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# Base-catalyzed 1–3 Prototropic Isomerization of Cycloheptatrienes[1]

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The base-catalyzed proton migration (from the 7- to 2-position) and proton exchange (at the 7-position) of cycloheptatrienes carrying an electron-withdrawing group were studied in a medium of aqueous sodium hydroxide or alcoholic potassium hydroxide. The order of the effect of the various substituents upon the relative rates is approximately: $CN > CONH_2 > COO^-$, Ph. The base-catalyzed prototropic isomerization proceeds through: i) the abstraction of a proton of the 7-position by the base, ii) the migration of the resulting carbanion to the allylic position (the rate-determining step), and iii) the recovery of a proton from the solvent. The kinetic study of the isomerization of 7-carboxycycloheptatriene (Ia) discloses the rate of the isomerization (*k*[the cycloheptatriene][base]) and the parameters ($E_a = 22.6$ kcal/mol, $\Delta H^{\neq} = 22.0$ kcal/mol, $\Delta S^{\neq} = -15.4$ e.u. at 60°). The structure of the cycloheptatrienyl anions formed as intermediates is discussed.

With reference to the migration of the double bonds in cycloheptatrienes, ter Borg *et al.*[4] first described the thermal 1–5 hydrogen shift mechanism, and Chapman, Borden and other groups[5] have recently reported the photochemical 1–7 hydrogen shift shown in Schemes 1 and 2. We have also

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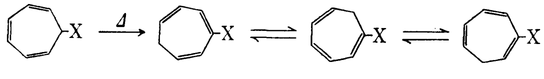
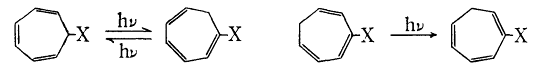
4) A. P. ter Borg, H. Kloosterziel and N. van Meurs, *Rec. Trav. Chim. Pays-Bas*, **82**, 717 (1963).

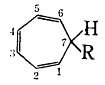
5) a) O. L. Chapman and G. W. Borden, *Proc. Chem. Soc.*, 221 (1963); b) A. P. ter Borg and H. Kloosterziel, *Rec. Trav. Chim. Pays-Bas*, **84**, 241 (1965); c) R. W. Murray and M. L. Kaplan, *J. Amer. Chem. Soc.*, **88**, 3527 (1966); d) G. W. Borden, O. L. Chapman, R. Swindell and T. Tezuka, *J. Amer. Chem. Soc.*, **89**, 2979 (1967); e) A. P. ter Borg, E. Razenberg and H. Kloosterziel, *Chem. Commun.*, **1967**, 1210.



Scheme 1. 1-5 H Shift

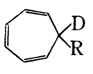


Scheme 2. 1-7 H Shift



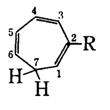
I

a: R=COOH
b: R=CN
c: R=CONH$_2$
d: R=Ph



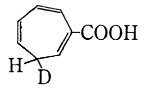
II

a: R=COOH
b: R=CN

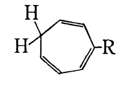


III

a: R=COOH
b: R=CN
c: R=CONH$_2$
d: R=Ph

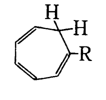


IV



V

a: R=COOH
b: R=CN
c: R=Ph



VI

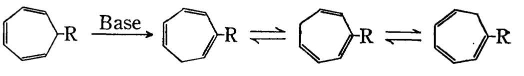
a: R=COOH
b: R=Ph

previously recognized the same mode of the thermal isomerization reaction on various cycloheptatrienes.[6] Now, however, we have found a new type of isomerization catalyzed by the base; this isomerization will be explained herein.

The proton migration in a basic medium was first observed by Buchner and his coworkers,[7] when 7-ethoxycarbonylcycloheptatriene was converted to 2-carboxycycloheptatriene (IIIa) on being refluxed with 10% alcoholic potassium hydroxide, although they did not mention the reaction mechanism. We ourselves have examined the behavior of carboxy-,[8] cyano-, carbamoil-, and phenyl-cycloheptatriene in basic media with the view of clarifying the mechanism of the base-catalyzed isomerization.

Upon heating the 7-substituted cycloheptatrienes mentioned above, the 3-, 1- and 2-substituted isomers were successively formed according to the 1–5 hydrogen shift mechanism; the chemical shifts and the couping constants of the hydrogen atom at the 7-position [H(7)] of each substance, shown in Table 1, were used for purposes of identification throughout the present work. As will be shown below, kinetic study proved that the base-catalyzed isomerization of cycloheptatrienes in dilute alkali generally took place much faster than the thermal 1–5 hydrogen shift.

The complete disappearance of the triplet signal at $\tau$ 7.52 due to H(7) in the NMR spectrum of 7-carboxycycloheptatriene (Ia), when the mixture was set aside in 2N sodium deuteroxide for 41 hr at room temperature indicated the proton exchange at the 7-position, while no deuterium exchange was observed when Ia was kept in a neutral medium such as deuterium oxide-dioxane (1 : 1) for 73 hr at the same temperature. The 7-*d*-7-carboxycycloheptatriene (IIa) thus formed was shown, on the evidence of the NMR (*i. e.* alterations of the signals due to H(7), (1), and (6)], to be isomerized to 7-*d*-2-carboxycycloheptatriene (IV) when warmed at 90°C for 10 hr in the same solvent (2N NaOD). The treatment of Ia with 2.5N sodium hydroxide at 110°C for 4 hr caused an isomerization affording 2-carboxycycloheptatriene (IIIa) in an 80% yield. The rate of the isomerization reaction of Ia to IIIa appears, from the results shown in Table 2, to depend upon the concentration of the base used (this was confirmed by the kinetic study; see below). The secondary isomerization (*i. e.*, IIIa to the other isomers, Va and VIa) was found to be considerably slower than the first-step isomerization under the same conditions, for the compound IIIa or Va remained almost unchanged when kept in 2N sodium hydroxide, even at a higher temperature such as 130°C. An enhancement of the rate of the secondary and subsequent-step isomerization of the carboxycycloheptatriene was, however, observed in a stronger base, as is shown in Tables 3 and 4; the data suggested that IIIa was successively converted to Va and the 1-substituted isomer (VIa). This was confirmed by examining the ratio of the products when IIIa or Va was treated with a concentrated base; these results are shown in Tables 5 and 6. Accordingly, the base-catalyzed proton transfer in the cycloheptatriene was considered to proceed by the step-by-step mechanism illustrated by Scheme 3; the last three compounds (IIIa, Va, and VIa) are at equilibrium.



