

Hemithioindigo-Based Trioxobicyclonadiene: 3D Multiswitching of Electronic and Geometric Properties

Fabien Kohl, Aaron Gerwien, Frank Hampel, Peter Mayer, and Henry Dube*



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ABSTRACT: Molecular photoswitches that offer simultaneous precise control over geometrical and electronic changes are rare yet highly sought tools for the development of responsive nanosystems. Here we present such an advantageous combination of property control within a novel multiphotoswitch architecture. Hemithioindigo-based trioxobicyclonadiene (HTI-TOND) offers a rigid three-dimensional molecular structure that undergoes different exotic rearrangement reactions upon photochemical and thermal signaling. Three to four different states with distinct geometric and electronic properties can be accessed reversibly in high yields within this molecular framework. Thus, a highly promising and unique switching tool has become available to instill the next level of addressability at the smallest scales.

Molecular switches are central building blocks in functional chemical systems that allow the introduction and control of precise changes at the smallest scales of matter. Photoswitches in particular offer distinct advantages because they use light as a fast and waste-free signal to affect the switching processes. For these reasons, photoswitches have risen to great prominence, and myriads of applications have been reported in which they have been employed as indispensable bases of responsive smart chemical systems.^{1–11} Many different types of photoswitches are being explored presently, which can roughly be divided into two classes, enabling either strong geometric or strong electronic changes upon switching. In the first case, the photochromism and electronic changes are typically not very large, with azobenzenes¹² and stilbenes^{13,14} being classical examples and imines,^{15,16} hydrazones,^{17–19} and indigoid photoswitches^{7,20} representing later additions. In the second case, geometry changes are oftentimes subtle, as can be seen for example in diarylethenes²¹ and dihydropyrans.^{22–25} Nevertheless, there are few examples in which both properties can be combined to some extent, and larger geometric changes are matched with severe electronic changes, such as in spiropyrans or the recently introduced Stenhouse dyes.^{26–28} Here strong photochromism and electronic changes are found in conjunction with distinct geometry changes. Such a combination is beneficial for virtually any application since both electronic changes (conjugation, polarity, photochromism, etc.) and geometry changes (proximity alterations, spatial distribution of functional groups, etc.) can then be controlled with the highest precision.

In this work, we present an entirely unexplored type of fundamental photoswitch, hemithioindigo^{7,20}-based trioxobicyclonadiene (HTI-TOND) **1** (Figure 1). HTI-TOND enables the desirable combination of concomitant geometry and electronic changes within a distinct molecular framework. It allows alteration between up to four different stable states **A** to **D** instead of the usual two states found in most fundamental

photoswitches. The TOND state is a highly rigid 3D molecular structure offering precise placement of functional groups in space. The other states are more flexible and in addition are differently conjugated, offering distinct electronic communication between molecular parts. The photoswitching processes employ two exotic reactions, a rare “forbidden” hetero-Diels–Alder/retro-Diels–Alder reaction (TOND **A** to **C/D** conversions) and an oxygen rearrangement reaction (**B** to **C/D** conversions), which are now introduced as novel mechanistic tools into the realm of photoswitching. In addition, a thermal oxygen-rearrangement reaction leading from TOND **A** to isomer **B** is also uncovered.

TOND-like structures are quite rare but are found in some natural products produced by fungi and bacteria.^{29–33} The simple methylated derivative was discovered in complexation with platinum in 1965 by Gibson et al.,³⁴ and its resolution was reported in 1977 by de Renzi et al.³⁵ Further TOND motifs have later been explored for synthetic accessibility^{36–39} and applications in, e.g., supramolecular chemistry,^{40–44} mainly by Kollenz and co-workers but also by others.^{45–47} To the best of our knowledge, no photochemistry has been reported to date. The HTI-TOND motif presented herein provides a hitherto not described aryl-substituted version of the TOND structure, enabling further functionalization on the periphery and in different spatial quadrants.

HTI-TOND system **1** was synthesized in four high-yielding steps that represent an alteration of a previously reported protocol for synthesizing highly substituted HTIs⁴⁸ (Scheme 1). Starting from commercially available thiosalicylic acid and

