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Environmentally friendly vapour phase synthesis of alkylquinolines

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2-methyl-8-ethylquinoline (MEQUI) was synthesized from ethylene glycol and an excess of 2-ethylaniline, operating in the vapour phase on K10 montmorillonite. Its structure was confirmed by ^{1}H-NMR (200 MHz) spectra recorded in $CDCl_3$ and DMSO. The synthesis of MEQUI is favoured by increasing the reaction temperature and amount of ethylene glycol, operating in a partially reducing atmosphere and feeding small amounts of water inside the organic feed. A possible reaction pathway proposed was confirmed by feeding a 2-ethylaniline/crotonaldehyde mixture.

Keywords: 2-methyl-8-ethylquinoline, vapour phase synthesis, acid-treated montmorillonite, 2-ethylaniline, ethylene glycol, crotonaldehyde

1. Introduction

Quinolines (including alkylquinolines) are an important class of heterocyclic compounds of high industrial interest, finding application as intermediates in the production of pharmaceuticals, herbicides, fungicides, acid-binding agents, corrosion or pickling inhibitors, etc. [1–3]. They are usually recovered from the methylnaphthalene fraction of coal tar by extraction with sulfuric acid, followed by precipitation with ammonia; however, today this source no longer seems able to cover completely the increasing market demand. Alternatively, quinolines can be obtained by different reactions [1,2], which have many drawbacks: for example, the most widely employed method, Skraup's synthesis, as well as other similar methods utilize high amounts of sulfuric acid and temperatures higher than 423 K, with a significant violence of the initial reaction [4].

In recent years many studies have been focused on the possibility of substituting liquid basic or acidic catalysts with solid compounds [5–11]: in fact, even though homogeneous catalysts are currently employed in many chemical processes of considerable practical importance, they have many drawbacks. In particular, their disposal, following neutralization and product work-up, is subject to increasing environmental constraints and alternatives are more and more urgently required. Increasing interest is today focused on reactions occurring in the vapour phase with heterogeneous catalysts that exhibit many advantages in comparison to liquid-phase syntheses (continuous production, simplified product recovery, catalyst regenerability, absence of acid waste stream, etc).

Cationic and anionic clays [8–10] represent economic and promising alternatives to liquid acids and bases, respectively, due to their wide availability, low cost and simple tailoring of the properties in order to fullfil specific requirements. However, the use of these catalysts in the synthesis of organic compounds has been only preliminarily investigated, mainly using home-made catalysts and operating in the liquid phase [5–8,10–13]. Reported in this paper is a study on the vapour phase synthesis of 8-methyl-2-ethylquinoline (as an example of alkylquinolines), carried out taking into account the possible scale-up of the process. The synthesis was performed starting from 2-ethylaniline and ethylene glycol (low price and widely available feedstocks) and using an acid-treated commercial clay as the catalyst.

2. Materials and methods

The catalytic tests were carried out using 2.0 ml (ca. 0.6 g, 425–850 μm particle size) of a commercial acid-treated montmorillonite (K10, Aldrich, Germany) (surface area 220–270 $m^2\ g^{-1}$), previously calcined at 573 K for 8 h. The tests were carried out in a fixed-bed glass microreactor (i.d. 7 mm, length 400 mm), placed in an elctronically controlled oven and operating at atmospheric pressure. The isothermal axial temperature profile of the catalytic bed during the tests was determined using a 0.5 mm J-type thermocouple, sliding in a glass capillary tube. The organic feedstock was introduced by an Infors Precidor model 5003 infusion pump, while the gas composition and flow was controlled using Brook mass flow meters. The products were condensed in two traps cooled at 268 K and collected in methanol, adding tridecane as an internal standard. The analyses were carried out using a Carlo Erba 4300 gas-phase chromatograph, equipped with FID and a wide bore SE 54 column (length 30 m, internal diameter 0.53 mm, film width 0.8 μm). The products were tentatively identified by GC-MS, using a Hewlett-Packard GCD 1800A system; the structures of the main products (preliminary isolated by preparative layer chromatography using commercial plates of silica gel and a $CHCl_3$: acetone = 9 : 1 (v/v) eluting mixture) were determined on the basis of the ^{1}H-NMR spectra recorded in $CDCl_3$ and DMSO by a 200 MHz spectrometer Varian Gemini 200.

3. Results and discussion

The catalytic results as a function of the different reaction conditions investigated are summarized in table 1. The yield values in 2-methyl-8-ethylquinoline (MEQUI) are referred to the amount of ethylene glycol in the feed, considering that this reagent was always totally converted in the reaction conditions investigated. Values of the 2-ethylaniline/ethylene glycol molar ratio higher than the stoichiometric one were generally used in agreement with that previously reported in the literature [14–16], taking into account the higher reactivity of ethylene glycol, in order to avoid its polymerization as well as the polyalkylation of the ethylaniline. The main identified by-products were aniline, 7-ethylindole, N-ethyl-2-ethylaniline and a not fully characterized diethylaniline, present in very low amounts.

