[Chem. Pharm. Bull. 32(1) 174—178 (1984)]

Determination of Rate Constants for Formation and Decomposition of Color Products in the Fujiwara Reaction Using Benzotrichloride

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(Received May 12, 1983)

The rate constants for the formation and the decomposition of color products in the Fujiwara reaction using benzotrichloride (α,α,α-trichlorotoluene) as the starting material were evaluated by means of simultaneous nonlinear least-squares fitting for the time course data of three compounds. The apparent rate constants for the formation of red and yellow compounds are 0.16 (s^{-1}) and 0.095 (s^{-1}), respectively, and those for the decomposition of these chromophores are 10.3 (s^{-1}) and 0.67 (s^{-1}), respectively. These results indicate that the red compound which is the main color compound in the Fujiwara reaction is very unstable and the yellow compound is rather stable. It was found that 40.3% of benzotrichloride is converted to the red compound, 23.9% to the yellow compound and 35.8% to other compounds.

Keywords——Fujiwara reaction; benzotrichloride; rate constant; MULTI; nonlinear least-squares; curve-fitting

The Fujiwara reaction[1] has been widely used for the colorimetric analysis of gem-polyhalogen compounds.[2-6] In the previous report,[7] the structures of the red and yellow compounds which are produced from benzotrichloride were determined, and the mechanism of their formation was discussed. The kinetics of the formation and decomposition of the color compounds, however, were not clarified.

In the present work, the rate constants for the formation and the decomposition of the color products were estimated by means of the nonlinear least-squares method and the conversion ratios of these compounds from benzotrichloride were evaluated to clarify the quantitative features of the Fujiwara reaction.

Experimental

Materials——Pyridine and benzotrichloride of analytical reagent grade (Nakarai Chemicals Ltd.) were further purified by distillation and stored with protection against light and moisture. Other chemicals of analytical reagent grade were used as supplied.

Apparatus——A Shimadzu GC-6A gas chromatograph equipped with a flame ionization detector was used to determine benzotrichloride. The column was a glass tube (1 m × 3 mm i.d.) packed with 10% polyethylene glycol (PEG) 20 M on Chromosorb W 100/120 mesh. The column temperature was maintained at 130 °C, and the injection port temperature was 200 °C. The carrier gas was helium at a flow rate of 65 ml/min, adjusted by means of a mass flow controller.

A high performance liquid chromatograph (TWINCLE, JASCO, Japan) equipped with a visible-wavelength detector was used in a reversed phase mode over Nucleosil $10C_{18}$ (M. Nagel) packed in a 25 cm × 4.6 mm i.d. stainless steel tube. The red compound was measured at 420 nm in the mobile phase of water–methanol (1 : 2 v/v), and the yellow compound at 370 nm in the mobile phase of water–methanol (1 : 1 v/v). All operations were carried out at ambient temperature.

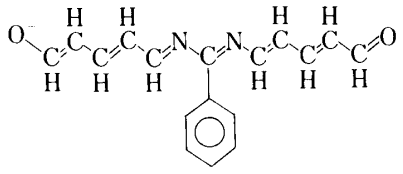
Sample Preparation——Pyridine solutions (60 ml each) containing 0.002, 0.003, 0.004, 0.0092, and 0.016 mol/l benzotrichloride were prepared. Eleven 3.0 ml aliquots of each solution were transferred into 25 ml flasks and 1.0 ml of 20% NaOH solution was added to each flask. They were heated for 3, 5, 10, 15, 20, 25, 30, 40, 50, 95, and 120 min on a boiling water bath with stirring, refluxed and then cooled in an ice bath to stop the reaction.

Procedure——The concentrations of unchanged benzotrichloride and the two color compounds were determined from the chromatographic peak heights. Standard solutions of benzotrichloride were prepared by dissolving the analytical grade substance in pyridine at concentrations ranging from 1.0×10^{-3} to 2.0×10^{-2} mol/l. The red and yellow compounds were isolated from the reaction solution and purified. The detailed procedures are described elsewhere.[7] The isolated red substance was dissolved in pyridine to make standard solutions in the range from 0.5×10^{-5} to 3.0×10^{-4} mol/l and similar solutions of the yellow substance were prepared in the range from 0.4×10^{-5} to 1.0×10^{-3} mol/l. The coefficients of correlation of all the calibration graphs thus obtained were above 0.997.

