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Stereospecificity and Absolute Stereochemistry of Bifunctional Amidine-Catalyzed 1,3-Proton Transfer in 1,3-Disubstituted Cyclohexenes

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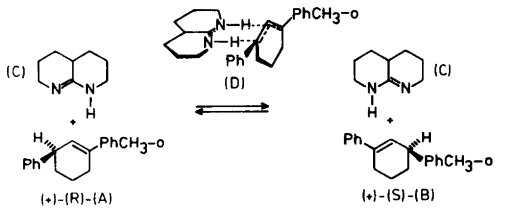
The stereochemistry of the reversible 1,3-proton transfer of 3-phenyl-1-(2-tolyl)cyclohexene ((A)) to 1-phenyl-3-(2-tolyl)cyclohexene ((B)), catalyzed by the bifunctional catalyst 1,2,3,4,4a,5,6,7-octahydro-1,8-naphthyridine ((C)), has been studied in benzene using a novel method. The stereospecificity was determined by reversibly rearranging partially-resolved (A) with (C) and by comparing *only* the specific rotation of the starting material (A) with that of (A) recovered after about $4t_{1/2}$. Since a large fraction of recovered (A)-molecules had reacted into (B) one or more times, the specific rotation of these molecules is affected by the stereospecificity of the reaction. A novel method, in which a reversible reaction is regarded as a series of irreversible processes, has been used to calculate the fraction of (A)-molecules that has been (B) one or more times and with these results an accurate lower limit for the stereospecificity of the 1,3-proton transfer is determined to be >98.4 %.

The absolute stereochemistry of this 1,3-proton transfer, *i.e.* if it takes place mainly suprafacially or antarafacially, was determined using resolved (A) and (B). Since (+)-(*R*)-(A) is found to rearrange mainly into (+)-(*S*)-(B), it is clear that the reaction takes place mainly suprafacially. The synthesis of (+)-(*R*)-(A) and (−)-(*R*)-(B) from (+)-(*R*)-3-phenylcyclohexanone and (+)-(*R*)-3-(2-tolyl)cyclohexanone are reported together with the synthesis, resolution and determination of the absolute configuration of the ketones.

As part of our studies of the mechanisms of two-proton transfer reactions,[1] proton transfers from carbon to nitrogen and from nitrogen to carbon have been investigated.[1a–f]

Recent ^{2}H-labelling studies indicate that the bicyclic *sec*-amidine (C) catalyzes the 1,3-proton transfer of 1,3,3-triphenylpropene to 1,1,3-triphenylpropene mainly by a bifunctional mechanism rather than a monofunctional one, [1e] *i.e.* the reaction uses structures similar to (D) in



Scheme 1.

Scheme 1. In order to further elucidate this type of two-proton transfer reaction we have designed and synthesized a reaction system (Scheme 1) which permits conclusions about the stereochemistry of the reaction to be drawn. The system allows the following questions to be answered: to what extent is the reaction stereospecific? Does the reaction preferentially take place antarafacially in the cyclohexene system or suprafacially as in the monofunctional catalysis of related systems?[1a,2]

Using a novel work-saving procedure, the reaction in benzene has been shown to be highly enantiospecific. Partially-resolved 3-phenyl-1-(2-tolyl)cyclohexene ((A)) was reversibly rear-

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ranged to 1-phenyl-3-(2-tolyl)cyclohexene ((B)) for about 4 reaction half-lifes and the remaining (A) was isolated by preparative GLC. A large fraction of the recovered (A)-molecules must have been (B)-molecules one or more times and these (A)-molecules may therefore potentially reveal the stereospecificity of the rearrangement. To estimate the enantiospecificity of the reaction, a new method was developed which transforms reversible reactions into a series of irreversible processes and this allows the calculation of the number of (A)-molecules that have been (B) one or more times.[3] By this method, an accurate lower limit of the stereospecificity could be estimated by comparing the specific rotation of the starting material with that of recovered (A). The method is described in detail in the preceding paper. The present reaction was found to be >98.4 % enantiospecific. Thus, for an accurate stereospecificity measurement of a reversible reaction, it is *only* necessary to know the specific rotation of *partially-resolved starting material* and the specific rotation of *recovered starting material* after some reaction. Obviously it is neither necessary to know the absolute configuration of the resolved product nor its specific rotation for estimation of the stereospecificity.

