Institute of Organic Chemistry (Director: G. Fodor)
Institute of General and Physical Chemistry (Director: Á. Kiss) of the University of Szeged (Hungary)

Preparation of some new quinoxaline derivatives

By Ödön Kovács and Erzsébet Tombácz

On synthesizing 1-aryl-2-alkylamino ethanols several quinoxaline derivatives were prepared. Namely the phenyl glyoxal derivatives obtained by this procedure as could be identified with o-phenylene diamine as quinoxaline derivatives because they crystallise readily. This was necessary because it did not succeed to isolate on the ring variously substituted phenyl glyoxals in crystalline form. On the other hand, the existence and structure of the employed glyoxal was proved by the crystalline quinoxaline derivatives obtained in this way (1).

It was observed that the o-hydroxy derivative of phenyl glyoxals did not yield quinoxalines but bis-o-hydroxy-phenyl-glyoxaliliden-o-oxy-phenylen diamine. Several quinoxaline derivatives were prepared for detailed spectroscopical examinations.

Quinoxaline. 5,8 g p-glyoxal and 46,8 ml acetic anhydride were boiled and refluxed for 22 hours. Subsequently to a yellowich-green transitory colour a dark brown solution resulted. On cooling brownish-white crystals formed, yield, 10,2 g. M. p. 106° C. The crystaline substance obtained in this way (0,05 mol), was dissolved in ethanol and mixed with the alcoholic solution of 5,4 g (0,05 mol) o-phenylen diamine. From the hot solution oily quinoxaline separates. The oily product was separated, thereafter in vacuo, distilled B. p. 222° C. 1,54 g quinoxaline in form of yellowish, -whitish oil was recovered getting gellike on standing. Yield 24%. M. p. 27° C (2).

2-3-dichloro-quinoxaline. 16,2 g (0,1 mol) dried 2-3-dihydroxy-quinoxalin and 41,2 g (0,2 mol) PCl_5 were mixed and the mixture was dissolved in as much phosphorous axychloride as was needed for it to dissolve. The solution was refluxed for 2 hours in a $CaCl_2$-ish tube. The excess solvent is distilled off in vacuo. On pouring the remainder into iced water 5,4 g (yield 27%) crystalline di-chloro-quinoxaline was obtained. It was crystallized in ethanol and purified with charcoal. White, silky crystals were recovered. M. p. 150° C (3).

2-(m-methoxy-phenyl)-quinoxaline. 22,2 g (0,1 mol) 2-(m-hydroxy-phenyl)-quinoxaline was dissolved in aqueous solution of NaOH, to this solution 13,8 g (0,11 mol) dimethyl sulphate was added. After shaking we obtained 13,8 g 2-(m-methoxy-phenyl)-quinoxaline. The crude product was recrystallized several times from ethanol. M. p. 85° C.

Analysis. Calcd. for $C_{15}H_{12}ON_2$: C, 74,76; H, 5,12; N, 11,86.
Found: C, 75,64; H, 4,98; N, 11,54.

2-(m-acetoxy-phenyl)-quinoxaline. 22,2 g (0,01 mol) 2-(m-hydroxy-phenyl)-quinoxaline was dissolved in 61,2 g acetic anhyride

(0,6 mol) and boiled on a waterbath for 4—5 hours. The excess acetic acid and acetic anhydride were distilled off in vacuo. On cooling, 24 g crystalline (2-(m-acetoxy-phenyl)-quinoxaline (yield 88%) was obtained. The raw product was purified with charcoal and recrystallized several times from ethanol. M. p. 207° C.

Analysis. Calcd. for $C_{16}H_{12}O_2N_2$: C, 72,69; H, 4,58; N, 10,61.
Found: C, 72,35; H, 4,26; N, 10,86.

2-(m-benzyl-oxy-phenyl)-quinoxaline. 22,2 g (0,1 mol) 2-m-hydroxy--phenyl-quinoxaline was dissolved in absolute alcohol and added to an alcoholic solution of metallic sodium of 2,3 g (0,1 mol) benzyl chloride was added. After boiling for 5 hours on the water-bath on cooling silky 2-(m-benzyl-oxy-phenyl)-quinoxaline crystals appared. It was recrystallized from ethanol and purified with charcoal. After recrystallization 23,7 g product was obtained. Yield: 76%. M. p. 118° C.

Analysis. Calcd. for $C_{21}H_{16}N_2O$: C, 80,73; H, 5,7; N, 8,98.
Found: C, 80,43; H, 4,96; N, 8,74.

2-(m-benzoyl-oxy-phenyl)-quinoxaline. 22,2 g (0,1 mol) 2-m-hydroxy-phenyl-quinoxaline was dissolved in an aqeous solution of 4,0 g NaOH (0,1 mol) and 15,4 g benzoylchloride was added. On shaking 2-(m-benzoyl-oxy-phenyl)-quinoxaline separated. The crude product was 20,6 g, yield 63%. It was crystallized from ethanol. M. p. 163° C.

