J. Chem. Soc., Faraday Trans. 1, 1982, **78**, 1079-1086

Enantiomer-differentiating Hydrogen Transfer from Fenchol to Menthone over Molten Indium Catalyst

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Received 13*th April*, 1981

The initial rate (r_0) of the hydrogen-transfer reaction from D-fenchol to menthone has been found to obey the following equation

$$r_{0,j} = k_j p_A$$

where k is the rate constant, p_A is the partial pressure of D-fenchol, and the subscript j denotes any one of the optical isomers (L-,D- and D,L-) of menthone. The reaction is enantiomer-differentiating: $k_L > k_D$, and the optical resolution of D,L-menthone takes place in the reaction between D-fenchol and D,L-menthone.

The experimental results are explained on the bases of an Eley–Rideal-type mechanism and stereochemically consistent transition-state models. Probable adsorption models for menthone are also proposed.

Heterogeneous enantiomer-differentiating reactions are closely related to biochemical enzymic reactions;[1] thus an unambiguous understanding of the mechanisms of the former reactions provides us with strong bases for studying those of the latter. A heterogeneous enantiomer-differentiating reaction is usually studied using a batch reaction system consisting of gas, liquid and solid (catalyst) phases.[2, 3] This introduces many difficulties in analysing the reaction rate, and therefore in clarifying the reaction mechanism: one must clarify the effects of agitation and mass transfer, effects of solvent and of solution pH, besides effects caused by the choice of catalyst used.

Recently, we[4, 5] have found that liquid metals such as liquid indium are able to catalyse certain kinds of vapour-phase enantiomer-differentiating reactions. Since kinetic formalism as a tool for investigating the mechanism of a vapour-phase heterogeneous catalytic reaction is firmly established,[6] this finding shows the potential merit in clarifying the mechanism of enantiomer differentiation.

In the present work, the kinetics of the enantiomer-differentiating hydrogen transfer from fenchol to menthone over a liquid-indium catalyst has been studied in order to discuss the reaction mechanism.

EXPERIMENTAL

MATERIALS

Special attention was paid to the purity of the reagents used. The purity of D-fenchol (the hydrogen-donating reagent) was better than 98.5% and that of cumene (the solvent for the reactants) was better than 98%. Both L-menthone and D,L-menthone (hydrogen-accepting reagents) were purified by means of column chromatography (silica gel, Wako-C-200, 100 g; benzene eluent) followed by distillation to remove benzene. The purity of the resulting menthone was better than 98%. The purity of indium metal (the catalyst) was 99.999%. The catalyst metal was fused, reduced and purified by a previously reported method.[7]

APPARATUS

The reaction apparatus used in the present work is shown schematically in fig. 1. This is essentially a conventional flow-type apparatus except for the reactor, which is of the rectangular-duct type. The use of a reactor of this type greatly facilitates kinetic measurements with liquid-metal catalysts.[8]

A cumene solution of the required concentrations of D-fenchol and L-menthone (or D,L-menthone) was supplied from an electrically driven micro-feeder into the reaction system. Within the preheating zone the feed solution was evaporated and mixed with a stream of purified helium. The mixture was then led to the reactor and subjected catalysis at the liquid-indium surface. The effluent from the reactor was cooled and the liquid products were separated from helium and the gaseous products (mainly hydrogen).

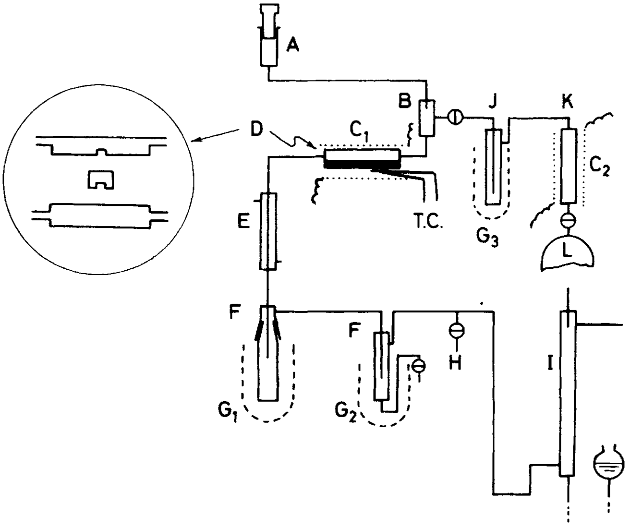

FIG. 1.—Reaction apparatus with a rectangular-duct-type reactor: (A) microfeeder, (B) preheater, (C_1), (C_2) electric furnaces, (D) rectangular-duct-type reactor (86 mm length, 20 mm width, 16 mm height), (E) cooler, (F) separator, (G_1), (G_2), (G_3) Dewar vessels, (H) sampling port, (I) soap-film flow meter, (J) trap containing molecular sieves, (K) vessel containing reduced copper catalyst, (L) helium reservoir.

