5-Oxazolones, IV[1]

Reactions of 5(4*H*)-Oxazolones with Triphenylphosphonium Methylides

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The Wittig reaction of ethyl (triphenylphosphoranylidene)acetate (2a) with the carbonyl group of trisubstituted 5(4*H*)-oxazolones 1a–c afforded ethyl 5(4*H*)-oxazolylideneacetates 3a–c and triphenylphosphane oxide. Starting from oxazolones 1d–i and ylide 2a, methyleneoxazoles 3d,e and ethyl 5-oxazoleacetates 4a–f were obtained besides ylides 5a–e deriving from the nucleophilic attack of the ylide at 1 and subsequent opening of the oxazole ring. Oxazolones 1a–c reacted also with triphenylphosphonium phenylmethylide (2b) to yield methyleneoxazoles 3f,g and ylides 5f–h. By treating triphenylphosphonium methylide (2c) and -methoxymethylide (2d) with 1a–c only open-chain compounds 5i–k and 5l–n, respectively, were obtained.

5-Oxazolone, IV[1]. – Reaktionen von 5(4*H*)-Oxazolonen mit Triphenylphosphonium-methyliden

Durch Wittig-Reaktion von (Triphenylphosphoranyliden)essigsäure-ethylester (2a) mit der Carbonylgruppe von trisubstituierten 5(4*H*)-Oxazolonen 1a–c werden 5(4*H*)-Oxazolylidenessigsäure-ethylester 3a–c und Triphenylphosphanoxid erhalten. Aus den Oxazolonen 1d–i und Ylid 2a bilden sich Methylenoxazole 3d,e und 5-Oxazolessigsäure-ethylester 4a–f neben Yliden 5a–e, die durch nucleophilen Angriff des Ylids auf 1 und nachfolgende Öffnung des Oxazolrings entstehen. Die Oxazolone 1a–c reagieren auch mit Triphenylphosphonium-phenylmethylid unter Bildung der Methylenoxazole 3f,g und Ylide 5f–h. Durch Umsetzung von Triphenylphosphonium-methylid (2c) und -methoxymethylid (2d) mit 1a–c wurden ausschließlich die offenkettigen Verbindungen 5i–k bzw. 5l–n erhalten.

The lactone group of 5(4*H*)-oxazolones is known to have a remarkable reactivity towards nucleophiles[2]. As a part of our continuing research program entailing the study of the reactions of oxazolones with the aim both to found entries to other heterocyclic systems and to develop synthetic pathways to classes of compounds of potential pharmacological interest, we have investigated the reactions of several substituted 5(4*H*)-oxazolones with triphenylphosphonium methylides.

5(4*H*)-Oxazolones **1a–c** were treated with an excess of ethyl (triphenylphosphoranylidene)acetate (**2a**) in refluxing anisol. The reaction took several hours to completion and ethyl 5(4*H*)-oxazolylideneacetates **3a–c** were produced with satisfactory yields. The reaction was too slow for practical use when attempted in lower boiling reaction solvents. However, when oxazolone **1d** was treated with **2a** a greater reactivity was qualitatively observed, allowing to perform the reaction in boiling benzene instead of anisol. After a reaction time of about 2 h a mixture of three products was obtained in which the expected oxazole **3d** was present in moderate yield besides a greater amount both of its isomerization product, i.e. 5-oxazolylacetate **4a**, and of ylide compound **5a**. Similarly, when starting from **1e** and **2a** compounds **3e**, **4b**, and **5b** were formed. However, in this particular case, **3e** could not be isolated as a pure substance, but was identified by ^{1}H NMR in a mixture with **4b**. In the case of products obtained from oxazolones **1f–h** the aromatization of the alkylidene product is clearly more easy owing to the presence of the phenyl substituent on C-4. Accordingly, only the oxazole derivatives **4c–e** were obtained. From the reaction mixtures obtained from **1g** and **1h** with ylide **2a** a substantial amount of open-chain ylides **5c,d** was also isolated besides the oxazole products. **1i** behaved similarly yielding both the 4-unsubstituted oxazole **4f** and the corresponding ylide **5e** on reaction with **2a**. Somewhat surprisingly compound **1f** reacted with **2a** to produce only the oxazole **4c**. No ylide compound could be found.

It is worth to note that other conjugation-stabilized phosphonium methylides such as triphenylphosphonium benzoylmethylide and ethyl 2-(triphenylphosphoranylidene)-propionate did not react appreciably with substrates **1a,c,f** and were not investigated further.

Starting from **1a,c** and **2b** (which was produced in situ from benzyltriphenylphosphonium chloride and phenyllithium) **3f,g** and the corresponding ylide products **5f,h** were obtained, respectively. Ylide **5g** was formed as the sole reaction product when **1b** was treated with **2b**. A similar behaviour was found by treating oxazolones **1a–c** with triphenylphosphonium methylide (**2c**) and triphenylphosphonium methoxymethylide (**2d**): only open-chain products **5i–k** and **5l–n**, respectively, were formed. Substrates **1d–i** did not react with **2b–d** even under more severe conditions.

