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Preliminary communication

A NOVEL ROUTE TO QUINOLINE DERIVATIVES FROM 1,3-PROPANEDIOL AND AMINOARENES: RUTHENIUM CATALYZED HETEROCYCLIZATION UNDER NON-ACIDIC CONDITIONS

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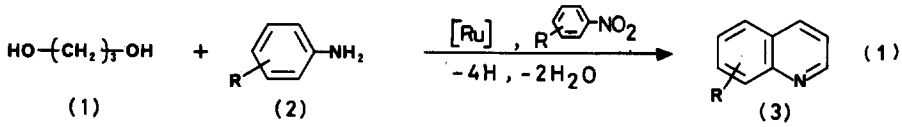
Summary

Ruthenium trichloride hydrate combined with tributylphosphine catalyzes the reaction between 1,3-propanediol and an aminoarene at 180°C, providing a novel route to quinoline derivatives under non-acidic conditions.

Transition metal catalyzed syntheses of quinoline derivatives under non-acidic conditions have been developed [1—3]. The Skraup synthesis is well known as a conventional method for building up a quinoline nucleus [4]. This method, however, requires a large amount of sulfuric acid with temperatures above 150°C and the reaction is often violent.

In this paper, we wish to report the first example of quinoline derivative synthesis from 1,3-propanediol (1) and aminoarenes (2) under non-acidic conditions (eq. 1).



(1) (2) (3) (1)

The reaction is catalyzed by a ruthenium complex and provides quinolines without a substituent at the N-hetero ring, which cannot be synthesized by Doebner—Miller type reactions [3, 5].

The general experimental procedure is as follows. Into a glass liner set in a stainless steel reactor were charged 1,3-propanediol (30 mmol), aminoarene (20 mmol), a hydrogen acceptor (20 mmol), $RuCl_3 \cdot nH_2O$ (mainly $n = 3$; 0.60

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mmol), tributylphosphine (1.20 mmol), and dioxane (5.0 ml) under argon. The reactor was heated to 180°C and kept at this temperature for 5 h.

Some representative results are listed in Table 1. The catalyst system, ruthebium trichloride hydrate and a tertiary phosphine, is highly active at 180°C (Runs 1 and 2). With ruthenium trichloride hydrate alone, quinoline is not obtained. As to the phosphine ligand, basic trialkylphosphines such as tributylphosphine produce good quinoline yield and selectivity as compared with PPh_3 (Run 1 and 3).

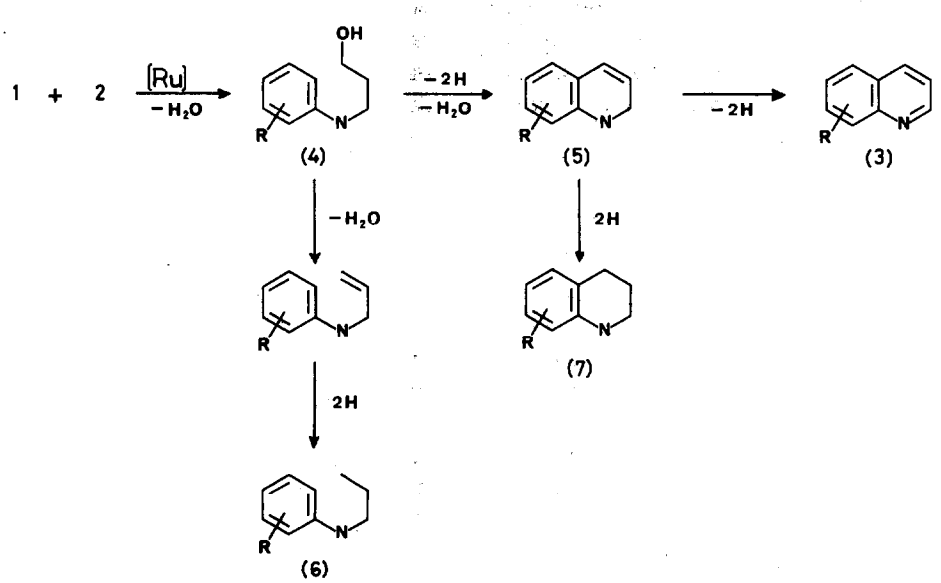
TABLE 1

Ruthenium catalyzed synthesis of quinoline derivatives from 1,3-propanediol and aminoarenes[a]