Ia IIIa Va VIa

Scheme 3 1-3 H$^+$ Shift

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[6] a) T. Nozoe and K. Takahashi, This Bulletin, **38**, 665 (1965); b) T. Nozoe, K. Takahashi and H. Yamamoto, *ibid.*, **42**, 3277 (1969).

[7] a) E. Buchner, *Ber.*, **29**, 106 (1896); b) *ibid.*, **30**, 632 (1897); c) *ibid.*, **31**, 2241 (1898); d) E. Buchner and F. Lingg, *Ber.*, **31**, 2447 (1898); e) W. Braun and E. Buchner, *ibid.*, **34**, 982 (1901).

[8] Structures of carboxycycloheptatrienes (norcaradienecarboxylic acid), tentatively assigned by Buchner (Ref. 7), have been revised by a) C. Grundmann and G. Ottmann, *Ann. Chem.*, **582**, 163 (1953); b) W. von Doering, G. Laber, R. Vonderwahl, N. F. Chamberlain and R. B. Williams, *J. Amer. Chem. Soc.*, **78**, 5448 (1956); c) H. Jungen and K. Rust, *Ann. Chem.*, **602**, 94 (1957).

Table 1. NMR Spectra of cycloheptatrienes

| Compound | $\tau$-Values for protons[a] | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | H(7) | H(1) | H(2) | H(3) | H(4) | H(5) | H(6) | Substituents |
| Ia | 7.52 tt<br>*J* 5.5, 1.1 | 4.69 ddt<br>*J* 8.0, 5.5, 1.0 | 3.75m | 3.40m | 3.40m | 3.75m | 4.69 ddt | −1.24 s |
| Ib | 7.13 tt<br>*J* 6.0, 0.8 | 4.67 ddt<br>*J* 9.0, 6.0, 0.8 | 3.72m | 3.32 tt<br>*J* 3, 0.7 | 3.32 tt | 3.72m | 4.67 ddt | — |
| Ic | 7.43 tbr<br>*J* 6.0, 0.9 | 4.55 ddt<br>*J* 9.3, 6.0, 1.3 | 3.68m | 3.33m | 3.33m | 3.68m | 4.55 ddt | 3.0—4.0m |
| Id | 7.33 tbr<br>*J* 5.5 | * | | | | | | |
| IIa | — | 4.70 dbr<br>*J* 8.7 | 3.74m | 3.39m | 3.39m | 3.74m | 4.70 dbr | −1.60 s |
| IIb | — | 4.63 dbr<br>*J* 9.5 | 3.70m | 3.27 tt<br>*J* 3, 0.7 | 3.27 tt | 3.70m | 4.63 dbr | — |
| IIIa | 7.65 t<br>*J* 7.0 | 3.42 t<br>*J* 7.0 | — | 2.85 dd<br>*J* 11.5, 0.7 | 3.35 dd<br>*J* 11.5, 5.3 | 3.80 dd<br>*J* 9.0, 5.3 | 4.64 dt<br>*J* 9.0, 7.0 | −2.40 s |
| IIIb | 7.62 t<br>*J* 7.0 | 3.97 t<br>*J* 7.0 | — | 3.46 dm<br>*J* 11.2, >1 | 3.20 ddt<br>*J* 11.2, 5.0, 0.3 | 3.74 ddd<br>*J* 9.3, 5.0, 0.3 | 4.58 dt<br>*J* 9.3, 7.0 | — |
| IIIc | 7.70 t<br>*J* 6.8 | | — | | | | | |
| IIId | 7.75 t<br>*J* 6.9 | | — | | | | | |
| IV | 7.67 dt<br>*J* 6.7, 3.0 | 3.40 d<br>*J* 6.7 | — | 2.82 dd<br>*J* 11.0, 1.0 | 3.31 dd<br>*J* 11.0, 5.5 | 3.78 dd<br>*J* 9.0, 5.5 | 4.63 dd<br>*J* 9.0, 6.7 | −1.26 s |
| Va | 7.72 t<br>*J* 6.8 | 4.40 dt<br>*J* 9.3, 6.8 | 3.31 d<br>*J* 9.3 | — | 2.30 d<br>*J* 6.0 | 3.72 dd<br>*J* 9.3, 6.0 | 4.63 dt<br>*J* 9.3, 6.8 | −2.05 s |
| Vb | 7.67 t<br>*J* 6.8 | 4.49 d<br>*J* 9.8, 6.8 | 3.77 d<br>*J* 9.8 | — | 2.83 d<br>*J* 5.5 | 3.72 dd<br>*J* 9.8, 5.5 | 4.38 dt<br>*J* 9.8, 6.8 | — |
| Vc | 7.77 t<br>*J* 6.8 | | | — | | | | |
| VIa | 7.37 d<br>*J* 6.7 | — | | | | | | |
| VIb | 7.34 d<br>*J* 7.0 | — | | | | | | |

a) In carbon tetrachloride as solvent, except compounds Ic and IIIc (deuteriochloroform).
br, broad; s, singlet; d, doublet; dd, double doublet; ddd, double doublet of doublets; t, triplet; dt, double triplet; ddt, double doublet of triplets; m, multiplet; dm, doublet of multiplets; *J* in Hz.
* The spectrum is too complicated to determine the accurate chemical shift remained blank.

