SYNTHESES AND STRUCTURE ELUCIDATION OF DIMETHYLAMINOVINYL SUBSTITUTED 1,3-OXAZINES AND PYRAZOLO[3,4-*d*][3,1]OXAZINE DERIVATIVES

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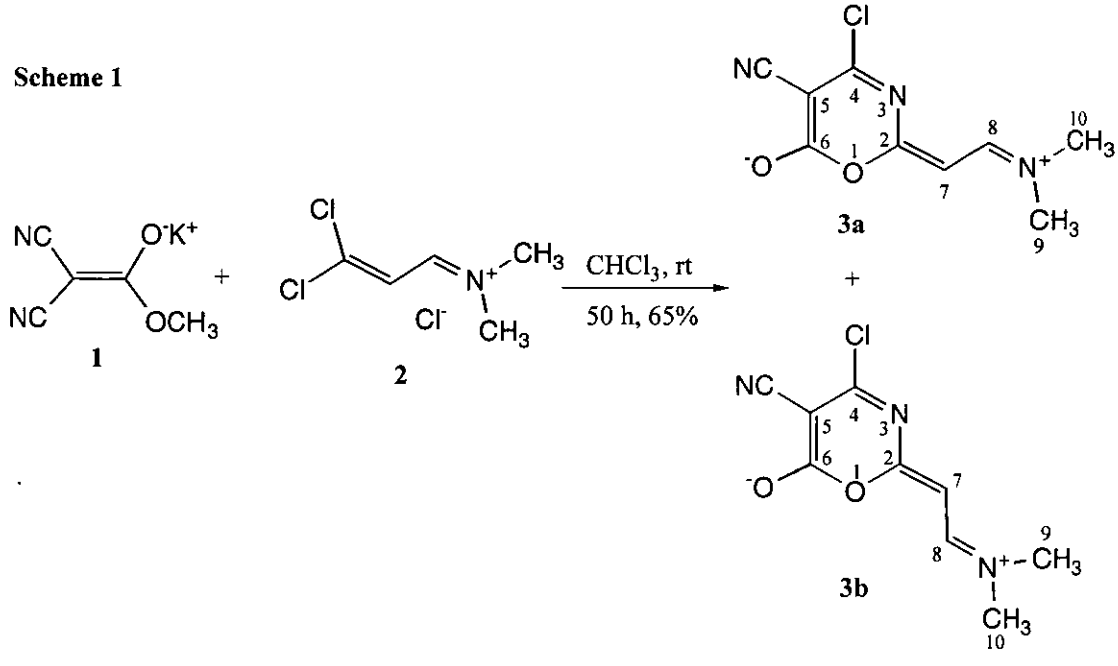
Dedicated on the 80th birthday of Professor Dr., Dr. h.c. Gerhard Fritz, Institut für Anorganische Chemie der Universität Karlsruhe (TH) with best wishes

Abstract - Potassium methyl dicyanoacetate (**1**) reacted with (3,3-dichloro-2-propenylidene)dimethylammonium chloride (**2**) to yield a mixture (1:1) of *E*- and *Z*-4-chloro-5-cyano-2-(*N,N*-dimethylimmonio)ethyliden-6-oxido-1,3-oxazines (**3**) which reacted further with different amines and arylhydrazines to 1,3-oxazine and pyrazolo[3,4-*d*][3,1]oxazine derivatives respectively. The products exist surprisingly only as *E*- configuration. The structures were elucidated unambiguously with a X-Ray diffraction analysis and NMR experiments.

In continuation of our investigation about reactions of alkyl dicyanoacetates and their salts,[1-11] which had previously been seldom used in organic syntheses in spite of their ready availability, we found that potassium methyl dicyanoacetate (**1**) reacted smoothly in chloroform at room temperature with (3,3-dichloro-2-propenylidene)dimethylammonium chloride (**2**), a new kind of iminium salts synthesized by Schroth *et al.*,[12,13] to give 4-chloro-5-cyano-2-(*N,N*-dimethylimmonio)ethylidene-6-oxido-1,3-oxazine (**3**) in 65% yield (Scheme 1).

Scheme 1



NMR experiments verified that the product (**3**) existed as a zwitterionic tautomer mixture with *E*- (**3a**) and *Z*- (**3b**) configurations. Thus, in the ^{1}H-NMR spectrum of **3**, the signals for the two CH-groups in the side chain were registered altogether as four doublets two for each. To be exact, the two in deep field at δ= 7.93 and 8.19 ppm are due to H-8 while the other two at δ= 4.97 and 5.07 ppm to H-7. These indicated the existence of tautomers of **3a** and **3b**. On the other hand, the four singlets for the dimethylamino group at 3.07, 3.08, 3.34 and 3.36 ppm are also consistent with the above-mentioned opinion. Furthermore, the evident of chemical shift difference between δ= 3.07, 3.08 ppm and δ= 3.34, 3.36 ppm suggested strongly the zwitterionic structure of **3**.

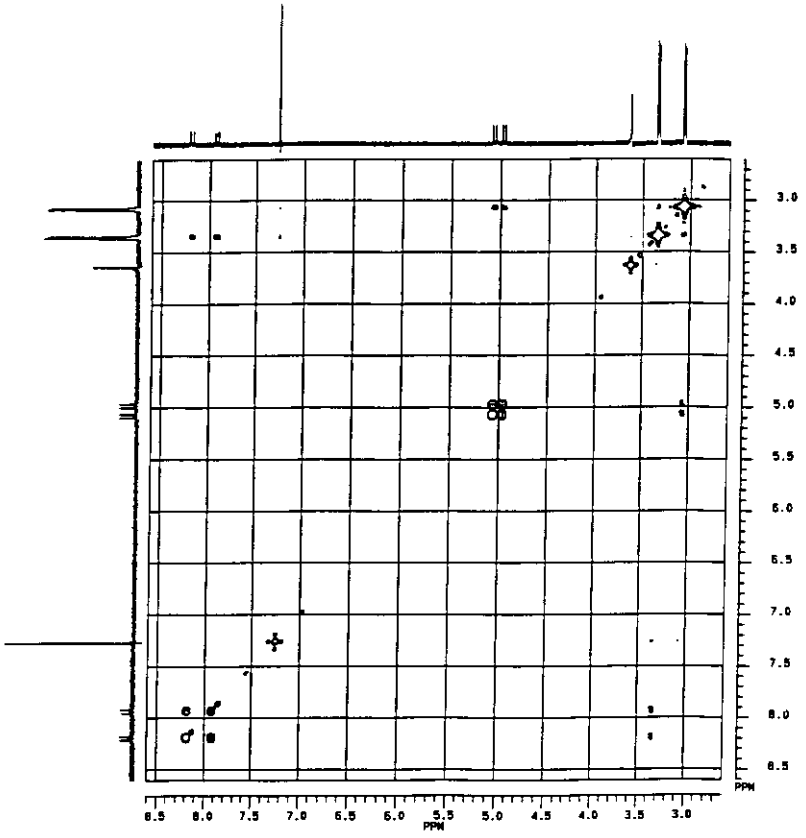


Figure 1. ^{1}H-NOESY spectrum of **3** (360.14 MHz, $CDCl_3$, 303K)