KINETIC STUDIES

Kinetic data were obtained by keeping the catalyst surface area (S) constant (*ca.* 18 cm^2) and varying the feed rate (F) of the reactants: the conversion (X_t) for the hydrogen-transfer reaction was measured as a function of the contact time (S/F). Thus the initial reaction rate (r_0) was determined from the initial slope of the curve representing the relation between X_t and S/F. Independent variables adopted in the rate study were the reaction temperature (T) and the respective partial pressures of fenchol (p_K) and menthone (p_A).

ANALYSIS

Analysis of the liquid products was carried out mainly by gas chromatography with an apparatus (Hitachi model 163) equipped with a capillary column (Unicon oil, 0.25 mm × 45 m) and a flame ionization detector. Each compound produced was identified by mass spectrometry (JEOL-JMS-D-300 gas-chromatographic mass spectrometer). In order to clarify if the optical resolution of D,L-menthone resulted from hydrogen transfer from D-fenchol to D,L-menthone, the specific optical rotation of the unreacted menthone remaining in the reaction products was measured at 15 °C with an automatic digital polarimeter (Union Giken PM-101). For this measurement menthone was separated from the products by the following method; first cumene (solvent) was removed by distilling the liquid products, and then menthone was separated from the residual mixture by means of column chromatography (silica gel column; benzene eluent). Finally benzene (eluent) was removed by distillation.

RESULTS

OVERALL REACTION

Product analyses revealed that (i) the liquid products were fenchone, menthol and neomenthol, (ii) the molar ratio of fenchol to (menthol + neomenthol) was always greater than unity, and (iii) the gaseous product was hydrogen. Both menthol and neomenthol could be accounted for as products of the hydrogen transfer from fenchol to menthone,[9] and the excess of fenchone and formation of hydrogen could be accounted for by the dehydrogenation of fenchol. Good mass balances were obtainable with these two reactions. Furthermore, separate experiments proved that no direct hydrogenation of menthone by gaseous hydrogen took place over the liquid-indium catalyst. Thus it was considered that the overall reaction is a composite of the following reactions:

$$\text{fenchol} + \text{menthone} \longrightarrow \text{fenchone} + \text{menthol and neomenthol} \qquad (1)$$

$$\text{fenchol} \longrightarrow \text{fenchone} + \text{H}_2. \qquad (2)$$

Frequently, a side reaction prevents one from obtaining precise kinetic data for the reaction of interest. However, this was not the present case. The dehydrogenation reaction (2) led to little difficulty in obtaining the conversion (X_t) for the hydrogen-transfer reaction (1): X_t was readily obtained from the concentrations of menthol and neomenthol in the products. Thus we were able to obtain the reliable kinetic data given below.

INITIAL RATE AND ENANTIOMER DIFFERENTIATION

Exemplified in fig. 2 is the relation between X_t and S/F at 410 °C. This figure illustrates two important aspects of the rate of the hydrogen-transfer reaction. First, the X_t against S/F plot is linear under the experimental conditions. This greatly facilitates evaluation of the initial rate (r_0), defined by $[\mathrm{d}X_t/\mathrm{d}(S/F)]_{S/F=0}$. Secondly, D-fenchol reacted with L-menthone at an increased rate than with D,L-menthone. This implies that the hydrogen-transfer reaction is enantiomer-differentiating: hydrogen transfer from D-fenchol to L-menthone is faster than that to D-menthone. In contrast to this, the rate of dehydrogenation of fenchol [reaction (2)] was found to be affected little by the change of the coexisting menthone species (from L- to D,L-).

The kinetic characteristics of hydrogen-transfer are best expressed in fig. 3. The reaction obeyed first-order kinetics with respect to the partial pressure of D-fenchol and zero-order kinetics with respect to the partial pressure of menthone. These characteristics were independent of the species (L- or D,L-) of menthone used as the hydrogen acceptor. However, the rate of hydrogen transfer to L-menthone ($r_{0,\mathrm{L}}$) was greater than that to D,L-menthone ($r_{0,\mathrm{D,L}}$).

