[Research Note]

Screening of Supports and Additives for Heteropoly Acid Catalysts for Friedel-Crafts Reaction by High-throughput Screening and Data Mining

Kohji OMATA*

Dept. of Applied Chemistry, Graduate School of Engineering, Tohoku University, Aoba 6-6-07, Aramaki, Aoba-ku, Sendai 980-8579, JAPAN

(Received September 14, 2010)

Friedel-Crafts alkylations are very important reactions which are widely used in the production of fine chemicals, intermediates, and petrochemicals. Solid catalysts should be developed for greening of these chemical processes. We previously developed a high-throughput screening system (HTS) and had been screening solid catalysts for benzylation of anisole by benzyl alcohol. In the present study, supports and additives for 12 tungstophosphoric acid (HPA) catalysts were screened by HTS and data mining tools using principal component analysis, radial basis function network, and support vector machine. These methods identified Re-HPA/activated carbon with the highest activity, which was experimentally confirmed.

Keywords

Friedel-Crafts reaction, High-throughput screening, Principal component analysis, Radial basis function network, Support vector machine

1. Introduction

The Friedel-Crafts reactions are very important reactions which are widely used in the production of fine chemicals, intermediates, and petrochemicals. Typical catalysts for the Friedel-Crafts reactions are available in the liquid phase. The usage of over-stoichiometric amounts of these acids generates several problems such as corrosion, separation, and waste disposal. Therefore, to develop environmentally benign processes, active and green solid acid catalysts are required. Ion-exchanged clays^{1,2)} are highly efficient catalysts and zeolites show unique shape selectivity in spite of the low activity imposed by the diffusivity limit. Among the H-type zeolites, β zeolite has properties as an anti-coking catalyst³⁾. Other mesoporous materials such as SBA-1⁴⁾ and transition metal oxides are other known types of catalysts^{5,6)}.

The high-throughput screening (HTS) approach is useful to estimate the catalytic properties of new materials. We previously developed the HTS method using test tubes and a dry bath to optimize the catalyst composition of oxides for benzylation of anisole by benzyl alcohol^{7,8)}. The ohmic heating was then replaced by rapid microwave heating to accelerate the screening, which showed that Fe or Sn containing montmorillonite have high activity⁹⁾. Then the development of successive catalyst screening revealed that phosphotungstate

(HPA) shows higher activity. In the present study, we describe the screening of support and additives for HPA catalyst for benzylation of anisole by benzyl alcohol using the HTS method with test tubes and data mining tools.

Catalytic phenomena are generally very complicated because many non-linear parameters are involved. Therefore, the catalytic activity or selectivity of a new catalyst is quite difficult to predict based on previous experimental results. We have been using RBFN^{10)~17)} to investigate the relationship between the activity and physicochemical properties of elements which are used as additives to catalysts. These properties should affect the catalytic properties such as surface area, metal dispersion, electronic state, morphology, thermal stability, affinity to supports, and others, and these catalytic properties then determine the catalytic activities. Therefore, the properties of elements should be correlated to the catalytic performance, although through quite complicated non-linear relationships. Catalysts were prepared using elements with known properties, and the parameters of a RBFN were tuned using the physicochemical properties and the catalytic performance. The tuning process is usually called “training” because of the association with the learning process of the human brain. The important point is that the variety of training elements are selected according to the orthogonal concept. For example, all elements can be clustered by the k-means clustering method, and some elements can be selected as the representative of each

* E-mail: omata@erec.che.tohoku.ac.jp

cluster. Then the relationship between the principal component of the physicochemical properties of elements and the activity of the catalyst containing the representative element can be quantified by RBFN and SVM. This procedure will be used in the present study.

