The Effect of the Constitution of Cyclic Ketones Upon the Equilibrium Constants of Their Cyanohydrins

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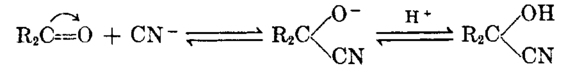
The mechanism of addition of anhydrous hydrogen cyanide to ketones, involves two steps.[2]



$$R_2C{=}O + CN^- \rightleftharpoons R_2C\begin{matrix}O^-\\CN\end{matrix} \underset{}{\overset{H^+}{\rightleftharpoons}} R_2C\begin{matrix}OH\\CN\end{matrix}$$

Since the over-all reaction velocity is independent of hydrogen ion concentration,[3] the first step is, therefore, the rate-determining one. The conversion obtainable in this reaction is largely a function of the structure of the ketone and is dependent upon the degree of dissociation of the cyanohydrin at equilibrium. In this work the dissociation constants of the cyanohydrins of some simple cyclanones, bicyclanones, and a 17-ketosteroid were measured using the process of Prelog and Kobelt.[4] The results obtained are given in Table I. The rate of reaction of some of the cyclic ketones with hydrogen cyanide are also shown in Figure 1.

TABLE I

THE DISSOCIATION CONSTANTS OF THE CYANOHYDRINS IN ALCOHOLIC SOLUTION AT 25°C.

The cyclic ketones	$K \times 10^2$ (mean value)	PK (− log K)	% of cyanohydrin after 24 hours (mean value)	Lit. $K \times 10^2$
Cyclohexanone	0.76	2.12	91	0.1[4]
2-Methylcyclohexanone	0.72	2.14	92	0.06[5]
2,2-Dimethylcyclohexanone	1.19	1.92	90	—
2,2,6-Trimethylcyclohexanone	1.29	1.90	90	—
Cyclopentanone	3.7	1.43	72	2.1[4]
Cycloheptanone	12.1	0.92	52	13.0[4]
trans-1-Decalone	1.17	1.93	91	—
trans-2-Decalone	1.23	1.91	91	—
cis-2-Decalone	1.87	1.73	87	—
1-Hexahydroindanone (mainly *cis*)	30.8	0.51	33	—
cis-8-Methyl-1-hexahydroindanone	200.0	−0.30	8	—
Estrone	2.03	1.69	89	—

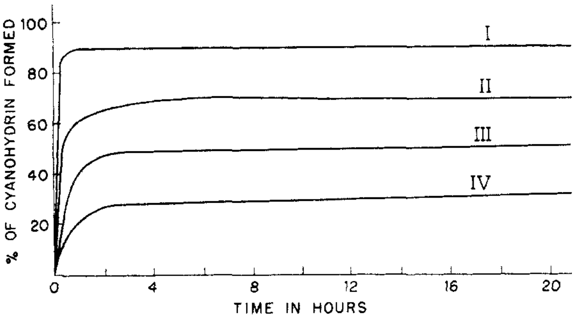
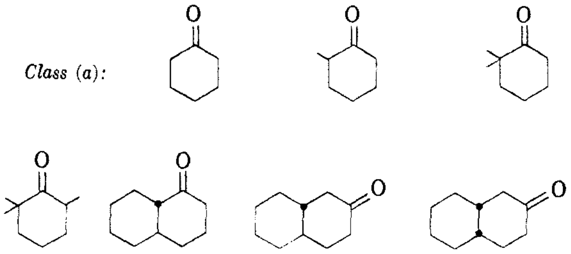


FIG. 1. THE RATE OF REACTION OF CYCLANONES WITH HYDROGEN CYANIDE. Curve I, cyclohexanone; Curve II, cyclopentanone; Curve III, cycloheptanone; Curve IV, 1-hexahydroindanone.

DISCUSSION

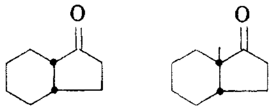
The cyclic ketones used can be divided into four classes:

Class (a):

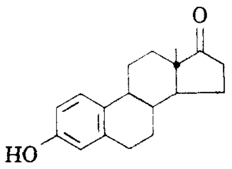


Class (b):

Class (c):



Class (d):



All class (a) compounds are of strainless ring structure, accordingly, the dissociation constants of their cyanohydrins are fairly low. The methyl groups do not appear to cause any steric hindrance nor to affect the polarization of the carbonyl group. This is in agreement with the dipole moment measurements.[6] The results of the 1- and 2-decalones are supported by the finding that their infrared absorption values are nearly the same as those of the aliphatic compounds.[7]

In class (b) compounds, the higher value of K of cycloheptanone is due to ring size effect. Regarding

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cyclopentanone, the deviation in its K value from that of cyclohexanone cannot be satisfactorily explained as in the case of the difference in their dipole moment values.[8]

In class (c) compounds, *cis*-1-hexahydroindanone is a strained molecule as shown from its model. The different behavior of this compound from that of *trans*-1-decalone is due to the size of the oxygenated ring and the stereochemical configuration of the junction of the two rings. In case of *cis*-8-methyl-1-hexahydroindanone, it seems that the steric hindrance of the angular methyl group has a further effect on the 1-ketone.

