Chemistry of Heterocyclic Compounds, Vol. 39, No. 4, 2003

THE BEHAVIOR OF DIMETHYLAMINO-SUBSTITUTED 2,5-DIARYLOXAZOLES AND 2,5-DIARYL-1,3,4-OXADIAZOLES UNDER VILSMEIER–HAACK CONDITIONS

L. D. Patsenker[1], I. G. Ermolenko[1], O. N. Lyubenko[1], I. A. Fedyunyaeva[1], N. A. Popova[1], O. S. Galkina[1], A. V. Mazepa[2], and B. M. Krasovitskii[1]

It has been shown that dimethylamino-substituted 2,5-diaryloxazoles and 2,5-diaryl-1,3,4-oxadiazoles undergo heterocyclization under Vilsmeier-Haack conditions with the participation of the dimethylamino group to form quinazolinium salts. The oxazole ring can also be formylated at the free 4 position. In alkaline medium the quinazolinium ring is readily hydrolyzed with desalkylation.

Keywords: 2,5-diaryloxazoles, 2,5-diaryl-1,3,4-oxadiazoles, dimethylamino-substituted, quinazolinium salts, heterocyclization, hydrolysis, Vilsmeier reaction.

The Vilsmeier-Haack reaction is a convenient and mild method for the formylation of a wide range of reactive aliphatic, aromatic, and heteroaromatic compounds substrates [1]. At the same time, in those cases where the electrophilic substitution is directed to a position *ortho* to a tertiary amino group, an alternative reaction may be observed. In place of the formation of an aldehyde there occurs a cyclization of the intermediate iminium adduct to a quinazolinium salt [2-5]. Such a heterocyclization may be considered as an example of the non-traditional occurrence of a reaction with a Vilsmeier reagent [6] and, in fact, as an example of a large class of reactions derived from an effect of a tertiary amino group [7, 8]. The formation of quinazolinium salts under Vilsmeier-Haack reaction conditions has been observed before, e.g. for 4-dimethylaminonaphthalic acid [2, 3] and 4-dimethylaminotoluene [4] derivatives. The mechanism of this unusual reaction was also determined and it was shown that the heterocyclization occurs in two stages *via* six-centered, synchronous transition states [9]. Formylation in the *ortho* position relative to the dimethylamino group does not always lead to cyclization. Hence we have previously shown that, for example, 4-dimethylaminobenzonitrile undergoes a simple 3-formyl substitution [10].

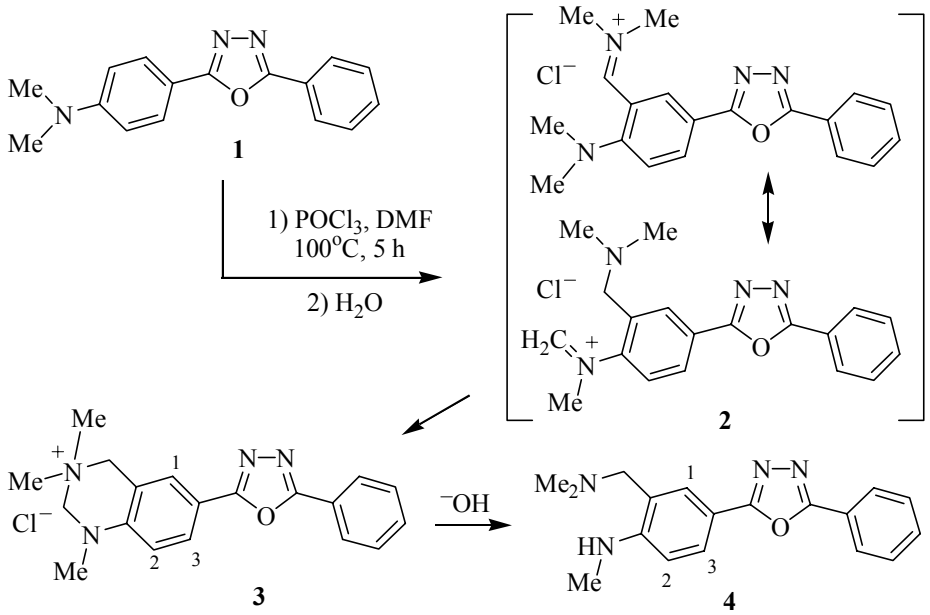
In our short communication [11] we have already noted that heterocyclization is observed in the formylation of 5-(4-dimethylaminophenyl)-2-(4-nitrophenyl)-1,3,4-oxadiazole, 2,5-di(4-dimethylaminophenyl)-1,3,4-oxadiazole, and 5-(4-dimethylaminophenyl)-2-(4-nitrophenyl)oxazole. The object of this work is a more detailed study of the behavior of different dimethylamino-substituted 2,5-diaryloxazoles and 2,5-diaryl-1,3,4-oxadiazoles under Vilsmeier–Haack reaction conditions.

---

[1] Institute of Monocrystals, Ukraine National Academy of Sciences, Kharkov 61001; e-mail patsenker@isc.kharkov.com. [2] A. V. Bogatsky Physico-Chemical Institute, Ukraine National Academy of Sciences, Odessa 65086; e-mail: tor@ukr.net. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 4, pp. 608-617, April, 2003. Original article submitted March 22, 2002.

