(s, 1, NH), 8.24 (s, 1, NH), 7.22 (m, 10, $2C_6H_5$), and 3.56 ppm (m, 4, NCH_2CH_2N); mass spectrum[15] (70 eV)—$C_{16}H_{16}N_4O_2$ (3.3) 0.2, $C_{10}H_9N_3O_2$ (7.8) 0.2, $C_9H_{11}N_3O$ (100) −1.1, $C_9H_{10}N_2O$ (17) −0.2, $C_9H_9N_2O$ (2.4) −0.2, $C_8H_{10}N_3$ (1.8) 0.2, $C_8H_7N_2$ (3.7) −1.3, C_7H_5NO (71) 0.0, C_7H_8N (27) −1.5, C_6H_5N (34) −0.8, C_6H_5 (30) −1.5.

Anal. Calcd for $C_{16}H_{16}N_4O_2$: C, 64.9; H, 5.43; N, 18.9. Found: C, 64.7; H, 5.38; N, 19.2.

The mother liquors (B) from crystallization of **15** were evaporated to dryness; the resulting solid was redissolved in a minimum of cold chloroform and preparatively chromatographed as above. The major band (R_f 0.31) was eluted from the plates with methanol in the usual manner yielding 0.213 g of **14**, mp 120–122°.

The basic aqueous filtrate above (A) was extracted twice with 25 ml of chloroform. After drying (anhydrous sodium sulfate) and filtering, the chloroform extract was evaporated to dryness. The residue was recrystallized from chloroform–hexane, yielding 0.530 g of **14**. The total yield of **14** from A and B was 0.743 g (42%): mp 120–122°; ir (KBr) 1715 (C=O) and 3350 cm^{-1} (NH_2); uv max (CH_3OH) 246 mμ (ε 18,500); nmr ($DCCl_3$) δ 7.33 (m, 5, C_6H_5), 4.00 (s, 2, NH_2), and 3.62 ppm (m, 4, NCH_2CH_2N); mass spectrum[15] (70 eV)—$C_9H_{11}N_3O$ (100) 0.5, $C_9H_{10}N_2O$ (4.3) −1.0, $C_9H_9N_2O$ (4.8) −4.0, $C_7H_8N_2$ (3.2) 0.0, C_7H_8NO (18) −0.3, C_7H_7N (30) −0.1, C_6H_5N (23) −0.5, C_6H_5 (90) −1.3.

Anal. Calcd for $C_9H_{11}N_3O$: C, 61.0; H, 6.26; N, 23.7. Found: C, 60.7; H, 6.32; N, 22.2.

3-Isopropylidenamino-1-phenyl-2-imidazolidinone (16). A.—In a separate experiment involving equimolar amounts of phenylisocyanate and hydrazinoethyl hydrogen sulfate executed as above, mother liquors (B) were evaporated to dryness and the residue was dissolved in acetone and chromatographed as above, giving rise to several bands. Eluting the major band with acetone and evaporating the solvent produces a solid that, after recrystallization from carbon tetrachloride–hexane, afforded 0.221 g (10%) of **16**: mp 54–56°; ir (KBr) 1725 (C=O) and 1650 cm^{-1} (C=N); uv max (CH_3OH) 248 mμ (ε 4500); nmr (CCl_4) δ 7.16 (m, 5, C_6H_5), 3.52 (s, 4, NCH_2CH_2N), 1.84 (s, 3, CH_3), and 1.96 ppm (s, 3, CH_3); mass spectrum[15] (70 ev)—217 (100), 202 (7.8), 175 (27), 161 (7.3), 147 (6.9), 133 (4.7), 118 (34), 106 (61), 91 (47), 77 (64).

Anal. Calcd for $C_{12}H_{15}N_3O$: C, 66.3; H, 6.96; N, 19.3. Found: C, 66.6; H, 6.89; N, 19.3.

B.—In 2 ml of acetone 51 mg (0.3 mmol) of **14** was dissolved and allowed to stand for 1.5 hr. The acetone was removed and the residue was dissolved in chloroform. Preparative tlc of the mixture yielded 23 mg (40%) of **16**.

Registry No.—Phenyl isocyanate, 103-71-9; **3a**, 109-84-2; **3b**, 3657-48-5; **4**, 18339-72-5; **5**, 18339-61-2; **6**, 18339-62-3; **7**, 18339-63-4; **9a**, 18339-64-5; **11a**, 18339-65-6; **12**, 18339-66-7; **13**, 18339-67-8; **14**, 18339-68-9; **15**, 18339-69-0; **16**, 18339-70-3.

Acknowledgment.—The authors wish to thank Dr. Emile Cherbuliez, Honorary Professor at the University of Geneva (Switzerland), for reviewing the manuscript.

