

# Molecular mechanics modeling of azobenzene-based photoswitches

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**Abstract** We present an extension of the generalized amber force field to allow the modeling of azobenzenes by means of classical molecular mechanics. TD-DFT calculations were employed to derive different interaction models for 4-hydroxy-4'-methyl-azobenzene, including the ground ( $S_0$ ) and  $S_1$  excited state. For both states, partial charges and the  $-N=N-$  torsion potentials were characterized. On this basis, we pave the way to large-scale model simulations involving azobenzene molecular switches. Using the example of an isolated molecule, the mechanics of cyclic switching processes are demonstrated by classical molecular dynamics simulations.

**Keywords** Molecular switch · TD-DFT · Force-field · Azobenzene

## Introduction

Derivatives of azobenzene ( $H_5C_6-N=N-C_6H_5$ ) belong to the most widely used molecular switches in opto- and nano-mechanical devices [1–4]. The great potential of azobenzenes in biochemistry and materials science is attributed to the  $-N=N-$  torsion, which gives rise to cis- and trans-isomerization,

accompanied by large structural rearrangements. In the electronic ground state, the cis–trans transformation is confined by a large energy barrier, thus stabilizing the  $-N=N-$  torsion angle either near  $10^\circ$  or near  $180^\circ$ . However, electronic excitation is known to change the torsion potential considerably, and actually leads to the stabilization of torsion angles half-way between the cis- and trans- configurations.

This peculiar phenomenon implies a reversible photoisomerization of azobenzenes, which has inspired many applications ranging from external control of cellular functions in biology [1, 2] to the manipulation of nanomaterials [3, 4]. Besides the large body of experimental characterization and application, relatively few theoretical studies have been dedicated to this important compound. Marx and coworkers pioneered ab-initio molecular dynamics studies of azobenzene models, including bridged azobenzene [5] and bulk phase systems [6]. While the latter study was performed within combined quantum/molecular mechanics models, computational efficiency is still limited by the need to perform quantum calculations on-the-fly.

In what follows, we parameterize a purely classical molecular mechanics force field for azobenzene, both in the ground ( $S_0$ ) and  $S_1$  excited state. The related torsion potentials are implemented in the generalized amber force field to allow wide application to a large manifold of azobenzene derivatives. By drastic reduction of computational costs, this approach will pave the way to large-scale simulation models, and thus to mimicking the switching of azobenzene in nanodevices and biological systems.

## Theory

An initial configuration of 4-hydroxy-4'-methyl-azobenzene was obtained from classical molecular mechanics modeling

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**Table 1** Charges derived from ESP fits to the  $S_0$  and  $S_1$  states, respectively. Atomic indices as in Fig. 1

Atom	Charge $S_0$	Charge $S_1$	Atom	Charge $S_0$	Charge $S_1$
C1	-0.1306	-0.1568	N9	-0.2474	-0.1886
H1	0.0513	0.0562	C10	0.4846	0.3514
C2	0.0883	0.1020	C11	-0.2910	-0.2580
C3	-0.1998	-0.2068	H11	0.1731	0.1758
H3	0.1627	0.1617	C12	-0.2285	-0.2236
C4	-0.3215	-0.2696	H12	0.1772	0.1722
H4	0.1789	0.1757	C13	0.2742	0.2803
C5	0.5474	0.3998	C14	-0.2285	-0.2236
C6	-0.3215	-0.2696	H14	0.1772	0.1722
H6	0.1789	0.1757	C15	-0.2910	-0.2580
C7	-0.1998	-0.2068	H15	0.1731	0.1758
H7	0.1627	0.1617	O16	-0.5241	-0.5359
N8	-0.3354	-0.2648	H16	0.3872	0.3888

using the generalized amber force field (GAFF) [7]. The molecular geometry was then optimized within (TD-) DFT calculations, both in the electronic ground state ( $S_0$ ) and the lowest singlet and triplet states ( $S_1, T_1$ ), respectively. We adopted the B3-LYP functional [8] and the def2-SVP basis set [9]. Based on the equilibrium geometries of an isolated 4-hydroxy-4'-methyl-azobenzene molecule in the  $S_0$  and  $S_1$  states, atomic partial charges were derived by fitting to the electrostatic potential (RESP charges [10], Table 1).