In order to correctly assign the signals, ^{1}H-NOESY and ^{1}H-COSY experiments of **3** were carried out. In the ^{1}H-NOESY spectrum (see Figure 1), the nOe between H-8 (δ= 7.93 and 8.19 ppm) and the signals of the methyl group at δ= 3.34 and 3.36 ppm indicates that the H-8 neighbors this methyl group and therefore the two signals at δ= 3.34 and 3.36 ppm must be assigned to the $NC^{10}\mathbf{H}_3$ group. On the other hand as expected, an other nOe between H-7 (δ= 4.97 and 5.07 ppm) and the signals of the other methyl group ($NC^{9}\mathbf{H}_3$) at δ= 3.07 and 3.08 ppm was registered. In consideration of oxygen possessing a higher electronegativity than nitrogen, the two dubletts at δ= 4.97 and 8.19 ppm should be assigned to the *Z*-structure (**3b**) while the other two at δ= 5.07 and 7.93 ppm to the *E*-structure (**3a**).

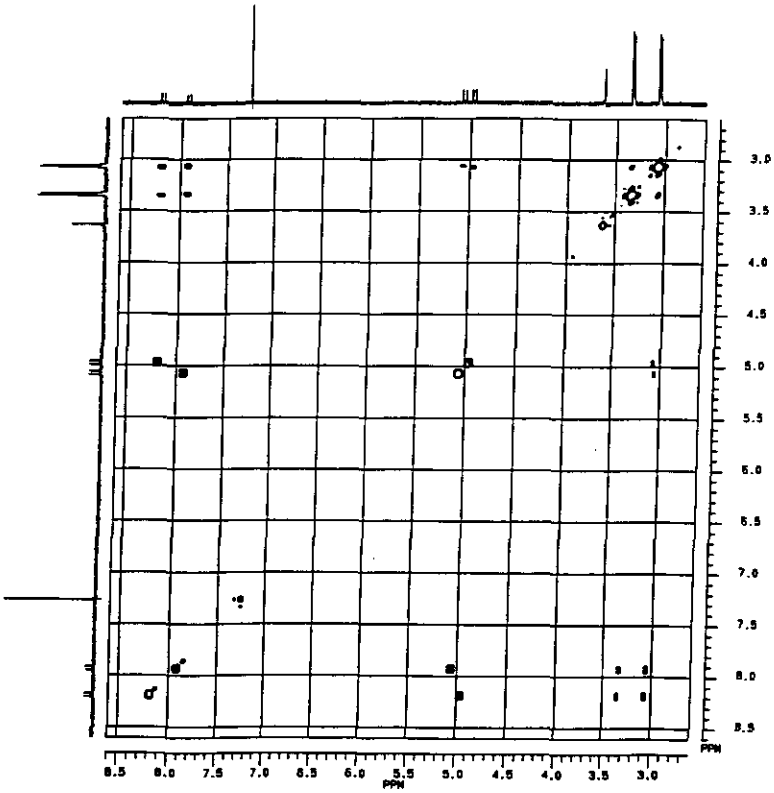
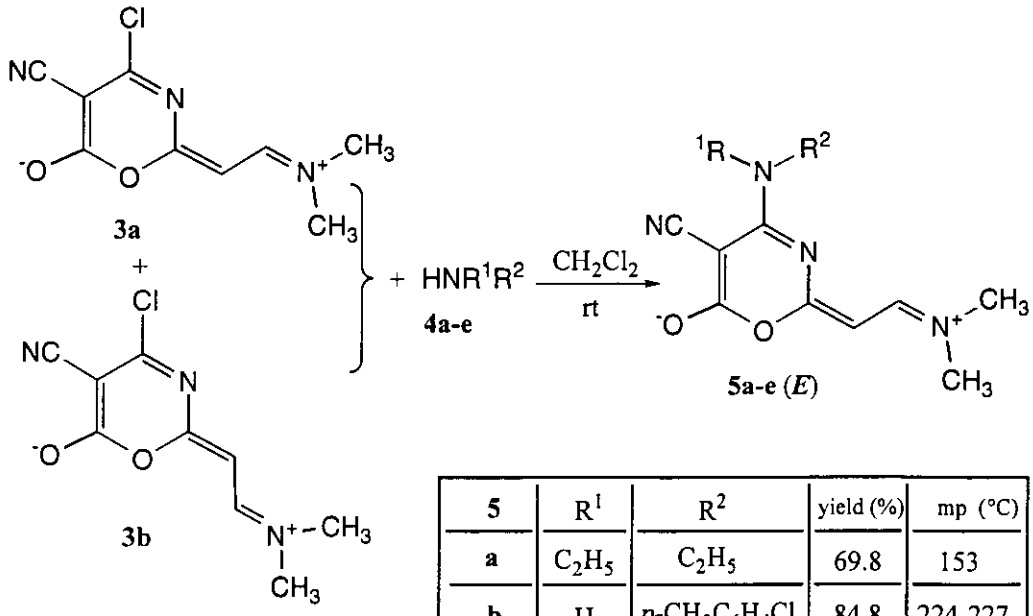


Figure 2. ^{1}H-COSY spectrum of **3** (360.14 MHz, $CDCl_3$, 303K)

As shown in ^{1}H-COSY spectrum of **3** (Figure 2), the H-7 at δ= 4.79 ppm coupled with the methyl group at δ= 3.08 ppm as well as the H-8 at δ= 8.19 ppm. This H-8 (8.19 ppm) coupled furthermore with the methyl group at δ= 3.36 ppm. In view of these facts, these four signals should be assigned to the *Z*-structure (**3b**). On the other hand, the H-7 at δ= 5.07 ppm coupled with methyl group at δ= 3.07 ppm and the H-8 at δ= 7.93 ppm. This H-8 (7.93 ppm) coupled with the methyl group at δ= 3.34 ppm as well. Therefore these four signals are due to the *E*-structure (**3a**). In a word, the signals of H-8 at δ= 8.19 ppm , H-7 at 4.79 ppm, $C^{10}\mathbf{H}_3$ at 3.36 ppm and $C^{9}\mathbf{H}_3$ at 3.08 ppm belong to the *Z*-structure (**3b**), while the signals of H-8 at 7.93 ppm , H-7 at 5.07 ppm , $C^{10}\mathbf{H}_3$ at 3.34 ppm and $C^{9}\mathbf{H}_3$ at 3.07 ppm to the *E*-structure (**3a**). According to intensities of the signals, the proportion between **3a** and **3b** is about 1:1. The relative great difference of the chemical shifts of $C^{9}\mathbf{H}_3$ and $C^{10}\mathbf{H}_3$ groups suggested strongly the zwitterionic structure.