A New Synthesis of 5-Acyl-2-oxazolin-4-ones and of β-Keto-α-hydroxy Acid Amides from the Reaction of 2,2,2-Trialkoxy-2,2-dihydro-1,3,2-dioxaphospholenes with Acylisocyanates

FAUSTO RAMIREZ[1] AND C. DAVID TELEFUS

Department of Chemistry of the State University of New York at Stony Brook, Stony Brook, New York 11790

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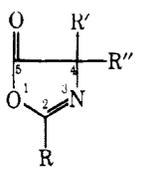
A new reaction leading to 5-acyl-2-oxazolin-4-ones and to the corresponding hydrolysis products, β-keto-α-hydroxy acid amides, is described. The reaction involves two steps: (1) the formation of a 2,2,2-trialkoxy-2,2-dihydro-1,3,2-dioxaphospholene from a trialkyl phosphite and an α-dicarbonyl compound and (2) the reaction of the phospholene with an acylisocyanate to yield the oxazolone and a trialkyl phosphate.

The 2-oxazolin-5-ones ("5-oxazolones" or azlactones[2]) (**1**) have been extensively investigated because of their application in the synthesis of α-amino acids. However, the 2-oxazolin-4-ones (**2**) have received little attention,[3-7] in spite of their potential use in the synthesis of α-hydroxy acid amides.



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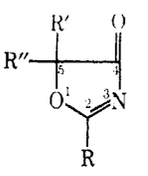

2

This paper describes a new reaction whose net effect is to convert an α-dicarbonyl compound (**3**) and an acylisocyanate[8,9] (**4**) into a 5-acyl-2-oxazolin-4-one (**6**), the precursor of a β-keto-α-hydroxy acid amide (**8**). The reagent employed in this reductive condensation is a trialkyl phosphite (**5**), which is first combined with the α-dicarbonyl compound to form a 2,2,2-trialkoxy-2,2-dihydro-1,3,2-dioxaphospholene.[10] Reac-

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(2) (a) H. E. Carter in "Organic Reactions," Vol. 3, R. Adams, Ed., John Wiley & Sons, Inc., New York, N. Y., 1946; (b) F. Korte and K. Heinz Buckel, *Chem. Ber.*, **93**, 104 (1960).

(3) (a) F. R. Japp and A. Findlay, *J. Chem. Soc.*, **75**, 1028 (1899); (b) C. F. Howell, N. R. Quinones and R. A. Hardy, *J. Org. Chem.*, **27**, 1679 (1962).

(4) (a) I. V. Smolanka, S. M. Khripak, and V. I. Staninets, *Ukr. Khim. Zh.*, **30** (3), 265 (1964); (b) H. Najer, R. Giudicelli, and J. Menin, *Bull. Soc. Chim. Fr.*, **8–9**, 1810 (1963).

(5) K. Hohenlohe-Oehringen, *Monatsh. Chem.*, **89**, 588 (1958).

(6) (a) J. C. Sheehan and P. T. Izzo, *J. Amer. Chem. Soc.*, **71**, 4059 (1949); (b) R. Neidlein, *Arch. Pharm.*, **298** (2), 124 (1965).

(7) (a) R. Filler, *Advan. Heterocycl. Chem.*, **4**, 71 (1965); (b) J. W. Cornforth in "Heterocyclic Compounds," Vol. 5, R. C. Elderfield, Ed., John Wiley & Sons, Inc., New York, N. Y., 1957.

(8) (a) A. J. Speziale and L. R. Smith, *J. Org. Chem.*, **28**, 1805 (1963); (b) O. Billeter, *Ber.*, **36**, 3218 (1903).

(9) P. A. S. Smith, "The Chemistry of Open-chain Organic Nitrogen Compounds," W. A. Benjamin, Inc., New York, N. Y., 1965, Chapter 6.

(10) The literature has been reviewed: (a) F. Ramirez, *Accounts Chem. Res.*, **1**, 168 (1968); (b) F. Ramirez, *Pure Appl. Chem.*, **9**, 337 (1964).

TABLE I

PROPERTIES OF ACYL ISOCYANATES AND OF THEIR UREA DERIVATIVES

RCONCO					RCONHCONHR′									
	Compd			Yield,		Compd		Molecular	Calcd, %			Found, %			
R	no.	Bp (mm), °C	Ir, μ[a]	%	R′	no.	Mp, °C	formula	C	H	N	C	H	N	Ir, μ
C_6H_5[b]	14	62–63 (3.5)	4.48, 5.90	80	[b]										
p-FC_6H_4	15	43–45 (0.7)	4.48, 5.90	95	C_6H_5	18	200–202[c]	$C_{14}H_{11}O_2N_2F$	65.1	4.3	10.8	65.1	4.4	10.7[d]	3.12, 5.90[e]
p-$CH_3OC_6H_4$	16	85–86[f] (0.7)	4.48, 5.90	90[g]	C_6H_5	19	221–223[h]	$C_{15}H_{14}O_3N_2$	66.7	5.2	10.4	66.8	5.2	10.6	5.82[i]
Cl_3C	17	42–43[j] (15)	4.50, 5.75	60	3,4-$Cl_2C_6H_3$	20	171–172[c,k]	$C_9H_6O_2N_2Cl_6$	30.8	1.4	8.0	31.0	1.5	7.5	5.80[i]

