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Short Communication

A Note on the Kinetics of a Prototropic Rearrangement*

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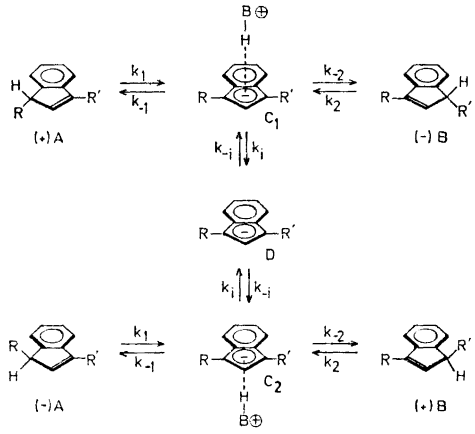
The stereochemistry of prototropic rearrangements in the indene ring-system has been studied from different viewpoints.[1–4] A kinetic treatment, based on the mechanism below, has been published [5] for the special cases where R=R′ ($k_1=k_2$ and $k_{-1}=k_{-2}$) and R′=H ($k_2=0$). The simple case with complete stereospecificity ($k_i=0$) has also been reported in detail [1–6] and the steric courses of such reactions were firmly established by the work of Cram and co-workers [3] and Bergson *et al.*[6,7] In this note, we will give some results of an investigation of a more general case where $k_1 \neq k_2 \neq 0$, $k_{-1} \neq k_{-2}$, $k_i \neq 0$ and $k_i \approx k_{-1} \approx k_{-2}$.



The substrates used in this study, 1-methyl-3-ethylindene (A, R=Me, R′=Et) and its tautomer (B), have been synthesized earlier.[6] With DMSO as solvent and piperazine or diethylamine as catalyzing base, the polarimetric behaviour of the reaction shows the characteristics (eqn. 1) of a partially stereospecific reaction. Eqn. (1) is, of course, independent of the actual mechanism proposed. This is also true for the time dependence of any linear function of the concentrations ([A]=[A$_+$]+[A$_-$] and [B]=[B$_+$]+[B$_-$]), *e.g.* the area, S, of the characteristic NMR-absorption peaks which was used in this study (eqn. 2).

$$\alpha = g_1 \exp(m_1 t) + g_2 \exp(m_2 t) \quad (1)$$

$$S = (S_0 - S_\infty) \exp(-k_r t) + S_\infty \quad (2)$$

The mechanistic interpretation of the rate constants $-m_1$, $-m_2$, and k_r, if the scheme above is adopted, is easily derived; m_1 and m_2 being the eigenvalues of the matrix $\mathbf{K}_\alpha$ and $-k_r$ is the trace of $\mathbf{K}_r$ (eqn. 5: one of the eigenvalues of $\mathbf{K}_r$ is zero). In this treatment we have assumed that the steady-state approximation is valid for the ion pairs (C_1 and C_2) and the symmetrical intermediate (D). The equilibrium constant, $K=[B]_\infty/[A]_\infty$, is related to the mechanistic rate constants or to the elements of $\mathbf{K}_\alpha$ according to eqn. (6). There is also a relation between the rearrangement rate constant, k_r, and the elements of $\mathbf{K}_\alpha$ (eqn. 7). Since m_1 and m_2 are eigenvalues of $\mathbf{K}_\alpha$, it is evident that $m_1+m_2=\lambda_1+\lambda_4$ and $m_1 m_2=\lambda_1\lambda_4-\lambda_2\lambda_3$.

* Part XV in the series "Proton-Mobility in the Indene Ring-System". Part XIV, *Arkiv Kemi* **29** (1968) 593.

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Table 1. Data from some polarimetric experiments. (Temp. 21.6°C. Solvent: DMSO-d_6. Piperazine concentration: 0.078 M. Total indene concentration: 1.00 M). The numerical calculations of the parameters were made according to Ref. 8. Equilibrium constant: 1.62±0.10 (from NMR analysis).