The chloro atom in **3** can be easily substituted by nucleophilic reagents, such as amines. Thus, amines (**4a-e**) reacted with **3** readily at room temperature to **5a-e** in satisfactory yields (see Scheme 2). Unexpectedly, **5a-e** were isolated only as *E*-configuration without exeption, eventhough the starting compound (**3**) consists of *E*- (**3a**) and *Z*- (**3b**) tautomers

Scheme 2



5	R^1	R^2	yield (%)	mp (°C)
a	C_2H_5	C_2H_5	69.8	153
b	H	*p*-$CH_2C_6H_4Cl$	84.8	224-227
c	H	*m*-$CH_2C_6H_4Cl$	45.5	231-234
d	H	*p*-$C_6H_4OCH_3$	24.0	>230
e	H	$N(CH_3)_2$	26.9	198-201

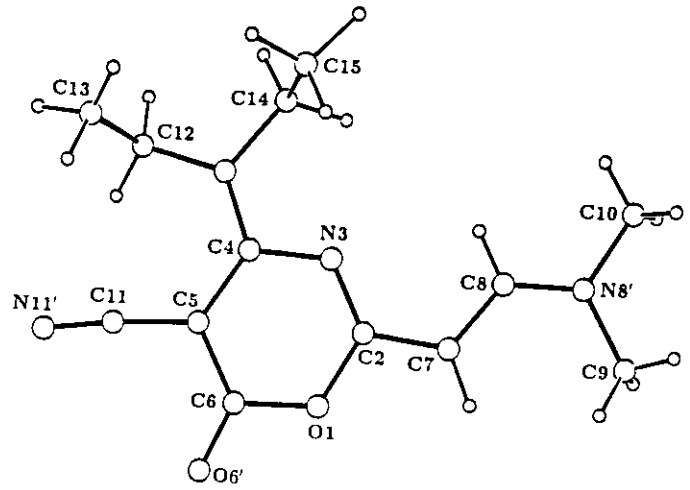
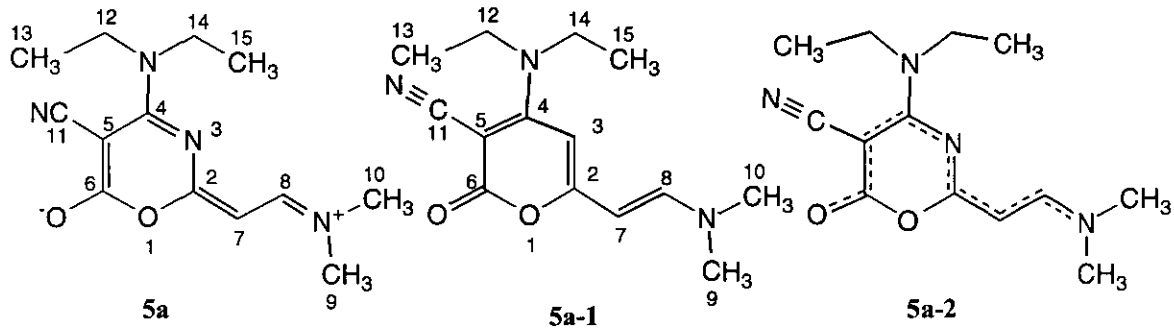


Figure 3. X-Ray structure of **5a**



5a **5a-1** **5a-2**

Table 1. Some important bond distances messured for **5a** and expected for **5a-1**

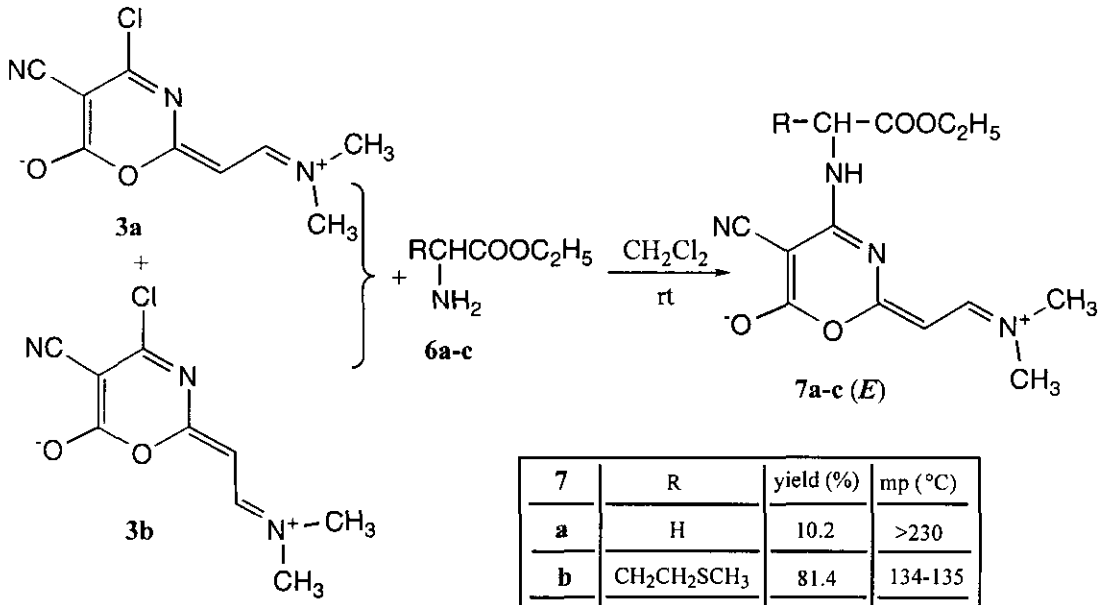
	bond distance (Å)			bond distance (Å)	
	5a (measured)	**5a-1** (from lit.,[14])		**5a** (measured)	**5a-1** (from lit.,[14])
C8-N8′	1.321(4)	1.355	C5-C6	1.422(4)	1.465
C7-C8	1.363(4)	1.312	C6-O6′	1.215(4)	1.205
C2-C7	1.412(5)	1.455	C6-O1	1.376(4)	1.339
C2-N3	1.291(4)	1.279	C5-C11	1.418(5)	1.427
N3-C4	1.352(5)	1.372	C11-N11′	1.130(6)	1.136
C4-C5	1.424(4)	1.369			

The structure of the products was confirmed unambiguously with X-Ray diffraction analysis besides the corresponding NMR data. The X-Ray structure of **5a**[15] (Figure 3) shows clearly that it possesses a *E*-configuration. In Table 1 the important bond distances measured for **5a** are summarized in the first column. Nearby are the expected values for the structure (**5a-1**) according to the literature.[14] The measured bond distances of C8-N8′, C2-C7, N3-C4 and C5-C6 in the first column are all obviously shorter than those of the corresponding typical single bonds given in the second column respectively. On the other hand, the measured bond distances of C7-C8, C2-N3, C4-C5 and C6-O6′are obviously longer than the expected typical double bonds. Therefore the structure of compound (**5a**) exists as a mesomeric equilibrium and would be best drawn as **5a-2**. Considering the zwitterionic structure suggested by ^{1}H-NMR determination of the product in which two separated singulets were registered at δ= 2.92 and 3.20 ppm for $C^9\mathbf{H}_3$ and $C^{10}\mathbf{H}_3$ respectively, we described it finally as **5a**. The C5-C11 bond distance measured as 1.418 (5)Å is consistent with a C_{sp1}-C_{sp2} single bond length reported in literature (1.427Å).[14] While the distance of *C11-N11′ [1.130(6)Å] tallies with that of a nitrile triple bond length* (1.136Å).[14] The relative great difference between the distance messured for C6-O1 [1.376 (4)Å] and a C_{sp2}-O bond length of typical δ-lactone (1.339Å)[14] indicates that **5a** does not possess a δ-lactone structure, which is consistent with the above-mentioned zwitterionic structure opinion.