[a] In CH_2Cl_2. The isocyanate band was flanked by weak shoulders at 4.30 and 4.60 μ. [b] References 6a and 8. [c] From CH_2Cl_2. [d] F, 7.5% (calcd 7.3%). [e] KBr pellet. [f] Solidified. [g] The CH_3O group had a ^1H nmr signal at τ 6.12. [h] From $HCON(CH_3)_2$. [i] Dilute CH_2Cl_2. [j] Reference 8a gave bp 80–85° (20 mm). [k] Reference 8a gave mp 175°.

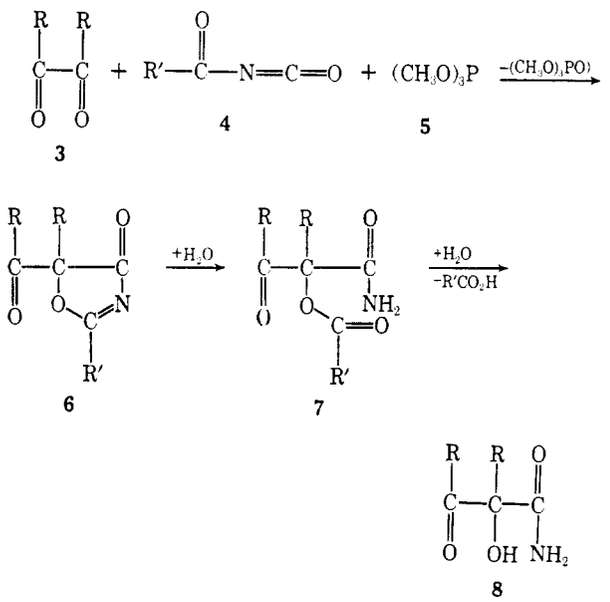
TABLE II

2-ARYL- AND 2-ALKYL-5-ACETYL-5-METHYL-2-OXAZOLIN-4-ONES

	Compd	Bp (mm) or	Molecular	Calcd, %			Found, %			Yield,	^1H nmr[a]		
R	no.	mp, °C	formula	C	H	N	C	H	N	%	τ (CH_3CO)	τ (CH_3)	Ir, μ[b]
C_6H_5	23	111–113 (0.04)	$C_{12}H_{11}O_3N$[c]	66.4	5.1	6.4	66.2	5.3	6.1	92	7.75[d]	8.22	5.67, 5.78
p-FC_6H_4	24	76–78[e]	$C_{12}H_{10}O_3NF$	61.3	4.3	5.9	61.5	4.5	5.7[f]	78	7.68[d]	8.12	5.62, 5.78
p-$CH_3OC_6H_4$	25	143–144[g]	$C_{13}H_{13}O_4N$	63.1	5.3	5.6	62.8	5.2	5.6	87	7.76[d,h]	8.23	5.68, 5.78
Cl_3C[i]	27	131–133[e,j]	$C_7H_8O_4NCl_3$[k]	30.4	2.9	5.1	30.3	2.9	5.1	60	7.62,[l] 7.68	8.32	3.10, 5.75,[m] 5.88

[a] Measured at 60 Mcps; nmr values were measured in parts per million *vs.* TMS = 10 (τ values). [b] In CH_2Cl_2 solution. [c] Mol wt (thermoelectric in CH_2Br_2) 214 (calcd 217). [d] In $CDCl_3$ solution. [e] From benzene–hexane. [f] F, 8.2% (calcd 8.1%). [g] From C_6H_6. [h] τ (CH_3O) 6.10. [i] Hydrate of the 2-oxazolin-4-one assumed to be 2-hydroxy-2-trichloromethyl-5-acetyl-5-methyloxazolidine-4-one. [j] Can be sublimed unchanged at 0.05 mm. [k] Mol wt (thermoelectric in dioxane) 272 (calcd 276). [l] In acetone-d_6; insoluble in other nmr solvents. The acetyl signal at τ 7.62 was accompanied by a second, much weaker, closely situated signal. One resolvable CH_3C signal only. The OH signal was broad at *ca.* τ 3.43. There was exchange of H and D with solvent. [m] In KBr pellet. The OH band at 3.10 μ is broad and strong.

