SUPPORTING MATERIAL

Steric and Electronic Influences on the Torsional Energy Landscape of Retinal

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Computational Methods

QM calculations were performed with Gaussian 03 (1) or Spartan'08 (2) on each model compound. Geometry optimizations used the 6-31G** basis set at the Hartree-Fock level; energies were computed for the optimized structures with second-order Møller-Plesset (MP2) perturbation theory to treat electron correlation. All optimizations were performed to default tolerances and all degrees of freedom were allowed to relax except for specific dihedrals as described below. To examine basis set effects, we computed single point energies for energy minima and maxima of the largest model compounds (MP2 level of theory with a cc-pVTZ basis set), and found only negligible changes in energy barriers of 3% or less. Molecular mechanics (MM) calculations were performed using the program CHARMM (3) without truncation of intermolecular forces. Torsional parameters for the methyl groups in retinal were fit to reproduce the QM energy surfaces described in the main text. Force field parameters for the remaining degrees of freedom were unchanged from those distributed with CHARMM.

Supporting Data

Table S1. Force field parameters, consistent with the CHARMM force field, for methyl rotation in neutral unsaturated alkenes based on the QM results in Figure 2. For comparison, previous MD simulations of retinal typically set the methyl torsion force constants to zero (4), i.e. they were not explicitly parameterized but rather relied solely on the non-bonded terms to determine the potential energy.

Atom types	K_ϕ	n	δ
CC2-CC1A-CT3-HA	0.0201	3	180
CC1A-CC1A-CT3-HA[a]	0.0640	3	180
CC1A-CC1B-CT3-HA[b]	0.0640	3	0

[a] CC1B-CC1B-CT3-HA uses the same force field parameters as CC1A-CC1A-CT3-HA.
[b] CC1B-CC1A-CT3-HA uses the same force field parameters as CC1A-CC1B-CT3-HA.

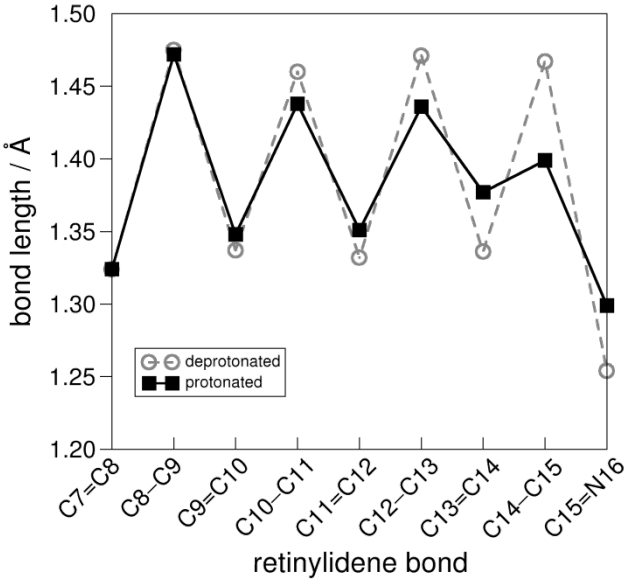

Figure S1. Protonation of the Schiff base decreases single bond length and increases double bond length. Data for bond lengths are taken from MP2 calculations performed on model compounds **8** (protonated) and **9** (deprotonated).

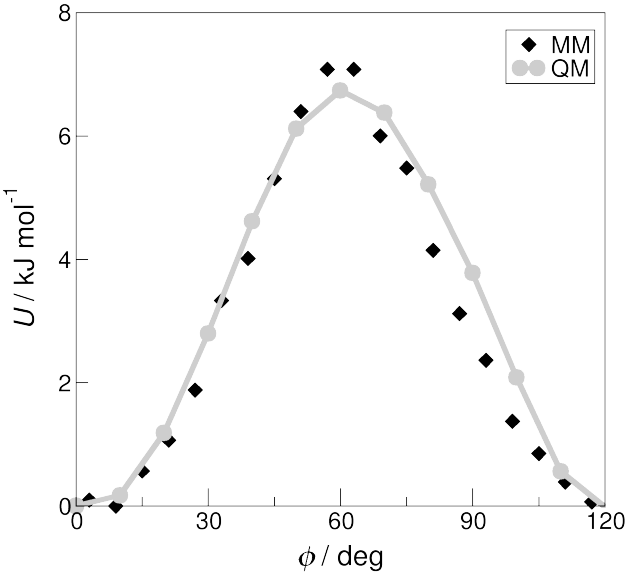

Figure S2. Comparison of QM (circles) and MM (diamonds) methyl torsion angle energies for C1-Me (equivalent to retinal C5-Me group) in compound **10**. Note that use of current CHARMM parameters for methyl dihedrals accurately reproduces the QM results.

Topologies of model compounds 1, 2, 5, 8, 9, and 10.

