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Catalysis of the Kemp Elimination by Natural Coals

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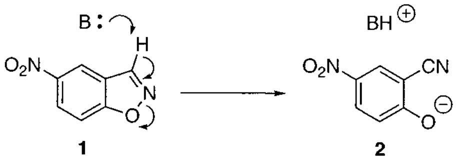
ABSTRACT



Commercially available coals were found to be efficient heterogeneous catalysts of the Kemp elimination reaction in aqueous solutions. A pH–rate profile study suggests that catalysis originates from specific catalytic groups and not simply from the large graphitic surface area. The low-quality lignite coals, which exhibit similar catalytic efficiency per weight to that of molecularly imprinted polymers, are better catalysts for this reaction in comparison with the bituminous coals.

The proton-transfer reaction, which is a key transformation in chemistry and biology,[1] represents an essential step in almost any biocatalyzed process. This step can become rate determining, especially when the proton is transferred to or from carbon. A well-studied model for proton transfer from a carbon atom is the Kemp elimination reaction.[2] This exothermic, concerted E_2 elimination of benzisoxazoles to salicylonitriles (e.g., **1** to **2**) is highly sensitive to the base strength. In the case of carboxylate bases, the reaction rate is strongly influenced by solvent polarity, primarily through desolvation−activation of the catalytic base.[3] This reaction has recently become a prime target for enzyme mimics because it is a simple, one-step transformation, which is highly sensitive to the medium. Efficient catalysis of this reaction by nonenzymatic systems could shed light on the importance of several catalytic factors that operate in concert within the preorganized environment of an enzyme active site.[4] The recently reported catalytic systems for this reaction include host molecules with rigid, preorganized clefts,[5] serum albumins,[6] polymeric amines,[7] imprinted polymers,[8] surfactant aggregates,[9] and specifically designed catalytic antibodies.[10]

Naturally occurring coals are versatile heterogeneous catalysts of several gas-phase reactions as well as of a few reactions carried out in solution.[11] The reported examples include various substitution, isomerization, and redox reactions. For example, the coal-catalyzed ligand substitution reactions with cobalt complexes[12] and solvolysis of phosphate

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esters[13] were attributed to the acidic and basic functional groups on the carbon surface. Conversely, the racemization of 1,1′-binaphthyl and its derivatives was found to be catalyzed by the graphitic surface and not by specific functional groups.[14]

In general, the coal catalytic activities stem from three main features: (a) a graphitic structure that is characterized by a highly porous hydrophobic surface area with a strong binding affinity toward aromatic molecules; (b) abundance of various functional groups, mostly containing oxygen, nitrogen, and sulfur, e.g., carboxylic acids, phenols, amines, various sulfur functional groups, and heteroaromatic rings; and (c) electronic conductivity. We reasoned that these features would render naturally occurring coals effective catalysts of the Kemp elimination reaction.

Here we show that commercially available coals indeed catalyze this reaction when mixed with **1** in a buffered solution and that catalysis originates from specific catalytic groups and not simply from the large graphitic surface area.

Three German lignites from three major mining areas in Germany (coals 1613, 1650, and 1551) and three bituminous coals (RSA, AUS, COL) were examined as potential catalysts of the Kemp elimination reaction.[15] All reactions were carried out by shaking a mixture of the coal powder and substrate **1** (0.5−2.0 mM) in phosphate buffer (50 mM, pH 7.4, 0.5 mL) containing acetonitrile (2% v/v) at 4 °C, and the progress of the reaction was monitored by HPLC. All coal samples were shaken in a buffer solution at room temperature for 2 days to reach equilibrium with solvent before using them as catalysts.

To compare the catalytic effect of these coal samples, we carried out a series of reactions using constant amounts of coal (10 mg) and varying concentrations of substrate **1**. Assuming that under these conditions there was a large excess of catalytic sites with respect to the substrate, we expected that the reaction would follow pseudo-first-order kinetics. Accordingly, we obtained the observed rate constants (k_{obs}) from the linear regression of the experimental rates as a function of substrate concentration (Table 1).