The structure of all products **3–5** was confirmed by analytical and spectroscopic data. As far as compounds **3a–e** are concerned, an IR absorption at about 1690–1720 cm^{-1} is a good evidence of the presence of the conjugated ester group. In the ^{1}H-NMR spectrum of **3a–g** a typical signal associated with the –CH= group is present in the δ = 5.2–5.8 region and the ^{13}C-NMR spectrum shows the res-

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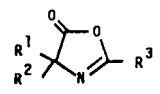

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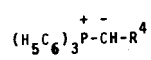
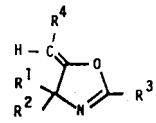


2

	R^1	R^2	R^3
1a	C_6H_5	C_6H_5	C_6H_4-OCH_3-4
b	C_6H_5	CH_3	C_6H_5
c	CH_3	CH_3	C_6H_5
d	CH_3	H	C_6H_5
e	$CH(CH_3)_2$	H	C_6H_5
f	C_6H_5	H	C_6H_4-OCH_3-4
g	C_6H_4-Cl-4	H	C_6H_5
h	C_6H_4-CH_3-4	H	C_6H_4-Cl-4
i	H	H	C_6H_5

	R^4
2a	$COOC_2H_5$
b	C_6H_5
c	H
d	OCH_3



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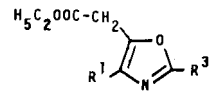
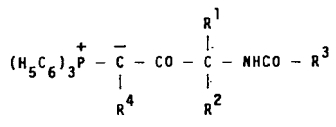


4

	R^1	R^2	R^3	R^4
3a	C_6H_5	C_6H_5	C_6H_4-OCH_3-4	$COOC_2H_5$
b	C_6H_5	CH_3	C_6H_5	$COOC_2H_5$
c	CH_3	CH_3	C_6H_5	$COOC_2H_5$
d	CH_3	H	C_6H_5	$COOC_2H_5$
e	$CH(CH_3)_2$	H	C_6H_5	$COOC_2H_5$
f	C_6H_5	C_6H_5	C_6H_4-OCH_3-4	C_6H_5
g	CH_3	CH_3	C_6H_5	C_6H_5

	R^1	R^3
4a	CH_3	C_6H_5
b	$CH(CH_3)_2$	C_6H_5
c	C_6H_5	C_6H_4-OCH_3-4
d	C_6H_4-Cl-4	C_6H_5
e	C_6H_4-CH_3-4	C_6H_4-Cl-4
f	H	C_6H_5



5

	R^1	R^2	R^3	R^4
5a	CH_3	H	C_6H_5	$COOC_2H_5$
b	$CH(CH_3)_2$	H	C_6H_5	$COOC_2H_5$
c	C_6H_4-Cl-4	H	C_6H_5	$COOC_2H_5$
d	C_6H_4-CH_3-4	H	C_6H_4-Cl-4	$COOC_2H_5$
e	H	H	C_6H_5	$COOC_2H_5$
f	C_6H_5	C_6H_5	C_6H_4-OCH_3-4	C_6H_5
g	C_6H_5	CH_3	C_6H_5	C_6H_5
h	CH_3	CH_3	C_6H_5	C_6H_5
i	C_6H_5	C_6H_5	C_6H_4-OCH_3-4	H
j	C_6H_5	CH_3	C_6H_5	H
k	CH_3	CH_3	C_6H_5	H
l	C_6H_5	C_6H_5	C_6H_4-OCH_3-4	OCH_3
m	C_6H_5	CH_3	C_6H_5	OCH_3
n	CH_3	CH_3	C_6H_5	OCH_3

onances associated with C-5 and C-α around δ = 164–167 and 91–106, respectively. To the exocyclic double bond the *Z* configuration was assigned mainly considering the positive NOE effect (8.5–10%) in the ^{1}H-NMR spectrum between the signal associated with the H atom on the double bond and the CH_3 signal in compounds **3b** and **3g**.

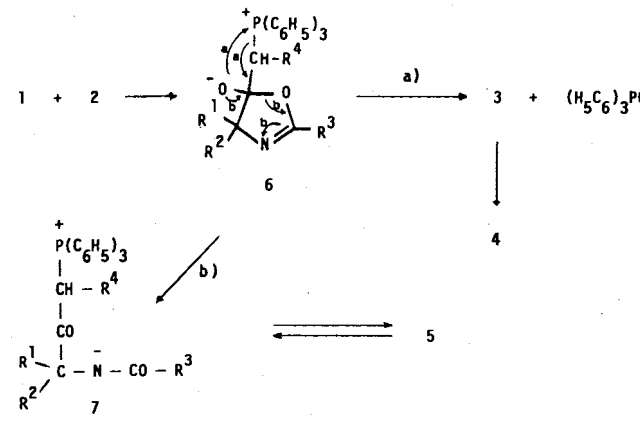
Compounds **5** show a broad carbonyl absorption (1670–1645 cm^{-1}) and an NH absorption at 3400–3200 cm^{-1}, which is confirmed by a signal at δ = 7.0–9.5 in the ^{1}H-NMR spectrum typical of aromatic amides. Expectedly, in the case of compounds **5i–k** the signal associated with the ylide H atom in the ^{1}H-NMR spectrum appears as a high-field[3] doublet ($J_{P,H}$ = 23–24 Hz), this atom being exchangeable with D_2O[4].