All topologies are in CHARMM format.

```
RESI 2MBD       0.00 ! 2-methyl, 1,3 butadiene
!
GROUP
ATOM C1  CC2   -0.42 !
ATOM H11 HE2    0.21 !
ATOM H12 HE2    0.21 !
ATOM C2  CC1A   0.00 !     H51    H52
GROUP                !        \  /
ATOM C3  CC1B  -0.15 ! H11     C5-H53
ATOM H31 HE1    0.15 !    \    /
ATOM C4  CC2   -0.42 !    C1=C2      H41
ATOM H41 HE2    0.21 !    /    \    /
ATOM H42 HE2    0.21 ! H12     C3=C4
GROUP                !         /    \
ATOM C5  CT3   -0.27 !       H31     H42
ATOM H51 HA     0.09 !
ATOM H52 HA     0.09 !
ATOM H53 HA     0.09 !

RESI 3MHT       0.00 ! 3-methyl 1,3,5 hexatriene
!
GROUP
ATOM C7   CC2  -0.42 !
ATOM H71  HE2   0.21 !
ATOM H72  HE2   0.21 !    H192    H193   H101    H121
ATOM C8   CC1A -0.15 !        \   /      |      /
ATOM H81  HE1   0.15 !    H191-C19       C11=C12
GROUP                !           \      /       \
ATOM C9   CC1B  0.00 !    H71     C9=C10         H122
ATOM C10  CC1B -0.15 !       \    /    \
ATOM H101 HE1   0.15 !       C7=C8     H101
GROUP                !       /    \
ATOM C11  CC1A -0.15 !    H72     H81
ATOM H111 HE1   0.15 !
ATOM C12  CC2  -0.42 !
ATOM H121 HE2   0.21 !
ATOM H122 HE2   0.21 !
GROUP                !
ATOM C19  CT3  -0.27 !
ATOM H191 HA    0.09 !
ATOM H192 HA    0.09 !
ATOM H193 HA    0.09 !

RESI 4MOT       0.00 ! 4-methyloctatetraene-all trans
                     !
GROUP
ATOM C9   CC2  -0.42 !
ATOM H91  HE2   0.21 !
ATOM H92  HE2   0.21 !
GROUP                !
ATOM C10  CC1B -0.15 !
ATOM H101 HE1   0.15 !
```

```
ATOM C11  CC1A -0.15 !             H202  H203  H151         H161
ATOM H111 HE1   0.15 !                 \  |        \       /
ATOM C12  CC1A -0.15 !             H201-C20         C15=C16
ATOM H121 HE1   0.15 !                        \       /       \
GROUP                !         H111          C13=C14         H162
ATOM C13  CC1B  0.00 !             \       /       \
ATOM C20  CT3  -0.27 !   H91        C11=C12         H141
ATOM H201 HA    0.09 !      \      /       \
ATOM H202 HA    0.09 !       C9=C10         H121
ATOM H203 HA    0.09 !      /      \
GROUP                !   H92       H101
ATOM C14  CC1B -0.15 !
ATOM H141 HE1   0.15 !
ATOM C15  CC1A -0.15 !
ATOM H151 HE1   0.15 !
ATOM C16  CC2  -0.42 !
ATOM H161 HE2   0.21 !
ATOM H162 HE2   0.21 !

RESI MAT        0.00 ! 13-methyl fragment of retinal, all-trans
                     ! with net zero charge
GROUP
ATOM C7   CC2  -0.42 !
ATOM H71  HE2   0.21 !  H71     H81
ATOM H72  HE2   0.21 !     \    /
ATOM C8   CC1A -0.15 !     C7=C8      H101
ATOM H81  HE1   0.15 !     /    \     /
GROUP                !  H72      C9=C10        H121
ATOM C9   CC1B  0.00 !           /    \       /
ATOM C19  CT3  -0.27 !   H191--C19     C11=C12         H141
ATOM H191 HA    0.09 !        / |     /       \       /
ATOM H192 HA    0.09 !     H192 |   H111       C13=C14           H161
ATOM H193 HA    0.09 !        H193            /       \         /
GROUP                !               H201--C20         C15=1NZ-C16--H162
ATOM C10  CC1B -0.15 !                   /  |        /         \
ATOM H101 HE1   0.15 !                H202   |     H151          H163
ATOM C11  CC1A -0.15 !                     H203
ATOM H111 HE1   0.15
ATOM C12  CC1A -0.15
ATOM H121 HE1   0.15
GROUP
ATOM C13  CC1B  0.00
ATOM C20  CT3  -0.27
ATOM H201 HA    0.09
ATOM H202 HA    0.09
ATOM H203 HA    0.09
GROUP
ATOM C14  CC1B -0.15 !changed
ATOM H141 HE1   0.15
ATOM C15  CC1A  0.23 !changed
ATOM H151 HE1   0.15
ATOM 1NZ  NS1  -0.60 !NS1 for deprotonated Schiff Base
ATOM C16  CT3  -0.05 !added
ATOM H161 HA    0.09 !added
ATOM H162 HA    0.09 !added
ATOM H163 HA    0.09 !added
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RESI MATH       1.00 ! 13-methyl fragment of retinal, all-trans
                     ! with net +1 overall charge
GROUP
ATOM C7   CC2  -0.42 !
ATOM H71  HE2   0.21 !  H71     H81
