Bismutite-based cooperative catalysts – Efficient heterogeneous systems for heterocyclization

PhD theses

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1. Introduction and main aims

Based on a general search in Scifinder (https://scifinder.cas.org) on the 2nd of January, 2023, in the last 10 years *ca.* a quarter of the 260000 publication related to catalysis focused on the production and/or transformation of heterocycles.[1] Most of them describe some kind of catalytic system (transition metal catalysis, Lewis acid catalysis, organocatalysis, biocatalysis, phase transfer catalysis, electrocatalysis), since the alternative route or mechanism they provide is much more economical and competitive than non-catalyzed processes.

Although the field of synthetic organic chemistry is dominated by homogeneous noble metal catalysis, heterogenized catalysts containing non-noble metal centers can also have many advantages. Not only can they offer the advantages of recyclability and robustness, which in itself can represent an economical and environmentally friendly alternative in catalyst selection, but also they can even be more effective candidates compared to their monometallic counterparts (enhanced selectivity and/or yield, milder reaction conditions, greener solvents), if the different metal centers are able to cooperate with each other.

Targeting this possibility, our primary hypothesis was that by modifying the Lewis acidic bismutite ($Bi_2O_2CO_3$) framework with copper, cobalt, manganese or nickel cations or oxide specimens, efficient multifunctional catalysts capable of promoting multi-step cyclization reactions in a heterogeneous manner can be produced. In addition, we hypothesized that their efficiency can be further enhanced by determining the structural factors that can most decisively affect the catalytic performance. Thus, the modified structures were thoroughly studied both structurally (XRD, Raman, XPS, *etc.*) and catalytically, in a series of catalytic tests, especially in cyclization reactions.

2. Experimental part

Syntheses of the modified bismutites

The transition metal ion modified bismutite structures were synthetized by a modified co-precipitation method, and were denoted by the formula of $MBi_2O_2CO_3$, regardless of the oxidation state of the metallic components. During the synthesis ammonia and sodium-carbonate solutions of a certain concentration (0.6 M) were added directly to bismuth- and transition metal nitrate-containing solutions of a certain concentration (3.75 mmol). Then stirring was continuous for 24 hours at 80 °C for $CuBi_2O_2CO_3$ and 100 °C for Co-, Mn-, $NiBi_2O_2CO_3$. The obtained, colored products were then filtered, washed and dried. With the exception of copper-bismutite, the fine powder solids were heat-treated at 290°C for 3 hours to remove any remaining traces of water before catalytic use.

Transition-metal free bismutites ($Bi_2O_2CO_3$) were prepared under the same conditions at 80 and 100 °C, but without the use of transition metal salt solutions.

The bismutite-supported transition metal oxide composites, used as reference compounds, were synthesized by a wet impregnation method. An ethanolic suspension was prepared from 1 equivalent (3.75 mmol) of as-prepared $Bi_2O_2CO_3$ and 2 equivalents of $CuO/MnO_2/$ in situ precipitated $Co(OH)_2/Ni(OH)_2$, from which the solvent was evaporated after 2 hours of ultrasonic treatment. For impregnated references, the $M–Bi_2O_2CO_3$ designation was used.

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[1]A general search of Scifinder (https://scifinder.cas.org) on the 2nd of January, 2023 found 265,839 "catalysis"-related English-language journals published between 2012 and January 2023, of which 71,525 were for production and/or transformation of heterocycles.

Instrumentation and characterization methods

The XRD patterns of the as-prepared bismutites were recorded on a Rigaku XRD MiniFlex II instrument by applying CuKα radiation ($\lambda = 0.15418$ nm) and 40 kV accelerating voltage at 30 mA. The interlayer distance (the interlayer space and the thickness of one layer) was calculated by the Bragg's law. The primary crystallite size was calculated by the Scherrer equation.

