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High-temperature reaction of SiO₂ with methanol: Nucleophilic assistance of some *N*-unsubstituted benzazoles



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ABSTRACT

SiO₂-containing materials (quartz, Pyrex glass, silica gel, and H-Y zeolite) react slowly with methanol at 350 °C under both supercritical and gas-phase conditions. The amount of SiO₂ reacted with supercritical methanol depends on the kind of the material and is varied from 0.05 wt% for quartz sand to 4.0 wt% for wide-porous silica gel for 5 h of the reaction. The main products of the reaction are methyl orthosilicates, mainly tetramethyl orthosilicate. *N*-Unsubstituted 1*H*-indole, 1*H*-benzimidazole, and 1*H*-indazole additives considerably increase the amount of reacted SiO₂-containing material. Noteworthy, quartz sand "solubility" is increased *ca* 14-fold when indole is used at the same reaction conditions. These benzazoles provide a nucleophilic assistance to the reaction between SiO₂ and methanol. During the assistance, the azole ring is methylated by methanol, and the participation of SiO₂-surface or tetramethyl orthosilicate molecule facilitates the alkylation reaction of benzazole used.

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1. Introduction

Traditionally, silicas (SiO₂) are a convenient and widely used supports for different catalysts in organic synthesis. The reasons for such popularity are their chemical inertness, high thermal stability, enhanced mechanical strength and capability to use it as granules or powder, easy regulation of pore sizes and specific surface areas, ability to absorb effectively water and/or different organic compounds, multiple regenerations without considerable loss of initial activity. Due to these physicochemical properties of SiO₂, quartz or Pyrex glassware is traditionally used for chemical reactions, in which chemists try to avoid the effects of reactor's wall material.

Silica-supported catalysts are commonly used in many important industrial processes such as oxidative coupling of methane (OCM) [1] or partial oxidation of the last into methanol and formaldehyde [2], syntheses from syngas to dimethyl ether [3], oxidized C₂-compounds [4], or higher alcohols [5], transformations of methanol into hydrocarbons [6,7], olefins (methanol-to-olefin process, MTO) [8–12], or dimethyl ether [13]. All of these catalytic processes have common feature since they occur in gas phase at temperature from 300 up to 800 °C and one of the chemical components of the reaction mixture is methanol (together with SiO₂). These temperatures are above the critical temperature of methanol. In the supercritical state, methanol exhibits high reactivity and can be used as an alkylating agent for catalytic *N*-/O-methylation of amines [14], diols [15], and phenols [16]. It is, however, not known if is SiO₂ indeed inert under supercritical and gas-phase conditions at high temperature in the presence of methanol?

In earlier studies [17,18], significant differences were found for oxidative transformation of methane to methanol when oxidation was conducted in stainless-steel or Pyrex-lined reactors at temperatures between 375 and 500 °C. Higher conversion and selectivity were obtained in the reaction carried out in Pyrex-lined (and quartz-lined too) reactor. The real origin of the differences remained unknown. Other studies have demonstrated that methoxide species CH₃O⁻ can be detected in methanol oxidation reaction over silica-supported catalyst, for example, over molybdenum oxide [19,20]. However, methoxide anion could not be formed by oxidation of methanol molecule. Only reduction $(CH_3OH \rightarrow CH_3O^- + [H^{\bullet}])$ or thermal dissociation $(CH_3OH \rightarrow CH_3O^- + H^+)$ can lead to methoxide species formation. At the same time, these species can be formed easily, for instance, by thermal dissociation of tetramethyl orthosilicate $(Si(OCH_3)_4 \rightarrow CH_3O^- + (CH_3O)_3Si^+)$. It is well known that chemical modification of silica by some alcohols at high temperature



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Fig. 1. Experimental set-up.

results in its surface alkoxylation and formation of isolated Si–OR functionality on the surface [21]. In this case, the internal lattice structure of silica remains unchanged. But there is no data on total chemical destruction of silica material by alcohols, when SiO₂ is "dissolved". We hypothesize that SiO₂ is able to react with methanol at high temperature without any catalyst/additives to give tetramethyl orthosilicate (TMOS), in spite of reaction of silica and lower alcohols in the presence of an alkali metal hydroxide. The last conversion results in the formation of tetraalkyl orthosilicates too and occurs at temperature above 200 °C [22–25]. The further studies to confirm this hypothesis are required.

In this paper, we conducted a detailed study of the hightemperature reaction between SiO_2 and methanol. In particular, we studied the reactivity of silica gel, quartz, Pyrex glass, and H-Y zeolite CBV-720 in supercritical methanol at 350 °C and determined the structures of the resulting products. Additionally, we have investigated the effect of some *N*-unsubstituted benzazoles, such as 1*H*-indole, 1*H*-benzimidazole, and 1*H*-indazole, on reactivity of SiO₂ in the high-temperature reaction with methanol.

2. Experimental

2.1. Reagents and solvents

The following solvents and reagents were used without additional purification: indole (\geq 99%, Aldrich), benzimidazole (\geq 98%, Aldrich), indazole (\geq 98%, Aldrich), methanol (\geq 99.8% with a water content \leq 0.05%, J. T. Baker[®]), ethanol (\geq 99.8% with a water content \leq 0.16%), and 2-propanol (\geq 99.7%, FCC, Aldrich).