Calculation——The computer calculation was carried out on a personal computer (PC-9801, NEC) with programing in BASIC. The program (MULTI)[8] allows the simultaneous nonlinear curve fitting of up to five time course equations. The damping Gauss–Newton method was adopted in the present study as the least-squares algorithm. The two-way analysis of variance (ANOVA) was also executed on the personal computer.

Results and Discussion

When benzotrichloride was used as a gem-polyhalogen compound in the Fujiwara reaction, red and yellow compounds having the structures **1** and **2**, respectively, and



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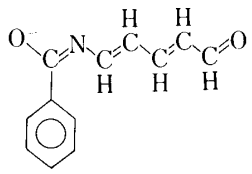

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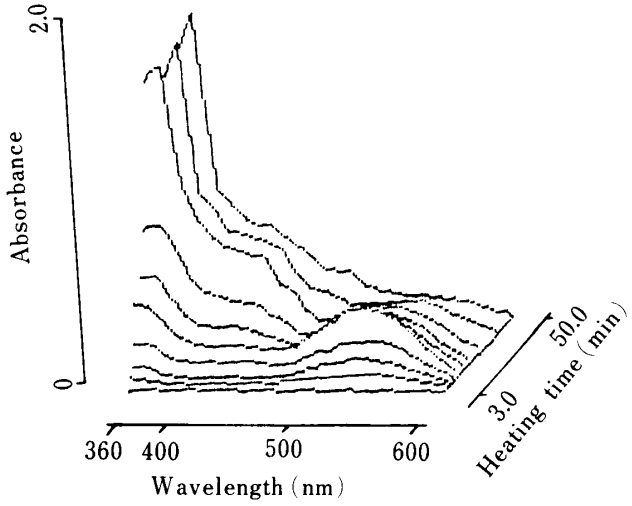

Fig. 1. Three-Dimensional Absorbance Curve of a Reaction Solution

glutaconaldehyde, which is the final product from the color products, were obtained as the major products. Figure 1 shows the three-dimensional absorbance curve of a solution obtained by the Fujiwara reaction. The ordinate is the absorbance. The two abscissas are wavelength (nm) and heating time (min). The concentration of red product ($\lambda_{max} = 530$ nm) increases first and then decreases with the heating time. The concentrations of yellow compound ($\lambda_{max} = 420$ nm) and glutaconaldehyde ($\lambda_{max} = 360$ nm) increase monotonously with the heating time.

Table I shows the time courses of benzotrichloride, red and yellow compounds for various initial concentrations (C_0) of benzotrichloride. When the red compound was heated in alkaline pyridine solution, the yellow compound and benzotrichloride were not produced.[7]

TABLE I. Concentrations[a] of Benzotrichloride, Red Compound and Yellow Compound

C_0[b]	Compound	Heating time (min)										
		3	5	10	15	20	25	30	40	50	95	120
0.2×10^{-2}	BTC[c]	192	189	186	180	180	180	154	143	140	107	93
	Red[d]	0.86	1.49	2.27	2.41	2.46	2.36	2.36	2.17	2.08	1.59	1.42
	Yellow[e]	0	0.51	1.84	3.43	4.88	5.68	6.87	8.20	10.1	12.3	12.6
0.3×10^{-2}	BTC	300	289	272	269	253	244	231	211	213	177	141
	Red	1.05	2.14	3.45	3.57	3.83	3.74	3.53	3.33	2.87	1.84	1.52
	Yellow	0.55	1.38	3.44	5.23	8.13	9.92	11.2	13.5	14.6	18.2	18.2
0.4×10^{-2}	BTC	410	391	387	359	346	353	315	315	289	219	143
	Red	2.37	3.60	5.36	5.74	5.83	5.64	5.64	4.64	4.69	3.55	2.70
	Yellow	2.28	3.42	5.14	10.4	12.9	15.6	17.5	21.6	25.2	29.5	33.2
0.92×10^{-2}	BTC	912	859	859	824	778	766	755	725	690	469	393
	Red	5.06	8.22	10.7	13.4	13.8	14.6	12.5	12.1	10.5	8.43	5.38
	Yellow	2.01	6.29	13.1	18.1	24.2	30.7	39.2	42.5	47.0	65.8	65.9
1.6×10^{-2}	BTC	1549	1544	1510	1459	1403	1358	1346	1239	1132	850	726
	Red	12.2	19.5	26.0	27.1	26.6	25.8	25.3	22.3	21.4	14.2	13.3
	Yellow	5.47	10.5	23.9	34.6	39.6	46.3	52.7	63.4	78.7	91.5	91.5

a) $\times 10^{-5}$ mol/l.
b) Initial concentration of benzotrichloride (mol/l).
c) Benzotrichloride.
d) Red compound.
e) Yellow compound.