Table 2. The action of aq. NaOH on Ia at 90°C for 3 hr

| Basicity (N) | Yield (%) | | | |
|---|---|---|---|---|
| | Ia | IIIa | Va | VIa |
| 0.2 | 90 | 5 | | |
| 1 | 40 | 40 | | |
| 4 | 20 | 68 | | |
| 10 | 15 | 60 | 10 | 5 |

Table 3. The action of 20% alc. KOH on Ia at 90°C

| Reaction Time (hr) | Yield (%) | | |
|---|---|---|---|
| | IIIa | Va | VIa |
| 2 | 86 | 14 | trace |
| 8 | 58 | 34 | 8 |

Table 4. The action of 45% alc. KOH on Ia at 130°C

| Reaction time (hr) | Yield (%) | | |
|---|---|---|---|
| | IIIa | Va | VIa |
| 1.5 | 25 | 31 | 44 |
| 14 | 22 | 28 | 50 |
| 37 | 20 | 26 | 53 |

Table 5. The action of 28% aq. NaOH on IIIa at 90°C

| Reaction time (hr) | Yield (%) | | |
|---|---|---|---|
| | IIIa | Va | VIa |
| 1 | 93 | 7 | |
| 3 | 85 | 15 | trace |
| 7 | 78 | 18 | 4 |
| 19 | 70 | 21 | 9 |
| 27 | 56 | 24 | 20 |

Table 6. The action of 20% alc. KOH on Va at 90°C

| Reaction time (hr) | Yield (%) | | |
|---|---|---|---|
| | IIIa | Va | VIa |
| 3 | 22 | 76 | 1.5 |
| 8 | 36 | 61 | 3 |

The effect of the substituents upon the relative rate of the isomerization was studied using other cycloheptatriene derivatives. The enhanced rates of the proton exchange and the isomerization resulted, to a great extent, in a cyano group. Upon the treatment of 7-cyanocycloheptatriene (Ib) with 4% sodium methoxide (in deuterium oxide) for 12 hr at room temperature, the proton exhange at the 7-position similarly took place to afford the deuterated compound (IIb) [no deuterium exchange occurred in deuterium oxide-dioxane (1 : 1)]. The 7-cyano compound (Ib) was readily converted to the 2-substituted isomer (IIIb) with 0.5% alcoholic potassium hydroxide (53% after three days at room temperature) or with 1.3% aqueous potassium hydroxide (80% after 2 hr at 45°C with stirring). Among the above reaction mixtures, a trace of 3-cyanocycloheptatriene (Vb), the secondary isomerization product, was detected (NMR). The rate of the initial isomerization was, however, much faster than those of the secondary or the subsequent isomerization, as was observed in the carboxycycloheptatriene system. It was found in the case of cyanocycloheptatriene that the hydrolysis of the cyano group took precedence over the secondary or tertiary isomerization in 2N aqueous sodium hydroxide; thus, the procedure is applicable to the preparation of IIIa and Va from the corresponding cyanocycloheptatrienes (see the Experimental section).

7-Carbamoilycycloheptatriene (Ic), when kept in 2.5N sodium hydroxide at 75°C for 10 min, gave a mixture consisting of the recovered Ic, the isomer (IIIc), Ia, and IIIa in a ratio of 13 : 14 : 68 : 5 (from NMR). Because Ia was confirmed not to isomerize to IIIa under the above conditions (*i. e.*, IIIa was derived from IIIc), the above ratio of the products suggested that the hydrolysis of the carbamoil group of Ic took place approximately 3.5 times faster than the isomerization of Ic to IIIc.[9]

Table 7. The action of 10% alc. KOH on Id at 84°C

| Reaction time (hr) | Yield (%) | | | |
|---|---|---|---|---|
| | Id | IIId | Vc | VIb |
| 0.7 | 40 | 33 | 11 | 11 |
| 1.5 | 16 | 50 | 17 | 16 |
| 4 | | 59 | 21 | 20 |

Among the isomerized products of 7-phenylcycloheptatriene[10] (Id), as is shown in Table 7, a small amount of the secondary and the tertiary isomers, Vc and VIb, was present, besides the main product, IIId, on treatment even with a dilute base. The conjugative effect of the aryl group could make the subsequent isomerization easier. The effect of the various substituents upon the relative rates of the isomerization was thus considered to be, by comparison with the semi-quantitative results mentioned above: $CN > CONH_2 > COO^-$, Ph (the rates of the last two appeared to be very similar).

Cycloheptatriene itself, when treated with a mixture of 10N sodium deuteroxide and dioxane (1 : 1) at 90°C for 8 hr, remained completely unchanged. Nor was any deuterium exchange (nor isomerization) observed when 7-methoxycycloheptatriene was refluxed with 9% alcoholic potassium hydroxide for 4 hr. These results showed that a hydrogen atom of a cycloheptatriene should be replaced by an electron-withdrawing group as a requirement for the base-catalyzed proton exchange followed by the isomerization; the isomerization and the exchange rates are in proportion to the acidity of the hydrogen atom of the 7-position of cycloheptatriene.