Similarly reacted α-amino acid esters (**6a-c**) with **3** at room temperature and afforded corresponding 6-

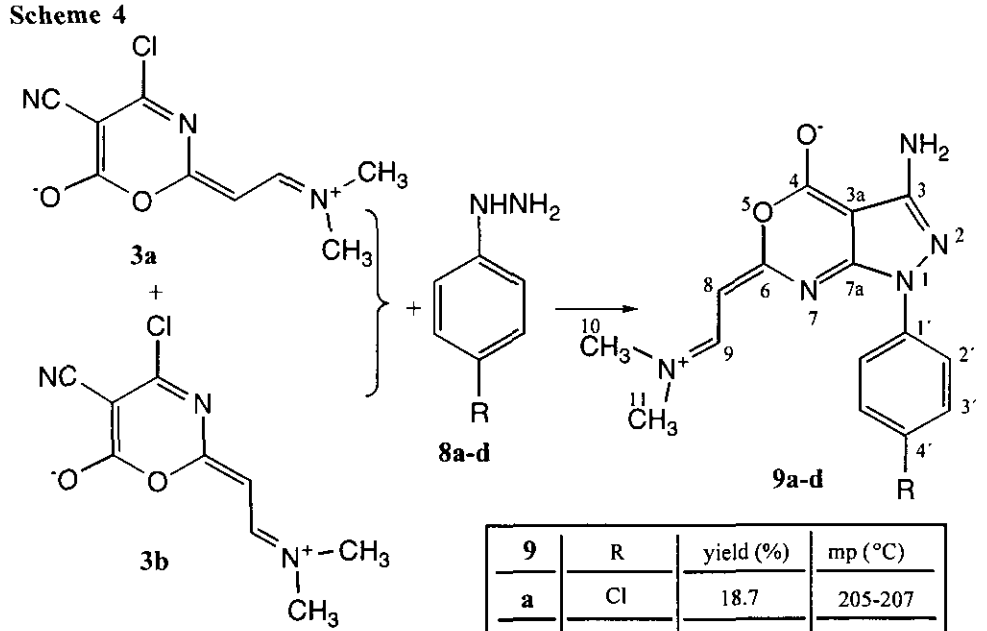
oxido-1,3-oxazines (**7a-c**) (Scheme 3). NMR data confirmed that the products (**7a-c**) existed also only as *E*-configuration.

Scheme 3



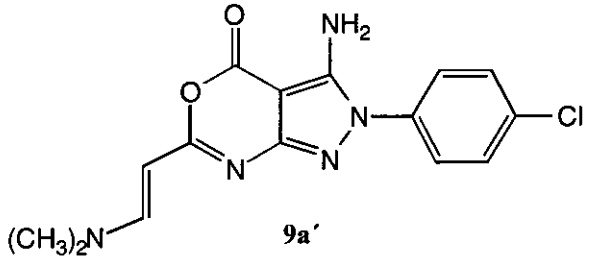
7	R	yield (%)	mp (°C)
a	H	10.2	>230
b	$CH_2CH_2SCH_3$	81.4	134-135
c	*p*-$CH_2C_6H_4OH$	62.9	193-196

Scheme 4



9	R	yield (%)	mp (°C)
a	Cl	18.7	205-207
b	OCH_3	43.4	231-234
c	CH_3	34.7	227-230
d	H	36.0	205

Besides we have found that **3** reacted in chloroform at room temperature with phenylhydrazine derivatives (**8a-d**) to yield the fused heterocyclic 3-amino-1-aryl-6-(*N,N*-dimethylimmonio)ethylidene-4-oxidopyrazolo[3,4-*d*][3,1]oxazines (**9a-d**) respectively (Scheme 4). NMR data indicate that **9a-d** possess *E*-structures. The aryl groups appear on N-1 position, since in the ^{1}H-NOESY spectrum of **9a** no nOe was observed between the amino group (δ= 4.60 ppm) and H-2′(δ= 7.37 ppm), eventhough **9a′** can theoretically also be formed through attack of N-2 of *p*-chlorophenylhydrazine on C-4 and the following nucleophilic addition of N-1 to the cyano group.



9a′

EXPERIMENTAL

Melting points were determined on a Reichert hot stage microscope and are uncorrected. IR spectra were measured with a Perkin-Elmer spectrophotometer 283 using potassium bromide and are given as cm^{-1}. UV spectra were recorded on a spectrophotometer Varian CARY 50 Scan and ^{1}H- and ^{13}C-NMR spectra on either a Bruker WM-250 (^{1}H-NMR: 250.13 MHz, ^{13}C-NMR: 62.89 MHz), Bruker WM-360 (^{1}H-NMR: 360.14 MHz, ^{13}C-NMR: 90.56 MHz) or a Varian XL 300 (^{1}H-NMR: 299.95 MHz, ^{13}C-NMR: 75.43 MHz) spectrometer in DMSO-d_6 or $CDCl_3$. The chemical shifts are reported in parts per million (ppm) downfield from internal tetramethylsilane. Electron impact MS spetra were obtained on a Varian MAT 311A instrument. Element analyses were performed on a Heraeus Vario EL CHNS apparatus.

(*E*)- and (*Z*)-4-Chloro-5-cyano-2-(*N,N*-dimethylimmonio)ethylidene-6-oxido-1,3-oxazine (3)

A suspension of (3,3-dichloro-2-propenylidene)dimethylammonium chloride (**2**; 2.70 g, 14.0 mmol) and potassium methyl dicyanoacetate (**1**; 2.34 g, 14.0 mmol) in water-free chloroform (150 mL) was stirred at rt for 50 h. The solid residue was filtered and washed with water to give yellow product. The filtrate was concentrated to about 70 mL. After cooling at -20°C a further portion of product was abtained. Recrystallization of the rough product with ethyl acetate gives yellow crystals; yield : 2.05 g (65.0%); mp 203-206°C. IR (KBr): 2218 (CN); 1740 (C=O); 1641, 1576, 1516 (C=C, C=N); 1477; 1432; 1253; 1041; 789. UV (MeCN): λ_{max}(log ε)= 411 (4.722); 273 (4.129); 203 (4.181). ^{1}H-NMR (360.14 MHz, $CDCl_3$): δ= 3.07 (s, 3/2H, H-9(**a**)); 3.08 (s, 3/2H, H-9(**b**)); 3.34 (s, 3/2H, H-10(**a**)); 3.36 (s, 3/2H, H-10(**b**)); 4.97 (d, J= 12.0 Hz, 1/2H, H-7(**b**)); 5.07 (d, J= 12.4 Hz, 1/2H, H-7(**a**)); 7.93 (d, J= 12.4 HZ, 1/2H, H-8(**a**)); 8.19 (d, J= 12.0 Hz, 1/2H, H-8(**b**)). ^{13}C-NMR (90.56 MHz, DMF, D_2O-Cap): δ= 37.8, 38.0, 45.8, 45.9 (4-, 4s, C-9, C-10); 80.1, 81.1 (2+, 2s, C-5); 86.6, 87.2 (2-, 2s, C-7); 114.2, 114.4 (2+, 2s,

CN); 156.7, 157.2 (2+, 2s, C-4); 158.4, 160.1 (2-, 2s, C-8); 163.5, 164.4 (2+, 2s, C-6); 167.0, 168.7 (2+, 2s, C-2). MS m/z (%): $[M+2]^+$: 227 (3); M^+: 225 (9); 98 (100); 55 (21); 42 (31). HRMS: Cacd for $C_9H_8N_3O_2Cl$: 226.1067. Found: 226.1068. *Anal.* Calcd for $C_9H_8N_3O_2Cl$: C, 47.91; H, 3.57; N, 18.62. Found: C, 47.71; H, 3.79; N, 18.32.

