

Experimental and Theoretical Conformational Analysis of 5-Benzylimidazolidin-4-one Derivatives – a ‘Playground’ for Studying Dispersion Interactions and a ‘Windshield-Wiper’ Effect in Organocatalysis

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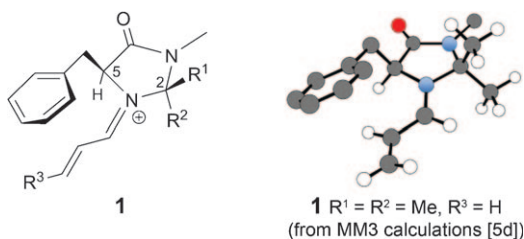
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The PF₆ salts of 5-benzyl-1-isopropylidene- and 5-benzyl-1-cinnamylidene-3-methylimidazolidin-4-ones **1** (*Scheme*) with various substituents in the 2-position have been prepared, and single crystals suitable for X-ray structure determination have been obtained of 14 such compounds, *i.e.*, **2–10** and **12–16** (*Figs. 2–5*). In nine of the structures, the Ph ring of the benzyl group resides above the heterocycle, in contact with the *cis*-substituent at C(2) (staggered conformation **A**; *Figs. 1–3*); in three structures, the Ph ring lies above the iminium π -plane (staggered conformation **B**; *Figs. 1* and *4*); in two structures, the benzylic C–C bond has an eclipsing conformation (**C**; *Figs. 1* and *5*) which places the Ph ring simultaneously at a maximum distance with its neighbors, the CO group, the N=C- π -system, and the *cis*-substituent at C(2) of the heterocycle. It is suggested by a qualitative conformational analysis (*Fig. 6*) that the three staggered conformations of the benzylic C–C bond are all subject to unfavorable steric interactions, so that the eclipsing conformation may be a kind of ‘*escape*’. State-of-the-art quantum-chemical methods, with large AO basic sets (near the limit) for the single-point calculations, were used to compute the structures of seven of the 14 iminium ions, *i.e.*, **3**, **4/12**, **5–7**, **13**, and **16** (*Table*) in the two staggered conformations, **A** and **B**, with the benzylic Ph group above the ring and above the iminium π -system, respectively. In all cases, the more stable computed conformer (‘isolated-molecule’ structure) corresponds to the one present in the crystal (overlay in *Fig. 7*). The energy differences are small (≤ 2 kcal/mol) which, together with the result of a potential-curve calculation for the rotation around the benzylic C–C bond of one of the structures, **16** (*Fig. 8*), suggests that the benzyl group is more or less freely rotating at ambient temperatures. The importance of intramolecular *London* dispersion (benzene ring in ‘contact’ with the *cis*-substituent in conformation **A**) for DFT and other quantum-chemical computations is demonstrated; the benzyl-imidazolidinones **1** appear to be ideal systems for detecting dispersion contributions between a benzene ring and alkyl or aryl CH groups. Enylidene ions of the type studied herein are the reactive intermediates of enantioselective organocatalytic conjugate additions, *Diels–Alder* reactions, and many other transformations involving α,β -unsaturated carbonyl compounds. Our experimental and theoretical results are discussed in view of the performance of 5-benzyl-imidazolidinones as enantioselective catalysts.

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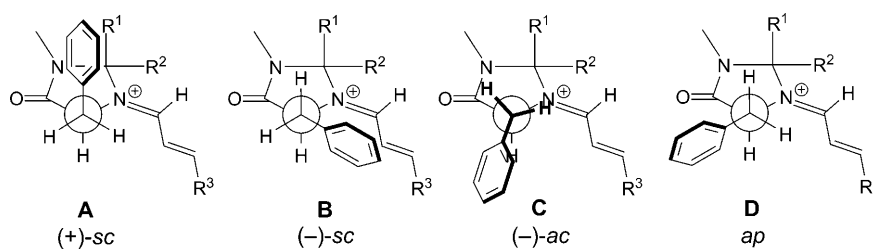
How Do the Reactive Intermediates of Organocatalysis with Amines Really Look like? – There is a rising interest in understanding the detailed mechanisms of organocatalysis [1–8]. The imidazolidinones [9], which *MacMillan* introduced as organocatalysts [5d], are mainly used for activation of α,β -unsaturated aldehydes, through iminium ions as reactive intermediates. In the (*S*)-phenylalanine-derived imidazolidinones **1**, the benzyl (Bn) group at C(5) is considered to provide the main contribution to steric shielding of the (*E*)-iminium-ion ‘top’ face, so that nucleophiles approach preferentially from the ‘bottom’ face. This is pictured in numerous papers by the *MacMillan* group, as shown in the presentation for **1** ($R^1 = R^2 = \text{Me}$, $R^3 = \text{H}$; results of an MM3 calculation [5b,d]).



A Challenge from Theory! – In 2004, *Houk* and co-workers [10] published results of DFT calculations of iminium ions **1** (with $R^1 = R^2 = R^3 = \text{Me}$, and $R^1 = \text{t-Bu}$, $R^2 = \text{H}$, $R^3 = \text{Me}$); the structures were computed with the functional B3LYP and 6-31G(d) basis sets (implemented in Gaussian 98, a level of theory, which *does not* account for *London* dispersion interactions, the weakest inter- and intramolecular forces). The surprising results of the calculations of the benzyl-trimethyl-imidazolidinone derivative (*Fig. 1*) were: *i*) of the *staggered* conformers **A**, **B**, and **D**, the one with the Ph group over the heterocycle, *i.e.*, **A**, was the most stable one, followed by conformer **B**, with the Ph group over the π -system (*cf.* **1**); *ii*) the least stable conformer, **D**, was the one with the Ph group next to the carbonyl O-atom; *iii*) an energy-minimum conformation, **C**, with an *eclipsed* $\text{PhCH}_2\text{--CH}$ bond was also found at only 1.3 kcal/mol above the most stable conformer **A**. For the 2-*t*-Bu derivative **1** ($R^1 = \text{t-Bu}$, $R^2 = \text{H}$, $R^3 = \text{Me}$), the most stable conformer, **B**, is the one with the Ph group above the π -system, and again, an *eclipsed* conformation, **C**, was found at only 0.7 kcal/mol above the global minimum (*Fig. 1*). A more recent computation (by *Platts* and *Tomkinson*, and co-workers [2a]) of the molecule **1**, $R^1 = R^2 = \text{Me}$, $R^3 = \text{Ph}$, using a DFT method with ‘*correct description of the weak interactions involved*’, confirmed the relative stability of the two *staggered* conformers **A** and **B** (*Fig. 1*).

Crystal Structures of Imidazolidinone-Derived Reactive Intermediates. – In January 2009, three single-crystal X-ray structures of 1-cinnamylidene-5-benzyl-3-methylimidazolidin-4-one iminium salts (cinnamylidene = 3-phenylprop-2-en-1-ylidene) were published [1c][2a]²). In the meantime, we have succeeded in obtaining

²) For *in situ* NMR detections of reactive intermediates in organocatalysis, see the publications by *B. List*, *D. G. Blackmond*, *S. H. Gellman*, *K. A. Jørgenson*, *W. W. Ogilvie* referenced in our previous publications [1].