Discussion

Although the above results show that in many cases the lactone carbonyl group of 5(4*H*)-oxazolones is satisfactorily reactive with respect to phosphonium ylides, some limitations should be noticed. The more important failures of the reaction were with triphenylphosphonium benzylmethylide and with ethyl 2-(triphenylphosphoranylidene)propionate. In the former case the known low reactivity of the ylide[5] can explain the result; in the second case steric hindrance is most probably responsible for the low reactivity. Also it is to be noted that negative results were obtained when oxazolones **1d–i** were treated with ylides more basic than **2a**. These ylides can deprotonate the oxazolone substrate at C-4 to a great extent thus lowering the reactivity of the carbonyl group.

Scheme 1 depicts the suggested mechanism of the reaction of oxazolones and phosphonium ylides.

Scheme 1



For the zwitterionic intermediate **6** two reaction pathways are open: according to a) triphenylphosphane oxide is eliminated producing compounds **3** which, if R^2 = H, show a trend to isomerize to the more stable aromatic oxazole **4**[6]. Indeed this isomerization process could be verified by following (NMR) the conversion of **3d** into **4a** in $CDCl_3$ solution and in the presence of a catalytical amount of pyridine. According to the path b) intermediate **6** rearranges to **7** through cleavage of the dihydrooxazole ring. The zwitterion **7** is in equilibrium with the isolated ylide form **5**. From the data thus far available an effect of the reaction temperature seems to exist with respect to the competition between pathways a) and b). In fact, path a) was observed in the case of substrates **1a–c** which were mandatorily treated at the high temperature of refluxing anisol with **2a** since lower

temperatures proved to be insuitable. In all other cases, where the lower thermal stability of the 4-H-substituted oxazolone substrate[8] (**1d–i**) or of the ylide[9] obliged to use a lower reaction temperature, which was permitted by the greater reactivity of the carbonyl group, both reaction pathways were observed. A confirmation was obtained by performing the reaction of **1d** with **2a** in refluxing dichloromethane instead of benzene: only compound **5a** was produced, as expected. Moreover, when **1b** was treated with ylide **2b** at higher temperature, i.e. in refluxing anisol, a small amount (about 5%) of the corresponding product **3** could be identified in the crude reaction mixture by ^{1}H NMR.

Evidence was found that path b) can be reversed at least partially and in particular cases. Indeed, by heating **5f** in refluxing toluene for several days, a mixture of **3f** and of **1a** was slowly formed. However, this reversibility cannot explain the prevailing of pathway a) at higher temperatures through a shifting of the equilibrium between **5** and **6**, since the reverse reaction appears to be too slow (several days against about 2 h which are required for the formation of **5f** from their precursors). Moreover, most of differently substituted compounds **5** remained practically unaffected when heated in anisol for long times.

The authors are grateful to Dr. *B. Gioia* for MS analyses.

Experimental

Melting points: Uncorrected, Büchi 150 (capillary) apparatus. – IR spectra: Perkin-Elmer 197 spectrophotometer. – ^{1}H-NMR spectra: $(CH_3)_4Si$ as internal standard in the solvent indicated; Varian EM 360 (for compounds **3** and **4**) and Bruker AC 200 (for compounds **5**) instruments. – ^{13}C-NMR spectra: 50.327 MHz, $(CH_3)_4Si$ as internal standard; Bruker AC 200 intrument. – ^{31}P-NMR spectra: 81.015 MHz, H_3PO_4 in D_2O as external standard; Bruker AC 200 instrument. – TLC: Ready-to-use silica gel plates with dichloromethane and ethyl ether as solvents. – Column chromatography: silica gel, petroleum ether (p.e. 40–60°C) as eluent,

