One-pot catalytic synthesis of higher aliphatic ketones

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Abstract

The catalytic synthesis of high molecular weight aliphatic ketones by reductive condensation of lower molecular weight ketones was achieved by using CO in the presence of a multifunctional catalyst containing copper dispersed on alumina. The useful combination of condensation, water gas shift and hydrogenation reactions in a one-pot reaction allowed high yields of methylisobutylketone from acetone.
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1. Introduction

High molecular weight aliphatic ketones obtained from lower ketones are important in a number of relevant applications. Methyl-isobutyl-ketone (MIBK), for instance, is a product widely used as painting and liquid–liquid extraction solvent due to similar polarity but higher stability towards aqueous acid or base than ethyl acetate [1]. For long time it has been manufactured from acetone, via a three-step process (Scheme 1). Acetone is first dimerised via aldol condensation to give diacetone alcohol (catalysed by base), which readily dehydrates in the presence of catalytic amount of H_2SO_4 or H_3PO_4 at 100 °C. Mesityl oxide is then catalytically (Pd or Ni, at 150–200 °C) hydrogenated to give MIBK.

A series of catalytic methods has been proposed aiming to reduce the number of steps of this process, mostly based on supported transition metals to catalyse the condensation of acetone to α,β unsaturated ketone followed by another catalytic reduction step [2–6], including a most recent process based on multifunctional Pd-polyoxometalate catalyst [7]. In general, the best results were obtained with a Pd–Zr–P multicomponent

catalytic system and with the Pd-acidic ion exchange resin process [8].

We now report an alternative, one-pot efficient process in which acetone and CO are reacted in the presence of a new catalytic system, consisting of copper dispersed on alumina, affording good yields of MIBK at 180 °C. The process is general and versatile as it could be applied for the synthesis of a variety of aliphatic low molecular weight ketones, operating in liquid phase. Taking acetone as typical substrate, the process can be represented as in reaction (1).

$$2\ CH_3\text{-}CO\text{-}CH_3 + CO \rightleftharpoons H_3C\text{-}\underset{\underset{CH_3}{|}}{CH}\text{-}CH_2\text{-}CO\text{-}CH_3 + CO_2 \quad (1)$$
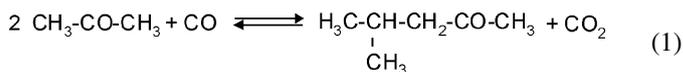
2. Experimental

2.1. Reagents and apparatus

Gamma-alumina gel was supplied by Aldrich (150 mesh ASTM, specific surface area 175 m^2/g); $Cu(NO_3)_2 \cdot 3H_2O$ (99% purity) and ammonium hydroxide solution (30–33% in water) from Fluka were used. MilliQ water was obtained by an Academic A-10 Millipore apparatus and used as a solvent for all experiments. Gaseous hydrogen, carbon monoxide and argon, from SIAD, were 99.99% pure.

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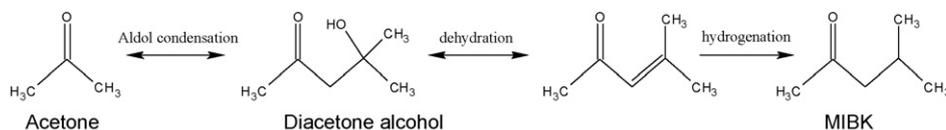
Scheme 1. Three step process for the synthesis of MIBK from acetone.

2.2. Catalytic system

2.2.1. Preparation procedure

Gamma-alumina gel (20 g) was added to a solution of 8 g of the blue aminocomplex prepared from $Cu(NO_3)_2 \cdot 3H_2O$ in 150 mL of water and 10 M ammonia (3 mL). The resulting suspension kept under continuous stirring was diluted with MilliQ water (2 L) to hydrolyse the cupramino complex and thus promoting adsorption on the alumina surface. The resulting solid was separated by filtration, washed with MilliQ water (3×1 L) and subsequently calcined at 350 °C for 3 h and finally reduced in a H_2 stream (20 mL/min) at 270 °C for 15 min.

2.2.2. Catalyst characterization

The resulting catalyst was 4.5% in weight in copper with a specific surface area of 270 m^2/g derived by BET analysis. Temperature programmed reduction (TPR) analysis was performed on a TPDRO-1100 (CE Instruments) equipped with a quartz reactor using H_2/Ar (5.1%, v/v) as reducing gas mixture flowing at 15 cm^3 min^{-1} with a thermal conductivity detector (TCD) for measuring the amount of H_2 uptake. Heating rate was 8 K min^{-1} from 315 to 673 K.

