# A Convenient Synthesis of New Arylethenylquinoxalines

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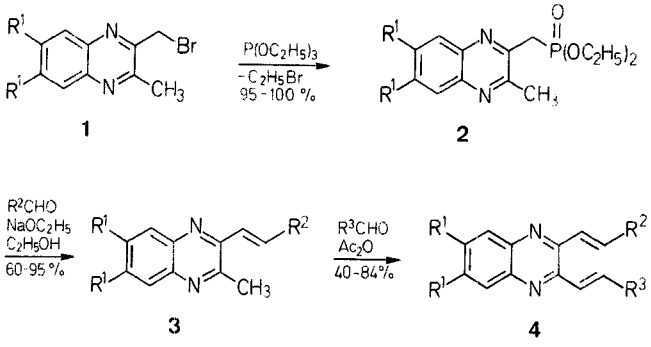
New 3-(2-arylethenyl)-2-methylquinoxalines **3** were prepared in high yields using standard procedures. These compounds serve as starting materials for the preparation of unsymmetrically substituted 2,3-bis-(2-arylethenyl)quinoxalines **4**, a new group of quinoxaline derivates.

Arylethenylquinoxalines have attracted considerable industrial attention. Thus 3-(2-arylethenyl)-2-methylquinoxalines **3** were claimed as pressure- and heat-sensitive color-formers,[1] and symmetrically substituted 2,3-bis(2-arylethenyl)quinoxalines were described as photoinitiators[2] and photosemiconductors[3] in lightsensitive mixtures.

Only a few examples for the preparation of 3-(2-arylethenyl)-2-methylquinoxalines **3** are given in the literature.[4] The scope of the reported synthesis is limited. Often low yields are obtained, due to the formation of bis-condensation products or a complete failure of the reaction. Moreover, to our knowledge, no attempt was made yet to synthesize 2,3-bis(2-arylethenyl)quinoxalines **4** having different substituents attached to the arylethenyl groups.

In this paper an easy high yield synthesis is reported for **3** as well as for unsymmetrically substituted 2,3-bis(2-arylethenyl)quinoxalines **4**, which are representatives of a new group of quinoxaline derivatives.

The reaction sequence is outlined below. 3-Bromomethyl-2-methylquinoxalines **1**, prepared according to a literature procedure,[5] were reacted with triethyl phosphite (Arbuzov-reaction) to yield the phosphonates **2** in nearly quantitative yields. The phosphonates **2** react smoothly with aromatic or heteroaromatic aldehydes under alkaline conditions (Horner-Emmons reaction) to give the 3-(2-arylethenyl)-2-methylquinoxalines **3** in good yields. By applying the conditions described in the experimental section, the products **3** usually separate from the hot or cooled reaction mixture in high purity.




**1** **2** **3** **4**

| 1, 2 | $R^1$ |
|---|---|
| **a** | H |
| **b** | $CH_3$ |
| **c** | Cl |

| 3 | $R^1$ | $R^2$ |
|---|---|---|
| **a** | H | 3,4-$(CH_3O)_2C_6H_3$ |
| **b** | H | 4-$CH_3C_6H_4$ |
| **c** | H | 3-$C_6H_5OC_6H_4$ |
| **d** | H | 4-$N(C_2H_5)_2C_6H_4$ |
| **e** | $CH_3$ | 3,4-$(CH_3O)_2C_6H_3$ |
| **f** | $CH_3$ | 2-methoxynaphthyl |
| **g** | Cl | 3,4-$(Cl)_2C_6H_3$ |
| **h** | Cl | 4-$N(C_2H_5)_2C_6H_4$ |

| 4 | $R^1$ | $R^2$ | $R^3$ |
|---|---|---|---|
| **a** | H | 3,4-$(CH_3O)_2C_6H_3$ | 4-$CNC_6H_4$ |
| **b** | H | 3,4-$(CH_3O)_2C_6H_3$ | $C_6H_5$ |
| **c** | H | 3,4-$(CH_3O)_2C_6H_3$ | 3-$CH_3OC_6H_4$ |
| **d** | H | 4-$CH_3C_6H_4$ | 3,4-$(Cl)_2C_6H_3$ |
| **e** | H | 3-$C_6H_5OC_6H_4$ | $C_6H_5$–CH=CH |
| **f** | H | 4-$N(C_2H_5)_2C_6H_4$ | 4-$NO_2C_6H_4$ |
| **g** | $CH_3$ | 3,4-$(CH_3O)_2C_6H_3$ | 4-$NO_2C_6H_4$ |
| **h** | $CH_3$ | 2-methoxynaphthyl | 3-$NO_2C_6H_4$ |
| **i** | Cl | 3,4-$(Cl)_2C_6H_3$ | 4-$CF_3C_6H_4$ |
| **j** | Cl | 4-$N(C_2H_5)_2C_6H_4$ | 4-$COOCH_3C_6H_4$ |

