



HAL
open science

Bending Enamine Patterns of Stabilized Pentalenes into “Polymethine Ylides”

Valentin Thery, Cyriac Barra, Alexandra Simeoni, Jacques Pecaut, Eder
Tomás-Mendivil, David Martin

► **To cite this version:**

Valentin Thery, Cyriac Barra, Alexandra Simeoni, Jacques Pecaut, Eder Tomás-Mendivil, et al.. Bending Enamine Patterns of Stabilized Pentalenes into “Polymethine Ylides”. *Organic Letters*, 2023, 25 (3), pp.560-564. <10.1021/acs.orglett.3c00037>. <hal-04234557>

HAL Id: hal-04234557

<https://cnrs.hal.science/hal-04234557v1>

Submitted on 10 Oct 2023

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire HAL, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



HAL Authorization

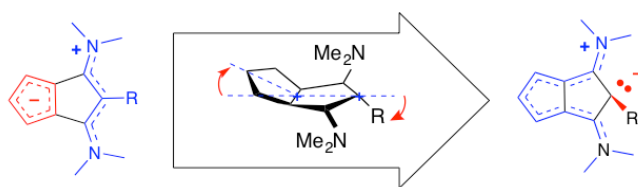
Bending Enamine Patterns of Stabilized Pentalenes into “Polymethine Ylides”.

Valentin They,[†] Cyriac Barra,[†] Alexandra Simeoni,[†] Jacques Pecaut,[‡] Eder Tomás-Méndivil,^{*†} and David Martin^{*†}

[†] Univ. Grenoble-Alpes, UMR CNRS-UGA 5250, CS 40700, 38058 Grenoble, France

[‡] Univ. Grenoble Alpes, CEA, CNRS, INAC-SyMMES, UMR 5819 38000 Grenoble, France

ABSTRACT: We report the synthesis and structural study of 2-substituted 1,3-bis(dimethylamino)pentalenes. The two-electrons donating substituents shift the formally anti-aromatic pattern toward more suited polarized structures. A subtle steric trade off can result either in planar cyclopentadienyl vinamidiniums, or in distorted structures featuring a pyramidalized ylidic carbon adjacent to a stabilized p-conjugated iminium (polymethine). This latter pattern mimics a postulated activated distorted geometry for key Breslow intermediates in the active site of thiamine-dependent enzymes. It highlights how the energetic drive to avoid anti-aromaticity can be used to access models for unconventional distorted conformations of organic molecules.



INTRODUCTION

Organic molecules can adopt unconventional geometries when constrained by high steric demand, rigid polycyclic scaffolds, or compression within molecular cages or crystallographic voids.¹⁻⁸ Similarly, the environments of active sites of enzymes are able to induce significant bond elongations, twists or out of plane distortions in small substrates.⁹ These reactive conformations can play a key role in enzymatic activations.¹⁰⁻¹⁴ They also constitute as many intriguing synthetic targets for a molecular chemist, who would like to pit one's wits against nature for the design and isolation of a chemical oddity.

In 2012, Tittman and coworkers considered such a distortion for enaminol **A** (Figure 1a),¹¹ a well-established intermediate in reactions involving thiamine-dependent enzymes.¹⁵⁻¹⁷ They showed that high resolution X-ray diffraction data of this compound within pyruvate oxidase from *Lactobacillus plantarum* could fit a model, in which **A** is in fast equilibrium with other tautomers, providing the C β carbon of the N-C α =C β enamine moiety of **A** does not feature a planar environment (**A'**, Figure 1a). An organic chemist would certainly consider it an audacious proposition, to say the least. Indeed, out-of-plane distortions of C=C double bonds in reactive alkenes are known, but mostly resulting from strained polycyclic structures.^{1,2} In the specific case of enamines,¹⁸ which feature a strongly polarized C=C double bond, a pyramidalized C β carbon would lead to an “iminium ylide”. As it is, the chimeric organic function appears paradoxical, as it bears a highly nucleophilic carbanion center conflicting with an electrophilic iminium moiety. Therefore, the design of viable versions is likely to require further stabilizing features.

Herein, we report a series of small organic molecules, which provides for few snapshots of the formal distortion of a π -conjugated enamine pattern into an ylidic iminium.