2. Experimental Method

2.1. HTS for Support of HPA Catalyst

Screening for the support of HPA catalyst was performed in test tubes used for the preparation and activity test of catalysts. A test tube (15 mm diameter) was charged with 12 tungsto (VI) phosphoric acid *n*-hydrate (Wako Pure Chemical Industries, Ltd., HPA) (15 mg) and ethanol (1 mL). Then a support (50 mg) was impregnated with the solution and dried at 90°C, followed by washing with ethanol (2 mL) three times at room temperature to remove the free HPA. Japan Reference Catalysts (Catalysis Society of Japan) such as H-type β zeolite (JRC-Z-HB25), H-type ZSM-5 (JRC-Z590H), magnesia (JRC-MGO-4-500A), zirconia (JRC-ZRO-1), silica A (JRC-SIO-5), alumina A (JRC-ALO-1A), alumina B (JRC-ALO-2), alumina C (JRC-ALO-7), were used as the support. Commercially available titania A (ST01, Ishihara Sangyo), titania B (anatase, Wako Pure Chemical Industries), silica B (P-10, Fuji Silysia Chemical Ltd.), silica C (ID, Fuji Davison), silica D (Q-15, Fuji Silysia Chemical Ltd.), activated carbon A (BAC-LP Kureha Corp.), and activated carbon B (GC Kuraray Coal, Kuraray Chemical Co., Ltd., AC) were also used. Activity tests were conducted in other test tubes in a dry bath at 130°C using anisole (2.0 g) and benzyl alcohol (0.2 g). After the reaction, the test tube was cooled quickly in water. The products were analyzed by gas chromatography (Shimadzu GC-8A, Ar carrier, Dexil 300 GC packed column at 170°C) equipped with a flame ionization detector. The main products were benzyl anisoles, with small amounts of dibenzyl ether. The yields of benzyl anisoles and dibenzyl ether were calculated on the basis of the benzyl group.

2.2. HTS for Additive of Supported HPA Catalyst

Screening of additives for HPA supported on activated carbon (HPA/AC) was conducted using statistical language R¹⁸⁾ as the data mining tools in the next three steps.

Step 1: preparation of input data

At first 64 elements were selected as candidates for the additives to supported HPA catalyst. Physicochemical properties^{19),20)} such as oxide formation enthalpy (FE, kJ/mol), 1st ionization energy (II, eV), 2nd ionization energy (2I, eV), electronegativity (EN, -), electric dipole polarizability (ED, Å³), boiling point (BP, K), melting point (MP, K), specific heat capacity (HC, J/g/K), heat of fusion (HF, kJ/mol), heat of vapor-

Table 1 Data File for Data Mining Saved with CSV Format

	A	B	...	P	Q	R
1	FE	II	...	VA	activity	symbol
2	417.98	5.139	...	1	17.9	Na
⋮	⋮	⋮	⋮	⋮	⋮	⋮
64	218.06	7.416	...	3		Pb
65	191.29	7.285	...	3		Bi

ization (HV, kJ/mol), thermal conductivity (TC, W/mK), covalent radius (CR, pm), density (DS, g/cm³), ionic radius (IR, pm), atomic weight (AW, g/mol), and valence of ion (VA, -) were used to characterize each element. For data mining, properties and activity were recorded in a 'data.csv' file with symbols as shown in **Table 1** illustrating a part of the csv file. Every property was normalized (mean = 0 and variance = 1) at the step of principal component analysis, so the units of properties were eliminated. Activity was also normalized to 0-1 for the response of the output of RBFN or SVM. Then, principal component analysis was conducted using the *prcomp*() function to find the important factors in the physicochemical properties of the elements. The contribution of 5 principal components accounted for over 85% of total eigenvalues, so these 5 components were used as input data.

