Technical Notes

Modeling the Chemical Conversion of Organic Compounds in Sodium Borohydride Reduction Reactions

Ruth M. Tinnacher and Bruce D. Honeyman*

Environmental Science and Engineering Division, Colorado School of Mines, Golden, Colorado 80401 U.S.A.

Abstract:

In this paper we propose a new modeling concept for the prediction of the chemical conversion of reducible species as a function of reductant concentration in sodium borohydride reduction reactions. This concept is applicable to organic compounds of unknown reactive group concentrations, such as mixtures of organic or colloidal materials. In addition to the prediction of chemical conversion, the calculation of model fitting parameters also provides values for an "apparent, conditional equilibrium constant" and an effective reactive group concentration. These models are derived on the basis of simple chemical principles and a chemical equilibrium assumption. The model-fitting parameters can be easily determined with standard mathematical software. Nevertheless, these models capture the overall behavior of the chemical reduction reaction sufficiently well for accurate predictive needs. This modeling concept can be applied in two possible ways. First, model predictions allow the transfer of experimental chemical conversion data to new, similar target compounds, assuming that the necessary requirements are fulfilled. This leads to shorter time-frames required for process development. Second, these models can be applied as heuristic tools in order to test the feasibility of a proposed overall reaction mechanism and/or effective reactive group concentration.

Introduction

Sodium borohydride (NaBH$_4$) is one of the primary reductants used for organic synthesis on the industrial scale[1] due to its safety, ease of handling, and high chemical yields. Most commonly, sodium borohydride is used to selectively reduce aldehydes, ketones, acid chlorides, and imines in presence of esters, epoxides, amides, nitriles, or nitro groups.[2] Under specifically optimized conditions, NaBH$_4$ is also able to transform other functional groups, such as esters and amides.[2] Examples of applications of sodium borohydride in the pharmaceutical and agrochemical industries include the production of female hormone estrogens, antihistamines, antiviral and antiasthmatic compounds, antidepressants, and plant growth regulators, to name a few.[2]

A considerable amount of general information is available on sodium borohydride reaction mechanisms and products.[1,3–6] However, for the development of a new application, detailed experimental investigations are usually necessary in order to determine the equilibrium constant for the specific reduction reaction (K). This constant can then be used to optimize chemical engineering processes, e.g., in terms of reductant concentrations, in order to achieve the desired levels of chemical conversion of reducible species in the reaction. A problem, however, arises for the determination of equilibrium constants and the prediction of chemical conversion levels, if the concentration of reactive groups involved in the reduction reaction (i.e., the "effective concentration") is unknown. For instance, this could be the case for heterogeneous mixtures of organic molecules or when it has to be questioned if all chemical reactive groups are available over the course of the reaction. The latter could be the result of potential steric limitations, for example, in reactions with colloidal material, polymers or surfactants.

Therefore, in this paper we propose a new modeling concept that is applicable to organic compounds with unknown, effective reactive group concentrations, one that allows for the prediction of the chemical conversion of reducible species in reduction reactions with sodium borohydride as a function of reductant concentration. This modeling tool is based on a chemical equilibrium assumption and does not include any kinetic parameters.

In addition, the fitting of model parameters in this mathematical framework will provide a value for an "apparent, conditional equilibrium constant" for a proposed, overall reduction reaction. In general, this constant will have some practical and predictive value for engineers; however, one should be aware of its limitations, especially from a chemical perspective. First, this value represents an "apparent" constant, as it is based on a postulated, overall reaction. Therefore, the detailed, underlying mechanisms of the reduction reaction do not have to be known in order to apply this modeling concept;

* Author for correspondence. Telephone: +1 303 273 3420. Fax: +1 303 273 3413. E-mail: honeyman@mines.edu.
(1) *The Sodium Borohydride Digest*; Rohm and Haas; http://www.rohmhaas.com/hydride/technical.html#. Accessed 03–14–07.
(2) Yadav, V. G.; Yadav, G. D.; Vyas, J. R. *Chim. Oggi* **2000,** *18,* 39.

(3) Gaylord, N. G. *Reduction with complex metal hydrides*; Interscience Publishers, Inc.: New York, 1956.
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(6) McMurry, J.; Castellion, M. E. *Fundamentals of organic and biological chemistry*; Prentice-Hall, Inc.: Upper Saddle River, NJ, 1999.

this should prove useful in practical applications. Second, this constant is defined as "conditional", which means that K is only strictly valid for the physical-chemical system conditions under which it has been determined (e.g., temperature, ionic strength, etc.). Finally, since the value of this constant is a result of modeling, it is dependent on the specific modeling approach and assumptions used in the process of its determination.

In addition to the prediction of the level of chemical conversion and the derivation of the apparent, conditional equilibrium constant, this chemical modeling concept can also be used as heuristic tool in order to test the feasibility of a proposed overall reaction mechanism and/or an assumed concentration of reactive groups involved in the reduction reaction. This modeling tool could potentially allow process engineers and researchers to shorten the time frame needed for development processes by transferring previously determined chemical conversion data to new, similar target compounds. Model predictions based on this concept could provide a good first-estimate of excess concentrations of reductant required for the optimum chemical conversion in new applications.