The experimental data mentioned above are summarized by the following rate equations:

$$r_{0,\mathrm{L}} = k_{\mathrm{L}}\,p_{\mathrm{A}}; \quad r_{0,\mathrm{D,L}} = k_{\mathrm{D,L}}\,p_{\mathrm{A}} \qquad (3a, b)$$

with

$$k_{\mathrm{L}} > k_{\mathrm{D,L}} \qquad (4)$$

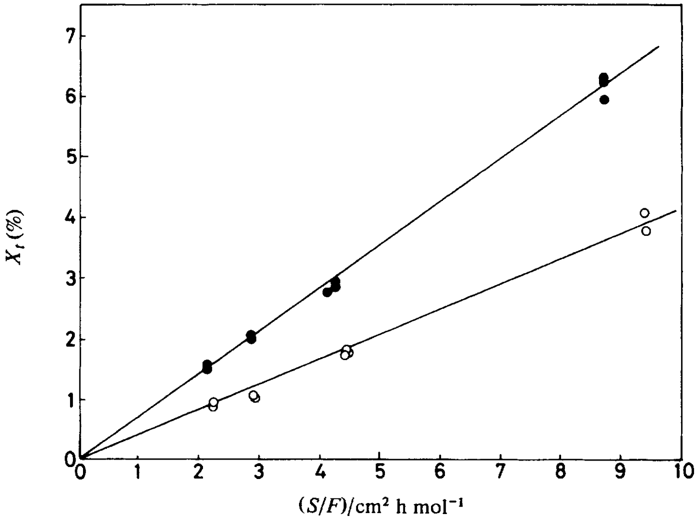

FIG. 2.—Conversion (X_t) for hydrogen transfer as a function of contact time (S/F) at 410 °C, p_A = 0.05 atm and p_K = 0.1 atm (1 atm = 101 325 Pa): ●, D-fenchol/L-menthone system; ○, D-fenchol/D,L-menthone system.

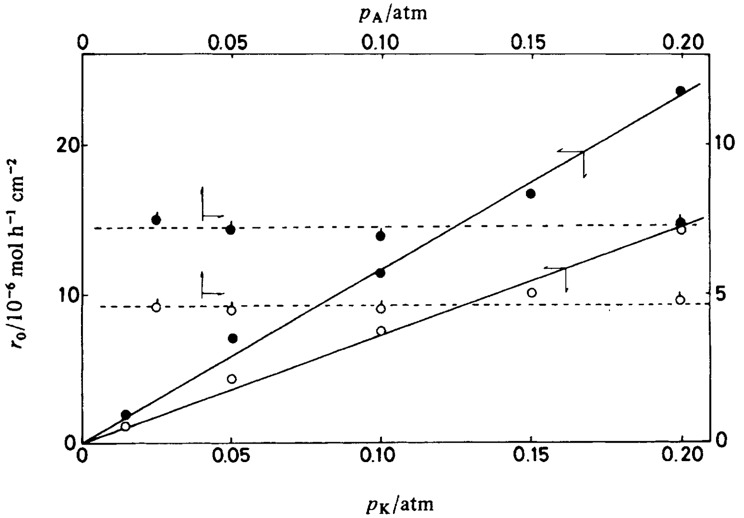

FIG. 3.—Characteristic features of the initial rate (r_0) of the hydrogen-transfer reaction at 410 °C: ●, ●, D-fenchol/L-menthone system; ○, ○, D-fenchol/D,L-menthone system; p_K = 0.05 atm for r_0/p_A relation, and p_A = 0.05 atm for r_0/p_K relation.

where k is the rate constant and the subscripts L and D,L indicate that the hydrogen acceptors are L-menthone and D,L-menthone, respectively.

The experimental data given in fig. 3 and the rate equations given above enabled us to evaluate the rate constant k_D defined by

$$r_{0,D} = k_D p_A \tag{5}$$

where the subscript D indicates that the hydrogen acceptor is D-menthone.

Thus a comparison between k_L and k_D becomes possible. The Arrhenius plots shown in fig. 4 reveal that

$$k_L > k_D \tag{6}$$

demonstrating the clear enantiomer-differentiating characteristics shown by the hydrogen-transfer reaction.

