Catalysis Communications 12 (2011) 1067–1070

Contents lists available at ScienceDirect

Catalysis Communications

journal homepage: www.elsevier.com/locate/catcom

Short Communication

Vapor phase synthesis of methylpyrazine using aqueous glycerol and ethylenediamine over $ZnCr_2O_4$ catalyst: Elucidation of reaction mechanism

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ARTICLE INFO

Article history:
Received 15 December 2010
Received in revised form 21 February 2011
Accepted 14 March 2011
Available online 22 March 2011

Keywords:
Hydrotalcite
Methylpyrazine
Glycerol
Ethylenediamine
$ZnCr_2O_4$

ABSTRACT

A novel method has been developed for the synthesis of methylpyrazine (MP) by using aqueous glycerol and ethylenediamine (EDA) over Zn–Cr catalyst derived from hydrotalcite precursors. The X-ray diffraction analysis of the oven-dried Zn–Cr samples synthesized at various pH ranging from 7 to 11 showed hydrotalcite phase whereas the calcined catalysts displayed ZnO and $ZnCr_2O_4$ phases. The cyclisation activity of Zn–Cr catalyst prepared at pH ~9 demonstrated 99.4% conversion of EDA and 94% of glycerol with ~72% selectivity to MP at a reaction temperature of 400 °C. This process demonstrates direct utilization of bio-glycerol for the synthesis of MP.

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1. Introduction

Fuel and energy crisis surge R&D, firstly on alternate fuels for future and secondly on clean fuels in the context of pollution abatement. Recent advancements in the development of bio-diesel production from non-edible oils seem a promising approach [1–3]. Bio-glycerol is a by-product that is inevitably formed in large amounts during bio-diesel production by transesterification of oils. On one hand generation of alternate fuels is a prime objective; on the other hand utilization or safe disposal of the by-products obtained in the process is equally important. Conversion of bio-glycerol into value added compounds and fine chemicals is extensively studied by several authors [4–6]. One of such processes is the production of 1,2-propylene glycol (PG) by hydrogenolysis of bio-glycerol over supported noble metal catalysts at high pressures [7,8].

Methyl pyrazine is an intermediate compound for the synthesis of 2-amido pyrazine, a well-known bacteriostatic and antitubercular drug. Conventionally methyl pyrazine is synthesized by cyclisation of ethylenediamine (EDA) and 1,2-propylene glycol (Scheme 1). Forni et al. have studied Pd-promoted zinc chromite catalyst for the synthesis of methyl pyrazine using EDA and 1,2-propylene glycol [9]. Studies pertaining to the same have been reported by others [10,11].

Synthesis of methylpyrazine using aqueous glycerol and EDA is not reported in the literature. This paper reports our exploratory research on the vapor phase synthesis of methylpyrazine, directly using aqueous glycerol and EDA (instead of the normal procedure that requires 1,2-propylene glycol and EDA) avoiding a process step i.e. the production of 1,2-propylene glycol by hydrogenolysis of bio-glycerol. Hence our methodology is exceptionally beneficial from the economical perspective in the transformation of bio-glycerol into useful compounds. Hydrotalcite like anionic clays are found to be new class of catalyst precursors for commodity and fine chemical synthesis. An excellent review recently by Centi et al. reports on the usage of layered materials for the synthesis of various chemical entities in domestic and industrial applications [12]. In the present investigation the Zn–Cr hydrotalcite precursors have been synthesized, characterized and the calcined form of catalysts is explored for the cyclisation of EDA and aqueous glycerol. Here we report for the first time, the synthesis of methylpyrazine using aqueous glycerol and ethylenediamine and a probable reaction mechanism has been proposed.