During rotation around the  $-N=N-$  bond in the electronic ground state, the molecule becomes a singlet-biradical. Thus, a spin-polarized ansatz for the wavefunction was employed to allow for symmetry breaking. This procedure has already proven to yield reasonable energies for singlet biradicals [11]. Moreover, the stability of the obtained ground-state wavefunctions was checked with respect to the MO coefficients.

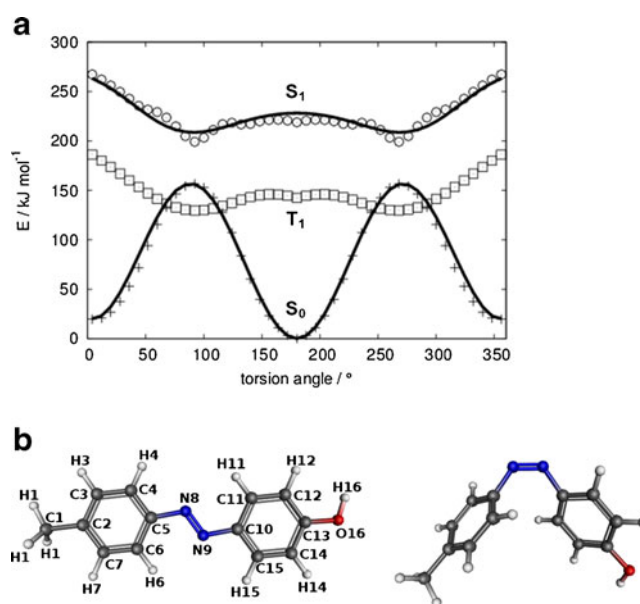
The molecular dynamics simulations were performed in the canonical ensemble using a time-step of 1 fs. Explicit summation is used for all non-bonded interactions. The cyclic switching of an isolated 4-hydroxy-4'-methyl-azobenzene molecule was explored for a series of 1,000 cycles, each comprising a 250 ps run at the electronic ground state followed by a 250 ps run in the  $S_1$  state. The relaxation period of 250 ps allowed after each excitation / decay event was chosen generously large in order to avoid coupling of the vibrational modes to the simulation procedure.

## Results

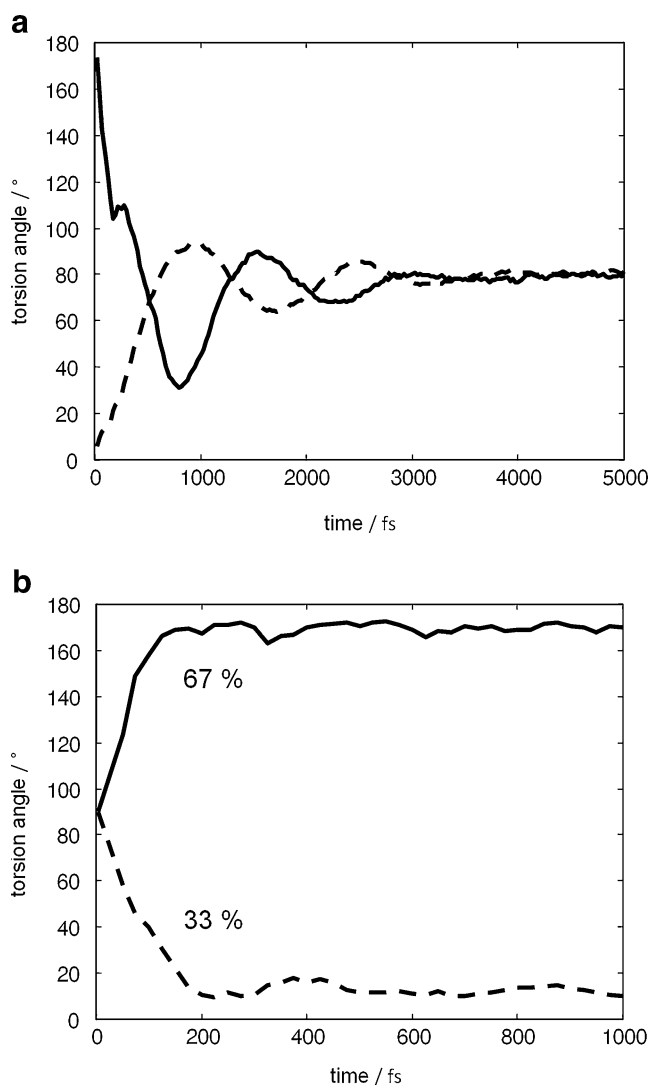
The main effects of electronic excitation in 4-hydroxy-4'-methyl-azobenzene may be devised in terms of the