	A	B	C	D
	(rel. energy [kcal/mol])			
Ref. [10]:				
R ¹ = R ² = R ³ = Me	0	0.3	1.3	3.5
R ¹ = ^t Bu, R ² = H, R ³ = Me	3.7	0	0.7	–
Ref. [2a]:				
R ¹ = R ² = Me, R ³ = Ph	0	1.2	–	–

Fig. 1. The three staggered conformations **A**, **B**, and **D**, and an eclipsed conformation, **C**, of the exocyclic C–C bond in N-enylidene 5-benzyl-3-methyl-imidazolidinones **1** and DFT-calculated relative energies of three specific molecules

suitable single crystals and in determining crystal structures of a whole series of such iminium salts, so that we have now a statistically significant number of structures (19 altogether), which allows us to discuss general trends. The preparation of the samples is outlined in the *Scheme*.

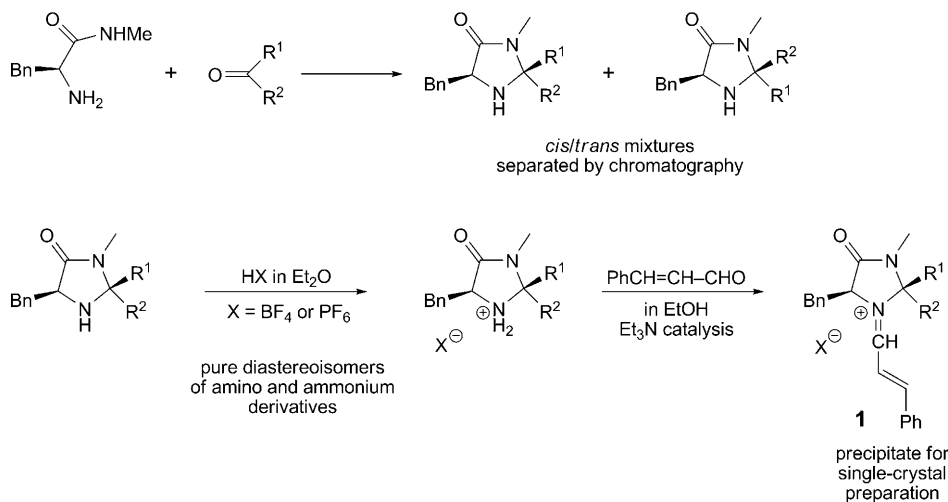
In most of the structures (11 out of 19), the benzylic Ph group is located over the heterocycle (see **2–10** in Figs. 2 and 3)³, with a C–H bond of the *cis*-substituent at C(2) pointing – more or less perpendicularly – towards the plane of the Ph ring. This conformation **A** is also present in a molecule without substituent at C(2) (isopropylidene salt **2**). Remarkably, conformer **A** is even found with substituents having no α -C,H group at C(2), but a β -C,H group (C(2)–C–C–H; see **4** and **6** in Fig. 2, and **9** and **10** in Fig. 3)! Not surprisingly, the C–F bond in the derivative **8** is *antiperiplanar* (*ap*) to the amide C–N(3) and *synclinal* (*sc*) or *gauche* to the iminium C=N(1) bond (with the more electropositive N-atom).

All 5-benzyl-imidazolidinone ammonium salts **11** studied so far have a (–)-*synclinal* conformation of the exocyclic PhCH₂–CH bond, placing the benzylic Ph ring and the heterocycle in a kind of a *gauche* arrangement (like in **B**; see Fig. 4). With the analogous *cis*-2,5-disubstituted cinnamylidene-imidazolidinones, this conformation was observed in the crystal structures of the compounds **12–14** (Ph, ⁱPr, and ^tBu substituent at C(2); Fig. 4).

The benzylic Ph group winds up in the space above the iminium π -system, with the two π -planes not parallel but at a certain angle. In contrast to the situation in conformers of type **A**, the Bn group is sterically shielding the ‘top’ face of the iminium system in conformers of type **B**. Note that the benzaldehyde-derived 2-Ph derivative adopts the conformation **A** in the crystal of the enantiomerically pure compound **4**

³) ... and, in all but two structures (*i.e.*, **9** and **10** in Fig. 3), the C=N bond has (*E*)-configuration!

Scheme. *Preparation of the Samples for X-Ray Crystal-Structure Determinations.* The single crystals are prepared by diffusion methods as described in our previous papers [1b–d]. Solutions of the analytically pure iminium salts contain (*E*)- and (*Z*)-isomers in ratios between >99:1 and 30:70 (by NMR analysis). The isomer which forms a single crystal from such solutions needs not be the major isomer. A discussion of the (*E/Z*)-isomerism of cinnamylidene derivatives of type **1** will be the subject of a separate communication. A full paper will follow with all the details of characterization of the compounds mentioned herein and of many others of the same structural type [1e].



(*Fig. 2*) and the conformation **B** in the crystal of the racemic form **12** (*Fig. 4*). This result may be interpreted as an indication that the energy difference between these two conformations is small.

In two cases, we found structures, in which the exocyclic $\text{PhCH}_2\text{--CH}$ bond is *quasi*-eclipsed (dihedral angles between 12 and 18° , see **15** and **16** in *Fig. 5*, and **C** in *Fig. 1*), with the Ph ring and the heterocycle being in a kind of an *anti*-arrangement. This *antiperiplanar* (*ac*) conformation was adopted in molecules **15** and **16** with a *cis*- ^iPr or *cis*- ^tBu , and *trans*-Me groups at C(2) of the 5-benzyl-imidazolidinone ring.

A Naive Interpretation of the Experimental Conformations. – A simple, classical text-book conformational analysis of the three staggered arrangements **A**, **B**, and **D** (*Figs. 1* and *6, a*) of 5-benzyl-1-enylidene-3-methyl-imidazolidin-4-ones, disregarding attractive or repulsive, other than steric (*Van der Waals*) forces, suggests that they are all ‘strained’: in **B** and **D**, there is 1,5-repulsion (see the blue dots in *Fig. 6, a*, and compare with a 1,3-diaxially substituted cyclohexane chair)⁴); in **A**, the benzylic Ph group and the *cis*-substituents across the ring are repelling each other as evident from the angles, which the benzylic C,C bonds form with the average plane of the heterocycle (see some $\text{C}(1''')\text{--C}(5)\text{--C}(2)$ angles in *Fig. 6, b*). All three unfavorable intramolecular

⁴) There are additional 1,5-repulsive distances between substituents on the exocyclic $\text{C}(1'')$ and the $\text{N}(3)\text{-Me}$ group in many imidazolidinone derivatives, as discussed in one of our previous papers (see *Fig. 10, c* and *d*, in [1b]).

