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The Wolff Rearrangement. V. Kinetic Isotope Effect of α-Diazoacetophenone*1

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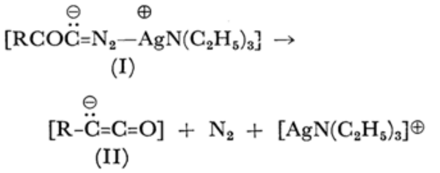
Kinetic isotope effect of the Wolff rearrangement of carbonyl-^{14}C and phenyl-1-^{14}C labeled α-diazoacetophenone was measured in *t*-butyl alcohol at 30°C, using a solution of silver benzoate in triethylamine as a catalyst. No apparent kinetic isotope effect was observed in both cases within experimental error. These results suggest that the elimination of nitrogen and the migration of phenyl group proceed in two steps in the rate-determining step.

In the previous papers of this series, we have reported the kinetic studies of the Wolff rearrangement of α-diazoacetophenone,1) and substituent effect of substituted α-diazoacetophenones catalyzed by silver benzoate in alcohols.2) From these results it was concluded that the rate-determining step of this reaction was that of elimination of nitrogen. In this case following two mechanisms are possible;

a) A concerted one-step mechanism in which elimination of nitrogen and migration of alkyl group proceed synchronously.

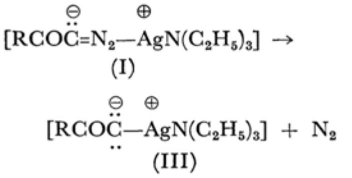
b) Two-step mechanism in which the elimination of nitrogen proceeds in the first step, followed by migration of alkyl group.

One-step mechanism

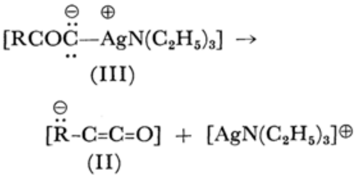


$$\underset{\text{(I)}}{[\mathrm{RCO}\overset{\ominus}{\ddot{\mathrm{C}}}{=}\overset{\oplus}{\mathrm{N_2}}{-}\mathrm{AgN(C_2H_5)_3}]} \rightarrow$$
$$\underset{\text{(II)}}{[\mathrm{R}{-}\overset{\ominus}{\ddot{\mathrm{C}}}{=}\mathrm{C}{=}\mathrm{O}]} + \mathrm{N_2} + [\mathrm{AgN(C_2H_5)_3}]^{\oplus} \qquad (1)$$

Two-step mechanism



$$\underset{\text{(I)}}{[\mathrm{RCO}\overset{\ominus}{\ddot{\mathrm{C}}}{=}\overset{\oplus}{\mathrm{N_2}}{-}\mathrm{AgN(C_2H_5)_3}]} \rightarrow$$
$$\underset{\text{(III)}}{[\mathrm{RCO}\overset{\ominus}{\underset{\cdot\cdot}{\ddot{\mathrm{C}}}}{-}\overset{\oplus}{\mathrm{Ag}}\mathrm{N(C_2H_5)_3}]} + \mathrm{N_2} \qquad (2)$$



$$\underset{\text{(III)}}{[\mathrm{RCO}\overset{\ominus}{\underset{\cdot\cdot}{\ddot{\mathrm{C}}}}{-}\overset{\oplus}{\mathrm{Ag}}\mathrm{N(C_2H_5)_3}]} \rightarrow$$
$$\underset{\text{(II)}}{[\overset{\ominus}{\ddot{\mathrm{R}}}{-}\mathrm{C}{=}\mathrm{C}{=}\mathrm{O}]} + [\mathrm{AgN(C_2H_5)_3}]^{\oplus} \qquad (3)$$

The kinetic isotope effect may be useful to distinguish these two mechanisms, in other words, to get the precise information on the transition state of this reaction. In this connection, Fry and his co-workers have studied the kinetic isotope effect of the Curtius rearrangement of phenyl-1-^{14}C, carbonyl-^{14}C and ^{15}N labeled benzazide.3) We have studied the kinetic isotope effect of the Wolff rearrangement of α-diazoacetophenone-(carbonyl-^{14}C) (IVa) and α-diazoacetophenone-(phenyl-1-^{14}C) (IVb), when triethylamine solution of silver benzoate was used as a catalyst.