Table 1. Preparation, physical and analytical data of compounds **3–5**

Starting Compounds	Reaction Solvent	Products	Yield[a] (%)	M.p.(°C)	Recryst. Solvent	Empirical Formula	M.w.	Calcd. (Found) C		H		N	
1a **2a**	anisol	**3a**	67	124-126	$CHCl_3/iPr_2O$	$C_{26}H_{23}NO_4$	413.4	75.53	(75.10)	5.61	(5.37)	3.39	(3.57)
1b **2a**	anisol	**3b**	62	63-64	$CHCl_3/iPr_2O$	$C_{20}H_{19}NO_3$	321.4	74.72	(74.75)	5.96	(6.05)	4.36	(4.27)
1c **2a**	anisol	**3c**	77	78	$CHCl_3/iPr_2O$	$C_{15}H_{17}NO_3$	259.3	69.47	(69.34)	6.61	(6.49)	5.40	(5.27)
1d **2a**	benzene	**3d**	b)	57	n-pentane	$C_{14}H_{15}NO_3$	245.2	68.57	(68.18)	6.17	(6.22)	5.71	(5.54)
		4a	57	oil[c]	-	$C_{14}H_{15}NO_3$	-	-	(68.84)	-	(6.09)	-	(6.02)
		5a	13	166	$CHCl_3/iPr_2O$	$C_{32}H_{30}NO_4P$	523.5	73.41	(73.01)	5.77	(5.80)	2.67	(2.57)
1e **2a**	benzene	**3e**	4[d]	-	-	$C_{16}H_{19}NO_3$	273.3	-	(-)	-	(-)	-	(-)
		4b	36[d]	71-72	Et_2O/n-pentane	$C_{16}H_{19}NO_3$	-	70.30	(69.97)	7.01	(7.03)	5.12	(5.04)
		5b	21	157-160	CH_2Cl_2/iPr_2O	$C_{34}H_{34}NO_4P$	551.6	74.03	(73.86)	6.21	(6.19)	2.54	(2.34)
1f **2a**	toluene	**4c**	67	57-59	iPr_2O	$C_{20}H_{19}NO_4$	337.4	71.20	(71.58)	5.68	(5.73)	4.15	(4.47)
1g **2a**	toluene	**4d**	29	110	Et_2O/n-pentane	$C_{19}H_{16}ClNO_3$	341.8	66.76	(66.40)	4.72	(4.54)	4.10	(4.03)
		5c	8	96-98	Et_2O/iPr_2O	$C_{37}H_{31}ClNO_4P$	620.0	71.67	(71.30)	5.04	(5.09)	2.26	(2.35)
1h **2a**	toluene	**4e**	27	96-97	iPr_2O	$C_{20}H_{18}ClNO_3$	355.8	67.51	(67.43)	5.06	(4.98)	3.94	(3.68)
		5d	11	145	Et_2O	$C_{38}H_{33}ClNO_4P$	634.1	71.97	(71.86)	5.25	(5.07)	2.21	(1.94)
1i **2a**	benzene	**4f**	37	46	n-pentane	$C_{13}H_{13}NO_3$	231.2	67.52	(67.14)	5.67	(5.90)	6.06	(5.91)
		5e	29	185	CH_2Cl_2/iPr_2O	$C_{31}H_{28}NO_4P$	509.5	73.07	(72.82)	5.54	(5.81)	2.75	(2.52)
1a **2b**	toluene	**3f**	22	165-166	Et_2O/n-pentane	$C_{29}H_{23}NO_2$	417.5	83.43	(83.53)	5.55	(5.69)	3.37	(3.42)
		5f	58	216-217(dec.)	CH_2Cl_2/iPr_2O	$C_{47}H_{38}NO_3P$	695.7	81.13	(80.93)	5.50	(5.37)	2.01	(2.05)
1b **2b**	toluene	**5g**	94	225-230(dec.)	$CHCl_3$ (hot)	$C_{41}H_{34}NO_2P$	603.7	81.57	(81.43)	5.68	(5.46)	2.32	(2.01)
1c **2b**	toluene	**3g**	23	98	Et_2O/n-pentane	$C_{18}H_{17}NO$	263.3	82.10	(81.94)	6.51	(6.67)	5.32	(5.31)
		5h	32	205	CH_2Cl_2/iPr_2O	$C_{36}H_{32}NO_2P$	541.6	79.83	(79.57)	5.95	(5.78)	2.59	(2.27)
1a **2c**	toluene	**5i**	46	240 (dec.)	CH_2Cl_2/iPr_2O	$C_{41}H_{34}NO_3P$	619.7	79.46	(79.10)	5.53	(5.23)	2.26	(2.46)
1b **2c**	toluene	**5j**	41	185	$CHCl_3/iPr_2O$	$C_{35}H_{30}NO_2P$	527.6	79.77	(79.62)	5.73	(5.81)	2.65	(2.81)
1c **2c**	toluene	**5k**	71	200	CH_2Cl_2/iPr_2O	$C_{30}H_{28}NO_2P$	465.5	77.40	(77.01)	6.06	(6.03)	3.01	(2.68)
1a **2d**	toluene	**5l**	44	205 (dec.)	$CHCl_3/iPr_2O$	$C_{42}H_{36}NO_4P$	649.7	77.64	(77.31)	5.58	(5.72)	2.16	(1.98)
1b **2d**	toluene	**5m**	22	175-177	CH_2Cl_2/Et_2O	$C_{36}H_{32}NO_3P$	557.6	77.54	(77.16)	5.78	(5.64)	2.51	(2.18)
1c **2d**	toluene	**5n**	54	127	CH_2Cl_2/iPr_2O	$C_{31}H_{30}NO_3P$	495.5	75.13	(74.90)	6.10	(6.09)	2.82	(2.41)

[a] Yields are not optimized. They are referred to **1**. – [b] Compound **3d** has been isolated only in one case (10%): In fact **3d** isomerizes quickly to **4a** in basic conditions, preventing its isolation in most cases. – [c] Isolated from *n*-pentane at –20°C as low-melting solid. – [d] Yield calculated on the mixture of **3e** and **4b**. On purification only pure **4b** could be obtained.

which is gradually mixed with ethyl ether. – MS: Varian MAT 311-A instrument.

5(4*H*)-Oxazolones **1b**[10], **1c**[11], **1d**[12], **1e**[13], **1f**[11], **1i**[14] are known compounds. Ylide **2a** is a commercial product. Ylides **2b**[15], **2c**[16], **2d**[17] are prepared as described in the literature.

