O/NMe$_2$ Exchange in the Reaction of 4-Benzylidene-5-oxazolones with Phosphorous Tris(dimethylamide)

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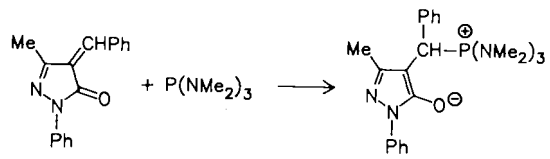
Eingegangen am 29. Juni 1988

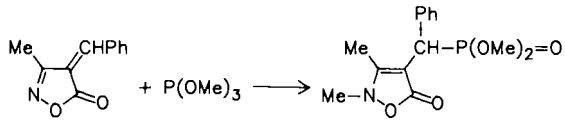
4-Benzylidene-5-oxazolones 5 do not react with P(OMe)$_3$; with P(NMe$_2$)$_3$ they give rise to 4-α-[bis(dimethylamino)phosphoryl]benzyl-5-dimethylaminooxazoles 6. This behavior differs from that of the corresponding pyrazolones and isoxazolones and is attributed to a decreased stability of the dipolar adduct resulting from a β attack of phosphorus.

The reaction of α,β-unsaturated carbonyl compounds with phosphorous esters and amides such as P(OMe)$_3$ and P(NMe$_2$)$_3$ attracts much interest[1] ever since it was first studied by F. Ramirez and co-workers[2]. It is normally initiated by the attack of phosphorus at the β position leading to a zwitterionic phosphonium enolate. In the case of P(NMe$_2$)$_3$ this primary product is mostly stable, whereas in the case of P(OMe)$_3$ it tends to escape the charge separation either by ring closure to form a 1,2λ^5-oxaphospholene or by shifting a methyl group. Oxo derivatives of heterocycles containing an alkylidene group in an adjacent position are special cases of α,β-unsaturated carbonyls. In general they behave like the acyclic representatives[1]. An example for the addition of P(NMe$_2$)$_3$ is provided by its reaction with 5-benzylidenethiazolidine-2,4-dione[3]; we now find another one in its reaction with the 4-benzylidene-5-pyrazolone **1**, leading to the zwitterionic product **2**.



1 **2**

The addition of P(OMe)$_3$ followed by the shift of a methyl group is demonstrated by its reaction with the 4-benzylidene-5-isoxazolone **3** thus yielding the 2-methyl-5-isoxazolone **4**[4].

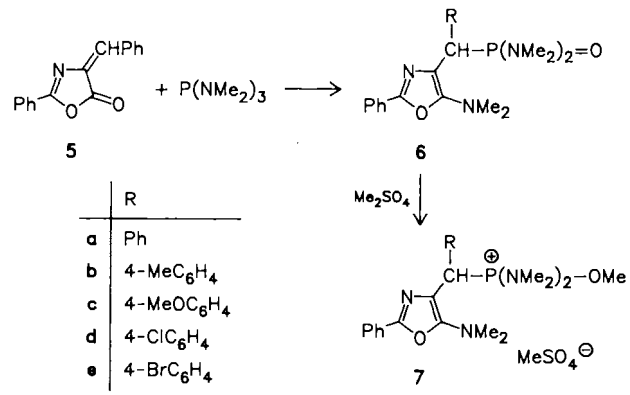


3 **4**

When we tried to extend the reaction with P(OMe)$_3$ and P(NMe$_2$)$_3$ to another group of heterocyclic enones, e.g. the 4-benzylidene-5-oxazolones **5**, we found them to behave differently. The *Z* isomers of the unsaturated azlactones **5** are readily accessible and are in general well-investigated[5]. No reaction with a phosphorus(III) compound seems to be reported, however[6].

In contrast to the 4-benzylidene-5-isoxazolone **3**, which reacts with P(OMe)$_3$ already at room temperature as described above, the essentially (except for the substituent in 3-/2-position) isomeric 4-benzylidene-5-oxazolone **5a** does not enter a reaction with P(OMe)$_3$ under the same conditions (see Experimental)[6].