General procedure for preparation of 5a-e and 7a-c:

To a suspension of 4-chloro-5-cyano-2-(*N,N*-dimethylimmonio)ethylidene-6-oxido-1,3-oxazine (**3**; 0.12 g, 0.5 mmol) in water-free dichlormethane (20 mL) was a solution of amines (**4a-e**) (5 mmol) or α-amino acid esters (**6a-c**) (5 mmol), which were set free from their corresponding hydrochlorides with $Ba(OH)_2$,[16] in water-free dichloromethane (20 mL) dropped during 30 min. The mixture was stirred at rt for 1-5 d. After removement of the solvent under reduced pressure, the residue was chromatographed on a silica column (70-230 mesh) using ethyl acetate as eluent to give the corresponding products (**5a-e**) and (**7a-c**). The products were then recrystallized with ethyl acetate.

(*E*)-5-Cyano-4-diethylamino-2-(*N,N*-dimethylimmonio)ethylidene-6-oxido-1,3-oxazine (5a) 69.8%. mp 153°C. IR (KBr): 2978 (C-H); 2196 (CN); 1704 (C=O); 1639, 1542 (C=C, C=N); 1464; 1436; 1414; 1362; 1261; 1109; 775. UV (MeCN): λ_{max}(log ε)= 363 (4.073); 256 (4.004); 225 (4.217). ^{1}H-NMR (360.14 MHz, DMSO-d_6): δ= 1.19 (t, J= 7.0 Hz, 6H, 2xCH_2**C**H_3); 2.92 (s, 3H, H-9), 3.20 (s, 3H, H-10), 3.69 (q, J= 7.0 Hz, 4H, 2x**C**H_2CH_3); 4.77 (d, J= 12.5 Hz, 1H, H-7); 7.85 (br d, J= 11.4 Hz, 1H, H-8). ^{13}C-NMR (90.56 MHz, DMSO-d_6): δ= 13.8 (-, s, 2xCH_2**C**H_3); 37.2, 45.1 (2-, 2s, C-9, C-10); 43.7 (+, s, 2x**C**H_2CH_3); 59.4 (+, s, C-5), 84.2 (-, br s, C-7); 118.2 (+, s, **C**N); 154.9 (-, br s, C-8); 161.0 (+, s, C-4). MS m/z (%): $[M+1]^+$: 263 (2); M^+: 262 (12); 98 (100); 55 (5); 42 (6). HRMS: Cacd for $C_{13}H_{18}N_4O_2$: 262.1431. Found: 262.1432. *Anal.* Calcd for $C_{13}H_{18}N_4O_2$: C, 59.53; H, 6.92; N, 21.36. Found: C, 59.75; H, 7.14; N, 21.05.

(*E*)-4-(*p*-Chlorobenzyl)amino-5-cyano-2-(*N,N*-dimethylimmonio)ethylidene-6-oxido-1,3-oxazine (5b) 84.8%. mp 224-227 °C. IR (KBr): 3302; 2924; 2205 (CN); 1729 (C=O); 1629, 1553, 1494 (C=C, C=N); 1392; 1247; 790. UV (MeCN): λ_{max}(log ε)= 367 (4.693); 293 (4.021); 255 (3.992); 218 (4.437). ^{1}H-NMR (250.13 MHz, DMSO-d_6): δ= 2.91 (s, 3H, H-9); 3.20 (s, 3H, H-10); 4.58 (d, J= 6.5 Hz, 2H, NHCH_2); 4.81 (d, J= 12.3 Hz, 1H, H-7); 7.30-7.40 (m, 4H, $H_{arom.}$); 7.90 (br, 1H, H-8); 8.50 (t, J= 4.9 Hz, 1H, N**H**). ^{13}C-NMR (62.89 MHz, DMSO-d_6): δ= 42.7, 50.5 (2-, 2s, C-9, C-10); 45.8 (+, s, NH**C**H_2); 64.9 (+, s, C-5); 121.7 (+, s, **C**N); 133.5 (-, s, C-3′); 134.6 (-, s, C-2′); 136.8 (+, s, C-4′); 143.7 (+, s, C-1′); 159.0 (-, br, C-8); 164.7 (+, s, C-6); 168.0 (+, br, C-2). MS m/z (%): $[M+2]^+$: 332 (8); M^+: 330 (22); 127 (5); 125 (15); 98 (100); 55 (16); 42 (17). *Anal.* Calcd for $C_{16}H_{15}N_4O_2Cl$: C, 58.10; H, 4.57; N, 16.94. Found: C, 58.18; H, 4.56; N, 16.67.

(*E*)-4-(*m*-Chlorobenzyl)amino-5-cyano-2-(*N,N*-dimethylimmonio)ethylidene-6-oxido-1,3-oxazine (5c) 45.5%. mp 231-234 °C. IR (KBr): 3310; 2936; 2199 (CN); 1723 (C=O); 1636, 1583, 1553, 1494 (C=C, C=N); 1392; 1255; 783. UV (MeCN): λ_{max}(log ε)= 367 (4.723); 294 (4.004); 256 (3.936); 216 (4.490). ^{1}H-NMR (360.14 MHz, DMSO-d_6): δ= 2.93 (s, 3H, H-9); 3.23 (s, 3H, H-10); 4.61 (d, J= 5.5

Hz, 2H, NHC**H**$_2$); 4.82 (d, J= 12.3 Hz, 1H, H-7); 7.30-7.39 (m, 4H, H$_{arom.}$); 7.94 (br, 1H, H-8); 8.50 (t, J= 5.2 Hz, 1H, N**H**). ^{13}C-NMR (62.89 MHz, DMSO-d$_6$): δ= 37.4, 45.3 (2-, 2s, C-9, C-10); 43.7 (+, s, NH**C**H$_2$); 59.7 (+, s, C-5); 84.0 (-, br, C-7); 116.5 (+, s, **C**N); 126.1 (-, s, C-5′); 126.9 (-, s, C-4′); 130.3 (-, s, C-6′); 132.9 (+, s, C-3′); 142.3 (+, br, C-1′); 156.8 (-, br, C-8); 159.6 (+, s, C-6). MS m/z (%): [M+2]$^+$: 332 (4); M$^+$: 330 (11); 127 (1); 125 (5); 98 (100); 55 (7); 42 (7). *Anal.* Calcd for $C_{16}H_{15}N_4O_2Cl$: C, 58.10; H, 4.57; N, 16.94. Found: C, 58.16; H, 4.56; N, 16.67.

