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Summary

6-Phenyl-2,4-dinitrophenol derivatives were prepared for their evaluation as herbicides.

Some of these compounds were found to be promising.

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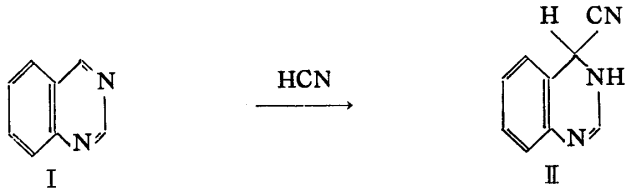
Eisaku Hayashi and Takeo Higashino: On the Reaction of Quinazoline with Acetophenone

(*Shizuoka College of Pharmacy*[*1])

In the previous paper of this series we have reported that the 4-position in quinazoline (I), owing to the overlapping of -M and -E effects of the nitrogen atoms of the ring and the effect of the fused benzene-ring, is very reactive to nucleophilic reagents.[1)]

Especially we attended to the formation of 3,4-dihydro-4-quinazolinecarbonitrile (II) on the reaction of I with hydrogen cyanide which is thought to be weaker of nucleophilic reagents at the activity.

In the present series of our work, the interests are focussed to attempting the reaction of I with carbanion as nucleophilic reagents.



I II

When I is made to react with acetophenone in the presence of sodium hydroxide solution at room temperature, an addition product agreed with $C_{16}H_{14}ON_2$ (III) in analytical values is obtained. In the ultraviolet spectrum of this compound, the two absorption peaks are located at 285 and 245 mμ. The former approximates to that of 3,4-dihydroquinazoline (IV) (290 mμ), and the latter does to that of acetophenone (242 mμ).[2)] Moreover, III shows the marked absorption bands at 3090 cm^{-1} for secondary amine and at 1665 cm^{-1} for carbonyl group in its infrared spectrum.

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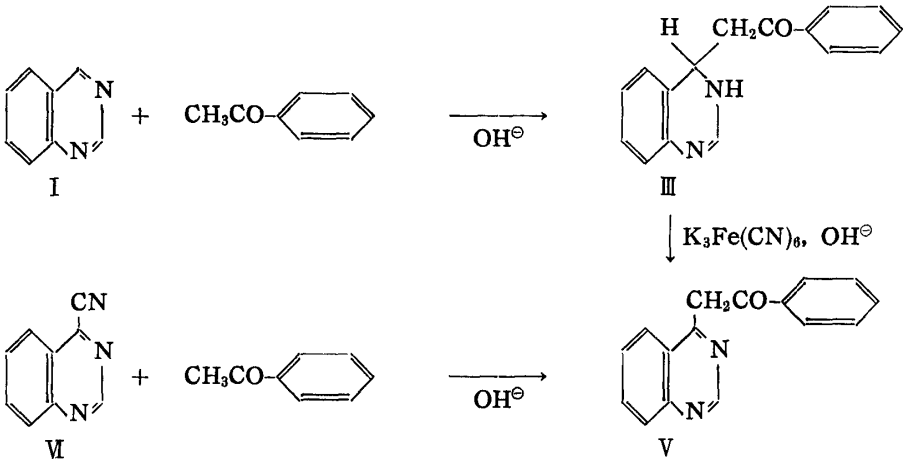
1) T. Higashino: Yakugaku Zasshi, **80**, 245 (1960).

2) J. Tanaka, S, Nagakura, M. Kobayashi: J. Chem. Phys., **24**, 311 (1956).

Those data should indicate Ⅲ to be 2-(3,4-dihydro-4-quinazolinyl)acetophenone.

In practice the structure of Ⅲ is determined to be 2-(3,4-dihydro-4-quinazolinyl)acetophenone, that is, the oxidation of Ⅲ with potassium ferricyanide in alkali gives 2-(4-quinazolinyl)acetophenone (Ⅴ) which is identical with an authentic sample prepared by the reaction of 4-quinazolinecarbonitrile (Ⅵ) with acetophenone in alkali[3] as follows:



The possible mechanism for this reaction is that the carbanion as nucleophilic reagent, which may be formed by treating acetophenone with sodium hydroxide solution, attacks the 4-position in I which is susceptible to nucleophilic reagents. Consequently, the addition product (Ⅲ) is formed *via* an intermediate such as Ⅲa type, as shown in Chart 1.

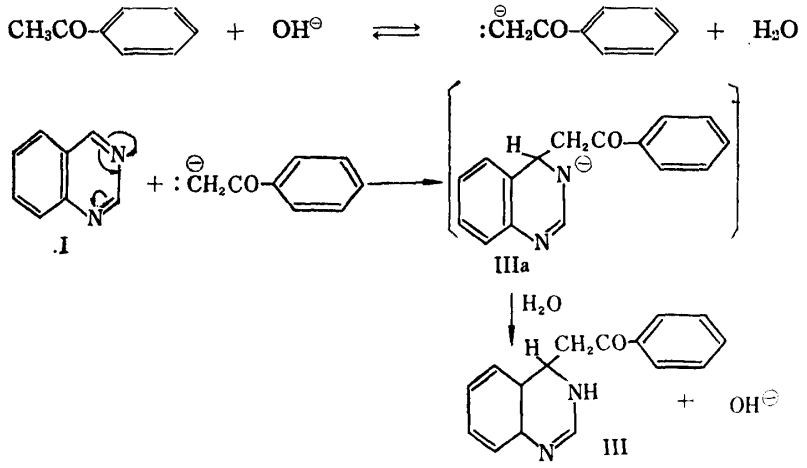


Chart 1.