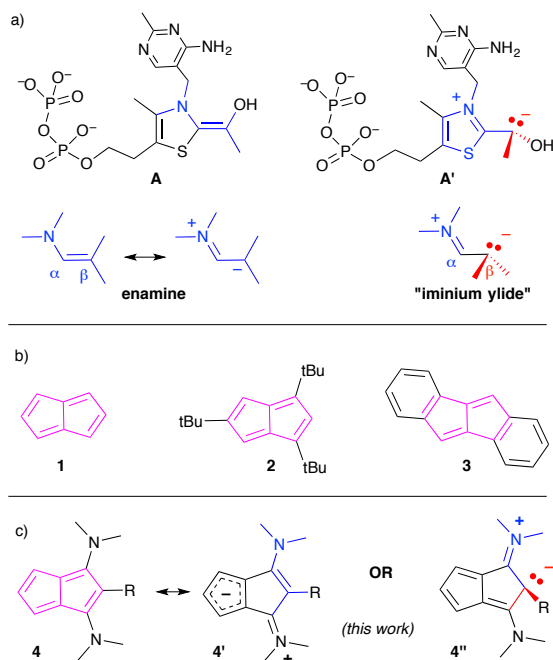


Figure 1: a) Enamines **A** are key intermediates in thiamine-dependent enzymatic catalysis. Distorted **A'** has been proposed to fit experimental X-ray diffraction data. b) Anti-aromatic pentalene **1** is highly reactive. Bulky derivative **2** and derivatives with benzo-fused pattern **3** can be isolated. c) Stabilized 1,3-di(amino)pentalenes **4** benefit from the aromaticity of a cyclopentadienyl moiety in limit form **4'**. This work unveils unforeseen alternative ylidic structures **4''**.

We came upon these molecular geometries while reexamining the electronic stabilization of pentalene derivatives. The parent pentalene **1** (Figure 1b) is a prototypical anti-aromatic hydrocarbon with 8 π -electrons.¹⁹ It is highly reactive, readily dimerizes and could only be characterized at cryogenic temperatures.²⁰ Few genuine pentalenes with high steric hindrance, such as 1,3,6-tri(*tert*-butyl)pentalene **2**, have been isolated.²¹⁻²⁶ In modern literature, "stable pentalenes" mostly refer to benzo-fused patterns **3**.²⁷ We were curious about a little-known design alternative, which was briefly investigated several decades ago by Hafner, Bangert and Orfanos.²⁸ They considered that the perturbation from electron-donating amino groups would shift the electronic situation towards a polarized electronic structure **4'**, better described as the association of an aromatic cyclopentadienyl and a vinamidinium moiety. Accordingly, they synthesized 1,3-bis(dimethylamino)pentalene **4a**,²⁸ whose identity was supported by ¹H NMR and reactivity (reversible protonation afforded the conjugate acid).