2-(4-Methoxyphenyl)-4,4-diphenyl-5(4H)-oxazolone (**1a**) is prepared starting from 2,2-diphenylglycine and 4-methoxybenzoyl chloride as described for the synthesis of 2,2,4-triphenyl-5(4*H*)-oxazolone[18]. Yield 81%, m.p. 145°C. – IR (nujol): 1800 cm^{-1} (C=O), 1650 (C=N). – ^1H NMR ($CDCl_3$): δ = 3.9 (s, 3H, OCH_3), 6.8–8.2 (m, 14H, Aryl H).

$C_{22}H_{17}NO_3$ (343.4) Calcd. C 76.95 H 4.99 N 4.08
Found C 76.51 H 4.86 N 3.97

4-(4-Chlorophenyl)-2-phenyl-5(4H)-oxazolone (**1g**): *N*-Benzoyl-2-(4-chlorophenyl)glycine is prepared by the Schotten-Baumann method from 2-(4-chlorophenyl)glycine[19] and benzoyl chloride: yield 57%, m.p. 180–181°C. – IR (nujol): 3340 cm^{-1} (NH), 1730, 1630 (C=O). – ^1H NMR (DMSO): δ = 5.7 (d, *J* = 7 Hz, 1H, CH), 7.3–8.1 (m, 9H, Aryl H), 9.1 (d, *J* = 7 Hz, 1H, NH). – The acylated glycine (5.0 g, 17 mmol) is suspended in Ac_2O (10 ml) under nitrogen and the suspension stirred at room temperature for 4 h. The yellow solid is filtered and washed with *n*-pentane yielding 4.4 g (95%); m.p. 150–155°C (dec.). – IR (nujol): 1650 cm^{-1} (mesoionic structure).

2-(4-Chlorophenyl)-4-(4-methylphenyl)-5(4H)-oxazolone (**1h**): *N*-(4-Chlorophenyl)-2-(4-methylphenyl)glycine is prepared by the Schotten-Baumann method from 2-(4-methylphenyl)glycine and 4-chlorobenzoyl chloride: yield 63%; m.p. 220°C. – IR (nujol): 3320 cm^{-1} (NH), 1720, 1620 (C=O). – ^1H NMR (DMSO): δ = 2.2 (s, 3H, CH_3), 5.5 (d, *J* = 7 Hz, 1H, CH), 7.1–8.0 (m, 8H, Aryl H), 9.0 (d, *J* = 7 Hz, 1H, NH). – The acylated glycine (12 g, 40 mmol) is suspended in anhydrous THF (100 ml). A solution of DCCD (8.4 g, 40 mmol) in THF (70 ml) is added dropwise in 10 min, and stirring is continued for 1 h. The solid is filtered and the organic layer is evaporated. The yellow solid is suspended in

Table 2. Spectral data of oxazoles **3** and **4**

Compd.	IR (Nujol; cm^{-1}) C=O	C=C	C=N	^1H NMR (δ) ($CDCl_3$)	^{13}C NMR (δ) ($CDCl_3$)
3a	1690	1670	1640	1.3 (t, J = 8 Hz, 3H, CH_3), 3.9 (s, 3H, OCH_3), 4.3 (q, J = 8 Hz, 2H, CH_2), 5.3 (s, 1H, H-α), 6.9-8.2 (m, 14H, Aryl H)	14.31 (CH_3), 55.39 (OCH_3), 60.06 (OCH_2), 84.62 (C-4), 96.73 (C-α), 160.60 (C-2), 164.39 (C-5), 170.37 (C=O)
3b	1710	1680	1650	1.3 (t, J = 8 Hz, 3H, $CH_2\underline{CH_3}$), 1,9 (s, 3H, CH_3), 4.2 (q, J = 8 Hz, 2H, CH_2), 5.2 (s, 1H, H-α), 7.3-8.2 (m, 10H, Aryl H)	14.34 ($CH_2\underline{CH_3}$), 28.02 (CH_3), 60.00 (OCH_2), 77.30 (C-4 93.16 (C-α), 160.78 (C-2), 164.48 (C-5), 173.17 (C=O)
3c	1700	1680	1650	1.3 (t, J = 8 Hz, 3H, $CH_2\underline{CH_3}$), 1.5 (s, 6H, CH_3), 4.2 (q, J = 8 Hz, 2H, CH_2), 5.2 (s, 1H, H-α), 7.3-8.3 (m, 5H, Aryl H)	14.30 ($CH_2\underline{CH_3}$), 28.7 (CH_3), 59.3 (OCH_2), 72.42 (C-4), 90.63 (C-α), 159.65 (C-2), 164.98 (C-5), 174.47 (C=O)
3d	1720	1670	1660	1.2 (t,J = 8 Hz, 3H, $CH_2\underline{CH_3}$), 1.5 (d, J = 8 Hz, 2H, CH_3), 4.2 (q, J = 8 Hz, 2H, CH_2), 5.3 (qq, J = 8 and 2 Hz, 1H, H-4), 5.7 (d, J = 2 Hz, 1H, H-α), 7.2-8.1 (m, 5H, Aryl H)	14.20 ($CH_2\underline{CH_3}$), 16.77 (CH_3), 59.91 (OCH_2), 66.66 (C-4 94.03 (C-α), 160.12 (C-2), 166.60 (C-5), 171.81 (C=O)
3e	1720	1660	1640	1.1-1.4 (m, 9H, $CH(\underline{CH_3})_2$, $CH_2\underline{CH_3}$), 2.0-2.6 (m, 1H, $\underline{CH}(CH_3)_2$) 4.2 (q, J = 8 Hz, 2H, CH_2), 5.1-5.4 (m, 1H, H-4), 5.8 (d, J = 2 Hz, 1H H-α), 7.2-8.1 (m, 5H, Aryl H)	a)
3f		1680	1640	3.7 (s, 3H, OCH_3), 5.5 (s, 1H, C-α), 6.7-8.1 (m, 19H, Aryl H)	55.61 (OCH_3), 76.82 (C-4), 106.34 (C-α), 156.98, 162.89 (C-5 and C-2)
3g		1680	1650	1.5 (s, 6H, CH_3), 5.5 (s, 1H, C-α), 7.1-8.3 (m, 10H, Aryl H)	29.89 (CH_3), 70.83 (C-4), 99.33 (C-α), 154.37, 160.68 (C-5 and C-2)