Wide-porous silica gel (ChromAnalyt, Ltd., Russia) with average pore diameter 141 Å, specific surface area 270–280 m² g⁻¹, pore volume 0.35 cm³ g⁻¹ was preliminary calcined at 250 °C for 2 h and then milled. The 0.8–1.0 mm fraction was used in experiments. Crashed quartz and Pyrex glass (1–1.3 mm fractions) were preliminary washed out with warm 10% aq. HCl (60 °C) for 2 h followed by multiple washing with distilled water to neutral pH. These solids were finally calcined at 500 °C for 3 h. H-Y Zeolite CBV-720 (mole ratio of SiO₂/Al₂O₃ is 30; average pore diameter is 24.28 Å; specific surface area is 780 m² g⁻¹) as a catalyst was commercial (Zeolyst International) and used without any conditioning.

Critical parameters of used alcohols are the following: for methanol – $T_{cr} = 240 \,^{\circ}$ C, $P_{cr} = 80 \,^{\circ}$ atm, $\rho_{cr} = 0.27 \,^{\circ}$ g cm⁻³; for ethanol – $T_{cr} = 244 \,^{\circ}$ C, $P_{cr} = 63 \,^{\circ}$ atm, $\rho_{cr} = 0.28 \,^{\circ}$ g cm⁻³; for isopropanol – $T_{cr} = 235 \,^{\circ}$ C, $P_{cr} = 47 \,^{\circ}$ atm, $\rho_{cr} = 0.27 \,^{\circ}$ g cm⁻³.

2.2. Experimental set-up

The scheme of experimental set-up is shown in Fig. 1. The set-up comprises a 285 mL high-temperature batch reactor (Autoclave Engineers), and Hastelloy C-276 alloy is the reactor's wall material (A). The autoclave is equipped with mechanical agitator MagneDrive[®] (Autoclave Engineers) and spinning catalytic basket Harshaw[®] (Autoclave Engineers) of volume *ca* 15 mL, two thermocouples (T₁) and (T₂), and sampling system with 6-port injector (S) Valco C1-2006 (VICI Valco Instruments Co. Inc.). The starting alcoholic solutions of benzazole were loaded by using a high-pressure syringe pump Teledyne ISCO 260D (C). Mixer speed and temperatures (T₁) and (T₂) are regulated by Sentinel controller (B), which additionally registers reaction pressure by electronic pressure sensor (P).

2.3. General experimental procedure

Initially, the removable catalytic basket was charged by one of selected solid SiO₂-containing materials: quartz sand – ~17.0 g, silica gel – ~6.7 g, Pyrex glass – ~17.0 g, zeolite – ~1.5 g. The amounts of solids loaded into the catalyst basket were different due to the different bulk density of these materials. Then the SiO₂-containing material was additionally dried directly in the basket at 180 °C for 0.5 h. After that, the weight of filled catalytic basket was measured with accuracy of \pm 0.5 mg (\pm 1.0 for silica gel only).

Before heating, the batch reactor (285 mL) with filled catalytic basket was charged by the required alcohol (methanol, ethanol, or isopropanol) that was pumped up from the vessel (5) (see Fig. 1). Finally, the reactor was purged with CO₂. The initial volume of methanol loaded was ~70 mL for runs with benzazoles or ~117 mL of the alcohol for all runs without using heterocycles. The heating time was 50–52 min to reach the reaction temperature from 25 °C. After heating the reactor up to 350 °C, benzazole solution (5.8 mmol in ~47 mL of methanol) was pumped into the reactor for 10 min. The starting point of the reaction time was at the end of pumping the benzazole solution or the reaching of reaction temperature (for the reaction without benzazole additives).

The reaction occurred at constant temperature of 350 ± 1 °C, mixer speed was 600 rpm in all experiments. During the reaction, samples of the reaction mixture were collected hourly to the sampler (7) by using a sampling system (S). An alcohol (methanol, ethanol, or isopropanol, 2.5–3 mL) was pumped into the reactor after each sampling to keep a constant reaction pressure. After cooling the reactor to room temperature (30 min), the final reaction mixture was poured into the vessel (6) through the port (3) (Fig. 1) and, along with other samples, analyzed by GC–MS (gas chromatography–mass spectrometry) and GC–AED (gas chromatography with an atomic emission detector) methods.

The catalytic basket with SiO₂-containing material was washed out with the same alcohol (50 mL) at 80 °C for 0.5 h. After opening the reactor, the catalytic basket was taken out, dried in the air for 10 h, and finished drying at 180 °C for 0.5 h. Then the final weight of filled catalytic basket was measured. The amount of reacted SiO₂ was determined as the difference between the initial weight and the final one of the filled basket.