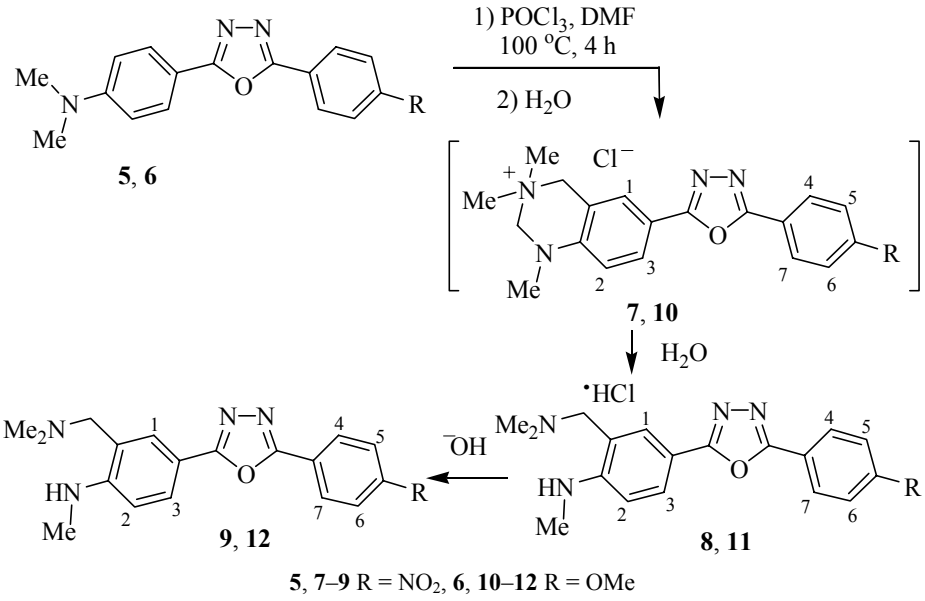
0009-3122/03/3904-0525$25.00

2,5-Diphenyloxazole, 2,5-diphenyl-1,3,4-oxadiazole and also their alkyl- alkoxy-, halo-, and nitro-substituted derivatives do not undergo formylation using the $POCl_3$–DMF complex under any kind of reagent ratio, even at temperatures where a strong tarring of the substrates begins. We have shown that the introduction of the strong electron-donor dimethylamino group into the *para* position of the phenyl leads to activation of the molecules and that an electrophilic substitution into the position *ortho* to this substituent becomes possible. In this way, the oxadiazole **1** gives the iminium intermediate **2** which cycloisomerizes to give the water soluble quinazolinium salt **3**. This salt is stable in aqueous solutions but when refluxed in a 1% aqueous solution of sodium carbonate it is hydrolyzed with desalkylation to give the 3-dimethylaminomethyl 4-methylamino-substituted compound **4**, which is insoluble in water. The methylene group is eliminated as a molecule of formaldehyde, the formation of which is identified by a qualitative reaction with fuchsin sulfurous acid (the Schiff reagent) [12].

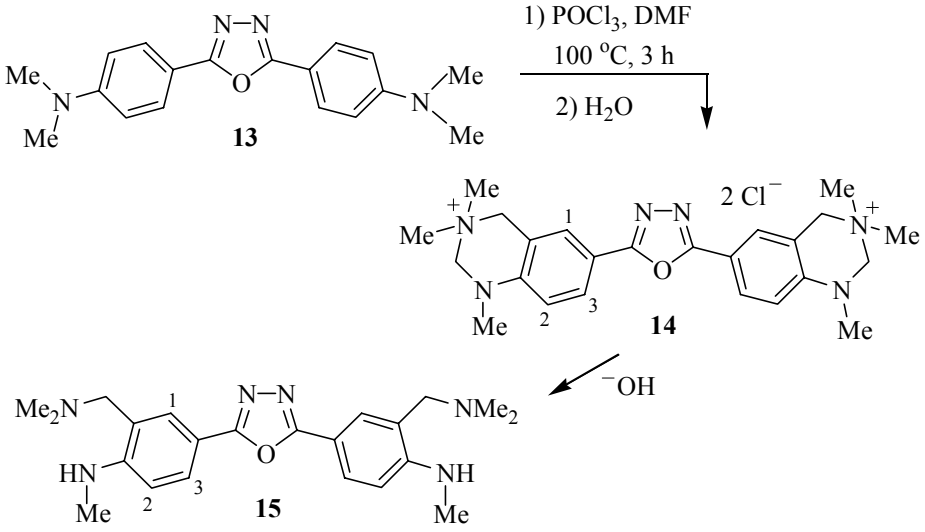


The nitro- and methoxy-substituted oxadiazoles **5** and **6** react similarly. However, the quinazolinium salt **7** proves to be so unstable that, even upon treatment of the reaction mixture with water and in the cold, decomposition occurs to give the hydrochloride **8** (which can readily be converted to the free base **9** using aqueous sodium carbonate solution). Such an unexpected instability of compound **7** had previously led us to an incorrect interpretation of its ^{1}H NMR spectrum and to assign it the structure 1,2,2-trimethyl-5-[5-(4-nitrophenyl)-1,3,4-oxadiazol-2-yl]-2,3-dihydro-1H-indazol-2-ium chloride [11]. With the aid of mass spectrometry and a counter synthesis (salt formation of the base **9** with HCl) in this work we have shown that it is, in fact, the hydrochloride **8** which is separated from the reaction mixture. In its mass spectrum there is absent any kind of evidence for the quaternary salt, or rather its thermolysis products formed by vaporization of the sample. At the same time, the mass spectrum is almost totally identical to that for the hydrolysis product **9**. The absence of a CH_3Cl peaks which are characteristic of quinazolinium salts and the high intensity of the ion peaks with *m/z* 36 and *m/z* 38 (HCl) led us to conclude that the compound discussed is actually the hydrochloride **8**.

The quinazolinium salt **10** is somewhat more stable and it could be separated from the reaction mixture. However, its hydrolysis to the hydrochloride **11** does occur partially. The mixture of compounds **10** and **11** obtained after the reaction can be separated chromatographically. Neutralization of an aqueous solution of the salt **11** gave the free base **12**.