a) Compound **3e** is obtained only in a mixture with **4b**

Compd.	IR (Nujol; cm^{-1}) C=O	^1H NMR (δ) ($CDCl_3$)
4a	1740	1.2 (t, J = 8 Hz, 3H, $CH_2\underline{CH_3}$), 2.15 (s, 3H, CH_3), 3.7 (s, 2H, CH_2-α), 4.2 (q, J = 8 Hz, 2H, CH_2), 7.3-8.2 (m, 5H, Aryl H)
4b	1730	1.1-1.4 (m, 9H,$CH(\underline{CH_3})_2$, $CH_2\underline{CH_3}$), 2.5-3.2 (sept, J = 8 Hz, 1H,CH), 3.7 (s, 2H, CH_2-α), 4.2 (q, J = 8 Hz, 2H, CH_2), 7.2 8.2 (m, 5H, Aryl H)
4c	1740	1.3 (t, J = 8 Hz, 3H, CH_3), 3.8, 3.q (two s, 5H, CH_2- , OCH_3), 4.2 (q, J = 8 Hz, 2H, CH_2), 6.8-8.1 (m, 9H, Aryl H)
4d	1730	1.2 (t, J = 8 Hz, 3H, CH_3), 3.8 (s, 2H, CH_2-α), 4.2 (q, J = 8 Hz, 2H, CH_2), 7.2-8.2 (m, 9H, Aryl H)
4e	1740	1.3 (t, J = 8 Hz, 3H, $CH_2\underline{CH_3}$), 2.4 (s, 3H, CH_3), 3.9 (s, 2H, CH_2-α), 4.2 (q, J = 8 Hz, 2H, CH_2), 7.1-8.2 (m, 8H, Aryl H)
4f	1740	1.2 (t, J = 8 Hz, 3H, CH_3), 3.7 (s, 2H, CH_2-α), 4.2 (q, J = 8 Hz, 2H, CH_2), 7.0 (s, 1H, H-4), 7.2-8.2 (m, 5H, Aryl H)

hot 2-propanol and filtered. Yield 76%; m.p. 164–165°C. – IR (nujol): 1660 cm^{-1} (mesoionic structure).

$C_{16}H_{12}ClNO_2$ (285.7) Calcd. C 67.27 H 4.20 N 4.90
Found C 66.18 H 4.33 N 5.01

Reaction of 5(4H)-Oxazolones **1a–c** *with Ethyl (Triphenylphosphoranylidene)acetate* (**2a**). – *General Procedure:* A solution of **1** (10 mmol) in anisol (50 ml) is refluxed. The ylide **2a** (12–13 mmol) is added in several portions in about 15 h until compound **1** disappears (TLC analysis). Anisol is evaporated, and the crude mixture is chromatographed. Reaction data are given in Table 1, spectroscopic data in Table 2.

Reaction of 5(4H)-Oxazolones **1d–i** *with Ethyl (Triphenylphosphoranylidene)acetate* (**2a**). – *General Procedure:* A mixture of **1** (10 mmol) and **2a** (20 mmol) is added to boiling toluene or benzene (50 ml) (as indicated in Table 1) in several portions in about 1 h, and then the mixture is refluxed for 30 min. After solvent evaporation the crude mixture is chromatographed. Reaction data are given in Table 1, spectroscopical data in Tables 2 and 3.

Reaction of 5(4H)-Oxazolones **1a–c** *with Ylides* **2b–d**. – *General Procedure:* The reaction is performed in a three-necked flask with magnetical stirrer, nitrogen inlet, and reflux condenser connected by a rubber tube to a two-necked flask with magnetical stirrer. In this flask the ylide reactant (11 mmol of **2a**, 15 mmol of **2c**, 15 mmol of **2d**) is prepared by treating the appropriate triphenylphosphonium halide in toluene suspension (20 ml) with 10% excess of phenyllithium (2 M solution in benzene/ethyl ether 70:30). The ylide solution is then added in several aliquots (by lifting and inclining the two-necked container) to a boiling toluene (30 ml) solution of the oxazolone compound (10 mmol) contained in the three-necked reactor. The addition is generally made in about 60–90 min, and stirring is continued for a further 30 min when the reaction is complete (TLC). After solvent evaporation the residue is taken up with dichloromethane (40 ml), and the organic layer is washed with water (40 ml), dried with Na_2SO_4, and evaporated under reduced pressure. The crude mixture is chromatographed. Reaction data are given in Table 1, spectroscopical data in Tables 2 and 3.

