Effects of Alkyl-substitution on the Base-catalysed 1,3-Proton Transfer in the Indene System

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Syntheses of 2-alkyl substituted, deuterated indenenes and their isomerization catalyzed by some tertiary aliphatic amines in pyridine solution, have been studied. Optically active 1,2-dimethylindene has been prepared and its rearrangement to 2,3-dimethylindene has been studied polarimetrically. Some steric and electronic consequences of substitution in the indene nucleus are discussed. The substitution pattern of the indene and the nature of the catalyst seem to influence the reaction rate in a complex way. Rate constants and activation parameters for the isomerization reactions are given.

The prototropic 1,3-shift in the indene system has been investigated in detail.¹⁻¹⁹ Base-catalyzed isomerization of 1-,¹⁻⁷ 1,2-,⁸ and 1,3¹⁰-alkyl substituted indenenes have been studied with regard to stereospecificity,^{3,19} intramolecularity and deuterium isotope effect.^{1,20,21} Recently, a report has been published²² concerning the influence of some β -substituents in alkylsubstituted methylindenenes on the isomerization rate.

This communication reports the results of some experiments with 2-alkyl substituted indenenes. The isomerization $1 \rightleftharpoons 2$ (Scheme 1), where R is a methyl or an ethyl group,

was studied by the NMR-technique. Further, optically active 1,2-dimethylindene 7 (Scheme 3)

Scheme 1.

was synthesized and its mutarotation to the non-chiral 2,3-dimethylindene was studied polarimetrically. As in previous investigations, aliphatic amines were used as catalysts and the reactions were run in pyridine solutions. The catalytic effect of 1,4-diazabicyclo[2.2.2]octane (DABCO) and triethylamine (TEA) were investigated. Earlier, it was found that the rearrangements under these conditions in the indene system were completely intramolecular and highly stereospecific.^{1,21}

In order to kinetically follow the reaction by NMR it was necessary to label the 2-alkylindenenes with deuterium in position 1 or 3. The 2-alkyl-3-deuterioindenenes 1 were prepared by reducing the corresponding 2-alkylindanones

Scheme 2.

Scheme 3.

with lithium aluminium deuteride, followed by dehydration with *p*-toluenesulphonic acid of the indanol obtained (Scheme 2). In order to get access to the 2-alkyl-1-deuterioindenes 2, 2-methylindene (or 2-ethylindene) was treated with butyllithium in dry ether at -30°C and the indenyllithium thus formed was decomposed with D₂O, followed by rapid acidification (Scheme 2). As judged from the NMR-spectrum, no rearranged product 1 was formed during this synthesis.

In the case of the 1,2-dialkylindene, the isomerization⁹ can be followed more accurately by the polarimetric technique since the indene mutarotates with the same rate as it isomerizes. The conventional synthesis of an optically active 1,2-substituted indene starts with the resolution of an α -alkyl- β -phenyl substituted alkanolic acid. This may be a complicated procedure since the molecule contains two asymmetric carbon atoms. An alternative route to the optically active indene was therefore undertaken. Optically active 3-methylindanone 3 was acylated in the 2-position with diethylcarbonate and the thallium salt of 2-carbethoxy-3-methylindanone 4 was prepared by treatment of 4 with thallous ethoxide. Alkylation with methyl iodide gave almost exclusively C-alkylation of the carbethoxy-indanone in good yield. Alkaline hydrolysis and decarboxylation gave the 1,2-dimethylindene 7 after some conventional steps (Scheme 3).

TREATMENT OF RATE DATA

The course of the reaction in Scheme 1 was measured by integration of the NMR-signals

from the vinylic proton and/or the saturated ring protons. The signal from the 2-alkyl group was used as an internal standard. In discussing the rate and equilibrium properties of the system, it should be remembered that the equilibrium constant 2/1 is equal to 2, due to the asymmetry of 2 (*cf.* Scheme 1). Using the notations given in the phenomenological reaction Scheme 4, we get the following rate equations:

$$\frac{d[(+)\text{A}]}{dt} = -(k_1 + k_D)[(+)\text{A}] + k_D[(-)\text{A}] + k_{-1}[\text{B}] \quad (1)$$

$$\frac{d[(-)\text{A}]}{dt} = k_D[(+)\text{A}] - (k_1 + k_D)[(-)\text{A}] + k_{-1}[\text{B}] \quad (2)$$

$$\frac{d[\text{B}]}{dt} = k_1[(+)\text{A}] + k_1[(-)\text{A}] - 2k_{-1}[\text{B}] \quad (3)$$

Scheme 4.

