ОПЕРАНДО ИССЛЕДОВАНИЯ: ИДЕНТИФИКАЦИЯ И УСТАНОВЛЕНИЕ ФУНКЦИЙ ИНТЕРМЕДИАТОВ В ХИМИЧЕСКИХ СИСТЕМАХ
Шмидт А.Ф., Курохтина А.А., Ларина Е.В.

Concept of operando spectroscopy

Operando *(working)* **spectroscopy** is an analytical methodology wherein the **spectroscopic characterization** of materials undergoing reaction is coupled simultaneously with measurement of **catalytic activity and selectivity**.

M. A. Bañares and I. E. Wachs, J. Raman Spectrosc., 2002, 33, 359-380.

Ex situ and *In situ* methods

ex situ analyses involve the removal of solvent and other compounds present in the reaction mixture, heating the samples and exposing them to vacuum or strong electric fields, *etc.*

in situ analyses are carried out directly in the reactor where the reaction proceeds, and exclude the uncontrolled influence of measurement conditions on the results of such measurements.

in situ investigation under real reaction conditions can be achieved using methods based on the following techniques:
- UV-vis spectroscopy,
- NMR spectroscopy,
- X-ray absorption (XAS, EXAFS, XANES),
- Raman spectroscopy,
- IR spectroscopy (TIRS, DRIFTS, ATR-IRS, PM-IRRAS),
- **Electron microscopy (ETEM, ESTEM, EELS/STEM).**
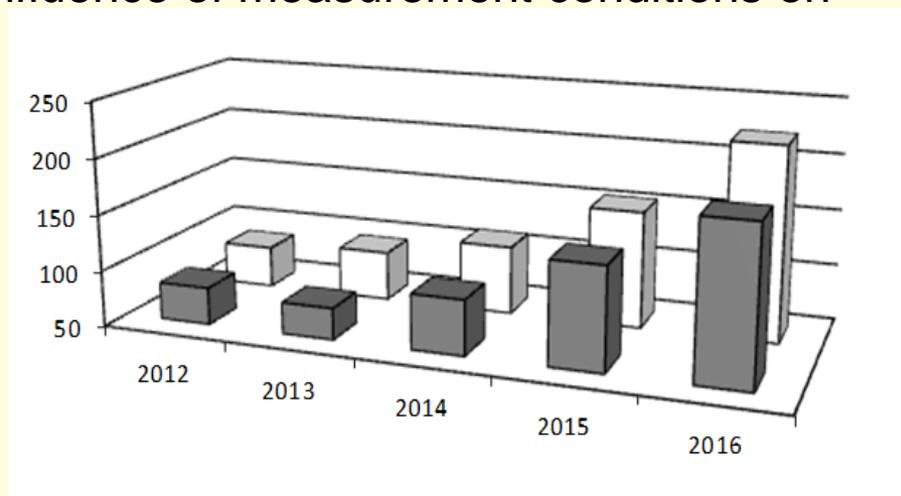
Number of publications containing the term "operando spectroscopy" in titles, abstracts, or keywords, as indexed in the Web of Science (white) and Scopus (grey) in 2012–2016.

Concept of operando studies

The concept of operando spectroscopy was represented by spectroscopic studies of catalysts (catalytic systems) under real reaction conditions, featuring simultaneous determination of structure/composition and activity/selectivity to obtain fundamental information on the [structure/composition]–[activity/selectivity] relationship

M. A. Bañares and I. E. Wachs, *J. Raman Spectrosc.,* 2002, **33**, 359-380.
M. A. Bañares, *Adv. Mater.,* 2011, **23**, 5293-5301.

$$[rate] = k_{app} \times [active\ species\ amount]^n$$

$$[TOF] = k_{app} \times [active\ species\ amount]^{n-1}$$

[active species amount]–[activity] relationships is required for evaluating apparent rate constants, i.e., obtaining fundamental information on [structure/composition]–[activity/selectivity] relationships

Two types of processes operating in a catalytic system → two types of kinetic data

1. Catalyst transformations under real conditions occurring outside the main catalytic cycle (**type 1 kinetic data**).
2. Catalyst transformations occurring in the main catalytic cycle, where catalytic reaction products are formed (**type 2 kinetic data**).
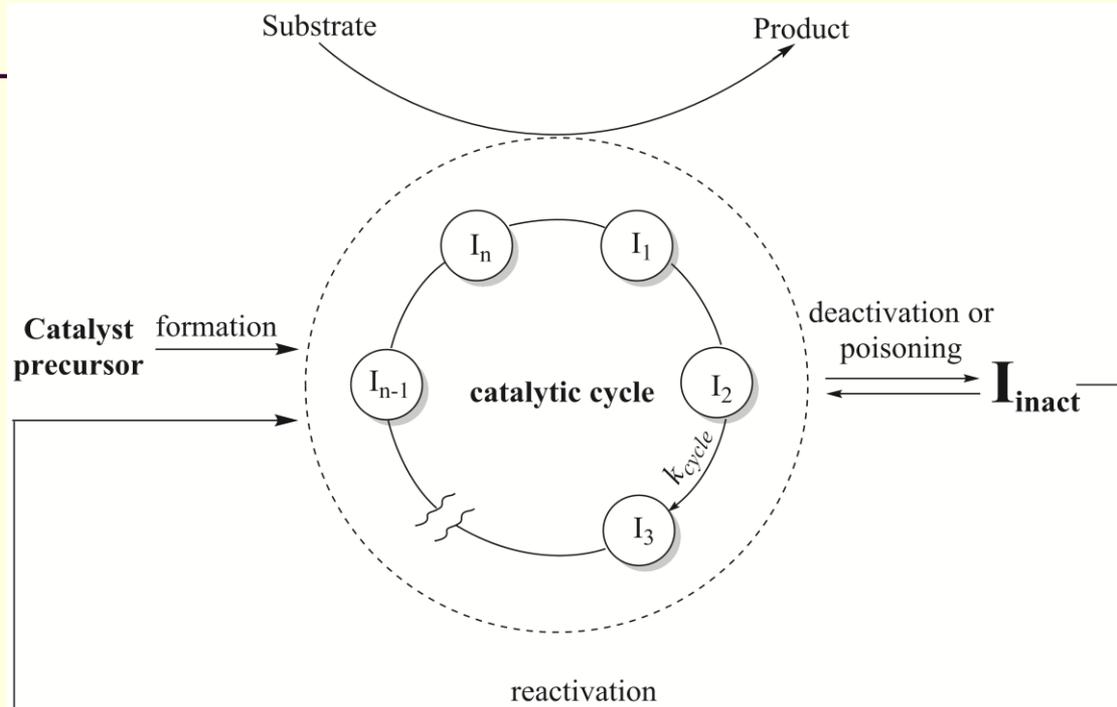
Schematic representation of key processes occurring in a catalytic system.

Operando studies should focus not only (and not as much) on *in situ* spectroscopic detection and identification of catalyst transformation products with simultaneous kinetic control of substrate conversion products to control catalytic activity, but also on the simultaneous kinetic control of observed catalyst species and substrate conversion products

Goals and tasks of operando studies

1. The obtaining of fundamental knowledge on full mechanisms operating in catalytic systems where **the roles of observed catalytic species** are precisely identified;

2. The construction of more reliable kinetic models that are able to play a key role in the development and optimization of processes (needs of chemical industry, commercialization of new catalytic processes and optimization of known ones).

The simultaneous acquisition of two types of kinetic data is actually the main experimental task of operando kinetic studies of catalytic processes (**operando kinetics**).

Requirements of operando studies

1. *In situ* methods

The tendency of performing all measurements using *in situ* techniques only can result in an unjustified complication of equipment and, as a consequence, in its high cost. In reality, some of these measurements can be carried out using *ex situ* methods, providing results well-suited for their purpose.

For instance, analyses of liquid and/or gas phases of the reaction mixture to determine the amounts of stable compounds present therein aiming at measuring the activity and selectivity of the catalytic system can be performed *ex situ* by periodical sampling for GC or GC-MS. If a large number of different products are formed in a catalytic reaction, methods involving prior component separation are considerably better suited than *in situ* spectroscopic measurements of such multi-component systems
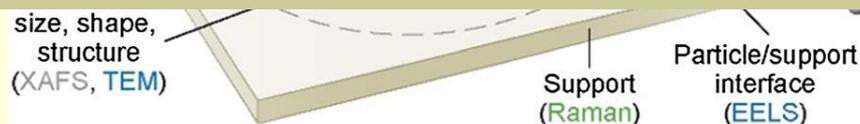
The four different beams (electron, X-ray, IR, and laser) probe different parts of the catalytic system (S. Zhao, Y. Li, E. Stavitski, R. Tappero, S. Crowley, M. J. Castaldi, D. N. Zakharov, R. G. Nuzzo, A. I. Frenkel and E. A. Stach, *ChemCatChem*, 2015, **7**, 3683-3691).

Requirements of operando studies

2. The reproduction of the reaction mixture composition

Researchers are willing to decrease the substrate/catalyst ratio (i.e., increase the catalyst content in the reaction mixture) to achieve higher quality of the obtained spectroscopic data and solve problems resulting from the insufficient detection limit of the used methods. Unfortunately, this compromise of operating catalytic systems under model conditions instead of real ones can dramatically influence the results.

Examples of the strong influence of the substrate/catalyst ratio on catalyst transformations outside the main catalytic cycle:

- A. F. Shmidt and A. Khalaika, *Kinet.Catal.*, 1998, **39**, 803-809.
- A. F. Schmidt and V. V. Smirnov, *J. Mol. Catal. A: Chem.*, 2003, **203**, 75-78.
- C. Amatore and A. Jutand, *J. Organomet. Chem.*, 1999, **576**, 254-278.
- C. Amatore and A. Jutand, *Acc. Chem. Res.*, 2000, **33**, 314-321.
- A. H. M. de Vries, J. M. C. A. Mulders, J. H. M. Mommers, H. J. W. Henderickx and J. G. de Vries, *Org. Lett.*, 2003, **5**, 3285- 3288.

The term "reaction mechanism"

1. A set of steps (usually called the mechanistic reaction scheme) that determines the mechanism structure, i.e., the interplay of reactants and intermediate species.

2. Information on the structures/compositions and reactivities of all reactants and

In our opinion, the absence of kinetic measurements and/or synchronization of two types of kinetic data in operando studies means that establishing the composition and structure of reaction intermediates and products is still considered **to be sufficient** for determining the reaction mechanism.