With P(NMe$_2$)$_3$ on the other hand, compounds **5a–e** give a clean reaction. As monitored by ^{31}P NMR, the reaction proceeds smoothly at ambient temperature. Its rate depends slightly on the nature of the benzylidene substituent in *p*-position and decreases in the order Cl, Br, H, Me, OMe. No intermediate can be observed. The products incorporate the two compounds in a 1:1 ratio. They are, however, not just zwitterionic adducts like **2**. In addition to the zwitterion formation, the phosphorus has attacked the carbonyl oxygen and transferred a dimethylamino group to the 5-position yielding the 5-aminooxazoles **6a–e**.



5 **6** **7**

	R
a	Ph
b	4-MeC$_6$H$_4$
c	4-MeOC$_6$H$_4$
d	4-ClC$_6$H$_4$
e	4-BrC$_6$H$_4$

The structure of compounds **6** follows unequivocally from their NMR spectra (Tables 1 and 2). The phosphorus chemical shift corresponds to that found for methyl- or ethylphosphoryl bis(dimethylamide) [δ(^{31}P) = 38] and deviates far from that of a tris(dimethylamino)phosphonium unit such as in **2** (Table 1). The ^{1}H-NMR spectrum shows the signals of three nonequivalent NMe$_2$ groups: a singlet for the one in 5-position and two doublets for the diastereotopic ones at phosphorus. Additional proof comes from ^{13}C-NMR as well as from IR spectra ($\nu_{P=O} \approx 1200$ cm^{-1}).

Dimethyl sulfate methylates the phosphoryl oxygen of **6d** (→ **7d**) instead of the oxazole nitrogen. The methylation is accompanied by the same downfield shift of the ^{31}P-NMR signal (ca. 20 ppm) as observed in the methylation of PhP(NMe$_2$)$_2$O[7].

Two pathways may be considered for the formation of **6**. The first involves the initial β attack of the P(NMe$_2$)$_3$ phosphorus leading to a dipolar adduct analogous to **2**. Interaction of the enolate end with the aminophosphonium end could then result in the exchange of substituents to give **6**. Dipolar adducts from the oxazolones **5** should be less favored than those deriving from the pyrazolone **1** or from the isoxazolone **3**, where the ring nitrogen in 2-

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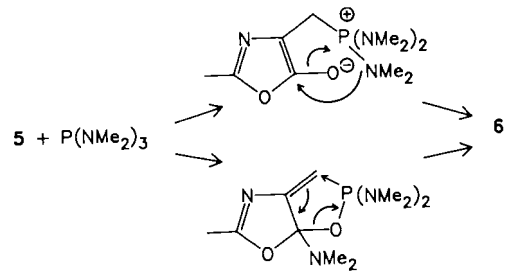
Table 1. $^{31}P\{^1H\}$- and ^1H-NMR spectra of the oxazoles **6a–e** and **7d** and of the zwitterionic pyrazole **2** in $CDCl_3$

δ (Atom) J [Hz]	6a	6b	6c	6d	6e	7d	2
P	35.7	34.8	33.1	32.8	34.2	54.8	61.0
4-CH	4.76(d)	4.71(d)	4.56(d)	4.72(d)	4.72(d)	5.33(d)	4.82(d)
^2J(PCH)	21.5	21.0	21.1	21.5	21.5	22.2	23.4
5-NMe	2.71	2.73	2.61	2.72	2.73	2.78	
P-NMe	2.64(d)	2.64(d)	2.52(d)	2.64(d)	2.65(d)	2.76(d)	2.50(d)
^3J(PNCH)	9.0	9.3	9.4	9.0	8.8	9.2	9.2
P-NMe	2.50(d)	2.51(d)	2.36(d)	2.51(d)	2.52(d)	2.75(d)	
^3J(PNCH)	9.8	9.8	9.1	9.5	9.8	9.8	
Me		2.42[a]	3.64[b]				1.92[c]

[a] 4-Me of R. – [b] 4-OMe of R. – [c] 5-Me.

position can effectively participate in the delocalization of the negative charge. The fact that **5** does not react with $P(OMe)_3$ may result from the lacking formation of a dipolar adduct.



The alternative pathway starts with the addition of $P(NMe_2)_3$ to the carbonyl group initiated by the nucleophilic attack of N on C-5. A corresponding addition has been reported as an intermediate step in other cases[8]. Subsequent β attack of phosphorus, and a presumably concerted opening of the C–O bond yields **6** without a charge separation being involved. This type of [2,3] sigmatropic rearrangement is well-known for allyl phosphinites[9]. The second pathway thus seems to provide the easier explanation for the product formed; it also accounts for the observed rate dependency.