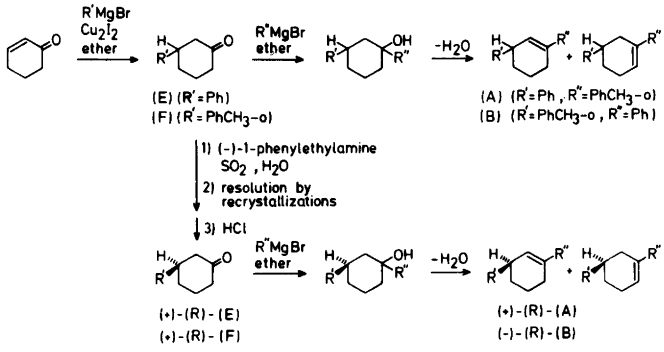
To answer the second question whether the rearrangement mainly takes place suprafacially or antarafacially, knowledge regarding at least the relative stereochemistry of (A) and (B) is needed. Therefore both resolved (A) and (B) of known absolute configuration have been prepared and used to show that the reaction takes place in a suprafacial manner. It is important to stress that by the procedure used, *i.e.* to first determine the stereospecificity and then the mode of rearrangement, it is only necessary to have partially-resolved (A) and to know the relative stereochemistry of (A) and (B).

RESULTS AND DISCUSSION

Racemic 3-phenyl-1-(2-tolyl)cyclohexene ((A)) was prepared according to Scheme 2 and purified by preparative GLC. The kinetics of the reversible rearrangement of (A) into 1-phenyl-3-(2-tolyl)cyclohexene ((B)), catalyzed by the bicyclic *sec*-amidine 1,2,3,4,4a,5,6,7-octahydro-1,8-naphthyridine ((C)), was studied in benzene at 125.21±0.10 °C by GLC (Scheme 1). The reaction mixture was 0.97 M in (C) and initially 0.031 M in (A). Analysis showed that the reaction is strictly a pseudo first-order reaction.[4] The equilibrium constant ($K=k_1/k_{-1}$) was determined after 10 half-lives to be 1.456±0.015 and the pseudo first-order rate constants obtained were $k_1=(1.94\pm0.05)\cdot10^{-6}$ s^{-1} and $k_{-1}=(1.33\pm0.05)\cdot10^{-6}$ s^{-1}. These kinetic data were used in the study of the reaction stereochemistry described below.

Resolved (A) *i.e.* (+)-(A) ($[\alpha]_{365}^{22.0}$ +66.96 ±0.26° (*c* 2.77, heptane)) was prepared according to Scheme 2 from optically active (E) which in turn had been resolved by recrystallizations of its (−)-1-phenylethylamine bisulfite addition compound from 90 % ethanol.

A mixture of 0.12 M of (+)-(A) and 0.96 M of (C) in benzene was reacted under the above conditions for about 4 half-lives (238.5 h). Analytical GLC showed the reaction mixture to have the composition 45.1 % (A) and 54.9 %(B). Separation by preparative GLC gave pure (+)-(A) with $[\alpha]_{365}^{22.0}$+66.93±0.42° (*c* 0.96, heptane) and pure (+)-(B) with $[\alpha]_{365}^{22.0}$+165.8±0.8° (*c* 1.22, heptane).



Scheme 2.

