ChemPubSoc Europe

DOI: 10.1002/ejoc.201600113

EurJOC European Journal of Organic Chemistry

Photoswitches

Internal C–C Bond Rotation in Photoisomers of α-Bisimines: a Light-Responsive Two-Step Molecular Speed Regulator Based on Double Imine Photoswitching

Lutz Greb,[a,b] Andreas Eichhöfer,[b] and Jean-Marie Lehn*[a,b]

Abstract: Benzil-based α-bisimines are implemented as photoswitches for the construction of a speed-regulating molecular device, in which, by application of light, three different states may be addressed, showing distinct frequencies of internal C–C bond rotation, spanning 12 orders of magnitude. Bond rotation barriers were determined experimentally and elucidated by DFT-methods.

Introduction

The control of molecular conformation and internal flexibility by external stimuli is an essential feature for the bottom up approach in the construction of nano-machineries – an active field embraced by the term molecular machines.[1] Due to its traceless application with high spatial control and usability for the generation of out-of-equilibrium states, light may be considered as the ideal multipurpose physical trigger. A plethora of light-driven switches have been described in the past decades, leading to numerous applications ranging, for example, from soft-matter technologies to photopharmacology.[2] The speeding up/slowing down of an internal bond rotational frequency by configurational switching can be considered as effecting molecular acceleration or braking action, respectively. The principles used for the construction of such systems mostly rely on steric effects, as it has been considered in seminal studies on molecular gearing.[3] A variety of photo-induced approaches for the control of rates of intramolecular single-bond rotation have emerged.[4,5] Usually, light irradiation causes a configurational change that results in a slowing down or stopping of internal motion. A greater challenge has been the induction of faster motion upon application of an external stimulus.[6] The reported molecular brakes function usually in two states – on and off – implementing photoswitches based on azo- or olefin functional groups. Although the light-induced *E*/*Z* isomerization of imines has been known for almost 70 years,[7] they have been only recently used as core units in molecular machines.[8] The thermal configurational relaxation of imines by in-plane nitrogen inversion may be easily tuned by varying the N substituent.[9] It has been noticed that the configuration around the C=N double bond may have an influence on the rotational flexibility of C substituents in imines,[10] and the mutarotation of optically active benzil monoimines was explained by hindered rotation around the internal C–C bond.[11]

α-Bisimines based on benzil can exist in either (*E*,*E*), (*E*,*Z*) or (*Z*,*Z*) configuration around the C=N double bonds (Figure 1). The bond-rotation barrier around the internal C–C bond should be strongly dependent on the position of the N substituent, with strongest hindrance in the (*Z*,*Z*) isomer and the lowest in the (*E*,*E*) configuration. The distribution over these states may be driven out of equilibrium by photochemical *E*/*Z* isomerization. Switching between the (*E*,*E*), (*E*,*Z*), and (*Z*,*Z*) configuration would represent a molecular rotational speed regulator with three different power settings.

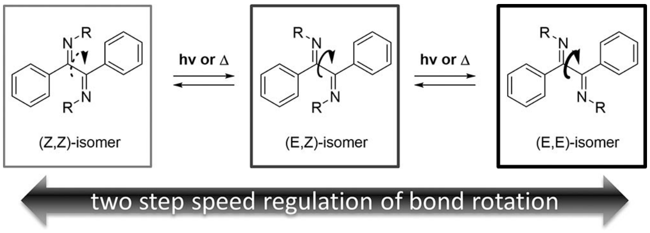

Figure 1. Internal C–C bond rotation in α-bisimines based on benzil.

We herein present a molecular double-photoswitch based on such an α-bisimine unit, capable to respond to light by *E*/*Z* isomerization into three different states displaying highly distinct internal C–C bond rotational rates. The dynamic processes have been elucidated by kinetic and DNMR studies and the pathways for the bond rotation were analyzed by density functional theory.

