Anomalous Equilibration of (*Z*)-*N*-[1-(1-Naphthyl)ethylidene]isopropylamine in [$^2H_4$]Methanol: a Kinetic Chimera involving an Apparent Equilibrium Overshoot

Derek R. Boyd,[a] Salim Al-Showiman,[b] W. Brian Jennings,*[b] and Valerie E. Wilson[b]

[a] *Department of Chemistry, Queen's University, Belfast BT9 5AG, N. Ireland*
[b] *Department of Chemistry, University of Birmingham, P.O. Box 363, Birmingham B15 2TT, U.K.*

Unexpected equilibrium overshoot observed during the isomerization of the title imine in [$^2H_4$]methanol is rationalised in terms of a biased kinetic deuterium isotope effect, and isomerization *via* an enamine intermediate.

As part of an investigation into imine isomerization, the equilibration of (*Z*)-*N*-[1-(1-naphthyl)ethylidene]isopropylamine, 1-$C_{10}H_7C(Me)$=$NCHMe_2$ (**1**), was studied by ^1H n.m.r. spectroscopy in several solvents by monitoring the integrated intensities of the isopropyl doublet signals of the *Z*- and *E*-isomers. Isomer equilibrations invariably follow standard reversible first-order kinetics, *i.e.* the plot of isomer abundance *vs.* time is a smooth curve terminating exponentially at the equilibrium distribution. However in the case of imine (*Z*)-(**1**) a quite anomalous plot was obtained for equilibration in [$^2H_4$]methanol solution at 20 °C (Figure 1a). The remarkable feature of the plot is that the the percentage of the *E*-isomer (initially zero) increases *beyond the equilibrium value*. This abnormal behaviour, which is reproducible, appears to breach accepted chemical principles. Thus, since the equilibrium *Z* : *E* distribution (78 : 22) is attained after *ca.* 115 min, why should the system then spontaneously diverge from the equilibrium ratio to give *Z* : *E* = 68 : 32 after 380 min, and then return again to the equilibrium distribution on long standing?

A clue to the dilemma was provided by the n.m.r. spectra as the vinylic methyl signal of both isomers (overlapping at δ 4.74) steadily decreased in intensity during the equilibrium and was barely evident at the end of the process. The *N*-isopropyl and 1-naphthyl signals maintained their total integrated intensities. As reported previously, α-protons in imines can undergo deuterium exchange in [$^2H_4$]methanol *via* imine–enamine tautomerism.[1—3] The degree of deuterium incorporation in the vinylic methyl group of (**1**) as a function of time is shown in Figure 1b. The equilibration of (*Z*)-(**1**) in CD_3OH solution gave a normal exponential plot of isomer abundance *vs.* time with no equilibrium overshoot.

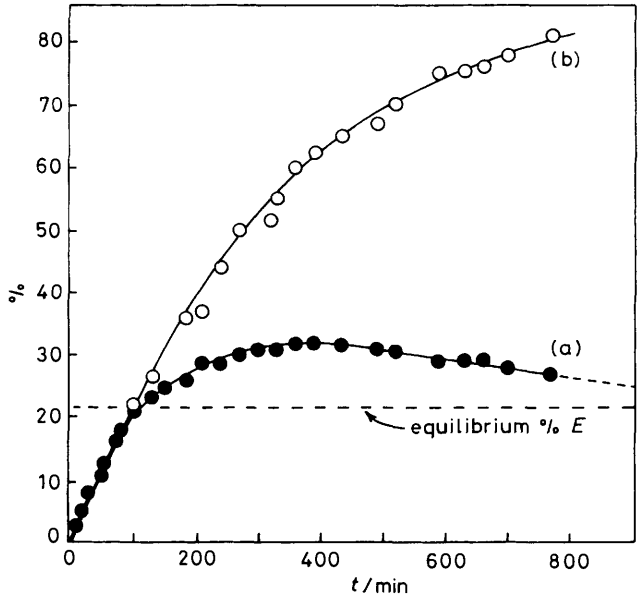
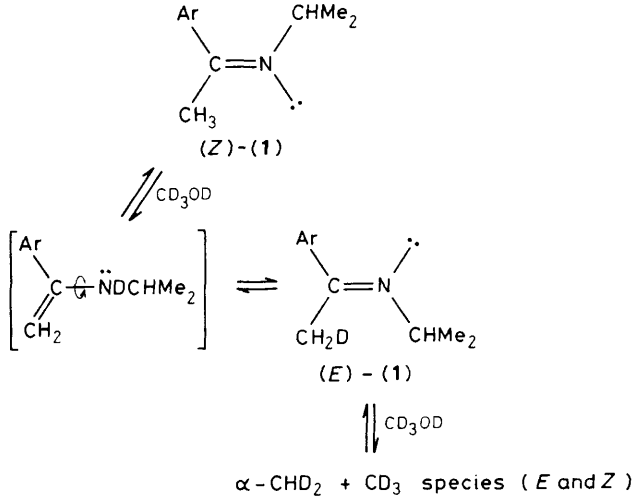


