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Received April 4, 1980

Reaction of quinazoline with trimethylsilyl cyanide and benzoyl chloride gave 2,4-dicyano-1,3-dibenzoyl-1,2,3,4-tetrahydroquinazoline as the major product. This compound undergoes monoalkylation with methyl iodide in the presence of sodium hydride. Reaction of cinnoline with trimethylsilyl cyanide and benzoyl chloride gave 1,2-dibenzoyl-4-cyano-1,2-dihydrocinnoline.

*J. Heterocyclic Chem.*, 17, 1211 (1980).

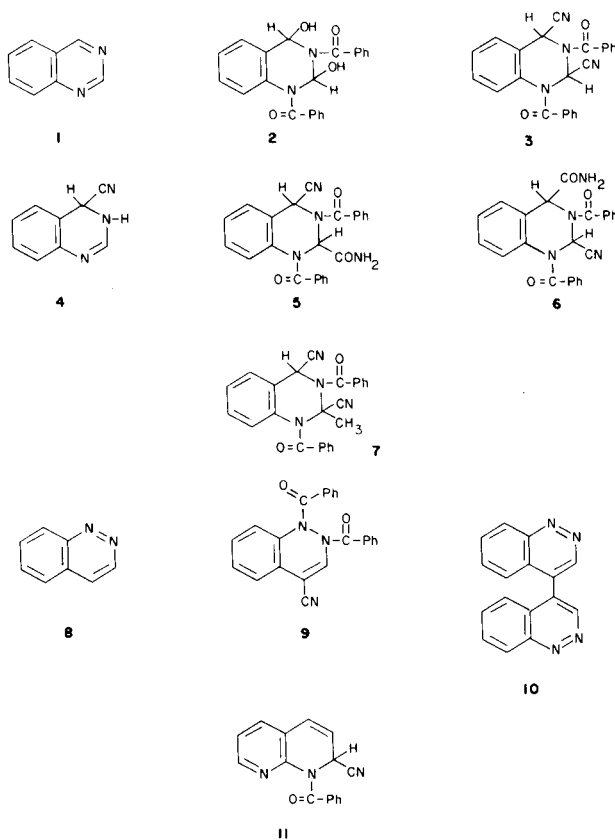
While the application of Reissert compound chemistry (1) to the diaza system, phthalazine has been extensively studied (2), the other related diaza compounds, quinazoline, quinoxaline, and cinnoline have received relatively little attention. Quinoxaline has been reported to undergo ring opening (3) to *o*-phenylenediaminedibenzamide when reacted with benzoyl chloride and potassium cyanide in methylene chloride-water. Quinazoline (1) has also been reported (4) to undergo ring opening to 2-formylbenzanilide under these same conditions.

Although the methylene chloride-water method of Reissert compound formation leads to ring opening (4) with quinazoline, we now find that application of the trimethylsilyl cyanide method (5) leads to a Reissert type compound. Reaction of quinazoline (1), benzoyl chloride, and trimethylsilyl cyanide in anhydrous methylene chloride gave a 25% yield of a compound,  $C_{22}H_{16}N_4O_2$ . Based on the spectral data and the analogy to the intermediate 2 proposed (4) in the ring opening of quinazoline, we propose 3 as the structure of this product. Compound 3 has a strong carbonyl absorption at  $1660\text{ cm}^{-1}$ . In addition to the aromatic multiplet the  $^1\text{H}$  nmr spectrum exhibited a multiplet at  $\delta$  6.77-6.60 and a singlet at  $\delta$  5.91 to account for the  $H_4$  and  $H_2$  protons. The mass spectrum showed loss of benzoyl, and then cyanide, followed by loss of cyanide and benzoyl, or benzoyl and cyanide. In addition to 3 a 10% yield of the hydrochloride of 4 was also isolated in this reaction. It is known that cyanide adds across the 3,4-bond in quinazoline (6).

When the reaction of quinazoline, benzoyl chloride, and trimethylsilyl cyanide was carried out in the presence of a catalytic amount of anhydrous aluminum chloride a more vigorous reaction took place and 3 was obtained in a 54% yield. In this case a 10% yield of a compound believed to be 5 or 6 was obtained.

Reaction of 3 with methyl iodide and sodium hydride in anhydrous dimethylformamide at room temperature gave rise to the monomethylation product 7.

Treatment of cinnoline (8) with benzoyl chloride and trimethylsilyl cyanide in anhydrous methylene chloride gave,



both in the presence or absence of anhydrous aluminum chloride, a 40% yield of a compound,  $C_{23}H_{15}N_3O_2$ . The spectral data is more consistent with structure 9 than with the isomeric structure having an *N*-cyano group and a *C*-benzoyl group. Hydrolysis of 9 with base gave rise to 4,4'-bicycinnolyl (10) (7).

We find that quinoxaline, 2-methylquinoxaline, and benzimidazole all give rise to *o*-phenylenediaminedibenzamide on attempted Reissert compound formation in methylene chloride-water, with or without the presence of a phase transfer catalyst.

