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1,3-Hydron Transfer in Some 5- or 7-Substituted 1-Methylindenes. Reaction Rates and Kinetic Isotope Effects

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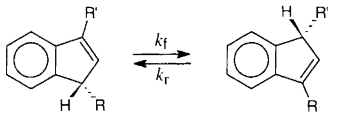
Rate constants and primary deuterium kinetic isotope effects (KIEs) have been determined for the base-catalysed 1,3-hydrotropic rearrangements of 1-methyl-5-nitroindene (**12**), 1-methyl-7-nitroindene (**13**), 5-methoxy-1-methylindene (**14**) and 5-fluoro-1-methylindene (**15**) in *o*-dichlorobenzene at 20 °C. The tertiary amine 1,4-diazabicyclo[2.2.2]octane (DABCO) was used as catalyst. The kinetics were followed by polarimetry using the isotopic quasi-racemate method. The rearrangement of **13** was also investigated by ^{1}H NMR kinetic experiments. The reaction rate correlates, as expected, with the electronic effect of the substituent ranging from a large increase for the 5-nitro substrate to a small decrease for the methoxy compound as compared with the unsubstituted 1-methylindene. The KIEs vary as predicted from the Melander–Westheimer postulate showing an increase with reaction rate from 5.57 to 8.56. The syntheses of the (+)-(*S*)-form of the 5- or 7-substituted indenes and the (−)-(*R*)-form of the deuteriated analogues are also reported.

The base-catalysed 1,3-hydrotropic rearrangement in the indene system (Scheme 1) has been used extensively since the early sixties by several workers as a model reaction for investigations of stereospecificity,[1,2] enantioselectivity,[3] competing elimination reactions,[4] kinetic methodology[1c,3a–d,5] and different aspects of kinetic isotope effects.[6]



Scheme 1.

An important feature was the discovery of the first non-enzymatic intramolecular[7] and stereospecific 1,3-hydron transfer reaction[1a,b] when amines were used as catalysts under suitable conditions. This hydron transfer is believed to occur via two or more hydrogen-bonded intermediates with a suprafacial shift of the hydron (Scheme 2).

The first studies[8] of the deuterium kinetic isotope effect (KIE) in the indene rearrangements were performed by means of simple NMR measurements, and later greater accuracy in KIE determinations was achieved by using optically active substrates.[9] A more systematic study of primary and secondary deuterium KIEs has also been reported[6a,b] for the rearrangement of 1-methylindene. These studies were performed in the solvents toluene and dimethyl sulphoxide, using different tertiary amines of varying basicity, including 1,4-diazabicyclo[2.2.2]octane (DABCO), as catalysts. In order to shed light on the eventual complication of internal ion-pair return for the interpretation of these results, the dependence of primary KIE on base and solvent was compared for the two substrates 1-methylindene and 1,3-dimethylindene.[6c,d]

To aid further investigations on isotope effects and enantioselectivity it was considered to be of great value to be able to manipulate the behaviour of the system by changing not only the solvent and the basicity of the catalyst but also the acidity of the indene substrate. Therefore it was decided to perform some kinetic studies on 1-methylindene substituted in the 5- or 7-position (Scheme 3). Such studies should show whether the KIE changes appreciably with the reaction rate. The increased acidity obtained by substitution by an electron withdrawing group would enable, e.g., the observation of a KIE maximum.[10] Because of the enhanced rate expected such substitution may also permit the study of sterically hindered, more slowly reacting bases. The rearrangement

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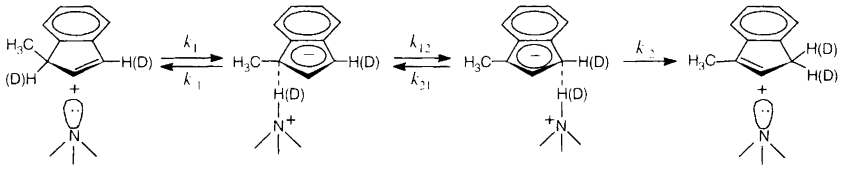
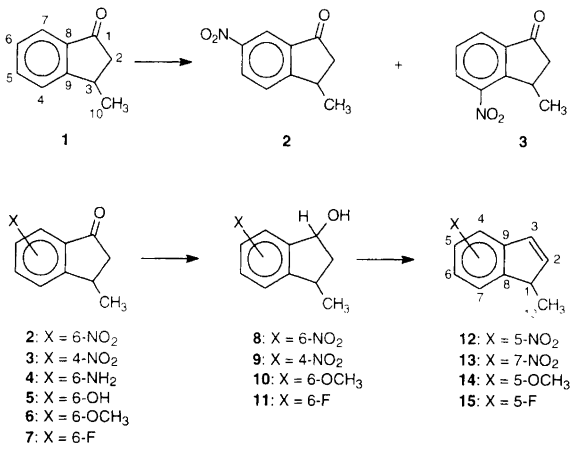


Scheme 2.

reactions reported in this study were all catalysed by the tertiary amine DABCO. A parallel investigation of enantioselectivity in this reaction system using the chiral catalyst dihydroquinidine has recently been reported[11]



1 **2** **3**

2: X = 6-NO_2
3: X = 4-NO_2
4: X = 6-NH_2
5: X = 6-OH
6: X = 6-OCH_3
7: X = 6-F

8: X = 6-NO_2
9: X = 4-NO_2
10: X = 6-OCH_3
11: X = 6-F

12: X = 5-NO_2
13: X = 7-NO_2
14: X = 5-OCH_3
15: X = 5-F

Scheme 3.

Results

Kinetics. The kinetic experiments were run under pseudo-first-order conditions. The polarimetric differential (isotopic quasi-racemate) method[6a,b] was used. This method permits both isotopic rate constants and their ratio to be determined simultaneously in one kinetic experiment, thus avoiding interexperimental errors. 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 may be obtained from the maximum (or minimum) value of the optical rotation and the corresponding reaction time (Fig. 1), or be evaluated by least-squares fitting of the model equation to the experimental data (*vide infra*). For the substrate **12** the KIE was also determined by ^{1}H NMR spectroscopy (*vide infra*).

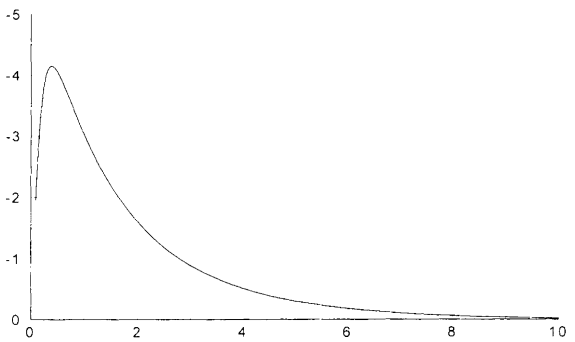


Fig. 1. Optical rotation (deg) vs. time (h) for a rearrangement of 1-methyl-5-nitroindene (**12**).

As in the earlier investigations[6] the deuteriated substrate was isotopically substituted in the 3-position as well as the reactive 1-postion to avoid a contribution to the optical rotation of the reaction mixture from an isotopically chiral product. Although the reactions are practically irreversible, a small amount of reverse reaction could introduce protium into the 1-position, but this is prevented by the presence of deuterium in the 3-position. The remote secondary isotope effect from this deuterium is expected to be negligible. The fluoroindene **15** was mistakenly not deuteriated in the 3-position. This causes the reaction product mixture to be optically active due to isotopic chirality. This optical rotation ($\alpha_\infty = 0.204$) was corrected for by appropriate adjustment of the pre-exponential factors in the fitting procedure.