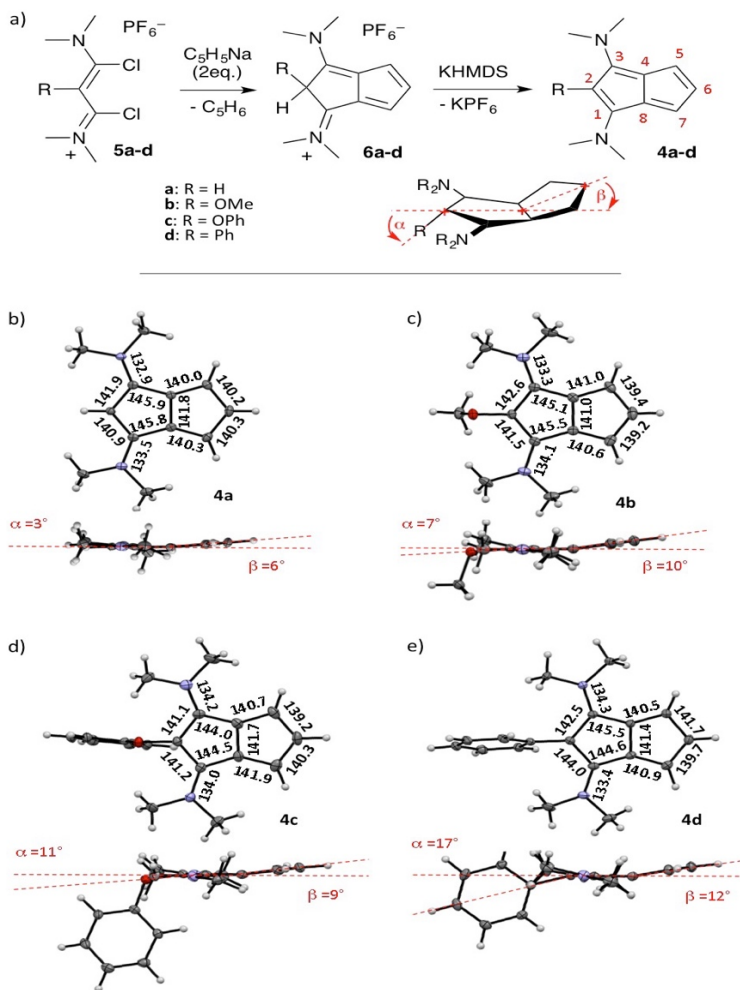


Figure 2: a) Synthesis and reactivity of stabilized pentalenes **4a-d**; numbering of pentalene rings and geometrical definition of bending angles α and β . b-e) Top and side views of ORTEP-representation of X-ray crystal structures of pentalenes **4a** (b), **4b** (c), **4c** (d) and **4d** (e), with thermal ellipsoids set at 50% probability. Co-crystallized solvent molecules are omitted for clarity. Bond lengths are indicated in pm.

The single crystal X-ray structure³³ of **4a** (Figure 2b) matches the envisioned polarized pattern **4'** with expected C–C bond lengths for a delocalized cyclopentadienyl and a vinamidinium moieties (140.0–141.8 pm), separated by longer single C3–C4 and C1–C8 bonds (149.8 and 149.9 pm, respectively). Note that the molecule remains slightly unsymmetrical, with a formal low C_s symmetry. For instance, there is no mirror perpendicular to the pentalene plane because methyl substituents at amino groups have different conformations. In the same line, C1–C2 is slightly longer than C2–C3 bond length (140.9 and 141.9 pm, respectively). We performed DFT calculations at several levels of theory and obtained optimized structures of **4a** only with a high C_{2h} symmetry.³⁴ When freezing the conformation at amino groups (see supporting information), relaxed optimizations reproduced well the solid-state geometry, affording transition states that are less than 0.3 kcal.mol⁻¹ higher in enthalpy than the corresponding unconstrained minimum. More generally, molecules **4a-d** are not positioned on an element of symmetry in the crystallographic cells. Therefore, we interpreted the slight differences between *in silico* and solid-state geometries as the result of the non-symmetrical environment for the molecules in the crystal structure. Note that Hafner mentioned preliminary low-resolution crystallographic data for **4a** in 1982.³⁵ The resulting geometry featured a more localized π -structure (for example, C3–C4 = 147 pm versus C1–C8 = 142 pm; C5–C6 = 137 pm versus C6–C7 = 143 pm). The proposed alternation of short and longer C–C bonds was somehow reminiscent of the structure of pristine anti-aromatic pentalenes.²² Our well-resolved structure (*R* index: 5.4%) shows that this was in fact the result of low-quality data and finally allows to rule out residual anti-aromatic character.

Whereas **4a** is mostly planar, experimental solid-state structures revealed that 2-substituted 1,3-bis(dimethyl)amino-pentalenes **4b-d** feature a significant pyramidalization at the C2 center and out-of-plane bending of the C4–C8 bond (Figures 2c-e). Importantly, DFT optimizations well reproduced the geometries, thus indicating that the crystallographic environment had no major role in inducing the distortions. An unbalance in sterics can induce significant *syn*-bending of C=C double bonds. This has been exemplified by various reports of bent structures of norbornadienes, sesquinorbornadienes or oxasesquinorbornadienes.² Therefore, we interpreted the bending (β) of the C4–C8 bond as a direct result of the pyramidalization (α), the cyclopentadienyl moiety being “pushed away” by the C2-substituent.

The pyramidalization (α) at C2 of **4b-d** suggests a significant weight for the ylidic limit form **4''**, with a lone pair at C2 (red, Figure 3b) next to a stabilized conjugated iminium, also called polymethine (blue). However, neither the geometric distortions, nor the difference in the electronic effect of substituents resulted in significant changes in the nature or the energy (in -6.1 – -6.2 eV range) of the highest molecular orbital of **4a-d**. In order to get further insights, we performed a relaxed scan optimization of model **4a** as a function of α (Figure 3a). Pyramidalization at C2 results in longer C1–C2 and shorter C1–C8 bonds, as expected for a gradual shift from **4a'** to ylidic limit form **4a''**. Furthermore, we computed Electron Localization Functions (ELF).³⁶ ELF is related to the Pauli exclusion principle and is a powerful mathematical bridge between quantum mechanics and intuitive chemical bonding concepts, such as electron pairing. Topological analysis of ELF affords partition of space into areas (so called basins), which can be attributed to bonds, core electrons, etc.^{37,38} The basin of a lone pair contains no nuclear center and is monosynaptic (it shares a boundary with only one core basin).³⁹ Such lone pair (red basins) is found at the C2 position of **4a**, even for modest distortions (Figure 3a).⁴⁰ As intuitively expected, the electronic population and volume of the corresponding basin grow when increasing α .