In class (d), the dissociation constant of estrone cyanohydrin was found to be very low when compared with that of *cis*-8-methyl-1-hexahydroindanone. This may be attributed to the difference in both the molecular size of the compound and the stereochemical configuration of the junction of the five and six-membered rings.

From the curves of the rate of reaction (Fig. 1), it is clear that the equilibrium, in the case of the strainless ring compounds, was attained in the first half an hour and that this time increased with the increase of the strain in the other cyclic ketones.

EXPERIMENTAL

Preparation and purification of the cyclic ketones. trans-1-Decalone and 1-hexahydroindanone (mainly cis isomer). These were prepared according to Robinson.[9–10] They were purified through their semicarbazones and then were distilled carefully.

cis and trans-2-Decalones. These were prepared by saponifying *cis/trans*-2-decalol acetate, then oxidizing the resulting alcohol with chromic acid. The stereoisomeric mixture of 2-decalone was purified through its bisulfite derivative, $\lambda_{max}^{ethanol}$ 283 mμ, ϵ_{max} = 18.8 (lit.[11]). The two isomers then were separated by fractional distillation using a fifty plate column. *cis*-2-Decalone, b.p. 105–106° (7 mm.), *semicarbazone* m.p. 184–185° (lit.[11–12]). *trans*-2-Decalone, b.p. 99° (7 mm.), *semicarbazone* m.p. 192–193° (lit.[12]).

Cyclopentanone, cyclohexanone, and cycloheptanone. These were purified from commercial samples through their semicarbazones and then were distilled carefully. The refractive indices of the final specimens, before measurements, are given in Table II. They are in close agreement with the best values in the literature.

Equilibrium constant determination. All measurements were made according to Prelog and Kobelt's method.[4] The solvent ethyl alcohol, the anhydrous hydrogen cyanide, and the standard mercuric nitrate solution, were similarly prepared; but the reaction mixtures were allowed to stand for 24 hours at 25° ± 0.05°.

TABLE II

THE REFRACTIVE INDICES OF THE CYCLIC KETONES

The cyclic ketones	n_D^{20}	Literature values		
Cyclopentanone	1.4365	n_D^{20}	1.4368	Vogel[13]
Cyclohexanone	1.4495	n_D^{20}	1.44977	Vogel[13]
Cycloheptanone	1.4600	n_D^{20}	1.45976	Vogel[13]
2-Methylcyclohexanone	1.4475	n_D^{20}	1.44766	Vogel[13]
trans-2-Decalone	1.4831	n_D^{20}	1.4828	Vogel[13]
2,2-Dimethylcyclohexanone	1.4480	n_D^{20}	1.4486	Adamson[14]
		n_D^{25}	1.4460	
2,2,6-Trimethylcyclohexanone	1.4478	n_D^{18}	1.4493	Cornubert[15]
trans-1-Decalone	1.4856	$n_D^{21.5}$	1.48487	Hückel[12]
cis-2-Decalone	1.4928	n_D^{20}	1.49265	Hückel[12]
1-Hexahydroindanone	1.4833	n_D	1.48117	Hückel[16]

Specimen results for *trans*-2-decalone are given in Table III, the concentrations being expressed in mmoles.

TABLE III

CYANOHYDRIN DISSOCIATION OF *trans*-2-DECALONE AT 25°

Time hr.	Initial concentration HCN	Ketone	Equilibrium concentration HCN	Cyanohydrin	Ketone	K × 10^2
24	8.76	3.605	5.49	3.27	0.335	1.124
24	8.76	2.598	6.415	3.345	.253	1.38
24	8.76	3.280	5.77	2.99	.29	1.12
24	8.76	2.60	6.46	2.36	.24	1.31
Mean value: K × 10^2 = 1.23 ± 0.13						

The rate of reaction of cyclopentanone, cyclohexanone, cycloheptanone, and 1-hexahydroindanone were determined by quick titration of a measured volume of the reaction mixture at various intervals. The curves obtained by drawing the percentage of the cyanohydrin formed, against the time in hours are shown in Figure 1.

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