Reissert compounds have been reported from both 1,6- and 1,7-naphthyridine (1). We now find that reaction of 1,8-naphthyridine with benzoyl chloride and potassium

cyanide in methylene chloride-water in the presence of a phase transfer catalyst gives rise to a Reissert compound (11).

## EXPERIMENTAL

### General.

All melting points were determined in a Thomas-Hoover capillary melting point apparatus and are uncorrected. Elemental analyses were performed by Spang Microanalytical Laboratory and mass spectra were obtained from the Midwest Center for Mass Spectrometry at the University of Nebraska. The infrared absorption spectra were determined with a Perkin-Elmer Model 710B spectrometer and <sup>1</sup>H nmr spectra were recorded on a 60 MHz R-24B Hitachi-Perkin-Elmer spectrometer.

### 2,4-Dicyano-1,3-dibenzoyl-1,2,3,4-tetrahydroquinazoline (3).

To a solution of 2.0 g. (0.015 mole) of quinazoline (1) in 25 ml. of anhydrous methylene chloride was added 3.0 g. (0.030 mole) of trimethylsilyl cyanide. After 2 minutes, 4.32 g. (0.03 mole) of benzoyl chloride was added and the mixture was stirred at room temperature for two days. The yellow solution was then poured onto a column of silica gel and eluted with methylene chloride. By evaporation of the eluent of the first light yellow band, was obtained 1.45 g. (25%) of crystalline 3, m.p. 189-191° from methylene chloride-hexane, ir (potassium bromide): 3070, 2975, 1660(s), 1600, 1490, 1370, 1350, 1285, 1260, 1145 cm<sup>-1</sup>; nmr (deuteriochloroform): δ 7.56-7.15 (m, 14H), 6.77-6.60 (m, 1H), 5.91 (s, 1H), 5.22 (s, from methylene chloride of crystallization).

Anal. Calcd. for C<sub>24</sub>H<sub>16</sub>N<sub>4</sub>O<sub>2</sub>·0.5CH<sub>2</sub>Cl<sub>2</sub>: C, 67.66; H, 3.94; N, 12.88. Found: C, 67.99; H, 3.96; N, 13.08.

Recrystallization from ethanol gave a compound with the same m.p. and ir. The <sup>1</sup>H nmr peak at δ 5.22 was missing; ms: m/e 392.1269 (C<sub>24</sub>H<sub>16</sub>N<sub>4</sub>O<sub>2</sub>) (2.56%), 287 (1.1), 270 (3.0), 261 (2.65), 235 (0.7), 155 (0.2), 130 (0.2), 129 (0.2), 105 (100).

Anal. Calcd. for C<sub>24</sub>H<sub>16</sub>N<sub>4</sub>O<sub>2</sub>: C, 73.45; H, 4.11; N, 14.28. Found: C, 73.39; H, 4.11; N, 14.24.

Further elution with methylene chloride and methanol-methylene chloride (1:9) gave 0.3 g. (10%) of the hydrochloride of 4, m.p. 211-214° from methanol; ir (potassium bromide): 3200-2400 (s, broad), 1660, 1610, 1575, 1480, 1445, 1340 cm<sup>-1</sup>; nmr (deuteriochloroform): δ 13.8-9.2 (very broad, exchangeable with deuterium oxide, 2H), 8.62 (s, H-2), 7.42 (broad s, 4 ArH), 6.68 (s, H-4); ms: m/e 157.0651 (C<sub>9</sub>H<sub>7</sub>N<sub>3</sub>) (2.96%), 156 (4.4), 130 (100), 129 (14.0), 103 (56.8), 76 (35.1).

Anal. Calcd. for C<sub>9</sub>H<sub>7</sub>ClN<sub>3</sub>: C, 55.82; H, 4.16; N, 21.70. Found: C, 55.76; H, 4.08; N, 21.50.

Compound 4 hydrochloride was stirred overnight in an open flask with equal volumes of 10% sodium hydroxide solution and chloroform. Concentration of the washed and dried chloroform layer gave 4-cyanoquinazoline, m.p. 114-116°, reported (6) m.p. 118-119°.

When the same reaction was repeated in the presence of a catalytic amount of anhydrous aluminum chloride, a vigorous reaction began. The reaction mixture was stirred at room temperature for two days and poured onto a column of silica gel and eluted with methylene chloride to give 3.2 g. (54.4%) of 3, identical in all respects to the compound described above. Elution with methylene chloride and 10% methanol in chloroform gave 0.63 g. of 5 or 6, m.p. 243-245° from glacial acetic acid; ir (potassium bromide): 3410, 3340 (w), 3280, 3205 (w), 3060 (w), 1715, 1680-1665 (s), 1640 (s), 1610, 1600, 1500, 1425, 1380 cm<sup>-1</sup>; ms: m/e 410.1386 (C<sub>24</sub>H<sub>16</sub>N<sub>4</sub>O<sub>2</sub>) (5.8%), 409 (0.4), 366 (19.7), 340 (0.5), 305 (1.2), 261 (1.6), 260 (4.6), 235 (7.8), 130 (0.8), 129 (0.4), 105 (100).