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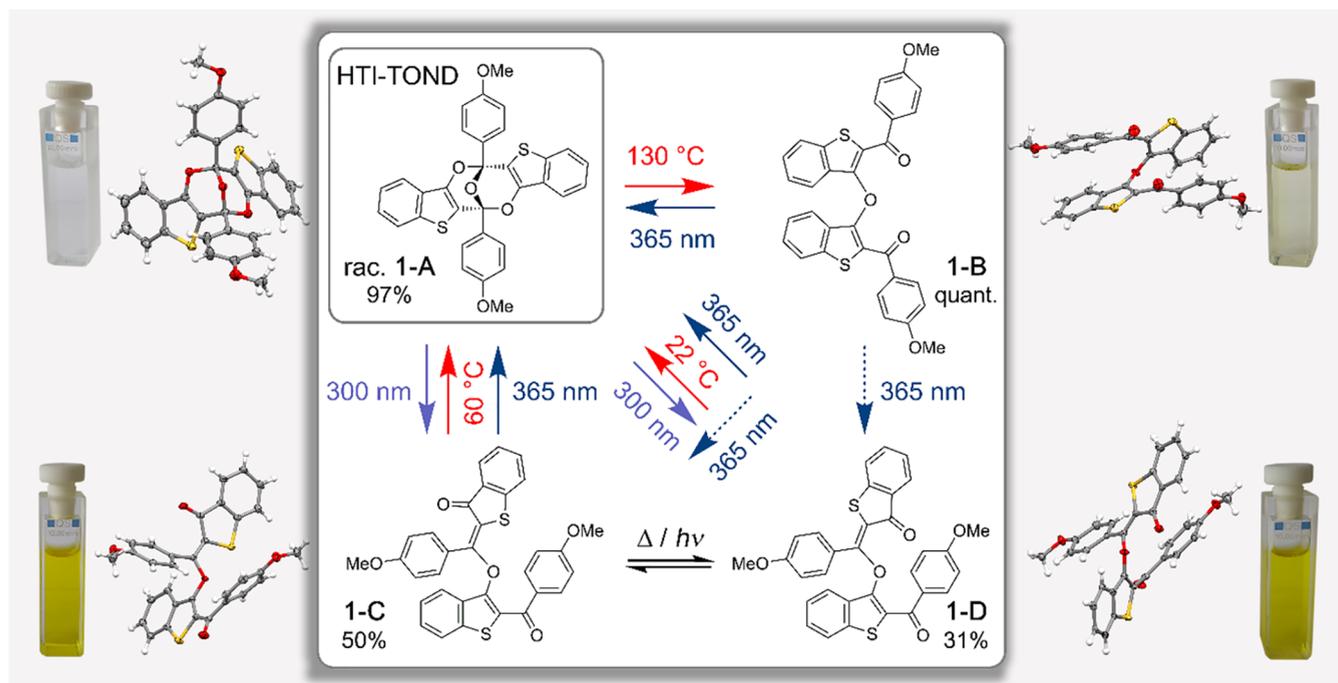
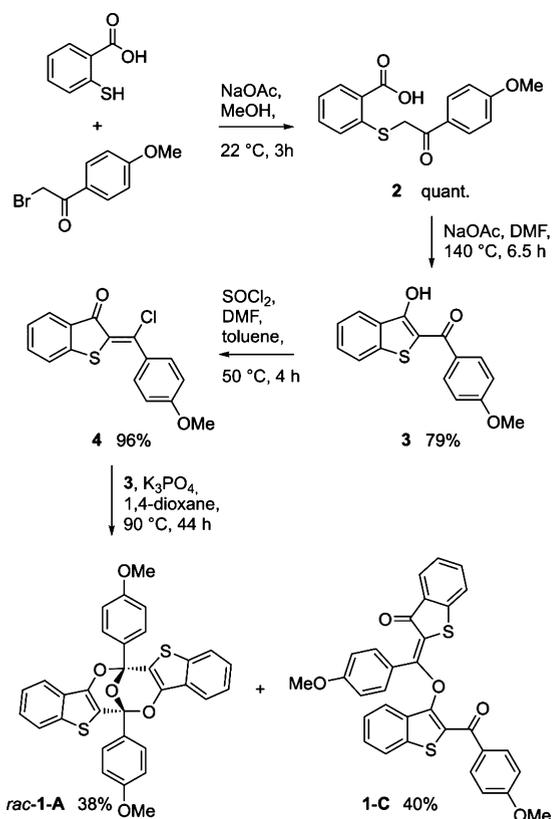


Figure 1. HTI-TOND 1 enabling switching between four different states A (racemic rigid TOND structure), B, C, and D with distinct geometric and electronic properties. Schematic structures, photo- or thermally induced net interconversions, and the corresponding structures in the crystalline state are shown alongside photographs of pure isomer solutions in toluene.