Table 3. Spectral data of phosphonium ylides **5**

Compd.	IR (Nujol; cm^{-1}) NH	C=O	^1H NMR (δ) ($CDCl_3$)[a]	^{31}P NMR (δ) ($CDCl_3$)
5a	3420	1660	0.51 (t,J = 7.1 Hz, 3H, $CH_2\underline{CH_3}$), 1.43 (d, J = 7 Hz, 3H, CH_3), 3.40-3.64 (m, 2H, CH_2), 5.60-5.75 (m, 1H, CH), 7.35-7.85 (m, 20H, Aryl H), 8.02 (d, J = 7.8 Hz, 1H, NH)	18.45
5b	3340	1660	0.81 (t, J = 7.2 Hz, 3H, $CH_2\underline{CH_3}$), 1.13 (d, J = 6.8 Hz, 6H, $CH(\underline{CH_3})_2$), 2.40-2.60 (m, 1H, $\underline{CH}(CH_3)_2$), 3.77-3.87 (m, 2H, CH_2), 5.93 (dd, J = 8.0 and 3.0 Hz, 1H, CH), 7.20 (d, J = 8.0 Hz, 1H, NH), 7.26-7.78 (m, 20H, Aryl H)	18.7
5c	3420	1670	0.54 (t, J = 7.0 Hz, 3H, CH_3), 3.50-3.65 (m, 2H, CH_2), 7.05 (d, J = 7.8 Hz, 1H, CH), 7.21-8.12 (m, 24H, Aryl H), 8.32 (d, J = 7.8 Hz, 1H, NH)	18.5
5d	3340	1665	0.51 (t, J = 7.1 Hz, 3H, $CH_2\underline{CH_3}$), 2.35 (s, 3H, CH_3), 3.45-3.59 (m, 2H, CH_2), 7.03 (d, J = 7.8 Hz, 1H, CH), 7.15-7.85 (m, 23H, Aryl H) 8.35 (d, J = 7.8 Hz, 1H, NH)	18.4
5e	3300	1645	0.82 (t, J = 7.1 Hz, 3H, $CH_2\underline{CH_3}$), 3.78-3.89 (m, 3H, OCH_3), 4.82 (s, CH_2), 7.26-7.80 (m, 21H, Aryl H and NH)	18.4
5f	3240	1660	3.76 (s, 3H, OCH_3), 6.15-7.66 (m, 34H, Aryl H), 9.45 (s, 1H, NH)	18.5
5g	3300	1650	2.08 (s, 3H, CH_3), 5.81-7.79 (m, 30H, Aryl H), 9.39 (s, 1H, NH)	18.6
5h	3320	1650	1.70 (s, 6H, CH_3), 6.93-7.74 (m, 35H, Aryl H), 8.58 (s, 1H, NH)	18.2
5i	3330	1670	3.60 (d, $J_{(P-H)}$ = 23.6 Hz, 1H, CH), 3.79 (s, 3H, OCH_3), 6.81-7.87 (m, 29H, Aryl H), 9.28 (s, 1H, NH)	17.0
5j	3320	1660	2.28 (s, 3H, CH_3), 3.52 (d, $J_{(P-H)}$ = 23.5 Hz, 1H, CH), 7.15-8.00 (m, 25H, Aryl H), 9.22 (s, 1H, NH)	18.6
5k	3300	1650	1.65 (s, 6H, CH_3), 3.88 (d, $J_{(P-H)}$ = 23.9 Hz, 1H, CH), 7.40-7.72 (m, 20H, Aryl H), 8.48 (s, 1H, NH)	17.9
5l	3260	1660	2.12 (s, 3H, $COCH_3$), 3.79 (s, 3H, OCH_3), 6.79-7.83 (m, 29H, Aryl H), 9.41 (s, 1H, NH)	13.4
5m	3370	1660	2.00 (s, 3H, CH_3), 2.37 (s, 3H, OCH_3), 7.10-8.00 (m, 25H, Aryl H), 9.28 (s, 1H, NH)	13.47
5n	3300	1660	2.00 (s, 6H, CH_3), 3.10 (s, 3H, OCH_3), 7.20-8.00 (m, 20H, Aryl H), 8.65 (s, 1H, NH)	12.8

[a] DMSO for compounds **5a**, **5c**, **5d**, **5k**.