We wish to thank the *Alexander von Humboldt Foundation* for supporting this investigation.

Experimental

Melting points were determined on a Lindström apparatus and are uncorrected. – Infrared spectra: Perkin-Elmer 325. – NMR spectra: Varian FT 80 and Jeol FX 90. – 4-Benzylidene-3-methyl-1-phenyl-5-pyrazolone (**1**) was prepared as described[10], the 4-benzylidene-2-phenyl-5-oxazolones (**5**) were prepared according to a procedure for **5a**[11]. – The reactions with $P(NMe_2)_3$ were carried out under argon.

3-Methyl-1-phenyl-4-⟨α-[tris(dimethylamino)phosphonio]benzyl⟩-pyrazol-5-olate (**2**): To a stirred suspension of 1.70 g (6.5 mmol) of **1** in 30 ml of dichloromethane was added 1.05 g (6.5 mmol) of $P(NMe_2)_3$. A clear solution was formed after 15 min at room temp. ^{31}P NMR indicated that the reaction was complete after 48 h. The solvent was then removed and the remaining solid recrystallized from acetonitrile yielding 1.65 g (61%) of **2** cream-colored crystals, m.p. 121–123°C. The solid substance turns red at room temp.

Table 2. $^{13}C\{^1H\}$-[a] and ^{13}C-NMR spectra of the oxazoles **6a–e** and of the zwitterionic pyrazole **2** in $CDCl_3$

δ (Atom) J [Hz]	6a	6c	6d	6e	2
C-2	154.4(dt)	153.4	154.6(t)	154.8	146.4(d)[b]
^4J(PCCNC)	0.7			0.7	7.0
^3J(CCCN)	4.8		4.4		
C-4	122.9(dd)	122.3(d)	122.4(dd)	122.4(d)	86.9(d)
^2J(PCC)	7.3	7.0	7.3	7.3	4.8
^2J(CCH)	7.0		7.0		
C-5	152.9(do)	152.1(d)	153.0(do)	153.2(d)	164.2(d)
^3J(PCCC)	10.6	10.6	10.3	10.3	4.0
^3J(CCCH)	4.0		3.7		
^3J(CNCH)	4.0		3.7		
2-C_i	127.7(t)	128.1	131.9[c]	127.7	141.8[d]
^3J(CCCH)	6.6				
2-C_o	125.1(ddd)	126.8	125.1(ddd)	125.3	118.2[d]
^1J(CH)	161.2		160.8		
^3J(CCCH)	7.7		6.0		
^3J(CCCH)	6.2		5.0		
2-C_m	128.0(ddd)	127.2	128.1(dtd)	128.3	127.9[d]
^1J(CH)	161.9		163.8		
^2J(CCH)	1.5		2.2		
^3J(CCCH)	6.6		5.9		
2-C_p	128.9(dt)	128.0	129.1(dt)	129.2	121.2[d]
^1J(CH)	160.8		161.2		
^3J(CCCH)	7.0		7.2		
4-CH	42.4(ddt)	40.3(d)	41.8(ddt)	42.1(d)	40.5(d)
^1J(PC)	109.5	110.7	110.0	109.5	101.1
^1J(CH)	122.0		123.1		
^3J(CCCH)	4.0		3.5		
R-C_i	136.8(ddt)	127.8(d)	135.5(ddt)	136.2(d)	136.7(d)
^3J(PCC)	4.8	5.1	4.4	4.8	2.2
^2J(CCH)	7.0		7.3		
^3J(CCCH)	7.5		7.7		
R-C_o	129.2(ddqd)	129.3(d)	130.6(dddd)	131.1(d)	129.0(d)
^3J(PCCC)	5.1	5.5	5.1	5.5	5.5
^1J(CH)	159.0		162.3		
^3J(CCCH)	7.3		7.0		
^3J(CCCH)	5.5		5.5		
R-C_m	127.5(dddd)	112.1	127.6(ddd)	130.7(d)	128.1(d)
^4J(PCCCC)	1.8			1.8	2.2
^1J(CH)	159.0		164.9		
^2J(CCH)	1.5		1.8		
^3J(CCCH)	7.0		5.9		
R-C_p	126.0(ddt)	157.0(d)	132.0[c]	120.3(d)	126.6(d)
^5J(PCCCCC)	2.6	2.2		3.3	2.9
^1J(CH)	160.1				
^3J(CCCH)	7.3				
Me		53.6[e]			14.0[f]
5-NMe	42.5(dqq)	41.4(d)	42.5(dqq)	42.7(d)	
^5J(PCCCNC)	1.5	1.1	1.1	1.1	
^1J(CH)	136.3		136,3		
^3J(CNCH)	4.4		4.4		
P-NMe	36.6(dqq)	35.6(d)	36.7(dqq)	36.9(d)	37.9(d)
^2J(PNC)	3.7	3.3	3.7	3.7	2.6
^1J(CH)	136.7		137.0		
^3J(CNCH)	4.0		4.0		
P-NMe	36.0(dqq)	35.0(d)	36.0(dqq)	36.1(d)	
^2J(PNC)	2.6	2.6	2.2	2.6	
^1J(CH)	134.1		136.7		
^3J(CNCH)	4.4		4.4		