Results and Discussion

Kinetic isotope effects of the Wolff rearrangement of (IVa) and (IVb) were determined as follows; Sampling of 10 m*l* of reaction mixture at every ten minutes after the initiation of the reaction, converting the unreacted IV in each sample into a 2,4-dinitrophenylhydrazone of phenacyl chloride by the reaction with 2,4-dinitrophenylhydrazine in the presence of hydrochloric acid, burning the purified hydrazone by modified van Slyke wet-oxidation method,4) and absorbing the carbon dioxide into an aqueous barium hydroxide solution to give barium carbonate, and counting the radio activity of the barium carbonate by G. M. counter after disk formation. The results obtained were

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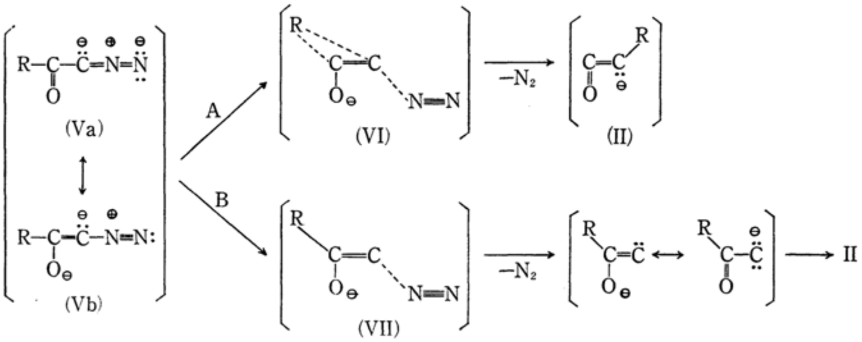
1) Y. Yukawa, Y. Tsuno and T. Ibata, This Bulletin, **40**, 2613 (1967).

2) Y. Yukawa, Y. Tsuno and T. Ibata, *ibid.*, **40**, 2618 (1967).

[*3] Triethylamine silver ion complex is omitted in V for simplicity, see Refs. 1 and 2.

3) A. Fry, private communication.

4) T. Noguchi, "Experimental Technique on Isotope," Vol. I, Nankodo, Tokyo (1955), p. 95.



given in Tables 1 and 2. Radio activity of each run was constant within experimental and counting error of ±2%, and no kinetic isotope effect was observed for IVa and IVb.

One of the most important factors of kinetic isotope effect is the variation of the zeropoint energy difference between the transition state and the reaction origin of the rate-determining step by means of heavy and light isotopic compounds. In other words, the partial bond breaking and bond formation with respect to labeled atom in the transition state causes the alternation of the vibrational frequency of that bond and consequently leads to the kinetic isotope effect. Generally, when bond breaking occurs in the transition state the normal kinetic isotope effect is expected, and bond formation causes the reverse one.

It may be considered from our results, in which no kinetic isotope effect was observed in both IVa and IVb, that bond breaking or bond formation with respect to both carbonyl-C-atom and phenyl-1-C-atom of α-diazoacetophenone is not happened in the transition state. Therefore two-step mechanism is preferred. The precise model of the transition state of this reaction may be shown by VII, in which the R-CO bond length is not changed from that of V*3 (path B). This may suggest that the bond energy effect observed in the substituent effect of para-electron releasing groups, such as *p*-methoxy and *p*-ethoxy, on reaction rate is not attributed to R-CO bond cleavage but to $C-N_2$ bond cleavage.

Experimental

Materials. *α-Diazoacetophenone-(carbonyl-^{14}C).* A mixture of 1.23 g (0.010 mol) of benzoic-^{14}C acid (sepcific activity 11.8 μc/mmol) and 2.5 g (0.021 mol) of purified thionyl chloride was refluxed for three hours. The excess thionyl chloride was evaporated under reduced pressure, and the last of the reagent was removed by azeotrope with two added 5 m*l* of absolute benzene. Benzoyl chloride obtained was used for diazoacetophenone formation without further purification. To 50 m*l* of etheral solution of diazomethane, prepared by the alkaline decomposition of 7.0 g (0.07 mol) of *N*-nitroso-*N*-methylurea, an etheral solution of previously synthesised benzoyl-^{14}C chloride was added drop by drop under stirring at −5°C. After standing overnight at room temperature, the ether was removed under reduced pressure at room temperature. Yellow crystals of IVa were obtained from the residue on standing in the refrigerator and purified by two recrystallization from petroleum ether. Mp 47.5—48.0°C, yield 0.85 g (58%).