2. Experimental

The Zn–Cr catalysts employed in this investigation were prepared by a simple coprecipitation method using $Zn(NO_3)_2 \cdot 6H_2O$ and $Cr(NO_3)_3 \cdot 9H_2O$ (Sigma–Aldrich, AR grade) with Zn:Cr = 2:1 (mole ratio), in order to get the hydrotalcite structure. The various samples were prepared at pH ranging from 7 to 11 using a mixture of 2 M NaOH + 1 M Na_2CO_3 as precipitating agent. The gels were washed thoroughly, filtered and oven-dried for 12 h at 120 °C, subsequently calcined in static air at 450 °C for 5 h. The surface properties of the fresh and the used samples were measured by N_2 adsorption at

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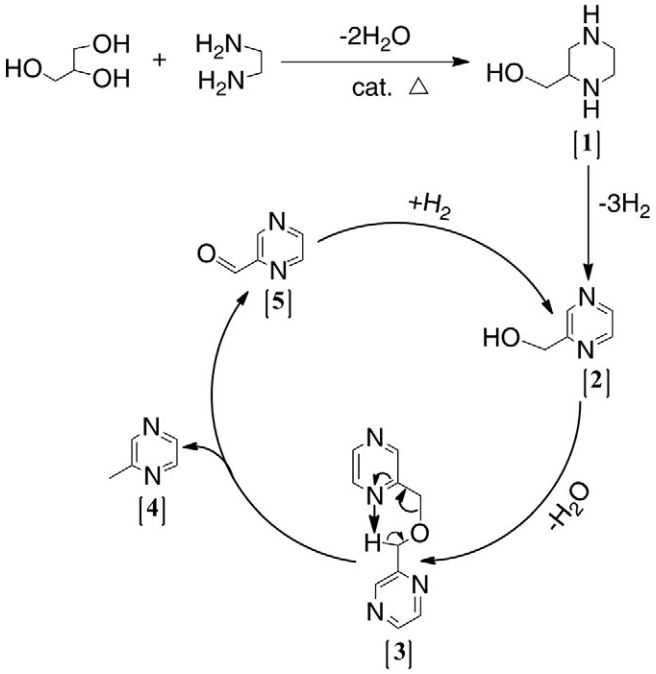
doi:10.1016/j.catcom.2011.03.021



Scheme 1. Proposed reaction mechanism for the formation of methylpyrazine during dehydrocyclization of glycerol and ethylenediamine over Zn–Cr catalyst.

−196 °C in a Autosorb 3000 physical adsorption apparatus. The specific surface areas were calculated applying the BET method. The temperature programmed desorption of NH_3 of Zn–Cr samples prepared by varying pH from 7 to 11 were measured using an Auto Chem 2910 (Micromeritics, USA). In a typical method about 0.1 g of calcined Zn–Cr sample was reduced at 400 °C 5 h in hydrogen at a flow rate of 30 mL min^{-1}. After the reductive pretreatment the sample was saturated with 10% NH_3 balance He at 60 °C at a flow rate of 50 mL min^{-1} subsequently flushed with He gas at 60 °C for 1 h. The TPD was carried out from 60 °C to 600 °C at a ramping rate of 10 °C min^{-1}. The amount of desorbed NH_3 was calculated using GRAMS/32 software. The carbon contents of the used Zn–Cr samples were measured using VARIO EL, CHNS analyser. The oven-dried and calcined forms of Zn–Cr catalysts were characterized by powder X-ray diffraction (XRD) analysis using a Rigaku miniflex X-ray diffractometer using Ni filtered Cu K_α radiation ($\lambda = 0.15406$ nm) from $2\theta = 2$ to 80°, at a scan rate of 2° min^{-1} with the beam voltage and a beam current of 30 kV and 15 mA respectively.