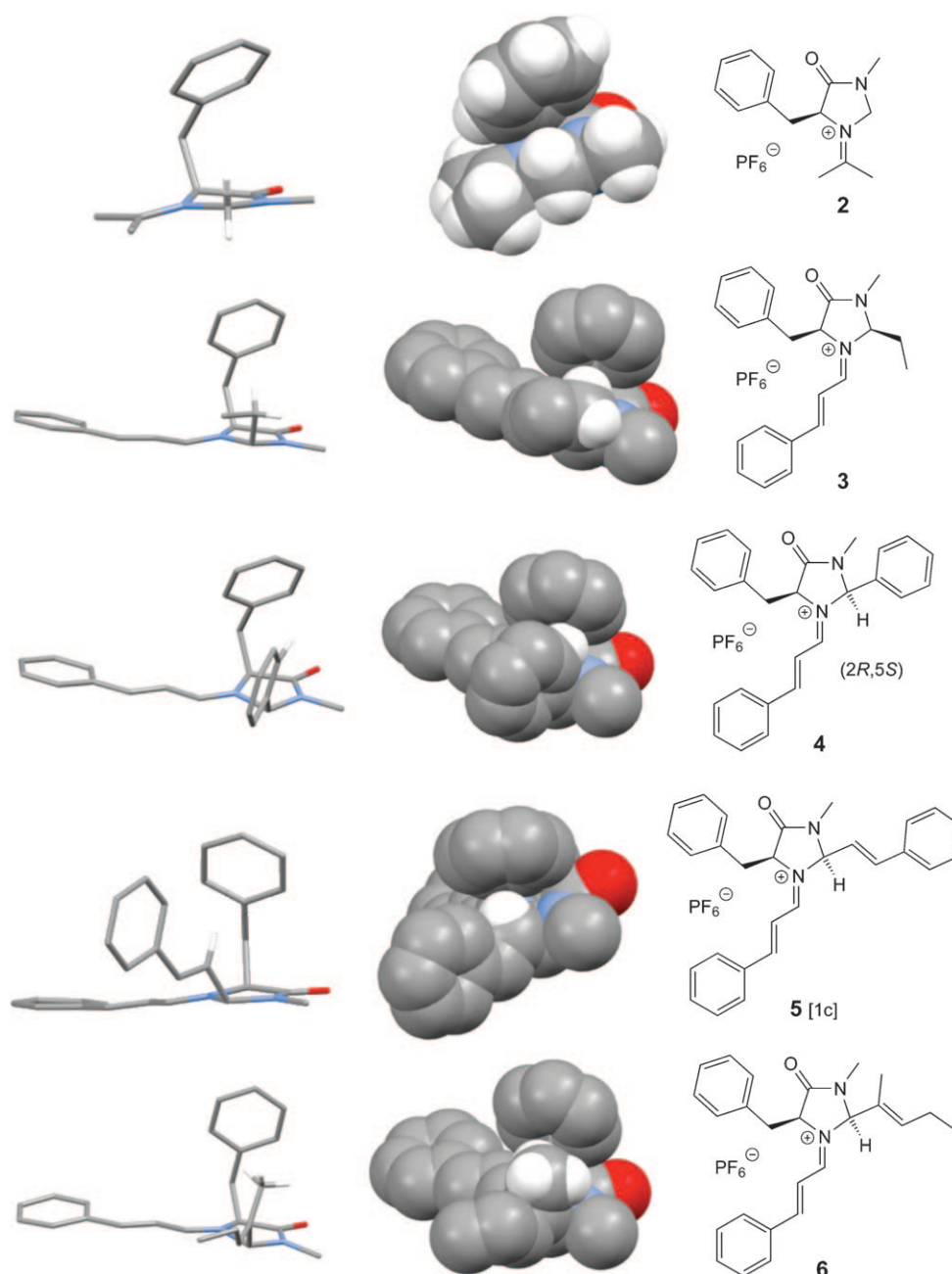


Fig. 2. Stick and space-filling presentations of iminium-salt structures with 2,5-cis-substitution of the imidazolidinone ring, and conformation **A** around the exocyclic $\text{PhCH}_2\text{-CH}$ bond. Compounds 2–6.

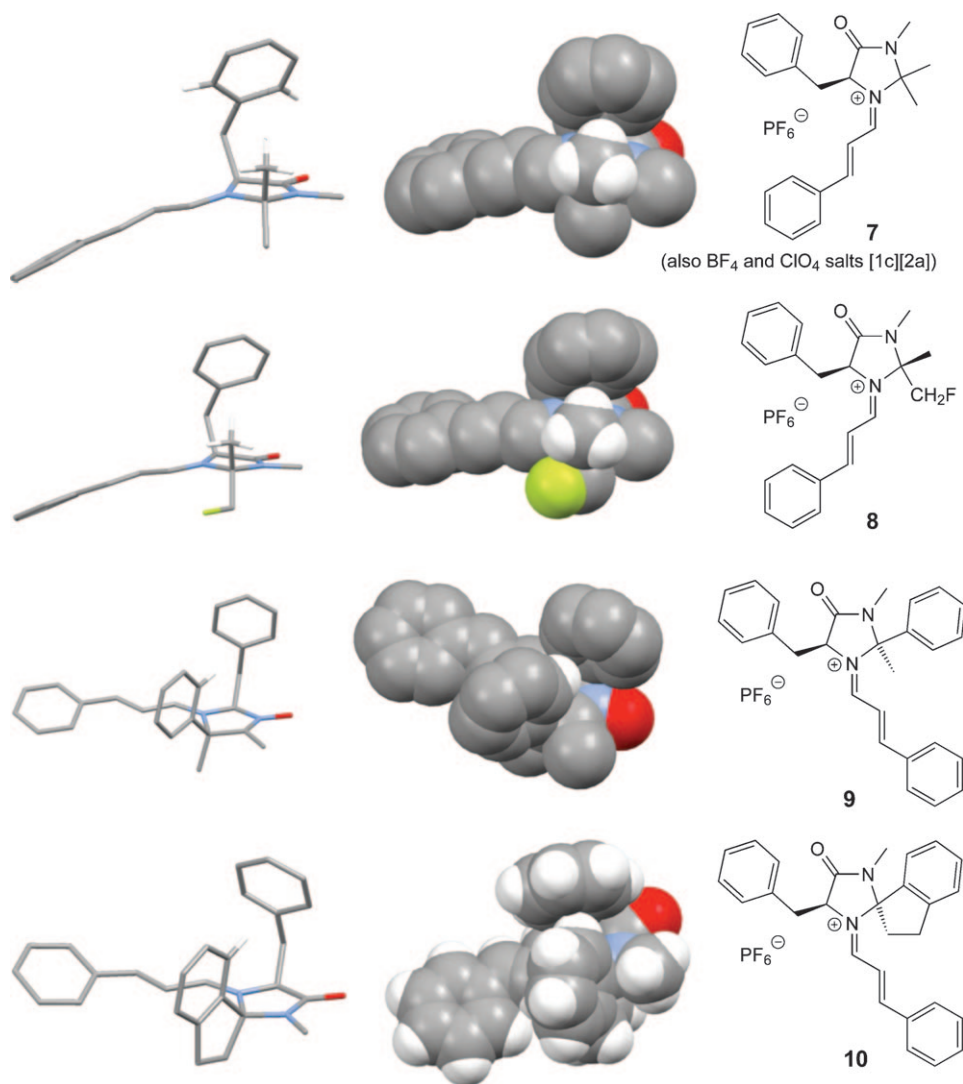


Fig. 3. Stick and space-filling presentations of (E)- and (Z)-cinnamylidene iminium-salt structures with two substituents at C(2) of the imidazolidinone, and conformation **A** around the exocyclic PhCH₂-CH bond. Compounds **7**–**10**.