The solvent *o*-dichlorobenzene was originally[6e] chosen because of its relatively high polarity (the dielectric constant $\varepsilon = 9.93$), chemical inertness and high boiling point. This solvent permitted the kinetics to be studied with reasonable reaction times for most reaction systems, since the rate of the reaction increases with solvent polarity but also because the solubilities of the amine catalysts used are higher in polar than in non-polar solvents.

According to ^{1}H NMR spectra of the equilibrated kinetic solutions the only product formed in the kinetic experiments was the 3-isomer of the substrates, and no remaining reactant 1-isomer was detected. A control experiment with no catalyst added to the reaction mixture was run to make sure that the reactant is stable under the appropriate conditions. The optical rotation did not change significantly during a time corresponding to >10 half-lives for the base-catalysed reaction.

In Table 1 are listed second-order rate constants (calculated by dividing the measured pseudo-first-order rate constants by the base concentration) and primary KIEs for the experiments where DABCO was used as catalyst.

Assuming pseudo-first-order kinetics, the optical rotation of the reaction mixture is given by eqn. (1) which describes the optical rotation as a sum of exponential terms corresponding to the contributions from the normal and isotopically labelled compounds, respectively. The equation also contains a constant term (a_0) for the rotation at infinite time. Ideally this should be very close to zero since the reaction products are achiral. On the basis of this kinetic model, the relations (2) and (3) for the minimum (or maximum) optical rotation and

Table 1. Second-order rate constants and primary KIEs for the rearrangement of 1-methylindene, 1-methyl-5-nitroindene (**12**), 1-methyl-7-nitroindene (**13**), 5-methoxy-1-methylindene (**14**) and 5-fluoro-1-methylindene (**15**) catalyzed by the base DABCO in *o*-dichlorobenzene at 20 °C.

Substrate[a]	[Base] (10^{-3} M^{-1})	k^H/[Base] (10^{-3} M^{-1} s^{-1})[b]	k^D/[Base] (10^{-3} M^{-1} s^{-1})[b]	k^H/k^D[c]
1-Methyl-5-nitroindene	0.082	11300	1320	8.56 [2]
1-Methyl-7-nitroindene	0.39	638	85.3	7.47 [2]
5-Fluoro-1-methylindene	24	6.61	0.978	6.76 [2]
1-Methylindene[d]	15–210	2.01	0.356	5.65 [8]
5-Methoxy-1-methylindene	83	0.465	0.0834	5.57 [2]

[a]The concentration of substrate was 0.1–0.4 M. [b]The rate constants are divided by the number (2) of nitrogen atoms in the amine used. [c]The number of kinetic runs is given in brackets. [d]Taken from Ref. 6(d).

the corresponding reaction time are derived. The pre-exponential factors a_1 and a_2 are complex functions of starting concentrations of the substrates, enantiomeric and isotopic purities and specific optical rotations.[6a] Eqns. (2) and (3) may be used to calculate the separate rate constants and the rate constant ratio, i.e., the kinetic isotope effect.

$$\alpha = a_1 e^{-k^H t} + a_2 e^{-k^D t} + a_0 \quad (1)$$

$$t_m = (k^H - k^D)^{-1} \times \ln(bS) \quad (2)$$

$$\alpha_m = a_1(bS)^{S/(1-S)} + a_2(bS)^{1/(1-S)} + a_0 \quad (3)$$

$$b \equiv a_1/(-a_2); \quad S \equiv k^H/k^D \quad (4)$$

The data given in Table 1 were obtained in this way using the experimentally determined values for a_1, a_2 and a_0 (=0). The validity of these rate constants was checked by insertion into eqn. (1). The resulting plot of α versus time shows a discrepancy, particularly pronounced for the nitro substrates, when compared with the experimental plot. This discrepancy is also evident by inspection of the residual plot ($\alpha - \alpha_{obs}$) which shows only a few changes of sign, thus indicating some systematic error.

It is also possible to include the linear parameters a_0, a_1 and a_2 in the set of fitted parameters. The resulting curve shows a better fit to the experimental data but the *a*-values obtained are unrealistic, e.g., the value of a_1 is changed 20% as compared with the fixed, experimentally determined, value.

In order to elucidate the kinetic behaviour for the substrate **12**, experiments were run with one single isotopic reactant at a time. At very low concentration of base (2.4×10^{-6} M) the pseudo-first order kinetic plot for reaction of unlabelled substrate **12** shows curvature, and a plot of the relative derivative of the optical rotation, $(d\alpha/dt)/\alpha$, shows a decrease in rate constant with time (Fig. 2) until a non-zero, almost constant, level is observed. With increased base concentration (4.9×10^{-5} M) the reaction time is much shorter and the reaction rate will show only a minor decrease during the course of the reaction. These observations were confirmed by following the kinetics by ^{1}H NMR spectroscopy in both deuterated *o*-dichlorobenzene and benzene solutions. Exploratory NMR kinetic experiments were

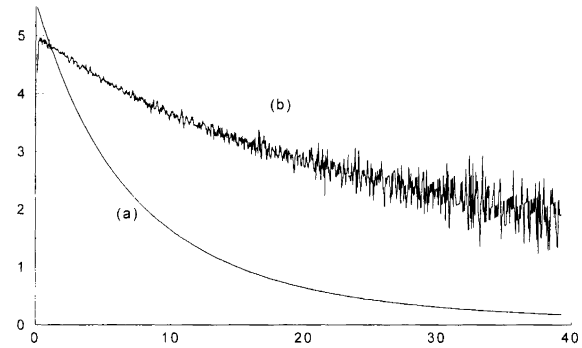


Fig. 2. Single-component experiment with labelled 1-methyl-5-nitroindene (**12**); (a) optical rotation (deg) vs. time (h) and (b) relative derivative (arbitrary scale) showing the decrease of rate constant.

performed in the cheaper solvent benzene-d_6. A stock solution of DABCO in benzene was prepared and was used in kinetic experiments on repeated occasions over a total time period of approximately 100 h. The observed rate constant decreases with time as the DABCO solution is stored, indicating the presence of some impurity capable of consuming the base. In a control experiment the solvent benzene was refluxed with DABCO, distilled off, washed and dried. The benzene handled in this way was then used for the preparation of a new base solution with a low concentration of DABCO (2.16×10^{-6} M). The kinetic experiments performed with this solution yielded a linear pseudo-first-order plot and an excellent residual plot. A kinetic isotope effect, in deuteriated *o*-dichlorobenzene at 20 °C, was also determined by ^{1}H NMR experiments. The concentration of DABCO (0.131 mM) was chosen high enough to yield pseudo-first-order plots for both the protic and deuteriated substrates. The mean value of the KIE is 8.9(5) (five experiments of each isotopic substrate) in good agreement with the polarimetrically determined value of 8.6 (Table 1).

For the polarimetric experiments an empirical model accounting for a first-order time dependent destruction of the base catalyst is suggested in eqns. (5) and (6). The function $f(t)$ accounts for the apparently exponential decay of the rate constant, from the initial value k^H to

the fraction $k^H\beta$.

$$\alpha = a_1 e^{-k^H f(t)t} + a_0 \quad (5)$$

$$f(t) = \beta + (1-\beta) \times e^{-\gamma t} \quad (6)$$

This model was tested and yielded a very good fit to the single-component experiments (Fig. 3). It should be noted that the residuals are at the level of the instrumental resolution throughout the experiment. This extremely good fit is only obtained with the full empirical model defined by eqns. (5) and (6). The $f(t)$-factor model [eqns. (5) and (6)] was then applied to the KIE experiments, using fixed values for a_1 and a_2 and the same correction function $f(t)$ for both k^H and k^D, eqn. (7). Moreover a time correction parameter δt was included to account for the uncertainty about the onset of the reaction. (Typically this parameter adopts a value of about 60 s). The KIE value obtained was 8.40, which is in good agreement with the min/max value of 8.56. Using the $f(t)$ correction the rate constants are referred to the initial conditions [$f(0) \equiv 1$], and the corresponding KIE value could be regarded as more reliable than those obtained by a fit of uncorrected k^H and k^D. For all substrates the KIE values obtained by the modified model were within reasonable error limits close to those reported in Table 1.

$$\alpha = a_1 e^{-k^H f(t)t} + a_2 e^{-k^D f(t)t} + a_0 \quad (7)$$

Discussion

According to the current mechanistic view[6b] (Scheme 2) the 1,3-proton transfer in indene and its alkyl-substituted analogues is believed to occur via ion-pair intermediates. 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, respectively.[12–14] The relationship between the phenomenological rate constant and the mechanistic rate constants is given by eqns. (8)–(10).