2.4. Reaction of quartz sand and supercritical alcohol both with and without the addition of benzazole additives

The reaction was carried out accordingly to *General experimental* procedure. The calculated initial reaction density of supercritical phase was $\rho = 0.33 \,\mathrm{g\,cm^{-3}}$. The reaction pressure at supercritical conditions depended on used alcohol: for methanol – 215 ± 1 , for ethanol – 153 ± 1 , for isopropanol – 120 ± 1 atm. Benzazole (1*H*-indole, 1*H*-benzimidazole, or 1*H*-indazole; 0.68 g) was only used for the reaction in supercritical methanol (*sc*-MeOH) and pumped

up into the reactor as methanol solution immediately after heating the reactor up to 350 $^\circ\text{C}.$

2.5. Reaction of silica gel, crashed Pyrex glass, and H-Y zeolite with sc-MeOH both with and without the indole additive

The reaction was carried out accordingly to *General experimental procedure*. The calculated initial reaction density of supercritical phase was $\rho = 0.33 \text{ g cm}^{-3}$. The reaction pressure at supercritical conditions was $215 \pm 1 \text{ atm}$. Methanol solution of 1*H*-indole (0.68 g) was introduced into the reactor immediately after heating up to $350 \degree$ C.

2.6. Gas-phase reaction of methanol and indole both with and without the quartz sand

Before heating, the reactor was provided with the removable catalytic basket that was empty for non-catalytic reaction or filled with ~17.0 g of quartz sand for catalytic one. Then the methanol solution of indole (0.22 g, 1.9 mmol, in ~37–38 mL) was loaded into the reactor. The calculated initial reaction density for gas phase was $\rho = 0.11$ g cm⁻³. The indole concentration was c = 0.007 mol L⁻¹ in gas phase. The reaction was carried out accordingly to *General experimental procedure* but without hourly collection of samples of the reaction mixture. The reaction pressure was 52–56 atm at 350 °C. The reaction time was 4 h. The starting point of the reaction time was at the end of heating the reactor up to the operating temperature.

After cooling the reactor to room temperature (30 min), the final reaction mixture was poured into to the vessel (6) through the port (3) (Fig. 1) and analyzed by GC–MS and GC–AED methods.

Quartz sand in the catalytic basket was washed out with methanol (50 mL) at $80 \,^{\circ}\text{C}$ for 0.5 h. After opening the reactor, the catalytic basket was taken out, dried in the air for 10 h, and finished drying at 180 $^{\circ}\text{C}$ for 0.5 h. Then the final weight of filled catalytic basket was measured. The amount of quartz sand that reacted was negligible.

2.7. Analysis of reaction mixtures

The identification of products was performed by GC–MS method on a gas chromatograph Varian Saturn 2000 with ion trap as detector using a 30 m-long quartz capillary column HP–5 with 0.25 mm i.d.; the film thickness of the stationary phase (5% diphenylsiloxane–95% dimethylsiloxane copolymer) was 0.25 μ m; helium with a constant flow rate of 1 mLmin⁻¹ was used as the carrier gas; the injector temperature was 300 °C; the temperature program: 50–200 °C (7 °Cmin⁻¹), 200–300 °C (20 °Cmin⁻¹), and 300 °C (20 min).

The qualitative analysis was carried out by comparing the retention time of the components and their complete mass spectra with corresponding data for pure compounds and with data from NIST and Wiley7 mass spectral libraries. The quantitative analysis of nitrogen-containing products was made by the GC–AED method on an Agilent 6890N gas chromatograph equipped with a jas 2370AA Atomic Emission Detector using a capillary low-bleed column HP–1MS (19091S-916), 60 m × 0.32 mm i.d. × 0.25 μ m (100% dimethylpolysiloxane). Table 1 shows the experimental conditions for the GC–AED analysis. Calculations of conversion and selectivity were based on mol nitrogen basis as a very sensitive and accurate GC method of the quantitative analysis [26].

3. Results and discussion

We have studied the reaction of SiO_2 with supercritical methanol at 350 °C and ~215 atm. It was *a priori* assumed that

Table 1

Temperature program and specific parameters for the GC-AED method.

GC experimental conditions				
Injection port	Split			
Injector temperature	280 °C			
Oven temperature program	40–280 °C (7 °C min ⁻¹), 280 °C (5 min)			
Column	Part no. 19091S-916, HP–1MS,			
	$60m \times 0.32mm$ i.d. \times 0.25 μm (100%			
	dimethylpolysiloxane)			
Inlet conditions	Column pressure – 13 psi, split flow –			
	100 mL min ⁻¹			
Split ratio	10:1			
Carrier gas	Helium, make-up flow – 230 mL min–1			
Injection volume	2 µL			
AED parameters				
Flow of spectrometer purge gas	500 mL min ⁻¹			
Transfer line/cavity temperatures	320 °C			
Data rate	5 Hz			
Nitrogen detection	At 388 nm using the CN molecular			
_	emission spectral band			
Reagent gases	O ₂ /H ₂ /CH ₄ -80:40:50 (psi)			

different forms of SiO_2 could react with MeOH at different reaction rates.

This assumption seems to be reasonable, since SiO₂-containing materials have different density, specific surface area, chemical impurities, and some other physical properties, which can have influence on chemical ones. Therefore, SiO₂-containing materials selected for the present study were wide-porous silica gel, quartz sand, crashed Pyrex glass, and commercial H-Y zeolite CBV-720. Nevertheless, the main comparative study was performed using silica gel and quartz sand. All experiments were conducted three or more times.