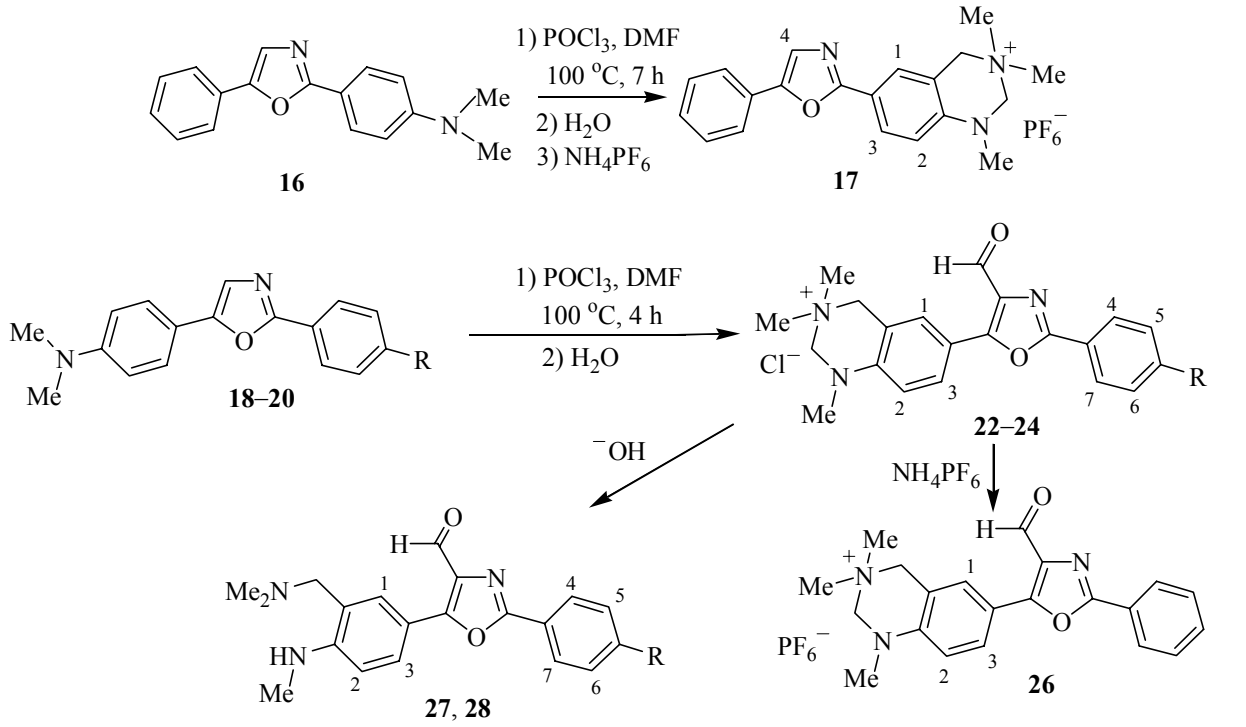
The oxadiazole **13** contains two dimethylamino groups and gives the bisquinazolinium salt **14** which is stable in water at room temperature. It is the most stable salt in the series of oxadiazoles and is hydrolyzed to the free base **15** only upon refluxing in a 1% solution of sodium carbonate.



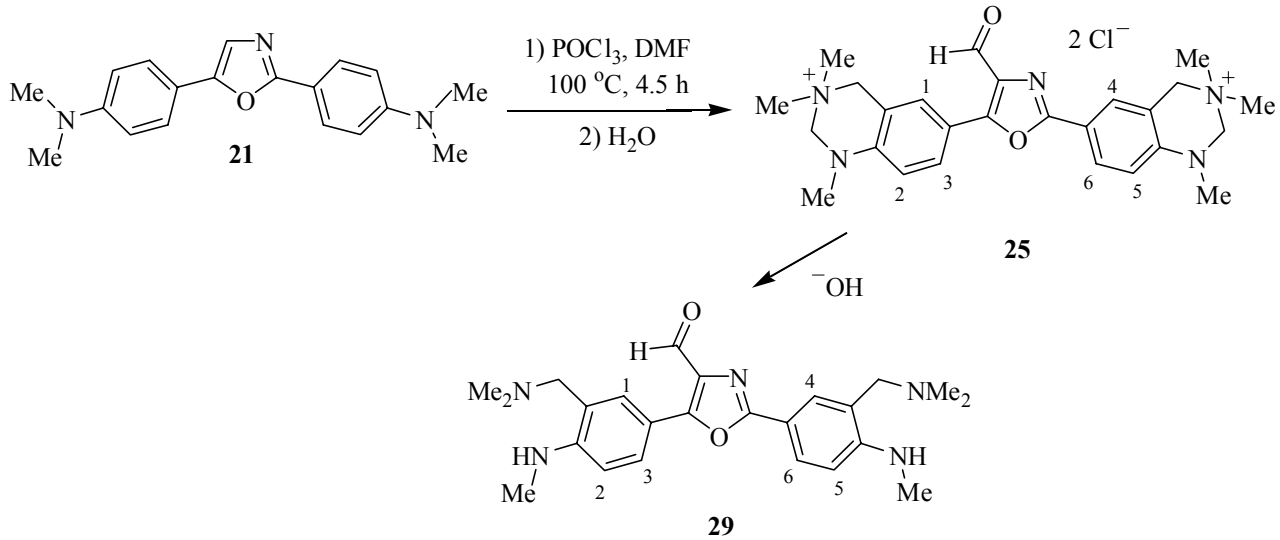
The oxazole **16** has a dimethylamino group in the 2-phenyl ring and also forms a quinazolinium salt but, due to its high water solubility, can only be separated as the hexafluorophosphate **17**. A formylation product (~8-10%) is formed as an admixture as observed in the ^{1}H NMR spectrum (δ CHO 10.09 ppm) and IR spectrum (νC=O 1680 cm^{-1}). It is most likely that the aldehyde group is situated at the *para* position of the 5-phenyl ring.

Through a conjugative effect a dimethylamino group in the 5-phenyl ring activates not only the benzene ring bound to it but also the free 4 position of the oxazole ring and, as a result, formylation is observed along with the heterocyclization. Hence the oxazoles **18-21** form the aldehydes **22-25**. Compounds **23-25** were separated and identified using ^{1}H NMR and IR spectroscopy. The quaternary salt **22** can be separated in the pure state only as the hexafluorophosphate **26**.

The reactivity of the investigated oxadiazoles **1**, **5**, **6**, **13**, and oxazoles **16**, **18-21** is quite similar. Chromatographic monitoring of the course of the reaction shows that they are converted almost quantitatively to the quinazolinium salts. However, the synthetic yields are not high due to the high solubility in water and the related difficulty in separation and purification and also, in some cases, their instability in aqueous solutions. Promotion of the separation and increase in the yields can be achieved by exchanging the chloride for hexafluorophosphate which markedly lowers the water solubility and increases their stability somewhat. Hence, where the chloride **22** could not be prepared in the pure state, the hexafluorophosphate **26** could be separated from the reaction mixture in 67% yield (without purification).



