

Conformational Behaviour of Non-fused Biheterocycles. Part 11.¹ 2,2'-Bi-imidazolyl

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The torsional potential of 2,2'-bi-imidazolyl has been analysed by means of *ab-initio* computations making use of minimal and split valence basis sets. The most significant geometrical parameters have been optimized, but the potential energy curve is essentially insensitive to geometry optimization. Only minor energy variations are involved in large amplitude motions between *cis* and perpendicular conformations, *transoid*-structures being significantly more stable. The general shape of the curve is not modified upon enlarging the basis set, but the relative stabilities of *cisoid*- and *transoid*-structures are increased by about 20%.

The conformational behaviour of non-fused biheterocycles consisting of two rings linked together by essentially single bonds has been the subject of several experimental investigations (for recent reviews see refs. 2–4) owing to the considerable interest of some compounds of this class in many fields of physical and chemical technologies.^{5,6} However, it is difficult to generate full rotational functions from experimental data since only the conformations in the vicinity of the energy minima can be well characterized, the rest of the potential energy curve remaining ill defined. Theoretical computations do not suffer from this type of problem and several studies^{2,7–11} have shown that non-empirical Hartree–Fock computations employing minimal or split valence basis sets provide useful results even in the rigid rotor approximation. Furthermore, the complete torsional potential is transferable with a high degree of accuracy among molecules with the same *ortho*-substituents irrespective of the nature of *meta*- and *para*-groups.

Although all the possible combinations between CH, N, O, and S *ortho*-groups both in bihexaheterocyclic^{2,8–16} and bipentaheterocyclic^{1,6,17–20} systems have been investigated, the combination of N and NH *ortho*-groups, which gives rise to particularly strong electrostatic interactions in view of the high degree of polarization of CN and NH bonds, remains to be investigated.

The transferability of the torsional potential, allows a complete definition of the conformational behaviour of the whole class of non-fused biheterocycles by studying just one prototype molecule, 2,2'-bi-imidazolyl. This molecule has been chosen owing to its wide use²¹ and also that of its derivatives²² for modelling the prosthetic group of some metalloenzymes.^{23,24}

Computational Procedure

As a first step a rigid geometry (hereafter referred to as RG) torsional potential was computed for 2,2'-bi-imidazolyl by the GAUSSIAN/82 package²⁵ using the STO-3G basis set,²⁶ the neutron diffraction structure of the imidazole ring,²⁷ and an inter-ring distance of 1.48 Å along the direction of the inter-ring bonds. The torsional angle, θ (that is the angle between the planes of the two rings), was spanned in steps of 30°. The imidazole–imidazole bond distance, R , the angles, α , formed by this bond with the CN(H) moieties of the two rings, and the CNH valence angles, β , (see Figure 1) were then optimized at each value of θ . The resulting curve gives rise to a partially flexible geometry (hereafter referred to as PFG) torsional

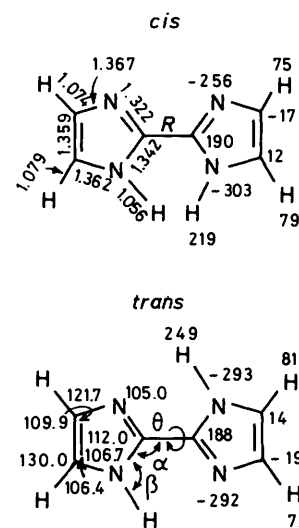


Figure 1. Schematic drawing of 2,2'-bi-imidazolyl at planar *cis* and *trans* conformations. The values of the fixed geometrical parameters (bond lengths in Å and valence angles in degrees from ref. 27) and the labelling of the variable geometrical parameters are reported on the left-hand side rings. STO-3G net charges (in millielectron) are reported on the right-hand side rings

potential. Both experimental and STO-3G optimized structures were finally employed for single-point computations with the split valence 3-21G basis set.²⁸

Results and Discussion

The structure, geometrical parameters, and net atomic charges of 2,2'-bi-imidazolyl are shown in Figure 1. The optimized values of the variable geometrical parameters for the different conformations are given in Table 1. It is noteworthy that both bond length and bond angle variations are quite small. In particular the variation of the valence angles are practically negligible except in the region $0^\circ \leq \theta \leq 30^\circ$, where the increase of α and β is particularly effective in reducing the strong repulsions between *ortho*-groups. For the same reason R is longer for *cisoid*- than for *transoid*-conformations. In this case, however, the largest increase is observed in the region $\theta \approx 90^\circ$ due to the lack of inter-ring conjugation.

