot Et_2O}$	$-\delta_{CCl_4}$	$\Delta = \delta_{CCl_4} - \delta_{C_6D_6}$	J_{POCCH}, Hz	Other data
 X = Cl, Br	 **12a**	*c*	5.66	−0.16	5.60	+0.05	2.5	Ir (CCl_4) 1667 cm^{-1}
	 **12b**	*c*	5.785	−0.035	5.77	−0.23	2.8	
7 + $ClP(=O)(OC_2H_5)_2$ →	**12a**		5.59 1.84 (vinyl CH_3)	−0.18 0.00	5.55 1.835	+0.03 +0.035		
	 **31a**	60	6.31	−0.19	6.13	+0.21	2.3	Ir (CCl_4) 1650 cm^{-1}
	 **31b**	40	6.56	−0.08	6.45	−0.25	2.8	
	 **32a**	97	6.36	−0.21	6.14	+0.17	1.6	Ir (CCl_4) 1625 cm^{-1}
	 **32b**	3	6.59	*d*	6.49	−0.23	2.8	
	 **15**		5.45	−0.14	5.39[e]	−0.24	2.2	^{31}P nmr +6.25 ppm
	 **37**		5.51	−0.15	5.38[e]	−0.32		
	 **43**		5.15	−0.22	5.18	−0.11 +0.09 (CH_2), +0.20 (CH_3)		Ir (film) 1695 cm^{-1}
	 **44**		5.54	−0.16	5.45	−0.30 +0.04 (CH_2), +0.24 (CH_3)		

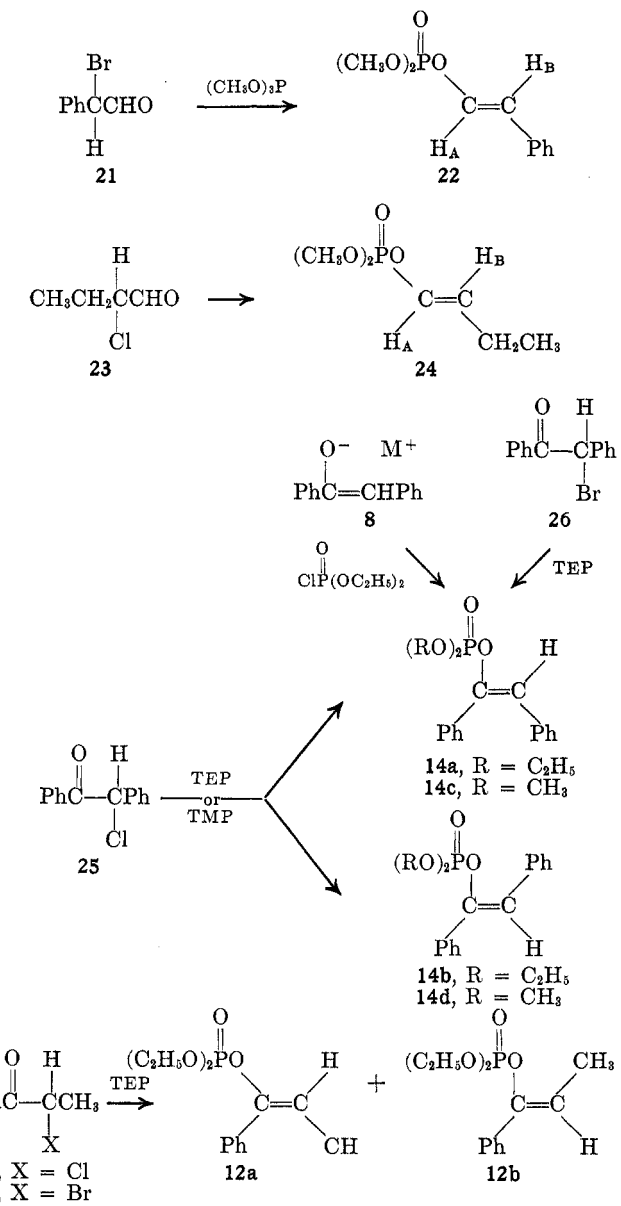
TMP, **21** →	$(CH_3O)_2P(=O)O$, H_B, Ph, H_A	**22**	6.37	−0.26	6.32[f]	−0.06	1.6	J_{AB} = 12 Hz
			H_A	−0.02		−0.20		
								Ir (CCl_4) 1652 cm^{-1}
TMP, **23** →	$(CH_3O)_2P(=O)O$, H_B, C_2H_5, H_A	**24**	H_B 5.385	−0.32	5.38[f]	−0.01	1.4	J_{AB} = 12.3 Hz
			H_A	−0.06		−0.13		
TMP, **27** →	$(CH_3O)_2P(=O)O$, H_B, Cl, H_A	**28a**	70 H_B 6.26	−0.23	6.14	+0.185	1.5	J_{AB} = 11.5 Hz
			H_A 6.87	−0.04	6.80	−0.04		
	$(CH_3O)_2P(=O)O$, Cl, H_B, H_A	**28b**	30 H_B 5.70	−0.30	5.605	+0.435	1.7	J_{AB} = 4.3 Hz