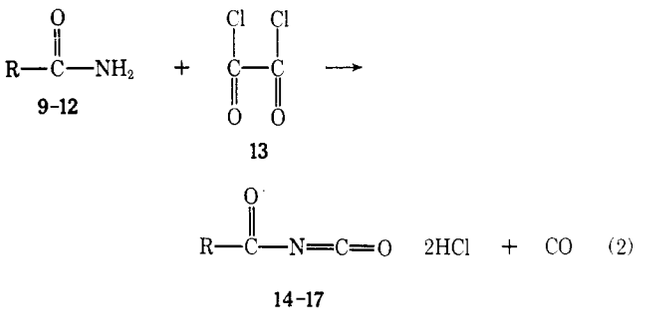
tion of the phospholene with the isocyanate produces the oxazolone **6** and a trialkyl phosphate (eq 1).



(1)

Results

Condensation of Acyl Isocyanates with 2,2,2-Trimethoxy-4,5-dimethyl-2,2-dihydro-1,3,2-dioxaphospholene (21).—The acyl isocyanates **14–17** were made from the corresponding amides **9–12** (eq 2) by the procedure of Speziale and Smith.[8a] The properties of the isocyanates and of the urea derivatives **18–20** are given in Table I. The dioxaphospholene **21** was prepared from biacetyl and trimethyl phosphite as previously described.[10]



(2)

The dioxaphospholene **21** reacted with benzoyl isocyanate (**14**) at 30°. The reaction had a 1:1 stoichiometry and produced trimethyl phosphate and 2-phenyl-5-acetyl-5-methyl-2-oxazolin-4-one (**23**) in good yield (eq 3). The properties of the 2-oxazolin-4-one **23** are given in Table II. Note in particular the two carbonyl bands in the infrared (ir) spectrum, and the ^1H nmr signals due to the acetyl and methyl groups on the heterocycle.

No intermediate was detected during the reaction, but we assume that the phospholene added to the isocyanate to form a dipolar adduct **22**, which underwent an intramolecular displacement of trimethyl phosphate by the acyl oxygen to yield the 2-oxazolin-4-one **23**.

The phospholene **21** reacted with aromatic acyl isocyanates having electron-withdrawing and electron-releasing groups, **15** and **16**, respectively, and gave the corresponding 2-oxazolin-4-ones **24** and **25**.

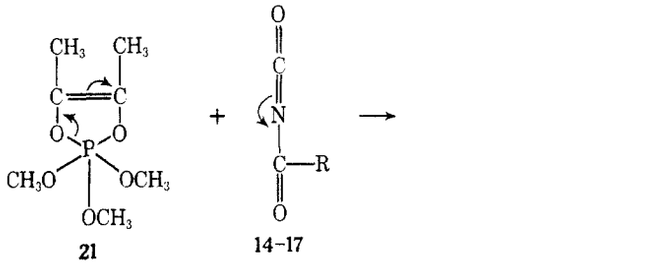
The 2-oxazolin-4-one **26** made from trichloroacetyl isocyanate (**17**) was very sensitive to moisture and was converted into a crystalline monohydrate assumed

TABLE III

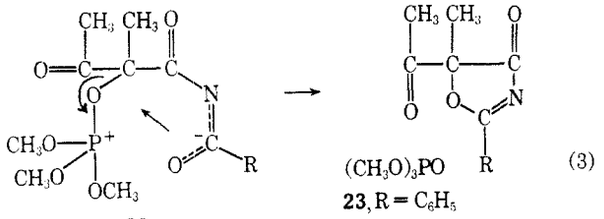
α-METHYL-α-HYDROXYACETOACETAMIDE AND O-ACYL DERIVATIVES $CH_3COC(CH_3)(OR)CONH_2$

R	Compd no.	Mp, °C	Molecular formula	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N	Yield, %	^{1}H nmr[a] τ (CH_3CO)	^{1}H nmr[a] τ (CH_3)	Ir, μ
C_6H_5CO	30	135–136[b]	$C_{12}H_{13}O_4N$	61.3	5.5	6.0	61.4	5.5	6.3	45	7.70[c]	8.16	5.81, 5.90,[d] 6.02
p-FC_6H_4CO	31	147–149[b]	$C_{12}H_{12}O_4NF$	56.9	4.7	5.5	57.1	4.8	5.6[e]	70	7.70[f]	8.15	5.78,[g] 5.80, 5.88
H	29	86–88[b]	$C_5H_9O_3N$	45.8	6.9	10.7	46.2	6.9	10.5	45	7.53[h]	8.36	2.85, 2.94, 5.78, 5.90[g]

[a] Nmr values were measured in parts per million *vs.* TMS = 0 (τ values). [b] From benzene. [c] In acetone-d_6. The 2 protons of the amide were at *ca.* τ 1.92. [d] In KBr pellet. [e] F, 7.4% (calcd 7.5%). [f] In $CDCl_3$ solution. [g] In CH_2Cl_2 solution. [h] A broad signal at τ 5.17 is attributed to OH.