To clarify the reaction mechanism, a kinetic study of the isomerization of 7-carboxycycloheptatriene (Ia) in a base was carried out. The disappear-

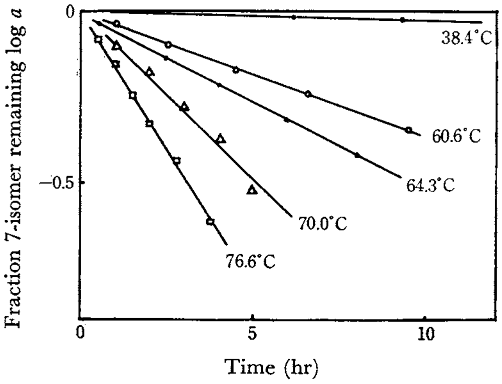

Fig. 1. Plots of the logarithm of the fraction of 7-isomer present *vs.* time at several temperatures.

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[9] Alkaline hydrolysis of Ic has been reported to afford IIIa but not Ia (Ref. 8a). Present experiment showed that the reaction would competitively undergo through: Ic→Ia→IIIa and Ic→IIIc→IIIa. Successful preparation of Ia from Ic was carried out by treatment with acid (see Experimental part).

[10] T. Nozoe, T. Mukai, T. Tezuka and K. Osaka, *Nippon Kagaku Zasshi*, **84**, 662 (1963). They reported that 7-phenylcycloheptatriene (Id), when refluxed with 10% ethanolic sodium hydroxide for 15 hr, gave an isomer which showed a triplet signal ($\tau$ 7.76, $J$=7.0 Hz) due to a methylene group of a phenylcycloheptatriene.

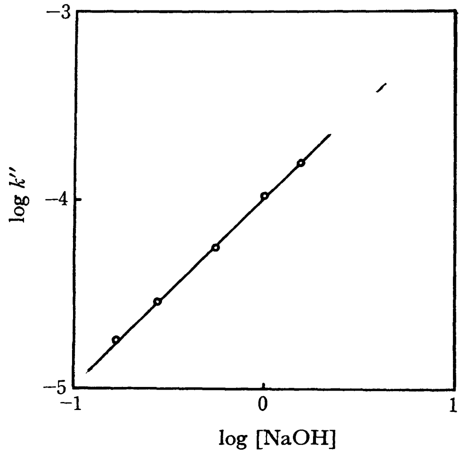


Fig. 2. Rate constants for the isomerization against a function of the base concentration.

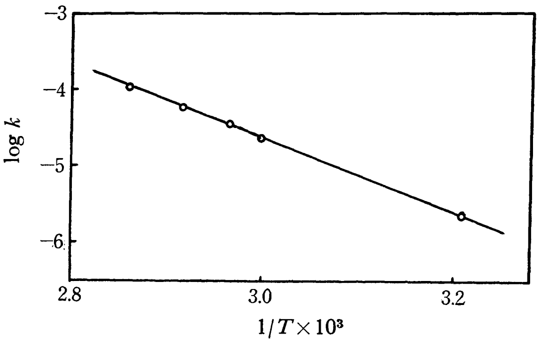


Fig. 3. Rate constants for the isomerization against a function of temperature.

Table 8. Observed and true rate constants ($k'$ and $k$) for the isomerization of Ia to IIIa in aq. NaOH

| Temp. (°C) | $k'$(sec$^{-1}$)[a] | $k$($l$/mol·sec)[b] |
|---|---|---|
| 76.6±0.1 | $1.07\times10^{-4}$ | $1.07\times10^{-4}$ |
| 70.0±.10 | $6.0\ \times10^{-5}$ | $6.0\ \times10^{-5}$ |
| 64.3±0.05 | $3.45\times10^{-5}$ | $3.46\times10^{-5}$ |
| 60.6±0.1 | $2.30\times10^{-5}$ | $2.31\times10^{-5}$ |
| 38.4±0.2 | $2.15\times10^{-6}$ | $2.16\times10^{-6}$ |

a) In 0.996N NaOH

b) Calculated from the equation $k$[Ia][NaOH]

Table 9. Rate constants ($k''$) for the isomerization of Ia in aq. NaOH at 76.1±0.1°C

| Basicity (N) | $k''$ (sec$^{-1}$) |
|---|---|
| 1.53 | $1.60\times10^{-4}$ |
| 0.996 | $1.05\times10^{-4}$ |
| 0.547 | $5.56\times10^{-5}$ |
| 0.275 | $2.81\times10^{-5}$ |

Table 10. Transition state parameters[a] for the base-catalyzed isomerization of Ia to IIIa

| $E_a$ kcal/mol | log $A$ sec$^{-1}$ | $\Delta F^{\neq}$ kcal/mol | $\Delta H^{\neq}$ kcal/mol | $\Delta S^{\neq}$ e.u. |
|---|---|---|---|---|
| 22.6 | 9.91 | 27.1 | 22.0 | −15.4 |

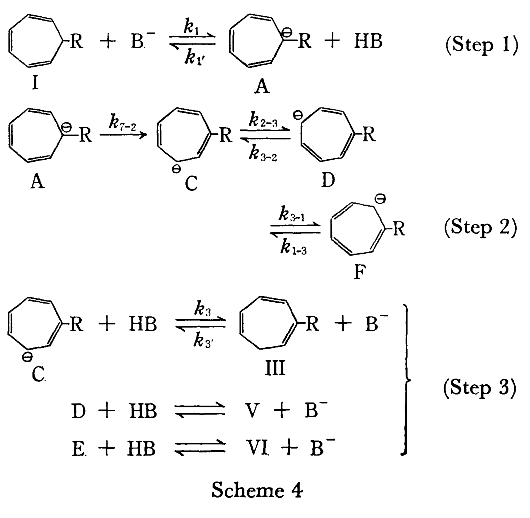
a) The transition state parameters are reported at 60°C.