The cyclisation activities over calcined Zn–Cr (HT) catalysts were performed at 300 to 400 °C at atmospheric pressure in a fixed-bed vertical quartz reactor (I.D = 0.8 cm, length = 46 cm) placed in a two-zone furnace operated in a down flow mode. The first one was pre-heating zone, which was maintained at 300 °C and the second one was catalyst bed temperature, both monitored by temperature controller cum programmers using K-type thermocouple. Glycerol (Fluka) and EDA supplied by SDFCL, India were used. Nitrogen (IOLAR-I grade, BOC, India) was used as a carrier gas. The cyclisation activities were carried out using −18/+23 sieved (BSS) catalyst particles. The carbon mass balance was done based on the inlet and outlet concentration of the organic moiety. Prior to the reaction about 0.2 g of calcined catalyst (sieved particles −18/+25 BSS) was reduced in 5% H_2 balance Ar at 400 °C for 5 h. A 20 wt.% aqueous glycerol solution was used and the glycerol to EDA mole ratio of 1:1 and flow rate of the reaction mixture of 2 mL h^{-1} along with N_2 as carrier gas at a flow rate of 1800 cc h^{-1} was maintained. The reaction mixture contained a glycerol:EDA:H_2O:N_2 = 1:1:20.5:20.4 (mole ratio) and the gas hourly space velocity (GHSV) = 18909 cc g^{-1} h^{-1}. The samples were collected after 3 h of continuous operation at each temperature and analyzed by gas chromatograph (Shimadzu, GC-17A) equipped with flame ionization detector (FID) using ZB-5 capillary column at a ramping rate of 10 °C min^{-1} from 60 to 280 °C. The samples were analyzed by GC-MS (QP5050A Shimadzu) using a ZB-5 capillary column with EI mode. The mass spectra confirmed the product distribution and the corresponding m/z values for **methylpyrazine**: $M^{+\cdot}$ m/z: 94, $(M\text{-}HCN)^{+\cdot}$ m/z: 67, $(M\text{-}CH_3CN)^{+\cdot}$ m/z: 53, $(M\text{-}C_3H_4N)^{+\cdot}$ m/z: 40; **pyrazine**: $M^{+\cdot}$ m/z: 80, $(M\text{-}HCN)^{+\cdot}$ m/z: 53; EDA: $(M\text{-}H)^{+}$ m/z: 59, $(M\text{-}NH_3)^{+\cdot}$ m/z: 43; **glycerol**: $(M\text{-}CH_2OH)^{+\cdot}$ m/z: 61; $\{M\text{-}(CH_2OH, H_2O)\}^{+\cdot}$ m/z: 43; **2,5-dimethylpyrazine**: $M^{+\cdot}$ m/z: 108; $(M\text{-}CH_3)^{+\cdot}$ m/z: 93; $(M\text{-}HCN)^{+\cdot}$ m/z: 81; $(M\text{-}CH_3CN)^{+\cdot}$ m/z: 67; $(M\text{-}C_3H_6N)^{+\cdot}$ m/z: 52; $(M\text{-}C_4H_4N)^{+\cdot}$ m/z: 42; **pyrazinealdehyde**: $M^{+\cdot}$ m/z: 108; $(M\text{-}H)^{+\cdot}$ m/z: 107; $(M\text{-}CO)^{+\cdot}$ m/z: 80; $(M\text{-}C_2N_2)^{+\cdot}$ m/z: 56; $\{M\text{-}(H,CO,C_2H_2)\}^{+\cdot}$ m/z: 53; and **2,3-dimethylpyrazine**: $M^{+\cdot}$ m/z: 108; $(M\text{-}CH_3CN)^{+\cdot}$ m/z: 67; $(M\text{-}C_4H_6N)^{+\cdot}$ m/z: 40. The methylpyrazine was isolated and analyzed by ^{1}H NMR spectra which revealed ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 8.32–8.5(m, 3 H); 2.56 (s, 3 H), attributed to methylpyrazine.

3. Results and discussion

The XRD patterns of all the Zn–Cr samples prepared by varying pH displayed similar hydrotalcite patterns in oven-dried form and ZnO–$ZnCr_2O_4$ phases over calcined samples. Fig. 1 shows the XRD patterns of the oven-dried (Zn–Cr prepared at pH = 9) sample revealed the

