# 2-(5-BROMO-2-FURYL)QUINOXALINE AND 3-(5-BROMO-2-FURYL)-2-QUINOXALONE

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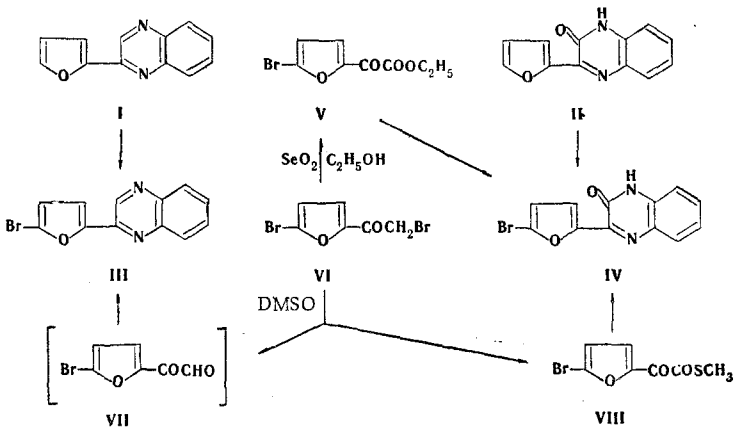
2-(5-Bromo-2-furyl)quinoxaline and 3-(5-bromo-2-furyl)-2-quinoxalone were obtained by the action of bromine on the corresponding quinoxaline derivatives and also by condensation of o-phenylenediamine with, respectively, (5-bromo-2-furyl)glyoxal or (5-bromo-2-furyl)glyoxylic acid esters.

In a continuation of our study of electrophilic substitution in the α-(2-furyl)quinoxaline series [1], we have accomplished the bromination of 2-(2-furyl)quinoxaline (I) and 3-(2-furyl)-2-quinoxalone (II). In both cases, the action of bromine, even when excess amounts of it are present, leads only to monobromo derivatives III and IV, in contrast to nitration, which gives a dinitro derivative in the case of II [1]. The position of the bromine atom in III and IV was proved by means of the PMR spectra.

The initial formation of stable complexes with bromine, which has been noted [2] for some quinoxalines, does not occur in the case of I and II, for salts identical to the products formed directly in the reaction of I and II, respectively, with bromine are obtained on treatment of III and IV with hydrobromic acid in acetone. Hydrobromides III and IV are labile and are converted to bases on heating in aqueous acetic acid or dimethylformamide (DMF).




The product (III) of the bromination of I proved to be identical to that prepared by condensation of o-phenylenediamine with (5-bromo-2-furyl)glyoxal (VII) [3].

We also synthesized 3-(5-bromo-2-furyl)-2-quinoxalone (IV) by condensation of o-phenylenediamine with the ethyl (V) and methylthio (VIII) esters of (5-bromo-2-furyl)glyoxylic acid. Ester V was obtained by oxidation of 5-bromo-2-bromoacetylfuran (VI) with selenium dioxide in absolute alcohol, in analogy with the synthesis of ethyl phenylglyoxylate [4]. Ester VIII was obtained along with (5-bromo-2-furyl)glyoxal by oxidation of 5-bromo-2-bromoacetylfuran under the conditions of the synthesis of the methylthio esters of other substituted glyoxylic acids [5].

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## EXPERIMENTAL

The melting points were determined with a Micro-Heiztisch Boëtius apparatus. Chromatography was carried out on Silufol $UV_{254}$ plates in the following systems: 1) benzene–ethyl acetate (1:1); 2) benzene–ethyl acetate (3:1). The PMR spectra were obtained with a Perkin-Elmer R-12A spectrometer (60 MHz) with cyclohexane ($\delta$ 1.44 ppm) as the internal standard. The IR spectra of hexachlorobutadiene (2000-4000 and 1300-1500 $cm^{-1}$) and Nujol (800-2000 $cm^{-1}$) pastes were recorded with a UR-20 spectrophotometer. The spectra were recorded with a UV-2 spectrophotometer.

2-(5-Bromo-2-furyl)quinoxaline (III). A solution of 1.02 g (20 mmole) of bromine in 5 ml of glacial acetic acid was added dropwise with vigorous stirring to a solution of 3.92 g (20 mmole) of I in 100 ml of the same solvent, after which stirring was continued for 2 h. The precipitated hydrobromide of base III was removed by filtration and washed with acetic acid and ether to give 6 g (85%) of orange crystals with mp 183-184° (dec.). Found: C 40.4; H 2.2; Br 44.4; N 7.9%. $C_{12}H_7BrN_2O \cdot HBr$. Calculated: C 40.5; H 2.3; Br 44.8; N 7.9%. Crystallization of the hydrobromide from hot aqueous acetic acid gave yellow crystals of base III with mp 123-124° (identical to the compound prepared through (5-bromo-2-furyl)glyoxal [3]) and $R_f$ 0.79 (system 1). UV spectrum (in alcohol), $\lambda_{max}$, nm (log $\varepsilon$): 220 (4.58, 268 (4.46), 288 (4.57), 370 (4.49). PMR spectrum (5% solution in acetone): $\delta$ 7.44 and 6.75 ppm (doublets, 3-H and 4-H of the furan ring, J = 3.6 Hz), 9.23, 8.04, and 7.76 ppm (3-H, 5-H and 8-H, and 7-H, respectively, of the quinoxaline ring). Found: C 52.1; H 2.6; Br 29.3; N 10.1%. $C_{12}H_7BrN_2O$. Calculated: C 52.3; H 2.6; Br 29.1; N 10.2%.

