Kinetics and Stereochemistry of Alkaline Cleavage of 1,1-Diacetyl-2-arylcyclopropane[1]

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The kinetics and the stereochemistry of alkaline cleavage of several 1,1-diacetyl-2-arylcyclopropanes (**1**) in ethanol–water mixture are reported. The rates can be expressed approximately by a third order equation, rate= k_2[**1**][OH^-]^2. With *para*-substituted derivatives (*p*-CH_3, H, *p*-Cl and *p*-Br) of 2-phenyl ring, the reaction constant ρ was obtained as +4.3 by plotting log k_2 against normal Hammett σ. At 0 °C, the main products were thermodynamically unstable *cis*-1-acetyl-2-arylcyclopropanes. The *cis* to *trans* ratio in the products decreased with increasing reaction temperature. The reaction mechanism has been discussed in relation to the cleavage reaction of unenolizable acyclic β-diketone. The large ρ value and preferred formation of *cis* product suggest that the substituent effects of 2-aryl group are transmitted through cyclopropane ring much more effectively to *trans* direction than to *cis* direction.

Pearson and Mayerle showed that the alkaline cleavage of dimethylacetylacetone, which belongs to unenolizable β-diketone, is second-order (rate=k_1-[ketone] [OH^-]).[2] The same kinetics and mechanism might be expected in the same cleavage of 1,1-diacetyl-2-arylcyclopropanes with hydroxide ion, since they are also unenolizable β-diketone, and the effects of the substituents at phenyl ring on the cleavage rates appear to provide a convenient tool to study the transmitting ability of the effects through cyclopropane ring. The present paper describes the stereochemistry and kinetics of alkaline cleavage of several 1,1-diacetyl-2-arylcyclopropanes in ethanol–water (75 : 25 by volume) mixture containing potassium hydroxide.

Cleavage of 1,1-diacetyl-2-phenylcyclopropane (**1**-H) with potassium hydroxide (0.05—0.6 M) gave *cis*- and *trans*-1-acetyl-2-phenylcyclopropane (**2**-H) with no detectable amount of by-product. Gas-chromatographic analysis showed that the *cis* to *trans* ratio in the products at 0 °C (concn of KOH=0.4 M) was 90 : 10, while the value decreased with increasing reaction temperature (40—60 °C) to 50 : 50. Considering that the *cis*-isomer should be thermodynamically much more unstable than *trans* isomer, it appears that the cleavage at lower temperatures predominantly gives kinetically controlled products. With *p*-methylphenyl (**1**-CH_3), *p*-chlorophenyl (**1**-Cl) and *p*-bromophenyl (**1**-Br) derivatives, almost the same results were obtained. Although the detailed analysis to determine whether the *trans* isomer was formed through the rearrangement of *cis*-isomer or directly from **1** was not performed, the change of *cis* : *trans* ratio with time appears to show that the *trans*-isomer resulted partly through rearrangement and in part directly, even at higher temperature (Fig. 1).

Curve IV in Fig. 1 was obtained by the estimation from the isomerization rate of *cis*-**2**-H to *trans*-**2**-H which will be reported in a succeeding paper.[3]

The rates of cleavage were determined by following the concentrations of potassium hydroxide. Quantitative analysis by gas chromatography could be applied to determine the *cis-trans* ratio of the products but not to the reaction mixture because of the partial decomposition of **1**-H.

In contrast to the reported case of 3,3-dimethyl-2,4-pentanedione,[2] the rates can be expressed approximately by a third-order equation, rate=k_2[**1**][OH^-]^2. The results are shown in Table 1.