α-Diazoacetophenone(phenyl-1-^{14}C). 1.11 g (0.009 mol) of commercial benzoic acid (phenyl-1-^{14}C labeled) (specific activity 18.7 μc/mmol) was chlorinated by 2.4 g (0.020 mol) of purified thionyl chloride to give phenyl-1-^{14}C labeled benzoyl chloride, according to the same method described in the previous part. IVb was obtained by the reaction of corresponding benzoyl chloride and four equivalents of diazomethane. Mp 47.5—48.0°C, yield 0.83 g (63%). The phenyl-1-labeled α-diazoacetophenone (0.83 g) was diluted isotopically by adding 1.40 g of unlabeled α-diazoacetophenone, and isotopically homogenized by two recrystallization from petroleum ether.

Specific Activity$=18.7\times0.83/(0.83+1.40)=6.96$ μc/mmol

Silver benzoate, t-Butyl Alcohol and Triethylamine. Reagent and solvents used here were prepared and purified by the method previously reported.[1)]

Quantitative Determination of α-Diazoacetophenone (IV). When IV was treated with 2,4-dinitrophenylhydrazine (VIII) in alcoholic solution in the presence of hydrochloric acid, 2,4-dinitrophenylhydrazone of phenacyl chloride[5)] was precipitated accompanying the evoluation of nitrogen. In order to utilize this reaction for the quantitative determination of unreacted diazoketone in the course of the Wolff rearrangement, it is ascertained that the formation of the hydrazone is almost quantitative under the same condition of the isotope effect determination reaction, as shown in Table 3.

Determination of Rate Constant and Kinetic Isotope Effect of the Wolff Rearrangement of IVa. *Determination of Reaction Rate.* To a solution of 0.813 g (5.5 mmol) of IVa (specific activity, 11.8 μc/mmol) dissolved in 100 m*l* of *t*-butyl alcohol contained in long necked reaction vessel, triethylamine (2.0 m*l*) solution of 0.100 g of silver benzoate was added at a time. After vigorous swirling, reaction vessel was immersed in the thermostated bath at 30.05+0.01°C. A 10 m*l* of alquot of the reaction mixture was pipetted into a 50 m*l* of flask containing 100 mg of VIII and 10 m*l* of concentrated hydrochloric acid and 10 m*l* of ethanol

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5) F. Arndt, B. Eistert and W. Partale, *Ber.*, **60**, 1364 (1927).

TABLE 1. REACTION RATE AND KINETIC ISOTOPE EFFECT OF THE WOLFF REARRANGEMENT OF IVa AT 30.05°C

No.	Time (min)	2,4-D weight (mg)	k_1[a] (10^{-4} min^{-1})	G. M. counting[c] (cpm)	counting ratio
1	10[b]	152.8		2636±17	100.0
2	20	136.4	114	2674±10	101.4±1.0
3	30	117.8	130	2636±14	100.0±1.1
4	40	107.0	118	2628±24	99.7±1.5
5	50	97.2	113	2632±26	99.8±1.6
6	60	85.3	117	2664±16	101.1±1.2
7	70	81.7	104	2670±17	101.3±1.2
			$k_1=116\pm6$		

a) Evolution of nitrogen gas accompanied with the reaction causes the error in volume of pipetting and then in rate measurement.

b) Initial sampling was made at ten minutes after the addition of the catalyst, because about ten minutes induction period was observed by the kinetic measurement using azotometer.

c) Counting was made by preset counting method of 10^4 count using Nuclear Chicago G. M. counter attached by Aloka G.M. tube for β-ray (membrane 1.3 mg/cm^2). Each sample was counted six times and average value was listed. These values listed were corrected for natural count (21 cpm).

TABLE 2. REACTION RATE AND KINETIC ISOTOPE EFFECT OF WOLFF REARRANGEMENT OF IVb

No.	Time (min)	2,4-D weight (mg)	k_1[a] (10^{-4} min^{-1})	G. M. counting[c] (cpm)	counting ratio
1	10[b]	150.4	—	1620±10	100.0
2	20	130.6	141	1647± 9	101.7±1.1
3	30	114.9	135	1617±11	99.8±1.3
4	40	102.0	129	1597± 9	98.6±1.1
5	50	90.9	126	1621± 9	100.1±1.1
6	60	81.1	123	—[d]	
7	70	70.8	126	1629± 6	100·6±1.0
			$k_1=130\pm5$		

Following reaction condition was applied:

IVb: 0.910 g, C_6H_5COOAg: 0.100 g, $(C_2H_5)_3N$: 2.00 m*l*, *t*-C_4H_9OH: 100 m*l*, at 30.05±0.02°C

a), b), c) These foot-notes are identical with those in Table 2.

d) Counting of this sample was not measured because of the experimental mistake.