---

[a] *Institut de Science et d'Ingénierie Supramoléculaires (ISIS), Université de Strasbourg,*
8 allée Gaspard Monge, 67000 Strasbourg, France
E-mail: lehn@unistra.fr
https://isis.unistra.fr/laboratory-of-supramolecular-chemistry-jean-marie-lehn/

[b] *Institut für Nanotechnologie (INT), Karlsruhe Institut für Technologie, Hermann-von-Helmholtz-Platz 1, 76344 Eggenstein-Leopoldshafen, Germany*

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201600113.

Results and Discussion

The bisimines **1**–**3** were synthesized in good yields by $TiCl_4$-mediated condensation of benzil (derivatives) with the corresponding amines (Figure 2a), being stable towards hydrolysis. ^{1}H NMR analysis of the non-*ortho*-substituted bisimines **1** and **2** established the (*Z*,*Z*) configuration around the C=N double bond as the exclusive thermodynamic product. Conversely, *ortho*-substitution at the aryl rings, as in compound **3**, rendered the (*E*,*E*) configuration the most stable, exclusive species. X-ray crystallographic analysis of (*Z*,*Z*)-**1** and (*E*,*E*)-**3** (Figure 2b) revealed that (*E*,*E*)-**3** occurs as the C–C *anti* conformer in the solid state, likely due to the diminished repulsion of the inwards oriented electron lone pairs at the nitrogen atoms and increased delocalization in the planar N=C–C=N system, whereas the more crowded (*Z*,*Z*)-**1** adopts a *gauche* conformation around the internal C–C bond. Accordingly, the internal C–C bond in (*E*,*E*)-**3** (1.50 Å) is shortened compared with the less conjugated (*Z*,*Z*)-**1** (1.52 Å). Irradiation of (*Z*,*Z*)-**1** with light of 254 nm and irradiation of (*Z*,*Z*)-**2** and (*E*,*E*)-**3** with light of > 280 nm led to significant, reversible *E*/*Z* isomerization, as was verified by ^{1}H NMR and UV/Vis spectroscopy (see Figure 3 and Supporting Information).[12] The thermal re-equilibration to the initial diastereomeric distribution occurred in all cases within 20 h at 20 °C (see inset in Figure 3 for **2**), corresponding to estimated N-inversion barriers of 22–24 kcal/mol, in agreement with literature data.[9a] The analysis of photostationary states (PSSs) and internal bond-rotation processes was limited to compound **2**. Irradiation of pure (*Z*,*Z*)-**2** with light of > 280 nm (125 W medium-pressure mercury lamp, 1 min) induced a switching to a PSS of 72 % (*E*,*E*)-**2** and 28 % (*E*,*Z*)-**2** (determined by ^{1}H NMR spectroscopy). By subsequent application of light of 365 nm (TLC handheld lamp) for 3 h, a PSS of 26 % (*E*,*E*)-**2**, 40 % (*E*,*Z*)-**2**, and 34 % (*Z*,*Z*)-**2** was obtained. Hence, by suitable choice of the irradiation wavelength or heat, the composition of the mixture can be controlled to have either (*Z*,*Z*)-**2**, (*E*,*E*)-**2**, or (*E*,*Z*)-**2** as the predominant configuration, thus conferring remarkable photoswitch features with three different switching states to such α-bisimines.

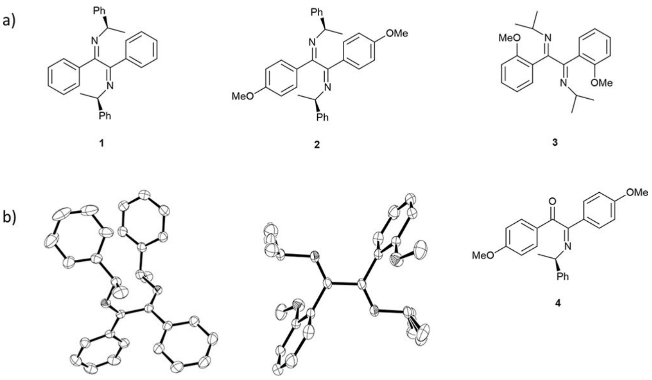

Figure 2. a) Structures of the α-bisimines (*Z*,*Z*)-**1**, (*Z*,*Z*)-**2**, and (*E*,*E*)-**3**, and of monoimine **4**. b) Solid-state molecular structures of (*Z*,*Z*)-**1** and (*E*,*E*)-**3**.