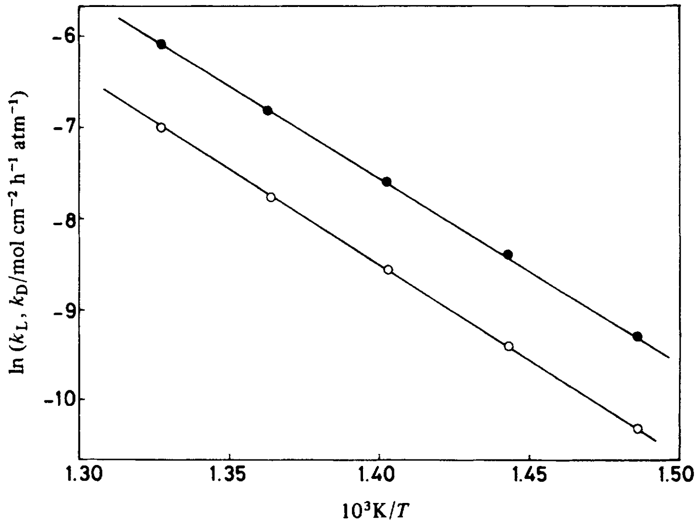

FIG. 4.—Arrhenius plots for k_L (●) and k_D (○).

$k_L = 1.2 \times 10^9 \exp(-40.3 \times 10^3/RT)$

$k_D = 1.2 \times 10^9 \exp(-41.6 \times 10^3/RT)$.

The inequality (6) suggests that the optical resolution of D,L-menthone takes place in the reaction between D-fenchol and D,L-menthone. In fact, the specific rotation of menthone separated from the reaction products was +2.08 ($C = 3.072$ g per 100 cm^3; ethanol solvent), indicating that optical resolution took place (optical yield ≈ 57%, the reaction temperature was 480 °C and the composition of the feed was menthone/cumene = 1.5 and cumene/fenchol = 18.6, both in molar ratios).

DISCUSSION

DERIVATION OF THE RATE EQUATION

The reaction mechanism deserves special discussion, since liquid-indium itself has no chirality and hence the enantiomer-differentiation observed in the hydrogen-transfer reaction over this catalyst might appear unusual. Thus the present discussion mainly treats this problem, and our first task is to disclose the relationship between the rate equation and the underlying microscopic processes.

It is possible to show that the following reaction mechanism well explains the experimental rate data. (1) The surface of the liquid-indium catalyst is almost completely covered by adsorbed menthone molecules (K): the adsorption is saturated and the number of adsorbed K molecules (n_K°) is assumed to be 10^{14} molecule cm^{-2}. The adsorbed K molecules are regarded as active centres with no translational or rotational freedom. (2) Chemisorption of fenchol molecules (A) upon active centres (adsorbed K molecules) limits the reaction rate.

Under the assumptions mentioned above we can obtain the following rate equation:[10]

$$r_0 = (p_A/\boldsymbol{k}T)\, n_K^\circ \boldsymbol{h}^4 [8\pi^2 I(2\pi m_A \boldsymbol{k}T)^{\frac{3}{2}}]^{-1} (f_v^\ddagger/f_v^A f_v^K) \exp(-E/\boldsymbol{R}T) \quad (7)$$

where $\boldsymbol{k}$ is Boltzmann's constant, $\boldsymbol{h}$ is Planck's constant, I is the moment of inertia of a fenchol molecule, m_A is the mass of a fenchol molecule, and f_v is a vibrational partition function (superscripts ‡, A and K denote the transition state, fenchol and menthone, respectively). Eqn (7) reduces to

$$r_0 = k_{th} p_A \quad (8)$$

where k_{th} is the rate constant by excluding p_A from the right-hand side of eqn (7).

It is clear that the theoretical rate equation is of a form identical with that of the experimental rate equations (3*a*) or (3*b*).

We can define the theoretical frequency factor A_{th} by

$$k_{th} = A_{th} \exp(-E/\boldsymbol{R}T). \quad (9)$$

With approximated values for n_K°, I, f_v^A, f_v^K and $f_v^\ddagger$, it is possible to show that the frequency factor A_{th} can take a value comparable to the experimental value: the details of calculation are not important for the discussion of enantiomer differentiation and are not presented here.

TRANSITION-STATE MODEL; ENANTIOMER DIFFERENTIATION

It is clear that the relation $k_L > k_D$ expressing the degree of enantiomer differentiation observed experimentally is explainable if we can justify the relation $k_{th,L} > k_{th,D}$. Stereochemistry tells that the relation is justified only when the following conditions are satisfied: (i) the transition state for hydrogen transfer to L-menthone is a diastereomer of the transition state for hydrogen transfer to D-menthone: (ii) the formation of the former transition state is easier than that of the latter. Whether these conditions are acceptable or not can be examined by making transition-state models.