However, it is important to note that values of fitting parameters and of calculated equilibrium constants and chemical conversion levels cannot be transferred indiscriminately. For the adaptation of the modeling results to a range of compounds, the following list of conditions needs to be fulfilled: (1) the reactive group concentration of the new target compound needs to be known or can be estimated; (2) the organic ligands need to be of comparable structure; (3) the chemical reaction conditions should be the same or at least very similar; and (4) the overall reaction mechanism needs to be known or accurately assumed.

The literature also provides various, more complex modeling approaches for the determination of chemical equilibria, e.g., based on Monte Carlo simulations[7] or statistical mechanics.[8] While these approaches provide solutions independent of specific system conditions, they also require more complicated modeling frameworks and substantially longer computation times.

Initially, the modeling framework described in this paper was developed for a specific application using a heterogeneous mixture of organic compounds: the reduction of fulvic acid (FA) with sodium borohydride for the radiolabeling of FA with tritium.[9] In the following we will briefly define fulvic acid and the chemical background of the reduction reaction and then present the model derivation based on this example. The general modeling concept, however, is not limited to this application and is transferable to various target compounds of unknown reactive group concentrations as well as reducing agents.

Chemical Background

Humic substances are a fraction of natural organic matter (NOM) and are found ubiquitously in soils, sediments, and waters. Humic substances represent a heterogeneous mixture of polyelectric acids, which cannot be further classified on the basis of a specific chemical structure; instead, they are purely operationally defined on the basis of their isolation and fractionation procedures.[10] In fact, all chemical and physical properties of humic substances, such as molecular size and weight, reactive group concentrations, and formation constants, follow statistical distributions within the mixture. While there is a certain degree of similarity among them, humic substances from various natural sources show differences in (average) chemical structures and reactivities. The complexity of these mixtures, the variability between samples from different sources, and their relatively large molecular size (500 Da for some aquatic humic substances to more than 10^6 Da for soil humic acids[11,12]), which can lead to the formation of micelles[13] and "colloidal-like" behavior,[11] all complicate the determination of effective, reactive group concentrations involved in specific reactions, as well as the transfer of reaction constants from one humic sample to another.

Fulvic acid (FA) is a water-soluble fraction of humic substances that is relevant for both natural and engineering systems due to its ability to associate with metals and organic compounds in solution, and to sorb onto surfaces. Hypothetical (average) model structures for fulvic acid have been developed, which indicate both aromatic and aliphatic structures, extensively substituted with oxygen and containing numerous functionalities, such as carboxylic and phenolic groups.[14]

Sodium borohydride reduction is usually described as a two-step process based on the following reaction:[15]
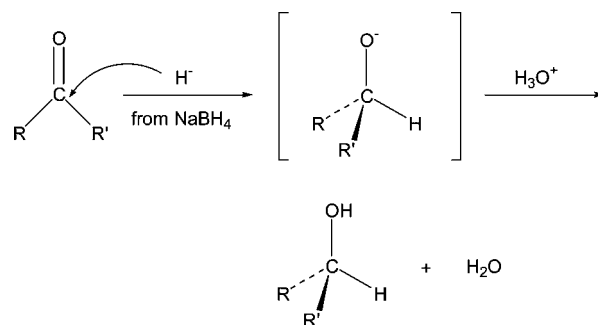
In the first step, sodium borohydride acts as a donor of a hydride ion in a nucleophilic addition reaction; in the second

(7) Carrero-Mantilla, J.; Llano-Restrepo, M. *Fluid Phase Equilib.* **2006**, *242*, 189.

(8) D'Abramo, M.; Aschi, M.; Marinelli, F.; Di Nola, A.; Amadei, A. *Journal of Molecular Structure: THEOCHEM* **2007**, *811*, 197.

(9) Tinnacher, R. M.; Honeyman, B. D. *Environ. Sci. Technol.* **2007**, *41*, 6776.
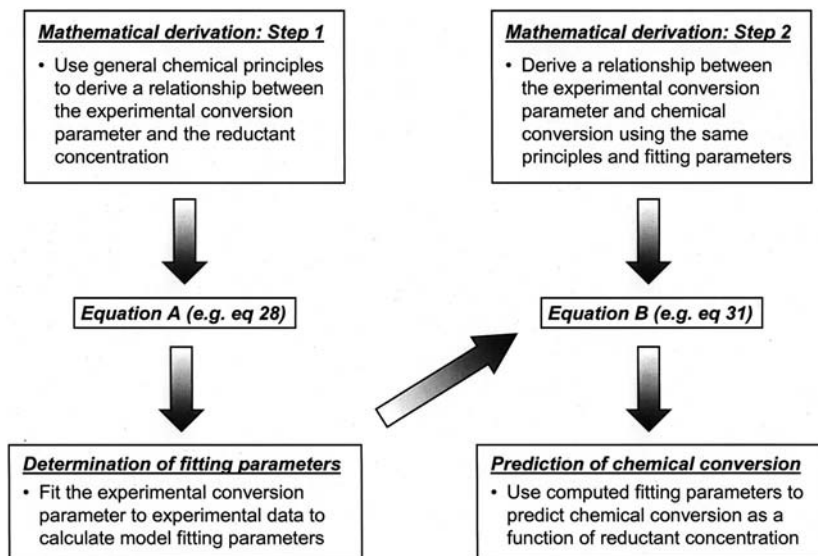
(10) Aiken, G. R.; McKnight, D. M.; Wershaw, R. L.; MacCarthy, P., An introduction to humic substances in soil, sediment, and water. In *Humic substances in soil, sediment, and water*, Aiken, G. R.; McKnight, D. M.; Wershaw, R. L.; MacCarthy, P., Eds. John Wiley & Sons: New York, 1985; pp 1.