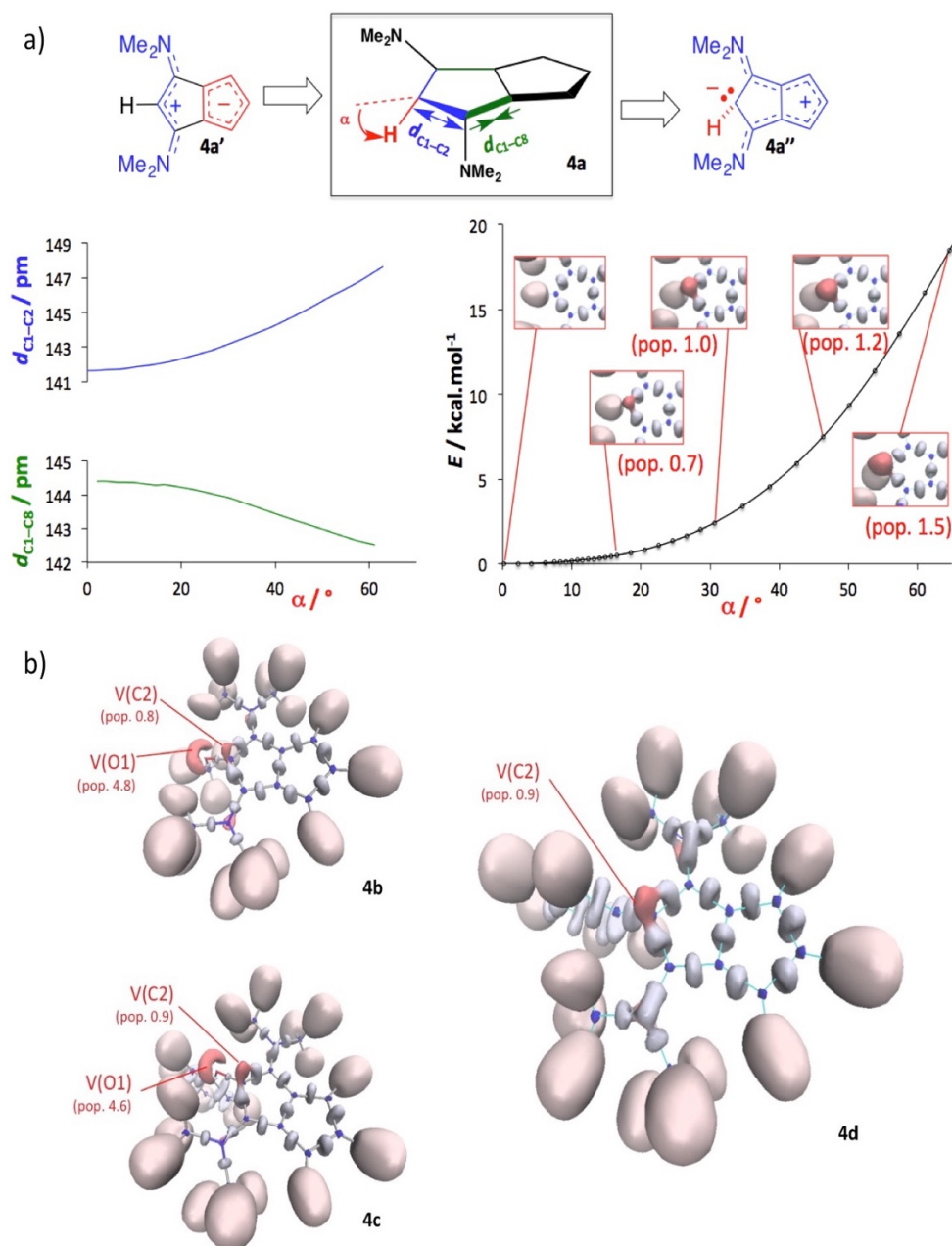


Figure 3: (a) Bond lengths (C1–C2 and C1–C8) and energy in relaxed optimization of **4a** as a function of α . Computed ELF isosurfaces at 0.80 isovalues in the vicinity of C2 are represented for some α values. The red volumes are monosynaptic basins corresponding to lone pairs. Other color codes are: blue for core electrons, beige for C-H bonds basins, grey for disynaptic basins (other bonds). (b) Representations of computed ELF at 0.80 isovalues for optimized structure of **4b-d**.