(Temkin, O. N., Homogeneous Catalysis with Metal Complexes, John Wiley & Sons, Ltd. 2012; 806 p).

No assumption concerning a reaction mechanism can be considered reliable "until it is shown to be consistent with the observed kinetics" (G. C. Bond and R. H. Cunningham, *J. Catal.*, 1997, **166**, 172-185).

"the most compelling evidence for the identity of the true catalyst will always be kinetic in nature", and only then can the two types of kinetic data on catalyst transformations outside and inside the main catalytic cycle be used to construct hypotheses on the role of one or another catalyst species in catalysis. (J. A. Widegren and R. G. Finke, *J. Mol. Catal. A: Chem.*, 2003, **198**, 317-341; R. Cano, A. F. Schmidt and G. P. McGlacken, *Chem. Sci.*, 2015, **6**, 5338-5346).

If all components of the reaction system are known

Initial compounds (including impurities) → **All intermediates** → **All products (including side products)**

Result: a required set of equations of component material balance and no information about the reaction mechanism

On the necessity of kinetic control of catalyst transformations in operando kinetic studies (mathematical viewpoint)

Molecular matrix of the system

$$B = \begin{bmatrix} \alpha_{11} & \alpha_{12} & & \alpha_{1k} \\ \alpha_{21} & \alpha_{22} & \dots & \alpha_{2k} \\ \dots & \dots & \dots & \dots \\ \alpha_{n1} & \alpha_{n2} & \dots & \alpha_{nk} \end{bmatrix}$$

where k is the number of chemical elements being a part of the components (i.e. chemical compounds) of the system; n is the number of the components (i.e. chemical compounds) of the system; α_{nk} – the number of gram-atoms of the element k in the component n.

Stoichiometric matrix of the system

$$A = \begin{bmatrix} \alpha_{11} & \alpha_{12} & & \alpha_{1n} \\ \alpha_{21} & \alpha_{22} & \dots & \alpha_{2n} \\ \dots & \dots & \dots & \dots \\ \alpha_{m1} & \alpha_{m2} & \dots & \alpha_{mn} \end{bmatrix}$$

In this case, n is the number of the components (i.e. chemical compounds) of the system; m is the number of the stoichiometric equations describing the conversions proceeding in the systems; α_{mn} is the stoichiometric coefficient of the component n in the stoichiometric equation m.

Based on the law of conservation of mass, the relation between the A and B matrices presents the follows:

$$A \times B = 0$$

On the insufficiency of the knowledge about the composition/structure of the components of the chemical systems for the establishing of the mechanism of their interconversions

Example 1 (very simple reaction)

Components: [Cat], [Alkane], [Cat●Alkane], [Alkene] and [H$_2$]:

$$[Cat] + [Alkane] = [Cat \bullet Alkane]$$

$$[Cat \bullet Alkane] = [Cat] + [Alkene] + [H_2].$$
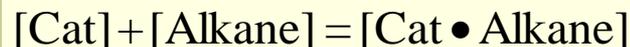
However, infinite number of linearly dependent stoichiometric equations (i.e. infinite number of *A* stoichiometric matrices) consistent also with the composition of the observed reaction components (i.e. with *B* molecular matrix) exists:

$$[Cat] + [Alkane] = [Cat \bullet Alkane]$$

$$[Cat \bullet Alkane] = [Cat] + [Alkene] + [H_2]$$

$$[Alkane] = [Alkene] + [H_2]$$
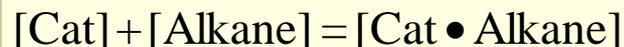
Example 2 (with consequent-parallel reactions).
Components: [Ni], [H$_2$], [C$_2$H$_4$], [C$_2$H$_6$], [Ni•H$_2$], [C$_2$H$_4$•Ni], [C$_2$H$_4$•Ni•H$_2$].

Molecular matrix of the system:

	$[Ni]$	$[H_2]$	$[C_2H_4]$	$[Ni \bullet H_2]$	$[C_2H_4 \bullet Ni]$	$[C_2H_4 \bullet Ni \bullet H_2]$	C_2H_6
Ni	1	0	0	1	1	1	0
H_2	0	1	0	1	0	1	1
C_2H_4	0	0	1	0	1	1	1

Stoichiometric matrix of the system:

$[Ni]$	$[H_2]$	$[C_2H_4]$	$[Ni \bullet H_2]$	$[C_2H_4 \bullet Ni]$	$[C_2H_4 \bullet Ni \bullet H_2]$	C_2H_6
0	1	1	0	0	0	−1
1	1	1	0	0	−1	0
1	0	1	0	−1	0	0
1	1	0	−1	0	0	0

The system of linearly independent stoichiometric equations:

the 1st variant of *A* matrix

$$[H_2] + [C_2H_4] = [C_2H_6]$$
$$[Ni] + [H_2] + [C_2H_4] = [C_2H_4 \bullet Ni \bullet H_2]$$
$$[Ni] + [C_2H_4] = [C_2H_4 \bullet Ni]$$
$$[Ni] + [H_2] = [Ni \bullet H_2]$$