The chiral N residues allowed for the experimental determination of the internal C–C bond-rotation frequency by kinetic analysis of the interconversion of atropisomers (Figure 4). The (*Z*,*Z*)-**2** atropisomers (*Z*,*Z*-**2a**/*Z*,*Z*-**2b**) were separated by column chromatography and the atropisomerization was followed at different temperatures by ^{1}H NMR spectroscopy, yielding an energy of activation for the internal bond rotation of 24.8 kcal/mol at 25 °C, translated to a rotational frequency of 4×10^{-6} s^{-1}. For compound (*E*,*Z*)-**2**, only one set of signals was visible at room temperature by ^{1}H NMR spectroscopy (in the enriched sample after the irradiation cycle > 280 nm/365 nm) indicating fast interconversion of both atropisomers. Cooling the sample to –80 °C led to significant broadening and splitting of different characteristic NMR signals. Line shape analysis of the RR′C*H*-N=C ^{1}H NMR signals yielded an energy of activation of about 10.0 kcal/mol at 25 °C for the internal bond rotation (see the Supporting Information).

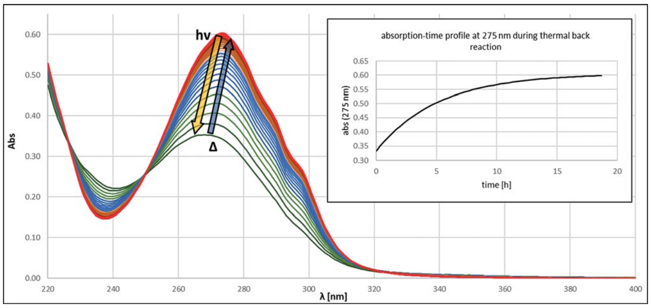

Figure 3. UV/Vis spectra of **2** before and after (1 min) irradiation with light > 280 nm and thermal back reaction (inset: time profile of thermal back reaction).

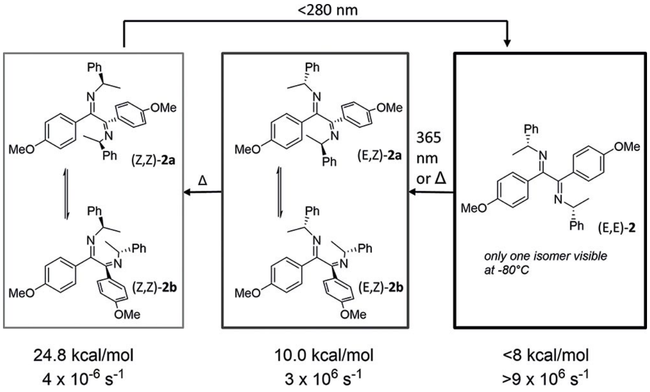

Figure 4. Atropisomers and experimentally determined rotation barriers and rotational frequencies of configurational diastereomers of **2**.

Consequently, the rotational frequency increases to 3.1×10^6 s^{-1} in the (*E*,*Z*) configuration. Bisimine (*E*,*E*)-**2**, visible in the ^{1}H NMR spectrum as a single compound at 25 °C, did not show any line broadening upon cooling the sample to –80 °C, hence indicating a rotational barrier below 8 kcal/mol (bond-rotation frequency of > 9×10^6 s^{-1}). Thus, highly distinct rotational rates around the internal C–C bond differing by 12 orders of magnitude were observed, which may be regulated by inducing different PSSs upon irradiation with UV light. Monoimine (*Z*)-**4** (see Figure 2), which was isolated during the preparation of bisimine **2**, was likewise investigated by line-shape analysis, yielding a barrier for the internal C–C bond rotation of 14.4 kcal/mol. This energy barrier is noticeably higher in comparison to the sterically similar (*E*,*Z*)-**2**. The origin of this higher barrier might be related to the stronger polarized C=O double bond in the N=C–C=O systems, in comparison with the less polarized N=C–C=N system, leading to a stronger electrostatic repulsion between the heteroatoms in a planar transition state.[13] In addition, it is known that α-dicarbonyls exhibit a diminished resonance energy stabilization in comparison to non-polarized dienes in planar configurations.[14] Thus, a reduced resonance energy stabilization in the transition states (with almost planar N=C–C=X) in (*Z*)-**4** might lead to an increased rotational energy barrier compared with **2**.

