[CONTRIBUTION FROM THE UNIVERSITY OF NEW MEXICO, LABORATORY OF PHARMACEUTICAL CHEMISTRY]

The Reaction of 2-Chloroquinoxaline With Substituted Acetonitriles

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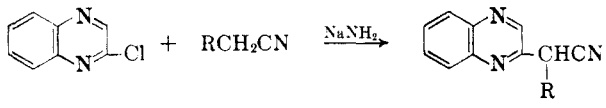
2-Chloroquinoxaline has been condensed with six substituted acetonitriles. The reaction, while general in nature, does not proceed as readily as that of 4-chlorocinnoline with the same nitriles. The six compounds prepared by this condensation have not previously been reported in the literature.

In previous papers we have reported the reaction of 4-chlorocinnoline with variously substituted acetonitriles.[1,2] In order to extend the data to other ring systems we now report the reaction of 2-chloroquinoxaline with six nitriles, namely: phenylacetonitrile, 2,4-dichlorophenylacetonitrile, *m*-methoxyphenylacetonitrile, 1-naphthylacetonitrile, diphenylacetonitrile, and 2-cyanomethyl-4,4-dimethyl-1-isopropyl-2-imidazoline. Sodium amide was used as the base to promote this nucleophilic reaction. The reaction has been shown to be a general reaction and is illustrated by the equation below.



We have found that the reaction did not take place with 2-chloroquinoxaline as readily as with 4-chlorocinnoline. This was determined by the size of the yields obtained. These could be compared since the reaction conditions were virtually identical.

Recently Mizuno, Adachi, and Ikeda[3] have reported a study of several active halogeno-heterocyclic systems with phenylacetonitrile and other compounds with active methylene groups. They indicate that "the chlorine-activating power" in 4-chlorocinnoline is considerably above that of 2-chloro-3-methylquinoxaline. Our work leads us to the same conclusion with regard to the 2-chloroquinoxaline.

EXPERIMENTAL

All melting points reported are uncorrected. Carbon and hydrogen analyses are by Weiler and Strauss, Oxford.

2-Chloroquinoxaline was readily prepared by the method of Gowenlock, Newbold, and Spring[4] and purified by vacuum distillation, m.p. 47–48°.

α-(2-Quinoxalyl)phenylacetonitrile. To 2.6 g. of phenylacetonitrile in 14 ml. of dry benzene was added 1.2 g. of sodium amide. After stirring the mixture for one hour 1.64 g. of 2-chloroquinoxaline in 15 ml. of dry benzene was added over a period of 30 minutes and the mixture was stirred an additional two hours. Water was added to hydrolyze the sodio derivative and the benzene layer was separated, dried over sodium sulfate, and the benzene evaporated. There was obtained 1.16 g. of yellowish-orange crystals which after crystallization from aqueous ethanol and chromatography on methanol deactivated alumina melted at 118–119°.

Anal. Calc'd for $C_{16}H_{11}N_3$: C, 78.34; H, 4.52. Found: C, 78.79; H, 4.43.

α-(2-Quinoxalyl)2,4-dichlorophenylacetonitrile. From 7.44 g. of 2,4-dichlorophenylacetonitrile, 2.4 g. of sodium amide, and 3.28 g. of 2-chloroquinoxaline there was obtained 3.1 g. of reddish-orange rosettes which upon purification as above melted at 149–151°.

Anal. Calc'd for $C_{16}H_9Cl_2N_3$: C, 61.21; H, 2.89. Found: C, 61.05; H, 2.99.

α-(2-Quinoxalyl)-m-methoxyphenylacetonitrile. From 2.94 g. of *m*-methoxyphenylacetonitrile, 1.2 g. of sodium amide, and 1.64 g. of 2-chloroquinoxaline there was obtained 0.77 g. of pale orange needles. After purification in the usual manner they melted at 110–110.5°.

Anal. Calc'd for $C_{17}H_{13}N_3O$: C, 74.16; H, 4.76. Found: C, 73.96; H, 4.95.

α-(2-Quinoxalyl)diphenylacetonitrile. From 7.22 g. of diphenylacetonitrile, 2.4 g. of sodium amide, and 3.28 g. of 2-chloroquinoxaline there was obtained 1.2 g. of colorless prisms which after purification melted at 129–131°.

Anal. Calc'd for $C_{22}H_{15}N_3$: C, 82.22; H, 4.71. Found: C, 82.38; H, 4.95.

α-(2-Quinoxalyl)-1-naphthylacetonitrile. From 3.34 g. of 1-naphthylacetonitrile, 1.2 g. of sodium amide, and 1.64 g. of 2-chloroquinoxaline there was obtained 0.97 g. of golden-brown prisms melting at 186–187° after crystallization from ethanol.

Anal. Calc'd for $C_{20}H_{13}N_3$: C, 81.31; H, 4.44. Found: C, 81.55; H, 4.46.

α-(2-Quinoxalyl)-4,4-dimethyl-1-isopropyl-2-imidazolinylacetonitrile. From 3.56 g. of 2-cyanomethyl-4,4-dimethyl-1-isopropyl-2-imidazoline, 1.2 g. of sodium amide, and 1.64 g. of 2-chloroquinoxaline there was obtained 1.9 g. of canary-yellow prisms after crystallization from ethanol, m.p. 176.5–177.5°.

Anal. Calc'd for $C_{18}H_{21}N_5$: C, 70.33; H, 6.89. Found: C, 70.95; H, 6.84.

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(1) Castle and Kruse, *J. Org. Chem.*, **17**, 1571 (1952).
(2) Castle and Cox, *J. Org. Chem.*, **19**, 1117 (1954).
(3) Mizuno, Adachi, and Ikeda, *Pharm. Bull.*, **2**, 225 (1954).
(4) Gowenlock, Newbold, and Spring, *J. Chem. Soc.*, 622 (1945).