The thermal behavior of the composites was studied on a Setaram Labsys derivatograph, employed under constant air flow conditions with 1 °C/min heating rate. The samples (30-35 mg) were placed into high-purity α-Al_2O_3 crucibles. For evolved gas analysis (EGA) a Pfeiffer QMS 200 mass spectrometer was used under oxygen flow (40 mL/min) with a 5 °C/min heating rate using *ca.* 100 mg of the samples.

To take the FT-IR spectra, a Bio-Rad Digilab Division FTS-65A/896 (mid-range spectra) instrument was used with 4 cm^{-1} resolution. The 4000−600 cm^{-1} wavenumber range were recorded with 256 scans for each spectrum, in ATR mode by utilizing a Harrick's single reflection diamond ATR accessory.

Raman spectra were also collected for the study of inorganic structural elements by a Raman Senterra II (Bruker) microscope at an excitation wavelength of 765 nm. 12.5 mW laser power was applied and 20 spectra with an exposition time of 20 s were averaged.

NIR and UV−Vis spectra were recorded on a SHIMADZU UV-3600i Plus UV−Vis−NIR spectrophotometer equipped with photomultiplier tube, InGaAs, and PbS detectors in the 50,000−6000 cm^{-1} wavenumber range with 4 cm^{-1} resolution recorded in reflection mode.

The XPS measurements were carried out with a SPECS instrument equipped with a PHOIBOS 150 MCD 9 hemispherical analyzer, under a main-chamber pressure in the high vacuum range ($10^{-9}-10^{-10}$ mbar). The analyzer was in fixed analyzer transmission mode with 40 eV pass energy for the survey scan and 20 eV pass energy for the high-resolution scans. The powdered sample was pressed into an indium foil and loaded into the chamber on a gold-coated sample holder. The Al Kα X-ray source was used at 14 kV and at 150 W power. Charge referencing was done to the adventitious carbon (284.8 eV) on the surface of the sample. XP spectra were evaluated by the CasaXPS commercial software package.

High resolution images from the morphology of the samples were taken by a Philips CM20 instrument running at an acceleration voltage of 200 kV, and a C_s-corrected scanning/transmission electron microscope of Themis instrument was used. The EDS mapping was monitored by Super-X detectors of the Themis instrument at 200 kV. The SAED patterns were evaluated using ProcessDiffraction software.[177]

Porosity and surface area studies were performed on a NOVA3000 instrument (Quantachrome, USA) gas adsorption system using nitrogen gas as the adsorbate. Porosity data were calculated by the Barrett−Joyner−Halenda method in the 0.05−0.35 relative pressure range. Before adsorption measurements, all the samples were outgassed under vacuum for 16 h at 25 °C. The specific surface areas were measured by the BET method by adsorption of N_2 at -196 °C. To remove any adsorbents from the surface of the samples, the samples were flushed with N_2 at 100 °C for 5 hours.

The ICP-MS measurements were performed on an Agilent 7700× instrument. During the sample preparation, a few milligrams of the samples measured by analytical accuracy were dissolved in 1.0 mL of concentrated nitric acid, and then they were diluted with distilled water to 50 mL and then filtered prior to the measurements. For the quantitative analyses, multielement standard was used (SigmaAldrich).

The basic sites were also characterized by using CO_2-temperature programmed desorption (TPD) technique, carried out on a Hewlett-Packard 5890 GC system equipped with a TCD detector. *Prior to* the measurements, a quartz tube was loaded with a portion of the sample (100 mg) followed by an initial purge in a He stream (50 mL/min) at room temperature for 10 min to remove impurities. The temperature was then raised to 650 K using the ramp rate

of 10 K/min and then held for 1 hour to remove water and other impurities. The temperature was then lowered to 373 K. Finally, the gas was changed to CO_2 in He (30 mL/min CO_2, 50 mL/min He) and circulated over the sample for 1 h. The gas was then removed from the sample by systematically increasing the temperature.

The surface acidity of the catalysts was characterized by NH_3-TPD. The samples were pre-treated as above to remove impurities and water. Ammonia was then adsorbed for 30 minutes. Finally, the sample was heated from room temperature to 823 K at a rate of 10 K/min and the desorbed gases were analyzed with a TC detector.

