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THE RUTHENIUM CATALYZED N-ALKYLATION AND N-HETEROCYCLIZATION OF ANILINE USING ALCOHOLS AND ALDEHYDES

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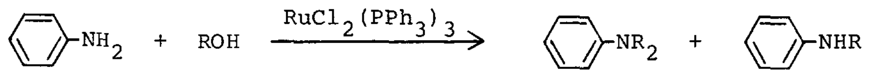
Summary: Aniline reacts with saturated and 2,3-unsaturated alcohols in the presence of ruthenium catalyst at 180°c to give N-alkylanilines and 2,3-alkylquinolines in good yields.

We recently reported the rhodium catalyzed N-heterocyclization of aminoarenes with aldehydes, affording a synthetic method of alkylquinolines1), and the rhodium and/or palladium catalyzed transformation of nitrobenzene into N-alkylanilines and alkylquinolines using aldehydes and carbon monoxide2).

In this communication we wish to report ruthenium catalyzed N-alkylation and N-heterocyclization of aniline using alcohols and aldehydes.

A typical procedure is described as follows. A mixture of aniline (40mmol), alcohol (20ml), and $RuCl_2(PPh_3)_3$ (0.4mmol, 1.0mol% based on aniline) was stirred under argon at 180°c for 5h using a 50ml stainless steel autoclave. Products were isolated by column chromatography or vacuum distillation and identified by NMR, IR and mass spectra.

Saturated alcohols combined with aniline in this procedure gave N,N-dialkyl and N-alkylaniline (eq.(1)). In this case N-heterocyclization did not occur. The results are shown in Table 1. Methanol had low reactivity for this reaction

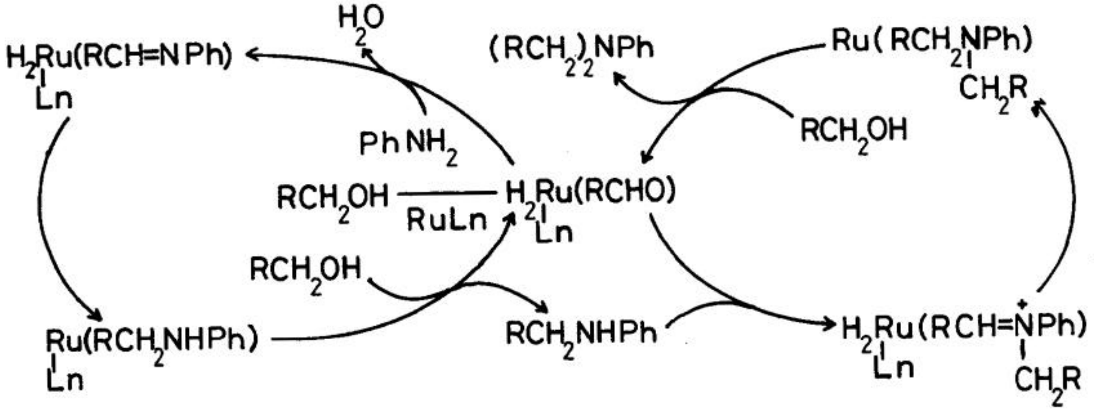


(1)

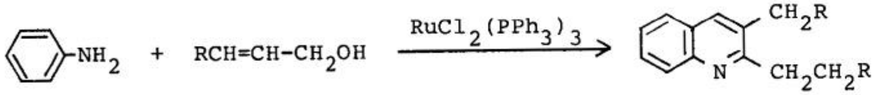
to give N-methyl and N,N-dimethylaniline in poor yields even with 2.0mol% catalyst. The reaction of ethanol gave N-ethyl and N,N-diethylaniline in excellent yields. Prolonging the reaction time with 0.5mol% catalyst was favorable to formation of N,N-diethylaniline indicating that the N-alkylation proceeded stepwise. Similarly N-alkylation proceeded smoothly when 1-propanol and 1-butanol were employed (Runs 7, 9). The N-alkylation did not proceed and all the aniline used was recovered when the reaction was carried out without the catalyst or with 1.0mol% $RuCl_3 \cdot nH_2O$. $RuH_2(PPh_3)_4$, which was reported as the most effective catalyst for the N-alkylation of aliphatic amines using alcohols[3], had low catalytic activity for the N-alkylation of aniline (Runs 6, 8). Secondary alcohols, such as 2-propanol and 2-butanol, gave only N-monoalkylaniline in poor yields (Runs 10, 11).