The ^{1}H-NMR spectra of MEQUI recorded in $CDCl_3$ and DMSO were compared with the corresponding spectra of known alkyl and dialkyl quinolines reported in the literature, in particular with that of 2,8-dimethylquinoline [17]. The main data determined for our compound were: ^{1}H-NMR ($CDCl_3$) $\delta = 1.40$ ppm (t, 3H, $CH_2C\underline{H}_3$), 2.75–2.80 ppm (s, 3H, $C\underline{H}_3$), 3.30–3.35 ppm (q, 2H, $C\underline{H}_2CH_3$), 7.25–7.65 ppm (m, 4H, aromatic protons $\underline{H}(3)$, $\underline{H}(6)$, $\underline{H}(7)$, $\underline{H}(5)$), 8.00–8.05 ppm (d, 1H, aromatic proton $\underline{H}(4)$); (ii) ^{1}H-NMR (DMSO) $\delta = 1.30$ ppm (t, 3H, $CH_2C\underline{H}_3$), 2.70 ppm (s, 3H, $C\underline{H}_3$), 3.25 ppm (q, 2H, $C\underline{H}_2CH_3$), 7.40–7.80 ppm (m, 4H, aromatic protons $\underline{H}(3)$, $\underline{H}(6)$, $\underline{H}(7)$, $\underline{H}(5)$), 8.25 (d, 1H, aromatic proton $\underline{H}(4)$). It must be noted that ^{1}H-NMR spectra of quinolines unsubstituted in position 2 are characterized by the presence of a doublet at $\delta = 8.6 \pm 0.2$ ppm (1H, aromatic proton $\underline{H}(2)$). The absence of such a signal confirms that our product cannot be 4-methyl-8-ethylquinoline. Furthermore, in the region between $\delta = 7.20$–7.70 ppm of the $CDCl_3$-spectrum of our product, the observed multiplet corresponding to 4H could be actually differentiated into d (1H), t (1H), d (1H) and d (1H) signals, as reported for 2,8-dimethylquinoline [17].

Table 1
Catalytic data as a function of the feedstock and reaction conditions employed

Run	Temperature (K)	Gas mixture	GHSV (h^{-1})	LHSV (h^{-1})	Yield [a] (%)
1	603	N_2	3 000	0.1 [b]	25
2	563	N_2	3 000	0.1 [b]	18
3	523	N_2	3 000	0.1 [b]	11
4	563	N_2	3 000	0.1 [c]	26
5	563	N_2	900	0.1 [b]	11
6	563	N_2	180	0.1 [b]	12
7	563	N_2	900	0.2 [c]	27
8	603	N_2	3 000	0.1 [d]	33
9	603	N_2	3 000	0.1 [e]	41
10	603	$H_2/N_2 = 1:9$ (v/v)	3 000	0.1 [b]	31
11	603	$H_2/N_2 = 1:9$ (v/v)	3 000	0.1 [f]	29

[a] In order to take into account the carbon number in the feed, the yield in 2-methyl-8-ethylquinoline (MEQUI) was calculated according to: (A) moles of MEQUI obtained / 0.5 moles of ethylene glycol fed × 100; (B) moles of MEQUI obtained/moles of crotonaldehyde fed × 100.

[b] 2-ethylaniline/ ethylene glycol (10.0 : 1.0 mol/mol).

[c] 2-ethylaniline/ethylene glycol/ water (10.0 : 1.0 : 0.1 mol/mol).

[d] 2-ethylaniline/ethylene glycol (5.0 : 1.0 mol/mol).

[e] 2-ethylaniline/ethylene glycol (1.0 : 2.0 mol/mol).

[f] 2-ethylaniline/crotonaldehyde (10.0 : 0.5 mol/mol).

From table 1 it is possible to note that the synthesis of MEQUI is favoured by increasing the reaction temperature (runs 1–3) and operating in the presence of small amounts of hydrogen in the gas phase (runs 1 and 10). The use of hydrogen only as the carrier gas gave rise to a significant decrease in activity and, mainly, selectivity. Another significant increase in the yield in MEQUI, can be achieved by increasing the amount of ethylene glycol in the feed, i.e. decreasing the 2-ethylaniline/ethylene glycol ratio (runs 1, 8 and 9). Comparison of runs 2 , 5 and 6 shows that a decrease in the gas hourly space velocity (GHSV) (i.e. an increase in contact time) gives rise to a decrease in the yield in MEQUI, without significant changes or any further decrease. On the contrary no significant changes are observed with increasing liquid hourly space velocity (LHSV) of the organic feed (runs 4 and 7). Finally, it is worth noting that the synthesis of MEQUI is significantly favoured by the addition of a small percentage of water to the organic feed (compare runs 2 and 4), with a positive effect similar to those previously reported in the literature for some vapour phase organic syntheses and attributed either to tailoring of the surface acidity of silica or silica/alumina supports [14,15,18] or suppression of coke and tar formation [19].