the 2nd variant of A matrix

$$[Ni] + [H_2] = [Ni \bullet H_2]$$
$$[Ni] + [C_2H_4] = [C_2H_4 \bullet Ni]$$
$$[Ni \bullet H_2] + [C_2H_4] = [C_2H_4 \bullet Ni \bullet H_2]$$
$$[C_2H_4 \bullet Ni] + [H_2] = [C_2H_4 \bullet Ni \bullet H_2]$$
$$[C_2H_4 \bullet Ni \bullet H_2] = [Ni] + [C_2H_6]$$
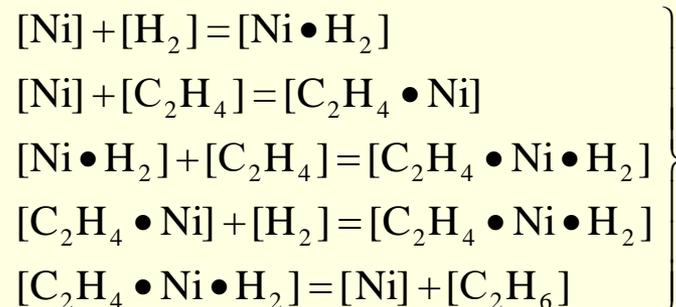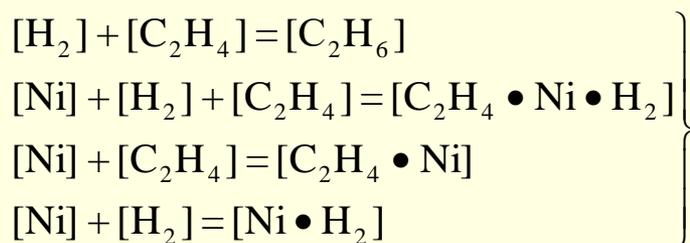
Synchronization of types 1 and 2 kinetic data
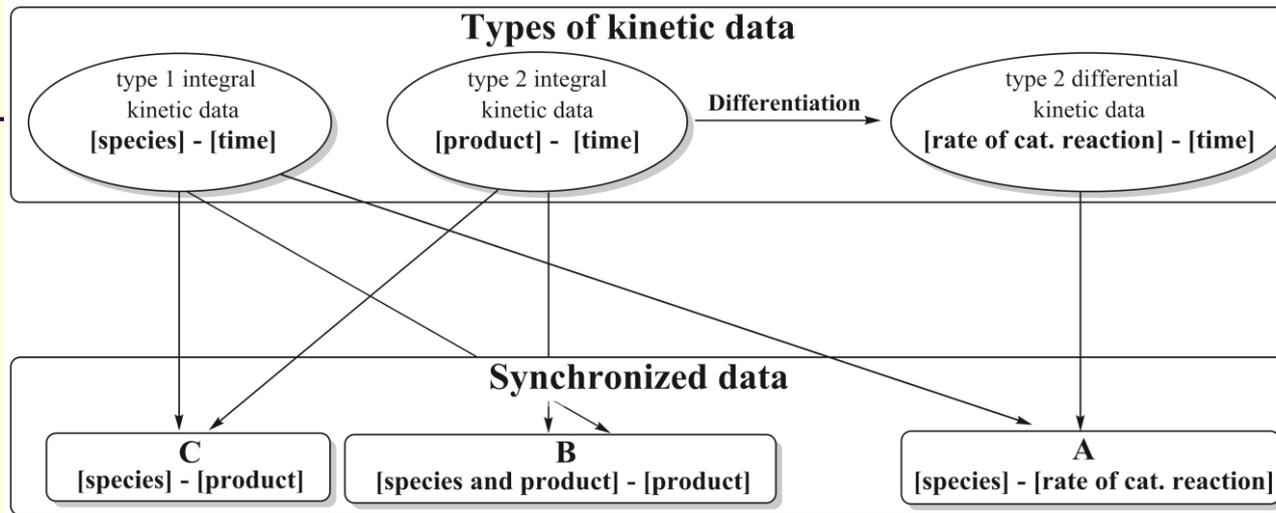
The example of complex mechanism of the catalytic reaction:
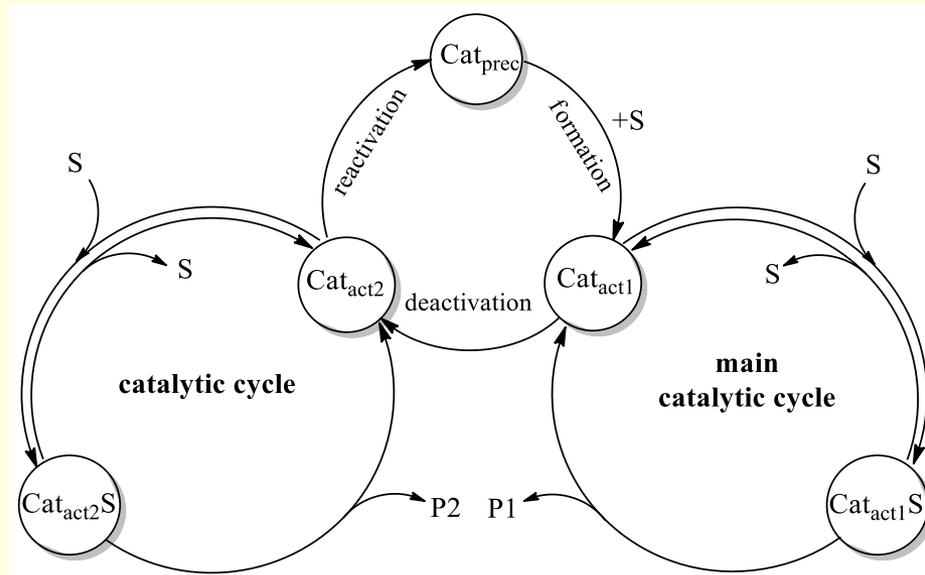
Catalytic system activity: synchronization of type 1 integral kinetic data with type 2 differential kinetic data
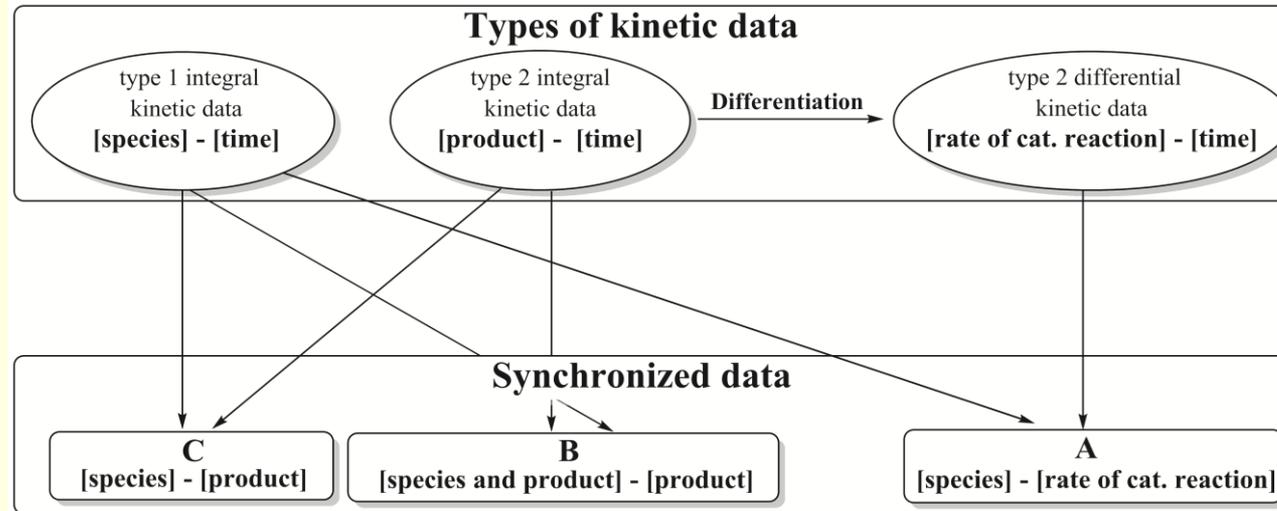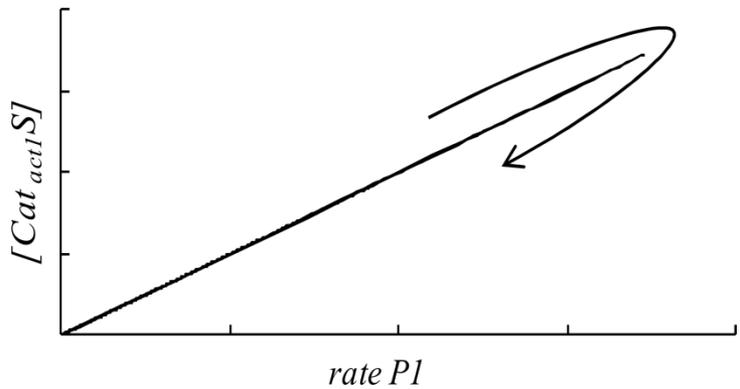
The participation of the species as catalytic cycle intermediate directly in the product formation step (i.e., the species are active)
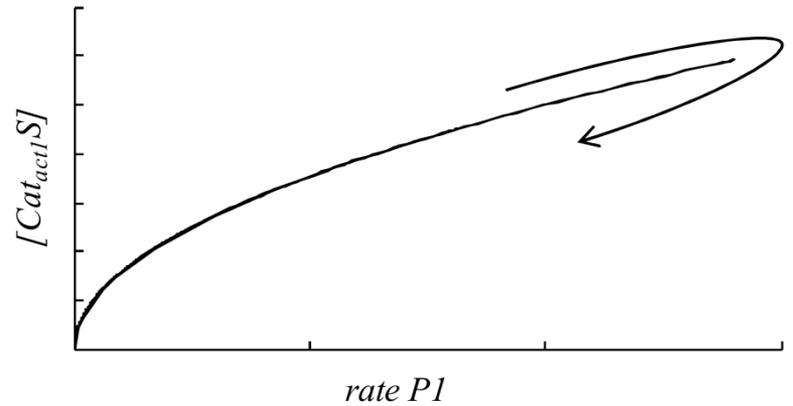
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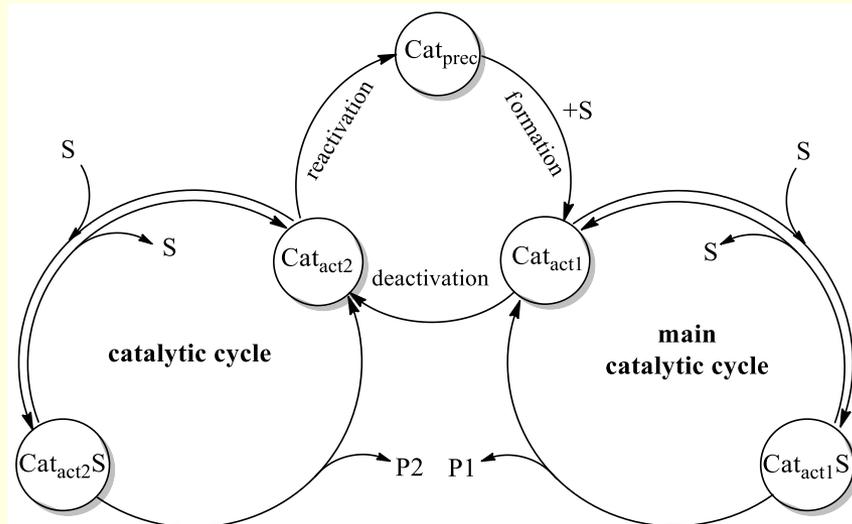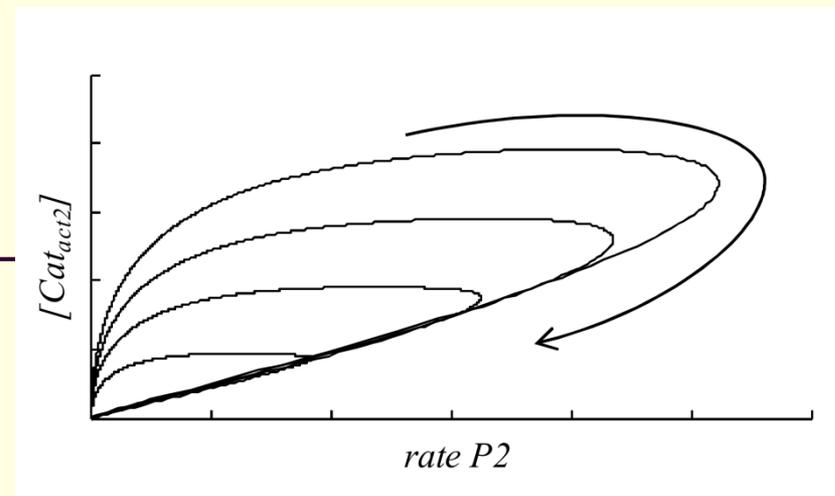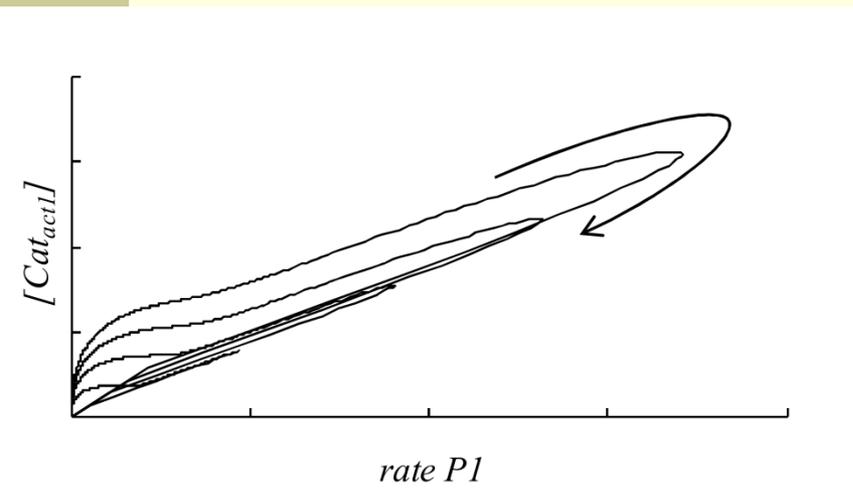
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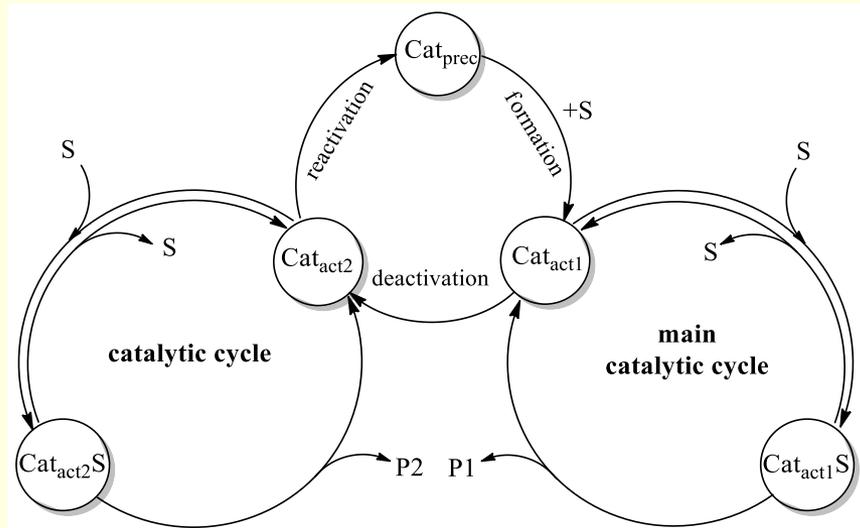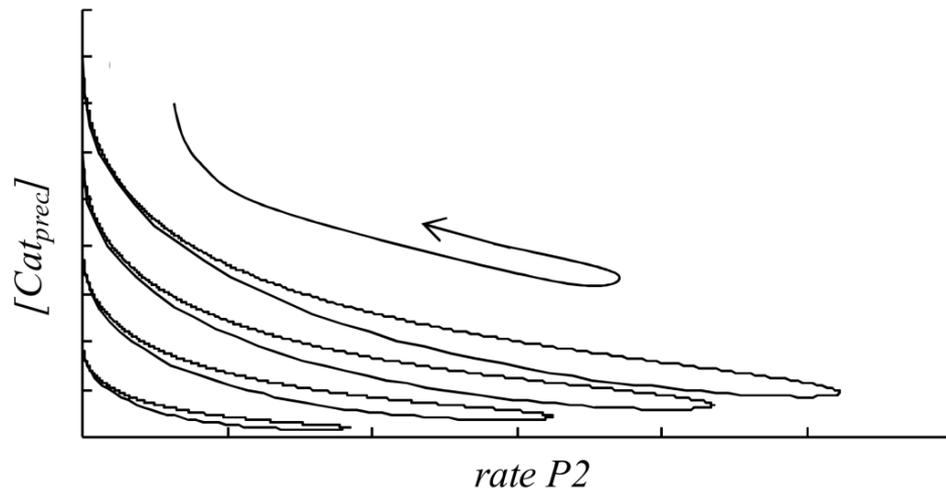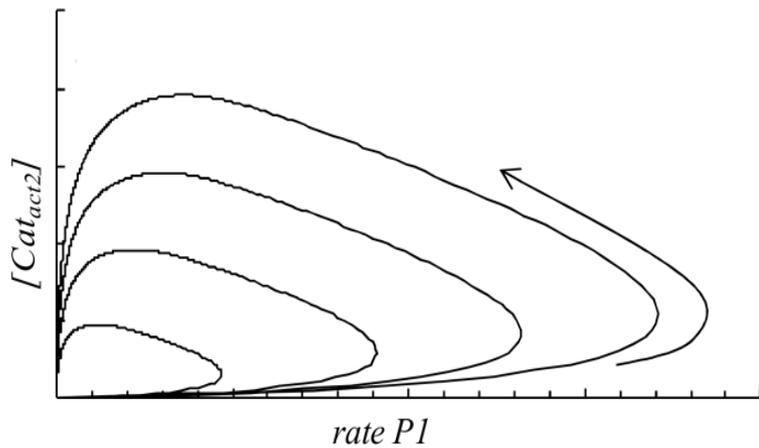
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The family of homo- and cross-coupling reactions of aryl halides with different reagents using ligand-free catalytic systems