All stationary points (minima and transition states) describing the internal C–C bond-rotation pathway of (*Z*,*Z*)/(*E*,*Z*) isomers of **2** and of (*Z*)-**4** were located by means of density functional theory at the B2PLYP/def2-TZVP level. The derived energy barriers for the C–C bond rotation are in good agreement with the experimentally determined ones, hence allowing us to account for the favored rotation pathways (Table 1).[15] In principle, the rotation around the internal C–C bond may proceed by N–R/N–R (*syn* path) or N–R/C–Ar slippage (*anti* path). For (*Z*,*Z*)-**2**, the *anti* path (26.1 kcal/mol) is favored over the *syn* path (34.0 kcal/mol), whereas in (*E*,*Z*)-**2** and (*Z*)-**4** the *syn*-path is the favored process. The internal C–C bond length in the minima and transition-state structures of (*Z*)-**4** are generally longer (1.53–1.54 Å) than the structures of **2** (1.52 Å), indicating a less-pronounced transition-state stabilization by resonance energy in the nearly planar N=C–C=O systems. In all cases, a geometrical flexibility along the C=N–C angle (towards N inversion) lowers the rotation barrier by concurrent angle enlargement from 120° in the minimum structures to 126–132° in the transition states. Motions in which bond rotation is coupled to trigonal N inversion have been described both by experimental and computational studies.[16] Analogously, the structural dynamics observed herein involve a coupling of bond rotation to planar N inversion.

Table 1. Calculated (D3-B2PLYP/def2-TZVP) energies and selected geometrical parameters in C–C bond rotation of (*Z*,*Z*)-**2**, (*E*,*Z*)-**2**, and (*Z*)-**4**.

Conformer	Rel. energy [kcal]	Torsional angle [°]	∠ C=N–C *Z*-conf. [°]	C–C length [Å]
Z,Z-**2a**	0.0	98.1	119.7	1.52
Z,Z-anti-TS	26.1	186.7	130.6	1.52
(Z,Z)-**2b**	0.6	271.0	120.4	1.52
(Z,Z)-anti-TS	34.0	12.3	131.8	1.55
(E,Z)-**2a**	0.0	80.4	120.7	1.52
(E,Z)-anti-TS	11.0	192.6	127.1	1.52
(E,Z)-**2b**	1.7	280.2	120.0	1.52
(E,Z)-syn-TS	9.6	21.5	125.7	1.52
(Z)-**4a**	0.0	97.0	120.2	1.53
(Z)-anti-TS	16.9	182.8	128.5	1.54
(Z)-**4b**	2.6	268.3	120.4	1.53
Z-syn-TS	14.7	20.2	125.0	1.54

Conclusions

In conclusion, we herewith present the unprecedented application of easily available imines as photoswitches with the ability to regulate internal C–C bond-rotation frequency over 12 orders of magnitude in 3 distinct states. The experimentally determined rotation barriers are in good agreement with the DFT calculated values, thus allowing for a more explicit insight into the rotational pathway. The described dynamic and structural features may serve as a starting point towards more advanced molecular machines based on imines. Moreover, the structural and dynamic behavior of α-bisimines could also serve as a guideline in the investigation of the conformational preference and dynamic/motional features of polyisocyanides,[17] as well as for the installation of oligo/poly-imine groups into materials (polymeric chains or particles).[18]

Experimental Section

Irradiation Experiments: A solution of bisimine (*Z*,*Z*)-**2** (1 mg) in 0.5 mL of MeOD in an NMR tube was placed in front (30 cm distance) of a medium-pressure mercury lamp (125 W) or under a TLC lamp (6 W, 365 nm) and irradiated for the given time. The diastereomer distribution was determined by ^{1}H NMR integration of characteristic signals, using the residual solvent signal as the internal standard. No byproducts of photo-induced decomposition were detected. CCDC 1425405 (for **1**) and 1425404 (for **3**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre. For further synthetic, NMR and computational details, see the Supporting Information.

