Proton-Mobility in the Indene Ring-System

III *. Kinetics of the Base-catalyzed Hydrogen Exchange between Indene and D₂O, and the Existence of Intramolecular Proton-Transfer

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Hydrogen exchange between indene and D_2O occurs at room temperature in pyridine solution with triethylamine as a catalyst. The exchange rate, obeying pseudo-first-order kinetics, was studied by the NMR-technique. The hydrogen atoms in the 1- and 3-positions of the indene molecule are substituted by deuterium, but in addition to this exchange reaction there is a rapid base-catalyzed proton-transfer between the 1- and 3-positions. The latter reaction could be studied separately using mono-deuteroindene.

Protium-deuterium and protium-tritium exchange experiments with indene have previously been made in different ways. Kharasch *et al.*[1] seem to be the first to have studied the exchange between indene and D_2O, and Koizumi[2] has also reported qualitative protium-deuterium exchange experiments. In his extensive works on hydrogen exchange, Shatenshtein[3] gives first-order rate constants for the reaction between indene and deuteroethanol or deuteroammonia. Furthermore, Avramoff and Sprinzak[4] found that protium-tritium exchange with indene is much more rapid in pyridine as a solvent than in ethanol, but only qualitative results are given.

In a previous note we reported[5] that protium-deuterium exchange and tautomeric rearrangements in the indene ring-system could easily be studied by the NMR-technique. This method is not only much simpler than those previously applied, but it also offers a possibility for a more detailed study of mechanisms.

We found that pyridine is a suitable solvent since it gives no interfering resonance signals and permits the use of fairly concentrated solutions of indene and D_2O. After addition of triethylamine (TEA) to a solution of indene and D_2O in pyridine, hydrogen exchange takes place at a rate convenient for kinetic studies at room temperature. Without TEA, the exchange is very slow, and can be neglected entirely in the following treatment.

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* The short communications by G. Bergson and A.-M. Weidler in *Acta Chem. Scand.* **17** (1963) 862 and **17** (1963) 1798 are regarded as Parts I and II, respectively, in this series.

EXPERIMENTAL RESULTS

The indene and triethylamine were redistilled shortly before use, and the pyridine, of *p.a.* quality, was dried over calcium hydride. D_2O (99.8 g/100 g) from Norsk Hydro was used in this investigation.

All kinetic runs were made with 2 M solutions of indene in pyridine at 30°C except when otherwise stated. With this indene concentration, homogeneous solutions containing D_2O concentrations as high as about 9 moles/l could be studied. The TEA concentrations used were 0.36, 0.72, and 1.08 moles/l. The proton magnetic resonance was measured by means of a Varian Associates A—60 analytical NMR-spectrometer; it was found that the A, K, and X-proton signals of indene, as well as the water signal, could be studied without interference from the peaks due to TEA and the aromatic protons in indene and pyridine. (Our assignment of the indene proton signals is based on the careful study by Elleman and Manatt.[6]) The close proximity of the aromatic peaks and the A-proton sextet makes, however, automatic integration of the latter difficult. Therefore, only the areas of the K- and X-protons signals were determined, except in a few cases when the areas of the A-, K-, and X-bands were determined by weighing.

As briefly reported earlier,[5] we found that the areas of the A- and X-signals gradually decreased, and the H_2O-signal increased. The area of the peak due to the K-proton, however, remained constant (*cf.* Table 1) apart from small

<div align="center">Table 1.</div>

Time, h	Area of K-band (Integration units)	Concentration in mole/l					
		H_2O-protons	A-protons	X-protons	(A+X)	A+X+H_2O	X/(X+A)
0.45	10.9	0.88	1.98	3.91	5.89	6.77	0.66
0.97	10.8	1.01	1.95	3.86	5.63	6.82	0.69
2.04	10.7	1.25	1.79	3.71	5.50	6.75	0.67
2.96	10.7	1.52	1.76	3.69	5.45	6.97	0.68
5.04	10.8	1.75	1.52	3.40	4.92	6.67	0.69
6.98	10.9	2.16	1.49	3.21	4.70	6.86	0.68
9.04	11.1	2.44	1.42	2.89	4.31	6.75	0.67
12.04	11.3	2.71	1.38	2.65	4.03	6.74	0.66

fluctuations. The most rational way of treating the data therefore seemed to be to regard the K-signal as an internal standard. From the known amount of indene added and the relative intensities of the K-, X-, and A-bands, the concentrations of X- and A-protons were thus calculated. The amount of H_2O-protons formed was determined empirically from a calibration curve obtained by integrating the water-peak and the K-signal in reference solutions made from varying known amounts of water and a constant amount of indene.

