CHEMISTRY LETTERS, pp. 1025-1026, 1979. Published by the Chemical Society of Japan

THE RHODIUM CATALYZED N-HETEROCYCLIZATION.
THE SYNTHESIS OF QUINOLINES FROM AMINOARENES AND ALDEHYDES

Yoshihisa WATANABE*, Michihiro YAMAMOTO, Sang Chul SHIM,
Take-aki MITSUDO, and Yoshinobu TAKEGAMI
Department of Hydrocarbon Chemistry, Kyoto University, Sakyo-ku, Kyoto 606

Aminoarenes react with aldehydes in the presence of a catalytic amount of a rhodium complex at 180°C to give substituted quinolines in good to excellent yields. Thus, quinaldine derivatives are readily prepared from aminobenzenes and ethanal.

During the course of our study on the rhodium catalyzed N-alkylation of amines by a carbon monoxide-water system,[1)] we found that a rhodium complex is an efficient catalyst for N-heterocyclization, preparation of quinolines from aminoarenes and aliphatic aldehydes. A rhodium complex also catalyzes the reaction between aniline and ethylene to give quinaldine but in poor yields.[2)] Skraup and its modified synthesis of quinolines from aminoarenes and carbonyl compounds have some disadvantages, uncontrolled violence of the reaction and an use of strong acids such as concentrated sulfuric acid.[3)] This communication deals with the reaction of aminoarenes with aldehydes in the presence of a rhodium complex in a neutral media, affording a novel method of heterocycle formation.

Typically, a mixture of a rhodium complex, $[Rh(norbornadiene)Cl]_2$(0.03 mmol), an amine(41 mmol), an aldehyde(88 mmol), nitrobenzene(13-60 mmol), and ethanol(20 ml) was stirred under an argon atmosphere at 180°C for 4 h, using an autoclave. Products were separated by vacuum distillation and analyzed by means of IR, ^1H NMR, and ^{13}C NMR spectra. The elemental analyses of the products gave satisfactory results. Some representative results are shown in Table.

The combination of aminoarenes, aldehyde, and nitrobenzene gave quinoline derivatives in good to excellent yields. N-Alkylaminoarenes were given as by-products in 5-30% yields. The presence of excess nitrobenzene highly reduced the formation of N-alkylaminoarenes. The nitrobenzene was confirmed to be partially reduced to aniline. A hydrogen transfer shoud take place for the formation of quinoline nucleus and then the nitrobenzene appears to act as an oxidizing agent in the reaction.

All ^1H NMR spectra(60 MHz in $CDCl_3$, Me_4Si as the internal standard) of these products exhibited no peak at δ 8.8 chraracteristic of 2-H of the quinoline nucleus.[4)] Quinaldine(1a) and 6-methoxyquinaldine(1b) were identified by comparing their IR and ^1H NMR spectra with those of authentic samples. The ^1H NMR spectra of the products from aniline-propanal and *p*-anisidine-propanal showed a typical pattern of the CH_3 and CH_3CH_2 group. Accordingly, 1c and 1d are believed to be 2-ethyl-3-methyl- and

Table. The rhodium-catalyzed synthesis of substituted quinoline from aminoarenes and aldehydes[a)]

Run	Amine	Aldehyde	Product	Isolated yield[b)] (%)	^1H or ^{13}C NMR[c)]
1	Aniline	Ethanal	Quinaldine (1a)	30	
2	*p*-Anisidine	Ethanal	6-Methoxy-quinaldine (1b)	34	
3	Aniline	Propanal	2-Ethyl-3-methyl-quinoline (1c)	59	δ(ppm) 1.33(t, 3H, $\underline{CH_3}CH_2$), 2.3 (s, 3H, $\underline{CH_3}$), 2.9(q, 2H, $CH_3\underline{CH_2}$) 7.2-8.1(m, 5H)
4	*p*-Anisidine	Propanal	2-Ethyl-3-methyl-6-methoxyquinoline (1d)	70	δ(Ppm) 1.3(t, 3H, $\underline{CH_3}CH_2$), 2.3 (s, 3H, $\underline{CH_3}$), 2.9(q, 2H, $CH_3\underline{CH_2}$), 3.8(s, 3H, $O\underline{CH_3}$), 6.6-8.0(m, 4H)
5	Aniline	Butanal	2-Propyl-3-ethyl-quinoline (1e)	82	(ppm) 14.2(q, $\underline{C}H_3$), 14.4(q, $\underline{C}H_3$), 22.5(t, $\underline{C}H_2$), 25.0(t, $\underline{C}H_2$), 37.5(t, $\underline{C}H_2$)

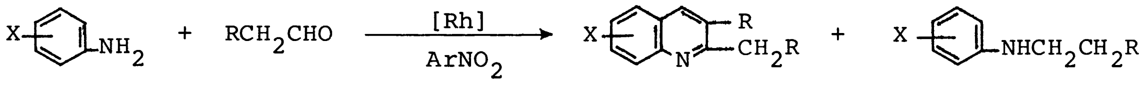
a) Under an argon atmosphere at 180°C for 4 h. $[Rh(norbornadiene)Cl]_2$, 0.03 mmol, Molar ratio: Amine(41 mmol)/aldehyde/nitrobenzene = 1.0/2.2-2.5/1.5.

b) Based on the amount of the amine used.

c) In $CDCl_3$, Me_4Si as the internal standard.

2-ethyl-3-methyl-6-methoxyquinoline respectively. Although the ^1H NMR spectrum of the product from aniline-butanal is complicated, its ^{13}C NMR spectrum(25.05 MHz in $CDCl_3$) exhibited five peaks charateristic of two kinds of CH_3 group and three kinds of CH_2 group. These may be reasonably assigned to the CH_3CH_2(14.4 and 25.0 ppm) and $CH_3CH_2CH_2$(14.2, 22.5, and 37.5 ppm) group. Thus, 1e is believed to be 2-propyl-3-ethylquinoline.

The results obtained here clearly demonstrate that the rhodium-catalyzed reaction between aminoarenes and aldehydes provides a facile route to N-heterocyclization, preparation of 2- and 2,3-substituted quinolines.



1 2

a X = H, R = H
b 6-CH_3O, H
c H, CH_3
d X = 6-CH_3O, R = CH_3
e H, CH_3CH_2

References

1) Y. Watanabe, M. Yamamoto, T. Mitsudo, and Y. Takegami, Tetrahedron Lett., 1978, 1289.

2) S. E. Diamond, A. Szalkiewicz, and F. Mares, J. Am. Chem. Soc., 101, 498(1979).

3) See, for example: R. H. F. Manske and M. Kulka, Organic Reactions, 7, 59(1960).

4) See, for example: W. Seiffert, Angew. Chem., 74, 250(1962).

(Received June 25, 1979)