ance of Ia in 0.996N sodium hydroxide, measured spectrophotometrically, exhibited good first-order kinetics over the temperature range of 38—77°C (see Fig. 1); the observed rate constants, $k'$, are shown in Table 8. The variation in the rates as a function of the concentration of the base was also studied at 76.0±0.1°C, the results being shown in Table 9. Assuming the observed first-order rate constants, $k''$, to be $k[\text{NaOH}]^n$, the slope of the straight line (Fig. 2), obtained by plotting log $k''$ against log [NaOH], indicated that $n$ equals 1.0; thus, the rate of the isomerization may be expressed in terms of the following equation:

$$v=k\ [\text{the cycloheptatriene}]\ [\text{base}]$$

The rate constants, $k$, for the isomerization at the various temperatures in the unit concentration of sodium hydroxide were calculated to be as is shown in Table 8. A plot of the $k$ values against $1/T$ was found to be linear (*cf.* Fig. 3), giving values for the transition-state quantities, $\Delta F^{\neq}$, $\Delta H^{\neq}$, and $\Delta S^{\neq}$ (from Eyring formulation). The results of these calculations are summarized in Table 10.

It can be postulated from the foregoing results that the base-catalyzed isomerization of cycloheptatrienes involved the carbanion formation (Step 1), the migration of the carbanion charge to the allylic position (Step 2), and finally the reformation of the isomerized cycloheptatriene by picking up a proton from the solvent (Step 3), as is illustrated by Scheme



Scheme 4

4. According to the reaction pathways shown here, the rates of the formation of three substances, A, C, and III, can be expressed as follows:

$$\frac{d[A]}{dt} = k_1[I][B^-] - k_{1'}[A][HB] - k_{7-2}[A] \qquad (1)$$

$$\frac{d[C]}{dt} = k_{7-2}[A] + k_{3-2}[D] - k_{2-3}[C] - k_3[C][HB] \qquad (2)$$

$$\frac{d[III]}{dt} = k_3[C][HB] - k_{3'}[III][B^-] \qquad (3)$$

where $k_1$, $k_1'$, $k_{7-2}$, $k_{2-3}$, $k_3$, and $k_3'$ are the rate constants of the reactions (Scheme 4); where [I], [A], [C], [D], and [III] are the concentrations (mol/*l*) of the corresponding substances in Scheme 4 and where $B^-$ and HB are, respectively, the anion of the base and the protonated anion (the solvent).

Although complete deuterium exchange was observed at the 7-position of Ia when it was dissolved in 2N sodium deuteroxide at room temperature, the heating of the solution at a higher temperature was required to cause the isomerization to give IV (as a single product; see above), indicating that Step 2 was the rate-determining process in the isomerization of IIa to IV (*i. e.*, $k_1$, $k_1'$, $k_3 \gg k_{7-2} \gg k_3'$, $k_{2-3}$). Upon the treatment of IIIa with 4N sodium deuteroxide at 100°C for 7 hr, the intensities of the methylene signal ($\tau$ 7.65) decreased to 0.75 H and the signals due to H(1) ($\tau$ 3.42, *t*) and H(6) ($\tau$ 4.64, d*t*) broadened in the NMR spectrum of the product, showing the formation of a mixture of IV and 7,7-$d_2$-2-carboxycycloheptatriene. This demonstrated that the proton exchange (with the solvent) at the 7-position preceded the isomerization reaction not only in 7-substituted cycloheptatrienes, but also in the 2-isomers (probably in the other isomers also), although the rates of both the exchange and the isomerization of the latter compounds were considerably slower than those of the former. Besides, the results in Table 5 and 6, as explained above, show that the compounds IIIa, Va and VIa were at equilibrium in stronger bases. Thus, the following relationship can be establisehd: $k_3$, $k_3' \gg k_{2-3}$, $k_{3-2}$, $k_{3-1}$, $k_{1-3}$.

Consequently, Eqs. (1)—(3) may be simplified as follows:

$$\frac{d[A]}{dt} = k_1[I][B^-] - k_{1'}[A][HB] \qquad (1')$$

$$\frac{d[C]}{dt} = k_{7-2}[A] - k_3[C][HB] \qquad (2')$$

$$\frac{d[III]}{dt} = k_3[C][HB] \qquad (3')$$

The formation of the intermediates, A and C, in dilute aqueous sodium hydroxide is considered to be a steady-state reaction; thus, $d[A]/dt \simeq 0$, and $d[C]/dt \simeq 0$. Therefore,

$$\frac{d[III]}{dt} = k_{7-2}[A] = k_{7-2}\frac{k_1[I][B^-]}{k_{1'}[HB]} = k[I][B^-]$$

where $k = k_1 \cdot k_{7-2}/k_{1'}[HB] = \text{const.}$

This equation, which is in agreement with our expermental results presented above, would seem to verify the assumption of the three-step isomerization mechanism shown in Scheme 4.

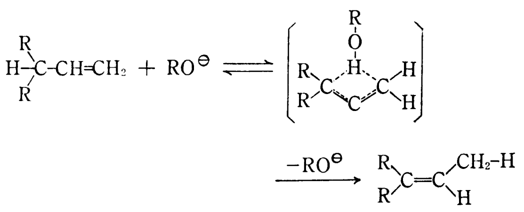
Similarly, when V is formed from III, the rate of the isomerization may be calculated as follows:

$$\frac{d[V]}{dt} = k'[III][B^-]$$

where; $k' = k_{3'} \cdot k_{2-3}/k_3[HB]$

Although $k'$ is probably much smaller than the $k$ shown above, the higher concentration of the base would facilitate the secondary isomerization reaction. This is also in accordance with our experimental results, which show that Va was formed from IIIa only in strong alkali (see above). The equilibrium relationship among the compounds III, V, and VI could be explained similarly. The determination of the equilibrium constants of each reaction in Scheme 4 would be of interest in connection with the relationship to the p$K_a$ values of H(7) of the compounds I, III, V, and VI.

