CHEMISTRY

# Roaming Reaction Pathways Along Excited States

The photodissociation of $NO_3$ into NO and $O_2$, an important atmospheric reaction, has no transition state but proceeds via an O atom roaming around the $NO_2$ core.

**Meredith J. T. Jordan and Scott H. Kable**

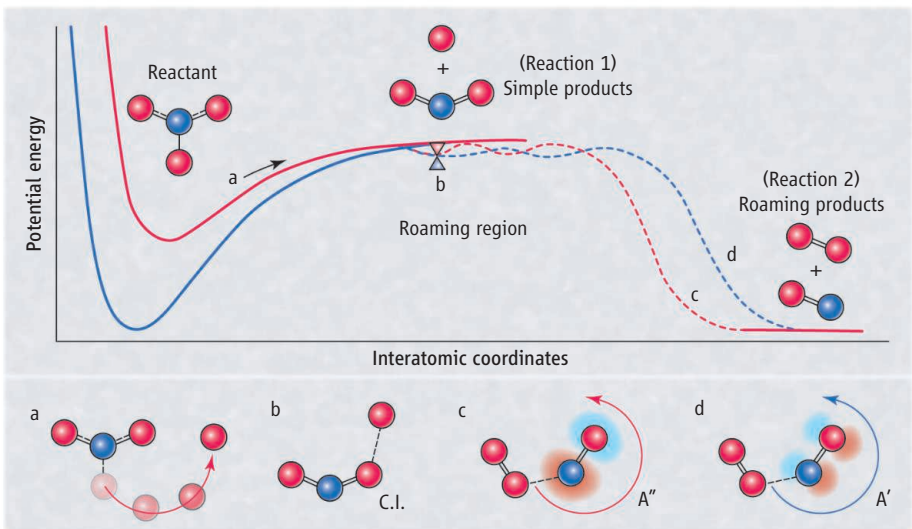
Transition state theory (TST) describes chemical reactions in terms of "reaction coordinates," usually the coordinates of atoms involved in breaking and forming bonds. Typically, there is an energetic barrier, the transition state (TS), between reactants and products. In 2004, a reaction mechanism was reported that seemingly defied the tenets of TST (*1*). In the photodissociation of $H_2CO$, one of the hydrogen (H) atoms "roamed" around the periphery of the HCO core, with no apparent reaction coordinate, and abstracted the other H atom to form $H_2$ and CO. The roaming products showed characteristic product-state distributions, distinct from those arising from a standard TS mechanism. On page 1075 of this issue, Grubb *et al*. (*2*) use detailed state-selective correlated experiments, together with theoretical calculations, to show that the photodissociation of $NO_3$ into NO and $O_2$, an important reaction in the atmosphere, occurs via roaming reactions on both the electronic excited state and the ground state of $NO_3$.

Roaming reactions are at odds with the simple TST picture of chemical reactivity. Since 2004, roaming has been implicated in dozens of photochemical reactions, in thermal reactions, and in shock tube studies (*3*). Indeed, a consensus is emerging that any barrierless bond-cleavage process might have a roaming mechanism alongside.

The $NO_3$ radical studied by Grubb *et al*. is an important oxidant in atmospheric chemical cycles. During the day, $NO_3$ is rapidly photolyzed, forming either $NO_2$ and O (reaction 1) or NO and $O_2$ (reaction 2):

$$NO_3 \rightarrow NO_2 + O \quad (1)$$
$$\rightarrow O_2 + NO \text{ (low rotation)} \quad (2a)$$
$$\rightarrow O_2 + NO \text{ (high rotation)} \quad (2b)$$

Reaction 1 is a straightforward barrierless N–O bond cleavage (*4*). The mechanism for reactional 2, however, has remained a mystery. No TS has been found at photon energies of relevance in the atmosphere. To add to the mystery, reaction 2 shows two distinct product state distributions, suggesting two distinct pathways (*5*). In reaction 2a, the NO is in a low rotational state, and the excess energy is carried by a highly vibrationally excited $O_2$. In reaction 2b, the excess energy is carried by a highly rotationally excited NO, and the $O_2$ is vibrationally cold. The product-state distributions from reaction 2a have the same characteristics as the roaming reaction in $H_2CO$ photolysis (*1*, *5*), which suggests that a similar roaming mechanism on the ground (X) state of $NO_3$ is responsible. Reaction 2b had been thought to arise from an undiscovered TS. Recently, however, it was proposed that roaming in the first excited (A) electronic state of $NO_3$ might be responsible (*6*).