steric neighborhoods in the staggered conformers **A**, **B**, and **D** are removed in the *ac*-conformation **C**: the benzylic Ph group is far remote from the *cis*-substituent at C(2) on the other side of the ring, and it has moved from a *quasi*-axial relationship with the iminium (**B** in Fig. 6, *a*) or with the C=O group (**D** in Fig. 6, *a*) into a *quasi*-equatorial position. The ‘energetic prize to pay’ for this relief is the *Pfizer* strain of eclipsing a H-atom each with the iminium N-atom, with the carbonyl C-atom and with the Ph C-atom (see Fig. 6, *c*). Thus, a partially eclipsed conformation of type **C** (Fig. 1) can become a

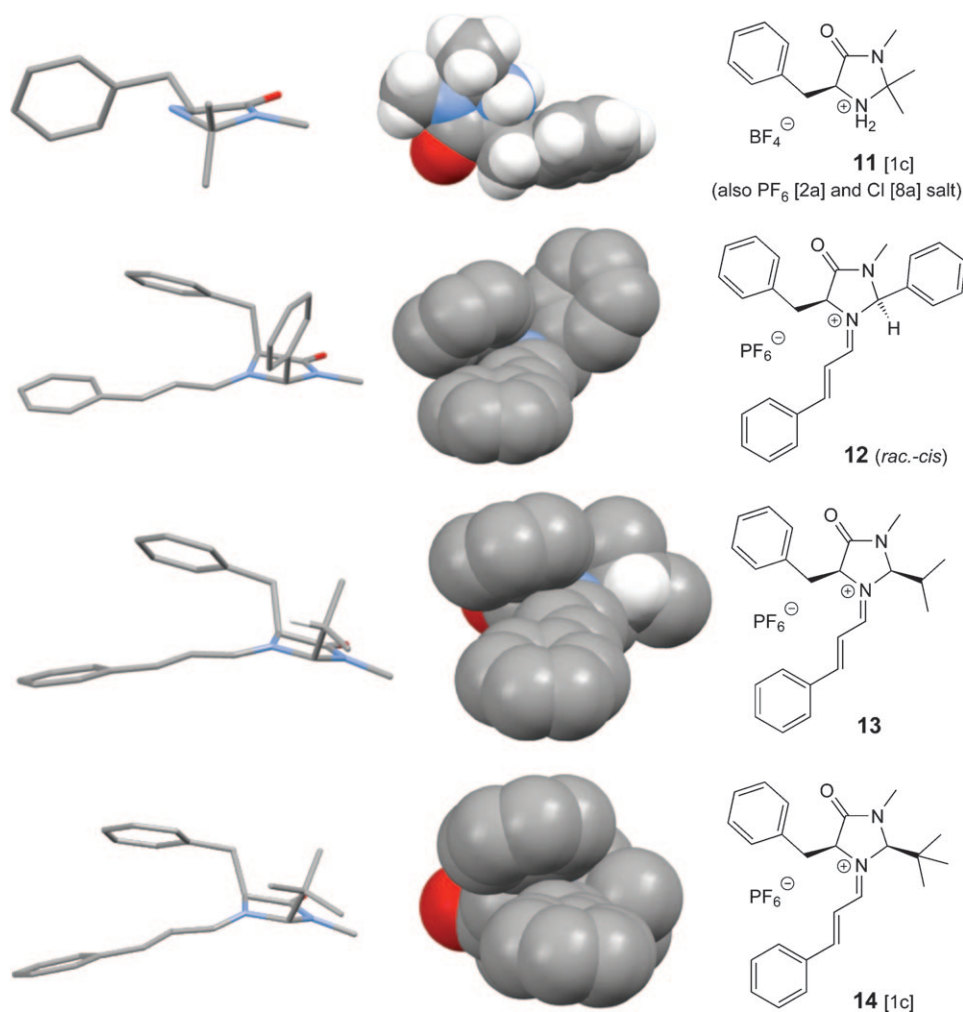


Fig. 4. Stick and space-filling presentations of ammonium and cinnamylidene iminium salts with conformation **B** around the PhCH₂–CH bond. Compounds **11**–**14**.

minimum, as seen in two of our X-ray crystal structures, and as predicted⁵⁾ by Houk's calculations (using a DFT version without dispersion corrections [10]).

Besides the purely steric considerations (repulsive part of the *Van der Waals* potential, also termed *Pauli* repulsion) used in the previous section for a simple conformational analysis, one must also consider *Coulomb* attractions (*cf.* between the benzylic Ph group and the positively charged iminium π -system in **B**), *Coulomb* repulsion (*cf.* between the negative electrostatic potentials of the Ph ring and of the

⁵⁾ The calculated Ph–C(1'')–C(5)–H dihedral angle is 10.1°, which is pretty close to the 12° value in the crystal structure of **15**.

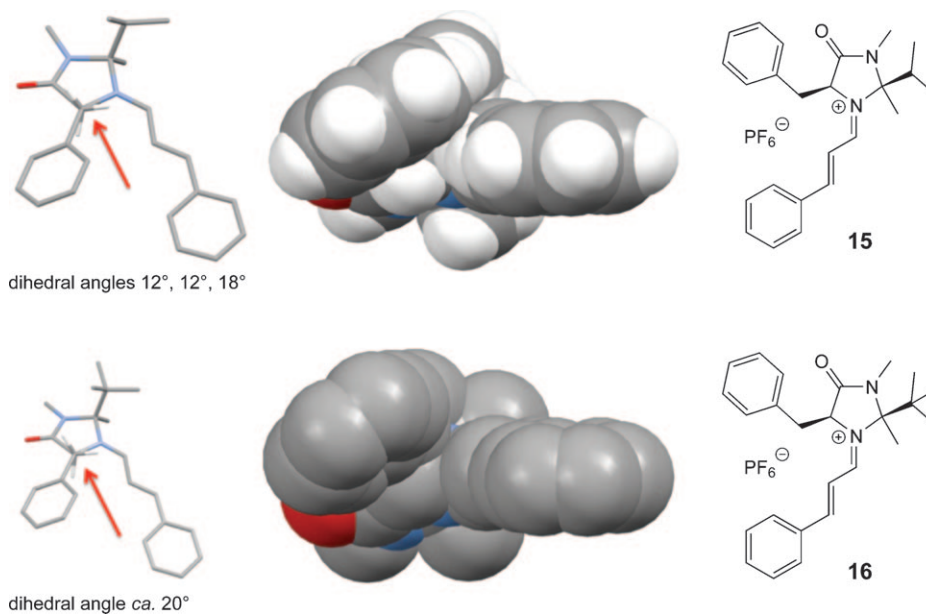


Fig. 5. Stick and space-filling presentations of cinnamylidene iminium-salt structures with geminally disubstituted C(2) of the imidazolidinone ring, and anticlinal (*ac*) conformation **C** around the exocyclic PhCH₂–CH bond. Compounds **15** and **16**.