(11) Gaffney, J. S.; Marley, N. A.; Clark, S. B., Humic and fulvic acids and organic colloidal materials in the environment. In *Humic and Fulvic Acids: Isolation, Structure, and Environmental Role*, Gaffney, J., S.; Marley, N. A.; Clark, S. B., Eds. American Chemical Society: Washington, D.C., 1996; pp 2.

(12) Wershaw, R. L.; Aiken, G. R., Molecular size and weight measurements of humic substances. In *Humic substances in soil, sediment, and water*, Aiken, G. R.; McKnight, D. M.; Wershaw, R. L.; MacCarthy, P., Eds. John Wiley & Sons: New York, 1985; pp 477.

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(15) McMurry, J. *Organic chemistry*; Brooks/Cole: Pacific Grove, CA, 2000.

Figure 1. Flow-chart describing the main steps of the modeling approach used to predict chemical conversion as a function of reductant concentration.

step, water protonates the tetrahedral alkoxide intermediate, which gives the alcohol product.

During the reduction of fulvic acid (FA) by sodium borohydride, FA carbonyl groups of aliphatic and aromatic ketones as well as quinones are selectively reduced to yield secondary alcohols and hydroquinones/phenols, respectively. The literature suggests, however, that the resulting FA hydroquinones are not stable in aerobic environments over time due to reoxidation with molecular oxygen or intramolecular redox processes.[16,17] Due to this instability, there is a need to clarify the term chemical conversion for this specific application. By definition, maximum chemical conversion is achieved when all FA reactive groups originally available for the reduction with $NaBH_4$ (ketones, as well as quinones) have been completely reduced.

In chemical conversion experiments, the UV–vis light absorbance of the reaction solutions after complete reaction was used to indirectly determine the chemical conversion of the reduction reaction. The UV–vis spectroscopic data were then used to determine the values of fitting parameters for the individual models. UV–vis spectral analysis was applied because the reduction of quinones is known to result in a decrease in light absorbance and visual color of FA. A blank containing FA but no $NaBH_4$ in solution was used to determine the absorbance value for a chemical conversion of zero; a sample containing FA and the maximum concentration of $NaBH_4$ represented solution absorbance at the maximum chemical conversion. For the selected wavelength, it could be assumed that the presence of sodium borohydride in solution did not contribute significantly to the measured absorbance values. Furthermore, the assumption was made that the number of transformed quinone groups is proportional to the total number of reduced FA carbonyl groups. While UV–vis absorbance was useful in this specific example, any type of chemical parameter

indicating chemical conversion can be used for this modeling concept in future applications.

This article is organized in the following manner. First, the mathematical derivations of one mathematical fitting equation and two chemical models are presented. Then, on the basis of the fitting of experimental efficiency data, these model equations are used to predict the chemical conversion as a function of $NaBH_4$ concentration in solution. Furthermore, apparent, conditional equilibrium constants are calculated based on the values of model fitting parameters. Finally, we provide a detailed description of the experimental setup that was used to test the chemical conversion of reducible reactive groups for FA reduction with sodium borohydride.

Model Development

General Modeling Approach. Three models were developed to describe chemical conversion in reduction reactions: one mathematical "curve fit" and two slightly different models based on chemical principles (chemical models 1 and 2). We describe the process used for developing a model on the basis of the prediction of the chemical conversion of reducible reactive groups in the reduction of FA with $NaBH_4$.[9] The general approach, however, is applicable to the evaluation of a wide range of compounds and reducing agents.

The mathematical curve fit model is used as a reference to compare its goodness-of-fit estimate with the fits of the two chemical models and is not intended to represent any specific chemical aspects of the system. In the case of the chemical models, however, the experimental parameter indicating the chemical conversion in the reduction reaction is linked to equations that are based on specific chemical attributes, such as the mass action expression for the labeling reaction, and the mass balance equations for $NaBH_4$ and FA-reactive group concentrations in solution. The essential difference between the two chemistry-based models lies in their description of FA-reactive group concentrations. In chemical model 1, the

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(17) Weber, E. J.; Spidle, D. L.; Thorn, K. A. *Environ. Sci. Technol.* **1996**, *30*, 2755.