Figure 1. (a) Plot of % *E*-isomer *vs.* time for the equilibration of (*Z*)-(**1**) in [$^2H_4$]methanol; (b) deuterium incorporation (%) at the α-methyl group of (**1**) during the equilibration.

The anomalous behaviour in CD_3OD can be rationalised in terms of an isomerization mechanism involving the intermediacy of the enamine tautomer (Scheme 1) coupled with a kinetic isotope effect.† Thus, the *E*-isomer *produced by this pathway* will *initially* contain a much higher proportion of deuterium in the vinylic methyl group than the *Z*-isomer starting material. As a consequence the deuterium isotope effects will selectively retard the back reaction (*E* → *Z*) by reducing the rate of proton–deuteron abstraction. Evidently this *biased* isotope effect is sufficient to cause the proportion of the *E*-isomer to increase beyond its equilibrium value during the equilibration. On prolonged standing the deuterium becomes equally distributed between the isomers and the true thermodynamic *E* : *Z* equilibrium is finally established.

The kinetic situation in (**1**) is complicated by the presence of three exchangeable α-protons, but the magnitude of the aggregate (primary plus secondary) isotope effect can be assessed to be *ca.* 3.4 by comparing the initial isomerization rate‡ of (*Z*)-(**1**) in CD_3OD ($k_{Z\rightarrow E} = 6.0 \times 10^{-5}\ s^{-1}$ at 20 °C) with the isomerization rate§ of (*Z*)-(**1**), previously deuteriated



Scheme 1. Ar = 1-naphthyl

† There is no significant thermodynamic isotope effect; thus the *Z*–*E* equilibrium constant for α-deuteriated (**1**) in [$^2H_4$]methanol was identical to that (0.28) for the non-deuteriated (**1**) in methanol within the precision of integration (±1%).

‡ The plot of $\ln[x_e/(x_e-x)]$ *vs.* time was linear over the initial 50 min.

§ A normal exponential equilibration plot was observed in this case, and the plot of $\ln[x_e/(x_e-x)]$ *vs.* time was linear over the period studied (4 h).

(98%) at the vinylic methyl group, measured in CD_3OD ($k_{Z \rightarrow E} = 1.75 \times 10^{-5}$ s^{-1} at 20 °C).

The observation of the isotope effect and the equilibrium overshoot for imine (**1**) establishes unequivocally that this imine isomerizes in methanol solution by enamine tautomerism rather than by a conventional intramolecular pathway.

A similar equilibrium overshoot was observed during the equilibration of (*Z*-*N*-[1-(1-naphthyl)ethylidene]-methylamine (**2**) in [$^2H_4$]methanol. A larger overshoot and a measurement of the primary isotope effect might be obtained in an imine containing only a single exchangeable α-proton. However, analogues of (**1**) and (**2**) where the α-methyl group is replaced by isopropyl exist almost completely in the *Z*-configuration. The observed equilibrium overshoot in these imine systems is related to isotope equilibrium perturbational effects observed in enzyme systems by Cleland *et al.*,[4] and to the reported effects observed by Cram[5] and coworkers and Bergman[6] during racemization or epimerization of substrates in CH_3OD. An equilibrium overshoot during a structural isomerization process has also been observed by More O'Ferrall and Vernon.[7]

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