XRD analysis was carried out with a Rigaku D III-MAX horizontal-scan powder diffractometer with Cu Kα radiation, equipped with a graphite monochromator and TEM images were obtained using a LEO 912 AB instrument.

2.3. Evaluation of the catalytic activity

A 100 mL steel reactor (AISI 316) equipped with a cock, pressure gauge and mechanical stirrer was purged with N_2 and charged with the catalyst thereby obtained (1 g) acetone (10 mL) and CO until reaching 40 bar after which the temperature was raised to 180 °C setting the reactor under vigorous agitation. At the end of the reaction, the reactor was rapidly cooled with a stream of water, venting off the gaseous mixture and recovering the catalyst by filtration. The filtrate

was analysed by GC–MS technique using a Shimadzu GCMS-QP 5050 instrument provided by a capillary polyethylene glycol 20 M column. Qualitative analysis of CO_2 in the gaseous product was performed using a Siemens Ultramat 23 instrument provided with an infrared detector.

3. Results and discussion

Reacting with carbon monoxide at 40 bar and 180 °C, acetone could be converted into the saturated condensation product, methylisobutylketone, (59.8–75.9%) and the unsaturated mesityl oxide, (2.3–4.9%), isopropanol (0.8–7.8%) and polycondensation products (Table 1) whereas CO_2 was the only compound detected beside the unreacted CO in the gaseous products. Under these conditions, the highest yield of MIBK, *i.e.* 61.3%, was obtained after 2 h reaction (Table 1, entry 2).

As expected, increasing the reaction time above 1 h lowers the overall yield of MIBK and favours the formation of other higher aliphatic ketones owing to competitive reactions. Hence, after 4 h we observed an acetone conversion of 99.6% with selectivities to DIBK and MIBK of ca. 29.7% and 59.8%, respectively, (Table 1, entry 4).

Table 2 shows how changing experimental conditions (T and P) yields and selectivities could be influenced.

For instance, a comparison between the results obtained at 180 °C (Table 1, entries 2 and 3) and those obtained at 140 °C (Table 2, entry 5) suggests that it is possible to increase the selectivity to MIBK from ca. 75% to 83.1%, decreasing the selectivity to the rest of reaction products by decreasing the reaction temperature. This could be explained by considering that a low reaction rate of the consecutive reactions takes place at 140 °C. On the contrary, raising the temperature from 180 °C (Table 1, entry 4) to 220 °C (Table 2, entry 6) and reducing the reaction time from 4 to 1 h afforded practically the same acetone conversion with selectivities to MIBK (ca. 58.6%) and to DIBK (ca. 29%) similar to those obtained at 180 °C. Finally, reducing the reaction pressure from 40 to 15 bar and keeping constant both reaction time and temperature resulted in

Table 1

Acetone conversion (5 mL) at different reaction time and product distribution in the one-pot reductive-conversion over Cu/Al_2O_3 (1 g) at $T = 180$ °C and $P = 40$ bar

Entry	Reaction time (h)	Conversion (%)	Selectivity[a] (%)						
			IPA	MOX	MIBK	MIBC	DIBK	DIBC	C12
1	0.5	36.7	7.8	7.9	75.9	–	8.4	–	–
2	1	77.3	2.1	0.4	74.6	2.3	18.8	0.4	1.5
3	2	88.8	1.1	0.1	69.1	0.9	25.9	0.2	2.7
4	4	96.0	0.8	–	59.8	4.0	29.7	1.1	4.6

[a] IPA = isopropanol; MOX = mesityl oxide; MIBK = mehtylisobutylketone; MIBC = methylisobutylcarbinol; DIBK = diisobutylketone; DIBC = diisobutylcarbinol.

Table 2
Acetone conversion at different reaction time and product distribution in the one-pot reductive-conversion over Cu/Al$_2$O$_3$

Entry	P_{CO} (bar)	T (°C)	Time (h)	Conversion (%)	Selectivity[a] (%)						
					IPA	MOX	MIBK	MIBC	DIBK	DIBC	C12
5	40	140	4	52.4	6.2	5.4	83.1	–	5.3	–	–
6	40	220	1	92.6	1.6	0.1	58.6	4.6	29.0	1.5	4.9
7	15	180	4	63.9	0.7	6.7	78.5	–	13.6	–	0.5

[a] IPA = isopropanol; MOX = mesityl oxide; MIBK = mehtylisobutylketone; MIBC = methylisobutylcarbinol; DIBK = diisobutylketone; DIBC = diisobutylcarbinol.

substrate conversion of 64% with a good selectivity to MIBK (ca. 78.5%), a lower selectivity to DIBK (13.6%) and a similar selectivity to unsaturated mesityl oxide (ca. 6.7%) (Table 2, entry 7).