Acknowledgments

L. G. thanks the A. v. Humboldt foundation for a postdoctoral fellowship. J.-M. L. thanks the ERC (Advanced Research Grant SUPRADAPT 290585) for financial support.

Keywords: Molecular machines · Molecular devices · Photochemistry · Imines · Bond rotation

[1] a) V. Balzani, A. Credi, F. M. Raymo, J. F. Stoddart, *Angew. Chem. Int. Ed.* **2000**, *39*, 3348–3391; *Angew. Chem.* **2000**, *112*, 3484; b) J.-P. Sauvage (Ed.), *Molecular Machines and Motors*, Springer, Berlin, **2001**; c) J. F. Stoddart, *Acc. Chem. Res.* **2001**, *34*, 410–411; d) S. Erbas-Cakmak, D. A. Leigh, C. T. McTernan, A. L. Nussbaumer, *Chem. Rev.* **2015**, *115*, 10081–10206; e) E. R. Kay, D. A. Leigh, F. Zerbetto, *Angew. Chem. Int. Ed.* **2007**, *46*, 72–191; *Angew. Chem.* **2007**, *119*, 72; f) W. R. Browne, B. L. Feringa, *Nat. Nanotechnol.* **2006**, *1*, 25–35.

[2] a) P. Ceroni, A. Credi, M. Venturi, V. Balzani, *Photochem. Photobiol. Sci.* **2010**, *9*, 1561–1573; b) S. Silvi, M. Venturi, A. Credi, *Chem. Commun.* **2011**, *47*, 2483–2489; c) B. L. Feringa (Ed.), *Molecular Switches*, Wiley-VCH, Weinheim, **2011**; d) C. Garcia-Iriepa, M. Marazzi, L. M. Frutos, D. Sampedro, *RSC Adv.* **2013**, *3*, 6241–6266; e) M.-M. Russew, S. Hecht, *Adv. Mater.* **2010**, *22*, 3348–3360; f) J. Broichhagen, J. A. Frank, D. Trauner, *Acc. Chem. Res.* **2015**, *48*, 1947–1960.

[3] a) H. Iwamura, K. Mislow, *Acc. Chem. Res.* **1988**, *21*, 175–182; b) A. Liden, C. Roussel, T. Liljefors, M. Chanon, R. E. Carter, J. Metzger, J. Sandstrom, *J. Am. Chem. Soc.* **1976**, *98*, 2853–2860.

[4] T. R. Kelly, M. C. Bowyer, K. V. Bhaskar, D. Bebbington, A. Garcia, F. Lang, M. H. Kim, M. P. Jette, *J. Am. Chem. Soc.* **1994**, *116*, 3657–3658.

[5] a) A. M. Schoevaars, W. Kruizinga, R. W. J. Zijlstra, N. Veldman, A. L. Spek, B. L. Feringa, *J. Org. Chem.* **1997**, *62*, 4943–4948; b) P. V. Jog, R. E. Brown, D. K. Bates, *J. Org. Chem.* **2003**, *68*, 8240–8243; c) J.-S. Yang, Y.-T. Huang, J.-H. Ho, W.-T. Sun, H.-H. Huang, Y.-C. Lin, S.-J. Huang, S.-L. Huang, H.-F. Lu, I. Chao, *Org. Lett.* **2008**, *10*, 2279–2282; d) K. Hirose, *J. Inclusion Phenom.*

Macrocyclic Chem. **2010**, *68*, 1–24; e) W.-T. Sun, S.-L. Huang, H.-H. Yao, I. C. Chen, Y.-C. Lin, J.-S. Yang, *Org. Lett.* **2012**, *14*, 4154–4157; f) Y. Jye-Shane, S. Wei-Ting, in *Organic Structures Design*, Pan Stanford, **2014**, pp. 137–183; g) W. S. Tan, P.-Y. Chuang, C.-H. Chen, C. Prabhakar, S.-J. Huang, S.-L. Huang, Y.-H. Liu, Y.-C. Lin, S.-M. Peng, J.-S. Yang, *Chem. Asian J.* **2015**, *10*, 989–997.