[a] Vinyl phosphates **14a** and **14b** were recovered in unchanged isomeric ratio after removal of the BF_3 with $NaHCO_3$. [b] No crossover of the vinyl protons in going from CCl_4 to C_6D_6 was demonstrated by examining **39**–**42** in mixtures of the solvents as well as in the pure solvents. [c] Vinyl phosphates **12a** and **12b** are obtained in 1.6:1 or 2.3:1 ratio from the α-chloro and α-bromo ketone, respectively. [d] Signal too weak for accurate value to be established. [e] δ_{CCl_4} for the vinyl proton of cyclohexene is −5.68, using the convention[5a] which expresses downfield shifts from TMS as negative. This establishes a cis phosphate "*Z*" value of +0.30 ppm. [f] These compounds are used to establish a geminal phosphate "*Z*" value of −1.42 ppm.

of the enolate **8** or reaction of the bromo ketone **26** with TEP gives only **14a**.

The minor isomers **14b** and **14d** represent examples of compounds with β-vinyl protons which are trans to phosphate. These cases give small BF_3 shifts (−0.02 and −0.04 ppm) and $\Delta = \delta_{CCl_4} - \delta_{C_6D_6}$ shifts which are positive (+0.30 and +0.28 for **14b** and **14d**). By similar reasoning, the reaction of α-chloro- or α-bromopropiophenone (**29**, **30**) with TEP gives the *E*-vinyl phosphate **12a** as the major isomer (Scheme III). The

SCHEME III



C_6D_6 shift for the trans methyl group in **12a** is only +0.035, a much smaller value than trans β-methyl shifts reported in other vinyl systems.[21]

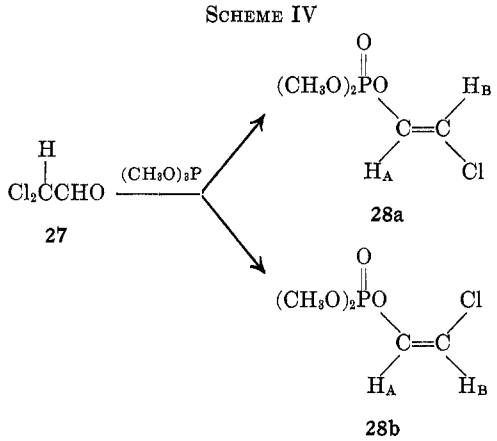
Vinyl phosphates bearing halogen atoms give ambiguous BF_3 shifts. Thus α,α-dichloroacetaldehyde (**27**) reacts with TMP to give 80:20 **28a** and **28b** (Scheme IV), as determined by J_{AB} (Scheme IV, Table II). The H_B protons of both isomers are deshielded by BF_3, however. The C_6D_6 shift is in the predicted manner, *i.e.*, H_{trans} is more shielded (+0.44) than is H_{cis} (+0.19). The situation is more complex for the iso-