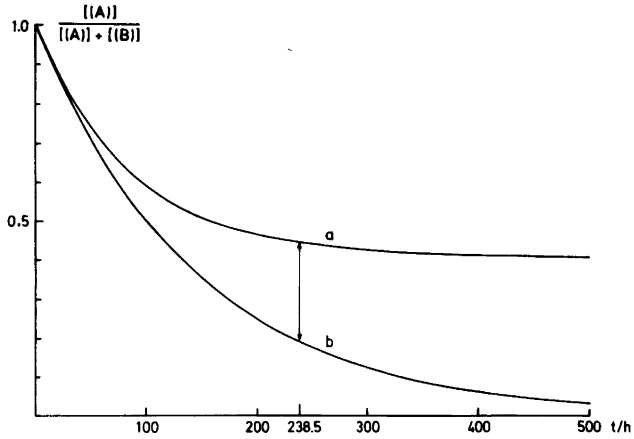


Fig. 1. Shows the time dependence of the fractions of (A) for the reversible reaction (A) $\underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}}$ (B) (curve a) and for the irreversible reaction (A) $\xrightarrow{k_1}$ (B) (curve b). The double arrow indicates the 57 % of compound (A) (remaining after 238.5 h of reaction) which has been (B) one or more times.

Calculations using the above kinetic data, solution of the rate equation for the above process $([(A)]-[(A)_\infty])=([(A)_o]-[(A)_\infty])e^{-(k_1+k_{-1})t}$ and solution of the equation in which the reverse reaction is ignored, $[(A)]=[(A)_o]e^{-k_1t}$, show that after 238.5 h 57 % of the recovered (A)-molecules have been (B)-molecules one or more times due to the reversibility (Figure 1). This result, together with the specific rotations of (A) recovered after reaction for 4 half-lives and that of the starting material, make it possible to conclude that the tautomeric rearrangement is >98 % enantiospecific.

A more accurate estimate of the enantiospecificity may be obtained if the fractions of recovered (A)-molecules that have been (B) not only once but twice, three times etc. could be calculated. This is made possible by regarding the reversible reaction (A) $\underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}}$ (B) as a series of irreversible processes, *i.e.*

$$(A)_{B0} \xrightarrow{k_1} (B)_{A1} \xrightarrow{k_{-1}} (A)_{B1} \xrightarrow{k_1} (B)_{A2} \cdots\cdots \xrightarrow{k_{-1}} (A)_{Bi-1} \xrightarrow{k_1} (B)_{Ai} \xrightarrow{k_{-1}} (A)_{Bi} \xrightarrow{k_1} (B)_{Ai+1} \xrightarrow{k_{-1}} \textit{etc.} \quad (1)$$

$(A)_{B0}$-molecules ((A)-molecules that have been (B) zero times) are of course irreversibly transformed into $(B)_{A1}$-molecules ((B)-molecules that have been (A) only once) and these in turn into $(A)_{B1}$. $(A)_{Bi}$ and $(B)_{Ai}$ denote those (A)- and (B)-molecules that have been (B) or (A) i times, respectively. $(A)_{Bi}$- and $(B)_{Ai}$-molecules can of course never become $(A)_{Bi-1}$- or $(B)_{Ai-1}$-molecules again. The solutions of the linear differential equations describing the time dependence of the concentrations of the species in eqn. (1) are reported in the preceding paper.[3b]

Using these solutions the following values have been obtained for the composition of (A) recovered after 238.5 h. 42.8 % of the (A)-molecules have never been (B), 48.7 % have been (B) once, 8.0 % twice, 0.5 % three times and only 0.02 % have been (B) four times. The fraction of (A) that has been (B) five or more times is found to be <0.003 %.

Thus having access for example to the $[(A)_{Bi}]$ for $i=1,2,3\ldots$, the stereospecificity could be estimated using eqn. (2) which is also derived in the preceding paper.[3b]

$$\frac{[\alpha_{(A)t}]}{[\alpha_{(A)0}]} = \frac{\sum_{i=0}^{\infty} [(A)_{Bi}]x^iy^i}{\sum_{i=0}^{\infty} [(A)_{Bi}]} \quad (2)$$

In eqn. (2), $[\alpha_{(A)t}]$ is the specific rotation of (A) that has been recovered after reaction time t and $[\alpha_{(A)0}]$ is that of the (A) starting material. The parameters x and y are the stereospecificities for

the reactions (A) →(B) and (B) → (A), respectively.