Scheme 1. Simple and High-Yielding Four-Step Synthesis of HTI-TOND 1



2-bromo-4'-methoxyacetophenone, a nucleophilic substitution reaction affords the corresponding thioether **2** quantitatively. Intramolecular condensation under mildly basic conditions

leads to hydroxythiophene derivative **3** in 79% yield, which subsequently is transformed into chlorinated HTI **4** in 96% yield after reaction with thionyl chloride. When precursors **3** and **4** are combined in the presence of K_3PO_4 at elevated temperatures, photoswitch **1** is obtained in 78% overall yield either as sole HTI-TOND A or as an isomeric mixture of 38% HTI-TOND A and 40% C, depending on the reaction duration. After application of different heating or irradiation steps, the four isomers of **1** (A to D) could be accumulated to varying degrees. Separation of the isomers using HPLC was possible because of their sufficiently high thermal stabilities. Identification and spectral assignment was facilitated by X-ray diffraction analysis in the crystalline state for all four isomers (see Figure 1).

The thermal behavior of the HTI-TOND system was first examined at different temperatures to establish its ground-state energy profile at the common temperature of 22 °C (Figure 2). The thermodynamically most stable state was found to be isomer B, which is obtained after prolonged heating to temperatures above 100 °C of, e.g., isomer A in toluene- d_8 solution. This reaction represents an unusual oxygen-rearrangement reaction in which not only two oxygen-carbon bonds are broken within the TOND structure but also new oxygen-carbon connectivity is established. An in-depth mechanistic investigation of this reaction will be the topic of a future dissemination. Heating a solution of either isomer C or D over prolonged times above 100 °C also leads to full conversion to pure isomer B. However, when the temperature is lowered, thermal isomer conversions become clearer. Starting from pure isomer C, HTI-TOND A is accumulated first as the direct isomerization product at 60 to 90 °C. When pure isomer D is heated, HTI-TOND A is also the direct isomerization product—even at ambient temperatures where no further thermal isomerization to B takes place. At the same time, a small amount of isomer C is also formed from D.

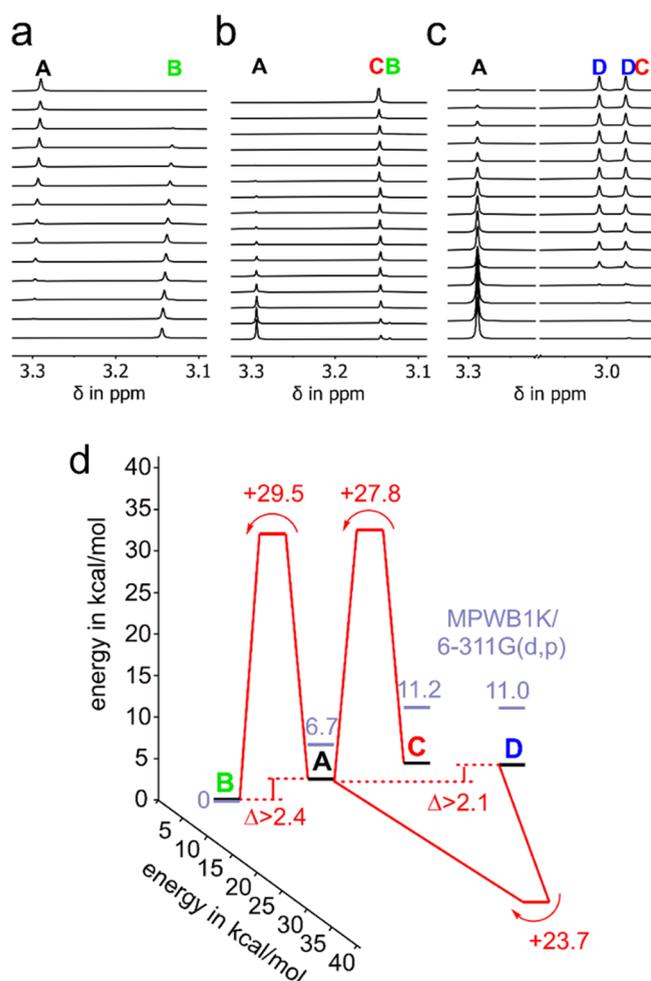


Figure 2. Thermal isomerization reactions of HTI-TOND system 1 and corresponding ground-state energy profile. (a–c) ^1H NMR spectra (400 MHz, toluene- d_8) showing thermal conversions of isomer HTI-TOND A at 100 °C, isomer C at 60 °C, and isomer D at 22 °C, respectively. Marked signals correspond to the OMe groups. (d) Experimental (red, all values correspond to 22 °C) and theoretical (violet) ground-state energy profile of 1.