TABLE 3. QUANTITATIVE DETERMINATION OF α-DIAZOACETOPHENONE (IV)

No.	Weight of IV (mg)	Weight of 2,4-D (mg) Calcd	Obs	Obs/Calcd (%)
1	22.8	52.2	52.1	99.8
2	32.5	74.5	75.2	100.9
3	41.8	95.8	95.8	100.0
4	52.0	119.1	119.7	100.6
5	60.6	138.8	139.2	100.3

at the intervals of ten minutes after the addition of the catalyst. The hydrazone solutions were allowed to stand overnight in the bath at 50—60°C, for the purpose of the complete precipitation of the hydrazone and aging of the crystals, then allowed to cool to room temperature, added 10 *ml* of water. Crystals of the hydrazone were collected on the precisely weighed fritted glass funnel, washed with 2 N hydrochloric acid until no yellow color of unreacted VIII-hydrochloride appeared in the filtrate, washed with distilled water and then dried for 12—15 hr at 80—90°C, and weighed.

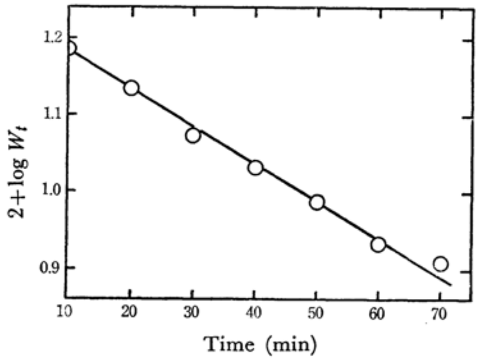

Fig. 1. The linear relationship between log W_t and time in the reaction of IVa.

The linear first-order plot was obtained between log *W* and time as shown in Fig. 1. The reaction rate *k* was calculated by the following equation,

$$k_t=2.303\times\log(W_0/W_t)$$

where W_0 and W_t were denoted the weight of the hydrazone at the time of $t=0$ and t respectively, and $t=0$ was the time of the first pipetting.

Measurement of Kinetic Isotope Effect. The hydrazone obtained from the rate measurement of IVa (shown in Table 1, Nos. 1—7) was recrystallized four times from a mixed solvent of ethyl acetate and ethanol (3 : 1), and solvent was evaporated completely in vacuum desiccator for a few days. About 15—16 mg of purified hydrazone was oxidized by modified van Slyke wet-oxidation method, and carbon dioxide was absorbed by 10 *ml* of saturated barium hydroxide solution to give barium carbonate. Carbon dioxide and barium hydroxide solution was kept separately until oxidation was complete (at 170°C, for 4 hr), in order to homogenize the distribution of carbon fourteen in barium carbonate. Barium carbonate was made as a disk of 1.7 cm in diameter, which had infinite thickness, by filtration (using metallic filter), and radio activity of these barium carbonate samples were counted by G. M. counter after drying.

Determination of Reaction Rate and Kinetic Isotope Effect of the Wolff Rearrangement of IVb. The same procedure described in the case of IVa was used for these measurements. Reaction conditions used and results obtained were given in Table 2 (Fig. 2). It was ascertained that the degree of the contamination of the commercial benzoic acid-(phenyl-1-^{14}C) (IX) used for the synthesis of IVb by the mixing of benzoic acid-(carbonyl-^{14}C) was no more than 0.44%, comparing the radio activity of the barium cabonate obtained by direct oxidation of IX with that obtained by Schmidt rearrangement of IX.

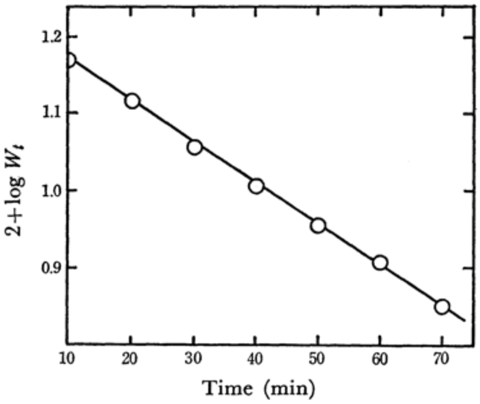

Fig. 2. The linear relationship between log W_t and time in the reaction of IVb.