If $[\text{A}] = [(+)\text{A}] + [(-)\text{A}]$, these equations can be written as:

$$\frac{d[\text{A}]}{dt} = -k_1[\text{A}] + 2k_{-1}[\text{B}] \quad (4)$$

$$\frac{d[B]}{dt} = k_1[A] - 2k_{-1}[B] \quad (5)$$

[The (+) and (-) signs have no configurational relevance.] Thus, deuterium migration, which brings (+)A to (-)A and *vice versa*, does not influence our kinetic measurements. Furthermore, if secondary isotope effects are neglected, *i.e.* if $k_{-1} = k_1$, the rate equations, in integrated form, will be:

$$[A] = ([A]_0 - [A]_\infty) \exp(-3k_1t) + [A]_\infty \quad (6)$$

$$[B] = ([B]_0 - [B]_\infty) \exp(-3k_1t) + [B]_\infty \quad (7)$$

If x and y denotes the area of the saturated and the vinylic protons, respectively, and λ is a proportionality constant we have

$$x = \lambda([A] + 2[B]) \quad (8)$$

$$y = \lambda[A] \quad (9)$$

Combining eqns. (6–7) with eqns. (8–9) we get:

$$x = (x_0 - x_\infty) \exp(-3k_1t) + x_\infty \quad (10)$$

$$y = (y_0 - y_\infty) \exp(-3k_1t) + y_\infty \quad (11)$$

Thus, the observed rate constant is $3k_1$. This fact is of importance for the comparison of the rate constants obtained for alkylindenes with different substitution pattern. Thus, if we consider a phenomenological reaction scheme equivalent to Scheme 4 for a 1- or a 1,2-substituted indene, the observed rate constant will be k_1 ,^{1,9} since the collapse ratio is large and for the symmetrically substituted 1,3-dimethylindene¹⁰ the observed rate constant will be exactly $2k_1$.

As pointed out before,¹⁴ however, the rearrangements proceed most probably *via* an ion-pair intermediate as in mechanistic reaction, Scheme 5.

Scheme 5.

In this case, a proper comparison should involve the mechanistic rate constant k'_1 , and it is easily shown that $k_{\text{obs}} = 3k'_1/2$ for 2-substituted indenenes and that $k_{\text{obs}} = k'_1$ in other cases of interest, *i.e.* the last expression is exactly valid for 1,3-dimethylindene and approximately valid for the 1-methylindene since the collapse ratio is large. The comparisons should thus be made according to the directions given in Table 1. These considerations should

Table 1.

Substrate:	Phenomenological Scheme 4 k_1	Mechanistic Scheme 5 k'_1
	$\frac{1}{2} k_{\text{obs}}$	$\frac{2}{3} k'_{\text{obs}}$
	k_{obs}	k_{obs}
	$\frac{1}{2} k_{\text{obs}}$	k_{obs}

be kept in mind when rate constants are to be compared. Enthalpies of activation can of course be calculated and compared directly, using k_{obs} . The entropies of activation will depend on which rate constant is chosen, but the experimental error will, in most cases, be larger than the difference between the entropy values calculated using different rate constants (*i.e.* k_{obs} , k_1 or k'_1). Finally, it should be noted that k_{obs} used in the present discussion is the second order rate constant, obtained by multiplying the experimentally observed pseudo-first order constant with $1/[\text{Base}]$.

RESULTS AND DISCUSSION

It was found earlier that the introduction of a methyl group in position 1 of the indene nucleus slows the TEA-catalyzed reaction at 30°C by a factor of 5.8.⁶ Introduction of a substituent in the 2-position of 1-methylindene further shows the reaction by a factor of 25.⁹ The retarding effect of a substituent in the 2-position is thus considerable. If 1-methylindene is substituted with a methyl group in the 3-

position, only a very slow rearrangement occurs with TEA.¹⁰

Turning to the DABCO-catalyzed reactions, it can be found from the present investigation and from earlier results in this field⁶ that 1-methylindene rearranges about 25 % slower than indene itself, but a further substitution to 1,2-dimethylindene slows the reaction rate by a factor about 7.⁹ Alkyl substitution to 1,3-dimethylindene shows that the mechanistic rate constant is about 40 times smaller than that for indene. The effect of alkyl-substitution on the reaction rate is thus markedly dependent on the situation of the substituent.

In the ground state, a 2-alkylindene should be more stable than a 1-alkylindene, due to hyperconjugation between the double bond and the methyl group, as well as between the double bond and the CH₂-group in position 1. In the transition state, the indene part is probably very much like the indenyl anion. In this anion, positions 1 and 3 have higher electron densities than position 2¹² and a 2-substituted indenyl anion is therefore expected to be more stable than a 1-substituted anion.

Starting with indene, the introduction of an alkyl substituent in the 1-position would thus raise the energy level of the ground state but also increase the energy level of the transition state (Fig. 1). In accordance with this view, the situation in the 2-alkylindene case should be a lower ground state energy level, but with a transition state of about the same magnitude as in indene. The introduction of a methyl group in the 1-position of 2-methylindene should also raise the energy of the ground state to about the same extent as a 1-methyl group does on substitution in indene. In the transition state, a 1-methyl substituent would act in the same direction, *i.e.* raising the energy level.

