Furazan ring opening upon treatment of benzofurazan with ethanolamine to yield quinoxalines

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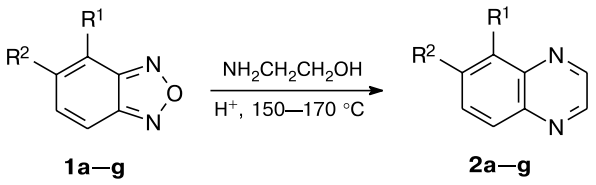
Heating of benzofurazans with ethanolamine in the presence of catalytic amount of *p*-toluenesulfonic acid leads to quinoxalines.

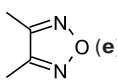
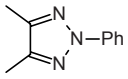
Key words: benzofurazans, ethanolamine, quinoxalines.

Study of chemical properties of benzofurazans showed that the heating of compounds **1a—g** with ethanolamine at 150—170 °C in the presence of catalytic amount of *p*-toluenesulfonic acid unexpectedly leads to quinoxalines **2a—g** (Scheme 1).

Scheme 1

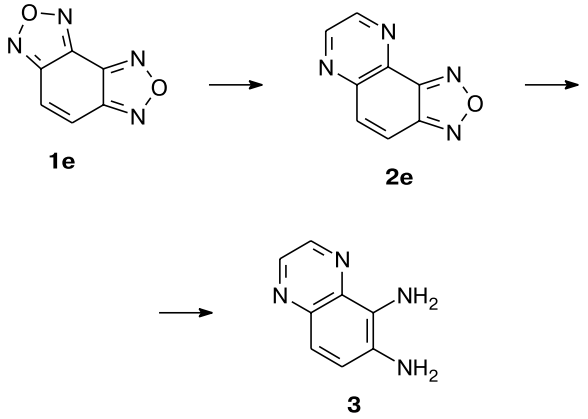


1, 2: R^1 = H, R^2 = H (**a**), Me (**b**), MeO (**c**); R^1 = NH_2, R^2 = H (**d**);

$R^1 + R^2$ =  (**e**),  (**f**), —CH=CH—CH=CH— (**g**)

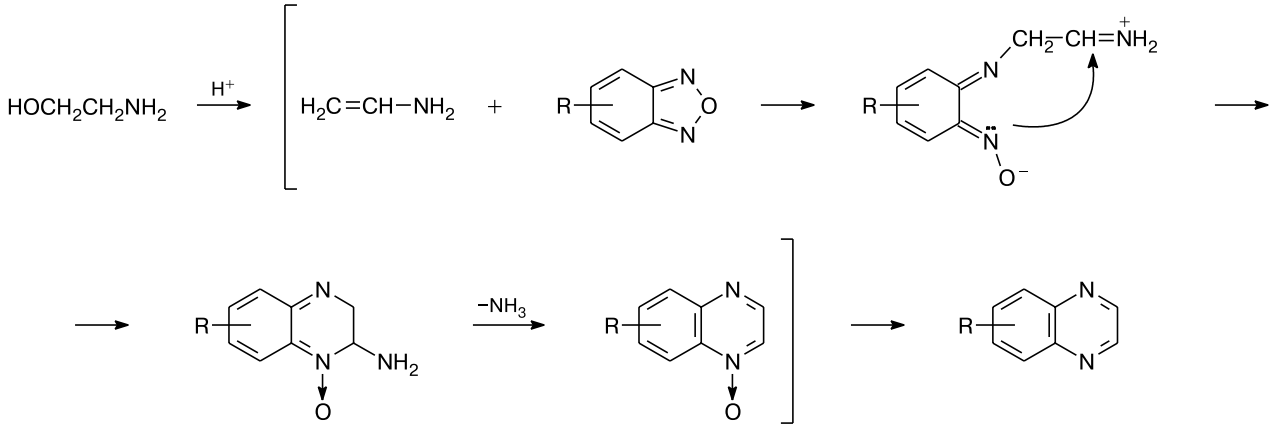
It should be noted that the reaction of benzo[1,2-*c*:3,4-*c*´]difurazan **1e** proceeds with generation of

Scheme 2



heat and leads to furazano[4,5-*f*]quinoxaline **2e** in 76% yield. Upon further heating of compound **2e** with ethanolamine at 150 °C, a reduction of its furazan ring takes place to form 5,6-diaminoquinoxaline **3** (Scheme 2).