Owing to the fact that no water was added as a reagent, and considering that almost no water was detected into the reaction products by G.C., the results reported in Tables 1 and 2 can be interpreted taking into account a simple reaction mechanism in which the heterogeneous copper catalyst mediates both hydrogen formation through the water gas shift reaction (Eq. (2)) and the hydrogenation of MOX (Eq. (3)). This is confirmed also by the presence of CO$_2$ which was qualitatively determined beside the organic products.

$$H_2O + CO = CO_2 + H_2 \qquad (2)$$

$$(CH_3)_2C = CHCOCH_3 + H_2 = (CH_3)_2CH-CH_2COCH_3 \qquad (3)$$
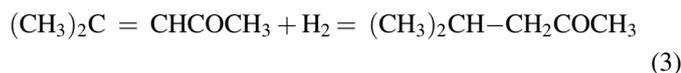
Hence, the H$_2$ needed for reducing the α,β unsaturated ketone is produced *in situ* by the action of supported Cu. As derived by GC analysis, all the water formed in the condensation of acetone to mesityl oxide and further condensations, is consumed in producing hydrogen used in the reduction of the

Nor CO has any influence on the reaction without the copper catalyst, as replacing carbon monoxide with N$_2$, the acetone conversion was 16.2% and the product consisted of 89% MOX. Moreover, reacting acetone with H$_2$ instead of CO we observed a high production of isopropanol (>50% selectivity) beside condensation products and water.

In the polyfunctional catalyst, the role of gamma-alumina could be compared to a "reactive sponge" whose H content may fall anywhere within the range $[0 < n < 0.6]$ for Al$_2$O$_3$·n(H$_2$O) as it can store and release water [9]. When a water molecule reaches the surface of gamma-alumina it breaks up. The H enters the material, and the O stays on the surface. Al atoms migrate from the centre of the material and combine with the O, thus extending the crystal matrix. Valence requirements determine that for every three H$_2$O molecules, six H move into the material, two Al move out, and the crystal extends by a stoichiometric Al$_2$O$_3$ unit.

Methylisobutylketone can further react with acetone and CO to give ketones of higher molecular weight mainly diisobutylketone (Eq. (4)) and 2,4,8-trimethylnonan-4-one (Eq. (5)). Therefore, CO pressure is an important parameter for the selectivity being able to control the dehydration step by means of reaction (2).

$$(4)$$

$$(5)$$
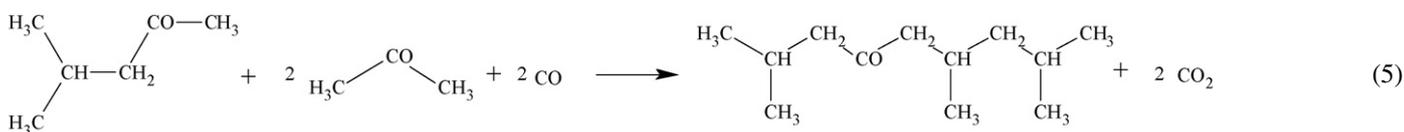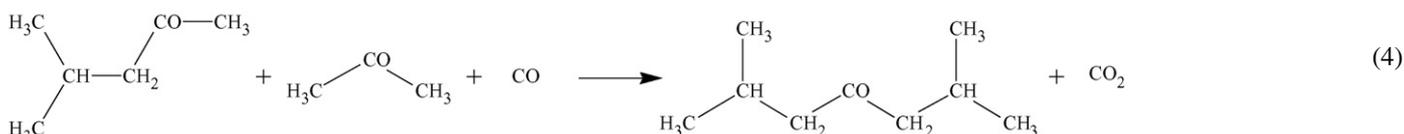
unsaturated ketone, thus shifting to the right the dehydration reaction.

Anhydrous gamma-alumina, in its turn, promotes the dehydration of diacetone alcohol to MOX as clearly shown by an experiment in which no Cu was deposited over alumina and the latter was used as the only catalyst under the reaction conditions of Table 1. In this case, in fact, after 4 h 17.1% of acetone was converted and 86.5% of the product was MOX.

A balance in the pressure of CO must be sought for which the formation of MIBK is the highest while the formation of other ketones is minimised.