The introduction of a methyl group in the 1-position does not always retard the proton abstraction rate (k'_1) when DABCO is used as a catalyst. This might seem puzzling since a retardation in reaction rate is quite obvious with TEA as catalyst. TEA should of course be sterically more hindering in the transition state than DABCO. However, a retardation in reaction rate would be expected also in the DABCO-case when a methyl group is introduced in the 1-position of 2-methylindene. Thus if $\Delta G^\ddagger_0$, $\Delta G^\ddagger_1$, $\Delta G^\ddagger_2$, and $\Delta G^\ddagger_{12}$ denote the

free energies of activation (as calculated from the k'_1 -values) for indene, 1-methylindene, 2-methylindene, and 1,2-dimethylindene, we get, using the values given in Table 2:

$$(\Delta G^\ddagger_1 - \Delta G^\ddagger_0)_{\text{DABCO}} = +0.1 \text{ kcal mol}^{-1};$$

$$(\Delta G^\ddagger_1 - \Delta G^\ddagger_0)_{\text{TEA}} = +1.0 \text{ kcal mol}^{-1}$$

$$(\Delta G^\ddagger_{12} - \Delta G^\ddagger_2)_{\text{DABCO}} = -0.1 \text{ kcal mol}^{-1};$$

$$(\Delta G^\ddagger_{12} - \Delta G^\ddagger_2)_{\text{TEA}} = +1.1 \text{ kcal mol}^{-1}$$

Thus, in the case of TEA the 1-methyl substituent increases the free energy of activation by 1.1 kcal mol⁻¹ whether or not a methyl group is present in the 2-position. With DABCO the introduction of a methyl substituent in the 2-position has little or no influence on the reaction rate, the average value for the difference in free energy of activation being 0.0 kcal mol⁻¹.

The difference between these values, 1.1 kcal mol⁻¹, may be ascribed to the difference in steric hindrance in the transition state (steric hindrance in the ground state being equal and negligible) between the 1-methyl and TEA and DABCO, respectively. If y'_1 denotes the steric hindrance in kcal mol⁻¹ between the 1-methyl group and the catalyst in the transition state, we get:

$$(y'_1)_{\text{TEA}} - (y'_1)_{\text{DABCO}} = +1.1 \text{ kcal mol}^{-1}$$

In the same way, one may use the activation energy differences between 2-methylindene (and 1,2-dimethylindene) and indene to estimate the difference in steric effects in the transition state between a 2-methyl group and TEA and DABCO, respectively. If y'_2 denotes the steric hindrance between the 2-methyl group and the catalyst in the transition state, we get:

$$(y'_2)_{\text{TEA}} - (y'_2)_{\text{DABCO}} = (\Delta G^\ddagger_2 - \Delta G^\ddagger_0)_{\text{TEA}} - (\Delta G^\ddagger_2 - \Delta G^\ddagger_0)_{\text{DABCO}}$$

and

$$(y'_2)_{\text{TEA}} - (y'_2)_{\text{DABCO}} = (\Delta G^\ddagger_{12} - \Delta G^\ddagger_0)_{\text{TEA}} - (\Delta G^\ddagger_{12} - \Delta G^\ddagger_0)_{\text{DABCO}} - \{(y'_1)_{\text{TEA}} - (y'_1)_{\text{DABCO}}\}$$

The right hand sides of these equations are, using the previously deduced value for the y'_1 -difference and the $\Delta G^\ddagger$ -values of Table 2, +0.4 and +0.6 kcal mol⁻¹. As an average value +0.5 kcal mol⁻¹ can be chosen and thus

$$(y'_2)_{\text{TEA}} - (y'_2)_{\text{DABCO}} = +0.5 \text{ kcal mol}^{-1}$$

A 2-methyl group thus causes a less pronounced selectivity between different catalysts than a

Table 2. Rate constants and activation parameters for the base-catalyzed tautomerization of some indene derivatives. Indene concentration: 2 M. Temperature: 30.0°C. Solvent: Pyridine.