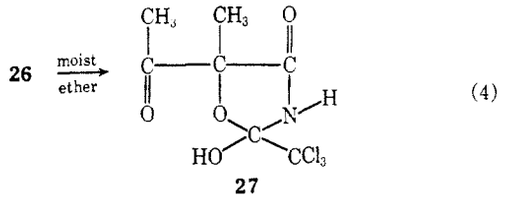
21 14–17



22 (3)

23, R = C_6H_5
24, R = *p*-FC_6H_4
25, R = *p*-$CH_3OC_6H_4$
26, R = Cl_3C

to be 2-hydroxy-2-trichloromethyl-5-acetyl-5-methyl-4-oxazolidinone (**27**) (eq 4). This material could be

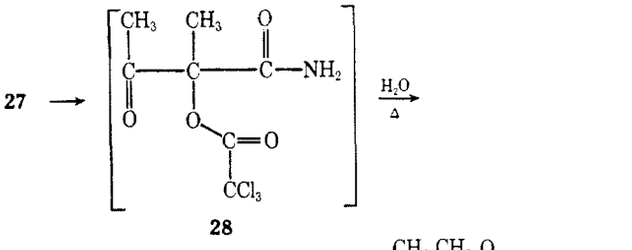


26 (4) **27**

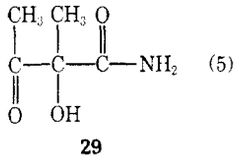
sublimed *in vacuo* without the loss of water and had a relatively strong band in the infrared at 3.10 μ, in addition to the two expected carbonyl bands (in a KBr pellet). The ^{1}H nmr spectrum and the results of further hydrolysis discussed in the next section are in agreement with structure **27**.

Reaction of 5-Acyl-2-oxazolin-4-ones with Water.—The "hydrate" **27**, of the 2-trichloromethyl-4-oxazolone (**26**), was converted into α-methyl-α-hydroxyacetoacetamide (**29**) by boiling water (eq 5); *cf.* Table III. The formation of other hydrolysis products was not excluded since the amide **29** was isolated only in 45% yield. The O-trichloroacetyl ester, **28**, if formed, was hydrolyzed under these conditions.

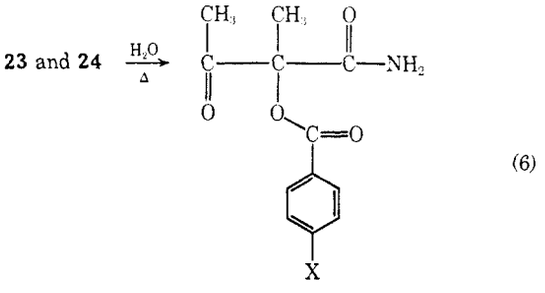
The 2-phenyl- and the 2-*p*-fluorophenyl-2-oxazolin-4-ones (**23** and **24**) were converted into the corresponding O-benzoyl and O-*p*-fluorobenzoyl esters **30** and **31**, of the hydroxyacetoacetamide **29** by boiling water (eq 6).



27 **28**



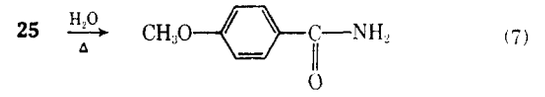
(5) **29**



23 and **24** (6)

30, X = H
31, X = F

The behavior of the 2-*p*-methoxyphenyl-2-oxazolin-4-one **25** toward boiling water was rather complex, but approximately 50% of *p*-methoxybenzamide **11** was isolated from this reaction (eq 7). A discussion of

