

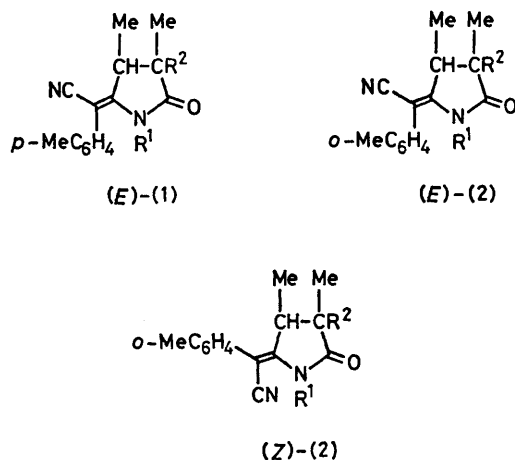
A *cis-trans* Equilibrium Isotope Effect in Arylcyanomethylenepyrrolidinones

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Summary The equilibration of three 5-arylcyanomethylene-3,4-dimethylpyrrolidin-2-ones in alkaline methanolic solutions by exchange of the C-3 hydrogen atom yields different *[cis]/[trans]* ratios for C-3-protio- than for the C-3 deuterio-compounds.

We present data on the *trans* \rightleftharpoons *cis* equilibration of the 5-(phenylcyanomethylene)-3,4-dimethylpyrrolidin-2-ones (*E*)-(1a), (*E*)-(2a), and (*Z*)-(2a) in alkaline methanol solution. These compounds were obtained by CN⁻ attack¹ on the corresponding pyrrolines.[†]



a; R¹ = R² = H **c;** R¹ = H, R² = D
b; R¹ = R² = D **d;** R¹ = D, R² = H

Under the experimental conditions chosen (see the Table), the C-H deuterium exchange proceeds slowly and only on the C-3 methine group. The exchange was followed by ¹H n.m.r. (60 MHz) spectroscopy. The methyl group resonances were identified from literature data,^{1,2} and from calculations of the anisotropy effect of the CN group.³ The results are summarized in the Table.

TABLE. *[cis]/[trans]* ratios for the equilibria of (1) and (2) in different solutions.^a

| Structure | CH ₃ OH, NaOCH ₃ | | CD ₃ OD, NaOCD ₃ ^b | |
|------------------|--|----------------------|--|---|
| | <i>[cis]/[trans]</i> | <i>[cis]/[trans]</i> | <i>[cis]/[trans]</i> ; (% deuteriated ^c at C-3) | <i>[cis]/[trans]</i> , extrapolated to 100% deuteriation at C-3 |
| (<i>E</i>)-(1) | 0.18 ± 0.05 | 0.15 ± 0.05 | 0.55 ± 0.04 (83 ± 2) | 0.67 ± 0.06 |
| (<i>E</i>)-(2) | 0.28 ± 0.05 ^d | 0.25 ± 0.05 | 0.54 ± 0.04 (78 ± 3) ^d | 0.54 ± 0.06 |
| (<i>Z</i>)-(2) | 0.20 ± 0.05 | — | 0.54 ± 0.04 (83 ± 4) | 0.65 ± 0.06 |

^a Calculated by ¹H n.m.r. spectroscopy. [sodium alkoxide] = 0.07 ± 0.01 mol l⁻¹, [(*E*)-(2)] = 0.22; [(*E*)-(1)] and [(*Z*)-(2)] = 0.12 mol l⁻¹. ¹H N.m.r. shifts are available on request from the authors. ^b The concentrations at equilibrium for the non-deuteriated isomer at C-3 (**d** series) show the same *[cis]/[trans]* ratio as the **a** series. ^c Calculated by ¹H n.m.r. spectroscopy, and from the mass spectra of compounds of the **c** series. ^d This value has been confirmed by ¹H n.m.r. spectroscopy at 200 MHz.

[†] All products were identified by i.r., ¹H n.m.r., and mass spectra. The compounds of the **b** series were identified by comparison with those of the **c** series, and were obtained by deuteration of the **a** series compounds. (*Z*)-(2a) was obtained as a byproduct of the reaction to give (*E*)-(2a), and separated by preparative t.l.c.

The relatively high proportion of *cis*-compound of the **a** series can be explained by a fixing of the five-membered ring in a twist-envelope conformation owing to the presence of the exocyclic CO and CC double bonds.⁴ The increase in the proportion of the *cis*-isomers of the **b** series at equilibrium represents a $\Delta G_{\text{H}}^{\circ} - \Delta G_{\text{D}}^{\circ}$ difference of 3.0–3.4 kJ mol⁻¹ for the *trans* \rightleftharpoons *cis* transformation. These values allow the observation of the increase in the deuteriated *cis*-isomer because $\Delta G_{\text{H}}^{\circ}$ is only about 4 kJ mol⁻¹. Nevertheless, the difference $\Delta G_{\text{H}}^{\circ} - \Delta G_{\text{D}}^{\circ}$ seems too large to be attributed to any single effect, e.g. dipole moment change,⁵ variation of the rotational entropy (0.02 J K mol⁻¹, calculated from the moments of inertia⁶ by means of the program COORD⁷), etc. Work is in progress to clear up this point.

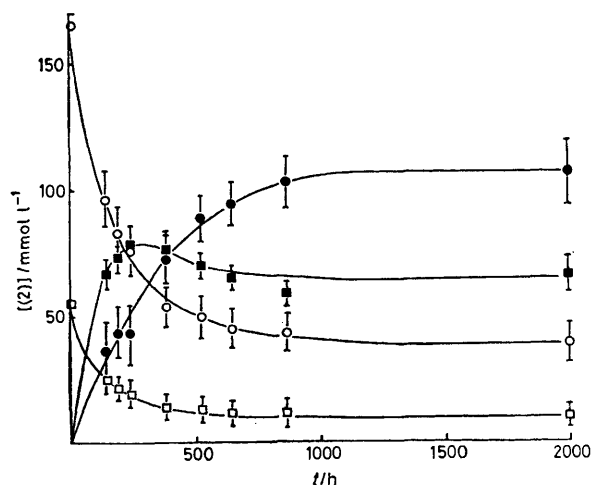


FIGURE. The variation of concentrations in the deuterium exchange experiment with (*E*)-(2a) at 37 °C: ○, *trans*-(*E*)-(2d); □, *cis*-(*E*)-(2d); ●, *trans*-(*E*)-(2b); ■, *cis*-(*E*)-(2b).

From the deuterium exchange the kinetic isotope effect can be observed qualitatively, since the time needed for equilibration is shorter for the protio-series than for the deuterio-series. The Figure shows the variation in con-

centration of the four components during the exchange experiment with (*E*)-(2) [the initial concentrations of *cis*- and *trans*-(*E*)-(2a) do not correspond to the equilibrium concentrations¹]. The concentration of the *cis*-deuteriated compound reaches a maximum before equilibrium and initially the rate of its formation is greater than the rate of the formation of the *trans*-deuteriated compound. We interpret this result on the basis of the different kinetic isotope effect during reprotonation to *cis*- or to *trans*-compounds.

The values obtained must be treated with some caution owing to the experimental technique used (60 MHz n.m.r. spectroscopy); however the dramatic isotope effect is easily detectable. The main aim of this report is not to give accurate [*cis*]/[*trans*] ratios but to point out this isotope effect to induce other workers to verify its existence in *trans* \rightleftharpoons *cis* systems where ΔG° is near zero.

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⁷ Quantum chemistry program exchange, program no. 136, Chem. Dept., Indiana University, Indiana.