On the Rearrangement of 1-Aralkylindenes

LENNART MEURLING

Department of Organic Chemistry, University of Uppsala, Box 531, S-751 21 Uppsala 1, Sweden

In connection with studies^{1,2} on the tautomerism of indene, an unusual effect of the triphenylmethyl group on the base-catalyzed prototropic rearrangement has been observed. 1-Benzyl-, 1-benzhydryl-, and 1-triphenylmethylindene were rearranged to the corresponding 3-substituted indenenes in benzene with diazabicyclo[2.2.2]octane (DABCO) as catalyst. The rate constants observed are given in Table 1, together with that found for the rearrangement of 1-methylindene. The trend of moderate increase in the rate constant observed on substituting the hydrogens in the methyl group by one and two phenyl groups is drastically changed for 1-triphenylmethylindene. This compound rearranges 30 times slower than 1-benzhydrylindene and about 5 times slower than 1-methylindene.

If one of the hydrogens in the methyl group of 1-methylindene is substituted, the transition state for proton abstraction (which is rate-determining in the rearrangement of 1-substituted indenenes) can adopt a conformation in which steric hindrance between the catalyst is of minor importance. Thus, in this case, the retarding effect of a methyl substituent (1-ethylindene) as well as the accelerating effect of the methoxy-, acetoxy-, and thioacetoxy groups can be qualitatively understood on the basis of electronic effects as shown by Ahlberg.³ Furthermore, in benzhydrylindene, rotation about the bond between the indenyl ring and benzylic carbon can minimize the steric interaction between the catalyst and the substrate, and electronic factors may thus account for the moderate rate acceleration found when going from 1-methylindene to benzhydrylindene (*cf.* Tafts' σ^* -substituent constants⁴).

The abrupt drop in the rearrangement rate which is observed when going to 1-triphenylmethylindene (Table 1) must to a large extent be ascribed to the lack of a conformationally favourable transition state. The series methyl-, benzyl-, benzhydryl-, and triphenylmethylindene is very suitable for the study of such effects, since the fully substituted compound deviates from the trend in the series. Successive substitution of the hydrogens of methylindene by methyl groups gives a monotonic decrease in the rate constant.

As regards the equilibrium constant between the 3- and the 1-substituted indene isomer, the triphenylmethyl group differs from the *t*-butyl group. The equilibrium constant, $[3\text{-}t\text{-butylindene}]/[1\text{-}t\text{-butylindene}]$, is 33 ± 1 ,⁵ a value smaller than that found for $[3\text{-methylindene}]/[1\text{-methylindene}]$ (about 100).⁵ This effect can, at least partly, be accounted for by the increased *peri*-interaction between the substituent and the aromatic hydrogen in the 3-isomer on going from methyl- to *t*-butylindene. In an analogous way, the equilibrium constant $[3\text{-triphenylmethylindene}]/[1\text{-triphenylmethylindene}]$ would be expected to be smaller than 33, but it is in fact larger than 50. It is possible that steric interactions also in the 1-isomer in this case may be responsible for this observation. However, all peculiarities of the triphenylmethyl group are still not understood.

Experimental. The aralkylindenes were prepared and purified according to procedures previously recorded.² Stock solutions of diazabicyclo[2.2.2]octane (Kebo), m.p. 158–159 °C, recrystallized twice from hexane, in benzene (Mallinckrodt), dried over molecular sieves and distilled, were prepared. The aralkylindenes were weighed into 10 ml flasks and base solution added, so that the substrate concentration was about 0.3 M. The flask was placed in a thermostat at a temperature of 35.0 ± 0.1 °C. Samples were withdrawn at intervals, quenched with 2 M hydrochloric acid and analyzed in the NMR-apparatus. The signals of the α -protons (*cf.* Ref. 1) of 1- and 3-aralkylindenes were examined and the corresponding integrals re-

Table 1. Comparison of the isomerization rates of 1-methylindene and some 1-aralkylindenes with diazabicyclo[2.2.2]octane in benzene at 35 °C.

Substrate	Conc. of catalyst [B] (mol/l)	k_1 pseudo-first order $\times 10^5$ (sec ⁻¹)	$k_1 \times 10^3/[B]$ (l mol ⁻¹ sec ⁻¹)
1-Methylindene	2.41×10^{-2}	11.3 ± 0.2	4.69 ± 0.09
1-Benzylindene	4.15×10^{-3}	2.56 ± 0.12	6.17 ± 0.35
1-Benzhydrylindene	4.40×10^{-3}	12.1 ± 0.6	27.5 ± 1.4
1-Triphenylmethylindene	2.64×10^{-2}	2.40 ± 0.15	0.91 ± 0.05

corded. The reaction was followed for at least 3 half-life times. No 1-substituted indene could be detected at equilibrium. From the equilibrium solutions, the 3-substituted indenenes were isolated and recrystallized from isopropanol. The distinct melting points of the indenenes isolated and the NMR-spectra showed that the products were uniform in character. The equilibrium constants were determined by the NMR-technique with the aid of a computer of average transients. All equilibrium constants were larger than 50. The experimental technique did not allow a more precise determination.

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Isoelectric Focusing in Deuterium Oxide Density Gradient

STIG FREDRIKSSON and SUNE PETTERSSON

Department of Physical Chemistry, Chalmers Institute of Technology and University of Gothenburg, S-402 20 Gothenburg, Sweden

The present paper is a preliminary report on the use of deuterium oxide as a substitute for sucrose when preparing density gradients for small isoelectric focusing columns. Full details of the technique used and the results obtained will be given elsewhere.

The isoelectric focusing column utilized in the present work is a modification of the 1.5 ml column described by Jonsson *et al.*¹ *Inter alia*, the bottom electrode of platinum wire has been exchanged for a sheet of palladium covering the bottom of the focusing chamber.

The D₂O density gradient has been created directly in the column by free interdiffusion of three D₂O solutions for 3 min.² The resulting D₂O concentration course, as obtained by measurement of the refractive index gradient,³ has a very high degree of linearity. The initial D₂O density gradient (0.018 g cm⁻⁴) is as strong as

the initial sucrose density gradient used by Jonsson *et al.* As expected, the stability in time is less for the D₂O density gradient than for the sucrose density gradient. However, the D₂O density gradient remaining after the column has been standing in an upright position for two hours (0.016 g cm⁻⁴), is still more than twice as strong as the sucrose density gradient obtainable in an LKB 110 ml column with 500 g of sucrose per litre as initial bottom concentration. Thus, the D₂O density gradient described should normally be quite sufficient for stabilization of protein zones. This conclusion is supported by results obtained in this laboratory at isoelectric focusing of β -lactoglobulin (*cf.* Fig. 1) and sperm whale myoglobin.

Fig. 1. Scan of 1.5 ml column¹ at 280 nm (solid curve) obtained after D₂O density gradient isoelectric focusing of 100 μ g β -lactoglobulin in 1 % Ampholine pH 4–6 for 75 min. Average field strength 30 V cm⁻¹. Superimposed are pH values of 60 μ l fractions of the column contents (circles).³ (A represents β -lactoglobulin A, and B β -lactoglobulin B.)

Isoelectric points evaluated from isoelectric focusing runs in D₂O density gradients were found to be about 0.1 pH unit higher than those obtained in sucrose density gradients. This increase seems to be the net result of two effects: the intrinsic pK_a values of the protolytic groups in proteins are higher in D₂O than in H₂O but simultaneously the pH meter reading in D₂O solution is lower than in H₂O solution for solutions of comparable acidity.

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