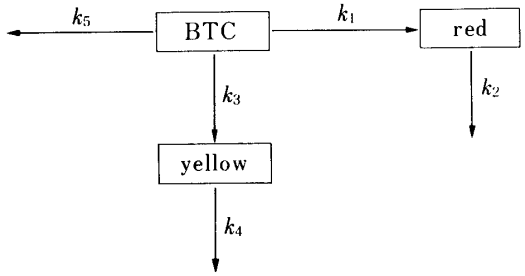

Fig. 2. A Model for the Fujiwara Reaction
The parameters from k_1 to k_5 are rate constants.

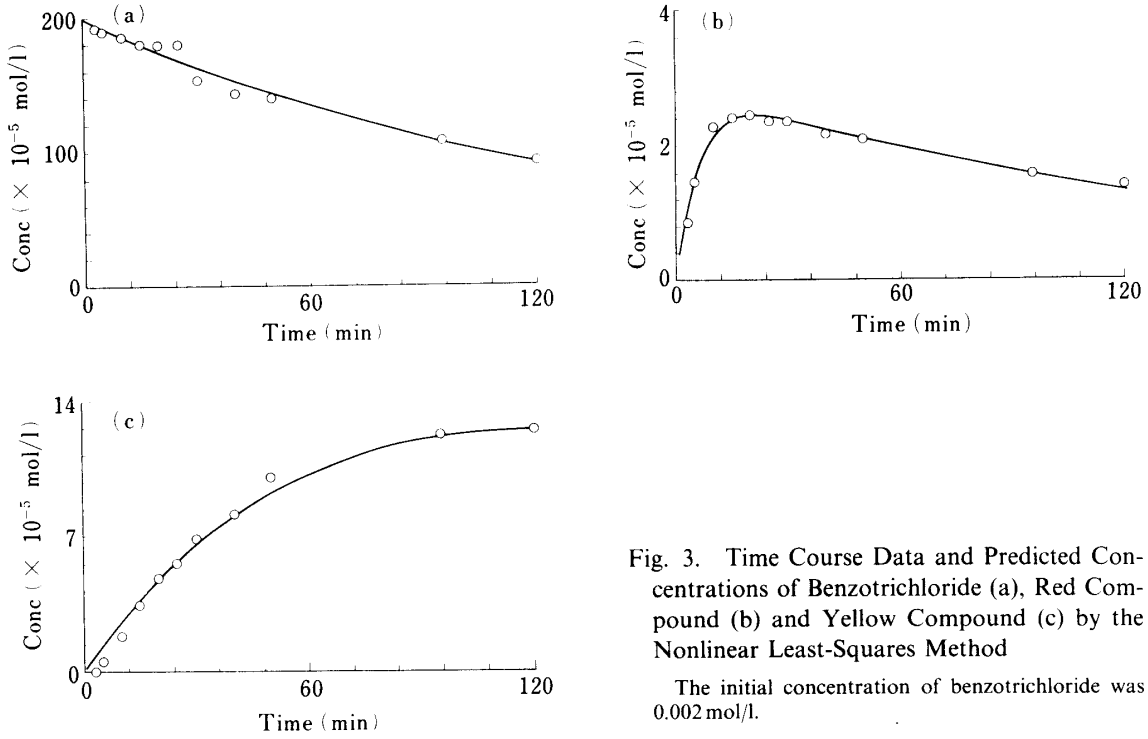

Fig. 3. Time Course Data and Predicted Concentrations of Benzotrichloride (a), Red Compound (b) and Yellow Compound (c) by the Nonlinear Least-Squares Method
The initial concentration of benzotrichloride was 0.002 mol/l.