Table 1. Observed Catalytic Parameters for the Different Coal Samples[a]

coal	k_{obs} (min^{-1})	$^{site}k_{cat}$ (min^{-1})
1650	0.0045	
1551	0.0041	0.82
1613	0.0033	0.10
AUS	0.0015	
COL	0.0014	0.0016
RSA	0.0009	0.0039

[a] The reactions were carried out using a shaker, and the progress of the reaction was monitored by HPLC equipped with a reverse phase, Supelcosil C18 column. Calculation of k_{obs} was corrected for the buffer-catalyzed reaction. Calculation of $^{site}k_{cat}$ was carried out according to Klotz.[16] The correlation coefficients (R^2) for the pseudo-first-order rate plots were between 0.96 and 0.99.

It has been shown that under conditions of excess catalyst a linear relationship exists between the reciprocal of k_{obs} and the reciprocal of catalyst concentration. From this relationship one can measure the Michaelis Menten parameters $^{site}k_{cat}$ and K_M.[16] Accordingly, we carried out the reaction with variable amounts of catalyst and used the linear correlation of a double reciprocal plot (of k_{obs} vs the catalyst weight) in order to estimate the apparent catalytic constant $^{site}k_{cat}$ (Table 1). The apparent K_M values in this heterogeneous system could not be determined in our case because the relationship between the catalyst weight and the active site concentration could not be estimated.

As expected for a heterogeneous catalyst, the catalytic efficiency was found to increase with increased coal surface area (Figure 1).[17] Probably a less expected finding is the apparently linear correlation between the kinetic data and the carbon content of the catalyst (Figure 2). We found that coals with decreased abundance of carbon atoms exhibit

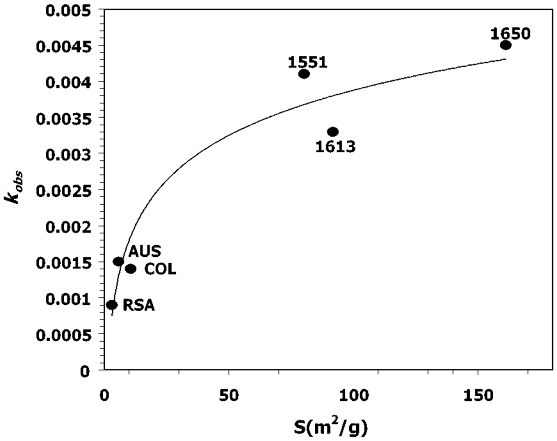

Figure 1. Dependence of catalytic efficiency on the surface area of different coals.

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(15) Lignites: coal 1613, source Lower Lusatia, East Germany, open-cast mine, Nochten; coal 1650, source Central Germany (Halle/Leipzig), open-cast mine, Profen; coal 1551, source Rhine/Ruhr (Rhenish brown coal), open-cast mine, Hambach. Bituminous coals: RSA, South Africa, Goodhope mine, Angloamerican's coal F-6486; AUS, Stewarton-lilyvale mine, BHP−Utha coal Ltd.; COL, El Cerrejon mine, Carbocol #4903/0985.

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(17) Coal: surface area (m^2/g), elemental analysis: 1613, 91.8, 62.3 (% C), 0.64 (% N), 24.8 (% O), 4.7 (% H); 1551, 80.2, 64.2 (% C), 0.78 (% N), 25.2 (% O), 4.5 (% H); 1650, 161.3, 59.9 (% C), 0.52 (% N), 18.5 (% O), 4.8 (% H); AUS, 5.8, 75.7 (% C), 4.3 (% H), 0.6 (%S); COL, 10.7, 67.5 (% C), 4. 31 (% H), 0.95 (% S); RSA, 3.15, 76.4 (% C), 4.0 (% H), 1.1 (% S).

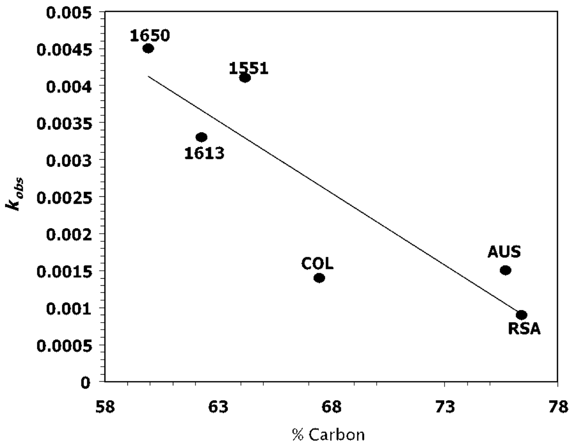


Figure 2. Dependence of catalytic efficiency on the carbon content of different coals.

increased catalytic efficiency. Assuming that the basic catalytic groups which are relevant to this reaction include carboxylate anions, phenols, amines, sulfur functionalities, and heteroaromatic rings, one would expect that decreased carbon/hetroatom proportions reflect an increased abundance of such catalytic sites. This may explain why the lignite coals, which are characterized by a larger surface area and a higher abundance of heteroatoms in comparison with the bituminous coals, are better catalysts for this reaction.