(*E*)-5-Cyano-2-(*N,N*-dimethylimmonio)ethylidene-4-(*p*-methoxyphenyl)amino-6-oxido-1,3-oxazine (5d) 24.0%. mp >230 °C. IR (KBr): 3245; 2945; 2214 (CN); 1735 (C=O); 1624, 1551, 1482 (C=C, C=N); 1394; 1352; 1253; 787. UV (MeCN): λ$_{max}$(log ε)= 373 (4.731); 257 (4.268); 211 (4.308). ^{1}H-NMR (250.13 MHz, DMSO-d$_6$): δ= 2.92 (s, 3H, H-9); 3.18 (s, 3H, H-10); 3.76 (s, 3H, OC**H**$_3$); 4.78 (d, J= 12.4 Hz, 1H, H-7); 6.92 (d, J= 8.8 Hz, 2H, H-3′); 7.32 (d, J= 8.8 Hz, 2H, C-2′); 7.78 (d, J= 12.4 Hz, 1H, H-8); 10.82 (s, 1H, N**H**). ^{13}C-NMR (62.89 MHz, DMSO-d$_6$): δ= 39.9, 47.1 (2-, 2s, C-9, C-10); 56.9 (-, s, O**C**H$_3$); 62.4 (+, s, C-5); 86.2 (-, s, C-7); 115.2 (-, s, C-3′); 117.7 (+, s, **C**N); 127.9 (-, s, C-2′), 131.9 (+, s, C-1′); 157.4 (-, br, C-8); 158.8 (+, s, C-4); 161.1(+, s, C-6); 163.2 (+, s, C-2). MS m/z (%): [M+1]$^+$: 313 (5); M$^+$: 312 (27); 268 (11); 98 (100); 71 (9); 55 (7); 42 (7). *Anal.* Calcd for $C_{16}H_{16}N_4O_3$: C, 61.53; H, 5.16; N, 17.94. Found: C, 61.52; H, 5.09; N, 17.65.

(*E*)-5-Cyano-2-(*N,N*-dimethylimmonio)ethylidene-4-(*N,N*-dimethylhydrazino)-6-oxido-1,3-oxazine (5e) 26.9%. mp 198-201 °C. IR (KBr): 3217; 2949; 2864; 2209 (CN); 1744 (C=O); 1695, 1636, 1559, 1507 (C=C, C=N); 1409; 1345; 772. UV (MeCN): λ$_{max}$(log ε)= 362 (4.666); 291 (3.960); 256 (3.993); 214 (4.204). ^{1}H-NMR (360.14 MHz, DMSO-d$_6$): δ= 2.90 (s, 3H, H-9); 3.18 (s, 3H, H-10); 4.96 (d, J= 12.0 Hz, 1H, H-7); 7.78 (d, J= 12.5 Hz, 1H, H-8); 9.28 (s, 1H, N**H**). ^{13}C-NMR (90.56 MHz, DMSO-d$_6$): δ= 42.4, 50.2 (2-, 2s, C-9, C-10); 51.7 (-, s, NHN(**C**H$_3$)$_2$); 88.9 (-, s, C-7); 121.3 (+, s, **C**N); 159.7 (-, s, C-8); 165.9 (+, s, C-6); 167.4 (+, s, C-2). MS m/z (%): [M+1]$^+$: 250 (1); M$^+$: 249 (7); 206 (14); 178 (11); 98 (100); 55 (10); 42 (15). *Anal.* Calcd for $C_{11}H_{15}N_5O_2$: C, 53.00; H, 6.07; N, 28.10. Found: C, 53.10; H, 6.05; N, 28.16.

(*E*)-5-Cyano-2-(*N,N*-dimethylimmonio)ethylidene-4-[(2-ethoxy-2-oxoethyl)amino]-6-oxido-1,3-oxazine (7a) 10.2%. mp >230 °C. IR (KBr): 3330; 2957; 2203 (CN); 1742, 1726 (C=O); 1638, 1603, 1553, 1507 (C=C, C=N); 1405; 1261; 782. UV (MeCN): λ$_{max}$(log ε)= 368 (4.723); 292 (3.936); 254 (3.870); 215 (4.362). ^{1}H-NMR (360.14 MHz, DMSO-d$_6$): δ= 1.20 (t, J= 7.1 Hz, 3H, OCH$_2$**C**H$_3$); 2.94 (s, 3H, H-9); 3.22 (s, 3H, H-10); 4.13 (q, J= 7.1 Hz, 2H, OC**H**$_2$CH$_3$); 4.82 (d, J= 12.1 Hz, 1H, H-7); 7.80 (br, 1H, H-8); 8.18 (br s, 1H, N**H**). ^{13}C-NMR (125.77 MHz, DMSO-d$_6$): δ= 14.1 (-, s, OCH$_2$**C**H$_3$); 37.5, 42.8 (2-, 2s, C-9, C-10); 45.4 (+, s, NH**C**H$_2$); 60.6 (+, s, O**C**H$_2$CH$_3$); 83.9 (+, s, C-5); 85.0 (-, s, C-7); 116.3 (+, s, **C**N); 155.5 (+, s, C-4); 157.1 (-, s, C-8); 168.7 (+, s, C-6); 169.5 (+, s, C-2). MS m/z (%): [M+1]$^+$: 293 (2); M$^+$: 292 (14); 98 (100); 55 (5); 42 (6). HRMS: Cacd for $C_{13}H_{16}N_4O_4$: 292.1173. Found: 292.1174. *Anal.* Calcd for $C_{13}H_{16}N_4O_4$: C, 53.42; H, 5.52; N, 19.17. Found: C, 53.24; H, 5.74; N, 18.92.