Run No.	$-m_1 \times 10^2$ (min^{-1})	$-m_2 \times 10^2$ (min^{-1})	g_1 (degrees)	g_2 (degrees)
1 [a]	1.146	0.161	4.332	−1.333
2 [b]	1.135	0.164	−1.580	−1.103
Mean value	1.140	0.163	–	–

[a] $\Delta B_0 = 0$ (*cf.* the text). [b] $\Delta A_0 = 0$.

$$\mathbf{K}_\alpha = -(k_{-1}+k_{-2}+k_i)^{-1}\begin{bmatrix} k_1(k_{-2}+k_i); & k_2k_{-1} \\ k_1k_{-2}; & k_2(k_{-1}+k_i) \end{bmatrix} = \begin{pmatrix} \lambda_1 & \lambda_2 \\ \lambda_3 & \lambda_4 \end{pmatrix} \quad (3)$$

$$\mathbf{K}_r = -(k_{-1}+k_{-2})^{-1}\begin{bmatrix} k_1k_{-2}; & -k_2k_{-1} \\ -k_1k_{-2}; & k_2k_{-1} \end{bmatrix} \quad (4)$$

$$k_r = (k_1k_{-2}+k_2k_{-1})/(k_{-1}+k_{-2}) \quad (5)$$

$$K = k_1k_{-2}/k_2k_{-1} = \lambda_3/\lambda_2 \quad (6)$$

$$k_r = -(\lambda_2+\lambda_3)(\lambda_1\lambda_4-\lambda_2\lambda_3)/[\lambda_2(\lambda_1-\lambda_3)+\lambda_3(\lambda_4-\lambda_2)] \quad (7)$$

The pre-exponential factors, g_1 and g_2, in eqn. (1) are functions of the specific optical rotations, the starting concentrations and the elements of $\mathbf{K}_\alpha$. As described previously,[6] the specific rotations can be eliminated, and information can be obtained about the rate constants without knowledge of the starting concentrations, provided two sets of pre-exponential factors are determined experimentally (eqns. 8 and 9). In the experiments, where ΔB is defined by $\Delta B = [B_+] - [B_-]$ and ΔA by $\Delta A = [A_+] - [A_-]$, superscript (1) refers to the condition $\Delta B = 0$, superscript (2) to $\Delta A = 0$, both conditions pertaining to the start. If the pre-exponential factors form the matrix $\mathbf{G}$, and $\mathbf{M}$ is a diagonal matrix with the elements m_1 and m_2, it is found that eqn. (10) is valid.

$$\alpha^{(1)} = g_{11}\exp(m_1t) + g_{12}\exp(m_2t) \quad (8)$$

$$\alpha^{(2)} = g_{21}\exp(m_1t) + g_{22}\exp(m_2t) \quad (9)$$

$$\mathbf{GMG}^{-1} = \begin{pmatrix} \lambda_1 & ; & \lambda_3\Delta A_0^{(1)}/\Delta B_0^{(2)} \\ \lambda_2\Delta B_0^{(2)}/\Delta A_0^{(1)} & ; & \lambda_4 \end{pmatrix} \quad (10)$$

Thus, from the observed equilibrium constant (determined in our case from NMR analysis) and the parameters in eqns. (8) and (9) (experimentally determined by polarimetry), the elements of $\mathbf{K}_\alpha$ can be calculated using eqns. (6) and (10). A test of the experimental procedure is provided by a comparison of the rearrangement rate constant predicted according to eqn. (7), with that obtained from independent NMR-kinetics. With the experimental conditions specified in Table 1, we obtained k_r (predicted) $= 1.10 \times 10^{-2}$ min^{-1} and k_r (observed, NMR) $= (1.15 \pm 0.10) \times 10^{-2} min^{-1}$.