molecules electrostatics and the change of the  $-N=N-$  torsion potential. The former gives rise to individual partial charges for the  $S_0$  and  $S_1$  states, respectively. Thus, two sets of partial charges were fitted to the electrostatic potential of an isolated 4-hydroxy-4'-methyl-azobenzene molecule (choosing the equilibrium geometries corresponding to the  $S_0$  and  $S_1$  states, respectively). To ensure the transferability to other azobenzene derivatives, only the most relevant partial charges, i.e., those of the nitrogen atoms and its neighbors were allowed to change upon electronic excitation.

Whilst adopting as many interaction models as possible from the generalized amber force field, the N–N bond, N–N–C and N–C–C valence angle, and, most importantly, the  $-N=N-$  torsion potential was re-parameterized. This was performed for both the  $S_0$  and the  $S_1$  state. However, since the TD-DFT calculations related to the  $S_1$  state are numerically less stable, the torsion potential was first fitted to the  $T_1$  state, and then a constant energy shift of 79.215 kJ mol<sup>-1</sup> was added to account for the difference in exchange energy. To derive the molecular mechanics parameters mimicking the torsion potential, we picked the equilibrium geometry of the molecule in the  $S_1$  state and implemented rotation around the N–N bond whilst keeping all other bond lengths and angles fixed (Fig. 1a). Thus, the corresponding force field terms are fitted without artificial coupling to inaccuracies arising from the force field



**Fig. 1** a Torsion potential for the rotation around the  $-N=N-$  bond. The dots, squares and stars reflect (TD)-DFT calculations whilst the solid curves indicate fitted molecular mechanics potentials, respectively. b Cis- and trans- configurations of 4-hydroxy-4'-methyl-azobenzene after relaxation to the corresponding minimum of the  $-N=N-$  torsion potential



**Fig. 2** **a** Average  $-N=N-$  torsion angle as a function of time upon electronic excitation to the  $S_1$  state. Relaxation from the cis- (*dashed curve*) and the trans- (*solid curve*) was sampled separately from a total of 1,000 runs. **b** Average  $-N=N-$  torsion angle as a function of time upon electronic decay from the  $S_1$  state. Relaxation to the cis- (*dashed curve*) and the trans- (*solid curve*) was sampled separately from a total of 1,000 runs

modeling of degrees of freedom other than the  $-N=N-$  torsion. Comparison of the DFT calculations and the off-the-shelf GAFF potential showed that rotation around the  $-N=N-$  bond is poorly reproduced. Setting the 1–4 interactions to zero, we fitted the torsion potential for the  $S_0$  and the  $S_1$  states as follows (Fig. 1a):

$N=N$  bond potential:

$$U_{gr} = 1/2 \times 6676.7 \text{ kJ mol}^{-1} \times [r_{N=N} - 1.2475]^2 \quad (S_0)$$

$$U_{ex} = 1/2 \times 7027.9 \text{ kJ mol}^{-1} \times [r_{N=N} - 1.2480]^2 \quad (S_1)$$

$N=N-C$  valence angle potential:

$$U_{gr} = 1/2 \times 640.15 \text{ kJ mol}^{-1} \times [\alpha_{N=N-C} - 110.1^\circ]^2 \quad (S_0)$$

$$U_{ex} = 1/2 \times 433.37 \text{ kJ mol}^{-1} \times [\alpha_{N=N-C} - 124.1^\circ]^2 \quad (S_1)$$

$N-C-C$  valence angle potential:

$$U_{gr} = 1/2 \times 445.33 \text{ kJ mol}^{-1} \times [\alpha_{N-C-C} - 103.4^\circ]^2 \quad (S_1)$$

