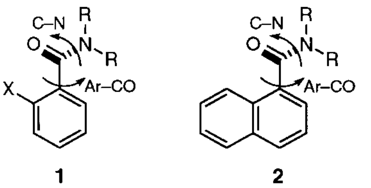
Concerted Rotation in a Tertiary Aromatic Amide: Towards a Simple Molecular Gear**

Jonathan Clayden* and Jennifer H. Pink

The design of molecular analogues of macroscopic mechanical components is an important part of any attempt to construct devices capable of doing mechanical work[1] or of storing or transmitting information on a molecular scale.[2] Recent developments in this field have included the design and synthesis of molecular brakes and switches,[3–5] ratchets,[6] turnstiles,[7] and gears,[8, 9] and we have shown that a series of conformationally interlocked tertiary amides can act as a device for the transmission of stereochemical information.[10] Subsequent to the pioneering studies of Mislow and Iwamura,[8] most investigations into molecular gears have addressed the question of concerted rotation in relatively complex triptycyl-based systems.[11] We have now studied a much simpler type of molecule as a possible molecular gear, a tertiary aromatic amide, and show here that two dynamic processes—rotation about the C–N and Ar–CO bonds—can be concerted.

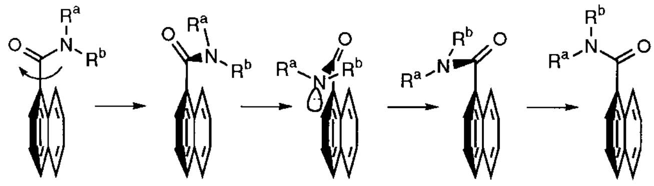
In the ground states of tertiary 2-substituted benzamides **1**[12] and 1-naphthamides **2**[13] (Scheme 1) the amido group lies perpendicular to the aromatic ring, and barriers to rotation about the aryl–CO bonds are typically greater than 65 kJ mol^{-1}.[14] In common with all amides, **1** and **2** also possess rotationally restricted C–N bonds, with barriers to exchange of the two R groups comparable in magnitude to the Ar–CO barrier.[15]



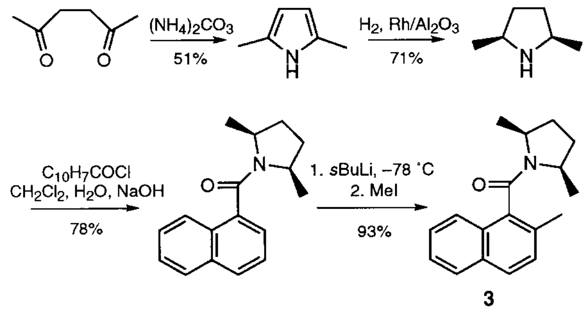
1 **2**

Scheme 1. Slow bond rotations in the tertiary aromatic amides **1** and **2**.

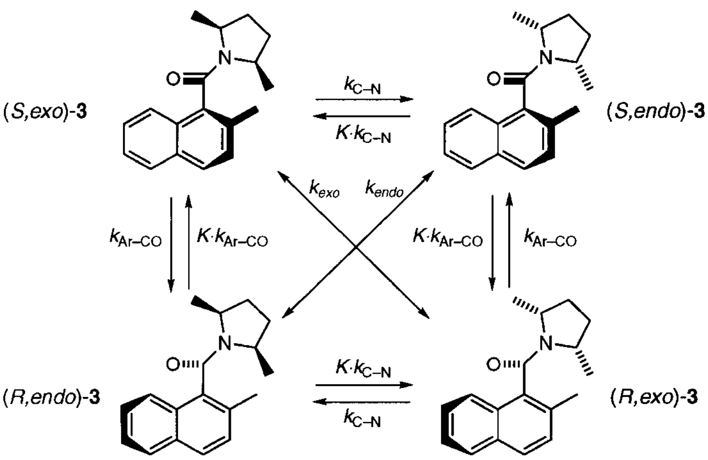
Variable-temperature NMR studies[16] permitted us to show that the barriers to rotation about both the aryl–CO and C–N bonds of *N,N*-diisopropylnaphthamide **2** (R = *i*Pr) are remarkably similar: 75 ± 1 kJ mol^{-1},[17] which raises the possibility that the two processes might in fact be concerted. Scheme 2 shows a mechanism for concerted Ar–CO and C–N rotation. At the transition state the carbonyl group loses conjugation with the lone electron pair on nitrogen, but this is compensated to some extent by increased conjugation with the aromatic ring.[18] Amide conjugation is regained most smoothly when motion of the alkyl substituents R^a and R^b is interlocked with rotation around the Ar–CO bond. Concerted rotation would imply correlation between two processes: isomerization of **2** to its enantiomer and exchange of the two groups carried by the nitrogen atom; indeed, such a correlation has been hinted at by one previous study.[19, 20]