(X)
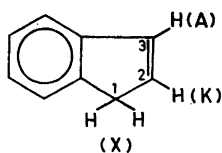
If A- and X-protons only are exchanged, self-consistency requires the sum of X-protons, A-protons and H_2O-protons to be independent of time. That this really is the case is shown in Table 1, where the results are given for an experiment starting from 2.00 mole/l of indene, 0.36 mole/l of TEA, 0.40 mole/l of H_2O, and 8.00 mole/l of D_2O at 25°C. Fig. 1 shows the results of an experiment where the A-proton peak was integrated automatically. Even in the latter case the self-consistency is fairly well shown.

Fig. 1. Concentration *vs.* time for different types of protons (run No. 3, Table 2).
O: X-protons. ▽: A-protons
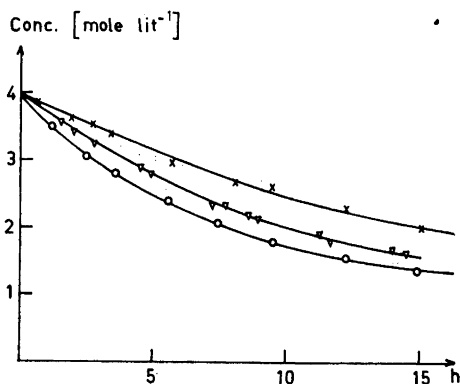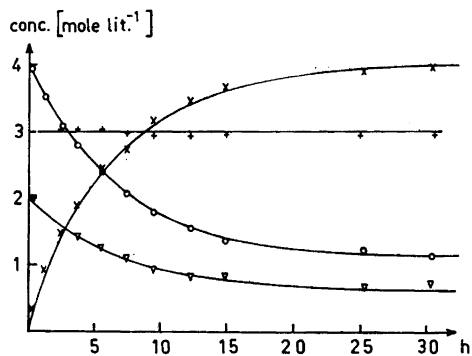×: H_2O-protons. +: $\frac{1}{2}(X + A + H_2O)$-protons.

Fig. 2. Concentration of X-protons *vs.* time for different TEA-concentrations. $d_0 = 16.5$ mole/l. $h_0 = 0$.
×: 0.36 mole/l TEA.
▽: 0.72 ,,
O: 1.08 ,,

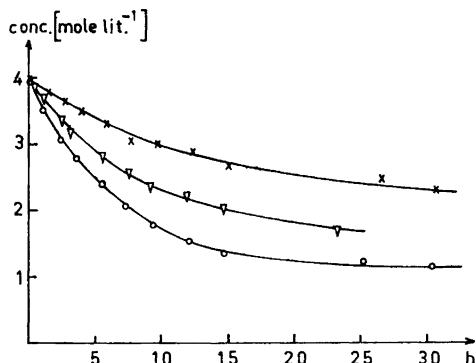*Fig. 3.* Concentration of X-protons *vs.* time for different d_0. TEA-concentration: 1.08 mole/l. $h_0 = 0$.
×: $d_0 = 5.5$ mole/l.
▽: $d_0 = 11.0$,,
O: $d_0 = 16.5$,,

An important observation is that the concentration ratio X/(X + A) is found to be independent of time, and, within the limits of experimental error, equal to 2/3, which is the value for pure indene (*cf.* Table 1).

The reaction rate is, as expected, a function of the amount of TEA added. This is borne out in Fig. 2. Furthermore, if the initial amount of D_2O is varied, the equilibrium concentration of X-protons should vary, which is the case. However, a closer analysis of the data presented in Fig. 3 also shows that the initial rate is a function of the starting amount of D_2O.

<center>ANALYSIS AND DISCUSSION OF THE EXCHANGE RATE</center>

Symbols:

B = concentration of catalyzing base,
H = concentration of (X + A)-protons,
D = concentration of (X + A)-deutrons,
x = concentration of X-protons,
y = concentration of X-deutrons,
h = concentration of H_2O-protons,
d = concentration of D_2O-deutrons.

The indices 0 and ∞ are used for concentrations at time 0 and at equilibrium, respectively.