Table 1. Summary of results for chemical conversion experiments

			Experimental results			
			total NaBH$_4$			
sample ID	total FA [mg]	total ketones [mol]	[mg]	[mol]	excess NaBH$_4$ conc. (x) [mol NaBH$_4$/mol ket.]	absorbance at 465 nm [ ]
blank	10.154	2.640E–05	0	0	0.000	0.775
1	10.039	2.610E–05	1.316	3.478E–05	1.333	0.650
2	10.136	2.635E–05	2.497	6.600E–05	2.504	0.542
3	10.196	2.651E–05	5.151	1.362E–04	5.136	0.480
4	10.153	2.640E–05	7.914	2.092E–04	7.924	0.445
5	10.143	2.637E–05	10.302	2.723E–04	10.326	0.432
6	10.197	2.651E–05	15.041	3.976E–04	14.996	0.425

			Modeling summary and results		
model	absorbance equation	fitting parameters	chemical conversion equation	K^a	
mathematical	ABS = $a_1 + b_1 \exp(-c_1 x)$	a_1 = 4.262E–01 b_1 = 3.517E–01 c_1 = 3.884E–01	$x_{FA}(x) = 1 - \exp(-c_1 x)$	n/a	
chemical 1	ABS = $\beta_0 - \beta_1 \{(x+1) - [(x+1)^2 - \gamma_1 x]^{1/2}\}$	β_0 = 8.031E–01 β_1 = 1.171E+03 γ_1 = 6.579E–04	$x_{FA}(x) = [2\{\beta_0 - ABS(x)\}]/(\beta_1\gamma_1)$	1.000E+00	
chemical 2	ABS = $\beta_0 - \beta_1\{(1 + \alpha x) - [(1 + \alpha x)^2 - \alpha\gamma_1 x]^{1/2}\}$ with $\alpha = 1/\alpha_0$	β_0 = 7.775E–01 β_1 = 2.234E–01 γ_1 = 3.289E+00 α = 3.094E–01	$x_{FA}(x) = [2\{\beta_0 - ABS(x)\}]/(\beta_1\gamma_1)$	5.622E+00	

^{a} K = apparent, conditional equilibrium constant.
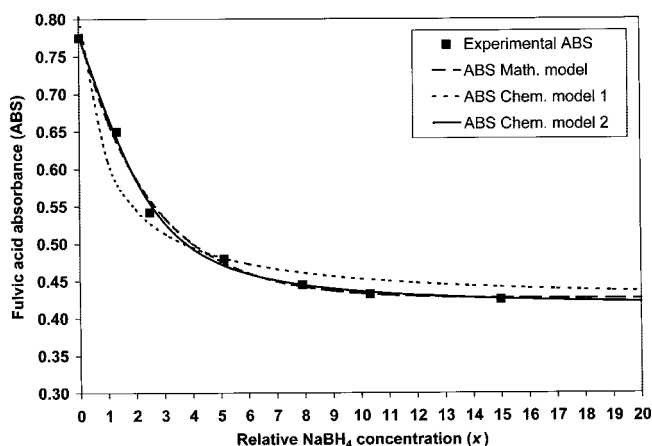
Figure 2. Fulvic acid solution absorbance at 465 nm after complete reaction (ABS) as a function of the initial, relative NaBH$_4$ concentration in solution (x): experimental data and model fitting curves.

Figure 3. Predicted chemical conversion functions (x_{FA}) for the mathematical curve fit and two chemical models (chemical models 1 and 2). See text for details.

concentration of reactive groups available for the reduction with NaBH$_4$ is fixed at a specific value, in order to test the general modeling concept. In chemical model 2, the same concept is then applied to a case of variable reactive group concentrations.

The general, stepwise modeling approach is the same for all types of models, and is explained for the chemical models in the following (see Figure 1). First, the mathematical modeling framework is developed in two steps. In the first step, a mathematical expression is derived in order to describe the relationship between the chemical parameter used to indicate the chemical conversion in the reduction reaction and the initial NaBH$_4$ concentration in solution (eq A). For this specific example, the UV–vis

absorbance of FA reaction solutions after complete reaction is used as the experimental conversion parameter, but various other chemical characteristics could be used for this purpose in future applications. In the second step, a mathematical relationship is found to link the experimental conversion parameter to the chemical conversion of reducible species (chemical conversion equation or eq B).

Following the above, the values of model parameters are determined by fitting eq A, derived in the first step, to experimental data using a standard mathematical software package (e.g., Mathematica 4.1). Finally, these fitting parameter values are used in the chemical conversion equation (eq B) in order to predict the chemical conversion of reducible species as a function of NaBH$_4$ concentration in solution. On the basis

of the calculated values of model fitting parameters, values for the apparent, conditional equilibrium constant can be determined. In addition, chemical model 2 also provides a calculated value for the effective reactive group concentration available in the reduction reaction.

Development of Mathematical Framework. *Step 1: Relationship between Experimental Conversion Parameter and NaBH₄ Concentration (Equation A). Mathematical Fit.* The mathematical curve fit model is based on the assumption that the relationship between FA absorbance (ABS) and reductant concentration can be described with three fitting parameters (a_1, b_1, c_1):

$$\text{ABS} = a_1 + b_1 \exp(-c_1 x) \tag{1}$$

The variable x represents the initial molar concentration of NaBH₄ relative to the concentration of FA-reactive groups initially available for the reduction with NaBH₄, and is defined as

$$x = \frac{[NaBH_4]_{Tot}}{[FA]_{Tot}} \tag{2}$$

with

$[NaBH_4]_{Tot}$ = total conc. of NaBH₄ [mol L⁻¹]
$[FA]_{Tot}$ = total reactive group conc. of FA [mol L⁻¹].