Also we have got three reaction products agreed with $C_{14}H_{18}O_2N_2$, $C_{16}H_{22}O_2N_2$, and $C_{20}H_{26}O_2N_2$ in those analytical values as I is made to react with acetone, 2-butanone and cyclohexanone respectively, but are in hope to determine the structures of those compound.

Experimental

Reaction of Quinazoline (I) with Acetophenone——A mixture of 1 g. of I, 4 ml. of acetophenone, and NaOH solution (0.5 g. of NaOH dissolved in 0.5 ml. of H_2O) was shaken for 4 hr. at room temperature.

3) T. Higashino: This Bulletin, **10**, 1048 (1962).

After neutralizing with dil. AcOH, the reaction mixture was extracted with $CHCl_3$. The $CHCl_3$ layer was extracted with 2*N* HCl in several times. The HCl layer was neutralized with K_2CO_3, and extracted with $CHCl_3$ and the $CHCl_3$ solution was dried with anhyd. K_2CO_3. The $CHCl_3$ solution was passed through a column of alumina to remove impurities. Distilling of $CHCl_3$ left white crystals, m.p. 151~152° (from benzene). Yield, 0.74 g. (39%). *Anal.* Calcd. for $C_{16}H_{14}ON_2$ (2-(3,4-dihydro-4-quinazolinyl)acetophenone): C, 76.78; H, 5.64; N, 11.19. Found: C, 76.74; H, 5.68; N, 11.22. IR ν_{max}^{KBr} cm^{-1}: 3090 (>NH), 1665 (>C=O). UV λ_{max}^{EtOH} mμ (log ε): 285 (3.80), 245 (4.12). 3,4-Dihydroquinazoline: UV λ_{max}^{EtOH} mμ (log ε): 290 (3.77).

Oxidation of 2-(3,4-Dihydro-4-quinazolinyl)acetophenone (III) with Potassium Ferricyanide——A mixture of 0.2 g. of III, K_2CO_3 solution (1 g. of K_2CO_3 dissolved in 3 ml. of H_2O), $K_3Fe(CN)_6$ solution (1 g. of $K_3Fe(CN)_6$ dissolved in 3 ml. of H_2O) and 5 ml. of benzene was vigorously shaken for 2 hr. at room-temperature. The benzene layer was dried with anhyd. K_2CO_3, filtered, and condensed to afford a residue. The residue was dissolved in 1 ml. of benzene and passed through a column of alumina to remove impurities. The crystals obtained by distilling benzene were recrystallized from benzene-petroleum (b.p. 60~80°) to afford 2-(4-quinazolinyl)acetophenone (V) as pale green needles, m.p. 160~161°. Yield, 0.07 g. (35%).

V was undepressed on admixture with an authentic sample, prepared by another route.[3]

Reaction of I with Acetone, 2-Butanone and Cyclohexanone——i) To a mixture of 3 g. of I, 3 g. of Me_2CO and NaOH solution (1.5 g. of NaOH dissolved in 1.5 ml. of H_2O), a quantity of MeOH was added to make a uniform solution. After allowing the reaction mixture to stand overnight at room temperature, 70 ml. of H_2O was added and extracted with $CHCl_3$. The $CHCl_3$ layer was dried with anhyd. Na_2SO_4, filtered, and condensed to afford white crystals. The crystals were washed with benzene and recrystallization from benzene-MeOH mixture afforded white crystals, m.p; 167~168° (decomp.). Yield, 3.6 g. (63%). *Anal.* Calcd. for $C_{14}H_{18}O_2N_2$: C, 68.27; H, 7.37; N, 11.37. Found: C, 68.39; H, 7.38; N, 11.46.

ii) Treatment of 1.3 g. of I, 1.5 g. of MeCOEt and NaOH solution (1 g. of NaOH dissolved in 1 ml. of H_2O) by the same method as described above afforded white crystals in 1.3 g. (62%) yield, m.p. 165° (decomp.) (from benzene-MeOH). *Anal.* Calcd. for $C_{16}H_{22}O_2N_2$: C, 70.04; H, 8.08; N, 10.21. Found: C, 69.98; H, 7.82; N, 10.05.

iii) Treatment of 1 g. of I, 3 g. of cyclohexanone and NaOH solution (0.5 g. of NaOH dissolved in 0.5 ml. of H_2O) by the same method as described above afforded white crystals in 0.78 g. (31%) yield, m.p. 235° (decomp.) (from benzene). *Anal.* Calcd. for $C_{20}H_{26}O_2N_2$: C, 73.59; H, 8.03; N, 8.53. Found: C, 73.34; H, 7.97; N, 8.66.

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Summary

Carbanion reacted as nucleophilic reagent with quinazoline.

Reaction of quinazoline with acetophenone in the presence of sodium hydroxide solution at room temperature afforded 2-(3,4-dihydro-4-quinazolinyl)acetophenone.

The mechanism for this reaction may be suggested as in Chart 1 in the text.

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