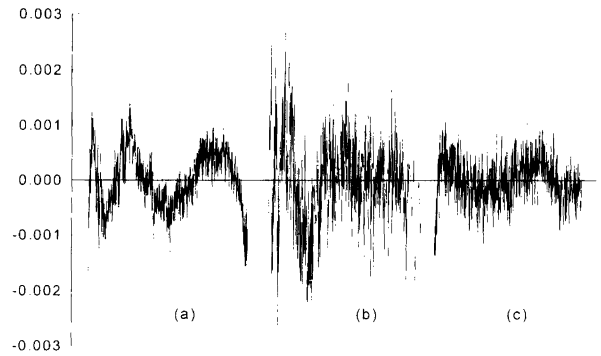


Fig. 3. Residuals (deg) for single-component experiments vs. time [modified model, eqns. (5) and (6)] with (a) unlabelled 1-methyl-5-nitroindene (**12**), low base concentration, (b) unlabelled 1-methyl-5-nitroindene (**12**), high base concentration, and (c) labelled 1-methyl-5-nitroindine [(1,3-$^2H_2$)-**12**], high base concentration. The duration of each curve corresponds to a complete reaction, about 40 h, 2 h and 20 h, respectively.

The rearrangement of the 1-isomer to the 3-isomer is irreversible for all substrates studied.[14]

$$k = k_1 \frac{1}{\left[1 + \left(\frac{k_{-1}}{k_{-2}}\right)\left(\frac{k_{-2}+k_{21}}{k_{12}}\right)\right]} \quad (8)$$

$$k = k_1 \frac{1}{\left[1 + \left(\frac{k_{-1}}{k_{-2}}\right)\left(\frac{k_{21}}{k_{12}}\right)\right]}, \quad \text{if } k_{21} \gg k_{-2} \quad (9)$$

$$k = k_1 \frac{1}{1+\sigma\chi}; \quad \sigma \equiv \frac{k_{-1}}{k_{-2}} \quad \text{and} \quad \chi \equiv \frac{k_{21}}{k_{12}} \quad (10)$$

Under circumstances when ion-pair equilibration is fast ($k_{21} \gg k_{-2}$) the observed KIE (k^H/k^D) is related to the KIE for the rate-determining ionization step according to eqn. (11). This equation also contains the ion-pair collapse ratio σ_L and the ion-pair equilibrium constant χ_L, L = H or D.

$$\frac{k^H}{k^D} = \frac{k_1^H}{k_1^D} \times \frac{1+\sigma^D\chi^D}{1+\sigma^H\chi^H} \quad (11)$$

The collapse ratio of the ion-pair intermediates and the ion-pair equilibrium constant in the rearrangement of 1-methylindene are not known. However, the collapse ratio has been assumed to be much smaller than unity, i.e., product is formed much faster than internal return of the ion-pair intermediates to starting material.[14] Under circumstances when this holds and the ion-pair equilibration is fast, the observed KIE can be identified with the KIE for the proton abstraction step. This identity also holds when the isotope effects on σ and χ are negligible. Experiments intended to shed light on the rate of ion-pair equilibration compared with the rate of ion-pair collapse are in progress.[15] The following discussion is based on the assumption that the observed KIE is equal to the KIE on proton abstraction.

The main effect of the nitro-substituent in the aromatic ring should be the resonance stabilization of the carbanion intermediate and, according to the Hammond postulate, a corresponding stabilization of the intermediate-like activated complex. The resulting increased acidity of the substrate is illustrated by the increase in reaction rate for both nitro compounds as compared with the unsubstituted compound. In Table 1 it is thus seen that for, e.g., the reaction of **12** catalysed by DABCO a 6000-fold increase of the second-order rate constant is observed. For **13** only a 300-fold increase in rate constant was observed, which might be attributed to a larger degree of steric hindrance to approach of the catalysing base for this compound. In the 7-position the nitro group is fairly close to the 1-methyl substituent, which could force the nitro group to be twisted out of the indene ring plane. This would to some extent prevent delocalization of the negative charge to the nitro group in the transition state of the proton abstraction step causing a less pronounced rate increase. The rates for the 5-substituted substrates, where steric hindrance is of

minor importance, are found to correlate with the Hammett σ-values[16] for the substituents (correlation coefficient = 0.997; for the nitro-subtituent, which is capable of interacting through resonance with a negative charge, the tabulated σ^--value was used). The magnitude of the Hammett reaction parameter, $\rho = 2.82$, supports the idea of a late ion-pair like TS.

On the basis of transition state theory the Melander–Westheimer postulate[17] predicts the maximal primary KIE for the proton-abstraction step to occur for the most symmetrical activated complex, i.e., when the proton is bound with equal strength to donor and acceptor. This takes place when the pK_a of the carbon acid equals that of the conjugate acid of the base catalyst ($\Delta pK_a = 0$).[18] For 1-methylindene* and DABCO the ΔpK_a is approximately 11, corresponding to a strongly asymmetric activated complex if this interpretation is valid. Despite this the KIE is rather high (Table 1). A case of very small variation of the primary deuterium KIE over a wide range of ΔpK has already been reported by Bordwell and Boyle[19] for deprotonation of nitroalkanes. The more acidic nitro-indene substrates are expected to display even stronger KIEs than 1-methylindene, since the ΔpK_a-value is diminished. The results given in Table 1 show that increased KIEs are indeed observed for both nitro-substrates **12** and **13**.

The fluoro compound **15**, which displays a very modest threefold rate increase, is also associated with a somewhat enlarged KIE. Thus KIEs for the series of substrates correlates with the rate constants as expected on the basis of the above discussion. However the variation is not especially pronounced. In particular, the KIE for the least acidic substrate, the methoxyindene **14**, is as high as 5.57, i.e., approximately the same as for 1-methylindene.

The different KIEs observed in the present kinetic study of substituted 1-methylindenes could in principle be caused by different extents of internal return from the first ion-pair intermediate formed back to starting material. If that is the case the observed KIE is not equal to the KIE for the rate-determining hydron-abstraction step. In eqn. (9) the complete rate expression, showing the relationship between the phenomenological and mechanistic rate constants for the proposed mechanism (Scheme 2), is given. In the interconversion between the ion-pair intermediates no covalent bonds are formed or broken. Therefore, the rate for this process may be expected to show low sensitivity to isotopic substitution. Using this assumption one obtains the relationship between the KIE for the rate-determining hydron-abstraction step and the observed KIE given by eqn. (12).

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

* The pK_a for 1-methylindene is estimated to 19.8 (in DMSO). Prof. F. G. Bordwell, *personal communication*.