TABLE III
CALCULATION OF VINYL PROTON NMR ABSORPTION IN VINYL PHOSPHATES

Compd	Vinyl proton (δ, CCl_4) Obsd	Calcd	Compd	Vinyl proton (δ, CCl_4) Obsd	Calcd
14a	6.33	6.34	**22**	H_A 7.08	7.08
14c	6.34			H_B 6.32	6.32
14b	6.69	6.59	**24**	H_A 6.32	6.43
14d	6.67			H_B 5.38	5.41
			28a	H_A 6.80	6.83
	H_B	4.91		H_B 6.14	6.02
11	5.21		**28b**	H_A 6.80	6.78
	H_C	5.16		H_B 5.605	5.82
12a	5.60	5.35	$(CH_3O)_2P(=O)O$, H, CH_3, CO_2CH_3	5.76[b]	5.47
			33a (major isomer, $J_{PH} \cong 1.5$ Hz)		
12b	5.77	5.60	$(CH_3O)_2P(=O)O$, CO_2CH_3, CH_3, H	5.47[b]	5.29
			33b (minor isomer, $J_{PH} \cong 0$ Hz)		
31a	6.13	5.96	^-O, $P(=O)O$, ^-O, CN, H_A, H_B	H_A 4.73 (D_2O)[c]	5.07 (D_2O)
31b	6.45	6.21	**34**	H_B 7.33 (D_2O)	7.22 (D_2O)
32a	6.14	5.93			
32b	6.49	6.18 (6.01)[a]	**40**	H_B 4.68	4.63
15	5.39	5.39		H_C 4.45	4.45

[a] Using Tobey's special values for crowded bromine.[5a] [b] Reference 26. [c] Reference 22.

SCHEME IV



meric diethyl 1-phenyl-2-bromovinyl phosphates (**31a** and **31b**) and the corresponding chloro compounds **32a**, **32b**. They are tentatively assigned the configurations shown in Table II on the basis of Tobey–Pascual shielding constants (Table III). The *E* isomer **31a** exhibits a larger negative BF_3 shift than does the *Z* isomer **31b** but the C_6D_6 shifts are reversed, *i.e.*, the apparent trans β-vinyl proton in **31b** is deshielded instead of being more shielded.[23] It was demonstrable that the addition of $BF_3 \cdot Et_2O$ caused no chemical change nor any isomerization of isomers under the conditions employed.

Prediction of Vinyl Proton Nmr Absorption in Vinyl Phosphates.—The assignment of vinyl phosphate stereochemistry by the above methods has led to the establishment of nmr shielding constants for a dialkyl phosphate group according to the methods of Tobey[5a] and Pascual[5b] as follows: geminal $OP(O)(OR)_2$, −1.42; cis, +0.30; and trans, +0.50 ppm. These values are reasonably related to those reported for *O*-acetyl[5a] and are to be used with −5.27 ppm as the base value for ethylene (δ 5.27).[5a] These phosphate "*Z*" values correlate the nmr absorption of β-vinyl protons in vinyl phosphates of known stereochemistry fairly well (Table III). Where both vinyl phosphates are available, this method allows the assignment of *E* or *Z* configuration to known or unknown cases. The stereochemical assignments thus made are in agreement, in a number of cases, with those made by the use of BF_3 shifts. Confirmation of the assigned stereochemistry of the dimethyl 1-methyl-2-carbomethoxyvinyl phosphates **33a** and **33b** is found.[24] There is even good agreement for the cis isomer of 2-cyanovinyl phosphate dianion (**34**)[22] although we do not generally expect the same "*Z*" values to apply to other phosphorylated groups.

Long-Range Phosphorus Proton Coupling Constants.—The $J_{^{31}POCCH}$ coupling constants for vinyl H_B in all of the vinyl phosphates examined are in the range of 1.4–2.8 Hz, assuming first-order analysis. For the isomeric pairs **12**, **14**, **28**, **31**, and **32** (assuming that the stereochemical assignment is correct in each case) trans $J_{^{31}PH} >$ cis $J_{^{31}PH}$. The larger coupling constant is thus found for the "zigzag path" of the trans isomer.[25a,c]

(23) The reasons for the ambiguous behavior of the halovinyl phosphates are not clear. Vinyl halides do not differ in their nmr benzene solvent shifts from other olefins.[21] Chloro and bromo compounds are claimed not to coordinate with BF_3.[20b]

(24) T. R. Fukuto, E. O. Hornig, R. L. Metcalf, and M. Y. Winton, *J. Org. Chem.*, **26**, 4620 (1961).