carbonyl O-atom in conformation **D**), and dispersion interactions (*cf.* between the benzylic Ph group and the *cis*-substituents on the other side of the heterocycle in conformation **A** [11]). To learn to which extent dispersion interactions contribute to the striking preponderance of structures of conformation **A** (Figs. 2 and 3), we have performed state-of-the-art quantum-chemical calculations of the seven structures **3**, **4**, **12**, **5**, **6**, **7**, **13**, and **16**.

Answers from Theory! – For all calculations, we have used the *Turbomole* [12] package of programs. All geometries have been optimized with B3LYP [13] and a triple zeta basis set (TZVPP [14], deprived of one f function for non-H-atoms and of one d function for the H-atoms, termed TZV2P), adding an empirical term for dispersion correction ('B3LYP-D') [15][16]. Single-point calculations on these geometries were performed using a larger basis set of quadruple zeta quality (def2-QZVP [17], deprived of one g function for non-H-atoms and one f function for the H-atoms, termed def2-QZVP-gf). Energies were obtained with second-order *Moller–Plesset* perturbation theory (MP2), also yielding improved, spin-component-scaled SCS-MP2 [18] energies. For comparison, density-functional calculations were conducted with the double hybrid (dispersion corrected) B2-PLYP-D [19][20] functional and B3LYP-D. All single-point calculations were performed with very large AO basis sets (near the limit). The results are collected in the *Table*. In *Fig. 7*, overlays of crystal structures and computed geometries are shown.

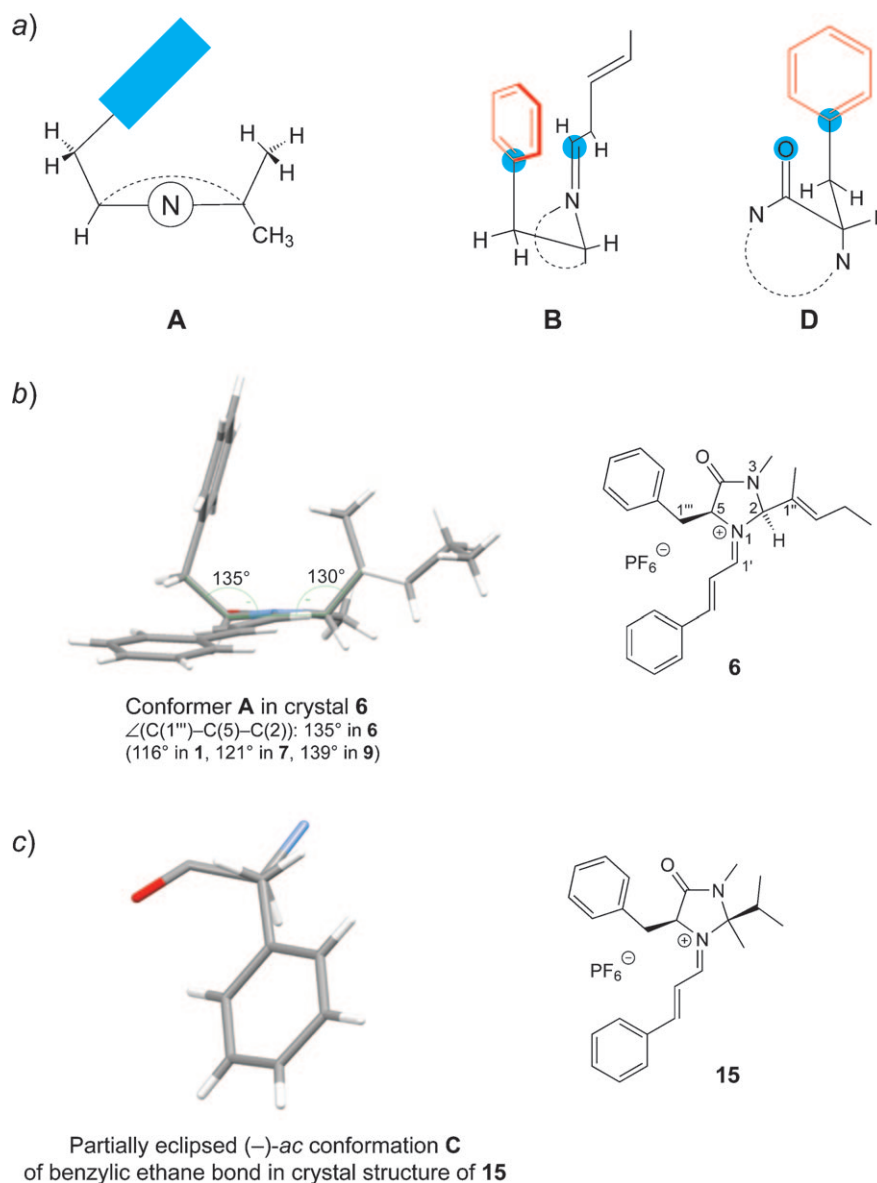


Fig. 6. Simple conformational analysis of the exocyclic $\text{PhCH}_2\text{-CH}$ bond in **A**, **B**, **C**, and **D**. a) The three staggered conformations **A**, **B**, and **D**; **A**: view along the $\text{C}=\text{N}^+$ bond axis with close proximity of the Ph ring and the *cis*-substituent at C(2); note that the *Van der Waals* thickness of a Ph ring is *ca.* 3.5 \AA , much thicker than the blue rectangle would indicate (*cf.* the space-filling presentations of the structures in Figs. 2–5); **B** and **D**: 1,5-repulsive neighborhoods of Ph and iminium C-atoms, and of Ph C-atom and $\text{C}=\text{O}$ O-atom. b) Widening of the angles of 2,5-substituents with respect to the heterocycle plane, due to repulsion (the ‘natural’ angle is *ca.* 125°). c) In an *anticlinal* conformation **C**, the 1,5-repulsions (in **B** and **D**) are eliminated (*cf.* structures **15** and **16** in Fig. 5), at the cost of eclipsing *Pfizer* strain between H-atoms, and N- and C-atoms.