Scheme 2. Concerted rotation in **2**.



Scheme 3. Synthesis of **3**.



Scheme 4. Stereoisomers of **3** and their interconversion.

The assignment problem associated with the individual methyl groups of **2** led us to design **3** as a better substrate for investigating concerted rotation; our synthesis of **3** is shown in Scheme 3. Amide **3** has a number of important features. It can exist in two diastereoisomeric conformations, *endo*-**3** and *exo*-**3**, which can interconvert by rotation about either the C–N bond or the Ar–CO bond (Scheme 4). Each diastereoisomers is chiral, and enantiomerization requires both Ar–CO *and* C–N rotation, either concerted or sequential. The 2-methyl group of **3** serves to slow these two processes to the point that the four conformers become atropisomers, and, indeed, we found them to be separable at room temperature by HPLC on a chiral stationary phase. Separation of a mixture

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of (±,*exo*)-**3** and (±,*endo*)-**3** on a Chiralpak-AD column produced three fractions, one of which contained both (*R*,*exo*)-**3** and (*R*,*endo*)-**3**, which were then readily separated by HPLC on achiral silica. Both (*S*,*exo*)-**3** and (*S*,*endo*)-**3** were obtained with a purity of greater than 96% from the Chiralpak-AD column. Relative configurations were assigned by NOE experiments; absolute stereochemistry was established by comparisons between the retention times of the two enantiomers on a chiral Whelk-O1 column and by use of the Pirkle model[19] for binding to this chiral stationary phase.

We then allowed samples of (*S*,*exo*)-**3** and (*S*,*endo*)-**3** to equilibrate with their stereoisomers by separate incubations in hexane at 33 °C, with analysis of the resulting product mixtures at regular intervals (Figures 1 and 2). Kinetic analysis is simplified by the fact that enantiomeric processes must have identical activation energies; moreover, the value of *K*, the quantitative ratio of (±,*exo*)-**3** to (±,*endo*)-**3** at equilibrium, could be determined accurately by HPLC to be (1.28 ± 0.02) and confirmed by NMR studies. Four mechanistic rate constants are involved: $k_{\mathrm{Ar-CO}}$ for rotation about the aryl–CO bond (*exo* to *endo*), $k_{\mathrm{C-N}}$ for rotation of the *exo* isomer about the C–N bond (*exo* to *endo*), and k_{exo} and k_{endo} for the proposed concerted isomerizations of the two diastereoisomers to the corresponding enantiomers. Rates for the reverse Ar–CO and C–N rotations (*endo* to *exo*) are then related to $k_{\mathrm{Ar-CO}}$ and $k_{\mathrm{C-N}}$ by the equilibrium constant *K*. Approximate values for all these rate constants were obtained when quartic curves were fitted to the early data points shown in Figures 1 and 2, and the gradient at $t = 0$ was derived. It is immediately clear from these plots that the rate at which both (*S*,*exo*)-**3** and (*S*,*endo*)-**3** enantiomerize is greater than the rate at which rotation occurs about the Ar–CO bond; therefore, rotation about the Ar–CO bond must be concerted to some degree with rotation about the C–N bond.