(25) (a) J. W. Emsley, J. Feeney, and L. H. Sutcliffe, "High Resolution Nuclear Magnetic Resonance Spectroscopy," Vol. 2, Pergamon Press, Oxford, 1966, pp 740, 741; (b) pp 735–739. (c) NOTE ADDED IN PROOF.—See E. Gaydou, J. Llinas, G. Peiffer, and A. Guillemonat, *Ann. Fac. Sci. Marseille*, **43**, 83 (1970), for relevant calculations.

The reported data for **33**, however, are $J_{^{31}PH} \cong$ 1.5 Hz for the cis β-vinyl proton in **33a** and *ca.* 0 for the trans vinyl proton in **33b** (based on ^{31}P nmr spectra),[25] in contradiction to our observations. In view of the complex nature of the factors influencing proton allylic coupling constants[25b,26] and since less is known about allylic phosphorus proton coupling, no generalization can safely be made.

Other Spectral Data for Vinyl Phosphates.—The ^{31}P nmr absorption of several vinyl phosphates is given in Table II.[27] The *Z* and *E* isomers of **14** were not sufficiently resolved at 24.29 MHz for an assignment to be made. The small positive shifts for **14c** and **15** are in accord with other vinyl phosphate data.[28] The ultraviolet spectra of **14a** and of the corresponding vinyl phosphinate **36** (see below) are more closely related to that of *cis*-stilbene (λ_{max} 280 nm) than that of *trans*-stilbene (λ_{max} 295 nm),[29] as expected.

Diphenyl Vinyl Phosphinates.—The reactions of α-halo ketones with ethyl diphenylphosphinate (**35**) lead, in many cases, to diphenyl vinyl phosphinates.[30] Preliminary studies indicate nmr behavior for these species similar to that of vinyl phosphates, as shown by **36** and **37** (Table II). The relationship of the stereochemistry of vinyl phosphate formation to the mechanistic pathways involved will be considered elsewhere.

Experimental Section[31]

All of the solvents used were dried by distillation from phosphorus pentoxide, calcium hydride, or lithium aluminum hydride. Reactions were conducted under an atmosphere of prepurified nitrogen. Organic solutions were dried over magnesium sulfate. The reactions of α-bromopropiophenone, α-chloropropiophenone, α-bromobenzyl phenyl ketone, and α-chlorobenzyl phenyl ketone with TEP have been previously recorded.[30c]

Phosphorylation of Enolates. Kinetic Control Methods. Procedure A.—Potassium (0.99 g, 0.025 g-atom) was added to triphenylmethane (6.1 g, 0.025 mol) in glyme (50 ml). The resultant mixture was stirred at 22° for 24 hr to give a dark red solution. Acetophenone (2.50 g, 0.021 mol) was added until the red color was just discharged. Diethyl phosphorochloridate (8.63 g, 0.050 mol) was then added, and the resultant mixture was stirred at 22° for 30 min, cooled, and filtered. Vpc analysis (on 3 or 5% SE-30 on Chromosorb W at *ca.* 180°), with the aid of a calibration curve for the vinyl phosphate **11**, indicated that **11** (61%) and the ketophosphonate **16** (11%) were formed.

Procedure B.—*n*-Butyllithium (2.5 *M* in hexane, 0.0065 mol) was treated with triphenylmethane (0.0065 mol) in THF to give lithium triphenylmethyl at 0°. The ketone (propiophenone or benzyl phenyl ketone, 0.005 mol) was added by syringe *via* a serum cap until the solution was light pink. Diethyl phosphorochloridate (0.006 mol) was added rapidly at 0° and the reaction was kept at 0° for 1 hr. After removal of the solvent, nmr analysis of the resultant mixture ($CDCl_3$) gave product ratios using triphenylmethane as an internal standard.

Equilibrium Control Method. Procedure C.—Using procedure B, *n*-butyllithium (0.005 mol), triphenylmethane (0.0055 mol), ketone (0.006 mol), and diethyl phosphorochloridate (0.006 mol), the ketone was added to give a colorless solution which was kept at 0° for 60 min before phosphorylation.

In several cases, the reaction mixture, from procedure A mainly, was chromatographed on silica gel with benzene and ether–benzene as eluents to give vinyl phosphates as isolable products.