Similarly, ELF for optimized geometry of **4b-d** feature basins for lone pairs at C2 (Figure 3b). Note that α increases throughout the **4b-d** series (**4b**: 7°; **4c**: 11°; **4d**: 17°), whereas populations (**4b**: 0.8; **4c**: 0.92; **4d**: 0.87) and volumes (**4b**: 38 Å³; **4c**: 42.3 Å³; **4d**: 40.2 Å³) of V(C2) afford a different ranking: **4b** < **4d** ≤ **4c**. Data for **4d** and **4c** correspond to the situation for **4a** with α about 20°. This shows that **4a**, **4b** and **4c-d** have an increasing ylidic character, **4c** and **4d** being roughly intermediate between a fully π -delocalized vinamidinium and an idealized pyramidalized polymethine ylide.^{41,42}

Only one minimum was found on the hypersurface of energy of **4a-c**. However, we identified two minima for **4d**: one reproducing the experimental solid-state structure (**4d''**), but also one corresponding to polarized planar pentalene **4d'** (Figure 4). In both forms, the nitrogen atoms have a planar environment. Although they can act as π -donors, they are not fully conjugated with the rest of the π -system. The corresponding torsions ($\phi_1, \phi_2 \approx \pm 20^\circ$) at the C–N bonds are likely the result of steric repulsions from the neighboring phenyl substituent. In **4d''**, the amino groups are paralleled ($\phi_1 \approx -\phi_2$). In this *C_s* geometry, the *N*-methyl groups hinder one face of the pentalene, pushing the phenyl group on the other side. Conversely, the geometry of **4d'** ($\phi_1 \approx \phi_2$) creates a pocket that allows for the alignment of the C–Ph bond in the plane of the pentalene ring. The two conformers are involved in a very fast equilibrium through transition state **TS1**, which is only few kcal.mol⁻¹ higher in energy. An alternative transition state **TS2** is higher in energy. It features a fully twisted amino group with an orthogonal non-conjugated lone pair. The maximum on the hypersurface of energy corresponds to **4d_{max}** (see Figure S2), in which the lone pairs of both amino groups are perpendicular to the π -system of the pentalene. In absence of stabilization from electron-donating substituents,⁴³ **4d_{max}** is a genuine anti-aromatic pentalene, with an alternation of single and double C-C bonds in the π -conjugated bicycle.