It is not immediately obvious how a contribution from the quotient denoted f in eqn. (12) will affect the observed KIE. However, some simplifications may be proposed. Firstly a normal isotope effect on the collapse of the intermediate to product, $k_{-2}^H > k_{-2}^D$, can be assumed. Secondly, the collapse ratio σ has been estimated to be small and therefore a more intermediate-like transition state for the more exothermic collapse to the product seems reasonable, according to the Hammond postulate. The isotopic sensitivity should thus be be smaller for k_{-2} than for k_{-1}, expression (13).

$$\frac{k_{-1}^H}{k_{-1}^D} > \frac{k_{-2}^H}{k_{-2}^D} \qquad (13)$$

Reformulation of inequality (13) gives relation (14). The conclusion is that the effects of internal ion-pair return on the 1,3-hydron transfer of 1-methylindene, and its aromatic substituted analogues, should give rise to an attenuation of the observed KIE.

$$\frac{k_{-1}^H}{k_{-2}^H} > \frac{k_{-1}^D}{k_{-2}^D} \Leftrightarrow \sigma^H > \sigma^D \qquad (14)$$

According to the discussion above, the lower KIEs obtained for some of the substrates studied, e.g., 1-methylindene and 5-methoxy-1-methylindene (see Table 1), may be caused by a higher degree of internal ion-pair return in these cases. Evidence of internal ion-pair return in similar systems has earlier been reported by Ahlberg and co-workers[13] and by Thibblin.[20]

Experimental

General. ^1H and ^{13}C NMR spectra were obtained with a Varian XL 300 or Unity 400 spectrometer. The spectra of the nitro compounds were run on the XL 300 spectrometer at 20 °C and the spectra of the other derivatives were run on the Unity 400 spectrometer at 25 °C. (^2H)Chloroform (>99.5 atom% ^2H, Dr Glaser AG Basel) was used as both solvent and internal standard, and the concentrations were ca. 0.15 M. IR spectra were obtained for KBr-plates or neat samples with a Perkin Elmer 1600 series FTIR spectrometer. Only the strongest and structurally most important peaks are listed. Analytical GLC was carried out on a Varian 3400 gas chromatograph, equipped with a flame-ionization detector and a Varian 4270 integrator, using a DB5–30W capillary column. Optical rotations were 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 a PC connected to the printer output of the polarimeter. The water-jacketed polarimetric cell (optical path length 10 cm, volume 0.9 ml) was connected to a HETO 02 PT 623 proportional regulating thermostat. A calibrated mercury thermometer, with an absolute accuracy of 0.02 °C, was used to measure the temperature at the outlet of the cell. The temperature did not deviate more

than 0.05 °C from the average value during the runs and was thus 20 ± 0.07 °C.

The nitro- and methoxy-indenes (**12, 13** and **14**) were purified by flash chromatography using Merck Kieselgel 60 (230–240 mesh) or Riedel-de Haen Kieselgel S (230–240 mesh). The mobile phases used were dichloromethane–pentane (60:40) for the nitro indenes and diethyl ether–pentane (2:98) for the methoxy-indenes. The fluoroindenes (**15**) were purified by preparative gas chromatography using a 1.5 m long and 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 gas as the carrier gas, at a flow rate of 100 ml min^{-1}. The injection temperature was 120 °C, the detection temperature 115 °C and the column oven temperature 115–120 °C. The amount of the isomeric 3-methyl-6-nitroindene in the purified 1-methyl-5-nitroindenes was determined by ^1H NMR spectroscopy. The isotopic purities of the deuteriated compounds were calculated from ^1H NMR data. The enantiomeric purities were determined by comparing the optical rotations of the phenylalkanoic acids or the 3-methylindanones (**1**) with literature values.[6a,14] The enantiomeric purities of the resolved nitroindenes were checked by HPLC on a 60 cm long and 1 cm wide column, packed with swollen microcrystalline triacetylcellulose (Merck 15–25 μm). Methanol–water (80:20) was used as the mobile phase. The specific rotations of the purified optically active 5- or 7-substituted indenes were measured in *o*-dichlorobenzene solution. The values, corrected for optical, isotopical and/or isomeric impurities when needed, are listed in Table 2. According to HPLC no significant racemization was observed in the syntheses of the optically active nitroindenes. The 1-methyl-5-nitroindenes (**12**) are sensitive to heat yielding the isomeric 3-methyl-6-nitroindenes. Typically, the product contained 1–9% of the 3-isomer. The percentage of the 3-isomer was determined with an accuracy of 0.5% by means of ^1H NMR spectroscopy.

*(S)-3-Methyl-6-nitroindan-1-one (S)-***2**. Essentially the procedure described for nitration of 1-indanone, by Ingold and Piggott,[21] was followed. 10.1 g (69.2 mmol) of (+)-(*S*)-3-methylindanone[6c] [(+)-(*S*)-**1**], [$0.10\alpha_{546}^{25.0} = +0.709$ (neat), lit.[14] for (−)-enantiomer, $\alpha_{546}^{25.0} = -7.41$ (neat, 1 dm)], was dissolved in 85 ml of concentrated sulphuric acid and cooled to 3 °C. A solution of 8.5 g (84 mmol) of potassium nitrate in 30 ml of concentrated sulphuric acid was added dropwise over 1.5 h while keeping the temperature below 8 °C. The reaction mixture was stirred at 3 °C for 1 h and then poured onto crushed ice, which gave a yellow precipitate. The nitro ketones were collected by filtration and washed with cold water until the washings were neutral. According to capillary GC, the crude product consisted of ca. 90% of (*S*)-**2** and ca. 10% of (*S*)-3-methyl-4-nitroindanone, [(*S*)-**3**]. Recrystallization three times from abs. ethanol yielded 8.7 g (45 mmol, 66%) of (*S*)-**2**.

NMR: δ_H 1.47 (3 H, d, $J_{3,10}$ 7.2 Hz, 10-H), 2.40 (1 H, dd, $J_{2cis,2trans}$ 19.4, $J_{2cis,3}$ 3.7 Hz, 2*cis*-H), 3.06 (1 H, dd, $J_{2cis,2trans}$ 19.4, $J_{2trans,3}$ 7.7 Hz, 2*trans*-H), 3.56 (1 H, m, $J_{2cis,3}$ 3.7, $J_{2trans,3}$ 7.7, $J_{3,10}$ 7.2 Hz, 3-H), 7.69 (1 H, d, $J_{4,5}$ 8.4 Hz, 4-H), 8.45 (1 H, dd, $J_{4,5}$ 8.4, $J_{5,7}$ 2.2 Hz, 5-H), 8.51 (1 H, d, $J_{5,7}$ 2.2 Hz, 7-H). δ_C 20.9, 33.1, 45.5, 118.7, 126.5, 128.9, 137.3, 147.7, 165.3, 203.8. IR: 1712, 1528, 1348 cm^{-1}.

*(+)-(S)-1-Methyl-5-nitroindene (+)-(S)-***12**. Essentially the procedure described for the synthesis of 6-nitroindene, by Miller and Frincke[22] was followed. The reaction was run under a nitrogen atmosphere. 8.0 g (42 mmol) of (*S*)-**2** was dissolved in 400 ml of methanol and cooled to 4 °C. Upon cooling some of the ketone precipitated again. 3.2 g (85 mmol) of sodium borohydride were added in small portions. When the evolution of hydrogen had ceased, the ice bath was removed, and the solution was stirred for 3 h at room temperature. The orange reaction mixture was poured into water and extracted with dichloromethane. The combined extracts were washed with water and brine, dried with sodium sulphate and concentrated to give 7.6 g (39 mmol) of the indanol (3S)-**8** which was used without purification. A solution of 1.0 g (5.2 mmol) of the crude indanol (3S)-**8** and 0.5 g of *p*-toluensulphonic acid monohydrate in 60 ml of benzene was heated to reflux and the water

Table 2. Specific rotations for some 5- or 7-substituted 1-methylindenes measured in *o*-dichlorobenzene solutions at 20 °C.[a,b]