In the course of our studies more than fifty different aryl- and hetarylaldehydes were investigated and only very few limitations of the scope of the reaction were observed. Araldehydes having acidic hydrogen, e.g. hydroxybenzaldehydes, should be protected, and in one case, using pentafluorobenzaldehyde, we observed nucleophilic displacement of one fluoro substituent. Even aldehydes with low carbonyl reactivity, e.g. 4-dialkylaminobenzaldehydes, or sterically hindered substrates, e.g. 2,6-disubstituted benzaldehydes, react in high yields. On the other hand, attempts to conduct the reaction with aromatic ketones, failed.

The compounds **3** are yellow to deep blue in color depending on the electronic configuration of the araldehyde used.

If the 3-(2-arylethenyl)-2-methylquinoxalines **3** are condensed with a further, differently substituted araldehyde in the presence of acetic acid anhydride, unsymmetrically substituted 2,3-bis(2-arylethenyl)quinoxalines **4** are obtained. The reaction proceeds best with araldehydes in which the carbonyl group is activated by the presence of electron-withdrawing groups in the ring.[4] With such compounds the yields of products **4** are high and there is no need for chromatographic separation of unreacted starting material as happens when less active aldehydes are employed.

In comparison with 3-(2-arylethenyl)-2-methylquinoxalines **3**, the 2,3-bis(2-arylethenyl)quinoxalines **4** show a bathochromic shift in their UV spectra. They exhibit broad absorption maxima with low absorption coefficients.

The new compounds **2**, **3** and **4** were characterized by microanalyses and their spectral data (Tables 1 and 2).

**Diethyl [(3-Methylquinoxaline-2-yl)methyl]phosphonate (2a); Typical Procedure:**

3-Bromomethyl-2-methylquinoxaline (**1a**;[5] 50 g, 0.21 mol) is added to triethyl phosphite (105 g, 0.63 mol), which is stirred at room temperature in a 500 ml flask equipped with a thermometer and a distillation bridge under the exclusion of moisture. The mixture is heated and at an initial temperature of 80 °C ethyl bromide begins to distil rapidly. The resulting solution is heated to 140 °C for 3 h. The excess of triethyl phosphite is distilled off under reduced pressure. By cooling to room temperature a tan-colored mass is obtained; yield: 61.5 g (~ 100%); m.p. 86–87 °C (*n*-hexane), colorless needles.

$C_{14}H_{19}N_2O_3P$ (294.3) calc. C 57.13 H 6.51 N 9.52 found 57.2 6.4 9.4

$^1$H-NMR ($CDCl_3$/TMS): $\delta$ = 1.26 (t, 6H, $CH_3$, $J$ = 7.4 Hz); 2.82 (s, 3H, $CH_3$); 3.59 (d, 2H, $CH_2$, $J_{HP}$ = 21.8 Hz); 4.11 (p, 4H, $CH_2$, $J$ = 7.4 Hz); 7.50–8.12 ppm (m, 4 $H_{arom}$).

**3-[2-(3,4-Dimethoxyphenyl)ethenyl]-2-methylquinoxaline (3a); Typical Procedure:**

To an alcoholate solution prepared from ethanol (200 ml) and sodium (1.15 g, 50 mmol) are added diethyl [(3-methylquinoxaline-2-yl) methyl]phosphonate (**2a**; 5.89 g, 20 mmol) and 3,4-dimethoxybenzaldehyde (3.66 g, 22 mmol) under exclusion of moisture. The resulting mixture is stirred under reflux for 3 h. During the heating a yellowish solid begins to separate. The mixture is cooled and left in a refrigerator overnight. The yellow solid is filtered off; yield: 4.9 g (80%); m.p. 142–143 °C (methanol).

$C_{19}H_{18}N_2O_2$ (306.4) calc. C 74.49 H 5.92 N 9.14 found 74.4 5.9 9.2

UV ($CH_2Cl_2$): $\lambda_{max}$ = 285, 383 nm.

$^1$H-NMR ($CDCl_3$/TMS): $\delta$ = 2.84 (s, 3H, $CH_3$); 3.90 (s, 3H, $OCH_3$); 3.94 (s, 3H, $OCH_3$); 6.82–8.05 ppm (m, 9H, CH + $H_{arom}$).

