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The Wolff Rearrangement. I. Kinetic Studies of the Decomposition of α-Diazoacetophenone[*1]

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Kinetic studies of the Wolff rearrangement of α-diazoacetophenone were performed in *t*-butyl alcohol, by the volumetric measurement of the evolved nitrogen, using a solution of silver benzoate in triethylamine as a catalyst. A pseudo-first-order rate constant was obtained accompanying the induction period. The effects of the concentrations of silver benzoate and triethylamine on the reaction rate were studied. The concentration of silver ions was determined by the gravimetric measurement of silver chloride in the course of the reaction. The silver ions were found to be consumed only in the initial stage of the reaction. On the basis of these results, a novel reaction mechanism, in which the active entity of the catalyst was thought to be a silver ion-triethylamine complex, was proposed.

Several reviews of the Wolff rearrangement have been published1−7) because of its usefulness in converting acids to derivatives of the homologous acids (Arndt-Eistert Synthesis). The rearrangement is catalyzed by silver oxide, silver nitrate,8,9) and silver benzoate,10) and also promoted by heat11) or ultraviolet light,12,13) particularly in the presence of copper-powder,14) cupric oxide,15) cuprous halide,10,16) and cuprous acetate.10) The products have been rationalized by assuming a ketene intermediate (III).7,17)

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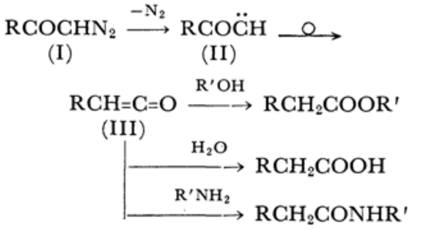

$$\underset{\text{(I)}}{\mathrm{RCOCHN_2}} \xrightarrow{-\mathrm{N_2}} \underset{\text{(II)}}{\mathrm{RCO\ddot{C}H}} \xrightarrow{\circ} \underset{\text{(III)}}{\mathrm{RCH{=}C{=}O}} \begin{cases} \xrightarrow{\mathrm{R'OH}} \mathrm{RCH_2COOR'} \\ \xrightarrow{\mathrm{H_2O}} \mathrm{RCH_2COOH} \\ \xrightarrow{\mathrm{R'NH_2}} \mathrm{RCH_2CONHR'} \end{cases} \quad (1)$$

Franzen[18] and Hugget[19] established the migration of the phenyl group of α-diazoacetophenone by tracer studies of carbonyl-^{14}C and -^{13}C compounds respectively. However, no kinetic study has yet been reported because of the heterogenity of the system. About twenty years ago, however, Newman and Beal[10] reported that homogeneous reaction conditions could be obtained by using a solution of silver benzoate in triethylamine as a catalyst; they proposed the free-radical chain mechanism of Eqs. (3)—(7).

We have, then, studied the catalytic Wolff rearrangement of α-diazoacetophenone kinetically under Newman's homogeneous conditions in order to clarify the reaction mechanism.

Experimental

Materials. *α-Diazoacetophenone.* This was prepared according to the method of Newman[20] and was purified by several recrystallizations from petroleum benzine, as pale yellow crystals (mp 47.5—48.0°C).

Silver Benzoate. Into an aqueous solution (200 m*l*) of 2.0 g (50 mmol) of sodium hydroxide, 6.1 g (50 mmol) of benzoic acid were dissolved, and the solution was heated at 80°C. Into this solution, there was then vigorously stirred a hot solution (200 m*l*) of 8.5 g (50 mmol) of silver nitrate. The silver benzoate precipitated was collected over hot filter, washed with 100 m*l* of hot water, dried under a vacuum, and stored in the dark.

Triethylamine. Commercial triethylamine was dried over metallic sodium and distilled under an atmosphere of nitrogen. A middle fraction (bp 87.9—88.0°C) was collected.

Isopropyl Alcohol and t-Butyl Alcohol. Commercial isopropyl alcohol and *t*-butyl alcohol were purified by distillation using an amount of metallic sodium sufficient to remove the water involved. Isopropyl alcohol: bp 82.3—82.5°C; *t*-butyl alcohol: bp 82.5—82.7°C.