Finally, other ketones can be successfully converted into higher homologues by varying the reaction time, depending on the specific substrate. As a consequence, while 3 h were enough to convert 68.1% of butan-2-one to 5-methylheptan-3-one (94.3%) and 3.6% butan-2-ol, 14 h were needed to convert
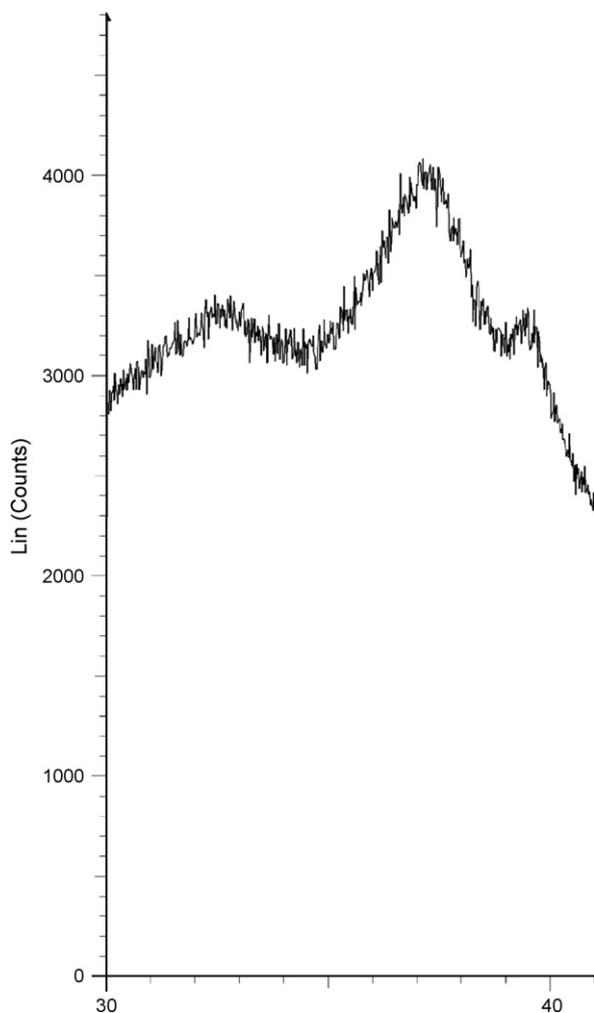
Fig. 1. XRD pattern of the Cu/Al$_2$O$_3$ catalyst.
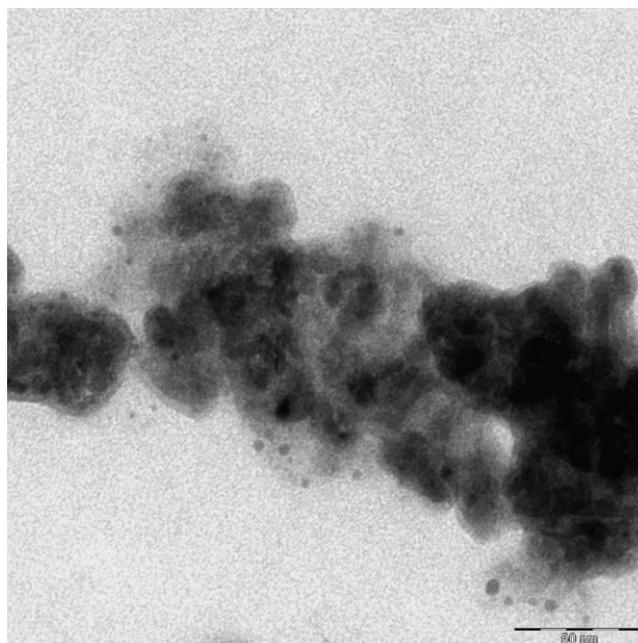
Fig. 2. TEM image of the Cu/Al$_2$O$_3$ catalyst.

Compared to other oxides used as Cu support, beside chemical activity related to its high surface area (220–250 m^2/g) [13], the optimal performance of γ-Al$_2$O$_3$ particles of relatively large size between 50 and 150 μm is consistent with the fact that this interphase is a surface fractal with low Haussdorf dimension [14]. For the alumina gel powders generally used in catalytic alcohol dehydrations [15] this result implies that particles of different diameter have largely different surface area as a low D value means that the surface area is strongly dependent on particle diameter.

The void phase (i.e., "nothing") [16] has a crucial importance in the performance of the catalysts as it is the large porosity of the silica gel to determine the large metal dispersion of supported metal nanoparticles, thus ensuring the high activity of supported metal catalysts. In practical applications, where such dispersion is of central importance, it is the task of chemist to design catalytic nanoarchitectures in which the support retains its stability during catalysis and upon longer reaction times in order to avoid pore collapse and sinterization of the metal particles.