Direct arylation of indole by iodobenzene

$$\text{indole} + \text{PhI} \xrightarrow[140^0C, \, DMF:H_2O=4:1]{PdCl_2} \text{2-Ph-indole}$$

Suzuki reaction

$$\text{PhI} + \text{PhB(OH)}_2 \xrightarrow[22\ ^0C, \, EtOH]{PdCl_2} \text{Ph-Ph}$$
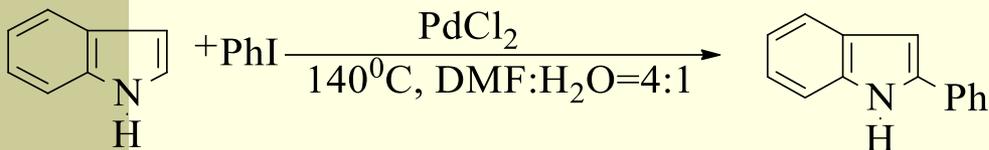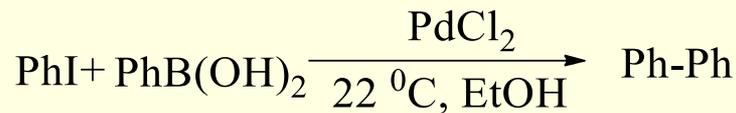
Heck reaction with benzoic anhydride

$$\text{Ph-CO-O-CO-Ph} + \text{=Ph} \xrightarrow[140^0C, \, NMP]{PdCl_2} \text{Ph-CH=CH-Ph} + \text{CH}_2\text{=C(Ph)}_2 + \text{Ph-CO-CH=CH-Ph} + \text{Ph-CO-CH}_2\text{-CH}_2\text{-Ph}$$
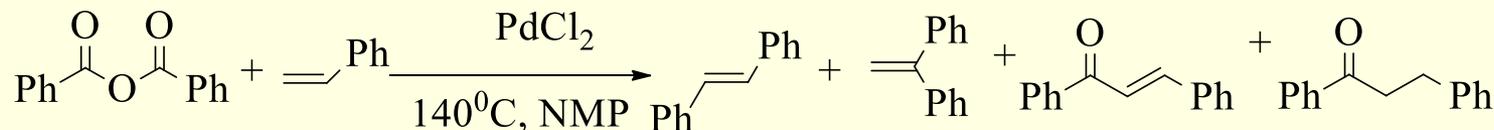
Heck reaction with bromobenzene
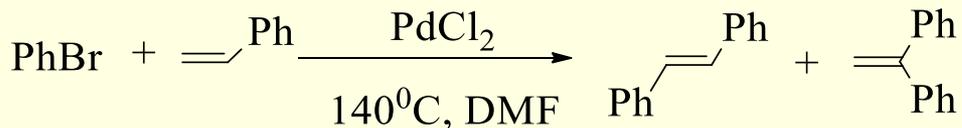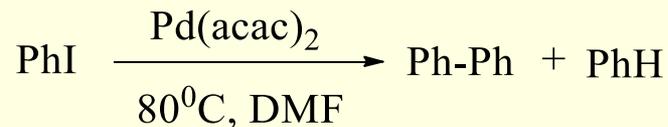
$$\text{PhBr} + \text{=Ph} \xrightarrow[140^0C, \, DMF]{PdCl_2} \text{Ph-CH=CH-Ph} + \text{CH}_2\text{=C(Ph)}_2$$

Reductive homocoupling of iodobenzene

$$\text{PhI} \xrightarrow[80^0C, \, DMF]{Pd(acac)_2} \text{Ph-Ph} + \text{PhH}$$

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The family of homo- and cross-coupling reactions of aryl halides with different reagents using ligand-free catalytic systems