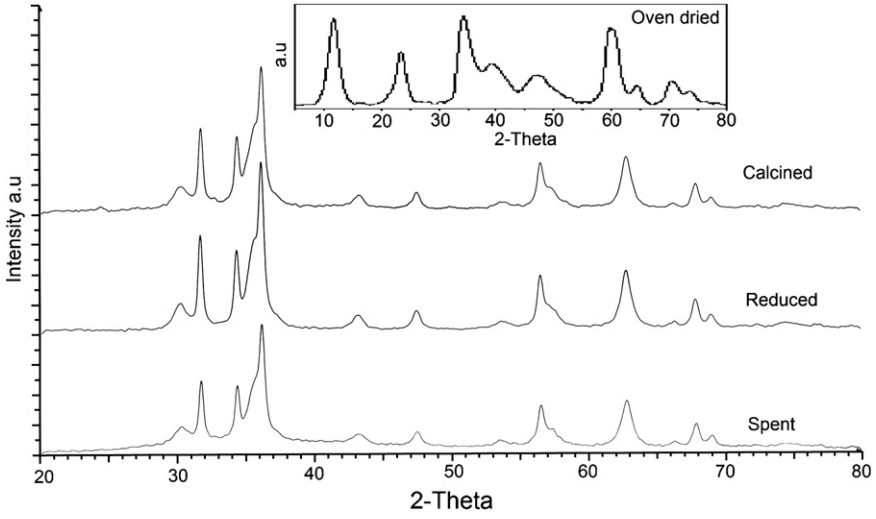


Fig. 1. XRD patterns of the Zn–Cr oven-dried, calcined in air at 450 °C/5 h and the used Zn–Cr catalyst prepared at pH = 9.

Table 1
Cyclisation activity of ethylenediamine and aqueous glycerol at a reaction temperature of 350 °C over Zn–Cr catalysts prepared at pH = 7 to 11 and calcined in air at 450 °C/5 h. Catalyst wt. = 0.2 g, feed rate = 2 mL h^{-1}; glycerol:EDA:H_2O:N_2 = 1:1:20.5:20.4 (mole ratio); and GHSV = 18909 cc g^{-1} h^{-1}.

[a]pH	BET–SA (m^2 g^{-1})		%Conv.	%Conv.	[b]Carbon (wt.%)	[c]NH_3 uptake	%Selectivity			[d]Specific rate × 10^8
	[e]Calcined	[f]Reduced	EDA	Glycerol		μmol g^{-1}	MP	Pyrazine	[g]Others	mol m^2 s^{-1}
7.0	31.7	35.2	57.5	43.7	2.83	360	65.2	18.8	15.9	6.8
8.0	38.1	40.8	69.4	55.6	2.68	284	64.0	18.5	17.4	7.4
9.0	45.3	37.6	74.0	71.3	1.91	101	69.2	16.5	14.2	10.4
10.0	56.4	56.2	56.2	59.4	2.76	302	66.2	18.3	15.4	5.7
11.0	63.4	60.0	44.5	28.3	2.75	466	55.7	21.5	22.8	2.6

[a] pH maintained during the preparation Zn–Cr LDH catalysts.
[b] Carbon contents of the used catalysts measured by CHN analysis.
[c] NH_3 uptakes measured by TPD of NH_3 of the fresh calcined and reduced catalysts.
[d] Specific rate is measured with respect to glycerol conversion and surface area of the reduced catalyst.
[e] BET–surface areas of the fresh calcined ZnO–$ZnCr_2O_4$ catalysts.
[f] BET–surface areas of the calcined and reduced (in 5%H_2 balance Ar at 400 °C/5 h) ZnO–$ZnCr_2O_4$ catalysts.
[g] Other compounds such as pyrazinealdehyde, 2,3-dimethyl pyrazine, and 2,5-dimethyl pyrazine.

