was also formed in each case, amounting to about 6% of the area of the internal standard.

Pentacovalent Phosphorus. II. Reactions of Dione and Lactone Dimers of Dimethylketene with Trivalent Phosphorous Acid Amides[1]

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Reactions of the dione 1 and lactone 2 dimers of dimethylketene with the phosphoramidites $(CH_3O)_2PN(CH_3)_2$ (3), $CH_3OP[N(CH_3)_2]_2$ (4), and $C_6H_5OP[N(CH_3)_2]_2$ (5) and with trisdimethylaminophosphine (6) were investigated. Carboxy esters resulted from reactions of 3 and 4 with either dimer while 5 and 6 gave carboxamides. The structures of these products are similar to those formed from dimethylketene dimers on reaction with trialkyl phosphites. Except for reactions of 3, identical products were formed from either 1 or 2 and a given phosphorus derivative. On reaction of 1 and 3, three products are formed in relative proportions dependent on reaction temperature. These reactions are discussed in terms of a postulated mechanism involving nucleophilic attack by phosphorus on carbonyl carbon of 1 or 2, followed either by ring expansion to a cyclic pentacovalent phosphorus intermediate or by ring opening to a phosphonium enolate species. Isomerization of 1 to 2 in the presence of 5 or 6 is also accommodated by the suggested reaction series. Possible kinetic control of carboxamide vs. carboxy ester formation is treated in terms of the structures and reaction patterns predicted for the postulated pentacovalent intermediates.

In the preceeding paper[3] we reported reactions of trialkyl phosphites and dimethyl methylphosphonite with the dimers (1 and 2) of dimethylketene. These results were interpreted in terms of transient pentacovalent phosphorus intermediates formed *via* ring expansion of the initial dimer–trivalent phosphorus adduct. Ultimate product formation was postulated to proceed *via* migration of an alkoxy group from pentacovalent phosphorus to the adjacent carbonyl group. Of interest in this regard is the question of the apparent relative migrational preference of different phosphorus substituents. This paper reports results of reactions of 1 and 2 with phosphorus amides having both methoxy and dimethylamino groups on phosphorus in the same molecule.


1   2   12
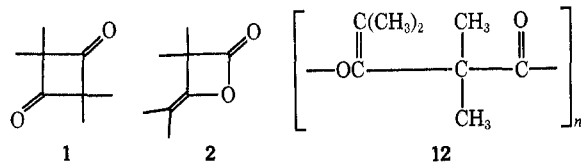
Results

Reactions were carried out neat under nitrogen. The trivalent phosphorus derivatives used (3–6) are shown in Table 1 in which products and yields are also recorded for the lactone reactions. The lactone reactions proceeded in a rather straightforward manner giving

reasonably high yields of vinyl products 7–11 similar to those which result with the trialkyl phosphites, as either the carboxamide or carboxylic ester. A side product in several instances is the same polymer 12 formed from lactone under the influence of methoxide.[4]
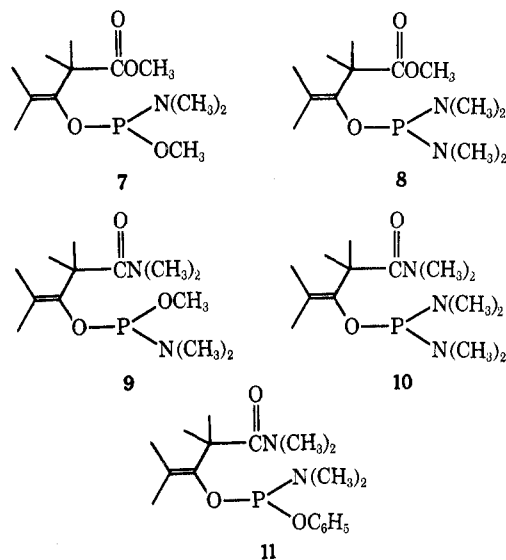
Reactions of the mixed amide esters, phosphoramidites $(CH_3O)_2PN(CH_3)_2$ and $CH_3OP[N(CH_3)_2]_2$, gave almost exclusively carboxyl ester products. Only with the diamino compound 4 at 115° is any carboxamide 9 formed. By contrast $C_6H_5OP[N(CH_3)_2]$ yields exclusively the carboxamide 11. Evidence for the structures of products 7–11 is given by their nmr and ir spectra and those of the sulfur and Arbuzov products (Table II). All show a weak ir band at about 1665 cm⁻¹ for

(1) A portion of this work was published in preliminary form: W. G. Bentrude and W. D. Johnson, *Tetrahedron Lett.*, 4611 (1967). This work was supported by Public Health Service Research Grant No. CA-11045 from the National Cancer Institute.

(2) National Institutes of Health Predoctoral Fellow, 1966–1969. This work taken in part from the Ph.D. Thesis of W. D. Johnson, University of Utah, 1969.

(3) W. G. Bentrude, W. D. Johnson, W. A. Khan, and E. R. Witt, *J. Org. Chem.*, 37, 631 (1972).

(4) R. H. Hasek, R. D. Clark, E. U. Elam, and J. C. Martin, *ibid.*, 27, 60 (1962).

TABLE I

REACTIONS OF PXYZ WITH LACTONE 2[a]

| Reactant PXYZ	X	Y	Z	Mol of PXYZ/ mol of 2	T, °C	Time, hr	% convn	% yield[b]	Product
3	CH_3O	CH_3O	$(CH_3)_2N$	1.0	115	6.5	100	95 (62)[c]	7
								0	12
4	CH_3O	$(CH_3)_2N$	$(CH_3)_2N$	1.1	25	240	100	100 (65)[c]	8
								0	12
					115	7	100	70	8
								10	9
								(10)	12
5	C_6H_5O	$(CH_3)_2N$	$(CH_3)_2N$	2.0	120	350	80	65 (30)	11
								>10[d]	12
6	$(CH_3)_2N$	$(CH_3)_2N$	$(CH_3)_2N$	2.0	115	19	100	60 (37)	10
								>10[d]	12

[a] Reactions run neat under nitrogen. [b] Based on reacted lactone. [c] Isolated yield in parentheses. [d] Not measured quantitatively but estimated to be considerably more than from reaction of 4.

the olefinic bond and an intense carbonyl band at 1725–1730 (carboxylic acid esters) or 1635–1640 cm⁻¹ (carboxamides). The trivalent derivatives have nmr absorptions readily assignable to vinyl methyls at δ 1.42–1.52 (J_{HP} = 3.0–3.5 Hz) and 1.64–1.76 (J_{HP} = 1.5–2.0 Hz) and geminal methyl absorptions at 1.28–1.41. The sulfur derivatives have similar absorptions at somewhat higher δ values. The *gem*-methyls sometimes appear as two peaks when phosphorus is an asymmetric center. The spectra of these products show them to be completely analogous to those formed from reactions of lactone with trialkyl phosphites which were well characterized in the preceeding paper.[3] Trivalent products 7–11 were very reactive with air (O₂) and sulfur. Quantitative elemental analyses were carried out on the sulfur derivative of each product 7–11, designated as 7s, 8s, etc., except for 9 which was not isolated but was readily characterized by its nmr spectrum. Phosphonium salt derivatives of 8 and 10 were isolated from their reactions with methyl iodide.

