Tetrahedron: Asymmetry Vol. 4, No. 12, pp. 2531-2534, 1993
Printed in Great Britain

0957-4166/93 $6.00+.00

The Isoinversion Principle for the Asymmetric Tautomerization of Photodienols.

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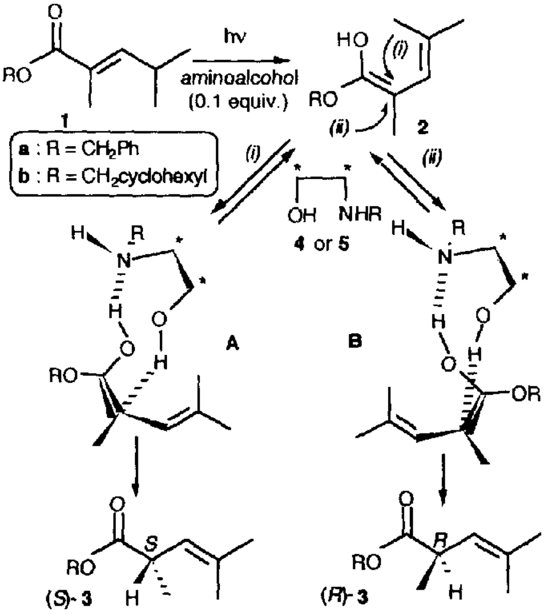
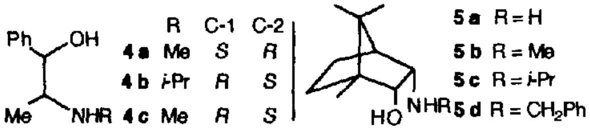
(*Received in UK* 18 *October* 1993)

Abstract: From the study of the tautomerization of prochiral dienols photogenerated in an organic solvent between -76 and +30°C in the presence of optically active aminoalcohols and in using the methodology developed by Scharf's group, the isoinversion temperature of the asymmetric process has been estimated to be -55°C.