Kinetic Measurement. The reaction rate was measured by reading the volume of nitrogen evolved into an azotometer. A solution of α-diazoacetophenone (I′) (0.73 g, 5.0 mmol) in 100 m*l* of a solvent was taken in a reaction vessel, immersed in a constant-temperature water bath (accuracy ± 0.01°C), and allowed to reach thermal equilibrium. The silver-amine catalyst was prepared by dissolving an exact amount of silver benzoate in a certain amount of triethylamine. The silver solution in a weighing bottle was dropped into the reaction vessel, and the reaction vessel was connected to the azotometer. The volume of nitrogen evolved was measured at moderate intervals until the volume of nitrogen reached 70—80% of the theoretical amount. The infinite volume, V_∞, of nitrogen was measured after ten times the time of the half-period had passed. During the measurement the reaction vessel was kept still, but a couple of pieces of crushed glass were added in the vessel in order to prevent the supersaturation of nitrogen. As the rate constant might be sensitive to a slight difference in reaction conditions, the same batches of solvents and catalyst were employed in each series of kinetic measurements.

Rearranged Product. After the reaction was over, the pieces of crushed glass and precipitated metallic silver were filtered off, and the solvent was removed under reduced pressure. The residue was hydrolyzed with an aqueous alcoholic solution of potassium hydroxide. On acidifying the alkaline layer with hydrochloric acid, phenylacetic acid was obtained in a 70% yield. Mp 76.0—77.0°C.

Quantitative Analysis of Unreacted Silver Ions. The rearrangement was carried out as has been described above, using 100 m*l* of isopropyl alcohol as a solvent; this is more convenient solvent for this treatment than *t*-butyl alcohol. After an appropriate time[*3] the reaction was stopped by cooling the solution in a dry ice - ethanol bath (at -70°C). Then the precipitated metallic silver was quickly separated out by centrifuge, and the silver ions remaining in the alcoholic layer were converted to silver chloride by adding 10 m*l* of concentrated hydrochloric acid; the unchanged I′ was also thus converted to phenacyl chloride. The amount of silver chloride was determined as follows: the mixture was evaporated to 5 m*l*[*4] under reduced pressure, and then cooled. The silver chloride was collected over a glass filter, washed several times with 5 m*l* of ethanol, dried for 2 hr in an air bath at 90°C, and weighed.

Results

The decomposition of α-diazoacetophenone (I′) has been carried out in *t*-butyl alcohol in the presence of various amounts of silver benzoate. The rates of the reaction were followed by reading the volume of the nitrogen collected. The amount of nitrogen evolved, in every case, is closely quantitative, and about 70% of the phenylacetic acid was obtained after hydration.

The catalytic decomposition of α-diazoacetophenone (I′) has an induction period of about 10% of the total course of the reaction. Except for the initial period, the reaction appeared to be of a pseudo-first-order with respect to the evolution of nitrogen. The rate constant, k, was thus calculated according to Eq. (2):

$$kt = 2.303 \times \log (V_\infty/(V_\infty - V_t)) \qquad (2)$$

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[*3] The reaction percentage was calculated from the volume of nitrogen evolved.

[*4] When the silver chloride was filtered out before the evaporation of the alcoholic layer, the amount of silver chloride obtained was decreased by a few percentage points.

where the reaction time, t, is taken from the apparent end of the induction period, where V_∞ indicates the total volume of nitrogen, and V_t the volume of nitrogen at time t. Some typical results are shown in Figs. 1 and 2.

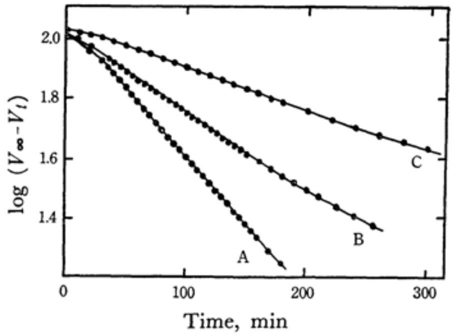

Fig. 1. Typical first-order plots of the Wolff rearrangement of I′ catalyzed by silver benzoate in t-butyl alcohol, at 30.00°C.