presence of HT phase layered double hydroxide (LDH) which is decomposed to form ZnO and $ZnCr_2O_4$ phases [13] upon calcination (Fig. 1) in air at 450 °C for 5 h. The lattice parameters corresponding to the HT structure are found to be $a = 3.10$ and $c = 22.5$ for Zn–Cr LDH. The basal spacing is calculated from the average of (**00l**) peaks ($d \sim 0.775$ nm), while the "a" dimension is calculated as twice the position of the (**110**) peaks ($a \sim 0.3106$ nm). This is in good agreement with the literature value [14,15]. The XRD patterns of the calcined catalyst indicated the presence of reflections at $2\theta = 36.2$, 31.7, 34.4, 56.6, and 62.8° and their corresponding 'd' values of 0.247, 0.281, 0.260, 0.162, and 0.147 nm are attributed to ZnO [**ICDD # 89–0510**] phase and diffraction lines at $2\theta = 35.7$, 30.3, 63.1, 57.4, and 43.4° with the 'd' values of 0.251, 0.294, 0.147, 0.160, and 0.208 nm are ascribed to the $ZnCr_2O_4$ [**ICDD # 22–1107**] phase. The BET–surface areas of the calcined and reduced Zn–Cr catalysts are reported in Table 1. It is observed that there is not much variation in the BET–surface areas of the calcined and reduced samples.

First, we examined the EDA and aqueous glycerol cyclisation activity over several ZnO–$ZnCr_2O_4$ catalysts (prepared at various pH ranging from 7 to 11) at a reaction temperature of 350 °C and the results are reported in Table 1. The ZnO–$ZnCr_2O_4$ samples prepared at pH ~ 9 shows relatively high EDA and glycerol conversion as well as selectivity towards methylpyrazine compared to other catalysts. Formation of about 18–20% of pyrazine along with by-products such as 2,3-dimethylpyrazine, 2,5-dimethylpyrazine, and pyrazinealdehyde, (~14–18%) were observed over all catalysts and slightly higher ~22% on the catalyst prepared at pH = 11. The better activity and selectivity of the ZnO–$ZnCr_2O_4$ (sample prepared at pH ~ 9) are explained based on the acidities of the catalysts (Table 1) measured by temperature programmed desorption (TPD) of NH_3. The TPD of NH_3 studies indicated that the sample prepared at pH ~ 9 is found to have lower acidity compared to other catalysts. It appears that strong acid sites are undesirable for the EDA and glycerol cyclisation reaction. The carbon content on the used catalysts (Table 1) showed *ca.* 1.91% over pH = 9 sample, which is lower compared to other samples.

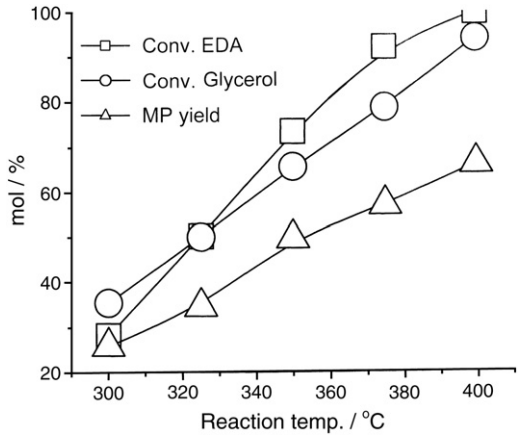
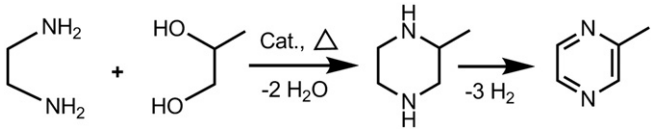


Fig. 2. Influence of reaction temperature over calcined Zn–Cr catalyst prepared at pH = 9, calcined in air at 450 °C/5 h. Catalyst wt. = 0.2 g, feed rate = 2 mL h^{-1}; glycerol:EDA:H_2O:N_2 = 1:1:20.5:20.4 (mole ratio); and GHSV = 18909 cc g^{-1} h^{-1}. Methylpyrazine yields were calculated with respect to glycerol conversions.