Run	Aminoarene	Hydrogen acceptor	Reaction temperature (°C)	Product	Yield (%)[b]
1	Aniline	Nitrobenzene	180	Quinoline	50 (90)
2	Aniline	Nitrobenzene	150	Quinoline	24 (73)
3[c]	Aniline	Nitrobenzene	180	Quinoline	37 (39)
4	Aniline	Diphenylacetylene	180	Quinoline	31 (48)
5	Aniline	Benzylideneacetone	180	Quinoline	4 (40)
6	Aniline	none	180	Quinoline	11 (17)
7	*p*-Toluidine	*p*-Nitrotoluene	150	6-Methylquinoline	29 (67)
8	*p*-Toluidine	*p*-Nitrotoluene	180	6-Methylquinoline	37 (38)
9	*P*-Anisidine	*p*-Nitroanisole	180	6-Methoxyquinoline	33 (37)

[a] 1,3-Propanediol (30 mmol), aminoarene (20 mmol), hydrogen acceptor (20 mmol), $RuCl_3 \cdot nH_2O$ (0.60 mmol), P-n-Bu_3 (1.20 mmol), dioxane (5.0 ml); reaction time 5 h. [b] Based on 1,3-propanediol charged, figures in parentheses show selectivities of the quinoline derivatives based on converted nitrogen compounds. [c] The catalyst is $RuCl_2(PPh_3)_3$ (0.60 mmol) instead of $RuCl_3 \cdot nH_2O$ P-n-Bu_3.

A nitroarene is used as hydrogen acceptor in the reaction. In this case, the hydrogenated nitroarene (aminoarene) enters the catalytic cycle to give the quinoline derivative. Diphenylacetylene is also used as a hydrogen acceptor, with considerable decrease in yield and selectivity of the product (Run 4).



Benzylideneacetone is not a suitable hydrogen acceptor presumably due to imine formation with aminoarene (Run 5). The reaction was complex when carried out in the absence of a hydrogen acceptor (Run 6), and *N*-propylaniline was produced, 7% yields, as well as traces of 1,2,3,4-tetrahydroquinoline (vide infra).

p-Toluidine and *p*-anisidine were converted to the corresponding quinoline derivatives in the presence of *p*-nitrotoluene or *p*-nitroanisole, respectively (Run 7—9). Glycerol instead of 1,3-propanediol did not give any quinoline by this procedure.

The formation of quinoline and other by-products is shown in Scheme 1. The first step is considered to be the formation of 3-anilinopropanol derivative 4. Similarly N-alkylation of aminoarenes using a primary alcohol in the presence of a ruthenium catalyst has been recently reported [6]. In that reaction, a hydrogen transfer from the alcohol mediated by a ruthenium complex was an important step, which would proceed via an alkoxoruthenium intermediate as indicated by eq. 2 [6, 7]. In the present reaction, similar hydrogen transfers

$$RCH_2OH \xrightarrow{[Ru]} RCH_2O{-}[Ru]{-}H \longrightarrow (RCHO)\,[Ru]H_2 \qquad (2)$$

from alcohol units seem to be the critical steps. Subsequently, the cyclization to 1,2-dihydroquinoline derivative 5 would occur and 5 is dehydrogenated to the quinoline 3. *N*-Propylaniline and 1,2,3,4-tetrahydroquinoline can be formed from 4 and 5, respectively, when the reaction system is rich in hydrogen.

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