Taking into account experimental errors in specific rotations and rate constants *etc.* and simulation using eqn. (2), yields that $x \cdot y > 0.9845$. If the enantiospecificities x and y are assumed to be equal, then $x=y=0.9922$, *i.e.* each of the reactions (A) → (B) and (B) → (A) is 99.22 % enantiospecific. If, on the other hand $x > y$ or $x < y$ we are only able to conclude that the smallest of the two stereospecificities must be >98.45 % and the larger is >99.22 %. In the present case it is obvious from the simulations that it is unnecessary for an accurate estimate to take into account those (A)-molecules that have been (B) more than three times.

By the above procedure it is thus possible to make an accurate estimate of a lower limit of the reaction enantiospecificity using only the specific rotations of partially-resolved starting material and that of starting material recovered after some reaction. Obviously for this estimate it is neither necessary to have access to completely resolved (A) or (B) nor to know their absolute or relative configurations.

However, the high enantiospecificity only tells us that the rearrangement is either mainly suprafacial or antarafacial. To be able to distinguish between these two possibilities it is necessary to know at least the relative configurations of the starting material (A) and the product (B).

To determine the rearrangement mode the following experiments were carried out. Ketones (E) and (F) of Scheme 2 were essentially completely resolved by the procedure indicated in the Scheme and the experimental section. Their absolute configurations were determined using the octant rule.[5] (+)-(E) and (+)-(F) were thus both shown to have the (*R*)-configuration. Assuming no change in stereochemistry, these compounds were converted into the corresponding cyclohexenes. Thus (+)-(*R*)-(E) ($[\alpha]_{589}^{22.0}$ +10.93±0.10° (*c* 2.83, CCl_4)) was reacted into (+)-(*R*)-(A) ($[\alpha]_{365}^{22.0}$+66.96±0.26° (*c* 2.77, heptane)) and (+)-(*R*)-(F) ($[\alpha]_{589}^{22.0}$ +40.25 ±0.16° (*c* 5.33, CCl_4)) was transformed into (−)-(*R*)-(B) ($[\alpha]_{365}^{22.0}$−167.3±2.2° (*c* 0.503, heptane)). It is interesting to note that (A) and (B) of the same configuration show opposite signs for the specific rotations despite the precursor ketones having the same sign. This difference is possibly due to steric crowding in (B) caused by the methyl group on the benzene ring in the 3-position.

On the basis of these results, it is concluded (since (+)-(A) rearranges by (C)-catalysis into (+)-(B), *i.e.* (+)-(*R*)-(A) yields (+)-(*S*)-(B)) that the *sec*-amidine catalyzed 1,3-proton transfer takes place mainly suprafacially. That this rearrangement makes use of a bifunctional mechanism (Scheme 1) rather than a monofunctional one is supported by ^{2}H-labelling experiments.

It is important to stress that by using the above procedure, *i.e.* to first determine the stereospecificity and then the mode of rearrangement, it is only necessary to have partially-resolved (A) and to know the relative stereochemistry of (A) and (B).

EXPERIMENTAL

General Methods. All glassware, including calibrated volumetric flasks used in the kinetics, the stereochemical experiment and the specific rotation measurements were treated with chromic acid, water, 2M ammonia, distilled water and finally dried at 170 °C for at least 24 h and stored in a desiccator.

The kinetics and the stereochemical experiments were carried out in a HETO 02PT 623 thermostat. The temperature was measured with a precalibrated mercury thermometer with an absolute accuracy ±0.10 °C.

Analytical GLC was performed with a Perkin-Elmer 900 Gas Chromatograph equipped with a 2 m×3 mm column containing 2 % Apiezon L on Varaport 30, 100/120 mesh at 276 kPa N_2. The oven temperature was programmed at 145−195 °C, 4°/min for the analysis of the kinetic mixtures; it was otherwise held at 175 °C.

The areas of the peaks were calculated by triangulation and/or using a disc. integrator. The error in the determination of the fraction of remaining substrate was estimated to ±0.6 %.

The preparative separations were made with a Varian Aerograph 920 equipped with a 1 m×6.3 mm column containing 20 % Carbowax 20M on Chromosorb W, AW, DMCS-treated, 60/80 mesh, a N_2-flow 75 ml/min and an oven temperature of 240 °C. The pure compounds were collected in glass tubes containing stainless steel[6] (see Fig. 2) to avoid aerosol formation. The optical rotation was measured on a Perkin-Elmer 241 Polarimeter.

