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REACTIONS OF 3-AMINO-SUBSTITUTED 5,6-DIHYDRO-2H-1,4-OXAZINES WITH α-HALO KETONES

N. A. Shtil'[1], A. M. Demchenko[2], A. P. Andrushko[1], and A. N. Krasovsky[1]

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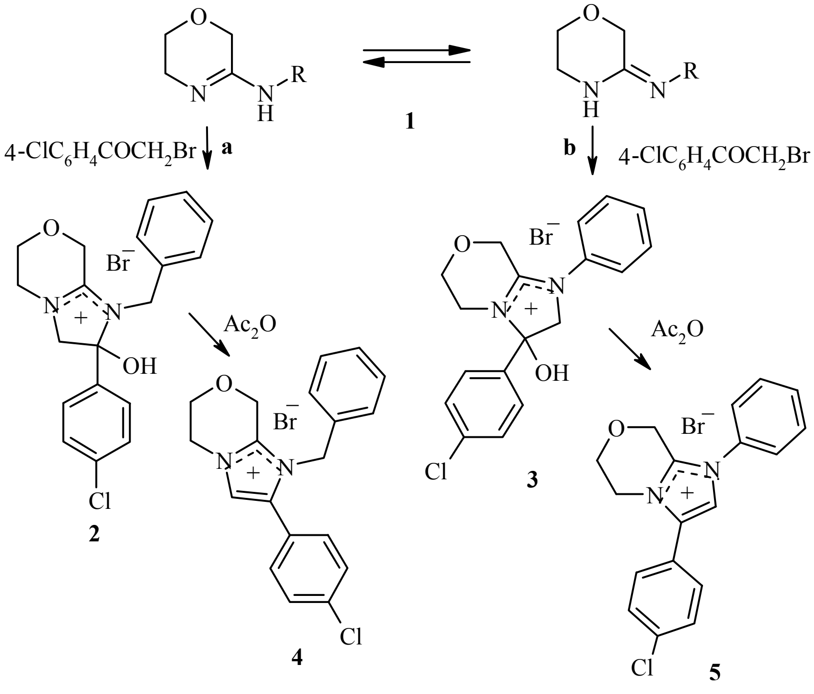
We have discovered that 3-amino-substituted 5,6-dihydro-2H-1,4-oxazines react with α-halo ketones either at the ring or exocyclic nitrogen atom depending on the nature of the substituent. Such behavior of 3-amino-substituted 1,4-oxazines may be attributed to the existence of amino (**1a**) or imine tautomeric form (**1b**) similar to 1,4-thiazines [1-3]. Thus, 3-benzylamino-5,6-dihydro-2H-1,4-oxazine forms derivatives at the ring nitrogen atom, while 3-phenyliminomorpholine forms derivatives at the exocyclic nitrogen atom (**3**).



a R = $C_6H_5CH_2$; **b** R = C_6H_5

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[1] Chernigov State Technological University, 14027 Chernigov, Ukraine; e-mail: demch@cn.relc.com.
[2] T. G. Shevchenko Chernigov State University, 14013 Chernigov, Ukraine; e-mail: demch@cn.ukrpack.net.
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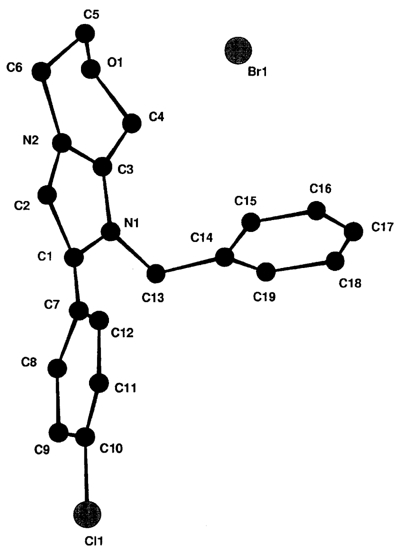

Fig. 1. Molecular structure of compound **4**.

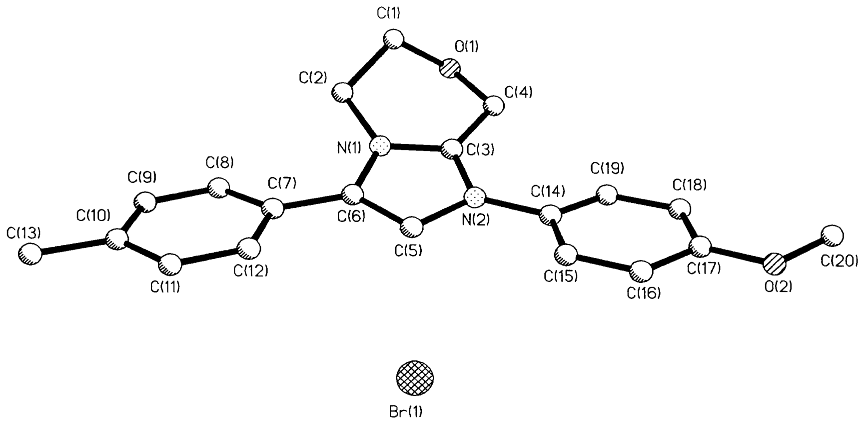

Fig. 2. Molecular structure of compound **5**.