Concerning the base-catalyzed allylic proton transfer, intramolecularity has been observed in various organic solvents and bases, as is explained in Scheme 5, where the isotopic exchange is much slower than the isomerization.[11] Scheme 5



Scheme 5

In our system, however, the rate of proton exchange was much faster than that of the isomerization (*i.e.*, $k_1$, $k_1' \gg k_{7-2}$; $k_3$, $k_3' \gg k_{2-3}$), and no clear evidence of intramolecularity was detected.

The rate-determining step of the isomerization (Step 2 in Scheme 4) involves p–$\pi$ bond rehybrization to form an allylic carbanion, the structure of which will now be discussed. According to the

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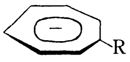
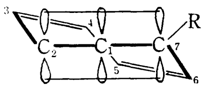
[11] D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press, New York (1965), p. 175; S. Bank, C. A. Rowe, Jr., and A. Schriesheim, *J. Amer. Chem. Soc.*, **85**, 2115 (1963); G. Bergson and A. M. Weidler, *Acta Chem. Scand.*, **17**, 862, 1798, 2691, 2724 (1963); R. B. Bates, R. H. Carnighan and C. E. Staples, *J. Amer. Chem. Soc.*, **85**, 3032 (1963); V. A. Mironov, E. V. Sobolev and A. N. Elizarova, *Tetrahedron*, **19**, 1939 (1963); W. R. Roth, *Tetrahedron Lett.*, **1964**, 1009; S. McLean and P. Haynes, *ibid.*, **1964**, 2385; Y. Kitahara, I. Murata and T. Muroi, This Bulletin, **38**, 1195 (1965).



F



G

molecular orbital theory, a cycloheptatrienyl anion which possesses eight electrons should exist as a triplet diradical in the ground state. The heptaphenylcycloheptatrienyl anion[12] has been reported to be a singlet because of the distortion by the phenyl groups. Dauben,[13] Doering,[14] and their co-workers have reported that they detected the $D_{7h}$ symmetrical (coplanar) cycloheptatrienyl anion by the deuterium exhcange, which occurred randomly on each carbon atom of the seven-membered ring. Under our circumstances, the migration of the anionic charge took place only to the allyclic position (*cf.* Scheme 4); this suggests that the rehybrization is limited within the three carbon atoms concerned, eliminating the possibility of a coplanar cycloheptatrienyl anion (F) as the structure of the intermediate anion. Thus, such a three-carbon coplanar anionic structure as is shown in the formula G seems most probable.

## Experimental

The NMR measurements were made at 25°C with a 60 Mc/sec Varian A-60 spectrometer.

**7-Carboxycycloheptatriene (Ia).** A mixture of 4.35 g of Ic (see below) and 110 m*l* of 2N sulfuric acid was heated at 120°C (bath) for 1 hr. The cooled mixture was brought to pH2 with 6N sodium hydroxide at 0°C, and then extracted with ethyl acetate. The dried extract (over $MgSO_4$) was evaporated and the residue was distilled, giving 3.65 g of Ia as a pale yellow oil, bp 98—100°C/2.5 mmHg $\lambda_{max}^{MeOH}$ m$\mu$ (log $\varepsilon$): 260 (3.52). $\nu_{max}^{neat}$ 3300—3020 mbr, 3026 m, 2910 m, 2700 w, 2600 w, 1710 s, 1600 m, 1417 m, 1392 w, 1300 m, 1220 m, 1202 m, 998 w, 930 w, 743 m and 705 s cm$^{-1}$.

**7-Cyanocycloheptatriene (Ib).** Although Doering and Knox[15] prepared Ib from tropylium bromide and potassium cyanide in a 87% yield, a slightly modified procedure was used. A mixture of 31.4 g of 7-ethoxycycloheptatriene[6a] and 120 m*l* of 2N hydrochloric acid was stirred at 0°C for 30 min, and then 26.0 g (1.7 equiv.) of potassium cyanide dissolved in 100 m*l* of cold water were slowly stirred in at 0°C (1 hr). After stirring for further 2 hr at room temperature, the mixture was extracted with ether; the dried extract (over $MgSO_4$) was freed from the solvent and distilled, giving 24.7 g of Ib as a colorless oil (92% yield) bp 105°C/27 mmHg. $\lambda_{max}^{MeOH}$ m$\mu$ (log $\varepsilon$): 259(3.70). $\nu_{max}^{neat}$ 3030 m, 2220 m, 1684 w, 1592 w, 1429 w, 1381 m, 1269 w, 1193 w, 1104 w, 1010 m, 975 w, 943 w, 802 w, 791 w, 745 s, 702 s and 685 s cm$^{-1}$.

(Found: C, 81.30; H, 6.08; N, 11.95%).

**7-Carbamoilcycloheptatriene (Ic).** The procedure followed that of Doering and Knox,[15] and Ic was obtained from Ib as colorless needles in a 47% yield (from ether), mp 140°C (lit,[7b,8a] 141°C). However, benzamide was also present (14%) as a by-product. $\nu_{max}^{KBr}$ 3390 s, 3205 s, 3012 m, 1661 s, 1639 sh, 1605 sh, 1429 s, 1387 m, 1269 m, 1209 w, 1140 w, 979 w, 735 s and 698 s cm$^{-1}$.