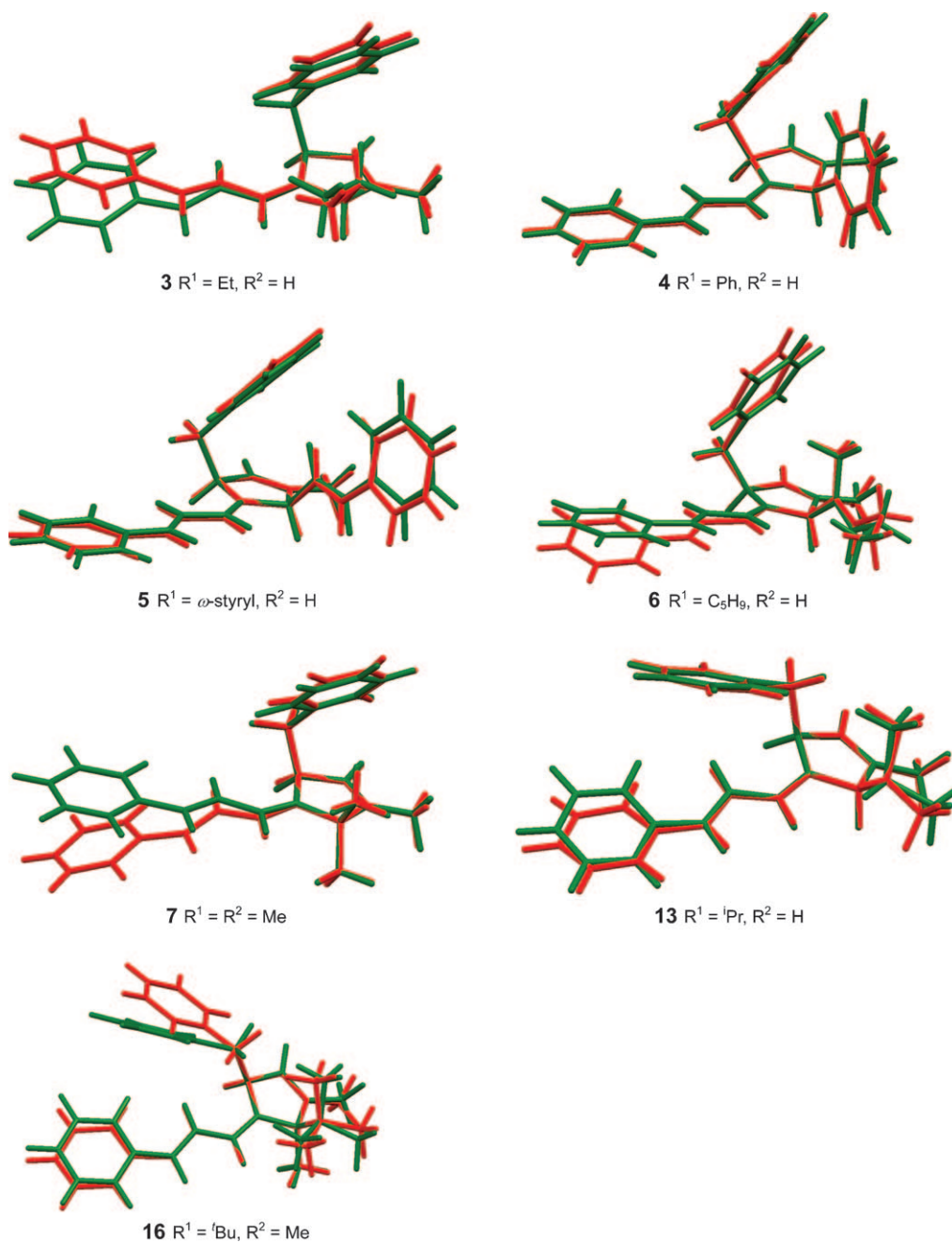
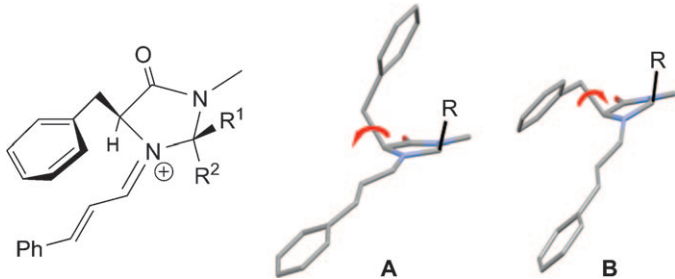


Fig. 7. Overlay of experimentally obtained and computationally optimized (B3LYP-D/TZV2P) geometries of the (E)-cinnamylidene iminium cations **3–7**, **13**, and **16**. Red: X-Ray; green: B3LYP-D. In all cases, the pairwise distances between the five ring atoms of the imidazolidinone ring were minimized in the overlay procedure.

Table. *Calculated Energy Differences* [kcal/mol] *between Conformer A* (benzylic Ph group above the heterocycle) *and Conformer B* (Bn group above the iminium π -system; $\Delta E = E(\mathbf{B}) - E(\mathbf{A})$) *for Seven 5-Benzyl-1-cinnamylidene-3-methylimidazolidin-4-ones*. The energies were obtained with the def2-QZVP-gf basis set. Geometries were optimized with B3LYP-D/TZV2P. **A** is more stable than **B**, except for **13** and **16**.



	R ¹	R ²	HF	MP2	SCS-MP2	B2-PLYP-D	B3LYP-D	B3LYP	B3LYP/ 6-31G(d)	E_{vdw}^a)
3	Et	H	0.6	0.1	0.2	0.3	0.7	0.2	0.3	0.5
4/12	Ph	H	1.2	0.7	0.7	0.9	0.9	0.8	1.5	0.1
5	C ₈ H ₇ (styryl)	H	0.5	2.5	1.9	2.3	2.4	0.2	1.2	2.2
6	C ₅ H ₉ (1-methylbut-2-enyl)	H	0.1	0.1	0.1	0.2	0.2	-0.2	0.2	0.4
7	Me	Me	1.8	1.0	1.1	1.4	1.6	1.1	1.3	0.4
7^b	Me	Me	2.0	2.7	1.7	2.4	2.0	-0.6	-2.0	2.6
13	ⁱ Pr ^c)	H	-0.3	-0.5	-0.5	-0.3	-0.1	-0.6	0.5	0.6
16	^t Bu	Me	-2.3	-1.4	-1.5	-1.8	-1.9	-2.5	-2.4	0.6

^a) ($s_6 = 1.05$). ^b) With (*Z*)-configured C=N bond. ^c) Energy corresponds to a conformation around the exocyclic CH-CHMe₂ bond in **13** that differs from the conformation found in the solid state.