	C_6H_5COOAg	$(C_2H_5)_3N$
A:	0.100 g	2.0 ml
B:	0.100 g	4.0 ml
C:	0.050 g	2.0 ml

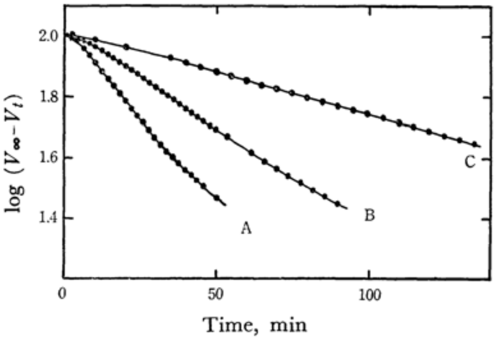

Fig. 2. Examples of the deviation from first-order plot according to the increase of the amount of silver benzoate.

	C_6H_5COOAg	$(C_2H_5)_3N$
A:	0.300 g	4.0 ml
B:	0.200 g	4.0 ml
C:	0.100 g	4.0 ml

When a smaller amount of silver benzoate (0.050—0.100 g) was used, the induction period covered about 10—20 min, during which time about 10 ml of the nitrogen was evolved; Eq. (2) was satisfied for a long time. However, if a larger amount (0.200—0.300 g) of the catalyst was employed, the extent which followed the first-order equation became narrower, as is shown in Fig. 2, and the reproducibility of the reaction rate became a little worse.

Secondly, the effect of the concentration of triethylamine on the rate was investigated, keeping the initial concentrations of silver benzoate (0.100 g, 0.44 mmol) and I′ (0.730 g, 5.0 mmol) constant. The results are listed in Table 1. The rate constant decreased in proportion to the decrease in the concentration of amine when 1.0—3.0 ml of triethylamine was used, while the rate converged to a constant as the amount of the amine increased to more than 3.0 ml. Similarily, the effect of the concentration of silver benzoate was investigated, keeping the amounts of triethylamine (2.0 and 4.0 ml) and I′ (5.0 mmol) constant. The results are summarized in Table 2. As Table 2 shows, the rate constant increased with the increase in the amount of silver benzoate in proportion to 1.46 and 1.33 powers of the catalyst amount.

The concentration of silver ions was followed by the gravimetric determination of silver chloride during the course of the reaction. The results in

TABLE 1. EFFECT OF TRIETHYLAMINE CONCENTRATION ON THE REACTION RATE OF THE WOLFF REARRANGEMENT OF I′ IN t-BUTYL ALCOHOL*

$(C_2H_5)_3N$ ml	$k\times10^4$ min^{-1}
1.0	93.4 ± 3.9
2.0	71.1 ± 0.8
3.0	63.0 ± 0.4
4.0	61.2 ± 0.4
5.0	62.1 ± 0.6

* Following reaction condition was used.
I′: 5.0 mmol, silver benzoate: 0.100 g (0.44 mmol), t-butyl alcohol: 100 ml, at 30.00°C.

TABLE 2. CORRELATION OF SILVER BENZOATE CONCENTRATION WITH REACTION RATE OF THE WOLFF REARRANGEMENT OF I′ IN t-BUTYL ALCOHOL*

C_6H_5COOAg g	$k\times10^4$, min^{-1}	
	$(C_2H_5)_3N$ 2.0 ml	$(C_2H_5)_3N$ 4.0 ml
0.050	30.1 ± 1.1	26.1 ± 0.6
0.100	71.1 ± 0.8	61.2 ± 0.4
0.150	145. ± 1.0	112. ± 3.
0.200	197. ± 3.	164. ± 10.
0.250	300. ± 9.	200. ± 16.
0.300	428. ± 13.	300. ± 23.