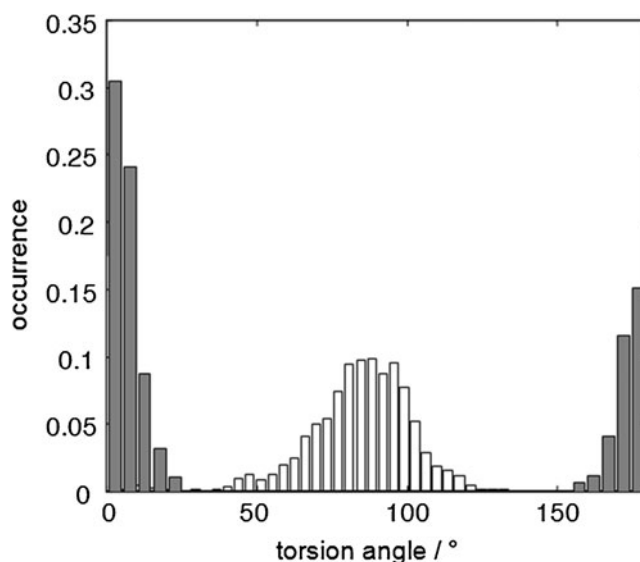
$$U_{ex} = 1/2 \times 569.39 \text{ kJ mol}^{-1} \times [\alpha_{N-C-C} - 123.5^\circ]^2 \quad (S_1)$$

$-N=N-$  torsion potential:

$$U_{gr} = 73.791 \text{ kJ mol}^{-1} \times [1 + \cos(2\phi - 180^\circ)] + 19.671 \text{ kJ mol}^{-1} \times [1 + \cos(\phi)] \quad (S_0)$$

$$U_{ex} = 3.567 \text{ kJ mol}^{-1} \times [1 + \cos(3\phi)] + 18.168 \text{ kJ mol}^{-1} \times [1 + \cos(2\phi)] + 19.4 \text{ kJ mol}^{-1} \times [1 + \cos(\phi)] \quad (S_1)$$

We furthermore fitted the molecular mechanics potential for the four adjacent  $-N-C-$  torsions as  $V = 10.779 \text{ kJ mol}^{-1} \times [1 + \cos(2\phi - 180^\circ)]$  taking the conventional weighted 1–4 interactions into account. Thus, these parameters can be used for both the  $S_0$  and  $S_1$  states. Fig. 1b illustrates the molecular geometry upon full relaxation to the (local) energy minima of the cis- and trans- conformers of the electronic ground state, respectively.



**Fig. 3** Occurrence profile of the  $-N=N-$  torsion angle as obtained from the endpoints of the 250 ps relaxation runs for  $S_1 \rightarrow S_0$  (*solid bars*) and  $S_0 \rightarrow S_1$  (*empty bars*) switching, respectively

To demonstrate the performance of this force field, cyclic switching of an isolated 4-hydroxy-4'-methyl-azobenzene molecule was explored from purely classical molecular dynamics simulations. Along this line, electronic excitation and decay was mimicked by switching between the two force field models periodically. From a total of 1,000 cycles, the average relaxation progress of the  $-N=N-$  torsion angle was sampled (Fig. 2). Both electronic excitation and decay leads to rapid reorganization within about 500 fs and 200 fs, respectively.

A prominent feature of electronic excitation in azobenzene is the stabilization of  $-N=N-$  torsion angles around  $90^\circ$ , i.e., near the transition state of the cis-trans isomerization of azobenzene in the ground state. Indeed, our molecular dynamics simulations related to molecular relaxation after electronic decay from the  $S_1$  state demonstrate clearly the accessibility of both, cis- and trans- configurations. Figure 3 shows the occurrence profile of the  $-N=N-$  torsion angle as obtained after each switching cycle, i.e., initial relaxation in the  $S_1$  ( $S_0$ ) state, followed by relaxation in the  $S_0$  ( $S_1$ ) state. From this it may be clearly seen that electronic excitation leads to torsion angles in-between the cis- and trans- conformers. Indeed, electronic decay from the  $S_1$  state yields both minima of the ground state potential energy landscape. However, the trans- is favored over the cis- conformer by a ratio of about 2:1. The balance is sensitive to the non-symmetry of 4-hydroxy-4'-methyl-azobenzene, but even for the symmetric azobenzene molecule the trans-conformer is energetically preferred [6].

## Conclusions

Based on the generalized amber force field we derived a purely classical molecular mechanics model of azobenzenes. TD-DFT calculations were used to provide reliable interaction models for both the ground ( $S_0$ ) and  $S_1$  excited state. Whilst clearly less accurate than full ab-initio or QM/MM based molecular dynamics simulations, we provide a basis for large-scale simulation models that might otherwise be inaccessible to current hardware. Using the example of an isolated molecule, we demonstrate cyclic cis-trans switching processes induced by electronic excitation and decay.

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