Indene derivative	Catalyst Nature	Conc. [B] mol l ⁻¹	k_{obs} sec ⁻¹	$k_{\text{obs}}/[\text{B}]$ l mol ⁻¹ sec ⁻¹	k' l mol ⁻¹ sec ⁻¹	$\Delta G^\ddagger$ kcal mol ⁻¹	$\Delta H^\ddagger$ kcal mol ⁻¹	$\Delta S^\ddagger$ cal mol ⁻¹ degree
Indene	DABCO	3.40×10^{-3}	$1.53 \times 10^{-4} c$	4.51×10^{-2}	3.02×10^{-2}	19.87 ± 0.05		
1-Methyl-	"	3.41×10^{-3}	$8.15 \times 10^{-5} b$	2.39×10^{-2}	2.39×10^{-2}	20.00 ± 0.03	10.9 ± 0.2^d	-30 ± 1
1,2-Dimethyl	"	2.21×10^{-3}	$7.32 \times 10^{-5} a$	3.31×10^{-2}	3.31×10^{-2}	21.20 ± 0.01	12.7 ± 0.2	-28 ± 1
2-Methyl	"	1.72×10^{-3}	$7.24 \times 10^{-5} c$	4.21×10^{-2}	2.82×10^{-2}	21.29 ± 0.05	11.4 ± 0.6	-33 ± 3
2-Ethyl	"	1.72×10^{-3}	$5.21 \times 10^{-5} c$	3.03×10^{-2}	2.03×10^{-2}	21.49 ± 0.05	11.4 ± 0.6	-33 ± 3
1,3-Dimethyl	"	2.79×10^{-1}	$2.13 \times 10^{-4} b$	7.65×10^{-4}	7.65×10^{-4}	22.06 ± 0.03	13.6 ± 0.2	-28 ± 1
Indene	TEA	5.40×10^{-3}	$5.75 \times 10^{-5} c$	1.06×10^{-2}	7.10×10^{-3}	20.74 ± 0.05	$-e$	
1-Methyl	"	2.57×10^{-1}	$3.15 \times 10^{-4} b$	1.23×10^{-3}	1.23×10^{-3}	21.79 ± 0.03	9.6 ± 0.2^f	-40 ± 1
1,2-Dimethyl	"	1.32	$6.61 \times 10^{-5} a$	5.01×10^{-5}	5.01×10^{-5}	23.72 ± 0.01	11.8 ± 0.2	-39 ± 1
2-Methyl	"	1.22×10^{-1}	$6.26 \times 10^{-5} c$	5.13×10^{-4}	3.44×10^{-4}	22.56 ± 0.05	9.8 ± 0.6	-42 ± 3
2-Ethyl	"	1.20×10^{-1}	$4.68 \times 10^{-5} c$	3.90×10^{-4}	2.61×10^{-4}	22.73 ± 0.05	9.2 ± 0.6	-45 ± 3

^a $2\sigma \approx 2\%$. ^b $2\sigma \approx 5\%$. ^c $2\sigma \approx 8\%$. ^d Ref. 14 Indene conc. ~ 0.1 M. ^e Ref. 3. ^f Ref. 6.

1-methyl substituent, and TEA exhibits a larger steric hindrance than DABCO. These conclusions are quite reasonable from the chemical point of view.

The above analysis invites an attempt to describe the substituent effects, both steric and electronic, by a linear model. This cannot lead anywhere, however, without further data. Important information can be obtained from the previous study of the rearrangement of 1,3-dimethylindene with DABCO. We may assume that the transition state is unsymmetrical, so that only one of the methyl groups gives rise to steric repulsion. Both methyl groups have other effects, however, which are mainly electronic on the ground state as well as on the transition state. Another important fact is the equilibrium constant between 3-methylindene and 1-methylindene. It has been found that 1-methylindene is present to about 1 % in equilibrium. The free energy difference between the ground states of these two indenenes must therefore be close to 2.8 kcal mol⁻¹. This difference is caused by substituent effects on the ground states, which for simplicity one may interpret as electronic (hyperconjugative) effects. Introducing the symbols given below, one gets the energy levels given in Fig. 1. The rate determining transition state for 3-methylindene is, of course, the same as for 1-methylindene. Referring to Fig. 1 we obtain the equations:

$$\Delta G^\ddagger_1 - \Delta G^\ddagger_0 = x'_1 + y'_1 + x^0_0 \quad (12)$$

$$\Delta G^\ddagger_{12} - \Delta G^\ddagger_0 = 2x'_1 + y'_1 + x^0_0 - x^0_1 \quad (13)$$

$$\Delta G_0 = x^0_0 + x^0_1 \quad (14)$$

$$\Delta G^\ddagger_2 - \Delta G^\ddagger_0 = x'_2 + y'_2 - x^0_1 \quad (15)$$

$$\Delta G^\ddagger_{12} - \Delta G^\ddagger_0 = x'_1 + y'_1 + x'_2 + y'_2 + x^0_0 - x^0_1 \quad (16)$$

The symbols have the following meaning:
 x^0_0 = effect on the ground state of introducing a ring-CH₃-group

x^0_1 = effect on the ground state of introducing a CH₃-group in hyperconjugation with a double bond

x'_1 = effect on the transition state of introducing a CH₃-group in the 1- or 3-position

x'_2 = effect on the transition state of introducing a CH₃-group in the 2-position

y'_1 = steric effect on the transition state of a CH₃-group in the 1-position

y'_2 = steric effects on the transition state of a CH₃-group in the 2-position

$\Delta G_0 = -RT \ln K_{eq}$, where K_{eq} is the equilibrium constant between 3-methylindene and 1-methylindene.