Appendix: ^{13}C NMR (δ) ($CDCl_3$): **5b** = 14.00, 16.46 ($CH(\underline{CH_3})_2$), 21.09 ($CH_2\underline{CH_3}$), 33.08 ($\underline{CH}(CH_3)_2$), 58.88 (d, $J_{(P-C)}$ = 8.03 Hz, CO-$\underline{C}$-N), 59.02 (OCH_2), 70.52 (d, $J_{(P-C)}$ = 109.96 Hz, C=P), 166.90 (d, $J_{(P-C)}$ = 11.48 Hz, C=O), 167.20 (NC=O), 194.12 (d, $J_{(P-C)}$ = 3.9 Hz, $\underline{C}OOC_2H_5$). **5d** = 14.00 (CH_3), 21.38 ($CH_2\underline{CH_3}$), 58.00 (d, $J_{(P-C)}$ = 9.0 Hz, CO-$\underline{C}$-N), 58.90 ($\underline{CH_2}CH_3$), 70.00 (d, $J_{(P-C)}$ = 110.5 Hz, C=P), 164.53 (NC=O), 166.56 (d, $J_{(P-C)}$ = 14.2 Hz, C=O), 191.23 ($\underline{C}OOC_2H_5$). **5g** : 21.23 (CH_3), 62.02 (d, $J_{(P-C)}$ = 12.8 Hz, CO-$\underline{C}$-N), 69.80 (d, $J_{(P-C)}$ = 107.1 Hz, C=P), 164.07 (NC=O), 186.06 (d, $J_{P-C)}$ = Hz 5.22, C=O). **5i**: 52.51 (d, $J_{(P-C)}$ = 112.0 Hz, C=P), 55.41 (OCH_3), 71.58 ($J_{(P-C)}$ = 14.6 Hz, CO-$\underline{C}$-N), 163.01 (d, $J_{(P-C)}$ = 11.3 Hz, C=O), 186.77 (NC=O). **5j**: 23.10 (CH_3), 49.00 (d, $J_{(P-C)}$ = 113.2 Hz, C=P), 63.15 (d, $J_{(P-C)}$ = 14.6 Hz, CO-$\underline{C}$-N), 164.85 (NC=O), 186.77 (C=O). **5m**: 20.09 (CH_3), 61.65 (d, $J_{(P-C)}$ = 11.3 Hz, CO-$\underline{C}$-N) 62.85 (OCH_3), 99.22 (d, $J_{(P-C)}$ = 129.2 Hz, C=P), 164.30 (NC=O), 183.93 (d, $J_{(P-C)}$ = 28.2 Hz, C=O).**5n**: 23.74 (CH_3), 58.36 (d, $J_{(P-C)}$ = 11 Hz, CO-$\underline{C}$-N), 65.08 (OCH_3), 100.34 (d, $J_{(P-C)}$ = 130 Hz, C=P), 165.48 (NC=O), 185.5 (d, $J_{(P-C)}$ = 26.2 Hz, C=O).

Spectral data:

5c: (FD), m/z = 619(M^+), 375, 245; (EI), m/z = 375 (100), 262 (15). **5d** (FD), m/z = 633(M^+), 375, 258; (EI) m/z = 375(79), 262(22), 139(100). **5i**: (FD), m/z = 619(M^+), 277.

Thermal Cyclization of **5f**: A solution of **5f** (820 mg, 1.2 mmol) in toluene (20 ml) is refluxed for several days until the starting compound disappeares (TLC: ethyl ether). After solvent evaporation the crude mixture is chromatographed yielding two fractions containing oxazolone **1a** and compound **3f**, identified by comparison with an authentical sample (TLC) and by their spectroscopical data (IR, ^{1}H NMR).

CAS Registry Numbers

1a: 114564-96-4 / **1b**: 95885-53-3 / **1c**: 7563-05-5 / **1d**: 13302-43-7 / **1e**: 5839-93-0 / **1f**: 28182-58-9 / **1g**: 114564-97-5 / **1h**: 114564-98-6 / **1i**: 1199-01-5 / **2a**: 1099-45-2 / **2b**: 16121-45-2 / **2c**: 3487-44-3 / **2d**: 20763-19-3 / **3a**: 114564-70-4 / **3b**: 114564-71-5 / **3c**: 114564-72-6 / **3d**: 114564-73-7 / **3e**: 114564-76-0 / **3f**: 114564-85-1 / **3g**: 114564-88-4 / **4a**: 114564-74-8 / **4b**: 114564-77-1 / **4c**: 114564-79-3 / **4d**: 114581-53-2 / **4e**: 114564-81-7 / **4f**: 114564-83-9 / **5a**: 114564-75-9 / **5b**: 114564-78-2 / **5c**: 114564-80-6 / **5d**: 114564-82-8 / **5e**: 114564-84-0 / **5f**: 114564-86-2 / **5g**: 114564-87-3 / **5h**: 114564-89-5 / **5i**: 114564-90-8 / **5j**: 114564-91-9 / **5k**: 114564-92-0 / **5l**: 114564-93-1 / **5m**: 114564-94-2 / **5n**: 114564-95-3 / 2,2-diphenylglycine: 3060-50-2 / 4-methoxybenzoyl chloride: 100-07-2 / 2-(4-chlorophenyl)glycine: 6212-33-5 / benzoyl chloride: 98-88-4 / *N*-benzoyl-2-(4-chlorophenyl)glycine: 56674-27-2 / *N*-(4-chlorophenyl)-2-(4-methylphenyl)glycine: 73842-45-2 / 2-(4-methylphenyl)glycine: 13227-01-5 / 4-chlorobenzoylchloride: 122-01-0

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[51/88]