Chemical Models. The assumptions and definitions for both chemical models are summarized in the following:

(1) The reduction of FA-reactive groups can be simplified to the following overall reaction

$$FA_{Ox} + NaBH_{4,Red} \rightleftarrows FA_{Red} + NaBH_{4,Ox} \tag{3}$$

and mass action expression, which represents an apparent, conditional equilibrium constant for the postulated overall reaction:

$$K = \frac{[FA_{Red}][NaBH_{4,Ox}]}{[FA_{Ox}][NaBH_{4,Red}]} \tag{4}$$

with

$[FA_{Ox}]$, $[FA_{Red}]$ = conc. of oxidized/reduced FA-reactive groups [mol L⁻¹]

$[NaBH_{4,Ox}]$, $[NaBH_{4,Red}]$ = conc. of oxidized/reduced forms of NaBH₄ [mol L⁻¹]

(2) Equimolar reduction of FA-reactive groups with sodium borohydride yields:

$$[FA_{Red}] = [NaBH_{4,Ox}] \tag{5}$$

(3) The mass balance equations for NaBH₄ and FA-reactive group concentrations in solution are given by:

$$[NaBH_4]_{Tot} = [NaBH_{4,Ox}] + [NaBH_{4,Red}] \tag{6}$$

$$[NaBH_{4,Red}] = [NaBH_4]_{Tot} - [NaBH_{4,Ox}] \tag{7}$$

$$[FA]_{Tot} = [FA_{Ox}] + [FA_{Red}] \tag{8}$$

(4) For the total concentration of FA-reactive groups available for the reduction with NaBH₄, the following assumptions are made:

(a) Chemical Model 1:

$[FA]_{Tot}$ is fixed with 2.6 mmol g⁻¹ FA, the total concentration of FA-ketone groups, $[FA\text{-}Ket]_{Tot}$.[18] Reduction reactions of NaBH₄ with any other potentially reactive groups of FA, e.g., quinones, are assumed to be negligible on the basis of their significantly lower concentration (0.08 mequiv g⁻¹ FA) in Suwannee River FA.[19] Therefore, it follows:

$$[FA]_{Tot} = [FA - Ket]_{Tot} = [FA - Ket_{Ox}] + [FA - Ket_{Red}] \tag{9}$$

and

$$[FA - Ket_{Ox}] = [FA - Ket]_{Tot} - [FA - Ket_{Red}] \tag{10}$$

$[FA]_{Tot}$ = total conc. of FA-reactive groups [mol L⁻¹]
$[FA\text{-}Ket]_{Tot}$ = total conc. of FA-ketone groups [mol L⁻¹]
$[FA\text{-}Ket_{Ox}]$ = conc. of oxidized FA-ketone groups [mol L⁻¹]
$[FA\text{-}Ket_{Red}]$ = conc. of reduced FA-ketone groups [mol L⁻¹]

(b) Chemical Model 2:

The concentration of FA-reactive groups can vary from the total number of FA-ketone groups by a factor of α_0:

$$[FA]_{Tot} = \alpha_0 [FA - Ket]_{Tot} \tag{11}$$

α_0 = coefficient and fitting parameter.

If α_0 is less than 1, this implies that not all FA-ketone groups are accessible during the reduction with NaBH₄. With $\alpha_0 > 1$, the concentration of FA-reactive groups is greater, and additional FA-functional groups may indeed be relevant for the reaction.

(5) There is a linear relationship between the chemical conversion of reducible FA-reactive groups (x_{FA}) and the measured light absorbance of the FA reaction solution (ABS):

$$x_{FA} = -k \times \text{ABS} + d \tag{12}$$

$$\text{ABS} = -\frac{x_{FA} - d}{k} = \frac{d}{k} - \frac{x_{FA}}{k} \tag{13}$$

In order to simplify this last equation, we define $a = 1/k$, which further gives

$$\text{ABS} = a(d - x_{FA}) \tag{14}$$

(6) The chemical conversion of reducible species is defined as the concentration ratio of reduced to total FA-reactive groups:

(18) Averett, R. C.; Leenheer, J. A.; McKnight, D. M.; Thorn, K. A. *Humic substances in the Suwannee River, Georgia: interactions, properties, and proposed structures; Water-Supply Paper 2373*; U.S. Geological Survey: Denver, 1994.
(19) Ratasuk, N. *Redox functional groups of humic substances. Ph.D. Dissertation*, University of Oklahoma, Norman, 2004.

$$x_{FA} = \frac{[FA_{Red}]}{[FA]_{Tot}} = 1 - \frac{[FA_{Ox}]}{[FA]_{Tot}} \quad (15)$$

This further yields for chemical model 1:

$$x_{FA} = \frac{[FA_{Red}]}{[FA - Ket]_{Tot}} \quad (16)$$

and for chemical model 2:

$$x_{FA} = \frac{[FA_{Red}]}{\alpha_0 [FA - Ket]_{Tot}} \quad (17)$$

The first step of the model derivation for chemical model 1 is described below; a summary of the derivation for chemical model 2 is provided in Supporting Information. First, an expression for the chemical conversion (x_{FA}) is derived to link x_{FA} to the apparent, conditional equilibrium constant for the reduction reaction (K) as well as to the relative molar concentration of NaBH$_4$ (x). The resulting expression for x_{FA} is substituted into the linear relationship between light absorbance and chemical conversion (eq 14). This provides the fitting equation for FA absorbance (ABS) as a function of x (eq A).

