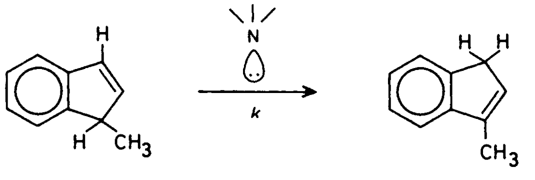
Primary ^{2}H Kinetic Isotope Effects in the Base-catalysed 1,3-Prototropic Rearrangement of 1-Methylindene and 1,3-Dimethylindene

Anita Hussénius, Olle Matsson,* and Göran Bergson*
Institute of Chemistry, University of Uppsala, P.O. Box 531, S-751 21 Uppsala, Sweden

Rate constants and primary deuterium kinetic isotope effects (p.d.k.i.e.s.) have been determined for the base-catalysed rearrangement of 1-methylindene (**1**) and 1,3-dimethylindene (**3**) in the solvent *o*-dichlorobenzene at 30 °C. The structurally similar tertiary amines 1-aza-adamantane, quinuclidine, 1,3-diaza-adamantane, DABCO, and 1,3,5-triaza-adamantane were used as catalysts. Substrate (**3**) gave a lower isotope effect than (**1**). The response in p.d.k.i.e. due to a change in basicity of the amine catalyst is very similar for (**1**) and (**3**). Despite its intermediate basicity, DABCO showed a significantly lower p.d.k.i.e. for both substrates. The p.d.k.i.e.s. obtained for the other bases, with a p*K* at or around 2.6, were almost constant. The consequences of a possible influence of internal ion-pair return on the rearrangement of the substrates are discussed and related to the measured p.d.k.i.e.s. The similarity between the substrates and the symmetry in the rearrangement of (**3**) permits some rationalizations to be made.

The kinetic isotope effect (k.i.e.) is a widely used tool for elucidating reaction mechanisms. Primary deuterium k.i.e.s. (p.d.k.i.e.s.) have been extensively utilized in the study of proton transfer reactions. The magnitude of the p.d.k.i.e. has been used to estimate the extent to which the proton is transferred from a carbon acid to base, in the activated complex of a rate-determining proton-abstraction step.[1] In interpreting observed primary k.i.e.s. several investigators have pointed out the importance of internal ion-pair return for proton-transfer reactions proceeding *via* carbanion intermediates.[2] A review was recently published by Koch.[2e]

In a recent paper we reported p.d.k.i.e.s. and secondary β-deuterium k.i.e.s. for the base-catalysed rearrangement of 1-methylindene (1) to 3-methylindene (2).[3]



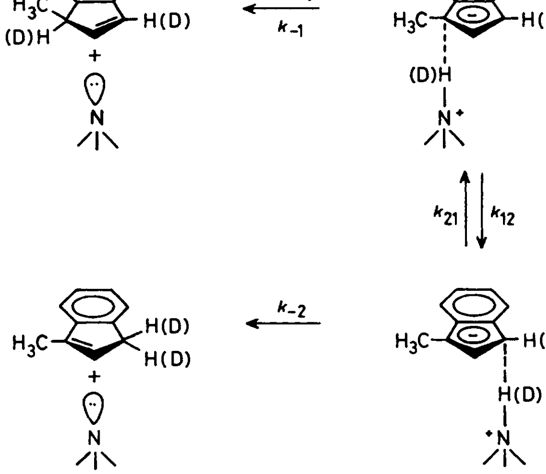
(1) (2)

The 1,3-proton transfer in indene and its alkyl-substituted analogues is believed to occur *via* one or, more likely, two ion-pair intermediate(s).[4] Experiments with optically active and isotopically labelled indenes have demonstrated that the proton transfer proceeds intramolecularly[5] and stereospecifically[6,7] when uncharged amines are used as catalysts. The suggested intermediates are tightly hydrogen-bonded complexes between the protonated amine and the carbanion, with the ammonium ion located above C-1 and C-3 of the indene moiety, respectively.[4] High stereospecificity is observed when the rates of rotation within the ion pair and of dissociation to free carbanion are slow, compared with collapse of the ion-pair to product or starting material.[5,6a] Cram and co-workers[7] showed that the tertiary amine DABCO gave almost complete stereospecificity even in such a polar solvent as dimethyl sulphoxide. The rearrangement of (1) to (2) may be regarded as irreversible.[8] The rearrangement rate is proportional to the concentration of the indene and the concentration of the catalysing base. A credible mechanism is shown in Scheme 1. The relationship between the phenomenological rate constant and the mechanistic rate constants is given by equations (1)–(3).† The k.i.e. for the rate-determining ionization step ($k_1^{\mathrm{H}}/k_1^{\mathrm{D}}$) is

$$k = k_1 \frac{1}{\left[1 + \left(\frac{k_{-1}}{k_{-2}}\right)\left(\frac{k_{-2} + k_{21}}{k_{12}}\right)\right]} \qquad (1)$$

$$k = k_1 \frac{1}{\left[1 + \left(\frac{k_{-1}}{k_{-2}}\right)\left(\frac{k_{21}}{k_{12}}\right)\right]}; \text{ if } k_{21} \gg k_{-2} \qquad (2)$$

$$k = k_1 \frac{1}{1 + \sigma\chi}; \ \sigma \equiv \frac{k_{-1}}{k_{-2}} \text{ and } \chi \equiv \frac{k_{21}}{k_{12}} \qquad (3)$$



Scheme 1.

---

† The derivation of equations (1)–(3) is given in an Appendix.