**Where the O atoms roam.** The schematic shows the energetics of the formation of products of $NO_3$ photodissociation from roaming on two electronic states. The structures corresponding to various points along the reaction (a to d) are shown below. (a) An O atom almost dissociating to $NO_2$ + O, but instead roaming around the core on the excited state in the van der Waals region. There is a conical intersection (C.I.) in the roaming region, which extensively mixes the ground and excited states (b). From here, the system can return to reactant in either state or produce products on either state. The A″ and A′ Λ-doublet states of the NO product (c and d) reveal which electronic state is responsible for the molecular products.

The pathways from the X and A states to products formed by reaction 1 and the roaming products formed by reaction 2a and reaction 2b are shown in the figure (the ground state in blue and the excited state in red). Photoexcitation results in rapid production of $NO_3$ in the A state (*6*). Slightly below the $NO_2$ + O asymptote is the roaming region, shown as dashed lines.

If the incipient O + $NO_2$ products have insufficient relative translational energy, the O atom roams around the $NO_2$ core in the region of van der Waals contact (see a in the figure). Morokuma and co-workers have identified several local minima and transition states in this region on both X and A states (*6*), illustrated by the wavy lines. They also identified a conical intersection (C.I.) in the roaming region that facilitates efficient internal conversion between the two electronic states (see b in the figure). Roaming pathways on both states lead to the same products, so the experimental challenge was to distinguish the two mechanisms.

Fortunately, $NO_3$ is a radical with an unpaired electron, and Grubb *et al*. used the alignment of this electron (in the pπ orbital of the NO fragment of $NO_3$) as a fingerprint of roaming on the X and A states (*5*). When the departing NO fragment spins away from its $O_2$ partner, the lobe of the pπ orbital may lie in, or out of, the NO plane of rotation (see c and d in the figure). These are manifest as spectroscopically distinct Λ-doublet states of the free NO radical. Grubb *et al*. found that reaction 2b (rotationally excited

School of Chemistry, University of Sydney, Sydney, NSW, 2006 Australia. E-mail: scott.kable@sydney.edu.au; m.jordan@chem.usyd.edu.au







Published by AAAS

NO) was associated almost exclusively with the A″ Λ-doublet state (see d in the figure), which is consistent only with reaction on the excited electronic state. NO formed via reaction 2a (rotationally cold) had a larger contribution from the A′ Λ-doublet component (d), in agreement with theoretical predictions for reaction on the ground state. Thus, all atmospheric production of NO + $O_2$ from $NO_3$ is mediated by roaming O atoms.

Grubb *et al*. not only solve a long-standing puzzle in atmospheric chemistry but also demonstrate roaming on an excited electronic state, which may be observed in other reactions. We can reflect on what properties of the A state of $NO_3$ might be important in supporting roaming. First, because of symmetry restrictions, the A state cannot radiate back to the ground state. Second, the only energetically accessible conical intersections between the A and X states are in the roaming region of configuration space. (*6*). Third, the A state is nested inside the X state and correlates with the same asymptotic products; no repulsive states cross the A state. These three factors together mean that the A state is metastable, and this long lifetime is likely to be crucial for roaming.

Roaming on the X and A states involves very large excursions on the potential energy surfaces in regions where the difference in electronic energy is very small. These dynamics are ripe for the breakdown of the Born-Oppenheimer approximation. Recently, roaming was also implicated in photoisomerization (*7*). If roaming contributes to dissociation, isomerization, and nonradiative curve crossings, and is as ubiquitous as it appears, then the challenge to incorporate roaming into reaction schemes and kinetic models is considerable indeed.


**References**

1. D. Townsend *et al*., *Science* **306**, 1158 (2004).
2. M. P. Grubb *et al*., *Science* **335**, 1075 (2012).
3. J. M. Bowman, B. C. Shepler, *Annu. Rev. Phys. Chem.* **62**, 531 (2011).
4. H. F. Davis *et al*., *J. Phys. Chem.* **97**, 2172 (1993).
5. M. P. Grubb *et al*., *J. Phys. Chem. A* **115**, 3218 (2011).
6. H. Xiao *et al*., *J. Phys. Chem. Lett.* **2**, 934 (2011).
7. M. L. Hause *et al*., *Nat. Chem.* **3**, 932 (2011).