Scheme 3



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Apparently, ethanolamine plays the role of a reducing agent similarly to ethylenediamine, which is a mild reducing agent.[1]

The sequence of processes in this synthesis of quinoxaline derivatives is not yet studied. It can be supposed that the enamine is initially formed from ethanolamine. Conversion of ethanolamines to enamines upon treatment with acids was confirmed in Ref. 2. Further attack of enamine at the nitrogen atom of the furazan ring leads to the ring opening followed by the pyrazine ring closure to form quinoxaline *N*-oxide similarly to the known "Beirut reaction".[3] *N*-Oxide oxygen atom, apparently, is readily eliminated upon treatment with ethanolamine, which, as it was shown above, is a reducing agent (Scheme 3).

The found way for the synthesis of quinoxalines from benzofurazans can serve as the alternative to the already existing methods.

Experimental

IR spectra were recorded on a Bruker Vector spectrometer in KBr pellets (concentration, 0.25%), ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM 400 spectrometer (400.13 and 100.63 MHz, respectively) as 5—10% solutions in $CDCl_3$, signals of residual protons of the solvent at δ 7.24 (^{1}H) and 76.90 (^{13}C) relatively to Me_4Si were used as the internal standard. Mass spectra were recorded on a Finnigan MAT-8200 instrument (ionization energy of electrons: 70 eV, direct inlet of a substance, the source of ions temperature: 180 °C). Monitoring of the course of the reaction and purity of compounds were performed by TLC on Sorbfil UV-254 plates with visualization in the UV light. Melting points were determined on the Kofler microheating stage.

Benzofurazans **1a,b,e** were synthesized according to the procedures described earlier[4—6] from the corresponding benzofuroxans by the reaction with triethyl phosphite. Compounds **1c**,[7] **1d**,[8] and **1f**[9] were obtained according to the known procedures. Compound **1g** was synthesized from the corresponding dioxime by its oxidation to furoxan[10] followed by the reduction to furazan with sulfur in ethylene glycol[11] in 60% yield. Structures of quinoxalines obtained were established by comparison of their melting points, IR and NMR spectra with those published in the literature.

Synthesis of quinoxalines 2a—g and 3 (general procedure). Ethanolamine (4 mL) and *p*-toluenesulfonic acid (0.1 g) were added to benzofurazan **1a—g** or **2g** (1 g). The mixture was heated until the starting compound disappeared (TLC monitoring). The mixture was cooled and poured in brine. The product was extracted with ethyl acetate (3×30 mL), the extract was washed with brine (3×30 mL) and dried with $MgSO_4$. The solvent was evaporated, the residue was subjected to chromatography on silica gel with chloroform as the eluent. Conditions of the reaction and yields of quinoxalines **2a—g** and **3** are given in Table 1.

1,2,5-Oxadiazolo[3,4-*f*]quinoxaline (2e). Found (%): C, 55.80; H, 2.29; N, 32.60. $C_8H_4N_4O$. Calculated (%): C, 55.82; H, 2.34; N, 32.55. MS, *m/z*: 172 $[M]^+$. ^{1}H NMR, δ: 7.88, 7.96 (both d, 1 H each, J = 10 Hz); 8.93, 8.98 (both d, 1 H each, J = 2 Hz). ^{13}C NMR, δ: 149.09; 147.84; 146.94 (CH); 146.02; 144.95 (CH); 135.90; 134.58 (CH); 118.31 (CH).

Table 1. Conditions of the reaction and yields of quinoxalines

Starting compound	*T*/°C	τ/h	Product	YIeld (%)	M.p./°C (lit. data)
1a	150—160	4	**2a**	87	29—30 (30.5)[12]
1b	150—160	5	**2b**	85	Oil (b.p. 248)[13]
1c	150—160	4	**2c**	72	55—57 (57.5)[13]
1d	165—170	12	**2d**	74	93—95 (90)[14—16]
1e	100—120	1	**2e**	75	164—165 *
1f	150—160	4	**2f**	89	194—195 *
1g	165—170	16	**2g**	78	54—56 (55—57)[1]
2e	150—160	1	**3**	66	144—145 (144—145)[12]

* Compounds were recrystallized from ethanol.

2-Phenyl-2*H*-triazolo[4,5-*f*]quinoxaline (2f). Found (%): C, 67.90; H, 3.65; N, 28.20. $C_{14}H_9N_5$. Calculated (%): C, 68.00; H, 3.67; N, 28.33. MS, *m/z*: 247 $[M]^+$. ^{1}H NMR, δ: 7.38 (m, 1 H, Ph); 7.48 (m, 2 H, Ph); 7.85, 8.03 (both d, 1 H each, J = 10 Hz); 8.36 (m, 2 H, Ph); 8.84, 8.86 (both d, 1 H each, J = 2 Hz). ^{13}C NMR, δ: 144.91; 144.56 (CH); 144.07; 143.83 (CH); 141.65; 139.80; 137.76; 129.46 (CH); 129.27 (CH); 128.93 (CH); 121.27 (CH); 120.22 (CH).

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