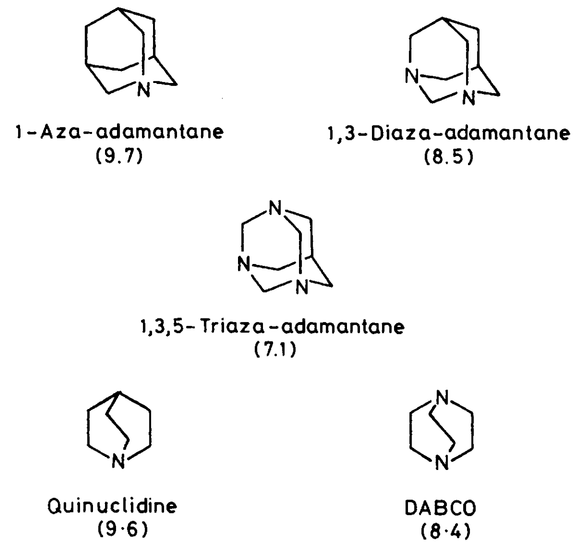
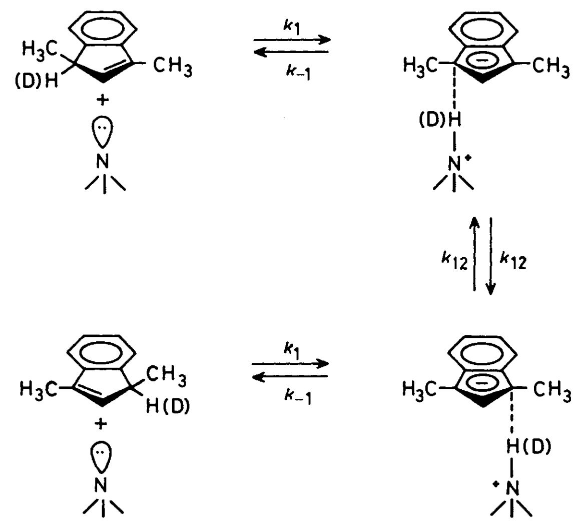


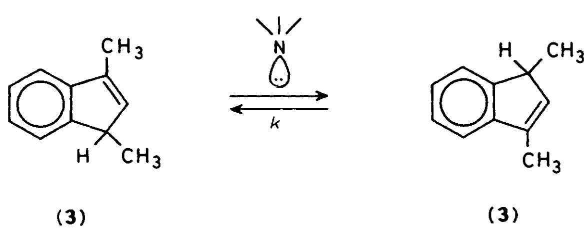
Figure 1. Amine catalysts used in the 1,3-prototropic rearrangement of (**1**) and (**3**). In parentheses are the pK values, statistically corrected for the number of nitrogens, measured in Me_2SO at 25 °C [taken from ref. (14)].



Scheme 2.

thus related to the observed k.i.e. (k^H/k^D) and the ion-pair collapse ratios ($\sigma = k^L_{-1}/k^L_{-2}$, L = H or D) according to equation (4). This equation also contains the ion-pair equilibrium constant χ. However, the collapse ratio of the ion-pair intermediates and χ in the rearrangement of (**1**) are not known, which makes it difficult to interpret the measured k.i.e.s.

$$\frac{k^H}{k^D} = \frac{k_1^H}{k_1^D} \cdot \frac{1 + \sigma^D\chi^D}{1 + \sigma^H\chi^H} \tag{4}$$



(**3**) (**3**)

Table 1. Observed second-order rate constants and p.d.k.i.e.s for the base-catalysed rearrangement of 1-methylindene[a] to 3-methylindene in *o*-dichlorobenzene at 30 °C.

Base	[Base]/ mol dm^{-3}	$k^H[B]^b$ / 10^{-3} dm^3 mol^{-1} s^{-1}	k^H/k^{Dc}
1-Aza-adamantane	0.013	67.6 ± 2	6.20
Quinuclidine	0.014–0.029	48.6 ± 1.5	6.18
1,3-Diaza-adamantane	0.070	4.83 ± 0.15	6.05
DABCO	0.001 1–0.093	3.77 ± 0.32	5.18
1,3,5-Triaza-adamantane	0.14	0.295 ± 0.009	5.90

[a] The substrate concentration was 0.3 mol dm^{-3}. [b] [B] = base concentration. The rate constants are divided by the number of nitrogen atoms in the amine used. [c] Error limits, obtained by estimation of the experimental errors involved, for k^H/k^D are ±0.08.

Table 2. Observed second-order rate constants and p.d.k.i.e.s for the base-catalysed rearrangement of 1,3-dimethylindene[a] in *o*-dichlorobenzene at 30 °C.

Base	[Base]/ mol dm^{-3}	$k^H/[B]^b$ / 10^{-3} dm^3 mol^{-1} s^{-1}	k^H/k^{Dc}
1-Aza-adamantane	0.12	1.92 ± 0.06	4.95
Quinuclidine	0.10–0.20	1.38 ± 0.06	4.93
1,3-Diaza-adamantane	0.30	0.131 ± 0.004	4.82
DABCO	0.015–0.61	0.103 ± 0.009	4.03
1,3,5-Triaza-adamantane	0.51–1.3	0.008 23 ± 0.0002	4.63

[a] The substrate concentration was 0.3 mol dm^{-3}. [b] [B] = base concentration. The rate constants are divided by the number of nitrogen atoms in the amine used. [c] Error limits, obtained by estimation of the experimental errors involved, for k^H/k^D are ±0.06.

At an early stage we pointed out[9] the usefulness of the 'symmetrically' substituted 1,3-dimethylindene, including a methyl-deuteriated form, for mechanistic studies of the 1,3-proton-transfer reaction. In the present investigation we have studied the rearrangement of both (**1**) and 1,3-dimethylindene (**3**) under the same experimental conditions.

The rearrangements have been catalysed by a series of structurally similar tertiary amines of varying basicity (Figure 1), including those used in the previous study.* The 3-system has the advantage, resulting from the 'symmetry,' that the observed primary k.i.e. is equal to the primary k.i.e. for the rate-determining ionization step, assuming fast equilibration of the intermediates [see Scheme 2, equations (5)–(7)]. The ion-pair

$$k = k_1 \frac{1}{\left(2 + \dfrac{k_{-1}}{k_{12}}\right)} \tag{5}$$

$$k = \tfrac{1}{2} k_1; \text{ if } k_{12} \gg k_{-1} \tag{6}$$

$$\frac{k^H}{k^D} = \frac{k_1^H}{k_1^D} \tag{7}$$

collapse ratio is here, by necessity, equal to unity. Thus, assuming fast equilibration of the ion-pair intermediates, the dependence of the p.d.k.i.e., for the proton-abstraction step, on the basicity of the catalysing base, may be determined in this system. Moreover, estimations of the importance of internal ion-

---

* Hexamethylenetetra-amine was not used in the present study. Because of its low solubility in *o*-dichlorobenzene the rate of rearrangement was too slow.

pair return in the rearrangement of (**1**) may eventually be made, by comparing the observed k.i.e.s for the two substrates.