Several reaction paths appear available in the dione-phosphoramidite reactions. With 4, 5, and 6 the same products result as in the lactone reactions including formation of 12. Reactions of 5 and 6 showed buildup of large amounts of lactone at intermediate times. *E.g.*, with 6 at 80°, about half the dione had been isomerized to lactone in 124 hr even though complete conversion of lactone to 8 required 400 hr.

By contrast, 3 in reaction with dione gave two products (13 and 14) which were not formed with lactone.

13

14   15
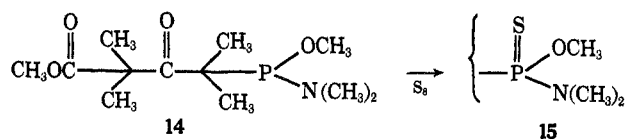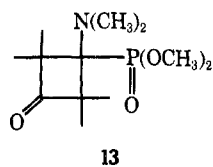
The relative amounts of 13 and 14 are reduced compared to 7 at higher temperatures as shown in Table III.

The cyclobutanone derivative 13 is somewhat unusual, but its proposed structure is fully born out by its ir spectrum which showed an intense band at 1780 cm⁻¹

expected for a cyclobutanone and absorptions at 1235 and 1250 cm⁻¹, one of which is likely a P=O stretching band. The nmr (C₆H₆) shows two sets of ring methyls at δ 1.38 and 1.48 and a dimethyl amino at δ 2.38 with J_{HP} of only 3.5 Hz. The reduced size of the coupling constant is consistent with the group not being directly bonded to phosphorus yet being in reasonably close proximity. Similar small J_{HP} values have been noted in analogous α-dimethylaminophosphonates.[5] The methoxyl groups on phosphorus appear in the expected range, δ 3.42 (J_{HP} = 11 Hz). The pentavalent structure of 13 was further shown by its failure to react with sulfur. Product 14 was isolated as its sulfur derivative 15. Its structure was shown clearly by its pmr (C₆H₆) spectrum (see Experimental Section) which was very comparable to the product of trimethyl phosphite reaction with 1 whose structure was proved rigorously in the preceeding paper.[3] It also showed the intense carbonyl infrared absorptions at 1745 and 1685 cm⁻¹ noted[3] for compounds of this type.

Discussion

These reactions involve essentially two features which deserve discussion: (1) the preservation or lack of preservation of dione or lactone structure in the products formed; (2) the distribution of products between carboxamides and carboxylic acid esters both of which could potentially result when both RO and $(CH_3)_2N$ are attached to the same phosphorus atom.

The first of the above aspects of these reactions may be treated in terms of a series of reactions (Scheme I) like that proposed[3] for the tertiary phosphite and dimethyl methylphosphonite reactions. Tables I and III show that, except for 3, all nucleophiles (4–6) gave the same product (24) on reaction with either 1 or 2. Reaction of dione 1 with 5 and 6 was accompanied by the formation of large amounts of 2. We suggest that this probably occurs by the sequence 6 → 20 → 21 → 2. It is well established[6] that the replacement of alkoxy substituents by amino groups in structures such as 17 and 20 stabilizes the ionic form 20 with the respect to the pentacovalent species 17. This facilitates conversion of 1 to 2. Completely consistent with these

(5) R. Burgada and J. Roussel, *Bull. Soc. Chim. Fr.*, 192 (1970); R. Burgada, *C. R. Acad. Sci., Ser. C*, **267**, 1854 (1968).

(6) D. B. Denney, D. Z. Denney, B. C. Chang, and K. L. Marsi, *J. Amer. Chem. Soc.*, **91**, 5243 (1969); F. Ramirez, C. P. Smith, J. F. Pilot, and A. S. Gulati, *J. Org. Chem.*, **33**, 3787 (1968).

TABLE II
SPECTROSCOPIC AND PHYSICAL DATA FOR

Product[a]	X	Y	Z	M	CH₃ₐ	CH₃_B	CH₃C	X	Y	Z	Solvent	Ir frequency,[b] cm⁻¹	Physical data
					\<Chemical shifts (multiplicity, J_{HP})\>								
7	CH₃O	(CH₃)₂N	CH₃O		1.43 (d, 3.5)	1.64 (d, 1.5)	1.28 (s)	3.37 (d, 13)	2.66 (d, 9.0)	3.63 (s)	Neat	2930, 1725, 1665, 1455, 1380, 1270, 1255, 1190, 1145, 1120, 1075, 1034, 970, 793, 740, 712, 683 (film)	Liquid, bp 68–70° (0.1 Torr)
7s	CH₃O	(CH₃)₂N	CH₃O	S	1.53 (d, 4.5)	1.71 (d, 3.5)	1.41 (s) 1.43 (s)	3.65 (d, 14)	2.90 (d, 13)	3.72 (s)	CDCl₃	2950, 1730, 1670 (w), 1465, 1385, 1250, 1190, 1147, 1113, 1076, 1035, 990, 856, 820, 752 (film)	Liquid
16	CH₃	(CH₃)₂N	CH₃O	O	1.41 (d, 3.5)	1.60 (d, 2.5)	1.30 (s)	1.41 (d, 16)	2.66 (d, 9.5)	3.60 (s)	CS₂	2930, 1725, 1665 (w), 1465, 1385, 1380, 1235, 1190, 1148, 1111, 1071, 992, 952, 907, 832, 775 (film)	Solid, mp 65–66°
8	(CH₃)₂N	(CH₃)₂N	CH₃O		1.42 (d, 3.5)	1.60 (d, 2.0)	1.26 (s)	2.60 (d, 9.0)	2.60 (d, 9.0)	3.54 (s)	Neat	2900, 1725, 1660 (w), 1450, 1380, 1270, 1192, 1135, 1110, 1068, 951, 778, 666 (film)	Liquid, bp 78–91° (0.15 Torr)
8s	(CH₃)₂N	(CH₃)₂N	CH₃O	S	1.52 (d, 4.5)	1.76 (d, 3.0)	1.42 (s)	2.75 (d, 12)	2.75 (d, 12)	3.73 (s)	CDCl₃	1730, 1670 (w), 1275, 1190, 1148, 1110, 1063, 988, 832, 760, 722 (Nujol)	Solid, mp 43–44°
10	(CH₃)₂N	(CH₃)₂N	(CH₃)₂N		1.43 (d, 3.0)	1.63 (d, 2.0)	1.25 (s)	2.63 (d, 9.0)	2.63 (d, 9.0)	2.92 (s)	Neat	2900, 1660 (s), 1640, 1470, 1390, 1275, 1200, 1112, 1068, 952, 797, 764, 744, 696, 666 (film)	Liquid, bp 87–88° (0.06 Torr)
10s	(CH₃)₂N	(CH₃)₂N	(CH₃)₂N	S	1.55 (d, 4.0)	1.76 (d, 3.0)	1.38 (s)	2.76 (d, 12)	2.76 (d, 12)	2.98 (s)	CDCl₃	1660 (s), 1630, 1295, 1190, 1110, 1070, 990, 980, 877, 848, 756, 738, 720 (Nujol)	Solid, mp 93.5–94.0°
11	C₆H₅O	(CH₃)₂N	(CH₃)₂N		1.52 (d, 3.5)	1.76 (d, 2.0)	1.38 (s) 1.41 (s)	7.1 (m)	2.74 (d, 9.5)	2.97 (s)	CDCl₃	2920, 1660 (s), 1630, 1580, 1485, 1390, 1220, 1110, 1068, 975, 860, 806, 763, 692 (film)	Liquid, bp 95–100° (0.1 Torr)
11s	C₆H₅O	(CH₃)₂N	(CH₃)₂N	S	1.56 (d, 4.5)	1.82 (d, 3.0)	1.62 (s) 1.74 (s)	7.2 (m)	2.58 (d, 12)	2.78 (s)	C₆H₆	2930, 1650 (s), 1635, 1580, 1490, 1390, 1208, 1110, 1100, 1068, 992, 916, 885, 856, 783, 762, 740, 688, 680 (film)	Liquid