Condensation products **2** and **3** are stable compounds. Heating these salts in acetic anhydride leads to dehydration, as indicated by IR and ^{1}H NMR spectra of the resultant imidazooxazinium bromides **4** and **5**. The unequivocal direction of the alkylation was demonstrated by X-ray diffraction structural analysis (Figs. 1 and 2). The X-ray diffraction data will be published in detail in a separate communication.

3-(4-Chlorophenyl)-3-hydroxy-1-phenyl-2,5,6,8-tetrahydro-3H-imidazo[2,1-*c*][1,4]oxazinium Bromide (3). Morpholinimine **1b** (1.76 g, 0.01 mol) was added to a solution of 4-chlorophenacyl bromide (2.34 g, 0.01 mol) in ethyl acetate (30 ml) and heated at reflux until the onset of precipitate formation (1-2 h). The mixture was then cooled. The precipitate was filtered off, washed with ether, and crystallized from ethanol to give **3** in 78% yield; mp 142°C. IR spectrum, ν, cm^{-1} (KBr pellets): 1620, 3060-3075. ^{1}H NMR spectrum, δ, ppm (400 MHz, DMSO-d$_6$, TMS): 3.05-4.00 (4H, m, OCH_2CH_2N); 4.53 (2H, s, OCH_2); 4.81-4.91 (2H, q, CH_2N); 7.55-7.82 (9H, m, arom); 8.36 (1H, s, OH). Found, %: N 6.58. $C_{18}H_{18}ClN_2O_2Br$. Calculated, %: N 6.84.

1-Benzyl-2-(4-chlorophenyl)-2-hydroxy-2,5,6,8-tetrahydro-3H-imidazo[2,1-*c*][1,4]oxazinium Bromide (2) was obtained analogously in 68% yield; mp 229°C. IR spectrum, ν, cm^{-1} (KBr pellets): 1620, 3050-3068. ^1H NMR spectrum (400 MHz, DMSO-d_6, TMS): 4.34-4.38 (2H, d, CH_2Ar); 3.52-4.11 (4H, m, OCH_2CH_2N); 4.13-4.29 (2H, q, OCH_2); 4.55-4.75 (2H, q, CH_2N); 7.11-7.72 (9H, m, arom); 8.10 (1H, s, OH). Found, %: N 6.88. $C_{19}H_{20}ClN_2O_2Br$. Calculated, %: N 6.61.

3-(4-Chlorophenyl)-1-phenyl-5,6-dihydro-8H-imidazo[2,1-*c*][1,4]oxazinium Bromide (5). Acetic anhydride (30 ml) was added to bromide **3** (4.10 g, 0.01 mol) and heated at reflux for 5 h. Then, acetic anhydride was evaporated in vacuum. The oily residue was washed with acetone, filtered, and crystallized from 2-propanol to give **5** in 65% yield; mp 146°C. IR spectrum, ν, cm^{-1} (KBr pellets): 1620. ^1H NMR spectrum (400 MHz, DMSO-d_6, TMS): 4.17, 4.36 (4H, tt, OCH_2CH_2N); 5.15 (2H, s, OCH_2); 7.67-7.80 (9H, m, arom); 8.42 (1H, s, CHN). Found, %: N 7.32. $C_{18}H_{16}ClN_2OBr$. Calculated, %: N 7.15.

1-Benzyl-2-(4-chlorophenyl)-5,6-dihydro-8H-imidazo[2,1-*c*][1,4]oxazinium Bromide (4) was obtained analogously in 60% yield; mp 218°C. IR spectrum, ν, cm^{-1} (KBr pellets): 1630. ^1H NMR spectrum (400 MHz, DMSO-d_6, TMS): 5.46 (2H, s, CH_2Ar); 4.24, 4.37 (4H, tt, OCH_2CH_2N); 5.18 (2H, s, OCH_2); 7.10-7.58 (9H, m, arom); 8.23 (1H, s, CHN). Found, %: N 6.54. $C_{19}H_{18}ClN_2OBr$. Calculated, %: N 6.90.

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