The information that can be gained about internal ion-pair return in the indene system is also of importance in connection with our attempts to understand the mechanism of asymmetric induction in the enantioselective rearrangement of (**1**), using chiral amine catalysts. Enantioselectivity in the indene system has been studied by Meurling and Bergson.[10] Recently, different p.d.k.i.e.s were observed for the (+)- and (−)-forms in the enantioselective rearrangement of (**1**) to (**2**), catalysed by (+)-(8*R*,9*S*)-dihydroquinidine in the solvent *o*-dichlorobenzene at 30 °C.[11] This solvent, which, for various reasons, is suitable in the enantioselective rearrangement experiments, was also used in the present investigation to permit a meaningful comparison of the results.

Results and Discussion

The results of the kinetic experiments, obtained by a polarimetric differential method, are listed in Tables 1 and 2. Using this method, the experiments start from an isotopic quasi-racemic mixture of the (−)-enantiomer of the protic substrate and the (+)-enantiomer of the deuteriated substrate (or *vice versa*). The rate constants and their ratio are determined from the observed optical rotation of the reaction mixture as a function of time. The method, which has been described elsewhere,[12] allows the rate parameters to be determined with high accuracy. Kinetic experiments using n.m.r. spectroscopy confirm the rate of rearrangement measured by polarimetry.

The deuteriated substrate (**1**) was also substituted with deuterium in the 3-position to avoid a possible contribution to the optical rotation of the reaction mixture from the chiral product 3-methyl(1-^{2}H)indene and also to avoid introduction of protium because of the slight possible degree of reversibility. The remote secondary isotope effect from this deuterium was neglected in the present interpretation of the results.

The second-order rate constants (calculated by division of the measured pseudo-first-order rate constants by the base concentration) and p.d.k.i.e.s displayed in Tables 1 and 2 are averages from three or more kinetic runs, and were calculated by least-squares fitting of the model two-exponential function to the experimental data corrected for protium content.[3,13]

The rearrangement of racemic 1-methyl-3-($^2H_3$)methylindene, catalysed by quinuclidine in deuteriated *o*-dichlorobenzene, was followed by n.m.r. spectroscopy. Two kinetic experiments were performed which gave observed rate constants, $k_{obs}/[\text{base}]$,* of 1.33×10^{-3} dm^3 mol^{-1} s^{-1} and 1.35×10^{-3} dm^3 mol^{-1} s^{-1}, respectively. These values are the same, within the error limits, as those obtained from the polarimetric experiments (Table 2, entry 2).

The thermodynamic basicity of the amines was determined in the solvent Me_2SO at 25 °C by Meurling.[14] Using these basicities, a linear correlation with the rate of rearrangement for (**1**) and (**3**) was found, with a correlation coefficient of 0.999 in both cases. This indicates that the relative p*K* values measured in Me_2SO are also valid in the solvent *o*-dichlorobenzene. Assuming this, one obtains a Brønsted β-coefficient of 0.90 for both substrates. Provided that the p*K*–p*K* plot for the two solvents has a slope of unity this value is consistent with an ion-pair-like transition state (TS).[15]

Except for DABCO, the isotope effect is relatively constant for the amines used. Only a very small increase in primary k.i.e., of the type predicted by the Melander–Westheimer model,[16] when proceeding from weaker to stronger bases, is observed. According to this model, a maximum p.d.k.i.e. is obtained for the case where the proton is bound with equal strength to donor and acceptor in the transition state. It has been suggested that this occurs when the pK_a of the carbon acid equals the pK_a of the conjugate acid of the base catalyst.[17] A small variation in the p.d.k.i.e. associated with k_1 has been reported by Streitwieser *et al.*[18] for the exchange of hydrocarbons, and by Bordwell and Boyle[19] for nitroalkanes. These results brought into question the idea that variation of pK_a of the carbon acid results in a variation of isotope effect, reflecting changes of TS symmetry. Wide ranges of pK_a were covered in these investigations. The deviation of DABCO has previously been observed for substrate (**1**) in other solvents.[3] Experiments with different concentrations of DABCO were performed (see Table 3), confirming the pseudo-first-order behaviour and yielding the same k.i.e. Association phenomena that change the properties of the catalysing base, as a possible reason for the attenuated isotope effects, can thus be ruled out. 1,3-Diaza-adamantane has almost the same pK_a value as DABCO, but follows the pattern of the other bases.

Table 3. Pseudo-first-order rate constants and p.d.k.i.e.s for the rearrangement of 1-methylindene[a] and 1,3-dimethylindene,[a] using DABCO as the catalyst, in *o*-dichlorobenzene at 30 °C.

Substrate	[DABCO]/ mol dm^{-3}	$k^H/10^{-3}$ s^{-1}	$k^{H\,b}/k^D$
1-Methylindene	0.093	0.758	5.13(2)
1-Methylindene	0.015	0.115	5.22(3)
1-Methylindene	0.0011	0.007 61	5.16(1)
1,3-Dimethylindene	0.61	0.132	4.02(1)
1,3-Dimethylindene	0.46	0.0962	4.03(2)
1,3-Dimethylindene	0.15	0.002 83	4.02(1)

[a] The substrate concentration was 0.3 mol dm^{-3}. [b] The number of kinetic runs are given in parentheses after each k.i.e. value.

The Two-intermediate Mechanism.—The complete rate expressions for substrates (**1**) and (**3**) are given by equations (1) and (5), respectively. These equations show the relationship between phenomenological and mechanistic rate constants for the mechanisms in Schemes 1 and 2. The schemes show stereospecific mechanisms, in which the hydrogen-bonded, substituted ammonium ion is conducted over one face of the allylic anion, from the C-1 to the C-3 position of the indene. The rearrangements of (**1**) and (**3**) were performed under conditions similar to those under which other dialkylindenes (*e.g.* 1-methyl-3-isopropylindene[6,7]) exhibit complete stereospecificity. In view of this, and since the rearrangement of (**3**) is accompanied by racemization owing to the enantiomeric relationship between reactant and product molecules, the postulated schemes seem well justified. The rate of interconversion between the two ion-pair intermediates may be expected to show low sensitivity to isotopic substitution, since no covalent bonds are formed or broken in this step. If this assumption is correct, the relationships between the k.i.e. for the rate-determining proton-abstraction step and the observed k.i.e. are given by equations (8) and (9) for the two substrates (**1**) and (**3**), respectively.

$$\frac{k^H}{k_D} = \frac{k_1^H\left[1 + \sigma^D\left(\frac{k_{-2}^D + k_{21}}{k_{12}}\right)\right]}{k_1^D\left[1 + \sigma^H\left(\frac{k_{-2}^H + k_{21}}{k_{12}}\right)\right]} = \frac{k_1^H}{k_1^D} f_1 \qquad (8)$$

$$\frac{k^H}{k^D} = \frac{k_1^H}{k_1^D}\frac{2k_{12} + k_{-1}^D}{2k_{12} + k_{-1}^H} = \frac{k_1^H}{k_1^D} f_3 \qquad (9)$$

---

* The concentration of quinuclidine was 0.0407 mol dm^{-3}.