$$ArX \; + \; Pd(0) \longrightarrow Ar\text{-}Pd\text{-}X$$

$$2Ar\text{-}Pd\text{-}X \longrightarrow Ar\text{-}Ar + Pd(0) + PdX_2$$
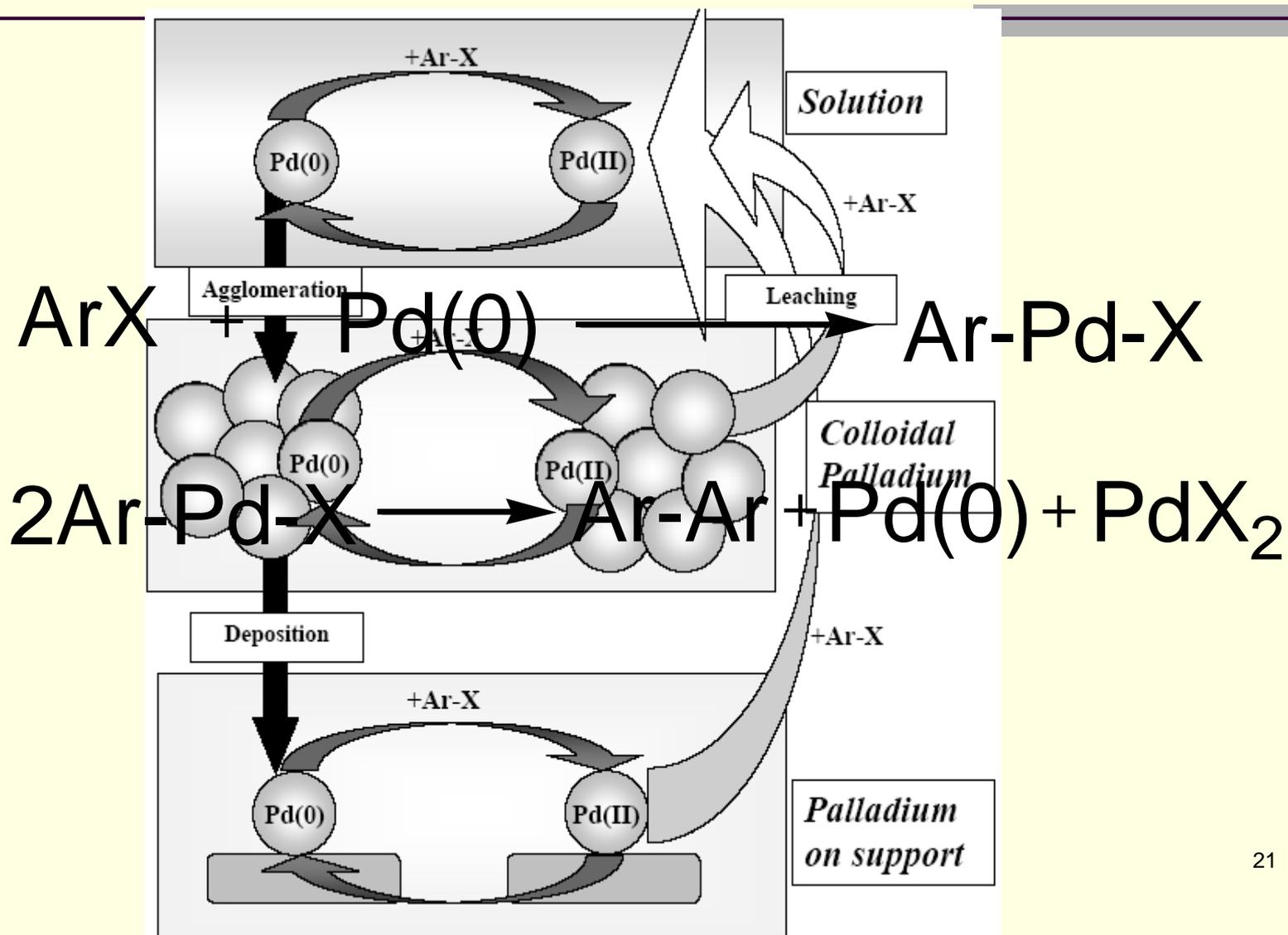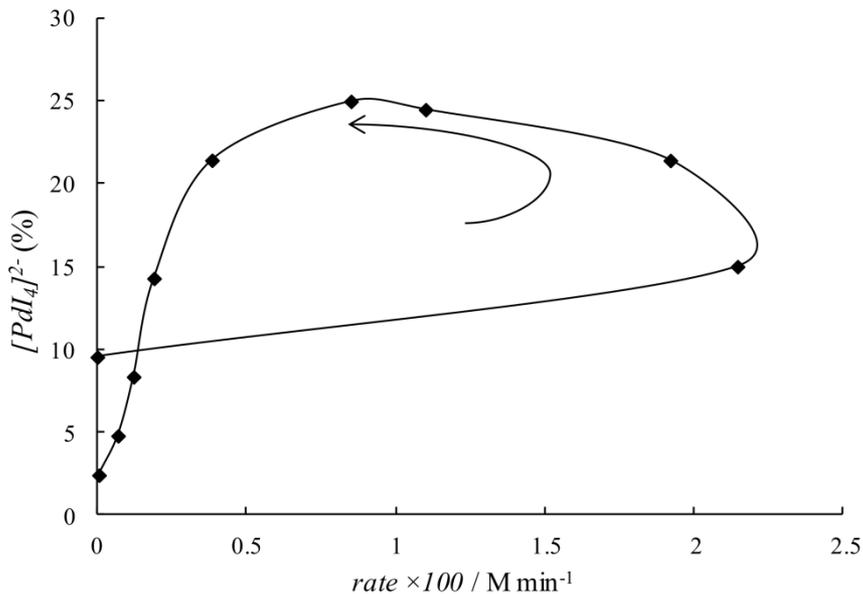
Percentage of $[PdI_4]^{2-}$ (relative to maximum possible concentration under the reaction conditions) vs. the rate of 2-phenylindole formation in the direct arylation of indole by iodobenzene using $PdCl_2$ as a catalyst precursor (reactions progress is indicated by an arrow)
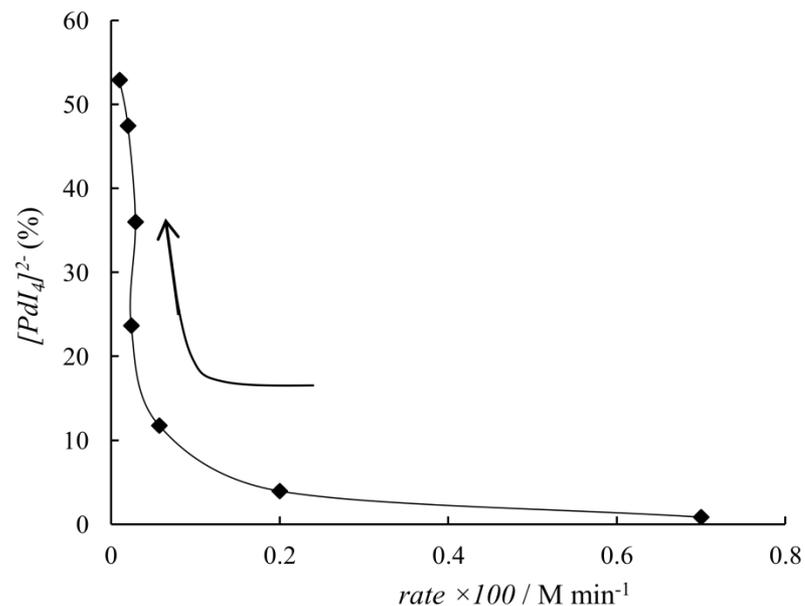
Percentage of $[PdI_4]^{2-}$ (relative to maximum possible concentration under the reaction conditions) vs. biphenyl formation rate in a Suzuki reaction of iodobenzene using $PdCl_2$ as a catalyst precursor (reactions progress is indicated by an arrow)
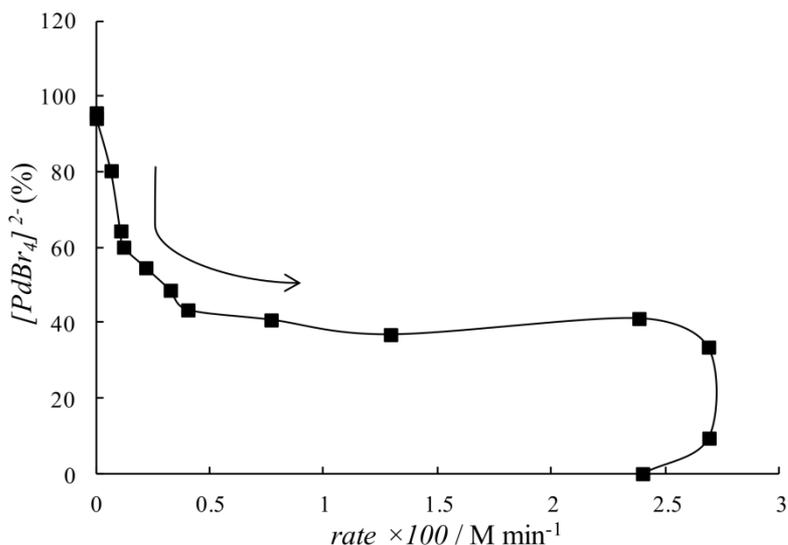
Percentage of $[PdBr_4]^{2-}$ (relative to maximum possible concentration under the reaction conditions) vs. stilbene formation rate in the Heck reaction of styrene and benzoic anhydride using NaBr-containing catalytic system and $PdCl_2$ as a catalyst precursor (reactions progress is indicated by an arrow)
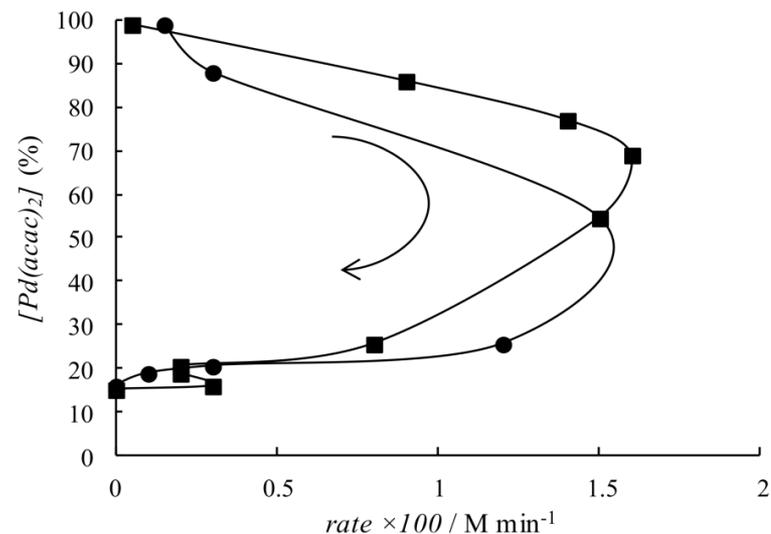
Percentage of $Pd(acac)_2$ (relative to maximum possible concentration under the reaction conditions) vs. rates of biphenyl (●) and benzene (■) formation in the reductive homocoupling of iodobenzene(reactions progress is indicated by an arrow)

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Catalytic system selectivity: synchronization of types 1 and 2 integral kinetic data
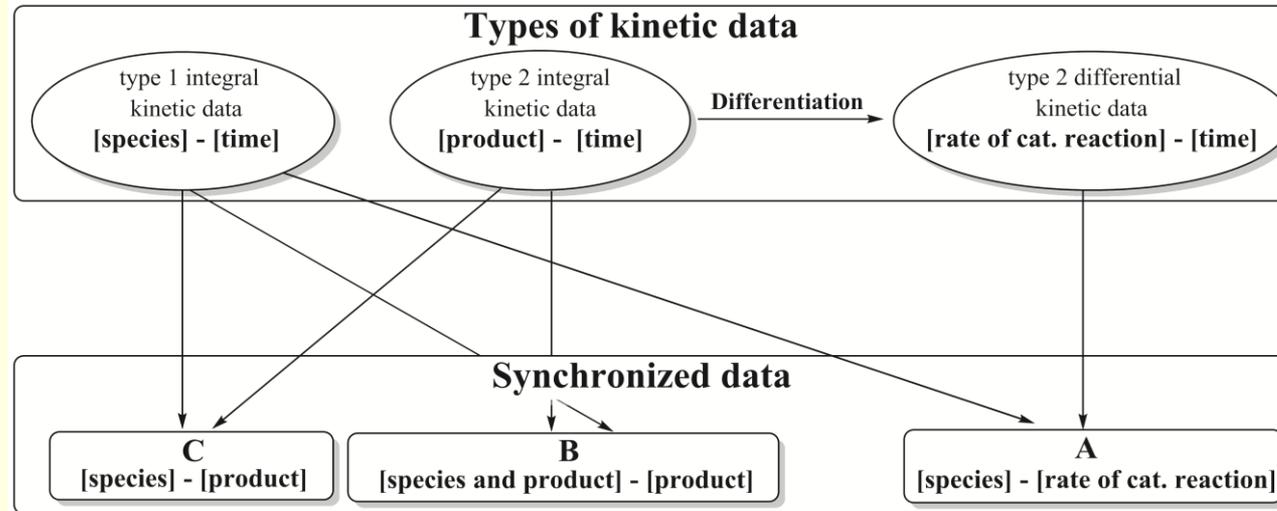
Differential selectivity

A. F. Schmidt, A. A. Kurokhtina and E.V. Larina, *Catalysis Science & Technology,* 2014**, 4,** 3439-3457*.*

$$Sel_{dif} = \frac{r_{P1}}{r_{P1} + r_{P2}} = \frac{1}{1 + r_{P2}/r_{P1}}$$

$$\frac{r_{P2}}{r_{P1}} = \frac{d[P2]/dt}{d[P1]/dt} = \frac{d[P2]}{d[P1]} = \frac{1 - Sel_{dif}}{Sel_{dif}}$$