Step 2: activity test

Based on the 5 principal components, elements in the periodic table were categorized into 7 groups by k-means clustering according to Hartigan-Wong²¹⁾ using the *kmeans*() function, because a category containing only one member appeared if the categorization included 8 or more groups. One or two elements from each category were selected as training elements and used for catalyst preparation. The representative elements of each category were selected because of the availability, solubility, decomposition temperature, toxicity, and so on. For impregnation on the supported HPA catalyst, Na, Mg, Mn, Zn, Pd, Sn, Cs, Pr, and W were selected as training elements. Bi and Re was selected as validation elements. Sodium acetate trihydrate, magnesium acetate tetrahydrate, manganese (II) acetate tetrahydrate, anhydrous zinc acetate, palladium (II) nitrate, cesium acetate, praseodymium (III) acetate dihydrate, tungstic acid, bismuth (III) acetate oxide (Wako Pure Chemical Industries), tin (II) acetate, and rhenium (VII) oxide (Strem Chemicals) were used as received without further purification. Support (AC, activated carbon B) was impregnated in an ethanol (1 mL) solution of HPA (8 mg) and the additive element salt (5 μmol). The solution was dried at 90°C and then the supported catalyst was transferred to another test tube followed by reaction without pretreatment.

Step 3: training and prediction

Finally the 5 principal components of the physicochemical properties and the results of activity tests of 9

Fig. 1 Flow Chart for Data Mining

Fig. 2 Screening of Support at 130°C for HPA Catalyst

catalysts were used to find the optimum inner parameters of the RBFN and SVM. Then the RBFN and SVM were used to predict the activity of additives on HPA/AC catalyst by virtual screening. These processes are diagrammed in Fig. 1 and the codes of R are listed in the Appendix section.

3. Results and Discussion

3.1. HTS for Support of HPA Catalyst

Figure 2 summarizes the results of the screening of supports. The catalysts were not calcined in air at high temperature to avoid the thermal damage, so to eliminate the time-consuming step in HTS, a part of the HPA would be liberated from the support during the liquid phase reaction. Therefore, catalysts were washed with ethanol three times before reaction to

Table 2 Screening of Additives for HPA/AC Catalyst

Additive	BA ^{a)} [%]	BE ^{a)} [%]
Cs	0.0	0.0
Mg	0.0	0.0
Mn	0.0	0.0
Zn	0.2	0.1
Na	0.4	0.2
Pr	28.0	4.1
Sn	56.1	5.6
Pd	57.0	5.2
W	62.8	4.4

a) Benzyl anisoles and benzyl ether at 130°C.

Table 3 Prediction of Benzyl Anisole Yield of HPA/AC Catalysts at 130°C

Additive	Experimental	by RBFN	by SVM
training data			
Sn	56.1	56.1	49.8
Pd	57.0	57.0	50.7
W	62.8	62.8	56.5
validation data			
Bi	59.4	66.1	54.7
Re	64.1	62.3	50.4

eliminate the free active species. The activities were apparently decreased by the ethanol washing treatment.

The order of activity of supported HPA was as follows: activated carbon > titania > alumina > silica > zeolite > zirconia > magnesia ≈ 0

3.2. HTS for Additives of Supported HPA Catalyst

8 mg HPA was charged with 5 μmol additive salt in 1 mL ethanol and then 50 mg activated carbon was impregnated. Ethanol washing treatment was eliminated to avoid the loss of additives. The weight of the HPA charge was determined because the weight of supported HPA on the activated carbon B was 0.2 g/g-carbon after ethanol washing. Without the additives, the yields of benzyl anisoles and benzyl ether were 58.2% and 4.7%, respectively. The results of screening are summarized in Table 2.

The 5 principal components of the physicochemical properties of the elements and the activities were used to tune the internal parameters of RBFN or SVM. After these properties and activities were correlated, RBFN and SVM could predict the activity of other additives on activated carbon. The order of activity predicted by RBFN was: Bi > W > Re > ... > Pd > ... > Sn, whereas that predicted by SVM was: W > Bi > Pd > Re > Sn. Both methods suggest that addition of Bi or Re would increase the product yield as shown in Table 3.

According to the activity test for validation of these predictions, yields of benzyl anisoles were 59.4% and 64.1% for Bi and Re, respectively. Therefore, catalyst containing Re was identified as a result of virtual screening by RBFN or SVM, although the activity was

Circles: benzyl anisoles, squares: benzyl ether. Closed symbols: Re-HPA/AC, open symbols: HPA.

Fig. 3 Effect of Reaction Temperature on the Activity of Re-HPA/AC

rather higher than predicted.