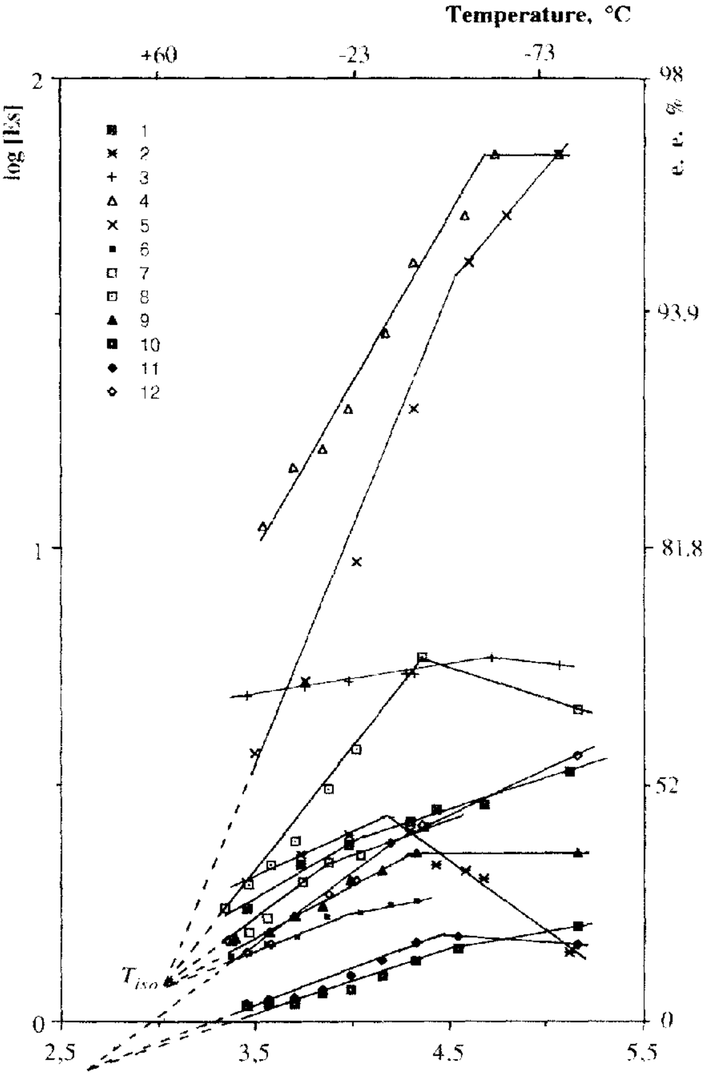


Enols play an important role in organic chemistry and intensive research work has been devoted to the keto-enol interconversion.[1] During the last few years, we have been largely concerned with the chiral proton donor-catalyzed enantioselective protonation of enols and dienols produced from Norrish-type II photoreactions.[2-4] Having established that i) a β-aminoalcohol as proton donor was required to observe a fair enantioselectivity, ii) no UV light is necessary for the tautomerization of the enol,[2f] we have assumed a model involving a nine membered transition state to rationalize the geometric constraints responsible for the enantioselective discrimination.[3] The acidity of dienols led us to consider the development of strong interactions between the enol and the aminoalcohol due to intermolecular hydrogen bond associations (scheme 1).[5,6] Therefore, we can expect that the transformation of the enol **2** into (S)-**3** and (R)-**3** involves at least two steps, one is the reversible formation of the diastereoisomeric intermediates **A** and **B**, the other is the protonation/rearrangement.



In this note, we disclose that the isoinversion principle developed on the basis of Eyring's theory[7] is applicable to the enantioselective process observed from the photodeconjugation of α,β-unsaturated esters in the presence of aminoalcohols. We report the determination of the difference of activation parameters $\Delta\Delta H^{\#}$ and $\Delta\Delta S^{\#}$ between the reaction paths leading to (*R*)-**3a** and (*S*)-**3a** from **2a** and catalytic amounts of **4a** or **5**[8] in methylene chloride. These results analyzed in conjunction with preceeding reports,[3b,7,9] have led us to determine the isoinversion temperature of the asymmetric tautomerization of dienols.

Fig. 1. Eyring diagram for the temperature dependence of the enantioselectivity in the tautomerization of dienols **2a** and **2b**.[a]



[a] For the signification of numbers 1 to 12, see Table.

The irradiation at λ = 254 nm and between -76 and +20°C of methylene chloride solutions of **1a** and any of the precedently cited aminoalcohols provided optically active **3a** in in 60-90% chemical yields. The enantiomeric excess (e.e.) of **3a**, determined by optical rotation and ^{1}H NMR in the presence of Eu(hfc)$_3$,[10] led us to plot log [Es] versus 1/T when considering that [Es] = [Major enantiomer] / [Minor enantiomer] (Fig. 1, curves 1 to 5).

From a given aminoalcohol, we can estimate that the concentration of each enantiomer is proportional to the rate constants k_R and k_S of protonation of the two enantiofaces of **2a**. Eq. 1 established from the Eyring equation,[7,11] would allow us to determine the discrimination parameters $\Delta\Delta H^{\#}$ and $\Delta\Delta S^{\#}$ for the portions of the curves of Figure 1 which correspond to straight lines. Each aminoalcohol affords two approximatively linear correlations[12] leading to two sets of activation parameters, one for T>T_{inv} and the other for T<T_{inv} (Table), T_{inv} (inversion temperature) having been described as the temperature where a change occurs in the dominance of enthalpy and entropy in the partial selectivity steps.[7] In other words, T_{inv} corresponds to the change of the slope of the said curve and is here comprised between -24 and -61°C.

$$\log [Es] = (-\Delta\Delta H^{\#} / 2.3\ R\ T) + (\Delta\Delta S^{\#} / 2.3\ R) = -\Delta\Delta G^{\#} / 2.3\ R\ T \qquad (1)$$

