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FORMATION OF CARBON–CARBON SINGLE BONDS FROM ISOCYANATES AND CYCLIC PENTAOXYPHOSPHORANES—VI[1]

SYNTHESIS OF 4-OXAZOLONES AND 4-THIAZOLONES, AND A NEW TYPE OF CHAPMAN REARRANGEMENT

F. RAMIREZ,*[2] C. D. TELEFUS and V. A. V. PRASAD
Department of Chemistry, State University of New York, Stony Brook, NY 11794, U.S.A.

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Abstract—The reaction of 4,5-dimethyl-2,2,2-trimethoxy-2,2-dihydro-1,3,2-dioxaphospholene with carbomethoxy, carbopropoxy and N,N-diphenylcarbamyl isocyanates yields, respectively, 2-methoxy-, 2-propoxy- and 2-diphenylamino-5-acetyl-5-methyl-2-oxazolin-4-one. The reaction with carbophenoxy isocyanate gives two products in a proportion which depends on experimental conditions: 2-phenoxy-5-acetyl-5-methyl-2-oxalin-4-one (1:1 stoichiometry) and 1,3-dicarbophenoxy-5-acetyl-5-methyl-hydantoin (1:2 stoichiometry). The 2-substituted 4-oxazolones are hydrolyzed to 5-acetyl-5-methyl-oxazolidin-2,4-dione. The alkyl group of the 2-alkoxy-4-oxazolones migrates to the adjacent nitrogen to give 3-alkyl-5-acetyl-5-methyl-oxazolidin-2,4-diones. The dioxaphospholene reacts with 2-substituted 2-thiazolin-4,5-diones to give 2-substituted 5-acetyl-5-methyl-2-thiazolin-4-ones, including rhodanine derivatives.

A new approach to the formation of C–C single bonds is based on the properties of the five-membered cyclic unsaturated pentaoxyphosphoranes, e.g. **1**.[3] These reagents are readily prepared from α-dicarbonyl compounds and trialkyl phosphites.[3] The biacetyl-TMP adduct† **1** yields 5-acyl-1,3-diaryl-hydantoins,[4,5] e.g. **2**, with two moles of aryl isocyanates, and 2-aryl-5-acyl-4-oxazolones,[6] e.g. **3**, with one mole of aroyl isocyanates. A hydantoin is obtained from p-toluenesulfonyl isocyanate.[6]

This type of reaction produces also 2-aryl-, and 2-amino-4-oxazolthiones,[1] **4** and **5**, from the corresponding aroyl and carbamyl isothiocyanates. The isomeric 4-thiazolones,[1] **6** and **7**, are made from 2-thiazoline-4,5-diones.

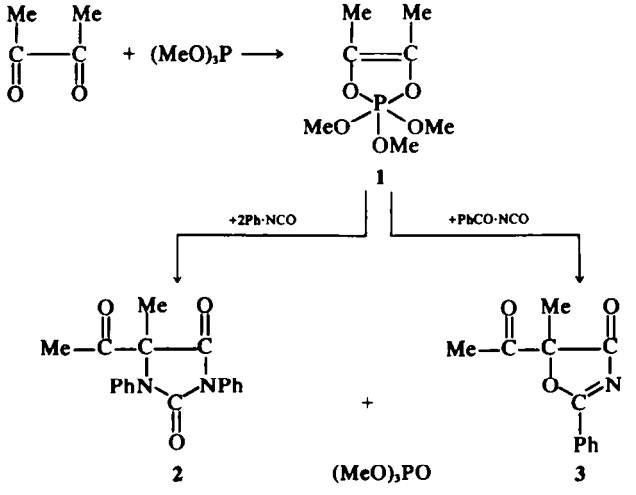
The heterocumulenes[7] and the 2-thiazolin-4,5-diones[8,9] required for these syntheses are readily available[10–13] from amides, thioamides[14,15] and thioureas.[15]

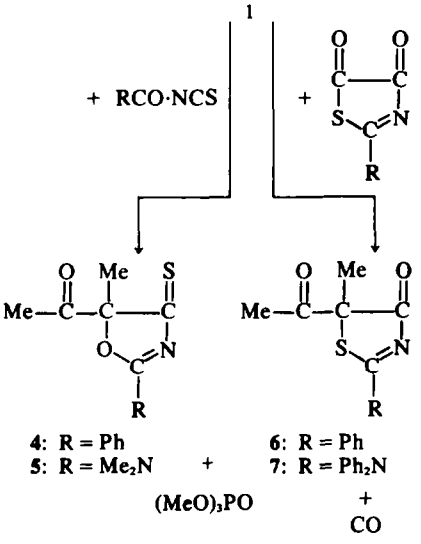
The hydantoins are one of the classical precursors of the α-aminoacids.[16–18] The 2-phenyl 4-oxazolones,[19,20] 4-oxazolthiones, and 4-thiazolones,[21] are easily hydrolyzed to the benzoate esters of the corresponding α-hydroxy-β-ketoamides,[6] α-hydroxy-β-keto-thioamides,[1] and α-mercapto-β-ketoamides.[1]

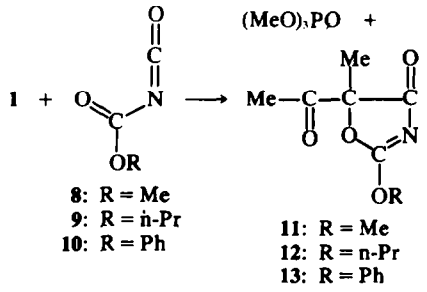
This investigation extends the synthetic scope of these new reactions, and explores further the mechanisms by which the various heterocycles are produced from compounds with P(5).†

†The following abbreviations will be used in this paper:

Biacetyl–TMP Adduct	= 4,5-Dimethyl-2,2,2-trimethoxy-2,2-dihydro-1,3,2-dioxaphospholene (1).
Hydantoin	= imidazolidin-2,4-dione.
4-Oxazolone	= 2-oxazolin-4-one.
4-Oxazolthione	= 2-oxazolin-4-thione.
4-Thiazolone	= 2-thiazolin-4-one.
P(4), P(5), P(6)	= Four-, five-, six-coordinate phosphorus.