(*E*)-5-Cyano-2-(*N,N*-dimethylimmonio)ethylidene-4-[(2-ethoxy-1-methylmercaptoethyl-2-oxoethyl)amino]-6-oxido-1,3-oxazine (7b) 81.4%. mp 134-135 °C. IR (KBr): 3313; 2985; 2201 (CN); 1730 (C=O); 1639, 1594, 1560, 1501 (C=C, C=N); 1404; 1274; 785. UV (MeCN): λ_{max}(log ε)= 368 (4.742); 292 (3.953); 256 (3.896); 215 (4.390). ^{1}H-NMR (360.14 MHz, $CDCl_3$): δ= 1.28 (t, J= 7.1 Hz, 3H, OCH_2CH_3); 2.11 (s, 3H, SCH_3); 2.05-2.23 (m, 2H, $CH_3SCH_2CH_2$); 2.57 (br, $CH_3SCH_2CH_2$); 2.95 (s, 3H, H-9); 3.22 (s, 3H, H-10); 4.22 (q, J= 7.1 Hz, 2H, OCH_2CH_3); 4.78 (d, J= 11.0 Hz, 1H, H-7); 4.98 (m, 1H, NHCH); 6.21 (d, J= 7.1 Hz, 1H, NHCH); 7.80, 8.03 (2br, 1H, H-8). ^{13}C-NMR (90.56 MHz, $CDCl_3$): δ= 14.2 (-, s, OCH_2CH_3); 15.5 (-, s, SCH_3); 28.5 (+, br s, $CH_3SCH_2CH_2$); 31.9 (+, s, $CH_3SCH_2CH_2$); 37.5, 45.8 (2-, 2s, C-9, C-10); 53.5 (-, s, NHCH); 61.9 (+, s, OCH_2CH_3); 88.5 (-, br, C-7); 115.7 (+, s, CN); 156.0 (-, br, C-8); 165.0 (+, br, C-6); 168.0 (+, br, C-2); 172.5 (+, s, COO). MS m/z (%): $[M+1]^+$: 367 (1); M^+: 366 (5); 292 (10); 98 (100); 61 (7); 55 (6); 42 (7). *Anal.* Calcd for $C_{16}H_{22}N_4O_4S$: C, 52.44; H, 6.05; N, 15.29; S, 8.75. Found: C, 52.47; H, 6.28; N, 15.10; S, 8.72.

(*E*)-5-Cyano-2-(*N,N*-dimethylimmonio)ethylidene-4-{[2-ethoxy-1-(*p*-hydroxyphenyl)-2-oxoethyl]-amino}-6-oxido-1,3-oxazine (7c) 62.9%. mp 193-196 °C. IR (KBr): 3311; 2937; 2208 (CN); 1734, 1690 (C=O); 1637, 1590, 1506 (C=C, C=N); 1412; 1269; 1221. UV (MeCN): λ_{max}(log ε)= 369 (4.724); 286 (4.067); 217 (4.441). ^{1}H-NMR (360.14 MHz, DMSO-d_6): δ= 1.54 (t, J= 7.1 Hz, 3H, OCH_2CH_3); 2.93 (s, 3H, H-9); 3.22 (s, 3H, H-10); 4.11 (q, J= 7.1 Hz, 2H, OCH_2CH_3); 4.76 (d, J= 12.2 Hz, 1H, H-7); 4.88 (br s, 1H, OH); 6.64 (d, J= 8.2 Hz, 2H, H-2′); 7.02 (d, J= 8.2 Hz, 2H, H-3′); 7.92 (br s, 1H, H-8); 9.24 (s, 1H, NH). ^{13}C-NMR (90.56 MHz, DMSO-d_6): δ= 14.0 (-, s, OCH_2CH_3); 35.5 (+, s, $HOC_6H_4CH_2$); 37.4, 44.4 (2-, 2s, C-9, C-10); 55.7 (-, s, NHCH); 59.7 (+, br, C-5); 60.7 (+, s, OCH_2CH_3); 83.7 (-, br, C-7); 114.9 (-, s, C-3′); 116.0 (+, s, CN); 127.2 (+, s, C-1′); 130.0 (-, s, C-2′); 155.8 (+, s, C-4′); 157.0 (-, br, C-8); 159.3 (+, br, C-4); 161.8 (+, br, C-6); 168.2 (+, br, C-2); 171.1 (+, s, COO). MS m/z (%): $[M+1]^+$: 399 (0.7); M^+: 398 (5); 325 (3); 220 (8); 107 (11); 98 (100); 45 (12); 44 (14). *Anal.* Calcd for $C_{10}H_{22}N_4O_5$: C, 60.29; H, 5.57; N, 14.06. Found: C, 60.39; H, 5.69; N, 13.69.

Gernal procedure for preparation of 9a-c:

Et_3N (0.3 mL) was added to a suspension of 4-chloro-5-cyano-2-(*N,N*-dimethylimmonio)ethylidene-6-oxido-1,3-oxazine (**3**; 0.22 g, 1.0 mmol) and corresponding arylhydrazine hydrochloride (**8a-c**) (1.0 mmol) in water-free dichloromethane (30 mL). The suspension was stirred at rt for 50-55 h. After removement of the solvent the residue was chromatographed with a silica column (70-230 mesh) using ethyl acetate as eluent to give **9a-c**. The products were then recrystallized with ethyl acetate.

(*E*)-3-Amino-1-(*p*-chlorophenyl)-6-(*N,N*-dimethylimmonio)ethylidene-4-oxidopyrazolo[3,4-*d*]-[3,1] oxazine (9a) 18.7%. mp 205-207 °C. IR (KBr): 3474, 3298, 3167 (NH); 2911; 1752 (C=O); 1630, 1550, 1507, 1495 (C=C, C=N); 1404; 1250. UV (MeCN): λ_{max}(log ε)= 377 (4.452); 265 (4.422). ^{1}H-NMR (250.13 MHz, $CDCl_3$): δ= 2.91 (br s, 3H, H-10); 3.15 (br s, 3H, H-11); 4.60 (s, 2H, NH_2); 4.89 (d, J= 12.8 Hz, 1H, H-8); 7.37 (dt, ^{3}J= 9.1 Hz, ^{4}J= 3.0 Hz, 2H, H-2′); 7.72 (d, J= 12.8 Hz, 1H, H-9); 7.96 (dt, ^{3}J= 9.1 Hz, ^{4}J= 3.0 Hz, 2H, H-3′). ^{13}C-NMR (90.56 MHz, DMSO-d_6): δ= 37.0, 44.7 (2-, 2s, C-10, C-11); 84.8 (-, s, C-8); 86.2 (+, s, C-3a); 121.3 (-, s, C-2′); 128.8 (-, s, C-3′); 128.9 (+, s, C-4′);

137.5 (+, s, C-1′); 152.2 (+, s, C-7a); 152.5 (+, s, C-3); 153.2 (-, s, C-9); 155.5 (+, s, C-4); 166.4 (+, br s, C-6). MS m/z (%): $[M+2]^+$: 333 (24); M^+: 331 (65); 289 (39); 287 (100); 166 (6); 111 (8); 98 (100); 70 (14); 55 (27); 42 (26). HRMS: Cacd for $C_{15}H_{14}N_5O_2Cl$: 331.0836. Found: 331.0836. *Anal.* Calcd for $C_{15}H_{14}N_5O_2Cl$: C, 54.31; H, 4.25; N, 21.11. Found: C, 54.24; H, 4.29; N, 20.81.