During the synthesis of phenothiazines, gas chromatographic measurements were carried out with a Thermo Scientific Trace 1310 Gas Chromatograph coupled with a Thermo Scientific ISQ QD Single Quadrupole Mass Spectrometer using a Thermo Scientific TG-SQC column (15m×0.25mm ID×0.25μm film). The operational parameters were as follows: column oven temperature: from 50 to 300 °C at 15 °C min^{-1}; injection temperature: 240 °C; ion source temperature: 200 °C; electrospray ionization: 70 eV; carrier gas: He at 1.5 mL min^{-1}; injection volume: 2 μL; split ratio: 1 to 33.3; and mass range: 25−500 m/z. The starting materials, the products, and the undesirable byproducts were identified using reference samples.

In the further catalytic studies, NMR spectroscopic measurements were carried out by a Bruker DRX500 instrument 500 MHz NMR spectrometer. Samples were dissolved in 0.7 mL of DMSO-d_6 or chloroform-d, and ^{1}H and ^{13}C spectra were taken at room temperature. Spectra were evaluated by MestReNova-14.1.0-24037 with fixing internally to the remaining resonance of the DMSO-d_6 (^{1}H: 2.50 ppm, ^{13}C: 39.52 ppm) or chloroform-d (^{1}H: 7.26 ppm, ^{13}C: 77.16 ppm).

Catalytic reactions

In an optimal procedure for the synthesis of phenothiazine 2 mL mixture of DMSO and distilled water in ration of 1:2, the corresponding 2-iodoaniline or its derivatives (0.5 mmol, 1.0 equiv.), 2-bromobenzenethiol (0.55 mmol, 1.1 equiv.), K_2CO_3 as the base (2.5 equiv.), and copper-containing bismutite as the catalyst (19 mg, corresponding to 5 mol % metal ion loading) were combined in a nitrogen-flushed Schlenk-tube equipped with a magnetic stirrer bar and was stirred continuously at 90 °C for 15h. Then, the mixture was cooled to room temperature, and the resultant liquid was extracted with 3×15 mL brine and 10 mL ethyl acetate. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure.

In order to find the mildest reaction conditions, the solvent, the temperature, the reaction time, the amount of the added base, and the catalyst loading were altered. In the reusability study, the solid catalyst was removed after the reaction by filtration for five identical rounds. The conversion and the selectivity values were determined after each reaction by using gas chromatography coupled with mass spectrometry (GC−MS) and by NMR spectroscopy. In the scope, 2-iodonaline derivatives with different electron donating and -withdrawing functional group were screened under the optimized reaction conditions.

In an optimal procedure for the synthesis of 2-phenylbenzimidazole 2 mL mixtures of DMSO and distilled water in ration of 1:9, the corresponding benzylamine or its derivative (0.5 mmol, 1 equiv.) and 2-aminoaniline (0.6 mmol, 1.2 equiv.) were combined in round-bottomed flasks equipped with a magnetic stirrer bar and a reflux condenser. The reaction mixtures were stirred for 8h at 90 °C with 10 mol% of $MnBi_2O_2CO_3$ and at 110 °C with 2.5 mol% of $CoBi_2O_2CO_3$. Then, as the mixtures were cooled to room temperature, the resultant liquids were each extracted with 3×15 mL brine (saturated sodium-chloride solution) and 10 mL ethyl acetate. The organic layers were dried over Na_2SO_4 and concentrated under reduced pressure.

To find the mildest reaction conditions for the maximum achievable product yield, the solvent, the temperature, the reaction time and the catalyst loading were altered for both catalysts. Afterwards, the reusability of the catalysts were investigated in a five-rounded

consecutive reaction series. Between the identical reactions, the catalysts were filtered from the reaction mixtures. The extensibility of heterocyclization was investigated from both reagents under optimized reaction conditions: by systematic pairing of benzylamine derivatives and 2-aminoaniline, 2-aminophenol or 2-aminothiophenol, different N-, O- and S-containing heterocycles were prepared. The conversion (C) and the selectivity (S) values were determined after each reaction by using NMR spectroscopy.