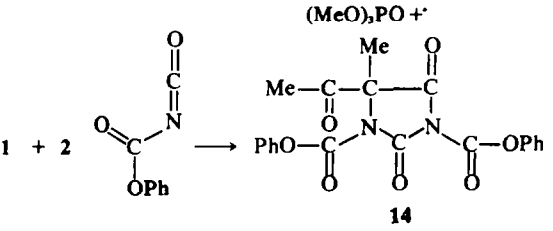


RESULTS

Reactions of the biacetyl-TMP adduct, **1**, *with carboalkoxy and carbamyl isocyanates.* The adduct,[3] **1**, reacts with carbomethoxy isocyanate[11] (**8**) to give the first example of a 2-alkoxy-4-oxazolone, **11**. This substance, **11**, can be isolated, but it cannot be purified since it undergoes a relatively rapid molecular rearrangement, as described below. The spectral properties of the 4-oxazolone, **11**, are summarized in Table 1.

The new carbopropoxy isocyanate (**9**), yields the corresponding 2-propoxy-4-oxazolone, **12**, which is considerably more stable than the 2-methoxy-analog, **11**.

The behavior of carbophenoxy isocyanate[11] (**10**) toward the adduct, **1**, is more complicated; two products are isolated regardless of the molar ratio of the reactants. When this ratio is 1:1, the major product is the 2-phenoxy-4-oxazolone, **13**, which is accompanied by *ca.* 19% of the hydantoin derivative, **14**. When the adduct, **1**, is allowed to react with two molar equivalents of the isocyanate, **10**, the major product is the hydantoin, **14**, (42%), although some oxazolone, **13**, is also formed. The two products, **13** and **14**, are easily separated. An attractive feature of **14** is the presence of the hydrolyzable carbophenoxy protective groups on the hydantoin nitrogens.

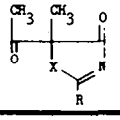


14

The course of the reaction of the adduct **1** and carbophenoxy isocyanate, **10**, can be followed by means of ^{31}P and ^{1}H NMR spectrometry, in CH_2Cl_2 solution. The first observable product is the imino-phospholane, **15**, which is characterized by a ^{31}P NMR shift at relatively

Table 1. Analyses and spectral data[a] of 5-acetyl-5-methyl-2-oxazolin-4-ones, and 5-acetyl-5-methyl-2-thiazolin-4-ones

Adduct.



Compd. No.	X	R	Mp°, Bp° (mm)	Formula	Calcd. % C	Calcd. % H	Calcd. % N	Found % C	Found % H	Found % N	^{1}H nmr $\tau(CH_3CO)$	^{1}H nmr $\tau(CH_3)$	Main ir bands in cm^{-1}	Yield %
11	O	CH_3O	—[b]	$C_7H_9O_4N$	...[b]	...	...	...	...	...	7.73	8.35[c]	1764, 1718, 1582	50
12	O	n-C_3H_7O	86-91 (0.1)	$C_9H_{13}O_4N$	54.3	6.6	7.0	54.3	6.6	7.0	7.75	8.28[d]	1779, 1724, 1587	69
13	O	C_6H_5O	136-138 (0.25)	$C_{12}H_{11}O_4N$	...[e]	...	...	...	...	...	7.72	8.22	1789, 1748, 1613, 1563	65
17	O	$(C_6H_5)_2N$	165-167[f]	$C_{18}H_{16}O_3N_2$	70.1	5.2	9.0	70.0	5.2	9.0	7.74	8.30	1745, 1709, 1569, 1558	92
21	S	$C_6H_5CH_2S$	112-114[g]	$C_{13}H_{13}O_2NS_2$	55.9	4.7	5.0[h]	56.0	4.7	5.1	7.60	8.32[i]	1733, 1698, 1481, 1351	80

[a] The ^{1}H NMR spectra were taken at 25° at 60 MHz in $CDCl_3$. The signals are in parts per million from TMS = 10 (τ values). The IR spectra were taken in CH_2Cl_2 solution.

[b] Distillation causes rearrangement to 5-acetyl-3,5-dimethyl-oxazolidin-2,4-dione.

[c] τ = 5·75 ppm (MeO).

[d] τ = 5·45 (triplet), 8·25 (multiplet) and 8·95 (triplet, $J_{HH} \sim 7$ Hz ($CH_3CH_2CH_2O$–).

[e] Analyzed as its "hydrate", 2-hydroxy-2-phenoxy-5-acetyl-5-methyl-oxazolidin-2,4-dione (**19**); See Experimental Section.

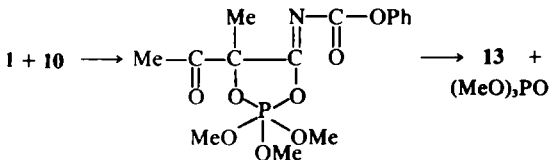
[f] From benzene-cyclohexane.

[g] From ethyl acetate–ether.

[h] S: calcd., 22·9; found, 22·7.

[i] τ = 5·50 ppm ($C_6H_5\underline{CH_2}S$).

high magnetic field,[4,5] δ $^{31}P = +54{\cdot}8$ ppm vs $H_3PO_4 = 0$. The three MeO-groups of the imino-phospholane, **15**, just as those of the adduct, **1**, are magnetically equivalent, due to relatively rapid permutational isomerization.[22] As the reaction proceeds, the imino-phospholane **15** is replaced by the oxazolone, **13**, and trimethyl phosphate.