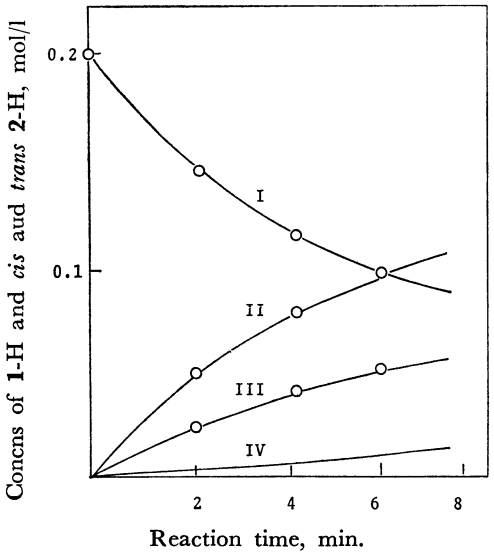


Fig. 1. Plot of the cleavage reaction of **1**-H in 75% ethanol at 25 °C. The initial concentrations of **1**-H and potassium hydroxide were 0.200 and 2.00 M, respectively. Curve I, II and III show the observed concentrations of **1**-H, sum of *cis* and *trans*-**2**-H, and *trans*-**2**-H, respectively.

Deviations from the third-order equation in lower concentration ranges of potassium hydroxide cannot be neglected and is considered to be due to the second-order term k_1[**1**] [OH^-] which must be added to the main term of the third-order.

The substituents at the *para* position of phenyl ring in **1** showed profound effects on the cleavage rates. Data with the substituents of methyl, chloro and bromo are given in the following table.

Hammett plot of the rates against normal σ values gave a straight line with a ρ value of +4.3. This large value shows that the substituent effect can be transmitted effectively through cyclopropane ring.

Pearson and Mayerle showed that the cleavage rates of acetylacetones by hydroxide ion consist of two terms; one is associated with one mole of ketone and

Table 1. Kinetical data of the cleavage reaction of **1**-H with potassium hydroxide in 75% ethanol[a)]

Initial concn of **1**-H (mol/l)	Initial concn of KOH (mol/l)	$k_2\times10^3$ (l^2/mol^2·s)	$k_1\times10^5$ (l/mol·s)
At 25.0°			
0.100	0.105	0.60	6.2
0.100	0.215	0.47	9.4
0.100	0.375	0.54	19.5
0.100	0.375	0.57	19.6[b)]
0.100	0.545	0.66	33.5
0.025	0.102	0.62	6.0
0.045	0.165	0.61	9.0
		mean 0.58	
At 30.0°			
0.100	0.112	1.7	
0.100	0.215	1.2	
0.100	0.400	1.2	
0.100	0.560	1.4	
		mean 1.4	
At 40.0°			
0.116	0.058	6.6	
0.116	0.111	3.7	
0.116	0.239	2.8	
0.116	0.474	2.5	
0.116	0.708	2.6	
0.035	0.071	6.0	
0.224	0.214	2.7	
		mean 2.9	
At 60.0°			
0.116	0.058	31	
0.117	0.116	16	
0.105	0.225	12	
0.036	0.073	21	
0.037	0.146	13	
0.030	0.178	12	
0.223	0.210	13	
		mean 15	

a) $\Delta H^{\neq}=13$ kcal/mol and $\Delta S^{\neq}=-18$ e. u. b) NaOAc (0.100 M) was added.

Table 2. Substituent effects on the cleavage rates at 40 °C

	$k_2\times10^3$ (l^2/mol^2·s)	Rel. rate	σ[4)]
1-CH_3	1.5	0.557	−0.170
1-H	2.82	1.00	0
1-Cl	8.12	2.88	+0.227
1-Br	8.78	3.11	+0.237

one mole of hydroxide ion (k_1, splitting of acetic acid from the monoanion formed by the addition of hydroxide ion to carbonyl) and the other with one mole of ketone and two moles of hydroxide ion (k_2, splitting of acetate ion from the dianion formed by proton abstraction from hydroxyl group of the monoanion with hydroxide ion), and the ratio of k_2/k_1 decreases by methyl substitution and becomes almost zero in the case of 3,3-dimethyl-2,4-pentanedione.[2)] The explanation for the changes of the ratio is not easy and they mentioned simply that this may be due to a weakening of carbon–carbon bond which renders less necessary the helping effect of double charged anion in cleaving. The difference of the reaction-order of the cleavage of 3,3-dimethyl-2,4-pentanedione and that of the present case is also difficult to explain. Binding the carbons of the two methyl groups in dimethylacetylacetone makes the carbon between the carbonyls a ring member of cyclopropane, reduces the steric requirement, and changes the character of the carbon. How it works in the reaction mechanism is difficult to predict, and remains unsolved.