3-Phenylcyclohexanone ((E)) and 3-(2-tolyl)-cyclohexanone ((F)). Ketones (E) and (F) were synthesized from 2-cyclohexen-1-one by a conju-

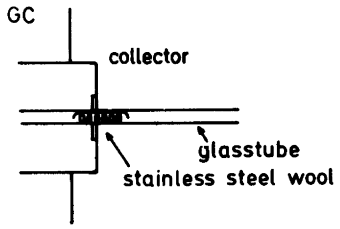


Fig. 2. Arrangement used in the preparative GLC to avoid aerosol formation.

gate addition of phenylmagnesium bromide and 2-tolylmagnesium bromide, respectively, using the method of Cope and Hecht.[7] The yields after distillation at 104–106 °C/2.7 Pa and 108–109 °C/2.7 Pa were 81 and 85 %, respectively.

(+)-(R)-3-Phenylcyclohexanone ((+)-(R)-(E)) and (+)-(R)-3-(2-tolyl)cyclohexanone ((+)-(R)-(F)). The method used for resolution of the ketones (±)-(E) and (±)-(F) is a modification of a method for resolving similar ketones.[8] 11.7 g (0.0965 mol) of (−)-1-phenylethylamine[9] ($[\alpha]_{589}^{22.0}$ −39.3° (neat) (lit.[9a] $[\alpha]_{589}^{22.0}$ −40.3°)) was dissolved in a mixture of 47.5 ml of 95 % ethanol, 47.5 ml ether and 1.9 ml of water. The solution was cooled by an ice–water mixture and reaction with sulfur dioxide, which was bubbled through the solution and allowed to proceed for about 1.5 h. The resulting homogeneous yellow liquid was stirred and 25.0 g (0.143 mol) of (±)-3-phenylcyclohexanone added dropwise. The reaction temperature was not allowed to exceed 30 °C. About 15 min after the addition and removal of the ice–water mixture, which lasted for *ca.* 20 min, the amine bisulfite compound started to crystallize and the solution decolourized. After another 10 minutes the whole solution had turned into a crystal porridge and SO_2 evolved. Two hours later (the last 1 h in an ice bath), 100 ml ether was added. The slurry formed was filtered and the crystals were washed with ether and dried. The yield of crude amine bisulfite compound was 30.9 g (85 % based upon (−)-1-phenylethylamine). Four recrystallizations from 90 % ethanol at <50 °C gave the (−)-1-phenylethylamine bisulfite addition compound of (+)-3-phenylcyclohexanone (13 % of the initial amount of salt (see Table 1)).

Table 1.

Recrystallization	% salt recovered	$[\alpha]_{589}^{22.0}$ for (+)-3-phenylcyclohexanone in CCl_4/°
1	59	3.2
2	51	8.4
3	64	10.6
4	69	10.9

Amine bisulfite compound (2.50 g) was added to 40 ml 20 % HCl and the mixture was stirred while kept at 40–45 °C. After about 2 h, all the salt had dissolved and the (+)-3-phenylcyclohexanone was extracted with 3×50 ml ether. The combined ether layers were washed with water and dried over $MgSO_4$. The yield of (+)-3-phenylcyclohexanone ($[\alpha]_{589}^{22.0}$+10.93±0.10° (*c* 2.83, CCl_4)) was 1.04 g (90 % based upon the decomposed amine bisulfite compound).

(+)-3-(2-tolyl)cyclohexanone was similarly resolved. The yield of amine bisulfite compound in this case was 91 % and, after two recrystallizations from 90 % ethanol at <50 °C, 27 % amine bisulfite compound was recovered. (+)-3-(2-tolyl)cyclohexanone with $[\alpha]_{589}^{22.0}$+40.25±0.16° (*c* 5.33, CCl_4) was obtained after hydrolysis of the amine bisulfite compound.

By using the octant rule[5] the absolute configuration of ketones (+)-(E) and (+)-(F) was shown to be the (R)-configuration. This result is consistent with that of Kretchmer[10] who obtained ketone (E) slightly resolved by asymmetric synthesis.