**2-[2-(4-Cyanophenyl)ethenyl]-3-[2-(3,4-dimethoxyphenyl)ethenyl]-quinoxaline (4a); Typical Procedure:**

Method A: A mixture of **3a** (6.1 g, 20 mmol), 4-cyanobenzaldehyde (5.2 g, 40 mmol) and acetic acid anhydride (30 ml) is refluxed with stirring and under the exclusion of moisture for 5 h. The dark solution is cooled and ethanol (100 ml) is added. The yellow precipitate is stirred for 1 h and collected; yield: 5.59 g (71%); m.p. 214–215 °C (ethanol/chloroform).

$C_{27}H_{21}N_3O_2$ (419.5) calc. C 77.31 H 5.05 N 10.02 found 77.1 5.0 10.0

IR (KBr): $\nu$ = 2226 $cm^{-1}$ (m, C≡N).

UV ($CH_2Cl_2$): $\lambda_{max}$ = 305, 350 (sh), 404 nm (sh).

$^1$H-NMR ($CDCl_3$/TMS): $\delta$ = 3.93 (s, 3H, $OCH_3$); 3.95 (s, 3H, $OCH_3$); 6.85–8.08 ppm (m, 15H, CH + $H_{arom}$).

**2-[2-(3,4-Dimethoxyphenyl)ethenyl]-3-(2-phenylethenyl)quinoxaline (4b); Typical Procedure:**

Method B: A mixture of **3a** (3.05 g, 10 mmol), benzaldehyde (3.18 g, 30 mmol) and acetic acid anhydride (15 ml) is refluxed with stirring for 18 h. The mixture is cooled to 80 °C and ethanol (50 ml) is added. The resulting mixture is refluxed for 15 min and the solvents are removed

**Table 1.** Selected Data of Compounds **2** and **3** Prepared

| Product | Yield[a] (%) | m.p. (°C)[b] (solvent) | Molecular Formula[c] | UV ($CH_2Cl_2$)[d] $\lambda_{max}$ (nm) | $^1$H-NMR ($CDCl_3$/TMS)[e] $\delta$ (ppm) |
|---|---|---|---|---|---|
| **2b** | 95 | 75 (*n*-hexane) | $C_{16}H_{23}N_2O_3P$ (322.3) | – | 1.26 (t, 6H, $J$ = 7.4 Hz); 2.43 (s, 6H); 2.82 (s, 3H); 3.61 (d, 2H, $J$ = 21.8 Hz); 4.13 (p, 4H, $J$ = 7.4 Hz); 7.72 (s, 2H) |
| **2c** | 95 | 193–194 (*n*-hexane) | $C_{14}H_{17}Cl_2N_2O_3P$ (363.2) | – | 1.27 (t, 6H, $J$ = 7.2 Hz); 2.83 (s, 3H); 3.61 (d, 2H, $J$ = 21.8 Hz); 4.14 (p, 4H; $J$ = 7.2 Hz); 8.07 (s, 2H) |
| **3b** | 92 | 129–130 ($CH_3OH/CH_2Cl_2$) | $C_{18}H_{16}N_2$ (260.3) | 285, 368 | 2.33 (s, 3H); 2.78 (s, 3H); 7.09–8.06 (m, 10H) |
| **3c** | 71 | 88–89 ($CH_3OH$) | $C_{23}H_{18}N_2O$ (338.4) | 283, 364 | 2.80 (s, 3H); 6.97–8.06 (m, 15H) |
| **3d** | 78 | 123–125 ($CH_3OH$) | $C_{21}H_{23}N_3$ (317.4) | 307, 440 | 1.19 (t, 6H, $J$ = 7.2 Hz); 2.80 (s, 3H); 3.34 (q, 4H, $J$ = 7.2 Hz); 6.52–8.06 (m, 10H) |
| **3e** | 84 | 175 ($C_2H_5OH$) | $C_{21}H_{22}N_2O_2$ (334.4) | 288, 383 | 2.45 (s, 6H); 2.83 (s, 3H); 3.92 (s, 3H); 3.96 (s, 3H); 6.93–8.01 (m, 7H) |
| **3f** | 82 | 175–176 ($CH_3OH/CH_2Cl_2$) | $C_{24}H_{22}N_2O$ (354.5) | 338, 388 | 2.47 (s, 6H); 2.81 (s, 3H); 4.02 (s, 3H); 7.24–8.64 (m, 10H) |
| **3g** | 94 | 218–219 ($C_2H_5OH/CHCl_3$) | $C_{17}H_{10}Cl_4N_2$ (384.1) | 283, 290, 374, 390sh | 2.85 (s, 3H); 7.26–8.13 (m, 7H) |
| **3h** | 76 | 138–140 ($C_2H_5OH$/toluene) | $C_{21}H_{21}Cl_2N_3$ (386.3) | 318, 352sh, 464 | 1.21 (t, 6H, $J$ = 7.0 Hz); 2.79 (s, 3H); 3.41 (q, 4H, $J$ = 7.0 Hz); 6.62–8.08 (m, 8H) |