Compound	$[\alpha]_{589}^{20.0}$	$[\alpha]_{578}^{20.0}$	$[\alpha]_{546}^{20.0}$
(+)-(*S*)-1-Methyl-5-nitroindene[c]	+151.4	+158.8	+184.2
(−)-(*R*)-(1,3-$^2H_2$)-1-Methyl-5-nitroindene[e]	−147.0	−154.3	−179.0
(+)-(*S*)-1-Methyl-7-nitroindene[c,e]	+789.8	+834.2	+990.7
(−)-(*R*)-(1,3-$^2H_2$)-1-Methyl-7-nitroindene[d]	−762.3	−805.2	−955.8
(+)-(*S*)-5-Methoxy-1-methylindene	+160.7	+168.8	+194.8
(−)-(*R*)-(1,3-$^2H_2$)-5-Methoxy-1-methylindene[c]	−165.8	−174.0	−200.9
(+)-(*S*)-5-Fluoro-1-methylindene	+164.8	+172.8	+199.0
(−)-(*R*)-(1-^2H)-5-Fluoro-1-methylindene[d]	−168.9	−177.2	−204.0

[a]The concentration of the indenes was 0.3–0.4 M. [b]The accuracy is ±1.1% for (+)-**12** and ±0.5% for the other compounds. [c]The values are corrected for the optical impurity. [d]The values are corrected for the protium content in the 1-position. [e]The rotation of (−)-(*R*)-**12** and (+)-(*S*)-**13** was also measured at the concentration 0.1 M yielding the same optical rotation as the measurement at the light concentration.

collected in a Dean–Stark apparatus. After 30 min, the reaction mixture was cooled, washed with sodium bicarbonate solution, water and brine, dried with sodium sulphate, and concentrated to give 0.9 g (5.0 mmol) of crude product. Purification yielded 0.82 g (4.6 mmol) of yellow, crystalline (*S*)-**12** (which contained a few per cent of rearranged 3-methyl-6-nitroindene). The yield for the two steps was 83%. NMR: δ_H 1.36 (3 H, d, $J_{1,10}$ 7.7 Hz, 10-H), 3.59 (1 H, m, $J_{1,2}$ 1.8, $J_{1,3}$ 1.6, $J_{1,10}$ 7.7 Hz, 1-H), 6.67 (1 H, dd, $J_{1,2}$ 1.8, $J_{2,3}$ 5.6 Hz, 2-H), 6.83 (1 H, dd, $J_{1,3}$ 1.6 Hz, $J_{2,3}$ 5.6 Hz, 3-H), 7.51 (1 H, d, $J_{6,7}$ 8.1 Hz, 7-H), 8.10 (1 H, dd, $J_{4,6}$ 2.2, $J_{6,7}$ 8.1 Hz, 6-H), 8.17 (1 H, d, $J_{4,6}$ 2.2 Hz, 4-H). δ_C 15.4, 45.3, 115.9, 120.3, 122.8, 129.2, 144.2, 145.0, 147.4, 155.9. IR: 1516, 1349 cm^{-1}.

(R)-(3-^{2}H)-3-Methyl-6-nitroindan-1-one (R)-(3-^{2}H)-**2**. (*R*)-(3-^{2}H)-**2** was prepared analogously to (*S*)-**2**. The optical rotation of the starting material, (*R*)-(3-^{2}H)-**1**, was $0.10\alpha_{546}^{25.0} = -0.634$ (neat). NMR: δ_H 1.47 (3 H, s, 10-H), 2.42 (1 H, d, $J_{2cis,2trans}$ 19.4 Hz, 2*cis*-H), 3.07 (1 H, d, $J_{2cis,2trans}$ 19.4 Hz, 2*trans*-H), 3.56 (0.012 H, m, 3-H), 7.70 (1 H, d, $J_{4,5}$ 8.3 Hz, 4-H), 8.48 (1 H, dd, $J_{4,5}$ 8.3, $J_{5,7}$ 2.2 Hz, 5-H), 8.54 (1 H, d, $J_{5,7}$ 2.2 Hz, 7-H). δ_C 20.9, 32.8 (t), 45.5, 119.0, 126.5, 129.0, 137.5, 148.0, 165.2, 203.8. IR: 1712, 1527, 1347 cm^{-1}.

(−)-(R)-(1,3-$^2H_2$)-1-Methyl-5-nitroindene (−)-(R)-(1,3-$^2H_2$)-**12**. (−)-(*R*)-(1,3-$^2H_2$)-**12** was prepared analogously to (+)-(*S*)-**12** except that sodium borodeuteride (>99.0 atom% D, Dr Glaser AG) was used instead of sodium borohydride in the reduction to introduce a deuterium into the 1-position. NMR: δ_H 1.34 (1 H, s, 10-H), 3.59 (0.012 H, m, 1-H), 6.66 (1 H, s, 2-H), 7.50 (1 H, d, $J_{6,7}$ 8.3 Hz, 7-H), 8.10 (1 H, dd, $J_{4,6}$ 2.1, $J_{6,7}$ 8.3 Hz, 6-H), 8.17 (1 H, d, $J_{4,6}$ 2.1 Hz, 4-H). δ_C 15.4, 44.9, 115.8, 120.4, 122.8, 129.0 (t), 144.0, 145.0, 147.4, 155.9. IR: 1515, 1342 cm^{-1}.

(S)-3-Methyl-4-nitroindan-1-one (S)-**3**. (*S*)-**3** was obtained as a by-product in the synthesis of (+)-(*S*)-**2**. It was isolated by flash chromatography [1:3 ethyl acetate–petroleum ether (b.p. 40–60 °C)] of the combined mother-liquors from the recrystallization of (+)-(*S*)-**2**. 10.1 g (69.2 mmol) of (+)-(*S*)-**1** yielded 0.82 g (4.2 mmol, 6.1%) of pure (*S*)-**3**. NMR: δ_H 1.35 (3 H, d, $J_{3,10}$ 7.0 Hz, 10-H), 2.45 (1 H, dd, $J_{2cis,2trans}$ 19.2, $J_{2cis,3}$ 1.7 Hz, 2*cis*-H), 3.02 (1 H, dd, $J_{2cis,2trans}$ 19.2, $J_{2trans,3}$ 7.8 Hz, 2*trans*-H), 4.25 (1 H, m, $J_{3,10}$ 7.0, $J_{2cis,3}$ 1.7, $J_{2trans,3}$ 7.8 Hz, 3-H), 7.60 (1 H, dd, $J_{5,6}$ 8.0, $J_{6,7}$ 7.5 Hz, 6-H), 8.03 (1 H, dd, $J_{5,7}$ 1.2, $J_{6,7}$ 7.5 Hz, 7-H), 8.41 (1 H, dd, $J_{5,6}$ 8.0, $J_{5,7}$ 1.2 Hz, 5-H). δ_C 21.6, 33.3, 45.3, 128.9, 129.5, 130.4, 139.0, 146.4, 153.9, 204.0. IR: 1716, 1526, 1359 cm^{-1}.

(+)-(S)-1-Methyl-7-nitroindene (+)-(S)-**13**. (+)-(*S*)-**13** was prepared analogously to (+)-(*S*)-**12**. 0.71 g (3.7 mmol) of the indanone gave 0.71 g (3.7 mmol) of (3S)-**9**. The crude indanol (3S)-**9** (0.70 g, 3.7 mmol) was dehydrated yielding 0.45 g (2.6 mmol) of (+)-(*S*)-**13**. The yield for the two steps was 69%. NMR: δ_H 1.29 (3 H, d, $J_{1,10}$ 7.3 Hz, 10-H), 4.25 (1 H, m, $J_{1,2}$ 1.9, $J_{1,3}$ 1.6, $J_{1,10}$ 7.3 Hz, 1-H), 6.65 (1 H, dd, $J_{1,2}$ 1.9, $J_{2,3}$ 5.5 Hz, 2-H), 6.77 (1 H, dd, $J_{1,3}$ 1.6, $J_{2,3}$ 5.5 Hz, 3-H), 7.41 (1 H, dd, $J_{4,5}$ 7.4, $J_{5,6}$ 8.2 Hz, 5-H), 7.61 (1 H, dd, $J_{4,5}$ 7.4, $J_{4,6}$ 1.0 Hz, 4-H), 7.94 (1 H, dd, $J_{4,6}$ 1.0, $J_{5,6}$ 8.2 Hz, 6-H). δ_C 14.1, 46.6, 120.2, 126.5, 127.9, 128.1, 143.8, 144.2, 145.3, 147.4. IR: 1523, 1346, (1330) cm^{-1}.