As can be seen from the values in the *Table*, the conformers **A** (Ph above the ring) and **B** (Ph above the iminium part) are very close in energy, in many cases the relative energy is actually close to the estimated error bars of the calculations for molecules of this size ($\pm 0.1 - 0.2$ kcal/mol for conformational energies). Note that all methods (except non-dispersion-corrected B3-LYP) yield qualitatively the same picture (*i.e.*, the same sign for the relative energy; the largest difference is *ca.* 1 kcal/mol for (*Z*)-**7**⁶) between MP2 and SCS-MP2): in the case of the 2-ⁱPr and 2-^tBu, 2-Me derivatives, **13** and **16**, respectively, the conformer **B** comes out to be more stable, while, in all other cases, conformer **A** is slightly or substantially (for **5** and **7**) more stable. As can be seen by the size and sign of the dispersion correction (last column), this is mainly due to the (absolutely) larger intramolecular dispersion energy for **A** compared to **B**. The effect is largest for **5** (*ca.* 2.2 kcal/mol) and decreases as expected for smaller substituents (*e.g.*, to 0.4 kcal/mol for **7**). Of course, there is also an intramolecular π -stacking-type stabilization in conformers of the type **B**, but the average distance of the Ph ring and the iminium part is rather large and can not compensate the R-Ph dispersive attractions in **A**. Very importantly, an uncorrected B3LYP calculation would yield a qualitatively

⁶) Note that the (*Z*)-isomer is less stable than the (*E*)-isomer, with a rather small energy gap (0.2–2.2 kcal/mol) between the two diastereoisomers.

wrong result in cases **6** and (*Z*)-**7**, because the dispersion correction dominates the energy difference.

The *Hartree–Fock* (*HF*) results in the *Table* are particularly intriguing, as this method is intrinsically ‘uncorrelated’ (*i.e.*, does not account for dispersion forces) but yields in most cases very similar results to those obtained with, *e.g.*, dispersion-corrected B3LYP-D! This can be explained as follows: beside the intramolecular dispersion energy (that favors conformer **A**), one must also consider the important polarization (induction) interaction between the Ph ring and the positively charged iminium part which is larger for **B**. Methods that underestimate this interaction would, therefore, also favor **A** over **B** (but for the wrong reasons). It is well-known that *HF* calculations strongly underestimate polarizabilities and also the corresponding non-covalent polarization interactions. This contribution in our case nearly seems to compensate for the also missing dispersion. Overall, seemingly good *HF* results are obtained. The B3LYP model, on the other hand, fairly well describes polarization effects, and thus we clearly see the effect of the missing dispersion that is hidden at the *HF* level. In general, such fortunate compensation effects cannot be expected, and this example demonstrates how important an equally good account is of the various types of non-covalent interactions.

In this context, we would also like to comment on the theoretical level typically employed in studies of such systems (*e.g.* B3LYP/6-31G(d), *cf.* [10]). Although, as noted above, the B3LYP functional itself is ‘dispersion-blind’, it seems empirically clear that B3LYP results, when used together with a small double-zeta type basis set as 6-31G(d), are better than expected even for systems with important ‘weak’ interactions⁷⁾. We attribute this to an intramolecular basis-set superposition error (BSSE) that artificially lowers the energies of interacting fragments. In this way, *London* dispersion effects are simulated to some extent, although one has to keep in mind that the BSSE decays exponentially with distance, while dispersion has an R^6 dependence. The computed B3LYP/6-31G(d) data in the *Table* support this view also for the problem investigated herein. For all (*E*)-isomers (and in particular for **5** and **6**), the B3LYP/6-31G(d) energy difference is closer to SCS-MP2 or B3LYP-D/def2-QZVP than to the B3LYP/def2-QZVP result. However, error compensations of this kind are far from being perfect as indicated by the wrong sign for ΔE in the case of (*Z*)-**7**.

The good superposition (*Fig. 7*) of calculated (gas phase) and measured (solid phase) structures, and the matching results of (solution phase) NMR investigations⁸⁾⁹⁾ indicate that we do not have to deal with counter-ion or crystal-packing effects in a discussion of the conformations **A–D**: the observed structures mainly reflect the *intramolecular* interactions.

7) For the S22 benchmark set of non-covalent interactions, the mean absolute deviations (MAD) of B3LYP/6-31G(d) and B3LYP/def2-QZVP are 2.8 and 3.7 kcal/mol, respectively. This clearly shows that the theoretically better (larger basis set) calculation seemingly provides a worse result.

8) The NMR spectra of 5-benzyl-1-cinnamylidene-imidazolidinone salts **1** in various solvents and at various temperatures [1b,c][2a] show strong shielding effects on the H-atoms of *cis*-substituents at C(2). The NMR spectra of the compounds **2–16** and of numerous analogues will be described and discussed in a forthcoming full paper.

9) Experimentally, rapid equilibration between various conformers of iminium ion **7** on the NMR time-scale can be concluded from temperature-dependent spectra (240–340 K) [2a].

To obtain an estimate for the barrier of rotation around the $\text{PhCH}_2\text{--CH}$ bond and to see whether up-to-date theory also finds an energy minimum for an *antiperiplanar* conformation **C**, we have calculated the potential curve for this rotation in molecule **16** (Fig. 8). The potential curve discloses why the calculation starting from the *antiperiplanar* X-ray structure (**C**; dihedral angle $\Phi(\text{H--C--CH}_2\text{--Ph}) = -20^\circ$) found the nearest minimum at $+14^\circ$ (**B**). The difference of the Bn orientation can be seen in the overlay of the calculated and measured structures of **16** (Fig. 7). However, the minimum-energy point of the rotation is the (*syn*)-*sc* structure (conformer **B**) with $\Phi = 60^\circ$. As the potential is rather flat between $\Phi = 0\text{--}60^\circ$, the environment (packing in the solid, solvent, counterions, etc.) will easily influence the orientation of the Bn group. It is remarkable that the staggered conformation **D** ($\Phi = 300^\circ$) of structure **16** is not an energy minimum at all, *i.e.*, the *gauche* arrangement of Ph and CO group lies (at 5.5 kcal/mol)¹⁰ on the slope between the eclipsing energy maximum ($\Phi = 240^\circ$) and the near-zero plateau between $\Phi = 0^\circ$ (**C**) and $\Phi = 60^\circ$ (**B**). We can also conclude from Fig. 8 that the rotation towards conformer **A** with $\Phi = 180^\circ$ (173.2° after full optimization) has to overcome a barrier of *ca.* 8.5 kcal/mol, allowing for rapid rotation⁸) at ambient temperature of the $\text{PhCH}_2\text{--CH}$ bond in iminium ion **16**.

Conclusions. – In the phenylalanine-derived imidazolidinones, which enantioselectively catalyze conjugate additions to α,β -unsaturated aldehydes and ketones, it has always been assumed, by practitioners, that the Bn group at C(5) provides steric shielding of one of the π -faces in the reactive intermediates, the enylidene iminium ions. Fourteen X-ray crystal structures of cinnamylidene iminium salts have now revealed that the preferred conformation **A** of the $\text{PhCH}_2\text{--CH}$ bond puts the Ph group above the heterocycle, in close proximity with the *cis*-substituent at C(2) of the imidazolidinone (nine structures; Figs. 2 and 3). The expected conformation **B** with the Ph group above the iminium π -system is detected only in three structures (Fig. 4). Furthermore, two iminium salts have a close-to-eclipsed conformation **C** around the $\text{PhCH}_2\text{--CH}$ bond with torsion angles ranging from 12 to 20° , and with the Ph ring pointing away from the heterocycle, and also from the iminium π -system (Fig. 5). A qualitative conformational analysis leads to the conclusion that, in essentially all conformations of the $\text{PhCH}_2\text{--CH}$ bond, there are unfavorable interactions, so that one might be tempted to suggest that this bond is energetically in a kind of ‘state of emergency’ (Fig. 6).