[a] Satisfactory C, H, and P analyses were obtained for these compounds (±0.4%) with the following exceptions. 7 and 8, which are readily air oxidized, were analyzed as their sulfur derivatives 7s and 8s. Only C and H analyses were obtained for 11s and 16 (for 16, calcd for H, 8.72; found, 8.20). [b] w indicates weak absorption; s signifies a shoulder.
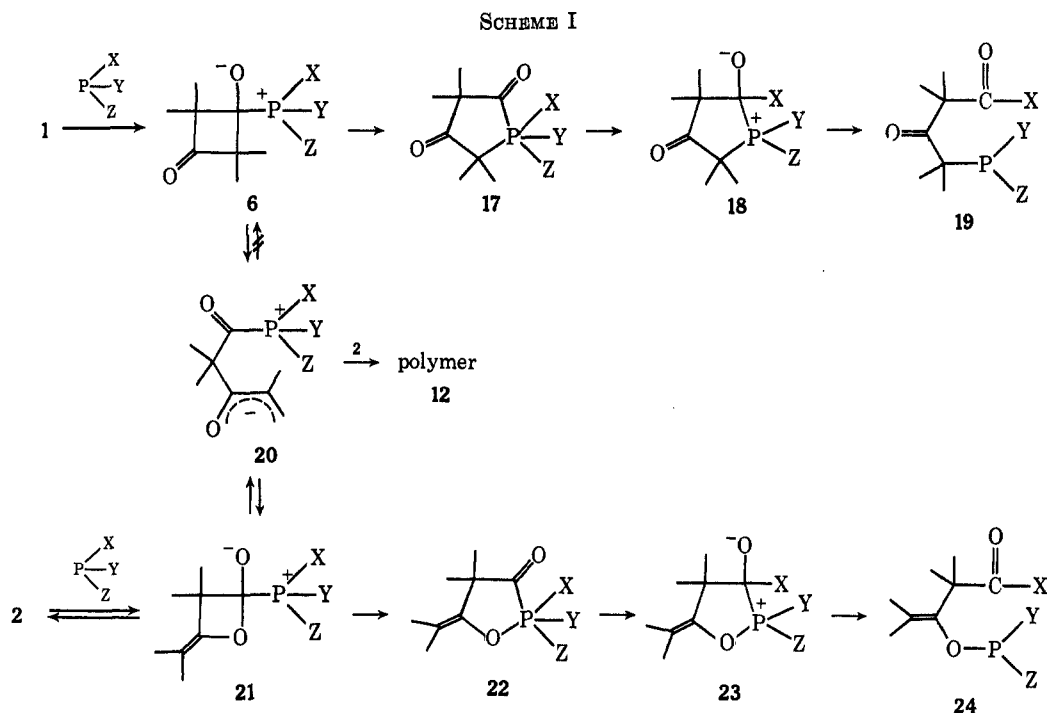
SCHEME I

TABLE III
REACTIONS OF PXYZ WITH DIONE 1[a]

Reactant PXYZ	Mol of PXYZ/ mol of 2	T, °C	Time, hr	% convn	Product	% yield[b]
3	1.0	115	56	100	13	0
					14	0
					7	80
3	1.2	80	232	50	13	10
					14	45
					7	35
3	1.1	65	525	50	13	65
					14	10
					7	15
4	1.1	85	400	90	8	95
					12	Trace
5	2.0	120	350	40	11	45
					12	c
					2	45
6	1.1	80	400	100	10	60
					12	25[d]
					2	50[e]

[a] Reactions run neat under nitrogen. [b] Based on reacted dione using vpc method. [c] Not measured quantitatively but considerably more than a trace. [d] Isolated yield. [e] After 124 hr, 50% conversion of 1.

ideas about the effects of substituents on the relative stabilities of 17 and 20 is the observation that only with a single dimethylamino substituent (3) is formation of 19 observed and then only at reduced temperatures. With 4, 5, and 6, apparently the amino substituents favor the route through 20 by stabilizing 20 at the expense of 17.

It will also be noted that the yield of polymer 12 from lactone is highest when intermediate 20, by which we believe 12 formation may be catalyzed, would be expected to be most readily formed from 21. A reasonable alternate explanation for the high degree of polymer formation in instances in which a positive charge is stabilized on phosphorus would be that 22 undergoes some dissociation to CH_3O^- or $(CH_3)_2N^-$ which then initiates the formation of 12.

Table I shows 3 is far more reactive toward the lactone than is trimethyl phosphite which requires 41 hr at 120° to completely convert lactone to product even when a 1-mol excess of phosphite is used.[3] This is consistent with the expected increased nucleophilicity of phosphorus on substitution of nitrogen in place of oxygen. Also consistent with phosphorus attack is the greatly reduced reactivity of the phenyl tetramethylphosphorodiamidite (5) with 2. In this instance 1 is converted to 2 and then only very slowly to 24 (11). Inspection of Table I shows in addition that 4 is also more reactive than trimethyl phosphite but no more reactive than 3. Substitution by a third dimethylamino (6) is accompanied by a decrease in reactivity compared to 3 and 4. At the same time, the amount of lactone which builds up on reaction of 6 with dione increases. These trends can be readily explained if the step 2 → 21 is normally endothermic and reversible. Dimethylamino substituents should lower the energy of 21 due to their electronic properties. This should speed up the process 2 → 21. At the same time increasing numbers of dimethylamino substituents may induce steric strain in intermediate 21. Thus, the rate of attack on 2 is maximized by replacing one or two methoxyls in trimethyl phosphite by dimethylaminos. A third dimethylamino results probably in a reduced rate of the reaction 22 → 23 (see later discussion) allowing the reverse of 2 → 21 to compete readily leading to a building of 2 on reaction of 6 with 1 as also occurs with 5. The reactivities of 3-6 with dione are not so readily comparable since they were not carried to similar levels of conversion. However, 6 is clearly more reactive than 4 as would be expected for nonreversible attack of more nucleophilic 6, both reactions giving rapid opening to 20. As expected 5 reacts very slowly.