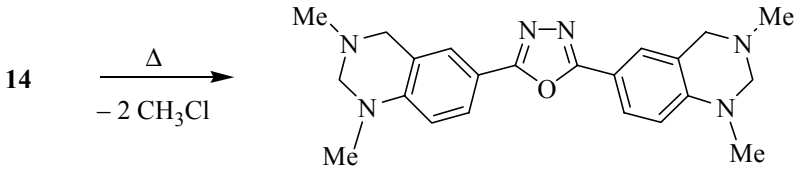
18, 22, 27 R = H, **19, 23, 28** R = NO_2, **20, 24** R = COOH



As in the case of the oxadiazoles, the quinazolinium salts in the oxazole series can be hydrolyzed to the corresponding 3-dimethylaminomethyl-4-methylamino-substituted compounds. Hence heating in aqueous sodium carbonate solution gave compounds **27-29**. It was not possible to deduce any kind of clear dependence between the structure of the investigated quaternary salts and the rate of their hydrolysis. In all cases the desalkylation occurs virtually quantitatively and without the formation of side products hence the lower synthetic yields must basically be due to their loss during the purification by recrystallization. A further quantity of the material can be obtained from the filtrates but this was not taken into account when calculating the synthetic yields.

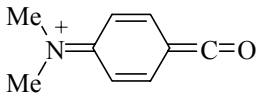
The ^{1}H NMR spectra of the quinazolinium salts showed characteristic signals for the two methylene groups in the heterocycle at 4.73-4.81 and 4.76-4.88 as well as the N–CH_3 group protons (3.18-3.20) and two methyl groups on the quaternary nitrogen atom (3.12-3.18 ppm). A doublet signal for one of the *ortho* protons of the dimethylaminophenyl fragment as seen in the starting compounds was absent. The hydrolysis products showed singlet signals for the methylamino group (2.83-2.87) and the dimethylamino groups (2.16-2.20) as well as resonances for the two methylene protons at 3.43-3.48 ppm. A formyl group proton signal was observed for the aldehydes in the region 10.01-10.05 ppm. The IR spectra of the synthesized compounds did not disagree with the structure proposed for them. The C=O stretching vibrations for the aldehydes were found at 1675-1685 cm^{-1}.

The mass spectra of the quaternary salts showed only the products of their thermal decomposition. It was notable that, in contrast to their hydrolysis, electron impact leads to desalkylation with elimination not of a methylene group in the quinazolinium ring but with loss of a methyl group at the quaternary nitrogen atom and retention of the heterocycle. Hence, for example, the salt **14** showed a mass spectrum corresponding to structure **30**. In addition, a peak for ions with *m/z* 50 was found in the spectrogram and this can be assigned to a molecule of CH_3Cl. In support of this there was also a characteristic isotopic peak at *m/z* 52 which points to the presence of a chlorine atom in these fragments. This allows us to suggest that the thermolysis of salt **14** accompanying its volatilization separates CH_3Cl molecules to form the nitrogen base **30**. A similar dependence is observed for other quinazolinium salts.

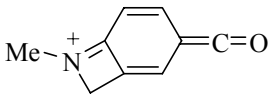


30

The overall direction of decomposition for compounds containing an azole ring is the fission of this heterocycle. It leads to the formation of fragment ions with *m/z* 148 (compounds **5** and **13**) and *m/z* 146 (compounds **9** and **15**) which very likely have a quinoid structure:



m/z 148



m/z 146

The basic, primary routes of fragmentation for the nitro substituted **5** and **19** are associated with the elimination of a nitro group (ions $[M-46]^+$). However, in the hydrolysis products **9**, **15**, and **28** fragmentation routes appear which are due to the loss of a dimethylaminomethylene fragment (ions $[M-CH_3]^+$ and $[M-(CH_3)_2N]^+$).

The quinazolinium salts are readily soluble in water and alcohol. The hydrolysis products are readily soluble in toluene, alcohol, and other organic solvents. With the exception of the nitro-substituted compounds,

all of those synthesized possess a strong, sky-blue fluorescence both in solutions and in the solid state and hence may be of interest as organic luminophores. A study of the spectroluminescent properties of these compounds is the subject of our next investigation.

EXPERIMENTAL

IR spectra were measured on a Specord IR-75 spectrometer for KBr tablets. ^{1}H NMR spectra were recorded on a Varian VXP-300 (300 MHz) instrument using DMSO-d_6 solvent and HMDS internal standard. Mass spectra were obtained on an MX-1321 spectrometer using direct sample introduction, ionizing intensity of 70 eV, and an ionizing chamber temperature of 200°C. Monitoring of the reaction course and the degree of purity of the products was carried out using TLC on Silufol UV-254 plates with chloroform–methanol (10:1) as eluent. The starting compounds **1**, **5**, **6**, **13**, **16**, and **18-21** were prepared by the methods reported in the studies [13, 14].

1,3,3-Trimethyl-6-(5-phenyl-1,3,4-oxadiazol-2-yl)-1,2,3,4-tetrahydroquinazolin-3-ium Chloride (3). $POCl_3$ (0.6 ml, 6.6 mmol) was added dropwise to a suspension of the oxadiazole **1** (0.55 g, 2.0 mmol) in DMF (2.5 ml, 32.5 mmol) at 60-70°C. The reaction product was stirred for 5 h at 100°C, cooled to room temperature, and poured onto a small amount of ice. Addition of acetone precipitated an oily material which crystallized after 12 h. Recrystallization from DMF gave a colorless crystalline material. Yield 0.22 g (30%); mp 272-273°C (DMF). IR spectrum, ν, cm^{-1}: 1610, 1585, 1450, 1430, 1390, 1300, 1210. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.15 (6H, s, $^+N(CH_3)_2$); 3.20 (3H, s, NCH_3); 4.79 (2H, s, CH_2); 4.86 (2H, s, CH_2); 7.15 (1H, d, *J* = 8.8, 2-H); 7.60-7.68 (3H, s, Ph); 7.91 (1H, s, 1-H); 8.04 (1H, dd, J_1 = 8.5, J_2 = 1.9, 3-H); 8.08-8.17 (2H, m, Ph). Found, %: C 63.81; H 9.72; Cl 9.56; N 15.50. $C_{19}H_{21}ClN_4O$. Calculated, %: C 63.95; H 5.89; Cl 9.96; N 15.71.