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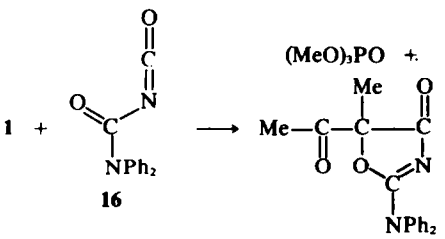
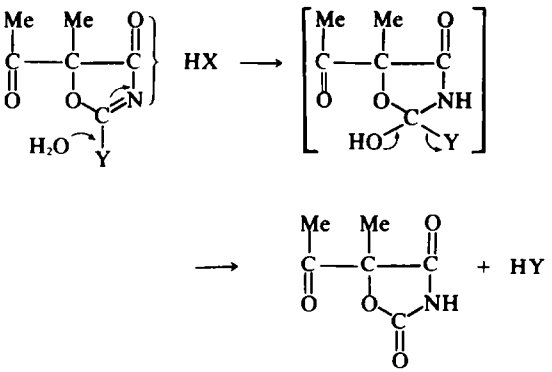
The biacetyl-TMP adduct, **1**, reacts with N,N-diphenylcarbamyl isocyanate (**16**) to give the first example of a 2-amino-4-oxazolone, **17**.



16 **17**

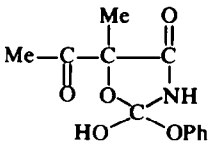
The 2-substituted 4-oxazolones, **11**, **12**, **13** and **17**, are easily hydrolyzed to the oxazolidindione, **18**. The alkoxy- and phenoxy- derivatives are cleaved rapidly by water in organic solvents, while the amino- derivative requires mild acid catalysis. It is assumed that these hydrolyses proceed as follows:



18

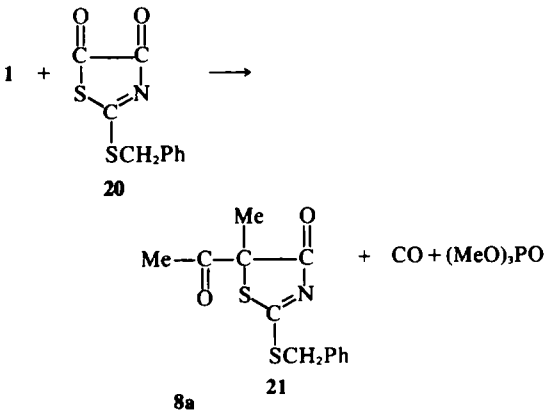
Y = MeO; n-PrO; PhO; Ph_2N

The relatively stable intermediate, **19**, can be isolated in the hydrolysis of the 2-phenoxy-4-oxazolone, **13**.



19

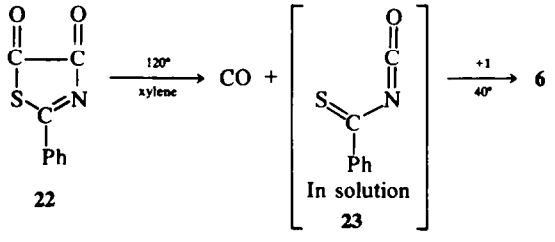
Reactions of the biacetyl-TMP adduct, **1**, *with 2-thiazolin-4,5-diones and with thioacyl isocyanates.* The 2-benzylmercapto-4-thiazolone, **21**, is obtained from the reaction of the biacetyl-TMP adduct, **1**, with the 2-benzylmercaptothiazolindione, **20**.[8,9] The benzyl protective group on sulfur enhances the synthetic capabilities of this rhodanine derivative, **21**, e.g. in transformations of the acetyl function.



20 **21**

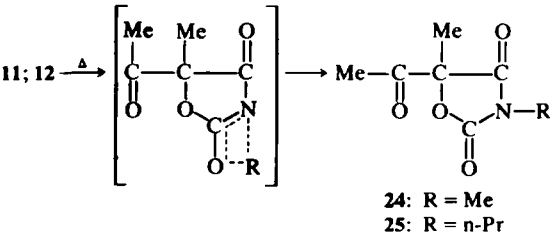
8a

Goerdeler *et al.* have reported the formation of thiobenzoyl isocyanate (**23**) as a distillate, from the pyrolysis of the phenyl-thiazolindione **22** in vacuum. We repeated this pyrolysis and obtained small amounts of a violet oil; however, treatment of this oil with the biacetyl-TMP adduct in CH_2Cl_2 gave polymeric material, and not the 2-phenyl-4-thiazolone, **6**, previously made[1] from the adduct **1** and the dione, **22**. Recently, Tsuge *et al.*[9b,c] carried out the pyrolysis of the dione **22** in xylene, and reported the formation of the unstable thiobenzoyl isocyanate (**23**) *in solution*. We added the adduct, **1**, to this solution and obtained, indeed, the 4-thiazolone, **6**, but in 45% yield, instead of the 75% yield realized from the dione itself, **22**, under comparable conditions.



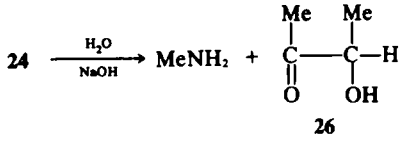
22 **23**

1,3 O → N *Alkyl migration in 2-alkoxy-2-oxazolin-4-ones.* The alkyl group of the 2-alkoxy-4-oxazolones **11** and **12**, migrates to the adjacent nitrogen upon heating. The Me-migration occurs at a significantly lower temperature than the Pr-migration, and the products are the corresponding 3-alkyl-5-acetyl-5-methyl-oxazolidin-2,4-diones, **24** and **25**.



24: R = Me
25: R = n-Pr

The cyclic N-methyl-N-acyl carbamate, **24**, is stable toward dilute aq-acid; however, **24** is degraded by dilute aq-alkali to methylamine and acetoin (**26**).