The expected increase in phosphorus nucleophilicity in 3, 4, and 6 may also play a role in determining the relative amounts of 19 to 24 from the dione reactions. Product 19, if a stronger nucleophile, would be more likely to undergo isomerization to 24 *via* the reverse of

steps 6 → 17 → 18 → 19. This process is observed[3] with the dione products analogous to 19 from reaction with triethyl and trimethyl phosphite. A sample containing a 35/65 ratio of 7/14, heated for 24 hr, showed the amount of 7 to be little changed although 14 was partly consumed by Arbuzov rearrangement.

As noted above, reactions of 3–5 can lead to either a carboxamide or carboxy ester. Within the context of Scheme I, this appears to depend upon the relative ease of transfer of methoxy or dimethylamino in 17 → 18 and 22 → 23. This of course assumes kinetic control of product formation. Several factors may influence


25

26   or   27
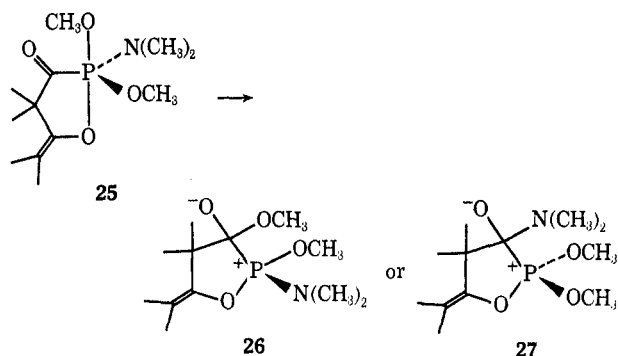
migrational aptitude. First, if the usual preference rules[7] for formation and reaction of pentacovalent phosphorus intermediates are obeyed, axial entrance and exit of substituents on phosphorus will be required. Second, the most electronegative substituent will occupy preferentially the axial position and thus be in a more favorable position to exit the bipyramid in migration. This suggests 25 as the most favored structure for the initially generated pentacovalent intermediate and predicts the observed migration of methoxy. A third factor could be the relative ease of ionization of a P–O and P–N bond. Consideration of stability of both the resulting anion and phosphonium ion predicts P–O cleavage to predominate. All of the above predict preferential methoxy migration as observed for reactions of 3 and 4.

Attempts to determine whether the variations in ratios of products of reaction of 4 with 2 result from kinetic or thermodynamic factors were not totally satisfying but indicated that 8/9 ratios were not readily changed once the products were formed. A mixture containing a 95/5 ratio of 8/9, heated at 115° for 18 hr, showed the ratios and amounts of 8 and 9 to remain unchanged even though at 115° the product ratio is usually about 85/15. However, a trace of $CH_3OP[N(CH_3)_2]_2$ and lactone were formed suggesting that 8 and/or 9 are formed reversibly. Similarly, an approximate 85/15 mixture, heated for about 300 hr at 60 and 92° showed little change in the 8/9 ratio although again a little of both 4 and 2 were formed. Thus, equilibration appears to be slow. A further indication that the carboxy ester is probably the product of kinetic control in reactions of 7 with 2 comes from consideration of bond strengths. The mean bond dissociation energies[8a] for P–O and P–N bonds to trivalent phosphorus favor the P–O bond by about 20 kcal/mol, whereas to

dissociate the C–O bond in CH_3OCH_3 requires[8b] only about 10 kcal/mol more energy than it does to cleave the C–N bond in $CH_3–N(CH_3)_2$.

The formation of carboxamide in the reaction of 5 with 1 or 2 appears to be somewhat anomalous in terms of the above-discussed influences on migrational aptitude. One possibility is that the phenoxy substituent has rendered phosphorus of such low nucleophilicity in 5 that preferential attack by nitrogen now occurs (structure 28). This requires nitrogen attack to be much slower than phosphorus attack in reactions of 3, 4, and 6 since carboxamides are not generally formed.

2 + 5 →   → 14

28
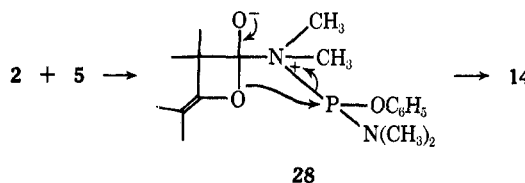
It has been argued[9] that, in compounds like 3–6, nitrogen (a hard base) may be more nucleophilic than phosphorus (a soft base) toward carbonyl centers (medium hard acids). In fact, we also could explain reactions of 3 and 4 with 1 and 2 in terms of attack of oxygen rather than nitrogen or phosphorus. That nitrogen could be more nucleophilic than phosphorus is conceivable but that oxygen rather than phosphorus or nitrogen attack predominates seems untenable. The formation, which we report elsewhere,[10] of a stable phosphorane intermediate of type 22 in reaction of a cyclic derivative analogous to 4 with 2 to give ultimately an *N,N*-dimethylcarboxamide is strong evidence for the correctness of Scheme I involving P attack even when a carboxamide results. Further, if both 5 and 6 reacted with 2 *via* nitrogen attack, the tremendous difference in reactivities (Table I) would not be expected. Nitrogen attack on reaction with 5 cannot be completely ruled out, however, since phosphorus would have greatly reduced nucleophilicity.

The reaction of 1 and 3 which forms 13 may reasonably be written by two sequences of intermediates starting with 29 or 30, and both have been proposed[9a,b,11] in reactions of other ketones which give this type of product. The phosphorus attack route is favored by the Russian workers.[11] Apparently the lowest activation enthalpy process, that which forms the cyclobutanone derivative 13, predominates at 65°. At 80°, increasing amounts of ring expansion of intermediate 29 (or phosphorus attack if 30 is the intermediate giving 13) and ring opening occur leading to products of type 19 and 24. In regard to the question of whether 13 results *via* 29 or 30, it may be significant that no product of type 13 is found from 5 where reduced phosphorus nucleophilicity may have resulted in nitrogen attack.

Based on relative reactivities of the phosphorus nucleophiles, Hudson, *et al.*,[9a] have argued for nitrogen

(7) F. H. Westheimer, *Accounts Chem. Res.*, 1, 70 (1968).

(8) (a) S. B. Hartley, W. S. Holmes, J. K. Jacques, M. F. Mole, and J. C. McConbroy, *Quart Rev., Chem. Soc.*, 17, 204 (1963); (b) J. A. Kerr, *Chem. Rev.*, 66, 465 (1966).