3.1. "Dissolution" of quartz and silica gel in sc-MeOH without additives

It was found out the reaction of quartz sand with supercritical methanol is slow. The conversion of the starting quartz is very small for 5 h of the reaction – less than 0.05 wt% (line "quartz only", Fig. 2). But silica gel is "dissolved" faster at the same reaction conditions (4 wt%, line "silica gel only"). Thus, 275 mg of silica gel from \sim 6.8 g of its initial amount is "dissolved" for 5 h of the reaction despite



Fig. 2. Reaction of silica gel and quartz with *sc*-MeOH for 5 h at 350 °C. Effect of benzazole additives on amounts of reacted SiO₂.

Main orthosilicates detected by GC-MS analysis in the reaction mixtures.					
RT (min) ^a	MS, m/z M ⁺	Formula	Orthosilicates		
3.07	152	Si(OMe) ₄	Tetramethyl orthosilicate ^b		
3.92	138	Si(OH)(OMe) ₃	Hydroxytrimethoxysilane ^c		
8 69	258	Si ₂ O(OMe) ₆	Hexamethyl diorthosilicate		

^a Retention time.

^b The relative concentration of TMOS is typically 85–98 wt% of all orthosilicates. ^c Si(OH)(OMe)₃ has usually a very low relative concentration in the reaction mixtures.

(hexamethoxydisiloxane)^d

 $^{\rm d}\,$ The relative concentration of hexamethoxy disiloxane is 1–8 wt% of all orthosilicates.

the fact that the initial total amount of silica gel was 2.5 times less than the starting weight of quartz sand. (Different starting amounts of silica gel and quartz sand loaded into the catalyst basket were limited due to different bulk density of these materials.) In addition, the crashed Pyrex glass manifested the "solubility", which is similar to quartz sand and strongly different from silica gel.

It is known that an alcohol chemisorbed on silica can react with its surface alkoxylating at elevated temperature. This esterification reaction occurs on both isolated silanol groups (\equiv Si–OH) and siloxane bridges (\equiv Si–OSi \equiv) and proceeds *via* cleavage of its Si–O bonds [27,28]. In our opinion, the significant difference between the reactivity of silica gel and quartz is due to the enhanced porosity and "friable" molecular packing of the first compared with quartz. Consequently, internal and external surfaces of silica gel have more amounts of free isolated Si–OH groups that actively interact with methanol and facilitate the following "dissolution" of SiO₂. An additional argument is that the reaction involving the opening of siloxane Si–O–Si bridges is favoured at higher temperature [29]. Due to the more fragile skeletal silica network, the contribution of this esterification pathway to the total "dissolution" process could be higher for silica gel too.

Our attempts to carry out the reaction of quartz both with supercritical ethanol and isopropanol have failed at the same reaction conditions. It was shown that the starting amount of quartz sand does not change within weighing accuracy (± 0.5 mg) after 5 h of the reaction in these alcohols. It is quite unexpected result since the esterification reaction of silica surface by ethanol or other lower alcohols is well-studied process to produce surface-alkoxylated silica [27–29]. Presumably, the ability of an alcohol to react with siloxane bridge disrupting the Si–O bond is crucial for the "dissolution" of SiO₂. Therefore, exclusively methanol demonstrated the considerable ability "to dissolve" the quartz sand.

3.2. Main reaction products obtained from quartz sand or silica gel in sc-MeOH

We determined the structure of main products in the reaction and quantified them. The GC–MS method was chosen for this purpose. NIST-2008 and Wiley 7N mass spectral libraries were used for the identification. It was shown that the reaction results in the formation of alkyl orthosilicates, mostly tetramethyl orthosilicate.

Table 2 shows the combined data on the GC–MS analysis of main orthosilicates identified in all reaction mixtures. Two orthosilicates were the main dissolved Si-containing compounds (about 99 wt% of all orthosilicates), which, in fact, were formed from SiO₂. These were TMOS (RT 3.07 min) and hexamethyl diorthosilicate (hexamethoxydisiloxane, RT 8.69 min). In addition, there was a very weak peak on chromatograms, which belonged to hydroxytrimethoxysilane (RT 3.92 min). The formation of hydroxytrimethoxysilane and hexamethyl diorthosilicate can be explained by the presence of water formed



Fig. 3. Orthosilicates content (recalculated to weight of Si per litre) *vs* time of keeping the reaction mixture. The lower curve – "quartz + methanol", the upper curve – "quartz + methanol + indole".

during the reaction $SiO_2 + 4CH_3OH \rightarrow Si(OMe)_4 + 2H_2O$, where methoxysilanols (for example, hydroxytrimethoxysilane) seem to be intermediates. The condensation of Si(OH)(MeO)_3 is known to result in dimerization and formation of hexamethoxydisiloxane: $2(MeO)_3Si-OH \rightarrow (MeO)_3Si-O-Si(OMe)_3 + H_2O$ [30]. Mono- and di-orthosilicates formed in these reactions may undergo further oligomerization. At room temperature, these processes are very slow and require prolonged period of time to form detectible amounts of these products.