We also calculated $\Delta\Delta H^{\#}$ and $\Delta\Delta S^{\#}$ corresponding to precedently reported results[3b,9] obtained from **2a**, **2b** and **4a**, **4b** or **4c** using various solvents (Fig. 1, curves 6 to 12). The extrapolation of the curves of figure 1 indicates common crossing points at high temperature: one for curves 5 to 9 obtained from **2a**, an other for curves 10 to 12 produced from **2b**. Each of these points represents an isoselective temperature (T_{iso}) which corresponds to the obtention of the same enantioselectivity from various systems.[7] From Eq. 2 and each diagram $\Delta\Delta H^{\#}_{(\text{higher T})}/\Delta\Delta S^{\#}_{(\text{higher T})}$ (Fig. 2), we can determine i) T_{iso} which corresponds to the slope of the linear correlation, and ii) the e.e. at T_{iso} which is calculated from the intercept on the ordinate.[7,13] Thus, T_{iso}**2a** = +58°C with 6% e.e; T_{iso}**2b** = +125°C with 12% e.e. and an inversed configuration of the major enantiomer. However, T_{iso}**2b** remains theoretical since other processes would occur at such a temperature. The inspection of the different curves does not indicate an isoselective point at low temperatures.

$$\Delta\Delta H^{\#}_{(\text{higher T})} = -\,2.3\;R\;T_{iso}\log[\text{Es}] + T_{iso}\;\Delta\Delta S^{\#}_{(\text{higher T})} \qquad (2)$$

Table

Ester/Aminoalcohol	**1a/4a**		**1a/5a**		**1a/5b**		**1a/5c**	
Solvent	CH_2Cl_2		CH_2Cl_2		CH_2Cl_2		CH_2Cl_2	
Temperature °C	$^{-76}/_{-22}$	$^{-22}/_{+20}$	$^{-76}/_{-31}$	$^{-31}/_{+20}$	$^{-74}/_{-57}$	$^{-57}/_{+20}$	$^{-74}/_{-60}$	$^{-60}/_{+13}$
$\Delta\Delta H^{\#}$ kJ mol^{-1}	-2.3	-5.0	+5.7	-3.65	+0.9	-1.2	0	-12.5
$\Delta\Delta S^{\#}$ J mol^{-1} K^{-1}	-1.9	-12.7	+31.4	-7.1	+18.7	+8.8	+34.7	-24.2
Curve/Fig. 1	1		2		3		4	
Ester/Aminoalcohol	**1a/5d**		**1a/4a**		**1a/4a**		**1a/4b**	
Solvent	CH_2Cl_2		pentane		octane		CH_2Cl_2	
Temperature °C	$^{-74}/_{-58}$	$^{-58}/_{+16}$	$^{-40}/_{-21}$	$^{-21}/_{+27}$	$^{-42}/_{-12}$	$^{-12}/_{+27}$	$^{-78}/_{-43}$	$^{-43}/_{+30}$
$\Delta\Delta H^{\#}$ kJ mol^{-1}	-9.4	-18.3	-1.5	-3.0	-3.0	-6.4	+2.6	-10.0
$\Delta\Delta S^{\#}$ J mol^{-1} K^{-1}	-12.6	-53.8	-1.9	-7.9	-5.6	-18.6	+25.7	-29.8
Curve/Fig. 1	5		6		7		8	
Ester/Aminoalcohol	**1a/4c**		**1b/4a**		**1b/4a**		**1b/4b**	
Solvent	hexane		hexane		CH_2Cl_2		CH_2Cl_2	
Temperature °C	$^{-78}/_{-40}$	$^{-40}/_{+25}$	$^{-78}/_{-48}$	$^{-48}/_{+20}$	$^{-78}/_{-48}$	$^{-48}/_{+20}$	$^{-78}/_{-45}$	$^{-45}/_{+30}$
$\Delta\Delta H^{\#}$ kJ mol^{-1}	0	-3.9	-1.4	-2.3	+0.6	-2.8	-3.6	-5.2
$\Delta\Delta S^{\#}$ J mol^{-1} K^{-1}	+6.5	-10.2	-3.6	-7.7	+5.8	-9.3	-8.2	-15.1
Curve/Fig. 1	9		10		11		12	