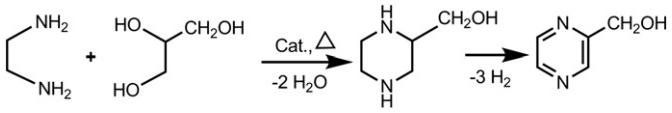
To gain an insight into the methylpyrazine yields, we performed experiments to check the influence of reaction temperature on the activity over ZnO–$ZnCr_2O_4$ catalyst prepared at pH ~ 9 and the data is represented in Fig. 2. It is interesting to note that there is not much change in selectivity towards MP with increase in reaction temperature. The extent of conversion of EDA is slightly higher than that of glycerol at all temperatures. The cyclisation activity of the ZnO–$ZnCr_2O_4$ catalyst showed (Fig. 2) almost 99.4% conversion of EDA and 94% glycerol with ~72% selectivity towards methylpyrazine at 400 °C. A number of experiments on the cyclisation activity over Zn–Cr catalysts are carried out under standard conditions using 20 wt.% aqueous glycerol and EDA. Based on the experimental data a plausible reaction mechanism (Scheme 1) is proposed in conjunction with earlier postulates for the formation of methylpyrazine [16].

A well-known mechanism on methylpyrazine formation is via dehydrocyclisation of EDA and 1,2-propylene glycol (Scheme 2) over mixed oxide catalysts is reported [10,11,17]. We anticipated that if EDA and glycerol undergo similar transformation, the end product could be pyrazylmethanol (Scheme 1, 2nd step or Scheme 3). On the contrary a large amount of methylpyrazine is obtained in this study along with some by-products. This is explained based on the conversion of pyrazylmethanol into methylpyrazine (see reaction mechanism Scheme 1) and pyrazinaldehyde [16].

Several reaction parameters are evaluated during the cyclisation of EDA and aqueous glycerol. We envisioned that the methylpyrazine could be formed by condensation followed by cyclisation of glycerol and EDA that proceeds through dehydrogenation, which undergoes homo-coupling (Scheme 1, 3rd step) reaction subsequently forming methylpyrazine and pyrazinealdehyde [18]. The high ratio of methylpyrazine compared to pyrazinealdehyde is probably due to the hydrogenation of pyrazinealdehyde [19] to form pyrazylmethanol (Scheme 1, 5th step) during the course of reaction, as one would expect equal proportions of pyrazinealdehyde and methylpyrazine for reaction Scheme 1. Pyrazine the main by-product obtained by



Scheme 2. Dehydrocyclization of EDA and 1,2-propylene glycol for the formation of methylpyrazine.



Scheme 3. Anticipated reaction mechanism for the formation of pyrazylmethanol.

hydrogenolysis of methylpyrazine is observed in the product mixture. Formation of the by-products such as 2,3-dimethylpyrazine and 2,5-dimethylpyrazine is probably due to disproportionation of methylpyrazine in presence of $ZnO–Cr_2O_3$ catalysts. However, phases due to any of the chromium oxides are not observed in the XRD analysis of calcined catalysts. They are either present in small amounts or below the X-ray detection limit. Formation of the second major product i.e. pyrazine (~18–20%) is explained by C–C cleavage (hydrogenolysis) reaction that is possible over $ZnCr_2O_4$ surface at high reaction temperatures or by the disproportionation of methylpyrazine to produce pyrazine and both 2,3-dimethylpyrazine and 2,5-dimethylpyrazine.

4. Conclusions

In summary, we have developed a new method for the synthesis of methylpyrazine; this constitutes a novel and more economical utilization of bio-diesel by-product (~10 wt.% in the bio-diesel process) i.e. bio-glycerol, which could provide a beneficial route for the synthesis of methylpyrazine derivatives that are useful for the pharma and drug industry. The cyclisation activity over $ZnO–ZnCr_2O_4$ catalyst (prepared at pH ~ 9) exhibited 99.4% conversion of EDA and 94% glycerol with ~65% yield towards methylpyrazine obtained at a reaction temperature of 400 °C.

This process may prove to be a starting point for the production of methylpyrazine and its derivatives using aqueous glycerol without development of new generation of industrial catalysts. The catalyst preparation condition such as pH has a large influence on the cyclisation activity. Further characterization of the catalyst studies are in progress.

Acknowledgements

Authors RS, CA, VK, RK and MS thank CSIR New Delhi for the award of Junior Research Fellowship.

Appendix A. Supplementary data

Supplementary data to this article can be found online at doi:10.1016/j.catcom.2011.03.021.

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