* Following reaction condition was utilized.
I′: 5.0 mmol, t-butyl alcohol: 100 ml, at 30.00°C

TABLE 3. THE QUANTITATIVE ANALYSIS OF SILVER ION IN THE COURSE OF THE WOLFF REARRANGEMENT*

Reaction, %	Deposited AgCl, %
7.3	75.0
8.0	71.2
20.9	71.9
51.2	71.9
78.6	72.7
100.	71.3

* Following reaction condition was applied.
I′: 5.0 mmol, silver benzoate: 0.100 g (0.44 mmol), triethylamine: 2.0 ml, isopropyl alcohol: 100 ml

Table 3 suggest that a certain quantity of silver ions is consumed rather simultaneously within the initial ten minutes, which may be comparable to the induction period. However, practically no more silver ions were consumed, and even at the end of the reaction about 70% of the initial amount still remained.

Discussion

Newman and Beal[10)] have proposed a free radical chain mechanism (Eqs. (3)—(7)) with regard to the silver salt-catalyzed Wolff rearrangement:

$$\underset{\text{(I)}}{\mathrm{RCOCHN_2}} + (\mathrm{C_2H_5})_3\mathrm{N} \rightleftarrows \underset{\text{(IV)}}{[\mathrm{RCO\ddot{C}{=}N_2}]^{\ominus}} + (\mathrm{C_2H_5})_3\mathrm{NH}^{\oplus} \qquad (3)$$

$$\underset{\text{(IV)}}{[\mathrm{RCO\ddot{C}{=}N_2}]^{\ominus}} + \mathrm{Ag}^{\oplus} \longrightarrow \underset{\text{(V)}}{[\mathrm{RCO\dot{C}{=}N_2}]} + \mathrm{Ag}\downarrow \qquad (4)$$

$$\underset{\text{(V)}}{[\mathrm{RCO\dot{C}{=}N_2}]} \xrightarrow{\circlearrowright} \underset{\text{(VI)}}{[\mathrm{R{-}\dot{C}{=}C{=}O}]} + \mathrm{N_2} \qquad (5)$$

$$\underset{\text{(VI)}}{[\mathrm{R{-}\dot{C}{=}C{=}O}]} + \underset{\text{(I)}}{\mathrm{RCOCHN_2}} \longrightarrow \underset{\text{(III)}}{\mathrm{RCH{=}C{=}O}} + \underset{\text{(V)}}{[\mathrm{R\dot{C}OC{=}N_2}]} \qquad (6)$$

$$\underset{\text{(III)}}{\mathrm{RCH{=}C{=}O}} + \mathrm{R'OH} \longrightarrow \mathrm{RCH_2COOR'} \qquad (7)$$

This proposal is based on the following experimental results:

1) Triethylamine is an inevitable reagent to promote the rearrangement, even when alcohol-soluble silver trifluoroacetate is used as a catalyst.

2) α-Diazoacetophenone does not change under the experimental conditions which lead to a successful Wolff rearrangement of α-diazoacetophenone.

3) The evolution of nitrogen is suppressed by the addition of hydroquinone to a reaction mixture that was reacting smoothly.

If the rearrangement proceeds through such a scheme, and if the reaction (4) proceeds during the whole course of the reaction, the quantity of silver ions must be gradually decreased as the reaction proceeds. Our observation indicates, however, that the only significant decrease in silver ions occurs within the initial ten minutes, and that about 70% of silver ions still remain in the reaction mixture at the end of the reaction. This strongly suggests that the reaction (4) proceeds only in the initial stage of the reaction. In Newman's mechanism the precipitation of metallic silver is inevitably accompanied by rearrangement. Assuming that silver ions or their amine complex would have no more catalytic action, the active species propagating the decomposition must be some free radicals, such as V and VI, in this mechanism. According to our experiments, the addition of another batch of the diazoketone to the mixture remaining after complete reaction gave rise to the evolution of nitrogen. Some active catalyst must therefore, be still alive in the solution after the complete decomposition of the diazoketone. The free radicals (V) and (VI) could not be expected to have such a long life as is suggested by Newman's mechanism, so this catalyst must be silver ions or their amine complex, $[\mathrm{Ag(C_2H_5)_3N}]^{\oplus}$.