[6] a) I. Alfonso, M. I. Burguete, S. V. Luis, *J. Org. Chem.* **2006**, *71*, 2242–2250; b) C. J. Welch, M. Biba, P. Pye, R. Angelaud, M. Egbertson, *J. Chromatogr. B* **2008**, *875*, 118–121; c) B. E. Dial, R. D. Rasberry, B. N. Bullock, M. D. Smith, P. J. Pellechia, S. Profeta, K. D. Shimizu, *Org. Lett.* **2011**, *13*, 244–247; d) B. E. Dial, P. J. Pellechia, M. D. Smith, K. D. Shimizu, *J. Am. Chem. Soc.* **2012**, *134*, 3675–3678.

[7] E. Fischer, Y. Frei, *J. Chem. Phys.* **1957**, *27*, 808–809.

[8] a) L. Greb, J.-M. Lehn, *J. Am. Chem. Soc.* **2014**, *136*, 13114–13117; b) L. Greb, A. Eichhöfer, J.-M. Lehn, *Angew. Chem. Int. Ed.* **2015**, *54*, 14345–14348; *Angew. Chem.* **2015**, *127*, 14553–14556.

[9] a) C. G. McCarty in *Carbon–Nitrogen Double Bonds*, Wiley, **1970**, pp. 363–464; b) D. Y. Curtin, C. G. McCarty, *Tetrahedron Lett.* **1962**, *3*, 1269–1274; c) J. M. Lehn, in *Top. Curr. Chem. Vol. 15/3*, Springer Berlin Heidelberg, **1970**, pp. 311–377.

[10] a) D. Casarini, L. Lunazzi, D. Macciantelli, *J. Chem. Soc. Perkin Trans. 2* **1992**, 1363–1370; b) A. Guerra, L. Lunazzi, *J. Org. Chem.* **1995**, *60*, 7959–7965.

[11] J. L. García-Ruano, M. A. Henao, D. Molina, R. Pérez-Ossorio, J. Plumet, *Tetrahedron Lett.* **1979**, *20*, 3123–3126.

[12] Photoswitching/re-equilibration cycles for **1** and **2** were repeated up to 5 times without visible (by ^{1}H NMR spectroscopy) decomposition. Partial photochemical side reactions where observed during photoswitching for **3**.

[13] S. Liu, *J. Phys. Chem. A* **2013**, *117*, 962–965.

[14] a) K. Eriks, T. D. Hayden, S. H. Yang, I. Y. Chan, *J. Am. Chem. Soc.* **1983**, *105*, 3940–3942; b) Q. Shen, K. Hagen, *J. Phys. Chem.* **1987**, *91*, 1357–1360; c) J. Liebman, *Struct. Chem.* **1992**, *3*, 449–450.

[15] For PES and all other computational details, see the Supporting Information.

[16] a) C. H. Bushweller, J. W. O'Neil, H. S. Bilofsky, *J. Am. Chem. Soc.* **1971**, *93*, 542–544; b) D. Casarini, L. Lunazzi, J. E. Anderson, *J. Org. Chem.* **1993**, *58*, 714–717.

[17] a) E. Schwartz, M. Koepf, H. J. Kitto, R. J. M. Nolte, A. E. Rowan, *Polym. Chem.* **2011**, *2*, 33–47; b) R. J. M. Nolte, *Chem. Soc. Rev.* **1994**, *23*, 11–19; c) W. Drenth, R. J. M. Nolte, *Acc. Chem. Res.* **1979**, *12*, 30–35; d) R. J. M. Nolte, R. W. Stephany, W. Drenth, *Rec. Trav. Chim. Pays-Bas* **1973**, *92*, 83–91.

[18] L. Greb, H. Mutlu, C. Barner-Kowollik, J.-M. Lehn, *J. Am. Chem. Soc.* **2016**, *138*, 1142–1145.

Received: February 1, 2016