It should be noted, that x^0_0 , x^0_1 , x'_1 and x'_2 are independent of the nature of the catalyzing base, whereas y'_1 and y'_2 are, of course, different for DABCO and TEA, as explained above.

Eqns. (12), (13), and (14) can be solved for y'_1 , and we get:

Fig. 1. Relative free energies between ground state and transition state for alkyindenenes. The symbols are explained in the text.

$$y'_1 = 2\Delta G^\ddagger_1 - \Delta G^\ddagger_{13} - \Delta G^\ddagger_0 - \Delta G_0 \quad (17)$$

The rate constant (7.65×10^{-4} l mol⁻¹ sec⁻¹) reported previously for the DABCO-catalyzed reaction for 1,3-dimethylindene, gives $\Delta G^\ddagger_{13} = 22.1$ kcal mol⁻¹. Using this value and the $\Delta G^\ddagger$ -values reported in Table 2 (together with $\Delta G_0 = -2.8$ kcal mol⁻¹ as given above), we find that $(y'_1)_{\text{DABCO}} = +0.8$ kcal mol⁻¹. Since we already have concluded that $(y'_1)_{\text{TEA}} - (y'_1)_{\text{DABCO}}$ was $+1.1$ kcal mol⁻¹, we now get $(y'_1)_{\text{TEA}} = +1.9$ kcal mol⁻¹.

Combination of eqns (12), (15), and (16) gives:

$$\Delta G^\ddagger_1 - \Delta G^\ddagger_0 = \Delta G^\ddagger_{13} - \Delta G^\ddagger_2 = x'_1 + y'_1 + x^0_0 \quad (18)$$

Using the average value for the free energy differences used above for the DABCO-case and the value $+1.1$ kcal mol⁻¹ for the TEA catalyzed reaction together with the y'_1 -values just obtained, we get $x'_1 + x^0_0 = -0.8$ kcal mol⁻¹. With the parameter values thus obtained, eqns (15) and (16) are best satisfied using $x'_2 - x^0_1 + (y'_2)_{\text{DABCO}} = +1.4$ kcal mol⁻¹. Thus, the data now available gives us the following parameters:

$$\begin{aligned} (y'_1)_{\text{DABCO}} &= +0.8 \text{ kcal mol}^{-1} \\ (y'_1)_{\text{TEA}} &= +1.9 \text{ kcal mol}^{-1} \\ x'_1 + x^0_0 &= -0.8 \text{ kcal mol}^{-1} \\ x^0_0 + x^0_1 &= -2.8 \text{ kcal mol}^{-1} \\ (x'_2 - x^0_1) + (y'_2)_{\text{DABCO}} &= +1.4 \text{ kcal mol}^{-1} \end{aligned}$$

Table 3 summarizes the activation free energy differences calculated using these parameter values and compares them with experimental results.

Thus, the eight parameters used in the model [eqns. (12)–(16)] have been fixed to six numerical values. An attempt can now be made, using chemical intuition, to create a set for all eight parameters. The steric parameters already given

makes it plausible to set $(y'_2)_{\text{DABCO}} = 0$, and the steric parameters would then be as follows:

$$\begin{aligned} (y'_1)_{\text{DABCO}} &= +0.8 \text{ kcal mol}^{-1}; \\ (y'_1)_{\text{TEA}} &= +1.9 \text{ kcal mol}^{-1} \\ (y'_2)_{\text{DABCO}} &= 0.0 \text{ kcal mol}^{-1}; \\ (y'_2)_{\text{TEA}} &= +0.5 \text{ kcal mol}^{-1} \end{aligned}$$

Using this value for $(y'_2)_{\text{DABCO}}$, we see that $x'_1 - x'_2 = +0.6$ kcal mol⁻¹. As long as $(y'_2)_{\text{DABCO}}$ is greater than -0.6 kcal mol⁻¹, which it seems safe to assume, the difference between x'_1 and x'_2 will be greater than zero. Thus, a 1-methyl group will have a more destabilizing effect on the transition state than a methyl group in the 2-position. This agrees well with the fact that the indenyl anion has a larger negative charge on the 1-carbon atom than on the 2-carbon atom. As mentioned before, the indene part of the transition state is probably very much like the indenyl anion.