(9) (a) R. Greenhalgh and R. F. Hudson, *Chem. Commun.*, 1300 (1968); (b) R. F. Hudson, R. J. G. Searle, and F. H. Devitt, *J. Chem. Soc. B*, 789 (1966); (c) R. F. Hudson and R. J. G. Searle, *ibid.*, 1349 (1968); (d) R. F. Hudson and R. J. G. Searle, *Chimia*, 20, 117 (1966).

(10) W. G. Bentrude, W. D. Johnson, and W. A. Khan, *J. Amer. Chem. Soc.*, 93, 923 (1971).

(11) A. N. Pudovik, I. V. Gur'yanova, S. P. Perevezentseva, and S. A. Terent'eva *Zh. Obshch. Khim.*, 39, 337 (1969); V. P. Evdakov, L. I. Mizrakh, and L. Yu Sandalova, *Dokl. Akad. Nauk SSSR*, 162, 573 (1965); A. N. Pudovik, S. A. Terent'eva, and E. S. Batyeva, *ibid.*, 175, 616 (1967).

29

30
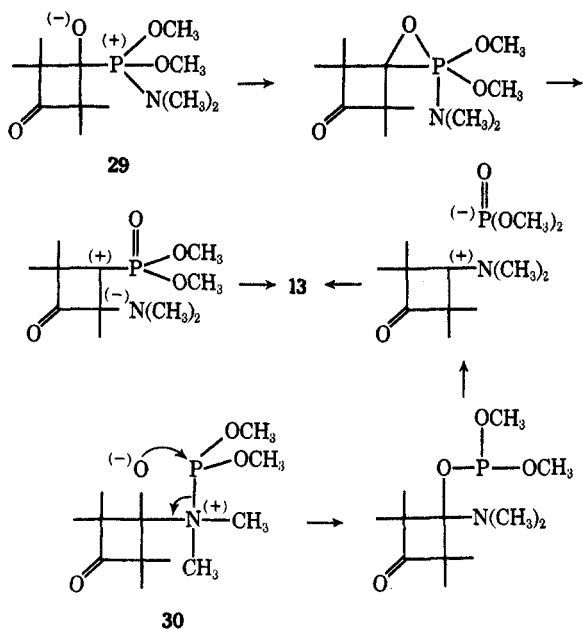
attack on carbonyl carbon in reactions with phenylisocyanate and benzaldehyde of **3** and its cyclic analog, 2-dimethylamino-1,3,2-dioxaphospholane. Rate-determining subsequent formation of a pentacovalent phosphorus intermediate was proposed. Apparently, some factor in our reaction system favors phosphorus attack at carbon in reactions of **3, 4,** and **6,** as we have not been able to write reasonable mechanisms for carboxy ester formation *via* nitrogen attack. While we do not argue with the kinetic evidence for nitrogen attack, we think that it is interesting that it is possible to write reasonable mechanisms similar to that of Scheme I for many of the reactions for which nitrogen attack might be suggested but for which no supporting evidence is available. Reactions 1–4[9d,12–14] as written require dialkyamino rather than alkoxy migration contrary to what we observe in reactions 1 and 2. Unfortunately, the relative importance of kinetic *vs.* thermodynamic factors in reactions 1–4 are difficult to assess.

In a recent paper[15] it has been proposed that reaction of $(RO)_2PN(CH_3)_2$ ($R = i\text{-}C_3H_7$) with β-propiolactone gives $ROP(O)(NMe_2)CH_2CH_2CO_2R$ by phosphorus attack at saturated carbon and $(RO)_2P(O)CH_2CH_2\text{-}CON(Me)_2$ by concerted P–N insertion in the lactone-C(=O)O– linkage followed by Arbuzov rearrangement. We believe that these results too could be accommodated *via* reactions similar to those of Scheme I. Further work relative to the importance of phosphorus *vs.* nitrogen attack in carbonyl systems appears needed.

Experimental Section

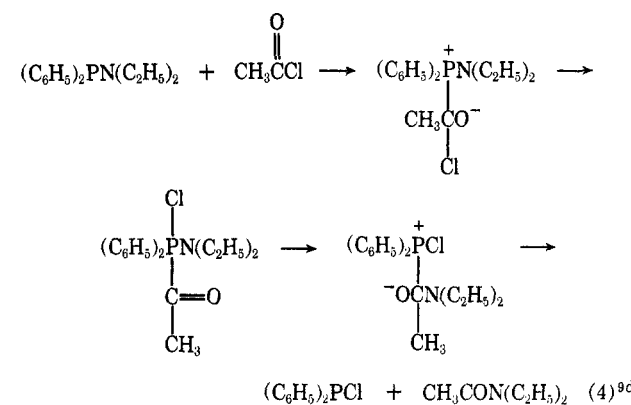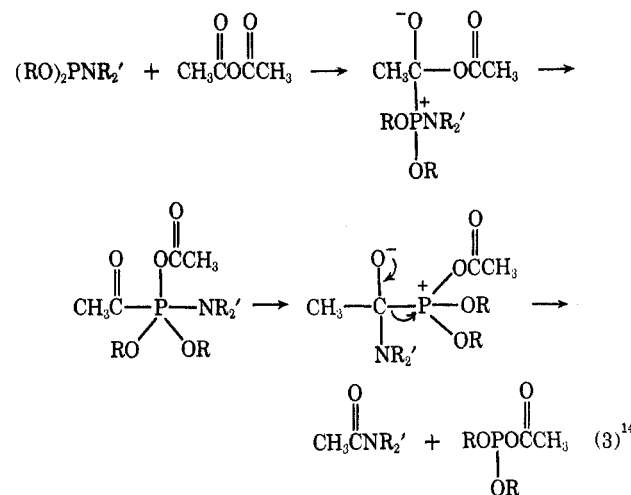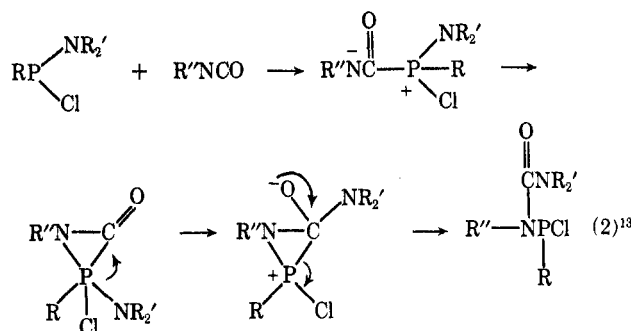All chemicals were commercial materials with the exception of the trivalent phosphorus compounds.
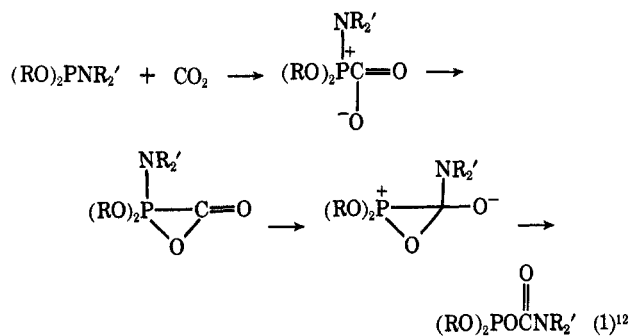
Pmr spectra were taken on either a Varian A-60 or A-56/60 spectrometer. Chemical shifts are in δ, parts per million downfield from TMS as internal standard. Ir spectra were recorded on a Perkin-Elmer 5A infrared spectrophotometer. Unless other-