When the yellow compound was heated in the solution, the red compound and benzotrichloride were not produced.[7] Therefore, it appears that the red and yellow compounds are produced directly from benzotrichloride, and benzotrichloride is not reproduced from them. The previous report[7] proved that both color compounds are finally decomposed to glutaconaldehyde as a major degradation product. Thus, the model in Fig. 2 was adopted to clarify the kinetic features of the Fujiwara reaction. The theoretical equations for the model in Fig. 2 are

$$C_1 = C_0 \cdot \mathrm{Exp}(-(k_1+k_3+k_5)\cdot t) \quad (1)$$

$$C_2 = k_1 \cdot C_0/(k_2-k_1-k_3-k_5)\cdot(\mathrm{Exp}(-(k_1+k_3+k_5)t)-\mathrm{Exp}(-k_2\cdot t)) \quad (2)$$

$$C_3 = k_3 \cdot C_0/(k_4-k_1-k_3-k_5)\cdot(\mathrm{Exp}(-(k_1+k_3+k_5)t)-\mathrm{Exp}(-k_4\cdot t)) \quad (3)$$

where C_1, C_2, and C_3 are concentrations of benzotrichloride, and the red and yellow compounds, respectively. Equations (1), (2), and (3) were simultaneously fitted to the time course data in Table I by means of MULTI. Figures 3a, b, and c show the experimental time course data and the concentrations predicted by the nonlinear least-squares method, when 0.002 mol/l of initial benzotrichloride was used. The open circles indicate the observed points and the line is predicted curve. Table II presents the apparent rate constants estimated by the least-squares method. The constant k_2 which is the decomposition rate constant of the red compound, is large, which shows that the compound is extremely unstable. The constant k_4,

TABLE II. Estimated Apparent Rate Constants of the Model in Fig. 2

Parameters	Initial concentration of benzotrichloride ($\times 10^{-2}$ mol/l)					
	0.2	0.3	0.4	0.92	1.6	Average
k_1	0.13	0.13	0.16	0.16	0.24	0.16
k_2	9.4	9.8	10.1	9.2	13.0	10.3
k_3	0.084	0.096	0.11	0.096	0.090	0.095
k_4	0.59	0.80	0.59	0.59	0.80	0.67
k_5	0.17	0.14	0.19	0.15	0.066	0.14

which is the decomposition rate constant of the yellow compound, is around 0.7 (s^{-1}), which shows that the yellow compound is rather stable.

The dependency of apparent rate constants on the initial concentration of benzotrichloride was verified by means of two-way analysis of variance (ANOVA). The calculated F-value between the rate constants for initial concentration of benzotrichloride was 1.12 which is insignificant at the 5% level, suggesting that the rate constants are independent of the initial benzotrichloride concentration. It is concluded that the reaction system can be regarded as linear under the present experimental conditions.

The conversion ratios from benzotrichloride to the color compounds were estimated by means of the following equations.

$$f_1 = k_1/(k_1+k_3+k_5) \quad (4)$$

$$f_2 = k_3/(k_1+k_3+k_5) \quad (5)$$

where f_1 and f_2 are the conversion ratios of benzotrichloride to red and yellow compounds, respectively. Thus, 40.3% of benzotrichloride is converted to the red compound, 23.9% to the yellow compound and 35.8% to the other degradation products, one of which was determined to be benzoic acid by means of mass spectrometry.

Conclusion

The rate constants were calculated from the concentration of each compound based on the model. The rate constant of decomposition of the red compound, which is the subject of analysis in the Fujiwara reaction, is about 60 (k_2/k_1) times faster than that of its formation. It is suggested that the time for which the color product is present in the reaction solution is brief.

References

1) K. Fujiwara, *Sitzungsber Abh. Naturforsch. Ges. Rostock*, **6**, 33 (1916).
2) J. H. Ross, *J. Biol. Chem.*, **58**, 641 (1923).
3) A. Seto and M. D. Schltze, *Anal. Chem.*, **28**, 1625 (1958).
4) P. J. Friedman and J. R. Cooper, *Anal. Chem.*, **30**, 1674 (1958).
5) K. Kakemi, T. Uno, and S. Ohashi, *Yakuzaigaku*, **18**, 24 (1958).
6) K. C. Leibman and J. D. Hindman, *Anal. Chem.*, **36**, 348 (1964).
7) T. Uno, K. Okumura, and Y. Kuroda, *J. Org. Chem.*, **46**, 3175 (1981).
8) K. Yamaoka, Y. Tanigawara, T. Nakagawa, and T. Uno, *J. Pharm. Dyn.*, **4**, 879 (1981).