Since the ruthenium catalysts were reported as an effective catalyst for the hydrogen transfer reaction[4], one of the possible reaction routes including hydrogen transfer from alcohol, formation of Schiff base, and hydrogenation of it is proposed in Scheme.

Scheme



On the other hand, the reaction of 2,3-unsaturated alcohols, such as allyl alcohol and crotyl alcohol, gave 2,3-alkylquinoline in good yields (eq.(2)). The results are shown in Table 2.



(2)

Allyl alcohol and crotyl alcohol isomerized to propanal and butanal respectively in the presence of $RuCl_2(PPh_3)_3$ as shown in eq.(3)

$$\underset{20\text{ml}}{RCH=CH\text{-}CH_2OH} \xrightarrow[180°c \qquad 5h]{RuCl_2(PPh_3)_3 \quad 0.4mmol} RCH_2CH_2CHO \qquad (3)$$

R=H 44%
$R=CH_3$ 53%

Therefore, this N-heterocyclization of aniline to quinoline is considered to proceed via the isomerization of the 2,3-unsaturated alcohols to the

Table 1. Ruthenium catalyzed N-alkylation of aniline using saturated alcohol a)

Run	Alcohol	Cat. b) (mol%)	Conv. b) /%	Product c)	Yield of Product /% b)d) N-alkyl	N,N-dialkyl
1	Methanol	2.0	59	R=CH_3	12	1
2	Ethanol	0.5	60	R=C_2H_5	53	7
3 e)	Ethanol	0.5	100	R=C_2H_5	54	37
4 f)	Ethanol	0.5	100	R=C_2H_5	4	69
5	Ethanol	1.0	100	R=C_2H_5	13	74
6 g)	Ethanol	1.0	23	R=C_2H_5	6	0
7	1-Propanol	1.0	100	R=$(CH_2)_2CH_3$	10	88
8 g)	1-Propanol	1.0	94	R=$(CH_2)_2CH_3$	9	0
9	1-Butanol	1.0	100	R=$(CH_2)_3CH_3$	15	79
10	2-Propanol	1.0	31	R=$CH(CH_3)_2$	25	0
11	2-Butanol	1.0	29	R=$CH(CH_3)C_2H_5$	28	0

a) Aniline(40mmol), Alcohol(20ml), Catalyst $RuCl_2(PPh_3)_3$, at 180°c, for 5h

b) Based on an amount of aniline used.

c) See eq.(1)

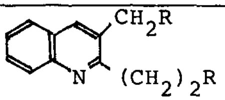
d) By GLC.

e) Reaction time 10h

f) Reaction time 17h

g) Catalyst $RuH_2(PPh_3)_4$

Table 2. Ruthenium catalyzed N-heterocyclization of aniline using 2,3-unsaturated alcohol and aldehyde a)

Run	Alcohol or Aldehyde	Conv. b) /%	Product 	Yield b)c) /%
1	Allyl alcohol	100	R=H	33
2	Crotyl alcohol	100	R=CH_3	45
3	Propanal	88	R=H	31
4	Butanal	100	R=CH_3	56

a) Aniline(40mmol), Alcohol or Aldehyde(20ml), $RuCl_2(PPh_3)_3$ (0.4mmol), at 180°c, for 5h

b) Based on an amount of aniline used.

c) By GLC.

corresponding aldehydes. Actually, the reaction of propanal and butanal with aniline in this procedure gave the 2,3-alkylquinolines in 31 and 56% yields (Table 2).

The results obtained here clearly demonstrate that this procedure is widely applicable to N-alkylation and N-heterocyclization of aminoarenes using alcohols and aldehydes under non-acidic condition.

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