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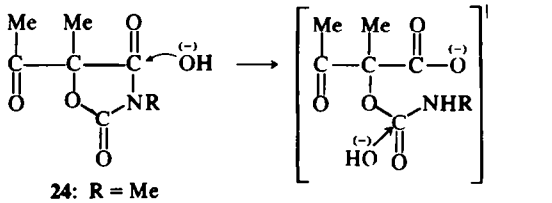
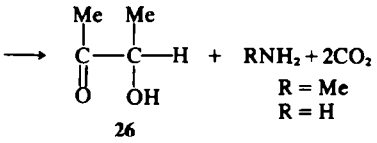
The alkaline hydrolysis of **24** is pictured as follows, although other sequences of steps are conceivable. A related hydrolysis is that of the 2-diphenylamino-4-oxazolone, **17**, which produced ammonia, acetoin (**26**) and diphenylamine, when carried out in dilute aq-alkali; presumably, the cyclic N-acyl carbamate, **27**, is an intermediate in this case: **17** → **27** → **26**.

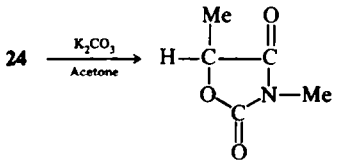


24: R = Me
27: R = H

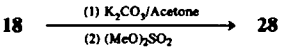


26

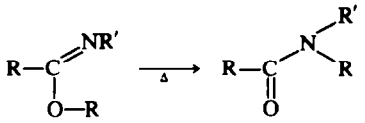
The rearrangement product, **24**, can be deacetylated to 3,5-dimethyl-oxazolidin-2,4-dione (**28**). The same substance, **28**, is obtained by deacetylation and simultaneous N-methylation of 5-acetyl-5-methyl-oxazolidin-2,4-dione (**18**).



28



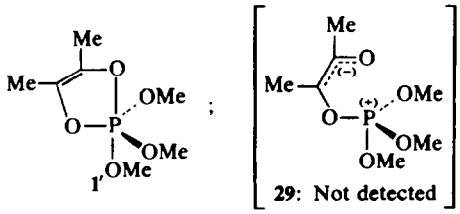
The 1,3 O → N alkyl migration of the 2-alkoxy-4-oxazolones, **11** and **12**, is related to the Chapman rearrangement,[23] which, however, takes place in O-alkyl imino carboxylate esters:



Radical[24] and ionic[25] mechanisms have been discussed for the Chapman rearrangement. The greater tendency for methyl vs propyl migration in the rearrangement of the oxazolones suggests that, in this case, reduced steric hindrance, rather than enhanced carbonium ion character of the alkyl group favors the migration.†[26]

DISCUSSION

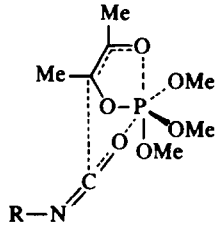
The 5-membered cyclic pentaoxyphosphoranes, e.g. **1'**, have a trigonal bipyramidal configuration with the ring in the apical-equatorial skeletal positions.[22] The ligands to the phosphorus exchange their skeletal positioning ("permutational isomerization") by intramolecular bond deformations, with the ring remaining apical-equatorial in all the permutational isomers.[22] There is no evidence that these P(5)[4] compounds exist in equilibrium with dipolar P(4) structures,‡[27-29] **29**, in non-polar solvents, in the temperature range of −30° to +30°, where the facile reactions with isocyanates take place.



1' ; **29**: Not detected

Although a reaction between the isocyanate and an undetectable P(4) structure, **29**, is not strictly ruled out, the weight of the present evidence favors these alternate possibilities:

(1) A concerted, one-step, mechanism via transition state **30**.



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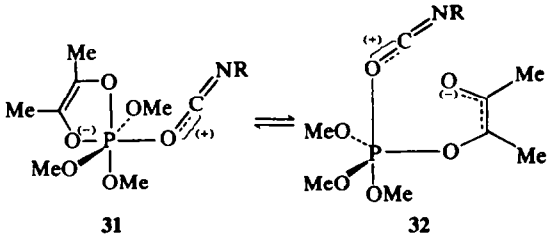
(2) A non-concerted mechanism in which the P(6) structure, **31**, and the dipolar P(5) structure, **32**, are intermediates.§[30]



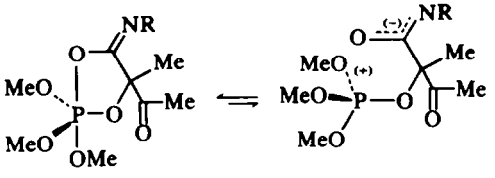
31 **32**

†As pointed out by Walling (Ref. 26), the substitution of an Me for an H of the Me radical *decreases* bond dissociation energies by about 4 kcal/mole. Thus, factors other than those reflected in bond dissociation energies appear to be required to explain these differences.

‡The existence of an equilibrium between P(5) and dipolar P(4) structures has been demonstrated in some related dioxytriaza-, dioxytricarbo-, and trioxydicarbo-phosphoranes (Ref. 27-29). The stability of P(5) structures increases markedly with the number of oxygen ligands.

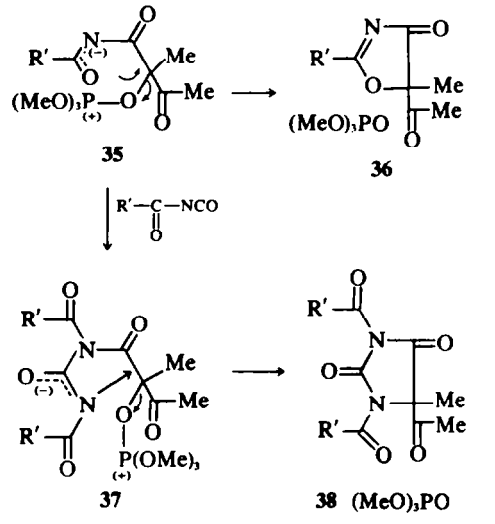
§Stable P(6) structures have been isolated from the addition of certain nucleophiles to cyclic pentaoxyphosphoranes related to **1'** but derived from hexafluorobiacetyl (Ref. 30). However, there is no evidence that stable P(6) structures can be obtained from the biacetyl-TMP adduct, **1'**. Yet, it is conceivable that the P(6) structure might be a transient intermediate or at least a transition state in the formation of intermediate.