Qualitative estimation of differential selectivity. The phase trajectories
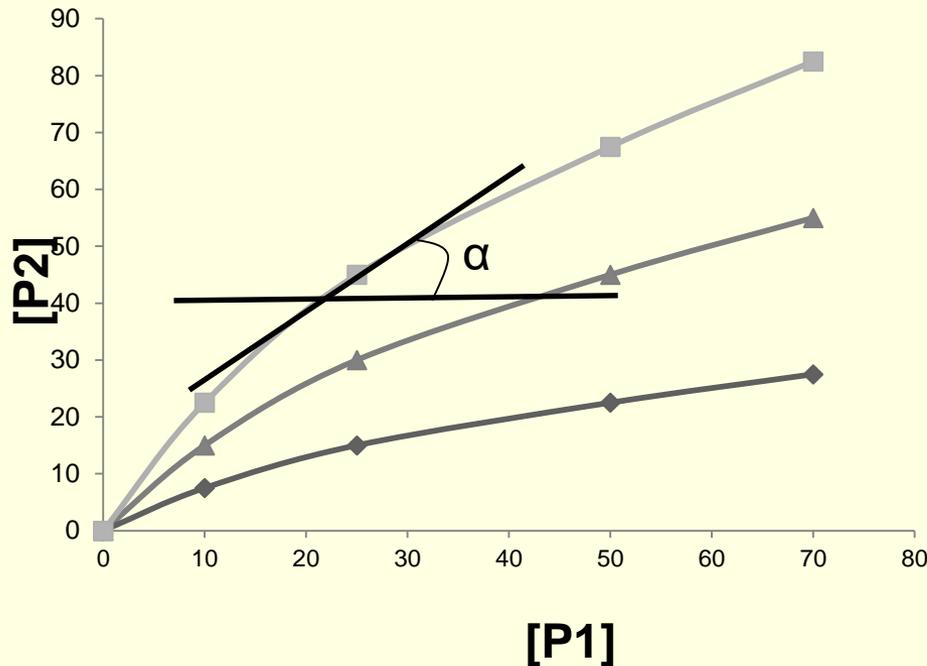
$$[P1] = f([P2])$$

$$r_{P1} = \frac{d[P1]}{dt}; \qquad r_{P2} = \frac{d[P2]}{dt}$$

$$\frac{r_{P2}}{r_{P1}} = \frac{d[P2]}{d[P1]}$$

$$tg\,\alpha = \frac{dP1}{dP2} = \frac{r_{P1}}{r_{P2}}$$
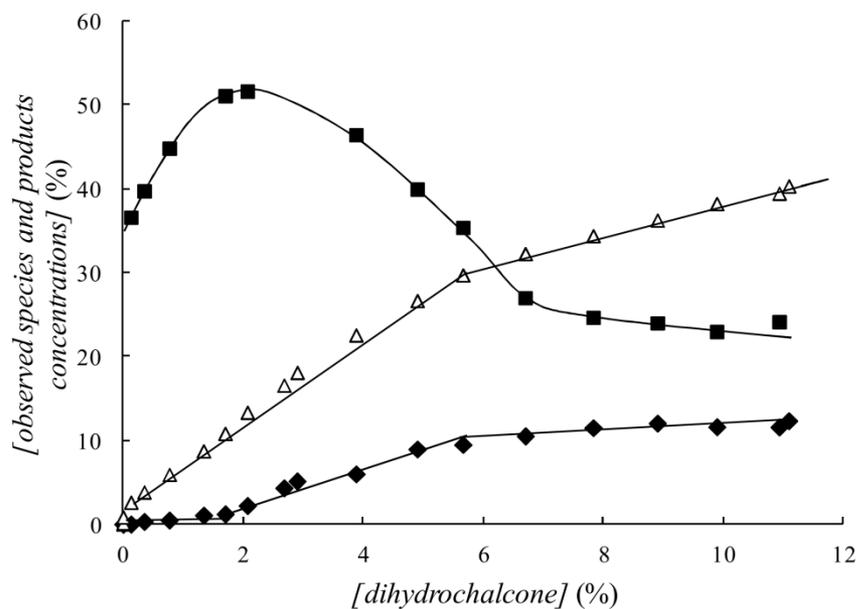
Percentages of $[PdBr_4]^{2-}$ (■), stilbene (△), and chalcone (♦) (relative to maximum possible concentrations under the reaction conditions) vs. percentage of dihydrochalcone using $PdCl_2$ as the catalyst precursor in the Heck reaction of styrene and benzoic anhydride

Using phase trajectories for elucidating the roles of observable catalyst species
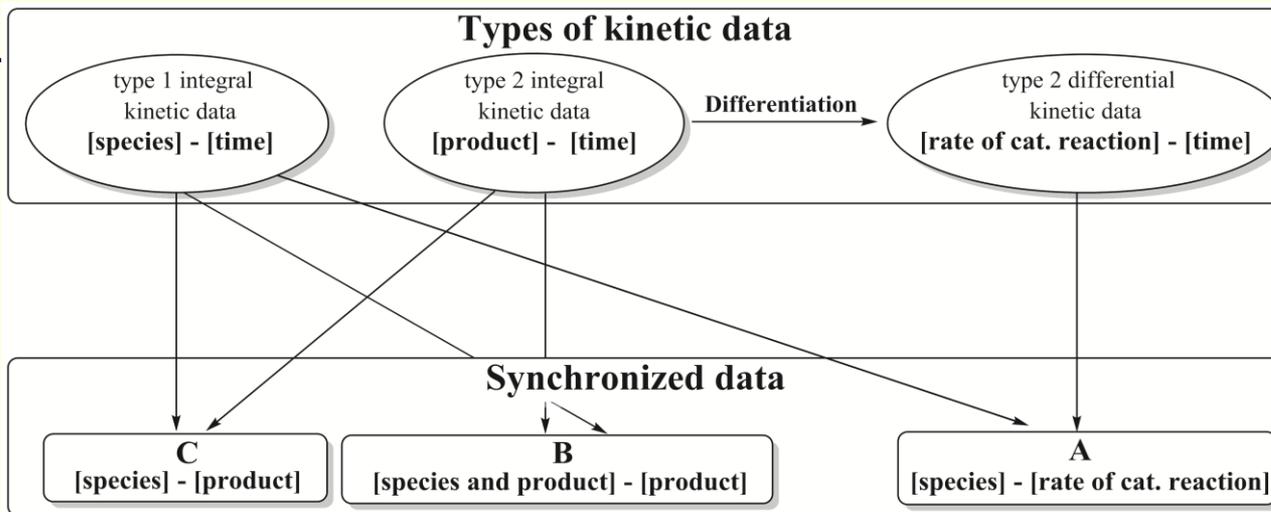
The example of complex mechanism of the catalytic reaction
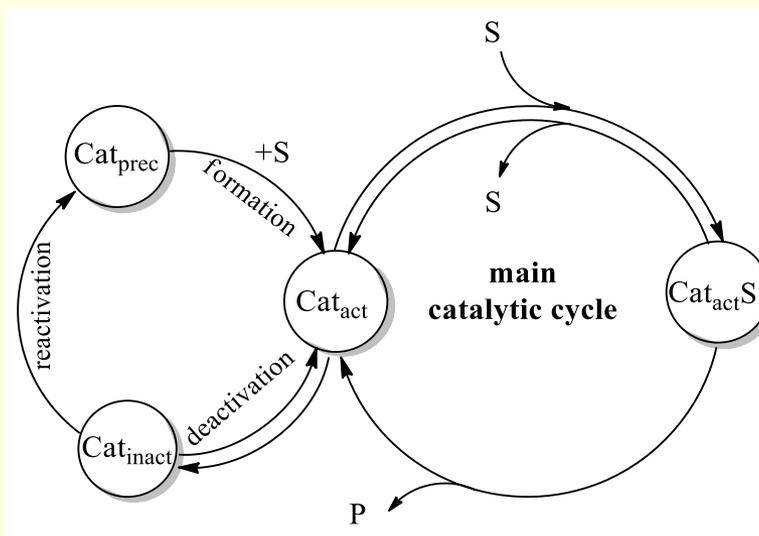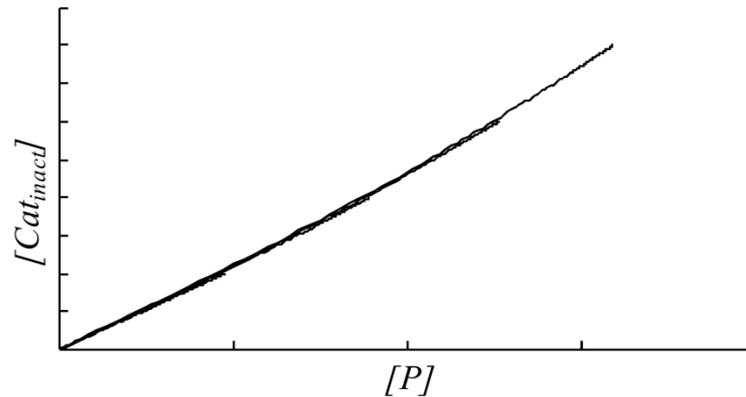
Simulated [species amount]–[product amount] dependences for inactive catalyst species (irreversible deactivation)

$$r_{cycle} = k_{cycle}[\text{I}] \qquad r_{deact} = k_{deact}[\text{I}]$$

where k_{deact} and k_{cycle} are the apparent rate constants of the deactivation of active species [I] and the catalytic reaction, respectively