In an optimal procedure for oxidative azo-coupling of anilines, aniline of 0.5 mL as reagent and solvent and the transition metal-containing bismutite of 10 mol% metal ion loading were combined in a round-bottomed flask equipped with a magnetic stirrer bar using a reflux condenser. The reaction mixture was stirred at 150 °C for 72h, then, the mixture was cooled to room temperature, and the resultant liquid was extracted with 2×15 mL distilled water, 1×15 mL brine and 10 mL portion of ethyl acetate. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure.

To find the highest azo-product yield, different solvents and solvent-free condition were investigated. During the scope, the corresponding aniline derivative (0.25 mmol, 1.0 equivalent) and the transition metal-containing bismutite as catalyst were combined in 0.5 mL aniline. The catalytic indicators were determined after each reaction by NMR spectroscopy.

In the optimal procedure for quinoline synthesis, 1 equiv. (0.5 mmol) aniline and 2 mL propane-1,3-diol were mixed in a round-bottom flask equipped with a magnetic stirrer bar and a reflux condenser with the catalyst powders of 10 mol% metal ion loading. The reaction mixtures were stirred for 72 h at 150 °C immersed in a silicon oil bath. After the reaction time was over, the mixture was cooled down to room temperature, and was extracted with 2×15 mL distilled water, 1×15 mL brine and 10 mL ethyl acetate. Then, the organic layer was dried over Na_2SO_4 and concentrated under reduced pressure.

During the scope, the corresponding aniline derivatives (0.25 mmol, 1.0 equivalent) and the transition metal-containing bismutite as catalyst were combined in propane-1,3-diol of 0.5 mL. The catalytic indicators were determined after each reaction by NMR spectroscopy.

For producing quinoxaline, the round-bottom flask was filled with 1 equiv. (0.5 mmol) 2-aminoaniline, 2 mL ethylene glycol and the corresponding bismutite catalyst of 10 mol% metal ion loading. The reaction mixtures were stirred for 24h hours with a magnetic stir bar in an oil bath of 110 °C, then the extracted samples (2×15 mL distilled water + 1×15 mL brine and 10 mL ethyl acetate) were concentrated under reduced pressure and analyzed by NMR spectroscopy.

In the versatility study, the corresponding 2-aminoaniline derivative (0.25 mmol, 1.0 equiv.) and the transition metal-containing bismutites as catalysts were combined in 0.5 mL ethylene glycol. The catalytic indicators were determined after each reaction by NMR spectroscopy.

The catalytic indicators were determined after each reaction by gas chromatography (GC-MS) or by NMR spectroscopy based on the following equations:

(1) $$C_{\text{starting material}} = \frac{n_{(0) \text{ starting material}}}{n_{(0) \text{starting material}} - n_{(t) \text{ starting material}}} \times 100$$

(2) $$S_{\text{product}} = \frac{n_{(t) \text{ product}}}{n_{(t) \text{ product}} + n_{(t) \text{ by-prodcut(s)}}} \times 100$$

(3) $$Y_{\text{product}} = S_{\text{product}} \times C_{\text{product}}$$

where C is the conversion of the starting materials, S and Y are the selectivity and yield of the desired products, n_0 is the corresponding initial volume of the reactants/products while n_t is the corresponding volume of the reactants or products at a given time.

3. Novel scientific results

T1. Interlamellar gallery and surface of Sillèn-type, layered bismuth-oxid subcarbonates (bismutites) were successfully modified with transition metal ion containing complex anions/non-stochiometric oxides.