[a] **6b**: 43.0 [d, ^5J(PCCCNC) = 1.5, 5-NMe], 37.1 [d, ^2J(PNC) = 3.7, P–NMe], 36.6 [d, ^2J(PNC) = 2.9, P–NMe]. – [b] C-3, ^3J(PCCC). – [c] Coupling not resolved due to overlapping. – [d] 1-Ph. – [e] 4-OMe of R. – [f] 5-Me.

within a few days; ^1H NMR indicates that is decomposes to a complex mixture.

2-Aryl-4-⟨α-[bis(dimethylamino)phosphoryl]benzyl⟩-5-dimethylaminooxazoles **6**: To a stirred suspension of 9.0 mmol of **5a–e** in 40 ml of dichloromethane was added 1.46 g (9.0 mmol) of $P(NMe_2)_3$. A clear dark solution resulted after ca. 15 min. As monitored by the ^{31}P-NMR signal of $P(NMe_2)_3$ the reaction was complete after less than 12 h in the case of **6d, e**, after 24 h in the case of **6a**, and almost complete after 96 h in the case of **6c**. After removing the

solvent under reduced pressure the solid residue was recrystallized from acetonitrile. – **6b, e** were not obtained in pure form.

6a: Crude yield 3.12 g (78%), colorless crystals, m.p. 139–141°C. – IR (KBr): ν = 1205 cm^{-1}.

$C_{22}H_{29}N_4O_2P$ (412.5)	Calcd.	C 64.06	H 7.09	N 13.58
	Found	C 63.75	H 7.19	N 14.02

6d: Crude yield 3.75 g (93%), colorless crystals, m.p. 136–138°C. – IR (KBr): ν = 1190 cm^{-1}.

$C_{22}H_{28}ClN_4O_2P$ (446.9)	Calcd.	C 59.13	H 6.31	N 12.54
	Found	C 58.95	H 6.45	N 12.61

6e: Crude yield 3.98 g (90%), pale yellow crystals, m.p. 128 to 130°C.

$C_{22}H_{28}BrN_4O_2P$ (491.4)	Calcd.	C 53.78	H 5.74	N 11.40
	Found	C 53.59	H 5.93	N 11.25

When **5a** in dichloromethane was stirred with the equivalent amount of $P(OMe)_3$ for 48 h at room temp., no change was observed in the ^{31}P NMR and **5a** was recovered unchanged.

Methylation of **6d**: To a solution of **6d** in $CDCl_3$ an excess of Me_2SO_4 was added. The NMR spectra, recorded after 30 min, showed **7d** to be the only product.

CAS Registry Numbers

1: 23901-60-2 / **2**: 116149-61-2 / **5a**: 842-74-0 / **5b**: 82309-33-9 / **5c**: 5429-22-1 / **5d**: 15601-44-2 / **5e**: 20345-16-8 / **6a**: 116149-62-3 / **6b**: 116149-63-4 / **6c**: 116149-64-5 / **6d**: 116149-65-6 / **6e**: 116149-66-7 / **7d**: 116149-68-9 / **7d** [P(V)]: 116149-69-0 / $P(NMe_2)_3$: 1608-26-0 / $P(OMe)_3$: 121-45-9

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