$$\frac{r_{deact}}{r_{cycle}} = \frac{k_{deact}}{k_{cycle}}$$
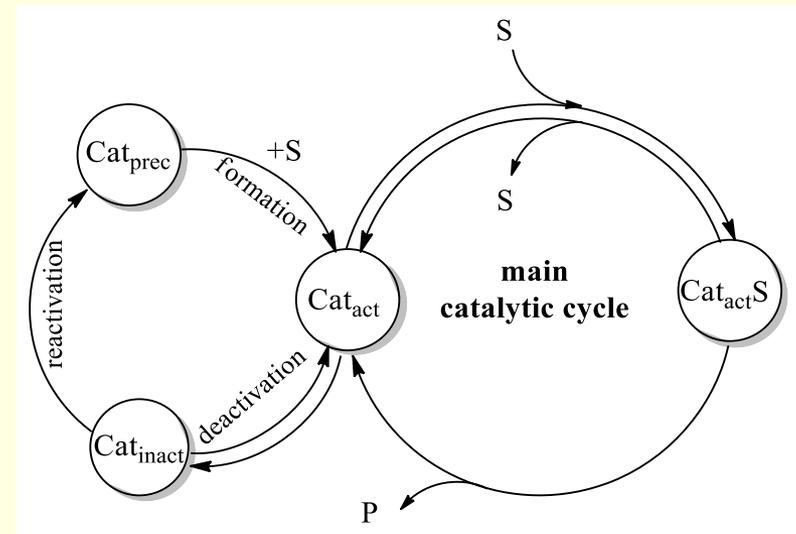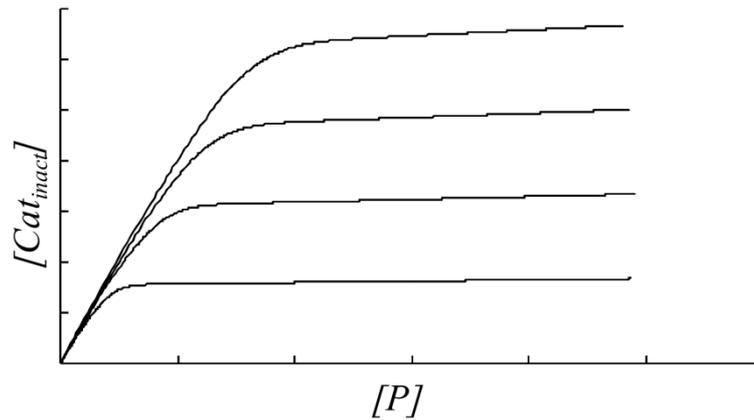
Simulated [species amount]–[product amount] dependences for inactive catalyst species (reversible deactivation)

$$r_{cycle} = k_{cycle} [I]$$

$$r_{deact} = k_{deact+}[I] - k_{deact-}$$

where k_{cycle} is the apparent rate constant of the catalytic reaction, and k_{deact+} and k_{deact-} are rate constants of direct and reverse deactivation, respectively

$$\frac{r_{deact}}{r_{cycle}} = \frac{(k_{deact+}[I] - k_{deact-})}{k_{cycle}[I]}$$
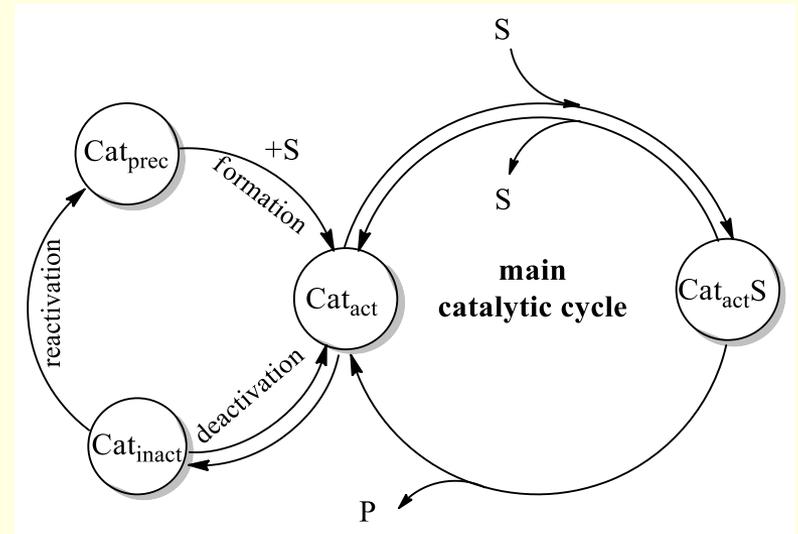
when $k_{deakt+}[I] \gg k_{deakt-}$: $\frac{r_{deact}}{r_{cycle}} = \frac{(k_{deact+}[I])}{k_{cycle}[I]} = \frac{k_{deact+}}{k_{cycle}}$
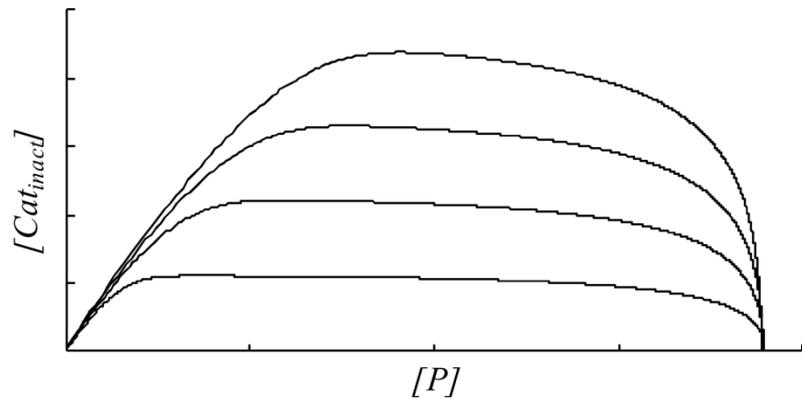
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Simulated [species amount]–[product amount] dependences for inactive catalyst species (deactivation is irreversible, but active species reactivation is possible as a result of a sequence of steps)
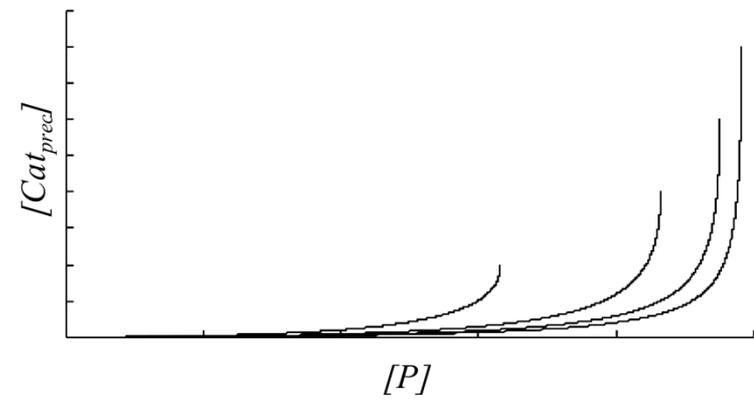
Simulated [species amount]–[product amount] dependences for inactive catalyst species (deactivation is irreversible and the observed inactive species are formed from the active one indirectly as a result of a sequence of steps)
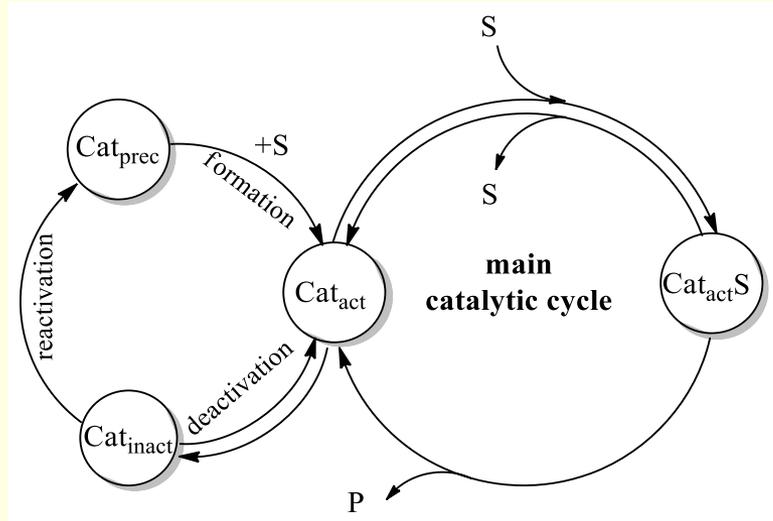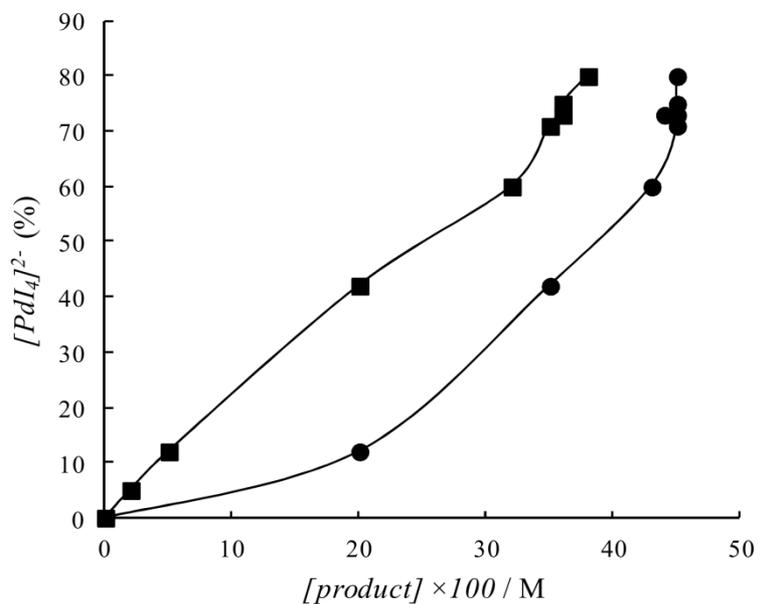
Percentage of $[PdI_4]^2$ (relative to maximum possible concentration under the reaction conditions) vs. concentrations of biphenyl (■) and benzene (●) in the reductive homocoupling of iodobenzene using Pd(acac)$_2$ as a catalyst precursor
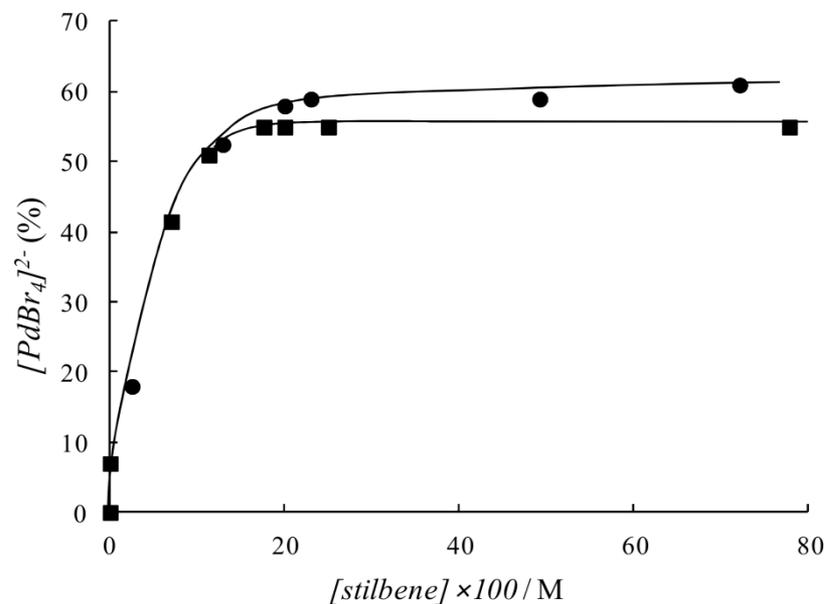
Percentage of $[PdBr_4]^{2-}$ (relative to maximum possible concentration under the reaction conditions) vs. stilbene concentration in the Heck reaction of styrene with bromobenzene using 0.8×10^{-2}M (■) and 1.6×10^{-2}M (●) PdCl$_2$ as a catalyst precursor
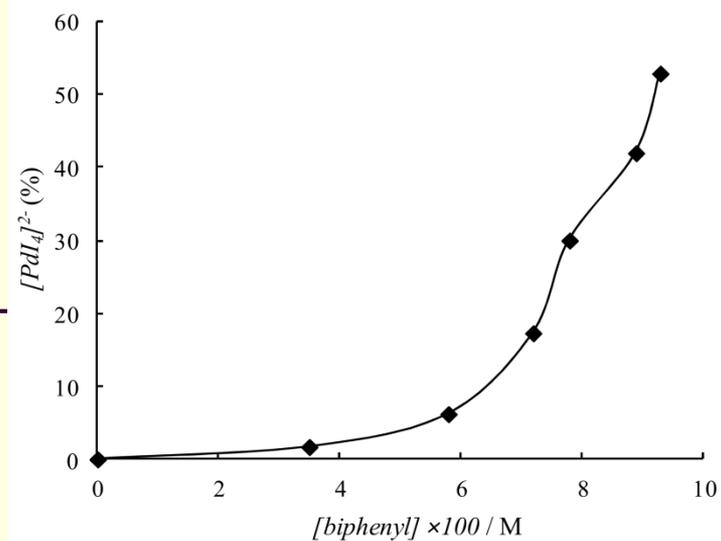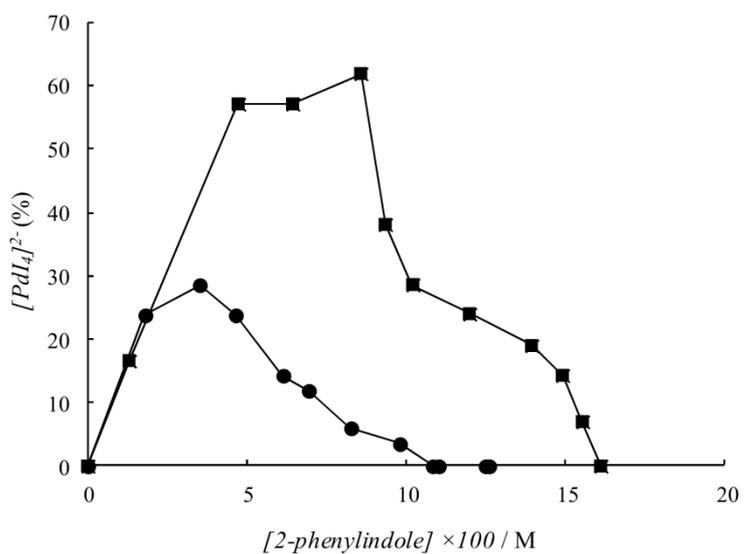
Percentage of $[PdI_4]^{2-}$ (relative to maximum possible concentration under the reaction conditions) vs. concentration of 2-phenylindole in the direct arylation of indole by iodobenzene using 1.6×10^{-2} M (●) and 3.2×10^{-2} M (■) levels of the catalyst precursor ($PdCl_2$)