One of the special features of the present cleavage is the formation of thermodynamically unstable *cis* product. A straightforward explanation may be as follows. First addition of hydroxide ion must occur at the *trans* acetyl group of **1** because of a larger steric hindrance of the adduct at *cis* acetyl group. Second attack of hydroxide ion forms dianion C (Fig. 2). Splitting of acetate anion from C forms carbanion F which gives *cis*-product through proton abstraction from the solvent.[4)]

If the addition of hydroxide ion to carbonyl is reversible and faster than the cleavage of C, as was pointed out by Pearson and Mayerle, other reaction pathways must be examined. Possible ones are depicted in Fig. 2. Equilibrium concentrations of A and C are higher than those of B and E, respectively,

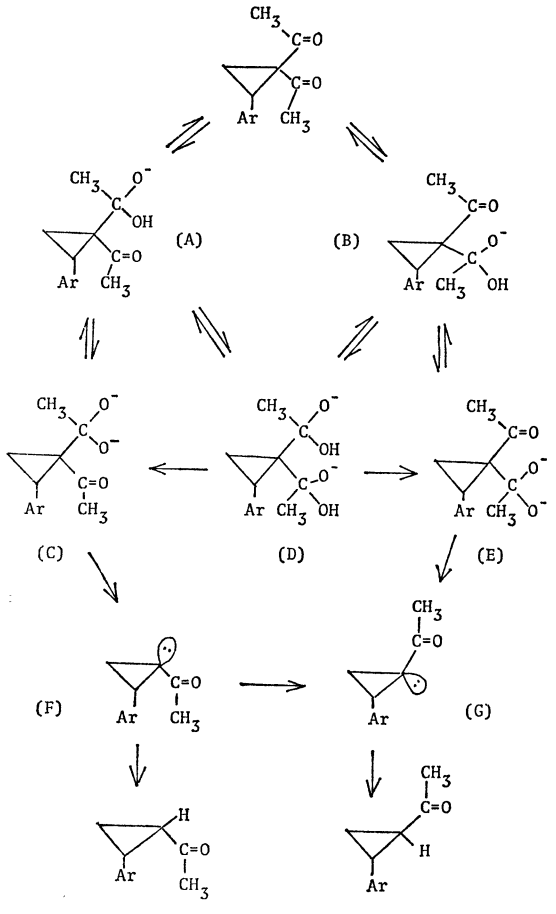


Fig. 2. Possible pathways of the cleavage of **1**.

because of the steric effects. The cleavage rate of E, however, must be faster than that of C because of the same effects. If the equilibria shown in Fig. 2 are attained rapidly, the relative rates of the cleavage of C and E determine the stereochemistry and the *trans* product must be obtained. To explain why the *cis* is the main product, at least at 0 °C, some other kind of factor than the steric which is more effective to accelerate the cleavage of C must be considered. An assumption that the substituent effects are transmitted more effectively to *trans* direction than to *cis* through cyclopropane ring may explain the present results. Although they may not be enough to rationalize the assumption, the fact that the carbanion formation by proton abstraction from ring methylene of *cis*-**2**-H with hydroxide ion proceeded much more rapidly than that from *trans*-**2**-H[3] appears to support the proposal.