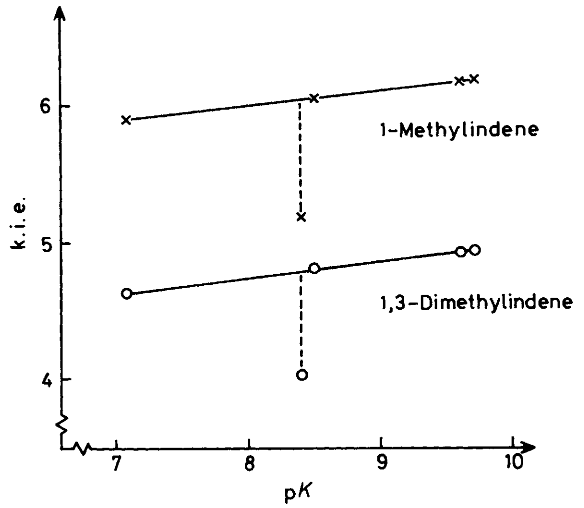


Figure 2. Observed primary k.i.e.s for the rearrangement of (1) and (3) *vs.* p*K* values of the amine catalysts. The dotted lines show the deviation of the amine DABCO.

Equation (9) shows that if internal ion-pair return is of importance in the rearrangement of (**3**), it will be manifested as an attenuation of the observed k.i.e.,* since it is reasonable to expect that the isotope effect on the ion-pair collapse is normal, *i.e.* $k^H_{-1} > k^D_{-1}$. For substrate (**1**), it is not quite obvious how a contribution from the quotient denoted f_1 in equation (8) affects the observed k.i.e. First, we can assume a normal isotope effect on the intermediate-collapse to product, $k^H_{-2} > k^D_{-2}$. Further, it is known that the forward reaction, from the ion-pair intermediate to product (**2**), is much faster than the backward reaction, from ion-pair to starting material (**1**) ($k_{-2} \gg k_{-1}$).[8,20] Therefore, according to the Hammond postulate, it seems reasonable to assume a more intermediate-like TS for the more highly exothermic collapse to (**2**). Thus, the isotopic sensitivity is assumed to be smaller for k_{-2} than for k_{-1}. Expression (10) should be valid if these rationalizations are correct.

$$\frac{k^H_{-1}}{k^D_{-1}} > \frac{k^H_{-2}}{k^D_{-2}} \qquad (10)$$

$$\frac{k^H_{-1}}{k^H_{-2}} > \frac{k^D_{-1}}{k^D_{-2}} \Leftrightarrow \sigma^H > \sigma^D \qquad (11)$$

Reformulation of inequality (10) gives relation (11). The conclusion is that the effect of internal ion-pair return on the 1,3-proton transfer of (**1**) should also give rise to an attenuation of the observed k.i.e.†

According to the discussion above, the lower k.i.e. for DABCO may be attributed to a higher degree of internal ion-pair return for this base. For the bases quinuclidine and DABCO, Thibblin[21] recently attributed different p.d.k.i.e.s to a small amount of internal return for the latter base, but quantitative estimates of the relevant collapse ratios are not given.

The data in Tables 1 and 2 show that, for all bases used, the rate constants for (**3**) are lower than for (**1**), in accordance with the lower acid strength expected for the former substrate. The difference in pK_a between the two substrates can be roughly estimated as 2.4, by comparison with the known pK_a values for indene (20.1, Me_2SO) and 3-methylindene (22.5, Me_2SO).[22] The value of Δp*K*, between the substrate and the conjugate acid of the base catalyst, is thus larger for (**3**) and the p.d.k.i.e.s are consistently lower. This could also, in principle, be a manifestation of a different degree of internal ion-pair return between the two substrates. The lower k.i.e. for (**3**) would then be due to a higher degree of reversibility of the ionization step for this substrate.

Approximation of Rapidly Equilibrating Intermediates.—The complete rate expressions, relating phenomenological and mechanistic rate constants, for the two substrates can be simplified by some assumptions. First, it seems reasonable to assume that the rate of interconversion between the ion-pair intermediates for substrate (**3**) is much faster than collapse to product ($k_{12} \gg k_{-1}$),[4] since no covalent bonds are formed or broken in this process. Moreover, simple extended Hückel calculations on the indenyl–ammonium ion-pair indicate that the ammonium ion, once formed, can slide between the 1- and 3-positions with very low activation energy.[4a] For the same reasons, a corresponding assumption for the (**1**)-system, $k_{21} \gg k_{-2}$ [see equations (2), (3)], is likely. This assumption of fast ion-pair isomerization is crucial, since it allows the observed k.i.e. for (**3**) to be identified with the k.i.e. for the rate-determining ionization step [equation (7)]. A case of slow equilibration of isomeric ion-pair intermediates of this type was, however, reported recently by Thibblin.[23]

As illustrated in Figure 2, the variation in p.d.k.i.e for the two substrates is almost constant for all bases used in this investigation. If there is no contribution to the k.i.e.s for (**3**) from internal return, the similarity in the k.i.e. pattern between the substrates provides strong support for the assumption that internal return is also negligible in the case of (**1**) [$\sigma \equiv (k_{-1}/k_{-2}) \ll 1$], since it cannot, according to the discussion above, amplify the observed k.i.e. Alternatively, there is no isotope effect on the ion-pair collapse ratio ($\sigma_H \approx \sigma_D$). In fact, an attempt to estimate the collapse ratio, σ, has been reported[20] and it has been assumed, on the strength of that investigation, that the collapse ratio is less than 0.05.[8] If that is the case, the observed k.i.e. for (**1**) equals the k.i.e. for the proton-abstraction step.