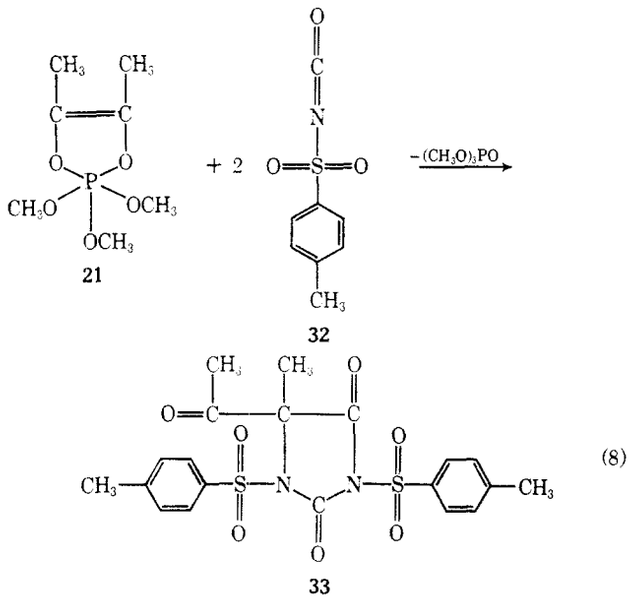


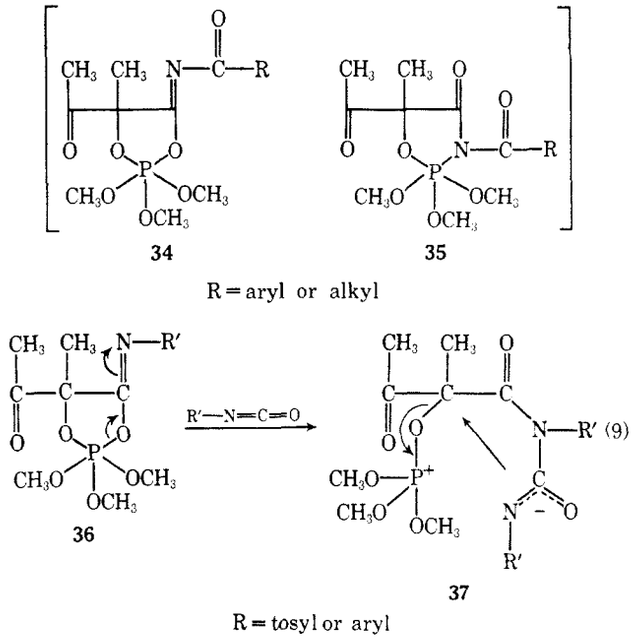
25 (7) **11**

the mechanisms of hydrolysis of 2-oxazolin-4-ones in general[3,6a,7] and of 5-acyl-2-oxazolin-4-ones in particular, at various pH values, will be postponed pending further studies now in progress.

Vigorous hydrolysis of the 2-phenyl-2-oxazolin-4-one (**23**) in aqueous hydrochloric acid gave benzoic acid and acetoin, $CH_3COCH(OH)CH_3$.

Reaction of the Dioxaphospholene with *p*-Toluenesulfonyl Isocyanate.—This reaction occurred at 30°, had a 1:2 phospholeneisocyanate stoichiometry, and yielded trimethyl phosphate and the N,N′-ditosylhydantoin, **33** (eq 8).





A comparison of the behavior of the acyl isocyanates, tosyl isocyanate, and phenyl isocyanate[11] toward the dioxaphospholene is instructive. The presence of an electron-withdrawing group, *i.e.*, R′ = acyl or tosyl (Ts), on the isocyanate, R′—N=C=O, increased its reactivity toward the nucleophilic phospholene.[12,13] However, the 1:1 adducts initially formed in these reactions behaved in different ways. The acyl isocyanate adduct, **22**, did not close to the 2,2,2-trimethoxy-4-imino-1,3,2-dioxaphospholane (**34**) or to the 2,2,2-trimethoxy-4-oxo-1,3,2-oxaazaphospholane (**35**); instead, it underwent an intramolecular displacement of phosphate to give the 2-oxazolin-4-ones **23**–**26**. The tosyl and phenyl isocyanate adducts, however, closed to the 1,3,2-dioxaphospholanes[11] **36**, which were, in turn, capable of nucleophilic addition to isocyanate yielding the 1:2 adducts, **37** (eq 9). The latter formed the hydantoins **33** by intramolecular displacement of phosphate.[11]

Experimental Section

The analyses were performed by the Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.

Acyl Isocyanates (Table I). Benzoylisocyanate (14).—Compound **14** was made from oxalyl chloride and benzamide in 1,2-$C_2H_4Cl_2$ solution (10–20 hr at reflux) following the procedure of Speziale and Smith.[8a] The new *p*-fluorobenzoyl isocyanate (**15**) and *p*-methoxybenzoyl isocyanate (**16**) were made as follows. Oxalyl chloride (1.25 molar equiv) was quickly added to a suspension of *p*-fluorobenzamide (**10**) or of *p*-methoxybenzamide (**11**) in CH_2Cl_2 (*ca.* 2.2 *M*) at 20°. The resulting clear solution was kept 12–20 hr at reflux, and the solvent was evaporated. The crude acyl isocyanates, **15** and **16**, were purified by distillation. They were characterized by their ir spectra and by the properties of the solid **ureas 18** and **19** made by reaction with 1 molar equiv of aniline in CH_2Cl_2. The application of this procedure to trichloroacetamide (**12**) gave an acyl isocyanate which boiled at a much lower temperature (*ca.* 40°) than that reported[8a] for **trichloroacetyl Isocyanate (17)**. Therefore, we repeated the preparation and the analysis of the urea **20** made from 3,4-dichloraniline and the acyl isocyanate; *cf.* Table I. The separation of trichloroacetylisocyanate (**17**) from solvent CH_2Cl_2 should be carried out by fractional distillation to avoid loss of volatile isocyanate. The acyl isocyanates, in general, must be protected from moisture.