It should be noted that the quantitative analysis of alkyl orthosilicates by the GC–MS method is not a simple routine procedure. The difficulty is that the amounts of detected orthosilicates in the reaction mixture for binary system "methanol+water" strongly depend on the time interval elapsed after the sampling prior to the GC–MS analysis. Recently, we demonstrated this for reaction mixtures "TMOS/water/indole" [31]. When the reaction mixture containing methanol (solvent), TMOS, water, and indole is kept at room temperature, TMOS starts to undergo hydrolysis and polycondensation reactions. A decrease of the amount of the detected orthosilicates is caused by oligomerization and gelification. The oligomeric orthosilicates formed from TMOS or Si₂O(OMe)₆ cannot be detected by the GC–MS method due to their large molecular weights and high boiling points (higher than injector temperature of chromatograph).

Fig. 3 shows the dependence of detected amounts of alkyl orthosilicates on the time of keeping the reaction mixture at room temperature. The lower curve refers to the reaction mixture obtained during the conversion of quartz sand in *sc*-MeOH, the upper curve – during the conversion of quartz sand in *sc*-MeOH with 1*H*-indole. Molar ratios of orthosilicates/water and orthosilicates/water/indole compounds were 1:25 and 1:3.6:3.7, respectively (taken into account the residual water content in methanol). Estimated concentrations of orthosilicates and water at starting point of curves were ~0.2/0.4 and ~2.0/0.9 gL⁻¹, correspondingly. The starting point of curves was at the end of the reaction after cooling the reactor to room temperature.

The dependence obtained shows that the initial amount of detected orthosilicates is reduced by three times for the first day of keeping (Fig. 3). Interesting to note, when molar ratio of orthosilicates/water/indole compounds was 1:2:1.4 at starting concentrations of orthosilicates and water being equal to $\sim 9/2 \text{ g L}^{-1}$, the amount of detected orthosilicates was reduced by half for first two days of keeping [31]. All these data mean that the initial molar ratio and concentration of orthosilicates, water, and



Fig. 4. Structures of benzazoles used as additives.

indole compounds strongly influence the oligomerization rate of orthosilicates.

3.3. Effect of indazole, benzimidazole, and indole on the reaction of quartz and silica gel with sc-MeOH

To convert SiO₂ (acidic oxide) into TMOS (ester of orthosilicic acid) at high temperature, it is usually needed an alkali hydroxides [22–25]. We assumed that organic bases, for example, *N*-unsubstituted benzazoles (1*H*-benzimidazole **1**, 1*H*-indazole **2**, and 1*H*-indole **3**, Fig. 4), will also promote the "dissolution" of SiO₂-containing materials in *sc*-MeOH at high temperature. The basicity of azoles used is as follows: benzimidazole > indazole \gg indole [32]. If the idea is correct, the rapidity of SiO₂ "dissolution" will correlate to the basicity of the azoles.

It was found out that the amount of "dissolved" quartz increases by 1.4 times with using the indazole (from 7.0 to 9.5 mg, line "quartz + indazole", Fig. 2). More significant effect is achieved when benzimidazole was used – the quartz "solubility" increases by \sim 5 times (line "quartz + benzimidazole"). It seems obvious that these two results of the reaction correlate with the basicity of selected benzazoles. However, the result of the reaction "quartz + indole" is quite unexpected. Contrary to our expectations, indole additives have a dramatic effect on the reactivity of quartz increasing its "solubility" in *sc*-MeOH by 14 times (line "quartz + indole"). Nevertheless, this result (0.6 wt% of starting amount of quartz sand) is not the best if we compare it with the "solubility" of silica gel without additives of benzazoles (4 wt%, line "silica gel only").

Interestingly, when indole was introduced in the reaction with *sc*-MeOH, the "solubility" of silica gel increases by 1.4 times only (line "silica gel + indole", Fig. 2) compared with the reaction of silica gel without additives. The possible reason is the following. Our preliminary data show that the amount of silica gel, which was "dissolved" in equal volume of *sc*-MeOH with considerable increasing the reaction time (up to 24 h), has the upper limit which is preferably determined by the water content in the reaction mixture. It is reasonable to assume that the reaction of SiO₂ with methanol resulting in formation of water together with TMOS is reversible. Therefore, the SiO₂ "dissolution" will be stopped when a certain concentration of water is reached in the reaction mixture. We observed this effect in several preliminary runs with silica gel, but this phenomenon requires further detailed study.

3.4. Correlation of quartz conversion in sc-MeOH with C-nucleophilicity of indole, benzimidazole, and indazole

Bearing in mind that the basicity of benzazoles did not have a crucial importance for the "dissolution" of SiO₂-containing materials, we tried to determine, which property of benzazoles has the key influence on the reactivity of SiO₂ in *sc*-MeOH. We believe that the property is the nucleophilicity of benzazoles, and not *N*-, but mainly *C*-nucleophilicity. *N*-Nucleophilicity of selected benzazoles correlates accurately with their basicity (see above), but *C*-nucleophilicity of these benzazoles is as follows: indole \gg benzimidazole > indazole. It means that the reactivity of indole is many times higher than that of benzimidazole (and much more – of indazole) in aromatic electrophilic substitution reactions, when these benzazoles act as a *C*-nucleophile.

Table 3

Conversion of benzazoles and ratio of main alkylation-type products in *sc*-MeOH with using quartz.^a

Benzazole	Benzazole conversion, mol.%	Ratio of <i>C-/N</i> -alkylation products, mol/mol
Indazole	10	$\sim 1/4$
Benzimidazole	48	$\sim 1/2$
Indole	54	$\sim 10/1$

^a Detected by the GC–MS method.