N,N-Dimethyl-2-methylamino-5-[5-(4-nitrophenyl)-1,3,4-oxadiazol-2-yl]phenylmethanamine Hydrochloride (8). $POCl_3$ (1.7 ml, 18.6 mmol) was added dropwise to a suspension of the oxadiazole **5** (1.3 g, 4.2 mmol) in DMF (10 ml, 130 mmol) at 60-70°C. The reaction product was stirred for 4 h at 100°C, cooled, and poured onto ice. The brown precipitate formed was recrystallized from DMF and then from ethanol to give yellow crystals. Yield 0.4 g (24%); mp 257.5-258.5°C (ethanol). IR spectrum, ν, cm^{-1}: 1610, 1580, 1550, 1525, 1510, 1370 (NO_2). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.77 (6H, s, $^+N(CH_3)_2$); 2.86 (3H, s, NCH_3); 4.38 (2H, s, CH_2); 6.83 (1H, d, *J* = 8.7, 2-H); 8.02 (1H, dd, J_1 = 8.5, J_2 = 2.0, 3-H); 8.11 (1H, s, 1-H); 8.34 (2H, d, *J* = 8.9, 4-, 7-H); 8.46 (2H, d, *J* = 8.9, 5-, 6-H). Found, %: C 55.61; H 5.30; Cl 8.77; N 17.64. $C_{18}H_{20}ClN_5O_3$. Calculated, %: C 55.46; H 5.13; Cl 9.11; N 17.97.

6-[5-(4-Methoxyphenyl)-1,3,4-oxadiazol-2-yl]-1,3,3-trimethyl-1,2,3,4-tetrahydroquinazolin-3-ium Chloride (10) and N,N-Dimethyl-5-[5-(4-methoxyphenyl)-1,3,4-oxadiazol-2-yl]-2-methylaminophenyl-methanamine Hydrochloride (11). $POCl_3$ (0.8 ml, 8.8 mmol) was added dropwise to a suspension of the oxadiazole **6** (0.6 g, 2.0 mol) in DMF (2.5 ml, 32.5 mmol) at 60-70°C. The reaction mixture was stirred for 4 h at 100°C, cooled, and poured onto ice. The grey precipitate formed was filtered off and separated by column chromatography on silica gel (eluent ethanol). The two fractions collected contained the quinazolinium salt **10** and the hydrochloride **11**. Both compounds gave colorless crystals after evaporation. Quinazolinium salt **10**, yield 0.2 g (27%); mp 248-250°C. IR spectrum, ν, cm^{-1}: 1610, 1480, 1420, 1340, 1310, 1250, 1180. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.15 (6H, s, $^+N(CH_3)_2$); 3.20 (3H, s, NCH_3); 3.85 (3H, s, OCH_3); 4.78 (2H, s, CH_2); 4.85 (2H, s, CH_2); 7.14 (1H, d, *J* = 8.9, 2-H); 7.18 (2H, d, *J* = 9.0, 5-, 6-H); 7.89 (1H, d, *J* = 1.5, 1-H); 8.02 (1H, dd, J_1 = 8.8, J_2 = 1.9, 3-H); 8.05 (2H, dd, J_1 = 9.0, J_2 = 1.9, 4-, 7-H). Found, %: C 61.89; H 5.48; Cl 8.85; N 14.07. $C_{20}H_{23}ClN_4O_2$. Calculated, %: C 62.09; H 5.69; Cl 9.18; N 14.49.

Hydrochloride 11. Yield 0.15 g (20%); mp 230°C. IR spectrum, ν, cm^{-1}: 1600, 1470, 1440, 1390, 1280, 1230. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.40 (6H, s, $N(CH_3)_2$); 2.85 (3H, s, NCH_3); 3.88 (3H, s, OCH_3); 4.25 (2H, s, CH_2); 6.74 (1H, d, *J* = 8.8, 2-H); 7.16 (2H, d, *J* = 8.6, 5-, 6-H); 7.85 (1H, s, 1-H); 7.92 (1H, d, *J* = 8.8,

3-H); 8.03 (2H, d, J = 8.6, 4-, 7-H). Found, %: C 61.29; H 5.98; Cl 8.85; N 14.64. $C_{19}H_{23}ClN_4O_2$. Calculated, %: C 60.88; H 6.14; Cl 9.47; N 14.95.

1,3,3-Trimethyl-6-[5-(1,3,3-trimethyl-1,2,3,4-tetrahydroquinazolin-3-ium]-6-yl)-1,3,4-oxadiazol-2-yl]-1,2,3,4-tetrahydroquinazolin-3-ium Dichloride (14). $POCl_3$ (1.4 ml, 15.3 mmol) was added dropwise to a suspension of the oxadiazole **13** (0.93 g, 3.0 mmol) in DMF (4 ml, 52.0 mmol) at 60-70°C. The reaction mixture was stirred for 3 h at 100°C, cooled to room temperature, and diluted with a small amount of 96% ethanol to give colorless crystals. Yield 0.9 g (60%); mp 318-320°C (ethanol). IR spectrum, ν, cm^{-1}: 1610, 1500, 1450, 1410, 1330, 1240. ^{1}H NMR spectrum, δ, ppm (J, Hz): 3.16 (12H, s, 2 $^+N(CH_3)_2$); 3.20 (6H, s, 2 NCH_3); 4.78 (4H, s, 2 CH_2); 4.84 (4H, s, 2 CH_2); 7.15 (2H, d, J = 8.8, 2-H); 7.86 (2H, s, 1-H); 8.01 (2H, dd, J_1 = 8.7, J_2 = 1.2, 3-H). Mass spectrum, *m/z* 390 $[M-2CH_3Cl]^+$. Found, %: C 58.46; H 6.37; Cl 14.41; N 17.12. $C_{24}H_{32}Cl_2N_6O$. Calculated, %: C 58.66; H 6.52; Cl 14.46; N 17.11.