For the derivation of x_{FA}, expressions for [NaBH$_{4,Red}$] and [FA-Ket$_{Ox}$] based on mass balance equations (eqs 7 and 10) are substituted in the mass action expression K (eq 4), so that

$$K = \frac{[FA - Ket_{Red}]}{[FA - Ket]_{Tot} - [FA - Ket_{Red}]} \times$$
$$\frac{[NaBH_{4,Ox}]}{[NaBH_4]_{Tot} - [NaBH_{4,Ox}]} \quad (18)$$

Then, the assumption of equimolar reduction (eq 5) is used to express [NaBH$_{4,Ox}$], and all terms are divided by [FA-Ket]$_{Tot}^2$, which leads to

$$K = \left(\frac{[FA - Ket_{Red}]}{[FA - Ket]_{Tot}}\right)^2 \Bigg/ \Bigg[\frac{[NaBH_4]_{Tot}}{[FA - Ket]_{Tot}} -$$
$$\frac{[FA - Ket_{Red}] \times \{[NaBH_4]_{Tot} + [FA - Ket]_{Tot}\}}{[FA - Ket]_{Tot}^2} +$$
$$\left(\frac{[FA - Ket_{Red}]}{[FA - Ket]_{Tot}}\right)^2 \Bigg] \quad (19)$$

Further, we use the definition of chemical conversion (eq 16) to express the equation in terms of x_{FA}:

$$x_{FA}^2(K - 1) - x_{FA}\left\{K \times \left(\frac{[NaBH_4]_{Tot}}{[FA - Ket]_{Tot}} + 1\right)\right\} +$$
$$K \times \frac{[NaBH_4]_{Tot}}{[FA - Ket]_{Tot}} = 0 \quad (20)$$

With the definition of x, the molar excess concentration of NaBH$_4$ in solution (eq 2), the equation further simplifies to

$$x_{FA}^2(K - 1) - x_{FA}\{K(x + 1)\} + Kx = 0 \quad (21)$$

which has the following two solutions:

$$x_{FA_{1,2}} = \frac{K(x + 1) \pm \sqrt{\{K(x + 1)\}^2 - 4(K - 1)Kx}}{2(K - 1)} \quad (22)$$

We determine the correct solution for x_{FA} by using the following condition: for [NaBH$_4$]$_{Tot} = 0$ and $x = $ [NaBH$_4$]$_{Tot}$/[FA-Ket]$_{Tot} = 0$ the valid chemical conversion value is $x_{FA} = 0$. Therefore, we find x_{FA_2} (negative sign) as solution, substitute this expression into the equation describing the linear relationship between absorbance and chemical conversion (eq 14), and further simplify the equation by defining

$$b = \frac{K}{K - 1} \quad (23)$$

It follows that:

$$\text{ABS} = ad - \frac{ab}{2}(x + 1) + a\sqrt{\frac{b^2}{4}(x + 1)^2 - bx} \quad (24)$$

Last, we implement the following parameters to simplify the numerical fitting process.

$$\beta_0 = ad \quad (25)$$

$$\beta_1 = \frac{ab}{2} \quad (26)$$

$$\gamma_1 = \frac{4}{b} \quad (27)$$

The resulting equation (eq A) is used for the fitting of the absorbance data for chemical model 1 (Mathematica 4.1):

$$\text{ABS} = \beta_0 - \beta_1\left\{(x + 1) - \sqrt{(x + 1)^2 - \gamma_1 x}\right\} \quad (28)$$

Step 2: Derivation of Chemical Conversion Equation (Equation B). *Mathematical Fit.* For the mathematical 'curve fit', the fitting parameters for the absorbance curve, a_1, b_1, and c_1, are linked to the chemical conversion function using the assumption of a linear relationship between chemical conversion and absorbance, with $a = 1/k$:

$$x_{FA} = -k \times \text{ABS} + d = -\frac{\text{ABS}}{a} + d \quad (12)$$

The combination of eq 1 with this linear relationship gives

$$x_{FA} = -\frac{a_1 + b_1 \times \exp(-c_1 x)}{a} + d \quad (29)$$

This equation is solved for the variables a and d by using two boundary conditions: 1) for $x \to 0$, $x_{FA} \to 0$, and 2) for $x \to \infty$, $x_{FA} \to 1$, which results in $a = b_1$ and $d = (a_1 + b_1)/b_1$.