The pH−rate profile study of the catalytic Kemp elimination reaction was carried out at a pH range between 4.5 and 8.5 using the lignite 1551 and the bituminous coal COL (Figure 3). Although the catalytic superiority of the lignite over the bituminous coal is preserved across the entire pH range, at higher pH values this superiority becomes more significant. This observation, together with the sigmoidal shape of the pH−rate profile for both catalysts, suggests that catalysis stems from specific catalytic groups and not simply from the large graphitic surface area. Unlike common titration curves of homogeneous acids and bases, which are characterized by steep sigmoid turning points, here we observe a very mild turning point at a pH range between 5.5 and 8.5. This observation probably reflects cumulative and average effects of various catalytic groups, each possessing a different pK_a value. A very similar curve that envelops several pK_a values (with visible turning points at pH 6.2 and 8.3) was observed when alkylated polyethylene imines were used to catalyze the Kemp elimination reaction.[7] By contrast, catalytic antibodies with carboxylate groups in their active site[10a] exhibit pK_a values of 5.5−6.0, and BSA, whose basic functional group is an amine, exhibits a distinct pK_a value of 8.95.[6b]

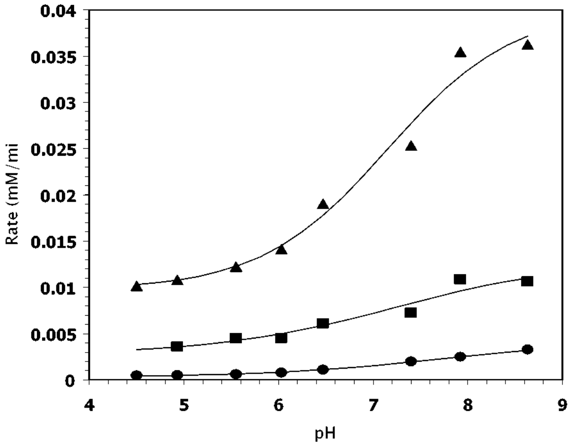
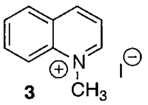


Figure 3. pH−rate profile of the reactions catalyzed by 1551 (▲), COL (■), and the buffer (●): coals (10 mg) were mixed with the appropriate buffer solution (0.49 mL) for 2 days at room temperature. An acetonitrile solution (10 uL) of substrate **1** (final concentration: 2.56 mM) was added and the mixture was shaken at 4 °C. The progress of the reaction was followed by HPLC.

We reasoned that adsorption of a hydrophobic salt onto the coal surface could enhance its catalytic efficiency, in analogy to the role played by cofactors in enzymatic catalysis. Thus, coals 1551 and COL (10 mg) were mixed with the appropriate buffer solution (0.49 mL) containing varying amounts of methylquinolinium iodide, **3**, and the mixture was shaken at room temperature for 2 days. The reaction rates with these pretreated catalysts were measured as described above. Indeed, the coal that was impregnated with methylquinolinium iodide was found to be a better catalyst than the coal itself (Figure 4). This effect can be attributed to the increase of a general base concentration on the surface of the catalyst and the stabilization of the negatively charged transition state by the hydrophobic methylquinolinium



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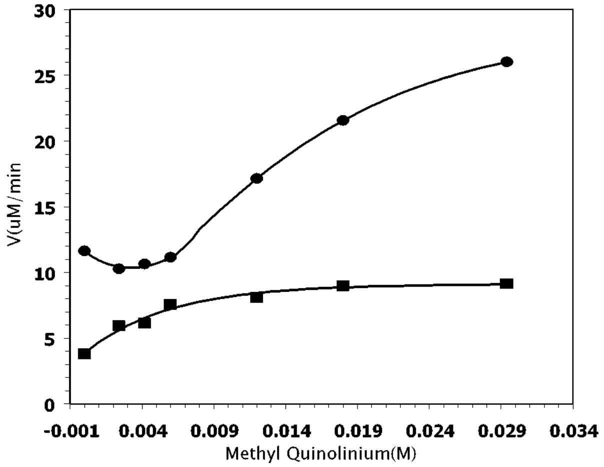