Because of the different activation energies for thermal isomerizations, HTI-TOND A or isomer B can be accumulated in high yields in thermal steps from isomers C and D if the temperature is controlled well. The corresponding Gibbs energies of activation ΔG^\ddagger as determined from kinetic analysis are given in Figure 2d. Since no thermal equilibria are established and isomer B is formed as the sole product after prolonged heating, only lower limits for the energy differences ΔG between isomers can be given by assuming 5% of a remaining isomer is not detected in the experiments. We further tested the effect of acid addition on the thermal behavior of 1. After addition of trifluoroacetic acid (TFA) to a solution of pure isomer C in toluene- d_8 solution, a significant acceleration of the thermal isomerization to exclusively HTI-TOND A took place even at ambient temperatures. Therefore, thermal reactions in the presence or absence of acid can be used to gain improved control to access the two most stable states A and B.

The experimental findings are generally in good agreement with the theoretical description conducted at the MPWB1K/6-

311G(d,p)/gd3bj level of theory, as shown in Figure 2d (for further details, see the Supporting Information).

The photochemistry of the HTI-TOND system 1 was investigated next by studying the photoreactions of the individual isomers separately (Figure 3). As depicted in Figure

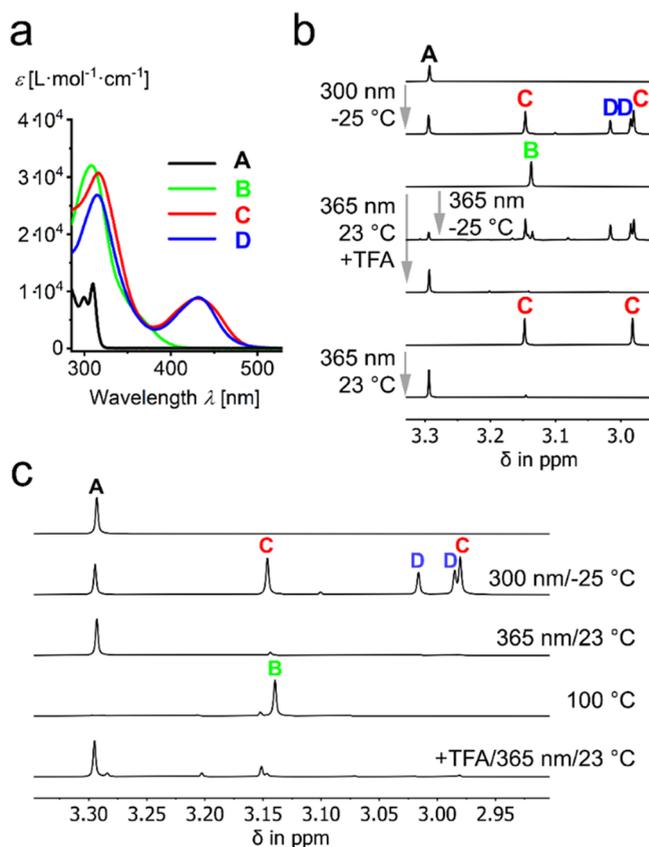


Figure 3. Photoisomerization and switching reactions of HTI-TOND system 1. (a) Molar absorptions of individual isomers A, B, C, and D of 1. (b) ^1H NMR (400 MHz, toluene- d_8) spectra showing photoconversions between individual isomers of 1 (MeO signals are shown). (c) Cycle experiment followed by ^1H NMR spectroscopy (400 MHz, toluene- d_8) in which isomers of 1 are converted in the sequence A \rightarrow C/D \rightarrow A \rightarrow B \rightarrow A.

3a, isomers A, B, and C/D show distinctly different molar absorptions, which are well-reproduced by the theoretical description (see the Supporting Information). The absorptions of isomers C and D appear to be most red-shifted but are not well-distinct from each other, which prevents effective photoswitching between just these two isomers. The absorption of HTI-TOND A resides only in the UV part of the absorption spectrum, and thus, photochemistry needs to invoke light of 300 nm. Irradiation at that wavelength in toluene- d_8 solution at -25 °C (to exclude thermal reactions of D) leads to the appearance of the spectral hallmarks of isomers C and D in the absorption and ^1H NMR spectra. In the photostationary state (pss), a mixture comprising 19% remaining HTI-TOND A and a total of 81% isomers C (50%, dominating species in solution) and D (31%) is formed. It is thus established that photoirradiation of HTI-TOND A with UV light leads to a rather exotic photochemical retro-hetero-Diels–Alder (RHDA) reaction that opens the TOND structure, yielding an intense yellow color of the solution. This photoreaction also delivers a different isomer than the

thermal reaction of HTI-TOND **A**, which establishes the latter as the branching point for the switching capacity of **1**.