Fig. 2. $\Delta\Delta H^{\#}/\Delta\Delta S^{\#}$ diagrams for the determination of isoselective points.[a]

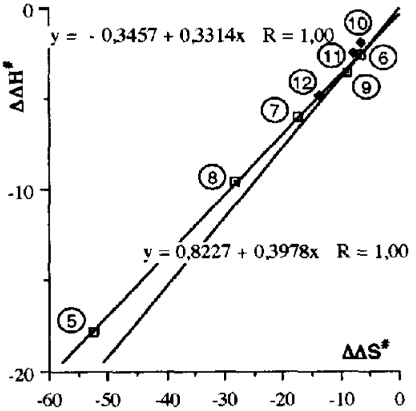
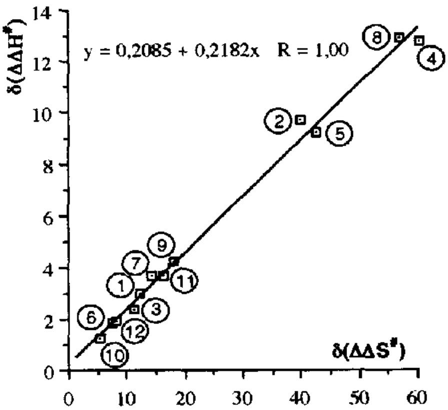


Fig. 3. $\delta\Delta\Delta H^{\#}/\delta\Delta\Delta S^{\#}$ diagram for the determination of the isoinversion temperature.[a]



[a] The circled numbers correspond to those as defined as "Curve/Fig. 1" in Table.

The relationship between $\delta\Delta\Delta H^{\#}$ and $\delta\Delta\Delta S^{\#}$ (Eq. 3, 4) of the different systems has been examined in using Scharf's methodology[7] (Fig. 3, Eq. 5). The

$$\delta\Delta\Delta H^{\#} = \Delta\Delta H^{\#}_{(\text{lower T})} - \Delta\Delta H^{\#}_{(\text{higher T})} \qquad (3)$$

$$\delta\Delta\Delta S^{\#} = \Delta\Delta S^{\#}_{(\text{lower T})} - \Delta\Delta S^{\#}_{(\text{higher T})} \qquad (4)$$

$$T_i = \partial(\delta\Delta\Delta H^{\#}) \,/\, \partial(\delta\Delta\Delta S^{\#}) = 218\ \text{K} \qquad (5)$$

linear correlation (correlation coefficient: 1) passing pratically through the origin demonstrates the isoinversion relationship, the slope of this line being precedently defined as the isoinversion temperature T_i. Therefore, the question submitted by Scharf's group in 1991[7] on the eventual application of the isoinversion principle to the enantioselective protonation of photodienols catalyzed by optically active β-aminoalcohols is now solved.[14] As stated by the German group for other reactions,[7] the systems which tautomerize dienols with high e.e. present a T_{inv} close to T_i.

Concerning the enantioselectivity of the tautomerization, we did not observe a relation between the value of T_i and the values of both T_{iso} and e.e. at T_{iso}. Indeed, the aminoalcohol **5d** allows us to reach a high e.e. from **2a** when working at $T \leq T_i$ (curve 5) although T_{iso}**2a** is relatively far from T_i and corresponds to a low calculated e.e..

In conclusion and from the isoinversion principle,[7] we can now work at around -55°C to test the efficiency of any chiral species on the asymmetric tautomerization of enols.

Acknowledgements: We gratefully acknowledge Pr Dr H.D. Scharf for the critical evaluation of our results.

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[12] Although some low temperature-correlations are determined in considering only two temperatures (Fig. 1), the strictly linear correlation issued from the diagram of Fig. 3 (*vide infra*) indicates that these lines are close to those which would be obtained in using more data.

[13] see also: B. Giese *Angew. Chem. Int. Ed. Engl.* **1977**, *16*, 125; *Acc.Chem. Res.* **1984**, *17*, 438.

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