Either mechanistic alternative† leads to the imino-1,3,2-dioxaphospholane, **33**, which is the first observable product of these reactions (a second permutational isomer of **33**, with the ring-termini reversed, is possible). The existence of a dipolar P(4) structure, **34**, in equilibrium with the P(5) form, **33**, is now reasonable due to the favorable charge delocalization in the amide anion.



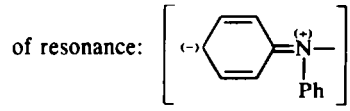
33 **34**

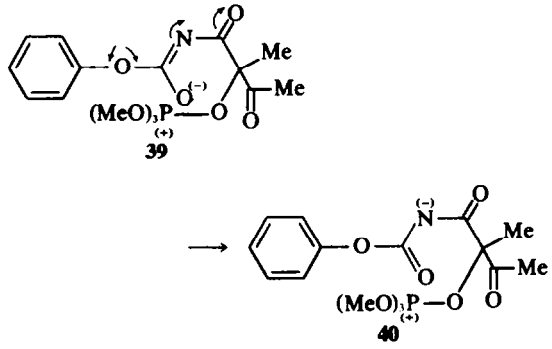
The reactions of phenyl and *p*-toluenesulfonyl isocyanates yield a dipolar P(4) structure (**34**: R = Ph, *p*-Me·C_6H_4·SO_2), with an ambident anion which reacts with a second molecule of the isocyanate to form the observed hydantoins. However, the reactions of benzoyl, carboalkoxy, and carbamyl isocyanates give a dipolar P(4) structure (**35**: R′ = Ph, RO, Ph_2N) with a trident anion which can follow two reaction paths. (a) Formation of a 2-substituted 4-oxazolone (**36**: R′ = Ph, MeO, *n*-PrO, PhO or Ph_2N). (2) Reaction with a second mole of isocyanate to give a hydantoin, **37**, which is analogous to the phenyl isocyanate case.



35 **36** **37** **38** $(MeO)_3PO$

4-Oxazolones, **36**, have been obtained from all the aroyl, carboalkoxy, carbophenoxy, and carbamyl isocyanates so far investigated. However, a hydantoin, **37**, was isolated only in the reaction of carbophenoxy isocyanate.‡ The cross-conjugation effect depicted in formula, **39**, which is not possible for the carboalkoxy and the benzoyl isocyanates, accounts for the lower tendency for 4-oxazolone formation vs hydantoin formation in carbophenoxy isocyanate (cf. **40**). The cross-conjugation effect may be less significant in the N,N-diphenylcarbamyl isocyanate case due to steric inhibition of resonance:

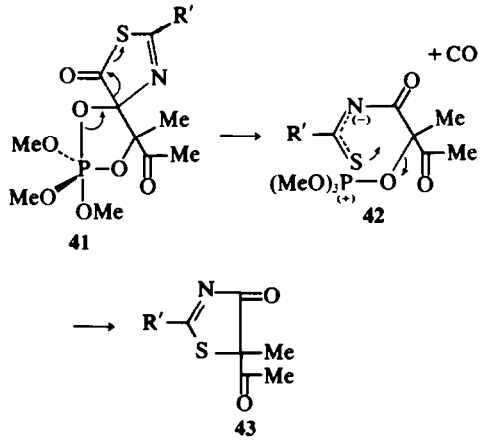




39 **40**

The formation of 4-oxazolthiones (**36**, with =S instead of =O; and R′ = Ph, Me_2N) is also understandable in these terms. The corresponding imino-1,3,2-thiaoxaphospholane (**33**; with S in place of one O in the ring) should be of a lower degree of stability, and it is not surprising that this type of P(5) intermediate has not been isolated in these reactions.

The formation of 4-thiazolones (**43**) from 2-thiazolin-4,5-diones is explained by a similar mechanism, except that the 1,3,2-dioxaphospholane, **41**, replaces the imino-phospholane, **33**, as the intermediate: **41** → **42** → **43**.



41 **42** **43**

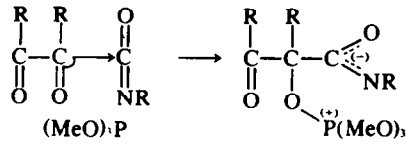
The formation of the 2-phenyl-4-thiazolone (**43**, R′ = Ph) from the preformed thiobenzoyl isocyanate (**23**) involves no new concept, as can be seen by a substitution of $S^{(-)}$ for $O^{(-)}$ in formula **35**.

It is apparent from this, and from the preceding papers,[1,4–6] that the oxyphosphorane C–C condensation reaction[3] achieves, in essence, the reversal of the usual electrophilic character of the carbonyl-carbon of α-diketones, and that the resulting nucleophilic

†The mechanistic alternatives, (1) and (2), differ, essentially, in the sequence by which the new P–O, and C–C bonds of the imino-dioxaphospholane, **33**, are formed from the adduct, **1′**, and the isocyanate. It is conceivable that both mechanisms may be operative in different types of pentaoxyphosphoranes, with different degrees of P(5) electrophilicities.

‡Since the yields of 4-oxazolones were not quantitative, relatively small amounts of hydantoins may have been formed in all cases; however, they could not be detected, in spite of the ease of isolation of hydantoins in general.

carbonyl–carbon adds to the carbon of a variety of heterocumulenes with synthetically useful results:



EXPERIMENTAL

Analyses by Schwarzkopf Microanalytic Laboratory, Woodside, N.Y., and Galbraith Laboratories, Knoxville, Tenn. All experiments with the Biacetyl-TMP Adduct (1) were carried out under anhydrous conditions; in those experiments, the by-product was $(MeO)_3PO$. The analytical and spectral data are given in Tables 1 and 2, except as noted in this Section.

Preparation of starting materials

Biacetyl-TMP adduct (1). Adduct 1 was made by dropwise addition of freshly distilled biacetyl (1·0 mole) to freshly distilled, anhydrous, trimethyl phosphite (1·02 moles) in dry CH_2Cl_2 (120 ml) at 0°, under N_2. The soln was stirred 3 hr at 0° and was evaporated; the residue was distilled to give adduct 1 b.p. 57–60° (0·2 mm) in 90% yield.