[a] Yield of isolated product.
[b] Uncorrected, measured with a Gallenkamp apparatus.
[c] Satisfactory microanalysis obtained: C ±0.25, H ±0.15, Cl ±0.30, N ±0.20.
[d] Recorded on a Perkin Elmer 554 UV spectrophotometer.
[e] Recorded on a Jeol FX 90Q spectrometer.

**Table 2.** Selected Data of Compounds **4** Prepared (Explanation to Footnotes as in Table 1)

| Product | Method | Yield[a] (%) | m.p. (°C)[b] (solvent) | Molecular Formula[c] | UV ($CH_2Cl_2$)[d] $\lambda_{max}$ (nm) | $^1$H-NMR ($CDCl_3$/TMS)[e] $\delta$ (ppm) |
|---|---|---|---|---|---|---|
| **4c** | B | 47 | 159–161 ($C_2H_5OH/CHCl_3$) | $C_{27}H_{24}N_2O_3$ (424.5) | 285sh, 322, 364, 408sh | 3.84 (s, 3H); 3.93 (s, 3H); 3.96 (s, 3H); 6.86–8.07 (m, 15H) |
| **4d** | A | 63 | 165–166 ($C_2H_5OH/CHCl_3$) | $C_{25}H_{18}Cl_2N_2$ (417.3) | 306, 344, 392 | 2.38 (s, 3H); 7.16–8.04 (m, 15H) |
| **4e** | B | 40 | 124–126 ($C_2H_5OH$) | $C_{32}H_{24}N_2O$ (452.6) | 280, 348sh, 402 | 7.01–8.07 (m, 24H) |
| **4f** | A | 77 | 209–210 ($C_2H_5OH/CHCl_3$) | $C_{28}H_{26}N_4O_2$ (450.5) | 326sh, 352, 430 | 1.19 (t, 6H, $J$ = 7.0 Hz); 3.40 (q, 4H, $J$ = 7.0 Hz); 6.52–8.33 (m, 16H) |
| **4g** | A | 84 | 228–229 ($CHCl_3$) | $C_{28}H_{25}N_3O_4$ (467.5) | 332, 360sh, 412sh | 2.49 (s, 6H); 3.93 (s, 3H); 3.96 (s, 3H); 6.87–8.31 (m, 13H) |
| **4h** | A | 78 | 242–243 ($C_2H_5OH/CHCl_3$) | $C_{31}H_{25}N_3O_3$ (487.6) | 276, 360, 410sh | 2.52 (s, 6H); 4.09 (s, 3H); 7.25–8.63 (m, 16H) |
| **4i** | A | 56 | 217–218 ($C_2H_5OH/CHCl_3$) | $C_{25}H_{13}Cl_4F_3N_2$ (540.2) | 304, 325sh, 394 | 7.25–8.14 (m, 13H) |
| **4k** | A/B | 47/66 | 113–114 ($C_2H_5OH$) | $C_{30}H_{27}Cl_2N_3O_2$ (532.5) | 308, 389, 414sh, 482 | 1.21 (t, 6H, $J$ = 7.0 Hz); 3.42 (q, 4H, $J$ = 7.0 Hz); 3.95 (s, 3H); 6.64–8.13 (m, 14H) |

under reduced pressure. The residue is chromatographed on silica gel using a toluene/dichloromethane mixture (1:1). The first yellow fraction is collected. Evaporation of the solvents leaves a yellow powder; yield: 2.45 g (62%); m.p. 165–167°C (ethanol).

$C_{26}H_{22}N_2O_2$ (394.5) calc. C 79.17 H 5.62 N 7.10; found 79.2 5.7 7.1

UV ($CH_2Cl_2$): $\lambda_{max}$ = 305, 349 (sh), 404 nm.

$^1$H-NMR ($CDCl_3$/TMS): $\delta$ = 3.93 (s, 3H, $OCH_3$); 3.96 (s, 3H, $OCH_3$); 6.86–8.09 ppm (m, 16H, CH + $H_{arom}$).

*Dedicated to Prof. Dr. Heinz Harnisch, Hoechst AG, on the occasion of his 60th birthday.*

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