A complete set of reasonable electronic parameters may be constructed if it is assumed that the stabilizing effect of the ground state (hyperconjugation) of the ring methylene group is equal to the stabilization between a methyl group and a double bond in the ground state. If this is true, we get the following values of the individual x -parameters:

$$\begin{aligned} x^0_0 &= -1.4 \text{ kcal mol}^{-1}; \\ x^0_1 &= -1.4 \text{ kcal mol}^{-1} \\ x'_1 &= +0.6 \text{ kcal mol}^{-1}; \\ x'_2 &= 0.0 \text{ kcal mol}^{-1} \end{aligned}$$

Steric repulsion between the catalyzing base and the substrates, as judged from models, seems to be approximately the same for 1- and 2-substituted indenenes. However, Plenat and Bergson found⁹ that the relative catalytic effect of TEA was more sensitive to the nature of the substrates, *i.e.* the substituted indenenes, than that of DABCO. For instance the ratio $k_{\text{DABCO}}/k_{\text{TEA}}$ was found to be 19:1 for 1-methylindene and 66:1 for 1,2-dimethylindene. In this investigation we found the corresponding ratio for 2-methylindene to be 8:1 and for indene 4:1. The introduction of a substituent in the nucleus of indene should of course present increased interaction between the substrate and TEA and it is obvious that a 1-methylsubstituent is more hindering than a 2-methyl group. However, it can be concluded from the

Table 3.

	DABCO		TEA	
	Exp.	Calc.	Exp.	Calc.
$\Delta G^\ddagger_1 - \Delta G^\ddagger_0$	0.1	0	1.0	1.1
$\Delta G^\ddagger_{13} - \Delta G^\ddagger_0$	2.2	2.0	—	3.1
$\Delta G^\ddagger_2 - \Delta G^\ddagger_0$	1.4	1.4	1.8	1.9
$\Delta G^\ddagger_{12} - \Delta G^\ddagger_0$	1.3	1.4	2.9	3.0

above mentioned considerations, that it is not the 1- or 2-substituents separately which are causing the substrate sensitivity for TEA, but a combination as reflected in the 1,2-dimethylindene case.

From Table 2 it can be seen that the enthalpies of activation are about the same for 1-methyl- and 2-methylindene; 10.9 and 11.4 kcal mol⁻¹ for the DABCO-catalyzed reactions and 9.6 and 9.8, respectively, for the TEA-catalyzed reaction. The activation enthalpies of the disubstituted indenenes were significantly higher, 12.7 kcal mol⁻¹ for 1,2-dimethylindene and 13.6 kcal mol⁻¹ for 1,3-dimethylindene in the DABCO-catalyzed reaction. As expected, there is no difference in $\Delta S^\ddagger$ between 1-, 1,2- and 1,3-dimethylindene (-30, -28, and -28 e.u.). Much of the difference in reactivity between these substrates can thus be attributed to differences in $\Delta H^\ddagger$. For this reason, it seems confusing that $\Delta S^\ddagger$ for the DABCO and TEA-catalyzed isomerization of 2-methylindene is larger than the corresponding reactions with 1-methylindene as a substrate. Even if the experimental errors are large, it must be concluded that the lower reacting power of the 2-substituted compounds is probably due to these differences in activation entropy. The origin of this difference is not clear at present.

EXPERIMENTAL

Instrumental. Melting points and boiling points are uncorrected. The NMR-spectra were recorded in CCl₄ at 34 ± 1°C on a Varian A 60 D spectrometer. Preparative GLC of the indenenes was performed on a Varian Aerograph Model 90-P4 with helium as carrier gas. The column used for purification was 0.6 m × 3/8", packed with 20 % Apiezon L on Chromosorb W, 60/80 mesh. The purities of the indenenes were checked on a Perkin-Elmer 900 gas chromatograph, equipped with a flame ionization detector, and with a 3 m × 1/8" column, packed with 5 % Apiezon L on 100/120 mesh Varaport. The polarimetric measurements were made with a Perkin-Elmer polarimeter 141 M and the infra-red spectra with a Perkin-Elmer Model 237 spectrophotometer.

Syntheses

2-Alkylindanones were prepared according to Cologne and Weinstein²⁴ by condensation of the appropriate arylalkylketone with formaldehyde

and subsequent dehydration of the ketols obtained with sulphuric acid. 2-Methylindanone-1: b.p.₁₁ = 112–113°C, n_D^{25} = 1.5520 (Lit.²⁴ b.p.₁₅ = 120°C, n_D^{25} = 1.5511). 2-Ethylindanone-1: b.p.₁₁ = 125–126°C, n_D^{25} = 1.5465 (Lit.²⁴ b.p.₁₅ = 127°C, n_D^{25} = 1.5457).

2-Alkyl-3-deuterioindenenes (1) Alkylindanone (0.05 mol) in 50 ml of dry ether was slowly dropped into a solution of 0.03 mol of LiAlD₄ (Merck, deuterium content min. 99 %) in 20 ml ether. After refluxing for 2 h and after the usual work-up procedure,⁵ the resulting indanols were dehydrated without further purification with 0.01 g of *p*-TsOH in 200 ml of dry benzene, using a Soxhlet extractor, filled with molecular sieves (Union Carbide, 5 Å). After half an hour of reflux the solution was chilled, extracted with 5 % aq. NaHCO₃ and then with a saturated NaCl solution and dried. The indenenes were distilled in vacuum and purified by preparative GLC. The deuterium content in the 3-position was 97 ± 1 % as judged by the NMR-spectrum.