**The Action of the Base on Ic.** A mixture of 100 mg of Ic and 1.2 m*l* of 2.5N sodium hydroxide was heated while being stirred at 70°C for 10 min. The cooled mixture was extracted with ethyl acetate; the organic layer was then washed with 0.5N sodium hydroxide, dried over $MgSO_4$, and evaporated to give 23 mg of colorless needles, which were found (from NMR) to be a mixture of Ic and IIIc (1 : 1.1). The above aqueous layer, combined with the washing, was brought to pH 2 with cold 2N sulfuric acid and extracted with ethyl acetate. The dried extract (over $MgSO_4$) was evaporated to give 61 mg of a yellow oil consisting of Ia and IIIa (15 : 1, from NMR).

**7-*d*-7-Carboxycycloheptatriene (IIa).** A solution of 136 mg of Ia dissolved in 1 m*l* of 2N sodium deuteroxide was set aside at room temperature for 41 hr and then stirred into 1.4 m*l* of cold 2N sulfuric acid at 0°C. The contents were, after having been stirred for 5 min, extracted with ethyl acetate; the dried extract was then evaporated *in vacuo*, giving 120 mg (88%) of IIa as a yellow oil (on the evidence of NMR).

**7-*d*-7-Cyanocycloheptatriene (IIb).** To a solution of 40 mg of sodium methoxide dissolved in 1.0 g of deuterium oxide, 50 mg of Ib were added. After having been set aside for 12 hr at room temperature with occasional shaking, the mixture was poured into 3 m*l* of cold 1N sulfuric acid and extracted with benzene. The evaporation of the extract *in vacuo* give 38 mg of IIb as a yellow oil (from NMR).

**2-Carboxycycloheptatriene (IIIa).** *a)* A mixture of 3.0 g of IIIb (see below) and 24 m*l* of 2.5N sodium hydroxide was refluxed for 3 hr with stirring. A small amount of a black tar formed was removed by decantation from the cooled mixture, which was then taken to pH2 with 6N sulfuric acid at 0°C and extracted with ether. The organic layer was extracted with cold 2N sodium hydroxide. After the acidification (pH 2) of the alkaline solution, the contents were extracted with ethyl acetate. The dried extract (over $MgSO_4$) was evaporated *in vacuo* and distilled at 103°C/3 mmHg, giving 1.27 g (43%) of IIIa as colorless needles. Sublimation at 80°C(bath)/0.1 mmHg gave the pure material, mp 71—72°C (lit[7c,8b] 71.5°C). $\lambda_{max}^{MeOH}$ m$\mu$ (log $\varepsilon$): 261(3.31). $\nu_{max}^{KBr}$ 3200—3100 mbr, 3012 m, 2976 sh, 2874 m, 2841 sh, 2653 m, 2545 m, 1692 sh, 1675 s, 1603 m, 1456 w, 1416 m, 1377 w, 1333 m, 1312 s, 1295 s, 1214 w, 1098 w, 925 w, 906 w, 882 w, 804 w, 760 m and 717 s cm$^{-1}$.

*b)* A mixture of 1.42 g of Ic and 8 m*l* of 2.5N sodium hydroxide was kept at 120°C (bath) for 1.5 hr, it was brought, after cooling, to pH 2 with cold 6N sulfuric acid, and then extracted with ether. The extract was twice shaken with cold 2N sodium hydroxide. The combined aqueous layer was taken to pH 2 with cold

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[12] R. Breslow and H. W. Chang, *J. Amer. Chem. Soc.*, **84**, 1484 (1962).

[13] H. J. Dauben, Jr., and M. R. Rifi, *ibid.*, **85**, 3041 (1963).

[14] W. von E. Doering and P. P. Gasper, *ibid.*, **85**, 3043 (1963).

[15] W. von E. Doering and L. H. Knox, *ibid.*, **79**, 352 (1957).

6N sulfuric acid and extracted with ethyl acetate. The evaporation of the organic layer *in vacuo* left a brown viscous tar which recrystallized from water, giving 0.68 g, (48%) of IIIa (from IR), mp 69—70°C.

*c)* A solution of 100 mg of Ia in 1 m*l* of 2.5N sodium hydroxide was heated at 120°C (bath); the cooled mixture was acidified (pH 2) with 2N sulfuric acid. The precipitate was filtered off and recrystallized from water, giving 80 mg of IIIa (from IR) as colorless plates mp 71—72°C.

**2-Cyanocycloheptatriene (IIIb).** The material Ib (1.00 g) in 50 m*l* of 0.5% alc. potassium hydroxide was set aside at room temperature for 3 days. After the addition of 100 m*l* of water, the mixture was extracted with ether. The dried extract (over $MgSO_4$) was evaporated at 20°C under reduced pressure and distilled, giving 0.53 g of IIIb as a colorless oil bp 105—108°C/23 mmHg. The NMR data are shown in Table 1.

**7-*d*-2-Carboxycycloheptatriene (IV).** *a)* A solution of 136 mg of Ia in 1 m*l* of 2N sodium deuteroxide was gently refluxed for 2 hr and then, after cooling, brought to pH 2 with cold 2N sulfuric acid. The precipitate was collected and sublimed at 80°C/0.1 mmHg, giving 90 mg of colorless plates, mp 48—50°C, which were shown to be IV (from NMR; *cf.* Table 1). $\nu_{\max}^{\mathrm{KBr}}$ 3200—3100 mbr, 3003 m, 2950 sh, 2841 m, 2646 m, 2525 m, 1686 sh, 1672 s, 1597 m, 1447 m, 1412 s, 1374 s, 1332 s, 1305 sh, 1292 s, 1209 w, 920 m, 904 w, 894 w, 880 w, 801 w, 758 m and 715 s $\mathrm{cm}^{-1}$.