3.3. Activity of Re-HPA/AC Catalyst

The effect of reaction temperature on the activity of Re-HPA/AC catalyst was investigated. The yield of benzyl anisoles increased rapidly over 120°C. The pseudo-first order rate constant of anisole formation was determined and the specific activation energy was estimated as 135.6 kJ/mol as shown in Fig. 3. This value is almost the same as that of clay supported catalyst¹⁾, which suggests that the diffusion steps are not rate-determining. HPA catalyst without support has an activation energy of 42.1 kJ/mol. The supported HPA showed much higher activity at high temperature, whereas the homogeneous HPA catalyst had higher activity under 120°C. The difference between these activation energies suggest that the contribution of liberated HPA from activated carbon is small in the activity of Re-HPA/AC catalyst.

4. Conclusion

Screening of a new catalyst for Friedel-Crafts benzylation of anisole was conducted using a HTS system and data mining tools. Many types of supports for HPA catalyst were screened in a short time, and an activated carbon supported phosphotungstate salt was discovered to show high activity. The relationship between the physicochemical properties of cation and the activity was quantified using a radial basis function network or support vector machine. These methods showed that the combination of Re and HPA on activated carbon provide optimum catalysis for the reaction, which was confirmed by experimental results.

Acknowledgment

This work was supported by a Grant-in-Aid for Challenging Exploratory Research (22656183).

Appendix

```

zz<-read.csv("data.csv")
pca<-prcomp(zz[1:64,1:16],scale=TRUE)
center<-pca$x[1:9,1:5]
max<-max(zz[1:9,17])
min<-min(zz[1:9,17])
response<-(zz[1:9,17]-min)/(max-min)
symbol<-data.frame(symbol=zz[,18])
prediction<-pca$x[1:64,1:5]
sigma2<-apply(apply(as.matrix(
  dist(center))^2,1,sort)[2:3,],2,mean)
weight<-t(solve(exp(as.matrix(dist(center))^2)/(-2)/sigma2)))%*%response
RBFN<-function(c,w,s,p) {
  tt<-matrix(data=p,nrow=9,ncol=
    5,byrow=T)
  response<-exp(apply((tt-c)^2/(-2)/
    s,1,sum))%*%w
  return(response)}
predicted<-NULL
for (i in 1:9) {predicted[i]<-RBFN(center,
  weight,sigma2,center[i,])}
plot(response,predicted)
predicted<-NULL
for (i in 1:64) {predicted[i]<-RBFN(center,
  weight,sigma2,pca$x[i,1:5])}
predicted<-data.frame(symbol=symbol,
  predicted=predicted*(max-min)+min)
(predicted<-predicted[order(-predicted
  [,2]),])
library(e1071)

```

```

z<-cbind(center,response)
model1=svm(response~.,data=z,cost=2,
scale=F)
plot(response,fitted(model1))
predicted<-NULL
predicted<-data.frame(predict(model1,
prediction))
predicted<-cbind(symbol,predicted*(max-
min)+min)
(predicted<-predicted[order(-predicted
[,2]),])

```

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要 旨

ハイスループットスクリーニングとデータマイニングによる Friedel-Crafts 反応用ヘテロポリ酸触媒の担体および添加物の探索

小俣 光司

東北大学大学院工学研究科応用化学専攻, 980-8579 仙台市青葉区荒巻字青葉6-6-07

Friedel-Crafts 反応は種々の中間体の合成や石油化学プロセスに欠かせない反応であるが、プロセスのグリーン化に対応した固体触媒の開発が求められているため、各種の HTS (High-Throughput Screening) 反応器を作製してベンジルアルコールによるアニソールのベンジル化反応の固体触媒の探索を進めている。本研究では12タングストリン酸 (HPA) 触媒に適した

担体を探索した後、担持触媒への最適添加元素をデータマイニングツールを用いてさらに探索した。添加物元素の物性値の主成分と活性の関係をラジアル基底関数ネットワークならびにサポートベクターマシンにより定量的に求めた結果、活性炭に担持した HPA に Re を添加した場合に高活性を示すことを見出した。