A general method for the modification of bismutites with transition metal ions has been developed, leading to the direct synthesis of modified bismutite structures using nitrate salts of the starting metals. In the modified co-precipitation method, the type of incorporation was determined by the quality of the (doping) metal ion. When treated with copper(II) ions, the interlayer space of the bismutite framework was modified by incorporation of azurite-type (hydroxycarbonato) complex. When manganese(II), cobalt(II), and nickel(II) salts were used, the bismuth oxide layers were modified. The transition metal-containing specimens were rather incorporated into the superficial layers of the bismutites, thus their distribution within the structure was highly heterogeneous. In contrast, the copper(II)-hydroxocarbonato complexes showed a homogeneous distribution. The latter can therefore be described as a new structural analogue of beyerite ($CaBi_2O_2CO_3$).

T2. The chemical environment, coordination mode and oxidation state of the doping metal ions were described by systematically combining different structural characterization and analytical methods. Based on the available data, the most probable structure and composition of bismutites were also given in each case.

XRD measurements proved that phase pure Sillèn-type bismutite structures were precipitated in every modified synthesis. Based on the diffraction patterns, formation of structural analogues of bismuth oxide subcarbonate were ascertained. The incorporation of doping metal ions and their distribution in the samples were detected by TEM-EDX. The oxidation states of metal ions and the superficial compositions were determined by XPS measurements. The transition metal ion contents of the bulk phase were determined by ICP-MS measurements. Structural building, inorganic components were identified by infrared and Raman spectroscopic measurements and the thermal behavior of the catalyst candidates was investigated by thermogravimetry. The surface and bulk spheres of $CuBi_2O_2CO_3$ proved to have identical composition, while the transition metal content showed enrichment in Mn-, Co- and $NiBi_2O_2CO_3$ on the surfaces, and in the manganese and cobalt systems this surface enrichment is also accompanied by the formation of interfacial sites.

T3. By modifying the interlamellar gallery of bismutite with copper(II) ions, an efficient and robust heterogeneous catalyst was prepared that can actively and selectively promote the formation of new C-S and C-N bonds even *via* a concerted mechanism. As a result, the catalyst has opened up a rapid concerted heterocyclization pathway for producing phenothiazines.

Due to the cooperative behavior of the bimetallic system, phenothiazine is prepared with quantitative conversion and outstanding selectivity under significantly milder reaction conditions (ligand-free reaction, shorter reaction time, lower temperature, less base addition). In addition, extensive substrate tolerance and a high degree of reusability were observed under optimal reaction conditions.

T4. We have demonstrated, that modification of the surface of bismutite with manganese(II) and cobalt(II) ions lead to the formation of reusable and robust heterogeneous systems capable of efficiently catalyzing the oxidative couplings of benzylamines and 2-aminoaniline, giving rise to 2-phenylbenzimidazole and its derivatives.

The interaction between the bismutite support and the incorporated transition metal ions has provided an effective cooperative catalytic surface that proved to be much more efficient in the oxidative coupling reaction tested than the individual components on their own or when the transition metal oxides were fixed to the support with only secondary binding forces. No oxidant was required to achieve product yields above 90 %. Moreover, stable performances were observed for both catalysts in the versatility and reusability studies.

T5. It was proven, that bimetallic systems formed by modifying the surface of bismutite ($MnBi_2O_2CO_3$ $CoBi_2O_2CO_3$ és $NiBi_2O_2CO_3$) can be used as efficient, multifunctional catalysts for tandem, oxidative coupling reactions with the formation of new C=N and C–C bonds that generate new heterocycles.

Manganese(II), cobalt(II) and nickel(II)-containing bismutites were successfully used in tandem oxidative couplings to produce azobenzene, quinoxaline and quinoline under solvent-free reaction conditions. The diol served as both reactant and solvent, and successful completion of the reaction did not require the use of an oxidant other than ambient air. In addition, the catalysts showed high selectivity for the formation of quinoline and quinoxaline products. The heterogeneous nature of quinoxaline synthesis in the presence of $CoBi_2O_2CO_3$ and the reusability of the catalyst were also successfully demonstrated and the mechanism of the oxidative dehydrogenation reaction of o-phenylenediamine and ethylene glycol catalyzed by $CoBi_2O_2CO_3$ was proposed by some control experiments.