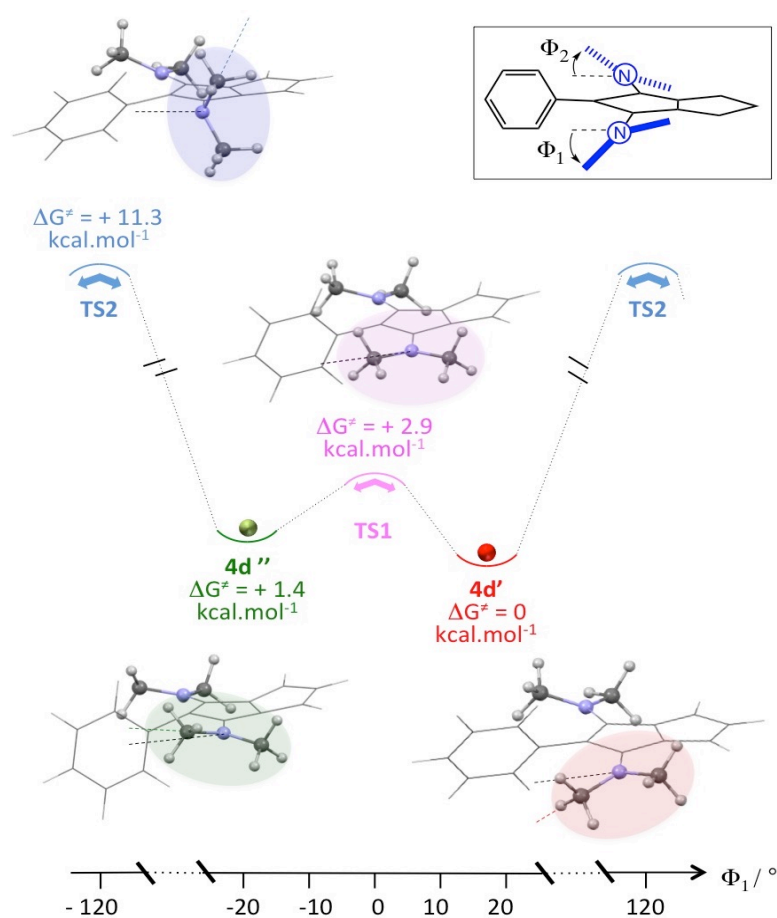


Figure 4: Computed conformational profile of **4d** as a function of ϕ_1 . Geometry of minima (**4d'** and **4d''**) and transition states (**TS1** and **TS2**) are shown with wireframes, dimethylamino groups being highlighted with a ball-and-stick style. Note the 240° periodicity; for instance, $\phi_1 = -120^\circ$ and $\phi_2 = 120^\circ$ both correspond to **TS2**, featuring a pyramidalized amino group with a lone pair parallel to C1-C2.

In conclusion, the two electron-donating amino substituents of **4a** shift the anti-aromatic pentalene pattern toward a more suited polarized structure **4a'**, as envisioned by Hafner et al. However, in 2-substituted pentalenes **4b-d**, steric hindrance precludes the full donation of the dimethylamino groups. This situation results in distorted geometries **4''**. Topological analysis of Electron Localization Functions indicates a lone pair at the pyramidalized C2 carbon atom, confirming a marked ylidic character for **4''**. In **4d**, both

conformations co-exist in fast equilibrium. These compounds provide for structural models for the postulated pyramidalized ylidic forms of Breslow intermediates in active site of thiamine-dependent enzymes, especially O-substituted derivatives **4b-c**.

The energetic drive to avoid anti-aromaticity usually triggers a pseudo Jahn-Teller distortion in cyclic unsaturated hydrocarbon backbones, resulting in two distinct valence tautomers with alternating single and double bonds.⁴⁴⁻⁴⁷ Here, a subtle trade-off with sterics provides access to unprecedented distorted forms with significant ylidic character. The introduction of anti-aromatic patterns is an unforeseen strategy for the design of unconventional, otherwise unattainable, distorted conformations of organic molecules.

Funding Sources

This work was supported by the French National Agency for Research (ANR-20-CE07-0010).

ACKNOWLEDGMENT

This work was supported by the French National Agency for Research (ANR-20-CE07-0010). Thanks are due to the CECCIC center of Grenoble for computer resources and the ICMG analytic platform (FR 2607). We acknowledge the CNRS and the University of Grenoble Alpes for a frictionless environment in the context of the Labex Arcane and CBH-EUR-GS (ANR-17-EURE-0003).