1,3,3-Trimethyl-6-(5-phenyl-1,3-oxazol-2-yl)-1,2,3,4-tetrahydroquinazolin-3-ium Hexafluorophosphate (17). $POCl_3$ (1.1 ml, 12.0 mmol) was added dropwise to a mixture of the oxazole **16** (0.52 g, 2.0 mmol) in DMF (2.5 ml, 32.5 mmol) at 60-70°C. The reaction mixture was held for 7 h at 100°C, cooled, and poured onto ice. NH_4PF_6 (0.32 g, 2.0 mmol) was added and a finely crystalline precipitate was formed. Purification by column chromatography on silica gel (eluent acetonitrile) gave colorless crystals. Yield 0.2 g (23%); mp 220-222°C. IR spectrum, ν, cm^{-1}: 1620, 1500, 830 (PF_6). ^{1}H NMR spectrum, δ, ppm (J, Hz): 3.12 (6H, s, $^+N(CH_3)_2$); 3.18 (3H, s, NCH_3); 4.73 (2H, s, CH_2); 4.76 (2H, s, CH_2); 7.09 (1H, d, J = 8.7, 2-H); 7.73 (1H, s, 4-H); 7.82 (1H, s, 1-H); 7.99 (1H, dd, J_1 = 8.6, J_2 = 1.9, 3-H); 7.86-7.30 (5H, m, Ph). Found, %: C 51.47; H 4.62; N 9.23. $C_{20}H_{22}F_6N_3OP$. Calculated, %: C 51.61; H 4.73; N 9.03.

6-[4-Formyl-2-(4-nitrophenyl)-1,3-oxazol-5-yl]-1,3,3-trimethyl-1,2,3,4-tetrahydroquinazolin-3-ium Chloride (23). $POCl_3$ (0.8 ml, 8.8 mmol) was added dropwise to a suspension of the oxazole **19** (0.62 g, 2.0 mmol) in DMF (2.5 ml, 32.5 mmol) at 60-70°C. The reaction mixture was stirred for 4 h at 100°C, cooled, and poured into iced water. The yellow-orange precipitate formed was recrystallized from DMF. Yield 0.27 g (32%); mp 273°C (DMF). IR spectrum, ν, cm^{-1}: 1685 (CO), 1610, 1580, 1510, 1345 (NO_2). Mass spectrum, *m/z* 378 $[M-CH_3Cl]^+$. ^{1}H NMR spectrum, δ, ppm J (Hz); 3.17 (6H, s, $^+N(CH_3)_2$); 3.21 (3H, s, NCH_3); 4.81 (2H, s, CH_2); 4.87 (2H, s, CH_2); 7.16 (1H, d, J = 8.8, 2-H); 8.10 (1H, s, 1-H); 8.26 (1H, dd, J_1 = 8.7, J_2 = 1.4, 3-H); 8.38 (2H, d, J = 8.8, 4-, 7-H); 8.44 (2H, d, J = 8.8, 5-, 6-H); 10.01 (1H, d, CHO). Found, %: C 58.69; H 4.71; Cl 7.89; N 12.71. $C_{21}H_{21}ClN_4O_4$. Calculated, %: C 58.81; H 4.90; Cl 8.28; N 13.07.

6-[2-(4-Carboxyphenyl)-4-formyl-1,3-oxazol-5-yl]-1,3,3-trimethyl-1,2,3,4-tetrahydroquinazolin-3-ium Chloride (24). $POCl_3$ (0.8 ml, 8.8 mmol) was added dropwise to a suspension of the oxazole **20** (0.62 g, 2.0 mmol) in DMF (2.5 ml, 32.5 mmol) at 60-70°C. The reaction mixture was stirred for 4 h at 100°C, cooled, and poured into iced water. The yellow precipitate formed was recrystallized from ethanol to give pale-yellow crystals. Yield 0.15 g (18%); mp ~360°C (ethanol). IR spectrum, ν, cm^{-1}: 1690 ($CO_{ald.}$), 1665 ($CO_{carboxy}$), 1610, 1565, 1500. ^{1}H NMR spectrum, δ, ppm (J, Hz): 3.16 (6H, s, $^+N(CH_3)_2$); 3.20 (3H, s, NCH_3); 4.78 (2H, s, CH_2); 4.83 (2H, s, CH_2); 7.16 (1H, d, J = 8.9, 2-H); 8.08 (1H, d, J = 2.0, 1-H); 8.14 (2H, d, J = 8.4, 4-, 7-H); 8.25 (2H, d, J = 8.5, 5-, 6-H); 8.25 (1H, d, J = 8.6, 3-H); 10.03 (1H, s, CHO). Found, %: C 61.52; H 5.01; Cl 7.81; N 9.53. $C_{22}H_{22}ClN_3O_4$. Calculated, %: C 61.75; H 5.15; Cl 8.30; N 9.82.

6-[4-Formyl-2-(1,3,3-trimethyl-1,2,3,4-tetrahydroquinazolin-3-ium-6-yl)-1,3-oxazol-5-yl]-1,3,3-trimethyl-1,2,3,4-tetrahydroquinazolin-3-ium Dichloride (25). $POCl_3$ (2 ml, 21.9 mmol) was added to a suspension of the oxazole **21** (0.8 g, 2.7 mmol) in DMF (4 ml, 52.0 mmol) at 60-70°C. The reaction mixture was stirred for 4.5 h at 100°C, cooled, and poured onto ice. A precipitate was formed upon addition of isopropanol and this was recrystallized from ethanol to give yellow crystals. Yield 0.1 g (8 %); mp ~360°C (ethanol). IR spectrum, ν, cm^{-1}: 1675 (CO), 1610, 1500, 1470, 1350. ^{1}H NMR spectrum, δ, ppm (J, Hz): 3.18 (12H, s, 2 $^+N(CH_3)_2$); 3.20 (6H, s, 2 NCH_3); 4.81 (4H, s, 2 CH_2); 4.88 (4H, s, 2 CH_2); 7.11 (1H, d, 5-H); 7.15 (1H, d, 2-H); 7.89 (1H, d, J = 1.6, 4-H); 8.02 (1H, d, J = 1.7, 1-H); 8.05 (1H, dd, J_1 = 8.7, J_2 = 1.6, 6-H); 8.16 (1H, dd, J_1 = 8.7, J_2 = 1.7, 3-H); 10.05 (1H, s, CHO). Found, %: C 60.05; H 6.19; Cl 13.54; N 13.18. $C_{26}H_{33}Cl_2N_5O_2$. Calculated, %: C 60.23; H 6.37; Cl 13.70; N 13.51.