We have found that selected benzazoles react with sc-MeOH in the presence of quartz at our reaction conditions to form CH₃substituted benzazoles, mainly - monoalkylated products. Table 3 shows qualitative results of the benzazoles reaction for 5 h. It is seen that conversions both of indole and benzimidazole are comparable and equal to one-half of their amounts loaded initially into the reactor. At the same time, the conversion of indazole is five times less than for other benzazoles. It is much more important to focus on the ratio of C-/N-alkylation products, which describes in some way the relationship of C-/N-nucleophilicity of used benzazole. *N*-Methylated products are principally formed from both indazole and benzimidazole. However, the contribution of C-alkylated products increases from indazole to benzimidazole (from 1/4 to 1/2, Table 3). Dramatically abrupt change of the ratio occurs in the reaction of indole (up to 10/1), when the C-methylated indoles as products dominate overwhelmingly. Thus, "the solubility" of quartz in sc-MeOH was directly proportional to the conversion of benzazoles into C-alkylated products, in other words - the reactivity of quartz sand in sc-MeOH correlates to the C-nucleophilicity of benzazoles. The auxiliary role of benzazoles is a nucleophilic assistance to the reaction of MeOH with solid SiO₂ surface, when SiO₂ is converted to TMOS together with methylation reaction of benzazoles by sc-MeOH.

3.5. Influence of SiO₂ ability "to be dissolved" on indole conversion in supercritical and gas-phase MeOH

Since the glassware and other SiO_2 -containing materials can slowly react with methanol at high temperature to give orthosilicate (TMOS), we believe that these materials should be used with caution for several chemical processes. For example, it is necessary to consider when some reactions carry out at similar conditions and both SiO_2 and methanol are starting reaction components. The problem is that tetramethyl orthosilicate, which is formed in the reaction of SiO_2 with methanol, could catalyze undesirable side reactions. Presently, the catalytic activity of TMOS in organic reactions is poorly studied.

Recently, the effective indole C₃-methylation by sc-MeOH was described by Kishida et al. [33]. The reaction carried out in Pyrex glass sealed tubes was determined by the authors as "without catalyst" conversion. Our attempts to repeat Kishida's results in batch reactor, in which corrosionresistant Hastelloy® C-276 alloy was the reactor's wall material, were failed. The indole conversion and selectivity of C_3 -methylation achieved by us were about three times lower. Then, it has been suggested that TMOS, which is formed at high temperature from Pyrex glass in sc-MeOH, has a catalytic effect on the indole C_3 -methylation. More recently, we have proved the idea by demonstrating the use of TMOS or TEOS (tetraethyl orthosilicate) significantly increases the selectivity of indole *C*₃-methylation by *sc*-MeOH (up to 95–96 mol%) [31]. The catalytic role of tetraalkyl orthosilicates was unequivocally established in this reaction.

To demonstrate the dependence of indole methylation reaction on the use of different SiO_2 -containing materials, we performed

Table 4

Comparative indole conversion and regioselectivity of C3-methylation catalyzed by different forms of SiO2.

SiO ₂ -containing catalyst	Indole conversion, mol.% ^d	3-Methylindole yield, mol.% ^d	3-Methylindole selectivity, %
Without catalyst in sc-MeOH ^a	29	18	62
Without catalyst in gas phase ^b	17	11	65
Quartz sand in sc-MeOH ^a	47	41	87
Quartz sand in gas phase ^b	19	17	88
After removal of quartz sand in sc-MeOH ^a	34	33	96
Crashed Pyrex glass in sc-MeOH ^a	40	35	87
Silica gel in sc-MeOH ^a	23	19	83
HY zeolite CBV-720 in sc-MeOH ^a	45	22	50
CeHY zeolite in gas phase (Ref. [34]) ^c	77	30	38

^a In supercritical methanol, molar ratio of methanol/indole is 500, 350 °C, 213-215 atm, 4 h.

^b In gas-phase methanol, molar ratio of methanol/indole is 500, 350 °C, 52–56 atm, 4 h.

^c In gas-phase methanol, molar ratio of methanol/indole is 6, HY zeolite impregnated by 3 wt% Ce⁺ salt, 350 °C, 4h.

^d Detected by the GC–MS method.



Scheme 1. The main products of indole monomethylation by sc-MeOH.



Fig. 5. Indole conversion in sc-MeOH with using different SiO₂-containing materials (mol%).

the reaction of *sc*-MeOH at 350 °C with using the crushed Pyrex glass, quartz sand, silica gel, and commercial H-Y zeolite CBV-720. Scheme 1 shows main products of the indole alkylation by *sc*-MeOH.

Figs. 5–6 and Table 4 show the indole conversion that was only 29% in non-catalytic reaction (line 1 in Table 4). This conversion



Fig. 6. Total yield of 3-methylindole 4 in sc-MeOH (mol%).

is higher than that silica gel is used as catalyst (line 7). The C_3 -methylation selectivity achieves $62 \mod \%$ (4 h) at non-catalytic conditions. It is seen that the graphical dependence is reaching a plateau after 5 h of the reaction.