REFERENCES

- (1) Borden, W. T., Pyramidalized alkenes. *Chem. Rev.* **1989**, *89*, 1095–1109.
- (2) Vazquez, S.; Camps, P., Chemistry of pyramidalized alkenes. *Tetrahedron* **2005**, *61*, 5147–5208.
- (3) Tani, K.; Stoltz, B. M., Synthesis and structural analysis of 2-quinuclidonium tetrafluoroborate. *Nature* **2006**, *441*, 731–734.
- (4) Scarso, A.; Trembleau, L.; Rebek, J., Encapsulation induces helical folding of alkanes. *Angew. Chem. Int. Ed.* **2003**, *42*, 5499–5502.
- (5) Scarso, A.; Trembleau, L.; Rebek, J., Helical folding of alkanes in a self-assembled, cylindrical capsule. *J. Am. Chem. Soc.* **2004**, *126*, 13512–13518.
- (6) Ajami, D.; Rebek, J., Compressed alkanes in reversible encapsulation complexes. *Nat. Chem.* **2009**, *1*, 87–90.
- (7) Takezawa H.; Shitozawa, K.; Fujita M., Enhanced reactivity of twisted amides inside a molecular cage. *Nat. Chem.* **2020**, *12*, 574–578.
- (8) Sivasankar, N.; Vasudevan, S., Stabilization of a distorted conformation of cyclohexane adsorbed in the voids of silicalite-1. *Catal. Lett.* **2004**, *97*, 53–58.
- (9) Neumann, P.; Tittmann, K., Marvels of enzyme catalysis at true atomic resolution: distortions, bond elongations, hidden flips, protonation states and atom identities. *Cur. Opin. Struct. Biol.* **2014**, *29*, 122–133.
- (10) Parikh, S. S.; Walcher, G.; Jones, G. D.; Slupphaug, G.; Krokan, H. E.; Blackburn, G. M.; Tainer, J. A., Uracil-DNA glycosylase–DNA substrate and product structures: Conformational strain promotes catalytic efficiency by coupled stereoelectronic effects. *Proc. Natl. Acad. Sci. USA.* **2020**, *97*, 5083–5088.
- (11) Meyer, D.; Neumann, P.; Koers, E.; Tittmann, K., Unexpected tautomeric equilibria of the carbanion-enamine intermediate in pyruvate oxidase highlight unrecognized chemical versatility of thiamin. *Proc. Natl. Acad. Sci. USA* **2012**, *109*, 10867–10872.
- (12) Fujihashi, M.; Ishida, T.; Kuroda, S.; Kotra, L. P.; Pai, E. F.; Miki, K., Substrate distortion contributes to the catalysis of orotidine 5'-monophosphate decarboxylase. *J. Am. Chem. Soc.* **2013**, *135*, 17432–17443.
- (13) Ludtke, S.; Neumann, P.; Erixon, K. M.; Leeper, F.; Kluger, R.; Ficner, R.; Tittmann K., Sub-Angstrom-resolution crystallography reveals physical distortions that enhance reactivity of a covalent enzymatic intermediate. *Nat. Chem.* **2013**, *5*, 762–767.
- (14) Vladimirova, A.; Patskovsky, Y.; Fedorov, A. A.; Bonanno, J. B.; Fedorov, E. V.; Toro, R.; Hillerich, B.; Seidel, R. D.; Richards, N. G. J.; Almo, S. C.; Rauschel, F. M., Substrate distortion and the catalytic reaction mechanism of 5-carboxyvanillate decarboxylase. *J. Am. Chem. Soc.* **2016**, *138*, 826–836.
- (15) Breslow, R., On the Mechanism of Thiamine Action. IV. Evidence from Studies on Model Systems. *J. Am. Chem. Soc.* **1958**, *80*, 3719–3726.
- (16) Kluger, R.; Tittmann, K., Thiamin diphosphate catalysis: Enzymic and nonenzymic covalent intermediates. *Chem. Rev.* **2008**, *108*, 1797–1833.
- (17) Jordan, F., Current mechanistic understanding of thiamin diphosphate-dependent enzymatic reactions. *Nat. Prod. Rep.* **2003**, *20*, 184–201.
- (18) Enamines are regarded as flexible at their amino moieties: Parasuk, W.; Parasuk, V., Proline- and thioproline-derived enamines: The theoretical study of torsional and ring-puckering conformations, *Comp. Theo. Chem.* **2011**, *964*, 133–140.
- (19) von Ragué Schleyer, P.; Jiao, H., What is aromaticity? *Pure Appl. Chem.* **1996**, *68*, 209–218.
- (20) Bally, T.; Chai, S.; Neuenschwander M.; Zhu Z., Pentalene: Formation, Electronic, and Vibrational Structure. *J. Am. Chem. Soc.* **1997**, *119*, 1869–1875.
- (21) Hafner, K.; Süß, H. U., 1,3,5-Tri-tert-Butylpentalene. A Stabilized Planar 8 π -Electron System. *Angew. Chem. Int. Ed.* **1973**, *12*, 575–577.
- (22) Kitschke, B.; Lindner, H. J., The crystal and molecular structures of two substituted pentalenes. *Tetrahedron Lett.* **1977**, *18*, 2511–2514.
- (23) Johnson, R. W., Electrochemistry and radical ions of 1,3,5-tri-tert-butylpentalene. *J. Am. Chem. Soc.* **1977**, *99*, 1461–1465.
- (24) Le Goff, E., The Synthesis of Hexaphenylpentalene. *J. Am. Chem. Soc.* **1962**, *84*, 3975–3976.
- (25) Hafner, K.; Suda, M. [6+2] Cycloadditions of Pentafulvene. A Facile Pentalene Synthesis. *Angew. Chem. Int. Ed.* **1976**, *15*, 314–315.
- (26) Suda, M.; Hafner, K., Synthesis of 4,6-di-tert-butyl-pentalene derivatives and their reversible dimerization. *Tetrahedron Lett.* **1977**, *18*, 2449–2452.
- (27) Konishi, A.; Yasuda, M., Breathing new life into nonalternant hydrocarbon chemistry: syntheses and properties of polycyclic hydrocarbons containing azulene, pentalene, and heptalene frameworks. *Chem. Lett.* **2021**, *50*, 195–212.
- (28) Hafner, K.; Bangert, K. F.; Orfanos, V., 1,3-Bis(dimethylamino)pentalene. *Angew. Chem. Int. Ed.* **1967**, *6*, 451–452.
- (29) Janousek, Z.; Viehe, H. G., Condensation of Dichloromethylenedimethylammonium Chloride (Phosgene Immonium Chloride) with N,N-Diakylcarboxamides. *Angew. Chem. Int. Ed.* **1971**, *10*, 574–575.
- (30) De Voghel, G. J.; Eggerichs, T. L.; Janousek, Z.; Viehe, H. G., Phosgene Immonium Salts XIII. Dichloromalonyl Cyanines and 3,5-Bis(dimethylamino)pyrazoles. *J. Org. Chem.* **1974**, *39*, 1233–1235.
- (31) Regnier, V.; Planet, Y.; Moore, C. E.; Pecaut, J.; Philouze, C.; Martin, D., Stable di- and tri-coordinated carbon(II) supported by an electron-rich β -diketiminato ligand. *Angew. Chem. Int. Ed.* **2017**, *56*, 1031–1035.
- (32) Tripathi M.; Regnier V.; Lincheneau C.; Martin D., Investigation of the full reversal of selectivity in the reaction of aniline with 1,3-dichloro-1,3-bis(dimethylamino)vinamidinium salts. *New J. Chem.* **2017**, *41*, 15016–15020.