6-(4-Formyl-2-phenyl-1,3-oxazol-5-yl)-1,3,3-trimethyl-1,2,3,4-tetrahydroquinazolin-3-ium Hexafluorophosphate (26). $POCl_3$ (1.6 ml, 17.5 mmol) was added dropwise to a mixture of the oxazole **18** (0.8 g, 3.0 mmol) in DMF (2.5 ml, 32.5 mmol) at 60-70°C. The reaction product was stirred for 9 h at 100°C, cooled, and poured onto ice. Addition of NH_4PF_6 (0.49 g, 3.0 mmol) precipitated a finely crystalline material. Purification by column chromatography on silica gel (acetonitrile eluent) gave yellow crystals. Yield 0.5 g (33%); mp 260-262°C. IR spectrum, ν, cm^{-1}: 1680 (CO), 1610, 1510, 850 (PF_6). ^1H NMR spectrum, δ, ppm (*J*, Hz): 3.12 (6H, s, $^+N(CH_3)_2$); 3.19 (3H, s, NCH_3); 4.73 (2H, s, CH_2); 4.77 (2H, s, CH_2); 7.15 (1H, d, *J* = 8.8, 2-H); 7.56-7.66 (3H, m, Ph); 8.05 (1H, d, *J* = 1.6, 1-H): 8.10-8.17 (2H, m, Ph); 8.22 (1H, dd, J_1 = 8.9, J_2 = 2.0, 3-H). Found, %: C 51.23; H 4.50; N 8.24. $C_{21}H_{22}F_6N_3O_2P$. Calculated, %: C 51.11; H 4.46; N 8.52.

General Method for the Hydrolysis of the Quinazolinium Salts. The quinazolinium salt (5 mmol) was refluxed in 1% aqueous sodium carbonate solution (10 ml) for 1 h. The precipitate formed was filtered off, washed with water, dried, and then purified chromatographically or by recrystallization from a suitable solvent.

N,N-Dimethyl-2-methylamino-5-(5-phenyl-1,3,4-oxadiazol-2-yl)phenylmethanamine (4). Purified by column chromatography on alumina (eluent benzene) to give colorless crystals. Yield 0.6 g (40%); mp 164-165°C. IR spectrum, ν, cm^{-1}: 1620, 1520, 1490, 1470, 1420, 1350, 1270. ^1H NMR spectrum, δ, ppm (*J*, Hz): 2.20 (6H, s, $N(CH_3)_2$); 2.85 (3H, d, *J* = 5.1, NCH_3); 3.48 (2H, s, CH_2); 6.62 (1H, q, J_1 = 14.8, J_2 = 9.9, J_3 = 4.6, NH); 6.71 (1H, d, *J* = 8.6, 2-H); 7.56-7.67 (3H, m, Ph); 7.73 (1H, d, *J* = 2.0, 1-H); 7.89 (1H, dd, J_1 = 8.6, J_2 = 1.9, 3-H); 8.05-8.14 (2H, m, Ph). Found, %: C 69.92; H 6.26; N 17.87. $C_{18}H_{20}N_4O$. Calculated, %: C 70.13; H 6.49; N 18.18.

N,N-Dimethyl-2-methylamino-5-[5-(4-nitrophenyl)-1,3,4-oxadiazol-2-yl]phenylmethanamine (9). Purified by recrystallization from a mixture of benzene–hexane (1:1) to give orange crystals. Yield 1.1 g (60%); mp 228-230°C (benzene–hexane, 1:1). IR spectrum, ν, cm^{-1}: 1610, 1585, 1555, 1500, 1350 (NO_2). ^1H NMR spectrum, δ, ppm (*J*, Hz): 2.18 (6H, s, $N(CH_3)_2$); 2.85 (3H, s, NCH_3); 3.45 (2H, s, CH_2); 6.65 (1H, s, NH); 6.71 (1H, d, *J* = 8.7, 2-H); 7.70 (1H, d, *J* = 1.9, 1-H); 7.90 (1H, dd, J_1 = 8.5, J_2 = 2.0, 3-H); 8.32 (2H, d, *J* = 8.9, 4-, 7-H); 8.41 (2H, d, *J* = 8.9, 5-, 6-H). Mass spectrum, *m/z* 353 [M^+]. Found, %: C 61.01; H 5.19; N 19.68. $C_{18}H_{19}N_5O_3$. Calculated, %: C 61.19; H 5.38; N 19.82.

N,N-Dimethyl-5-[5-(4-methoxyphenyl)-1,3,4-oxadiazol-2-yl]-2-methylaminophenylmethanamine (12). Purified by recrystallization from a mixture of benzene–hexane (1:1) to give colorless crystals. Yield 0.85 g (50%); mp 150-152°C (benzene–hexane, 1:1). IR spectrum, ν, cm^{-1}: 1620, 1480, 1440, 1410, 1330, 1300, 1250. ^1H NMR spectrum, δ, ppm (J, Hz): 2.16 (6H, s, $N(CH_3)_2$); 2.83 (3H, s, NCH_3); 3.43 (2H, s, CH_2); 3.85 (3H, s, OCH_3); 6.61 (1H, d, *J* = 5.0, NH); 6.70 (1H, d, *J* = 8.6, 2-H); 7.16 (2H, d, *J* = 8.9, 5-, 6-H); 7.71 (1H, d, *J* = 1.7, 1-H); 7.87 (1H, dd, J_1 = 8.4, J_2 = 1.5, 3-H); 8.03 (2H, d, *J* = 8.7, 4-, 7-H). Found, %: C 67.21; H 6.29; N 16.35. $C_{19}H_{22}N_4O_2$. Calculated, %: C 67.45; H 6.51; N 16.57.

N,N-Dimethyl-5-[5-(3-dimethylaminomethyl-4-methylaminophenyl)-1,3,4-oxadiazol-2-yl]-2-methylaminophenylmethanamine (15). Purified by recrystallization from benzene–hexane (1:1) to give colorless crystals. Yield 1.25 g (63%) with mp 183-184°C (from a mixture of benzene–hexane, 1:1). IR spectrum, ν, cm^{-1}: 1610, 1510, 1440, 1410, 1330, 1290. ^1H NMR spectrum, δ, ppm (J, Hz): 2.17 (12H, s, 2 $N(CH_3)_2$); 2.84 (6H, s, 2 NCH_3); 3.44 (4H, s, 2 CH_2); 6.57 (2H, s, 2 NH); 6.69 (2H, d, *J* = 8.6, 2-H); 7.68 (2H, s, 1-H); 7.85 (2H, dd, J_1 = 8.5, J_2 = 1.3, 3-H). Mass spectrum, m/z 394 [M^+]. Found, %: C 66.87; H 7.49; N 21.12. $C_{22}H_{30}N_6O$. Calculated, %: C 67.01; H 7.61; N 21.32.