Attempted Reaction of an Enolate with Vinyl Phosphates.—A mixture of the potassium enolate of acetophenone (procedure A), from acetophenone (2.40 g, 0.020 mol) and diethyl cyclohexenyl phosphate (**15**, 4.68 g, 0.020 mol) was heated at reflux in glyme for 30 min and distilled to give **15** and two minor components (by vpc on 5% SE-30). Similar treatment of the above enolate with diethyl 1-phenylvinyl phosphate (**11**) gave only acetophenone and **11**.

Vinyl Phosphates.—Pertinent data are given in Tables II and III. The nmr spectra (CCl_4) were consistent with assigned structures, generally exhibiting δ 7.1–7.7 (m, 5 or 10, phenyl, when present), *ca.* 3.95 (m, 4, CH_2CH_3), *ca.* 0.82 (t, 3, CH_2CH_3) as well as vinyl absorption as in Table II, or (for dimethyl phosphates) 3.5 ppm (CH_3O).

Diethyl 1-phenyl-2-chlorovinyl phosphate (31): 73% from TEP and dichloroacetophenone; bp 140° (0.3 mm).

Anal. Calcd for $C_{12}H_{16}O_4ClP$: C, 49.58; H, 5.55. Found: C, 49.65; H, 5.57.

Diethyl 1-phenyl-2-bromovinyl phosphate (32): 91% from TEP and dibromoacetophenone; bp 140–145° (0.05 mm).

Anal. Calcd for $C_{12}H_{16}O_4BrP$: C, 43.01; H, 4.81. Found: C, 43.25; H, 4.90.

Dimethyl 2-phenylvinyl phosphate (22): 74% from 2-chloro-2-phenylacetaldehyde and TMP; bp 135–140° (0.75 mm).

Anal. Calcd for $C_{10}H_{13}O_4P$: C, 52.64; H, 5.74; P, 13.57. Found: C, 52.46; H, 5.62; P, 13.44.

Dimethyl 2-ethylvinyl phosphate (24): 11% from crude 2-chlorobutyraldehyde and TMP; bp 60–80° (0.6 mm); mass spectrum[32] (70 eV) *m/e* calcd for $C_6H_{13}O_4P$, 180.0559 (found, 180.0575).

Diethyl cyclopentenyl phosphate (43): 68% from TEP and 2-chlorocyclopentanone; bp 85–87° (0.1 mm) [lit.[33] bp 104–105° (1 mm)].

Diethyl cycloheptenyl phosphate (44): 74% from TEP and 2-bromocycloheptanone; bp 117–120° (0.1 mm); vpc (10% SE-30) one peak.

Anal. Calcd for $C_{11}H_{21}O_4P$: C, 53.22; H, 8.33. Found: C, 53.10; H, 8.49.

Diethyl 1-methylvinyl phosphate (40): 83% from TEP and chloroacetone; bp 90–91° (5 mm) [lit.[34] 65–66° (1.5 mm)].

Attempted Synthesis of the Diethyl Phosphate of 1-Hydroxy-1-halo-1,2-diphenylethane.—Treatment of the erythro bromohydrin **19** [from the reaction of *trans*-stilbene epoxide (**18a**) with HBr or from *trans*-stilbene, *N*-bromosuccinimide, NaOAc, and HOAc[35]] with diethyl phosphorochloridate and triethylamine (or with collidine), with $POCl_3$ and triethylamine, or with $POCl_3$ and triethyl phosphate (followed by ethanol for the latter two reactions) gave none of the desired phosphate **20** (Scheme II). Attempts at reacting **18a** with diethyl phosphate and *p*-TSA, or with diethyl phosphorochloridate and aluminum chloride,[36] were also unsuccessful.

Reduction of Dimethyl 1,2-Diphenylvinyl Phosphate.—Ammonia (100 ml, purified by distillation from Li wire) was added to a nitrogen-filled flask containing **14c,d** (3.04 g, 0.0100 mol) in anhydrous diethyl ether (20 ml) and *tert*-butyl alcohol (1.52 g, 0.0200 mol) at 22°. Lithium wire (0.14 g, 0.0200 g-atom) was added in pieces by means of an erlenmeyer flask connected with Gooch tubing. The ammonia was allowed to evaporate overnight. Then, after addition of saturated aqueous $NaHCO_3$ (100 ml) and diethyl ether (100 ml), the phases were separated. The organic layer, combined with an ether extraction (100 ml) of the aqueous layer, was washed with 1 *N* NaOH (100 ml), dried, filtered, and evaporated *in vacuo* to give *trans*-stilbene (1.73 g, 0.0096 mol, 96%); ir and nmr (CCl_4) were identical with those

(26) G. P. Newsoroff and S. Sternhell, *Tetrahedron Lett.*, 6117 (1968).