Isomer **B** possesses an absorption that reaches the 400 nm mark with its tail. It can thus be irradiated with light of longer wavelengths (e.g., 365 nm in toluene(- d_8)) at different temperatures, leading to population of isomers **C** and **D** in roughly equal amounts first and then to almost complete conversion to HTI-TOND **A** after prolonged irradiation times. Low-temperature irradiation of **B** shows that this behavior is due solely to photoconversions, including a less efficient photoreaction from **B** to **A**, resulting in a pss with up to 97% **A** accumulated. The dominating photochemical reaction from **B** to **C/D** represents again a rather exotic oxygen-rearrangement reaction, which also differs from the corresponding thermal rearrangement leading from HTI-TOND **A** to **B**. The mechanism is again not clarified at this point and is currently under investigation in our laboratory. When toluene(- d_8) solutions of pure isomer **C** are irradiated at a wavelength of 300 or 365 nm at different temperatures, isomer **D** is populated initially as the product of *Z/E* photoisomerization, but conversion to HTI-TOND **A** over prolonged irradiation times is also observed. Likewise, irradiation of isomer **D** leads to almost complete conversion to isomer **A** after prolonged irradiation times with 365 nm or longer-wavelength light.

Taking the photochemistry of **1** together, irradiation of isomer **B** with 365 nm light populates isomer **A** almost quantitatively. Isomers **C** and **D** can be accumulated in up to 81% yield after irradiation of HTI-TOND **A** with 300 nm light and thus serve as a thermally stable third state. When in turn isomers **C** and **D** are irradiated with 365 nm light, they readily convert back to **A** photochemically. Some degradation is observed in the photoreactions (see the [Supporting Information](#)), but in the presence of acid the overall switching processes are facilitated and proceed more rapidly.

Overall, it is thus possible to access three different states of **1** in high percentages and convert them reversibly into each other using light of different wavelengths and heat as signals. The fourth isomer **D** cannot be enriched to the degree of being the dominant species in solution at present. However, up to 30% **D** can be obtained by irradiation of isomer **A** at low temperatures. HTI-TOND isomer **A** serves as the branching point, from which isomers **B** and **C/D** can be obtained in high yields either thermally or photochemically, respectively. To illustrate, we have conducted a cycle experiment interconverting the isomers in the sequence $A \rightarrow C/D \rightarrow A \rightarrow B \rightarrow A$ (Figure 3c). Additionally, the interconversion sequence $A \rightarrow B \rightarrow A$ was conducted four times (see the [Supporting Information](#)), evidencing multiple switching cycle capacity.

In summary, we have presented a unique molecular photoswitch that allows multistate switching in different sequences by a combination of light and heating signals. During switching the rigidity and electronic character of the molecular architecture are altered significantly, leading from colorless to deep-yellow solutions. Unusual RHDA and rearrangement photo- and thermal reactions are employed for the isomerization processes, which now enter the stage of photoswitching together with a unique molecular 3D structure as a novel motif for responsive nanosystems. We believe that this photoswitching system offers highly interesting and distinctive possibilities for responsive molecular functions in all chemistry-related fields. Applications as well as mechanistic elucidations are currently under investigation in our laboratory.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/jacs.1c12364>.

Synthesis details; photochemical, photophysical, and thermal behavior; theoretical description; and crystal structural data ([PDF](#))

Accession Codes

CCDC 2123730–2123732 and 2123787 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, U.K.; fax: +44 1223 336033.

■ AUTHOR INFORMATION

Corresponding Author

Henry Dube – Department of Chemistry and Pharmacy, Friedrich-Alexander Universität Erlangen-Nürnberg, 91058 Erlangen, Germany; orcid.org/0000-0002-5055-9924; Email: henry.dube@fau.de

Authors

Fabien Kohl – Department of Chemistry and Pharmacy, Friedrich-Alexander Universität Erlangen-Nürnberg, 91058 Erlangen, Germany

Aaron Gerwien – Department of Chemistry and Center for Integrated Protein Science (CIPSM), Ludwig-Maximilians Universität München, 81377 Munich, Germany

Frank Hampel – Department of Chemistry and Pharmacy, Friedrich-Alexander Universität Erlangen-Nürnberg, 91058 Erlangen, Germany

Peter Mayer – Department of Chemistry and Center for Integrated Protein Science (CIPSM), Ludwig-Maximilians Universität München, 81377 Munich, Germany

Complete contact information is available at: <https://pubs.acs.org/10.1021/jacs.1c12364>

Notes

The authors declare no competing financial interest.

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