5-(3-Dimethylaminomethyl-4-methylaminophenyl)-2-phenyl-1,3-oxazole-4-carbaldehyde (27). Purified by recrystallization from benzene to give yellow crystals. ^1H NMR spectrum, δ, ppm (*J*, Hz): 2.19 (6H, s, $N(CH_3)_2$); 2.88 (3H, s, NCH_3); 3.47 (2H, s, CH_2); 6.69 (1H, s, NH); 6.71 (1H, d, *J* = 8.2, 2-H); 7.43-7.68 (3H, m, Ph); 7.90 (1H, d, *J* = 2.0, 1-H); 8.12 (1H, d, 3-H); 8.04-8.10 (2H, m, Ph).

5-(3-Dimethylaminomethyl-4-methylaminophenyl)-2-(4-nitrophenyl)-1,3-oxazole-4-carbaldehyde (28). Purified by column chromatography on alumina (eluent toluene) to give dark-red colored crystals. Yield 1.25 g (65%); mp 215-216°C. IR spectrum, ν, cm^{-1}: 1685 (CO), 1610, 1580, 1510, 1340 (NO_2). ^1H NMR

spectrum, δ, ppm (*J*, Hz): 2.18 (6H, s, $N(CH_3)_2$); 2.88 (3H, s, NCH_3); 3.47 (2H, s, CH_2); 6.73 (1H, d, *J* = 8.9, 2-H); 6.77 (1H, s, NH); 7.94 (1H, s, 1-H); 8.16 (1H, d, *J* = 8.7, 3-H); 8.34 (2H, d, *J* = 8.7, 4-, 7-H); 8.40 (2H, d, *J* = 8.7, 5-, 6-H); 10.06 (1H, s, CHO). Mass spectrum, *m/z* 380 [M^+]. Found, %: C 62.95; H 5.08; N 14.57. $C_{20}H_{20}N_4O_4$. Calculated, %: C 63.16; H 5.26; N 14.73.

2,5-Di(3-dimethylaminomethyl-4-methylaminophenyl)-1,3-oxazole-4-carbaldehyde (29). Purified by recrystallization from benzene–hexane (1:1) to give colorless crystals. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.16 (12H, s, 2 $N(CH_3)_2$); 2.84 (3H, d, *J* = 3.9, NCH_3); 2.86 (3H, d, *J* = 3.9, NCH_3); 3.44 (2H, s, CH_2); 3.46 (2H, s, CH_2); 6.53 (2H, s, 2 NH); 6.67 (1H, d, *J* = 8.2, 5-H); 6.70 (1H, d, *J* = 8.3, 2-H); 7.70 (1H, d, *J* = 1.9, 4-H); 7.84 (1H, d, *J* = 1.9, 1-H); 7.88 (1H, dd, J_1 = 8.3, J_2 = 1.9, 6-H); 8.04 (1H, dd, J_1 = 8.6, J_2 = 2.0, 3-H); 10.0 (1H, d, CHO).

The authors express their gratitude to chemical sciences candidate S. V. Iksanova (Institute of Organic Chemistry, Ukraine National Academy of Sciences, Kiev) for measurement of the ^{1}H NMR spectra.

The work was carried out with the support of the Ukraine National Academy of Sciences (grant No. 0801051062).

REFERENCES

1. K. V. Vatsuro and G. L. Mishchenko, *Named Reactions in Organic Chemistry* [in Russian], Khimiya, Moscow (1976), p. 115.
2. B. M. Krasovitskii, L. I. Kormilova, I. G. Ermolenko, L. D. Patsenker, and V. N. Baumer, *Functional Materials,* **4**, 280 (1997).
3. L. D. Patsenker, I. G. Yermolenko (Ermolenko), Ye. Ye. Artyukhova (E. E. Artyukhova), V. N. Baumer, and B. M. Krasovitskii, *Tetrahedron*, **56**, 7319 (2000).
4. O. Meth-Cohn, and D. L. Taylor, *J. Chem. Soc., Chem. Commun.*, **14**, 1463 (1995).
5. Y. Cheng, O. Meth-Cohn, and D. Taylor, *J. Chem. Soc., Perkin Trans. 1*, 1257 (1998).
6. C. M. Marson and P. R. Giles, *Synthesis using Vilsmeier Reagents*, CRC Press, Boca Raton, Ann Arbor, London, Tokyo (1994).
7. O. Meth-Cohn and B. Tarnowski, *Adv. Heterocycl. Chem.*, **31**, 207 (1976).
8. O. Meth-Cohn, *Adv. Heterocycl. Chem.*, **65**, 1 (1996).
9. L. D. Patsenker, *Teor. i Eksp. Khim.*, **36**, 201 (2000).
10. L. D. Patsenker, E. E. Artyukhova, I. G. Ermolenko, and I. A. Borovoi, *Ukraine Patent 42307A*; Bulletin. Promislova Vlasnist (Industrial Ownership), No. 9, 4.74 (2001).
11. L. D. Patsenker, I. G. Ermolenko, I. A. Fedyunyaeva, N. A. Popova, and B. M. Krasovitskii, *Khim. Geterotsikl. Soedin.*, 705 (2000).
12. Houben-Weyl, *Methods of Organic Chemistry*, Khimiya, Moscow (1967), Vol. 2, pp. 431, 461.
13. N. A. Popova, E. G. Yushko, B. M. Krasovitskii, V. I. Minkin, A. E. Lyubarskaya, and M. L. Gol'berg, *Khim. Geterotsikl. Soedin.*, 26 (1983).
14. V. N. Kerr, F. N. Hayes, D. G. Ott, R. Lier, and E. Hansbury, *J. Org. Chem.*, **24**, 1864 (1959).