Table 1. Geometric parameters (see text and Figure 1 for the definition and units) optimized at the STO-3G level for various conformations of 2,2'-bi-imidazolyl. The dipole moments (μ/D) obtained at the STO-3G and 3-21G levels are also reported

θ	R	α	β	$\mu(\text{STO-3G})$	$\mu(3-21G)$
0°	1.488	123.89	127.83	6.95	7.64
30°	1.490	123.05	127.36	6.78	7.48
60°	1.494	122.43	126.82	6.22	6.89
90°	1.498	122.45	126.56	5.20	5.78
120°	1.492	122.47	126.16	3.76	4.18
150°	1.484	122.39	125.54	1.98	2.20
180°	1.480	122.35	125.13	0.00	0.00

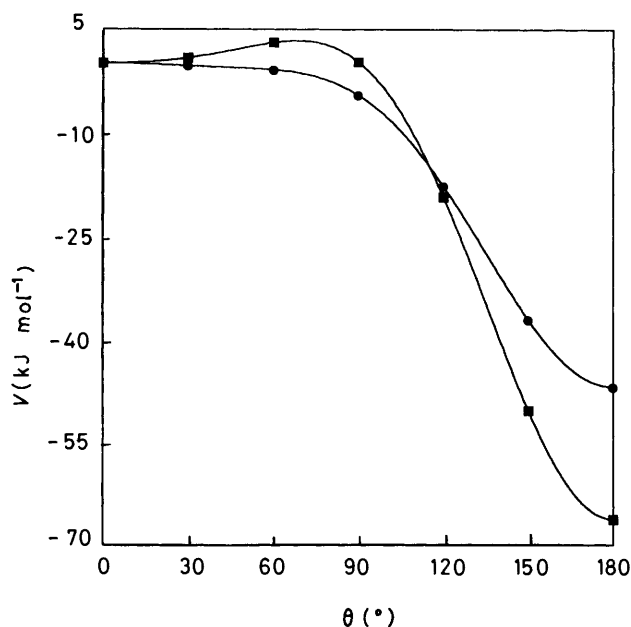


Figure 2. Torsional curves of 2,2'-bi-imidazolyl obtained by STO-3G/PFG (●) and 3-21G/PFG (■) computations

The potential energy curves for internal rotation around the central C-C bond are drawn in Figure 2. Four different curves were generated, corresponding to RG or PFG models and to the use of STO-3G or 3-21G basis sets.

As in analogous systems^{8,9,11} the potential constants of the PFG model are generally well reproduced by the rigid geometry computations irrespective of the basis set. However, at the STO-3G level partial geometry optimization leads to the disappearance of the *gauche* minimum, as already reported for systems with similar H...H non-bonded interactions such as butadiene²⁹ or 1,4-diazabutadiene.³⁰

The torsional curve is very flat in the region $0^\circ < \theta < 90^\circ$, but the *cis*-conformation always corresponds to an energy maximum. A shallow minimum at $\theta \approx 70^\circ$ is found by three of the four levels of computation employed. The presence of these two extreme points should not cause any observable effect on view of the very small energy differences involved.

According to all the models employed the *cis*-conformation is significantly less stable than the *trans*-form, which is the absolute minimum of the curve. However, the energy difference between the two forms increases by about 20% going from STO-3G to 3-21G basis sets. Although the results obtained by split valence basis sets are generally considered more reliable in conformational studies of aromatic molecules (see however ref. 31), in the present case this conclusion is partially invalidated by the well known overestimation of the strength of hydrogen

bridges by split valence basis sets.³² Since the STO-3G basis set usually provides reasonable values for these strengths, the *cis-trans* energy difference obtained at this level might be more reliable.

The different sets of conformational energies $V(\theta)$ [expressed as the total energies $E(\theta)$ minus the energy $E(0^\circ)$ of the planar *cis* conformation] have been fitted to a truncated Fourier expansion:

$$V(\theta) = \frac{1}{2} \sum V [1 - \cos(j\theta)] \quad (1)$$

This fitting allows a quantitative comparison of different molecules and/or provides the location of the extreme points on the potential curve.^{2,8,18} Furthermore, the physical origin of the low-order potential constants has been well recognized.⁸

The conformational energies and their six-term Fourier expansions are given in Table 2 together with the location and relative energies of the minima and maxima on the torsional curves obtained from these expansions. The potential constants V_4 , V_5 , and V_6 are negligible (*i.e.* smaller than 1 kJ mol⁻¹) irrespective of the geometry and the basis set used. This gives further support to our previous suggestion⁸ that three potential constants are sufficient to describe accurately the conformational behaviour of *all* non-fused biheterocycles. However, the choice of the appropriate expansion is not straightforward since the best fitting is obtained in the present case including the terms V_1 , V_2 , and V_3 , whereas inclusion of the V_4 term in place of V_3 leads to better results for several other molecules.^{19,20} Indeed, the relative weight of odd and even potential constants is reversed in 2,2'-bi-imidazolyl with respect to all the other systems studied up to now thus leading to a much more asymmetric torsional potential.