(R)-(3-^{2}H)-3-Methyl-4-nitroindan-1-one (R)-(3-^{2}H)-**3**. (*R*)-(3-^{2}H)-**3** was obtained as a by-product in the synthesis of (*R*)-(3-^{2}H)-**2** and it was isolated in the same way as (*S*)-**3**. NMR: δ_H 1.35 (3 H, s, 10-H), 2.46 (1 H, d, $J_{2cis,2trans}$ 19.2 Hz, 2*cis*-H), 3.02 (1 H, d, $J_{2cis,2trans}$ 19.2 Hz, 2*trans*-H), 4.25 (0.012 H, m, 3-H), 7.60 (1 H, dd, $J_{5,6}$ 8.0, $J_{6,7}$ 7.5 Hz, 6-H), 8.05 (1 H, dd, $J_{5,7}$ 1.1, $J_{6,7}$ 7.5 Hz, 7-H), 8.41 (1 H, dd, $J_{5,6}$ 8.0, $J_{5,7}$ 1.1 Hz, 5-H). δ_C 21.6, 33.0, 45.2, 129.0, 129.6, 130.4, 139.1, 146.4, 153.9, 204.1. IR: 1716, 1534, 1352 cm^{-1}.

(−)-(R)-(1,3-$^2H_2$)-1-Methyl-7-nitroindene (−)-(R)-(1,3-$^2H_2$)-**13**. (−)-(*R*)-(1,3-$^2H_2$)-**13** was prepared analogously to (+)-(*S*)-**13** except that sodium borodeuteride (>99.0 atom% D, Dr Glaser AG) was used instead of sodium borohydride in the reduction to introduce a deuterium into the 1-position. NMR: δ_H 1.28 (3 H, s, 10-H), 4.25 (0.012 H, m, 1-H), 6.64 (1 H, s, 2-H), 7.41 (1 H, dd, $J_{4,5}$ 7.4, $J_{5,6}$ 8.2 Hz, 5-H), 7.60 (1 H, dd, $J_{4,5}$ 7.4, $J_{4,6}$ 1.0 Hz, 4-H), 7.94 (1 H, dd, $J_{4,6}$ 1.0, $J_{5,6}$ 8.2 Hz, 6-H). δ_C 14.0, 46.2 (t), 120.1, 126.5, 127.6 (t), 127.9, 143.8, 144.0, 145.2, 147.4. IR: 1522, 1349, (1336) cm^{-1}.

(S)-6-Amino-3-methylindan-1-one (S)-**4**. The reduction used in the preparation of (*S*)-**4** is a modification of the procedure described for 2-aminofluorene by Kuhn.[23] 6.1 g (32 mmol) of (*S*)-**2** were suspended in 230 ml of ethanol (78%). A solution of 2.3 g of calcium chloride in 5 ml of water was added to the suspension together with 60 g of activated zinc dust and the mixture was refluxed for 5 h. The zinc dust and the zinc oxide were filtered from the boiling solution using Celite and extracted with boiling ethanol. 200 ml of water were added and the solution was extracted with ether. The combined organic layers were washed with brine, dried with sodium sulphate and concentrated to give 4.7 g (29 mmol, 91%) of crude (*S*)-**4**. The yellow crystalline amine was used without purification. NMR: δ_H 1.34 (3 H, d, $J_{3,10}$ 7.1 Hz, 10-H), 2.23 (1 H, dd, $J_{2cis,2trans}$ 19.0, $J_{2cis,3}$ 3.2 Hz, 2*cis*-H), 2.90 (1 H, dd, $J_{2cis,2trans}$ 19.0, $J_{2trans,3}$ 7.2 Hz, 2*trans*-H), 3.32 (1 H, m, $J_{2cis,3}$ 3.2, $J_{2trans,3}$ 7.2, $J_{3,10}$ 7.1 Hz, 3-H), 3.80 (2 H, br s, NH_2), 6.95 (1 H, s, 7-H), 6.95–6.98 (1 H, m, 4-H or 5-H), 7.26–7.30 (1 H, m, 4-H or 5-H). δ_C 21.6, 32.1, 46.0, 107.4, 122.9, 125.8, 137.5, 146.0, 150.7, 206.6. IR: 3457, 3347, 1684, 1323 cm^{-1}.

(R)-(3-^{2}H)-6-Amino-3-methylindan-1-one (R)-(3-^{2}H)-**4**. (*R*)-(3-^{2}H)-**4** was prepared analogously to (*S*)-**4**. NMR: δ_H 1.34 (3 H, s, 10-H), 2.23 (1 H, d, $J_{2cis,2trans}$ 19.0 Hz, 2*cis*-H), 2.90 (1 H, d, $J_{2cis,2trans}$ 19.0 Hz, 2*trans*-H), 3.32 (0.028 H, m, 3-H), 3.78 (2 H, brs, NH_2), 6.95 (1 H, s, 7-H), 6.95–6.98 (1 H, m, 4-H or 5-H), 7.26–7.30 (1 H, m, 4-H or 5-H). δ_C 21.5, 31.7 (t), 45.9, 107.4, 122.9, 125.8, 137.6, 146.0, 150.6, 206.6. IR: 3457, 3347, 1684, 1323 cm^{-1}.

(S)-6-Hydroxy-3-methylindan-1-one (S)-**5**. Essentially the procedure described for the synthesis of 6-hydroxyindanone, by Ingold and Piggott, was followed.[21] To a suspension of 4.5 g (28 mmol) of (*S*)-**4** in 70 ml of 1 M sulphuric acid, a solution of 1.9 g (28 mmol) of sodium nitrite in 5 ml of water was added. The reaction mixture was heated at 100 °C until the evolution of nitrogen had ceased. The mixture was filtered from the brown precipitate that had formed during the reaction and both the yellow solution and the precipitate were extracted with ether. The combined organic layers were washed with water and brine, dried with sodium sulphate and concentrated to give a brown crude product. Purification by flash chromatography (70:30 diethyl ether–pentane) yielded 2.2 g (14 mmol, 49%) of slightly yellow crystalline (*S*)-**5**. NMR: δ_H 1.37 (3 H, d, $J_{3,10}$ 7.0 Hz, 10-H), 2.30 (1 H, dd, $J_{2cis,2trans}$ 19.0, $J_{2cis,3}$ 3.2 Hz, 2*cis*-H), 2.96 (1 H, dd, $J_{2cis,2trans}$ 19.0, $J_{2trans,3}$ 7.2 Hz, 2*trans*-H), 3.38 (1 H, m, $J_{2cis,3}$ 3.2, $J_{2trans,3}$ 7.2, $J_{3,10}$ 7.0 Hz, 3-H), 5.88 (1 H, s, OH), 7.19 (1 H, dd, $J_{4,5}$ 8.3, $J_{5,7}$ 2.5 Hz, 5-H), 7.23 (1 H, dd, $J_{4,7}$ 0.6, $J_{5,7}$ 2.5 Hz, 7-H), 7.37 (1 H, dd, $J_{4,5}$ 8.3, $J_{4,7}$ 0.6 Hz, 4-H). δ_C 21.5, 32.3, 46.1, 108.4, 123.5, 126.3, 137.7, 152.7, 155.6, 206.8. IR: 3253, 1675, 1302 cm^{-1}.