2-Methyl-3-deuterioindene (1a). Yield 68 % (calc. on the ketone) b.p.₁₁ = 76–77°C, n_D^{25} = 1.5637 (Lit.²⁵ gives for 2-methylindene b.p._{1,3} = 64–65°C, n_D^{25} = 1.5645). NMR: (Shifts in δ) 6.7–7.3, 4 H, complex; 3.11, 2 H, s (singlet); 2.09, 3 H, s.

2-Ethyl-3-deuterioindene (1b). Yield 76 % (calc. on ketone) b.p.₁₁ = 82–85°C, n_D^{25} = 1.5590 (Lit.²⁵ gives for 2-ethylindene b.p._{1,1} = 62°C, n_D^{25} = 1.5598). NMR: 6.7–7.3, 4 H, complex; 3.09, 2 H, s; 2.32, 2 H, q, J = 7.5 cps; 1.15; 3 H, t, J = 7.5 cps.

2-Alkyl-1-deuterioindenenes (2). 2-Alkylindene²⁵ (0.02 mol) in 10 ml of dry ether was treated with 0.03 mol of butyllithium in ether solution at -30°C and held at this temperature for 1.5 h. D₂O, 5 ml (Norsk Hydro, 99.8 % D) was added with vigorous stirring during 5 min. The temperature was never allowed to exceed -15°C. After acidification with 2 M HCl, the ether layer was separated and the acidic phase extracted with ether. After drying of the extracts, the solvent was evaporated and the residue distilled in vacuum. The indenenes were further purified by preparative GLC. No rearrangement occurred during the synthesis, since the deuterium content was more than 96 % in the 1-position as judged by the NMR-spectrum.

2-Methyl-1-deuterioindene (2a). Yield 82 %, b.p.₁₀ = 74–75°C, n_D^{25} = 1.5643. NMR: 6.7–7.3, 4 H, complex; 6.42, 1 H, t, J = 2.5 cps; 3.07, 1 H, complex; 2.08, 3 H, d, J = 2.5 cps.

2-Ethyl-1-deuterioindene (2b). Yield 77 %, b.p.₁₀ = 81–83°C, n_D^{25} = 1.5592. NMR: 6.7–7.3, 4 H, complex; 6.39, 1 H, t, J = 2.5 cps; 3.05, 1 H, complex; 2.30, 2 H, q, J = 7.5 cps; 1.15, 3 H, t, J = 7.5 cps.

An interesting fact is that in the spectra of 2-alkyl-3-deuterioindenenes, the signal from the X-protons (methylene) appeared at a shift which was 0.04 ppm higher than the corresponding signal from the 1-deuterium-substituted

analogues. This effect was also demonstrated in the rearrangement, since at equilibrium, the amount of *1a* and *2a* (or *1b* and *2b*) could be seen as separate entities. This isotope effect is not unusual,²⁶ and still larger shifts are found in ¹⁹F spectroscopy. Bovey²⁷ reports that in the spectrum of a 1:16 v/v mixture of cyclohexane and cyclohexane-*d*₁₁, the signal from the remaining H appeared at a shift 0.057 ppm from the sharp resonance of cyclohexane. The same effect, although to a lower extent, can be observed when the spectra from 1-deuterio- and 3-deuterioindenes are examined. The origin of this isotope effect is thought to result from differences in zero point vibrational functions, which are associated with different isotopic masses. A more extensive theoretical treatise is given elsewhere.²⁸

(-)-3-Methyl-2-carbethoxy-indanone-1 (4). (-)-3-Methylindanone-1 (3) {[α]_D²⁵ = +1.8° (c = 31.6, benzene)}, 10 g (69 mmol), obtained by ring-closure of (+)- β -phenyl-butyric acid, {[α]_D²⁵ = +57.6° (c = 2.8, benzene)}⁵ in 75 ml of dry benzene, was dropped into 6.5 g (270 mmol) of NaH (BDH, puriss) and 75 g (630 mmol) of diethyl carbonate in 50 ml of dry benzene at +65°C for 2 h, and maintained at that temperature for another hour. The solution was chilled to +10°C, acetic acid was added to pH 6, the mixture chilled to $\pm 0^\circ\text{C}$ and the pH adjusted to 1 with hydrochloric acid. The organic phase was extracted twice with 5% NaHCO₃ and with NaCl aq. sat., After evaporation of the benzene, the residue was distilled under vacuum, yield: 83% b.p._{0.5} = 131–133°C, n_D^{25} = 1.5435, [α]_D²⁵ = -105° (c = 2.0, benzene). NMR: About 30% of the product was present as the enol. Shifts: 10.52, s; 6.7–7.3, complex; 4.23, q; 3.14, d; 1.21, d; 1.23, complex. IR: C=O, 1720 cm⁻¹ (ester), 1670 cm⁻¹ (ketone).