The V_2 term reflects the tendency of the molecule to adopt a planar conformation in order to maximize its conjugative stability. Its value is similar to those of 2,2'-bipyrryl (14 kJ mol⁻¹) and 2,2'-bithienyl (16 kJ mol⁻¹). In contrast, the V_1 term, which takes into account the asymmetry of electrostatic interactions between *ortho*-groups,¹¹ is particularly large in 2,2'-bi-imidazolyl (41.6 kJ mol⁻¹ vs. 10.3 kJ mol⁻¹ for 2,2'-bipyrryl and 2.3 kJ mol⁻¹ for 2,2'-bithienyl). In fact for 2,2'-bi-imidazolyl the repulsive interactions between N...N and NH...HN *ortho*-groups, which exist in *cisoid*-conformations, are substituted by attractive NH...N interactions in *transoid*-conformations. This effect is strongly reduced in 2,2'-bipyrryl and, especially, 2,2'-bithienyl due to the low polarity of CH and CS bonds.

Although the *cisoid* energy minimum does not correspond to a planar conformation, the relative stability of planar *cis*- and *trans*-structures deserves some further comment in view of the prevalence of these structures in the solid state. The preference between these two structures can be justified by taking into account steric and electrostatic interactions between *ortho*-groups. As in other similar molecules steric energy differences are small and the preferred planar conformation is mainly determined by electrostatic terms. However, inspection of the atomic net charges reported in Figure 1 indicates a significant electron redistribution between *cis*- and *trans*-conformations. The energy variation E_{ct} caused by this modification is given by:³³

$$E_{ct} \approx \sum \sum a_{ij} [q_i(\text{cis}) - q_i(\text{trans})] \quad (2)$$

The net charges on the different atoms are estimated as:^{33,34}

$$q_i \approx \frac{1}{2} q^{\text{Mull-TO-3G}}$$

and the terms a_{ij} for CN and NH bonds are taken as equal to those of CC and CH bonds (which are already available³³).

Table 2. Total energies of planar *cis*-conformations [$E(0^\circ)$ in a.u.], conformational energies [$V(\theta) = E(\theta) - E(0^\circ)$ in kJ mol⁻¹], and potential constants (V_i in kJ mol⁻¹) in the Fourier expansions [cf. equation (1)] obtained for 2,2'-bi-imidazolyl by different methods (see text). RG and PFG abbreviations refer to computations employing rigid and partially flexible geometries, respectively (see text)

	STO-3G/RG	STO-3G/PFG	3-21G/RG	3-21G/PFG
$E(0^\circ)$	-442.829 31	-442.829 41	-445.936 76	-445.936 99
$V(30^\circ)$	-1.42	-1.45	-0.36	-0.03
$V(60^\circ)$	-1.01	-1.55	2.61	2.56
$V(90^\circ)$	-4.19	-5.04	-0.20	-0.04
$V(120^\circ)$	-17.85	-18.60	-19.74	-20.16
$V(150^\circ)$	-36.98	-37.80	-48.83	-50.57
$V(180^\circ)$	-46.34	-47.49	-64.37	-67.12
V_1	-41.63	-42.50	-56.84	-59.12
V_2	19.14	18.84	32.16	33.35
V_3	-4.17	-4.46	-6.72	-7.23
V_4	-0.86	-0.61	-0.89	-0.33
V_5	-0.54	-0.53	-0.80	-0.77
V_6	-0.16	-0.14	0.21	0.17
$\theta_{\min.} (^\circ)$	39	—	26	22
$V_{\min.}$	-1.60	—	-0.37	-0.15
$\theta_{\max.} (^\circ)$	64	—	72	71
$V_{\max.}$	-0.96	—	3.14	3.16

With these rough estimates we obtain an energy difference between *cis*- and *trans*-conformations of 2,2'-bi-imidazolyl of 46.2 kJ mol⁻¹, in remarkable agreement with the PFR/STO-3G value of 46.3 kJ mol⁻¹. This result gives further support to the previous discussion about the reliability of conformational energies and suggests some caution against the widespread use of constant net charges in empirical conformational studies.