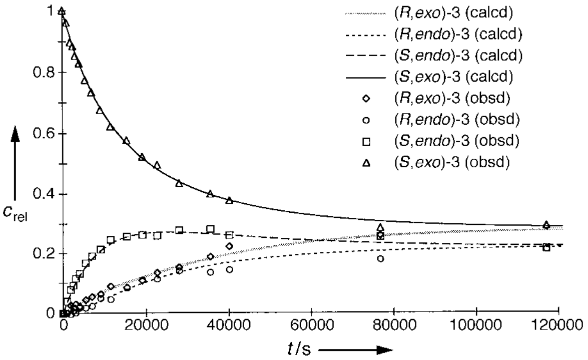

Figure 1. Equilibration of (*S*,*exo*)-**3**.

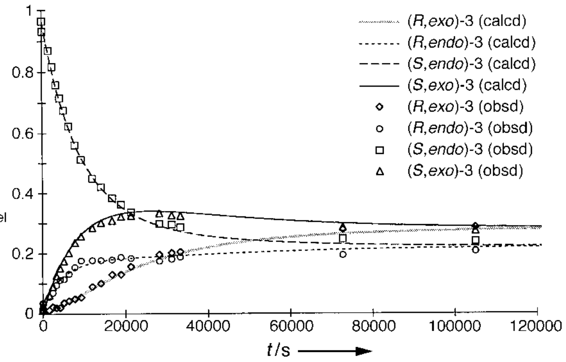

Figure 2. Equilibration of (*S*,*endo*)-**3**.

The system was modeled through a calculation of its evolution over time intervals of 250 s;[21] small adjustments to the derived rate constants $k_{\mathrm{Ar-CO}}$, $k_{\mathrm{C-N}}$, k_{exo}, and k_{endo} permitted the resulting plots to be fitted to the experimental data. The correspondence between the modeled and observed evolution of the system is shown in Figures 1 and 2, and provides strong evidence for the validity of our kinetic analysis. Table 1 presents the rate constants for the four processes at 33 °C along with the corresponding calculated free energy of activation $\Delta G^{\neq}$. The fact that k_{exo} and k_{endo} are not zero confirms that concerted rotation takes place; because k_{exo} and k_{endo} are an order of magnitude larger than $k_{\mathrm{Ar-CO}}$, at least 90% of the rotations about the Ar–CO bond are concerted with rotation about the C–N bond. As $k_{\mathrm{C-N}}$ has the same value as $k_{\mathrm{exo}} + k_{\mathrm{endo}}$, C–N rotations must also be free to occur without coupling to other rotations, and must occur about as frequently as concerted C–N and Ar–CO rotations. Unconcerted Ar–CO rotations are presumably rare for steric reasons; although unconcerted C–N rotations are not sterically hindered, rotation of the two bonds in concert permits the carbonyl group to exchange N-C=O conjugation, which must be lost at the transition state, for Ar-C=O conjugation.

Table 1. Kinetic parameters for the equilibrations of (*S*,*exo*)-**3** and (*S*,*endo*)-**3**.

	k (33 °C) [10^{-5} s^{-1}]	$\Delta G^{\neq}$ [a] [kJ mol^{-1}]
$k_{\mathrm{C-N}}$	3.9 ± 0.8	100.8 ± 0.5
$k_{\mathrm{Ar-CO}}$	0.1 ± 0.05	110 ± 1.5
k_{exo}	1.0 ± 0.1	104.3 ± 0.3
k_{endo}	2.9 ± 0.6	101.6 ± 0.5

[a] Determined at 33 °C from the Eyring equation..

The lower energy barrier for concerted isomerization of the *endo* isomer to the corresponding enantiomer is not unexpected: The amido nitrogen atom can pass over the 2-position of the naphthyl ring without steric crowding between the pyrrolidine methyl groups and the naphthyl 2-methyl group. Concerted isomerization of the *exo* isomer to the corresponding enantiomer requires the pyrrolidine methyl groups to straddle the naphthyl 2-methyl group, or the amido nitrogen atom to pass over the more rigidly bonded hydrogen atom at the 8-position of the naphthyl ring.