The substitution of these expressions for the variables a and d in eq 29 leads to the chemical conversion equation for the mathematical model:

$$x_{FA}(x) = 1 - \exp(-c_1 x) \qquad (30)$$

Chemical Models. For both chemical models, the linear relationship between light absorbance and chemical conversion has already been used in their mathematical derivations. Therefore, expressions for the variables a and d can be directly derived from the original definitions of the absorbance fitting parameters, β_0, β_1, and γ_1 (eqs 25–27). The resulting expressions for $a = \beta_1 \gamma_1 / 2$ and $d = 2\beta_0 / \beta_1 \gamma_1$ are combined with eq 12 to give the chemical conversion function (eq B) for chemical models 1 and 2:

$$x_{FA}(x) = \frac{2\{\beta_0 - \text{ABS}(x)\}}{\beta_1 \gamma_1} \qquad (31)$$

Results and Discussion

Fitting of Absorbance Data. The light absorbance data at 465 nm show an exponential-type decrease in absorbance with increasing NaBH$_4$ concentrations in solution (Table 1, Figure 2). All three model fits follow the general trend of the absorbance data reasonably well. This implies that, despite their simplicity, the proposed chemical models are able to capture the chemical system behavior. For a more detailed model analysis, the root mean square (rms) was used as a goodness-of-fit estimate to compare model fits based on the overall variance of residuals:

$$\text{rms} = \sqrt{\frac{\sum_{i=1}^{N} (\text{ABS}_i - \text{ABS}_{i,\text{exp}})^2}{(N - P)}} \qquad (32)$$

with

ABS$_i$ = model fit of absorbance value [ ]
ABS$_{i,\text{exp}}$ = experimental absorbance value [ ]
N = number of data points [ ]
P = number of model fitting parameters [ ]

The smaller the rms value is for a particular model, the more closely this model captures the data points. Based on calculations, chemical model 2 provides the best fit (rms = 1.076×10^{-2}) of the absorbance data, the mathematical curve fit the second best (rms = 1.175×10^{-2}), and chemical model 1 the third best fit (rms = 4.006×10^{-2}). In addition to a higher rms value, chemical model 1 also shows structure in the residuals (data not reported). The improved fit of chemical model 2 over chemical model 1 indicates that the actual concentration of FA-reactive groups involved in the reduction reaction may be larger than the FA-ketone group concentration ($\alpha_0 > 1$), probably including some quinone groups as well. In

fact, based on the results of chemical model 2, ketone groups provide only approximately 30% of the total number of FA-reactive groups involved in the reduction with NaBH$_4$ ($\alpha = 0.3$, $\alpha_0 = 3.2$). However, the reported quinone concentration for Suwannee River FA[19] seems rather low compared to the broad range of concentrations, e.g., from 0.28 to 4.2 mequiv g^{-1} FA, found for various other types of fulvic acids in the literature.[20] On the other hand, an improved fit of chemical model 2 is also expected due to the addition of one more fitting parameter in comparison to the other two models. Therefore, additional data points and replicates are needed to support this conjecture, which goes beyond the scope of this study.

Prediction of Chemical Conversion. Due to the exponential-type decrease in solution absorbance with increasing NaBH$_4$ concentrations, the predicted chemical conversion curves follow an exponential-type increase (Table 1, Figure 3). We can conclude from the experimental and mathematical work that at least a 10-fold molar NaBH$_4$ excess concentration, equivalent to approximately equal masses of FA and NaBH$_4$, is required to ensure maximum chemical conversion of FA-reactive groups.

Calculation of Apparent, Conditional Equilibrium Constants. Previously, we have defined the parameters b (eq 23) and γ_1 (eq 27). By combining these two expressions, we find an equation for the apparent, conditional equilibrium constant K as a function of the fitting parameter γ_1, which is valid for both chemical models.

$$K = \frac{4}{4 - \gamma_1} \qquad (33)$$

A comparison of the computed values of K is provided in Table 1.

Summary and Conclusions

Two types of chemical models were developed to describe the chemical conversion of reducible fulvic acid reactive groups in a reduction reaction with sodium borohydride as a function of reductant concentration. The common modeling concept represents a relatively simple, engineering approach, based on general chemical principles such as the mass action expression, mass balance equations and a chemical equilibrium assumption. This concept is applicable to organic compounds of unknown, effective reactive group concentrations, such as organic mixtures or colloidal materials. In addition to the prediction of chemical conversion, the calculation of model fitting parameters also provides values for "apparent, conditional equilibrium constants", which are valid for the specific reaction conditions under which they have been determined.

Model fitting parameters can be determined easily and quickly using a standard mathematical software package, such as Mathematica. Nevertheless, the chemical models seem to capture the overall behavior of the chemical reduction reaction sufficiently well when compared to a mathematical fit of the same experimental data.

In general, this modeling concept can be applied in two possible ways. First, model predictions allow the transfer of

(20) Stevenson, F. J., Reactive Functional Groups of Humic Substances. In *Humus chemistry Genesis, Composition, Reactions*, Wiley-Interscience Publications: New York, 1982; pp 221.

existing, experimental chemical conversion data to new, similar target compounds assuming that the necessary requirements are fulfilled. This can provide a good first-estimate of reductant concentrations required for the optimum chemical conversion in new applications. On the other hand, in cases of an unknown overall reaction mechanism or unspecified effective reactive group concentrations involved in the reduction reaction, the modeling concept can be used in order to test the feasibility of a proposed overall reaction or reactive group concentration.