10.1126/science.1218767

CELL SIGNALING

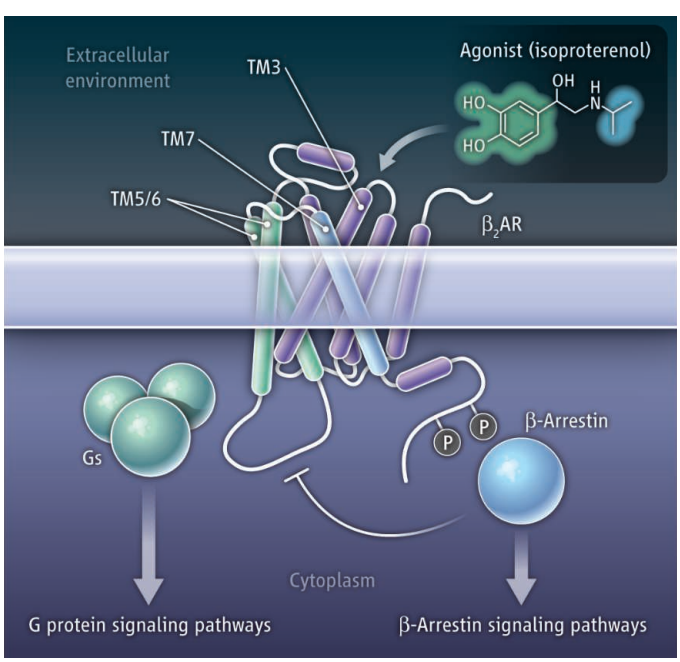
# Structural Origins of Receptor Bias

Agonists can elicit pathway-specific conformational changes in a G protein–coupled receptor.

**Stephen R. Sprang and Jackson Chief Elk**

Humans express more than 800 G protein–coupled receptors (GPCRs), through which myriad physiological, immune, and neurophysiological processes are regulated (*1*). These receptors are embedded in the cell's plasma membrane and bind to extracellular chemical stimuli (agonists). This interaction induces conformational changes in the receptor that converge at intracellular sites that bind to either heterotrimeric guanine nucleotide–binding proteins (G proteins) or to β-arrestin proteins that block G protein binding and lead to receptor desensitization and internalization, as well as provide a scaffold for protein regulatory complexes that control gene expression (*2*). Many agonists induce functionally selective or biased states of the receptor, wherein one pathway is activated with greater efficacy than another (*3*). Thus, GPCRs are not simple on-off switches, but can adopt multiple conformational states to control diverse processes. On page 1106 of this issue, Liu *et al*. (*4*) provide clues as to how a GPCR called the $\beta_2$-adrenergic receptor ($\beta_2$AR) can tune its conformation to achieve a balance of functional outcomes, as directed by the chemical structure of the receptor agonist.

Like all GPCRs, the polypeptide chain of the $\beta_2$AR traverses back and forth across the membrane, forming a series of seven-transmembrane (TM) α helices (see the figure). Ligands occupy a site that is deep within the receptor but accessible to the extracellular environment. Adrenergic receptor agonists are typically composed of a cyclic aromatic "head" group and an alkyl-amine "tail." Crystal structure analyses of the $\beta_1$AR and $\beta_2$AR reveal that the head group reinforces contacts between TM5 and TM6, whereas the amine substituent stabilizes interactions between TM3 and TM7 (*5*, *6*). Conformational changes upon ligand binding follow a common theme in the three activated GPCRs, including the $\beta_2$AR, that have so far been crystallized (*7*–*9*). Local structural perturbations induced by agonist binding are transduced into a concerted outward displacement of TM5 and TM6, which opens a pocket on the intracellular surface of the receptor that accepts the G protein. Binding of β-arrestin to GPCRs requires the addition of phosphate groups at specific sites on the intracellular surface of the receptor by GPCR protein kinases. This phosphorylation occurs at a separate site, beyond TM7, toward the C terminus of the receptor. Structural changes




**Functionally selective.** Binding of agonists to the $\beta_2$AR results in conformational changes that displace TM5 and TM6 (green) and/or TM7 (blue). The conformational changes permit G protein (Gs) binding or receptor phosphorylation (P) and β-arrestin binding. β-arrestin binding blocks G protein signaling. The aromatic moiety of the agonist (isoproterenol shown) contacts TM5 and TM6, whereas the hydroxylamine substituent interacts with TM3 and TM7.

CREDIT: C. BICKEL/*SCIENCE*

Center for Biomolecular Structure and Dynamics, University of Montana, Missoula, MT 59812, USA. E-mail: stephen.sprang@umontana.edu

# Roaming Reaction Pathways Along Excited States

Meredith J. T. Jordan and Scott H. Kable

*Science* **335** (6072), 1054-1055.
DOI: 10.1126/science.1218767