Isocyanates. They were prepared by an adaptation of the procedure of Speziale *et al.*[10,11] Oxalyl chloride (115 mmoles) was added rapidly to a stirred suspension of the carbamate, or the N,N-disubstituted urea (104 mmoles) in CH_2Cl_2 (100 ml) at 20°. The mixture was kept *ca.* 15 hr at reflux. The solvent was evaporated, and the residue was purified by vacuum distillation. A solid derivative was made by addition of 1 molar equiv of aniline to the isocyanate in CH_2Cl_2 at 20°, followed by recrystallization of the urea.

MeO·CO·NCO[11] (8): b.p. 38–43° (90 mm); 47% yield from $MeO{\cdot}CN{\cdot}NH_2$. *n-PrO·CO·NCO* (9): b.p. 46–48° (22 mm); 65% from $n\text{-}PrO{\cdot}CO{\cdot}NH_2$; IR bands at 2222 and 1754 cm^{-1} (CH_2Cl_2); *urea derivative from aniline*: m.p. 119–122° (hexane); IR bands at 1740 and 1709 cm^{-1} (CH_2Cl_2); (Found: C, 58·9; H, 6·4; N, 12·5. Calcd. for $C_{11}H_{14}O_3N_2$: C, 59·5; H, 6·3; N, 12·6%). *PhO·CO·NCO*:[11] b.p. 66–68° (2 mm); 56% from $PhO{\cdot}CO{\cdot}NH$; IR bands at 2222, 1751 and 1740 cm^{-1} (CH_2Cl_2); *urea derivative from aniline*: m.p. 156–159° (benzene–hexane); IR bands at 1740 and 1709 cm^{-1} (CH_2Cl_2). *$Ph_2N{\cdot}CO{\cdot}NCO$*: b.p. 115–116° (0·15 mm); 58% from $Ph_2N{\cdot}CO{\cdot}NH_2$; IR bands at 2222 and 1700 cm^{-1} (CH_2Cl_2); *urea derivative from aniline*: m.p. 133–138° (CH_2Cl_2–pentane); IR bands at 1709 and 1660 cm^{-1} (CH_2Cl_2). (Found: C, 72·5; H, 5·2; N, 12·8. Calcd. for $C_{20}H_{17}O_2N_3$: C, 72·5; H, 5·1; N, 12·7%).

2-Thiazolin-4,5-diones. 2-Phenyl- and 2-benzylmercapto-2-thiazoline-4,5-diones, 22 and 20, were prepared as described by Goerdeler *et al.*,[8,9] from oxalyl chloride and thiobenzamide (commercially available), and benzyl dithiocarbamate,[15] respectively.

Reactions of the adduct (1) *with isocyanates*

Carbomethoxy isocyanate (8) *preparation of 2-methoxy-5-acetyl-5-methyl-2-oxazolin-4-one* (11). A soln of 1 (25·4 g; 121 mmoles) in CH_2Cl_2 (25 ml) was dropped into a soln of 8 (12·2 g; 121 mmoles) in CH_2Cl_2 (50 ml) at 0°. The yellow soln was stirred 1 hr at 0°, and *ca.* 16 hr at 20°. The solvent was evaporated at 20 nm, and the residue was freed from $(MeO)_3PO$ by careful short-path distillation at 1·5 mm and a bath temp below 70°. The remaining *4-oxazolone*, 11, could not be purified; all attempted distillations caused the molecular rearrangement described below.

Carbopropoxy isocyanate (9) *preparation of 2-propoxy-5-acetyl-5-methyl-2-oxazolin-4-one* (12). A soln of 1 (9·3 g; 44·4 mmoles) in CH_2Cl_2 (20 ml) was dropped into a soln of 9 (5·72 g; 44·4 mmoles) in CH_2Cl_2 (30 ml), at 20°. The mixture was stirred *ca.* 19 hr at 20°; the solvent was removed at 20 mm, and $(MeO)_3PO$ (6·0 g; 97% of the theory) was distilled at 3 mm (bath at 65°; short-path distillation). The crude *4-oxazolone*, 12, was purified by short-path distillation without appreciable rearrangement.

Carbophenoxy isocyanate (10)

(a) *Optimum conditions for the preparation of 2-phenoxy-5-acetyl-5-methyl-2-oxazolin-4-one* (13). A soln of 10 (3·98 g; 24·4 mmoles) in CH_2Cl_2 (20 ml) was dropped, over a 25 min period, into a stirred soln of 1 (5·12 g; 24·4 mmoles) in CH_2Cl_2 (50 ml), at −20°. The mixture was kept 15 min at −20°, and then allowed to reach 20°; the IR spectrum of an aliquot showed the absence of isocyanate. After 14 hr at 20°, the solvent was evaporated, and the trimethyl phosphate (3·0 g; 88% of the theory) was distilled at *ca.* 100° (0·02 mm). The residue was treated with a mixture of benzene and ether (10 ml of each), and was filtered to remove *1,3-dicarbophenoxy-5-acetyl-5-methyl-hydantoin* (14; 0·92 g; 19% based on adduct). The filtrate was evaporated and the residue was distilled to yield *2-phenoxy-5-acetyl-5-methyl-2-oxazolin-4-one* (13; 3·8 g; 65% based on adduct 1).

The 4-oxazolone, 13, was very sensitive to moisture; treatment of 13 with moist ether resulted in a new crystalline compound with the probable structure of *2-phenoxy-2-hydroxy-5-acetyl-5-methyl-oxazolidin-4-one* (19). (Found: C, 56·6; H, 5·1; N, 5·6. Calcd. for $C_{12}H_{13}O_5N$: C, 57·4; H, 5·2; N, 5·6%). The ^1H NMR spectrum of the "hydrate" 19 (in $CDCl_3$) had the following signals (τ in ppm): m at 3·0 (aromatic ^1H); broad signal at 4·5 (OH); s at 7·75 (MeCO); s at 8·34 (MeC). The IR spectrum had bands at: 3571–3390 (NH), 3333–2632 (OH), 1779 (C=O), 1733 (sh, C=O) cm^{-1} (CH_2Cl_2). The "hydrate" had the odor of phenol and underwent slow spontaneous decomposition to 5-acetyl-5-methyl-oxazolidin-2,4-dione (18; see below).