The One-intermediate Mechanism.—In the discussion so far we have assumed the existence of two ion-pair intermediates in the prototropic rearrangement of the indenes (**1**) and (**3**). This assumption is based on experimental evidence from the study of competing elimination and proton transfer by Thibblin,[21] where related indenes were used, and also on the extended Hückel calculations by Wold and Bergson[4a] referred to above. However, the one-intermediate mechanism cannot be totally ruled out. This alternative would, of course, greatly simplify the interpretation for substrate (**3**). The observed k.i.e. may then be directly identified with the ionization isotope effect. For substrate (**1**), equation (12) gives the relationship between observed and ionization k.i.e.s.

$$\frac{k^H}{k^D} = \frac{k^H_1}{k^D_1} \cdot \frac{1 + \sigma^D}{1 + \sigma^H} \qquad (12)$$

The conclusion is the same as that drawn from the discussion based on equation (8): internal return has the effect of attenuating the observed k.i.e., and thus cannot account for the higher k.i.e. observed for substrate (**1**) as compared with substrate (**3**). Considering the great similarity in the response to change of base shown in Figure 2, it appears unlikely that the amount of internal return is different for the bases used.

---

* This holds also for the case $k^H_{12} \neq k^D_{12}$, as long as the isotope effect on the ion-pair equilibration is normal.

† When $\chi^H \neq \chi^D$ no definite conclusion can be drawn.

Table 4. Optical rotations of (–)-1-methylindene and (+)-1-methyl(1,3-$^2H_2$)indene. The specific rotations were measured in *o*-dichlorobenzene solution.[a]

λ/nm	$0.1\alpha^{30.0}$ (neat)	$[\alpha]^{30.0}$
589	–19.15	–195.8
	+19.63	+197.5
578	–20.06	–204.2
	+20.58	+207.2
546	–23.16	–235.7
	+23.77	+239.3
436	–43.17	–439.9
	+44.40	+447.4
365	–78.20	–794.8
	+80.57	+810.7

[a] The accuracy is ±0.5%.

Table 5. Optical rotations of (–)-1,3-dimethylindene and (+)-1,3-dimethyl(1-^2H)indene. The specific rotations were measured in *o*-dichlorobenzene solution.[a]

λ/nm	$0.1\alpha^{30.0}$ (neat)	$[\alpha]^{30.0}$
589	–14.86	
	+15.26	+163.3
578	–15.55	–167.6
	+15.99	+170.9
546	–17.96	–193.3
	+18.48	–197.7
436	–33.67	–362.8
	+34.72	+372.3
365	–61.4	–662.1
	+63.6	+681.3

[a] The accuracy is ±0.5%.

Tunnelling.—We have avoided a discussion about contributions from tunnelling to the experimental isotope effects.[24] It is known, that small amounts of internal return appear to have an effect on the temperature dependence of the observed k.i.e., which is indistinguishable from that caused by tunnelling.[25] If the question about the rate of ion-pair equilibration can be resolved, the substrate (3) appears to be a good candidate for an investigation on tunnelling, since the temperature dependence of k_1 and the associated k.i.e. can be determined.

Experimental

General.—The ^1H n.m.r. and the proton noise-decoupled ^{13}C n.m.r. spectra were obtained with a Varian XL 300 spectrometer, operating at 300 MHz and equipped with a 5 mm switchable probe. All spectra were run at 20 °C. $SiMe_4$ was used as an internal standard. ^1H N.m.r. (^{13}C n.m.r.) spectra were obtained using a spectral width of 4 kHz (16.5 kHz), 30 016 data points, pulse width 30 deg. (50 deg.) and duration of 90 deg. pulse 21.6 μs (17.0 μs), data-acquisition time of 3.75 s (0.91 s) and 16 (3 000) scans. [$^2H_6$]Benzene (> 99.8 atom% ^2H, Riedel-de Haen AG) was used as the solvent. Analytical g.l.c. was run on a Hewlett–Packard 5830A gas chromatograph equipped with electronic integrator (GC Terminal 18850 A) or a Hewlett–Packard 5880A (Terminal 5880A Series), each equipped with a flame-ionization detector.

Purification of the substrates was carried out by preparative gas chromatography on a 1.5 m long and $\frac{3}{8}''$ wide column, packed with 15% Apiezon L on Chromosorb W (AW, DMCS), 60–80 mesh. A Varian Aerograph Model 90 P gas chromatograph with a thermal conductivity detector was used, with helium as the carrier gas, at a flow rate of 100 cm^3 min^{-1}.

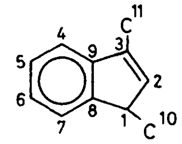
Optical rotation was measured with a Perkin-Elmer 241 photoelectric polarimeter. The kinetic runs were performed with the same instrument, equipped with an automatic data-acquisition system consisting of an ABC 80 with a floppy disc unit FD 2U. The water-jacketed polarimetric cell (optical path length 10 cm, volume 0.9 cm^3) was connected to a HETO 02 PT 623 proportional regulating thermostat. The temperature was measured with a calibrated mercury thermometer with an absolute accuracy of 0.02 °C at the outlet of the cell. The temperature did not deviate more than 0.02 °C from the average value during the runs and was thus 30.00 ± 0.04 °C.

Indenes.—The synthesis of the optically active and isotopically substituted 1-methylindenes has been described earlier.[12a] (–)-(*R*)-1,3-Dimethylindene, (+)-(*S*)-1,3- dimethyl-(1-^2H)indene and 1-methyl-3-($^2H_3$)methylindene were prepared from the corresponding 3-methylindanones,[12a] which were subjected to a Grignard reaction with methylmagnesium iodide yielding the 1,3-dimethylindanols.[9] After having been recrystallized twice from hexane, the optically active indanols were dehydrated with toluene-*p*-sulphonic acid as described in ref. 12(*a*). The 1-methyl-3-($^2H_3$)methylindene was dehydrated by being heated under reduced pressure. The crude 1,3-dimethylindenes were distilled under reduced pressure under nitrogen, b.p. 80–82 °C/1.3 kPa. Yields ranged from 49–75%. All indenes were finally purified by preparative gas chromatography using injection temp. 110–120 °C, detection temp. 115–120 °C and column oven temp. 105–110 or 115–120 °C for the 1-methylindenes and the 1,3-dimethylindenes, respectively. The fractions were collected in ice-cooled glass traps and the purified substrates were stored under nitrogen in the freezer.

The optical rotation of each batch of purified indene was measured in a short polarimetric microcell (optical path length 1 cm, volume 0.09 cm^3, neat). Optical rotations measured neat and in *o*-dichlorobenzene are collected in Tables 4 and 5.