Experimental Section

Reagents. All reaction solutions were prepared with auto-claved UV-water (Barnstead EASYpure UV compact ultrapure water system), which was made oxygen-free by boiling and purging with nitrogen gas for 45 min. Suwannee River fulvic acid (International Humic Substances Society, Cat. No. 1R101F-1) was selected as organic compound; (nonradioactive) sodium borohydride powder was purchased from Fisher Scientific (>98% purity, S678–25).

Experimental Setup of Chemical Conversion Experiment. Sodium borohydride is known to decompose in neutral and acidic aquatic solutions, leading to the production of hydrogen gas.[1] Since solution conditions, such as pH and temperature, affect $NaBH_4$ degradation, the reduction of FA was performed at alkaline pH and only slightly elevated temperature. Furthermore, due to the instability of FA quinone reduction products over time, all chemical conversion experiments were performed in an oxygen-free glovebox environment with oxygen-free UV-water, and sample exposure to oxygen prior to spectral analysis was minimized.

Solutions containing aliquots of 10 mg of freeze-dried FA and various weights of $NaBH_4$ (from approximately 1.25 to 15 mg) were adjusted to pH values of 9.6 ± 0.06 with a NaOH solution. FA standard solutions containing no $NaBH_4$ were prepared in the same manner. After pH adjustments at room-temperature, all solutions (10 mL total volume) were allowed to equilibrate in a heated water bath at 60 °C for 4 h. After equilibration, the loss of UV-water due to evaporation was corrected based on weight-difference for all sample and standard solutions. Within 10 min after sample removal from the glovebox, solutions were scanned for light absorbance on a Hach DR/4000 U spectrophotometer over a wavelength range from 200 to 800 nm (10 mm far UV quartz cell: Hach Co. 48228-00, 1-Q-10). Light absorbance values of FA solutions at 465 nm were used to determine the degree of FA reduction at individual $NaBH_4$ concentrations. This particular wavelength was chosen because it showed significant absorbance differences between samples of different expected levels of chemical conversion of reducible FA reactive groups (Figure S1, Supporting Information), and its use for this type of organic material is well established in literature.[21] However, when absorbance data sets at different wavelengths (400 and 450 nm) were processed in the same manner, the predicted efficiency values were within five percentage points of the predicted values based on 465 nm absorbance data (data not reported). Oxygen-free UV-water adjusted to pH 9.6 ± 0.03 provided the baseline for all UV–vis spectroscopic analyses.

Symbols Defined

Symbol	= description [unit]
a, b	= fitting parameters
a_1, b_1, c_1	= fitting parameters
ABS	= UV absorbance of reaction solution at 465 nm
ABS_i	= model fit of UV absorbance of reaction solution at 465 nm
$ABS_{i,exp}$	= experimental UV absorbance of reaction solution at 465 nm
d	= fitting parameter
$[FA_{Ox}]$	= concentration of oxidized FA-reactive groups [mol L^{-1}]
$[FA_{Red}]$	= concentration of reduced FA-reactive groups [mol L^{-1}]
$[FA]_{Tot}$	= total concentration of FA-reactive groups [mol L^{-1}]
$[FA\text{-}Ket_{Ox}]$	= concentration of oxidized FA-ketone groups [mol L^{-1}]
$[FA\text{-}Ket_{Red}]$	= concentration of reduced FA-ketone groups [mol L^{-1}]
$[FA\text{-}Ket]_{Tot}$	= total concentration of FA-ketone groups [mol L^{-1}]
k	= fitting parameter
K	= apparent, conditional equilibrium constant for the reduction reaction
N	= number of data points
$[NaBH_{4,Ox}]$	= concentration of oxidized form of $NaBH_4$ [mol L^{-1}]
$[NaBH_{4,Red}]$	= concentration of reduced form of $NaBH_4$ [mol L^{-1}]
$[NaBH_4]_{Tot}$	= total concentration of $NaBH_4$ [mol L^{-1}]
P	= number of model fitting parameters
rms	= root mean square, goodness-of-fit estimate
x	= relative molar $NaBH_4$ concentration
x_{FA}	= chemical conversion of reducible FA-reactive groups [ ] or [%]
α, α_0	= coefficients and fitting parameters
β_0, β_1, γ_1	= fitting parameters

Supporting Information Available

Spectral data of fulvic acid solutions after reduction with various amounts of sodium borohydride; mathematical derivation for chemical efficiency model 2. This information is available free of charge via the Internet at http://pubs.acs.org.

(21) MacCarthy, P.; Rice, J. A., Spectroscopic methods (other than NMR) for determining functionality in humic substances. In *Humic substances in soil, sediment and water*, Aiken, G. R.; McKnight, D. M.; Wershaw, R. L.; MacCarthy, P., Eds. John Wiley & Sons: New York, 1985; pp 527.