If the mechanistic scheme above is adopted it is also possible to calculate the collapse ratio (k_{-2}/k_{-1}) and the degree of stereospecificity $((k_{-1}+k_{-2})/(k_{-1}+k_{-2}+k_i))$ according to eqns. (11) and (12). The data in Table 1 give the values 0.65 and 0.85, respectively, for these quantities. These figures are quite reasonable chemically.

$$k_{-2}/k_{-1} = \lambda_3(\lambda_2-\lambda_4)/\lambda_2(\lambda_3-\lambda_1) \quad (11)$$

$$(k_{-1}+k_{-2})/(k_{-1}+k_{-2}+k_i) = [\lambda_3(\lambda_1-\lambda_3)+\lambda_3(\lambda_4-\lambda_2)]/(\lambda_1\lambda_4-\lambda_2\lambda_3) \quad (12)$$

They should, however, be regarded as approximate since the experimental uncertainties have not been fully assessed.

It is quite clear, however, that the stereospecificity is significantly lower than 100 % when the secondary amines used in this investigation serve as catalysts. This is interesting since Cram *et al.*[3] found very high stereospecificity when a tertiary amine (DABCO) was used in a similar indene rearrangement in DMSO. Cram's observation is in full agreement with results obtained by our method for the reaction A⇌B with DABCO in DMSO. Further studies and a more detailed report will be published later.

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Studies on Orchidaceae Alkaloids

XIV.* A Phthalide Alkaloid from *Dendrobium pierardii* Roxb.

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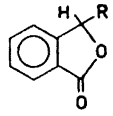
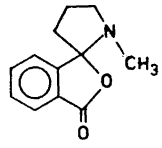
An optically active alkaloid, pierardine, 3-(3-dimethylaminopropyl)phthalide, has been isolated from *Dendrobium pierardii* Roxb. Its structure (I) resembles that of shihunine (II),[2-4] isolated from *Dendrobium lohohense* Tang *et* Wang.

The free base I was obtained as a viscous oil by purification through its hydrochloride. The molecular formula, $C_{13}H_{17}NO_2$, was established by high resolution mass spectrometry of the base and elemental analysis of its hydrochloride and its methiodide.

The presence of a phthalide group in I was indicated by its UV spectrum, which is almost superimposable on that of phthalide,[5] and supported by its IR spectrum showing a strong carbonyl band at





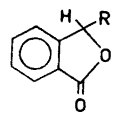
I $R=-CH_2CH_2CH_2N(CH_3)_2$ II

III $R=-CH_2CH_2CH_2\overset{\oplus}{N}(CH_3)_2\ O^{\ominus}$

IV $R=-CH_2CH=CH_2$

V $R=-CH_2CH_2CH_3$

1777 cm^{-1} in carbon tetrachloride, shifted to 1767 cm^{-1} in acetonitrile. The NMR spectrum shows four aromatic protons (τ 2.0–2.7, multiplet) and a one proton signal at τ 4.46 (multiplet) due to the benzylic hydrogen in the phthalide group. On basis of the above evidence, the following partial structure of I was indicated:



A 6 H singlet (τ 7.81) in the NMR spectrum and the base peak *m/e* 58 in the mass spectrum strongly suggest the presence of the $-CH_2N(CH_3)_2$ grouping in I. Oxidation of I with hydrogen peroxide afforded an oily *N*-oxide, which gave an NMR spectrum in which the 6 H singlet was shifted to τ 6.77. Without further purification the *N*-oxide was pyrolyzed giving the nitrogen free compound IV. The NMR spectrum of IV shows four aromatic protons, four protons in the region τ 3.9–5.1 and two allylic protons centered at τ 7.35. Catalytic hydrogenation of IV afforded V, which was indistinguishable from 3-propylphthalide (IR, NMR and MS) obtained by catalytic hydrogenation of propylidenephthalide, and hence pierardine has structure I. Attempts to elucidate the absolute configuration of pierardine are in progress.

Experimental. All melting points are corrected. Mass spectra were measured on an LKB 9000 spectrometer (ionization energi 70 eV), and with a double focussing Atlas SM 1 mass spectrograph. IR spectra were recorded

* No. XIII of this series, see Ref. 1.