Analysis. Calcd. for $C_{21}H_{14}O_2N_2$: C, 77,27; H, 4,33; N, 8,59.
Found: C, 77,10; H, 4,54; N, 8,80.

2-(p-methoxy-phenyl)-quinoxaline. 22,2 g (0,1 mol) 2-p-hydroxy--phenyl-quinoxaline was dissolved in an aqueous solution of 4,4 g sodium hydroxide and 13,8 g (0,11 mol) dimethyl sulphate was added. The methylated product separated on shaking. The crude product was recrystallized several times from ethanol and yielded 18,3 g 2-(p-methoxy-phenyl)-quinoxaline in long needles. Yield: 81%. M. p. 102° C. (1).

2-(p-acetoxy-phenyl)-quinoxaline. 22,2 g (0,1 mol) p-hydroxy--phenyl-quinoxaline was dissolved in 6,12 (0,6 mol) acetic anhydride and boiled for 4—5 hours on the water-bath. The excess acetic acid and acetic anhydride were both distilled off in vacuo. The acetylated product separated on cooling in crystals. The raw product was recrystallised a few times from ethanol. 23,4 g p-acetoxy-phenyl--quinoxaline was obtained. Yield: 86%. M. p. 125° C.

Analysis. Calcd. for $C_{16}H_{12}O_2N_2$: C, 72,69; H, 4,58; N, 10,61.
Found: C, 72,34; H, 4,28; N, 10,85.

2-(p-benzyloxy-phenyl)-quinoxaline. 22,2 g (0,1 mol) 2-p-hydroxy-phenyl-quinoxaline was dissolved in an aeqeous solution of 4,0 g sodium hydroxide (0,1 mol), 13,8 g benzylchloride was added

and the mixture boiled for 6 hours. On cooling yellow, silky crystals separated. To remove the sodium chloride the filtered product was washed with water several times. Weight 23,6 g, 76% yield. Then the crystals were purified and recrystallised a few times from ethanol. M. p. 130° C.

Analysis. Calcd. for $C_{21}H_{16}N_2O$: C, 80,73; H, 5,7; N, 8,98.
Found: C, 80,42; H, 4,95; N, 8,76.

2-(p-benzoyloxy-phenyl)-quinoxaline. 22,2 g (0,1 mol) p-hydroxy-phenyl-quinoxaline was dissolved in an aquesous solution of 4,0 g sodium hydroxide and 15,4 g (0,11 mol) benzoylchloride added. On shaking 21,3 g 2-(p-benzoyloxy-phenyl)-quinoxaline was separated, yield 65%. The crude product was recrystallised from ethanol. M. p. 152° C.

Analysis. Calcd. for $C_{21}H_{14}O_2N_2$: C, 77,27; H, 4,33; N, 8,59.
Found: C, 77,15; H, 4,47; N, 8,89.

3-4-(dimethoxy-phenyl)-quinoxaline. 23,8 g (0,1 mol) 3-4-(dihydroxy-phenyl)-quinoxaline was dissolved in an aqueous solution of 8,4 g sodium hydroxide (0,21 mol) and 26,5 g (0,21 mol) dimethyl sulphate was added. On shaking 12,5 g 3-4-(dimethoxy-phenyl)-quinoxaline was separated. Yield: 47%. The crude product was filtered and crystallised several times from ethanol. M. p. 120° C.

Analysis. Calcd. for $C_{16}H_{14}O_2N_2$: C, 72,14; H, 5,30; N, 10,53.
Found: C, 71,88; H, 5,14; N, 10,25.

3-4-(dibenzoyloxy-phenyl)-quinoxaline. 23,8 g (0,1 mol) 3-4-dihydroxy-phenyl-quinoxaline was dissolved in an aqueous solution of 8,0 g (0,2 mol) sodium hydroxide and 29,4 g (0,21 mol) benzoyl chloride added. On shaking 27,7 g 3-4-(dibenzoyloxy-phenyl)-quinoxaline was separated. Yield: 62%. The crude product was crystallised from ethanol with charcoal. M. p. 172° C.

Analysis. Calcd. for $C_{28}H_{18}O_4N_2$: C, 75,31; H, 4,07; N, 6,28.
Found: C, 75,05; H, 3,74; N, 5,92.

3-4-(dibenzyloxy-phenyl)-quinoxaline. 23,8 g (0,1 mol) 3-4-dihydroxy-phenyl-quinoxaline was dissolved in absolute alcohol and an alcoholic solution of sodium ethoxide from 4,6 g sodium (0,2 mol) added. Finally 27,8 g benzylchloride was added. The solution was boiled for 5 hours on the water-bath, on cooling yellow, silky crystals of 3-4-(dibenzyloxy-phenyl)-quinoxaline formed. On recrystallising several times from ethanol 33,7 g of a pure product was obtained. Yield: 71%. M. p. 118° C. (1).

References.

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2. *Organic Syntheses:* 24. p. 61.
3. *Hinsberg, Pollack:* Ber. 29, 784; Ber. 41. 20 31.