The substrates **1** have been prepared by demercurations of 3,3-diacetyl-2-arylpropylmercuric acetates (**3**-H, **3**-Cl, **3**-Br and **3**-CH_3 for phenyl, *p*-chlorophenyl, *p*-bromophenyl and *p*-tolyl, respectively). Although **1**-H can be obtained by the demercuration of the corresponding chloride of **3**-H with potassium hydroxide as was reported previously,[5] applications of the same method to the others gave only poor yields. It was found, however, that the demercuration of **3** proceeded smoothly in dimethyl sulfoxide (DMSO) at about 120 °C and gave much better yields of **1**. At higher temperatures than 120 °C, the yields of **1** became low because of the formation of isomeric dihydrofurans. **3** were prepared by the reactions of acetylacetone with β-acetoxy-β-arylethylmercuric acetates (**4**-H, **4**-Cl, **4**-Br and **4**-CH_3 for phenyl, *p*-chlorophenyl, *p*-bromophenyl and *p*-tolyl, respectively), which were obtained by acetoxymercuration of styrenes, in acetic acid containing perchloric acid or boron trifluoride.[5] Typical examples of the results are shown in Table 3.

Table 3. Preparation of **1** by the demercuration of **3**

	Temp. °C	Time min	Yield of **1** %[a]	Mp, °C
1-H	120	30	35	57.5—59.0
1-CH_3	111—120	15	34	57.6—59.0
1-Cl	110—115	35	57	74.6—75.5
1-Br	120	10	33	72.2—73.2

a) After recrystallization from *n*-heptane.

Experimental

*Preparation of **1** through **4** and **3**.* The following example shows the typical experimental procedure for the preparation of **1**. Into a mixture of acetic acid (300 ml) and mercuric acetate (1.0 mol), styrene (1.0 mol) was added and stirred at room temperature for 1 hr, and then acetylacetone (2.0 mol) was added. Under keeping the mixture below 40 °C, 60% perchloric acid (160 g) was added dropwise and stirred for 2 hr. The reaction mixture was poured into 20% aqueous solution of sodium acetate (1000 g). Crystals of **3**-H formed were collected, washed with ether, and recrystallized from ethanol (1.2 l), 370 g (0.80 mol). Purified **3**-H (0.80 mol) was dissolved into hot DMSO (660 ml) and kept at 120 °C for 30 min. After removing metallic mercury formed, the reaction mixture was poured into saturated aqueous solution of sodium chloride (1.5 l). Brownish raw crystals were collected and recrystallized from *n*-heptane (1.8 l) to give pure **1**-H (56 g, 35% yield), mp 57.5—59.0 °C.

Starting from *p*-substituted styrenes, which were prepared by reduction of the corresponding acetophenones and subsequent dehydration,[6] **3** were obtained in 75—80% yields and then **1** in 33—57% yields. Purifications of **3** were essential to get better yields of **1** (Table 4).

Table 4. Analyses of **1**

	Found (%)			Calcd (%)		
	C	H	X	C	H	X
1-H	76.85	7.17		77.20	6.98	
1-Cl	65.87	5.48	14.86	65.91	5.54	14.98
1-Br	55.27	4.76	28.67	55.54	4.66	28.42

Because of the lack of the sufficient amount of the material, **1**-CH_3 was not analyzed.

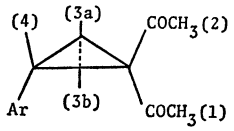
IR spectra were recorded on HITACHI EPI-G2. IR of **1**-H (KBr): $\nu_{C=O}$, 1700(s) and 1680(s); δ_{C-H} of CH_3, 1370(s) and 1360(s); $\delta_{C=O}$, 1260(s); δ C-H of benzene ring, 780(s), 740(m), and 700(s). NMR spectra (in deuteriochloroform with TMS as an internal standard) were recorded on a Varian Associates HR-220 at 220 MHz at room temperature. δ values are summarized in Table 5.