4. Practical use of the results

The results presented here are fundamental in nature. Nevertheless, regardless of the type of modification (intercalation or surface modification), bismutites modified with transition metals offer numerous applications in a highly active and selective manner in various heterocyclization reactions. It is expected that these composites can be used in many industrial processes aiming at a more environmentally friendly and economic production of various heterocyclic compounds.

5. Publications

Papers related to the Theses published in refereed journals

[1] **M. Kocsis**; S. B. Ötvös; G. F. Samu; Z. Fogarassy; B. Pécz; Á. Kukovecz; Z. Kónya; P. Sipos; I. Pálinkó; G. Varga:
Copper-Loaded Layered Bismuth Subcarbonate - Efficient Multifunctional Heterogeneous Catalyst for Concerted C-S/C-N Heterocyclization, *ACS Appl. Mater. Interfaces* **13**, 42650-42661 (2021).
   Impact factor: 10.383   Independent citation: 2

[2] **M. Kocsis**; M. Szabados; S. B. Ötvös; G. F. Samu; Z. Fogarassy; B. Pécz; Á. Kukovecz; Z. Kónya; P. Sipos; I. Pálinkó; G. Varga:
Selective production of imines and benzimidazoles by cooperative bismuth(III)/transition metal ion catalysis, *Journal of Catalysis* **414**, 163-178 (2022)
   Impact factor: 7.251   Independent citation: 1

3] **Kocsis, M.**; Baán, K.; Ötvös, S.B.; Kukovecz, Á.; Kónya, Z.; Sipos, P.; Pálinkó, I.; Varga, G.:
Sustainable synthesis of azobenzenes, quinolines and quinoxalines via oxidative dehydrogenative couplings catalysed by reusable transition metal oxide–Bi(III) cooperative catalysts
Catalysis Science and Technology, (2023)
   Impact factor: 5.140_{2022} Independent citation: —

Other papers published in refereed journals

[1] S. B. Ötvös; R. I. Mészáros; G. Varga; **M. Kocsis**; Z. Kónya; Á. Kukovecz; P. Pusztai; P. Sipos; I. Pálinkó; F. Fülöp:
A Mineralogically-Inspired Silver-Bismuth Hybrid Material: An Efficient Heterogeneous Catalyst for the Direct Synthesis of Nitriles from Terminal Alkynes. *Green Chem.* **20**, 1007–1019 (2018).
   Impact factor: 9.405   Independent citation: 9

[2] G. Varga; **M. Kocsis** Á. Kukovecz; Z. Kónya; I. Djerdj.; P. Sipos; I. Pálinkó:
Cu^{I}BiOI Is an Efficient Novel Catalyst in Ullmann-Type C-N Couplings with Wide Scope—A Rare Non-Photocatalyic Application. *Mol. Catal*. **493**, 111072 (2020).
   Impact factor: 5.062   Independent citation: 3

[3] R. I. Mészáros; S. B. Ötvös; G. Varga; É. Böszörményi; **M. Kocsis**; K. Karádi; Kónya Z. Kónya; Á. Kukovecz; I. Pálinkó; F. Fülöp:
A Mineralogically-Inspired Silver–Bismuth Hybrid Material: Structure, Stability and Application for Catalytic Benzyl Alcohol Dehydrogenations under Continuous Flow Conditions. *Mol. Catal.* **498.** (2020).
   Impact factor: 5.062   Independent citation: —

Papers non-related to the Theses published as full papers in conference proceedings

[1] Z. Timár, **M. Kocsis**, G. Varga, P. Sipos, I. Pálinkó:
Intercalation of CaAl-layered double hydroxide with benzoate or acetate ion *Modern Trends in Coordination, Bioinorganic, and Applied Inorganic Chemistry*, XXVI. International Conference on Coordination and Bioinorganic Chemistry, ISBN: 978-80-89597- 65-9, Smolenice, Szlovákia, 2017, 131–137.

full journal papers

related to the topic of the Theses: 3   total: 7

cumulative impact factor
related to the topic of the Theses: 22.774   total: 42.303

independent citations
related to the topic of the Theses: 3   total: 15