The following relations are obviously valid:

$$d = d_0 - (H_0 - H) \tag{1}$$

$$h = h_0 + (H_0 - H); \quad \text{thus: } d + h = d_0 + h_0 \tag{2}$$

and $y = x_0 - x$ $\tag{3}$

An examination of the exchange data shows that the concentration of X-protons as a function of time can be expressed by the formula:

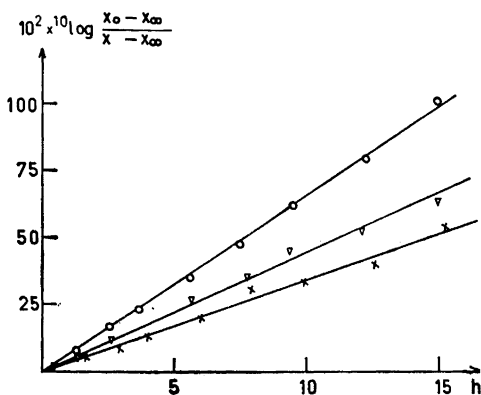$$x = (x_0 - x_\infty)\exp(-kt) + x_\infty \tag{4}$$

Fig. 4. Illustration of the validity of formula (4). $d_0 = 16.5$ mole/l. $h_0 = 0$. TEA-concentrations as in Fig. 2.
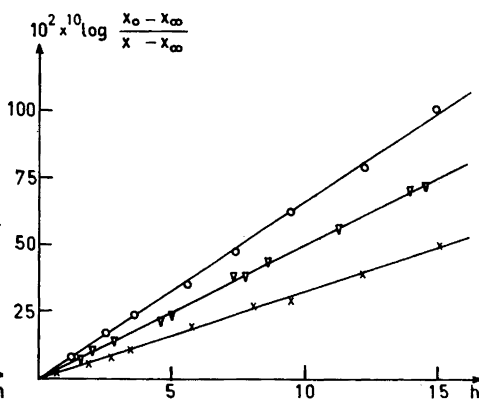
*Fig. 5.* Illustration of the validity of formula (4). TEA-concentration: 1.08 mole/l. $h_0 = 0$. d_0 as in Fig. 3.

The validity of the function (4) is shown in Figs. 4 and 5, from which it is evident that the parameter k depends on the TEA concentration and on the initial concentration of D_2O.

The experimentally observed function (4) is simply a solution of the rate equation for a first-order reversible exchange of X-protons:

$$\frac{dx}{dt} = -\lambda_1 x + \lambda_2 y \qquad (5)$$

with $\lambda_1 + \lambda_2 = k$.

It would be wrong, however, to draw any conclusions about the mechanism of the exchange reaction from this simple rate-law. It is quite well-known that if isotope effects can be neglected, the exchange will always follow first-order kinetics irrespective of mechanism.[7] Some information of the reaction mechanism can be obtained, however, by analyzing the factors determining the parameter k. In doing this, let us investigate the kinetic consequences of the following postulated sequence of reactions:
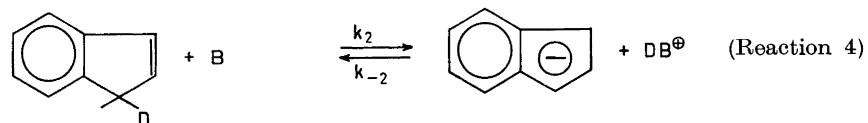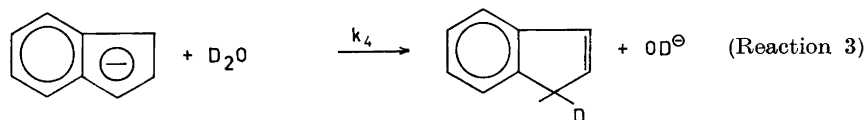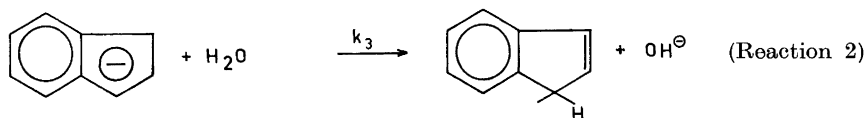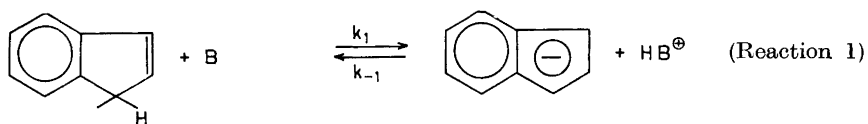
It is evident that the concentration of X-protons (or deutrons), which are the "acidic" ones, should enter the rate equations. The situation is somewhat complicated, however, by the fact that the removal of an X-proton does not necessarily result in an increase of X-deutrons, but may also lead to the creation of an A-deutron (reaction 5). An X-deutron can also be formed without the help of D_2O, as illustrated by reaction 6.