The nature of the copper precursor dispersed on alumina was investigated by XRD and TEM techniques. Temperature

86.1% of MIBK to 93% 2,4,8-trimethylnonan-4-one and 4.2% methylisobutylcarbinol.

Although copper catalysts have been previously employed in hydrogenation reactions using dihydrogen [10], or alcohols [11] as a hydrogen source, the coupling of water gas shift reaction with a hydrogenation reaction is to our knowledge new and promising for further application.

After reduction, copper species on alumina consist mainly of zero-valent copper as derived by XPS-Auger studies [12], having a mean specific Cu(0) area of 20–30 m^2/g [13].

Table 3
Comparison among different catalytic systems and conditions in acetone conversion to MIBK

Catalytic system	Bibliographic reference	T (°C)	P (bar)	Conversion (%)	Selectivity (%) MIBK
Cu/Al$_2$O$_3$	Present work	180	40 (CO)	88.8	69.1
Pd/MgO	[18]	200	1 (H$_2$)	64.0–31.0	50.0–65.0
Ni/Al$_2$O$_3$	[19]	100	1 (H$_2$)	71.0	66.0
Pd/SAPO	[20]	200	36 (H$_2$)	25.9	80.8
Pd/(Nb$_2$O$_5$/SiO$_2$)	[21]	160	20 (H$_2$)	30.0–35.0	88.0–92.0
Pd/Nb$_2$O$_5$	[5]	160	20 (H$_2$)	45.6	92.5
Cu/MgO	[22]	280	1 (H$_2$)	60.0–80.0	60.0–75.0
Pd/CsPW	[7]	180	5 (H$_2$)	42.0	87.0
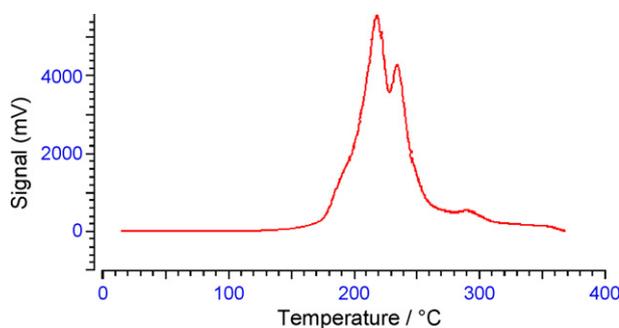
Fig. 3. TPR profile of Cu/Al$_2$O$_3$ catalyst.

programmed reduction (TPR) analysis was also performed in order to determine the reducibility of the immobilized copper species.

The XRD spectrum of the air calcined sample gave broad diffuse diffraction lines assigned to the CuO phase (Fig. 1) indicating poor crystallinity while the TEM images did not allow the statistic determination of the diameters. However, the presence of spherical particles of ca. 8–15 nm resulted evident (Fig. 2).

In the TPR profile, a large reduction peak between 180 and 320 °C, embodying two principal absorptions centred at 218 and 235 °C, was observed (Fig. 3).

Copper species which are reduced at higher temperatures between 350 and 400 °C are assigned to ions immobilized on alumina by strong adsorption [17]. On the other hand, species that are reduced at lower temperatures (210–240 °C) are predominantly formed during drying by precipitation from the liquid enclosed in the pore volume. Hence, the catalyst Cu/Al$_2$O$_3$ here employed in the synthesis of higher aliphatic ketones consists of copper species which are easily reducible, ensuring the availability of all copper for catalytic activity.

Compared with previous bifunctional catalytic systems employing H$_2$ as a reducing agent, acetone condensation in the presence of CO allows higher yields in MIBK.

Table 3 summarises the best performance (conversions and selectivities) observed in the present research which are compared with previous literature data.

4. Conclusions

In conclusion, the one-pot synthesis of higher aliphatic ketones from ketones of low molecular weight was achieved in the presence of alumina-supported copper catalyst and using CO instead of dihydrogen as a reagent. The process is competitive with other one-step processes previously reported, owing to the high conversion ensured by the removal of water through the shift reaction. The process is versatile towards different ketones and could be conducted also in gaseous phase. Therefore, in place of the traditional three-step homogeneous catalytic process using mutually destructive acid and base catalysts, a new one-pot heterogeneous catalytic process based on the cheap Cu metal is now available. Chemical and economic considerations suggest that the copper process is competitive with respect to the single step palladium processes and offers a practical alternative to the chemical industry to achieve another among the most fundamental chemical syntheses [23].

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