The purity of the indenes was checked by g.l.c. on a 2.9 m long and $\frac{1}{8}''$ wide column, packed with 5% Apiezon L on 80/100 mesh Chromosorb W (AW, DMCS). A solution of the indene in diethyl ether was injected at column oven temp. 120 °C (150 °C), injection temp. 130 °C (160 °C), and detection temp. 160 °C (180 °C) for the 1-methylindenes (1,3-dimethylindenes). All samples used in the measurements showed only one peak. The isotopic purities of the deuteriated compounds were calculated from ^1H n.m.r. data.

N.M.R. Data.—(–)-(*R*)-1,3-*Dimethylindene* (0.45 mol dm^{-3}). δ_H 1.12 (3 H, d, $J_{1,10}$ 7.5 Hz, 10-H), 1.96 (3 H, dd, $J_{1,11}$ 1.6, $J_{2,11}$ 1.9 Hz, 11-H), 3.23 (1 H, split q, $J_{1,10}$ 7.5, $J_{1,2}$ 1.9 Hz, 1-H), 5.92 (1 H, m, $J_{1,2}$ 11.9, $J_{2,11}$ 1.6 Hz, 2-H), and 7.21 (4 H, m, aromatic); δ_C 12.9 (C-11), 16.4 (C-10), 43.9 (C-1), 119.3, 122.7, 125.1, 126.6, 136.1, 138.4 (C-3, C-8, or C-9), 145.5 (C-3, C-8, or C-9), and 150.0 (C-3, C-8, or C-9).



(+)-(*S*)-1,3-*Dimethyl*(1-^2H)*indene* (0.52 mol dm^{-3}). δ_H 1.11 (3 H, s, 10-H), 1.96 (3 H, d, $J_{2,11}$ 1.6 Hz, 11-H), 3.23 (0.012 H, m, 1-H), 5.91 (1 H, 'q', $J_{2,11}$ 1.6 Hz, 2-H), and 7.22 (4 H, m, aromatic); δ_C 12.9 (C-11), 16.3 (C-10), 43.5 (C-1, t), 119.3, 122.7, 125.1, 126.6, 136.1, 138.4 (C-3, C-8, or C-9), 145.6 (C-3, C-8, or C-9), and 150.0 (C-3, C-8, or C-9).

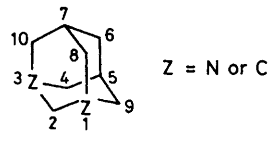
1-*Methyl*-3-($^2H_3$)*methylindene* (0.40 mol dm^{-3}). δ_H 1.12 (3 H, d, $J_{1,10}$ 7.5 Hz, 10-H), 1.94 (0.031 H, m, 11-H), 3.23 (1 H, qd, $J_{1,10}$ 7.5, $J_{1,2}$ 1.9 Hz, 1-H), 5.92 (1 H, d, $J_{1,2}$ 1.9 Hz, 2-H), and 7.21 (4 H, m, aromatic); δ_C 16.4 (C-10), 43.9 (C-1), 119.3, 122.7, 125.1, 126.6, 136.2, and 138.4 (C-3, C-8, or C-9), 145.6 (C-3, C-8, or C-9), and 150.1 (C-3, C-8, or C-9).

Catalysts and Solvent.—All handling of the purified amines was carried out in a glove box, in which the atmosphere was circulated through molecular sieves (5 Å) in the presence of Ascarite to lower the amount of carbon dioxide in the atmosphere. The glove box was flushed with nitrogen before use. The flasks containing the stock solutions of the amines were stored in larger bottles filled with dry nitrogen and containing silica gel together with KOH pellets.

The preparation and purification of quinuclidine (1-azabicyclo[2.2.2]octane) and 1,4-diazabicyclo[2.2.2]octane (DABCO) have been described earlier.[3] 1-Aza-adamantane was prepared from ethyl 9,9-ethylenedithio-3-tosyl-3-azabicyclo[3.3.1]nonane-7-carboxylate[26,]* according to the method described by Speckamp *et al.*[27] The 1-aza-adamantane was purified by sublimation twice, under nitrogen, at 80 °C at normal pressure, m.p. 250–252 °C. The purity was checked by analytical g.l.c., using a glass column (1 m × 0.003 m) packed with 3% PS 400 on Chrom W (HP 80/100) and a carrier gas (N_2) flow of 40 cm^3 min^{-1}. Injection temp. 250 °C, detection temp. 200 °C, and column oven temp. 80 °C.

1,3-Diaza-adamantane was synthesized from 3,5-dimethylpyridine. Oxidation of 3,5-dimethylpyridine to the corresponding dicarboxylic acid was performed with potassium permanganate analogously to the oxidation of 3-methylpyridine.[28] The pyridine-3,5-dicarboxylic acid was esterified under Fischer conditions.[29] In the following steps the procedure outlined by Stetter *et al.*[30] was followed. The 1,3-diaza-adamantane was purified by sublimation twice, at 80 °C/2.7 kPa, m.p. 260–261 °C. The purity was checked by analytical g.l.c. using a glass column (1.5 m × 0.003 m) packed with 10% Carbowax–1% KOH on Chrom W (AW, DMCS) and a carrier gas (N_2) flow of 30 cm^3 min^{-1}. Injection and detection temp. 250 °C, and a column oven temp. 150 °C.

N.M.R. Data.—The ^{1}H n.m.r. spectra have been reported.[14]



1-*Aza-adamantane* (0.38 mol dm^{-3}). δ_C 28.2 (C-3, C-5, and C-7), 37.4 (C-4, C-6, and C-10), and 59.6 (C-2, C-8, and C-9).

1,3-*Diaza-adamantane* (0.41 mol dm^{-3}). δ_C 21.1 (C-5 and C-7), 36.2 (C-6), 58.8 (C-4, C-8, C-9, and C-10), and 75.5 (C-2).