(-)-2,3-Dimethyl-2-carbethoxyindanone (5). (-)-3-Methyl-2-carbethoxyindanone-1, 12 g (0.054 mol) in 100 ml of dry ether was treated dropwise with 13.4 g (0.054 mol) of thallous ethoxide at room temperature. After 5 min, the thallium salt of 3-methyl-2-carbethoxy-indanone-1 precipitated as a yellow powder, which was filtered and washed with a small amount of ether. Yield: quantitative, m.p. 156–157°C. The salt was boiled under reflux with 50 g (0.350 mol) of methyl iodide (Kebo, puriss.). After filtration of the thallium(III) iodide obtained, the residue was distilled under vacuum. Yield: 87%, n_D^{25} = 1.5282, b.p.₁ = 135–136°C, [α]_D²⁵ = -67° (c = 2.6, benzene). NMR: 6.7–7.3, 4 H, complex; 3.52, 1 H, q; 3.86, 2 H, complex; 1.31, 3 H, d; 1.20, 6 H, complex. IR: C=O 1745 cm⁻¹ (ester), 1690 cm⁻¹ (ketone).

(-)-2,3-Dimethylindanone-1 (6). (-)-2,3-Dimethyl-2-carbethoxyindanone (5) 8 g (0.034 mol) was stirred at room temperature with 100 ml of 5% NaOH for 24 h. To the homogeneous solution 100 ml of 4 M H₂SO₄ was added and the mixture refluxed for 2 h. After ether ex-

traction and evaporation of the solvent the residue was distilled. Yield: 87%, b.p.₁₀ = 118–119°C, n_D^{25} = 1.5428. (Lit.⁹ gives for the racemic compound b.p.₁₃ = 121°C, n_D^{17} = 1.5548), [α]_D²⁵ = +3.0° (c = 10.0 benzene) NMR: 6.7–7.3, 4 H, complex; 2.31, 1 H, p; 1.72, 1 H, 1.10, 3 H, d; 0.95, 3 H, d. IR: C=O 1725 cm⁻¹ (ketone).

(+)-1,2-Dimethylindene (7). (+)-2,3-Dimethylindanone, 4.0 g (0.025 mol) was dissolved in 50 ml of methanol and sodium borohydride, 1.0 g (0.027 mol) in 75 ml 0.1 M NaOH was added slowly to the solution maintained at 20–25°C by external cooling. After evaporation of the solvent, 100 ml of water was added, the mixture extracted with ether, the ether phases dried over anhydrous MgSO₄ and the solvent evaporated. Without any further purification, the indanol was dissolved in 150 ml of dry benzene and dehydrated by the same route as the 2-alkyl-3-deuterioindenes. The crude indene was flash-distilled and purified *via* preparative GLC. Yield: 2.5 g, 69%, b.p.₁₁ = 82–86°C, n_D^{25} = 1.5655 (lit. gives for the racemic compound b.p.₁₃ = 86–87°C, n_D^{25} = 1.5642). [α]_D²⁵ = +115° (c = 2.0, benzene). NMR: 6.6–7.3, 4 H, complex; 6.25, 1 H, p; 3.01, 1 H, p; 1.96, 3 H, q; 1.18, 3 H, d.

Kinetics

The kinetic experiments were performed in a thermostat having an accuracy of $\pm 0.05^\circ\text{C}$. Diazabicyclooctane (KEBO), m.p. 156–158°C, was recrystallized twice from hexane (spectrograde). Triethylamine (Merck) was distilled over sodium. Pyridine (Mallinckrodt) was dried over calcium hydride and distilled and degassed with oxygen-free N₂. Stock solutions of the aliphatic amines were prepared and added to the substrate, such that the indene concentration was 2 M. At specific intervals, samples were withdrawn from the reaction bottle, quenched with dilute hydrochloric acid and the indenenes extracted with carbon tetrachloride. The samples were diluted with carbon tetrachloride to give concentrations approximately 2 M in indene. The NMR-spectra were recorded and the average of at least three integrals of A- and X-protons was recorded. The internal standard was the CH₃-group of 2-methylindene or the -CH₂-group in 2-ethylindene. About 15 observations during 3 half-lives were recorded. The rate constants were calculated by means of a least-squares plot. The isomerizations were studied at 20.0, 30.0, and 40.0°C.

In a test run the isomerization of 1-methylindene and 3-deuterioindene, respectively, with DABCO as a catalyst was studied. These runs were undertaken at 30.0°C. The internal standard was *t*-BuOH, 0.1 M, which has a very small retarding effect on the reaction rate.

The polarimetric measurements were performed with 0.5 M optically active 1,2-dimethyl-

indene and inactive 1,2-dimethylindene added so that the total concentration was 2 M. The mutarotation was followed by means of an automatic data collecting system, equipped with a paper tape punch. About 200 observations were made over at least 3 half-life times. The rate constants were calculated *via* a least-squares plot performed by the computer programme PROGAE¹⁴.

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