Reaction of 2,2,2-Trimethoxy-4,5-dimethyl-2,2-dihydro-1,3,2-dioxaphospholene (21) with 1 Molar Equiv of Acyl Isocyanates. Preparation of 2-Aryl- and 2-Alkyl-5-acetyl-5-methyl-2-oxazolin-4-ones (23–26) (Table II).—A solution of the phospholene[10–12] **21** in CH_2Cl_2 (1.6–2.5 *M*) was added, dropwise, to a solution of the acyl isocyanate in CH_2Cl_2 (1.6–2.5 *M*, 1 molar equiv) at 20°. The reaction was mildly exothermic, and the solution was stirred 4–10 hr at 20°.

The solvent and the trimethyl phosphate were removed by distillation at 20 and 1 mm, respectively. The oxazolone was purified by distillation (if liquid) or by trituration with cold ether followed by recrystallization from benzene (if solid). The 2-trichloromethyloxazolone **26** was very sensitive to moisture and was converted into the stable, crystalline **2-hydroxy-2-trichloromethyl-5-acetyl-5-methyloxazolidine-4-one (27)** by treatment with moist ether, prior to recrystallization from benzene.

The reaction of the phospholene **21** with *2 molar equiv* of benzoyl isocyanate (**14**) gave the same oxazolone **23** plus unreacted isocyanate.

Hydrolysis of 2-Aryl- and 2-Alkyl-5-acetyl-5-methyl-2-oxazolin-4-ones (Table III).—A suspension of the oxazolone in water was kept 8–12 hr at reflux temperature. The solid which separated on cooling was filtered and was purified by recrystallization from benzene. The **2-phenyl-2-oxazolin-4-one 23** and the **2-*p*-fluorophenyl-2-oxazolin-4-one 24** gave the corresponding O-benzoyl and O-*p*-fluorobenzoyl esters **30** and **31** derived from **α-methyl-α-hydroxyacetoacetamide (29)**. The **2-trichloromethyl-2-oxazolin-4-ones (26** and **27)** gave α-methyl-α-hydroxyacetoacetamide (**29**), under the same conditions. The **2-*p*-methoxyphenyl-2-oxazolin-4-one 25** gave a mixture of products from which *p*-methoxybenzamide (**11**) was isolated in *ca.* 40% yield.

When the 2-phenyl-2-oxazolin-4-one **23** was heated 10 hr with 10% aqueous HCl, benzoic acid and acetoin were produced.

Reaction of 2,2,2-Trimethoxy-4,5-dimethyl-2,2-dihydro-1,3,2-dioxaphospholene (21) with 2 Molar Equiv of *p*-Toluenesulfonyl Isocyanate (32).—A solution of the phospholene **21** (40 g) in CH_2Cl_2 (50 ml) was added dropwise to freshly distilled *p*-$CH_3C_6H_4SO_2NCO$ (80 g) in CH_2Cl_2 (50 ml). The reaction was exothermic. After 8–10 hr at 20°, the solvent was evaporated and the residue was stirred with cold ether (*ca.* 50 ml) and filtered. The crude hydantoin (**50 g**, mp 160–170°) was recrystallized from $CHCl_3$–hexane to give 5-acetyl-5-methyl-1,3-di(*p*-toluenesulfonyl)hydantoin (**33**), mp 178–179° (*ca.* 50% yield).

(11) F. Ramirez, S. B. Bhatia, and C. P. Smith, *J. Amer. Chem. Soc.*, **89**, 3030 (1967).

(12) (a) F. Ramirez, N. Ramanathan, and N. B. Desai, *ibid.*, **84**, 1317 (1962); (b) F. Ramirez, H. J. Kugler, and C. P. Smith, *Tetrahedron Lett.*, 3153 (1968); (c) F. Ramirez, H. J. Kugler, A. V. Patwardhan, and C. P. Smith, *J. Org. Chem.*, **33**, 1185 (1968), and references therein.

(13) A. J. Kirby, *Tetrahedron Lett.*, 3001 (1966).

Anal. Calcd for $C_{20}H_{20}O_7N_2S_2$: C, 51.7; H, 4.3; N, 6.0; S, 13.8. Found: C, 51.4; H, 4.4; N, 6.2; S, 13.9.

The ^1H nmr spectrum had signals at τ 7.70 (three acetyl protons), 8.00 (three methyl protons on hydantoin ring), and 7.55 (methyl protons on benzene ring). The ir spectrum (in CH_2Cl_2) had bands at 5.60, 5.73 and 5.81 (sh) μ.