Quantum-chemical methods of wave-function and density-functional type can describe the experimental findings accurately, when the important intramolecular dispersion effects are accounted for. This comprises optimized structures that compare very well with those from X-ray analyses, as well as conformational energies. In all investigated cases, the experimentally observed crystal structure also corresponds to the most stable conformer computed under isolated-molecule conditions (Fig. 7). The computed conformational energies for phenyl-iminium π -stacked and Ph-substituent-contact rotamers, **B** and **A**, respectively, vary in a small range of $+/-2$ kcal/mol for typical organic substituents at C(2) of the heterocycle. The relative intramolecular dispersion contribution as well as phenyl–iminium polarization interactions appear to

¹⁰) Cf. the 3.5 kcal/mol for **D** in the *Houk* calculation (Fig. 1) [10].

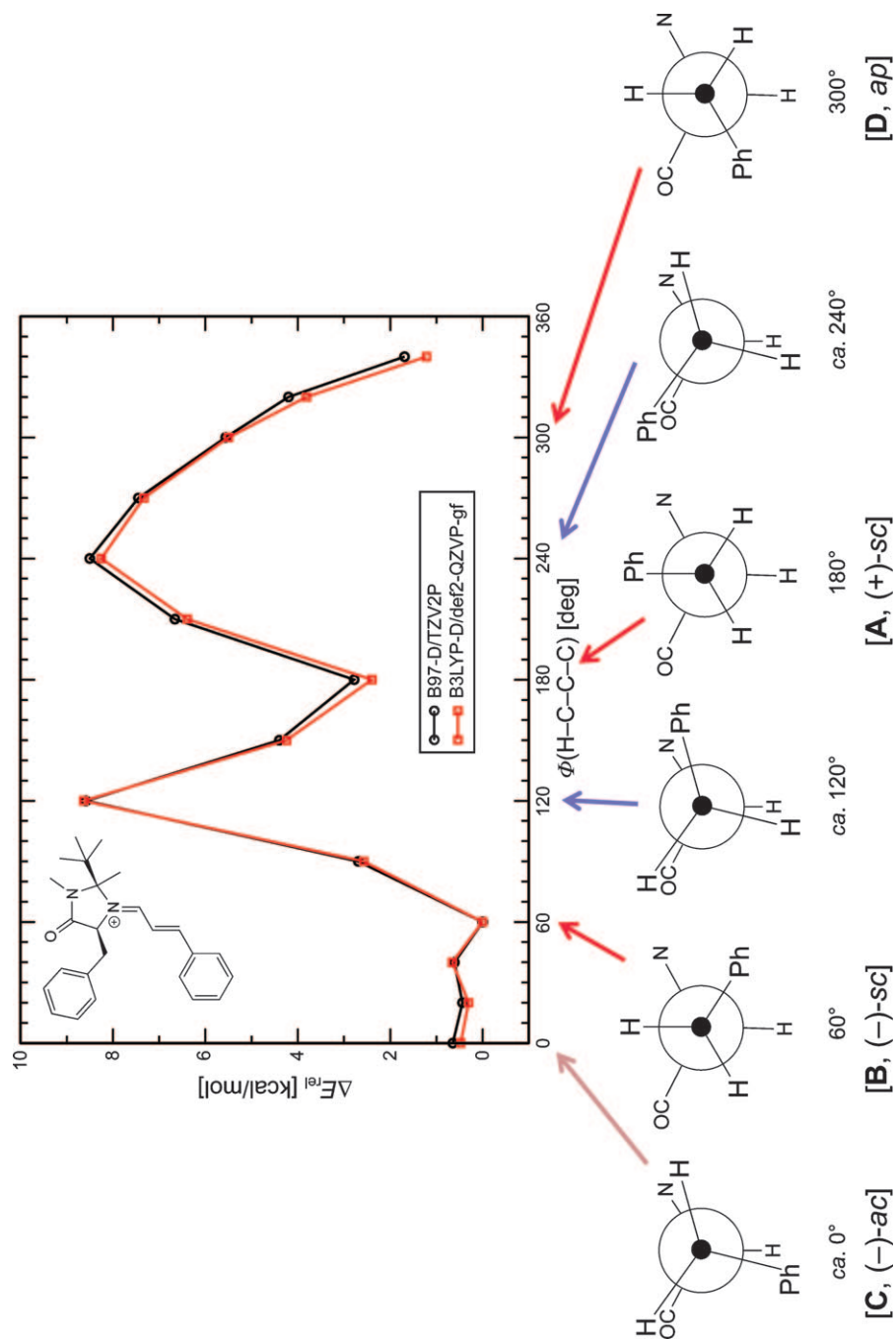


Fig. 8. Potential energy [kcal/mol] for the rotation of the *Bn* group in **16** around the benzylic C–C bond. Geometries were optimized at fixed dihedral angle $\phi(\text{H-C-C-Ph})$ with B97-D/TZV2P, and single-point calculations on these partially optimized geometries were performed with B3LYP-D/def2-QZVP-gf.

be of about the same magnitude, and must be considered in accurate and predictive theoretical treatments. The popular B3LYP density-functional level can only be recommended when augmented with dispersion corrections as, *e.g.*, in the standard DFT-D approach.

The calculated potential-energy profile of the PhCH₂–CH bond in structure **16**, with a *cis*-*t*Bu and a *trans*-Me substituent at C(2) of the imidazolidinone ring (*Fig. 8*), shows a peculiar plateau between $\Phi = 0^\circ$ (eclipsed conformation **C**) and $\Phi = 60^\circ$ (*gauche* relationship **B** between the Ph group and the iminium N-atom), suggesting that stacking interaction, 1,5-repulsion, and the ‘cost’ of eclipsing balance each other. There is a conformational-energy minimum at $\Phi = 180^\circ$ when the Ph group is in contact with the *t*Bu group, whereas the staggered conformation ($\Phi = 300^\circ$) with *gauche*-arrangement between Ph and C=O groups is not a minimum in the calculated potential-energy profile of structure **16**.

Overall experimental and theoretical results lead to the conclusion that the Bn group in 2-benzyl-imidazolidinone iminium ions is more or less freely-rotating (small energy differences of and low rotational barriers between conformers) at ambient temperatures, the conditions of organocatalysis, providing the desired steric shielding of one face of the iminium π -system, in what could be called a ‘windshield-wiper’ effect.

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