(S)-6-Methoxy-3-methylindan-1-one (S)-**6**. Essentially the method described for synthesis of 7-methoxyindanone, by Loudon and Razdan, was followed. A mixture of 2.1 g (13 mmol) of (*S*)-**5**, 4.9 g of potassium carbonate, 14.4 g (101 mmol) of methyl iodide and 135 ml of acetone was refluxed for 4.5 h. The acetone was evaporated off, 200 ml of water were added and the product was extracted with ether. The combined ether layers were washed with water and brine, dried with magnesium sulphate and concentrated to give 2.7 g crude (*S*)-**6**. Purification by flash chromatography (3:2 pentane–ether) yielded 1.9 g (12 mmol, 83%) of crystalline (*S*)-**6**. NMR: δ_H 1.37 (3 H, d, $J_{3,10}$ 7.0 Hz, 10-H), 2.29 (1 H, dd, $J_{2cis,2trans}$ 19.0, $J_{2cis,3}$ 3.2 Hz, 2*cis*-H), 2.96 (1 H, dd, $J_{2cis,2trans}$ 19.0, $J_{2trans,3}$ 7.2 Hz, 2*trans*-H), 3.38 (1 H, m, $J_{2cis,3}$ 3.2, $J_{2trans,3}$ 7.2, $J_{3,10}$ 7.0 Hz, 3-H), 3.84 (3 H, s, OCH_3), 7.16 (1 H, d, $J_{5,7}$ 2.5 Hz, 7-H), 7.20 (1 H, dd, $J_{5,7}$ 2.5, $J_{4,5}$ 8.4 Hz, 5-H), 7.39 (1 H, d, $J_{4,5}$ 8.4 Hz, 4-H). δ_C 21.5, 32.2, 46.0, 55.6, 104.6, 124.1, 126.0, 137.6, 152.9, 159.4, 206.3. IR: 1708, 1491, 1294, 1277 cm^{-1}.

(+)-(S)-5-Methoxy-1-methylindene (+)-(S)-**14**. (+)-(*S*)-**14** was prepared in a manner similar to that described for 5-methoxyindene, by Winter *et al.*[25] 1.8 g (10 mmol) of (*S*)-**6** dissolved in 35 ml of dry ether was added dropwise to a suspension of 0.19 g (5.1 mmol) of lithium aluminium hydride in 85 ml of ether and the mixture was refluxed for 1 h. The solution was cooled and the excess of lithium aluminium hydride was destroyed with water. The layers were separated and the water layer was extracted with ether. The combined organic layers were washed with brine, dried with sodium sulphate and concentrated to give 1.7 g (9.6 mmol, 94%) of crude (3S)-**10** which was used without purification. (Recrystallization from *n*-hexane isolated one of the diastereoisomers (1.2 g, 7 mmol), but both of them could be used for the dehydration.) A solution of 0.50 g (2.8 mmol) of (3S)-**10** and 0.04 g of *p*-toluenesulphonic acid monohydrate in 35 ml of benzene was refluxed for 30 min. The mixture was cooled and washed with sodium bicarbonate solution, water and brine, dried with sodium sulphate and concentrated to give 0.42 g of crude brown (+)-(*S*)-**14**. Purification by flash chromatography (2:98 ether–pentane) yielded 0.34 g (2.1 mmol, 76%) of colourless liquid (+)-(*S*)-**14**. NMR: δ_H 1.29 (3 H, d, $J_{1,10}$ 7.5 Hz, 10-H), 3.45 (1 H, m, $J_{1,10}$ 7.5, $J_{1,2}$ 1.7, $J_{1,3}$ 1.7 Hz, 1-H), 3.83 (3 H, s, OCH_3), 6.50 (1 H, dd, $J_{1,2}$ 1.7, $J_{2,3}$ 5.5 Hz, 2-H), 6.72 (1 H, dd, $J_{1,3}$ 1.7, $J_{2,3}$ 5.5 Hz, 3-H), 6.76 (1 H, dd, $J_{6,7}$ 8.0, $J_{4,6}$ 2.2 Hz, 6-H), 6.92 (1 H, d, $J_{4,6}$ 2.2 Hz, 4-H), 7.29 (1 H, d, $J_{6,7}$ 8.0 Hz, 7-H). δ_C 16.2, 44.4, 55.5, 106.7, 110.5, 122.9, 130.0, 141.4, 142.7, 145.3, 158.9.

(R)-(3-^{2}H)-6-Hydroxy-3-methylindan-1-one (R)-(3-^{2}H)-**5**. (*R*)-(3-^{2}H)-**5** was prepared analogously to (*S*)-**5**. NMR: δ_H 1.36 (3 H, s, 10-H), 2.30 (1 H, d, $J_{2cis,2trans}$ 9.6 Hz, 2*cis*-H), 2.96 (1 H, d, $J_{2cis,2trans}$ 9.6 Hz, 2*trans*-H), 3.38 (0.028 H, m, 3-H), 6.59 (1 H, brs, OH), 7.19 (1 H, dd, $J_{5,7}$ 2.5, $J_{4,5}$ 8.3 Hz, 5-H), 7.23 (1 H, dd, $J_{4,7}$ 0.6, $J_{5,7}$ 2.5 Hz, 7-H), 7.37 (1 H, dd, $J_{5,7}$ 2.5, $J_{4,5}$ 8.3 Hz, 5-H). δ_C 21.4, 31.9, 46.0, 108.4, 123.8, 126.3, 137.6, 152.7, 155.8, 207.4. IR: 3253, 1684, 1305 cm^{-1}.

(R)-(3-^{2}H)-6-Methoxy-3-methylindan-1-one (R)-(3-^{2}H)-**6**. (*R*)-(3-^{2}H)-**6** was prepared analogously to (*S*)-**6**. NMR: δ_H 1.36 (3 H, s, 10-H), 2.28 (1 H, d, $J_{2cis,2trans}$ 19.0 Hz, 2*cis*-H), 2.95 (1 H, d, $J_{2cis,2trans}$ 19.0 Hz, 2*trans*-H), 3.38 (0.028 H, m, 3-H), 3.83 (3 H, s, OCH_3), 7.16 (1 H, d, $J_{5,7}$ 2.5 Hz, 7-H), 7.20 (1 H, dd, $J_{5,7}$ 2.5, $J_{4,5}$ 8.4 Hz, 5-H), 7.39 (1 H, d, $J_{4,5}$ 8.4 Hz, 4-H). δ_C 21.4, 31.8 (t), 45.9, 55.6, 104.6, 124.1, 126.0, 137.6, 152.8, 159.4, 206.2. IR: 1708, 1491, 1294, 1277 cm^{-1}.