$$(RO)_2PNR_2' + CO_2 \longrightarrow (RO)_2\overset{+}{P}C=O \longrightarrow$$

$$(RO)_2POCNR_2' \quad (1)^{12}$$

$$RP\overset{NR_2'}{\underset{Cl}{}} + R''NCO \longrightarrow R''NC-\overset{+}{P}-R \longrightarrow$$

$$R''—NPCl \quad (2)^{13}$$

$$(RO)_2PNR_2' + CH_3COCCH_3 \longrightarrow CH_3C-OCCH_3 \longrightarrow$$

$$CH_3CNR_2' + ROPOCCH_3 \quad (3)^{14}$$

$$(C_6H_5)_2PN(C_2H_5)_2 + CH_3CCl \longrightarrow (C_6H_5)_2\overset{+}{P}N(C_2H_5)_2 \longrightarrow$$

$$(C_6H_5)_2PCl + CH_3CON(C_2H_5)_2 \quad (4)^{9d}$$

wise noted, recorded bands (cm^{-1}) are of medium to strong intensity. Preparative vpc work was done with a Varian Aerograph A90-P3 gas chromatograph on a 10 ft by $^3/_8$ in. 20% SE-30 on Chromosorb W column operated isothermally at 200 ml/min. Analytical vpc data were obtained with a thermal conductivity F & M 810 Model gas chromatograph using temperature programmed conditions, 120 ml/min flow and a 6 ft by 0.25 in. 20% SE-30 on 60–80 mesh Chromosorb W column. Quantitative estimates of reactant conversions and product yields were made by measuring the total area of reactants before reaction and that of remaining reactants and/or products formed. Identical injection sample sizes and chromatographic conditions

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were utilized. Percentage yields of products were calculated on the basis of limiting starting material consumed using the measured areas and assumed equal sensitivity of all peaks. In some cases sensitivities were measured and found to be within 10% of each other. This accuracy was deemed sufficient for the purposes of the experiment in which, generally, relative yields of products of a given system under different conditions are of greatest interest.

Analyses were performed by the Schwartzkopf Microanalytical Laboratory, Woodside, N. Y., and by Galbraith Laboratories, Knoxville, Tenn. Melting points are uncorrected.

Dimethyl dimethylphosphoramidite (3) was prepared by mixing tris(dimethylamino)phosphine (50.0 g, 0.309 mol), 750 ml of benzene, and 1 g of dimethylamine hydrochloride and heating to reflux temperature. Methanol (19.8 g, 0.618 mol) in 250 ml of benzene then was added dropwise with constant stirring. After 17 hr of heating, vpc analysis showed that the reaction contained the optimum amount of desired product (~5% $CH_3OP[N(CH_3)_2]_2$). The solvent was removed under reduced pressure, and the residue was distilled through a heated helices-packed column to yield pure **3** (18.8 g, 0.137 mol): 44% yield; bp 86–89° (190 torr) [lit.[16] 50–51° 45 Torr)]; pmr (neat) δ 2.57 (6 H, d, J_{HP} = 9.0 Hz, $N(CH_3)_2$), 3.34 (6 H, d, J_{HP} = 12 Hz, $POCH_3$).

Methyl Tetramethylphosphorodiamidite (4).—Phosphorus trichloride (175 g, 2.00 mol), pyridine (158 g, 2.00 mol), and 1 l. of ether were mixed and cooled in an ice bath. Methanol (64.0 g, 2.00 mol) in 700 ml of ether was added dropwise with vigorous stirring. After the mixture was warmed to room temperature, the solid amine hydrochloride was removed by filtration, and the solvent was removed under reduced pressure. Distillation yielded CH_3OPCl_2: 60.0 g (0.452 mol); 23% yield; bp 42° (100 Torr) [lit.[17] 58° (300 torr)]. To the ice-cooled CH_3OPCl_2 (60.0 g) in 750 ml of ether was added dropwise with vigorous stirring dimethylamine (100 g, 2.22 mol) in 250 ml of ether. The addition funnel containing the dimethylamine solution was wrapped with aluminum foil which contained Dry Ice to prevent the dimethylamine from evaporating. After the mixture warmed to room temperature, the solid amine hydrochloride was removed by filtration, and the solvent was removed under reduced pressure. The residue was distilled twice through a heated helices-packed column to give the desired product (11.4 g, 0.0752 mol): 17% yield (based on CH_3OPCl_2); bp 95–96° (135 Torr) [lit.[18] 53–54° (24 Torr)]; pmr (neat) δ 2.51 (12 H, d, J_{HP} = 9.0 Hz, $PN(CH_3)_2$), 3.30 (3 H, d, J_{HP} = 12.5 Hz, $POCH_3$).

Phenyl Tetramethylphosphorodiamidite (5).—Tris(dimethylamino)phosphine (24.5 g, 9.15 mol) in 350 ml of anhydrous benzene was heated to reflux under nitrogen. Phenol (14.2 g, 0.15 mol) dissolved in 100 ml of anhydrous benzene was added dropwise. After addition, refluxing and stirring were continued for 15 hr. Benzene was distilled off under reduced pressure, and the residual liquid was distilled through a small Vigreux column to yield pure **5** (28.25 g, 0.133 mol): 86.6% yield; bp 52–53° (0.1 Torr); pmr (neat) δ 2.52 (12 H, d, J_{HP} = 9.0 Hz, $PN(CH_3)_2$), 7.0 (5 H, m, OC_6H_5). **5** was converted to its sulfide for analysis.

Anal. Calcd for $C_{10}H_{17}N_2OPS$: C, 49.17; H, 7.01; P, 12.68. Found: C, 48.68; H, 6.86; P, 12.80.

Reactions of Dione 1 with Phosphoramides 3–6.—The starting materials were mixed neat under a nitrogen atmosphere in a flask. The stopper was wired tightly in place and the flask was heated at the temperature indicated. At intervals the flask was opened under nitrogen, and the contents were monitored by vpc, 10°/min program rate. Details concerning these reactions appear below.

Phosphoramidite 3 (2.99 g, 21.4 mmol) and **1** (2.92 g, 21.4 mmol) were heated at 115° for 56 hr at which time vpc analysis showed reaction to be complete to give **7** in 80% yield based on dione. About 10% of an unidentified shorter retention time peak and several minor very long retention time products were noted. **7** was identified by its vpc retention time and by comparison of ir and pmr spectra of the reaction product mixture with those of authentic **7** from reaction of **3** with lactone **2**.