(b) *Optimum conditions for the preparation of 1,3-dicarbophenoxy-5-acetyl-5-methyl-hydantoin* (14). A soln of 1 (3·80 g; 18·1 mmoles) in CH_2Cl_2 (3 ml) was dropped into a soln of 10 (5·90 g; 36·2 mmoles) in boiling CH_2Cl_2 (10 ml; *ca.* 40°). The mixture was kept 0·5 hr at reflux, cooled to 20° and filtered; the solid was washed with ether (2 × 25 ml) to yield 14 (3·0 g; 42% based on adduct; m.p. 179–180° from CH_2Cl_2: CCl_4). (Found: C, 60·6; H, 4·0; N, 7·1. Calcd. for $C_{20}H_{16}O_7N_2$: C, 60·4; H, 4·0; N, 7·1%). The ^1H NMR spectrum of 14 (in CH_2Cl_2) had the following signals (τ in ppm): s at 7·57 (MeO), and s at 7·87 (MeC), in addition to the aromatic multiplet. The IR spectrum had bands at: 1805 (C=O), 1789 (C=O), 1751 (C=O), 1730 (C=O), cm^{-1} (CH_2Cl_2).

(c) *Investigation of the course of the reaction by ^{31}P and ^1H NMR and IR spectrometry.* The isocyanate 10 (0·101 g; 6·2 mmoles) and 1 (0·130 g; 6·2 mmoles) were mixed with CH_2Cl_2

Table 2. Analyses and spectral data of 2-R-5-acetyl-5-methyl-oxazolidin-2,4-diones

Compd. No.	R	Mp°, Bp° (mm)	Formula	Calcd. % C	Calcd. % H	Calcd. % N	Found % C	Found % H	Found % N	^1H nmr τ_{CH_3CO}	^1H nmr τ_{CH_3}	τ_R	Main ir bands, in cm^{-1}
18	H	81–82[a]	$C_6H_7O_4N$	45.9	4.5	8.9	45.9	4.4	8.9	7.62	8.20	...[b]	3333, 1795, 1779, 1730
24	CH_3	77–78 (0.1)	$C_7H_9O_4N$	49.1	5.3	8.2	48.8	5.3	7.8	7.67	8.23	6.92	1812, 1748, 1733
25	n-C_3H_7	60–62 (0.03)	$C_9H_{13}O_4N$	54.0	6.6	7.0	54.0	6.6	7.0	7.67	8.24	...[c]	1812, 1742, 1724

[a]From CH_2Cl_2–n-pentane.
[b]N–H proton not detected.
[c]τ = 6·45 (triplet), 8·3 (multiplet) and 9·07 ppm, $J_{HH} \sim 7$ Hz ($CH_3CH_2CH_2$).

(0·4 ml) at −20° in an NMR tube. The mixture was kept 10 min at −20°, and was then allowed to reach 20° when the ^{31}P NMR spectrum was immediately recorded; it had the following signals = +54·8: +51·9: +48·4: −1·74 ppm vs H_3PO_4 = 0, in the relative proportions of 5·2:1·7:1·0:1·2. The following assignments are made, respectively: 4 - (N - *carbophenoxy*)*imino* - 5 - *acetyl* - 5 - *methyl* - 2,2,2 - *trimethoxy* - 2,2 - *dihydro* - 1,3,2 - *dioxaphospholane* (**15**): ?: 4,5 - dimethyl - 2,2,2 - trimethoxy - 2,2 - dihydro - 1,3,2 - dioxaphospholene (**1**): trimethyl phosphate. The ^1H NMR spectrum of a comparable soln was consistent with these assignments. The formation of **13**, at the expense of **15**, could also be noted. The ^1H spectrum taken after 20 hr at 20° disclosed the formation of **13** as the major product, plus $(MeO)_3PO$.

N,N-*Diphenylcarbamyl isocyanate* (**16**)

Preparation of 2-*diphenylamino*-5-*acetyl*-5-*methyl*-2-*oxazolin*-4-*one* (**17**). A soln of **1** (5·75 g; 27·3 mmoles) in CH_2Cl_2 (15 ml) was dropped into a soln of **16** (6·5 g; 27·3 mmoles) in CH_2Cl_2 (50 ml), at 20°. The mixture was stirred *ca.* 13 hr at 20°; the solvent was evaporated at 20 mm, and the resulting solid was triturated with ether (2 × 10 ml). The 4-*oxazolone* (**17**; 7·7 g; 95%; crude m.p. *ca.* 150–160°) was filtered off and purified by recrystallization.

Hydrolyses of 2-*alkoxy*-, *and* 2-*diphenylamino*-5-*acetyl*-5-*methyl*-2-*oxazolin*-4-*ones* (**11**, **12** *and* **17**) *to* 5-*acetyl*-5-*methyl*-*oxazolidin*-2,4-*dione* (**18**)

2-*Methoxy*-4-*oxazolone* (**11**). A soln of crude **11** (4·0 g), water (1·2 g) and MeCN (25 ml) was kept 8 hr at reflux. The solvent was evaporated at 20 mm, and the remaining water was removed by azeotropic distillation with benzene. The residue was recrystallized from CH_2Cl_2-n-pentane to give 0·86 g (23% yield) of the *oxazolidindione*, **18**.

2-*Propoxy*-4-*oxazolone* (**12**). A soln of distilled **12** (3·68 g; 18·5 mmoles) and water (0·70 g; 37 mmoles) in MeCN (40 ml) was kept 12 hr at reflux. The work-up was as in the previous experiment. The crude *oxazolidindione* (**18**; 2·1 g; 72%) was purified as indicated in Table 2 (50% yield of product melting at 81–82°).