Percentage of $[PdI_4]^{2-}$ (relative to maximum possible concentration under the reaction conditions) vs. concentration of biphenyl in the Suzuki reaction with iodobenzene using $PdCl_2$ as a catalyst precursor
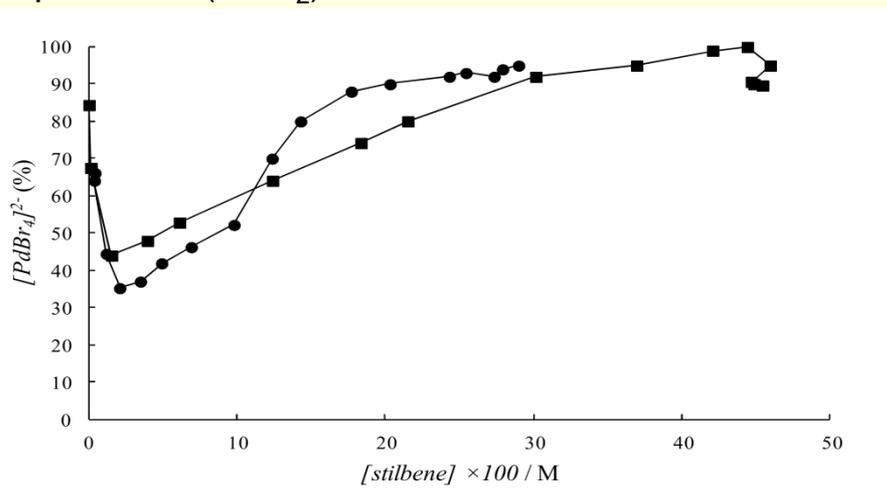
Percentage of $[PdBr_4]^{2-}$ (relative to maximum possible concentration under the reaction conditions) vs. concentration of stilbene using Na_2PdBr_4 (■) and $PdBr_2$ (●) as catalyst precursors in the Heck reaction of styrene with benzoic anhydride

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Establishing active species
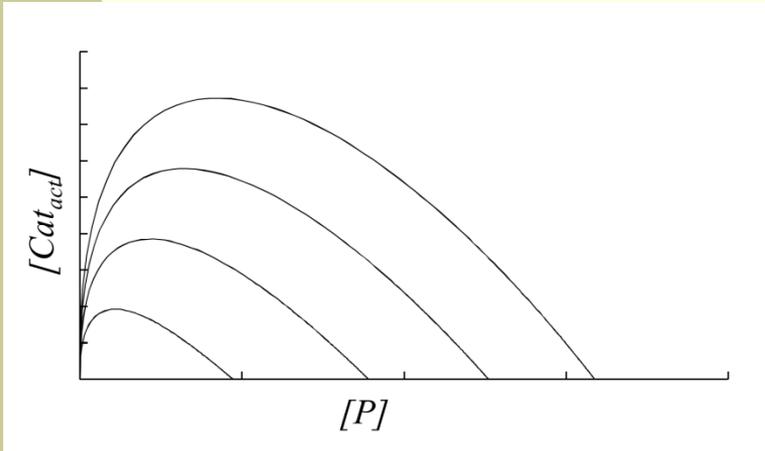
Simulation of [species amount]-[product amount] dependences for active catalyst species
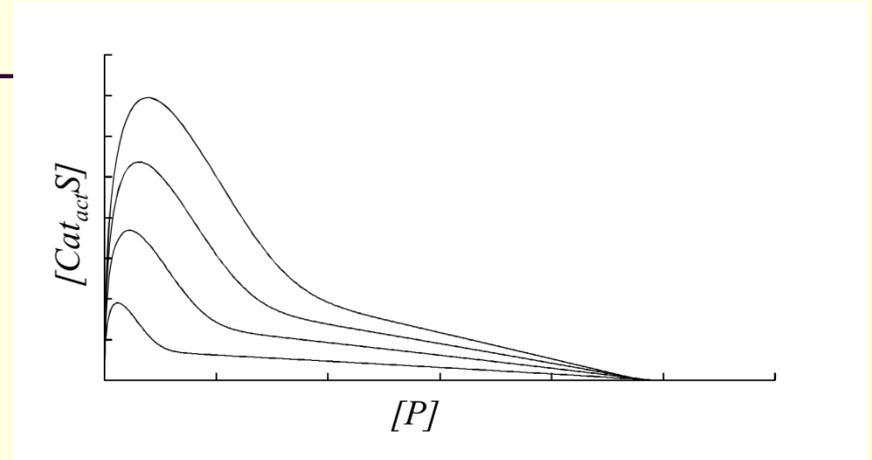
Simulation of [species amount]-[product amount] dependences for active catalyst species
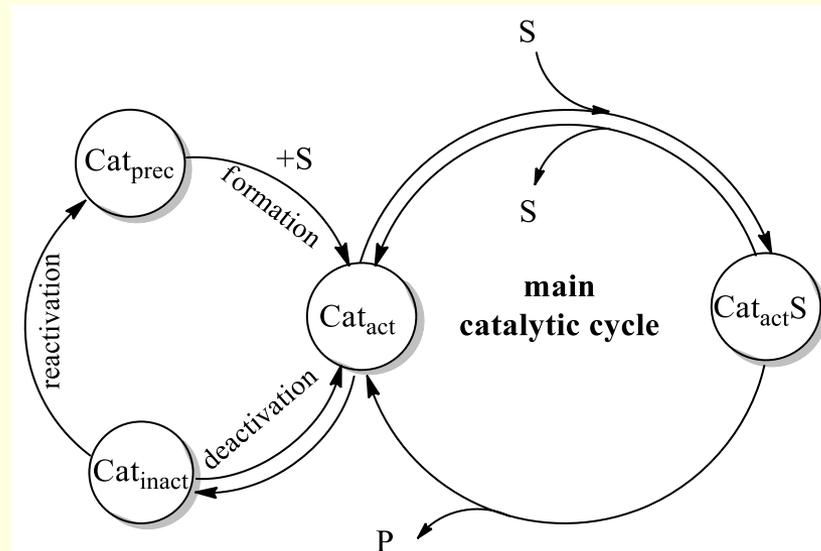
Conclusions

1. The establishing of the roles of the observed products of catalyst transformations in catalysis instead of their simple detecting should be considered as the main goal of operando studies from the fundamental as well as applied viewpoints.

2. The importance of simultaneous kinetic control of the reaction products and observed catalyst species is not taken into account very often. This does not allow using all possibilities of operando studies.

3. Only the synchronization of integral and differential kinetic data on the accumulation of the reaction products and observed catalyst species allows elucidating the roles of the latter in catalysis.

4. Operando kinetic studies allow obtaining information not only on main catalytic cycle but also on catalyst transformations occurring outside it (formation, deactivation and reactivation).

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