(1,3-$^2H_2$)-5-Methoxy-1-methylindene (−)-(R)-**14**. (−)-(*R*)-**14** was prepared analogously to (+)-(*S*)-**14** except that lithium aluminium deuteride (>99% D, Dr Glaser AG) was used in the reduction to introduce a deuterium into the 1-position. NMR: δ_H 1.28 (3 H, s, 10-H), 3.45 (0.028 H, m, 1-H), 3.83 (3 H, s, OCH_3), 6.50 (1 H, s, 2-H), 6.76 (1 H, dd, $J_{4,6}$ 2.2, $J_{6,7}$ 8.0 Hz, 6-H), 6.92 (1 H, d, $J_{4,6}$ 2.2 Hz, 4-H), 7.29 (1 H, d, $J_{6,7}$

8.0 Hz, 7-H). δ_C 16.1, 43.9 (t), 55.4, 106.7, 110.5, 122.9, 129.8 (t), 141.5, 142.6, 145.2, 158.9.

(S)-6-Fluoro-3-methylindan-1-one (S)-7. The fluoroindanone (*S*)-7 was prepared in a manner similar to that described for 5-fluoro-1-indanone by Allinger and Jones,[26] but the decomposition of the fluoroborate salt was modified.[27] To a mixture of 6.0 g (37 mmol) of the aminoindanone (*S*)-**4** in 7.0 ml of concentrated hydrochloric acid and 5.2 ml of water, a solution of 2.5 g of sodium nitrite in 3.5 ml of water was added, keeping the temperature below 5 °C. 7.0 g of 48% fluoroboric acid were added and the mixture was kept at 0 °C for 45 min. The reaction was then cooled to −30 °C after which the salt was collected and washed with 9 ml of cold methanol, 9 ml of cold ether and then dried in a desiccator over concentrated sulphuric acid. The diazonium fluoroborate was obtained as a brown powder in a yield of 6.8 g (26 mmol) 70%. The dry diazonium salt was added in portions to 110 ml of dry refluxing toluene, each portion being added after the initial evolution of gas from the previous portion had subsided. The solution was heated under reflux for 1.5 h after the last addition. The toluene solution was decanted from the insoluble tar and washed with water, 1 M sodium hydroxide and water again. After being dried over sodium sulphate the solution was concentrated and the crude product obtained was purified by flash chromatography (15:85 ethyl acetate–*n*-hexane) yielding 2.3 g (14 mmol, 38%) of liquid (*S*)-**7**. NMR: δ_H 1.39 (3 H, d, $J_{3,10}$ 7.2 Hz, 10-H), 2.31 (1 H, dd, $J_{2cis,2trans}$ 19.2, $J_{2cis,3}$ 3.4 Hz, 2*cis*-H), 2.98 (1 H, dd, $J_{2cis,2trans}$ 19.2, $J_{2trans,3}$ 7.4 Hz, 2*trans*-H), 3.42 (1 H, m, $J_{3,10}$ 7.2, $J_{2cis,3}$ 3.4, $J_{2trans,3}$ 7.4 Hz, 3-H), 7.28–7.37 (2 H, m, 5-H and 7-H), 7.47 (1 H, dd, $J_{F,4}$ 4.6, $J_{4,5}$ 8.4 Hz, 4-H). δ_C 21.4, 32.4, 46.0, 109.2(d), 122.4(d), 126.7(d), 138.1, 155.4, 162.3(d), 205.3. IR: 1712, 1485, 1264, 1247 cm^{-1}.

(S)-5-Fluoro-1-methylindene (S)-15. The fluoroindene (*S*)-**15** was prepared in the same way as the nitroindenes (**12** and **13**). The benzene solution was concentrated by distillation since the fluoroindene **15** is quite volatile. 2.7 g (16 mmol) of (*S*)-**7** gave 2.5 g (15 mmol, 91%) of crude (3S)-**11** which was used without purification. Dehydration of 0.50 g (3.0 mmol) of the indanol yielded after purification by flash chromatography (pentane) 0.34 g (2.3 mmol, 76%) of (*S*)-**15**. The indene was further purified by preparative gas chromatography. NMR: δ_H 1.30 (3 H, d, $J_{1,10}$ 7.6 Hz, 10-H), 3.46 (1 H, m, $J_{1,10}$ 7.6, $J_{1,2}$ 2.0, $J_{1,3}$ 2.0 Hz, 1-H), 6.56 (1 H, dd, $J_{1,2}$ 2.0 Hz, $J_{2,3}$ 5.6 Hz, 2-H), 6.72 (1 H, dd, $J_{1,3}$ 2.0, $J_{2,3}$ 5.6 Hz, 3-H), 6.88 (1 H, m, $J_{4,6}$ 2.4, $J_{6,F}$ 9.6, $J_{6,7}$ 8.0 Hz, 6-H), 7.03 (1 H, dd, $J_{4,F}$ 9.0, $J_{4,6}$ 2.4 Hz, 4-H), 7.31 (1 H, dd, $J_{6,7}$ 8.0, $J_{7,F}$ 5.0 Hz, 7-H). δ_C 16.0, 44.5, 108.0 (d), 111.2(d), 123.2, 129.5, 143.5, 144.5, 145.6, 162.2 (d).

(R)-(3-^2H)-6-Fluoro-3-methylindanone (R)-(3-^2H)-7. (*R*)-(3-^{2}H)-**7** was prepared analogously to (*S*)-**7**. NMR: δ_H 1.39 (3 H, s, 10-H), 2.31 (1 H, d, $J_{2cis,2trans}$ 19.2 Hz, 2*cis*-H), 2.98 (1 H, d, $J_{2cis,2trans}$ 19.2 Hz, 2*trans*-H), 3.42 (0.012 H, m, 3-H), 7.28–7.37 (2 H, m, 5-H and 7-H), 7.47 (1 H, dd, $J_{F,4}$ 4.6, $J_{4,5}$ 8.4 Hz, 4-H). δ_C 21.4, 32.0(t), 45.8, 109.2(d), 122.4(d), 126.7(d), 138.2, 155.3, 162.3(d), 205.2 IR: 1712, 1485, 1264, 1247 cm^{-1}.

(R)-(1,3-$^2H_2$)-5-Fluoro-1-methylindene (R)-15. (*R*)-**15** was prepared analogously to (*S*)-**15** except that sodium borodeuteride (>99% D, Dr Glaser AG) was used instead of sodium borohydride to introduce a deuterium into the 1-position. NMR: δ_H 1.30 (3 H, s, 10-H), 3.46 (0.012 H, m, 1-H), 6.56 (1 H, s, 2-H), 6.88 (1 H, m, $J_{4,6}$ 2.4, $J_{6,F}$ 9.6, $J_{6,7}$ 8.0 Hz, 6-H), 7.03 (1 H, dd, $J_{4,F}$ 9.0, $J_{4,6}$ 2.4 Hz, 4-H), 7.31 (1 H, dd, $J_{6,7}$ 8.0, $J_{7,F}$ 5.0 Hz, 7-H). δ_C 15.9, 44.1 (t), 108.0 (d), 111.2 (d), 123.2 (d), 129.4 (t), 143.3, 144.5, 145.6 (d), 162.3 (d).

Catalyst and solvent. The purification of 1,4-diazabicyclo[2,2,2]octane (DABCO)[6b] and *o*-dichlorobenzene[6c] have been described earlier. All handling of the purified amine was carried out in a glove box, in which the atmosphere was circulated through molecular sieves (5 Å). 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.

Kinetic procedure. The polarimetric kinetic procedure has been described in detail in an earlier paper.[6b] The NMR kinetic experiments were performed in the following way. 1-Methyl-5-nitroindene or (1,3-$^2H_2$)-1-methyl-5-nitroindene (10–20 mg) was weighed into a small vial. DABCO solution (0.8 ml) was added to a 5 mm NMR tube and placed in the probe of the NMR spectrometer at 20 °C for approximately 20 min. The thermostatted DABCO solution was then poured into the vial containing the substrate and a clock was started when half of the base solution had been added. The mixture was rapidly shaken and transferred to the NMR tube which was placed in the probe of the spectrometer and the acquisition was started. A preacquisition delay array of time intervals between each recorded spectrum was used. Each pulse sequence, consisting of four scans, took 20 s. The kinetics were followed by measuring the integrals of the methyl group at the 1-position in the substrate and the 3-position in the rearranged product. The observed rate constant was obtained from the slope of a plot of ln [**12**] versus time by least squares fitting. For the experiments in which a base solution with high concentration of DABCO (0.131 mM) was used, the correlation coefficient between the fitted line and the experimental data was $\geqslant$0.999 in all cases.

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