The same reactants (25.5 mmol of **3**, 21.4 mmol of **1**) gave predominantly product **7**, **14**, and **13** after 232 hr at 80° (50%

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conversion of **1**) in 35, 45, and 10% yields. Distillation [75–76° (0.15 Torr), 40% combined yield] failed to separate the products. Addition of sulfur and gentle warming gave products **15** and **7s** and left **13** unchanged. **15** and **7s** were separated by preparative vpc. **15**: pmr (C_6H_6) δ 1.48 and 1.59 (3 H each, s, $CO(CH_3)_2CO$), 1.53 (3 H, d, J_{HP} = 19 Hz, $PC(CH_3)_2$), 1.54 (3 H, d, J_{HP} = 17.5 Hz, $PC(CH_3)_2$), 2.62 (6 H, d, J_{HP} = 9.0 Hz, $PN(CH_3)_2$), 3.30 (3 H, d, J_{HP} = 13 Hz, $POCH_3$), 3.30 (3 H, s, CO_2CH_3); ir (film) 2950, 1745, 1720 (w), 1685, 1465, 1385, 1225, 1180, 1156, 1138, 1029, 990, 896, 806, 730, 679 cm^{-1}.

Anal. Calcd for $C_{12}H_{24}NO_4PS$: C, 46.58; H, 7.81; P, 10.01. Found: C, 46.37; H, 8.08; P, 9.57.

At 70° in 525 hr **3** (39.4 mmol) and **1** (35.7 mmol) gave approximately 50% conversion of **1** to **7**, **14**, and **13** in 15, 10, and 65% yield, respectively. Distillation yielded small amounts of **13**, bp 100–105° (0.15 Torr), purified by vpc: pmr (C_6H_6) δ 1.38 (6 H, s, ring CH_3), 1.48 (6 H, s, ring CH_3), 2.38 (6 H, d, J_{HP} = 3.5 Hz, $N(CH_3)_2$), 3.42 (6 H, d, J_{HP} = 11 Hz, $POCH_3$); ir (film) 2950, 1780, 1470, 1250, 1235, 1033, 830, 742 cm^{-1}.

Anal. Calcd for $C_{12}H_{24}NO_4P$: C, 51.98; H, 8.72; P, 11.17. Found: C, 51.82; H, 8.74; P, 11.05.

All the reactions showed the presence of a small amount of **2** formed in steady concentrations throughout the reaction.

Phosphoramidites 4, 5, and **6** reacted with **1** under conditions recorded in Table III in generally routine fashion to give the same products as they did with **2**. Reactions with **4** showed formation of a small amount (<5%) of lactone **2** which persisted throughout the reaction. With **5** at 40% conversion of **1**, a 45% yield of lactone **2** was noted by vpc along with the product **8** (45%) shown to be identical with that from **5** and **2** by vpc, ir, and pmr measurements. A small amount of solid **12** was observed to precipitate out of the reaction but was not isolated. Reaction with **6** (8.40 g, 5.15 mmol) showed half of **1** (6.82 g, 48.7 mmol) converted to **2** in 124 hr at 80°. Complete conversion of **1** to products took 400 hr at which time all **2** was consumed as well to a 60% yield of **10**. From the reaction was isolated 1.5 g (25% yield) of polymer **12** which was recrystallized from diglyme, mp 197–199° (lit.[4] mp 198–200°). **10** was distilled to give 3.2 g, 10.6 mmol (24% yield), of a viscous, colorless liquid, bp 92–93° (0.07 Torr).

Reactions of Lactone 2 with Phosphoramides 3–6.—The procedure was the same as with the dione, except as given below. Spectroscopic data for products appear in Table II. Products **7–11** were warmed with S_8 to convert them to the corresponding sulfides on which elemental analyses were obtained.

Phosphoramidite 3 (5.11 g, 3.65 mmol) and **2** (5.00 g, 3.65 mmol) at 100° for 6.5 hr gave 100% conversion of reactants to **7** in 95% yield by vpc. Distillation yielded pure **7** as a viscous, colorless liquid, 6.25 g, 22.5 mmol (62%), bp 68–70° (0.1 Torr). When heated gently with sulfur, **7** yielded the thio compound **7s**, collected by preparative vpc as a viscous, slightly yellow liquid. Reaction of **7** with excess methyl iodide at room temperature yielded the methylphosphonate **16** as a white solid, mp 65–66° (from hexane).

Dry air bubbled through **7** at room temperature for 4 hr gave an approximate 85% yield of what is probably the corresponding oxide, the phosphoramidate, a viscous, colorless liquid which was not further purified. A pmr spectrum of unpurified oxide differed from that of **7** only in slight changes in chemical shifts and coupling constants as expected for a simple oxidation at phosphorus.

Phosphoramidite 4 (3.00 g, 20.0 mmol) and **2** (2.50 g, 17.9 mmol) at room temperature for 10 days gave a 100% conversion of **2** to a quantitative yield of **8** (by vpc). Distillation yielded pure **8**, a colorless, viscous liquid, bp 79–81° (0.15 Torr). At 115° vpc analysis showed the same reactants to yield **8** (70%) along with material assigned structure **9** (10%). The latter was not obtained in pure, isolated form, but its structure was deduced from a pmr spectrum of **8** in which **9** was the only impurity. Peaks assignable to **9** were observed at δ 2.84 (s, $CON(CH_3)_2$) and 3.38 (d, J_{HP} = 13 Hz, $POCH_3$). Assignment was based on comparison with the pmr spectrum of **10**. **8** reacted readily with sulfur to give **8s**, white crystals, mp 43–44° (hexane). With excess methyl iodide at room temperature, **8** gave the methyl phosphonium salt, a white solid, which was washed six times with pentane: mp 130–132°; pmr ($CDCl_3$) δ 1.42 (6 H, s, gem CH_3), 1.61 (3 H, d, J_{HP} = 3.5 Hz, vinyl CH_3), 1.78 (3 H, d, J_{HP} = 3.0 Hz, vinyl CH_3), 2.42 (3, H, d, J_{HP} = 15 Hz, PCH_3), 2.97 (6 H, d, J_{HP} = 11 Hz, $N(CH_3)_2$), 3.76 (3 H, s, OCH_3); ir

(Nujol) 1730, 1665 (w), 1320, 1245, 1170, 1145, 1103, 1072, 1013, 968, 923, 912, 880, 857, 834, 805, 770, 735 cm^{-1}.

Phosphoramidite 5 (2.00 g, 9.44 mmol) and **2** (0.66 g, 4.7 mmol) for 350 hr at 120° showed 80% conversion of **2** to **11** (65% yield by vpc) isolated by distillation as a viscous, colorless liquid (0.40 g, 1.1 mmol), 30%, bp 95–100° (0.1 Torr). A considerable amount of polymer **12** precipitated from solution during reaction but was not quantitatively measured. **11** reacted rapidly on warming with sulfur to give the thio compound **11s**, a pale yellow liquid isolated by preparative vpc.