1,3,5-Triaza-adamantane was prepared by reductive dehalogenation of 7-bromo-1,3,5-triaza-adamantane[31] with lithium aluminium hydride under Dubois conditions.[32] Compared with the method used in ref. 35, this procedure gave a higher yield and a product that was easier to purify. To a 500 cm^3 three-necked round-bottomed flask, containing lithium aluminium hydride (16.7 g, 0.440 mol) and tetrahydrofuran (200 cm^3; h.p.l.c. grade, passed through activated basic aluminium oxide, distilled from calcium hydride and stored over 4 Å molecular sieves), was added 7-bromo-1,3,5-triaza-adamantane (10.0 g, 0.0458 mol) in small portions. The reaction mixture was refluxed under nitrogen for 4 h. The reaction was followed by g.l.c. on a glass column (1 m × 0.003 m) packed with 3% PS 400 on Chrom W (HP 80/100), using an injection and detection temp. of 270 °C and a column oven temp. of 150 °C. After the mixture had cooled to room temperature, the excess of lithium aluminium hydride was destroyed by adding water (14 cm^3), 15% aqueous sodium hydroxide (14 cm^3), and water (42 cm^3). The salts were filtered off and then refluxed with benzene in a flask equipped with a Dean–Stark water separator. The combined organic layer was dried with calcium oxide (analytical grade, newly heated) and evaporation of the solvents gave the crude 1,3,5-triaza-adamantane, which was recrystallized from benzene–heptane (1:5, v:v), yield (3.8 g, 60%), 99.8% pure (calculated as g.l.c. peak area). One more recrystallization gave >99.9% pure product. M.p. 259–260 °C.

o-Dichlorobenzene (Merck, p.a.) was passed through a column of activated basic aluminium oxide (Fluka) and then distilled in a Fischer Spaltrohr distillation apparatus at reduced pressure. The purity of the fractions was checked by g.l.c. on a 4.5 m long and $\frac{1}{8}''$ wide copper column, packed with 15% Carbowax 20 M on Varaport, at a carrier gas flow of 30 cm^3 min^{-1}. Injection and detection temp. 200 °C, column oven temp. 150 °C.

Kinetic Procedure.—The polarimetric differential kinetic procedure, evaluation of rate parameters, and error analysis have been described in detail in an earlier paper.[3]

N.M.R. Kinetics.—A solution of quinuclidine in deuteriated *o*-dichlorobenzene (Ciba–Geigy, >99.5 atom% D) was prepared in a 2 cm^3 calibrated volumetric flask. The racemic 1-methyl-3-($^2H_3$)methylindene (0.040 cm^3) was weighed in a 5 mm n.m.r. tube. The base solution and the n.m.r. tube containing the substrate was thermostatted at 30 °C. Quinuclidine solution (0.6 cm^3) was withdrawn by means of a nitrogen-filled syringe and added to the substrate (under nitrogen). The n.m.r. tube was rapidly shaken and placed in the pre-thermostatted (30 °C) probe of the spectrometer. A clock was started when half of the base solution had been added. A preacquisition delay array of time intervals between each recorded spectrum was used. Each pulse sequence, consisting of 16 scans, took 1 min (acquisition time 3.749 s and pulse 7 μs). The kinetics were followed by measuring the integrals of methyl groups at the 1- and 3-positions (1.12 and 1.96 ppm, respectively). The observed rate constant was obtained from the slope of a plot of $\ln([A] - [A]_\infty)$ *vs.* time, by least-squares fitting {[A] is the concentration of starting material, *i.e.*, 1-methyl-3-($^2H_3$)methylindene, and $[A]_\infty$ the concentration at infinite time, *i.e.*, at equilibration}. Two n.m.r.–kinetic experiments were performed. The correlation between the fitted line and the experimental data was >0.999 in both cases.

Acknowledgements

We thank Dr. Rolf Danielsson for his kind help in connecting the microcomputer to the polarimeter, and for writing the program for the data collection and transmission. We also thank Dr. Lennart Meurling for the gift of an 1-aza-adamantane precursor, and Dr. Stefan Sjöberg and Mr. Kenneth Granberg for help with the synthesis of 1,3-diaza-adamantane. This investigation is part of a project financially supported by the Swedish Natural Science Research Council (through grant K-KU 2446-115). A fellowship from Stiftelsen Bengt Lundqvists Minne to one of us (A. H.) is gratefully acknowledged.

---

* This substrate was a gift from Dr. L. Meurling.

References

1 R. A. More O'Ferrall in 'Proton Transfer Reactions,' eds. E. F. Caldin and V. Gold, Chapman and Hall, London, 1975, pp. 216–227.

2 (*a*) L. Melander and W. H. Saunders, Jr., 'Reaction Rates of Isotopic Molecules,' Wiley, New York, 1980, p. 158; (*b*) D. J. Cram, C. A. Kingsbury, and B. Rickborn, *J. Am. Chem. Soc.*, 1961, **83**, 3688; (*c*) A. Thibblin, I. Onyido, and P. Ahlberg, *Chem. Scr.*, 1982, **19**, 145; (*d*) A. Thibblin, *J. Am. Chem. Soc.*, 1983, **105**, 853; (*e*) H. F. Koch in 'Comprehensive Carbanion Chemistry, Part C,' eds. E. Buncel and T. Durst, Elsevier, 1987, p. 321.

3 O. Matsson, *J. Chem. Soc., Perkin Trans. 2*, 1985, 221.

4 (*a*) S. Wold and G. Bergson, *Ark. Kemi*, 1967, **28**, 245; (*b*) J. Almy and D. J. Cram, *J. Am. Chem. Soc.*, 1969, **91**, 4459.

5 G. Bergson and A.-M. Weidler, *Acta Chem. Scand.*, 1963, **17**, 862.

6 (*a*) G. Bergson and A.-M. Weidler, *Acta Chem. Scand.*, 1963, **17**, 1798; (*b*) A.-M. Weidler and G. Bergson, *ibid.*, 1964, **18**, 1487.

7 J. Almy, R. T. Uyeda, and D. J. Cram, *J. Am. Chem. Soc.*, 1967, **89**, 6768.

8 L. Meurling and G. Bergson, *Chem. Scr.*, 1974, **6**, 104.

9 L. Ohlsson, I. Wallmark, and G. Bergson, *Acta Chem. Scand.*, 1966, **20**, 750.

10 (*a*) See ref. (8) and ref. (9); (*b*) L. Meurling, *Chem. Scr.*, 1975, **7**, 90; (*c*) L. Meurling, G. Bergson, and U. Obenius, *ibid.*, 1976, **9**, 9.

11 O. Matsson, L. Meurling, U. Obenius, and G. Bergson, *J. Chem. Soc., Chem. Commun.*, 1984, 43.

12 (*a*) G. Bergson, O. Matsson, and S. Sjöberg, *Chem. Scr.*, 1977, **11**, 25; see also (*b*) A. J. Bennet and M. L. Sinnott, *J. Am. Chem. Soc.*, 1986, **108**, 7287.