Poor catalytic efficiency is demonstrated by H-Y zeolite (this result is not shown on Figs. 5–6, see line 8 in Table 4), those use leads to ~45% of indole conversion (4h). Selectivity on 3-methyl-1*H*-indole **4** (3-MI, skatole) is much lower (about 50 mol%, 4h) due to increasing the amount of 1-methyl-1*H*-indole **5** (~7–9 mol%) as well as di-, tri- and poly-methylated indoles (cf. Ref. [33]).

Apparently, the acidity and other properties of zeolite CBV-720 proved to be too strong to provide acceptable selectivity of alkylation by methanol. It appears that HY zeolite is similar to usual Friedel-Crafts catalyst (a strong Lewis acid) at our reaction conditions. The catalytic activity of TMOS formed from this zeolite during the reaction is insufficient to that the product of indole C_3 methylation would be the main one. Earlier, it has been shown under gas-phase conditions that the use of modified HY zeolites in the reaction of indole with methanol can lead to high selectivity of the C₃-alkylation (96% for 4 h at 300 °C), but only at low conversion of starting indole (\leq 35%) [34]. The highest catalytic efficiency at 350 °C has been demonstrated by HY zeolite modified with Ce+ ions (line 9 in Table 4). However, the yield of 3-MI 4 was only 30% at high conversion of indole (77%). This confirms our conclusion that zeolites are not guite effective catalysts for the indole alkylation by alcohols at high temperature (above $300 \circ C$).

Catalysis by wide-porous silica gel gives 83 mol% of the selectivity on C_3 -alkylation (4 h), although the indole conversion is only 23% for the same reaction time (line 7 in Table 4). Dependences on Figs. 5–6 demonstrate that the use of SiO₂ slows down the indole conversion during first 5 h compared with non-catalytic reaction, but then the conversion increases more rapidly. In addition, the selectivity of the reaction with SiO₂ is higher by 20% (after 4 h) than that without catalyst.

Interestingly, graphical dependences of the indole conversion and the yield of skatole **4** vs the reaction time, which were obtained for catalysis by silica gel, are nearly straight within chosen range of reaction times.

The crashed Pyrex glass as a catalyst shows linear dependences too. The indole conversion grows up to 40% (4 h), and the selectivity on 3-MI **4** (87 mol%, line 6 in Table 4) is noticeably higher compared to other reactions listed above (Figs. 5–6). Such selectivity of the indole C_3 -alkylation was comparable with Kishida's one achieved for the reaction in Pyrex glass sealed tube [33].

Quartz sand demonstrates the best catalytic result in the alkylation reaction (Figs. 5–7). The conversion of indole reaches 47% at C_3 -selectivity of 87 mol% for 4 h of reaction (line 3 in Table 4). Increasing of the reaction time up to 19 h (Fig. 7) leads to the complete indole conversion (99% and higher) accompanied by slight



Fig. 7. Comparison of catalytic methylation by using *sc*-MeOH with quartz in reactor volume and after preliminary removal of quartz from reactor.

decrease of the selectivity from 88 (2 h) to 82 mol% (19 h). The higher yield of 3-MI **4** is achieved for 15–17 h of the reaction (about 81 mol%), and then concentration of the C_3 -methylated indole **4** in the reaction mixture begins to decrease due to its further alkylation. Thus, we have demonstrated for the reaction of indole alkylation that the catalytic efficiency of SiO₂ depends strongly on the type of SiO₂-containing material.

It seemed to be important to determine whether quartz sand has catalytic effect in gas-phase reaction of indole with methanol. We scaled down for three times initial concentrations of indole and methanol that were earlier used for the reaction in supercritical MeOH. It was necessary to decrease the reaction density inside the reactor lower than critical value. At the same time, the amount of quartz sand as a catalyst was no change.

Gas-phase reaction that occurred at the same $350 \,^{\circ}$ C showed that the products distribution does not differ from one obtained in *sc*-MeOH. However, both non-catalytic and catalytic conversions of indole are significantly decreased in gas-phase reaction. The reaction without using the quartz sand gave 17% of conversion for 4 h with 65 mol% of selectivity to 3-methylindole **4** (line 2 in Table 4). The selectivity was reaching up to 88 mol% when quartz sand was used (at 19% of indole conversion, line 4). The selectivity

observed is the main evidence of SiO_2 catalytic activity in gas phase. In addition, the emergence of TMOS in the reaction mixture (GC–MS data) shows that SiO_2 is also reacting with methanol in the gas-phase conditions at high temperature.

The comparison of experimental data obtained at gas-phase and supercritical conditions suggests that the reaction of SiO₂ with methanol at 350 °C is faster at high pressures, i.e. the higher the density of the reaction medium (and partial pressure of methanol) is, the quicker and more actively the desilication of zeolites, silicas or glasses occurs. The effect of the reaction temperature assumes to be the same: the higher the temperature is, the faster the reaction of SiO₂ with methanol is. Interestingly, such desilication may be yet another reason for the catalyst deactivation in the MTO process or the one-step DME synthesis. It is well known that catalysts or catalyst systems in aforementioned processes are usually deactivated due to sintering of active copper sites at high reaction temperature, forming of coke on the surface of the catalyst, and poisoning by some contaminants [35-38]. At the same time, if the desilication of SiO₂-containing catalysts takes place under the action of methanol at high temperature and pressure, the partial destruction of active sites of catalysts should occur by crushing the catalyst matrix.