Phosphoramidite 6 (11.6 g, 71.4 mmol) and **2** (5.00 g, 35.7 mmol) gave complete conversion of **2** to products in 19 hr at 115° yielding 60% of **10** (by vpc) and several minor unidentified products. A large amount of **12** also was formed. Distillation yielded pure **10**, a colorless viscous liquid, 4.0 g, 13 mmol (37%), bp 87–88° (0.06 Torr). Reaction of **10** with sulfur gave a solid which was recrystallized several times from hexane, mp 93.5–94°. With excess methyl iodide, **10** formed the methyl phosphonium salt, a white solid, which was washed several times with

pentane to give a white solid: mp 175–177°; pmr (CDCl$_3$) δ 1.38 (6 H, s, gem CH$_3$), 1.64 (3 H, d, J_{HP} = 3.5 Hz, vinyl CH$_3$), 1.80 (3 H, d, J_{HP} = 2.5 Hz, vinyl CH$_3$), 2.45 (3 H, d, J_{HP} = 15 Hz, PCH$_3$), 2.98 (6 H, d, J_{HP} = 11 Hz, PN(CH$_3$)$_2$), 2.94 (6 H, s, CON(CH$_3$)$_2$); ir (Nujol) 1665, 1620 (w), 1315, 1255, 1175, 1111, 1095, 1059, 1011, 975, 950, 926, 910, 877, 859, 806, 734, 672 cm^{-1}.

Anal. Calcd for C$_{15}$H$_{33}$N$_3$O$_2$PI: C, 40.45; H, 7.47. Found: C, 40.54; H, 7.35.

Registry No.—**1**, 933-52-8; **2**, 3173-79-3; **3**, 20217-54-3; **4**, 17166-16-4; **5**, 26546-75-8; **6**, 1608-26-0; **7**, 20217-34-9; **7s**, 32687-54-0; **8**, 20217-52-1; **8 MeI**, 32654-72-1; **8s**, 32687-56-2; **10**, 20217-33-8; **10 MeI**, 32687-58-4; **10s**, 32687-24-4; **11**, 32687-25-5; **11s**, 32687-26-6; **13**, 32654-70-9; **15**, 32687-27-7; **16**, 32687-28-8.

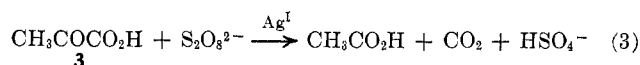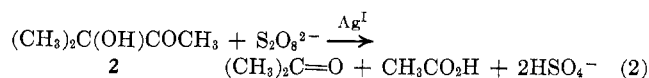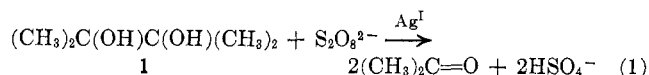# Kinetic Analysis of Silver-Catalyzed Oxidative Cleavage Reactions by Peroxydisulfate Ions[1]

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The rates of the silver(I)-catalyzed oxidative cleavage reactions of pinacol (**1**), 2-methyl-2-hydroxy-3-butanone (**2**), and pyruvic acid (**3**) by potassium peroxydisulfate have been measured at various concentrations of the reactants. The observed rates indicate that two reaction paths are operative in these cleavage reactions. In path I, the oxidative cleavage is performed by silver(III). Path II is a free-radical chain reaction that involves silver(II) as the oxidative cleaving agent. Oxidative cleavage by path II is faster than path I and predominates at lower substrate concentrations, whereas the slower path I is more likely if the substrate concentration is high or if the substrate reacts rapidly with silver(III).

The silver(I)-catalyzed oxidative cleavage reactions of glycols by peroxydisulfate was demonstrated by Greenspan and Woodburn.[2] Kinetic studies of the cleavage reactions of α-hydroxy acids and esters show that the rate laws for the cleavage reactions are dependent on the concentrations of the reagents and, in some instances, the reaction rates are inversely related to the substrate concentration.[3-8] Our investigations were directed toward finding an explanation for the kinetic behavior of these oxidative cleavage reactions. A mechanistic rationale for the kinetics of the oxidative cleavage reactions of pinacol (**1**), 2-methyl-2-hydroxy-3-butanone (**2**), and pyruvic acid (**3**) yielding the products shown in eq 1, 2, and 3, respectively (see Experimental Section), is presented in this article.

$$(CH_3)_2C(OH)C(OH)(CH_3)_2 + S_2O_8{}^{2-} \xrightarrow{Ag^I} $$
$$\underset{\textbf{1}}{} \quad 2(CH_3)_2C{=}O + 2HSO_4{}^- \quad (1)$$

$$(CH_3)_2C(OH)COCH_3 + S_2O_8{}^{2-} \xrightarrow{Ag^I} $$
$$\underset{\textbf{2}}{} \quad (CH_3)_2C{=}O + CH_3CO_2H + 2HSO_4{}^- \quad (2)$$

$$\underset{\textbf{3}}{CH_3COCO_2H} + S_2O_8{}^{2-} \xrightarrow{Ag^I} CH_3CO_2H + CO_2 + HSO_4{}^- \quad (3)$$

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(1) This work was supported by a grant (AM-08517) from the National Institutes of Health.

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Kinetic Data.[3]—In the absence of Ag^I, the rate of reaction of the peroxydisulfate with compounds **1**, **2**, and **3** at 30° in a sulfate–bisulfate buffered solution (pH 1.4) is negligible. Upon addition of Ag^I, immediate reaction ensues. Preliminary studies by us, as well as the previously cited investigations by others,[3-8] showed that the rate laws for the reactions depended markedly on the relative concentrations of the reagents. Initial rates for the oxidative cleavage reactions of **1**, **2**, and **3** at various initial concentrations of Ag^I, the substrate, and peroxydisulfate are shown in Tables I, II, and III, respectively.

Examination of the oxidative–cleavage rates for pinacol in Table I reveal the following. (1) At the higher [Ag^I] and pinacol concentrations, the cleavage rates are essentially zero order in substrate and first order in Ag^I. (2) At the higher [Ag^I] but lower substrate concentrations, the reaction rates are half-order in both Ag^I and the substrate. (3) At the lowest [S$_2$O$_8{}^{2-}$], the reaction rates are zero order in pinacol and half order in [Ag^I]. (4) At low [Ag^I] but higher (S$_2$O$_8{}^{2-}$) and pinacol concentrations, the reaction rates are zero order in substrate but approach three-halves order in [Ag^I]. (5) The kinetic order of S$_2$O$_8{}^{2-}$ is considerably greater than unity except at low substrate concentrations. (6) At low [Ag^I], the reaction rate appears to be inversely related to the pinacol concentration.

The oxidative cleavage rates of the hydroxy ketone **2** and pyruvic acid (**3**) show some of the characteristics observed for the pinacol reaction. The most significant difference is that the inverse concentration effect