Racemic 3-phenyl-1-(2-tolyl)cyclohexene ((A)) and 1-phenyl-3-(2-tolyl)cyclohexene ((B)). 3-phenyl-1-(2-tolyl)cyclohexanol was made by addition of 2-tolylmagnesium bromide to the ketone (E) according to the procedure of France *et al.*[11] Compound (A) was then obtained after water-elimination achieved by adding a solution of 1.1 g of the alcohol in 10 ml 1,3-dimethylbenzene dropwise to a refluxing solution of a catalytical amount of *p*-toluene sulfonic acid (*ca* 0.1 g) in 15 ml 1,3-dimethylbenzene. After refluxing for about 15 min, 20 ml water was added and the organic phase was separated. The water-phase was extracted with ether and the combined organic phases were washed with water and dried over $MgSO_4$. 0.65 g of a product mixture of (A) and 5-phenyl-1-(2-tolyl)cyclohexene in the ratio 1:3 was obtained after distillation at 136–140 °C/1.3 Pa. Pure (A) was obtained by preparative GLC. ^{1}H NMR (100 MHz, $CDCl_3$): δ 1.45–2.17, 2.30, 2.36 (9 H, m, m, s), 3.54 (1 H, m), 5.61 (1 H, dt), 7.15, 7.26 (9 H,s, q).

(B) was similarly synthesized from ketone (F) and phenylmagnesium bromide. The product mixture consisted of (B) and 1-phenyl-5-(2-tolyl)cyclohexene in the ratio 1:2.7. ^{1}H NMR (100 MHz, $CDCl_3$): δ 1.45–2.18, 2.39, 2.51 (9 H, m, s, m), 3.77 (1 H, m), 6.11 (1 H, dt), 7.00–7.53 (9 H, m).

(+)-(R)-3-phenyl-1-(2-tolyl)cyclohexene ((+)-(R)-(A)) and (−)-(R)-1-phenyl-3-(2-tolyl)cyclohexene ((−)-(R)-(B)). Optically active (+)-(A) and (−)-(B) was prepared and purified as for racemic (A) and (B) from the optically active ketones (+)-(*R*)-(E) ($[\alpha]_{589}^{22.0}$ +10.93±0.10° (*c* 2.83, CCl_4)) and (+)-(*R*)-(F) ($[\alpha]_{589}^{22.0}$+40.25 ±0.16° (*c* 5.33, CCl_4)), respectively. No change of the absolute configuration at the asymmetric carbon is expected to occur in the synthesis of (A) and (B) and therefore both the obtained cyclohexenes (+)-(A) and (−)-(B) must have the (*R*)-configuration. Pure (+)-(*R*)-(A) with $[\alpha]_{365}^{22.0}$−66.96±0.26° (*c* 2.77, heptane) and pure (−)-(*R*)-(B) with $[\alpha]_{365}^{22.0}$ −167.3 ±2.2° (*c* 0.503, heptane) was obtained.

1,2,3,4,4a,5,6,7-Octahydro-1,8-naphthyridine ((C)). The amidine (C) was made according to Janné and Ahlberg[12] with the modification that *ca.* 5 % excess of transdecahydro-1,8-naphthyridine was used.

Kinetics and stereochemical experiments. All preparations of the solutions used in the kinetics and the stereochemical experiments were made in a N_2-filled dry-box to avoid contamination by oxygen and moisture.

A benzene solution of 0.99 M in (C) was prepared and this solution was used in making the reaction solutions for the kinetics and the stereochemical experiments.

The kinetic solution, which was 0.97 M in (C), 0.031 M in (B) and 0.030 M in the internal standard octadecane, was distributed into 0.5 ml ampoules (0.1 ml in each). The reaction was carried out in a thermostat at 125.21±0.10 °C. The ampoules were then broken at suitable times and the reaction mixture was quenched with 1M HCl. The organic phase was washed with water and after separation by centrifugation analyses was made by analytical GLC.