Figure 4. Dependence of catalytic efficiency of coals 1551 (●) and COL (■) on added methylquinolinium iodide.

cation.[7] As shown in Figure 4, the additional catalytic effect reaches saturation at high concentrations of **3** and is more pronounced with coal 1551 than with COL. While coal 1551 reaches saturation only when the concentration of **3** exceeds 0.05 M, COL is already saturated at 0.007 M. This difference in the adsorbance capacity correlates well with the difference in the surface area of these two coals (80 and 11 m^2/g, respectively). The cocatalytic effect of **3** with coal 1551 is observed only beyond the concentration of 0.007 M, probably reflecting partial inhibition of the coal catalytic groups.

It is interesting to compare the efficiency of our coal catalysts with molecularly imprinted polymers (MIP) because both are heterogeneous catalysts. Although the work of Liu and Mosbach[8] refers to a the nonsubstituted substrate, **4**, which is less reactive than **1**, it appears that both catalysts are comparable in terms of their catalytic efficiency per weight (Figure 5).

In conclusion, we have shown here that commercially available coals are efficient heterogeneous catalysts of the Kemp elimination reaction in aqueous mixtures. The pH−rate profile suggests that catalysis originates from specific catalytic groups, with pK_a values ranging from 5.5 to 8.5, and not simply from the large graphitic surface area. Interestingly, the coals of lower commercial value are the more efficient catalysts. Thus, the lignite coals, which are characterized by both larger surface area and higher abundance of heteroatoms in comparison with the bituminous coals, are better catalysts for this reaction. The efficiency of these catalysts per weight is comparable with that of a heterogeneous MIP.

All previously reported catalysts of the Kemp elimination reaction combine a general base with a hydrophobic environment. Further rate enhancement can be achieved by stabilization of the delocalized, negatively charged transition state. This work suggests that the various coals possess generic hydrophobic pockets with basic functional groups, as is the case with serum albumins,[6] alkylated polyethylene imine,[7] imprinted polymers,[8] and surfactant aggregates.[9] These nonspecific catalysts can achieve remarkable rate enhancements of up to 10^4. Yet, to reach higher rate accelerations, it is necessary to use specific catalysts that mimic the enzymatic precision. Specific positioning of the general base at the appropriate distance and relative orientation with respect to the substrate is required for more effective catalysis. Indeed, high catalytic efficiency (rate acceleration of 3.4×10^8) has been achieved with the appropriately designed catalytic antibody 34E4, which represents an encouraging step toward ideal enzyme mimics.[10a]

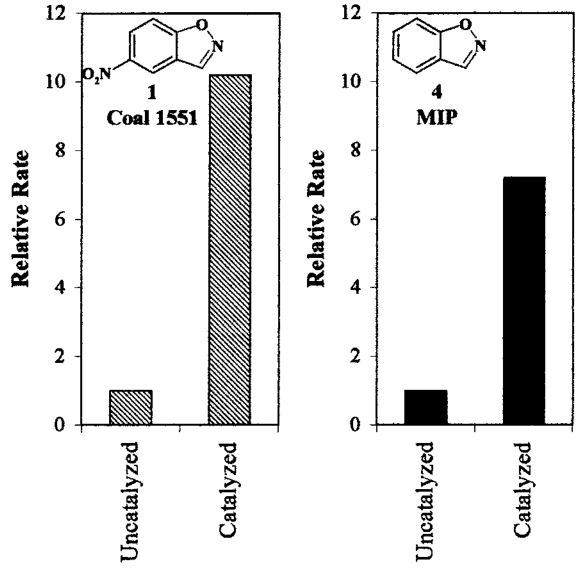

Figure 5. Comparison of the catalytic efficiency of coal 1551 (left) and MIP2 (data taken from ref 8). The reaction was carried out under the conditions used for MIP2 and substrate **4**: coal 1551 (10 mg) in ethanol−water (1:3, v/v, 8 mL) with substrate **1** (3.075 mM).

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