Anal. Calcd. for C<sub>24</sub>H<sub>16</sub>N<sub>4</sub>O<sub>2</sub>: C, 70.23; H, 4.42. Found: C, 69.88; H, 4.80.

### Alkylation of 3 with Methyl Iodide.

To 1.0 g. (0.0025 mole) of 3 and 0.72 g. (0.005 mole) of methyl iodide in

10 ml. of anhydrous dimethylformamide was added in small portions, 0.24 g. (0.0050 mole) of 50% sodium hydride in oil dispersion. The mixture was stirred at room temperature for 2 hours and poured into 250 g. of ice. Filtration and recrystallization from ethanol gave 0.63 g. (62%) of 7, m.p. 203-205°, ir (potassium bromide): 3070, 2980, 1675, 1600, 1360, 1295, 1280 cm<sup>-1</sup>; nmr (deuteriochloroform): δ 7.52-7.19 (m, 14H), 6.78-6.62 (m, 1H), 2.44 (s), 2.23 (s) (methyl groups in ratio 1:2).

Anal. Calcd. for C<sub>25</sub>H<sub>18</sub>N<sub>4</sub>O<sub>2</sub>: C, 73.87; H, 4.46; N, 13.79. Found: C, 73.87; H, 4.41; N, 13.75.

### 1,2-Dibenzoyl-4-cyano-1,2-dihydrocinnoline (9).

To a stirred solution of 1.0 g. (0.0077 mole) of cinnoline (8) and 1.52 g. (0.0154 mole) of trimethylsilyl cyanide in 2 ml. of anhydrous methylene chloride was added a catalytic amount of aluminum chloride and 2.16 g. (0.0154 mole) of benzoyl chloride. The mixture was stirred at room temperature for 36 hours and a bright yellow solid was filtered and recrystallized from methylene chloride-methanol to give 1.12 g. (40%) of 9, m.p. 241-243°; ir (potassium bromide): 3060, 1660, 1605, 1350, 1330, 1170, 940 cm<sup>-1</sup>; ms: m/e 365.1180 (C<sub>23</sub>H<sub>15</sub>N<sub>3</sub>O<sub>2</sub>) (12.71%), 364 (0.95), 288 (5.47), 287 (29.35), 271 (11.89), 262 (7.23), 261 (40.14), 260 (5.01), 258 (7.0), 218 (19.53), 157 (13.92), 130 (8.2), 129 (25.58), 111 (5.38), 109 (3.57), 106 (7.28), 105 (100).

Anal. Calcd. for C<sub>23</sub>H<sub>15</sub>N<sub>3</sub>O<sub>2</sub>: C, 75.60; H, 4.14; N, 11.50. Found: C, 75.23; H, 4.27; N, 11.62.

The same compound was obtained in comparable yield when aluminum chloride was not used in the above reaction.

### Reaction of 9 with Base.

A mixture of 0.35 g. of 9 in 10 ml. of ethanol and 10 ml. of 5% sodium hydroxide solution was heated on the steam bath for 30 minutes. The alcohol was removed *in vacuo*, water was added, and the mixture was extracted with chloroform. Concentration of the dried chloroform extract and recrystallization from ethanol gave 4,4'-bicinnolinyl (10), m.p. 235-236°, reported (7) m.p. 232-234°; ir (potassium bromide): 1600, 1545, 1480, 1430, 1380, cm<sup>-1</sup>; nmr (deuteriochloroform): δ 9.25 (s, 2H), 8.65 (d, 2H), 8.0-7.15 (m, 6H); ms: m/e 258.0910 (C<sub>16</sub>H<sub>10</sub>N<sub>4</sub>) (100%).

Anal. Calcd. for C<sub>16</sub>H<sub>10</sub>N<sub>4</sub>: C, 74.40; H, 3.90; N, 21.69. Found: C, 74.32; H, 3.92; N, 21.67.

### 1-Benzoyl-2-cyano-1,2-dihydro-1,8-naphthyridine (11).

To a mixture of 1.0 g. (0.0077 mole) of 1,8-naphthyridine in 20 ml. of methylene chloride, 2.0 g. (0.0308 mole) of potassium cyanide in 3 ml. of water, and 0.1 g. of benzytriethylammonium chloride was added over 30 minutes 4.33 g. (0.031 mole) of benzoyl chloride. The mixture was stirred at room temperature for 3 hours and worked up in the usual manner to give after chromatography on silica gel using benzene as the eluent and recrystallization from chloroform-*n*-hexane 0.42 g. (21%) of 11, m.p. 170-171°; ir (potassium bromide): 3065, 2955, 1665, 1595, 1560, 1430, 1330, 1290 cm<sup>-1</sup>; nmr (deuteriochloroform): δ 7.86-6.59 (m, 9H), 6.24-5.93 (m, 2H).

Anal. Calcd. for C<sub>16</sub>H<sub>11</sub>N<sub>3</sub>O: C, 73.54; H, 4.24; N, 16.08. Found: C, 73.37; H, 4.27; N, 16.01.

## REFERENCES AND NOTES

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