It was interesting to establish the origin of catalytic effect on the indole alkylation. Is it the surface area of SiO_2 -containing material (heterogeneous catalysis) or the action of TMOS-methanol binary system (homogeneous catalysis) as we demonstrated earlier [31]?

At first, the reaction was carried out between quartz sand and *sc*-MeOH at 350 °C for 2 h, after that the catalytic basket with quartz sand was removed from the reactor. When the reactor was bolted and heated up to 350 °C, the concentrated indole solution in methanol was loaded by using a high-pressure syringe pump. Finally, the reaction was carried out for 6 h under supercritical conditions in the presence of compounds formed preliminary after contact of quartz sand with *sc*-MeOH (TMOS and some other methyl orthosilicates). A comparison of the reactions in presence of quartz and after its removal from the reactor is shown in Fig. 7. One can see that the removal of quartz from the reactor resulted in decreasing the final indole conversion for 4 h of the reaction (from 47 down



Scheme 2. The proposed nucleophilic assistance of indole for participation of SiO₂-surface in catalysis.



Scheme 3. The further plausible transformations of methyl-hydroxylated SiO₂-surface.

to 34 mol%, line 5 in Table 4). Nevertheless, the selectivity of C_3 -methylation became extremely high (96%) and the same as if the reaction would be catalyzed homogeneously by TMOS [31].

Thus, it could be concluded that the high selectivity of the reaction is the result of homogeneous catalysis by TMOS. The last is formed from quartz (in general – from any SiO₂-containing material) at high temperature during the "dissolution" in *sc*-MeOH. At the same time, the solid quartz surface is also involved in the overall catalytic conversion. This participation could be as follows (Scheme 2). At first stage, methanol reacts with isolated Si—OH groups of SiO₂-containing material to methylate partially its surface. At second step, the chemically modified surface participates for indole alkylation as a part of catalytic binary system (\equiv SiOCH₃+MeOH, cf. Ref. [31]).

At least, two pathways of the alkylation could be realized (Scheme 2). The pathway (A): an alkylating agent is MeOH; 1Hindole is coordinated to the solid surface by hydrogen bonding of indole N–H with oxygen atom of \equiv SiOCH₃ group of modified surface (as shown in Scheme 2) or with oxygen atom of silanol \equiv Si-OH group of initial unmodified SiO₂-surface. The role of methoxylated SiO₂-surface is to adopt H atom of indole H-N bond and to facilitate the HO–CH₃ bond rupture due to Lewis acid properties. The pathway (**B**): an alkylating agent is methoxylated SiO₂-surface (isolated \equiv Si-OCH₃ group); 1*H*-indole is coordinated to the solid surface by hydrogen bonding of indole N-H with oxygen atom of siloxane \equiv Si-O-Si \equiv bridge (as shown in Scheme 2). The role of MeOH molecule is nucleophilic assistance for indole methylation by =SiO-CH₃ moiety. The result of such auxiliary is the facilitation of \equiv SiO-CH₃ and \equiv SiO-Si \equiv bonds cleavage and the additional methoxylation of SiO2-surface. The consolidated result on the participation of both indole and methanol molecules is a "loosening" of initial SiO₂-surface structure and formation of new well-developed "methyl-hydroxylated" one. The last is more friable and much less chemically robust than the unmodified SiO₂-surface and could reversible reacts with MeOH (easier and faster) to give TMOS or can eliminate (release) H₂O and MeOH molecules to form a poor-developed SiO₂-surface which can also be converted into Si(OCH₃)₄ under the reaction conditions, but slower than "methylhydroxylated" surface (Scheme 3).

4. Conclusions

We have demonstrated that different SiO_2 -containing materials react with methanol at $350 \,^{\circ}C$ under both supercritical and gas-phase conditions. The amount of the material reacted with supercritical methanol can be varied from 0.05 wt% for quartz sand to 4.0 wt% for silica gel for 5 h of the reaction. SiO₂ reacts in this case

as an acidic oxide to give mainly tetramethoxysilane-tetramethyl ester of orthosilicic acid. Surprisingly, the additive of aromatic azaheterocycles, such as N-unsubstituted indole, benzimidazole, and indazole, is able to increase considerably the amount of reacted SiO₂-containing material. The key role of tested benzazoles is the nucleophilic assistance for the reaction of SiO₂ and methanol. At the same time, tetramethyl orthosilicate that is formed from SiO₂ under these reaction conditions has appreciable catalytic activity on methylation reaction of benzazole, especially on indole alkylation, and promotes (facilitates) the conversion of benzazole to Cand/or N-methylated derivatives. We hypothesize that the methylation process of benzazole is the aromatic electrophilic substitution by methanol or methoxylated solid SiO₂-surface as a methylating agent and proceeds via cyclic, multi-centred transition state. Importantly, both ethanol and isopropanol do not undergo this reaction with SiO₂ at the same experimental conditions.

These data suggest that all SiO₂-containing materials (including silica-supported catalysts too) are chemically destroyed by methanol at 350 °C and above, especially in the presence of different nucleophilic additives. Additionally, methyl orthosilicates can catalyze some reactions (for example, undesirable ones) between different chemical components of the reaction mixture.

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