*b)* A mixture of 109 mg of IIIa and 1 m*l* of 4N sodium deuteroxide was heated at 100°C(bath) for 7 hr and then treated much as above, giving 97 mg of pale yellow plates, mp 51—55°C. The product was found to be a mixture of IV and 7,7-$d_2$-2-carboxycycloheptatriene on the evidence of the NMR spectrum (see the main text).

**3-Carboxycycloheptatriene (Va).** A mixture of 10.0 g of Vb (see below) and 80 m*l* of 2.5N sodium hydroxide was stirred at 20°C for 5 hr, then at 90°C(bath) for 1 hr, and finally at 130°C(bath) for 2 hr. The cooled mixture was brought to pH 2 the careful addition of 2N sulfuric acid and extracted with ethyl acetate. The dried extract (over $MgSO_4$) was freed from the solvent and distilled, giving 7.47 g of colorless needles (70% yield), bp 106—107°C/0.2 mmHg, which sublimed at 80°C(bath)/0.1 mmHg and afforded Va as colorless needles, mp 56—57°C (lit,[7c,8b] 59.5°C). $\lambda_{\max}^{\mathrm{MeOH}}$ m$\mu$ (log $\varepsilon$): 279(3.79). $\nu_{\max}^{\mathrm{KBr}}$ 3200—3100 mbr, 3030 m, 2967 m, 2865 m, 2825 m, 2660 m, 2545 m, 1675 s, 1610 m, 1536 m, 1435 s, 1408 w, 1395 w, 1340 m, 1294 s, 1236 w, 1200 w, 1190 sh, 1100 w, 968 w, 951 sh, 939 w, 800 w, 770 w and 740 s $\mathrm{cm}^{-1}$.

**3-Cyanocycloheptatriene (Vb).** The compound Ib (146 g) was heated at 155°C(bath) for 2 hr under a nitrogen atmosphere (1 atm) in a flask stopped with a nitrogen balloon. (This method is frequently used because of convenience and safety in large-scale experiments on thermal isomerization). The distillation of the product gave 130 g of a pale yellow liquid (94%) bp 53°C/0.4 mmHg. This consisted of Vb (more than 90%) and 1-cyanocycloheptatriene (less than 10%), togethe with a trace of the unreacted Ib. (The percentage was derived from the NMR integration.)

**Thermal Isomerization of Carboxycycloheptatrienes.** When 110 mg of Ia was heated in a sealed tube at 150°C for 3 hr, the NMR spectrum showed the presence of Ia and Va in the ratio of 1 : 1, plus a trace of VIa. The compound IIIa gave a mixture of IIIa and VIa (4 : 1) when heated at 150°C for 5 hr. Similarly, Va afforded a mixture of Va and VIa (*ca.* 1 : 3) when heated at 180°C for 4 hr.

**Reaction Rate Measurements.** *a) The Base-catalyzed Isomerization of Ia to IIIa in 0.996N Sodium Hydroxide.* An aqueous solution of Ia (*ca.* $1\times10^{-2}$ mol/*l*) in 0.996N sodium hydroxide was prepared. About 1.2 m*l* of the solution in a sealed tube was kept in the vapour of carbon tetrachloride (76.6±0.1°C), methanol (64.3±0.05°C), chloroform (60.6±0.1°C), and dichloromethane (38.4±0.2°C), and in an oil bath equipped with a thermostat (70±1°C). The tubes were taken out at regular intervals, and 1 m*l* of the solution was added to 10 m*l* of a mixture of 1.5N hydrochloric acid and methanol (1 : 9 v/v.). Then 1 m*l* of the dilute solution was added to 10 m*l* of methanol. The reference solution was prepared in a similar manner. The fraction of the 7-substituted cycloheptatriene remaining was calculated from:

$$a = \frac{E_\infty - E}{E_\infty - E_0}$$

where $E_0$, $E_\infty$, and $E$ are the extinctions of Ia, IIIa and the reaction mixture respectively, at 230 m$\mu$ (measured with Hitachi recording spectrophotometer, Model EPS-3). The rate constant, $k'$, was determined from a plot of log $a$ *vs.* the time (Fig. 1).

*b) The Base-catalyzed Isomerization of Ia to IIIa in Various Strengths of the Basicity at 76.1±0.1°C.* A solution ($2\times10^{-3}$ mol/*l*) of Ia in a given concentration of sodium hydroxide was heated in a sealed tube at 76.1±0.1°C (in a carbon tetrachloride vapour bath). Measurements were carried out much as in the foregoing experiment except that 1 m*l* of the reactant was diluted with 9 m*l* of methanol and 1 m*l* with hydrochloric acid strong enough to make the mixture slightly acidic (pH 2). The results are shown in Table 9.

*c) Thermal Isomerization of Ia to Va.* A solution of 5.839 mg of Ia dissolved in 50 m*l* of isooctane was prepared. About 1.1 m*l* of the solution sealed in a tube were heated at 99.9±0.1°C (water vapor bath). The tube was taken out at regular intervals, 1 m*l* of the solution was diluted with 10 m*l* of isooctane, and the extinction was measured at 280 m$\mu$. The rate constant ($k=1.5\times10^{-6}$ $\mathrm{sec}^{-1}$), calculated much as above, was sought in order to compare it with that of the base-catalyzed isomerization of Ia in 1N sodium hydroxide at the same temperature, the latter being obtainable from Fig. 3 ($k=8.53\times10^{-4}$ *l*/mol·sec). The base-catalyzed isomerization was, therefore, found to be 5—$6\times10^2$ times the thermal reaction under the above conditions. This tendency could generally be the case for the isomerization of cycloheptatrienes with electron-withdrawing substituents. Accordingly, it was concluded that the thermal 1—5 hydrogen shift did not interfere with the measurement of the reaction rate of the base-catalyzed isomerization.

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