Registry No.—**14,** 4461-33-0; **15,** 18354-35-3; **16,** 4695-57-2; **17,** 3019-71-4; **18,** 18354-38-6; **19,** 18354-39-7; **20,** 6077-66-3; **23,** 18354-41-1; **24,** 18354-42-2; **25,** 18354-43-3; **27,** 18354-44-4; **29,** 18354-48-8; **30,** 18354-45-5; **31,** 18354-46-6; **33,** 18354-47-7.

A γ-Pyran Derivative from Pulegone and Ethyl Acetoacetate. Reformulation of a Bicyclo[3.3.1]nonenone Structure

JOSEPH WOLINSKY AND HELEN S. HAUER

Department of Chemistry, Purdue University, Lafayette, Indiana 47907

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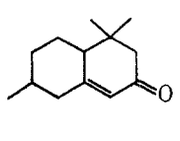
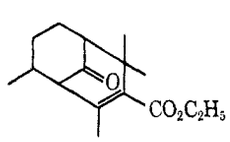
The crystalline solid isolated from the zinc chloride catalyzed condensation of pulegone and ethyl acetoacetate and previously identified as 3-carbethoxy-2,4,4,8-tetramethylbicyclo[3.3.1]-2-nonen-9-one is now reformulated as 3-carbethoxy-2,4,4,7-tetramethyl-5,6,7,8-tetrahydro-1,4-benzopyran by a reconsideration of its spectral properties and by hydrogenation to a tetrahydro derivative and dehydrogenation to 3-carbethoxy-2,4,4,7-tetramethyl-1,4-benzopyran.

Some time ago it was shown[1] that pulegone acetone, produced by the zinc chloride catalyzed condensation of pulegone with ethyl acetoacetate, has the constitution represented by I rather than three alternative structures proposed by other investigators.[2,3] In the meantime, Chow[4] reported the isolation of another crystalline product from the pulegone condensation, referred to here as compound B, and argued that it possessed structure II.



I



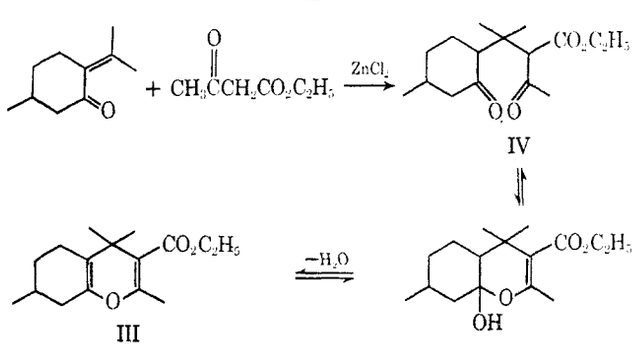
II

The exclusive reduction of the carbethoxy group in compound B by excess lithium aluminum hydride and the alleged formation of a hydrazide rather than a normal 2,4-dinitrophenylhydrazone derivative were but two of the many observations recorded by Chow[4] which do not agree with the behavior expected for a compound such as II. We have reexamined this matter and wish to report that compound B is the carbethoxypyran III and is most likely formed according to the sequence outlined in Scheme I.

When the reaction of pulegone with ethyl acetoacetate was conducted for 10 hr pulegone acetone (I) was the only crystalline product isolated. When the condensation was stopped after 2 hr, column chromatography afforded a new crystalline solid, mp 37–38°, whose physical and spectral properties were essentially identical with those of compound B reported by Chow.[4] There can be no question that the solid that we isolated is identical with the compound described by Chow.[4]

Compound B is converted into pulegone acetone by the action of zinc chloride in acetic acid[4] suggesting that its formation is reversible and that diketo ester IV eventually undergoes an irreversible intramolecular aldol condensation followed by decarbethoxylation to give I. This accounts for the fact that compound B is not found when the condensation is extended for 10 hr. Since the cyclization of IV to III produces water, it was reasoned that the yield of III might be improved if water was removed so as to prevent the hydrolysis of III to IV. When acetic anhydride was added to the reaction mixture, in order to consume the water which formed, the yield of III rose from 5 to 18% and little or no pulegone acetone formed. Unfortunately, the yield of III could not be further improved; the remainder of the material was largely accounted for as a nonvolatile, presumedly polymeric, oil.

SCHEME I



(1) J. Wolinsky and M. A. Tyrell, *Chem. Ind.* (London), 1104 (1960).
(2) P. Barbier, *C. R. Acad. Sci., Paris,* **127,** 870 (1898).
(3) L. G. Jupp, G. A. R. Kon, and E. H. Lockton, *J. Chem. Soc.,* 1639 (1928).
(4) Y. L. Chow, *Tetrahedron Lett.,* 1337 (1964).