2-*Diphenylamino*-4-*oxazolone* (**17**). A mixture of purified **17** (1·26 g), 10% HCl aq (15 ml), and acetone (15 ml), was kept 4 hr at reflux, and was filtered. The insoluble solid was treated with KOH aq, and extracted with CH_2Cl_2, yielding Ph_2NH after removal of CH_2Cl_2. The acetone filtrate was evaporated to give the *oxazolidindione*, **18**.

Reaction of the adduct, **1**, *with* 2-*benzylmercapto*-2-*thiazolin*-4,5-*dione* (**20**)

Preparation of 2-*benzylmercapto*-5-*acetyl*-5-*methyl*-2-*thiazolin*-4-*one* (**20**). The adduct **1** (4·2 g; 20 mmoles) was added to a soln of **20** (4·74 g; 20 mmoles) in CH_2Cl_2 (50 ml) at 20°. The reaction was slightly exothermic. The mixture was kept 0·5 hr at reflux, was concentrated to one-half its volume, and was diluted with hexane (15 ml). The yellow 4-*thiazolone* (**21**; 4·46 g; 80% yield of crude) was filtered off and recrystallized.

Pyrolysis of 2-*phenyl*-2-*thiazolin*-4,5-*dione* (**22**) *and reaction of the pyrolysis product* [*thiobenzoyl isocyanate* (**23**)] *with the biacetyl*-*TMP adduct* (**1**)

The dione (**22**; 1 g) was suspended in xylene (15 ml; dried over Na), and the mixture was heated to 120°. Gas evolution was noted at *ca.* 95°. The resulting red-violet xylene soln, said[9] to contain **23**, was added to a soln of **1** (1 molar equiv) in hexane (10 ml) at 20°. (The reaction was not exothermic). The mixture was kept 6 hr at 45°, and was evaporated in vacuum. The residue was treated with a mixture of benzene:hexane:ether (7 ml:3 ml:2 ml), and the crystalline 2-*phenyl*-4-*thiaxolone*, **6**, (48% of the theory) was filtered.

Molecular rearrangement of 2-*alkoxy*-5-*acetyl*-5-*methyl*-2-*oxazolin*-4-*ones* (**11** *and* **12**) *to* 3-*alkyl*-5-*acetyl*-5-*methyl*-*oxazolidin*-2,4-*diones* (**24** *and* **25**)

2-*Methoxy*-4-*oxazolone* (**11**). This substance, **11**, was transformed into 5-*acetyl*-3,5-*dimethyl*-*oxazolidin*-2,4-*dione* (**24**) when heated 5 hr at 125°. The pure **24** was isolated in 50% yield after distillation.

2-*Propoxy*-4-*oxazolone* (**12**). This substance, **12**, required heating for 2·5 hr at 170° for complete rearrangement into 3-*propyl*-5-*acetyl*-5-*methyl*-*oxazolidin*-2,4-*dione* (**25**).

Alkaline degradation of 5-*acetyl*-3,5-*dimethyl*-*oxazolidin*-2,4-*dione* (**24**). A mixture of **24** (1·0 g) and 5% NaOH aq was kept *ca.* 13 hr at reflux. Methylamine was evolved. The soln contained acetoin according to the ^1H NMR spectrum. The N-methyl-dione, **24**, was recovered unchanged after 2 hr at reflux in 5% HCl aq.

Alkaline degradation of 2-*diphenylamino*-5-*acetyl*-5-*methyl*-2-*oxazolin*-4-*one* (**17**). A mixture of **17** (0·78 g), 10% NaOH aq (10 ml), and glyme (20 ml), was kept 18 hr at reflux. Ammonia was evolved. The glyme was distilled off, and the residue was filtered to give Ph_2NH (85% of the theory) and an aqueous soln containing acetoin, as shown by comparison of the ^1H NMR spectrum with that of an authentic sample.

Deacetylation of 5-*acetyl*-3,5-*dimethyl*-*oxazolidin*-2,4-*dione* (**24**)

Formation of 3,5-*dimethyl*-*oxazolidin*-2,4-*dione* (**28**). A mixture of **24** (11·85 g), K_2CO_3 (12·0 g) and acetone (80 ml) was kept 5 hr at reflux. The mixture was filtered, the inorganic solid was washed with acetone, and the acetone layer was evaporated. The residue was distilled to give 3,5-*dimethyl*-*oxazolidin*-2,4-*dione* (**28**; 2·7 g; 30% yield; b.p. 53–54° at 0·12 mm). The ^1H NMR spectrum ($CDCl_3$) had the following signals: τ = 8·40 (d, J_{CH_3CH} = 8 Hz); 5·05(q, J_{CH_3CH} = 8 Hz), 6·98 (s, MeN). The main IR bands were at 1808 and 1730 cm^{-1} (CH_2Cl_2). (Found: C, 46·4; H, 5·6; N, 10·7. Calcd. for $C_5H_7O_3N$: C, 46·5; H, 5·4; N, 10·8%).

Deacetylation and N-*methylation of* 5-*acetyl*-5-*methyl*-*oxazolidin*-2,4-*dione* (**18**)

Preparation of 3,5-*dimethyl*-*oxazolidin*-2,4-*dione* (**28**). A mixture of **18** (0·89 g; 5·7 mmoles), K_2CO_3 (0·86 g), and acetone (5 ml) was stirred 4 hr at 20°. Dimethyl sulfate (0·71 g; 5·7 mmoles) was added, and the mixture was kept 6 hr at reflux, was diluted with ether (10 ml), and was filtered. The filtrate was diluted with water (10 ml), and extracted with ether (3 × 10 ml). The combined ether-extracts were dried (molecular sieves 4A), and evaporated to give 3,5-*dimethyl*-*oxazolidin*-2,4-*dione* (**28**), with spectral properties (IR and ^1H NMR) identical to those of the analytical sample.

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