On the basis of the above data, a possible reaction pathway may be proposed (figure 1), in which MEQUI is formed by cycloaddition, and following dehydrogenation reactions, with the preliminary formation of crotonaldehyde as an intermediate, in agreement with the pioneering work of Doebner and Von Miller [20]. To confirm the role of crotonaldehyde as an intermediate, a 2-ethylaniline/crotonaldehyde (10.0 : 0.5 mol/mol) mixture was fed, the composition of which took into account the differences in carbon atom number between

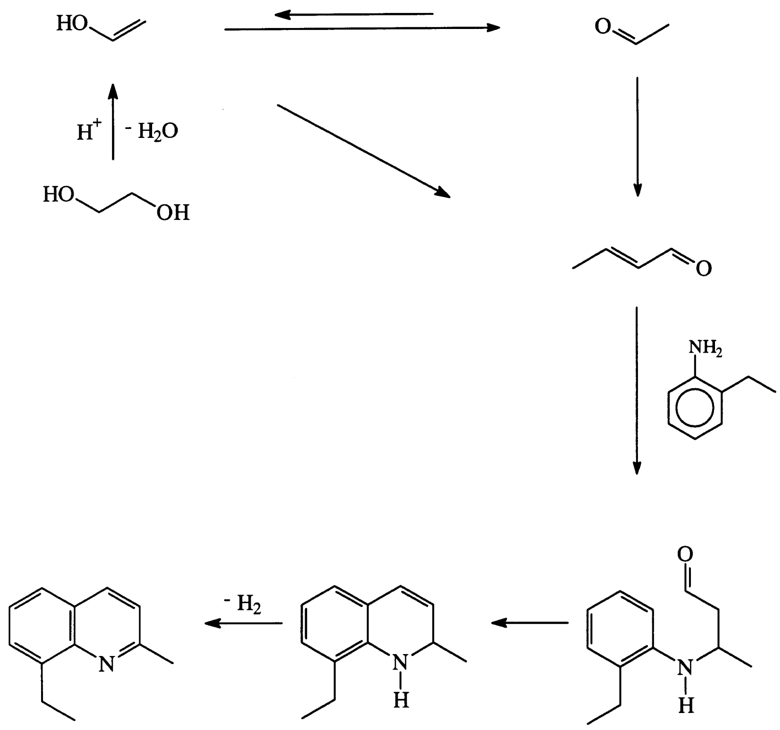

Figure 1. Reaction pathway for the synthesis of 2-methyl-8-ethylquinoline.

ethylene glycol and crotonaldehyde. Runs 10 and 11 of table 1 confirm the hypothesis on the role of crotonaldehyde, showing similar yields in MEQUI, regardless of the mixture fed. However, it is intriguing to note that in previous papers [21,22] it has been reported that the interaction of aniline and crotonaldehyde in the gas phase over an aluminosilicate catalyst gave mainly 4-methylquinoline, in agreement with Skraup's original suggestion.

It must be pointed out that the formation of 2-methyl-8-ethylquinoline seems to be clearly favoured in comparison to the isomer 4-methyl-8-ethylquinoline, on the basis of the calculated heats of formation (93.6 and 262.3 kJ/mol, respectively) and on the assumption that the entropy changes during the reaction are similar for both products [23]. However, it is not possible to exclude that a different and competitive reaction pathway may occur when aniline is the reagent and the catalyst contains Al^{3+} ions, with an ortho alkylation of the aromatic ring [24] followed by the closure reaction. This pathway does not favour 2-ethylaniline due to steric hindrance and the deactivating effect of the ethyl group.

4. Conclusions

Quinolines and/or alkylquinolines can be synthesized operating in the vapour phase with heterogeneous catalysts, with evident advantages from the industrial and environmental points of view. In particular, 2-methyl-8-ethylquinoline (MEQUI) was obtained using a commercial acid-treated clay (K10) and starting from widely available organic feedstocks, its synthesis being favoured at higher temperatures and operating in a partially reducing atmosphere, with high amounts of ethylene glycol and a small percentage of water in the feed. The industrial relevance of the vapour-phase synthesis of quinolines and/or alkylquinolines is confirmed by a very recent patent [25], in which the preparation of 8-methylquinoline with high selectivity and yield is reported.

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