One of our noticeable findings is that silver nitrate, in the absence of triethylamine, also has a catalytic action on the rearrangement of α-diazoacetophenone in either an ethanol or an isopropyl alcohol solution, thus leading to esters of phenylacetic acid. Furthermore, in these cases no precipitation of metallic silver is observed. Because of the low solubility of silver nitrate in these alcohols, the reaction may be correspondingly slower than that of a silver benzoate-catalyzed reaction. On the other hand, the addition of triethylamine to this solution resulted in the precipitation of metallic silver, with a considerable increase in the rate. Triethylamine is not necessarily essential to the rearrangement, but in effect it contributes to some deposition of metallic silver independently of the rearrangement. From these results, it seems significant that the reaction essentially needs catalysis by certain silver ions, perhaps in the complex form, but the reduction of the ions or the complex seems not to be essential to the real course of the decomposition. This suggests that the formation of metallic silver is due to reaction with some co-catalyst present in the solution.

Newman reported that the inhibition of the reaction was effected by the addition of hydroquinone to the reaction mixture. Hydroquinone seems not to act as a scavenger of free radical intermediates, but as a reducing agent of silver ions. The presence of some co-catalyst might be supported by the fact that the formation of metallic silver, which has already been established as having no catalytic action, is observed only in the initial stage of the reaction. One possible co-catalyst is oxygen dissolved in the reaction system. The rearrangement carried out in an atmosphere of argon was found still to be accompanied by the precipitation of metallic silver. When a certain amount of α-diazoacetophenone was added in a closed system to the clear part of the reaction mixture (the supernatant solution of the reaction mixutre) after the reaction had been allowed to proceed to completion, the evolution of nitrogen was observed again, with no precipitation of metallic silver. In ordinary reactions, the removal of a trace of oxygen involved is very difficult, and the amount of precipitated metallic silver varies to some extent with the reaction conditions. Therefore, a trace of oxygen can be one of the possible co-catalysts for the production of metallic silver. These results appear to be better elucidated in terms of the following scheme:

$$\underset{\text{(I)}}{RCOCHN_2} + (C_2H_5)_3N \rightleftarrows \underset{\text{(IV)}}{[RCO\ddot{C}{=}N_2]^\ominus} + (C_2H_5)_3NH^\oplus \tag{3}$$

$$\underset{\text{(IV)}}{[RCO\ddot{C}{=}N_2]^\ominus} + [AgN(C_2H_5)_3]^\oplus \longrightarrow \underset{\text{(VII)}}{[RCO\ddot{C}{=}N_2^\ominus{-}^\oplus AgN(C_2H_5)_3]} \tag{8}$$

$$\underset{\text{(VII)}}{[RCO\ddot{C}{=}N_2^\ominus{-}^\oplus AgN(C_2H_5)_3]} \longrightarrow \underset{\text{(VIII)}}{[RCO\underset{\cdot\cdot}{\ddot{C}}{}^\ominus{-}^\oplus AgN(C_2H_5)_3]} + N_2 \tag{9}$$

$$\underset{\text{(VIII)}}{[RCO\underset{\cdot\cdot}{\ddot{C}}{}^\ominus{-}^\oplus AgN(C_2H_5)_3]} \xrightarrow{\Omega} \underset{\text{(IX)}}{[R{-}\ddot{C}{=}C{=}O]^\ominus} + [AgN(C_2H_5)_3]^\oplus \tag{10}$$

$$\underset{\text{(IX)}}{[R{-}\ddot{C}{=}C{=}O]^\ominus} + BH \longrightarrow \underset{\text{(III)}}{RCH{=}C{=}O} + B^\ominus \tag{11}$$

$$\underset{\text{(III)}}{RCH{=}C{=}O} + R'OH \longrightarrow RCH_2COOR' \tag{7}$$