References

- Part 10, N. Russo, M. Toscano, V. Barone, and C. Minichino, *J. Chim. Phys.*, 1987, **84**, 735.
- V. Barone, F. Lejl, C. Cauletti, and M. N. Piancastelli, *Mol. Phys.*, 1983, **49**, 599.
- A. Almendinger, O. Bastiansen, L. Fernholt, B. N. Cyvin, S. J. Cyvin, and S. Samdal, *J. Mol. Struct.*, 1985, **128**, 59.
- K. Vinodgopal and W. R. Leenstra, *J. Phys. Chem.*, 1985, **89**, 3824.
- G. Brewer and E. Suin, *Inorg. Chem.*, 1985, **24**, 4580.
- A. I. Nazzari, G. B. Street, and K. J. Wynne, *Mol. Cryst. Liq. Cryst.*, 1985, **125**, 303.
- E. Ortí, J. Sánchez-Marín, and F. Tomás, *J. Mol. Struct., THEOCHEM.*, 1984, **108**, 199.
- V. Barone, F. Lejl, and N. Russo, *Int. J. Quantum Chem.*, 1986, **29**, 541.
- E. Von Nagy-Felsobuki, *Chem. Phys. Lett.*, 1986, **127**, 245.
- J. Almlöf, *Chem. Phys.*, 1974, **6**, 135.
- G. H. Penner, *J. Mol. Struct., THEOCHEM.*, 1986, **137**, 191.
- V. Barone, F. Lejl, L. Comisso, N. Russo, C. Cauletti, and M. N. Piancastelli, *Chem. Phys.*, 1985, **96**, 435.
- M. Yagi, K. Makiguchi, A. Ohnuki, K. Suzuki, J. Higuchi, and S. Nagase, *Bull. Chem. Soc. Jpn.*, 1985, **58**, 252.
- V. Barone, C. Cauletti, F. Lejl, M. N. Piancastelli, and N. Russo, *J. Am. Chem. Soc.*, 1982, **104**, 4571.
- V. Barone, F. Lejl, N. Russo, and P. L. Cristinziano, unpublished results.
- V. Barone, L. Comisso, F. Lejl, and N. Russo, *Tetrahedron*, 1985, **41**, 1915.
- E. Ortí, J. Sánchez-Marín, and F. Tomás, *J. Mol. Struct., THEOCHEM.*, 1985, **124**, 307.
- E. Ortí, J. Sánchez-Marín, and F. Tomás, *Theor. Chim. Acta*, 1986, **69**, 41.
- E. Ortí, J. Sánchez-Marín, M. Merchan, and F. Tomás, *J. Phys. Chem.*, 1987, **91**, 545.
- V. Barone, F. Lejl, N. Russo, and M. Toscano, *J. Chem. Soc., Perkin Trans. 2*, 1986, 907.
- M. S. Haddad and D. N. Hendrickson, *Inorg. Chem.*, 1978, **17**, 2622.
- P. G. Rasmussen, O. H. Bailey, and J. C. Bayón, *Inorg. Chem.*, 1984, **23**, 338.
- V. Casellato, P. A. Vigato, and M. Vidali, *Co-ord. Chem. Rev.*, 1977, **23**, 31.
- D. M. Kurtz, Jr, D. F. Shriver, and I. M. Klotz, *Co-ord. Chem. Rev.*, 1977, **24**, 145.
- J. S. Binkley, M. J. Frisch, D. J. DeFrees, K. Raghavachari, R. A. Whiteside, H. B. Schlegel, E. M. Fluder, and J. A. Pople, GAUSSIAN 82, Carnegie-Mellon University, 1982.
- W. J. Hehre, R. F. Steward, and J. A. Pople, *J. Chem. Phys.*, 1969, **51**, 2657.
- B. M. Craven, R. K. McCullan, J. D. Bell, and H. C. Feeman, *Acta Crystallogr., Sect. B*, 1977, **33**, 2585.
- J. S. Binkley, J. A. Pople, and W. J. Hehre, *J. Am. Chem. Soc.*, 1980, **102**, 939.
- G. R. De Maré and D. Nesius, *J. Mol. Struct., THEOCHEM.*, 1984, **109**, 103.
- V. Barone and N. Russo, unpublished results.
- S. Marriott and R. D. Topsom, *Aust. J. Chem.*, 1986, **39**, 1157.
- P. G. Jasien and W. J. Stevens, *J. Chem. Phys.*, 1986, **84**, 3271.
- S. Fliszár, 'Charge Distributions and Chemical Effects,' Springer, Berlin, Heidelberg, New York, 1983.
- V. Barone, C. Minichino, N. Russo, and S. Fliszár, *Can. J. Chem.*, in the press.

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