(27) Performed on a JEOLCO C-60H nmr spectrometer by Professor Grace Borowitz, Upsala College.

(28) F. Ramirez, K. Tasaka, N. B. Desai, and C. P. Smith, *J. Org. Chem.*, **33**, 25 (1968).

(29) H. H. Jaffé and M. Orchin, "Theory and Applications of Ultraviolet Spectroscopy," Wiley, New York, N. Y., 1962, pp 431–434.

(30) (a) I. J. Borowitz, E. W. R. Casper, and R. K. Crouch, *Tetrahedron Lett.*, 105 (1971); (b) H. Parnes and R. K. Crouch, Yeshiva University, unpublished results.

(31) The instrumental techniques used have mainly been recorded previously.[30c] More recent nmr spectra were recorded on a Varian A-60A spectrometer and infrared spectra were recorded on a Perkin-Elmer 257 infrared spectrophotometer.

(32) Mass spectra were kindly done by R. Foltz, Battelle Memorial Institute, on an AEI MS-9 mass spectrometer on NIH Contract 69-2226.

(33) B. A. Arbusov, V. S. Vinogradova, and N. A. Polezhaeva, *Dokl. Akad. Nauk SSSR*, **121**, 641 (1958); *Chem. Abstr.*, **53**, 1180 (1959).

(34) A. J. Speziale and R. C. Freeman, *J. Org. Chem.*, **23**, 1883 (1958).

(35) H. O. House, *J. Amer. Chem. Soc.*, **77**, 3070 (1955).

(36) R. W. Upson, *ibid.*, **75**, 1763 (1953).

of the genuine sample. A similar reaction but with ethanol (2 equiv), added 30 min after the Li, gave the same result. A reaction with excess Li (36 equiv) and *tert*-butyl alcohol (26 equiv, initially present) gave an oil whose nmr spectrum ($CDCl_3$) showed vinyl protons at δ 5.4, 5.7 but no aromatic absorption; *i.e.*, the phenyl rings were reduced to cyclohexyl groups. Reaction of **14c,d** at −78° (Dry Ice–acetone bath) with Li (2 equiv) and methanol (initially present) gave phenyl benzyl ketone (33%) and no stilbenes.[37]

(37) This cleavage of a vinyl phosphate to the enolate of phenyl benzyl ketone, which is then protonated by methanol, is related to other cleavage reactions of enol phosphorylated species which are currently under investigation in our laboratory.[30a]

Registry No.—**11**, 1021-45-0; **12a**, 10409-51-5; **12b**, 10409-50-4; **14a**, 10409-53-7; **14b**, 10409-52-6; **14c**, 31327-09-0; **14d**, 31327-10-3; **15**, 4452-32-8; **22**, 31327-12-5; **24**, 31327-13-6; **28a**, 31327-14-7; **28b**, 31327-15-8; **31a**, 31327-16-9; **31b**, 31327-17-0; **32a**, 31327-18-1; **32b**, 31428-82-7; **36**, 31327-21-6; **37**, 30758-41-9; **38**, 31327-19-2; **39**, 31327-22-7; **40**, 5954-28-9; **41**, 1733-53-5; **42**, 31327-25-0; **43**, 30842-23-0; **44**, 31327-27-2.

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α-Anions. IV. Positional and Stereochemical Isomerization of 2- and 3-Unsaturated Carboxylic Acid Dianions[1a]

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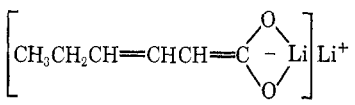
The stable dianions (carbanions of carboxylate salts) of the geometric isomers of 2- and 3-hexenoic acids were prepared and the nature of the carbanions was determined by deuteration and alkylation. Each of the four geometric anions, *i.e.*, *cis*- and *trans*-2-hexenoate dianions and *cis*- and *trans*-3-hexenoate dianions, on reprotonation gave 3-hexenoic acid exclusively. The results suggest the carbanion species of the 3-alkenoic acid salts to be more stable than the carbanion species of the 2-alkenoic acid salts. The geometric transformations that evolved provided further insights into the nature of the isomerizations. *trans*-2-Hexenoic acid gave a mixture of the cis-3 isomer (67%) and trans-3 isomer (33%), whereas *cis*-2-hexenoic acid gave the trans-3 isomer exclusively. The dianions from *cis*- and *trans*-3-hexenoic acids showed no indication of either positional or geometric isomerization since reprotonation regenerated the acids unchanged. A mechanistic scheme is described in terms of a polarized dianion of the following structure to explain these phenomena.



