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DISCUSSION

THE COMPLEMENTARITY PRINCIPLE IN CHEMICAL REACTIONS

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New reactions are usually discovered in the course of experiments. On the other hand, there is another "method" for discovering new reactions to be discussed below, in which the course and mechanism of a reaction can be predicted and the predicted structure as though known in advance is confirmed by physicochemical methods of analysis.

The theoretical basis for such prediction is the complementarity principle proposed by Niels Bohr. "When viewpoints differ to the point of inconsistency, it may be that such viewpoints give a true picture of things only when taken together". "Contradictions do not contradict each other but only supplement each other". [1]. The principle of complementarity was discovered in 1927 but the argument between Joseph Proust and Claude Berthollet on the law of definite proportions (1801-1807) may be considered a manifestation of this principle in chemistry. We first encountered this principle relative to chemical reactions and the experimental discovery of reactions.

We will take below different viewpoints as an already studied reaction and a still unknown reaction. In the former (A), the most characteristic features are determined in order to distinguish the latter (B) by directly opposite features. Hence, concepts are formed about the still unknown reaction and the number of possible pathways for its accomplishment is reduced to a minimum and sometimes to a single pathway. If the known reaction A is general, then new reaction B is most likely the same. The special nature of reaction A is reflected in limitations in syntheses according to scheme B. These are examined together for a more complete description of the properties of compounds and, primarily, of reactants, while in the case of identical structure of reactants, they combine into a single common reaction. An important role is given to orienters – indicators. We shall illustrate the manifestation and use of the complementarity principle by two "pairs" of reactions, in which type-B are described by us for the first time.

1. Reduction of isatins to give indoles (A) and the indolinedione-indole rearrangement (B) [2, 3] (Scheme 1). The most characteristic features of the reduction of isatins **1** to give indoles **2** are that isatins and the reducing agents B_2H_6, $NaBH_4$, and $LiAlH_4$ are the reactants. The reduction of both CO groups proceeds without opening of the five-membered ring. The orienter for prediction and discovery of the indolinedione-indole rearrangement was the well-known method for the purification of isatins: the impure preparation

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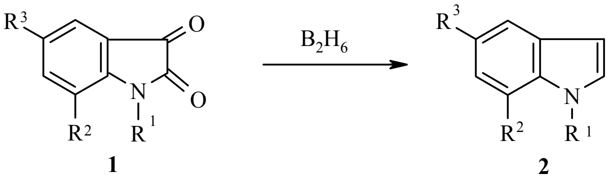
is dissolved in an aqueous solution of an equimolar amount of NaOH, the five-membered ring immediately opens to give the sodium salt of isatinic acid, the insoluble impurities are filtered off, and purified isatin is precipitated from the aqueous layer upon acidification

In the case of the indolinedione-indole rearrangement, the five-membered ring of the key N-acylmethylisatin **3** obtained from isatins and halomethyl ketones is readily opened upon dissolution in aqueous alkali (NaOH) and alcoholic solutions of sodium alcoholate (BuONa in BuOH). The sodium salt of isatinic acid and its incomplete orthoester have the same arrangement of functional groups so that cyclization to give 2-acylindole-3-carboxylic acid through aldol and ester condensation mechanisms is unavoidable. Thus, isomerization is used instead of reducing agents.

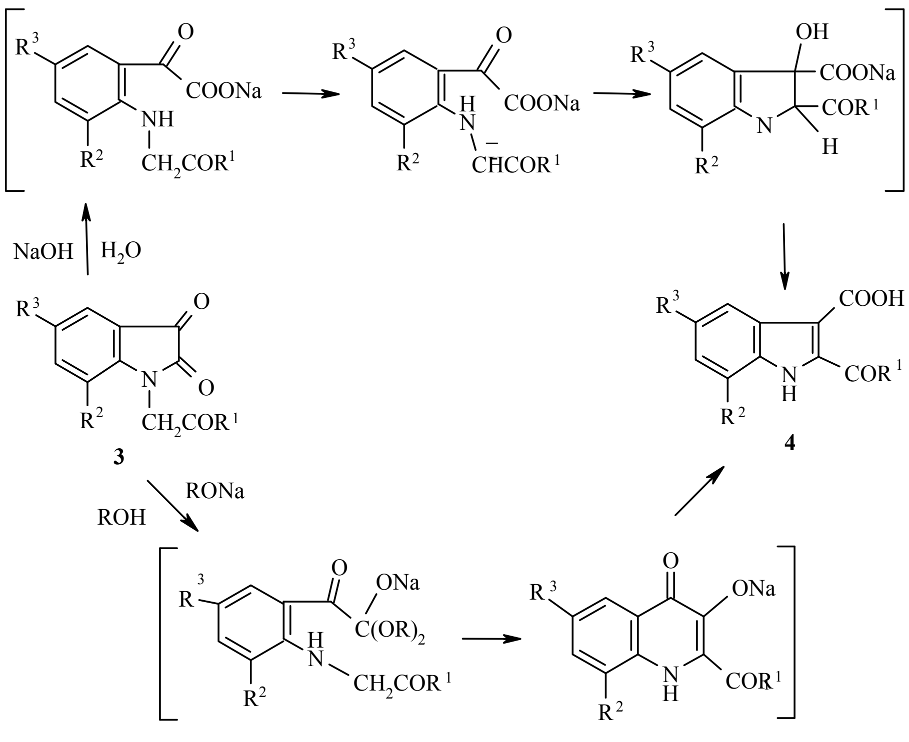
Scheme 1

Reaction A:



$R^1 = R^2 = R^3 = H$; $R^1 = Me$, $R^2 = R^3 = H$; $R^1 = R^3 = H$; $R^2 = F, Br, I, NO_2$; $R^1 = H$, $R^2 = R^3 = Br$

Reaction B:



$R^1 = Me, Et, Pr, CHMe–CH_2Me, CH_2CHMe_2, CHEt_2, Ph, 4\text{-}BrC_6H_4, 4\text{-}Cl$; $R^2 = H, Me$;
$R^3 = H, Me, MeO, Cl, Br$

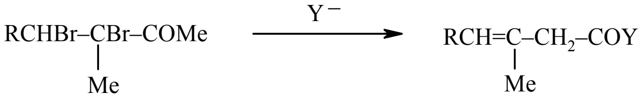
Both reactions are general and are considered together in describing the transformations of the oxidized form of indole into the reduced form. In this case, we may also note limitations of each of the reactions. The limitation in the first reaction is the impossibility of synthesizing indoles with aldehyde and ketone groups in the benzene ring. The limitation in the second reaction is the impossibility of synthesizing acids such as **4** with alkyl or aryl substituents at the nitrogen atom.

2. Favorsky Rearrangement (A) and Synthesis of Enamines of β-Diketones (B) [4, 5] (Scheme 2). The successive loss of the α- and β-halogen atoms as HBr is one of the characteristic features of the Favorsky rearrangement of α,β-dibromo ketones. The final product is a β,γ-unsaturated carboxylic acid. The orienter for the development of reaction B is the mechanism of the Favorsky rearrangement.

The most characteristic features of enamine synthesis are as follows. Even in the case of a 10-fold excess of amine (imidazole, 1,2,4-triazole, piperidine, diethylamine), which serves both as a reactant and base, the β-bromine atom is the first to be lost at temperatures from -20 to 110-120°C followed by the α-bromine atom. The final product is an enamine of a β-diketone. The rearrangement and enamine synthesis are general in nature. Taken together, these reactions give a more general concept of the properties of α,β-dibromo ketones than when examined separately.

Scheme 2

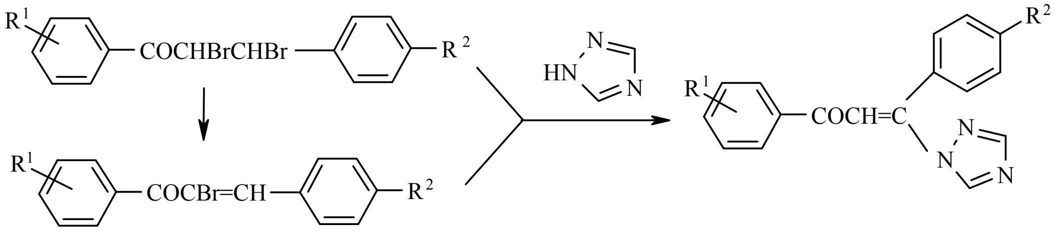
Reaction A:



$$\mathrm{RCHBr{-}\underset{\underset{\displaystyle Me}{|}}{C}Br{-}COMe} \xrightarrow{Y^-} \mathrm{RCH{=}\underset{\underset{\displaystyle Me}{|}}{C}{-}CH_2{-}COY}$$

R = Alk, Ar; Y = OH, AlkO, NH_2, NR^1_2; R^1 = H, Alk

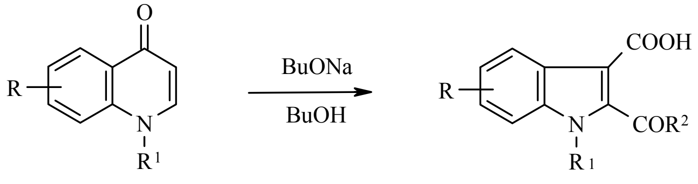
Reaction B:



$R^1 = R^2 = H$; $R^1 = 4\text{-Cl}$, $R^2 = H$; $R^1 = 4\text{-Cl}$, $R^2 = \text{Cl}$; $R^1 = 2,4\text{-Cl}_2$, $R_2 = NO_2$;
$R^1 = H$, $R^2 = \text{OMe}$; $R^1 = 4\text{-Cl}$, $R^2 = \text{OMe}$; $R^1 = 4\text{-Cl}$, $R^2 = NO_2$

3. Modification of the indolinedione-indole rearrangement. In light of their role in chemical transformations, reactants and intermediates are seen as opposites. This is the basis for a conclusion concerning modifications in the indolinedione-indole rearrangement.

The one-step isomerization of 1-alkyl-, 1-aryl-, or 1-H-2-acyl-3-hydroxy-4-quinolones to give 1-alkyl-, 1-aryl-, or 1-H-2-acylindole-3-carboxylic acids is called the quinolone-indole rearrangement.



R – substituents at C(5)–C(8); R^1 = H, alkyl, aryl

The same quinolones but without a substituent at the nitrogen atom preceded as intermediates the formation of the final products in Scheme 2 and, thus, this reaction is already confirmed experimentally. The original and modified rearrangements proceed through a single mechanism under identical conditions, while the final products differ only by the substituents at the nitrogen atom. We should note significantly that the N-alkyl derivatives of the acids are obtained in a multistep synthesis. Thus, the most important limitation in the first of these reactions is removed.

Other examples of application of the complementarity principle in chemical reactions are devoted to various areas of chemistry. Such examples are not treated in this communication.

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