3-(5-Bromo-2-furyl)-2-quinoxalone (IV). A. Compound II was brominated in the form of a suspension via the method described above to give an almost quantitative yield of the hydrobromide of IV as orange needles with mp 248-249°. Recrystallization from glacial acetic acid–ether gave a product with mp 254-256° (dec.). Found: Br 42.8; N 7.8%. $C_{12}H_7BrN_2O_2 \cdot HBr$. Calculated: Br 43.0; N 7.5%. A 0.87-g sample of the hydrobromide was dissolved in 10% sodium hydroxide solution, and base IV was precipitated by acidification with acetic acid. The precipitate was removed by filtration and washed with water to give 0.51 g (75%) of yellow crystals with mp 268-269° (dec., from aqueous acetic acid). Compound IV was also obtained from its hydrobromide by direct recrystallization from DMF–water. The compound had $R_f$ 0.61 (system 1). UV spectrum (in a solution made up of 2 vol. % DMF and 98 vol.% alcohol), $\lambda_{max}$, nm (log $\varepsilon$): 380 (4.64), 400 (4.50); $\lambda_{min}$ 275 (3.68). PMR spectrum (in tetrahydrofuran): $\delta$ 7.82 and 6.89 ppm (doublets, 3-H and 4-H of the furan ring, J = 3.5 Hz), 7.48 ppm (unresolved $A_2B_2$ multiplet, 5-H, 6-H, 7-H, and 8-H of the quinoxaline ring). Found: C 49.4; H 2.3; Br 28.0; N 9.5%. $C_{12}H_7BrN_2O_2$. Calculated: C 49.5; H 2.4; Br 27.5; N 9.6%.

B. A 13.4-g (50 mmole) sample of VI was added to a solution of 5.85 g (50 mmole) of selenium dioxide in 50 ml of absolute alcohol, and the mixture was stirred and refluxed for 9 h. The selenium was removed by filtration, and the filtrate was vacuum-evaporated. A solution of 1 g (10 mmole) of o-phenylenediamine in 20 ml of alcohol was added to $^1/_{10}$ of the volume of the crude ethyl (5-bromo-2-furyl)glyoxylate (V), and the mixture was heated on a water bath for 30 min. It was then diluted with water to precipitate 0.97 g (67%, based on VI) of IV with mp 268-269° (dec., from DMF–water) and $R_f$ 0.61 (system 1).

C. A mixture of 0.10 g (0.4 mmole) of VIII and 0.44 g (0.44 mmole) of o-phenylenediamine in 3 ml of alcohol was heated to the boiling point and diluted with water, and the precipitate was removed by filtration to give 0.11 g (94%) of yellow flakes with mp 268-269° (dec.) and $R_f$ 0.61 (system 1).

Methyl (5-Bromo-2-furyl)glyoxylate (VIII) and (5-Bromo-2-furyl)glyoxal (VII). A mixture of 5.4 g (0.02 mole) of freshly prepared [3] VI and 20 ml (0.3 mole) of dimethyl sulfoxide was held at −40 to −50° for 2 h and then at room temperature for 24 h. It was then poured over ice (100 g) and water (50 ml), and the precipitated VIII was removed by filtration, washed with water, and dried to give 1.95 g (39%) of yellow needles with mp 93-94° (from dilute alcohol) and $R_f$ 0.80 (system 2, black spot). UV spectrum (in alcohol): $\lambda_{max}$ 318 nm, log $\varepsilon$ 4.45. IR spectrum, $cm^{-1}$: 3160 and 3150 ($\nu_{CH}$ of the furan ring), 2940 ($\nu_{CH_3}^{as}$), 2867 ($\nu_{CH_3}^{s}$), 1682 and 1665 (inflection, ketone $\nu_{CO}$ and $\nu_{CO-S}$), 1450 ($\delta_{CH_3}^{as}$), 1360 ($\delta_{CH_3}^{s}$), and 1300 ($CH_3-S$). PMR spectrum (in acetone): $\delta$ 2.32 ppm ($CH_3$), 6.47 and 7.64 ppm (doublets, 3-H and 4-H of the furan ring). Found: Br 32.1; S 12.6%. $C_7H_5BrO_3S$. Calculated: Br 32.1; S 12.9%.

Glyoxal VII, which was present in the filtrate along with traces of VIII [$R_f$ 0.74 and 0.80 (system 2)], was converted to 2-(5-bromo-2-furyl)quinoxaline (III) by addition of 4.75 g (40 mmole) of o-phenylenediamine in 100 ml of water. The precipitate was removed by filtration, washed with hot water, and dried to give 2.7 g of III [49%, based on VI, contaminated with 5-10% IV (according to TLC and the PMR spectrum)].

Compound III was washed out of 0.4 g of this mixture by treatment with 20 ml of alcohol to give 0.01 g of undissolved IV with $R_f$ 0.61 (system 1). Treatment of the filtrate with charcoal and evaporation gave 0.27 g of residual III with mp 121-123° and $R_f$ 0.79 (system 1).

## LITERATURE CITED


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