The isomeric 3-olefinic acids I and 2-olefinic acids II, have been reported by Linstead and Noble[2] to equilibrate (eq 1) in the pure state and in organic solvents,

$$\underset{\text{I}}{\text{RCH=CHCH}_2\text{COOH}} \rightleftharpoons \underset{\text{II}}{\text{RCH}_2\text{CH=CHCOOH}} \quad (1)$$

water, and alkaline solutions. The acids were induced to isomerize at elevated temperatures (100–200°), and the rates were greatly accelerated at these temperatures by alkali. The 2-olefinic isomer II was produced in the equilibrium as the thermodynamically favored acid, *i.e.*, the proportions of 2-olefinic to 3-olefinic were 70:30 for the *n*-hexenoic and *n*-pentenoic acids and 98:2 for *n*-butenoic acid.

In a continuation of our studies on the chemistry of α-metalated carboxylic acids (RCHLiCOOLi),[3-5] we have examined the carbanions derived by reaction of lithium diisopropylamide with isomeric 2- and 3-alkenoic acids. Crotonic acid produced a dianion that on quenching with hydrochloric acid yielded 3-butenoic acid quantitatively and exclusively. This unexpected shift of the conjugated double bond into the β,γ position is counter to the results reported for the thermodynamic equilibrium of the isomeric acid pair for which α,β-alkenoic acid predominates.[6] Since butenoic acid isomers provide limited stereochemical information, the longer chain 2- and 3-hexenoic acids were chosen for a more detailed investigation of the transformation.

The dianions of cis and trans isomers of 2- and 3-hexenoic acids were prepared by reaction of the individual geometric isomers with lithium diisopropylamide in tetrahydrofuran (THF) solution at 0°; the solution was then quickly warmed to room temperature and allowed to stir for 30 min.[3,5] The dianions were quenched with dilute hydrochloric acid and the recovered acids, after their conversion to methyl esters with diazomethane, were examined by glpc for determinations of geometric and positional isomerization. The *trans*-2-hexenoic acid (III) gave a mixture of 67% *cis*-3-hexenoic acid (IV) and 33% *trans*-3-hexenoic acid (V) in a combined yield of 98% (eq 2).[7] Prolonged heating (4 hr) of this dianion mixture at 45–50° induced no change in its isomeric composition. Similar treatment of the *cis*-2-hexenoic acid (VI) gave *trans*-3-hexenoic acid (V) exclusively (eq 3). The complete isomeriza-

(1) (a) Presented at the 161st National Meeting of the American Chemical Society, Los Angeles, Calif., March 28–April 2, 1971. (b) Eastern Marketing and Nutrition Research Division, Agricultural Research Service, U. S. Department of Agriculture.

(2) R. P. Linstead and E. G. Noble, *J. Chem. Soc.*, 610 (1934).

(3) P. E. Pfeffer and L. S. Silbert, *J. Org. Chem.*, **35**, 262 (1970).

(4) P. E. Pfeffer and L. S. Silbert, *Tetrahedron Lett.*, 699 (1970).

(5) P. E. Pfeffer, L. S. Silbert, and J. M. Chirinko, Jr., *J. Org. Chem.*, in press.

(6) A photochemical transformation of crotonic acid to 3-butenoic acid has previously been reported to occur in 59% yield after prolonged irradiation and equilibration of crotonic and isocrotonic acids: P. J. Kropp and H. J. Krauss, *ibid.*, **32**, 3222 (1967).

(7) A cis,trans mixture of α,β-unsaturated acids has been reported to isomerize photochemically to their β,γ isomers composed of a cis/trans ratio of 0.5: R. R. Rando and W. von E. Doering, *ibid.*, **33**, 1671 (1968).