13 (*a*) J. P. Chandler, *QCPE*, 1976, **11**, 307; (*b*) see ref. 3.

14 L. Meurling, *Chem. Scr.*, 1975, **7**, 23.

15 See *e.g.* (*a*) H. Maskill, 'The Physical Basis of Organic Chemistry,' Oxford University Press, 1985, p. 415. For a critical discussion of the interpretation of the Brønsted coefficient see (*b*) F. G. Bordwell and W. J. Boyle, Jr., *J. Am. Chem. Soc.*, 1971, **93**, 511; (*c*) A. J. Kresge in 'Proton Transfer Reactions,' eds. E. F. Caldin and V. Gold, Chapman and Hall, London, 1975, pp. 179—199; (*d*) A. Pross in 'Advances in Physical Organic Chemistry, Vol 21,' eds. V. Gold and D. Bethell, Academic Press, London, 1985, pp. 99–196; (*e*) M. Godfrey, *J. Chem. Soc., Perkin Trans. 2*, 1988, 139.

16 (*a*) L. Melander, 'Isotope Effects on Reaction Rates,' Ronald Press, New York, 1960, pp. 24–31; (*b*) F. H. Westheimer, *Chem. Rev.*, 1961, **61**, 265.

17 R. P. Bell and D. M. Goodall, *Proc. R. Soc. London, Ser. A*, 1966, **294**, 273.

18 A. Streitwieser, Jr., W. B. Hollyhead, G. Sonnichsen, A. H. Pudjaatmaka, C. J. Chang, and T. C. Kruger, *J. Am. Chem. Soc.*, 1971, **93**, 5096.

19 F. G. Bordwell and W. J. Boyle, Jr., *J. Am. Chem. Soc.*, 1971, **93**, 512.

20 G. Bergson and L. Ohlsson, *Acta Chem. Scand.*, 1967, **21**, 1393.

21 A. Thibblin, *Chem. Scr.*, 1983, **22**, 182.

22 F. G. Bordwell and M. J. Bausch, *J. Am. Chem. Soc.*, 1983, **105**, 6188.

23 (*a*) See ref. 21; (*b*) A. Thibblin, *J. Chem. Soc., Chem. Commun.*, 1984, 92.

24 L. Melander and W. H. Saunders, Jr., 'Reaction Rates of Isotopic Molecules,' Wiley, New York, 1980, ch. 5.2.

25 H. F. Koch and D. B. Dahlberg, *J. Am. Chem. Soc.*, 1980, **102**, 6102.

26 W. N. Speckamp, J. Dijkink, and H. O. Huisman, *Chem. Commun.*, 1970, 197.

27 W. N. Speckamp, J. Dijkink, A. W. J. D. Dekkers, and H. O. Huisman, *Tetrahedron*, 1971, **27**, 3143.

28 A. W. Singer and S. M. McElvain, *Org. Synth.*, Coll. Vol. 3, 1955, 751.

29 E. Fischer and A. Speier, *Chem. Ber.*, 1895, **28**, 3252.

30 (*a*) H. Stetter and H. Hennig, *Chem. Ber.*, 1955, **88**, 789; (*b*) H. Stetter and R. Merten, *Chem. Ber.*, 1957, **90**, 868.

31 V. Galik, M. Safa'r, and S. Landa, *Collect Czech. Chem. Commun.*, 1975, **40**, 442.

32 B. Ancian, B. Tiffon, and J. E. Dubois, *J. Chem. Phys.*, 1981, **74**, 5857.

Received 6 *June* 1988; *Paper* 8/01109E

Appendix

Derivation of equations (1)–(3), *for the rearrangement of* 1-*methylindene* **(1)** *to* 3-*methylindene* **(2)** *via two ion-pair intermediates* ($\mathbf{I}_1$ *and* $\mathbf{I}_2$):

Mechanistic scheme:

$$(\mathbf{1}) \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathbf{I}_1 \underset{k_{21}}{\overset{k_{12}}{\rightleftharpoons}} \mathbf{I}_2 \xrightarrow{k_{-2}} (\mathbf{2})$$

Phenomenological scheme:

$$(\mathbf{1}) \xrightarrow{k} (\mathbf{2})$$

Rate equations for the disappearance of **(1)**, $\mathbf{I}_1$ and $\mathbf{I}_2$, with the steady-state approximation applied on the intermediates:

$$-\frac{\mathrm{d}[(\mathbf{1})]}{\mathrm{d}t} = k_1[(\mathbf{1})] - k_{-1}[\mathbf{I}_1] = k[(\mathbf{1})] \qquad (1')$$

$$\frac{-\mathrm{d}[I_1]}{\mathrm{d}t} = -k_1[(\mathbf{1})] + (k_{-1} + k_{12})\cdot [\mathbf{I}_1] - k_{21}[\mathbf{I}_2] = 0 \qquad (2')$$

$$\frac{-\mathrm{d}[\mathbf{I}_2]}{\mathrm{d}t} = -k_{12}[\mathbf{I}_1] + (k_{21} + k_{-2})[\mathbf{I}_2] = 0 \qquad (3')$$

Reformulation of equation (3′) gives equation (4′), which, upon insertion into equation (2′) gives equation (5′).

$$[\mathbf{I}_2] = \frac{k_{12}}{k_{21} + k_{-2}}[\mathbf{I}_1] \qquad (4')$$

$$[\mathbf{I}_1] = k_1 \frac{k_{21} + k_{-2}}{k_{-1}k_{21} + k_{-1}k_{-2} + k_{12}k_{-2}}[\mathbf{1}] \qquad (5')$$

Insertion of equation (5′) into equation (1′) gives the relation between the phenomenological rate constant (k) and the mechanistic rate constants, *i.e.* equations (1)–(3).

$$k = k_1 \frac{1}{\left[1 + \left(\frac{k_{-1}}{k_{-2}}\right)\left(\frac{k_{-2} + k_{21}}{k_{12}}\right)\right]} \qquad (1)$$

$$k = k_1 \frac{1}{\left[1 + \left(\frac{k_{-1}}{k_{-2}}\right)\left(\frac{k_{21}}{k_{12}}\right)\right]}; \text{ if } k_{21} \gg k_{-2} \qquad (2)$$

$$k = k_1 \frac{1}{1 + \sigma\chi}; \ \sigma \equiv \frac{k_{-1}}{k_{-2}} \text{ and } \chi \equiv \frac{k_{21}}{k_{12}} \qquad (3)$$