- (33) X-ray crystallographic data (cif files) were deposited at the Crystallographic Data Centre (deposition numbers: CCDC 2208540-2208546).
- (34) DFT calculations were performed with the Gaussian09 software package: Gaussian 09, Revision D.01, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson G. A., *et al.*, Gaussian 09, Gaussian Inc., Wallingford CT, **2009**.
- (35) Hafner, K., New aspects of the chemistry of nonbenzenoid polycyclic conjugated π -electron systems. *Pure Appl. Chem.* **1982**, *54*, 939–956.
- (36) Becke A. D.; Edgecombe K. E., A simple measure of electron localization in atomic and molecular systems. *J. Chem. Phys.* **1990**, *92*, 5397–5403.
- (37) Silvi B.; Savin A., Classification of chemical bonds based on topological analysis of electron localization functions. *Nature* **1994**, *371*, 683–686.
- (38) Savin, A.; Nesper, R.; Wengert, S.; Fässler, T. E., ELF: The Electron Localization Function, *Angew.Int. Ed. Engl.* **1997**, *36*, 1808–1832.
- (39) Chesnut, D. B. An Electron Localization Function Study of the Lone Pair. *J. Phys. Chem. A* **2000**, *104*, 11644–11650.
- (40) ELF computation were performed with the Topmod suite of software: Zoury, S.; Krokidis, X.; Fuster F.; Silvi, B., Computational tools for the electron localization function topological analysis. *Comp. Chem.* **1999**, *23*, 597–604.
- (41) Chamorro, E.; Fentealba P.; Savin, A., Electron Probability Distribution in AIM and ELF Basins. *J. Comput. Chem.* **2003**, *24*, 496–504.
- (42) Savin, A., On the significance of ELF basins. *J. Chem. Sci.* **2005**, *117*, 473–475.
- (43) For chameleonic behaviors of amino groups, see: Vatsadze, S. Z.; Loginova, Y. D.; dos Passos Gomes, G.; Alabugin, I. V., Stereoelectronic Chameleons: The Donor–Acceptor Dichotomy of Functional Groups. *Chem. Eur. J.*, **2017**, *23*, 3225–3245.
- (44) Berger, R. J. F.; Viel, A., The symmetry principle of antiaromaticity. *Z. Naturforsch.* **2020**, *75*, 327–339.
- (45) Bersuker, I. B., Pseudo-Jahn-Teller Effect - A Two-State Paradigm in Formation, Deformation, and Transformation of Molecular Systems and Solids. *Chem Rev.* **2013**, *113*, 1351–1390.
- (46) Ni, Y.; Sandoval-Salinas, M. E.; Tanaka, T.; Phan, H.; Herng, T. S.; Gopalakrishna, T. Y.; Ding, J.; Osuka, A.; Casanova, D.; Wu, J., [n]Cyclopara-biphenylmethine Polyradicaloids: [n]Annulene Analogs and Unusual Valence Tautomerization. *Chem* **2019**, *5*, 108–121.
- (47) Peeks, M. D.; Anderson, H. L., Watching Bonds Move in a Large Antiaromatic Ring. *Chem* **2019**, *5*, 9–17.