Illustrated in fig. 5 are the probable transition-state models for the following hydrogen transfer reactions:

D-fenchol + L-menthone → A1 → L-fenchone + L-menthol
D-fenchol + D-menthone → A2 → L-fenchone + D-menthol
D-fenchol + D-menthone → B1 → L-fenchone + D-neomenthol
D-fenchol + D-menthone → B2 → L-fenchone + L-neomenthol

where A1, A2, B1 and B2 are the transition states defined in fig. 5.

One basic assumption used in making these models is that the hydroxy group in the fenchol molecule combines with the carbonyl group in the menthone molecule to form the state shown in fig. 5(*c*). In addition it is implicitly assumed that the

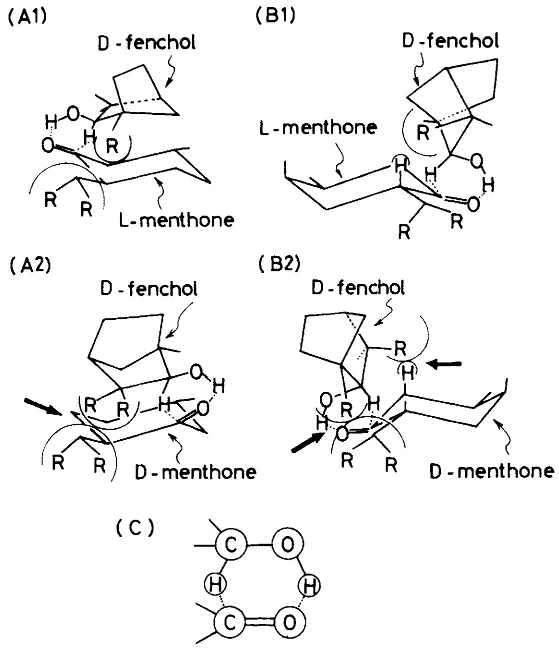

FIG. 5.—Transition-state models: arrow indicates an area of large steric hindrance.

formations of both menthol and neomenthol obey identical kinetic rules, while the structures of the transition states of these reaction are stereochemically different from each other.

From geometries of these models, it is apparent that A1 is a diastereomer of A2, and B1 is a diastereomer of B2. Futhermore, both in the formation of A2 and in the formation of B2, points of large steric hindrance appear in the areas indicated by the arrows in fig. 5. On the other hand, little steric hindrance appears in forming A1 and B1. Thus the relation $k_{\mathrm{th,L}} > k_{\mathrm{th,D}}$ representing enantiomer differentiation is reasonable.

In principle, it is expected that the differences in the structures of mutually corresponding pairs of diastereomers (A1 and A2; B1 and B2) should bring about differences both in the frequency factors and in the activation energies. At first sight the experimental result shown in fig. 4 seems to indicate that $A_{\mathrm{L}} = A_{\mathrm{D}}$ and $E_{\mathrm{L}} < E_{\mathrm{D}}$. However, the difference in activation energies is < 8 kJ mol^{-1} and its accuracy is uncertain. Therefore we can draw no conclusion from the experimental result.

ADSORPTION MODEL

Following from the reaction mechanism discussed above, the reactive menthone molecule adsorbed on the catalyst surface should be oriented according to the following restrictions: (i) the carbonyl group must be activated by contacting with the catalyst surface; (ii) the same group is open to attack by the fenchol molecule impinging from the gas phase.

Illustrated in fig. 6 are the probable adsorption models obtained by taking these

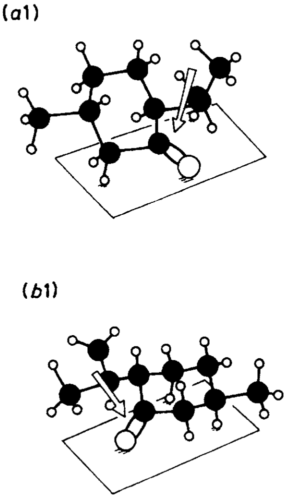

FIG. 6.—Possible models for the reactive L-menthone molecule adsorbed on the liquid-indium catalyst: arrow indicates the direction from which the fenchol molecule attacks: ○, hydrogen; ●, carbon; ◯, oxygen.

restrictions into consideration. The models are for adsorbed L-menthone: the mirror image of each gives the corresponding adsorbed state for D-menthone. From the adsorbed state *a*1, the transition state A1 results, yielding finally L-menthol. On the other hand, the transition state B1 and finally D-neomenthol result from the adsorbed state *b*1.

The authors thank Prof. S. Imaizumi for helpful discussions. Partial financial support for this work by a grant for scientific research from the Japanese Ministry of Education is also acknowleged. We are most grateful to a referee for his helpful and scholarly comments.

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