*Alkaline Cleavage of **1**.* Into 100 ml volumetric flask, **1**-H (2.02 g, 0.01 mol), ethanol-water (75 : 25 by volume) mixture and potassium hydroxide dissolved in the same mixture (25 ml of 1.6 M solution) were added. After keeping the flask at 20 °C for 5 hr, the mixture was neutralized with hydrochloric acid (32.6 ml of 1 M). This result showed that 74% of the theoretical amount of potassium hydroxide were consumed. After ethanol was removed by distillation, the mixture was extracted with ether and dried over sodium sulfate. After removing ether, the product was analyzed by gas chromatography (YANACO GC-550 TPH, 1.5 m of 3 mmφ, Apiezon-L grease, helium). No other peak than **1**-H and *cis*- and *trans*-**2**-H was observed. The product was distilled *in vacuo*, bp 107—110 °C/7 mmHg. By column chromatography (Wakogel C-200, 30 mmφ × 40 cm, hexane-ethyl acetate (90: 10 by volume)), *cis*- and *trans*-**2**-H were isolated. Repeating the same procedure, pure *cis*- and *trans*-**2**-H were obtained. IR of *trans*-**2**-H was identical with that reported by Pierre *et al.*[7] IR of *cis*-**2**-H (bp 123—124 °C/11 mmHg) showed no absorption at 1358(m) and 1190(m) cm^{-1} which were observed in *trans*-**2**-H. IR (liq. film): $\nu_{C=O}$, 1703(s) and 1698(s); $\delta_{CH\ of\ CH_3}$, 1388(s); $\delta_{C=O}$, 1170(s); $\delta_{CH\ of\ benzene\ ring}$, 770(m), 720(w), and 695(m). Found: C, 82.61; H, 7.81%. Calcd for $C_{11}H_{12}O$: C, 82.46; H, 7.55%.

The cleavage products of *para*-substituted **1** gave the same pattern of gas chromatograms as that of **1**-H, showing that the reaction proceeded as in the case of **1**-H. Since sufficient amounts of pure *trans* products could not be isolated, NMR spectra were obtained for only *cis*-products and are shown in the following table. The differences of the chemical shift of **1**-H due to the anisotropy of aromatic ring made possible the discrimination of *cis*- and *trans*-**2**.

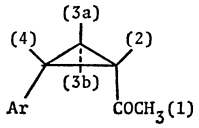
Kinetics. The rates were determined by following the potassium hydroxide concentrations by the titration

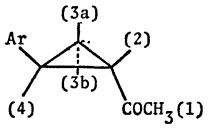
Table 5. δ Values



	H-1	H-2	H-3a	H-3b	H-4
1-H	1.77 s	2.27 s	1.57 d. of d. J=5.2 and 9.1	2.22 d. of d. J=5.2 and 7.8	3.24 d. of d. J=7.8 and 9.1
1-Br	1.80 s	2.20 s	1.57 d. of d. J=9 and 4	2.22 d. of d. J=8 and 4	3.13 d. of d. J=9 and 8
1-CH_3	1.80 s	2.27 s	1.65 d. of d. J=9 and 4	2.22 d. of d. J=8 and 4	3.23 d. of d. J=9 and 8

Table 6. NMR spectra





	H-1	H-2	H-3a	H-3b	H-4
cis-**2**-H	2.01 (s)	2.43 (m)	1.30 (m)	1.83 (m)	2.69 (m)
2-Cl	2.04 (s)	2.1—2.7	1.32 (m)	1.79 (m)	2.2—2.8
2-Br	2.05 (s)	2.44 (m)	1.30 (m)	1.79 (m)	2.61 (m)
2-CH_3	2.00 (s)	2.39 (m)	1.26 (m)	1.80 (m)	2.64 (m)
trans-**2**-H	2.30 (s)	2.21 (m)	1.38 (m)	1.67 (m)	2.52 (m)

with hydrochloric acid as usual. By plotting log of initial rates at constant concentrations of **1**-H against log[KOH], straight lines were obtained. The slopes of the lines were 1.99, 2.17 and 2.21 at 40, 30 and 20 °C. The third-order rate constants were obtained by the usual method of calculation.

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