(Reaction 5)

(Reaction 6)
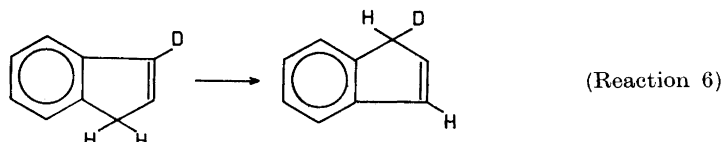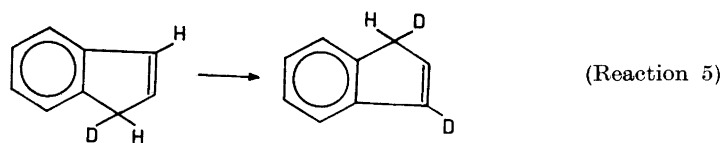
These considerations are, of course, independent of the mechanism involved. Therefore, the time derivative of the total proton concentration (X- plus A-type) must enter the rate equations. Thus, if we consider the above scheme, we get:

$$\frac{\mathrm{d}H}{\mathrm{d}t} = -k_1 xB + k_{-1}A_H\ominus + k_3 A\ominus h \tag{6a}$$

or $$\frac{\mathrm{d}D}{\mathrm{d}t} = -k_2 yB + k_{-2}A_D\ominus + k_4 A\ominus d \tag{6b}$$

where $A_H\ominus$ and $A_D\ominus$ denote an anion or an ion-pair derived from the indene molecule by the abstraction of a proton and a deuteron respectively. $A\ominus$ is the sum of $A_H\ominus$ and $A_D\ominus$.

The steady-state approximation for $A_H\ominus$ and $A_D\ominus$ gives:

$$A_H\ominus = k_1 xB/(k_{-1} + k_3 h + k_4 d) \tag{7}$$

and $$A_D\ominus = k_2 yB/(k_{-2} + k_3 h + k_4 d) \tag{8}$$

Combining (7), (8), and (6a) we get:

$$\frac{\mathrm{d}H}{\mathrm{d}t} = -k_1 k_4 Bxd/(k_{-1} + k_3 h + k_4 d) + k_2 k_3 Bhy/(k_{-2} + k_3 h + k_4 d) \tag{9}$$

The observed relation between x and H:

$$H = (3/2)x, \text{ and therefore } \frac{\mathrm{d}H}{\mathrm{d}t} = \tfrac{3}{2}\frac{\mathrm{d}x}{\mathrm{d}t} \tag{10}$$

makes it possible to analyze this rate equation further.

We consider the two limiting cases: (1°) $k_3 h$ and $k_4 d \ll k_{-1} \sim k_{-2}$ and (2°) $k_3 h$ and $k_4 d \gg k_{-1} \sim k_{-2}$.

Case 1. Eqn. (9) reduces to:

$$\frac{\mathrm{d}H}{\mathrm{d}t} = -\frac{k_1}{k_{-1}} k_4 Bxd + \frac{k_2}{k_{-2}} k_3 Bhy \tag{11}$$

If $k_1 k_4 B/k_{-1} = k_2 k_3 B/k_{-2} = k'$, eqn. (11) can be written as:

$$\frac{dH}{dt} = -k'd_0 x + k'(h_0 + \tfrac{3}{2} x_0)(x_0-x) \tag{12}$$

or by using the relation (10):

$$\frac{dx}{dt} = -\tfrac{2}{3} k'd_0 x + \tfrac{2}{3} k'(h_0 + \tfrac{3}{2} x_0)(x_0-x) \tag{13}$$

since $-xd + yh = -xd_0 + (h_0 + \tfrac{3}{2}x_0)(x_0-x)$. Therefore, k is given by

$$k = \tfrac{2}{3}k'(d_0 + h_0 + \tfrac{3}{2}x_0) \tag{14}$$

Case 2. Eqn. (9) reduces to:

$$\frac{dH}{dt} = \frac{-k_1 k_4 Bxd + k_2 k_3 Bhy}{k_3 h + k_4 d} \tag{15}$$

This equation can give first-order kinetics only if $k_3 = k_4$ and $k_1 = k_2$. Thus:

$$\frac{dH}{dt} = \frac{-k_1 B d_0 x + k_1 B(h_0 + \tfrac{3}{2}x_0)(x_0-x)}{h_0 + d_0} \tag{16}$$

and therefore:

$$k = \frac{2k_1 B}{3(h_0 + d_0)}(d_0 + h_0 + \tfrac{3}{2}x_0) \tag{17}$$

From Table 2 it is evident that the dependence of k on d_0 is in agreement with case 1 but not with case 2, since k' calculated from eqn. (14), is essentially constant in runs 1, 2, and 3 where the base concentration is fixed, whereas k_1 as evaluated from eqn. (17) is not constant. One might expect k'/B to be independent of the TEA-concentration, but this is not exactly the case as shown by the comparison of runs 3, 4, and 5 in Table 2. This discrepancy may arise from the fact that acid-base equilibrium between TEA and water has not been considered here, or it may be an effect due to changes in the character of the reaction medium since rather large amounts of TEA are used. This point is a subject for further study.

The physical meaning of case 2 is that the recombination rate of the ion-pair is much lower than the rate of reaction with water, and it may be identified

Table 2.

Run No.	TEA mole/l	d_0 mole/l	$10^2 \times k$ h^{-1}	$10^2 \times k'$* l mole^{-1}h^{-1}	$10^2 \times (k'/B)$ l^{2}mole^{-2}h^{-1}	$10^2 \times k_1$** l mole^{-1}h^{-1}
1	1.08	5.5	7.5	0.98	0.90	5.0
2	1.08	11.0	10.6	0.93	0.86	9.5
3	1.08	16.5	14.8	0.99	0.92	15.1
4	0.72	16.5	11.1	0.74	1.02	16.9
5	0.36	16.5	7.0	0.47	1.29	21.3

* calc. from eqn. (14). ** Calc. from eqn. (17).

as the well-known step-wise mechanism where the rate determining step is the abstraction of a hydrogen ion from the indene molecule. Case 1, which is valid in our system, means that the recombination rate of the ion-pair is much higher than the rate of reaction with water. Kinetically it is impossible, however, to distinguish this case from the pure concerted mechanism involving a simultaneous attack of base and water on the indene molecule since we cannot decide whether k'/B is a single constant or composed of k_1, k_4, and k_{-1}. Thus, our reaction scheme (reactions 1—4) contains formally all possible mechanisms from step-wise to concerted, and there is a continuous transition, determined by the life-time of the ion-pair, between these two extremes. It must be remarked that, in this connection, we use the term ion-pair without any specific physical definition and only as a word for the pair indenylanion-HB$\oplus$ without regard to the distance between its components.

The observed constant ratio between the X- and (A+X)-proton concentrations is, however, not in agreement with the assumption of a pure concerted mechanism being the only one operating in the system (nor with a step-wise mechanism). This is so because an A-deutron can be created only from a pre-existing X-deutron in the indene molecule as, e.g., through reaction 5 above. Therefore, the concentration of X-deutrons determines the rate of formation of A-deutrons, which rate accordingly tends to zero as $t \to 0$. Thus, the observed constant ratio cannot be accounted for. A proton-transfer from the 1- to the 3-position must therefore occur, which is intramolecular in the sense that it does not involve the participation of protons (or deutrons) in the medium.

The entire set of observations can thus be described by case 1 of our reaction scheme, i.e. by the formation of a shortlived ion-pair, whose recombination rate is much higher than its reaction with water. Alternatively, the hydrogen exchange between indene and D_2O might proceed via a pure concerted mechanism independent of the intramolecular proton-transfer, the latter being a separate reaction.