Although amide **3** displays a degree of gearing between the Ar–CO and C–N rotations, the barrier to gear slippage is low; a better interpretation of the dynamics of **3** might be that Ar–CO rotation is "gated"[22] by C–N rotation. Simple "two-toothed" molecular gears have received little attention alongside their three-[8] and four-toothed[9] cousins, but they seem particularly well suited for use as devices for the storage and transmission of binary information.

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High-Pressure Soft X-Ray Absorption Spectroscopy: A Contribution to Overcoming the "Pressure Gap" in the Study of Heterogeneous Catalytic Processes

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Thomas Schedel-Niedrig,* and Robert Schlögl

*Dedicated to Professor Sir John Meurig Thomas
on the occasion of his 65th birthday*

X-ray absorption spectroscopy (XAS) is an important tool in the study of gas–solid reactions and their products.[1] In the past few years in situ techniques have attained great importance in the field of heterogeneous catalysis.[2] Studies under reaction conditions close to those found in practice are necessary, because the structure of a catalyst under reaction conditions can be significantly different from that after the reaction or ex situ. To allow any relevant interpretation, an in situ measurement requires the simultaneous detection of spectroscopic data together with the conversion from the gas phase. Silver, copper, or molybdenum catalysts are used in technical processes for the conversion of methanol into formaldehyde.[3] These are well-suited to the study of the principles of chemical reactions on various surfaces due to the apparent clarity of the possible courses of reaction.[4] The oxidation of methanol on pure silver has shown, for example, that catalytic reactions under model conditions in ultra high vacuum (UHV) can take a different course to those under practicle conditions.[5–7] Three different types of atomic oxygen were identified by surface science studies of silver that was subjected to oxygen under pressure in a manner that is used in practice;[5, 8–10] their positions are shown in Figure 1. The critical oxygen pressure at which qualitative differences to the UHV model conditions in the surface chemistry of the Ag–O system were observed was 0.1 mbar. The only differences observed up to an oxygen partial pressure of 1000 mbar were in the reaction kinetics of the formation processes involved. With increasing temperature, atomic oxygen is initially formed on the surface (O_α). At a critical level of pressure and temperature, it then migrates under the surface to occupy interstitial sites in the silver crystal (O_β).[11] On increasing the temperature still further, a new form of oxygen is formed from the O_β species and, parallel to this, directly from the gas phase. The new form is incorporated into the top atomic layer of the crystal (O_γ) and interacts strongly with the silver centers. This state differs from that of a metal oxide—silver oxide is no longer thermodynamically stable at temperatures of formation above 600 K—both in structure and in that its existence is strictly limited to a single atomic layer. [5, 8–10]

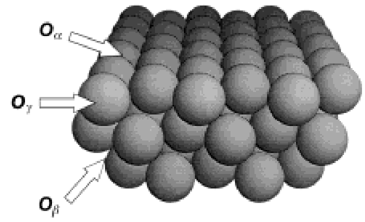

Figure 1. Schematic depiction of the Ag(111) surface treated with oxygen. The atomic oxygen species O_α, O_γ, and O_β were characterized by surface-sensitive spectroscopic techniques.[5–13] The chemisorbed O_α species and the O_γ species bonded in the surface layer are responsible for the oxide hydrogenation and the dehydrogenation of methanol.[12, 13] The O_β species acts as a reservoir for both surface species during the catalytic oxidation of methanol.

The oxidation of a methanol molecule can either occur by dehydrogenation with loss of one hydrogen molecule and the formation of formaldehyde [Eq. (1)], or by oxide hydrogenation or total oxidation with loss of hydrogen and simultaneous uptake of oxygen to give water and formaldehyde or water and carbon dioxide [Eqs. (2) and (3)].

$$CH_3OH \xrightarrow[Ag]{O_\gamma} CH_2O + H_2 \qquad (1)$$

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