ATOM H72  HE2   0.21 !     \    /
ATOM C8   CC1A -0.15 !     C7=C8      H101
ATOM H81  HE1   0.15 !     /    \     /
GROUP                !  H72      C9=C10        H121
ATOM C9   CC1B  0.00 !           /    \       /
ATOM C19  CT3  -0.27 !   H191--C19     C11=C12         H141
ATOM H191 HA    0.09 !        / |     /       \       /
ATOM H192 HA    0.09 !     H192 |   H111       C13=C14         2HZ1
ATOM H193 HA    0.09 !        H193            /       \       /
GROUP                !               H201--C20         C15=1NZ
ATOM C10  CC1B -0.15 !                    /  |        /       \
ATOM H101 HE1   0.15 !                H202   |     H151        C16--H161
ATOM C11  CC1A -0.15 !                     H203               / \
ATOM H111 HE1   0.15                                      H162  H163
ATOM C12  CC1A -0.15
ATOM H121 HE1   0.15
GROUP
ATOM C13  CC1B  0.00
ATOM C20  CP   -0.27
ATOM H201 HA    0.09
ATOM H202 HA    0.09
ATOM H203 HA    0.09
GROUP
ATOM C14  CC1B -0.15 !changed
ATOM H141 HE1   0.15
ATOM C15  CC1A  0.37 !changed
ATOM H151 HR1   0.20 !changed
ATOM 1NZ  NS2  -0.40 ! NS2 for protonated Schiff Base
ATOM 2HZ1 HC    0.38
ATOM C16  CT3   0.18 !added
ATOM H161 HA    0.09 !added
ATOM H162 HA    0.09 !added
ATOM H163 HA    0.09 !added

RESI RTC5       0.00 ! retinal C5-methyl fragment,
                     ! nomenclature from PDB based on retinol
!
GROUP
ATOM C1   CT    0.00 !
ATOM C2   CT2  -0.18 !
ATOM H21  HA    0.09 !
ATOM H22  HA    0.09 !
ATOM C3   CT2  -0.18 !
ATOM H31  HA    0.09 !
ATOM H32  HA    0.09 !
ATOM C4   CT2  -0.18 !
ATOM H41  HA    0.09 !
ATOM H42  HA    0.09 !
ATOM C5   CC1A  0.00 !
ATOM C6   CC1A  0.00 !
GROUP                !
ATOM C7   CC1B -0.15 !
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```
ATOM H71  HE1   0.15 !
ATOM C8   CC1B -0.15 !
ATOM H81  HE1   0.15 !
ATOM C9   CC1A  0.00 !
ATOM C10  CC1A -0.42 !
ATOM H101 HE1   0.21 !
ATOM H102 HE1   0.21 !  H162 H163  H171 H172
GROUP                !      \  |    |  /
ATOM C16  CT3  -0.27 !  H161-C16    C17-H173            H191 H192
ATOM H161 HA    0.09 !          \  /                      \   /
ATOM H162 HA    0.09 !    H21    C1         H71    H81      C19
ATOM H163 HA    0.09 !       \  /  \         |      |       /  \
GROUP                !    H22-C2    C6------C7=====C8----C9    H193
ATOM C17  CT3  -0.27 !        |     ||                    ||
ATOM H171 HA    0.09 !    H31-C3    C5   H181            C10-H101
ATOM H172 HA    0.09 !       /  \  /  \  /               |
ATOM H173 HA    0.09 !    H32    C4    C18-H182          H102
GROUP                !          /  \     \
ATOM C18  CT3  -0.27 !        H41  H42   H183
ATOM H181 HA    0.09 !
ATOM H182 HA    0.09 !
ATOM H183 HA    0.09 !
GROUP                !
ATOM C19  CT3  -0.27 !
ATOM H191 HA    0.09 !
ATOM H192 HA    0.09 !
ATOM H193 HA    0.09 !
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References

1. Frisch, M. J., G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery, Jr., T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez, and J. A. Pople. 2004. Gaussian 03. Gaussian, Inc., Wallingford, CT.
2. Wavefunction, Inc. 2008. Spartan'08. Wavefunction, Inc., Irvine, CA.
3. Brooks, B. R., C. L. Brooks III, A. D. Mackerell, Jr., L. Nilsson, R. J. Petrella, B. Roux, Y. Won, G. Archontis, C. Bartels, S. Boresch, A. Caflisch, L. Caves, Q. Cui, A. R. Dinner, M. Feig, S. Fischer, J. Gao, M. Hodoscek, W. Im, K. Kuczera, T. Lazaridis, J. Ma, V. Ovchinnikov, E. Paci, R. W. Pastor, C. B. Post, J. Z. Pu, M. Schaefer, B. Tidor, R. M. Venable, H. L. Woodcock, X. Wu, W. Yang, D. M. York, and M. Karplus. 2009. CHARMM: the biomolecular simulation program. *J. Comp. Chem.* 30: 1545-1614.
4. Feller, S. E., K. Gawrisch, and T. B. Woolf. 2003. Rhodopsin exhibits a preference for solvation by polyunsaturated docosohexaenoic acid. *J. Am. Chem. Soc.* 125: 4434-4435.