TAUTOMERISM OF 1-D-INDENE

The rapid proton-transfer within the indene molecule proposed as responsible for the constant X/(X+A) concentration ratio found in the exchange experiments, could be studied directly by subjecting 1-d-indene to basic conditions. Considering the tautomeric proton-transfer reaction below (reaction 7), and denoting the tautomeric species by M and N, we get the following rate equation:

$$\frac{dM}{dt} = -k'' \ (M-2N) \tag{18}$$

if isotope effects are neglected and remembering that N has two X-type protons. If we start from pure M, we have the following subsidary conditions:

(Reaction 7)

$$\left. \begin{array}{l} M + N \ = x_0 \\ M + 2N = x \end{array} \right\} \tag{19}$$

(M)　　　(N)
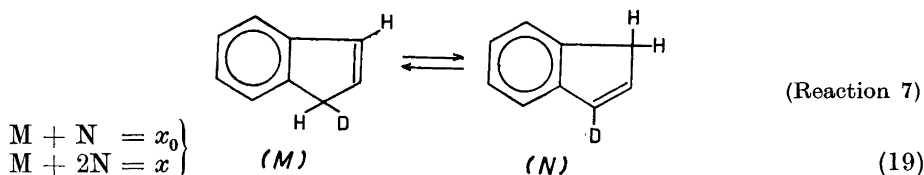
which leads to the following form of the rate equation with x as variable:

$$\frac{\mathrm{d}x}{\mathrm{d}t} = k'' \, (4x_0 - 3x) \tag{20}$$

or

$$\frac{\mathrm{d}x}{\mathrm{d}t} = -3k'' \, (x - x_\infty) \tag{21}$$

By deuterating indenylsodium with D_2O, we succeeded in preparing the desired 1-d-indene (M), the structure of which was established by analyzing its NMR-spectrum. The A- and K-signals each consists of two doublets, the peak separations being consistent with coupling constants $J_{AK} = 5.5 \pm 0.1$, $J_{KX} = 1.9 \pm 0.1$ and $J_{AX} = 1.8 \pm 0.1$ cps, in good agreement with those found for ordinary indene.[6] The X-signal has an additional fine-structure due to D—H coupling. The intensity ratio for the A-, K-, and X-protons was as expected 1:1:1.

The 1-d-indene was quite stable, and only slow changes in the spectrum were observed in pyridine solution. The NMR-spectrum of a 2 M solution in pyridine, containing 0.72 mole/l TEA, showed a X/K-proton peak ratio of about 4/3, 6 min after mixing, indicating that the tautomeric equilibrium had been established already after this time. In order to be able to follow the rate of the proton-transfer, we used a TEA concentration as low as 5.4×10^{-3} mole/l, and a half-life period of about 200 min was observed. Application of the rate-law (21) is shown in Fig. 6. From the slope of the line, k'' was found to be 7.1×10^{-2} h^{-1}. The bimolecular rate constant, obtained by dividing k'' with the base concentration, becomes 13.2 lit. mole^{-1} h^{-1}, which should be compared with $k'd_0/B$ in the exchange experiments; the latter quantity is always < 0.2 lit. mole^{-1} h^{-1}. Thus the intramolecular proton-transfer is sufficiently rapid compared to the hydrogen exchange to be responsible for the constant X/(A+X)-proton concentration ratio.
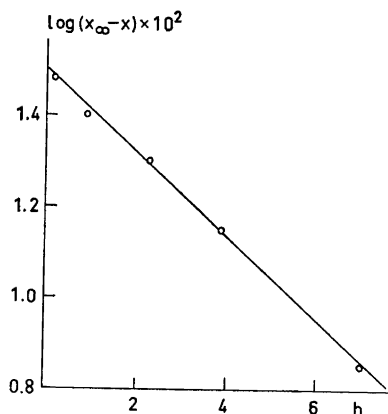

Fig. 6. Illustration of the validity of the integrated rate-law (21).

The investigation of 1-*d*-indene is being continued and further details about this and other deuterated indenes both with regard to tautomeric changes and NMR-spectra will be published later.

DISCUSSION

Intramolecular proton transfer is a new concept within the domain of tautomeric rearrangements. The first observation of such a transfer was made by Cram and Uyeda [8] in the rearrangement of 2-phenylbutene-3 to 2-phenyl-butene-2, where at least 54 % of the rearrangement involves intramolecular proton transfer. Our studies of the racemization and rearrangement rates of 1-methylindene,[5] which started prior to our knowledge of Cram's paper, indicated a similar mechanism, and our recent investigation of 1-methyl-3-isopropylindene [9] showed that the proton transfer is not only almost completely intramolecular but also *stereospecific*. The investigations of the proton-mobility of the indene ring system are to be continued.

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