(*E*)-3-Amino-1-(*p*-methoxyphenyl)-6-(*N,N*-dimethylimmonio)ethylidene-4-oxidopyrazolo[3,4-*d*]-[3,1]oxazine (9b) 43.4%. mp 231-234 °C. IR (KBr): 3431, 3335 (NH); 2918; 1733 (C=O); 1635, 1546, 1506 (C=C, C=N); 1414; 1263; 1246. UV (MeCN): λ_{max}(log ε)= 369 (4.531); 259 (4.364). ^{1}H-NMR (360.14 MHz, DMSO-d_6): δ= 2.86 (s, 3H, H-10); 3.14 (s, 3H, H-11); 3.76 (s, 3H, O**CH$_3$**); 4.79 (d, J= 12.6 Hz, 1H, H-8); 5.64 (s, 2H, N**H$_2$**); 6.99 (dd, ^{3}J= 9.2 Hz, ^{4}J= 2.6 Hz, 2H, H-3′); 7.73 (d, J= 12.6 Hz, 1H, H-9); 7.83 (dd, ^{3}J= 9.2 Hz, ^{4}J= 2.4 Hz, 2H, H-2′). ^{13}C-NMR (90.56 MHz, DMSO-d_6): δ= 37.1, 44.8 (2-, 2 br s, C-10, C-11); 55.4 (-, s, O**CH$_3$**); 84.9 (-, s, C-8); 85.6 (+, s, C-3a); 114.2 (-, s, C-3′); 122.0 (-, s, C-2′); 132.0 (+, s, C-1′); 151.2 (+, s, C-7a); 152.4 (+, s, C-3); 152.9 (-, s, C-9); 155.8 (+, s, C-4); 166.0 (+, s, C-6). MS m/z (%): $[M+1]^+$: 328 (12); M^+: 327 (65); 283 (100); 164 (6); 98 (66); 70 (10); 55 (14); 43 (15); 42 (14). HRMS: Cacd for $C_{16}H_{17}N_5O_3$: 327.1331. Found: 327.1331. *Anal.* Calcd for $C_{16}H_{17}N_5O_3$: C, 58.71; H, 5.24; N, 21.39. Found: C, 58.58; H, 5.25; N, 21.08.

(*E*)-3-Amino-6-(*N,N*-dimethylimmonio)ethylidene-4-oxido-1-(4′-tolyl)pyrazolo[3,4-*d*][3,1]oxazine (9c) 34.7%. mp 227-230 °C. IR (KBr): 3444, 3338, 3225 (NH); 2917; 1746 (C=O); 1631, 1549, 1507 (C=C, C=N); 1395; 1362; 1248; 1115; 816; 778. UV (MeCN): λ_{max}(log ε)= 371 (4.543); 261 (4.390). ^{1}H-NMR (250.13 MHz, DMSO-d_6): δ= 2.32 (s, 3H, C$_6$H$_4$C**H$_3$**); 2.89 (s, 3H, H-10); 3.17 (s, 3H, H-11); 4.85 (d, J= 12.6 Hz, 1H, H-8); 5.70 (s, 2H, N**H$_2$**); 7.25 (d, J= 8.4 Hz, 2H, H-2′); 7.76 (d, J= 12.6 Hz, 1H, H-9); 7.87 (d, J= 8.4 Hz, 2H, H-3′). ^{13}C-NMR (90.56 MHz, $CDCl_3$): δ= 21.0 (-, s, C$_6$H$_4$CH$_3$); 86.7 (-, s, C-8); 87.1 (+, s, C-3a); 121.3 (-, s, C-2′); 129.4 (-, s, C-3′); 135.7 (+, s, C-4′); 136.2 (+, s, C-1′); 151.8 (+, s, C-3); 151.9 (+, s, C-7a); 152.2 (-, s, C-9); 157.0 (+, s, C-4); 169.2 (+, s, C-6). MS m/z (%): $[M+1]^+$: 312 (11); M^+: 311 (62); 267 (100); 98 (84); 91 (20); 70 (10); 55 (23); 42 (22). *Anal.* Calcd for $C_{16}H_{17}N_5O_2$: C, 61.73; H, 5.50; N, 22.49. Found: C, 61.58; H, 5.64; N, 22.11.

(*E*)-3-Amino-6-(*N,N*-dimethylimmonio)ethylidene-4-oxido-1-phenylpyrazolo[3,4-*d*][3,1]oxazine (9d)

A solution of 4-chloro-5-cyano-2-(*N,N*-dimethylimmonio)ethylidene-6-oxido-1,3-oxazine (**3**; 0.22 g, 1.0 mmol) and phenylhydrazine (**8d**, 0.5 mL, 4.2 mmol) in water-free dichloromethane (40 mL) was stirred at rt for 2 d. After removement of the solvent the residue was chromatographed with a silica column (70-230 mesh) using ethyl acetate as eluent. The abtained product was recrystallized with ethyl acetate to give 107 mg (36.0%) of **9d**. mp 205 °C. IR (KBr): 3422, 3294, 3198 (NH); 1748 (C=O); 1631, 1550, 1518, 1495 (C=C, C=N); 1399; 776. UV (MeCN): λ_{max}(log ε)= 373 (4.433); 261 (4.273). ^{1}H-NMR (250.13 MHz, $CDCl_3$): δ= 2.89 (br s, 3H, H-10); 3.12 (br s, 3H, H-11); 4.59 (s, 2H, N**H$_2$**); 4.89 (d, J= 12.8 Hz, 1H, H-8); 7.22 (t, J= 7.4 Hz, 1H, H-4′); 7.41 (t, J= 7.5 Hz, 2H, H-3′); 7.72 (d, J= 12.8 Hz, 1H, H-9); 7.96 (dd, ^{3}J= 7.4 Hz, ^{4}J= 1.0 Hz, 2H, H-2′). ^{13}C-NMR (90.56 MHz, $CDCl_3$): δ= 37.6, 45.2 (2-, 2s, C-

10, C-11); 86.6 (-, s, C-8); 87.3 (+, s, C-3a); 121.2 (-, s, C-2′); 124.7 (-, s, C-4′); 125.8 (-, s, C-3′); 138.7 (+, s, C-1′); 152.0 (+, s, C-3); 152.3 (+, s, C-7a); 152.4 (-, s, C-9); 157.0 (+, s, C-4); 166.3 (+, s, C-6). MS m/z (%): $[M+1]^+$: 298 (16); M^+: 297 (84); 253 (100); 227 (7); 149 (4); 98 (88); 77 (11); 70 (9); 55 (15); 42 (16). HRMS: Calcd for $C_{15}H_{15}N_5O_2$: 297.1226. Found: 297.1226. *Anal.* Calcd for $C_{15}H_{15}N_5O_2$: C, 60.60; H, 5.09; N, 23.55. Found: C, 60.58; H, 5.30; N, 23.20.

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15. Crystal data: $C_{13}H_{18}N_4O_2$, pale yellow prism, dimension 0.15x0.20x0.25 mm, monoclinic, space group: $P2_1/a$ (#14), a= 14.003 (2) Å, b= 6.601 (1) Å, c= 15.788 (2) Å, ß= 108.18 (1)°. V= 1386.5(5) $Å^3$, Z= 4, F_{000}= 560e, μ(Mo-Kα)= 0.081 mm^{-1}. Intensity data were collected using a graphite monochromated Mo-Kα (λ= 0.71073 Å) radiation and applying ω–2θ scan technique. Up to $\sin\theta/\lambda$= 0.62$Å^{-1}$ 2702 independent reflections were measured out of which 1495 reflections with I≥2.0 $\sigma(I)$

were graded as observed. The structure was solved by conventional direct methods (SIR) and refined (244 parameters) by full matrix least-squares technique using anisotropic temperature factors for non-hydrogen atoms and isotropic ones for the hydrogen atoms. The final R-value was 0.057.

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