BH: $(C_2H_5)_3NH^\oplus$, $RCOCHN_2$, $R'OH$, *etc.*

The reaction of the diazoketone-anion (IV), formed by the rapid equilibrium (3), with the amine complex of silver ions leads to the complex intermediate (VII)*5 (Eq. (8)). This complex (VII) releases nitrogen gas and forms an anion-complex (VIII) (Eq. (9)). This anion-complex (VIII) rearranges to the ketene-anion, (IX), reproducing the silver-amine complex (Eq. (10)), which is also repeatedly used as a catalyst by reactions (8) and (9). The ketene-anion (IX) and an acid, BH, form a ketene (III) (Eq. (11)); the subsequent addition of an alcohol gives the ester (Eq. (7)):

$$\underset{\text{(VII)}}{[RCO\ddot{C}{=}N_2^\ominus{-}^\oplus AgN(C_2H_5)_3]} + \text{Co-catalyst} \longrightarrow \underset{\text{(X)}}{[RCO\dot{C}{=}N_2{-}\text{Co-catalyst}]} + Ag\downarrow + N(C_2H_5)_3 \tag{12}$$

$$\underset{\text{(X)}}{[RCO\dot{C}{=}N_2{-}\text{Co-catalyst}]} \longrightarrow \underset{\text{(V)}}{[RCO\dot{C}{=}N_2]} + \text{Co-catalyst} \tag{13}$$

On the other hand, in the presence of a co-catalyst such as oxygen, the production of metallic silver and the diazoketone-co-catalyst complex (X) might be expected (Eq. (12)). If the complex X is decomposed to the co-catalyst and a diazoketone-radical (V) (Eq. (13)), ketene will be formed on the nitrogen left in accordance with Newman's mechanism (Eqs. (5) and (6)). It seems reasonable to consider that the reaction (12) occurs only in the initial stage of the reaction, and that the step (5) is not faster than the step (9). Moreover, the regeneration of the co-catalyst would promote Eq. (12), and a further consumption of silver ions would occur. The reaction of the intermediate complex (X) is considered to lead to some side reactions, but the details of these side reaction are not yet apparent. Since the reaction steps (3) and (8) are in rapid equilibria, the rate-determining step of this rearrangement must be the reaction (9), indicating that the reaction is pseudo-first-order with respect to diazoketone.

The effect of the amount of silver benzoate on the reaction rate is also explained by Eq. (8). As has been noted before, the dependency of the rate on the concentration of silver ions was found to be a little higher than first-order. However, if the deposition of silver metal in the initial stage is essentially independent of the decomposition of diazoketone, the real reaction rate might be closer to a first-order dependency on the concentration of silver ion. The effect of triethylamine may be explained by either the solvent effect on the stability of the complex VII, resulting in a slight retardation of the reaction (9), or the so-called solvent effect due to the variation in the polarity of the reaction medium. Even in the absence of amine, the reaction might proceed through the ketocarbene-ketene intermediate, as is shown in Eq. (1).

Perhaps Newman's mechanism can not be neglected in the initial stage, in which the precipitation of metallic silver occurs, but it is not generally applied throughout the reaction. Other problems of interest are whether the elimination of nitrogen and the migration of R group occur in two steps (Eqs. (9) and (10)) or in one concerted step (Eq. (14)), and the nature of the electronic structure of the transition state or the intermediate.

$$\underset{\text{(VII)}}{[RCO\ddot{C}{=}N_2^\ominus{-}^\oplus AgN(C_2H_5)_3]} \xrightarrow{\Omega} \underset{\text{(IX)}}{[R{-}\ddot{C}{=}C{=}O]^\ominus} + N_2 + [AgN(C_2H_5)_3]^\oplus \tag{14}$$

In order to clarify the problem, the substituent effect on the reaction rate and the kinetic isotope effect of carbonyl-^{14}C- and phenyl-1-^{14}C-labeled α-diazoacetophenone have been studied. The results will be presented in subsequent reports.

The authors wish to express their hearty thanks to Professor Matsuji Takebayashi for his valuable discussions.

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*5 Instead of the $[AgN(C_2H_5)_3]^\oplus$ of the complex (VII) and (VIII) $Ag^\oplus[N(C_2H_5)_3]_2$ can play the same role. The precise structure of the complex (VII), that is, the nature and the position of the bond formed between silver ions and the diazoketone-anion, is not clear.