The stereochemical experiment was carried out in an 1 ml ampoule containing 0.9 ml 0.96 M of (C) and 0.12 M of (+)-(*R*)-(A) $[\alpha]_{365}^{22.0}$ +66.96±0.26° (*c* 2.77, heptane). After about 4 $t_{1/2}$ (238.5 h) at 125.21±0.10 °C, the reaction was quenched and the reaction mixture was washed and analyzed as above. The analysis showed that the composition of the mixture was 45.1 % (A) and 54.9 % (B). Separation was carried out with preparative GLC.

The product composition differs from that obtained in the kinetic experiment (44.4 % (A) and 55.6 % (B)). This presumably depends on the difference in the amidine (C) concentration in the two experiments. In the kinetic experiment about 2 % of the benzene is vapour in the ampoules. In the stereochemical experiment, on the other hand, the fraction of benzene vapour is only about 0.06 %.

The specific rotation of the separated (A) and (B) was measured (their purity was controlled by analytical GLC) and found to be $[\alpha]_{365}^{22.0}$ +66.93±0.42° (*c* 0.96, heptane) and $[\alpha]_{365}^{22.0}$ +165.77±0.88° (*c* 1.22, heptane), respectively.

The kinetics and stereochemical experiments were repeated and the results were within the reported experimental error.

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REFERENCES

1. a. Ahlberg, P. and Ladhar, F. *Chem. Scr. 3* (1973) 31; b. Niemeyer, H. M. and Ahlberg, P. *Chem. Commun.* (1974) 799; c. Niemeyer, H. M., Goscinski, O. and Ahlberg, P. *Tetrahedron 31* (1975) 1699; d. Janné, K. and Ahlberg, P. *Acta Chem. Scand. B 30* (1976) 245; e. Janné, K. and Ahlberg, P. *Chem. Commun.* (1976) 1040; f. Ek, M. and Ahlberg, P. *Chem. Scr. 16* (1980) 62; g. Engdahl, K.-Å., Bivehed, H., Ahlberg, P. and Saunders, W. H., Jr. *Chem. Commun.* (1982) 423; h. Engdahl, K.-Å., Bivehed, H., Ahlberg, P. and Saunders, W. H., Jr. *J. Am. Chem. Soc. 105* (1983) 4767.
2. a. Bergson, G. and Weidler, A.-M. *Acta Chem. Scand. 17* (1963) 1798; b. Almy, J. and Cram, D. J. *J. Am. Chem. Soc. 91* (1969) 4459 and references therein.
3. a. Ahlberg, P. and Ek, M. *Chem. Commun.* (1979) 624; b. Ek, M. and Ahlberg, P. *Acta Chem. Scand. B 38* (1984) 203.
4. a. Frost, A. A. and Pearson, R. G. *Kinetics and Mechanism,* 2nd Ed., Wiley, New York 1970; b. Hammett, L. P. *Physical Organic Chemistry,* 2nd Ed., McGraw-Hill, New York 1970; c. Ritchie, C. D. *Physical Organic Chemistry: The Fundamental Concepts,* Dekker, New York 1975.
5. Mislow, K. In Breslow, R., Ed., *Introduction to Stereochemistry,* Benjamin, California 1965, p. 157.
6. Teranishi, R., Flath, R. A., Mon, T. R. and Stevens, K. L. *J. Gas Chromatogr. 3* (1965) 206.
7. Cope, A. C. and Hecht, S. S. *J. Am. Chem. Soc. 89* (1967) 6920.
8. a. Adolphen, G., Eisenbraun, E. J., Kern, G. W. and Flanagan, P. W. K. *Org. Prep. Proced. 2* (1970) 93; b. Adams, R. and Garber, J. D. *J. Am. Chem. Soc. 71* (1949) 522.

9. a. Theilacker, W. and Winkler, H.-G. *Chem. Ber. 87* (1954) 690; b. Ladhar, F. *Unpublished recipe.*
10. Kretchmer, R. A. *J. Org. Chem. 37* (1972) 2744.
11. France, H., Heilbron, I. M. and Hey, D. H. *J. Chem. Soc.* (1939) 1288.
12. Janné, K. and Ahlberg, P. *Synthesis* (1976) 452.

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